A thesis submitted in part fulfilment of the requirements of the degree of Doctor of Philosophy

Stereoselective Synthesis of Artificial *C*-Nucleosides

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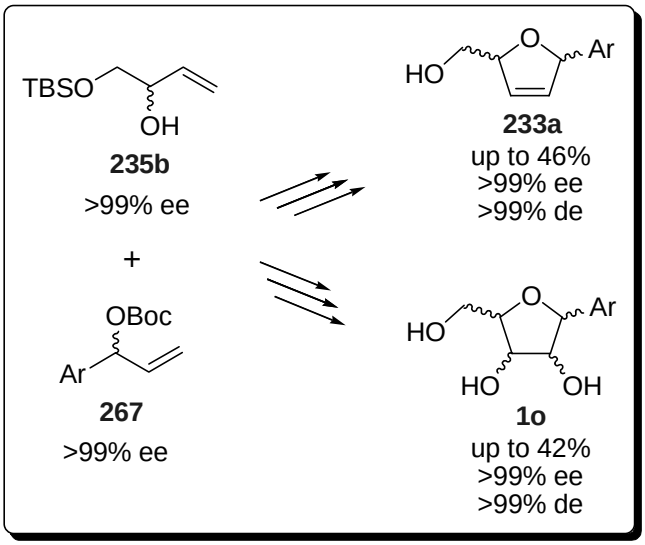
Abstract

Reported herein is a conceptually new synthetic route to 1'-aryl-*C*-ribofuranosides and their 2',3'-didehydro-2',3'-dideoxy (D4) analogues. We have successfully implemented a divergent synthetic route capable to reach two important, biologically significant groups of compounds. The first two strategic transformations are common for both families of target compounds (asymmetric allylic substitution, and ring-closing metathesis). D4 *C*-nucleoside analogues are synthesised in a three-step procedure, and 1'-aryl ribofuranoses are constructed in a four-step procedure.



The target compounds were prepared in an excellent enantio- and diastereopurity, in good overall yields. The yield in the synthesis of 1'-aryl-2',3'-didehydro-1',2',3'-trideoxyribofunanoses is up to 46% over all the reaction steps. The overall yield of the 1'-arylribofuranoses is up to 42%.

All the strategic transformations rely on catalytic oranometallic reactions employing group 8a transition metals. All the reactions have been optimized with a view of maximal atom efficiency and environmental impact.

In summary, our new methodology is perfectly suitable for the synthesis of 1'-arylribofuranoses, and their D4-analogues, bearing non-*ortho*-substituted aromatics and hereroaromatics, lacking coordinating (nitrogen) substituents or heteroatoms. In this point of view the most promising target application is the synthesis of lipophilic isosters of ribonucleosides for the RNA-studies.

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Abbreviations

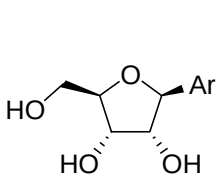
Å	Ångström
AAS	Asymmetric Allylic Substitution
Aq	Aqueous
Ac	Acetyl
AcOEt	Ethyl Acetate
AEGIS	Artificially Expanded Genetic Information Systems
Ar	Aryl
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	1,1'-Binaphthyl-2,2'-diol
Bn	Benzyl
Boc	*tert*-Butyloxycarbonyl
$(Boc)_2O$	di-*tert*-Butyl dicarbonate
bp	Boiling point
Bu	Butyl
n-Bu	*normal*-Butyl
s-Bu	*sec*-, *secondary*-Butyl
t-Bu	*tert*-, *tertiary*-Butyl
Bz	Benzoyl
cat	Catalytic
cHx	Cyclohexyl
CI	Chemical ionization
CM	Cross-metathesis
CMV	Cytomegalovirus
conc	Concentrated
Cp	Cyclopentadienyl
Cy	Cyclohexyl
D4	2',3'-Didehydro-2',3'-dideoxy (analogues of nucleosides)
dd	2',3'-Dideoxy (analogues of nucleosides)
DCM	Dichloromethane
de	Diastereoisomeric excess
DIBAL-H	Diisobutylalane (di-*iso*-butylaluminium hydride)
DMAP	Dimethylaminopyridine
DME	1,2-Dimethoxyethane

DMF	*N*,*N*-Dimethylformamide
DMPS	Dimethylphenylsilyl
DMSO	Dimethylsulfoxide
DNA	2'-*β*-D-Deoxyribonucleic acid
DP	Diphosphate (i.e. nucleoside diphosphate)
dRf	2'-*β*-D-Deoxyribofuranos-1'-yl
ee	Enantiomeric excess
EI	Electron Impact
equiv	Equivalents
FIV	Feline Immunodeficiency Virus
GC	Gas Chromatography
HHV	Human Herpes Virus
HIV	Human Immunodeficiency Virus
HMDS	Bis(trimethylsilyl)azane
HPLC	High Perfomance Liquid Chromatography
HSV	Herpes Simplex Virus
HWE	Horner-Wadsworth-Emmons reaction
LTMP	Lithium 2,2,6,6-tetramethylpiperidide
mCPBA	3-Cloroperoxybenzoic acid
Me	Methyl
Mes	2,4,6-Trimethylphenyl
mp	Melting point
MS	Mass Spectroscopy
Ms	Methylsulfonyl
NA	Nucleic acid
NMO	*N*-Methylmorpholine *N*-oxide
NMR	Nuclear Magnetic Resonance
Np	Naphthyl
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
PCR	Polymer Chain Reaction
Ph	Phenyl
i-Pr	Prop-2-yl
PMA	Phosphomolybdic acid
PMB	4-Methoxybenzyl
RCM	Ring-closing metathesis

R&D	Research and Development
Rf	*β*-D-Ribofuranos-1'-yl
RNA	Ribonucleic acid
rt	Room temperature (ambient temperature)
SIV	Simian Immunodeficiency Virus
TBDPS	*tert*-Butyldiphenylsilyl
TBS	*tert*-Butyldimethylsilyl
TCDI	Di(1*H*-imidazol-1-yl)methanethione (thiocarbonyl diimidazol)
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TIPS	Triisopropylsilyl
TLC	Thin Layer Chromatography
TMAD	*N*,*N*,*N*',*N*'-Tetramethylamidoazodicarboxylate
TMS	Trimethylsilyl
Tol	4-Methylbenzoyl
TP	Triphosphate (i.e. nucleoside triphosphate)
Ts	4-Methylbenzenesulfonyl
VZV	Varicella-Zoster Virus

Preface

C-Nucleosides **1** are natural products (Ar: aryl, heteroaryl). They occur in functional RNA, like *transfer*-RNA. In spite of a very low content of these compounds in natural matrix, Cohn successfully isolated pseudouridine **1a** in 1959, as the first *C*-nucleoside ever, in 0.2-0.3% yield from yeast RNA.[1]



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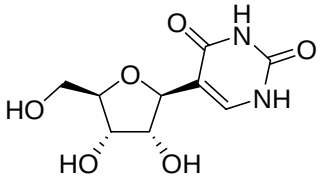


1a

The very low content in natural resources hindered any practical applications of these compounds. Methods of modern synthetic chemistry were utilised in the development of several synthetic approaches to the natural *C*-nucleosides. More interestingly, synthetic chemistry enabled introduction of various aryls and heterocycles as the artificial nucleobase moiety.

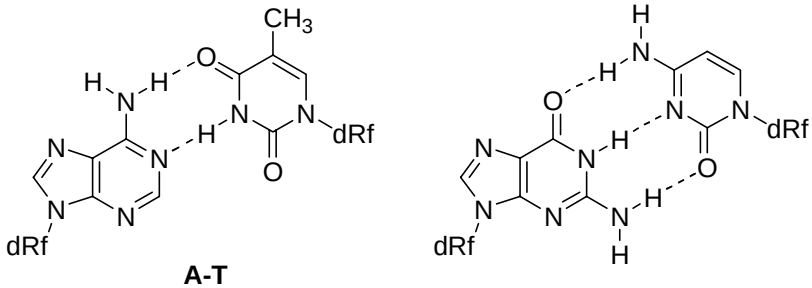
Nucleosides bearing artificial or modified nucleobases can be used in chemical biology as tools for studying and the modulation of biological progresses,[2] as well as for the preparation of artificial bio-analogue systems.[3] Several Artificial Expanded Genetic Information Systems (AEGIS) were successfully developed.[4] A new scientific inter-discipline has emerged: Synthetic Biology.[5] The ultimate goals of synthetic biology are systems where high-level behaviours of living systems are mimicked by artificial chemical systems.[6] Various artificial nucleobases were designed for these purposes.

Among these compounds, *C*-nucleosides **1** play an important role.[7] They are characterized by replacement of a relatively unstable C-N glycosidic bond by a stable C-C bond and, therefore, exhibit *in vivo* stability against nucleosidase enzymes.[8] These improved properties, combined with high potential of versatility in the substitution patterns,[9] have the promise of far reaching applications in chemical biology[3] and medicinal chemistry.[10,11]

Herein we report on a principally novel synthetic method for artificial *C*-nucleosides.

1. Artificial Nucleosides in Chemical Biology

The structure of duplex DNA is based on the complementary Watson-Crick hydrogen bonding patterns of **A**-**T** and **G**-**C** pairs.[12] The replacement of the natural nucleobases by diverse surrogates has become very popular in recent years.[13] The original aim just to investigate the structure and function of nucleic acids (NA) was extended towards three main goals. (1) Formation of stabilized duplexes.[14] (2) Design of universal nucleobases not discriminating between the complementary bases.[15] (3) Extending the genetic alphabet.[16]

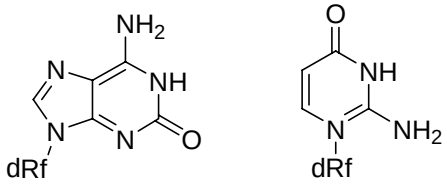


dRf: 2'-deoxyribofuranosyl

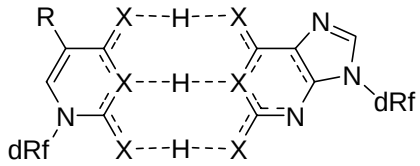
Efforts to expand the genetic alphabet are focused on a stable and replicable third base-pair.[17] Recent progress has resulted in the development of several candidates that are both stable in the DNA duplex and replicated by DNA polymerases with various degrees of efficiency and fidelity. The candidate base-pairs draw upon unnatural hydrogen-bonding topologies as well as upon shape complementarity,[18] hydrophobic forces,[19] metal-bridged[20] base-pairs and even covalent cross-links.[21]

1.1. Artificial Base-Pairs Based on Hydrogen-Bonding

The concept of hydrogen bonding patterns and shape complementarity was introduced by Benner (e.g., isoguanosine, iso-**G**; isocytidine, iso-**C**).[18]



Further development led to the introduction of other donor-acceptor (**D**-**A**) purine-pyrimidine (**pu**-**py**) pairs[22] and finally to a generalization of Watson-Crick nucleobases pairs.[23] In the most general form, the Watson-Crick base-pair joins a six-membered heterocyclic ring **py** (in nature, a pyrimidine) with a fused five/six-membered ring system **pu** (in nature, a purine) *via* three H-bonds. Two inter-base H-bonds are formed between exocyclic functional groups; one is formed between heteroatoms of the heterocycles. Donor hydrogen-bonding patterns are assigned **D**, whereas the acceptor hydrogen-bonding patterns are assigned **A**. With three H-bonds, eight (2^3) H-bonding patterns and sixteen independently replicable bases are conceivable within the Watson-Crick geometry. Only six of them are readily accessible (Table 1).



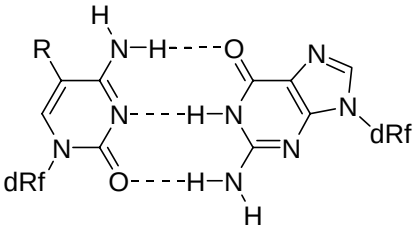
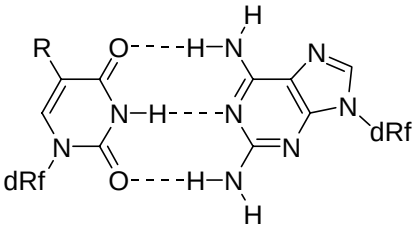
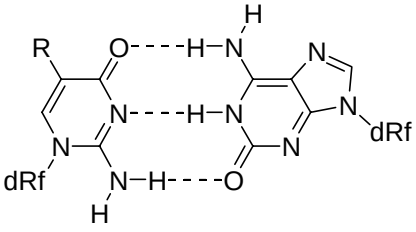
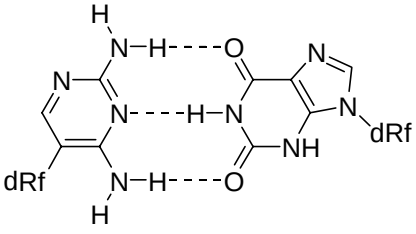
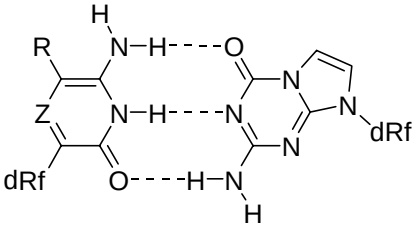
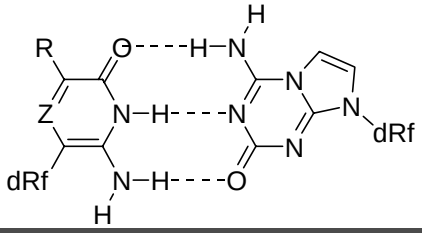
py **pu**

R: H, CH_3
X = heteroatom

Dotted lines in the picture indicate the position of double bonds to complete the valence to the heteroatoms, and make the heterocycles aromatic.

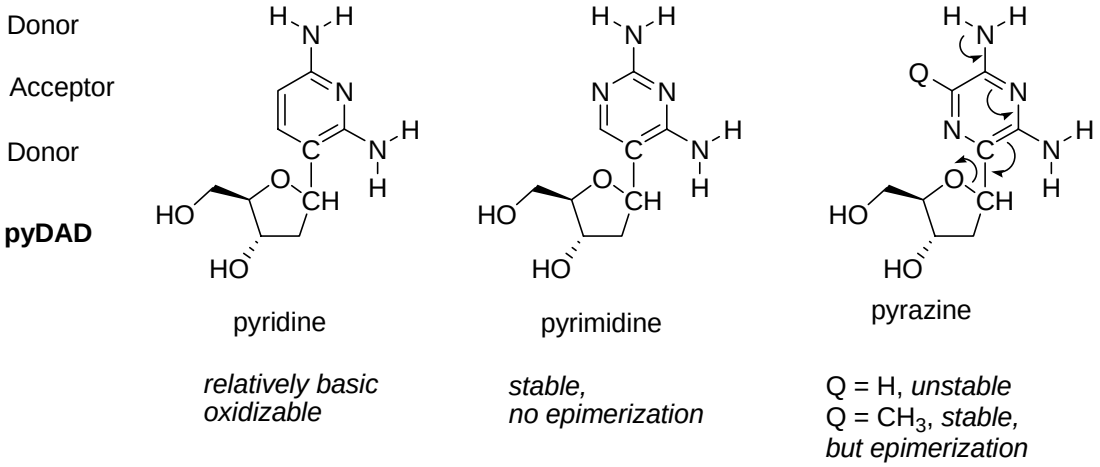
In practice, pyrimidine analogs presenting **pyADD**, **pyDAD**, and **pyDDA** H-bonding patterns are difficult to prepare.[24] In order of good stacking capabilities, they need to be aromatic, therefore the ring systems requires a junction to the carbohydrate as a *C*-glycoside, thus forming *C*-nucleoside. Several heterocycles might solve this problem. The 6-aminopyridin-2(1*H*)-one structure, which formally presents the correct H-bonding pattern, did not appear to be suitable, and is readily oxidized (Table 1, entries 5, and 6; Z = CH). Adding an N-atom to yield the 2-aminopyridin-4(3*H*)-one decreases the susceptibility to oxidation, but creates an unacceptable tautomeric ambiguity.[25]

Table 1. Generalised Watson-Crick base-pairs
(R = H, CH_3; Z = N, CH)

entry	bonding pattern	base-pair	bonding pattern
1	**pyDAA** Donor Acceptor Acceptor		**puADD** Acceptor Donor Donor
2	**pyADA** Acceptor Donor Acceptor		**puDAD** Donor Acceptor Donor
3	**pyAAD** Acceptor Acceptor Donor		**puDDA** Donor Donor Acceptor
4	**pyDAD** Donor Acceptor Donor		**puADA** Acceptor Donor Acceptor
5	**pyDDA** Donor Donor Acceptor		**puAAD** Acceptor Acceptor Donor
6	**pyADD** Acceptor Donor Donor		**puDAA** Donor Acceptor Acceptor

Finally, the **pyADD** and **pyDDA** patterns were implemented in the pyrazine ring. Also the original purine ring has to be changed to pyrrolo[3,2-a]triazol ring (Table 1, entries 5, and 6; Z = N). Although different heterocycles can support individual hydrogen-bonding patterns, only some representations of the same pattern are more suitable in artificial genetic systems than others (Figure 1).[26]

Figure 1. *C*-glycosidic heterocycles able to implement the **pyDAD** hydrogen-bonding pattern



The ability of NA polymerase enzymes to catalyse the template-directed synthesis of duplex oligonucleotides containing some of these artificial base-pairs has been investigated.[27,28] The most important result is that the *C*-nucleoside linkage itself has no influence on the enzymatic recognition of base-pairs with DNA polymerases.[29] The iso-**G** and iso-**C** base-pairs were successfully incorporated into DNA as self-complementary base-pairs with the Klenow fragment of DNA polymerase I (KF) from *Escherichia coli*.[30] Furthermore, an additional set of codon-anticodon (iso-**C**):(iso-**G**) was introduced and successfully used to incorporate iodotyrosine (an unnatural amino acid) into a polypeptide.[31] These encouraging results have triggered a quest for replication of an AEGIS by Polymerase Chain Reaction (PCR). A polymerase suitable for amplifications of a six-letter genetic alphabet was found in HIV reverse transcriptase. One variant of the clinic mutant was found suitable (Y188L), and it has been engineered further. These improvements eliminated the "self-repair" exonuclease activity, and generated doubly-changed HIV reverse transcriptase (Y188L-E478Q). This mutant was able to amplify a DNA containing a **pyDAD-puADA** pair in the PCR reaction. These artificial base-pairs were retained through multiple cycles of amplification. Longer PCR incubation times were needed to produce full-lenght strands than in the case of natural base-pairs. This successful PCR amplification was the first example of a six-letter genetic code replication.[32] A successful practical application was also developed, based on polymerase incorporation of AEGIS components. EraGen Biosciences (www.eragen.com) have developed a process, where a primer having a fluorescently tagged iso-**C** is targeted against a specific region of the SARS-virus DNA sequence. In a real time PCR a polymerase incorporates a fluorescence-quencher-tagged iso-**G** opposite iso-**C**, thus quenching fluorescence in the case when SARS virus is present.

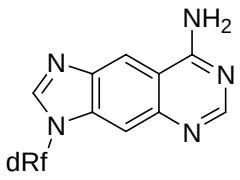
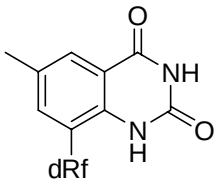
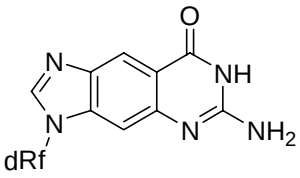
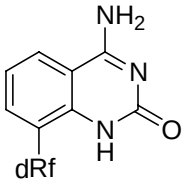
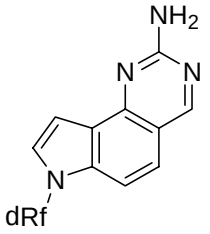
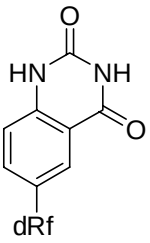
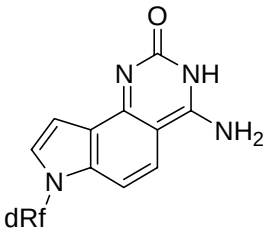
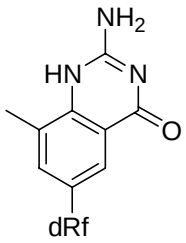
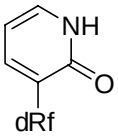
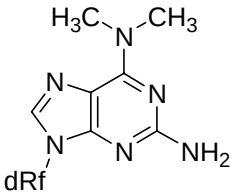
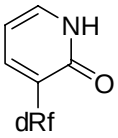
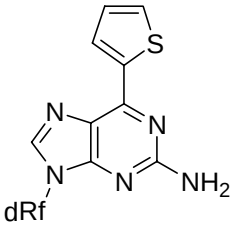
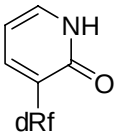
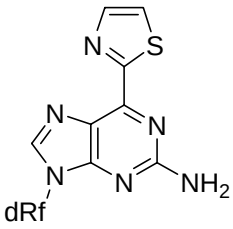
The above stated studies have shown a very important result. An incorporation of *C*-nucleosides into a DNA duplex does not determine the duplex stability.[33] Further progress in the field of artificial base-pairs with H-bonding patterns based on *C*-nucleosides is shown in a table (Table 2).

The natural base-pair analogues in which the fusion of a benzo-ring increases their size by ca. 2.4 Å (x**A**, x**T**, x**C**, x**G**) were reported three decades ago.[34] Kool introduced the idea of size-expanded genetic systems using these structures.[35,36] These *linear* expanded analogues form stable base-pairs and are selectively incorporated into DNA opposite the template strand.[37] More recently, a double helix of size-expanded DNA (xDNA) containing all the size-expanded base-pairs have been prepared.[38] This work has shown that a new, expanded helix adopts β-structure, the right-handed-twisting variant that is the most common natural form of DNA. In a similar manner, *angular* expanded analogues (y**A**, y**T**, y**C**) were introduced, which exhibit even better duplex stability when incorporated into DNA.[39]

Hirao introduced the nucleobase **y**,[40] and **v**.[41] The d**y**TP is incorporated into DNA more efficiently than any natural substrate opposite template d**x**.[42] Further optimization of the complementary base gave structure **s**. The d**y**TP was incorporated into DNA opposite template d**s** with higher efficiency and a threefold higher selectivity than the opposite template d**x**.[43] The efficiency and fidelity of **y**-**v** pairing were as high as in natural base-pairs. The RNA transcript containing two consecutive **y** bases was successfully transcribed from DNA template containing two **v** bases.

It is apparent that unnatural base-pairs that are paired using H-bonding patterns offer promising approaches to expanding the genetic alphabet. However, there are some inherent limitations to their selective replication in DNA, due to the range of tautomeric forms of the unnatural bases.[44]

Table 2: Artificial base-pairs with H-bonding patterns

	base-pair[a]		
dx**A**			dx**T**
dx**G**			dx**C**
dy**A**			dy**T**
"dy**G**^{45}"			dy**C**
d**y**			d**x**
d**y**			d**s**
d**y**			d**v**

[a]For all the references see the text below

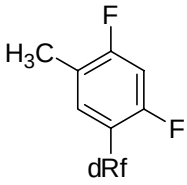
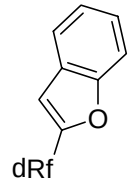
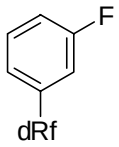
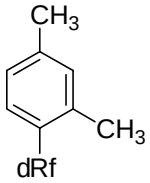
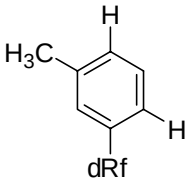
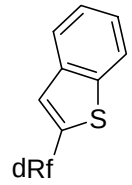
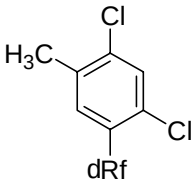
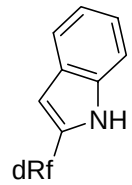
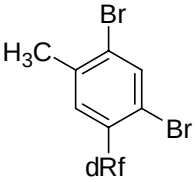
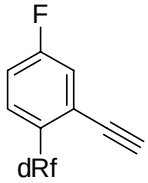
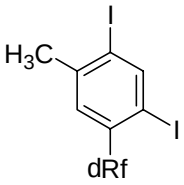
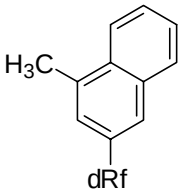
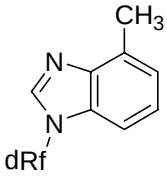
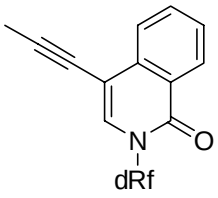
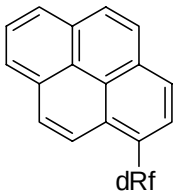
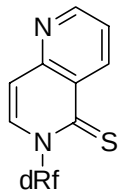
1.2. Artificial Base-Pairs Based on Hydrophobic Interactions

Kool observed that H-bonds are not absolutely necessary and introduced a new concept of hydrophobic interactions.[19] The first nucleoside analogue was difluorotoluene **F**, as an isostere of thymine.[46] Furthermore, corresponding thimidine isoster d**F** triphosphate (d**F**TP), lacking the functionality for H-bonding, was selectively incorporated by DNA polymerases into DNA, opposite d**A** in the template.[47] These results encouraged further research in this kind of base-pairs analogues. They are mainly *C*-nucleosides (Table 3). Also mechanistic aspects of DNA replications were intensively studied.[48]

Many other hydrophobic *C*-nucleosides were synthesised as molecular probes for NA structural and functional studies, as well as for extension of the genetic alphabet. The most significant contributions to this area were from the Berdis,[49] Hirao,[50] Kool,[51] Kuchta,[52] and Romesberg[53] labs.[54] These hydrophobic artificial nucleobases are expected to selectively pair with each other within a DNA duplex. The self-pairs are based on hydrophobic, and more dominantly on packing interactions. A very interesting example has been published, where non-hydrogen bonded, non-shape complementary, but stable and selective base-pair was formed. In this case only the interstrand packing interactions of pentafluorophenyl- and phenyl- pseudonucleobase[55] contributed to the observed stability.[56] Contributions of all these interactions were investigated in an extensive theoretical study.[57] The unwinding free energy of 128 DNA octamers was correlated with the sum of interaction energies among DNA bases and their solvation energies, utilizing advanced level of theory, high accurate calculations. The results shows the importance of inter- and more importantly intramolecular stacking energies for the DNA duplex stabilization. These interactions are diminished when pairing a hydrophobic base-pair with a natural nucleobase, due to forced desolvation of a hydrophilic natural nucleobase. This enhanced the selectivity and stability of a hydrophobic self-pair or different, but hydrophobic base-pair.

Many nucleotides bearing these artificial nucleobases were successfully replicated.[64,65,67] However, the utility was limited by insufficient rate of insertion of the next correct nucleobase, i.e. NA strand extension. More recently, significant improvements in this field were achieved, mainly utilising artificial nucleobases with a relatively small aromatic surface. The minor groove hydrogen bonds interactions are expected to be the main interaction for a successful polymerase-mediated extension in these cases.[58]

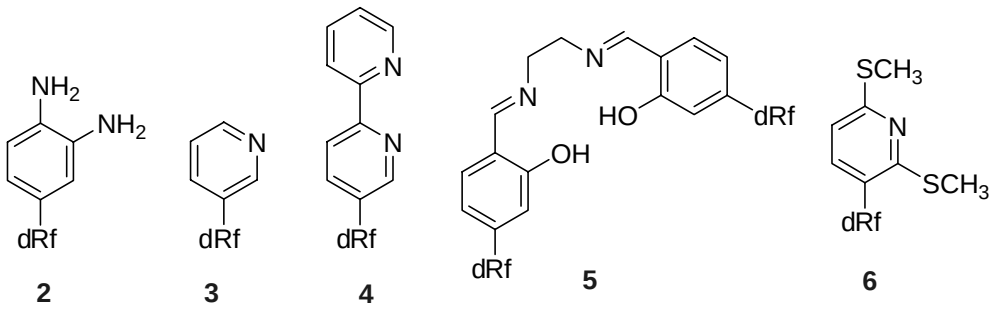
Table 3. Artificial base-pairs with hydrophobic bonding patterns

sign (pairs with)	nucleoside	sign (pairs with)	nucleoside
d**F** (d**A**, d**Z**, d**Q**)		**BFr**[59] self-pair	
3FB[60] self-pair		**DM5**[61] self-pair	
d**H**[62]		**BTp**[59] self-pair	
d**L**[62] (d**I**)		**IN**[59] self-pair	
d**B**[62] (d**I**)		d**F**[63] (d**A**)	
d**I**[62] self-pair		**3MN**[64,65] self-pair	
d**Z**[66] (d**F**)		**PICS**[65,67] self-pair	
d**P**[68] (a-basic)		**SNICS**[59] self-pair	

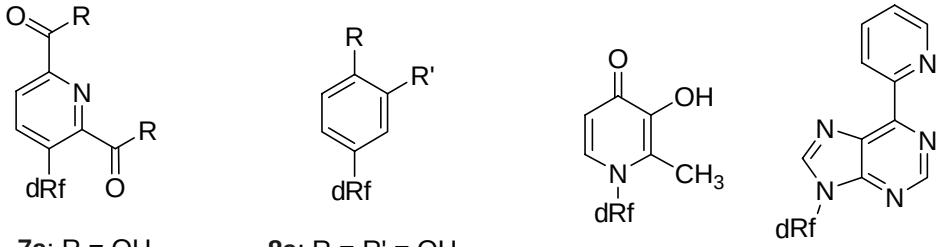
1.3. Artificial Base-Pairs Based on Metal Bridges

Unnatural nucleobases that have the ability to bind metal ions can replace their natural analogues in DNA.[20] Metal-containing base-pairs could be incorporated into DNAs at desired positions. When the bond energy of metal coordination is compared with that of H-bonding, one ligand-metal bond should compensate for two or three H-bonds. Metal ions incorporated in this way could serve at least five purposes. (1) They could regulate thermal stability of high-order structures of DNA (duplex, triplex, etc.). (2) They could allow one-dimensional metal arrays in direct-stacked contact along the DNA helix axis with interesting chemical and physical properties, with applications far beyond chemical biology, such as molecular wires[69] or single-molecule magnets.[70] (3) They could be used to generate metal-dependent functions such as redox or photochemical catalysts. (4) They could be able to assemble DNA duplexes at the junctions to form two- or three-dimensional DNA networks. (5) Finally, DNA could be labelled with metal ions for genetic analytical use.

Interactions of the DNA helix with various metal salts and complexes have been well known, as well as the effect of subsequent stability enhancement, presumably due to the metal coordination.[71] The first artificial metal ligand-type nucleoside **2** (so called "ligandoside") was described in 1999 by Shionoya.[72] Since then, other nucleosides having mono- to tri-dentate ligands for metal-mediated base-pairing have been reported. The *C*-glycosidic connection is the preferred feature in this class of artificial nucleosides. To date, *C*-nucleosides **2**-**8** and *N*-nucleoside **9** and **10** have been reported. A salen-based *C*-nucleoside was recently developed. This new "ligandoside" **5** features an interesting combination of metal coordinating groups, and a covalent cross-link.[73]



2 **3** **4** **5** **6**

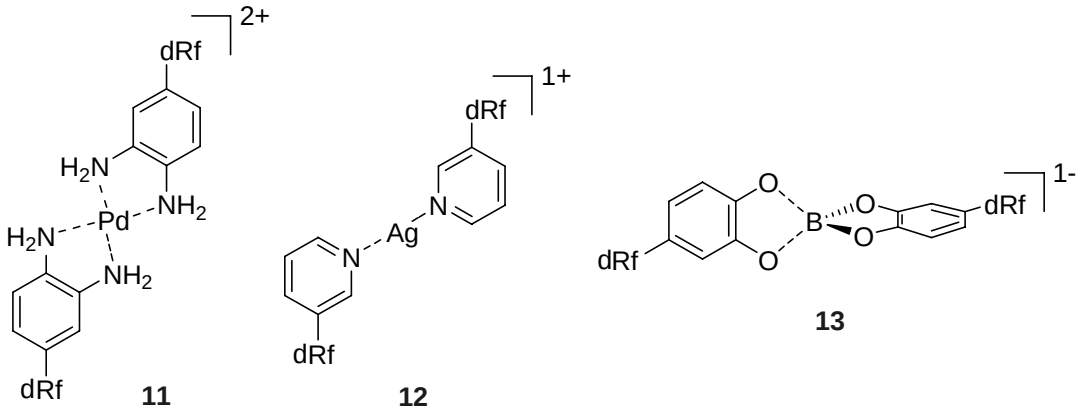


7a: R = OH
7b: R = NH_2
7c: R = NHMe

8a: R = R' = OH
8b: R = NH_2, R' = OH
8c: R = OH, R' = NH_2

9 **10**

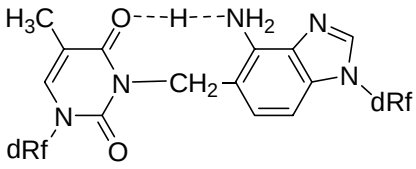
The pseudonucleobase moiety can form a stable metal complex in a linear, trigonal-planar, square-planar, tetrahedral or octahedral geometry. Among these geometries, a linear, trigonal-planar and square-planar mimic a flat, H-bonded natural base-pair geometry, and just square-planar **11**, linear **12** and tetrahedral **13** have been synthesized. To date, complexes of Ag(I),[74] B(III),[75] Co(II),[76] Cu(II),[77] Fe(III),[78] Hg(II),[79] Mn(III),[78] Ni(II),[76,78] and Pd(II)[72,80] have been reported.



11 **12** **13**

1.4. Artificial Base-Pairs Based on Covalent Cross-Linking

The concept of covalently cross-linked DNA with molecular architecture similar to the Watson-Crick H-bonded base-pairs was introduced by Leonard in 1986.[81] Since then, several papers with this unique structural motif have appeared.[21,82]



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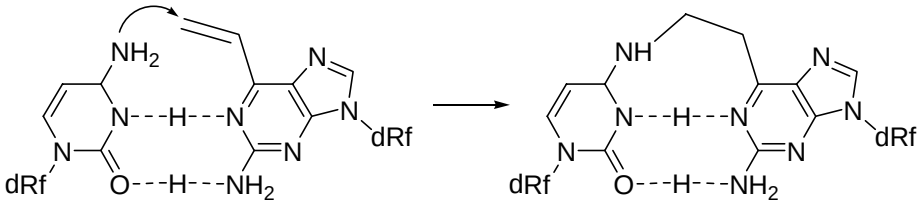
These base-pairs were incorporated into the DNA as cross-linked structures **14** from the very beginning[21a] or formed the crosslink sequence-selectively inside the DNA. As an example, the d**G**-d**C** pair analogue **15** is formed after the attack of vinyl functionality by the deoxycytidine amino group (Scheme 1).[21b]

Scheme 1. Formation of sequence selective cross-link inside the DNA

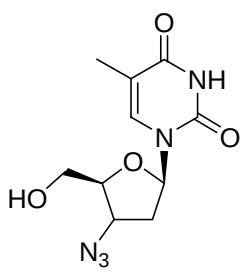


d**C** **15**

2. Artificial Nucleosides in Medicinal Chemistry

The nucleoside analogues have also an important impact on medicinal chemistry as antineoplastics and virostatic drugs.[83,84]

The current stock pile for the chemotherapy of viral infections consists of 37 licensed antiviral drugs. Among them are seven inhibitors of nucleoside reverse transcriptase (NRTIs), mainly for treatment of retroviral HIV infection. There are zidovudine **16**, didanosine **17**, zalcitabine **18**, stavudine **19**, abacavir **20** and L-nucleosides lamivudine **21** and emtricitabine **22**.



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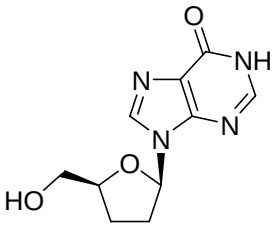

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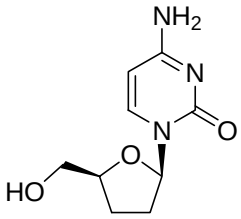

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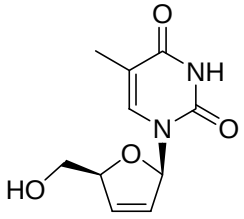

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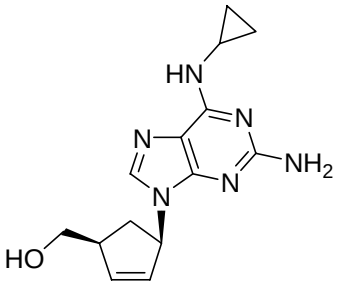

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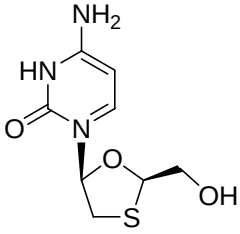

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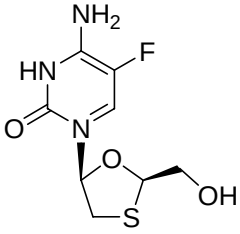


22

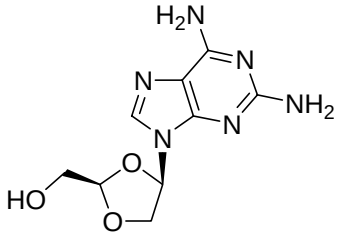
The mode of action of these drugs has been extensively studied, and comprehensive reviews have been published.[85] In general, after the transport of the parent drug inside the cell, all NRTIs are transformed into the corresponding 5'-mono-, di- and tri-phosphate, using cellular/viral phosphokinase enzymes. The 5'-triphosphate itself is the active drug. In the case of DNA viruses (human herpes virus, varicella-zoster virus, cytomegalovirus), the virus-encoded nucleoside kinase accomplished the formation of the antiviral drug monophosphate that is metabolised further to the corresponding di- and tri-phosphate by cellular kinase enzymes. The monophosphorylation step is the rate-limiting step in this case, and thus contributes significantly to the overall antiviral activity. On the other hand, retroviruses (human immunodeficiency virus 1, human immunodeficiency virus 2, simian immunodeficiency virus, feline immunodeficiency virus) do not encode their own nucleoside kinase and antiretroviral drugs are phosphorylated, diphosphorylated, and triphosphorylated directly by cellular kinase enzymes.

The mechanism of action of these drugs is based on the substrate competition of the natural nucleoside triphosphate and the drug triphosphate and subsequent inhibition of viral reverse transcriptase (for RNA viruses) or viral DNA-polymerase (for DNA viruses) catalysed viral DNA polymerization reaction. The termination of the viral DNA-chain elongation is due to the lack of 3'-hydroxy group functionality, required for the connection of the next nucleoside triphosphate. The evolution difference between eukaryotic and viral DNA-polymerase (or viral reverse transcriptase) is one of the most important principles

enabling chemotherapy of a viral infection. The antiviral activity is the result of a higher affinity of the drug-triphosphate to viral DNA polymerase (reverse transcriptase) than to the cellular DNA polymerases α, β, γ, δ and ε.

This affinity ratio means that there is always certain inhibition of the cellular polymerases. The most sensitive is the mitochondrial polymerase γ. The result is a mitochondrial toxicity with various adverse effects. The most important are peripheral neuropathy (sensory disorders, itching, and pain), bone marrow suppression, liver failure, and myopathy.[86]

There are also several NRTIs drugs in current clinical trials. Amdoxovir **23**, dOTC **24**, FdOTC **25**, reverset **26** and alovudine **27**. Various combinations of these and/or already licensed drugs are also being investigated.[11a]



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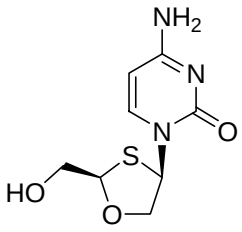

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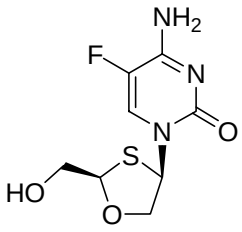

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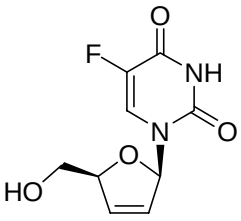

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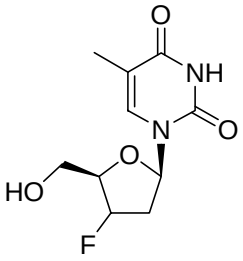
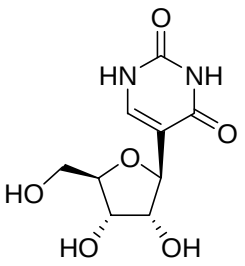


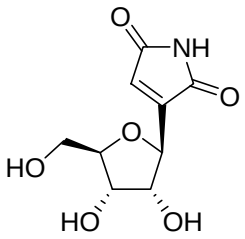
27

Intensive research in this area promises further development in terms of high activity, selectivity and low toxicity.[87] The use of *C*-nucleosides could improve the stability, i.e., the halftime of decomposition inside the cells.

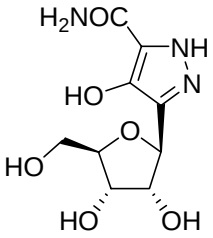
The *C*-nucleosides themselves have become important among modern antineoplastics.[88] This series is dominated by the ribose structural pattern as a carbohydrate part; representative examples are pseudouridine **1a**,[89] showdomycin **1b**,[90] pyrazofurin **1c**[91] and thiazofurin **1d**.[92]



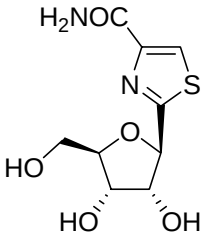
1a



1b



1c



1d

The mechanism of action of these drugs is very similar to the antivirals. The difference is in targeting the modified human DNA polymerase of tumour cells, instead of the viral polymerase. Obviously this is far more challenging and intensive research in this field is highly desirable.[93]

3. Synthetic Routes to *C*-Nucleosides

Since the Cohn discovery of the first *C*-nucleoside pseudouridine **1a**, these natural products and their artificial analogues became an important part of research. The low natural abundance of *C*-nucleosides together with a high desire for their analogues led to a focused interest in this class of compounds. Many synthetic strategies have been developed and summarised in excellent reviews.[94] Different approaches may be employed to classify these strategies. We would like to present the following scheme in this chapter, regarding the structural features of *C*-nucleosides.

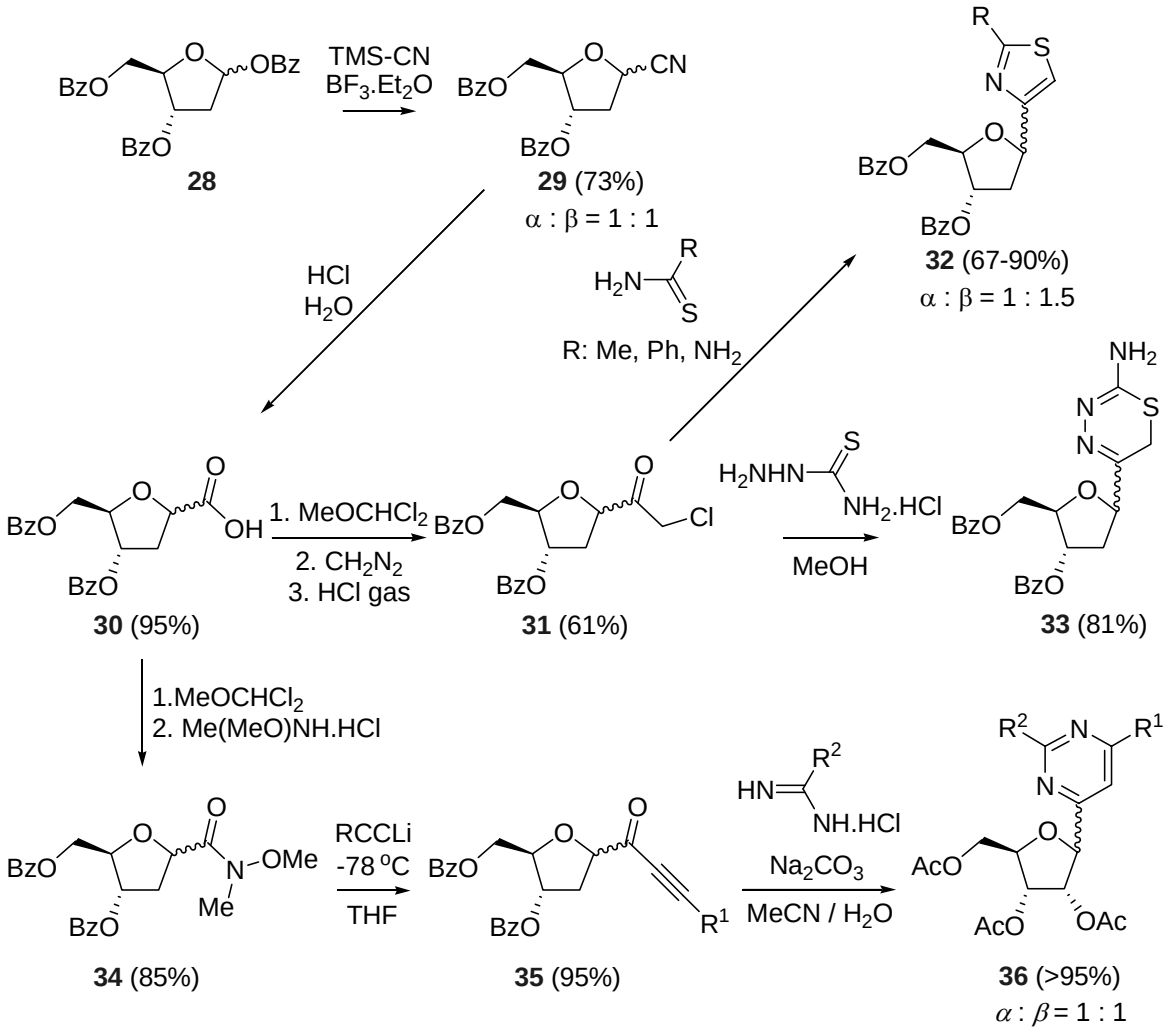
(1) Connection of an appropriate functional group to an anomeric position of a preformed carbohydrate moiety, followed by a construction of the aglycon unit. (2) Connection of an appropriate functional group to a preformed aglycon, followed by a construction of the carbohydrate moiety. (3) A direct coupling of a preformed carbohydrate moiety with an aglycon. (4) Chemical modification of an existing *C*-nucleoside.

3.1. Construction of an Aglycon Unit upon a Carbohydrate Moiety

3.1.1. Introduction of the CN Group

The first synthetic strategy for the introduction of the appropriate functional group onto a preformed carbohydrate is often utilized to construct heterocycles.[95] A classical example is the introduction of the CN-group (Scheme 2). For example, Baldwin and co-workers introduced the CN group in the reaction of fully benzoylated carbohydrate **28** with trimethylsilyl cyanide.[96] The resulting mixture of nitrile anomers **29** was hydrolyzed to carboxylic acid **30**. This precursor was converted into a chloroacetyl derivative **31** by reaction with α,α-dichloromethyl methyl ether, diazomethane, and HCl respectively. Subsequent cyclization with thioamide nucleophiles gave substituted thiazoles **32** in moderate to good yield. Cyclization with semithiocarbazide afforded aminothiadiazole **33** as a mixture of anomers in good yield. Acid **30** can be converted into amide **34** whose reaction with lithium acetylide afforded acetylene **35**. Treatment of the latter derivative with amidoimidates produced pyrimidines **36** as a 1:1 mixture of anomers in good yield.[97]

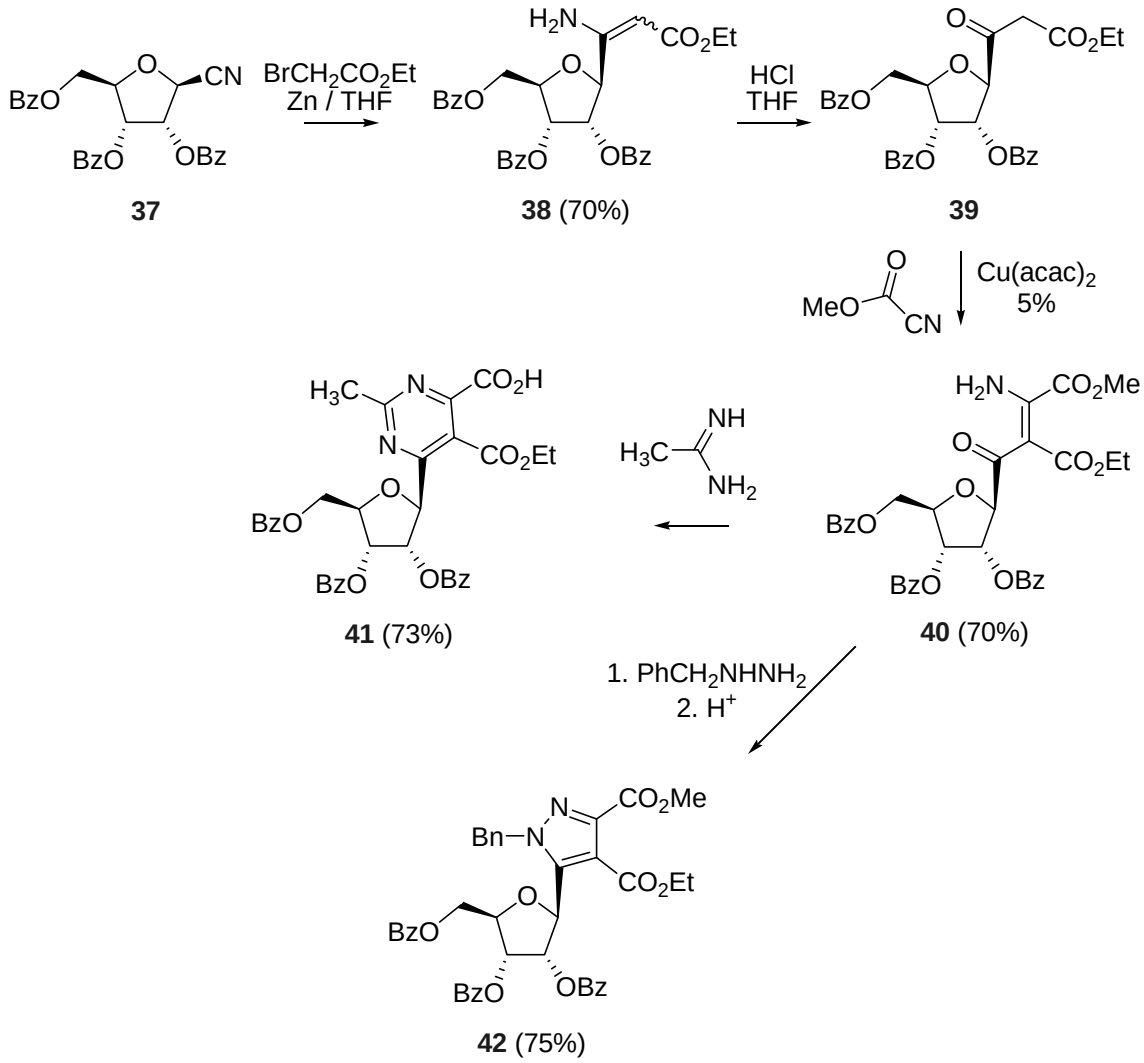
Scheme 2. Introduction of the CN group followed by heterocylic ring construction



The above presented cyano-group introduction is a non-stereoselective reaction, affording an equimolar mixture of both anomers. However, the carboxylic acid **30** is suitable for a chromatographic separation of the anomers. Thus, there is a possibility to carry out the subsequent reactions with pure diastereoisomers.

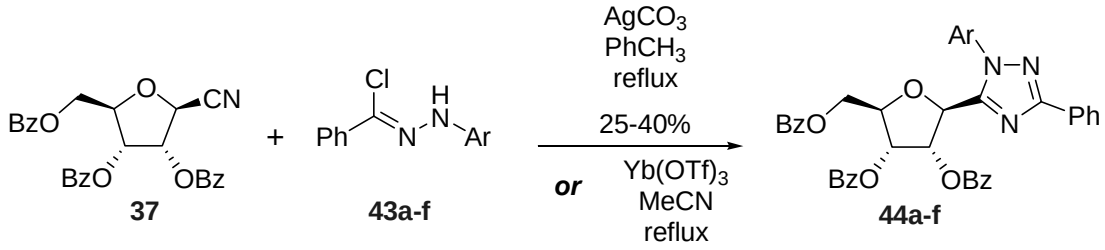
Protected 1-cyano-*β*-D-ribofuranose **37** was employed in the synthesis of pyrimidines by Veronse *et al* (Scheme 3).[98] To the nitrile group was added the Reformatsky organozinc reagent to form β-iminoester **38**.[99] After hydrolysis, the resulting unstable β-ketoester **39** was immediately treated with methyl cyanoformate is the presence of copper(II) catalyst to afford diester **40** in good overall yield. Subsequent cyclization of **40** with amidoimidates or benzylhydrazine furnished the protected pyrimidine- **41** and pyrazole- *C*-nucleoside **42**, respectively.

Scheme 3. Construction of pyrimidines **41**, and pyrazoles **42**



Al-Masoudi *et al* reported a procedure employing *β*-cyano functionality in a cycloaddition reaction.[100] Protected 1-cyano-*β*-D-ribofuranose **37** was treated with various hydrazonyl chlorides **43** in the presence of Lewis acids to afford 1,2,4-triazoles **44** in good yields when ytterbium triflate was used (Scheme 4).

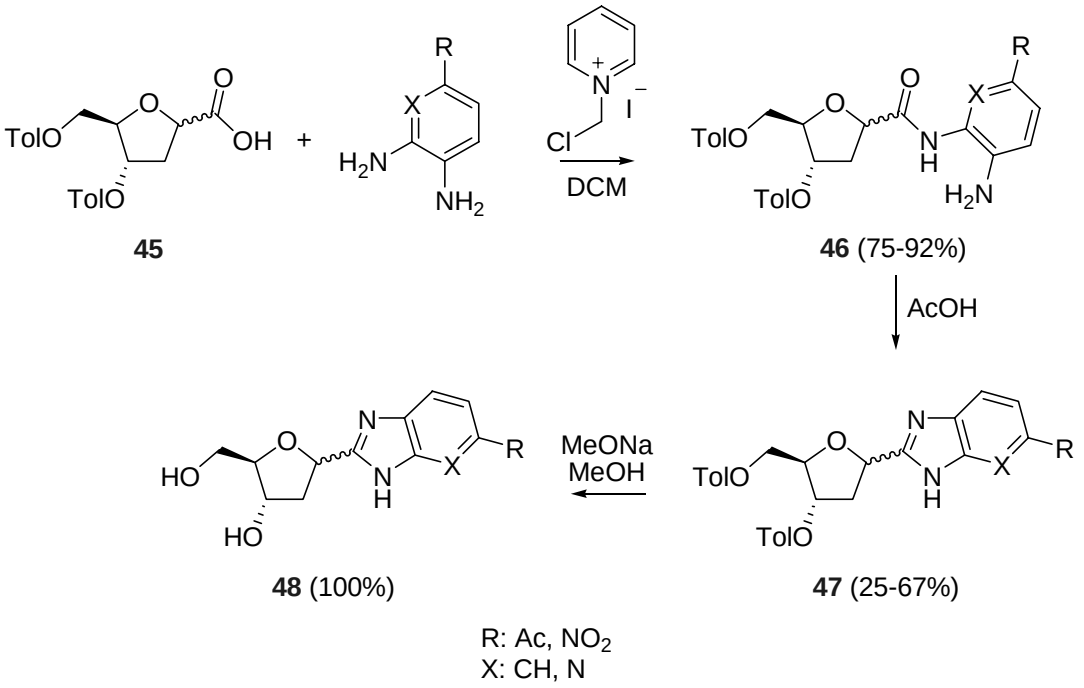
Scheme 4. Cycloaddition on nitrile, construction of 1,2,4-triazoles **44**



44a (74%) Ar = 2,4,6-$Cl_3C_6H_2$
44b (66%) Ar = *p*-ClC_6H_4
44c (66%) Ar = *p*-FC_6H_4
44d (58%) Ar = *p*-OHC_6H_4
44e (63%) Ar = *p*-$NO_2C_6H_4$
44f (64%) Ar = 2,4-$F_2C_6H_3$

Benhida *et al* reported a similar approach employing the tolylated acid **45** in the reaction with a variety of diamines using MuKaiyama reagent (chloromethylpyridinium iodide) in dichloromethane.[101] The resulting amides **46** were cyclized under acidic conditions to the corresponding benzo- and pyrido-imidazoles **47**. Basic deprotection with sodium methanolate afforded *C*-nucleosides **48** in moderate overall yields (Scheme 5).

Scheme 5. Construction of imidazole rings; X = CH or N

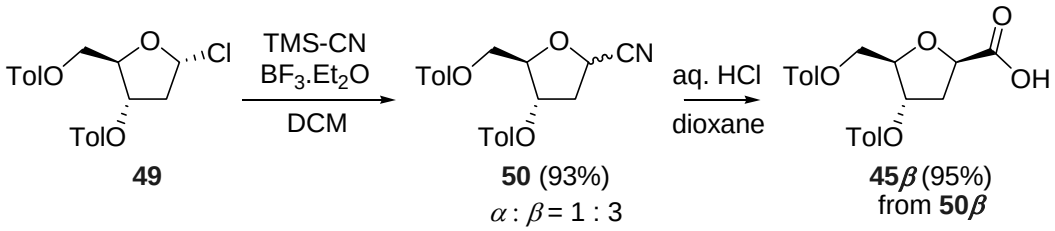


R: Ac, NO_2
X: CH, N

The diastereoselectivity of the above reactions fully depends on the initial cyano group introduction. Benhida *at al* reported a moderate diastereoselectivity (50% de) when α-chlorodeoxyribose **49** was used as a starting material. The resulting mixture of anomers

proved to be separable, and the desired 1-cyano-β-deoxyribofuranose **50β** was employed in the subsequent reaction sequences (Scheme 6).[101]

Scheme 6. Preparation of diastereopure acid **45β**



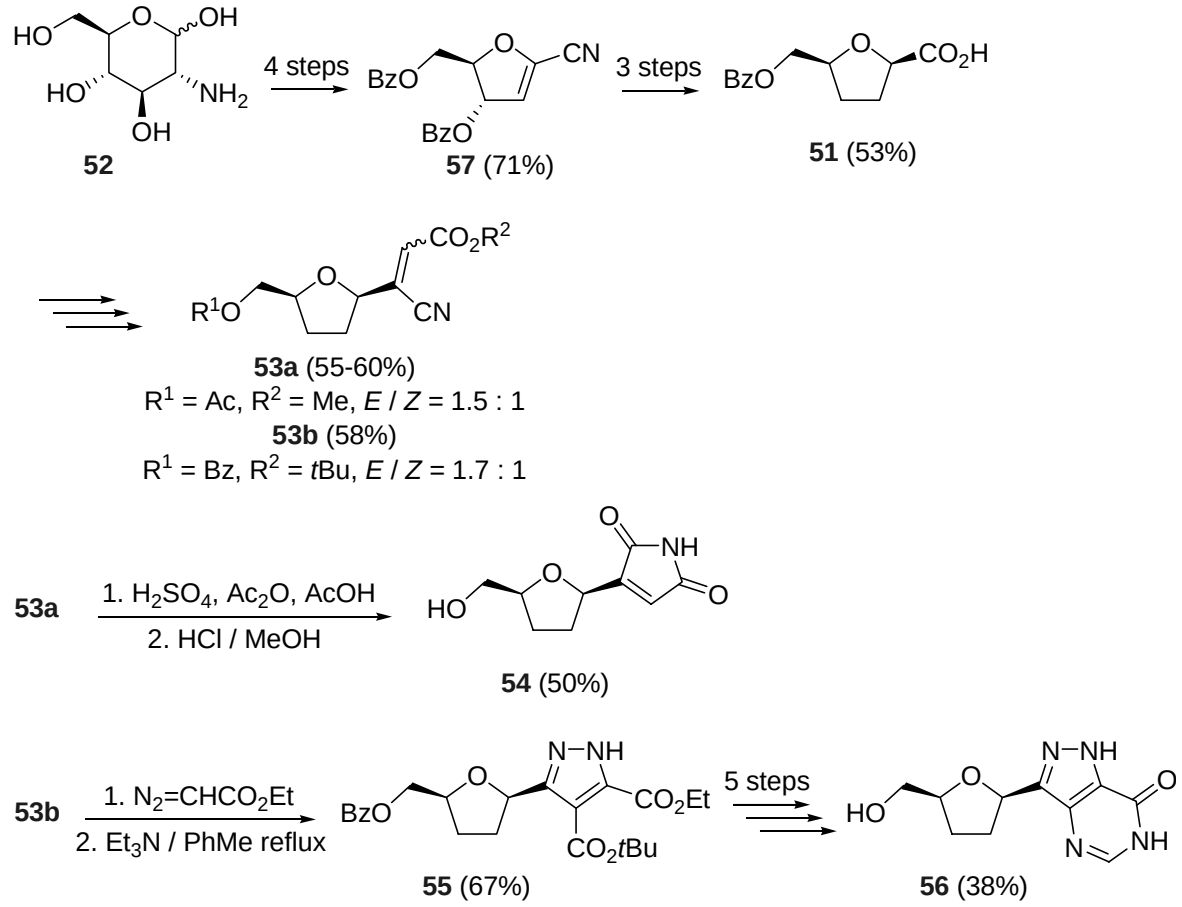
49

50 (93%)
$\alpha : \beta = 1 : 3$
(separable diastreoisomers)

45β (95%)
from **50β**

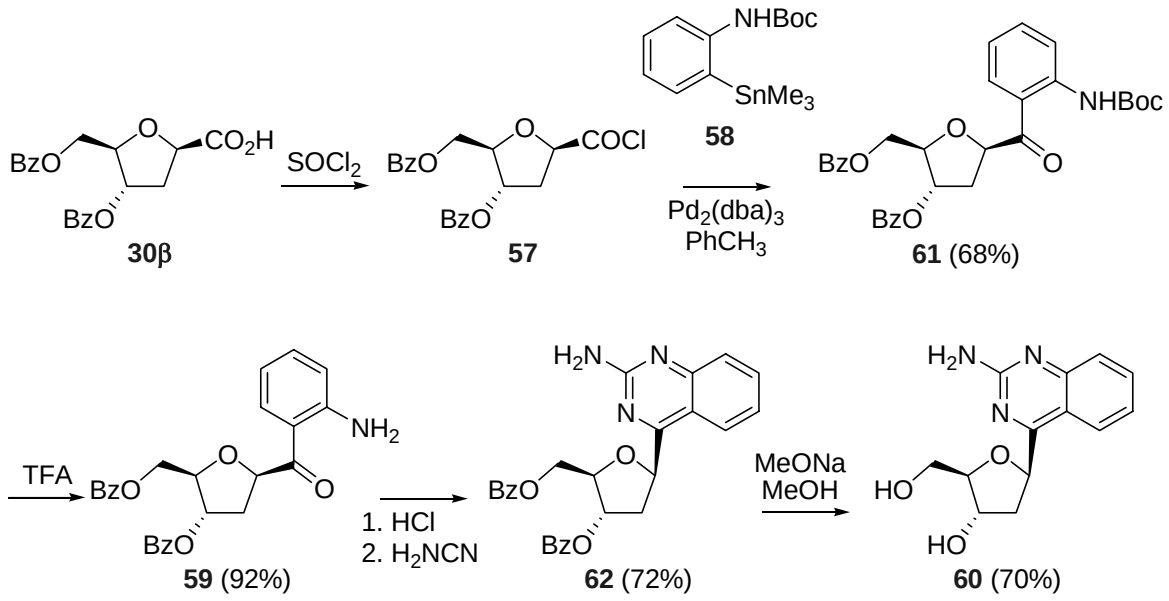
This strategy was also employed in the synthesis of dideoxynucleosides. Jung *et al* reported the synthesis utilising the purified β-anomer of protected acid **51**, readily available from glucosamine **52** in seven steps and 37% overall yield.[102] The acid **51** was converted into the common intermediate, cyanoester **53** by a cyanation reaction, followed by the Wittig-type reaction with the appropriate triphenylphosphorane. Various ester functionalities were utilised in the cyanoester **53**. Cyanoester **53** was either cyclised and deprotected to afford dideoxyshowdomycin **54** in the way of Ohno's synthesis of showdomycin,[103] or submitted to cyclization reaction with ethyl diazoacetate to give pyrazol diester **55**. Dideoxyformycin B **56** was finalised and deprotected in five following steps (Scheme 7).

Scheme 7. Construction of dideoxyshowdomycin **54** and dideoxyformycin B **56**



More recently Gold *et al*. reported a procedure employing the purified *β*-anomer of protected acid **30**.[104] The acid **30*β*** was converted to the corresponding acid chloride **57** and submitted to palladium-catalysed Stille coupling reaction with 2-trimethylstannyl aniline **58**. Removal of the protecting group gave aniline **59** in high yield. The cyclization with cyanamide, followed by deprotection, furnished the benzopyrimidine 2'-deoxyriboside **60** (Scheme 8).

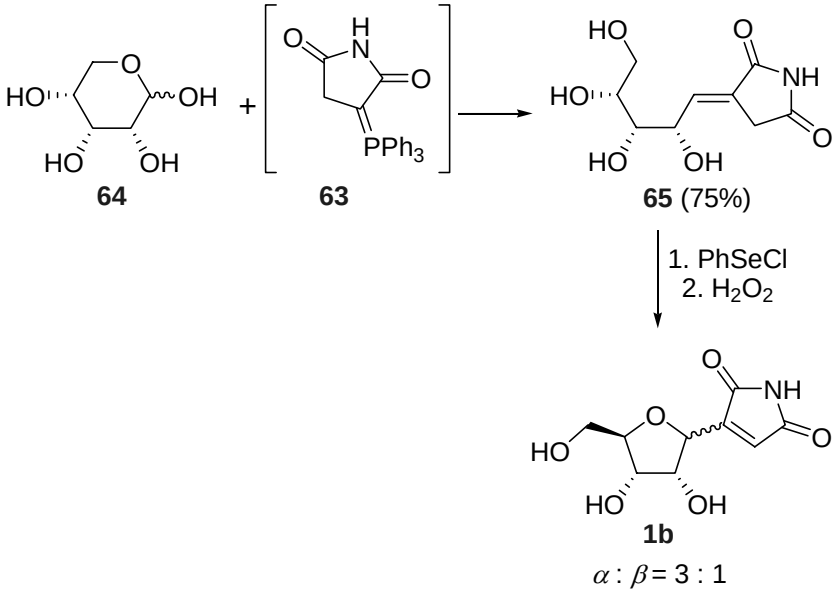
Scheme 8. Construction of diastereopure benzopyrimidines **60**



3.1.2. Wittig-Type Reaction

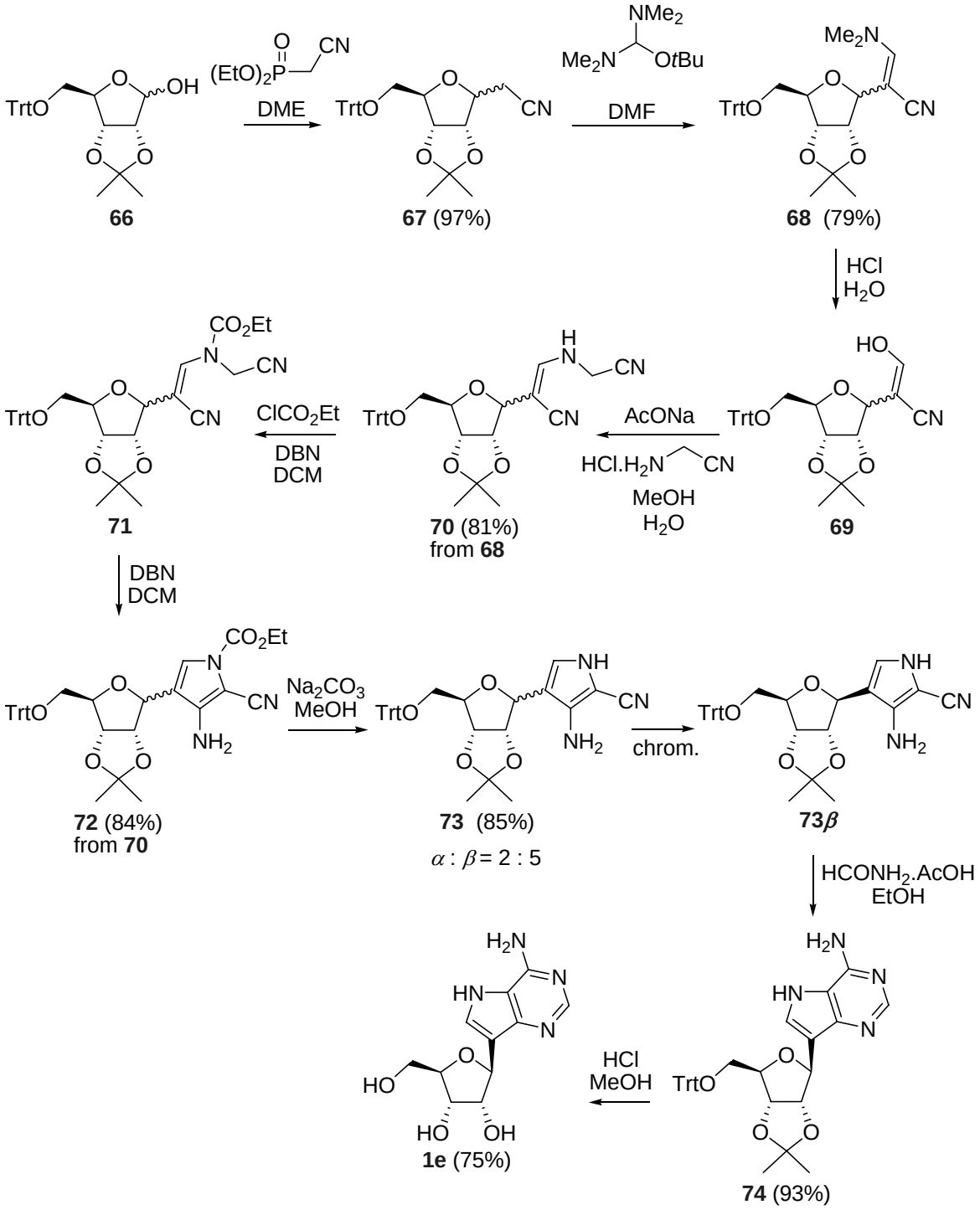
Another important approach within the aglycon building-up strategy is the Wittig-type reaction.[105] This approach is based on the reaction of a phosphorus ylide with an aldehyde function on the carbohydrate moiety. The reaction of ylide **63** with D-ribose **64** in boiling tetrahydrofuran produced compound **65** in 75% yield. Selenoetherification, followed by oxidative elimination, yielded showdomycine **1b*β*** and epishowdomycine **1b*α*** as a 1:3 mixture (Scheme 9).[106]

Scheme 9. Wittig-type chemistry in the synthesis of Showdomycin **1b**



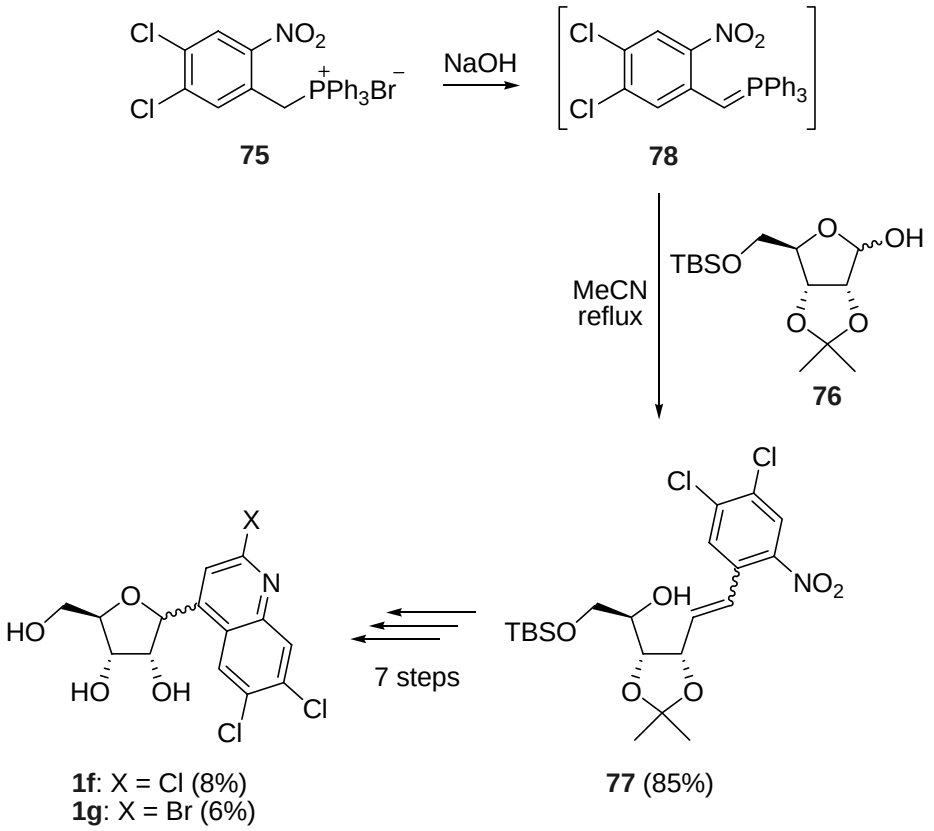
The classical synthesis of 9-deazaadenosine **1e** commenced with the functionality introduction *via* Horner-Wadsworth-Emmons reaction (Scheme 10).[107] Protected ribose **66** produced ribosylacetonitril **67** on reaction with diethyl methylencyanophosphonate. The subsequent reaction with *tert*-butoxy bis(dimethylamino)methane in DMF gave enamine **68**. Acidic hydrolysis and alkylation of enol **69** with aminoacetonitrile hydrochloride in an acetate buffer produced bis-nitrile **70** in good yield over two steps. Protection of the secondary amino function with ethylchloroformate afforded intermediate **71** and subsequent cyclization with an excess of base produced the functionalized pyrrole **72** in good yield. After deprotection, the pyrrole-anomers **73** were separated using column chromatography. Pure *β*-D-anomer **73*β*** was cyclized with formamide acetate in boiling ethanol to produce the protected adenosine **74**. Deprotection afforded the *C*-analogue of adenosine **1e** in 22% overall yield, after 10 steps from protected ribose **66**.

Scheme 10. Classical synthesis of 9-deazaadenosine **1e**



Wittig-type chemistry was used by Townsend *et al* to construct polyhalogenated quinolines as potential antiviral agents (Scheme 11).[108] Phosphonium bromide **75** was treated with sodium hydroxide and then directly coupled with protected ribose **76** to afford alkene **77** in a good combined yield of two isomers (85%, *Z*:*E* = 12:1). This mixture was elaborated in seven steps to the desired *C*-nucleosides **1f**, and **1g** bearing bromodichloroquinoline, and trichloroquinoline aglycon, respectively. However, the overall yield was low.

Scheme 11. Construction of polyhalogenated quinoline **1f-g**

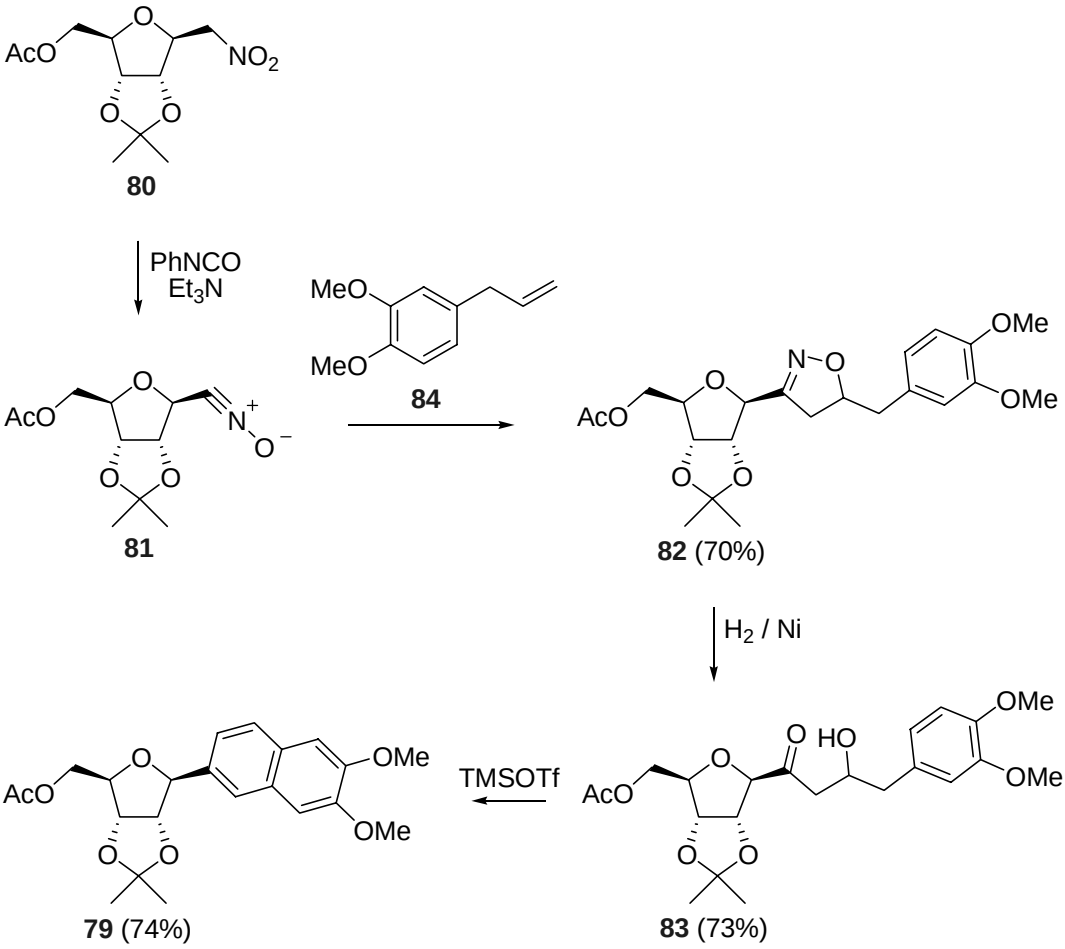


3.1.3. Cycloaddition

Cycloaddition reactions have become an important strategy to be considered in the construction of aglycons. The first attempts were related to the total synthesis of showdomycin, where Diels-Alder cycloaddition reaction was used to construct the carbohydrate moiety with an appropriate functional group in the anomeric position.[103] In the same year (1984) Kozikowski *et al* employed a 1,3-dipolar cycloaddition reaction in the synthesis of artificial nucleoside analogues bearing an isooxazoline ring instead of ribose, and in the total synthesis of (±)-blastomycinone.[109]

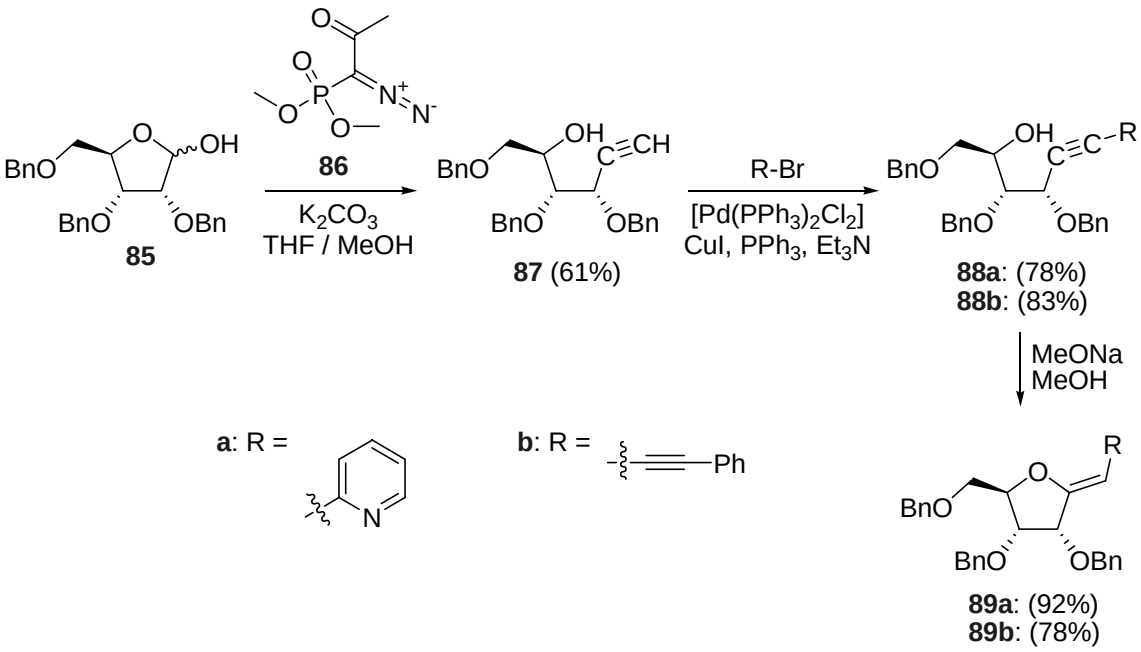
With this experience in hand, Kozikowski *et al* soon reported the first example of 1,3-dipolar cycloaddition in the synthesis of dimethoxynaphthyl *C*-nucleoside **79**.[110] Starting with the nitromethylene derivative **80**, conversion to the nitrile oxide **81** was achieved as shown, and cycloadition with the substituted allyl benzene afforded isooxazoline **82**. Reduction of the latter product with Raney nickel then gave ketoalcohol **83** that was cyclized to the aryl *C*-nucleoside **79** on treatment with trimethylsilyl triflate (Scheme 12).

Scheme 12. 1,3-Dipolar cycloadition in construction of aglycon unit



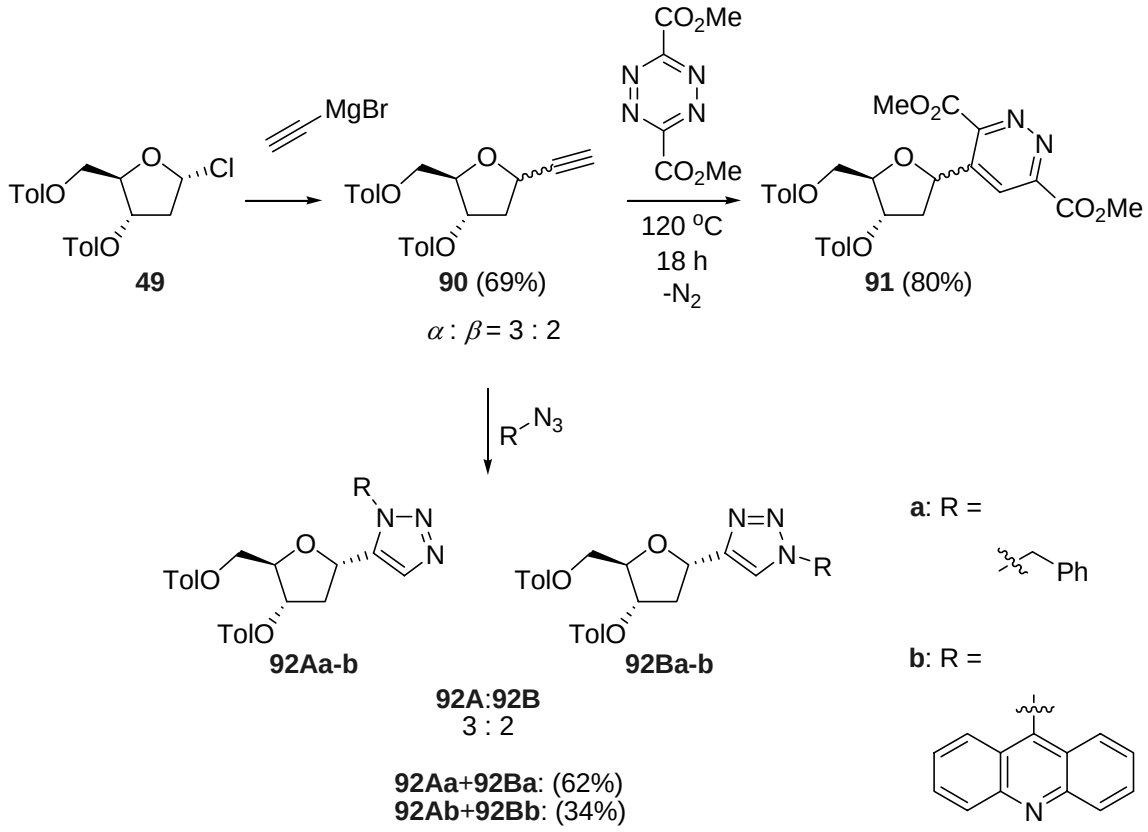
More recent procedures employ reactions involving an alkynyl glycoside, either as an intermediate or directly for the cycloaddition reaction. Vasella *et al* reported a procedure of *exo*-glycals (Scheme 13).[111] The triple bond was introduced directly to the hemiacetal carbon of the protected carbohydrate **85**. The proposed Corey-Fuchs's procedure of alkynylation failed and Ohira's method was used instead, utilizing phosphonate **86**. The resulting alkyne **87** was submitted to palladium-catalysed cross-coupling reaction with 2-bromopyridine and (bromoethynyl)benzene under the Sonogashira reaction condition to afford alkynes **88a** and **88b** in good yield. Base-catalysed cyclization gave desired protected *exo*-glycals **89a** and **89b** in good yield.

Scheme 13. Cycloaddition in construction of *exo*-glycals



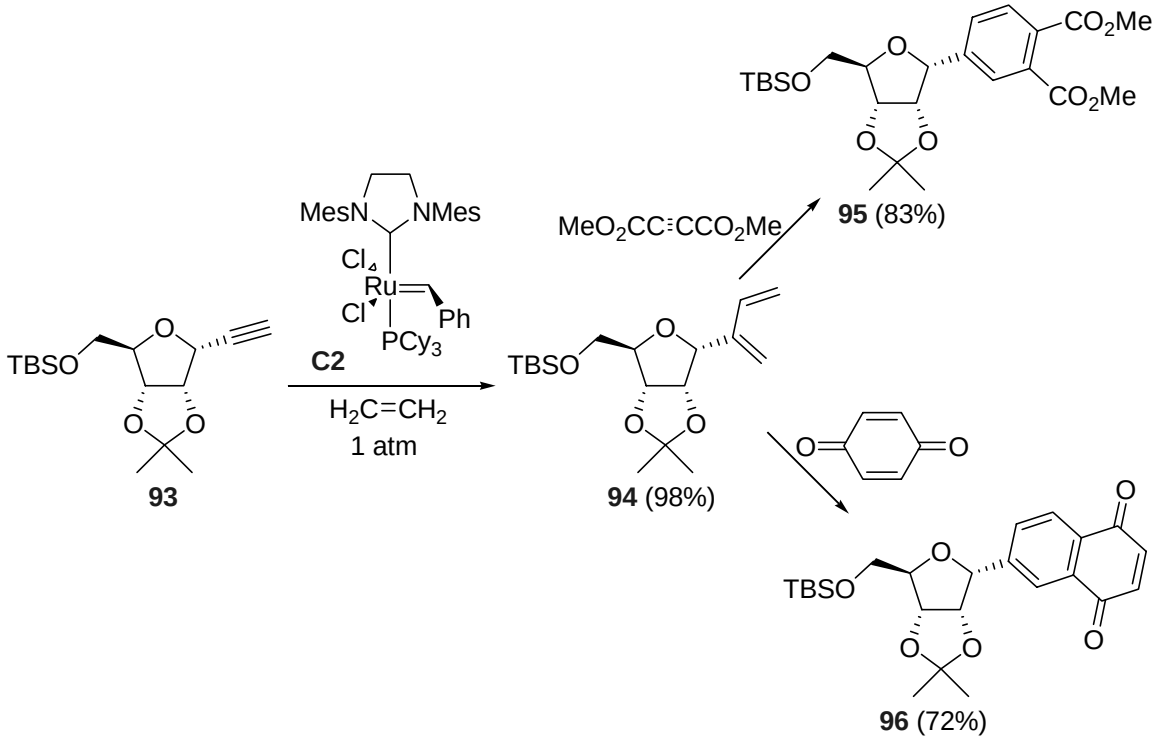
Other procedures have utilised an ethynyl group connected to the anomeric C-atom. The key intermediate, ribofuranosylethyne **90** may be prepared with various degrees of stereoselectivity. Unfortunately, the α-anomer is the predominant product in all the procedures. Wamhoff *et al* reported synthesis of pyridazine- and triazole- *C*-nucleosides (Scheme 14).[112] An *alpha* anomer of chlororibose **49** was reacted with ethynylmagnesium bromide to afford tolylated ribofuranosylethyne **90** as a mixture of anomers. A strong influence of the protecting groups was expected. The ester-based protecting groups (Ac, Bz, Tol) were responsible for a strong neighbouring effect during ethenyl group introduction. The anomeric mixture of **90** was submitted to the Diels-Alder cycloaddition reaction. In the presence of dimethyl [1,2,4,5]-tetrazine-3,6-dikaboxylate, the cycloadduct was formed and spontaneously decomposed under the Diels-Alder reaction conditions and gave pyridazine **91**. The anomeric mixture of **90** was reacted with azides in [3+2] cycloaddition reaction to afford practically equimolar (^{1}H-NMR) mixtures of two possible regioisomers **92Aa-b** and **92Ba-b** in moderate yield. The regioselectivity was not influenced by steric effects as shown in the case of azidoacridine.

Scheme 14. Cycloaddition in construction of pyridazines **91** and triazoles **92**



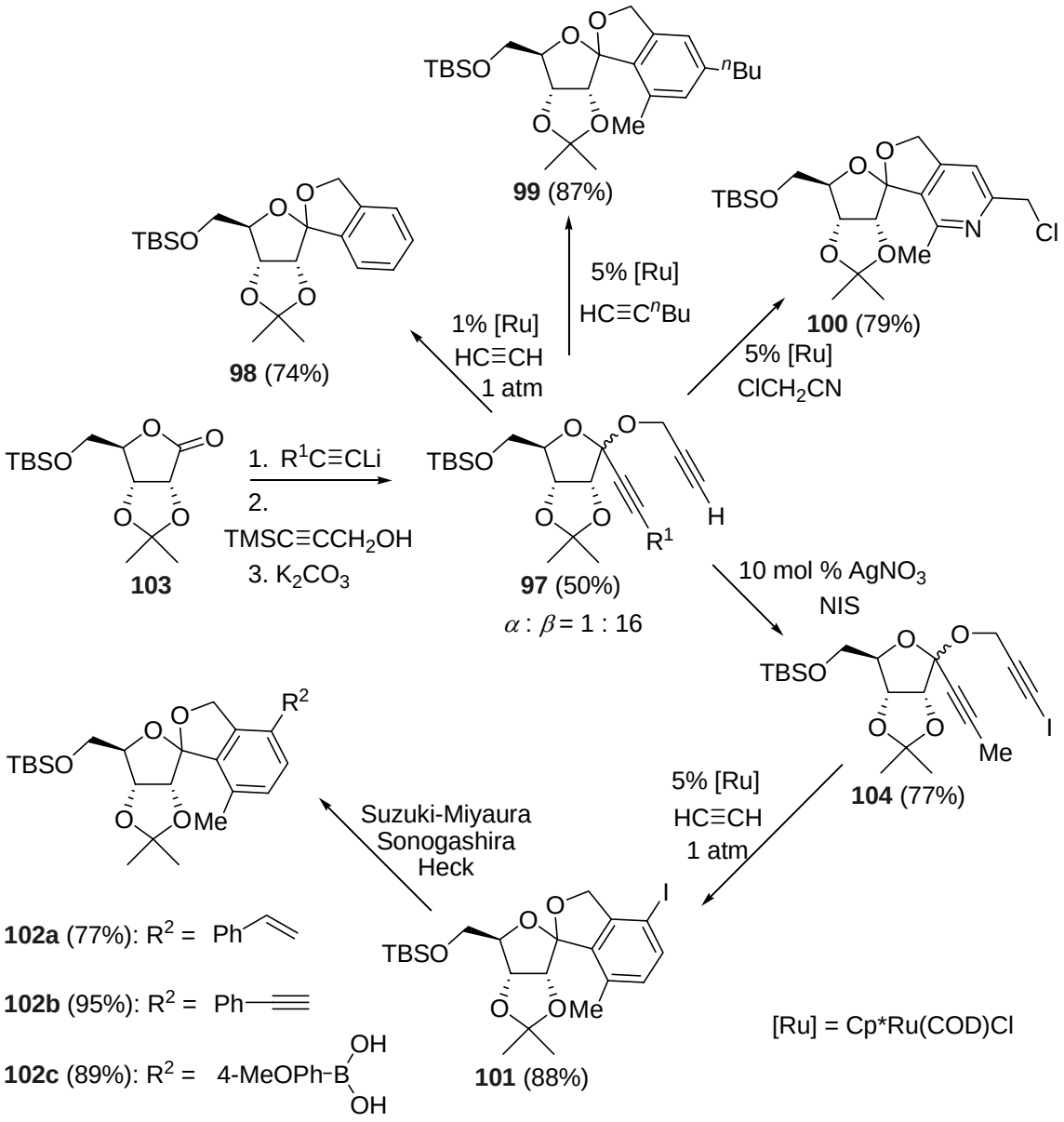
Kaliappan *et al* reported a very efficient procedure leading to *C*-aryl glycosides (Scheme 15).[113] Application of this method to the ribofuranosides was also investigated. The synthetic strategy is based on a cross-enyne metathesis followed by Diels-Alder cycloaddition reaction. Protected ribofuranosylethyne **93** was reacted with ethylene in the means of cross-enyne metathesis catalysed by Grubbs 2nd generation catalyst **C2**. The expected product **94** was isolated in high yield and reacted either with dimethyl ethynyldicarboxylate or benzoquinone to afford α-*C*-nucleosides **95** and **96**, respectively. Both the cross-metathesis and the cycloaddition were carried out in toluene at 80 °C and a two-reactions-one-pot procedure was effected, without any significant difference in the isolated yield.

Scheme 15. Cross-enyne metathesis followed by Diels-Alder cycloaddition



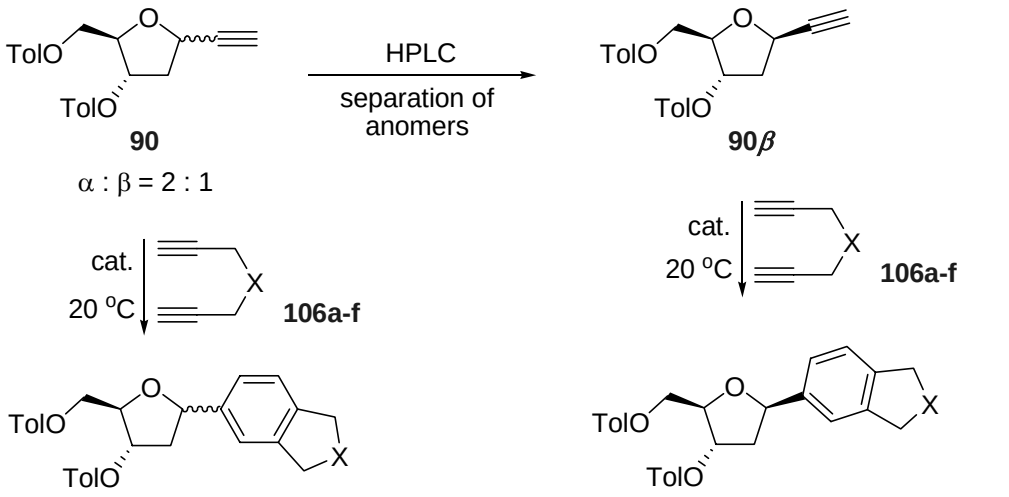
Another atom efficient method was recently published by Yamamoto *et al* (Scheme 16),[114] according to which spirocyclic *C*-nucleosides are formed in a cyclotrimerization reaction. The main advantage here is the presence of three flexible substitution sites upon the newly formed benzene or pyridine ring. The synthesis of predominantly *β*-anomer of di-alkyne **97** was optimized and the latter derivative was cyclized: (1) under ethyne atmosphere to afford unsubstituted benzene (R^1 = H) derivative **98**, with hexyne to produce disubstituted benzene **99** (R^1 = Me), or with chloroacetonitrile to furnish the corresponding pyridine **100**. Iodination, followed by cyclotrimerization, gave intermediate **101** with the third position suitable for further functionalization. The products of Heck **102a**, Sonogashira **102b**, and Suzuki-Miyaura **102c** coupling reaction were prepared in good yield.

Scheme 16. Cyclotrimerization in construction of spirocyclic *C*-arylribosides **102**



Cyclotrimerization leading to standard *C*-nucleosides was reported by Kotora *et al* (Scheme 17).[115] The anomeric mixture of tolylated ribofuranosylethyne **90** was reacted with a range of diynes to afford the expected products of cyclotrimerization **105a-f**. Various transition metal complexes were investigated to promote the reaction. As the authors were aware of the practical importance of *β*-*C*-nucleosides, HPLC separation of the desired anomer **90** was carried out. The pure *β*-anomer **90*β*** gave in cyclotrimerization comparable or improved yields of cycloadducts **105a*β*-105f*β***.

Scheme 17. Cyclotrimerization in construction of spirocyclic *C*-arylribosides **105**



105a (86%) X = $C(CO_2Et)_2$
105b (57%) X = $C(CO_2Me)_2$
105c (57%) X = $C(CO_2Et)CO_2Me$
105d (52%) X = $C(CO_2Et)CN$
105e (17%) X = NTs
105f (32%) X = O

105aβ (95%) X = $C(CO_2Et)_2$
105bβ (81%) X = $C(CO_2Me)_2$
105cβ (62%) X = $C(CO_2Et)CO_2Me$
105dβ (52%) X = $C(CO_2Et)CN$
105eβ (45%) X = NTs
105fβ (32%) X = O

cat.: various complexes of Co, Ir, Ni, Rh, and Ru

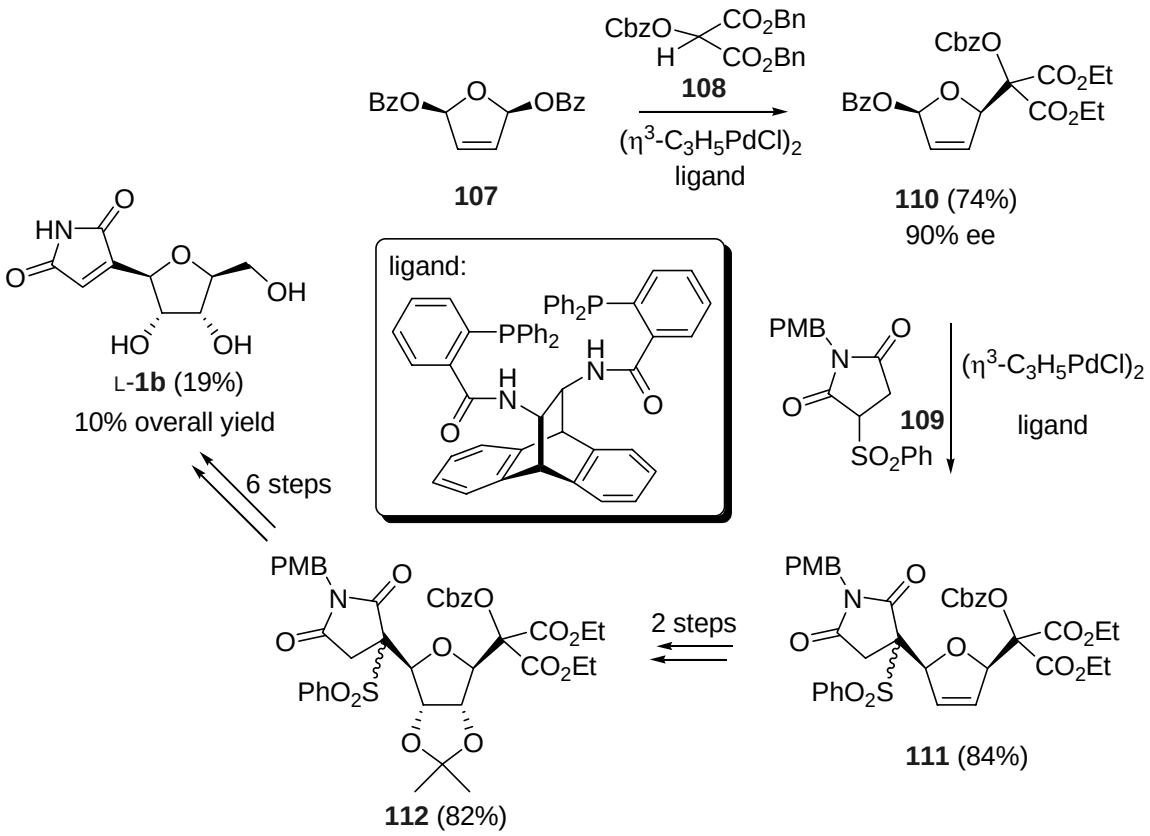
3.1.4. Other Methods of Construction of an Aglycon Unit

Other procedures leading to structures fulfilling the definition of *C*-nucleoside have been developed. However, the practical utility of these procedures is low, as their versatility is low and/or the compounds produced are of a very limited use. Only a brief selection of these methods is presented herein.

Trost *et al* reported the palladium-catalysed asymmetric allylic substitution-based synthesis of L-showdomycin L-**1b** (Scheme 18).[116] This synthesis relies on desymetrization of the enantiopure benzylated dihydrofuran **107**, upon which were constructed both the hydroxymethyl and maleimide moieties. The hydroxymethyl part was introduced in the form of the activated maleic diester **108**, whereas the maleimide moiety in the form of sulfonylsuccinimide **109**. In theory, either part, **108** or **109**, can be introduced in either order. However, the hydroxymethyl precursor **108** was introduced first, followed by the introduction of imide **109** due to the side-products and poor enantioselectivity in the case of the reverse order. The unnatural L-configuration of the final product resulted from the enantioselectivity of the introduction of precursor **108**. Whereas the presented L-configured intermediate L-**110** was obtained in high enantioselectivity of 90% ee, the natural D-configured intermediate D-**110** was attained in more than 76% ee on average. Only the

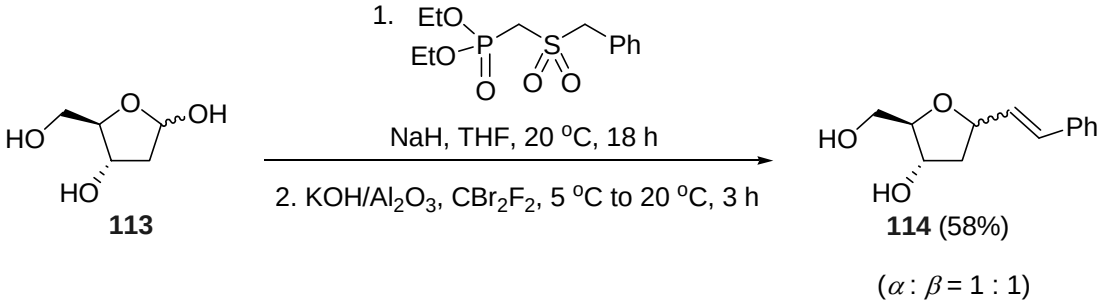
highly advanced "Trost-design" ligands were utilised in this study.[117] Once the building blocks had been attached to the dihydrofurane ring, they were elaborated further to the final target of L-showdomycin L-**1b** in ten steps and 10% overall yield. Although the authors claimed this method to be "a versatile route to the preparation of biologically interesting natural and unnatural *C*-nucleosides", this has not been utilised since published in 1999. The main disadvantage is the long elaboration of suitable precursors towards desired structures, combined with the highly complex, commercially unavailable ligands for the palladium-catalysed allylic substitution.

Scheme 18. Allylic substitution in the synthesis of L-Showdomycin



Fully unprotected 2'-deoxyribose **113** was reacted in a two-step-one-pot reaction protocol to give an equimolar mixture of anomers of *C*-nucleoside **114**. The reaction itself consists of four consecutive steps involving Horner-Wadsworth-Emmons olefination, followed by cyclization, tandem bromination, and Ramberg-Bäcklund reaction (Scheme 19).[118]

Scheme 19. HWE/cyclization-tandem-halogenation/Ramberg-Bäcklund reaction

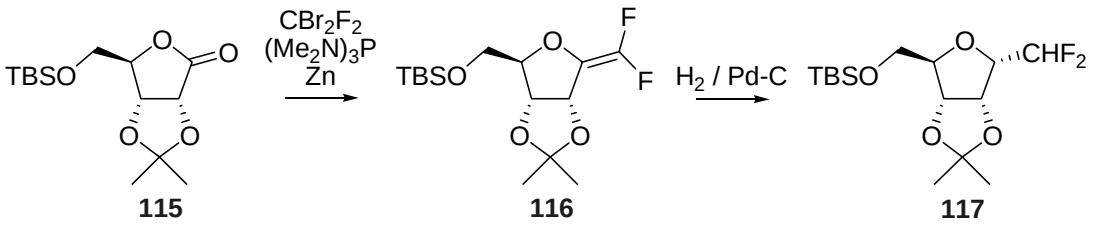


113 **114** (58%)

(α : β = 1 : 1)

Protected ribonolactone **115** was functionalized by carbenoid chemistry: Reaction with tris(dimethylamino)phosphine, dibromodifluoromethane and zinc dust in refluxing tetrahydrofuran produced the difluoro enol ether **116**. Hydrogenation then afforded the desired difluormethyl analogue **117** (Scheme 20).[119]

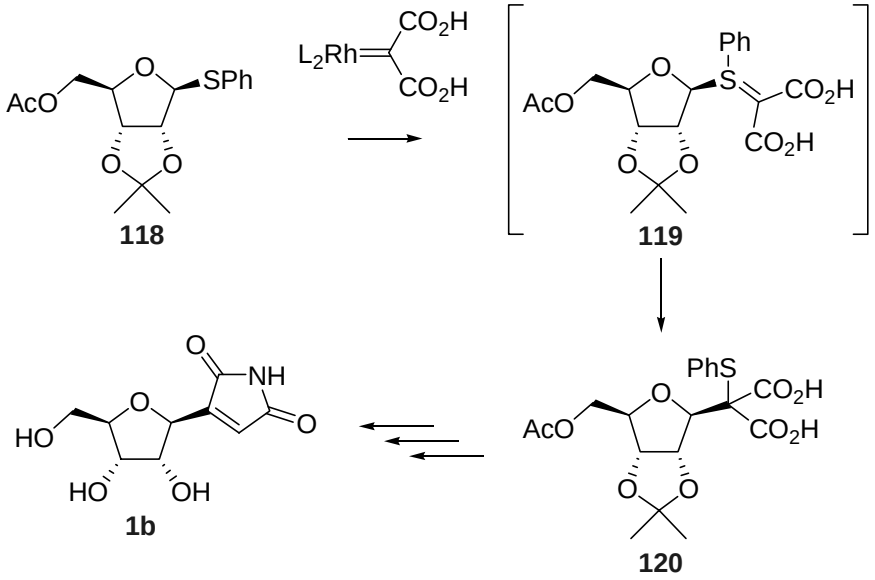
Scheme 20. Functionalization of protected ribonolactone with difluorocarbene



115 **116** **117**

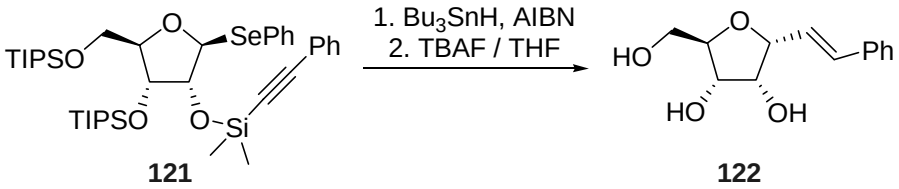
The thionucleoside **118** was reacted with the rhodium-based carbene to yield intermediate **119**, which then underwent a rearrangement to produce **120**, which was elaborated further to afforded Showdomycin **1b** (Scheme 21).[120]

Scheme 21. Functialization of protected thioribose *via* carbene insertion



Stork *et al* has used his intramolecular radical cyclization method for the silicon-tethered alkynes to stereoselectively synthesize *C*-ribofuranosides. Owing to the mechanism of the reaction, the diastereoselectivity strictly depends on the alkyne position: with the ribose substrate **121**, the α-anomer **122** becomes the only product of the reaction (Scheme 22).[121]

Scheme 22. The radical cyclization in the aglycon unit construction



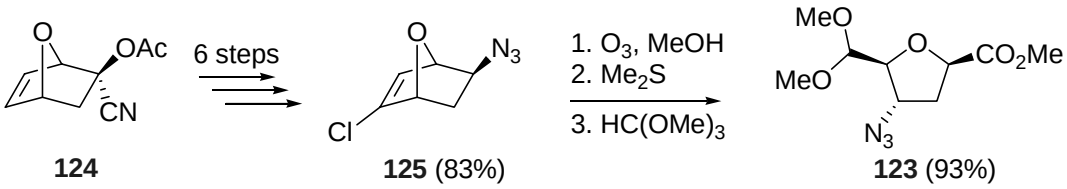
3.2. Construction of a Carbohydrate Moiety upon an Aglycon Unit

The logical complement to the synthetic strategy based on construction of an aglycon unit upon a carbohydrate moiety is the construction of a carbohydrate moiety upon an aglycon, or the synthesis of a carbohydrate moiety followed by aglycon construction. These strategies are not common as they require constructing up to four stereogenic centres.

This strategy includes several total syntheses of *C*-nucleosides, as these always start with the carbohydrate moiety containing all the stereochemistry required.[122] Vogel *et al* reported synthesis of the *C*-nucleoside intermediate **123**, containing all the structural features and

stereochemistry required in the biologically attractive 3'-azido-2',3'-dideoxy-*C*-nucleosides (Scheme 23).[123] The enantiopure cyanoacetate **124** was transformed in six steps to azidochloride **125**. Ozonolysis of the bicyclic structure **125** followed by an aldehyde function protection furnished azidoester **123**. The ester functionality of this common intermediate was elaborated further into a range of *C*-nucleosides.

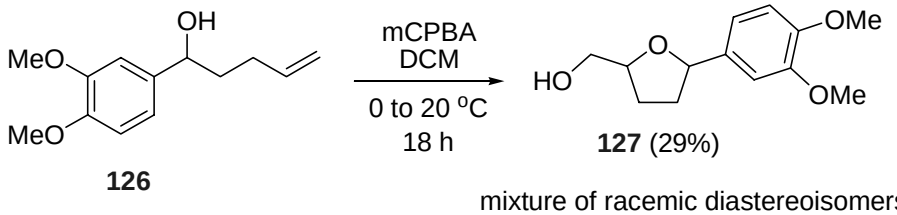
Scheme 23. Total synthesis of a carbohydrate part of 3'-azido-2',3'-dideoxy *C*-nucleosides



124 **125** (83%) **123** (93%)

2',3'-Dideoxy-*C*-nucleosides should receive a special attention among *C*-nucleosides analogues. They possess a structural feature of 2,5-disubstituted tetrahydrofuran, and thus they share synthetic methodology with a variety of natural compounds.[124] Non-stereoselective synthesis of racemic diastereoisomers was reported (Scheme 14).[125] Unsaturated alcohol **126** was submitted to the epoxidation, followed by an *in-situ* non-stereoselective oxirane-ring opening cyclization to give 2,5-disubstituted tetrahydrofuran **127**.

Scheme 24. Non-stereoselective synthesis of 2,5-disubstituted tetrahydrofurane



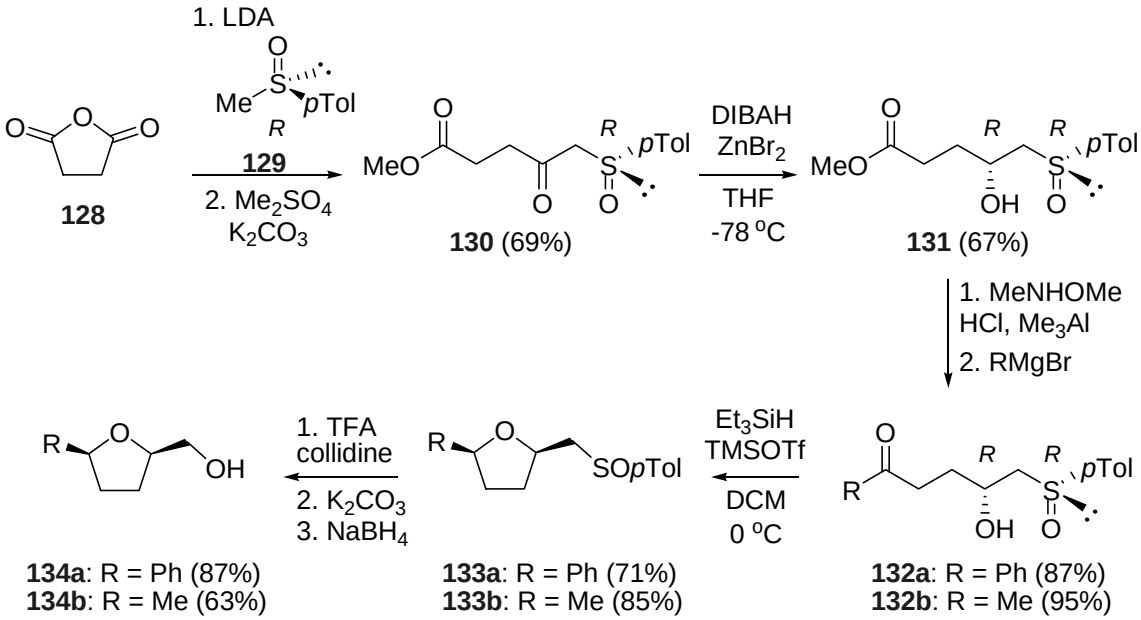
126 **127** (29%)

mixture of racemic diastereoisomers

A stereoselective synthesis of tetrahydrofurans (and tetrahydropyrans) was developed by Carreño *et al* (Scheme 25).[126] Succinic anhydride **128** was reacted with a lithium salt of the enantiopure (*R*)- or (*S*)- methyl *p*-tolylsulfoxide **129**. The resulting acid was reacted with dimethy sulfate to give ester of β-ketosulfoxide **130**. Highly diastereoselective reduction of β-ketosulfoxide **130** was achieved using diisobutylaluminium hydride (DIBAL-H) with (or without) an addition of $ZnBr_2$ as a Lewis acid. The reported diastereoselectivity exceeded 98% de for both anomers. Hydroxysulfinyl ester **131** was transformed into the corresponding Weinreb amide as a versatile intermediate suitable for reactions with a

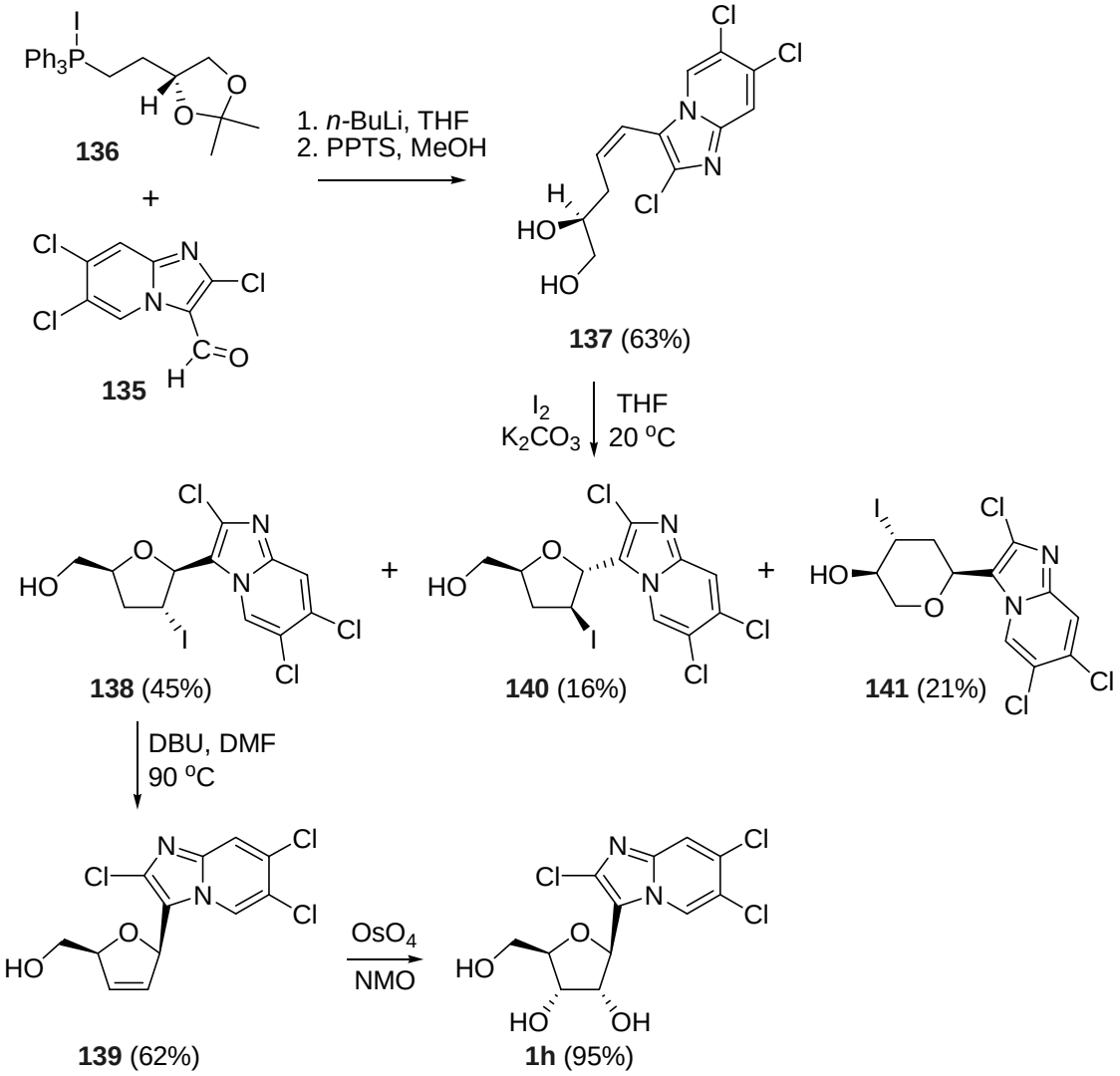
variety of arylmagnesium bromides to afford hydroxysulfinyl ketones **132**. The reductive cyclization gave tetrahydrofurans **133a-b**. The diastereoselectivity of the cyclization was determined in the crude reaction mixture only in the case of phenyl substituent (72% de). Only the major diastereoisomers **133a-b** were isolated. The Pummerer reaction, followed by reduction, released the 5'-hydroxyl functionality of the desired 2',3'-dideoxy-*C*-nucleosides **134a-b**.

Scheme 25. Hydroxysulfinyl ketones in stereoselective synthesis of 2,5-disubstituted tetrahydrofurans



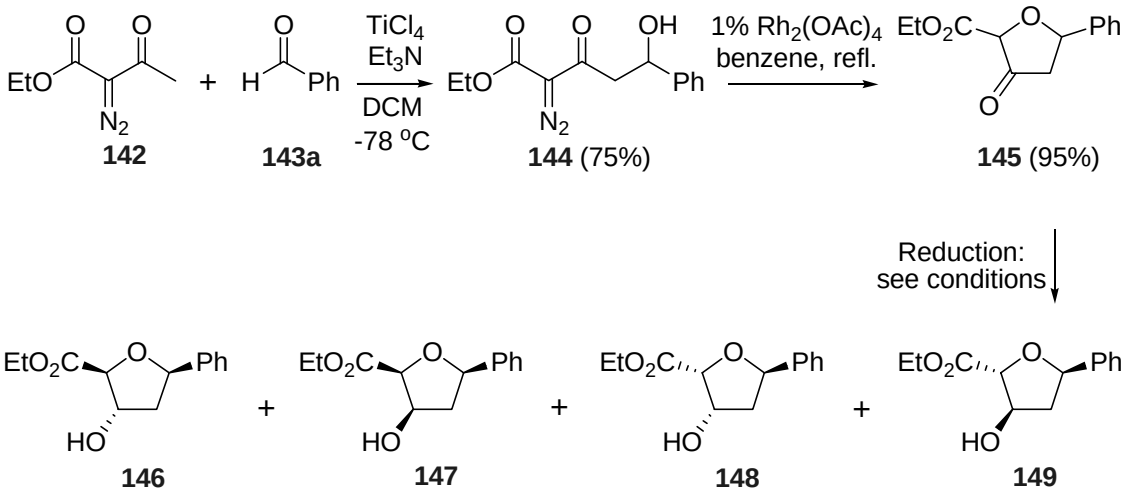
The classical route of construction of the carbohydrate moiety upon an aglycon was reported by Townsend *et al* (Scheme 26).[127] The 2,6-dichloro-3-formylimidazo[1,2-*a*]pyridine **135** bearing a formyl functionality was reacted with phosphonium iodide **136** in Wittig olefination reaction and deprotected to afford diol **137**. Iodocyclization of diol **137** was extensively optimized to yield a procedure where desired iodotetrahydrofuran **138** was in majority. Elimination of iodine, followed by standard stereoselective oxidation of dihydrofuran **139**, gave ribofuranose **1h** in 17% yield over all four reaction steps.

Scheme 26. Construction of a carbohydrate moiety upon an aglycon unit



The last course within this strategy employs carbene chemistry. The first attempts have been reported by Calter *et al.*[128] Aldol reaction of **142** with arylaldehyde **143a** was employed as the key step followed by Rh-catalysed cyclization of the resulting **144** *via* the corresponding metallocarbene (Scheme 27). Full reduction of ketoester **145** can, a priori, afford racemic diastereoisomers **146-149**, but the configuration of the natural 2'-deoxy-*β*-D-ribofuranoside **146** was not observed under any reduction conditions. The *cis*-ketoester **145** was also isolated as a single diastereoisomer prior to reduction, but this compound is configurationally unstable.

Scheme 27. Carbene in carbohydrate moiety construction, non-specific reduction

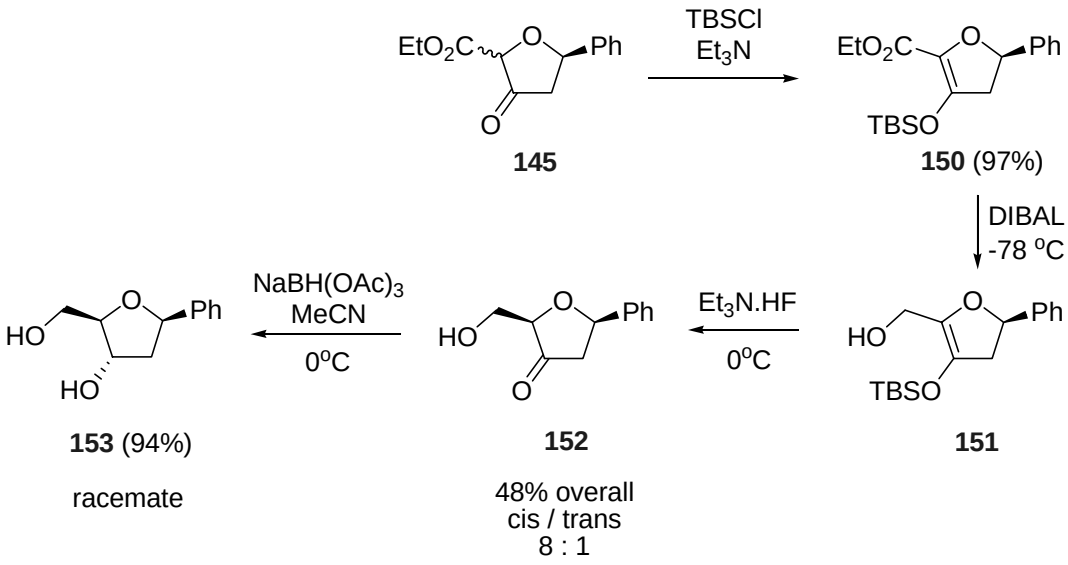


Reduction conditions:	**146**	**147**	**148**	**149**
$NaBH_4$, MeOH, 0 °C:	0	1	0.1	1
L-Selectride, -78 °C:	0	2	1 .0	0
L-Selectride, Et_3N, -78 °C:	0	1	1.7	0

racemic diastereoisomers

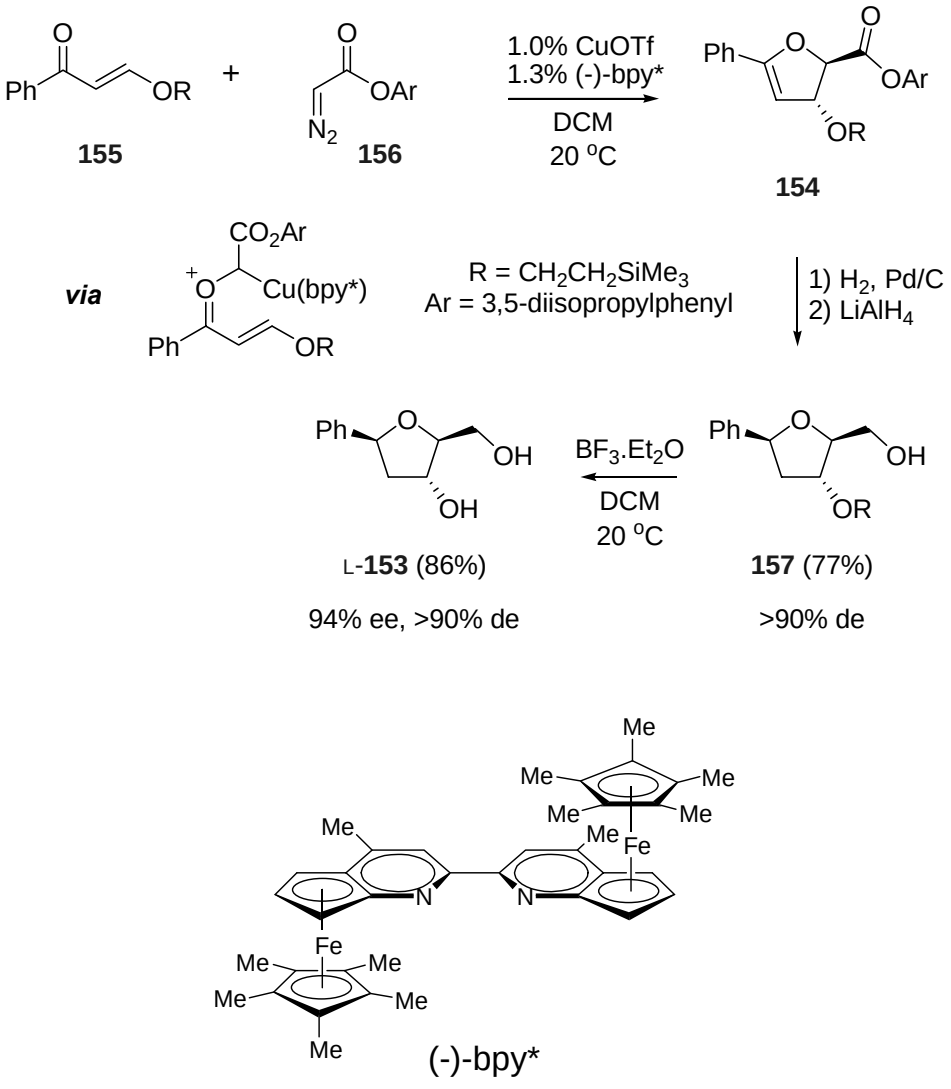
The sequential reduction of **145** was also investigated (Scheme 28). Ketoester **145** was transformed into the corresponding silyl enol ether **150** and the ester function was reduced with DIBAL-H to afford the primary alcohol **151**. Diastereoselective cleavage of the silylenolether group in **151** was performed using triethylammonium fluoride to produce ketone **152** in moderate yield and good diatereoselectivity (77% de). Final reduction of **152** with sodium triacetoxyborohydride afforded racemic diol **153** with the configuration of natural 2'-deoxy-*β*-D-ribofuranose.

Scheme 28. Carbene in carbohydrate moiety construction, two subsequent reductions



There have been several attempts to follow this strategy, however only with modest success, prohibiting practical use.[129] Carbene cycloaddition approach was developed very recently by Fu *et al* (Scheme 29).[130] The principal difference here is the disconnection of the resulting dihydrofuran (**145** *vs.* **154**). Copper-catalysed cycloaddition of enone **155** with diazoester **156** is the key-reaction. Dihydrofuran **154** is then stereoselectively hydrogenated to tetrahydrofuran (>90% de), followed by reduction of the ester function to primary hydroxyl functionality and deprotection, to afford the desired 2'-deoxy-*C*-nucleoside L-**153** in good overall yield (66%, 4 steps) and good stereoselectivity. However, the practical utility of this efficient procedure is limited by the availability of the ligand (-)-bpy* used in the copper-catalysed cycloaddition.

Scheme 29. Copper-catalyzed asymmetric [4+1] cycloaddition of enones with diazo compounds to form 2'-deoxy-*C*-nucleoside L-**153**



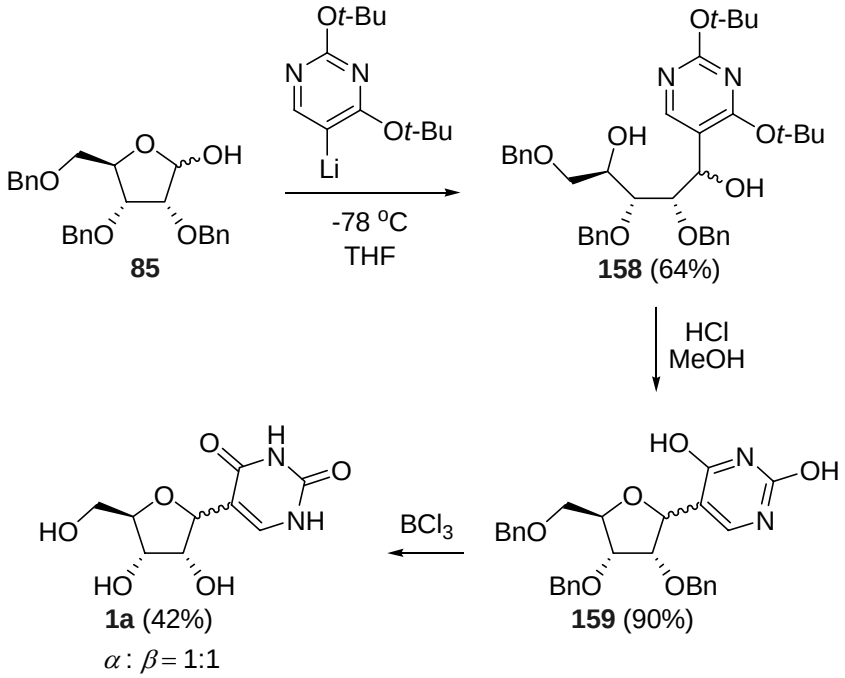
3.3. Direct Coupling of a Carbohydrate Moiety with a Preformed Aglycon Unit

The synthetic strategy of the direct coupling of a protected carbohydrate moiety with a preformed aglycon nucleophile represents the most common synthetic approach to the construction of *C*-nucleoside backbone.[94d] There are six different reaction tactics within this synthetic approach of direct coupling. (1) Nucleophilic addition to an aldehyde function of a carbohydrate; (2) Nucleophilic addition to 1,2-anhydrofuranoses; (3) Nucleophilic addition to halogenoses; (4) Nucleophilic addition to furanolactones; (5) Heck coupling; (6) Coupling mediated by Lewis acids.

3.3.1. Nucleophilic Addition to an Aldehyde Function of a Carbohydrate

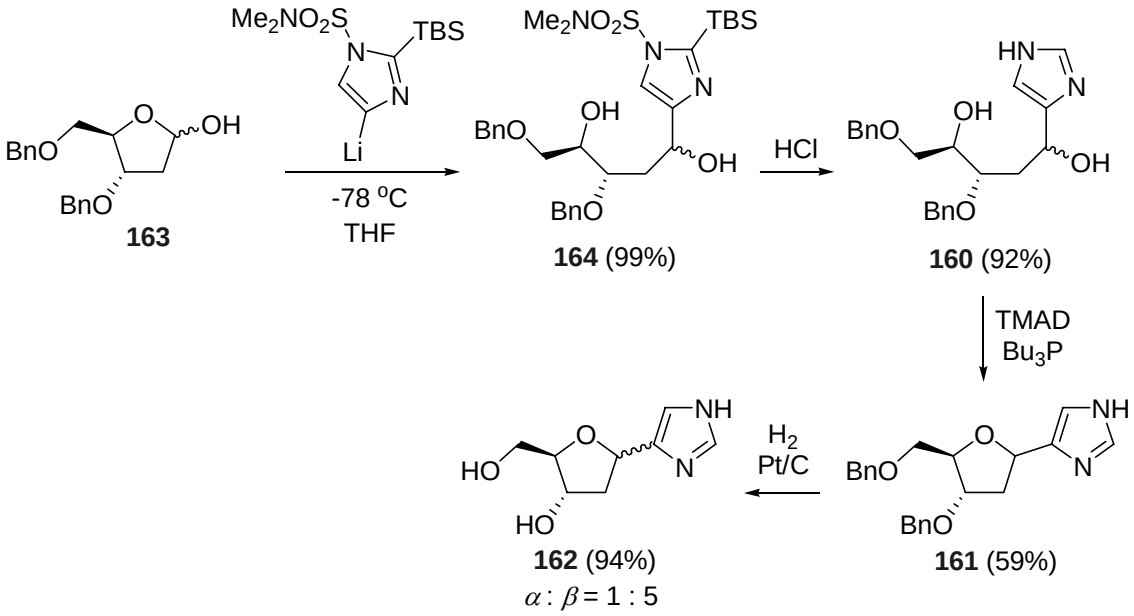
Addition of organometallic reagents to the aldehyde functionality in the carbohydrate moiety leads to a mixture of diastereoisomeric diols in good yields. Subsequent cyclization proceeds under acidic conditions in a non-diastereoselective fashion (Scheme 30).[131]

Scheme 30. Coupling of protected ribofuranose **85** and organolithium derivate with acid-catalysed cyclization



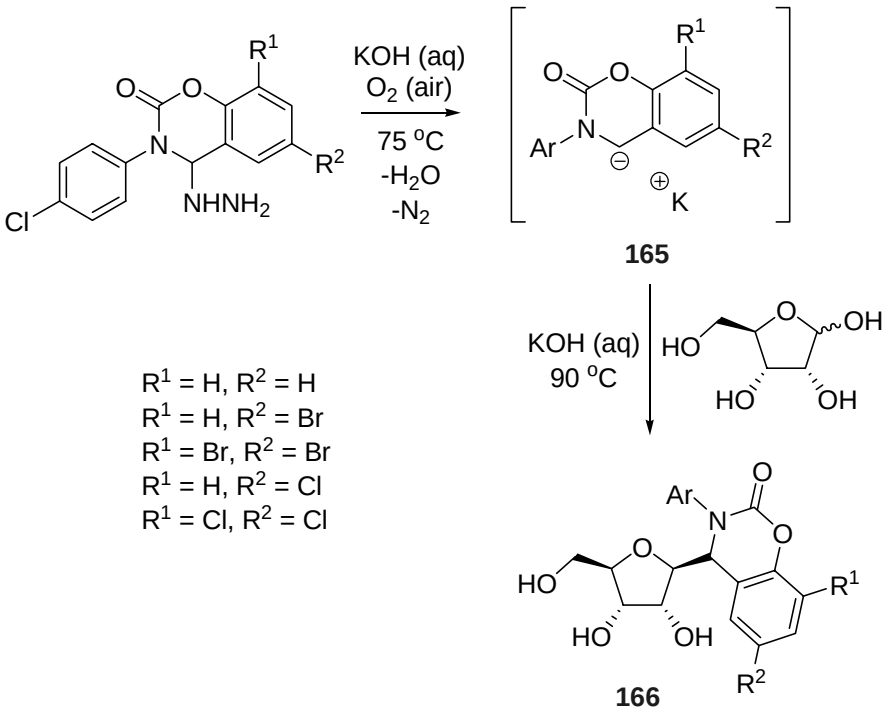
The intermediate diol **160** has been cyclized diastereoselectively under Mitsunobu conditions to produce **161**. The subsequent deprotection afforded the 2'-deoxyribofuranoside **162** in 50% overall yield, and 66% de (Scheme 31).[132] An optimized Mitsunobu-based cyclization procedure was published recently. The corresponding pyrazole derivatives were prepared with up to 92% de.[133]

Scheme 31. Coupling of protected 2'-deoxyribofuranose and organolithium nucleophile with cyclization under Mitsunobu conditions.



Yadav *et al* recently communicated on an interesting one-step procedure leading to benzoxazinone *C*-nucleosides (Scheme 32).[134] The dehydrazinative[134] glycosilation of unprotected ribose with intermediate **165** in aqueous media features of atom-efficient, environmentally bening process. However, the limited range of aglycons possessing activated benzyl functionality together with the absence of some experimental details (isolated yields) may hinder the possible practical applications of this method.

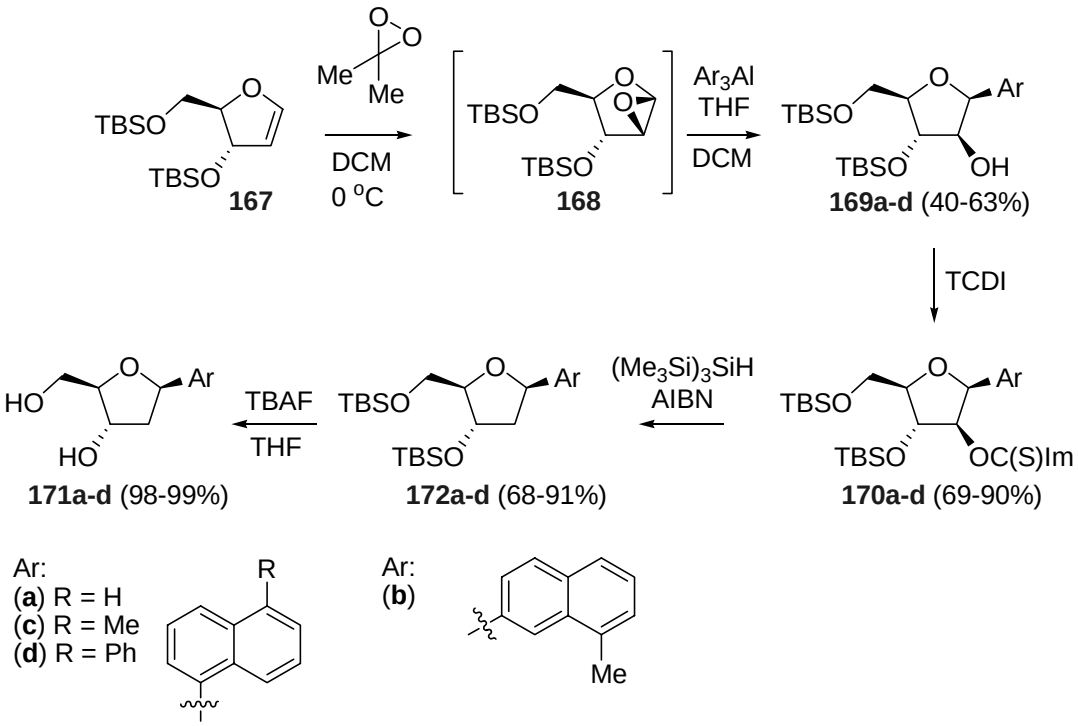
Scheme 32. Dehydrazinative glycosylation to benzoxazinone *C*-nucleosides



3.3.2. Nucleophilic Addition to 1,2-Anhydrofuranoses

A very innovative method was recently published by Seitz *et al* (Scheme 33).[135] Furanose glycal **167** was epoxidized by dimethyldioxirane to furnish anhydrofuranose **168**. The oxirane ring was stereoselectively opened by various triarylalanes to afford arabinofuranoses **169**. The using of triarylalanes is preferred over aryldimethylalanes, as it gives substantially better isolated yield. Arabinofuranose **169** was deoxygenated in 2'-position using the Barton two-step procedure. Final deprotection gave 2'-deoxyribofuranose-*C*-nucleosides **170** in moderate overall yields and excellent diastereoselectivity. The need of three equivalents of the aryl building block (Ar_3Al) may be prohibitive in the case of more complex aryl moieties.

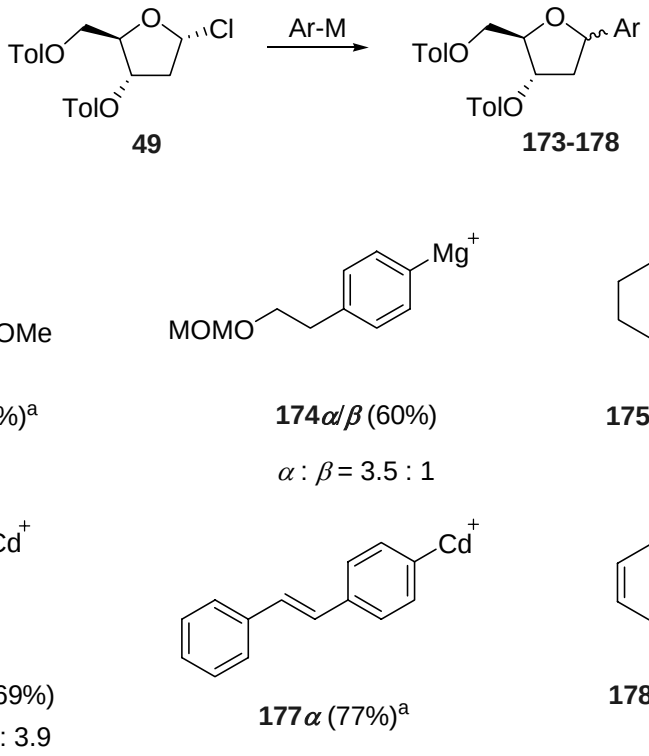
Scheme 33. Nucleophilic addition to the protected 1,2-anhydrofuranose



3.3.3. Nucleophilic Addition to Halogenoses

A coupling reaction of protected carbohydrate with a soft organometallic reagent is the oldest method for the *C*-glycoside bond construction.[136] Naturally it has become an important method for *C*-nucleosides synthesis. Both protected ribosyl, and 2-deoxyribosyl bromides or chlorides may be used as starting materials. Among them, Hoffer's chlorosugar (1-chloro-2-deoxy-3,5-bis[*O*-(*p*-toluoyl)]-α-D-ribofuranose **49**)[137] became one of the most widely used building blocks. The typical reaction procedure features of a coupling reaction of halogenose and an organometallic reagent based on cadmium, zinc, mercury, magnesium, and even lithium. Yields are generally low, determined by the nature of the organometallic reagent (Scheme 34).[138,139]

Scheme 34. Coupling of Hoffer's chlorosugar with various organometallic reagents



49 **173-178**

173β (2%)[a] **174**α/β (60%) **175**α (41%)[a]

α : β = 3.5 : 1

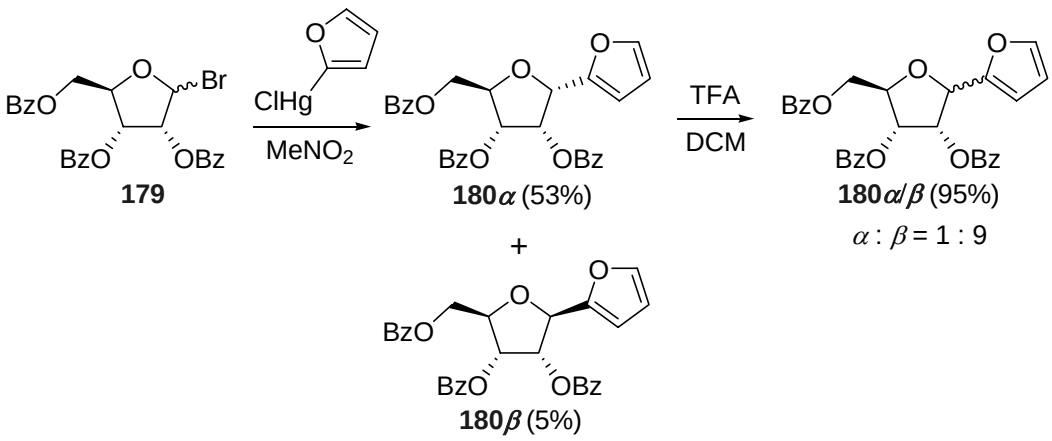
176α/β (69%) **177**α (77%)[a] **178**α/β (0%)

α : β = 1 : 3.9

[a]Only one diastereoisomer was isolated.

The α-anomer is the major product in all the cases, regardless on any variation of metal, solvent, temperature or other possible reaction conditions. The acid-catalysed epimerization is required as an additional step in order to obtain the more often desired, naturally configured β-anomer (Scheme 35).[140] Furanylmercury chloride was reacted with bromo ribose **179** to give separable anomeric mixture with predominant α-anomer **180**α, which was isolated and submitted to the acid-catalysed epimerization to afford β-anomer in 80% de purity.

Scheme 35. Furanylmercury-bromose coupling followed by epimerization



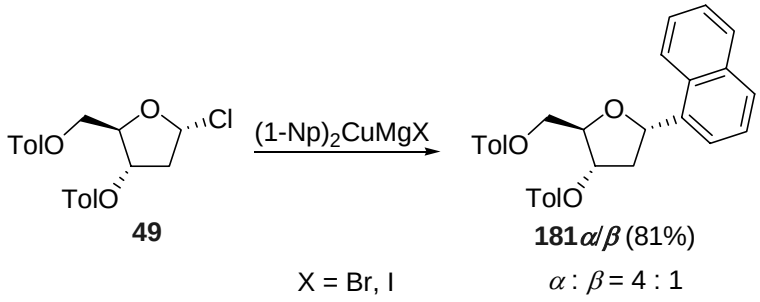
179 **180**α (53%) **180**α/β (95%)

α : β = 1 : 9

180β (5%)

In spite of the unfavourable stereochemical outcome, the synthetic approach utilizing the halogenose-coupling reaction has been optimized further. Seitz *et al* reported an environmentally friendly organometallic reagent based on mixed magnesium-cuprate (Normant cuprate). This organometallic reagent substantially improved the isolated yield of the anomeric mixture, which again in combination with subsequent epimerization has made this method competitive (Scheme 36).[141,142]

Scheme 36. Coupling of Hoffer's chlorosugar with Normant reagent

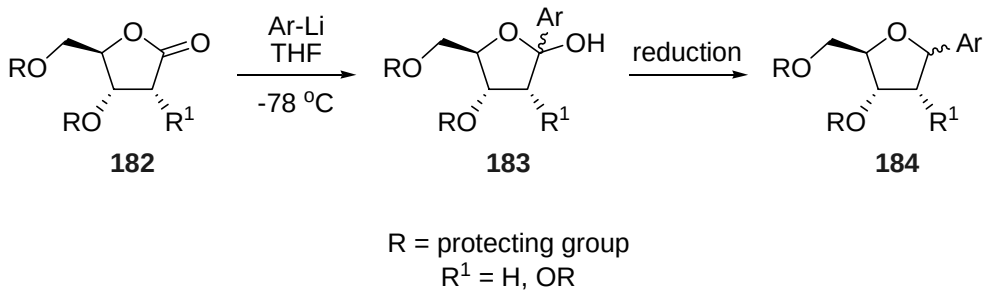


3.3.4. Nucleophilic Addition to Furanolactones

Addition of aglycon organometallic nucleophilic reagent accros the lactone functionality is the most frequent synthetic tactic to construct a new C-C anomeric bond in the case of *C*-ribonucleosides, and one of the most frequent approaches to the synthesis of 2'-deoxy-*C*-ribonucleosides (together with Heck coupling).

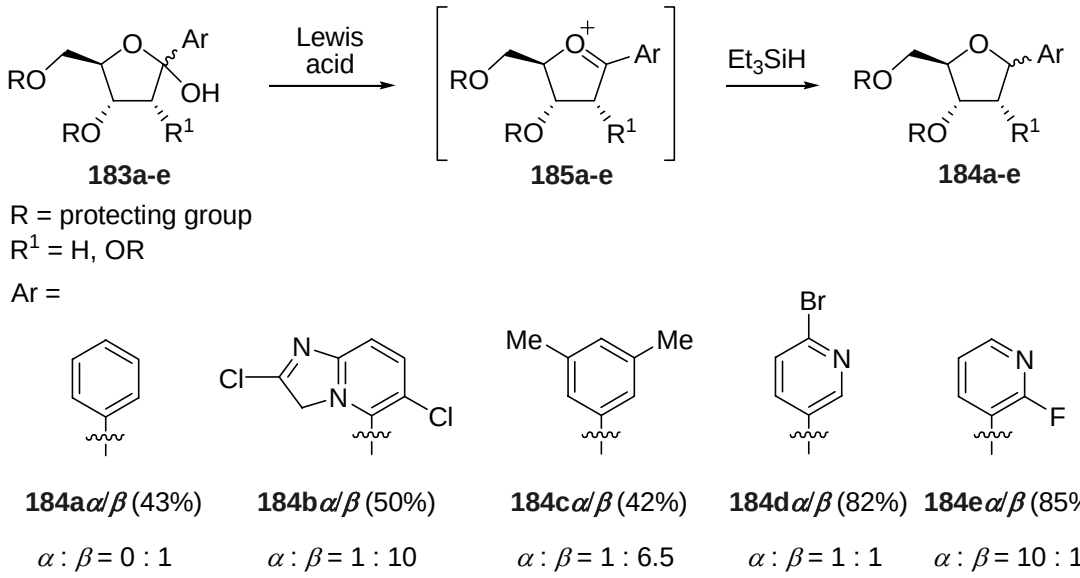
Protected lactone **182** is reacted with aryl (heteroaryl) lithium reagent at low temperature to give hemiketal **183**. Subsequent reduction of the hemiketal function to afford the desired *C*-nucleoside **184** was developed in two possible reaction pathways (Scheme 37).

Scheme 37. Coupling of ribonolactones with organometallic reagents



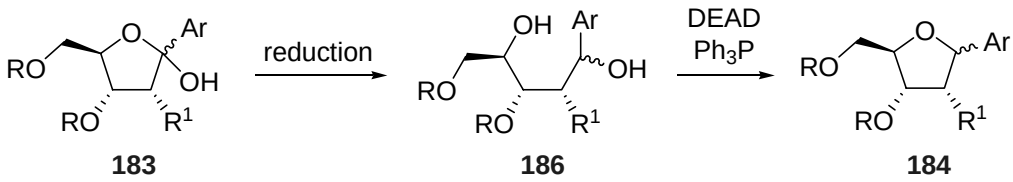
The older method features deoxygenation of hemiketal **183** by Lewis acid, followed by reduction of the oxonium intermediate **185** (Scheme 38).[143] The most common Lewis acid is boron trifluoride etherate. Reduction of the planar intermediate **185** utilises triethylsilane in most cases. The reduction prceeds in a non-stereoselective fashion yielding equimolar mixtures of anomers, though various degrees of stereoselectivity, based on nature of the aglycon unit, were reported.[144]

Scheme 38. Lewis acid mediated deoxygenation followed by silane reduction

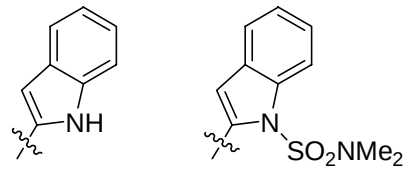


Nucleophile addition to lactones proved to be a favourite method for the *C*-nucleosides construction, utilising easily accessible building blocks, but having unsatisfactory stereoselectivity. To overcome this particular problem, an alternative sequence of hemiketal **183** transformation has been developed. Hemiketal **183** is reduced by complex hydride to afford diol **186** that is cyclised under Mitsunobu conditions to the desired nucleoside analogue **184** (Scheme 39).[145,146]

Scheme 39. Reduction followed by Mitsunobu-type cyclization



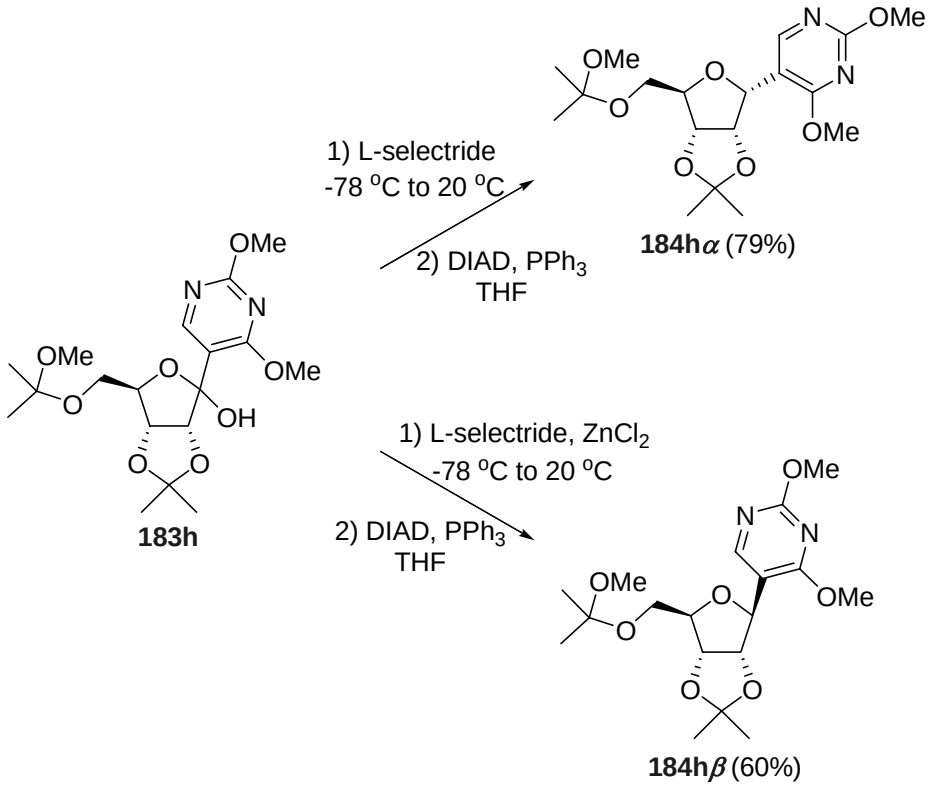
Stereoselectivity of the above reaction sequence can be controlled in different ways. Benhida *et al* reported stereoselective reduction of hemiketals **183f-g** and Mitsunobu cyclization of diols **186f-g** bearing indole, imidazole, and benzimidazole heteroaryl moiety.[145] The stereoselectivity was controlled by the presence and the nature of the *N*-protecting group on heterocycle. They observed that the choice of an appropriate protecting group on the heterocyle moiety resulted in a highly stereoselective (up to 80% de) borohydride reduction of the hemiketal **183g** to the corresponding diol **186g** in quantitative yield, which upon Mitsunobu cyclization gave the α-anomer. On the other hand, removal of the protecting group allowed the total stereocontrol during the Mitsunobu cyclization step, leading to the β-anomer **184f** exclusively.



f $\alpha : \beta = 0 : 100$ **g** $\alpha : \beta = 100 : 0$

A more general stereocontrol was reported by Hanessian *et al* (Scheme 40).[146] Stereoselective reduction of hemiketal **183h** was performed using L-selectride alone or with an addition of zinc chloride. The neighbouring effect of the protecting groups was also the essential part of the successful stereocontrol. The stereoselective reduction was followed by standard Mitsunobu-type cyclization. This methodology was applied to the synthesis of the α- and β-anomers of pseudouridin **1a**. Starting from unprotected ribonolactone, the target structures were prepared in five steps as single diastereoisomers in good overall yield **1a*α*** (65%), and **1a*β*** (46%).

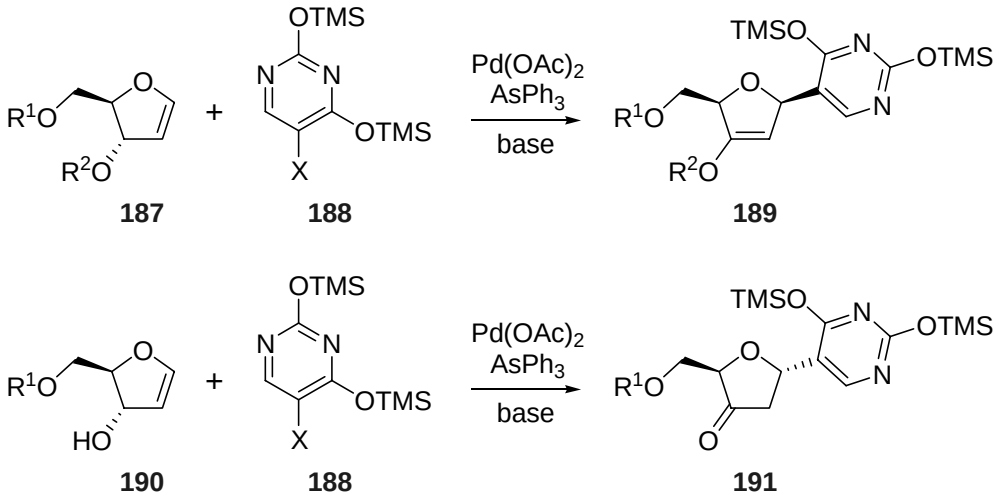
Scheme 40. L-selectride stereoselective reduction followed by Mitsunobu-type cyclization



3.3.5. Heck Coupling

Heck-type coupling reaction between the anomeric carbon of carbohydrate derivatives and (hetero)aromatics is the most important method for the synthesis of 2'-deoxy-*C*-nucleosides in the last 30 years.[94f] Daves *et al* reported the utility of the palladium-catalysed Heck coupling reaction for the synthesis of *C*-nucleosides for the first time.[147] Heck reaction is highly regioselective and stereoselective in the formation of C-C bonds. New *C*-glycosidic bond is formed on the least sterically hindered face of the glycal ring. An appropriate protecting group at the 3-hydroxyl function of the glycal controls the anomeric configuration of the resulting *C*-nucleoside. Such a protection results in an exclusive formation of β-anomer. A free, unprotected 3-hydroxyl function drives the attack of the organopalladium species to occur from the opposite direction to give α-anomer exclusively (Scheme 41).[148]

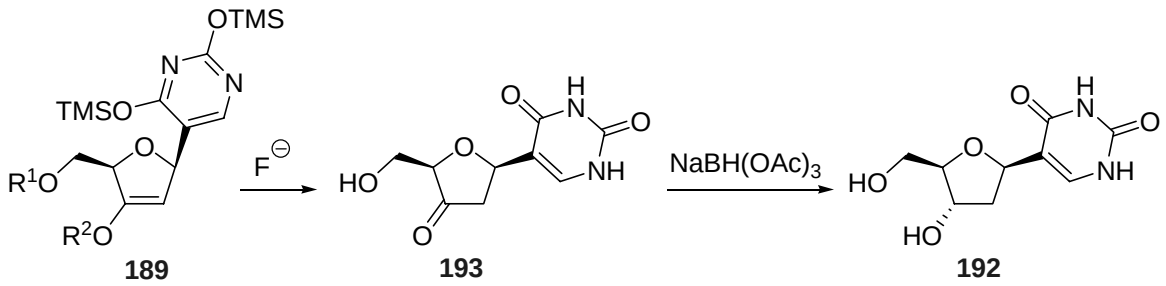
Scheme 41. Heck-type coupling reaction of furanoid glycals with aglycon precursor



R^1 = H, DMPS, TBDPS, TBS, TIPS
R^2 = DMPS, TBDPS, TBS, TIPS
X = HgOAc, I, Sn(^{n}Bu)$_3$

The carbonyl functionality is then restored in the Heck-type coupling product **189** by fluoride mediated desilylation of the corresponding silyl enol ether, and subsequently reduced by sodium triacetoxyborohydride with high stereoselectivity to afford the desired 2'-deoxy-*C*-nucleoside **192** (Scheme 42).[149]

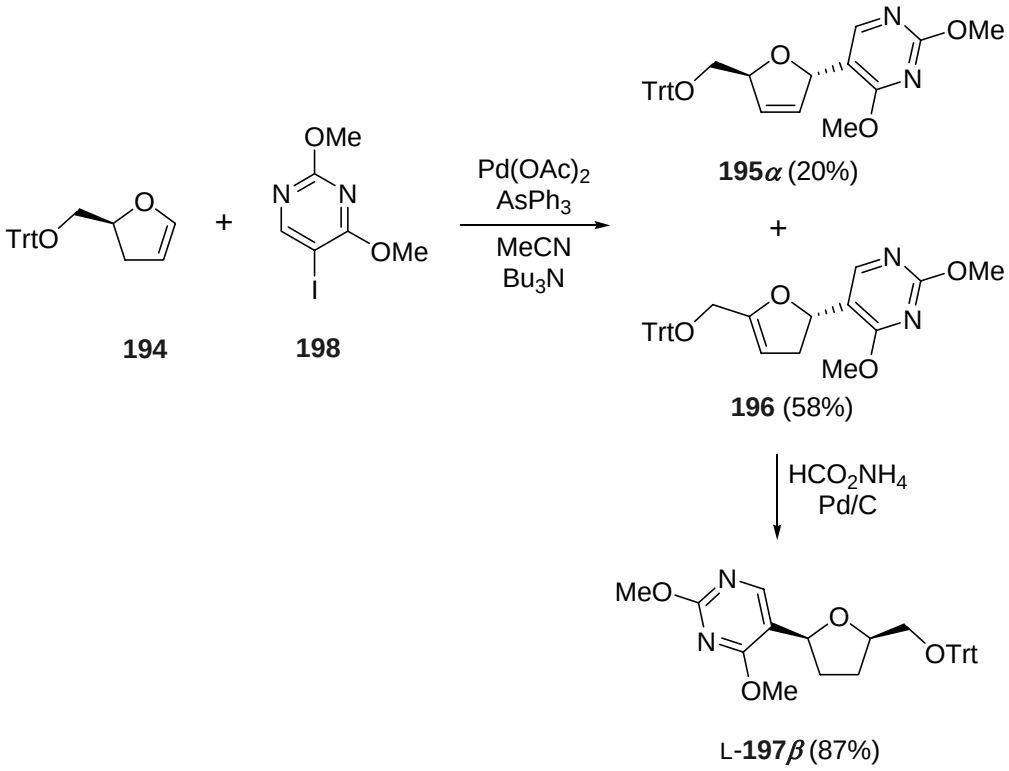
Scheme 42. Heck-enol deprotection followed by stereoselective reduction



Furthermore, the Heck reaction was used in the stereoselective synthesis of 2',3'-dideoxy-*C*-nucleosides (Scheme 43).[150] Enantiopure 2,3-dihydrofurane **194** was reacted with iodopyrimidine to give a mixture of 2,3- and 2,5-dihydrofurans **195*α***, and **196**, respectively. Although the major product **196** lost its original chiral centre, this was restored in a stereoselective hydrogenation that occurred from the least hindered face of the dihydrofuran ring. However, the restored chirality was of the opposite configuration, thus leading to L-unnatural configuration of the carbohydrate moiety in L-**197*β***. The reaction

sequence gave a comparable yield of the naturally configurated D-**197*β*** in the reaction with the opposite enantiomer of the tritylated hydroxymethyldihydrofurane **194**.

Scheme 43. Heck-type coupling in the synthesis of 2',3'-dideoxy *C*-nucleosides

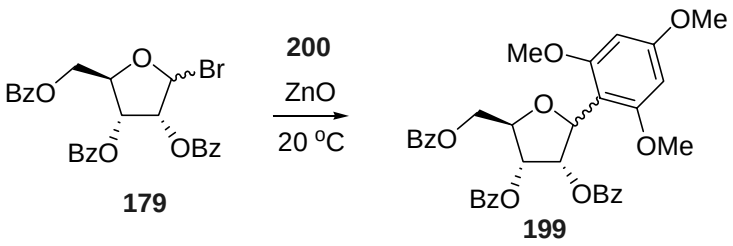


Several general observations have been made for the Heck-type coupling reaction of the glycal to the aglycon.[151] Palladium acetate and $Pd_2(dba)_3$ are the most widely used sources of palladium and $AsPh_3$ is the most frequent ligand of choice. Standard solvents for Heck reaction (DMF, MeCN, THF) have been employed in most of the cases. The most frequent bases are Bu_3N, Et_3N, *i*Pr_2NEt. Inorganic bases, like sodium bicarbonate ($NaHCO_3$) have been used only in several cases.

3.3.6. Coupling Mediated by Lewis Acids

Coupling reactions of a preformed carbohydrate and a (hetero)aryl catalysed by Lewis acids provide a simple method for the formation of *C*-nucleosides. The method was developed in the synthesis of *C*-glycosides of hexopyranoses.[152,153] Šorm *et al* utilised the Lewis-acid-mediated coupling reaction in the synthesis of showdomycin (*vide infra*, page 63). Condensation of benzylated bromose **179** with *sym*-trimethoxybenzene in the presence of zinc chloride gave *C*-nucleoside **199** (Scheme 44).[154]

Scheme 44. Lewis acid catalysed condensation used in the first synthesis of showdomycin **1b**

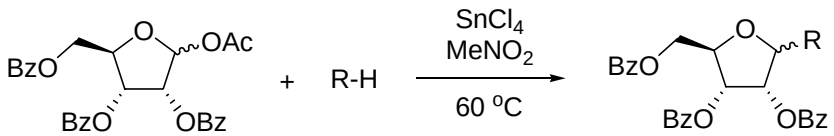


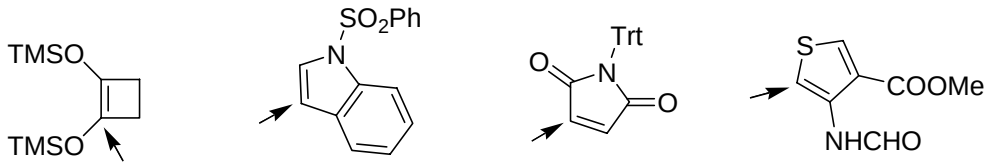
200: 1,3,5-trimethoxybenzene

The authors applied this protocol to a broad range of electron-rich benzenes to afford equimolar mixtures of anomers of the products.[155]

The simplicity of the process is balanced with poor regioselectivity of the aglycon attack and with non- or low stereoselectivity of new anomeric C-C bond formation. Reactions are fully controlled by the nature of the aglycon unit. Some reference examples are shown in the reaction of protected ribofuranose **201** with a range of aglycon units **202a-202f** (Scheme 45).[156,157]

Scheme 45. Coupling reaction of aglycon and preformed carbohydrate catalysed by Lewis acid



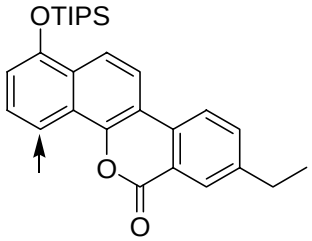


202a (92%)
$\alpha : \beta = 0 : 100$

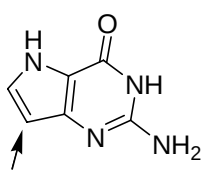
202b (49%)
$\alpha : \beta = 1 : 1$

202c (56%)
$\alpha : \beta = 2 : 3$

202d (60%)
$\alpha : \beta = 2 : 3$



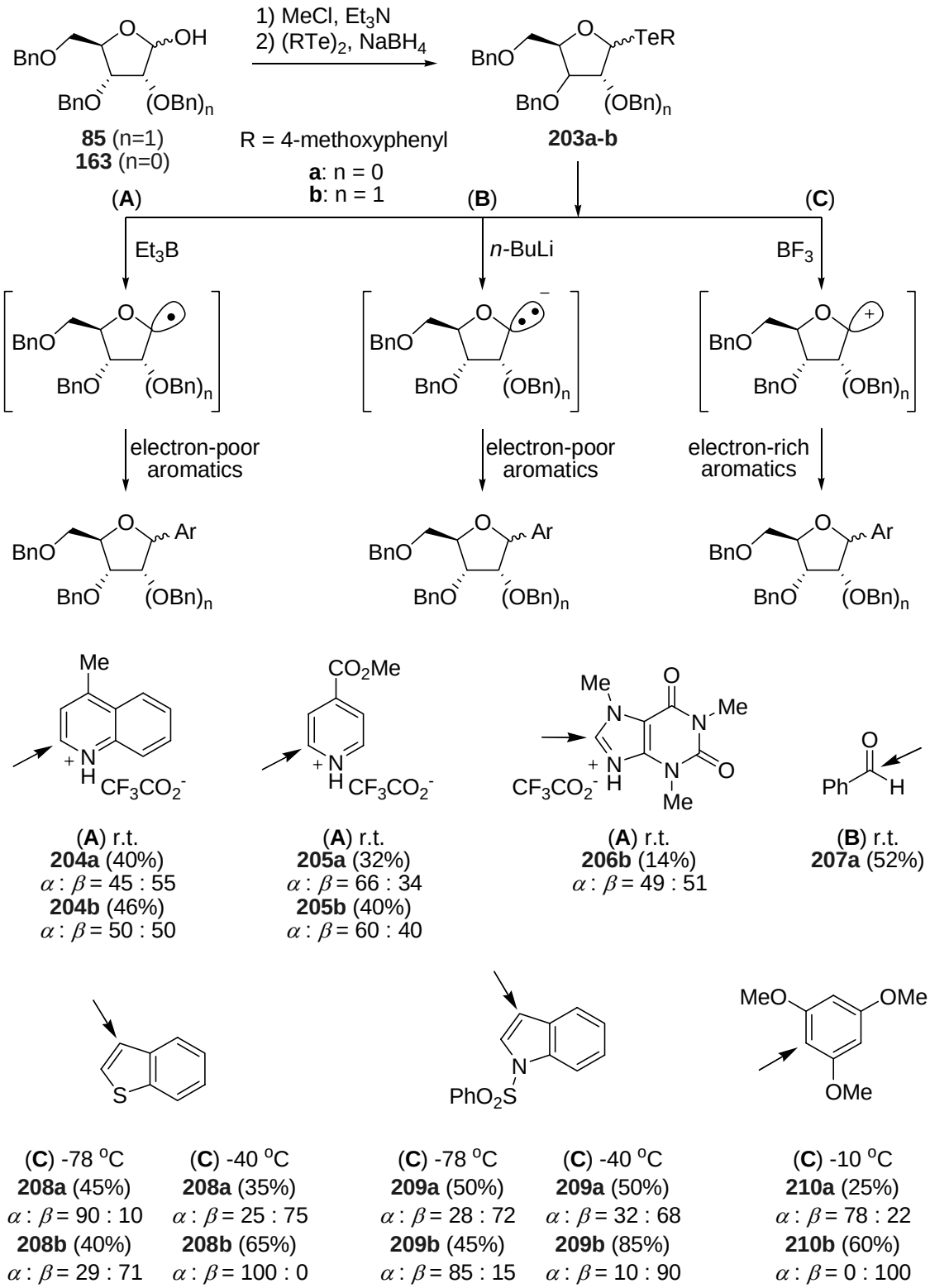
202e (60%)
$\alpha : \beta = 1 : 1$



202f (45%)
$\alpha : \beta = 0 : 100$

Tellurides are known as useful building blocks reactive toward electrophiles, nucleophiles, and radicals.[158] Togo and Yokoyama reported a procedure based on coupling reaction of carbohydrate anomeric radical, anion, and cation with aglycon unit (Scheme 46).[159] Ribofuranose derivatives **85** and **163** were transformed to the corresponding anisyl tellurides and directly treated with either triethylborane, buthyllithium, or boron trifluoride, respectively, and reacted with appropriate aryl- or heterocyclic- aglycon unit. No stereoselective reaction was observed. The reactions of a mixtures of anomers (route **A**) gave essentially the same results as in the cases where pure α- and β-anomer of telluride **203a**, and **203b** had been separated and employed in the reaction. The reactions of radical cation (route **C**) resulted in certain degree of stereoselectivity. However, these were of the same value as were the thermodynamic equilibrium ratio of epimerization mediated by boron trifluoride itself.

Scheme 46. Tellurides in *C*-nucleosides synthesis

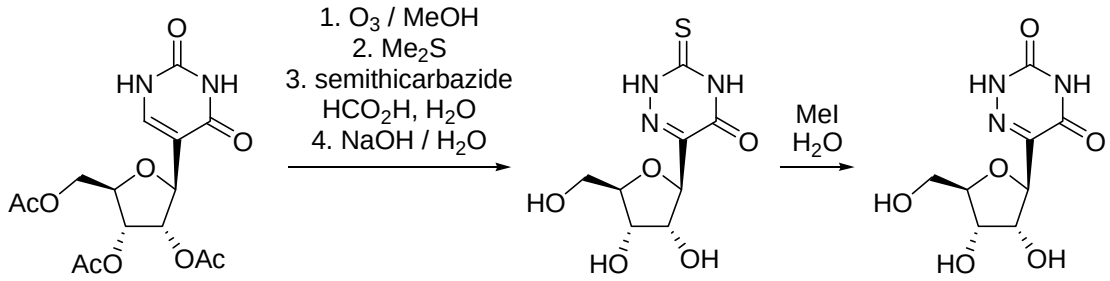


3.4. Chemical Modification of Existing *C*-Nucleosides

The last synthetic strategy is based on modification of functional groups in the naturally occurring or synthetic *C*-nucleosides. The modification(s) may include either aromatic part or carbohydrate part of the *C*-nucleoside, or both. The C-C bond between an aglycon and a carbohydrate moiety is kept intact during all the transformations.[160]

This strategy was employed in the syntheses of analogues of the naturally occurring pseudouridine (Scheme 47).[161] Protected pseudouridine **211** was transformed into thiatriazolon **212**, which was hydrolyzed to 6-aza analogue of pseudouridine **1j**. This approach faded as the natural sources were very limited, both in quantity and structural diversity.

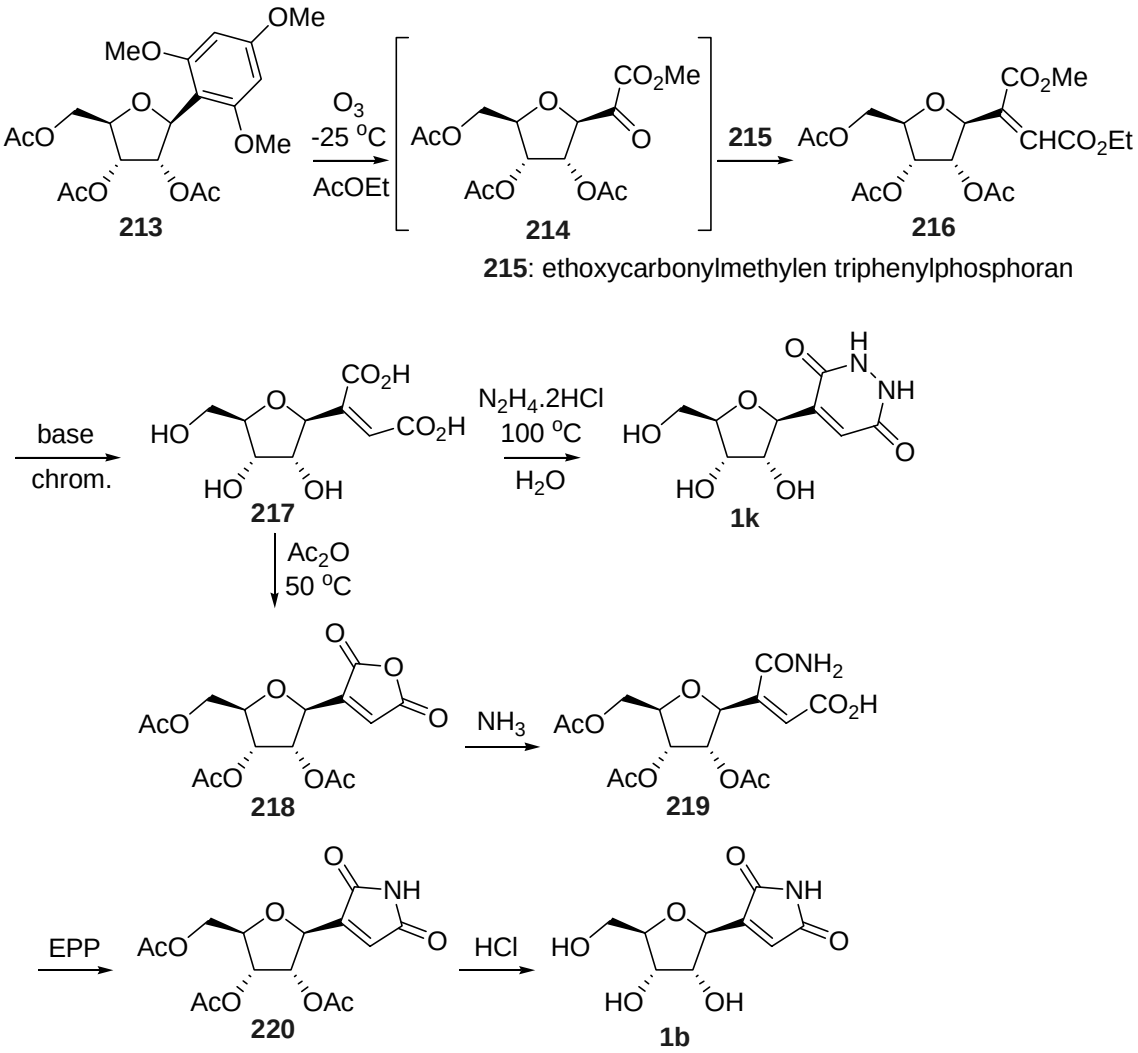
Scheme 47. Modification of protected pseudouridine **211**



211 **212** **1j**

Šorm *at al* reported the first synthesis of showdomycin (Scheme 48).[154] The parent *C*-nucleoside structure **213** was obtained by Lewis acid catalysed condensation (*vide supra*, page 59) followed by separation of *β*-anomer (by crystallization). The protected *C*-nucleosides **213** was ozonolyzed in ethyl acetate at -25 °C with reductive workup. The resulting ketoester **214** was directly treated with phosphoran **215** in refluxing benzene, yielding the unsaturated ester **216**. The *cis* to *trans* isomers ratio on the new double bond was 10:1. After alkaline hydrolysis the desired *cis* isomer was separated by ion-exchange chromatography. Diacid **217** was treated with hydrazine dihydrochloride to give pyridazine **1k**. The conversion of diacid **217** to showdomycin **1b** was accomplished in four steps and 14% yield as follows: diacid **217** was dehydrated to afford anhydride **218**, followed by ammonolysis to produce maleamic acid **219**, dehydration by ethyl polyphosphate in dimethylformamide, and final deprotection by 2% HCl in methanol.

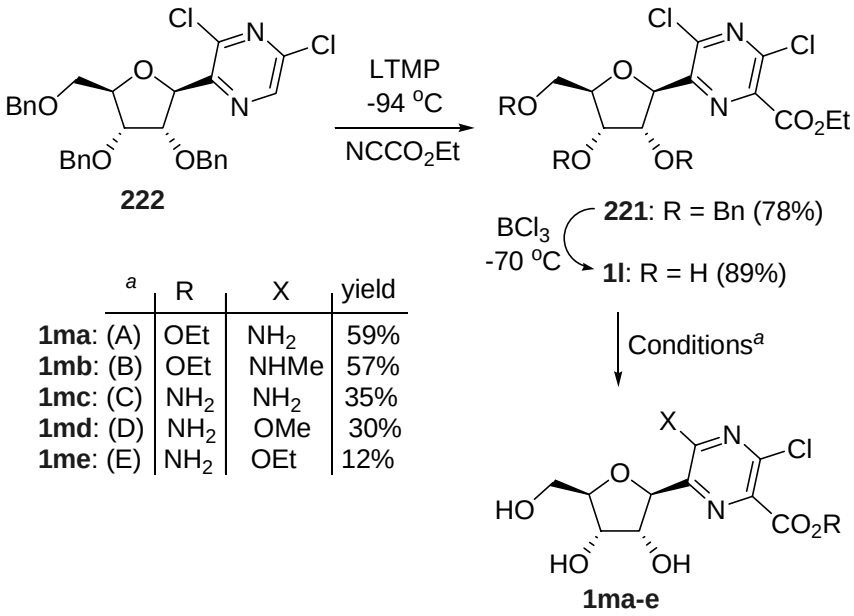
Scheme 48. First synthesis of showdomycin **1b** and its pyridazine analogue **1k**



Renaissance of this method has begun in late 1990's. Many stereoselective methods were developed to construct *C*-nucleosides as shown in previous paragraphs of this chapter. *C*-Nucleosides possessing a structure of a common intermediate can be stereoselectively synthesized and then transformed into a plethora of final structures.

Townsend *et al* reported preparation and subsequent derivatization of pyrazinoic ester **221**.[162] Protected pyrazine *C*-nucleoside **222** was selectively lithiated by lithium 2,2,6,6-tetramethylpiperidide at low temperature and carboxylated using ethyl cyanoformate. This was an optimized procedure as many of standard carboxylation procedures failed. The resulting ester **221** was debenzylated and the resulting ribose **1l** was submitted to a variety of functionalization. A range of potential chemotherapeutics **1ma-1me** was prepared in three steps (Scheme 49).

Scheme 49. Pyrazinoic-ester *C*-Nucleosides **1m**

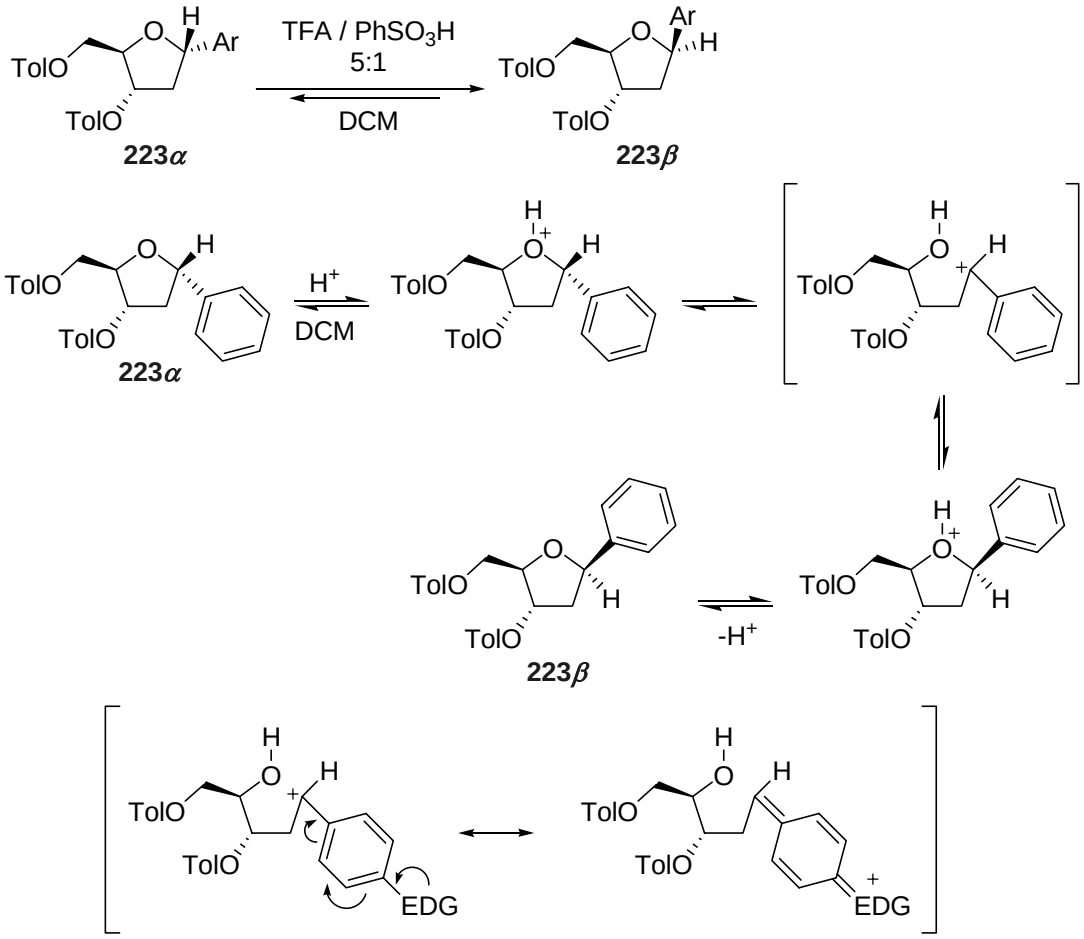


[a]	R	X	yield
1ma: (A)	OEt	NH_2	59%
1mb: (B)	OEt	NHMe	57%
1mc: (C)	NH_2	NH_2	35%
1md: (D)	NH_2	OMe	30%
1me: (E)	NH_2	OEt	12%

[a]Conditions: (A) 2 equiv of NH_3 / 1,4-dioxane, 40 °C, 42 h;
(B) 2 equiv of $MeNH_2$ / THF, 20 °C, 30 h;
(C) sat. NH_3 / EtOH, 4 °C, 48 h;
(D) sat. NH_3 / MeOH, 20 °C, 48 h;
(E) sat. NH_3 / EtOH, 20 °C, 70 h;

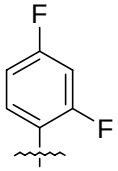
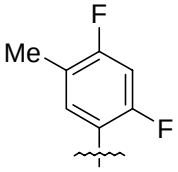
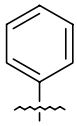
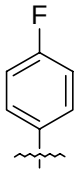
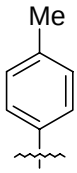
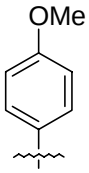
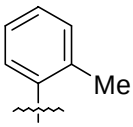
Epimerization plays an important role among possible modifications of *C*-nucleosides. Many presented procedures constructing the anomeric C-C bond are not perfectly stereoselective, thus controlled epimerization would be highly desirable. Optimized procedures were reported for *C*-nucleosides bearing both, electron-donating-group (EDG) and electron-withdrawing-group (EWG).[9,163]

Scheme 50. Epimerization of *C*-nucleosides **223**



Stivers *at al* have presented two procedures either for EDG or EWG substituted aglycon.[163] Epimerization is possible just by using a catalytic amount of TFA (5%) in the case of EDG groups. Stronger acidic conditions are required for EWG substituted aglycons. A catalytic amount of a mixture of TFA and benzensulfonic acid proved to be optimal (Scheme 50). Examples of thermodynamic equilibrium distribution of an epimerization are shown in table (Table 4).

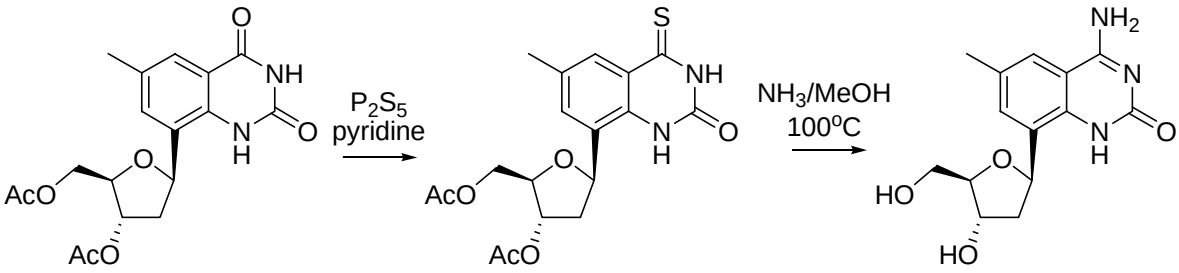
Table 4. Epimerization of *α-C*-nucleosides (Scheme 50)

compound	Ar	conditions	α-isomer[a] (%)	β-isomer[a] (%)
223a		20 mol % catalyst 40 °C, 40 h	37	58
223b		12 mol % catalyst 40 °C, 20 h	35	54
223c		12 mol % catalyst 40 °C, 20 h	38	54
223d		12 mol % catalyst 40 °C, 20 h	27	65
223e		5 mol % catalyst 40 °C, 20 h	30	64
223f		5 mol % catalyst 23 °C, 2 h	20	78
223g		5 mol % catalyst 40 °C, 20 h	32	63

[a]Isolated yield

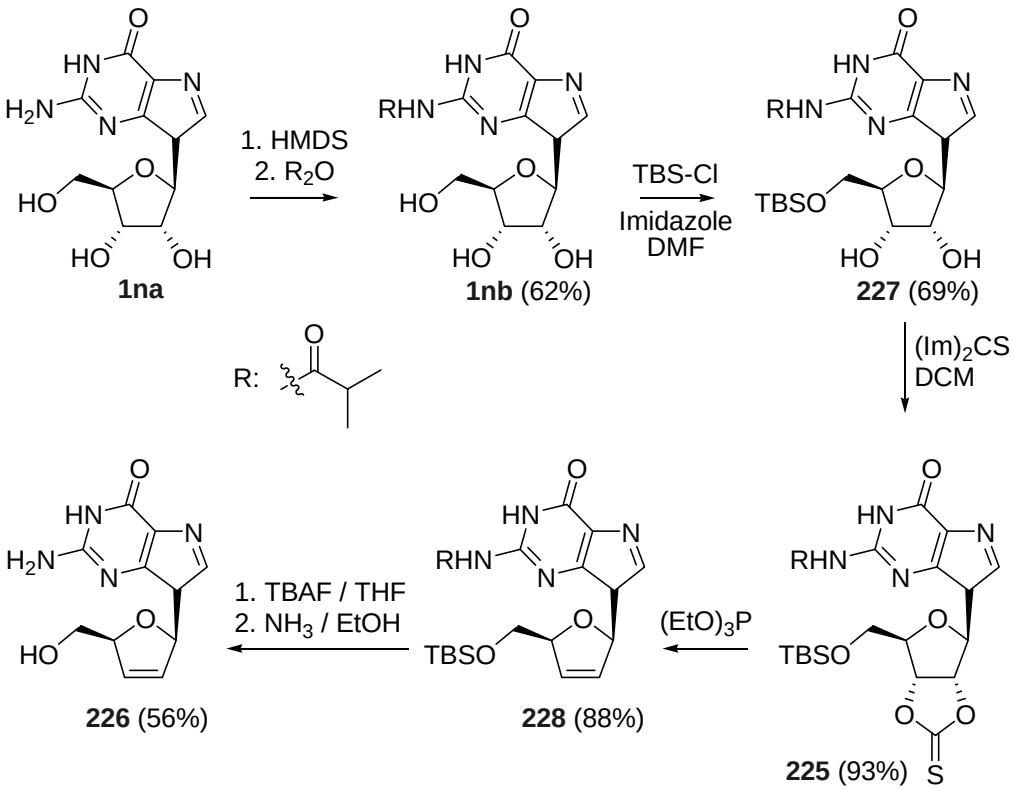
Recently, the strategy of *C*-nucleoside modification was employed in the syntheses of the artificial DNA-nucleoside analogue dx**C** from dx**T**.[37c] Starting dx**T** was transformed into its 4-thia analogue **224**, subsequent amonolysis afforded dx**C** in 74% overall yield.

Scheme 51. Synthesis of d**xC**



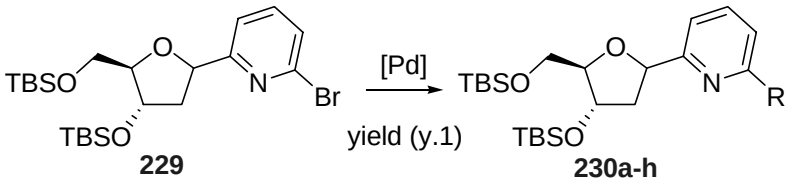
The carbohydrate-moiety modification procedures were also important since the discovery of *C*-nucleosides.[164] Modification of the carbohydrate part of an easily accessible *C*-nucleoside remains the major way to compounds possessing modified (artificial) carbohydrate, such as the D4 modification. Sartorelli *et al* reported a preparation of D4-9-deazaguanosine.[165] 9-Deazaguanosine **1na** was treated with bis(trimethylsilyl)azane in anhydrous DMF, followed by pyridine and isobutyranhydride to afford the *N*-protected 9-deazaguanosine **1nb**. Standard protection of the primary hydroxyl function with *tert*-butyldimethylsilyl was followed by formation of the cyclic thiocarbonate **225** using thiocarbonyl diimidazole in dichloromethane. Deoxygenation with triethyl phosphite, followed by two consequent deprotection steps, yielded D4 9-deazaguanosine **226**.

Scheme 52. Modification of the carbohydrate moiety, synthesis of D4 9-deazaguanosine **226**



A very innovative approach to *C*-nucleosides modifications has been published by Hocek *et al*.[166] Protected 2'-deoxy-*C*-nucleoside **229** bearing a bromopyridine nucleobase was submitted to a wide range of palladium catalysed reactions. These involved simple hydrogenolysis (**a**), cross-coupling reactions with trimethylalane (**b**), and triethylalane (**c**), Suzuki-Miyaura coupling with phenylboronic acid (**d**), Negishi coupling with benzylzinc chloride (**e**), and Hartwig-Buchwald aminations with lithium bis(trimethylsilyl)amide (**f**), methylamine (**g**), and dimethylamine (**h**). The subsequent deprotection of **230a-h** gave 2'-deoxyribonucleosides **231a-h** with a broad range of substitution patterns. This modular approach is a good example of modern trends in synthetic approach to the modification of existing *C*-nucleosides (Scheme 52).[167]

Scheme 52. Modification of the sugar moiety



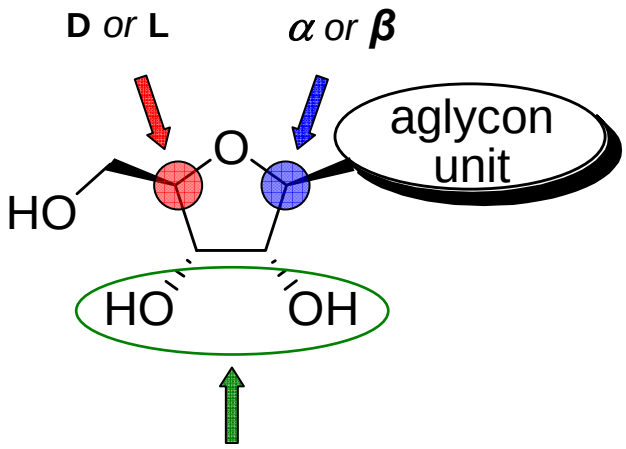
230, **231**	R	y. 1	y. 2
a:	H	81%	84%
b:	Me	78%	80%
c:	Et	90%	74%
d:	Ph	72%	56%
e:	Bn	77%	66%
f:	NH_2	83%	68%
g:	NHMe	50%	78%
h:	$NHMe_2$	48%	57%

4. Novel Synthetic Approach to *C*-Nucleosides

In the previous chapter, we have discussed several powerful synthetic methods commonly used in *C*-nucleoside synthesis. Nevertheless, any synthetic methodology has certain restrictions, and therefore new synthetic approaches are highly desirable. Any new, practically useful concept proposal has to be competitive with any of the state-of-the-art methods frequently used.

4.1. General Considerations

We have reanalysed the general structure of *C*-nucleosides. *C*-Nucleosides are compounds featuring two parts; (1) the polysubstituted tetrahydrofuran ring bearing up to four stereogenic centres (carbohydrate part). The most important one is that on the carbon 4'-bearing the hydroxymethyl substituent. The absolute configuration at this carbon directs the structure either to D- (4'-*R*) or L- (4'-*S*) family of carbohydrates, with the principal consequence to the biological relevance of the compound. The second most important centre is at the carbon 1'-bearing the aglycon unit. Here the relative configuration of the aglycon-connecting C-C bond to the position of hydroxymethyl group in 4'-position directs the structure either to α- (*trans*) or β- (*cis*) anomer of *C*-nucleoside. Positions 2',3'- may be free or mono- and di- hydroxylated. Hydroxyl group(s) is(are) in the (deoxy)*ribo* relative configuration in all the relevant cases.



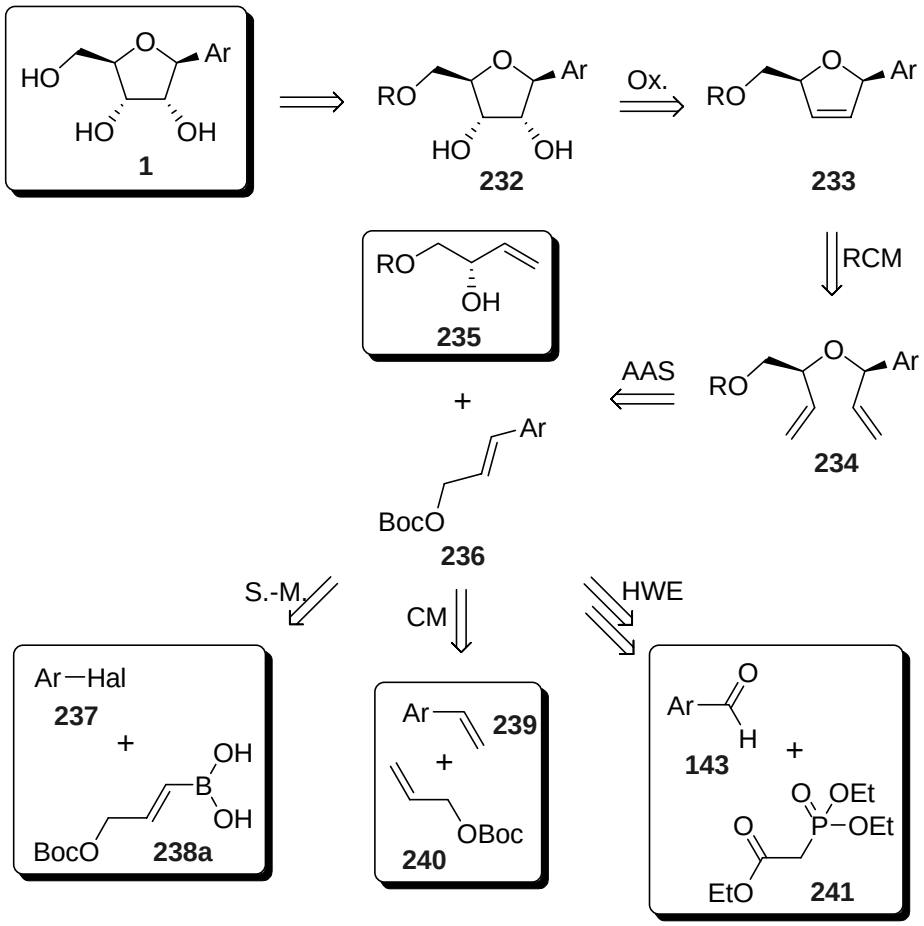
(2) The second part is the aglycon unit (pseudonucleobase). This has to be an aromatic, mono- to poly- cyclic structure, bearing substituents of varying nature and number, may

include a range of heteroatoms in the core cycle except the position where connected to the 1'-carbon of carbohydrate part.

4.2. Retrosynthetic Analysis

We have considered *C*-ribofuranosides **1** as our primary target structure. The retrosynthetic analysis was designed with all the aspects of modern and viable synthetic methodology (Scheme 54).[168]

Scheme 54. Novel (retro)synthetic analysis of *C*-nucleosides **1**



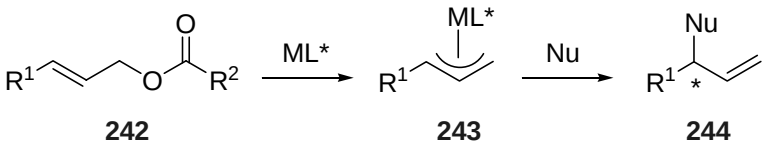
The retrosynthesis starts with introducing a 5'-OH protecting group to form **232**. The second retrosynthetic step, and the first of the strategic ones, is *cis*-vicinal dihydroxyl functionality removal to form a double bond in dihydrofuran **233**. The stereochemical outcome of the reaction is perfectly directed by the relative configuration of the substituents in the positions 2'- and 5'- of the dihydrofuran ring **233**. Moreover, dihydrofuran **233** features the structure of D4 nucleoside analogues, and thus forms an important target in itself. This highly enhances the utility of the proposed reaction

sequence. Dihydrofuran **233** is then disconnected in ring-closing metathesis (RCM) to form diallyl ether **234**. The key-step of the proposed synthesis is the disconnection of the diallyl ether **234** in the way of asymmetric allylic substitution (AAS). Extensive optimization of this reaction had been expected. We have finished the retrosynthetic analysis with commercially available butenediol **235** (R = H) and readily available arylpropenols **236** in four steps. Furthermore, we envisaged an extensive comparative study on the starting arylpropenols **236**, in order to obtain these in as short synthesis as possible in the cases where they are not commercial.

4.3. Metal-Catalysed Asymmetric Allylic Substitution

Asymmetric allylic substitution is a versatile method for the construction of a new chiral centre, starting with achiral allylic substrates, such as **242** (Scheme 55). This transformation is catalysed by chiral complexes of transition metals, such as palladium,[169,170] molybdenum,[171] tungsten,[171b,172] ruthenium,[173] rhodium,[174] iridium,[175] nickel,[176] platinum,[177] iron,[178] and copper,[179] and typically proceeds through the π-allyl intermediate **243**. To date, asymmetric allylic substitution has evolved into a powerful synthetic tool for the enantioselective formation of C-C, C-N, and C-O bonds.[169-179] Among the leaving groups, esters (**242**, R^2 = alkyl), carbonates (**242**, R^2 = OR') and, in particular, *tert*-butyl carbonates (**242**, R^2 = O*t*-Bu), have an important position.

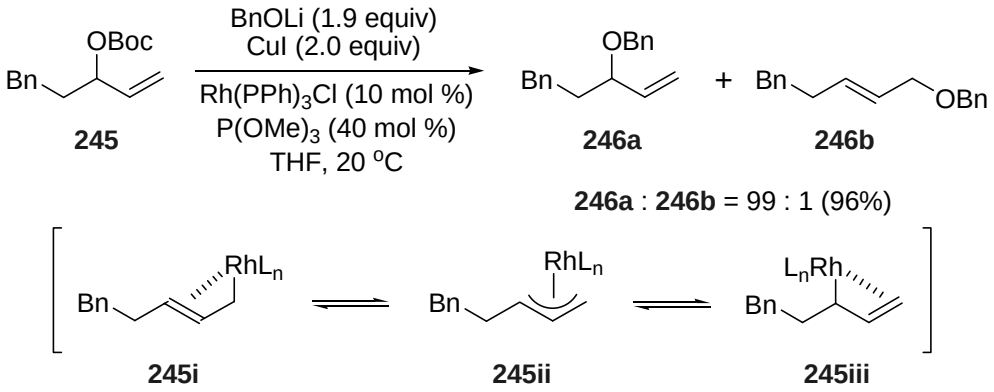
Scheme 55. Metal-catalysed asymmetric allylic substitution.



242 **243** **244**

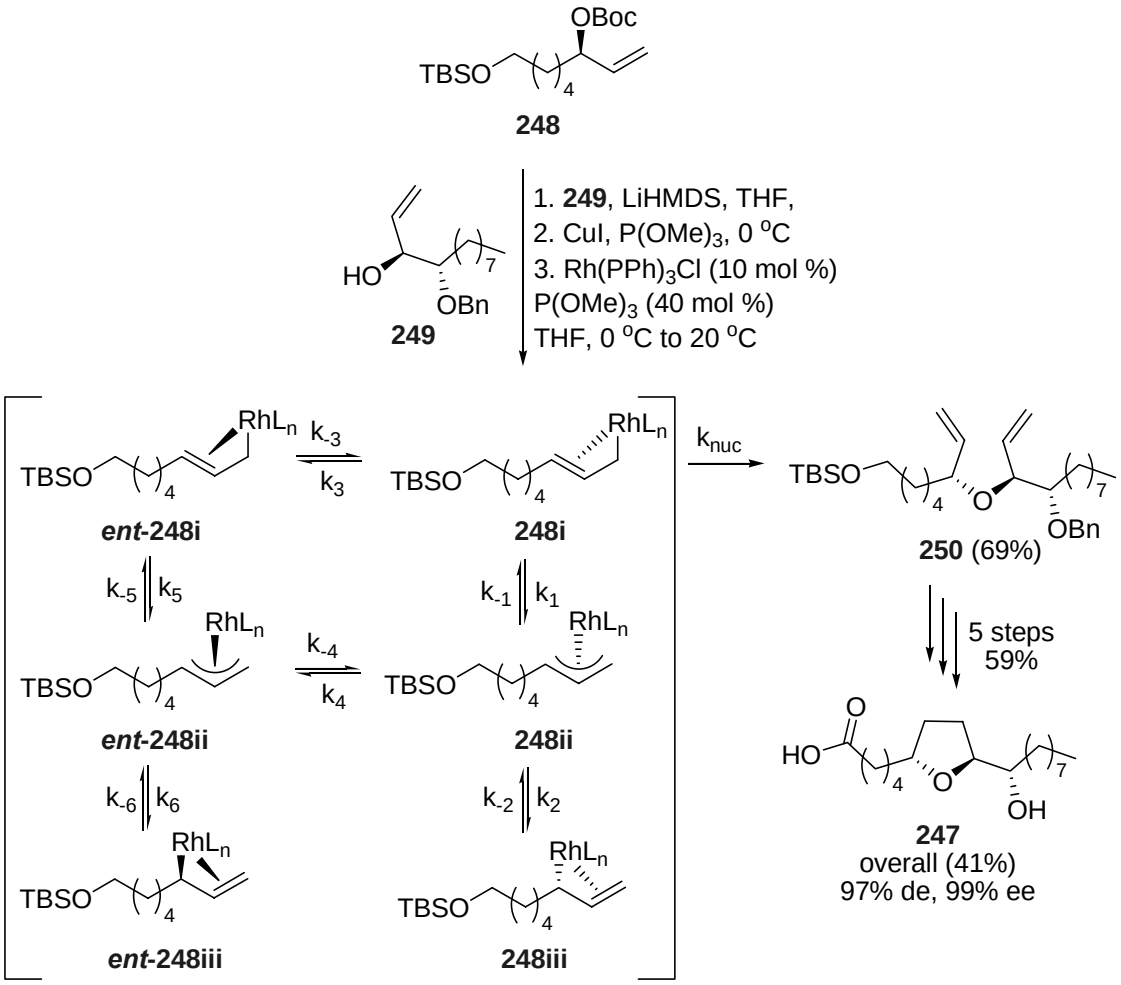
Aliphatic alkoxides are generally difficult to be successfully reacted in AAS reaction. Evans *et al* reported rhodium-catalysed allylic etherification using copper(I) alkoxides.[174a] This approach proved to be beneficial, avoiding a range of side-reactions when usual *hard* alkali alkoxides were used. The transmetallation of an alkali-metal alkoxide diminished the nucleophile basicity, thus promoting the etherification on a *soft* allylic electrophile.[180] The reaction exhibited excellent regioselectivity, using phosphite-modified Wilkinson catalyst (Scheme 56).

Scheme 56. Regioselectivity of Rh-catalysed allylic substitution



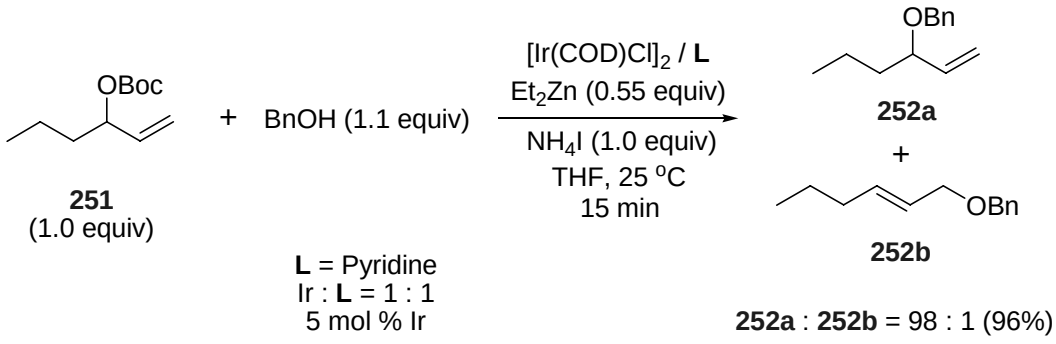
Evans and co-workers employed their new catalytic system in the enantioselective synthesis of guaric acid **247** (Scheme 57).[181] Formation of strongly coordinated σ-π complex of rhodium species and the allyl system was proposed. A double-inversion mechanism has been expected in this case but not rigorously proven. In general, the reaction can proceed through either an *enyl* complex **248i** or (distorted) π-allyl complexes **248ii** and **248iii**. Stereocontrol of the reaction through control of dynamic equilibrium of the intermediates **248i-iii** was not successful due to complexity of these reactions. Considerably easier approach was applied. The reaction conditions were optimised in order to perform an allylation of the nucleophile faster than racemisation of the rhodium complexes occurs (i.e. $k_{nuc} >> k_3$, $k_{nuc} >> k_1 \cdot k_4$). Enantiopure branched carbonate **248** together with configurational stability of the catalyst-substrate complex resulted in excellent stereoselectivity of the reaction.

Scheme 57. Stereoselectivity of Rh-catalysed allylic substitution



The first regioselective allylic etherification of aliphatic Zn-alkoxides catalysed by iridium species was reported by Lee *et al* (Scheme 58).[182] Carbonate **251** was reacted with a model substrate (benzyl alcohol) in the presence of diethylzinc. A fast reaction gave the expected products **252a** and **252b** in excellent regioselectivity in favour of the branched product **252a**.

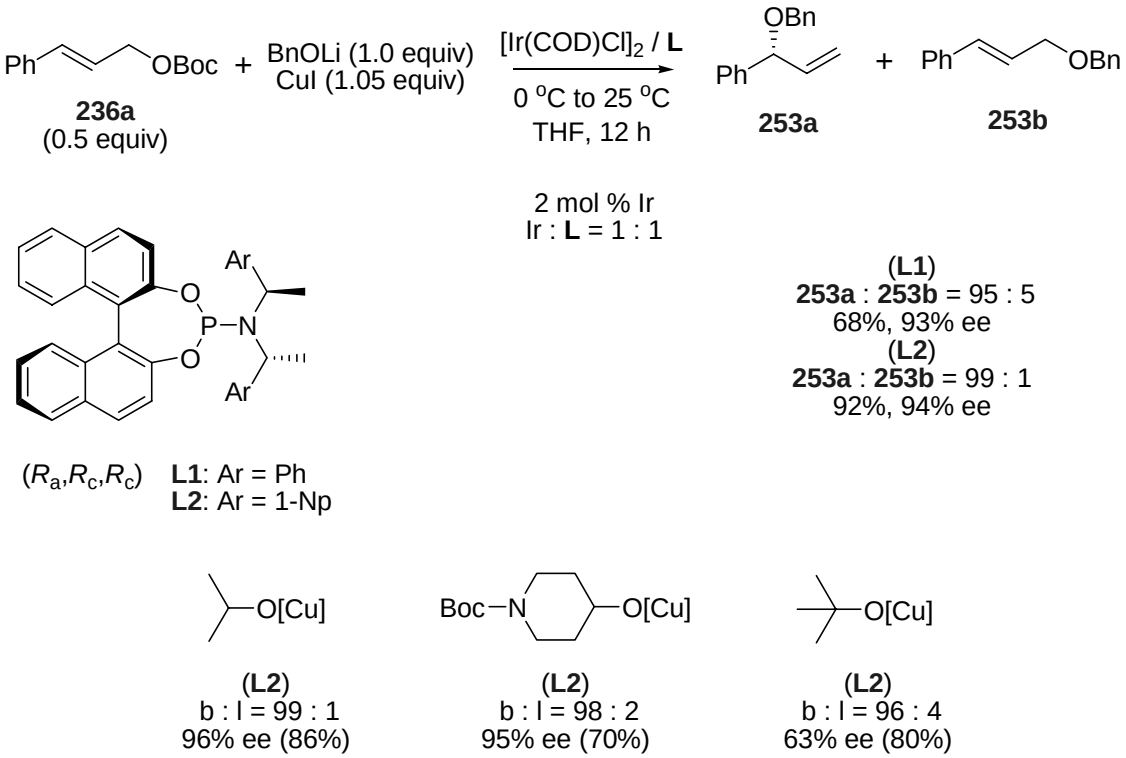
Scheme 58. Regioselectivity of Ir-catalysed allylic substitution of Zn-alkoxides



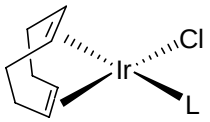
The extensive work of Hartwig *et al* proved Cu(I)-alkoxides superior over the Zn-alkoxides.[183] Linear carbonates **236** were used as the allylating agent in all cases. Stereoselective formation of an *enyl* catalyst-substrate complex was based on chiral ligands, thus forming a chiral iridium catalyst. This is the key difference when compared with branched carbonates such as **248**. Chiral σ-π complex of matal species and the allyl system bears the chirality induced either by starting non-racemic carbonate in the case of branched carbonates (e.g. **248**) or by chiral catalyst in the case of linear carbonates (e.g. **236**).

Primary and secondary alkoxides were successfully reacted in iridium-catalysed reaction utilising phosphoramidites ligands **L1** and **L2**. Reactions with tertiary alkoxides exhibited high regioselectivities and good yields, however enantioselectivites were comparatively lower than in the case of primary or secondary alkoxides (Scheme 59).

Scheme 59. Stereoselectivity of Ir-catalysed allylic substitution of Cu-alkoxides

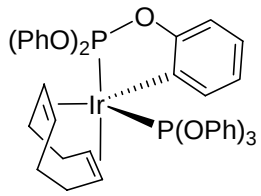


Several catalytically active species can be expected in the reaction.[175a] Complex **K1** was generally considered to be the active catalyst in the cases when $[Ir(COD)Cl]_2$ was used as a precatalyst.



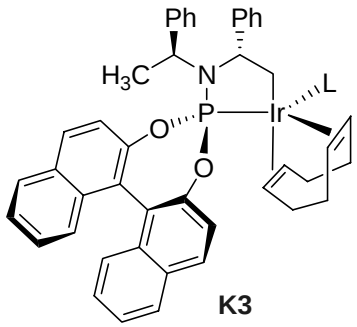
K1

An interesting observation was made in an attempt to isolate a catalyticaly active species or its complex with a substrate. In the allylation reaction of dimethyl malonate, catalysed by $[Ir(COD)Cl]_2 - P(OPh)_3$ was isolated metalacycle **K2** arising from the reaction of the corresponding complex **K1** with sodium malonate nucleophile.



K2

In this point of view, any Ir-catalysed allylic substitution requires close attention to the reaction conditions. The following two general procedures were developed (THF, rt): (1) The catalyst is prepared by mixing $[Ir(COD)Cl]_2$ and ligand in a 1:2 ratio. A simple complex **K1** is formed by ligand exchange and consecutive breaking of chloro bridges. (2) Treatment the former mixture with a base in order to induce the C-H activation and metalacycle formation (a type of **K2** complex). Hartwig *et al* reported preparation of the metalacyclic complex **K3** based on the opposite enantiomer of the phosphoramidite ligand **L1**. Its structure was confirmed by X-ray diffraction. Initial kinetic study showed roughly one order of magnitude increase in reaction rate when metalacyclic catalyst was used.[184]



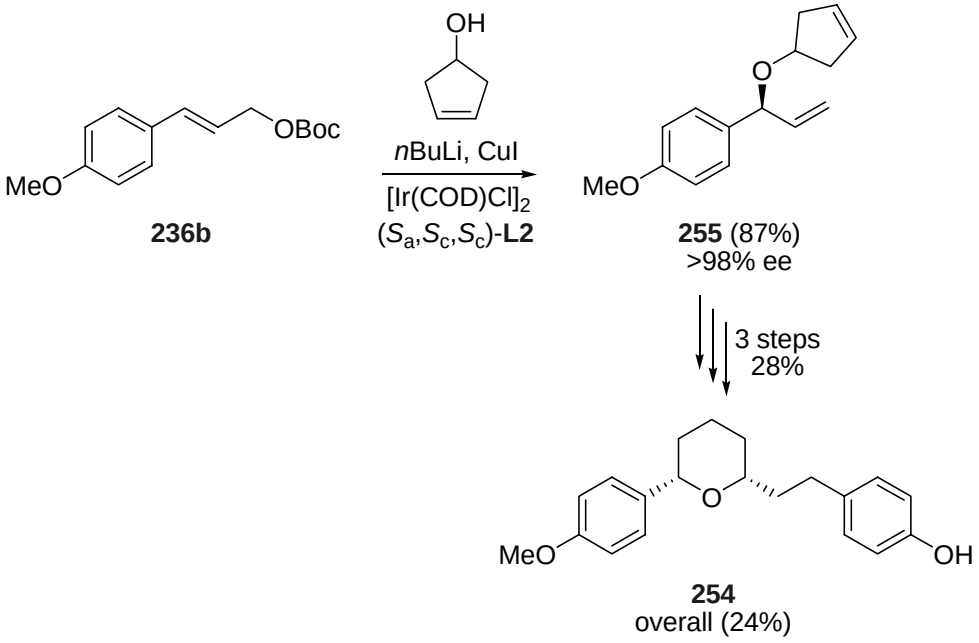
K3

Effects of such catalyst activation and ligand steric properties on the enantioselective allylation of amines and phenoxides were then further investigated.[185]

The only synthesis based on the iridium-catalysed allylation of aliphatic alkoxides reported to date is a very innovative stereoselective synthesis of the tetrahydropyranic antibiotic centrolobine **254** (Scheme 60).[186] The synthesis started with reaction of carbonate **236b**

with 3-cyclopentenol. The allylation product was obtained in good yield (87%) and excellent enantioselectivity of more than 98% ee. Phosphoramidite ligand **L2** was utilised in this reaction. Subsequent ring rearrangement metathesis, followed by isomerization of a terminal double bond and then by a one-pot cross-metathesis/catalytic hydrogenation gave centrolobine **254** in three preparative steps in good overall yield

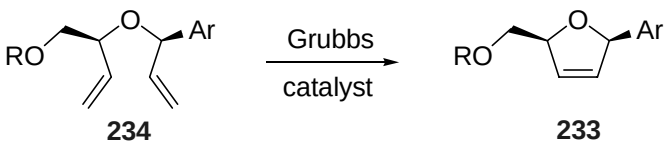
Scheme 60. Stereoselective synthesis of Centrolobine



4.4. Ring-Closing Metathesis (RCM)

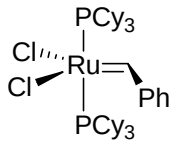
Ring-closing metathesis is a powerful method for the construction of unsaturated rings.[187] The reaction proposed in our synthetic scheme starts with diallyl ether **234** to afford dihydrofuran **233**. Protected dihydrofuran **233** features all the key structural motifs of the target *C*-nucleoside; i.e. defined stereocentres in positions 1 and 5 (Scheme 61).

Scheme 61. Ring-closing metathesis in the proposed *C*-nucleosides synthesis

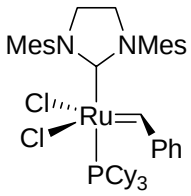


Only Grubbs ruthenium-based catalysts were considered during retrosynthetic analysis. This simplification was based on the fact that our system is one of the most common systems employed in RCM with a range of successful examples. Commercially available

ruthenium-based Grubbs 1st generation **C1**, and Grubbs 2nd generation catalyst **C2** have been used in this study.



C1

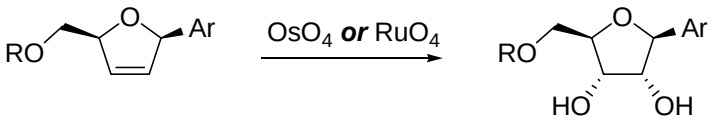


C2

4.5. Vicinal Dihydroxylation

The transition-metal-catalysed dihydroxylation of olefins represents a powerful synthetic tool for generation of two C-O bonds with precisely defined relative configuration. The reaction proceeds with high degree of stereospecificity. *Vicinal* dihydroxyl function is introduced from the least stericaly hindered face of the double bond. Metal tetroxide is used in a catalytic amount with a reoxidant such as metal chlorates, potassium ferricyanide, hydrogen peroxide, *tert*-butyl peroxide, or the most common, *N*-methylmorpholine *N*-oxide (NMO). Osmium tetroxide is one of the most reliable reagents for this catalytic transformation.[188] All these features fulfilled our requirements for the proposed transformation in our *C*-nucleoside synthesis (Scheme 62).

Scheme 62. *cis*-Vicinal dihydroxylation in the proposed *C*-nucleoside synthesis



233 **234**

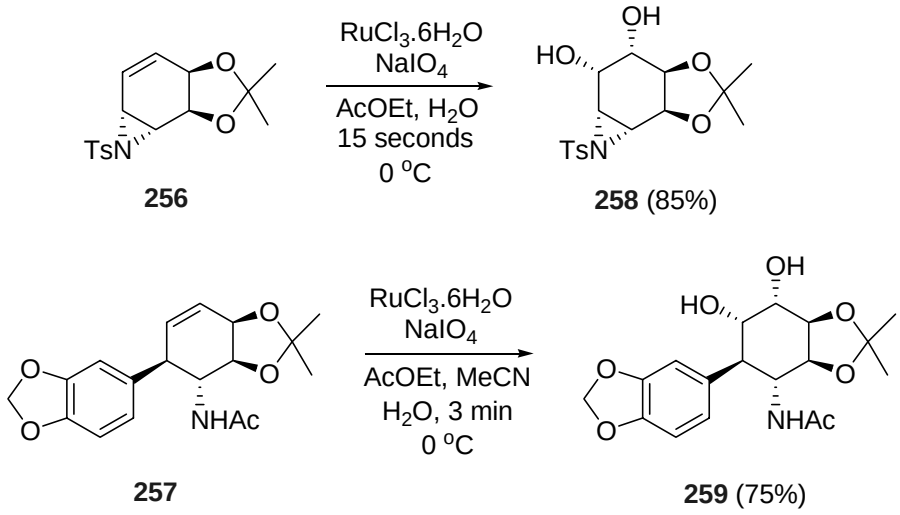
Osmium tetroxide has been successfully applied in many dihydroxylations reactions in the past century. However, OsO_4 is an expensive, highly toxic, non-polar volatile solid, which prevents its use on a large scale considering environmental issues. Kobayashi *et al* reported one successful solution of these particular problems, using microencaptulation process to capture this reagent, and form a recoverable and reusable polymer-supported catalyst.[189]

The second alternative has emerged in use of an isoelectronic, less expensive and much less toxic ruthenium tetroxide (RuO_4) as the dihydroxylation catalyst.[190] RuO_4 exhibits a dramatically higher reactivity compared to OsO_4. Reactions catalysed by RuO_4 were

considered as non-selective for a long time. Sica *et al* reported the first successful application of RuO_4 as a selective catalyst in *vicinal* dihydroxylation of olefins.[191] Several further improvements of the Sica's original procedure have then followed.[192]

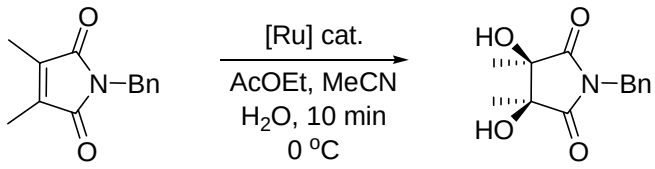
Ruthenium tetroxide successfully competes with osmium tetroxide in dihydroxylation reactions since this discovery. Hudlický *et al* employed RuO_4-catalysed dihydroxylation reaction in the synthesis of complex natural products (Scheme 63).[193] Olefins **256**, and **257** were stereoselectively dihydroxylated, using 10 mol %, and 7 mol % of ruthenium respectively. Due to its reactivity and very short reaction times, these reactions are called *flash dihydroxylation*.

Scheme 63. Ruthenium-catalysed *cis*-vicinal dihydroxylation reaction



Further improvement of the RuO_4-catalysed dihydroxylation was reported be Plietker *et al*.[194] Combination of RuO_4 with a Lewis acid generated a new bimetallic catalytic system, which not only further enhanced the reaction selectivity, but also surpassed the OsO_4. A redox-active Lewis acid, such as $CeCl_3$, aids both the Ru-catalyst reoxidation and the subsequent hydrolysis of the Ru(VI) ester, together with a deceleration of the undesired scission reaction of the resulting diol. The use of a catalytic amount of $CeCl_3$ (10%) broadened the reaction scope together with the further decreasing of Ru-loading to 0.25 mol %. Tetrasubstituted, electron-deficient double bonds were successfully dihydroxylated in high yields under these conditions (Scheme 64).

Scheme 64. Ru-Ce bimetallic *cis*-vicinal dihydroxylation reaction

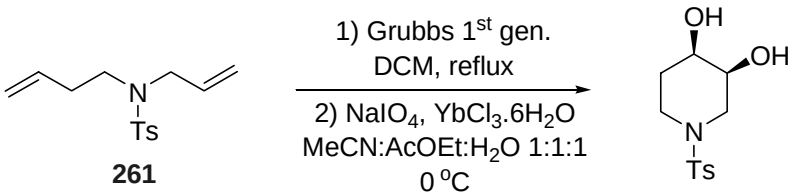


260 (89%)

[Ru] cat.:
12 mol % Ru (0.1M $RuCl_3$ in water)
10 mol % $CeCl_3.7H_2O$
1.5 equiv $NaIO_4$

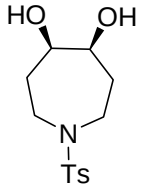
A very innovative combination of metathesis and Ru-catalysed dihydroxylation was recently reported by Blechert *et al* (Scheme 65).[195] The presented reaction protocol features two reactions catalysed by Ru-species, which increases the synthetic efficiency and economy, together with lowering the negative environmental impact. Diene **261** was submitted to the ring-closing metathesis to afford the expected cyclohexene product. The reaction solvent was then evaporated, since dichloromethane, the usual metathesis solvent proved to be incompatible with the subsequent dihydroxylation protocol. The resulting residue, containing the metathesis product together with the residues of the metathesis catalyst, was then dissolved in a mixture of acetonitrile and ethyl acetate, cooled to 0 °C, and a cold solution of a mixture of $NaIO_4$ and a catalytic amount (10%) of Lewis acid in water was added. The authors claimed better results when $YbCl_3$ was used instead of $CeCl_3$. The reaction gave a product of *vicinal* dihydroxylation **262** in good yield. However, the reaction yields varied in a wide range, even for relatively similar substrates (Scheme 65).

Scheme 65. Two-step-one-pot procedure of RCM-*cis*-vicinal dihydroxylation reaction

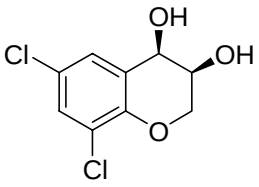


261

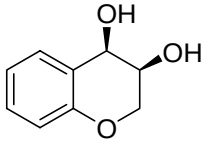
262a (88%)



262b (21%)



262c (63%)



262d (33%)

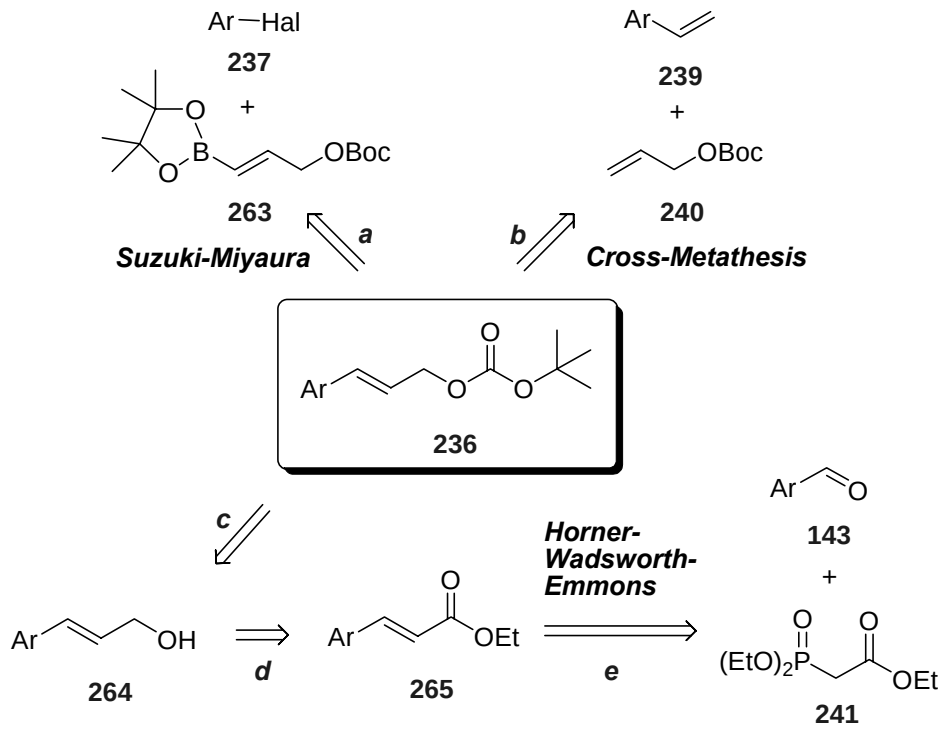
5. Results and Discussion

5.1. Linear Carbonates

Conversion of an alcohol to the corresponding Boc derivative is well established synthetic transformation.[196] Expedient synthesis of even a small library of desirable carbonates may actually become considerably more cumbersome than expected. With 3-aryl allyl alcohols, in particular, there is little choice in diversity with a view of matching the portfolio of the commercially available aryl building blocks with a suitable methodology.

We have now developed two new methods for the construction of *tert*-butyl (*E*)-3-arylprop-2-en-1-ol carbonates **236** from commercially available starting materials that are suitable for parallel synthesis techniques (routes *a* and *b*; Scheme 66). For comparison, some of the materials have been synthesized *via* an optimized conventional approach to these compounds, based on the Horner-Wadsworth-Emmons reaction (HWE; route *c*).

Scheme 66. Retrosynthetic analysis of *tert*-butyl 3-arylprop-2-en-1-yl carbonates. For Ar, see the following Schemes

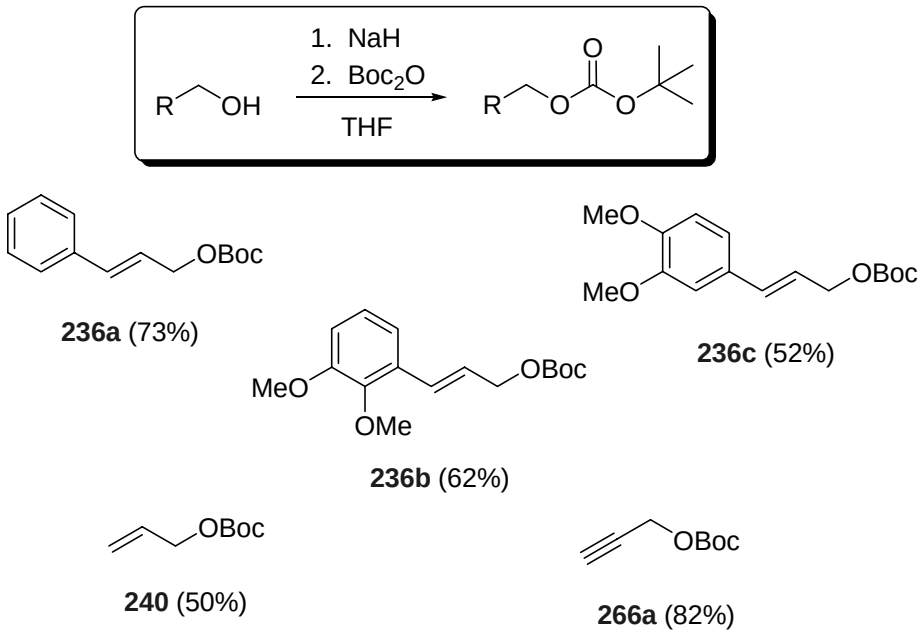


Our retrosynthetic analysis of the target carbonates **236** was based upon the desire to develop a one-step synthetic protocol suitable for parallel synthesis (Scheme 66). The main interest was laid upon the disconnection (***a***) employing the commercially available aryl halides **237** and the common building block **263**. Route (***b***) is based on the (*E*)-double bond disconnection *via* a cross-metathesis reaction of the commercially available styrenes **239** and the Boc-protected allyl alcohol **240** as common building blocks. The last part of our investigation was focused on the optimization of the Boc derivatization of the cinnamyl-type alcohols **264** (***c***). Some of these alcohols are commercially available or easy to make from the corresponding cinnamic acids. Others can be synthesized using the Horner-Wadsworth-Emmons reaction. Optimization of the latter sequence, starting with the commercially available aldehydes **143** and the phoshonate reagent **241**, into a three-step-one-purification protocol (***c***-***e***) is also reported.

5.1.1. Boc Derivatization

The Boc-derivatization of cinnamyl alcohol **264a** was investigated under various conditions (Scheme 67).[196] The procedure employing Boc anhydride and NaOH with a phase-transfer catalyst failed,[196a] whereas reactions with Boc anhydride in dichloromethane catalysed by $V(O)(OTf)_2$[196b] gave only the symmetric carbonate $(PhCH{=}CHCH_2O)_2CO$ in high yield. On the other hand, by following the procedure, in which Boc anhydride is added to a solution of the corresponding alkoxide in THF,[196c,d] we were able to isolate the desired product **236a** in about 40% yield along with the symmetric carbonate $(PhCH{=}CHCH_2O)_2CO$. A modified protocol, in which the alcoholate solution was transferred to an excess of the solution of Boc anhydride, afforded **236a** in high yield and was then employed throughout this study (Scheme 67).

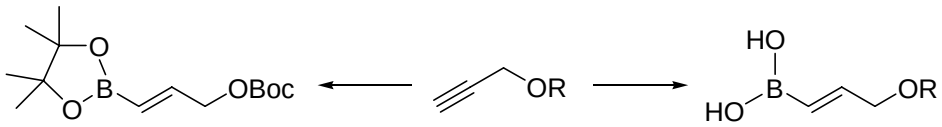
Scheme 67. Formation of *tert*-butyl carbonates **236**.



5.1.2. Suzuki-Miyaura Coupling

The preparation of the building block **238a** was based upon the procedure for the preparation of boronic acid **238b** (Scheme 68).[197] In our hands, the established protocol was successful only for propargyl alcohol **266b** to produce **238b** (Table 5, entry 1), and failed in the case of the Boc derivative **266a** (entries 2, and 3). Alternative hydroboration conditions were also investigated:[198] thus, for instance, treatment of alkyne **266a** with boron dibromide proved fruitless (entry 4) and an attempted reaction with dicyclohexylborane, followed by addition of trimethylammonium *N*-oxide, gave only moderate yield (entry 5). On the other hand, employing dicyclohexylborane as catalyst,[199] with a stoichiometric amount of catecholborane, furnished the desired product **238a** in good yield (entry 6).[200] Finally, the reaction of **266a** with pinacolborane, catalysed by dicyclohexylborane, afforded vinyl boronate **263** in an excellent isolated yield (entry 7). In the latter protocol, the high purity of the hydroborating reagents proved to be crucial for attaining high yields.

Scheme 68. Hydroboration; for conditions, see Table 5.



263 **266a**, R = Boc **238a**, R = Boc
266b, R = H **238b**, R = H

Table 5. Hydroboration of **266a** and **266b**.

entry	conditions	alkyne	product	yield (%)[a]
1	Catecholborane (2 equiv) neat, 70 °C, 1 h	**266b**	**238b**	40
2	Catecholborane, THF 70 °C, 12 h	**266a**	**238a**	0
3	Catecholborane, neat 70 °C, 12 h	**266a**	**238a**	0
4	$Br_2BH{\cdot}Me_2S$, DCM 0 °C to 20 °C, 6 h	**266a**	**238a**	0
5	cHx_2BH, TMANO, THF 0 °C to 20 °C, 1.5 h	**266a**	**238a**	40
6	Catecholborane, cHx_2BH (10%), neat 20 °C, 12 h	**266a**	**238a**	62
7	Pinacolborane, cHx_2BH (10%), neat 20 °C, 12 h	**266a**	**263**	95

[a]Isolated yields.

The procedure, published for the Suzuki-type coupling reactions of hydroxy boronic acid **238b** in the presence of thallium ethoxide in aqueous medium,[201] was applied to the coupling of the Boc-protected acid **238a** with *p*-iodotoluene but gave only traces of the desired product **236d** (Scheme 69; Table 6, entry 1). By contrast, simple standard conditions for the aqueous Suzuki-Miyaura coupling reactions, employing K_2CO_3 as a base, resulted in the formation of **236d** in good yield (entry 2).[202]

A considerable drawback of the latter protocol is the behavior of the acid **238a**: when freshly prepared, it is a white solid, which in the air (moisture) melts to a very viscous oil, containing variable amount of the corresponding oligomers; upon prolonged standing, both forms (oil or solid) become a sticky brown-grey solid, containing products of decomposition. These features, in conjunction with the lower yield of the hydroboration, drew our attention to boronate **263**, a colourless, bench stable liquid that can be distilled.[203]

Initially, we chose alkali carbonates in aqueous 1,2-dimethoxyethane (DME) as the reaction medium for the **237d** + **263** coupling. An overnight heating with alkali carbonates gave the product **236d** in about 10% yield (Table 6, entries 3 and 4). Higher loading of the iodide **237d** and the base led to an improvement (entries 5 and 6), whereas a significant decrease of the yield was observed when potassium *tert*-butoxide was employed (entry 7), although the use of a toluene-water two-phase system resulted in some improvement (entry 8). The reaction failed when higher amount of water (>80%) was used in the solvent mixture, or when thallium ethoxide was used as a base, or when DMF was chosen as a solvent. Best results were attained when the reaction time was kept short (entry 9). Other published conditions did not lead to any further improvement.[204] Furthermore, the recyclable microencapsulated palladium[205] gave lower yields along with a relatively high amount of unidentified side-products (entries 10 and 11), whereas the use of an advanced ligand,[206] such as S-Phos (2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl), resulted in no reaction or gave just traces of product **236d** (entry 12).

Scheme 69. Suzuki-Miyaura coupling.

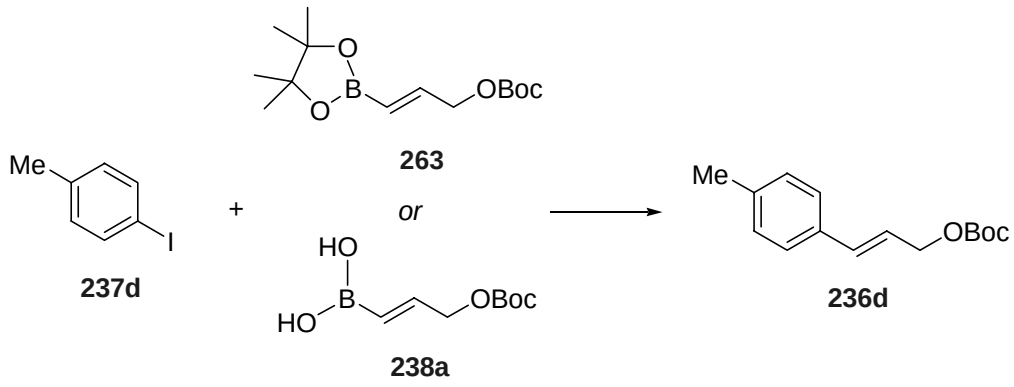


Table 6. Suzuki-Miyaura coupling optimization.[a]

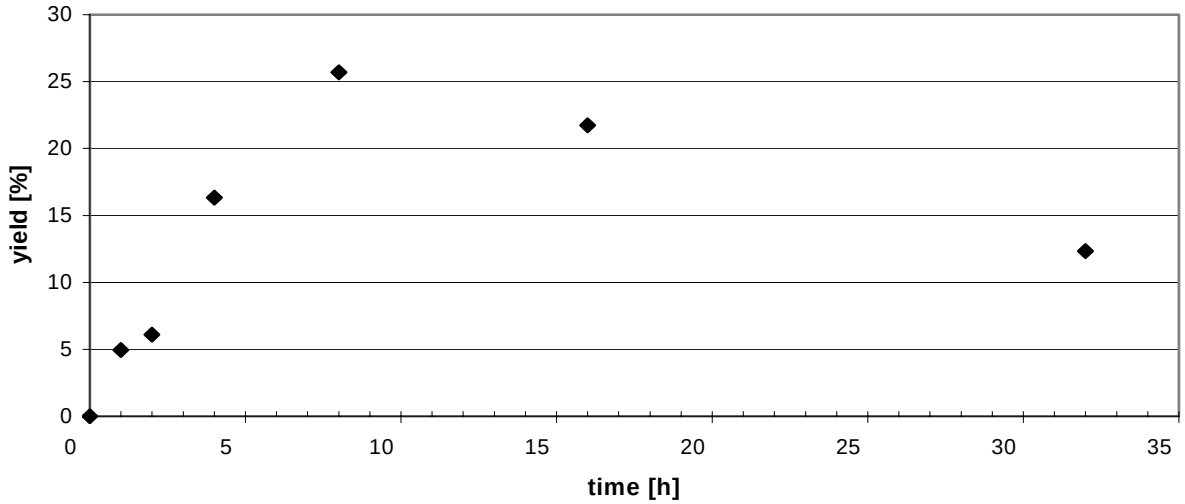
entry	**237d** (equiv)	allyl carbonate	catalyst (mol %)	base (equiv)	solvent	conditions	yield[b] (%)
1	2.0	**238a**	$(Ph_3P)_4Pd$ (5)	EtOTl (2.1)	DME - H_2O (7:3)	20 °C, 1 h	traces[c]
2	0.7	**238a**	$(Ph_3P)_4Pd$ (10)	K_2CO_3 (1.8)	DME - H_2O (20:3)	85 °C, 20 h	61
3	1.0	**263**	$(Ph_3P)_4Pd$ (10)	Na_2CO_3 (5.3)	DME - H_2O (7:5)	100 °C, 15 h	8
4	1.0	**263**	$(Ph_3P)_4Pd$ (10)	K_2CO_3 (2.5)	DME - H_2O (20:3)	80 °C, 18 h	12
5	1.8	**263**	$(Ph_3P)_4Pd$ (9)	K_2CO_3 (7.8)	DME - H_2O (20:3)	85 °C, 18 h	33
6	3.3	**263**	$(Ph_3P)_4Pd$ (5)	K_2CO_3 (5.5)	DME - H_2O (4:1)	100 °C, 20 h	40
7	1.9	**263**	$(Ph_3P)_4Pd$ (5)	*t*-BuOK (4.8)	DME - H_2O (4:1)	100 °C, 20 h	6
8	2.2	**263**	$(Ph_3P)_4Pd$ (5)	*t*-BuOK (5.2)	Toluene - H_2O (4:1)	100 °C, 20 h	26
9	5.0	**263**	$(Ph_3P)_4Pd$ (5)	K_2CO_3 (4.0)	DME - H_2O (1:1)	80 °C, 2 h	42
10	1.4	**263**	Pd(0) EnCat™ (5)	K_2CO_3 (3.3)	DME - H_2O (1:1)	80 °C, 14.5 h	25
11	0.9	**263**	Pd(0) EnCat™ (4)	K_2CO_3 (2.7)	DME - H_2O (1:1)	80 °C, 2 h	16
12	0.9	**263**	$(Ph_3P)_4Pd$ (5) S-Phos (5)	K_2CO_3 (2.0)	DME - H_2O (1:1)	20 °C, 1 h	5

[a]Reactions were performed on 1 mmol scale, using 10 mL of the solvent mixture; all the equivalents are based on the boronate (boronic acid). [b]Isolated yield. [c]The yield was determined by ^{1}H-NMR spectroscopy in the reaction mixture after the work up.

Having identified potassium carbonate as the optimal base, a DME-water mixture (1:1) as the optimal solvent system, and $(Ph_3P)_4Pd$ as the most suitable pre-catalyst (entry 2), we then investigated the role of the reaction time in the range of 1-32 h at 40 °C (Chart 1). The acquired data clearly show an increase in yield of **236d** with a maximum reached in 8 h.

Our data suggest that both the product **236d** and the starting boronate **263** are unstable under the reaction conditions.

Chart 1. Suzuki-Miyaura coupling of **237d** with **263**; isolated yields *vs* reaction time.[a]



[a] Reactions were performed on 1 mmol scale; conditions: aryl iodide (0.9 equiv), K_2CO_3 (3 equiv), DME / H_2O (1:1, 10 mL), 40 °C, $(PPh_3)_4Pd$; isolated yields.

A deeper insight was obtained *via* monitoring the reaction by ^{1}H-NMR spectroscopy. The coupling was performed at a higher temperature (80 °C), with sampling every 20 min (Chart 2). The spectra plot showed an increasing amount of the product **236d**, reaching the maximum in about 2 h. After this point, both signals begun to slowly disappear in the baseline noise. We concluded that, at the temperatures ranging from 40 °C to 80 °C, boronate **263** is sufficiently reactive to form a significant amount of the product **236d**, whose formation is estimated to be one order of magnitude faster than the rate of its decomposition. These results also show that 80 °C for 2 h are optimal reaction parameters for this process.

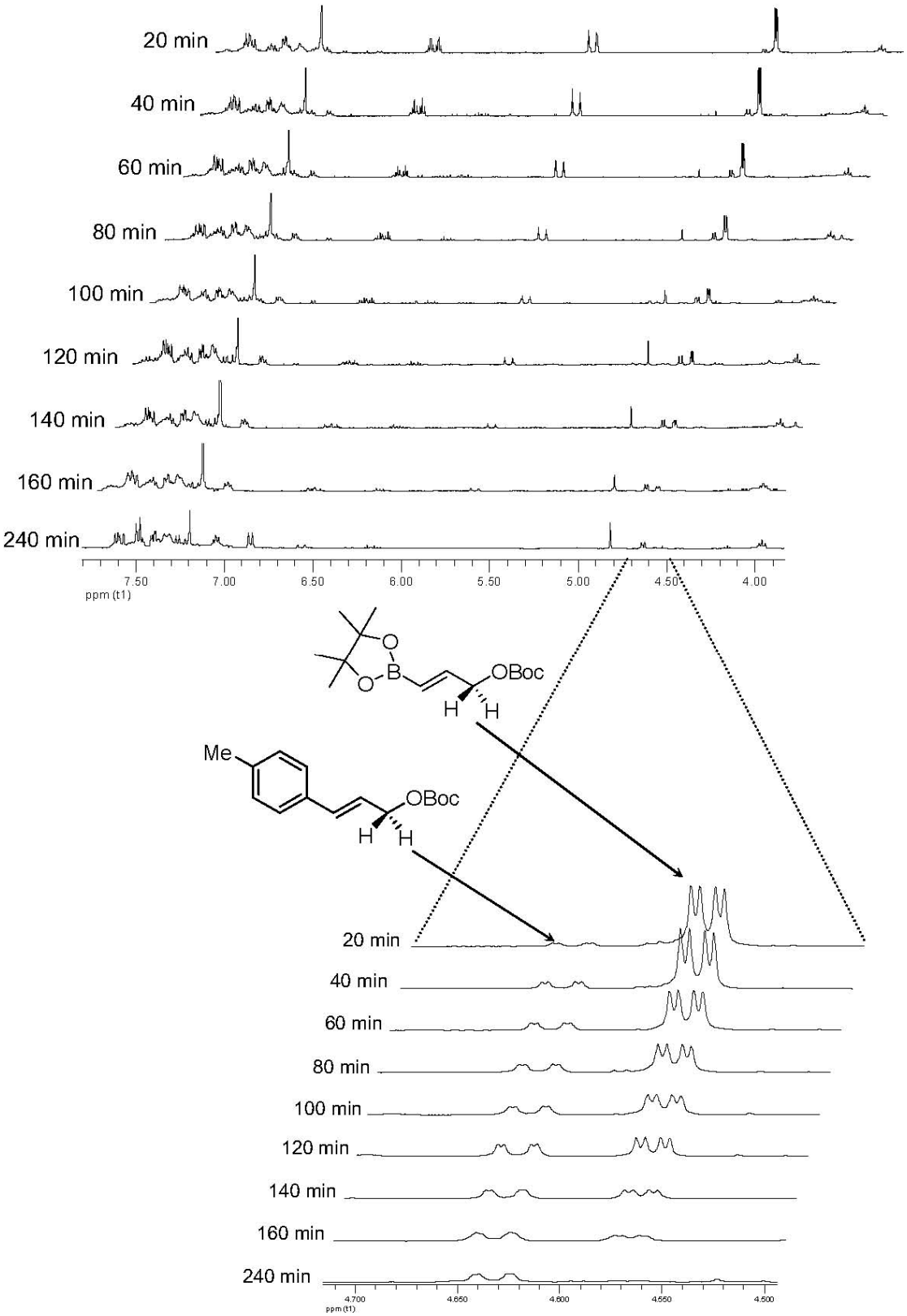


Chart 2: ^{1}H-NMR spectra plot based on Scheme 5. The reaction was performed on a 1 mmol scale; conditions: aryl iodide (0.9 equiv), K_2CO_3 (2.5 equiv), DME-H_2O(1:1, 10 mL), 80 °C, $(PPh_3)_4Pd$ (5.4 mol %).

The last sets of parameters to be optimized were the ratios of the starting iodide and the base employed (Table 7). We also proved the need for higher amounts of water (50%), combined with higher dilution. Under these conditions, the reactions were homogeneous (compare entries 2 *vs* 3). The other results show the highest yields when either excess of boronate **263** (entry 4) or iodide **237d** (entry 6) were used along with an excess of base. Further increased loading of the base (entries 6 and 7) had a more negative effect than further increase in the loading of the iodide (entries 5 and 6).

Table 7. The influence of the molar ratios on the Suzuki-Miyaura Coupling of **237d** with **263**.[a]

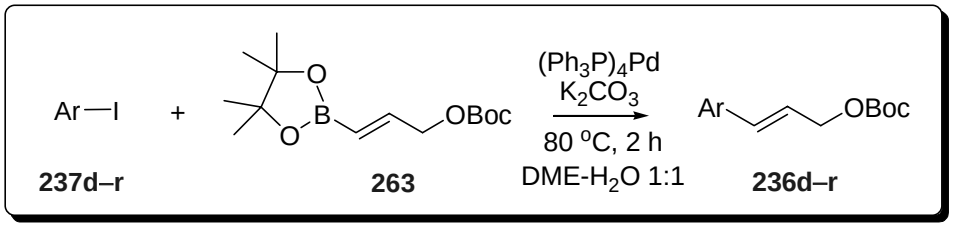
entry	iodide (equiv)	base (equiv)	solvent	Pd(0) (mol%)	yield[b] (%)
1	1.4	2.9	2 mL, DME / H_2O (9:1)	5.2	11[c]
2	0.8	1.7	2 mL, DME / H_2O (9:1)	5.2	9[c]
3	0.8	2.3	10 mL, DME / H_2O (1:1)	4.0	20
4	0.6	1.7	10 mL, DME / H_2O (1:1)	3.1	36
5	4.7	2.9	10 mL, DME / H_2O (1:1)	5.6	33
6	3.1	3.0	10 mL, DME / H_2O (1:1)	6.0	36
7	4.6	4.6	10 mL, DME / H_2O (1:1)	4.8	24

[a]Reactions were performed on 1 mmol scale; conditions: 2 h, 80 °C, $(PPh_3)_4Pd$; all equivalents are based on the boronate. [b]Isolated yield. [c]The yield was determined by ^{1}H-NMR spectroscopy in the reaction mixture after the work up.

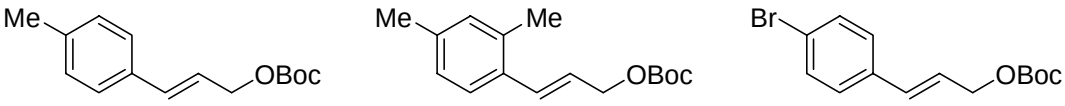
The optimized reaction protocol was employed in the synthesis of a series of various carbonates **236d-r** (Scheme 70).[207] The results fully correspond to the previous observations as well as to the common reactivity of aryl halides in the Suzuki-Miyaura coupling reaction. The highest yields were attained with electron-poor aryl iodides lacking *ortho* substituents. Aryl bromides did not successfully react in any variation of the reaction conditions. This effect can be utilized in the distinguishing of the reaction site of polyhalogenated substrates; thus, for example, 4-bromoiodobenzene (**237f**) was selectively reacted at the C-I bond to produce **236f**. In some cases, the excess of aryl iodide was successfully recovered (**236e**, **236j**, **236l**, and **236n**). 3-Iodopyridine (**237q**) was also successfully reacted to afford **236q**. Despite the low to moderate yields, the main synthetic utility of this method is in the fast reaction and mild reaction conditions. An aqueous work

up procedure gave generally mixtures containing mainly the unreacted starting iodide (in excess) and the desired product. With the subsequent simple chromatography, the whole reaction-purification procedure did not exceed 3 h, which is very convenient for automation. These advantages were demonstrated in the reaction of salicylate **237r**[208] that afforded the highly substituted carbonate **236r**.

Scheme 70. Suzuki-Miyaura coupling of aryl and heteroaryl halides **237** with vinyl boronate **263**.



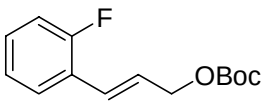
237d–r **263** **236d–r**



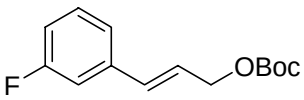
236d (42%)

236e (12%)

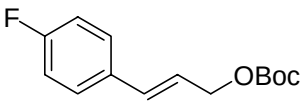
236f (41%)



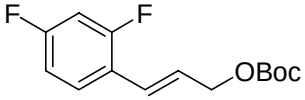
236g (10%)



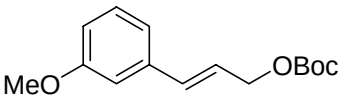
236h (40%)



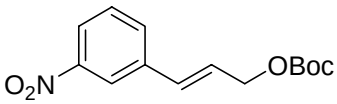
236i (29%)



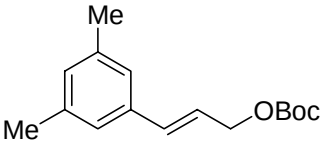
236j (15%)



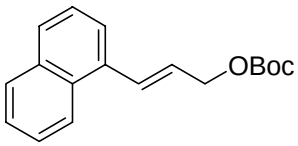
236k (25%)



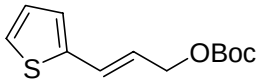
236l (57%)



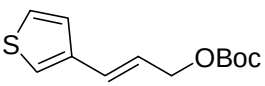
236m (33%)



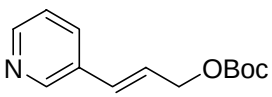
236n (56%)



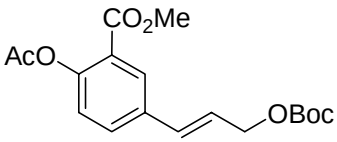
236o (31%)



236p (44%)



236q (18%)

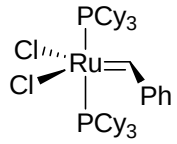


236r (22%)

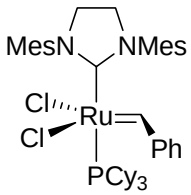
5.1.3. Alkene Cross Metathesis

Alkene cross metathesis reaction[209] was investigated as an alternative synthetic approach to the carbonates **236** (Scheme 71). Many of the starting vinyl aromatics **239** are commercially available or are readily accessible in one step by the well-developed vinylation of aryl halides **237**,[210] which renders this approach attractive.

Employing styrene (**239a**) and allyl *t*-butyl carbonate (**240**) as model substrates, a brief screening of the reaction conditions has been conducted to find an optimal protocol. The second-generation Grubbs catalyst **C2** gave generally twice as high yields as the Grubbs first-generation catalyst **C1**, along with the full conversion of allyl carbonate **240** (Table 8, entries 1 and 2).



C1



C2

In both cases *trans*-stilbene was isolated as the major product as a result of self-metathesis of **239a**. On the other hand, self-metathesis of allyl carbonate **240** was observed only as a very minor side reaction. Higher yields of the desired product **236a** were attained by increasing the excess of styrene (entries 6 and 7), which is an acceptable scenario in the case of cheap, commercially available vinyl aromatics.

Various vinyl aromatics were then submitted to the optimized cross metathesis protocol (Scheme 72).[207] The reaction showed reversed electronic demands to the Suzuki-Miyaura coupling and did not work for electronically poor substrates, such as nitrostyrene or pentafluorostyrene, and for vinyl pyridines. On the other hand, the reaction proceeded successfully with *ortho*-substituted styrenes to produce **236e** and **236g**.

Scheme 71. Synthesis of carbonates **236** *via* cross-coupling metathesis.

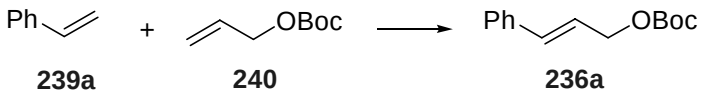
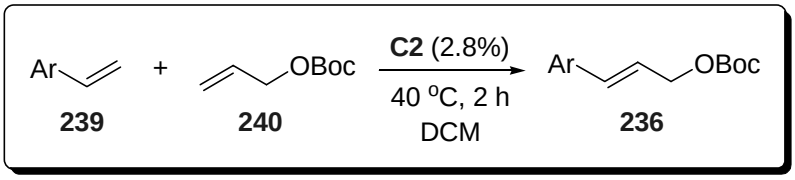


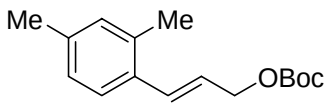
Table 8. Screening of the cross-metathesis reaction.[a]

entry	**239a** (equiv)	catalyst (mol %)	time (h)	yield (%)[b]
1	2.0	Grubbs 1st (5.6)	12	17
2	2.0	Grubbs 2nd (2.7)	2	36
3	0.5	Grubbs 2nd (0.7)	2	21
4	0.4	Grubbs 2nd (0.8)	2	23
5	0.2	Grubbs 2nd (0.4)	2	16
6	5.0	Grubbs 2nd (2.4)	2	37
7	10.0	Grubbs 2nd (2.7)	2	43

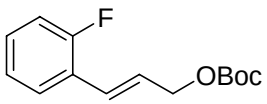
[a]Reactions were performed on 1 mmol scale; conditions: DCM (2 mL), 40 °C; all the equivalents are based on allyl carbonate. [b]Isolated yields.

Scheme 72. Ru-Catalyzed cross metathesis of styrenes **239** with allyl carbonate **240**.

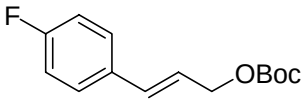




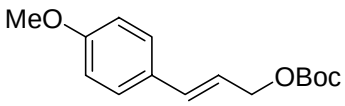
236e (52%)



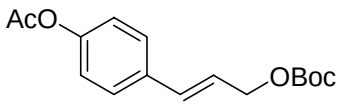
236g (29%)



236i (27%)



236s (35%)



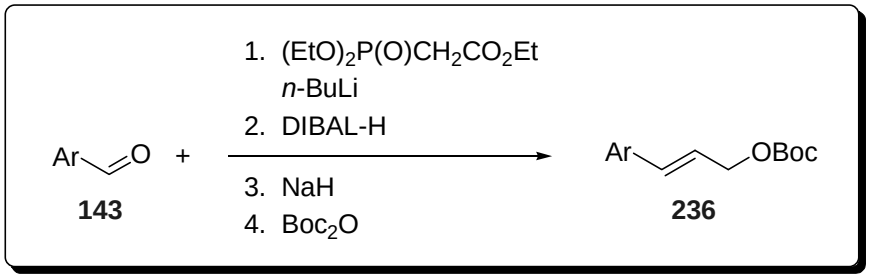
236t (36%)

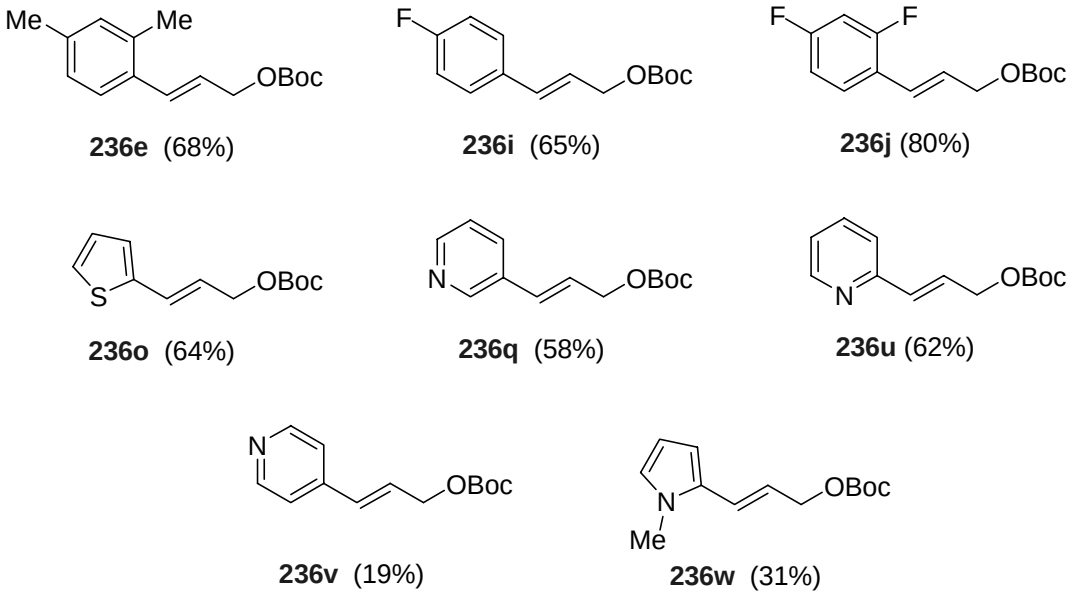
5.1.4. Horner-Wadsworth-Emmons Reaction

Optimization of the conventional synthetic approach[211] to carbonates **236** was also investigated (Schemes 66 and 73). Commercially available aryl aldehydes **143** were reacted with phosphonate **241** to afford the corresponding ethyl acrylates **265** (see Scheme 66, page 81). The reaction proved to be clean and highly stereoselective; no (*Z*)-isomers were detected by ^{1}H-NMR spectroscopy. The acrylates **265** were then reduced with DIBAL-H directly after the aqueous work-up without further purification. The resulting aryl propenols **264** were obtained again in sufficient purity and were directly transformed into the desired Boc derivatives **236**, using our optimized protocol (*vide supra*, page 82); the crude products were then subjected to the only purification (by chromatography) required in this sequence.

This classical synthetic approach proved to be very robust for a number of structural patterns (Scheme 73). The only difficulties were observed in the reaction sequences of aldehydes **143v** and **143w**. Pyridine aldehyde **143v** reacted well in the HWE reaction but the subsequent reduction at room temperature resulted in the formation of intractable products only. Reduction at low temperature (-80 °C) gave propenol **264v** in about 40% yield (over two steps) but additional purification of the propenol **264v** was necessary. Carbonate **236v** was obtained from the latter product (48%) by using the standard Boc derivatisation procedure. Pyrrole carbonate **236w** was prepared by the standard reaction sequence. The problematic part was the final purification, due to the low stability of the pyrrole moiety.[212] Even if the chromatography was carried out on a column of neutral alumina and with triethylamine as co-eluent, the blue colour of pyrrole-based oligomers was observed upon the stationary phase. Also the final pyrrole carbonate **236w** proved unstable at room temperature, as it underwent spontaneous polymerization. Despite these particular problems, this optimized HWE approach proved to be a very convenient method for a gram scale (all reactions were carried out on 20 mmol scale) synthesis of carbonates **236** bearing various structural patterns including the *ortho*-substituents and aromatic/heteroaromatic moieties with diverse electronic properties.

Scheme 73. Horner-Wadsworth-Emmons approach to carbonates **236**.





236e (68%) **236i** (65%) **236j** (80%)

236o (64%) **236q** (58%) **236u** (62%)

236v (19%) **236w** (31%)

5.1.5. Conclusions

We have systematically investigated new synthetic routes to *tert*-butyl (*E*)-3-arylprop-2-enol carbonates (**236a-w**) based on Suzuki-Miyaura reaction and alkene cross metathesis and compared them with an optimized conventional approach based on HWE reaction. All these three approaches were shown to be complementary. The Suzuki-Miyaura coupling reaction is a versatile method for aryls lacking an *ortho* substituent and for non-coordinating heterocycles, bearing preferentially electron-withdrawing functionalities. This method employs a wide range of commercially available aryl iodides and its main advantage relates to polyfunctional substrates, such as methyl acetylsalicylate (**237r → 236r**). The cross metathesis is a universal method with preference for electronically neutral or electron-donating groups, highlighted by the tolerance to *ortho* substituents.[213] Both these methods give moderate and reproducible yields within the limitations spelt out here. These one-step reactions are fast and atom-economic, yielding relatively clean products that are easy to purify, which makes this approach amenable to the use in parallel synthesis of large sets of derivatives with diverse functionality. The

HWE-based reaction sequence, optimized to a three-step-one-purification protocol, represents a robust method for the standard preparation of carbonates **236** that can be easily scaled up. Comparing the three methods shows that each has its merit so that they are complementary and none is a clear, general winner. Thus, for instance, the synthesis of **236r** would be rather difficult *via* the classical HWE approach in view of the required protection-deprotections step, selective reactivity, etc. On the other hand, some of the low yields obtained *via* the Suzuki-Miyaura coupling (e.g., **236e**) would direct the strategy either toward cross-metathesis or HWE approach.

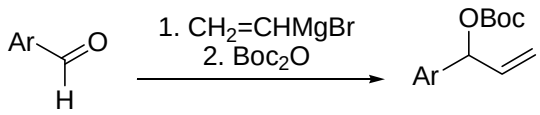
5.2. Branched Carbonates

5.2.1. Racemic Branched Carbonates

The branched carbonates **267** were prepared by a published, one-pot procedure.[214] Aryl aldehyde was treated with vinylmagnesium bromide, and the resulting magnesium alkoxide was directly transferred to a solution of an excess of Boc anhydride (Scheme 74). Various aryl aldehydes **143** were employed in the reaction (Scheme 74, Table 9). The unexpected product **236** was obtained as a side- or main product in several cases. These linear carbonates **236** were most likely formed *via* [3,3] sigmatropic rearrangement (Scheme 75).

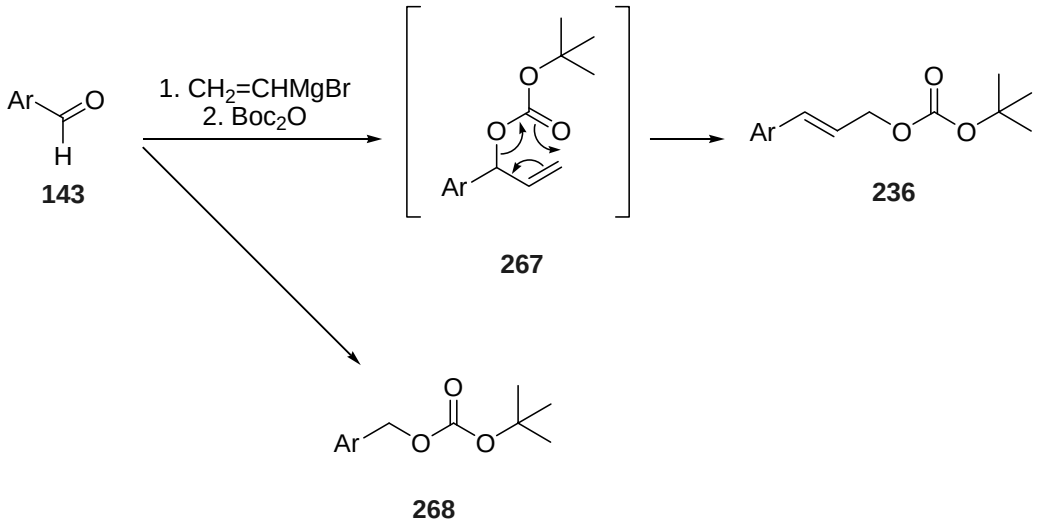
The second unexpected product **268** was identified by means of elemental analysis; its formation pathway was not investigated. None of these side-products (**236** or **268**) were mentioned in the original procedure. The amount of the side-products can be correlated with the electronic properties of the aryl substituent (Table 9).

Scheme 74. Synthesis of the carbonates **267**



143 **267**

Scheme 75. Rearrangement of the carbonates **267**



In some cases, the desired product **267** was not formed and only the products **236** and **268** were detected (entries 6, and 9). Only aldehyde **143q** gave carbonate **267q** selectively (entry 7). The mixtures of all the possible carbonates are not convenient for the preparative synthesis due to the difficult separation (physical properties of the compounds **267** and **236** are essentially the same).

Table 9. Synthesis of the *tert*-butyl 1-arylprop-2-en-1-ol carbonates.[a]

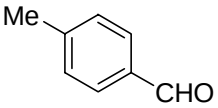
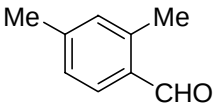
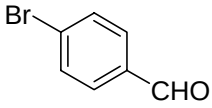
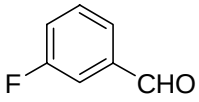
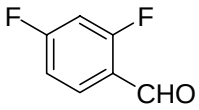
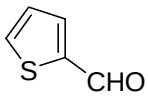
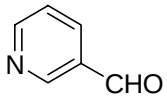
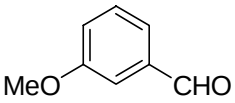
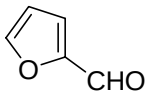
entry	aryl aldehyde	ratio[b] **267**:**236**:**268** (%)
1	 **143d**	67.0 : 26.5 : 6.5[c]
2	 **143e**	29.2 : 63.5 : 7.3[c]
3	 **143f**	39.4 : 0.0 : 60.6
4	 **143h**	50.5 : 0.0 : 49.5

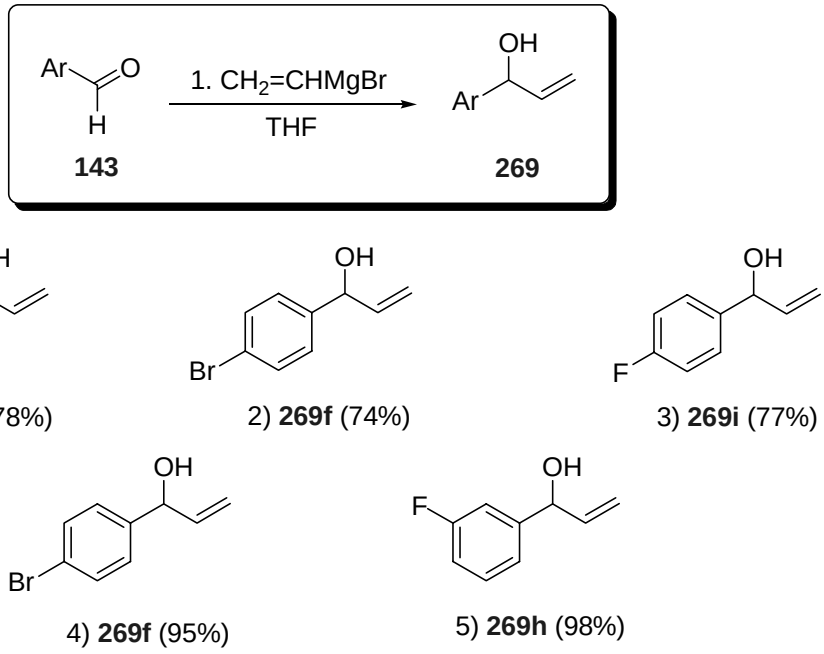
Table 9. Synthesis of the *tert*-butyl 1-arylprop-2-en-1-ol carbonates.[a]

entry	aryl aldehyde	ratio[b] **267**:**236**:**268** (%)
5	 **143j**	23.8 : 0.0 : 76.2
6	 **143o**	0.0 : 74.1 : 25.9
7	 **143q**	100 : 0.0 : 0.0
8	 **143x**	68.0 : 0.0 : 32.0
9	 **143y**	0.0 : 97.1 : 2.9

[a]Reaction was performed on 50 mmol scale. [b]Ratio based on isolated yields. [c]Ratio based on the ^{1}H-NMR spectroscopy of the crude reaction mixture.

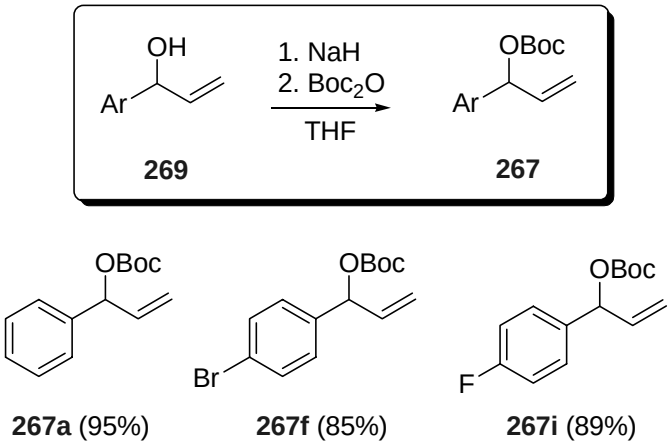
The preparation of carbonates **267** proved to be optimal in two subsequent steps, with isolation of the intermediate 1-arylpropenol **269** (Scheme 76, and 77). Several 1-arylpropenols **269** were prepared in sufficient yield (74-78%; Scheme 76, entries 1, 2, and 3). These results were in contrast with our expectation for such a simple transformation. The lower yield was caused by collecting of only the most intensive (UV-light) fractions during the chromatography separation of the desired product. During the reaction-yield-investigation we have realised, only the aqueous work-up is a sufficient purification procedure when small (5-7%) excess of vinylmagnesium bromide is used during the reaction with an aldehyde **143**. The resulting 1-arylpropenols **269** were isolated in high yield (95-98%; Scheme 76, entries 4, and 5), and in a good quality (no detectable impurity in ^{1}H/^{13}C-NMR spectra), fully compatible with the further proposed chemical transformations. The only notable difference is the intensive colour of the products isolated without the chromatography separation step.

Scheme 76. Synthesis of the allyl alcohols **269**



Using neat sodium hydride instead of its suspension in mineral oil further improved the isolated yields of carbonates **267** up to 95% (Scheme 77).

Scheme 77. Synthesis of carbonates **267**



5.2.1. Non-Racemic Branched Carbonates.

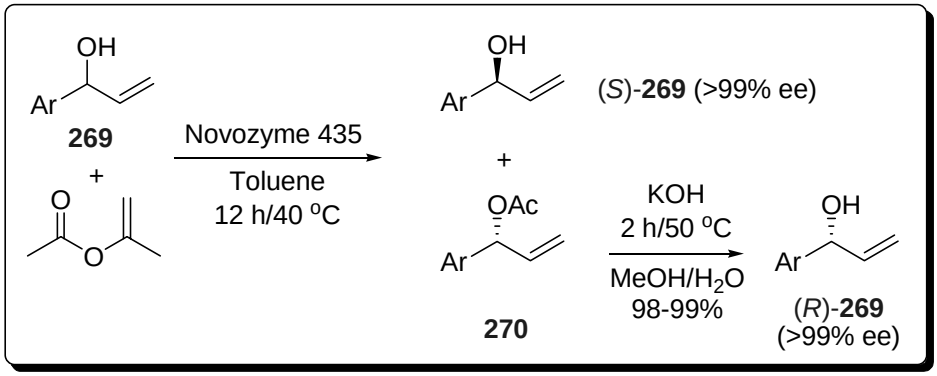
The non-racemic 1-arylpropenols **269** were prepared by means of enzymatic resolution.[215] The highly active, acrylic resin supported recombinant lipase formulation Novozyme™ 435 was added to a suspension of the corresponding 1-arylpropenol **269**, isopropenyl acetate, and 4 Å molecular sieves in dry toluene (Scheme 78). The enantioselectivity of the lipase-catalysed reaction can be described by enantiomeric ratio, the *E*-value. The *E*-value

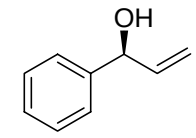
is defined as the ratio of specificity constant for the two enantiomers and can be expressed in terms of ee_S and ee_R only (Equation 1).[215a]

$$E = \frac{\ln\left(\frac{1-ee_S}{1+\frac{ee_S}{ee_R}}\right)}{\ln\left(\frac{1+ee_S}{1+\frac{ee_S}{ee_R}}\right)} \qquad \text{Equation 1}$$

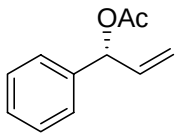
The *E*-values of the Novozyme™ 435 was rather high in all the resolution reactions. The observed values of $E>1000$ indicate a very good selectivity of the lipase formulation Novozyme™ 435 for the resolution of 1-arylpropenols **269**. The reactions yielded mixtures of (*S*)-alcohol and (*R*)-acetate in all cases. These were separated by column chromatography. The acetates were hydrolysed in aqueous methanolic solution of potassium hydroxide in practically quantitative yields. The enantiopurities of the (*S*)-alcohols and (*R*)-ester-liberated alcohols were determined by GC and/or HPLC. The absolute configuration was determined by comparison (chiral GC) with the commercially available enantiopure standard ((*S*)-1-phenylpropenol (*S*)-**269a**). The absolute configurations of the other 1-arylpropenols **269** were correlated to the known 1-phenylpropenol, by comparison of the absolute sign of the optical rotation value, by the HPLC behaviour, and by the chemical correlation of the diastereoisomers produced in the later reactions.

Scheme 78. Resolution of 1-arylpropenols **269**

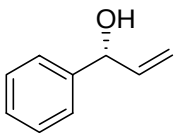




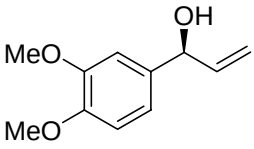
(*S*)-**269a** (45%)



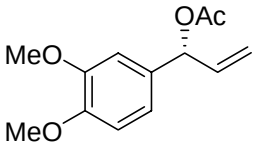
(*R*)-**270a** (47%)



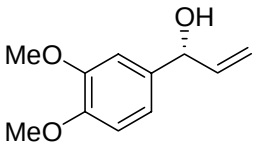
(*R*)-**269a** (44%)



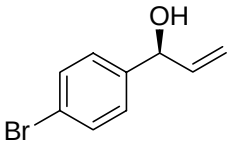
(*S*)-**269c** (22%)



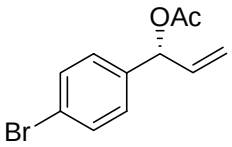
(*R*)-**270c** (46%)



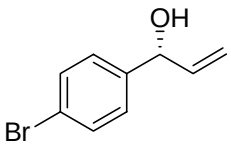
(*R*)-**269c** (45%)



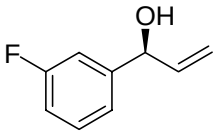
(*S*)-**269f** (22%)



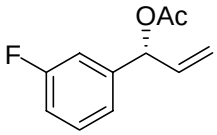
(*R*)-**270f** (43%)



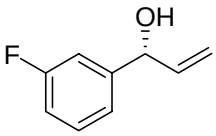
(*R*)-**269f** (42%)



(*S*)-**269h** (40%)



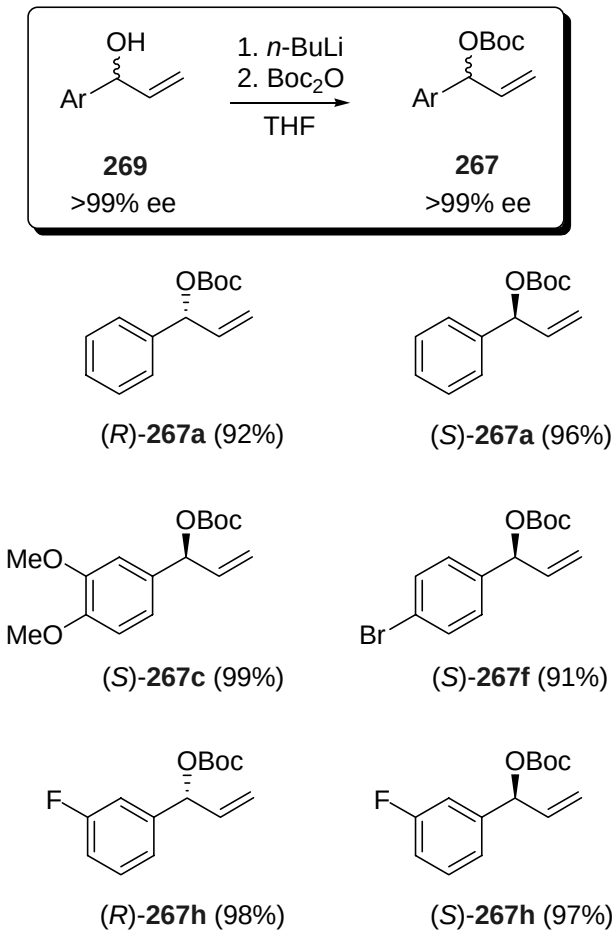
(*R*)-**270h** (44%)



(*R*)-**269h** (41%)

The synthesis of the corresponding non-racemic carbonates **267** was further optimized. *n*-Buthyllithium was used as a base instead of sodium hydride. High yields and excellent purities of the desired products were attained without chromatography separation (Scheme 79). The main advantage of this procedure is that it allows an accurate base addition (1.05 equiv), together with the use of a very small excess of Boc anhydride (1.01 to 1.02 equiv). The high purities of the resolved starting 1-arylpropenols **269** were also of a key importance for the high purity of the resulting carbonates **267**.

Scheme 79. Synthesis of the non-racemic carbonates **267**



5.2.3. Conclusions

We have successfully prepared various non-racemic 1-arylpropenols **269** and their carbonates **267**. Several published procedures[214,215] were tested and optimized. We presented a very robust synthetic procedure leading to enantiopure carbonates **267**. Carbonates **267** bring the wealth of aryl moieties of commercially available aryl aldehydes, together with the chirality source easily available in any of the required absolute configuration. Thus carbonates **267** are the key group of starting materials for our novel *C*-nucleosides synthetic methodology development.

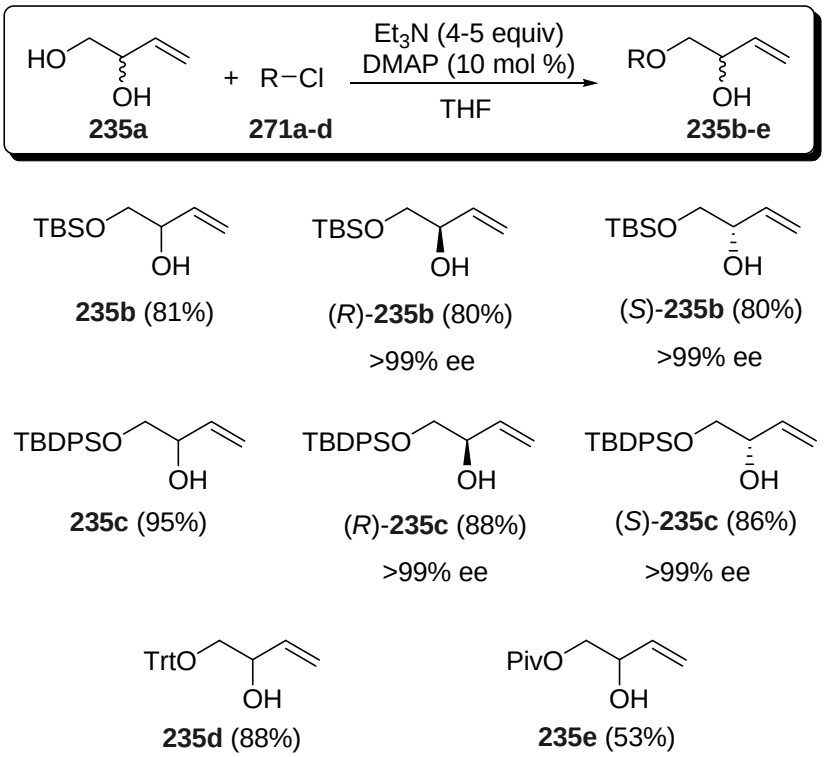
5.3. Iridium-Catalysed Asymmetric Allylic Substitution (AAS)

5.3.1. Synthesis of Protected Butenediols for AAS

One of the main advantages of the proposed synthetic strategy leading to *C*-nucleosides is the common building block of the nucleophilic part in the AAS reaction. Any synthetic sequence always starts with protected 3-buten-1,2-diol **235**. Diol **235** is protected at the

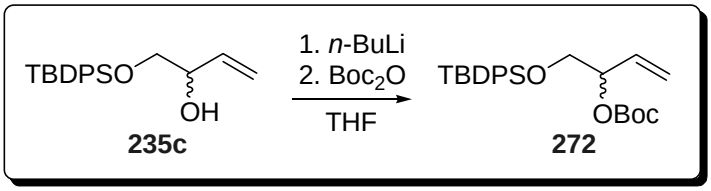
primary hydroxyl in order to enable only the secondary hydroxyl function to react in AAS reaction. Various protecting groups were investigated. Standard synthetic procedures were employed for the introduction of the protecting groups (Scheme 80).[216] Either racemic, or enantiopure, commercially available diol **235a** was used. In the proposed *C*-nucleoside synthetic scheme the (*R*)-enantiomer will give rise to the unnatural L-*C*-nucleosides, whereas the (*S*)-enantiomer will produce the natural configuration of D-*C*-nucleosides. The protection of the enantiopure diol **235a** proceeded without any loss of enantiopurity. The cheaper racemic diol **235a** is suitable for the AAS reaction condition optimization. The protecting groups were selected in order to achieve high selectivity in the primary hydroxyl function protection. These were pivaloyl, trityl, *tert*-butyldiphenylsilyl, and *tert*-butyldimethylsilyl. During the course of the AAS reaction investigation we have realised that only the *tert*-butyldimethylsilyl was suitable for all the proposed synthetic sequence (*vide infra*, page 116).

Scheme 80. Synthesis of the protected butenediols **235b-e**



The carbonates **272** and (*R*)-**272** were prepared for the complete AAS reaction investigation (Scheme 81). The optimized procedure for the Boc function introduction was employed (*vide supra*, page 100).

Scheme 81. Synthesis of the carbonates **272**



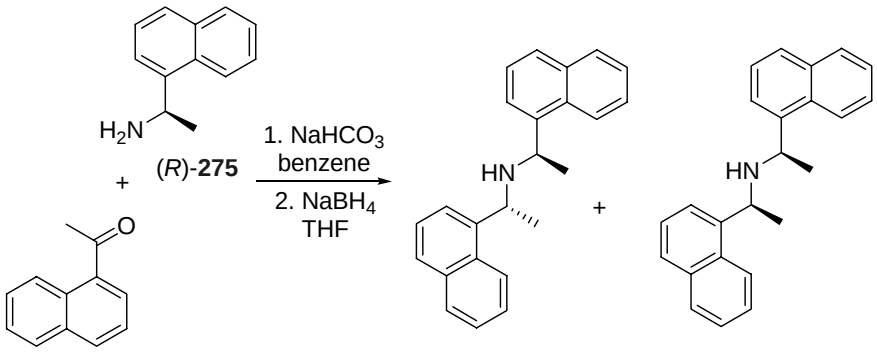
272 (94%) (*R*)-**272** (95%)

>99% ee

5.3.2. Synthesis of Ligands for AAS

Several Feringa's type phosphoramidite ligands were used through the AAS reaction investigation and optimisation. Some of them were prepared by published procedures.[217,218] The required amine (*R*,*R*)-**273** was prepared by reductive amination of ketone **274** using the commercially available enantiopure amine (*R*)-**275** and sodium borohydride at room temperature (Scheme 82), followed by separation of the resulting diastereoisomers by column chromatography on silica gel.[219]

Scheme 82. Synthesis of naphthylethylamines **273**

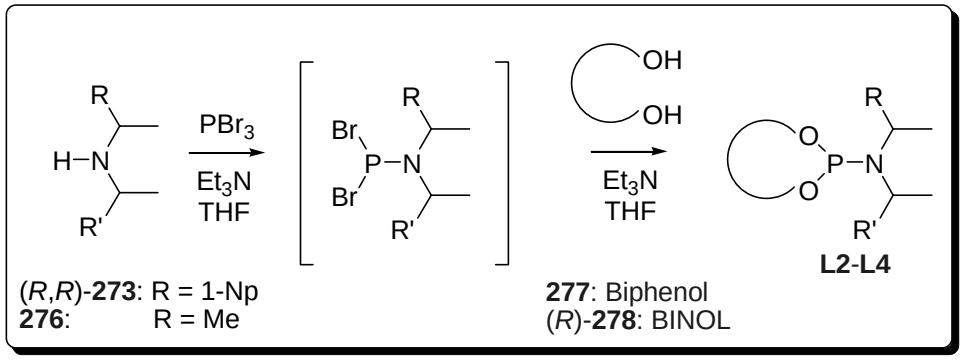


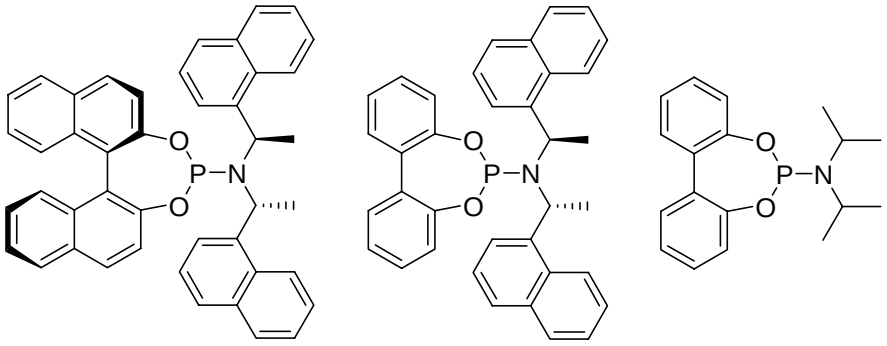
274 (*R*,*R*)-**273** (*R*,*S*)-**273**

Attempted synthesis of the phosphoramidite ligand **L4**, using Feringa's method, failed.[217] The reason was the use of chromatography on silica gel (as described in the reference) which, in our hands, proved to be incompatible with this class of compounds. Using chromatography on Al_2O_3, as reported by Alexakis, gave the desired product.[220] Phosphoramidite **L4** was prepared by adding amine **276** and diol **277** consecutively to phosphoric tribromide (Scheme 83). Ligands (*R*,*R*)-**L3** and (R_a,R_c,R_c)-**L2** were synthesized

in the same way, starting from amine (*R*,*R*)-**273** and the respective phenols **277** and (*R*)-**278**. The yields correspond with the published results[217] and were not optimized.

Scheme 83. Synthesis of the phosphoramidites **L2**-**L4**





(R_a,R_c,R_c)-**L2** (39%) (*R*,*R*)-**L3** (34%) **L4** (48%)

5.3.3. Optimization of the AAS Conditions

Initial conditions for the iridium-catalysed intermolecular allylic etherification were published by Hartwig.[183] According to the original procedure, solid aliphatic lithium alkoxide and copper(I) iodide are mixed, followed by addition of a solvent at 0 °C; a solution of a mixture of the catalyst and the ligand is then added at 0 °C, finally followed by the addition of the allyl carbonate at 0 °C. The reaction temperature profile is a gradient from 0 °C to 20 °C during 16 h. All these procedures need to be carried out under inert/anhydrous conditions.

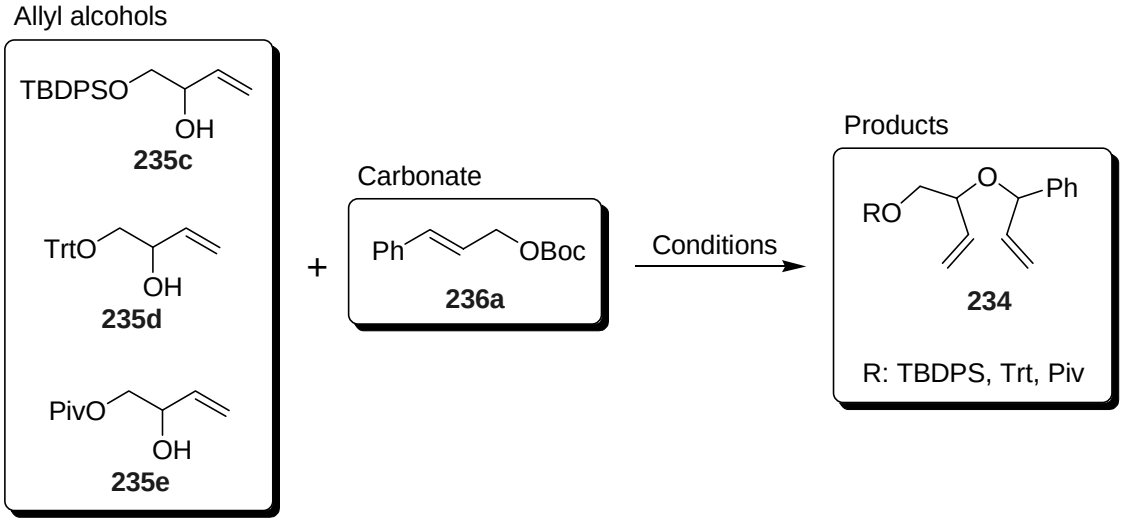
Our reaction system required further development and optimization in order to improve the reaction of our more complex allylic, secondary and sterically hindered alcohol **235c**. This optimization included finding the right conditions for the deprotonation of the alcohol and optimizing the source of the metal for the alkoxide formation, the time to the alkoxide

formation, the reaction temperature profile, as well as identifying the influence of the ligand, various additives, and the activation of the metal catalyst and its loading.

Various methods for the formation of alkoxide from **235c** were investigated, namely deprotonation by *n*-butyllithium, vinylmagnesium bromide, phenylmagnesium bromide, and phenylzinc bromide. The solution of alkoxide from **235c** thus generated was then directly transferred (*via* cannula) to the suspension of a Cu(I) salt in THF at 0 °C or at 20 °C, with CuI and CuBr·Me_2S, employed as the source of Cu(I), respectively. For the formation of the alkoxide from **235c**, the protocol using *n*-butyllithium at 0 °C for 10 min, followed by transmetallation with CuI at 20 °C for 30 min, proved to be optimal. Appearance of a bright yellow solution of the corresponding copper alkoxide is indicative of the successful transmetallation. The quality of the CuI also proved to be of the key importance. The optimized CuI treatment includes drying of the perfectly ground CuI in the reaction flask at 140 °C overnight, and until the reaction is set up. No difference was noticed when non-degassed solvent was used.

With the successful procedure for the copper alkoxide formation, we started to optimize the rest of the reaction conditions (Scheme 84, Table 10). These included the reaction temperature profile, and the protecting group in racemic butenediol **235**. These initial optimisations were monitored only by ^{1}H-NMR spectroscopic analysis of the worked-up reaction mixture. In conflict with the original procedure,[183] we have found at least ambient temperature (20 °C) necessary for the reaction to proceed to full conversion. The observed *de* dropped down to 40% de as a consequence of this temperature change, when the most complex ligand (R_a,R_c,R_c)-**L2** was used (entry 20). No significant improvement was observed when the "activated" catalyst was used.[185] The catalyst was "activated" by heating $[Ir(COD)Cl]_2$ and ligand **L4** or (R_a,R_c,R_c)-**L2** with propylamine at 50 °C for 20 min to generate the metalacyclic structure **K3** (*vide supra*, page 76), followed by evaporation of the volatile materials before the addition of the reaction solvent and the two reagents. The reaction was tested in the case when only the ligand was added without the metal source (entry 19). Only small conversion up to 10% was observed in this case. TBDPS protecting group showed the best performance under the same reaction conditions (entries 20, 21, and 22). The conversion dropped dramatically when trityl protecting group was used (entry 21), followed by further significant decresing in the case of pivaloyl protecting group (entry 22).

Scheme 84. The initial screening of diallylic ether **234** formation



Ligands

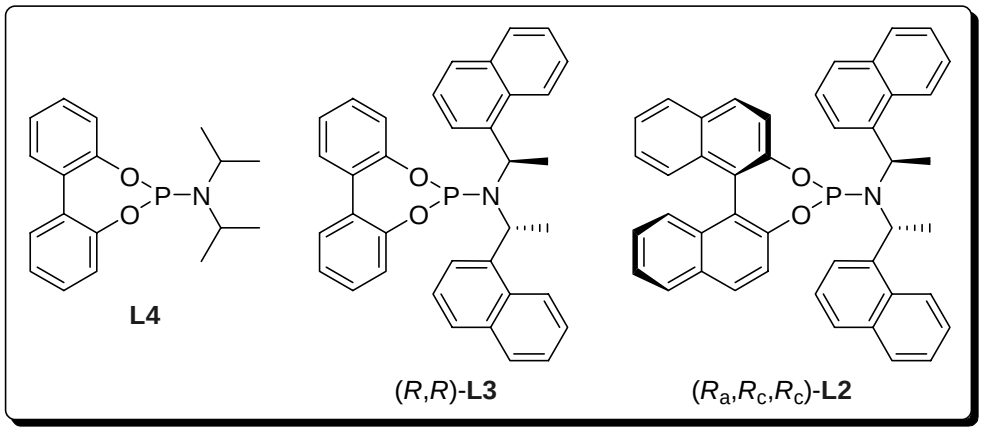


Table 10. Allylic substitution reaction, Scheme 84.[a]

entry	allyl alcohol	ligand (mol %)	pre-cat.[b] (mol % Ir)	cond.[c]	temperature profile	conv. (%)[d]
1	**235c**	**L4** 2.2%	2.0%	S	0 °C/4 h 0 °C to 20 °C/12 h	10
2	**235c**	**L4** 2.2%	2.0%	S	0 °C/1 h 0 °C to 20 °C/15 h	49
3	**235c**	**L4** 4.4%	3.0%	A	20 °C/5 h	5
4	**235c**	**L4** 4.4%	3.0%	A	0 °C/15 min 20 °C/4 h 45 min	6
5	**235c**	**L4** 4.4%	3.0%	A	0 °C/30 min 20 °C/4 h 30 min	8
6	**235c**	**L4** 4.4%	3.0%	A	0 °C/1 h 20 °C/4 h	11
7	**235c**	**L4** 4.4%	3.0%	A	0 °C/5 h	30
8	**235c**	**L4** 2.2%	2.0%	S	20 °C/16 h	18

Table 10. Allylic substitution reaction, Scheme 84.[a]

entry	allyl alcohol	ligand (mol %)	pre-cat.[b] (mol % Ir)	cond.[c]	temperature profile	conv. (%)[d]
9	**235c**	**L4** 2.2%	2.0%	S	0 °C/15 min 20 °C/15 h 45 min	22
10	**235c**	**L4** 2.2%	2.0%	S	0 °C/30 min 20 °C/15 h 30 min	26
11	**235c**	**L4** 2.2%	2.0%	S	0 °C/1 h 20 °C/15 h	32
12	**235c**	**L4** 2.2%	2.0%	S	0 °C/4 h 0 °C to 20 °C/15 h	25
13	**235c**	(R_a,R_c,R_c)-**L2** 4.1%	4.2%	A	0 °C/5 h	5
14	**235c**	(R_a,R_c,R_c)-**L2** 4.0%	4.0%	A	20 °C/5 h	83
15	**235c**	(R_a,R_c,R_c)-**L2** 4.1%	4.2%	S	0 °C/4 h 0 °C to 20 °C/15 h	56
16	**235c**	(R_a,R_c,R_c)-**L2** 4.1%	4.2%	S	20 °C/16 h	98 (93)[e]
17	**235c**	(R_a,R_c,R_c)-**L2** 1.0%	1.0%	S	20 °C/16 h	49
18	**235c**	(*R*,*R*)-**L3** 1.0%	1.0%	S	20 °C/16 h	74
19	**235c**	(R_a,R_c,R_c)-**L2** 2.0%	n.a.	S	20 °C/16 h	10
20	**235c**	(R_a,R_c,R_c)-**L2** 2.0%	2.0%	S	20 °C/16 h	95 40% de
21	**235d**	(R_a,R_c,R_c)-**L2** 2.0%	2.0%	S	20 °C/16 h	25
22	**235e**	(R_a,R_c,R_c)-**L2** 2.0%	2.0%	S	20 °C/16 h	12

[a]Reactions were performed on 1 mmol scale, conditions: 1 equiv CuI, 1 equiv *n*-BuLi, 0.55 equiv carbonate, THF. [b][Ir(COD)Cl]$_2$ was used as a pre-catalyst. [c]Conditions "S" (= standard), conditions "A" (= activated). The catalyst was activated by heating [Ir(COD)Cl]$_2$ and an appropriate ligand with propylamine at 50 °C for 20 min, followed by evaporation of the volatile materials. [d]Conversion based on the ^{1}H-NMR spectroscopy integrals of the worked-up reaction mixture (based on the carbonate). [e]Isolated yield (%), average from 2 independent runs.

We decided to investigate most of the possible catalytic systems for the AAS reaction, as a consequence of the above stated initial results (Scheme 85). Rhodium can be employed as an alternative catalyst. A simple rhodium catalyst was described in the allylic ether formation.[181] The advantage of this method resides in the formation of the ether from carbonates **267**, **272** and alcohols **235**, **269** with retention of configuration at both stereocentres. Surprisingly, formation of alkene **279** was observed in the cases when rhodium was used. Selectivity of the formation of **279** was found to strongly depend on the ligand employed. We have investigated the influence of the additional commercial ligands

such as (*S*)-BINAP, (S_a,S_c,S_c)-**L1**, (*R*,*R*)-**L5**, (*t*-BuO)$_2$PN(*i*Pr)$_2$ **L6**, and (MeO)$_3$P **L7**. Conditions without any additional ligand were also investigated.

The difference between rhodium and iridium was demonstrated in the reaction in the reaction with the branched carbonate **267a** without any additional ligand. Whereas rhodium catalysed reaction gave preferentially alkene **279a** (Scheme 85, Table 11, entry 1), iridium catalysed reaction gave only the expected product of allylic substitution **234ca** (entry 2). Also the reactivity of the linear and branched carbonate significantly differs in the reaction without any additional ligand. Whereas the branched carbonate **267a** gave a significant amount of product **234ca** (entry 4), the linear carbonate **236a** proved to be unreactive under these conditions (entry 3). Moreover, the successful recovery of starting **236a** (88%) indicates that no iridium complex of **236a** was formed. The phosphine ligand ((*S*)-BINAP) significantly enhanced the amount of the undesired product **279a**, whereas the amount of the product **234ca** was decreased or entirely eliminated (compare entries 1 *vs.* 9 and 2 *vs.* 10). No enrichment in any diastereoisomer was observed in these cases. The reactions with silane **235c** were successfully promoted by using (S_a,S_c,S_c)-**L1** as the catalyst (entries 7, and 8). Only trace of the excess of one diastereoisomer was observed in the later case. This is a significant difference to compare with the less sterically hindered silane **235b**, where only modest amount of the product was isolated along with recovered starting material (Scheme 86, Table 12, entries 11, and 12). The non-sterically hindered phosphoramidite (*R*,*R*)-**L5** decreased the reaction rate. In the case of the linear carbonate **236a** the reaction did not proceed and only the starting material was recovered (entry 11). The reaction rate of the branched carbonate **267a** decreased (entry 12). Also in these two cases, no enrichment in any diastereoisomer was observed. The non-chiral, relatively bulky ligand **L6** improved the reaction. In the case of the linear carbonate **236a**, only the starting **236a** (98%) was recovered. In the case of the branched carbonate **267a** the isolated yield of **234ca** increased (compare entries 3 *vs*. 13 and 4 *vs*. 14). Trimethylphosphite ligand **L7** promoted formation of the undesired product **279a** (entries 17, and 18). The alkene **279a** was formed exclusively in these cases, and it was isolated along with a substantial amount of the unreacted branched carbonate **267a**.

The 4'-fluoro analogue **267i** gave the results consistent with the previous observations for the non-fluorinated carbonate **267a** for both rhodium and iridium catalysed reaction (entries 5 and 6), but generally with 20% increase in yields.

Scheme 85. Diallylic ether **234** formation investigation I.

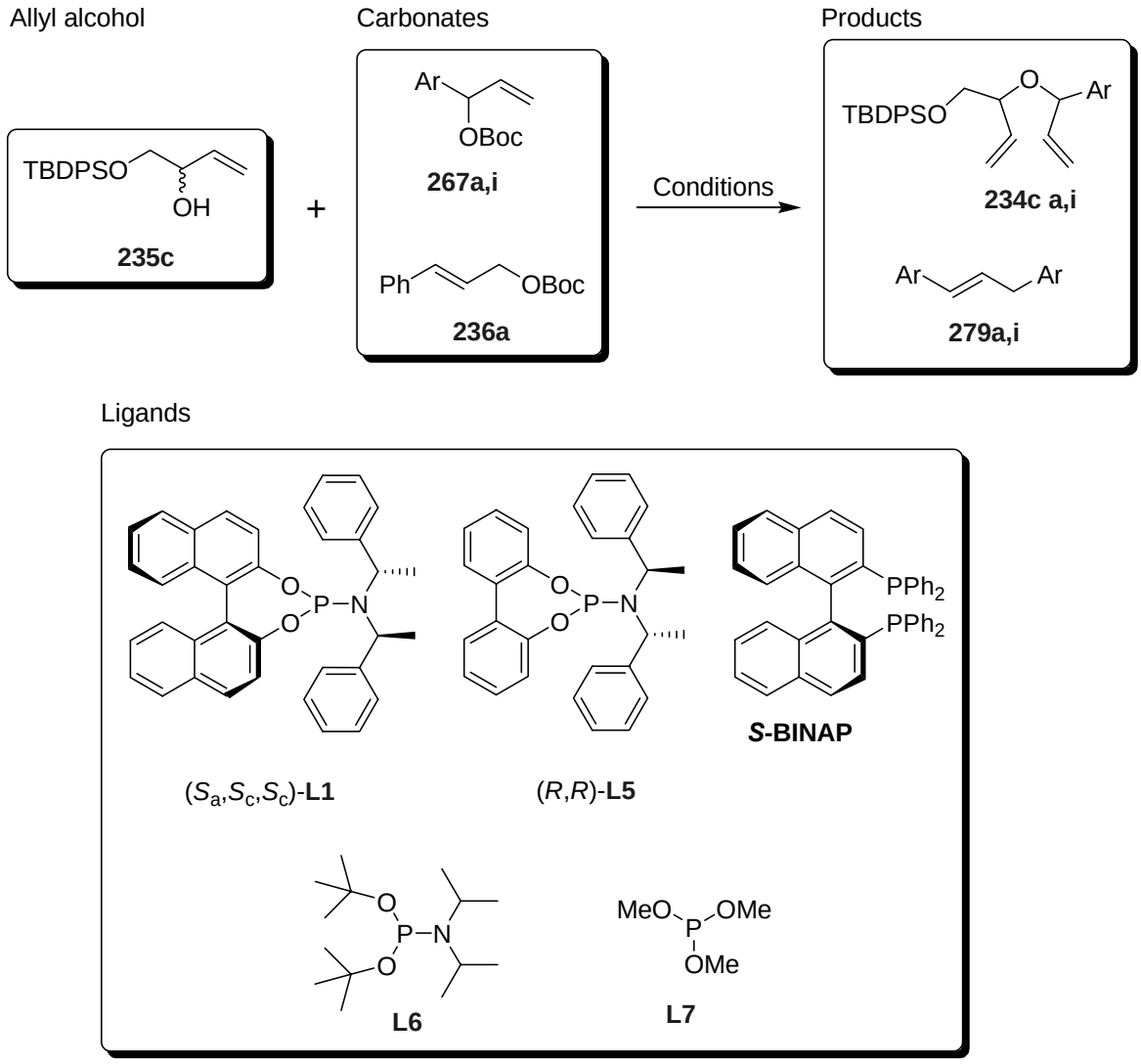


Table 11. Allylic substitution reaction, Scheme 85.[a]

entry	allyl alcohol	carbonate	conditions	com-pound	yield[b] (%)	re-covered[b] (%)
1	**235c**	**267a**	$[Rh(COD)Cl]_2$, 9.5% Rh 20 °C	**234ca**	12	-
				279a	23	-
2	**235c**	**267a**	$[Ir(COD)Cl]_2$, 4.2% Ir 20 °C	**234ca**	52	-
3	(*R*)-**235c**	**236a**	$[Ir(COD)Cl]_2$, 3.0% Ir 20 °C	**236a**	-	88
4	(*R*)-**235c**	**267a**	$[Ir(COD)Cl]_2$, 3.0% Ir 20 °C	**234ca**	54	-
5	(*R*)-**235c**	**267i**	$[Rh(COD)Cl]_2$, 4.0% Rh 20 °C	**279i**	43	-
				234ci	31	-
6	(*R*)-**235c**	**267i**	$[Ir(COD)Cl]_2$, 3.7% Ir 20 °C	**234ci**	77	-

Table 11. Allylic substitution reaction, Scheme 85.[a]

entry	allyl alcohol	carbonate	conditions	com-pound	yield[b] (%)	re-covered[b] (%)
7	**235c**	**236a**	$[Ir(COD)Cl]_2$, 2.1% Ir (S_a,S_c,S_c)-**L1** 1.8% 20 °C	**234ca**	73 0% de	-
8	**235c**	**267a**	$[Ir(COD)Cl]_2$, 2.1% Ir (S_a,S_c,S_c)-**L1** 1.8% 20 °C	**234ca**	66 6.3% de	-
9	(*R*)-**235c**	**267a**	$[Rh(COD)Cl]_2$, 3.7%Rh *S*-BINAP 3.2% 20 °C	**279a**	18	-
10	(*R*)-**235c**	**267a**	$[Ir(COD)Cl]_2$, 2.6% Ir *S*-BINAP 2.4 % 20 °C	**234ca** **279a**	5 33	- -
11	(*R*)-**235c**	**236a**	$[Ir(COD)Cl]_2$, 1.8% Ir (*R*,*R*)-**L5** 2.9% 20 °C	**236a**	-	99[c]
12	(*R*)-**235c**	**267a**	$[Ir(COD)Cl]_2$, 1.8% Ir (*R*,*R*)-**L5** 2.9% 20 °C	**267a** **234ca**	- 19	57 -
13	**235c**	**236a**	$[Ir(COD)Cl]_2$, 1.9% Ir **L6** 2.0% 20 °C	**236a**	-	98
14	**235c**	**267a**	$[Ir(COD)Cl]_2$, 1.9% Ir **L6** 2.0% 20 °C	**234ca**	62	-
15	**235c**	**267a**	$Rh(PPh_3)_3Cl$, 4.9% Rh **L7** 20% 0 °C	**267a**	-	77
16	**235c**	**267a**	$Rh(PPh_3)_3Cl$, 4.8% Rh **L7** 120% 0 °C	**267a**	-	41
17	**235c**	**267a**	$Rh(PPh_3)_3Cl$, 6.2% Rh **L7** 20% 20 °C	**267a** **279a**	- 46 (77)[d]	40 -
18	**235c**	**267a**	$Rh(PPh_3)_3Cl$, 6.2% Rh **L7** 120% 20 °C	**267a** **279a**	- 20 (40)[d]	51 -

[a]Reactions were performed on 1 mmol scale, conditions: CuI (1 equiv), *n*-BuLi (1 equiv), carbonate (0.55 equiv), THF. [b]Isolated yield. [c]Yield based on the ^{1}H-NMR spectroscopy integrals of the crude reaction mixture. [d]Yield based on the starting carbonate recovered.

The reactions of the *tert*-butyldimethylsilyl protected butenediol **235b** were investigated (Scheme 86, Table 12). The reactions without any additional ligand were investigated. These gave generally higher yields to compare with reactions of butenediol **235c** (entries 1 to 10). The phosphoramidite (S_a,S_c,S_c)-**L1** promoted the reaction in the case of the linear

carbonate **236a** (entry 11) but a substantial part of the starting material was also recovered. The reaction rate of the branched carbonate **267a** decreased (entry 12). In both cases, any enrichment of any diastereoisomer was below experimental error of the measurement. This is a significant difference to compare with the more sterically hindered silane **235c**, where practically doubled yield of the product was isolated without any recovered starting material (Scheme 85, Table 11, entries 7, and 8). The phosphoramidite (*R*,*R*)-**L5** decreased the reaction rate. In the case of the linear carbonate **236a**, the reaction did not proceed and only the starting material was recovered (entry 13). The reaction rate of the branched carbonate **267a** decreased (entry 14). Also in these two cases, no enrichment in any diastereoisomer was observed. The non-chiral, relatively bulky ligand $(t\text{-BuO})_2\text{PN}(i\text{Pr})_2$ **L6** improved the reaction (entries 15, and 16). All these observations were consistent with previously recorded data for **235c**.

Scheme 86. Diallylic ether **234** formation investigation II.

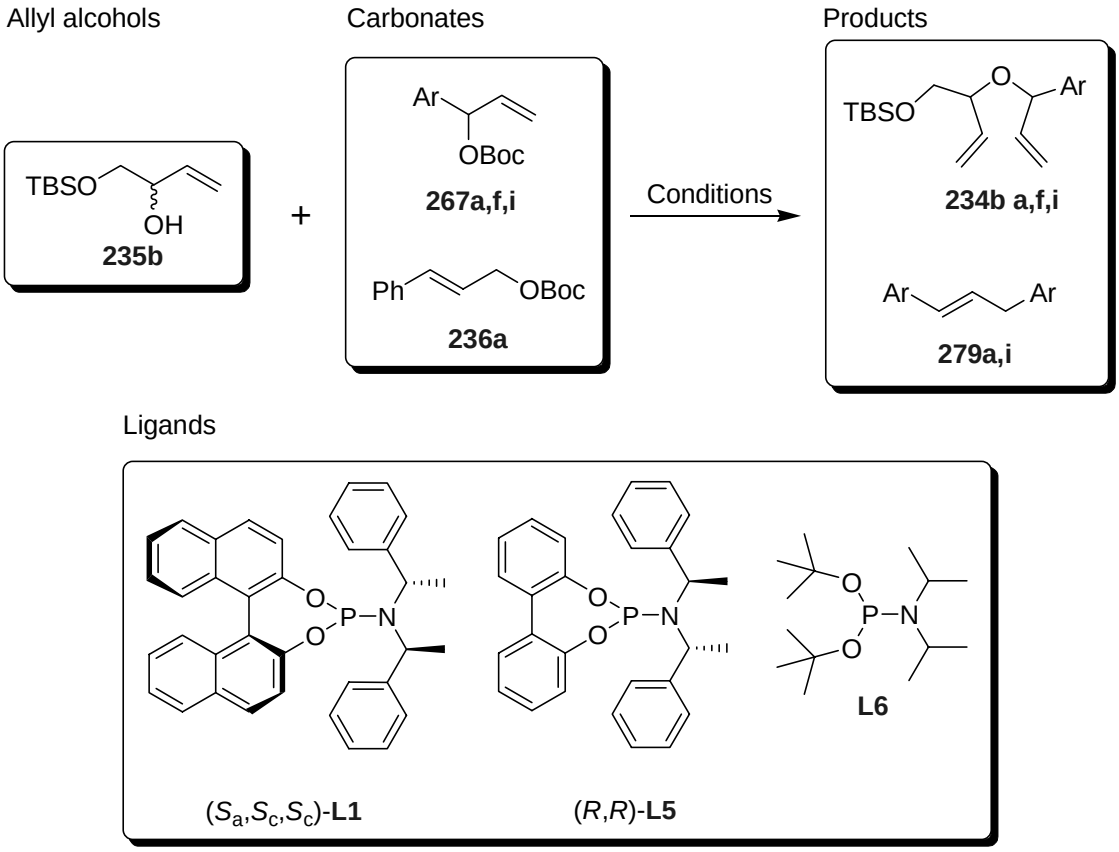


Table 12. Allylic substitution reaction, Scheme 86.[a]

entry	allyl alcohol	carbonate	conditions	com-pound	yield[b] (%)	re-covered[b] (%)
1	**235b**	**236a**	$[Rh(COD)Cl]_2$, 2.3% Rh 20 °C	**236a**	-	99[c]
2	**235b**	**267a**	$[Rh(COD)Cl]_2$, 2.3% Rh 20 °C	**267a**	-	99[c]
3	**235b**	**236a**	$[Ir(COD)Cl]_2$, 1.9% Ir 20 °C	**236a**	-	99
4	**235b**	**267a**	$[Ir(COD)Cl]_2$, 1.9% Ir 20 °C	**234ba**	84	-
5	**235b**	**267a** 0.7 eq	$[Ir(COD)Cl]_2$, 2.0% Ir 20 °C	**234ba**	76	-
6	**235b**	**267a** 0.8 eq	$[Ir(COD)Cl]_2$, 2.0% Ir 20 °C	**234ba**	74	-
7	**235b**	**267i** 0.9 eq	$[Ir(COD)Cl]_2$, 2.0% Ir 20 °C	**234bi**	74	-
8	**235b**	**267i** 1.0 eq	$[Ir(COD)Cl]_2$, 2.0% Ir 20 °C	**234bi**	65	-
9	(*R*)-**235b**	(*S*)-**267a**	$[Ir(COD)Cl]_2$, 2.8% Ir 20 °C	**234ba**	79	-
10	(*R*)-**235b**	**267f**	$[Ir(COD)Cl]_2$, 1.8% Ir 20 °C	**234bf**	75	-
11	**235b**	**236a**	$[Ir(COD)Cl]_2$, 2.1% Ir (S_a,S_c,S_c)-**L1** 1.8% 20 °C	**236a** **234ba**	- 38 0% de	31 -
12	**235b**	**267a**	$[Ir(COD)Cl]_2$, 2.1% Ir (S_a,S_c,S_c)-**L1** 1.8% 20 °C	**234ba**	41 2.8% de	-
13	**235b**	**236a**	$[Ir(COD)Cl]_2$, 2.0% Ir (*R*,*R*)-**L5** 2.2% 20 °C	**236a**	-	86
14	**235b**	**267a**	$[Ir(COD)Cl]_2$, 2.0% Ir (*R*,*R*)-**L5** 2.2% 20 °C	**234ba**	75 0% de	-
15	**235b**	**236a**	$[Ir(COD)Cl]_2$, 2.2% Ir **L6** 2.1% 20 °C	**236a**	-	93
16	**235b**	**267a**	$[Ir(COD)Cl]_2$, 2.2% Ir **L6** 2.1% 20 °C	**234ba**	84	-

[a]Reactions were performed on 1 mmol scale, conditions: CuI (1 equiv), *n*-BuLi (1 equiv), carbonate (0.55 equiv), THF. [b]Isolated yield. [c]Yield based on the ^{1}H-NMR spectroscopy integrals of the crude reaction mixture.

The reactions employing slightly different retrosynthetic disconnection of the target diallyl ether were also investigated during the extensive allylic substitution investigation sumarised in the previous schemes and tables (Scheme 85, 86 and Table 11, 12). The difference is based on disconnecting the 4'-O bond of the target ribofuranose ring rather

than the 1'-O bond. The reaction was investigated under various conditions, employing allyl alcohol **269a** and branched carbonate **272** (Scheme 87, Table 13). No expected product was either isolated or detected in the crude reaction mixture. Various amount of the starting carbonate **272** was recovered in all cases

Scheme 87. Diallylic ether **234** formation investigation III.

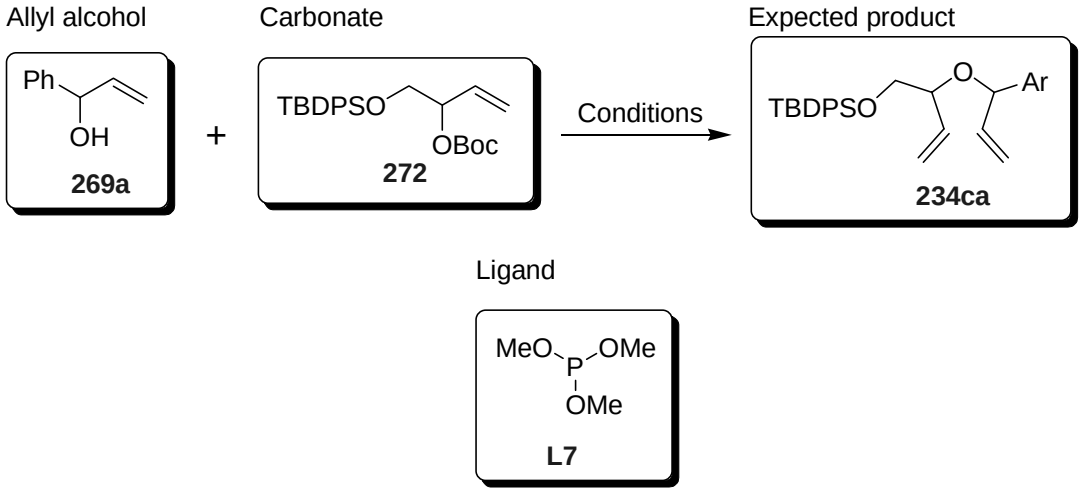


Table 13. Allylic substitution reaction, Scheme 87.[a]

entry	conditions	isolated compound	re-covered[b] (%)
1	$Rh(PPh_3)_3Cl$, 4.6% Rh **L7** 20% 0 °C	**272**	32
2	$Rh(PPh_3)_3Cl$, 4.6% Rh **L7** 120% 0 °C	**272**	66
3	$Rh(PPh_3)_3Cl$, 5.2% Rh **L7** 20% 20 °C	**272**	28
4	$Rh(PPh_3)_3Cl$, 5.2% Rh **L7** 120% 20 °C	**272**	94
5	$[Rh(COD)Cl]_2$, 4.0% Rh 20 °C	**272**	16
6	$[Ir(COD)Cl]_2$, 3.6% Ir 20 °C	**272**	34

[a]Reactions were performed on 1 mmol scale, conditions: CuI (1 equiv), *n*-BuLi (1 equiv), carbonate (0.55 equiv), THF. [b]Isolated yield.

5.3.4. Conclusions

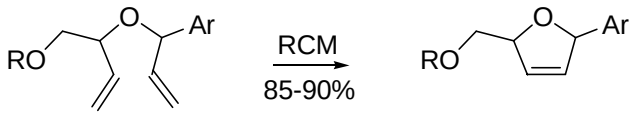
In summary, the optimal procedure for the formation of the diallyl ether **234** utilises only the metal source ($[Ir(COD)Cl]_2$), adding 2 mol % of iridium, without any additional ligand. The successful procedure requires reaction temperature of 20 °C for at least 16 h. The reaction employs enantiopure allyl alcohol **235** and branched allyl carbonate **267** as the sources of chirality. The best reaction conditions were tested with a range of substrates and carbonate equivalence ratio. All the reactions performed have shown very consistent performance. The optimal equivalence ratio of the carbonate for efficient reaction should be in the range of 0.8-0.9 equiv.

5.4. Optimization of the Final Reaction-Sequence Steps and Completion of the Synthesis of Artificial *C*-Nucleosides and Their Analogues

5.4.1. Proof of the Synthetic Concept Using Diastereoisomeric Mixtures

The diallyl ethers obtained in the AAS investigation were submitted to the standard RCM reaction procedure (Scheme 88).[187] The reaction was briefly screened for optimal conditions. Grubbs 1st generation **C1** and Grubbs 2nd generation **C2** catalysts were used in the reaction. No significant difference was noticed in the performance of these catalysts in our simple RCM to construct the five-membered ring. Therefore, Grubbs 1st generation catalyst **C1** was chosen as an optimal catalyst, in loadings as low as 1%. Diastereoisomeric mixtures of racemic D4 1'-arylribofuranose analogues **233** were produced in good yields.

Scheme 88. Preliminary RCM reaction of diallyl ethers **234**



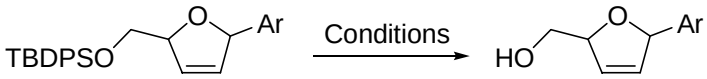
234 **233**

R: TBDPS; TBS

These diastereoisomeric mixtures of D4 analogues were used for the optimization of the 5'-OH deprotection conditions (Scheme 89, Table 14). The initial reaction conditions using TBAF gave the expected product in 40-50% yield along with a number of decomposition products, which made the separation tedious. Therefore, milder reaction conditions were investigated, employing various complex salts of hydrogen fluoride (entries 2 to 5). The pyridine-hydrogen fluoride complex gave no reaction, unless used in high excess (entry 2,

and 3). The best results were obtained with the $Et_3N{\cdot}3HF$ complex (entry 4, and 5). Only this reaction procedure enabled a recovery of the starting material, but the amount recovered (1.8%) indicated that also in this case decomposition took place. This is an important issue in the D4 nucleoside analogues preparation. The higher sensitivity of dihydrofuranes is known, and it has to be considered in the synthetic strategy planing.[221]

Scheme 89. Deprotection of the D4 *C*-nucleosides analogues



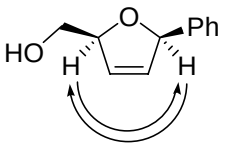
233c **233a**

Table 14. Deprotection of the intermediates **233c**, Scheme 89.[a]

entry	Ar	reagent (equiv)	conditions	yield (%)[b]
1	Ph	TBAF (3.5)	20 °C, 16 h	44
2	Ph	Py·HF (2.8)	20 °C, 20 h	0
3	Ph	Py·HF (11)	20 °C, 16 h	52
4	Ph	$Et_3N.3HF$ (3.2)	20 °C, 16 h	56
5	4-F-Ph	$Et_3N.3HF$ (3.0)	20 °C, 16 h	58

[a]Reactions were performed on 0.5 mmol scale. [b]Isolated yield of an equimolar mixture of racemic diastereoisomers.

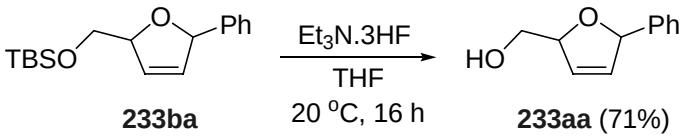
The mixture of diastereoisomers could be separated by column chromatography after the deprotection step. The deprotected D4 nucleoside analogue **233aa** was successfully isolated as two separated diasteroisomers. Configuration of one was assigned as *cis*-**233aa** by NOE-NMR experiments. However, because of the very low intensity of the NOE enhancement (1-2%), this should be considered just as a preliminary method for the stereochemistry assignment. No NOE enhancement was recorded for any of the ^{1}H-NMR signals of the second diastereoisomer.



NOE: 1-2%

We decided to change the protecting group of the primary hydroxyl functionality of butene-1,2-diol to *tert*-butyldimethylsilyl (TBS) group. This proved to be beneficial in the allylic substitution and, most importantly, in the deprotection step. The introduction of TBS proved selective in favour of the primary hydroxyl function (*vide supra*, page 102). The utility of TBS was confirmed in the deprotection of D4 analogue **233ba** (Scheme 90). The isolated yield was roughly 20% higher than in the case of TBDPS.

Scheme 88. Final deprotection of the D4 *C*-nucleosides analogues



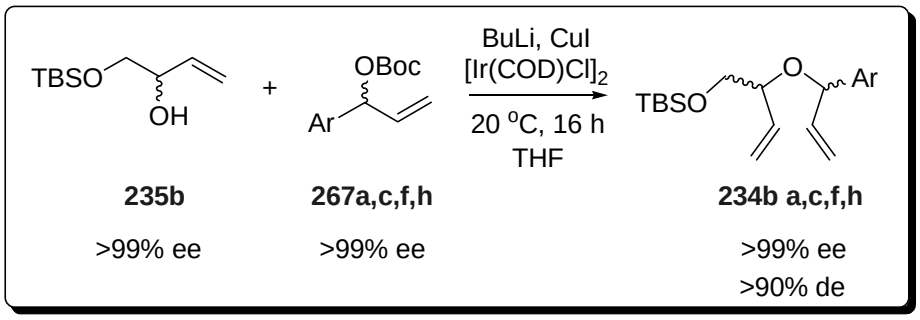
233ba **233aa** (71%)

5.4.2. Synthesis of Diallylethers

The best conditions developed for AAS (*vide supra*, page 114) were utilised in the synthesis of various diallyl ethers **234** (Scheme 91). All the carbonates **267** bearing substituted benzene ring gave the expected products in comparable yields; however, pyridine-derived and *ortho*-substituted carbonates **267** did not successfully react. The corresponding carbonates decomposed and only small amounts of the starting silyl protected butenediol were recovered in these cases.

The AAS reaction proved to be very robust within these limitations. All the reactions performed showed practically the same yield. Racemic starting materials were used in some cases. Protected, enantiopure diols **235b** were reacted with enantiopure carbonates **267** to give enantiopure diallyl ethers with high diastereoselectivity. The diastereopurity of the diallyl ether produced was determined by ^{1}H-NMR spectroscopy only. The *de* purity can be claimed up to 90% de due to this method. Very weak, or entirely no ^{1}H-NMR integral intensities of the second diastereoisomer were recorded.

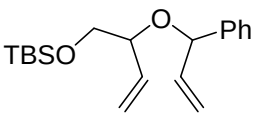
Scheme 91. Optimised AAS: Formation of diallyl ethers **234**



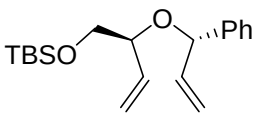
235b >99% ee

267a,c,f,h >99% ee

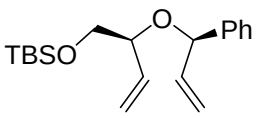
234b a,c,f,h >99% ee, >90% de



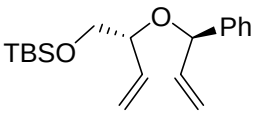
234ba (72%)



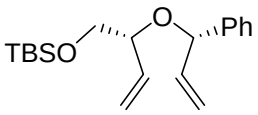
(2*S*,1'*S*)-**234ba** (79%)



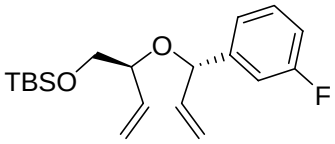
(2*S*,1'*R*)-**234ba** (82%)



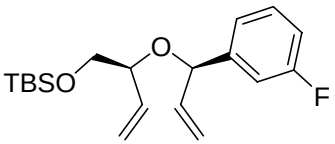
(2*R*,1'*R*)-**234ba** (83%)



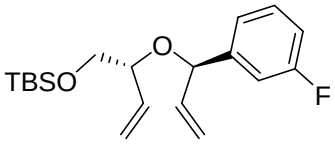
(2*R*,1'*S*)-**234ba** (77%)



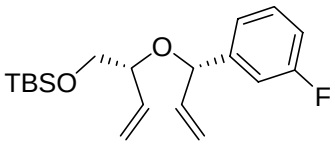
(2*S*,1'*S*)-**234bh** (78%)



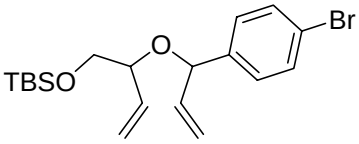
(2*S*,1'*R*)-**234bh** (74%)



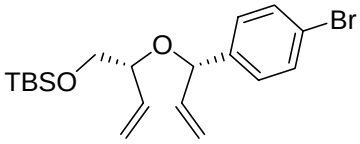
(2*R*,1'*R*)-**234bh** (72%)



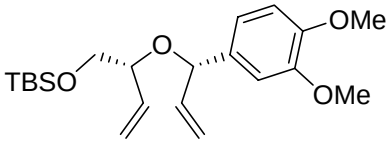
(2*R*,1'*S*)-**234bh** (73%)



234bf (75%)



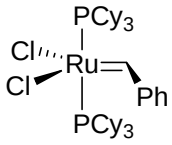
(2*R*,1'*S*)-**234bf** (85%)



(2*R*,1'*S*)-**234bc** (70%)

5.4.3. Synthesis of Artificial 2',3'-Didehydro-2',3'-Dideoxy-*C*-Nucleosides

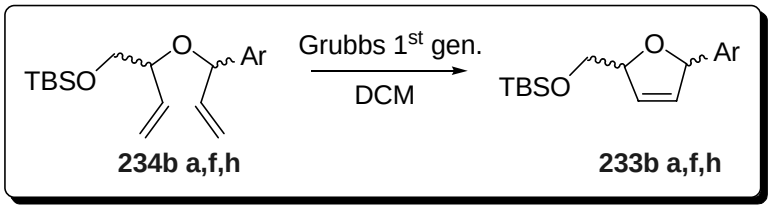
Diallyl ethers **234** were submitted to the optimized RCM reaction conditions (Scheme 92). Diallyl ether **234** was dissolved in degassed dichloromethane, and a catalytic amount (1-2%) of Grubbs 1st generation catalyst **C1** was added under a stream of argon.



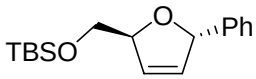
C1

The reaction mixture was heated at 50 °C for 3 hours. Conversion of the starting material was monitored by TLC in a couple of the first runs. The optimal reaction time of 3 hours proved to be sufficient for all the diallyl ethers **234** employed. All reactions furnished protected D4 *C*-nucleosides analogues **233** in good yield.

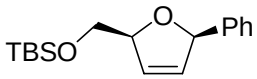
Scheme 92. RCM and D4 analogues **233** formation



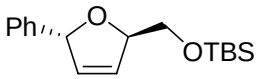
234b a,f,h **233b a,f,h**



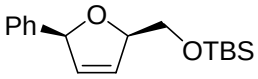
D-**233ba**α (56%)



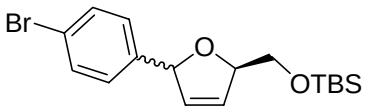
D-**233ba**β (78%)



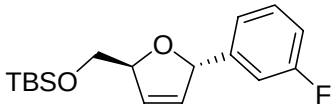
L-**233ba**α (91%)



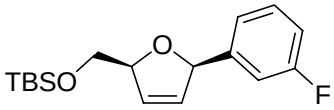
L-**233ba**β (86%)



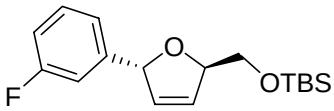
L-**233bf**α/β (84%)



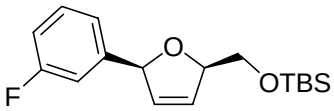
D-**233bh**α (95%)



D-**233bh**β (96%)



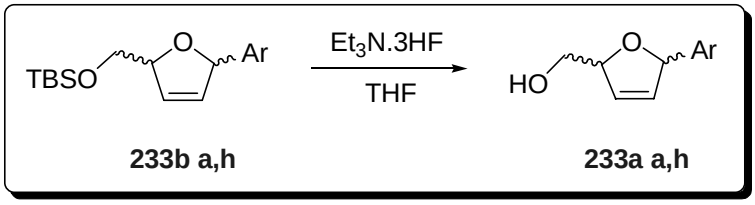
L-**233bh**α (97%)



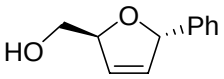
L-**233bh**β (95%)

The protected D4 nucleosides analogues **233** are not only the key intermediates for the synthesis of target ribofuranosides, but also represent protected final product of significant biological importance (see the Chapter 1). The 5'-*O*-protected enantiopure 2',3'-didehydro-1',2',3'-triideoxy-1'-aryl ribofuranoses were deprotected using the optimized reaction conditions (Scheme 93). All the possible combinations of the enantiopure D4 *C*-nucleosides analogues bearing phenyl and 3-fluorophenyl moiety were successfully prepared and isolated in good yields.

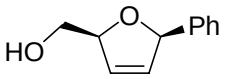
Scheme 93. D4 analogues **233** deprotection



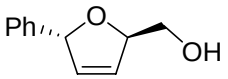
233b a,h **233a a,h**



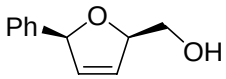
D-**233aa**α (66%)



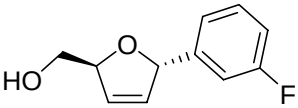
D-**233aa**β (68%)



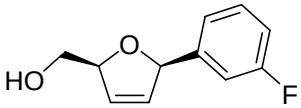
L-**233aa**α (71%)



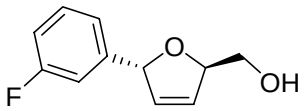
L-**233aa**β (54%)



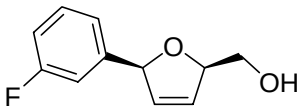
D-**233ah**α (88%)



D-**233ah**β (61%)



L-**233ah**α (76%)



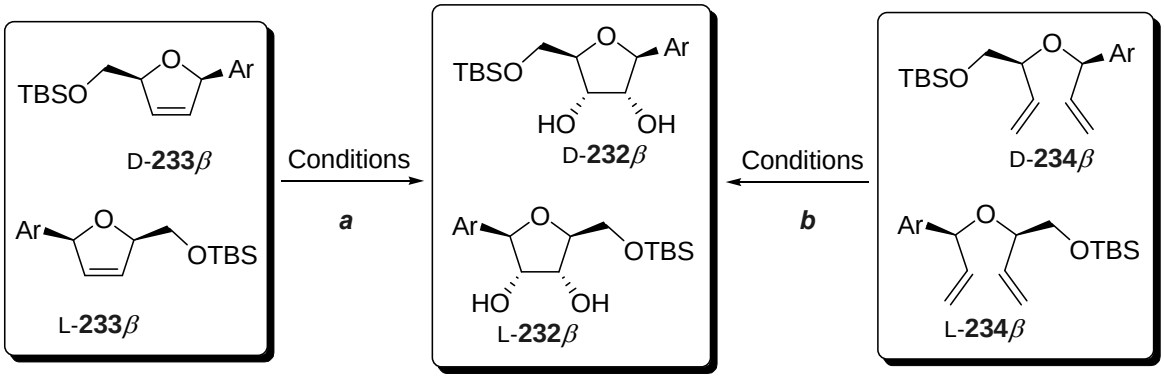
L-**233ah**β (66%)

This deprotection step represents not only the possible divergent route broadening the synthetic utility of our new *C*-nucleosides synthetic approach, but also provides a tool to determine the enantiopurity of our products. Both the previous intermediates, diallyl ethers **234** and ring-closed metathesis products **233** were not suitable for HPLC or GC analysis, either for stability reasons or no resolution. All four diastereoisomers of 1'-phenyl substituted D4 nucleoside analogue were submitted to the GC analysis. The results we obtained were compared with the chromatograms recorded for racemic mixture of diastereoisomers and with the chromatograms recorded for each racemic diastereoisomer. All the samples showed high diastereopurity and enantiopurity in values of >99% ee, and >99% de. Based on these values we could propose the diastereoselectivity of the first step, the AAS reaction, was higher than the ^{1}H-NMR spectroscopy-estimated 90% de. But in this case we have to keep in mind that deprotected D4 *C*-nucleosides analogues are as far as three chromatography separations from the diastereoselective reaction step, and a various *de* enhancement may occur.

5.4.4. Synthesis of Artificial Ribofuranosides and Completion of the Synthesis

The vicinal dihydroxylation of the double bond was the last strategic transformation to be investigated in our novel synthetic route to *C*-nucleosides. There are two possible tactics to construct the target structure of 5'-*O*-protected ribofuranose (Scheme 94). The first one, the route (***a***) is a more conventional way of direct vicinal dihydroxylation of the double bond in D4 *C*-nucleoside analogues **233**.[187,193] This transformation can be performed by catalytic oxidation either by more common osmium tetroxide, or by less toxic and far more reactive ruthenium tetroxide.[190,193] The second possibility, route (***b***), is a novel method recently developed by Blechert.[195] This innovative procedure employs ruthenium catalyst for both, the RCM reaction step, and then in the oxidation step as a two-reaction-one-pot procedure.

Scheme 94. Formation of protected ribofuranose **232**



All the above stated reaction tactics were investigated in various combinations of the reaction conditions. The vicinal dihydroxylation (***a***) utilising osmium tetroxide in catalytic amount, and *N*-methyl morpholine *N*-oxide as a stoichiometric oxidant in a mixture of THF-water (9:1) gave the expected product D-**232** (Table 15, entry 1). Although the reaction yield was lower than expected, the reaction conditions were not optimized in this particular case.

Our main interest was laid upon the optimization of a less toxic, environmentally friendly ruthenium tetroxide oxidation. This was optimized in a number of experiments with model compounds (e.g., 2-cyclohexenone). Basically, two different reaction protocols were reported: (1) Plietker's procedure utilises catalytic amount of a ruthenium source together with certain amount of Lewis acid ($CeCl_3$) and a stoichiometric amount of various inorganic oxidants, most frequently $NaIO_4$.[194] A minor modification of this procedure was

recently reported. Blechert *at al* reported a RCM reaction procedure with a subsequent utilising of the ruthenium metathesis catalyst as a ruthenium source for the Plietker's procedure of vicinal dihydroxylation in a two-reaction-one-pot procedure.[195] Neither of these two modifications were successful in our hands at the level claimed by the authors. We are aware that the practical success in heterogeneous reaction is determined by the efficiency of the phase transfer. This parameter is of key importance, and may be difficult to keep, especially in a variety of reaction scales. (2) Hudlicky's procedure does not utilise any Lewis acid additive, and runs the reaction with a higher ruthenium catalyst loading (10%).[193]

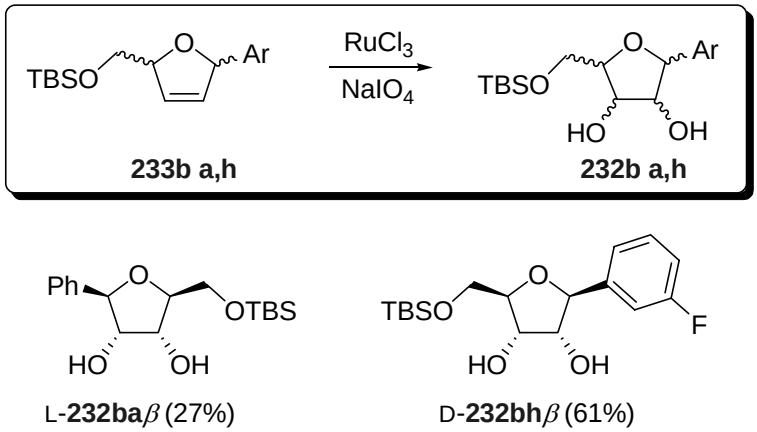
Table 15. Formation of the protected ribofuranoses **232**, Scheme 94, sumarised in Schemes 95 and 96.[a]

entry	Ar (config.)	route	oxidation catalyst (mol %)	conditions	yield (%)[b]
1	Ph (D-)	***a***	OsO_4 (9.0)	20 °C, 19 h	34
2	Ph (D-)	***b***	**C1** (5.0) $RuCl_3 \cdot H_2O$ (5.0)	50 °C, 3 h 0 °C, 20 s	25
3	Ph (L-)	***a***	$RuCl_3 \cdot H_2O$ (10.3)	0 °C, 40 s	27 (88)[c]
4	3-F-Ph (D-)	***a***	$RuCl_3 \cdot H_2O$ (12.2)	0 °C, 45 s	61
5	3-F-Ph (D-)	***a***	$RuCl_3 \cdot H_2O$ (12.0)	0 °C, 80 s	16
6	3-F-Ph (L-)	***b***	**C1** (1.5) $RuCl_3 \cdot H_2O$ (10)	50 °C, 3 h 0 °C, 15 s	34
7	4-Br-Ph (L-)	***b***	**C1** (1.4) $RuCl_3 \cdot H_2O$ (10.7)	50 °C, 3 h 0 °C, 10 s	31

[a]Reactions were performed on 1.0 mmol scale. $NaIO_4$ 1.5 equiv. [b]Isolated yield. [c]Yield based on the starting alkene recovered.

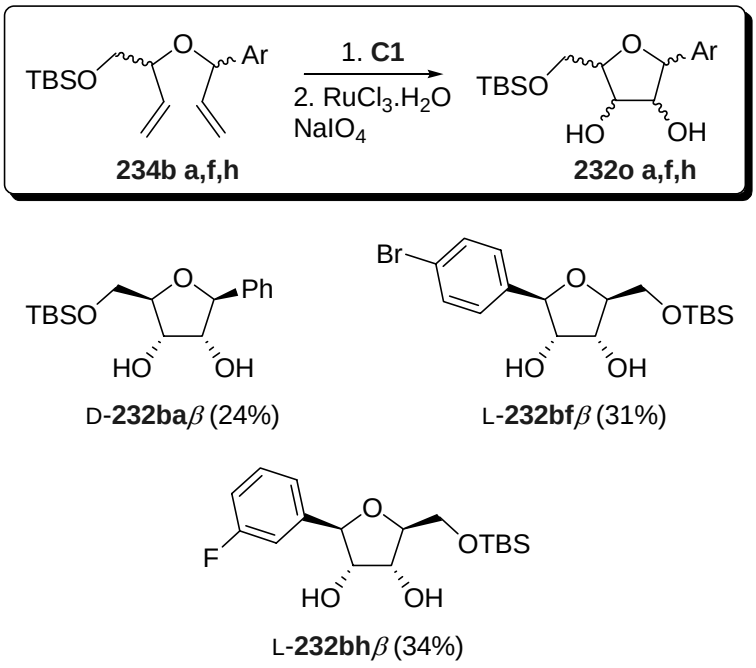
Furthermore, in this procedure the results were very much dependent on the level of homogeneity. Finally, a combination of these two protocols proved to be optimal. The optimized reaction procedure starts as proposed by Blechert and after the RCM reaction step the solvent was changed, but the oxidation was performed *via* Hudlicky's procedure, without any Lewis acid, and with an additional ruthenium source in the form of $RuCl_3 \cdot H_2O$ (up to 10% Ru in total), using $NaIO_4$ as the stoichiometric (re)oxidant (Table 15, Schemes 95, 96).

Scheme 95. Oxidation of dihydrofurans **233**, formation of ribofuranisides **232b**



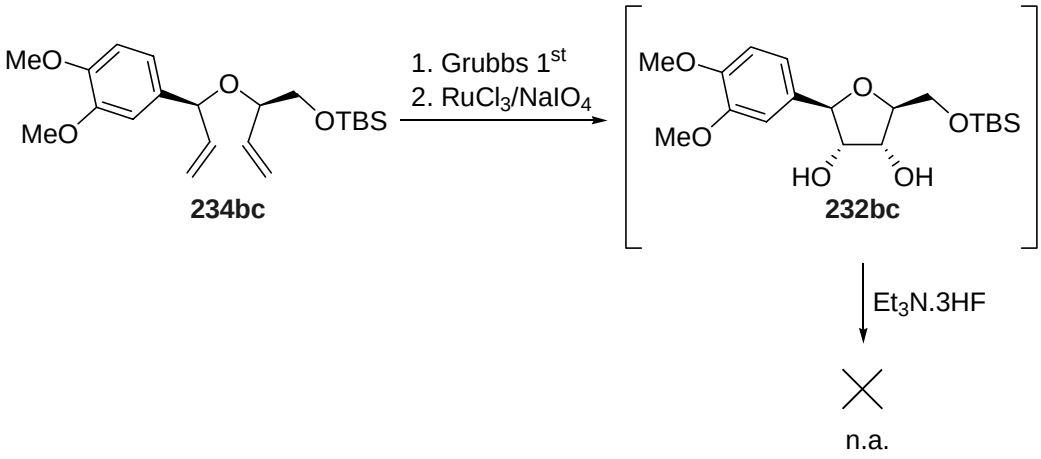
Any other reaction conditions, such as the Hudlicky procedure with a Lewis acid added, different reaction solvents, reaction time, reaction temperature, and various combinations of them did not lead to any improvement. We suggest a high potential for possible optimization of the oxidation step, but only in terms of improved homogeneity control. Remarkable results were recorded in the case when the unreacted starting material was successfully recovered (Table 15, entry 3), or in the case of an improved homogeneity (entry 4). Note the high reaction rate of the ruthenium oxidation and the significant drop in the isolated yield once the reaction time was prolonged (entry 4 *vs*. 5).

Scheme 96. Tandem RCM-oxidation, formation of ribofuranisides **232b**



A synthesis of deprotected ribofuranose **1oc** *via* a 5'-*O*-protected ribofuranose L-**232bc** in a three-step-one-pot reaction protocol was attempted (Scheme 97). Diallyl ether **234bc** was dissolved in degassed dichloromethane and a catalytic amount (2%) of Grubbs 1st generation catalyst **C1** was added in a stream of argon. Once the RCM reaction was completed, the solvent was removed. The residue was dissolved in a mixture of ethyl acetate and acetonitrile (1:1), and the oxidation step was performed as stated in the above paragraph. The reaction solvent was changed for the third time (THF) and a complex $Et_3N{\cdot}3HF$ was added according to the optimized deprotection procedure. However, the resulting reaction mixture was far too complex to isolate the target structure.

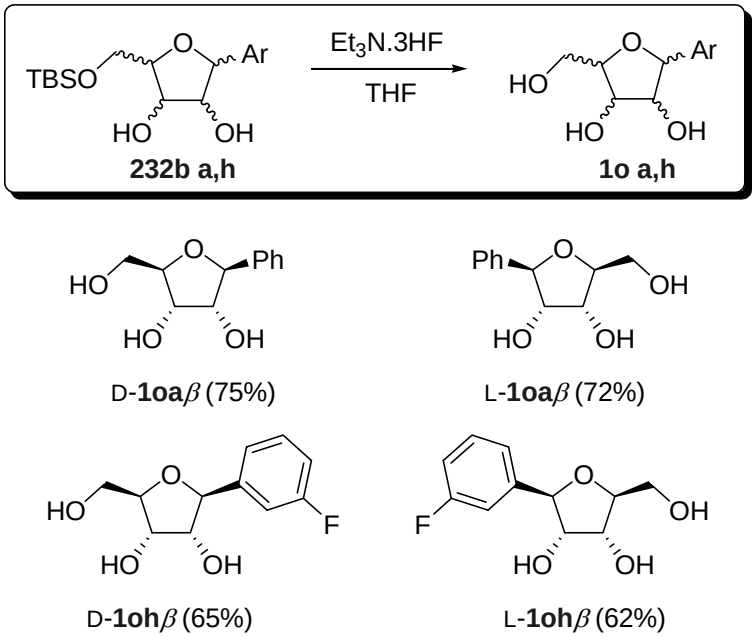
Scheme 97. Attempted synthesis of ribofuranose **1oc**



This is one of the practical limitations of our new synthetic procedure. We suggest to isolate the 5'-*O*-protected intermediate, as the oxidation step introduces side-products, which cannot be taken further through the ribofuranose synthesis.

The enantiopure 1'-aryl ribofuranoses **1o** were obtained in the deprotection step, utilising an optimized reaction protocol (*vide supra*, page 116). Both enantiomers of D-, and L-ribofuranoses bearing phenyl, and 3-fluorophenyl aromatic moiety were prepared in good yields (Scheme 98).

Scheme 98. Deprotection of ribofuranisides **232b**



Both enantiomers of *β*-1'-phenyl ribofuranose **1oa** were isolated as crystalline compounds suitable for X-ray diffraction analysis (Figure 2, and 3). In this very last stage of the successful synthesis the absolute stereochemistry of the products was thus confirmed. Knowing the configuration of the 4'-carbon brought from the starting butenediol **235** configuration on all the remaining stereocentres can be assigned. The observed configuration fully corresponds to our initial expectations and to the chirality brought from the starting branched carbonates **267**.

5.4.5. Conclusions

D4 *C*-nucleoside analogues were synthesised in a three-step procedure, and 1'-aryl ribofuranoses were constructed in a fourth-step procedure. The enantiopurity and diastereopurity of all the products is based on the enantiopurity of the starting materials, and a conservation of this chirality throughout all the transformations employed. The target compounds were prepared in excellent enantio- and diastereopurity, in good overall yields. The yield in the synthesis of 1'-aryl-2',3'-didehydro-1',2',3'-trideoxyribofunanoses **233a** is up to 46% over all the reaction steps. The yield of 1'-arylribofuranoses **1o** is up to 42%.

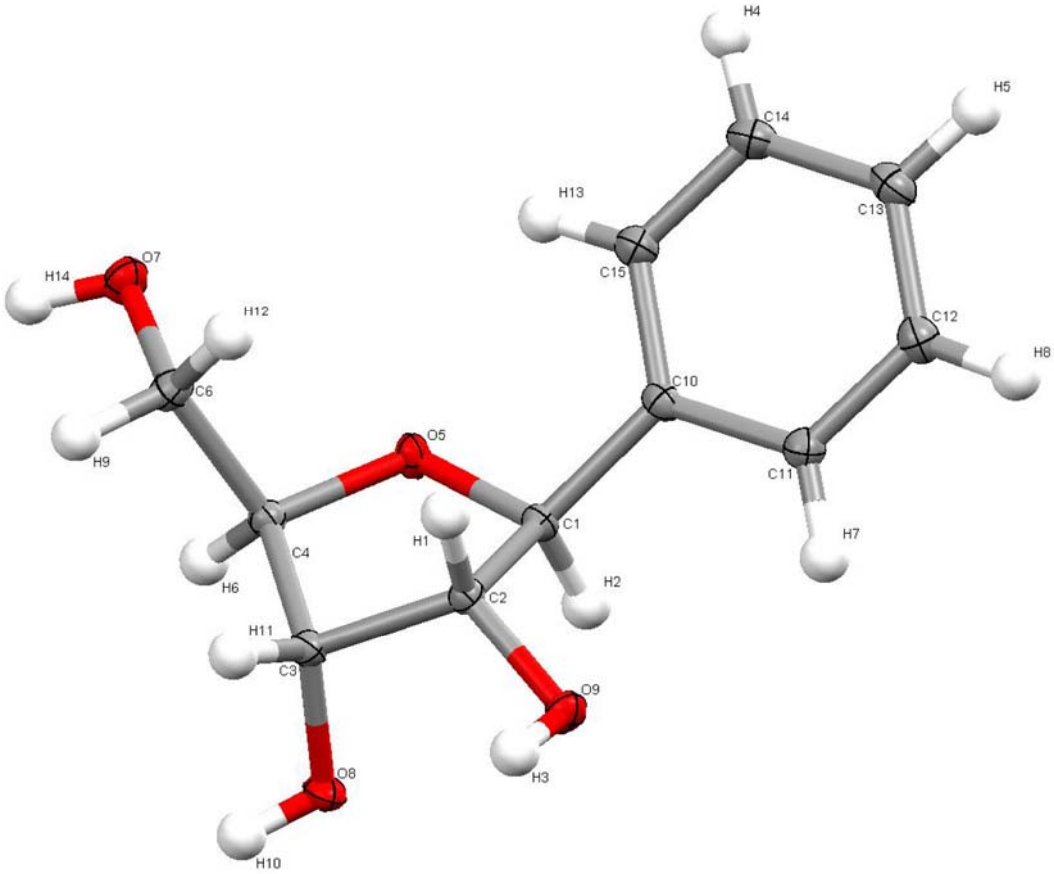


Figure 2: ORTEP drawing of 1'-deoxy-1'-phenyl-β-D-ribofuranose, with the atom numbering scheme. Thermal elipsoids are drown at the 50% probability level.

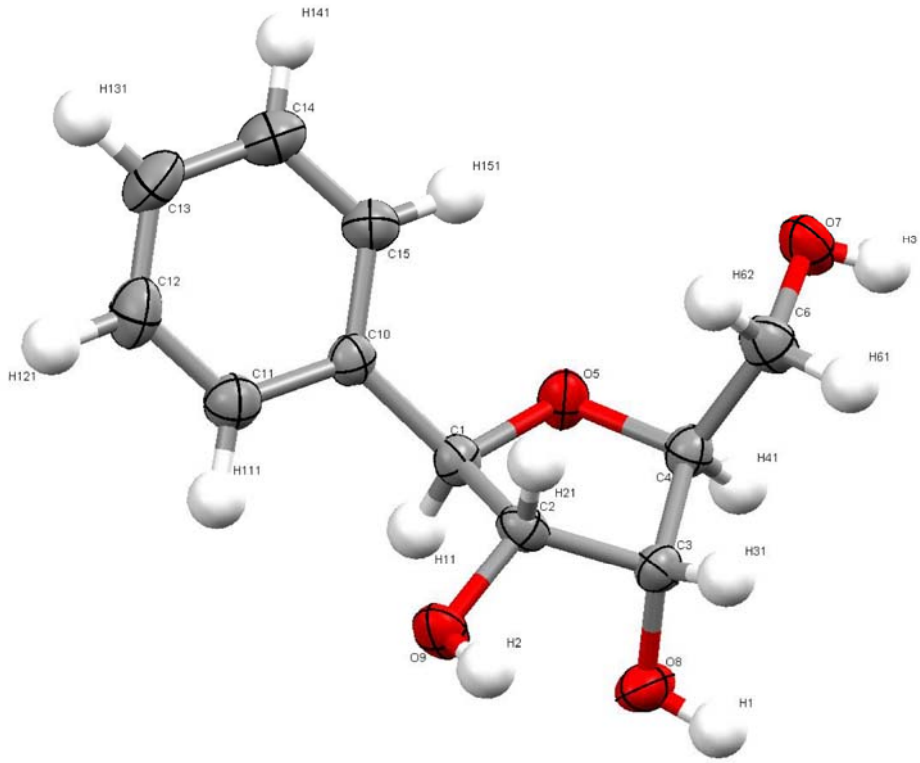


Figure 3: ORTEP drawing of 1'-deoxy-1'-phenyl-β-L-ribofuranose, with the atom numbering scheme. Thermal elipsoids are drown at the 50% probability level.

5.5. Conclusions

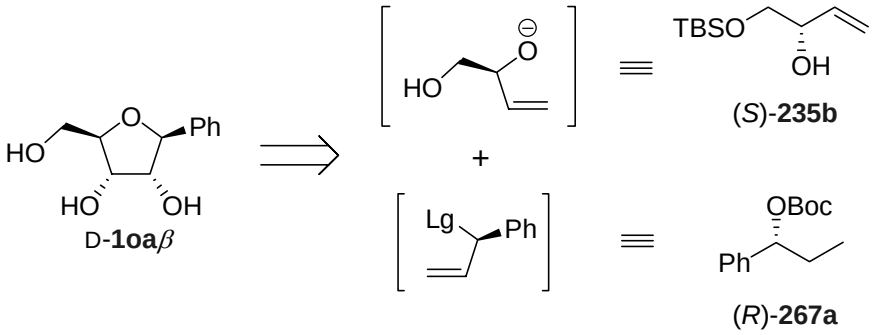
We have systematically investigated a conceptually new synthetic route to *C*-nucleosides. This synthetic concept is based on a divergent reaction sequence containing three strategic steps and, as the very last step, the deprotection.

All the strategic reactions are catalytic oranometallic reactions employing group 8a. transition metals. All the reactions were, from the beginning, optimized with a view of maximal atom efficiency. The point of an environmental impact was strongly considered through all the optimization processes, and only the reaction variations with the lowest toxicity and with the lowest environmental impact were chosen, and optimized further.

The successful implementation of a divergent synthetic route enabled us to access two important, biologically significant groups of compounds. The two first strategic transformations are common for both target families of compounds (AAS, and RCM reactions). D4 *C*-nucleoside analogues were synthesised in a three-step procedure, and 1'-aryl ribofuranoses were constructed in a fourth-step procedure.

The enantiopurity and diastereopurity of all the products is based on the enantiopurity of the starting materials, and a conservation of this chirality throughout all the transformations employed. From this point of view, the most important is the first strategic connection, utilizing an excellent memory effect of the iridium catalyst in the allylic substitution. The right choice of the right enantiomer of the starting material is very straightforward. For example in the case of 1'-aryl ribofuranose, there are fourth stereocentres at carbons 1', 2', 3', and 4'. The configuration of the centres 2', and 3' (*syn*) is introduced in the last strategic step, and fully depends on the configuration of the centres 1', and 4'. These later ones are based on the configuration in the two starting materials. Thus full chirality control can be easily achieved.

Scheme 99. Chirality source retention in novel ribofuranisides **1o** synthesis

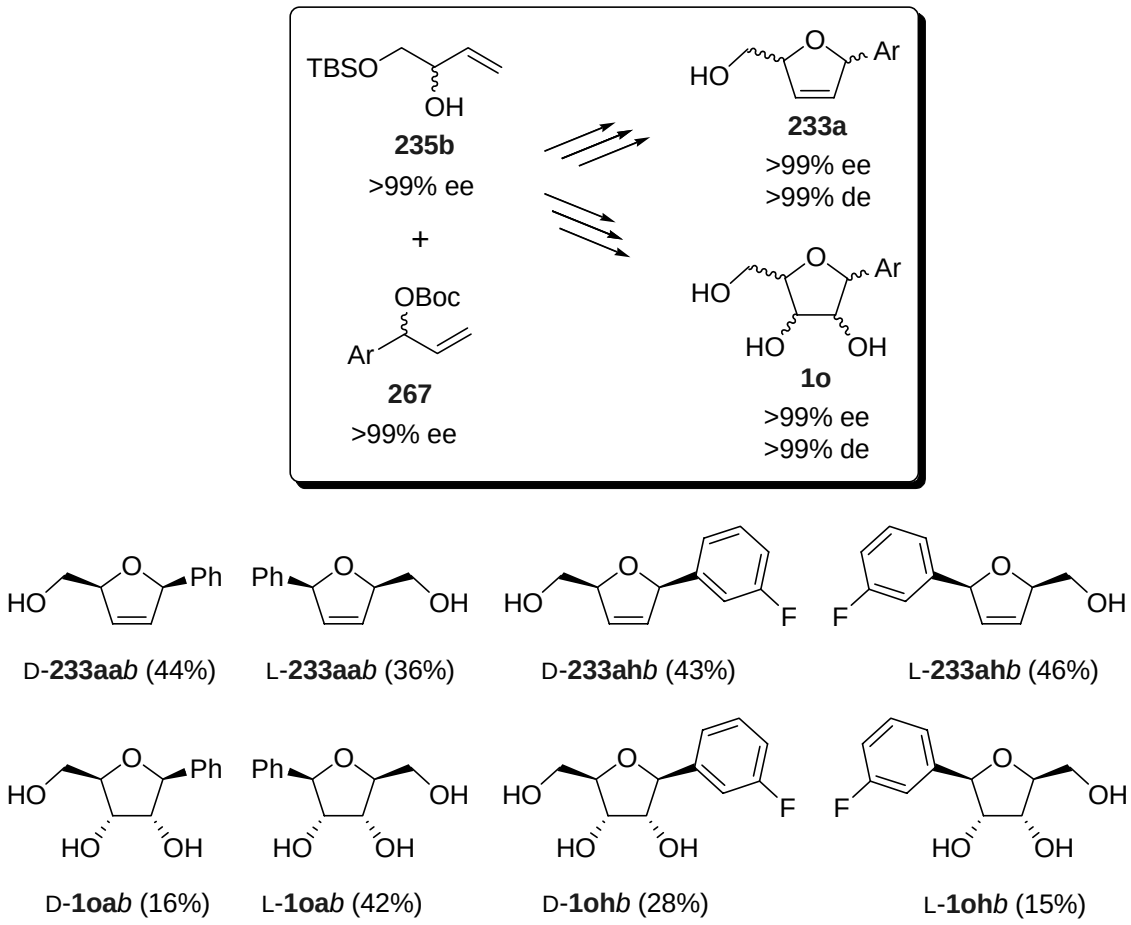


In summary, diol (*S*)-**235** leads to the D-ribofuranoses and diol (*R*)-**235** leads to the L-ribofuranoses. The combinations of enantiomers of the diol and the carbonate (*S*)-,(*S*)-, and (*R*)-, (*R*)- led to the *alpha* ribofuranoses, whereas mixed configuration of (*S*)-,(*R*)-, and (*R*)-, (*S*)- led to the *beta* ribofuranoses (Scheme 99).

We have successfully developed new synthetic methodology enabling to prepare two important classes of biologically significant compounds, utilising one common (retro)synthetic concept (Scheme 100). The target compounds were prepared in excellent enantio- and diastereopurity, in good overall yields. The yield in the synthesis of 1'-aryl-2',3'-didehydro-1',2',3'-trideoxyribofunanoses is up to 46% over all the reaction steps. The yield of 1'-arylribofuranoses depends in particular on successful undertaking of the oxidation step. In the first attempt we can predict about 15% overall yield, about 30% overall yield in the case the phase transfer in a heterogeneous reaction mixture was well managed, and finally the overall yield up to roughly 42%, in the case of good phase transfer control and a recovery of an unreacted starting material (kinetic control).

All the reaction steps were investigated in detail and optimized. We were aware of the key importance of the starting materials resources, and an extensive account on all the starting materials was reported herein. All the starting materials utilised are either commercially available or easy to prepare in high yields and excellent stereoselectivity.

Scheme 100. Total overall preparative yields of *C*-nucleosides and their analogues



Our new synthetic methodology is fully comparable with current state-of-the-art synthetic routes to *C*-nucleosides. This is particularly interesting in the term of a small number of reaction steps and a good overall yield. Our synthetic protocol enables to produce *C*-nucleosides with any stereochemistry required, with a variety of structural features in the aglycon unit, thus providing unprecedented synthetic tool. Despite not fully optimised oxidation step, the overall yield is fully comparable with the most common synthetic methods. Future work of our research will be focused on the optimisation of the oxidation step as it could enhance the overall yield of the synthesis up to 70%.

Every synthetic methodology has its limitations. In summary of all the above results, our new methodology is perfectly suitable for the synthesis of 1'-arylribofuranoses, and their D4-analogues, bearing non-*ortho*-substituted aromatics and heteroaromatics, lacking coordinating (nitrogen) substituents or (ring)heteroatoms. From this point of view the most promising target application is the synthesis of lipophilic isosters of ribonucleosides for the RNA-studies.

6. Experimental

6.1. General Methods

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were recorded in $CHCl_3$ at 25 °C unless otherwise indicated with an error of <±0.1 on an Autopol IV (Rudolph Research Analytical) polarimeter. The $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. The NMR spectra were measured in chloroform-d_1. Residual solvent peaks (δ 7.26, ^{1}H; δ 77.00, ^{13}C) and CCl_3F (δ 0.00, ^{19}F) were used as internal standards unless otherwise indicated. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. Complete assignment of all NMR signals was performed using a combination of H,H-COSY, H,C-HSQC and H,C-HMBC experiments. IR spectra were recorded for a thin film between NaCl plates or for $CHCl_3$ solutions. Mass spectra (EI or CI-isobutane, unless otherwise specified) were measured on a dual sector mass spectrometer using direct inlet and the lowest temperature enabling evaporation. All reactions were performed under an atmosphere of dry, oxygen-free argon in oven-dried glassware three times evacuated and backfilled with the argon three times. Reaction temperature -83 °C refers to the cooling bath filled with an ethyl acetate – liquid nitrogen mixture. Solvents and solutions were transferred by syringe-septum and cannula techniques. All solvents for the reactions were of reagent grade and were dried and distilled immediately before use as follows: tetrahydrofuran (THF) from sodium/benzophenone; dichloromethane from calcium hydride. Solvents for the palladium- and ruthenium-catalysed reactions were degassed *in vacuo* and stored over molecular sieves (4 Å) under argon atmosphere. Yields are given for isolated products showing one spot on a TLC plate and no impurities detectable in the NMR spectrum. The identity of the products prepared by different methods was checked by comparison of their ^{1}H-NMR spectra, and ultimate elemental composition (microanalysis).

6.2. General Procedures

General Procedure A: *tert*-Butyloxycarbonylation of Alcohols to Produce Carbonates 236. An alcohol (100.0 mmol, neat or 5M solution in THF if solid) was added slowly to a suspension of sodium hydride (6.0 g, 150 mmol, 60% suspension in mineral oil, 3× washed with dry THF) in THF (100 mL) at room temperature and the mixture was stirred for 1 h.

The resulting solution was added slowly to a solution of *tert*-butoxy-(*tert*-butoxycarbonyloxy)methanone (Boc anhydride, 25.0 g, 115 mmol) in THF (400 mL) at room temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (100 mL) and the product was extracted into ether (500 mL). The organic layer was dried (Na_2SO_4) and evaporated.

General Procedure B: Suzuki-Miyaura Coupling Reaction to Produce Carbonates 236. A flask containing aryl iodide **237** (3.00 mmol), K_2CO_3 (415 mg, 3.00 mmol) and $(Ph_3P)_4Pd$ (60.0 mg, 0.052 mmol) was sealed and three times evacuated and backfilled with argon. Boronate **263** (neat, 280 mg, 1.00 mmol), DME (5 mL), and water (5 mL) were added and the mixture was stirred at 80 °C for 2 h. The resulting solution was cooled to room temperature, diluted with Et_2O (80 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4) and evaporated.

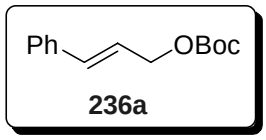
General Procedure C: Suzuki-Miyaura Coupling Reaction to Produce Carbonates 236. A flask containing K_2CO_3 (415 mg, 3.00 mmol) and $(Ph_3P)_4Pd$ (60.0 mg, 0.052 mmol) was sealed and three times evacuated and backfilled with argon. Aryl halide **237** (3.00 mmol), boronate **263** (neat, 285 mg, 1.00 mmol), DME (5 mL), and water (5 mL) were added and the mixture was stirred at 80 °C for 2 h. The resulting solution was cooled to room temperature, diluted with Et_2O (80 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4) and evaporated.

General Procedure D: Cross Metathesis Reaction to Carbonates 236. A flask containing benzylidene[1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene]dichloro(tricyclohexylphosphine)ruthenium (2^{nd} generation Grubbs catalyst; **C2**; 23.9 mg, 0.028 mmol) was sealed and three times evacuated and backfilled with argon. Dichloromethane (2.0 mL), neat allyl carbonate **240** (1.00 mmol), and neat vinyl aromate **239** (0.40 to 5.00 mmol) were added and the mixture was stirred at 40 °C for 2 h. The resulting solution was cooled to room temperature and evaporated.

General Procedure E: Horner-Wadsworth-Emmons Based Reaction Sequence to Carbonates 236. *n*-Butyllithium (11 mL, 22 mmol, 2.0M solution in pentane) was added slowly to a solution of triethylphosphonoacetate **241** (4.49 g, 20.0 mmol) in THF (20 mL) at –83 °C. After 5 min, aldehyde **143** (20.0 mmol) was added slowly and the resulting mixture was stirred at -83 °C for 10 min and then at room temperature for 2 h. The reaction

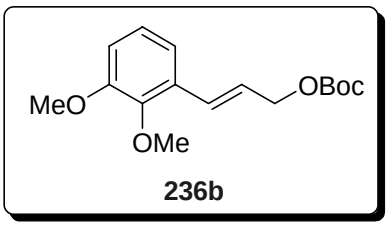
was quenched with brine (10 mL), the mixture was diluted with ether (100 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. The crude ethyl ester **265** was dissolved in THF (20 mL), cooled to 0 °C, and DIBAL-H (40 mL, 60 mmol, 1.5M solution in toluene) was added slowly at this temperature. The resulting mixture was stirred at room temperature for an additional 2 h and than the reaction was quenched with a saturated aqueous solution of potassium-sodium tartrate (50 mL). The resulting solution was stirred at 40 °C and a solid potassium-sodium tartrate (approximately 15 g) was added in portions, until the solution became homogeneous. The resulting mixture was diluted with ether (300 mL), washed with a saturated aqueous solution of potassium-sodium tartrate (3 × 100 mL), dried (Na_2SO_4), and evaporated. The crude allyl alcohol **264** was dissolved in THF (20 mL) and slowly added to a suspension of sodium hydride (1.21 g, 30.3 mmol, 60% suspension in mineral oil, 3 × washed with dry THF) in THF (20 mL) at room temperature and the mixture was stirred for 1 h. The resulting solution was added slowly to a solution of Boc anhydride (4.84 g, 22.2 mmol) in THF (50 mL) at room temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (10 mL) and the mixture was diluted with ether (250 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated.

6.3. Synthesis of Linear Carbonates



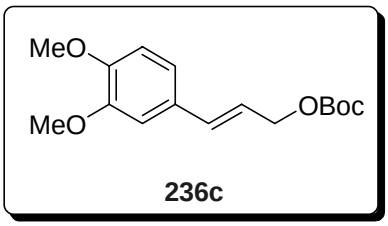
236a

***tert*-Butyl (*E*)-3-Phenylprop-2-en-1-yl Carbonate (236a).** Fractional distillation of the crude product obtained by procedure **A** produced **236a** as a colourless oil (34.07 g, 73%): bp 114 °C at 270 Pa; ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.54 (s, 9H, *t*-Bu), 4.76 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 6.5 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.1 Hz, 2H, 1-H), 6.33 (dt, ^3J = 15.9 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.5 Hz, 1H, 2-H), 6.71(dt, $^3J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.1 Hz, 1H, 3-H), 7.27-7.32 (m, 1H, H-arom), 7.33-7.38 (m, 2H, H-arom), 7.43 (dd, $J_{H,H}$ = 7.2 and 1.5 Hz, 2H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.65 (C(*C*H_3)$_3$), 67.32 (CH_2-1), 82.03 (*C*(CH_3)$_3$), 122.74 (CH-2), 126.51, 127.94 and 128.46 (CH-arom), 134.25 (CH-3), 136.03 (C-arom), 153.21 (CO carbonate); MS (CI-NH_3) *m*/*z* (%) 252 (M+NH_4^+, 2), 151 (1), 134 (3), 117 (2), 88 (3); IR ($CHCl_3$): ν 2980 (m), 1740 (s), 1449 (w), 1369 (m), 1275 (s), 1254 (s), 1163 (s), 1117 (m), 1085 (w), 967 (m) cm^{-1}. Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.93; H, 7.78.



236b

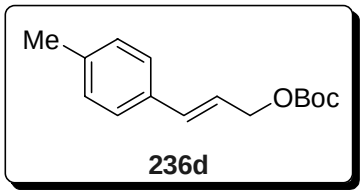
***tert*-Butyl (*E*)-3-(2',3'-Dimethoxyphenyl)prop-2-en-1-yl Carbonate (236b).** The crude product obtained by procedure **A** was chromatographed on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (90:10) to afford **236b** as a yellow oil (1.064 g, 49%, 62% based on the recovered allylic alcohol). Continued elution with a mixture of hexanes and ethyl acetate (80:20) gave the starting allylic alcohol **264b** (272 mg, 19% recovered). **236b**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.49 (s, 9H, *t*-Bu), 3.79 (s, 3H, CH_3O-2'), 3.84 (s, 3H, CH_3O-3'), 4.73 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.5 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.31 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 16.1 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.5 Hz, 1H, 2-H), 6.82 (dd, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 8.0 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ = 1.4 Hz, 1H, 4'-H), 6.98 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 16.1 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 7.00 (t, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 8.0 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ = 8.0 Hz, 1H, 5'-H), 7.07 (dd, $^{3}J_{6'\text{-H},5'\text{-H}}$ = 8.0 Hz, $^{4}J_{6'\text{-H},4'\text{-H}}$ = 1.4 Hz, 1H, 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.71 ($C(CH_3)_3$), 55.70 (CH_3O-3'), 60.87 (CH_3O-2'), 67.75 (CH_2-1), 82.05 ($C(CH_3)_3$), 111.74 (CH-4'), 118.26 (CH-6'), 123.96 (CH-5'), 124.19 (CH-2), 128.72 (CH-3), 130.29 (C-1'), 146.84 (C-2'), 152.89 (C-3'), 153.27 (CO carbonate); IR (neat) ν 2979 (w), 2835 (w), 1740 (s, CO carbonate), 1478 (m), 1369 (m), 1272 (s), 1255 (s), 1161 (s), 1117 (m), 1090 (m), 1070 (m), 1008 (m) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 294 (M^+, 15), 238 (M^+-$(CH_3)_2C{=}CH_2$, 100), 194 (M^+-$(CH_3)_2C{=}CH_2$-CO_2, 5), 177 (MH^+-$(CH_3)_2C{=}CH_2$-CO_2-H2O, 85); HRMS (EI) 294.1469 [$C_{16}H_{22}O_5$ (M^+) requires 294.1467]. Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.14; H, 7.66.



236c

***tert*-Butyl (*E*)-3-(3',4'-Dimethoxyphenyl)prop-2-en-1-yl Carbonate (236c).** The crude product obtained by procedure **A** was chromatographed on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (90:10) to furnish **236c** as a yellow oil (638 mg, 33%, 52% based on the recovered allylic alcohol). Continued elution with a mixture of hexanes and ethyl acetate (75:25) gave the starting allylic alcohol **264c** (440 mg, 35% recovered). **236c**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.49 (s, 9H, *t*-Bu), 3.86 (s, 3H, CH_3O), 3.87 (s, 3H, CH_3O), 4.69 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.6 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.1 Hz, 2H,

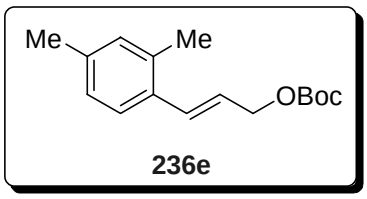
1-H), 6.15 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 15.8 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.6 Hz, 1H, 2-H), 6.59 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 15.8 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.1 Hz, 1H, 3-H), 6.80 (d, $^3J_{5'\text{-H},6'\text{-H}}$ = 8.1 Hz, 1H, 5'-H), 6.91 (dd, $^3J_{6'\text{-H},5'\text{-H}}$ = 8.1 Hz, $^4J_{6'\text{-H},2'\text{-H}}$ = 1.9 Hz, 1H, 6'-H), 6.93 (d, $^4J_{2'\text{-H},6'\text{-H}}$ = 1.9 Hz, 1H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.71 (C(CH$_3$)$_3$), 55.73 and 55.81 (CH_3O), 67.56 (CH_2-1), 82.07 (C(CH$_3$)$_3$), 108.81 (CH-2'), 110.94 (CH-5'), 119.97 (CH-6'), 120.78 (CH-2), 129.16 (C-1'), 134.39 (CH-3), 148.93 and 149.12 (C-arom), 153.30 (CO carbonate); IR (neat) ν 2979 (w), 1739 (s, CO carbonate), 1515 (m), 1369 (m), 1269 (s), 1256 (s), 1160 (s), 1027 (m), 966 (m), 856 (m) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 295 (MH^+, 10), 294 (M^+, 50), 238 (M^+-$(CH_3)_2C{=}CH_2$, 100), 224 (32), 193 (MH^+-$(CH_3)_2C{=}CH_2$-CO_2, 15), 177 (MH^+-$(CH_3)_2C{=}CH_2$-CO_2-H_2O, 100); HRMS (EI) 294.1466 [$C_{16}H_{22}O_5$ (M^+) requires 294.1467]. Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.14; H, 7.67.



236d

***tert*-Butyl (*E*)-3-(4'-Methylphenyl)prop-2-en-1-yl Carbonate (236d).** A flask containing 4-iodotoluene (109 mg, 0.50 mmol), boronic acid **238a** (151 mg, 0.75 mmol), K_2CO_3 (187 mg, 1.35 mmol) and $(PPh_3)_4Pd$ (57.0 mg, 0.049 mmol) was sealed, three times evacuated and backfilled with argon. DME (5 mL) and water (0.7 mL) were then added and the reaction mixture was stirred at 85 °C for 20 h. The resulting solution was co-distilled three times with toluene and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (100:0 to 97:3) to afford **236d** as a colourless oil (76 mg, 61%):

A crude product obtained using procedure **B** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (100:0 to 97:3) to furnish **236d** as a colourless oil (89 mg, 36%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.51 (s, 9H, *t*-Bu), 2.34 (s, 3H, CH_3), 4.71 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 6.6 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.25 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.6 Hz, 1H, 2-H), 6.64 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.3 Hz, 1H, 3-H), 7.13 (d, $^3J_{3'\text{-H},2'\text{-H}}$ = 8.1 Hz, 2H, 3'-H), 7.29 (d, $^3J_{2'\text{-H},3'\text{-H}}$ = 8.1 Hz, 2H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 21.22 (CH_3), 27.76 (C(CH$_3$)$_3$), 67.63 (CH_2-1), 82.16 (C(CH$_3$)$_3$), 121.73 (CH-2), 126.54 (CH-2'), 129.26 (CH-3'), 133.36 (C-1'), 134.48 (CH-3), 137.97 (C-4'), 153.33 (CO carbonate); IR (neat) ν 2979 (m), 1736 (s, CO carbonate), 1453 (m), 1368 (m), 1273 (s), 1155 (s) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 266 (M+NH_4^+, 35), 165 ([M+NH_4^+]-Boc, 30), 148 (M+H^+-Boc, 45), 131 (40), 52 (100). Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.25; H, 7.98.

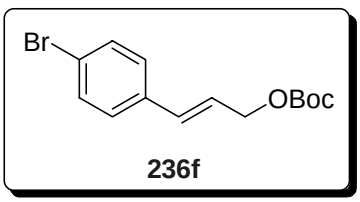


236e

***tert*-Butyl (*E*)-3-(2',4'-Dimethylphenyl)prop-2-en-1-yl Carbonate (236e).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5) to give **236e** as a yellowish oil (27 mg, 11%).

The crude product obtained by procedure **D** was chromatographed on a column of silica gel (3 × 10 cm) with hexanes to yield the corresponding stilbene derivative (123 mg); continued elution with a mixture of hexanes and ethyl acetate (98.5:1.5) gave **236e** as a colourless oil (150 mg, 52%).

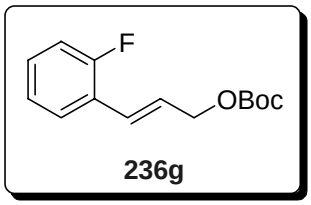
The crude product obtained by procedure **E** was chromatographed on a column of silica gel (5 × 15 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to produce **236e** as a colourless oil (3.60 g, 68%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 2.30 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.72 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.6 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.14 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.7 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.6 Hz, 1H, 2-H), 6.85 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.7 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 6.97 (s, 1H, 3'-H), 6.98 (d, J_{HH} = 7.6 Hz, H-arom), 7.34 (d, J_{HH} = 7.6 Hz, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 19.63 (CH_3), 21.06 (CH_3), 27.78 ($C(CH_3)_3$), 67.84 (CH_2-1), 82.12 ($C(CH_3)_3$), 123.19 (CH-2), 125.79 and 126.83 (CH-arom), 131.04 (CH-3'), 132.41 (CH-3), 132.44, 135.53 and 137.74 (C-arom), 153.35 (CO carbonate); IR (neat) ν 2980 (m), 2932 (m), 1742 (s, CO carbonate), 1613 (w), 1369 (s), 1276 (s), 1254 (s), 1162 (s), 1089 (m), 858 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 508 (2), 468 ([2M+NH_4^+]-*t*BuOH, 5), 386 ([2M+NH_4^+]-*t*BuOH-CO_2, 4), 280 ([M+NH_4^+], 3), 179 ([M+NH_4^+]-Boc, 3), 162 (MH^+-Boc, 5), 145 (MH^+-Boc-OH, 42), 52 (100). Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.18; H, 8.48.



236f

***tert*-Butyl (*E*)-3-(4'-Bromophenyl)prop-2-en-1-yl Carbonate (236f).** The crude product obtained by procedure **B** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to afford **236f** as white crystals (113 mg, 33%): mp 57-58 °C; ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 4.70 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.4 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.28 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.4 Hz, 1H,

2-H), 6.60 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.3 Hz, 1H, 3-H), 7.24 (d, $^{3}J_{a\text{-H},b\text{-H}}$ = 8.4 Hz, 2H, H_a-arom), 7.44 (d, $^{3}J_{b\text{-H},a\text{-H}}$ = 8.4 Hz, 2H, H_b-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.75 (C(*C*H_3)$_3$), 67.13 (CH_2-1), 82.30 (*C*(CH_3)$_3$), 121.88 (C-4'), 123.73 (CH-2), 128.10 (C_aH-arom), 131.68 (C_bH-arom), 132.98 (CH-3), 135.10 (C-1'), 153.24 (CO carbonate); IR ($CHCl_3$) ν 2983 (m), 1740 (s, CO carbonate), 1487 (m), 1370 (m), 1277 (s), 1256 (s), 1216 (s), 1157 (s), 1073 (m), 845 (m), 755 (s) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 642/644/646 ([2M+NH_4^+], 10), 524/526/528 ([2M+NH_4^+]-*t*BuOH-CO_2, 65), 330/332 ([M+NH_4^+], 100), 229/231 ([M+NH_4^+]-Boc, 35), 212/214 (MH^+-Boc, 15), 195/197 (MH^+-Boc-OH, 4), 52 (43). Anal. Calcd. for $C_{14}H_{17}BrO_3$: C, 53.69; H, 5.47. Found: C, 53.60; H, 5.47.

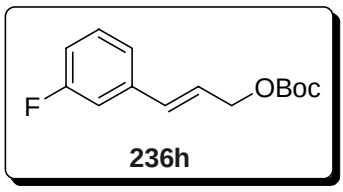


236g

***tert*-Butyl (*E*)-3-(2'-Fluorophenyl)prop-2-en-1-yl Carbonate (236g).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (100:00 to 98.5:1.5) to give **236g** as a colourless oil (25 mg, 10%).

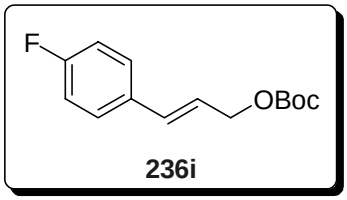
The crude product obtained by procedure **D** was chromatographed on a column of silica gel (3 × 10 cm) with hexanes to yield the corresponding stilbene derivative (17 mg); continued elution with a mixture of hexanes and ethyl acetate (98.5:1.5) provided **236g** as a colourless oil (70 mg, 29%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.51 (s, 9H, *t*-Bu), 4.74 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.3 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.4 Hz, 2H, 1-H), 6.38 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 16.1 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.3 Hz, 1H, 2-H), 6.82 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 16.1 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.4 Hz, 1H, 3-H), 7.03 (ddd, $^{3}J_{HF}$ = 10.7 Hz, $^{3}J_{3'\text{-H},4'\text{-H}}$ = 8.2 Hz, $^{4}J_{3'\text{-H},5'\text{-H}}$ = 1.2 Hz, 1H, 3'-H), 7.10 (dt, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 7.6 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ = 7.6 Hz, $^{4}J_{5'\text{-H},3'\text{-H}}$ = 1.2 Hz, 1H, 5'-H), 7.22 (ddd, $^{3}J_{4'\text{-H},3'\text{-H}}$ = 8.2 Hz, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 7.6 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ = 1.8 Hz, 1H, 4'-H), 7.45 (dd, $^{3}J_{6'\text{-H},5'\text{-H}}$ = 7.6 Hz, $^{4}J_{6'\text{-H},4'\text{-H}}$ = 1.8 Hz, 1H, 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.76 (C(*C*H_3)$_3$), 67.47 (CH_2-1), 82.30 (*C*(CH_3)$_3$), 115.75 (d, $^{2}J_{CF}$ = 22.1 Hz CH-3'), 123.97 (d, $^{2}J_{CF}$ = 12.1 Hz, C-1'), 124.10 (d, $^{4}J_{CF}$ = 3.6 Hz, CH-5'), 125.55 (d, $^{4}J_{CF}$ = 5.1 Hz, CH-2), 126.63 (d, $^{3}J_{CF}$ = 3.6 Hz, CH-3), 127.61 (d, $^{3}J_{CF}$ = 3.6 Hz, CH-6'), 129.34 (d, $^{3}J_{CF}$ = 8.8 Hz, CH-4'), 153.28 (CO carbonate), 160.34 (d, $^{1}J_{CF}$ = 250.3 Hz, CF-2'); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –118.21; IR ($CHCl_3$) ν 2979 (m), 1743 (s, CO carbonate), 1489 (m), 1457 (m), 1370 (m), 1256 (s), 1163 (s), 969 (m), 858 (m), 755 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 522 ([2M-NH_4^+], 1), 404 ([2M+NH_4^+]-*t*BuOH-CO_2, 3), 270 ([M+NH_4^+], 95), 214 ([M+NH_4^+]-CH_2=C(CH_3)$_2$, 20),

169 ([M+NH_4^+]-Boc, 20), 152 (MH^+-Boc, 22), 135 (MH^+-Boc-OH, 5), 52 (100). Anal. Calcd. for $C_{14}H_{17}FO_3$: C, 66.65; H, 6.79. Found: C, 66.77; H, 6.91.



236h

***tert*-Butyl (*E*)-3-(3'-Fluorophenyl)prop-2-en-1-yl Carbonate (236h).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99.2:0.8) to furnish **236h** as a yellowish oil (103 mg, 40%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 4.72 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 6.3 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.29 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.3 Hz, 1H, 2-H), 6.63 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.3 Hz, 1H, 3-H), 6.94 (dddd, $^3J_{HF}$ = 8.5 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 8.4 Hz, $^4J_{4'\text{-H},6'\text{-H}}$ = 2.5 Hz, $^4J_{4'\text{-H},2'\text{-H}}$ = 0.9 Hz, 1H, 4'-H), 7.08 (ddd, $^3J_{2'\text{-H,F}}$ = 10.1 Hz, $^4J_{2'\text{-H},4'\text{-H}}$ = 2.5 Hz, $^4J_{2'\text{-H},6'\text{-H}}$ = 1.9 Hz, 1H, 2'-H), 7.14 (ddd, $^3J_{6'\text{-H},5'\text{-H}}$ = 7.8 Hz, $^4J_{6'\text{-H},2'\text{-H}}$ = 1.9 Hz, $^4J_{6'\text{-H},4'\text{-H}}$ = 0.9 Hz, 1H, 6'-H), 7.27 (ddd, $^3J_{5'\text{-H},4'\text{-H}}$ = 8.4 Hz, $^3J_{5'\text{-H},6'\text{-H}}$ = 7.8 Hz, $^4J_{5'\text{-H,F}}$ = 6.0 Hz, 1H, 5'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.75 ($C(CH_3)_3$), 67.02 (CH_2-1), 82.35 ($C(CH_3)_3$), 113.06 (d, $^2J_{CF}$ = 21.8 Hz CH-2'), 114.84 (d, $^2J_{CF}$ = 21.4 Hz, CH-4'), 122.50 (d, $^4J_{CF}$ = 2.8 Hz, CH-6'), 124.38 (CH-2), 130.02 (d, $^3J_{CF}$ = 8.5 Hz, CH-5'), 132.93 (d, $^4J_{CF}$ = 2.5 Hz, CH-3), 138.51 (d, $^3J_{CF}$ = 7.8 Hz, C-1'), 153.25 (CO carbonate), 163.00 (d, $^1J_{CF}$ = 245.4 Hz, CF-3'); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.84; IR ($CHCl_3$) ν 2980 (m), 1741 (s, CO carbonate), 1584 (m), 1370 (m), 1276 (s), 1255 (s), 1161 (s), 1117 (m), 966 (m), 859 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 522 ([2M+NH_4^+], 15), 404 ([2M+NH_4^+]-*t*BuOH-CO_2, 25), 386 (10), 310 (10), 270 ([M+NH_4^+], 100), 169 ([M+NH_4^+]-Boc, 5), 152 (MH^+-Boc, 5), 135 (MH^+-Boc-OH, 2), 52 (5). Anal. Calcd. for $C_{14}H_{17}FO_3$: C, 66.65; H, 6.79. Found: C, 66.49; H, 6.81.



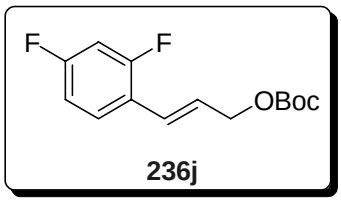
236i

***tert*-Butyl (*E*)-3-(4'-Fluorophenyl)prop-2-en-1-yl Carbonate (236i).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to give **236i** as a yellowish oil (72 mg, 29%).

The crude product obtained by procedure **E** was chromatographed on a column of silica gel (5 × 15 cm) with a mixture of hexanes and ethyl acetate (100:0 to 98.5:1.5) to

afford **236i** as a colourless oil (3.273 g, 65%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 4.70 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.5 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.21 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.5 Hz, 1H, 2-H), 6.63 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 6.94 (dd, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 8.8 Hz, $^{3}J_{3'\text{-H,F}}$ = 8.7 Hz, 2H, 3'-H and 5'-H), 7.28 (dd, $^{4}J_{2'\text{-H,F}}$ = 5.4 Hz, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 8.8 Hz, 2H, 2'-H and 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.76 (C(*C*H_3)$_3$), 67.32 (CH_2-1), 82.26 (*C*(CH_3)$_3$), 115.51 (d, $^{2}J_{CF}$ = 21.7 Hz, CH-3'), 122.64 (d, $^{6}J_{CF}$ = 2.2 Hz, CH-2), 128.19 (d, $^{3}J_{CF}$ = 8.1 Hz, CH-2'), 132.34 (d, $^{4}J_{CF}$ = 3.2 Hz, C-1'), 133.23 (CH-3), 153.30 (CO carbonate), 162.56 (d, $^{1}J_{CF}$ = 247.6 Hz, CF-4'); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –114.15; IR (neat) ν 2981 (m), 2936 (w), 1740 (s, CO carbonate), 1601 (m), 1510 (s, CF), 1370 (m), 1275 (s), 1255 (s), 1159 (s), 850 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 522 ([2M+NH_4^+], 10), 404 ([2M+NH_4^+]-*t*BuOH-CO_2, 100), 348 (10), 270 ([M+NH_4^+], 40), 169 ([M+NH_4^+]-Boc, 7), 152 (MH^+-Boc, 9), 135 (MH^+-Boc-OH, 8), 52 (1). Anal. Calcd. for $C_{14}H_{17}FO_3$: C, 66.65; H, 6.79. Found: C, 66.39; H, 6.95.

The crude product obtained by procedure **D** was chromatographed on a column of silica gel (3 × 10 cm) with hexanes to yield the corresponding stilbene derivative (73 mg); continued elution with a mixture of hexanes and ethyl acetate (100:0 to 98.5:1.5) gave **236i** as a colourless oil (65 mg, 27%).

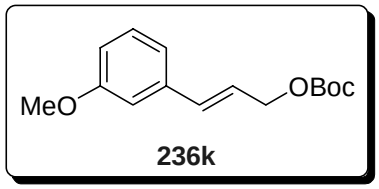


236j

***tert*-Butyl (*E*)-3-(2',4'-Difluorophenyl)prop-2-en-1-yl Carbonate (236j).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1 to 98.5:1.5) to afford **236j** as a yellowish oil (31 mg, 11%).

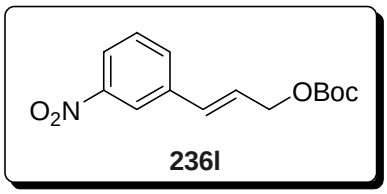
The crude product obtained by procedure **E** was chromatographed on a column of silica gel (5 × 15 cm) with a mixture of hexanes and ethyl acetate (100:0 to 98.5:1.5) to furnish **236j** as a colourless oil (4.32 g, 80%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 4.72 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.3 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.1 Hz, 2H, 1-H), 6.31 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 16.1 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.3 Hz, 1H, 2-H), 6.74 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 16.1 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.1 Hz, 1H, 3-H), 6.79 (ddd, $^{3}J_{HF}$ = 11.4 and 10.8 Hz, $^{4}J_{3'\text{-H},5'\text{-H}}$ = 2.4 Hz, 1H, 3'-H), 6.84 (dddd, $^{3}J_{HF}$ = 11.3 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ = 8.7 Hz, $^{4}J_{5'\text{-H},3'\text{-H}}$ = 2.4 Hz, $^{5}J_{HF}$ = 1.0 Hz, 1H, 5'-H), 7.41 (ddd, $^{3}J_{6'\text{-H},5'\text{-H}}$ = 8.7 Hz, $^{4}J_{HF}$ = 8.5 and 6.4 Hz, 1H, 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.77 (C(*C*H_3)$_3$), 67.35 (CH_2-1), 82.37 (*C*(CH_3)$_3$), 104.09 (t, $^{2}J_{CF}$ = 25.6 Hz, CH-3'), 111.52 (dd, $^{2}J_{CF}$ = 21.5 Hz, $^{4}J_{CF}$ = 3.6 Hz, CH-5'), 125.23 (dd, $^{4}J_{CF}$ = 5.1 Hz, $^{6}J_{CF}$ = 2.1 Hz, CH-2), 125.74 (dd,

$^{3}J_{CF}$ = 2.9 Hz, $^{5}J_{CF}$ = 1.5 Hz, C-3), 128.48 (dd, $^{3}J_{CF}$ = 9.5 and 5.2 Hz, CH-6'), 137.50 (d, $^{2}J_{CF}$ = 25.6 Hz, C-1'), 153.26 (CO carbonate), 162.40 (d, $^{1}J_{CF}$ = 250.1 Hz, CF), 162.52 (d, $^{1}J_{CF}$ 250.2 Hz, CF); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –110.66 (d, $^{4}J_{FF}$ = 7.9 Hz), -113.92 (d, $^{4}J_{FF}$ = 7.9 Hz); IR (neat) ν 2981 (m), 2934 (m), 1742 (s, CO carbonate), 1615 (m), 1503 (s, CF), 1370 (m), 1275 (s), 1255 (s), 1161 (s), 966 (m), 853 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 288 ([M+NH_4^+], 30), 187 ([M+NH_4^+]-Boc, 5), 170 ([M+NH_4^+]-*t*BuOH-CO_2, 5), 153 ([M+NH_4^+]-*t*BuOH-CO_2-NH_3, 5), 52 (100). Anal. Calcd. for $C_{14}H_{16}F_2O_3$: C, 62.22; H, 5.97. Found: C, 62.35; H, 6.15.



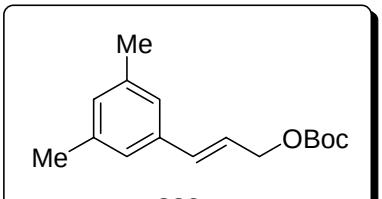
236k

***tert*-Butyl (*E*)-3-(3'-Methoxyphenyl)prop-2-en-1-yl Carbonate (236k).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99.2:0.8) to give iodo-3-methoxybenzene **237k** (366 mg, 51% recovered). Continued elution with a mixture of hexanes and ethyl acetate (98.5:1.5) furnished **236k** as a yellowish oil (73 mg, 25%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 3.81(s, 3H, CH_3O), 4.72 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.4 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.29 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.4 Hz, 1H, 2-H), 6.64 (d, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, 1H, 3-H), 6.82 (ddd, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 8.1 Hz, $^{4}J_{4'\text{-H},2'\text{-H}}$ = 2.5 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ = 0.9 Hz, 1H, 4'-H), 6.92 (dd, $^{4}J_{2'\text{-H},4'\text{-H}}$ = 2.5 Hz, $^{4}J_{2'\text{-H},6'\text{-H}}$ = 1.7 Hz, 1H, 2'-H), 6.98 (ddd, $^{3}J_{6'\text{-H},5'\text{-H}}$ = 7.9 Hz, $^{4}J_{6'\text{-H},2'\text{-H}}$ = 1.7 Hz, $^{4}J_{6'\text{-H},4'\text{-H}}$ = 0.9 Hz, 1H, 6'-H), 7.24 (dd, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 8.1 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ = 7.9 Hz, 1H, 5'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.77 (C(*C*H_3)$_3$), 55.18 (CH_3O), 67.35 (CH_2-1), 82.22 (*C*(CH_3)$_3$), 111.83 (CH-2'), 113.77 (CH-4'), 119.30 (CH-6'), 123.22 (CH-2), 129.54 (CH-5'), 134.22 (CH-3), 137.62 (C-1'), 153.31 (CO carbonate), 159.76 (CH-3'); IR (neat) ν 2979 (m), 2938 (m), 1740 (s, CO carbonate), 1598 (m), 1580 (m), 1369 (m), 1275 (s), 1255 (s), 1159 (s), 857 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 546 ([2M+NH_4^+], 18), 428 ([2M+NH_4^+]-*t*BuOH-CO_2, 63), 282 ([M+NH_4^+], 100), 181 ([M+NH_4^+]-Boc, 45), 164 (MH^+-Boc, 40), 147 (MH^+-Boc-OH, 10), 52 (25). Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.03; H, 7.80.



236l

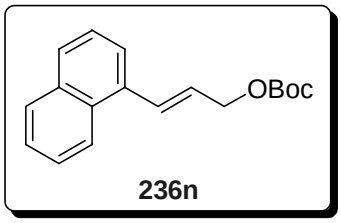
***tert*-Butyl (*E*)-3-(3'-Nitrophenyl)prop-2-en-1-yl Carbonate (236l).** The crude product obtained by procedure **B** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to afford iodo-3-nitrobenzene **237l** (562 mg, 73% recovered). Continued elution with a mixture of hexanes and ethyl acetate (97.5:2.5) furnished **236l** as a yellowish oil (134 mg, 43% of theory, 57% based on the recovered iodide): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.49 (s, 9H, *t*-Bu), 4.74 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.0 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.4 Hz, 2H, 1-H), 6.42 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 16.0 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.0 Hz, 1H, 2-H), 6.70 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 16.0 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.4 Hz, 1H, 3-H), 7.48 (dd, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 8.1 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ = 7.8 Hz, 1H, 5'-H), 7.67 (ddd, $^{3}J_{6'\text{-H},5'\text{-H}}$ = 7.8 Hz, $^{4}J_{6'\text{-H},2'\text{-H}}$ = 1.8 Hz, $^{4}J_{6'\text{-H},4'\text{-H}}$ = 0.9 Hz, 1H, 6'-H), 8.08 (ddd, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 8.1 Hz, $^{4}J_{4'\text{-H},2'\text{-H}}$ = 2.2 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ = 0.9 Hz, 1H, 4'-H), 8.21 (dd, $^{4}J_{2'\text{-H},4'\text{-H}}$ = 2.2 Hz, $^{4}J_{2'\text{-H},6'\text{-H}}$ = 1.8 Hz, 1H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.69 ($C(CH_3)_3$), 66.53 (CH_2-1), 82.45 ($C(CH_3)_3$), 121.14 (CH-2'), 122.49 (CH-4'), 126.40 (CH-2), 129.48 (C-5'), 131.23 (CH-3), 132.27 (C-6'), 137.93 (C-1'), 148.52 (C-3'), 153.13 (CO carbonate); IR (neat) ν 2981 (m), 2935 (m), 1742 (s, CO carbonate), 1531 (s, C-N), 1369 (m, N-O), 1351 (s, N-O), 1276 (s), 1255 (s), 1160 (s), 966 (m), 859 (m), 732 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 576 ([2M+NH_4^+], 5), 458 ([2M+NH_4^+]-*t*BuOH-CO_2, 1), 297 ([M+NH_4^+], 100), 241 (3), 52 (23). Anal. Calcd. for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.14; N, 5.02. Found: C, 60.13; H, 6.15; N, 4.88.



236m

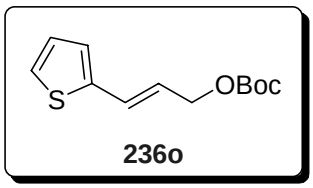
***tert*-Butyl (*E*)-3-(3',5'-Dimethylphenyl)prop-2-en-1-yl Carbonate (236m).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to yield 3,5-dimethyliodobenzene **237m** (252 mg, 35% recovered). Continued elution with a mixture of hexanes and ethyl acetate (99:1) afforded **236m** as a yellowish oil (87 mg, 33%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.51 (s, 9H, *t*-Bu), 2.31 (s, 6H, CH_3), 4.71 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.5 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.27 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.5 Hz, 1H, 2-H), 6.61 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 6.91 (s, 1H, 4'-H), 7.02

(s, 2H, 2'-H and 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 21.19 (CH_3), 27.76 (C(CH_3)$_3$), 67.55 (CH_2-1), 82.09 (C(CH_3)$_3$), 122.44 (CH-2'), 124.52 (CH-2' and CH-6'), 129.77 (CH-4'), 134.64 (CH-3), 136.08 (C-1'), 137.98 (C-3' and C-5'), 153.35 (CO carbonate); IR (neat) ν 2979 (m), 2920 (w), 1740 (s, CO carbonate), 1602 (w), 1369 (m), 1274 (s), 1254 (s), 1163 (s), 853 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 542 ([2M+NH_4^+], 15), 424 ([2M+NH_4^+]-*t*BuOH-CO_2, 100), 280 ([M+NH_4^+], 42), 179 ([M+NH_4^+]-Boc, 40), 162 (MH^+-Boc, 52), 145 (MH^+-Boc-OH, 30), 52 (30). Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.06; H, 8.39.



236n

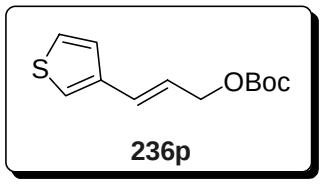
***tert*-Butyl (*E*)-3-(Naphthalen-1'-yl)prop-2-en-1-yl Carbonate (236n).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to give 1-iodonaphthalene **237n** (629 mg, 81% recovered). Continued elution with a mixture of hexanes and ethyl acetate (98.5:1.5) afforded **236n** as a yellowish oil (93 mg, 32%, 56% based on recovered iodide): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.54 (s, 9H, *t*-Bu), 4.85 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 6.4 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.34 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 15.6 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.4 Hz, 1H, 2-H), 7.44 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 15.6 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.3 Hz, 1H, 3-H), 7.46 (m, 1H, 3'-H), 7.50 (m, 1H, 6'-H), 7.52 (m, 1H, 8'-H), 7.61 (d, J_{HH} = 7.2 Hz, 1H, 4'-H), 7.81 (d, J_{HH} = 8.2 Hz, 1H, 2'-H), 7.86 (dd, J_{HH} = 7.71 Hz, $^4J_{6'\text{-H},8'\text{-H}}$ = 2.0 Hz, 1H, 6'-H), 8.11 (dd, J_{HH} = 7.2 Hz, $^4J_{8'\text{-H},6'\text{-H}}$ = 2.0 Hz, 1H, 8'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.77 (C(CH_3)$_3$), 67.52 (CH_2-1), 82.23 (C(CH_3)$_3$), 123.68 (CH-7'), 124.12 (CH-4'), 125.51 (CH-2), 125.79 (CH-8'), 126.11 and 126.12 (CH-3'/6'), 128.33 (CH-2'), 128.47 (CH-5'), 131.07 (C-10'), 131.64 (CH-3), 133.50 (C-1'), 133.95 (C-9'), 153.35 (CO carbonate); IR (neat) ν 2979 (m), 1740 (s, CO carbonate), 1369 (m), 1276 (s), 1254 (s), 1160 (s), 857 (m), 791 (m), 777 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 586 ([2M+NH_4^+], 10), 468 ([2M+NH_4^+]-*t*BuOH-CO_2, 65), 302 ([M+NH_4^+], 30), 201 ([M+NH_4^+]-Boc, 25), 184 (MH^+-Boc, 25), 167 (MH^+-Boc-OH, 100), 52 (10). Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.16; H, 6.92.



236o

***tert*-Butyl (*E*)-3-(Thiophen-2'-yl)prop-2-en-1-yl Carbonate (236o).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to yield **236o** as a yellowish oil (77 mg, 31%).

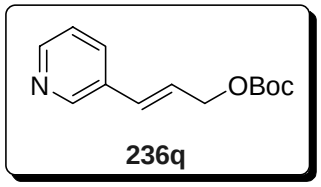
The crude product obtained by procedure **E** was chromatographed on a column of silica gel (5 × 15 cm) with a mixture of hexanes and ethyl acetate (100:0 to 99:1) to produce **236o** as a colourless oil (3.07 g, 64%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 4.67 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.5 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.12 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.7 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.5 Hz, 1H, 2-H), 6.79 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.7 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.3 Hz, 1H, 3-H), 6.96 (dd, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 5.0 Hz, $^{3}J_{4\text{-H},3'\text{-H}}$ = 3.6 Hz, 1H, 4'-H), 6.99 (dd, $^{3}J_{3'\text{-H},4'\text{-H}}$ = 3.6 Hz, $^{4}J_{3'\text{-H},5'\text{-H}}$ = 1.1 Hz, 1H, 3'-H), 7.18(dd, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 5.0 Hz, $^{4}J_{5'\text{-H},3'\text{-H}}$ = 1.1 Hz, 1H, 5'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.75 (C(*C*H$_3$)$_3$), 67.08 (CH_2-1), 82.23 (*C*(CH$_3$)$_3$), 122.29 (CH-2), 124.94 (CH-5'), 126.50 (CH-3'), 127.34 (CH-4'), 127.53 (CH-3), 141.13 (C-1'), 153.26 (CO carbonate); IR (neat) ν 2980 (m), 2933 (w), 1741 (s, CO carbonate), 1650 (w), 1369 (m), 1274 (s), 1254 (s), 1161 (s), 956 (m), 857 (m), 700 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 380 ([2M+NH_4^+]-*t*BuOH-CO_2, 1), 258 ([M+NH_4^+], 5), 157 ([M+NH_4^+]-Boc, 5), 140 (MH^+-Boc, 5), 123 (MH^+-Boc-OH, 25), 52 (100). Anal. Calcd. for $C_{12}H_{16}O_3S$: C, 59.97; H, 6.71. Found: C, 59.75; H, 6.96.



236p

***tert*-Butyl (*E*)-3-(Thiophen-3'-yl)prop-2-en-1-yl Carbonate (236p).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to afford **236p** as a yellowish oil (110 mg, 44%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 4.68 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.6 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.3 Hz, 2H, 1-H), 6.14 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.8 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.6 Hz, 1H, 2-H), 6.67 (ddt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.8 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.3 Hz, $^{4}J_{3\text{-H},4'\text{-H}}$ = 0.6 Hz, 1H, 3-H), 7.19 (dd, $^{4}J_{2'\text{-H},4'\text{-H}}$ = 2.9 Hz, $^{4}J_{2'\text{-H},5'\text{-H}}$ = 1.3 Hz, 1H, 2'-H), 7.20 (dd, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 5.1 Hz, $^{4}J_{5'\text{-H},2'\text{-H}}$ = 1.3 Hz, 1H, 5'-H), 7.27 (ddd, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 5.1 Hz, $^{4}J_{4'\text{-H},2'\text{-H}}$ = 2.9 Hz, $^{4}J_{4'\text{-H},3\text{-H}}$ = 0.6 Hz, 1H, 4'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.73 (C(*C*H$_3$)$_3$), 67.40 (CH_2-1), 82.15 (*C*(CH$_3$)$_3$),

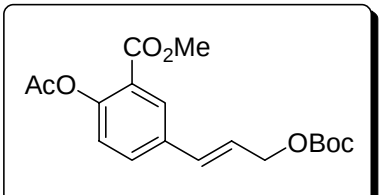
122.59 (CH-2), 123.10 (CH-2'), 124.91 (CH-5'), 126.13 (CH-4'), 128.62 (CH-3), 138.78 (C-3'), 153.27 (CO carbonate); IR (neat) ν 2981 (m), 1741 (s, CO carbonate), 1369 (m), 1275 (s), 1254 (s), 1163 (s) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 240 (M^+, 5), 205 (20), 184 (M^+-$(CH_3)_2C{=}CH_2$, 50), 166 (M^+-*t*BuOH, 100), 140 (M^+-$(CH_3)_2C{=}CH_2$-CO_2, 20), 123 (30), 121 (40), 119 (25), 83 (40); HRMS (EI) 240.0822 [$C_{12}H_{16}O_3S$ (M^+) requires 240.0820].



236q

***tert*-Butyl (*E*)-3-(Pyridne-3'-yl)prop-2-en-1-yl Carbonate (236q).** The crude product obtained by procedure **C** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (60:40) to furnish **236q** as a brown oil (44 mg, 18%).

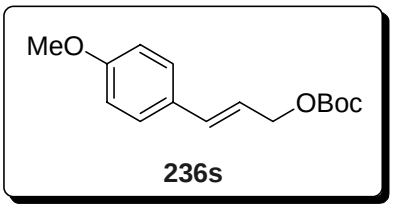
The crude product obtained by procedure **E** was chromatographed on a column of silica gel (5 × 15 cm) with ethyl acetate to afford **236q** as a brown oil (2.22 g, 48%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.45 (s, 9H, *t*-Bu), 4.68 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 6.2 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.4 Hz, 2H, 1-H), 6.31 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 16.0 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.2 Hz, 1H, 2-H), 6.60 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 16.0 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.4 Hz, 1H, 3-H), 7.19 (dd, $^3J_{5'\text{-H},4'\text{-H}}$ = 8.0 Hz, $^3J_{5'\text{-H},6'\text{-H}}$ = 4.8 Hz, 1H, 5'-H), 7.64 (ddd, $^3J_{4'\text{-H},5'\text{-H}}$ = 8.0 Hz, $^4J_{4'\text{-H},2'\text{-H}}$ = 2.1 Hz, $^4J_{4'\text{-H},6'\text{-H}}$ = 1.6 Hz, 1H, 4'-H), 8.43 (dd, $^3J_{6'\text{-H},5'\text{-H}}$ = 4.8 Hz, $^4J_{6'\text{-H},4'\text{-H}}$ = 1.6 Hz, 1H, 6'-H), 8.55 (d, $^4J_{2'\text{-H},4'\text{-H}}$ = 2.1 Hz, 1H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.62 ($C(CH_3)_3$), 66.77 (CH_2-1), 82.26 ($C(CH_3)_3$), 123.31 (CH-5'), 125.26 (CH-2), 130.20 (CH-3), 131.68 (C-3'), 132.87 (CH-4'), 148.34 (CH-2'), 148.93 (CH-6'), 153.08 (CO carbonate); IR (neat) ν 2980 (w), 1744 (s, CO carbonate), 1280 (s), 1255 (m), 1161 (m) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 236 (MH^+, 100), 180 (MH^+-$(CH_3)_2C{=}CH_2$, 20), 120 (10), 118 (MH^+-$(CH_3)_2C{=}CH_2$-H_2O, 10); HRMS (EI) 236.1289 [$C_{13}H_{18}O_3N$ (MH^+) requires 236.1287]. Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.03; H, 7.35; N, 5.89.



236r

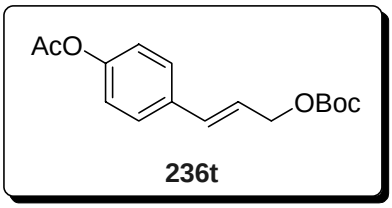
Methyl 2-Acetoxy-5-(*E*)-3'-*tert*-butoxycarbonyloxy-prop-1'-en-1'-yl Benzoate (236r). The crude product obtained by procedure **B** was chromatographed on a column of silica gel

(3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to yield the deacetylated iodide (192 mg); continued elution with a 95:5 mixture gave the starting iodide **237r** (195 mg, 20% recovered). Finally, elution with a 90:10 mixture afforded **236r** (84 mg, 22%) as a yellow oil: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.48 (s, 9H, *t*-Bu), 2.32 (s, 3H, CH_3CO), 3.85 (s, 3H, CH_3O), 4.70 (dd, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 6.2 Hz, $^{4}J_{3'\text{-H},1'\text{-H}}$ = 1.0 Hz, 2H, 3'-H), 6.29 (dt, $^{3}J_{2'\text{-H},1'\text{-H}}$ = 15.9 Hz, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 6.2 Hz, 1H, 2'-H), 6.64 (dt, $^{3}J_{1'\text{-H},2'\text{-H}}$ = 15.9 Hz, $^{4}J_{1'\text{-H},3'\text{-H}}$ = 1.0 Hz, 1H, 1'-H), 7.04 (d, $^{3}J_{3\text{-H},4\text{-H}}$ = 8.4 Hz, 1H, 3-H), 7.54 (dd, $^{3}J_{4\text{-H},3\text{-H}}$ = 8.4 Hz, $^{4}J_{4\text{-H},6\text{-H}}$ = 2.2 Hz, 1H, 4-H), 8.01 (d, $^{4}J_{6\text{-H},4\text{-H}}$ = 2.2 Hz, 1H, 6-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 20.86 (CH_3CO), 27.67 ($C(CH_3)_3$), 52.15 (CH_3O), 66.88 (CH_2-3), 82.26 ($C(CH_3)_3$), 123.12 (C-1), 123.19 (CH-3), 124.53 (CH-2'), 129.79 (CH-6), 131.46 (CH-4), 132.00 (CH-1'), 134.28 (C-5), 150.07 (C-2), 153.16 (CO carbonate), 164.54 (CO benzoate), 169.55 (CO acetate); IR ($CHCl_3$) ν 2980 (m), 1740 (s), 1731 (s), 1369 (s), 1275 (s), 1187 (s), 1081 (s) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 350 (M^+, 1), 319 (4), 294 (M^+-$(CH_3)_2C{=}CH_2$, 14), 252 (100), 220 (30), 191 (30), 159 (25), 158 (18), 103 (15); HRMS (EI) 350.1367 [$C_{18}H_{22}O_7$ (M^+) requires 350.1366]. Anal. Calcd. for $C_{17}H_{22}O_7$: C, 61.71; H, 6.33. Found: C, 61.53; H, 6.47.



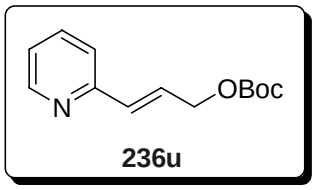
236s

***tert*-Butyl (*E*)-3-(4'-Methoxyphenyl)prop-2-en-1-yl Carbonate (236s).** The crude product obtained by procedure **D** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to give **236s** as a colourless oil (88 mg, 35%), followed by corresponding stilbene derivative (21 mg). **236s**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 3.81 (s, 3H, CH_3O), 4.70 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.7 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.16 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.8 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.7 Hz, 1H, 2-H), 6.62 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.8 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 6.85 (d, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 8.8 Hz, 2H, 3'-H), 7.33 (d, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 8.8 Hz, 2H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.78 ($C(CH_3)_3$), 55.26 (CH_3O), 67.74 (CH_2-1), 82.11 ($C(CH_3)_3$), 113.97 (CH-3'), 120.54 (CH-2), 127.88 (CH-2'), 128.93 (C-1'), 134.25 (CH-3), 153.37 (CO carbonate), 159.56 (C-4'); IR (neat) ν 2979 (m), 1742 (s, CO carbonate), 1610 (m), 1514 (m), 1370 (m), 1275 (s), 1253 (s), 1164 (s), 1034 (m), 849 (m) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 282 ([M+NH_4^+], 0.5), 264 (M^+, 1), 208 (5), 175 (20), 147 ([M+NH_4^+]-NH_3-*t*BuOH-CO_2, 100). Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.32; H, 7.89.



236t

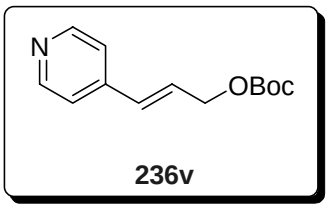
***tert*-Butyl (*E*)-3-(4'-Acetyloxyphenyl)prop-2-en-1-yl Carbonate (236t).** The crude product obtained by procedure **D** was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to yield the starting acetate **239t** (46 mg, 28% recovered). Continued elution with a 92.5:7.5 mixture afforded **236t** (75 mg, 36% based on recovered starting acetate) as a colourless oil; the corresponding stilbene derivative (8 mg) was eluted with an 85:15 mixture. **236t**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 2.29 (s, 3H, CH_3CO), 4.70 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 6.4 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.24 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.9 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 6.4 Hz, 1H, 2-H), 6.64 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.9 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 7.04 (d, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 8.6 Hz, 2H, 3'-H), 7.39 (d, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 8.6 Hz, 2H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 21.06 (CH_3CO), 27.73 ($C(CH_3)_3$), 67.25 (CH_2-1), 82.19 ($C(CH_3)_3$), 121.67 (CH-3'), 123.13 (CH-2), 127.57 (CH-2'), 133.27 (CH-3), 133.94 (C-1'), 150.34 (C-4'), 153.26 (CO carbonate), 169.28 (CO acetate); IR (neat) ν 2981 (m), 1740 (s, CO carbonate), 1507 (m), 1370 (m), 1275 (s), 1255 (s), 1194 (s), 1164 (s) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 602 ([2M+NH_4^+], 1), 484 ([2M+NH_4^+]-*t*BuOH-CO_2, 2), 310 ([M+NH_4^+], 10), 175 ([M+NH_4^+]-NH_3-*t*BuOH-CO_2, 100). Anal. Calcd. for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.60; H, 7.02.



236u

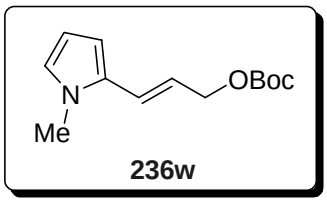
***tert*-Butyl (*E*)-3-(Pyridine-2'-yl)prop-2-en-1-yl Carbonate (236u).** The crude product obtained by procedure **E** was chromatographed on a column of silica gel (5 × 15 cm) with ethyl acetate to afford **236u** as a brown oil: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.46 (s, 9H, *t*-Bu), 4.74 (d, $^{3}J_{1\text{-H},2\text{-H}}$ = 4.7 Hz, 2H, 1-H), 6.69 (d, $^{3}J_{3\text{-H},2\text{-H}}$ = 15.8 Hz, 1H, 3-H), 6.75 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 15.8 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 4.7 Hz, 1H, 2-H), 7.09 (ddd, $^{3}J_{5'\text{-H},4'\text{-H}}$ = 7.6 Hz, $^{3}J_{5'\text{-H},6'\text{-H}}$ = 4.8 Hz, $^{4}J_{5'\text{-H},3'\text{-H}}$ = 1.0 Hz, 1H, 5'-H), 7.24 (ddd, $^{3}J_{3'\text{-H},4'\text{-H}}$ = 7.8 Hz, $^{4}J_{3'\text{-H},5'\text{-H}}$ = 1.0 Hz, $^{5}J_{3'\text{-H},6'\text{-H}}$ = 0.9 Hz, 1H, 3'-H), 7.58 (ddd, $^{3}J_{4'\text{-H},3'\text{-H}}$ = 7.8 Hz, $^{3}J_{4'\text{-H},5'\text{-H}}$ = 7.6 Hz, $^{4}J_{4'\text{-H},6'\text{-H}}$ = 1.8 Hz, 1H, 4'-H), 8.51 (ddd, $^{3}J_{6'\text{-H},5'\text{-H}}$ = 4.8 Hz, $^{4}J_{6'\text{-H},4'\text{-H}}$ = 1.8 Hz, $^{5}J_{6'\text{-H},3'\text{-H}}$ = 0.9 Hz, 1H, 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.66 ($C(CH_3)_3$), 66.57 (CH_2-1), 82.13 ($C(CH_3)_3$), 121.74 (CH-3'), 122.37 (CH-5'), 127.49 (CH-3), 132.66 (CH-2), 136.37 (CH-4'), 149.46

(CH-6'), 153.15 (CO carbonate), 154.48 (C-2'); IR (neat) ν 2980 (w), 1741 (s, CO carbonate), 1278 (s), 1254 (s), 1161 (s) cm^{-1}; MS (CI-isobutane, 150 °C) *m*/*z* (%) 236 (MH^+, 100), 180 (MH^+-$(CH_3)_2C{=}CH_2$, 20), 120 (MH^+-$(CH_3)_2C{=}CH_2$-H_2O, 40); HRMS (CI-isobutane) 236.1289 [$C_{13}H_{18}O_3N$ (MH^+) requires 236.1287). Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.22; H, 7.27; N, 6.07.



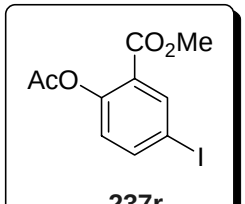
236v

***tert*-Butyl (*E*)-3-(Pyridine-4'-yl)prop-2-en-1-yl Carbonate (236v).** A solution of the allyl alcohol **264v** (60 mg, 0.44 mmol) in THF (2 mL) was added slowly to a suspension of sodium hydride (54 mg, 1.30 mmol, 60% suspension in mineral oil, 3 × washed with dry THF) in THF (3 mL) at room temperature and the mixture was stirred for 1 h. The resulting solution was added slowly to a solution of Boc anhydride (226 mg, 1.04 mmol) in THF (7 mL) at room temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (5 mL), the mixture was diluted with ether (100 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (60:40) to furnish **236v** as a yellow oil (50 mg, 48%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.49 (s, 9H, *t*-Bu), 4.73 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 5.7 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 6.48 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 16.0 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 5.7 Hz, 1H, 2-H), 6.59 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 16.0 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 7.22 (d, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.0 Hz, 2H, 3'-H and 5'-H), 8.54 (d, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.0 Hz, 2H, 2'-H and 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.71 ($C(CH_3)_3$), 66.47 (CH_2-1), 82.53 ($C(CH_3)_3$), 120.96 (CH-3' and CH-5'), 127.94 (CH-2), 131.01 (CH-3), 143.47 (C-4'), 150.16 (CH-2' and CH-6'), 153.11 (CO carbonate); IR (neat) ν 2980 (m), 1742 (s, CO carbonate), 1596 (m), 1369 (m), 1277 (s), 1255 (s), 1162 (s), 1119 (m), 849 (m) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 235 (M^+, 10), 179 (M^+-$(CH_3)_2C{=}CH_2$, 45), 135 (M^+-$(CH_3)_2C{=}CH_2$-CO_2, 10), 118 (MH^+-$(CH_3)_2C{=}CH_2$-CO_2-H_2O, 30), 28 (100); HRMS (EI) 235.1207 [$C_{13}H_{17}NO_3$ (M^+) requires 235.1208]. Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.20; H, 7.34; N, 5.81.



236w

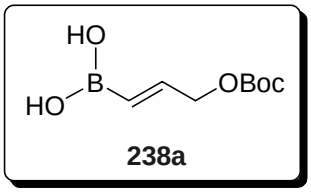
***tert*-Butyl (*E*)-3-(*N*-Methylpyrrol-2'-yl)prop-2-en-1-yl Carbonate (236w).** The crude product obtained by procedure **E** was chromatographed on a column of neutral alumina (3 × 15 cm) with a mixture of hexanes, ethyl acetate and Et_3N (74:25:1) to give **236w** as a brown oil (200 mg, 31%): ^{1}H-NMR (400.1 MHz, C_6D_6) δ 1.35 (s, 9H, *t*-Bu), 2.72 (s, 3H, CH_3), 4.60 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 6.6 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.2 Hz, 2H, 1-H), 5.94 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 15.7 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.6 Hz, 1H, 2-H), 6.16 (dd, $^3J_{4'\text{-H},3'\text{-H}}$ = 3.7 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 2.6 Hz, 1H, 4'-H) 6.20 (dd, $^3J_{5'\text{-H},4'\text{-H}}$ = 2.6 Hz, $^4J_{5'\text{-H},3'\text{-H}}$ = 1.6 Hz, 1H, 5'-H), 6.31 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 15.7 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.2 Hz, 1H, 3-H), 6.41 (dd, $^3J_{3'\text{-H},4'\text{-H}}$ = 3.7 Hz, $^4J_{3'\text{-H},5'\text{-H}}$ = 1.6 Hz, 1H, 3'-H); ^{13}C-NMR (100.6 MHz, C_6D_6) δ 27.76 (C(*C*H_3)$_3$), 33.32 (CH_3), 67.92 (CH_2-1), 81.16 (*C*(CH_3)$_3$), 108.30 (CH-3'), 108.47 (CH-4'), 119.72 (CH-2), 123.58 (CH-5'), 123.85 (CH-3), 130.53 (C-2'), 154.17 (CO carbonate); MS (EI, 150 °C) *m*/*z* (%) 237 (M^+, 80), 181 (M^+-$(CH_3)_2C{=}CH_2$, 80), 137 (M^+-$(CH_3)_2C{=}CH_2$-CO_2, 52), 120 (80), 57 (100); HRMS (EI) 237.1362 [$C_{13}H_{19}NO_3$ (M^+) requires 237.1365].



237r

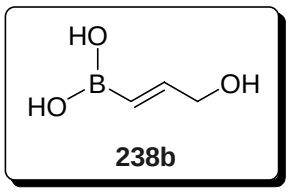
Methyl 2-Acetoxy-5-iodobenzoate (237r).[208] Concentrated H_2SO_4 (10 drops) was added to a solution of 5-iodosalicylic acid (1.515 g, 5.73 mmol) in methanol (10 mL) and the resulting mixture was heated at 80 °C for 8 h. The mixture was cooled and poured slowly into an ice-water mixture (100 mL). White crystals which precipitated were collected by filtration and washed to neutral pH with 5% aqueous sodium hydrogencarbonate and distilled water, consecutively. The crude crystals were dissolved in acetic anhydride (3 mL, 31 mmol), concentrated H_2SO_4 (5 drops) was added, and the reaction mixture was stirred at room temperature for three days. The reaction mixture was then diluted with $CHCl_3$ (40 mL) and the resulting solution was washed with 5% aqueous sodium hydrogencarbonate three times. The organic layer was dried (Na_2SO_4) and evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (92:8) to give **237r** as a white solid (1.544 g, 84%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.34 (s, 3H, CH_3CO), 3.87 (s, 3H, CH_3O), 6.86 (d, $^3J_{3\text{-H},4\text{-H}}$ = 8.5

Hz, 1H, 3-H), 7.85 (dd, $^{3}J_{4\text{-H},3\text{-H}}$ = 8.5 Hz, $^{4}J_{4\text{-H},6\text{-H}}$ = 2.2 Hz, 1H, 4-H), 8.32 (d, $^{4}J_{6\text{-H},4\text{-H}}$ = 2.2 Hz, 1H, 6-H); consistent with the literature data.[208]



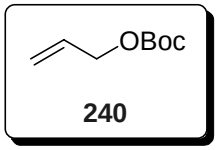
238a

1-(*tert*-Butyloxycarbonyl)prop-2-en-1-ol-3-yl Boronic acid (238a). Cyclohexene (165 mg, 2.01 mmol) was added to a mixture of a 1.0M solution of borane in THF (1.0 mL, 1.0 mmol) and THF (1 mL) at 0 °C and the mixture was stirred for 1.5 h. The resulting solution was evaporated in vacuum to form a white solid, to which were added neat catecholborane (1.34 g, 11.2 mmol) and then carbonate **266a** (1.50 g, 9.6 mmol) at room temperature (spontaneous heating is desired for high yield) and the resulting mixture was stirred at room temperature overnight. The reaction was quenched with water (10 mL) and the mixture was stirred for 2 h. The resulting suspension was filtered off, yielding **238a** as a white solid (710 mg, 36%). The filtrate was extracted with ethyl acetate (3 × 20 mL) and combined organic layers were dried (Na_2SO_4) and evaporated. The residue was chromatographed on a column of silica gel (5 × 5 cm) with a mixture of hexanes and ethyl acetate (80:20), which eluted catechol. Continued elution with ethyl acetate afforded boronic acid **238a** as a white foam 504 mg, 26%). The combined yield of boronic acid **238a** was 1.210 g (62%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.48 (s, 9H, *t*-Bu), 4.69 (dd, $^{3}J_{1\text{-H},2\text{-H}}$ = 4.5 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.7 Hz, 2H, 1-H), 5.76 (dt, $^{3}J_{3\text{-H},2\text{-H}}$ = 17.9 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.7 Hz, 1H, 3-H), 6.91 (dt, $^{3}J_{2\text{-H},3\text{-H}}$ = 17.9 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 4.5 Hz, 1H, 2-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ 27.70 (C(*C*H_3)$_3$), 67.49 (CH_2-1), 82.40 (*C*(CH_3)$_3$), 122.45 (CH-3), 149.18 (CH-2), 153.15 (CO carbonate); MS (EI) *m*/*z* (%) 384 (3(M+H^+-H_2O-*t*Bu), 20), 322 (3(M+H^+-H_2O-*t*Bu-$H_2O.CO_2$), 10), 278 (3(M+H^+-H_2O-*t*Bu-$H_2O.CO_2$-CO_2), 10), 216 (7), 177 (8); HRMS (EI) 384.0844 [$C_{12}H_{15}O_{12}B_3$ trimer (M+H^+-H_2O-*t*Bu) requires 384.0842]; IR ($CHCl_3$) ν 3328 (m), 2977 (w), 1748 (s), 1645 (w), 1394 (m), 1349 (m), 1279 (m), 1248 (m), 1159 (m), 1138 (m), 1113 (m), 1074 (m) cm^{-1}. Anal. Calcd. for $C_8H_{15}BO_5$: C, 47.56; H, 7.48. Found: C, 47.68; H, 7.34.



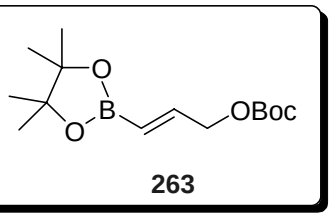
238b

Prop-2-en-1-ol-3-yl Boronic acid (238b).[197] Neat catecholborane (13.25 g, 110.5 mmol) was added slowly to neat propargyl alcohol (2.76 g, 50.8 mmol) at room temperature over a period of 15 min. After the addition has been completed, the mixture was heated at 70 °C for 1 h. White precipitate that was formed during the course of the reaction was dissolved in a small amount of a mixture of MeOH and CH_2Cl_2 (1:1) and chromatographed on a column of silica gel (5 × 5 cm): a mixture of hexanes and ethyl acetate (50:50) eluted catechol; continued elution with a mixture of CH_2Cl_2 and MeOH (90:10) furnished boronic acid **238b** as a white foam (2.08 g, 40%): ^{1}H-NMR (400.1 MHz, CD_3OD) δ 4.10 (dd, $^3J_{1\text{-}H,2\text{-}H}$ = 4.2 Hz, $^4J_{1\text{-}H,3\text{-}H}$ = 1.9 Hz, 2H, 1-H), 5.80 (dt, $^3J_{3\text{-}H,2\text{-}H}$ = 17.8 Hz, $^4J_{3\text{-}H,1\text{-}H}$ = 1.9 Hz, 1H, 3-H), 6.60 (dt, $^3J_{2\text{-}H,3\text{-}H}$ = 17.8 Hz, $^3J_{2\text{-}H,1\text{-}H}$ = 4.2 Hz, 1H, 2-H); ^{13}C-NMR (100.6 MHz, CD_3OD) δ 64.78 (CH_2-1), 123.10 (CH-3), 151.75 (CH-2).



240

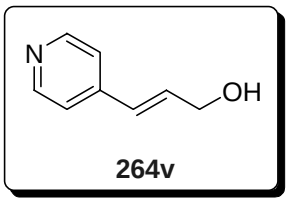
***tert*-Butyl Prop-2-en-1-yl Carbonate (240).**[222] Fraction distillation of the crude product obtained by procedure **A** yielded **240** as a colourless oil (7.89 g, 50%): bp 40 °C at 270 Pa; ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.46 (s, 9H, *t*-Bu), 4.53 (ddd, $^3J_{1\text{-}H,2\text{-}H}$ = 5.8 Hz, $^4J_{1\text{-}H,3\text{-}Ha}$ = 1.4 Hz, $^4J_{1\text{-}H,3\text{-}Hb}$ = 1.3 Hz, 2H, 1-H), 5.22 (ddd, $^3J_{3\text{-}Hb,2\text{-}H}$ = 10.5 Hz, $^2J_{3\text{-}Hb,3\text{-}Ha}$ = 2.8 Hz, $^4J_{3\text{-}Hb,1\text{-}H}$ = 1.3 Hz, 1H, 3-Hb), 5.31 (ddd, $^3J_{3\text{-}Ha,2\text{-}H}$ = 17.2 Hz, $^2J_{3\text{-}Ha,3\text{-}Hb}$ = 2.8 Hz, $^4J_{3\text{-}Ha,1\text{-}H}$ = 1.4 Hz, 1H, 3-Ha), 5.90 (ddt, $^3J_{2\text{-}H,3\text{-}Ha}$ = 17.2 Hz, $^3J_{2\text{-}H,3\text{-}Hb}$ = 10.5 Hz, $^3J_{2\text{-}H,1\text{-}H}$ = 5.8 Hz, 1H, 2-H). Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.70; H, 8.96.



263

Pinacolyl 1-(*tert*-Butyloxycarbonyl)prop-2-en-1-ol-3-yl Boronate (263). Cyclohexene (164 mg, 2.00 mmol) was added to a mixture of a 1.0M solution of borane in THF (1.0 mL, 1.0 mmol) and THF (1 mL) at 0 °C and the mixture was stirred for 1.5 h. The resulting solution was evaporated in vacuum to form a white solid, to which was added neat pinacolborane (1.41 g, 11.0 mmol). Carbonate **266a** (1.56 g, 10.0 mmol) was then

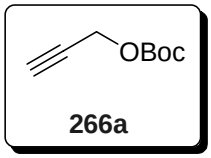
slowly added and the reaction mixture heated spontaneously. The resulting mixture was stirred at room temperature overnight, the reaction was quenched with water (2 mL) and the mixture was stirred for 1 h. The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the combined organic layers were dried (Na_2SO_4) and evaporated to yield boronate **263** (2.70 g, 95%): bp 110-111 °C at 270 Pa; ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.20 (s, 12H, CH_3), 1.42 (s, 9H, *t*-Bu), 4.58 (dd, $^3J_{1\text{-H},2\text{-H}}$ = 4.8 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.8 Hz, 2H, 1-H), 5.63 (dt, $^3J_{3\text{-H},2\text{-H}}$ = 18.1 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.8 Hz, 1H, 3-H), 6.55 (dt, $^3J_{2\text{-H},3\text{-H}}$ = 18.1 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 4.8 Hz, 1H, 2-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 24.65 ($C(CH_3)_2$), 27.65 ($C(CH_3)_3$), 67.76 (CH_2-1), 82.03 ($C(CH_3)_3$) , 83.27 ($C(CH_3)_2$), 120.25 (CH-3), 145.66 (CH-2), 153.13 (CO carbonate); MS (CI) *m/z* (%) 285 (9, $M+H^+$), 284 (2, M+), 229 (100, $M+H^+$-*t*Bu), 228 (25, M^+-*t*Bu), 185 (7, $M+H^+$-*t*Bu-CO_2), 119 (20), 101 (35);HRMS (CI) 285.1871 [$C_{14}H_{26}BO_5$ $(M+H)^+$ requires 285.1873]; IR ($CHCl_3$) 2980 (s), 1744 (s), 1648 (m), 1458 (w), 1370 (m), 1350 (m), 1329 (m), 1278 (s), 1255 (s), 1165 (m), 1145 (s), 1118 (m) cm^{-1}; Anal. Calcd. for $C_{14}H_{25}BO_5$: C, 59.18; H, 8.87. Found: C, 59.32; H, 8.83.



264v

(*E*)-3-(Pyridine-4'-yl)prop-2-en-1-ol (264v). *n*-Butyllithium (1.1 mL, 2.2 mmol, 2.0M solution in pentane) was added slowly to a solution of triethylphosphonoacetate **241** (450 mg, 2.01 mmol) in THF (5 mL) at –83 °C and the mixture was stirred for 5 min. Pyridine-4-carbaldehyde **143v** (214 mg, 2.00 mmol) was then slowly added and the resulting mixture was stirred at –83 °C for an additional 10 min and then at room temperature for 2 h. The reaction was quenched with brine (5 mL), the mixture was diluted with ether (100 mL) and washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. The crude ethyl ester **265v** was dissolved in THF (5 mL), cooled to -83 °C, DIBAL-H (3.2 mL, 4.8 mmol, 1.5M solution in toluene) was added slowly, and the resulting mixture was stirred for an additional 2 h at this temperature. The reaction was quenched with MeOH (5 mL) and then a saturated aqueous solution of potassium-sodium tartrate (10 mL) was added. The resulting mixture was stirred at 40 °C and a solid potassium-sodium tartrate (approximately 2 g) was added in portions, until the solution became homogeneous. The resulting mixture was diluted with ether (100 mL), washed with an aqueous saturated solution of potassium-sodium tartrate (3 × 50 mL), dried (Na_2SO_4), and evaporated. The residue was chromatographed on a column of silica gel (3 × 10 cm) with ethyl acetate to afford **264v** as a white solid (105 mg, 39%): mp 90-91 °C ($CHCl_3$);

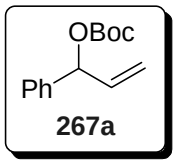
^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.52 (s, 1H, OH), 4.39 (m, 2H, 1-H), 6.58-6.60 (m, 2H, 2-H and 3-H), 7.24 (d, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 6.2 Hz, 2H, 3'-H and 5'-H), 8.52 (d, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 6.2 Hz, 2H, 2'-H and 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 62.86 (CH_2-1), 120.95 (CH-3' and CH-5'), 127.66 and 133.94 (CH-2 and CH-3), 144.30 (C-4'), 149.99 (CH-6'); IR ($CHCl_3$) 3019 (m), 1220 (m), 1211 (m), 784 (m) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 135 (M^+, 75), 117 (M^+-H_2O, 20), 106 (85), 93 (100); HRMS (EI) 135.0686 [C_8H_9NO (M^+) requires 135.0684].



266a

***tert*-Butyl Prop-2-yn-1-yl Carbonate (266a).** Fraction distillation of the crude product obtained by procedure **A** gave **266a** as a colourless liquid (25.60 g, 82%): bp 47-49 °C at 270 Pa ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.47 (s, 9H, *t*-Bu), 2.50 (t, $^{4}J_{3\text{-H},1\text{-H}}$ = 2.5 Hz, 1H, 3-H), 4.64 (d, $^{4}J_{1\text{-H},3\text{-H}}$ = 2.5 Hz, 2H, 1-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.6 ($C(CH_3)_3$), 54.2 (CH_2-1), 75.2 (CH-3), 77.2 (C-2), 82.9 ($C(CH_3)_3$), 152.6 (CO carbonate); MS (CI) *m*/*z* (%) 157 ($M+H^+$, 100), 139 (5), 119 (5), 101 (20), 81 (22); HRMS (CI) 157.0862 [$C_8H_{13}O_3$ $(M+H)^+$ requires 157.0865]; IR ($CHCl_3$): ν 3296 (m), 2983 (w), 1747 (s), 1395 (m), 1371 (m), 1280 (m), 1256 (m), 1158 (m), 1097 (m) cm^{-1}; Anal. Calcd. for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.54; H, 7.80.

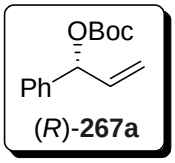
6.4. Synthesis of Branched Carbonates



267a

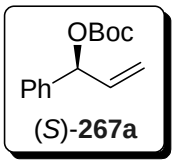
(±)-*tert*-Butyl 1-Phenylprop-2-en-1-yl Carbonate (267a). Phenylpropenol (±)-**269a** (3.405 g, 25.37 mmol) was added slowly to a suspension of sodium hydride (1.6 g, 40 mmol, 60% suspension in mineral oil, 3 × washed with dry THF) in THF (35 mL) at room temperature and the mixture was stirred for 1 h. The resulting solution was added slowly to a solution of Boc anhydride (6.024 g, 27.60 mmol) in THF (100 mL) at room temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (15 mL), diluted with ether (300 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave (±)-**267a** as a colourless oil

(5.672 g, 95%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.48 (s, 9H, *t*-Bu), 5.26-5.33 (m, 2H, 3-H), 6.00-6.09 (m, 2H, 1-H and 2-H), 7.29-7.40 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.76 ($C(CH_3)_3$), 79.18 (CH-1), 82.28 ($C(CH_3)_3$), 117.10 (CH_2-3), 126.97 (CH-2'), 128.14 (CH-4'), 128.51 (CH-3'), 136.18 (CH-2), 138.69 (C-1'), 152.71 (CO carbonate); MS (EI, 150 °C) *m*/*z* (%) 234 (M^+, 80), 178 (M^+-$(CH_3)_2C{=}CH_2$, 98), 177 (100); HRMS (EI) 234.1258 [$C_{14}H_{18}O_3$ (M^+) requires 234.1256]. Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.64; H, 7.72.



(*R*)-**267a**

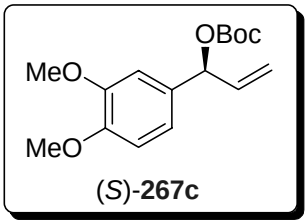
(*R*)-*tert*-Butyl 1-Phenylprop-2-en-1-yl Carbonate (*R*)-(267a). *n*-Butyllithium (6.5 mL, 13.0 mmol, 2.0M solution in pentane) was added to a cold (0 °C) solution of phenylpropenol (*R*)-**269a** (1.742 g, 12.98 mmol) in THF (15 mL). The resulting solution was stirred at 0 °C for 10 min and then transferred (*via* cannula) to a solution of Boc anhydride (2.974 mg, 13.63 mmol) in THF (30 mL) at 20 °C, and the mixture was stirred at this temperature for 3 h (TLC monitoring). The reaction was quenched with brine (20 mL), the mixture was diluted with ether (200 mL), washed with brine (3 × 100 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave (*R*)-**267a** as a colourless oil (2.804 g, 92%): $[\alpha]_D$ +29.2 (*c* 0.94, $CHCl_3$), >99% ee, chiral HPLC (Chiracel OJ-H, hexane/2-propanol 99:1, 0.500 mL.min^{-1}) t_R = 14.59 min ((*R*)-**267a**), t_R = 19.13 min ((*S*)-**267a**).



(*S*)-**267a**

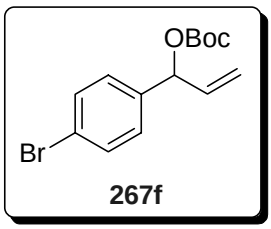
(*S*)-*tert*-Butyl 1-Phenylprop-2-en-1-yl Carbonate (*S*)-(267a). *n*-Butyllithium (2.5 mL, 5.0 mmol, 2.0M solution in pentane) was added to a cold (0 °C) solution of phenylpropenol (*S*)-**269a** (675 mg, 5.03 mmol) in THF (5 mL). The resulting solution was stirred at 0 °C for 10 min and then transferred (*via* cannula) to a solution of Boc anhydride (1.221 mg, 5.59 mmol) in THF (25 mL) at 20 °C, and the mixture was stirred at this temperature for 3 h (TLC monitoring). The reaction was quenched with brine (15 mL), the mixture was diluted with ether (50 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave (*S*)-**267a** as a colourless oil (1.132 g, 96%): $[\alpha]_D$

-25.6 (*c* 0.99, $CHCl_3$), >99% ee, chiral HPLC (Chiracel OJ-H, hexane/2-propanol 99:1, 0.500 mL.min^{-1}) t_R = 14.59 min ((*R*)-**267a**), t_R = 19.13 min ((*S*)-**267a**).



(*S*)-**267c**

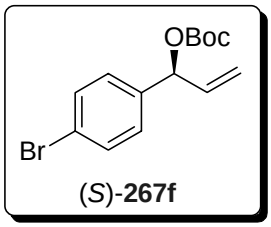
(*S*)-*tert*-Butyl 1-(3',4'-dimethoxyphenyl)prop-2-en-1-yl Carbonate (*S*)-(267c). *n*-Butyllithium (7.3 mL, 14.6 mmol, 2.0M solution in pentane) was added to a cold (0 °C) solution of 1-(3,4-dimethoxyphenyl)prop-2-en-1-ol (*S*)-**269c** (2.837 g, 14.60 mmol) in THF (15 mL). The resulting solution was stirred at 0 °C for 10 min and then transferred (*via* cannula) to a solution of Boc anhydride (3.20 g, 14.7 mmol) in THF (70 mL) at 20 °C, and stirred at this temperature for 3 h (TLC monitoring). The reaction was quenched with brine (20 mL), diluted with ethyl acetate (200 mL), washed with brine (3 × 80 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave (*S*)-**267c** as a light yellow oil (4.26 g, 99%): $[\alpha]_D$ -42.2 (*c* 1.66, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.45 (s, 9H, *t*-Bu), 3.84 (CH_3O), 3.86 (CH_3O), 5.22 (ddd, $^3J_{3\text{-Ha},2\text{-H}}$ = 10.4 Hz, J_{HH} = 1.7 Hz, J_{HH} = 1.3 Hz, 1H, 3-Ha), 5.29 (ddd, $^3J_{3\text{-Hb},2\text{-H}}$ = 17.1 Hz, J_{HH} = 1.5 Hz, J_{HH} = 1.2 Hz, 1H, 3-Hb), 5.94-5.96 (m, 1H, 1-H), 6.01 (ddd, $^3J_{2\text{-H},3\text{-Hb}}$ = 17.1 Hz, $^3J_{2\text{-H},3\text{-Ha}}$ = 10.4 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 5.9 Hz, 1H, 2-H), 6.82 (d, $^3J_{5'\text{-H},6'\text{-H}}$ = 8.2 Hz, 1H, 5'-H), 6.87 (d, $^4J_{2'\text{-H},6'\text{-H}}$ = 2.0 Hz, 1H, 2'-H), 6.91 (dd, $^3J_{6'\text{-H},5'\text{-H}}$ = 8.2 Hz, $^4J_{6'\text{-H},2'\text{-H}}$ = 2.0Hz, 1H, 6'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.67 (C(*C*H_3)$_3$), 55.75 (2 × CH_3O), 78.96 (CH-1), 82.17 (*C*(CH_3)$_3$), 110.02 (CH-2'), 110.78 (CH-5'), 116.67 (CH_2-3), 119.69 (CH-6'), 131.04 (CH-1'), 136.10 (CH-2), 148.85, and 148.86 (C-3', and C-4'), 152.62 (CO carbonate); MS (CI) *m*/*z* (%) 295 ([M+H$^+$], 90), 177 (100); HRMS (CI) 295.1537 [$C_{16}H_{23}O_5$ (M+H$^+$) requires 295.1545].



267f

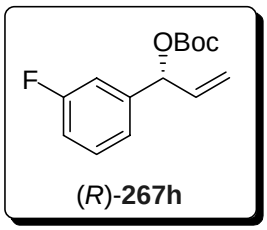
(±)-1-(4'-Bromophenyl)prop-2-en-1-yl *tert*-Butyl Carbonate (±)-(267f). 1-(4'-Bromophenyl)prop-2-en-1-ol (±)-**269f** (13.94 g, 65.4 mmol) was added slowly to a suspension of sodium hydride (2.51 g, 104.6 mmol, neat) in THF (70 mL) at room temperature and the mixture was stirred for 10 min. The resulting solution was added slowly to a solution of Boc anhydride (16.24 g, 74.4 mmol) in THF (100 mL) at room

temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (20 mL), diluted with ether (300 mL), washed with brine (3 × 100 mL), dried (Na_2SO_4), and evaporated. Gradient chromatography on a column of silica gel (10 × 10 cm) with a mixture of hexanes and ethyl acetate (100:0 to 98:2) gave (±)-**267f** as a yellowish oil (17.44 g, 85%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 5.27-5.36 (m, 2H, 3-H), 5.97-6.06 (m, 2H, 1-H and 2-H), 7.28 (d, $^3J_{HH}$ = 8.6 Hz, 2H, H-arom), 7.52 (d, $^3J_{HH}$ = 8.6 Hz, 2H, H-arom); MS (CI-NH_3, 145 °C) *m*/*z* (%) 642/644/646 ([2M+NH_4^+], 3), 524/526/528 ([2M+NH_4^+]-*t*BuOH-CO_2, 25), 330/332 ([M+NH_4^+], 30), 229/231 ([M+NH_4^+]-Boc, 35), 212/214 (MH^+-Boc, 100), 195/197 (MH^+-Boc-OH, 85). Anal. Calcd. for $C_{14}H_{17}BrO_3$: C, 53.69; H, 5.47. Found: C, 53.72; H, 5.51.



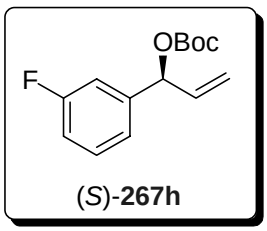
(*S*)-**267f**

(*S*)-1-(4'-Bromophenyl)prop-2-en-1-yl *tert*-Butyl Carbonate (*S*)-(267f). *n*-Butyllithium (6.0 mL, 12.0 mmol, 2.0M solution in pentane) was added to a cold (0 °C) solution of 1-(4-bromophenyl)prop-2-en-1-ol (*S*)-**269f** (2.575 g, 12.08 mmol) in THF (15 mL). The resulting solution was stirred at 0 °C for 10 min and then transferred (*via* cannula) to a solution of Boc anhydride (2.65 g, 12.1 mmol) in THF (60 mL) at 20 °C, and stirred at this temperature for 3 h (TLC monitoring). The reaction was quenched with brine (20 mL), diluted with ethyl acetate (200 mL), washed with brine (3 × 80 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave (*S*)-**267f** as a light yellow oil (3.45 g, 91%): $[\alpha]_D$ -22.6 (*c* 1.99, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.50 (s, 9H, *t*-Bu), 5.27-5.36 (m, 2H, 3-H), 5.97-6.06 (m, 2H, 1-H and 2-H), 7.28 (d, $^3J_{HH}$ = 8.6 Hz, 2H, H-arom), 7.52 (d, $^3J_{HH}$ = 8.6 Hz, 2H, H-arom); MS (CI-NH_3, 145 °C) *m*/*z* (%) 642/644/646 ([2M+NH_4^+], 3), 524/526/528 ([2M+NH_4^+]-*t*BuOH-CO_2, 25), 330/332 ([M+NH_4^+], 30), 229/231 ([M+NH_4^+]-Boc, 35), 212/214 (MH^+-Boc, 100), 195/197 (MH^+-Boc-OH, 85). Anal. Calcd. for $C_{14}H_{17}BrO_3$: C, 53.69; H, 5.47. Found: C, 53.72; H, 5.51.



(*R*)-**267h**

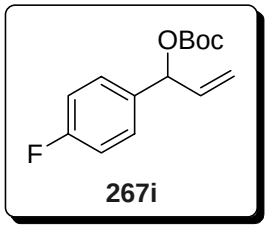
(*R*)-*tert*-Butyl 1-(3'-fluorophenyl)prop-2-en-1-yl Carbonate (*R*)-(267h). *n*-Butyllithium (16 mL, 32 mmol, 2.0M solution in pentane) was added to a cold (0 °C) solution of 1-(3-fluorophenyl)prop-2-en-1-ol (*R*)-**269h** (4.679 g, 30.74 mmol) in THF (30 mL). The resulting solution was stirred at 0 °C for 10 min and then transferred (*via* cannula) to a solution of Boc anhydride (7.10 g, 32.5 mmol) in THF (100 mL) at 20 °C, and stirred at this temperature for 3 h (TLC monitoring). The reaction was quenched with brine (20 mL), diluted with ether (300 mL), washed with brine (3 × 100 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave (*R*)-**267h** as a light yellow oil (7.60 g, 98%): $[\alpha]_D$ +14.2 (*c* 4.43, $CHCl_3$), >99% ee, chiral HPLC (Chiracel OJ-H, hexane/2-propanol 99:1, 0.500 mL.min^{-1}) t_R = 10.20 min ((*R*)-**267h**), t_R = 12.06 min ((*S*)-**267h**); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.48 (s, 9H, *t*-Bu), 5.25-5.36 (m, 2H, 3-H), 5.99 (ddd, $^3J_{2\text{-H},3\text{-Ha}}$ = 16.1 Hz, $^3J_{2\text{-H},3\text{-Hb}}$ = 10.7 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.2 Hz, 1H, 2-H), 6.05 (m, 1H, 1-H), 6.98 (dddd, $^3J_{4'\text{-H},F}$ = 8.5 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 8.5 Hz, $^4J_{4'\text{-H},2'\text{-H}}$ = 2.6 Hz, $^4J_{4'\text{-H},6'\text{-H}}$ = 1.0 Hz, 1H, 4'-H), 7.08 (ddd, $^3J_{2'\text{-H},F}$ = 9.6 Hz, $^4J_{2'\text{-H},4'\text{-H}}$ = 2.6 Hz, $^4J_{2'\text{-H},6'\text{-H}}$ = 1.0 Hz, 1H, 2'-H), 7.14 (dddd, $^3J_{6'\text{-H},5'\text{-H}}$ = 7.6 Hz, $^4J_{6'\text{-H},2'\text{-H}}$ = 1.0 Hz, $^4J_{6'\text{-H},4'\text{-H}}$ = 1.0 Hz, $^5J_{6'\text{-H},F}$ = 0.4 Hz, 1H, 6'-H), 7.31 (ddd, $^3J_{5'\text{-H},4'\text{-H}}$ = 8.5 Hz, $^3J_{5'\text{-H},6'\text{-H}}$ = 7.6 Hz, $^4J_{5'\text{-H},F}$ = 5.8 Hz, 1H, 5'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.74 (C(*C*H_3)$_3$), 78.37 (d, $^4J_{CF}$ = 1.9 Hz, CH-1), 82.59 (*C*(CH_3)$_3$), 113.89 (d, $^2J_{CF}$ = 22.4 Hz, CH-2'), 115.05 (d, $^2J_{CF}$ = 21.2 Hz, CH-4'), 117.65 (CH_2-3), 122.52 (d, $^4J_{CF}$ = 3.0 Hz, CH-6'), 130.07 (d, $^3J_{CF}$ = 8.2 Hz, CH-5'), 135.71 (CH-2), 141.35 (d, $^3J_{CF}$ = 7.1 Hz, C-1'), 152.60 (CO carbonate), 162.89 (d, $^1J_{CF}$ = 246.4 Hz, CF-3'); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.06.



(*S*)-**267h**

(*S*)-*tert*-Butyl 1-(3'-fluorophenyl)prop-2-en-1-yl Carbonate (*S*)-(267h). *n*-Butyllithium (15 mL, 30 mmol, 2.0M solution in pentane) was added to a cold (0 °C) solution of 1-(3-fluorophenyl)prop-2-en-1-ol (*S*)-**269h** (4.50 g, 29.6 mmol) in THF (30 mL). The resulting solution was stirred at 0 °C for 10 min and then transferred (*via* cannula) to a solution of Boc anhydride (6.92 g, 31.7 mmol) in THF (100 mL) at 20 °C, and stirred at

this temperature for 3 h (TLC monitoring). The reaction was quenched with brine (20 mL), the mixture was diluted with ether (300 mL), washed with brine (3 × 100 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave (*S*)-**267h** as a light yellow oil (7.24 g, 97%): $[\alpha]_D$ -14.1 (*c* 3.58, $CHCl_3$), >99% ee, chiral HPLC (Chiracel OJ-H, hexane/2-propanol 99:1, 0.500 mL.min^{-1}) t_R = 10.20 min ((*R*)-**267h**), t_R = 12.06 min ((*S*)-**267h**); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.48 (s, 9H, *t*-Bu), 5.25-5.36 (m, 2H, 3-H), 5.99 (ddd, $^3J_{2\text{-H},3\text{-Ha}}$ = 16.1 Hz, $^3J_{2\text{-H},3\text{-Hb}}$ = 10.7 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.2 Hz, 1H, 2-H), 6.05 (m, 1H, 1-H), 6.98 (dddd, $^3J_{4'\text{-H},F}$ = 8.5 Hz, $^3J_{4'\text{-H},5'\text{-H}}$ = 8.5 Hz, $^4J_{4'\text{-H},2'\text{-H}}$ = 2.6 Hz, $^4J_{4'\text{-H},6'\text{-H}}$ = 1.0 Hz, 1H, 4'-H), 7.08 (ddd, $^3J_{2'\text{-H},F}$ = 9.6 Hz, $^4J_{2'\text{-H},4'\text{-H}}$ = 2.6 Hz, $^4J_{2'\text{-H},6'\text{-H}}$ = 1.0 Hz, 1H, 2'-H), 7.14 (dddd, $^3J_{6'\text{-H},5'\text{-H}}$ = 7.6 Hz, $^4J_{6'\text{-H},2'\text{-H}}$ = 1.0 Hz, $^4J_{6'\text{-H},4'\text{-H}}$ = 1.0 Hz, $^5J_{6'\text{-H},F}$ = 0.4 Hz, 1H, 6'-H), 7.31 (ddd, $^3J_{5'\text{-H},4'\text{-H}}$ = 8.5 Hz, $^3J_{5'\text{-H},6'\text{-H}}$ = 7.6 Hz, $^4J_{5'\text{-H},F}$ = 5.8 Hz, 1H, 5'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.74 ($C(CH_3)_3$), 78.37 (d, $^4J_{CF}$ = 1.9 Hz, CH-1), 82.59 ($C(CH_3)_3$), 113.89 (d, $^2J_{CF}$ = 22.4 Hz, CH-2'), 115.05 (d, $^2J_{CF}$ = 21.2 Hz, CH-4'), 117.65 (CH_2-3), 122.52 (d, $^4J_{CF}$ = 3.0 Hz, CH-6'), 130.07 (d, $^3J_{CF}$ = 8.2 Hz, CH-5'), 135.71 (CH-2), 141.35 (d, $^3J_{CF}$ = 7.1 Hz, C-1'), 152.60 (CO carbonate), 162.89 (d, $^1J_{CF}$ = 246.4 Hz, CF-3'); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.06.

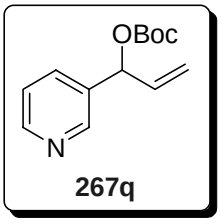


267i

(±)-*tert*-Butyl 1-(4'-Fluorophenyl)prop-2-en-1-yl Carbonate (±)-(267i). 1-(4'-Fluorophenyl)prop-2-en-1-ol (3.030 g, 20.00 mmol) was added slowly to a suspension of sodium hydride (1.6 g, 40 mmol, 60% suspension in mineral oil, 3 × washed with dry THF) in THF (40 mL) at room temperature and the mixture was stirred for 1 h. The resulting solution was added slowly to a solution of Boc anhydride (4.810 g, 22.04 mmol) in THF (70 mL) at room temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (15 mL), diluted with ether (200 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave (±)-**267i** as a colourless oil (4.146 g, 82%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.47 (s, 9H, *t*-Bu), 5.26 (dd, J_{HH} = 9.1 Hz, $^2J_{3\text{-Ha},3\text{-Hb}}$ = 1.2 Hz, 1H, 3-Ha), 5.30 (dd, J_{HH} = 15.7 Hz, $^2J_{3\text{-Hb},3\text{-Ha}}$ = 1.2 Hz, 1H, 3-Hb), 6.01 (m, 2H, 1-H and 2-H), 7.04 (t, $^3J_{3'\text{-H},F}$ = 8.7 Hz, $^3J_{3'\text{-H},2'\text{-H}}$ = 8.7 Hz, 2H, 3'-H), 7.35 (dd, $^3J_{2'\text{-H},3'\text{-H}}$ = 8.7 Hz, $^4J_{2'\text{-H},F}$ = 5.3 Hz, 2H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.74 ($C(CH_3)_3$), 78.39 (CH-1), 82.42

(*C*(CH_3)$_3$), 115.41 (d, $^2J_{CF}$ = 21.6 Hz, CH-3'), 117.24 (CH_2-3), 128.91 (d, $^3J_{CF}$ = 8.3 Hz, CH-2'), 134.53 (d, $^4J_{CF}$ = 3.2 Hz, C-1'), 135.97 (CH-2), 152.62 (CO carbonate), 162.53 (d, $^1J_{CF}$ = 246.7 Hz, CF-4'); IR (NaCl, neat) ν 2982 (m), 1742 (s, CO carbonate), 1511 (s), 1276 (s), 1254 (s), 1157 (s) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 252 (M^+, 5), 196 (M^+-(CH_3)$_2$C=CH_2, 45), 135 (90), 57 (100); HRMS (EI) 252.1163 [$C_{14}H_{17}O_3F$ (M^+) requires 252.1162]. Anal. Calcd. for $C_{14}H_{17}O_3F$: C, 66.65; H, 6.79. Found: C, 66.60; H, 6.74.

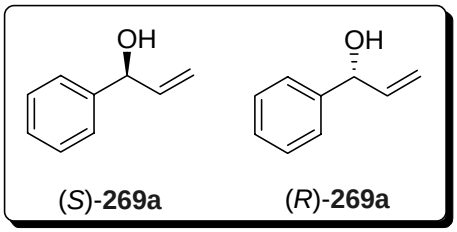
Procedure utilising neat sodium hydride: 1-(4'-Fluorophenyl)prop-2-en-1-ol (1.135 g, 7.45 mmol) was added slowly to a suspension of sodium hydride (350 mg, 14.58 mmol, neat) in THF (20 mL) at room temperature and the mixture was stirred for 15 min. The resulting solution was added slowly to a solution of Boc anhydride (1.880 g, 8.61 mmol) in THF (50 mL) at room temperature and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (15 mL), diluted with ether (200 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave (±)-**267i** as a colourless oil (1.674 g, 89%).



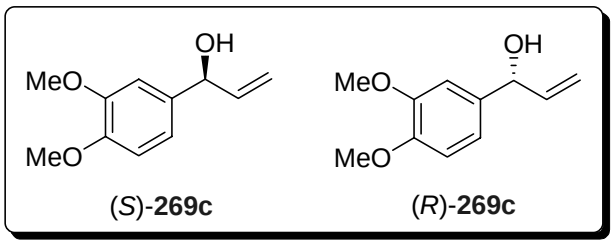
267q

(±)-*tert*-Butyl 1-(Pyridin-3'-yl)prop-2-en-1-yl Carbonate (±)-(267q). Vinylmagnesium bromide (70 mL, 70 mmol, 1.0M solution in THF) was added slowly to a solution of pyridine-3-carbaldehyde (6.830 g, 63.77 mmol) in THF (60 mL), and the resulting solution was stirred at 0 °C for 1 h. Then the solution was added slowly (*via* cannula) to a solution of Boc anhydride (15.454 g, 70.81 mmol) in THF (100 mL) at 0 °C and the mixture was stirred at room temperature overnight. The reaction was quenched with brine (15 mL), diluted with ether (200 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4) and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (85:15) gave (±)-**267q** as a brown oil (3.94 g, 26%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.41 (s, 9H, *t*-Bu), 5.25 (dd, $^3J_{3\text{-Ha},2\text{-H}}$ = 10.3 Hz, $^2J_{3\text{-Ha},3\text{-Hb}}$ = 1.0 Hz, 1H, 3-Ha), 5.29 (dd, $^3J_{3\text{-Hb},2\text{-H}}$ = 16.8 Hz, $^2J_{3\text{-Hb},3\text{-Ha}}$ = 1.0 Hz, 1H, 3-Hb), 5.97 (ddd, $^3J_{2\text{-H},3\text{-Hb}}$ = 16.8 Hz, $^3J_{2\text{-H},3\text{-Ha}}$ = 10.3 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.0 Hz, 1H, 2-H), 6.00 (m, 1H, 1-H), 7.23(ddd, $^3J_{5'\text{-H},4'\text{-H}}$ = 7.9 Hz, $^3J_{5'\text{-H},6'\text{-H}}$ = 4.8 Hz, J_{HH} = 0.8 Hz, 1H, 5'-H), 7.63 (dddd, $^3J_{4'\text{-H},5'\text{-H}}$ = 7.9 Hz, $^4J_{4'\text{-H},2'\text{-H}}$ = 2.2 Hz, $^4J_{4'\text{-H},6'\text{-H}}$ = 1.7 Hz, J_{HH} = 0.4 Hz, 1H, 4'-H), 8.50 (dd, $^3J_{6'\text{-H},5'\text{-H}}$ =

4.8 Hz, $^{4}J_{6'\text{-H},4'\text{-H}}$ = 1.7 Hz, 1H, 6'-H), 8.57 (d, $^{4}J_{2'\text{-H},4'\text{-H}}$ = 2.2 Hz, 1H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 27.60 (C(CH_3)$_3$), 76.72 (CH-1), 82.60 (C(CH_3)$_3$), 117.94 (CH_2-3), 123.27 (CH-5'), 134.17 (C-3'), 134.53 (CH-4'), 135.16 (CH-2), 148.66 (CH-2'), 149.47 (CH-6'), 152.35 (CO carbonate); IR (NaCl, neat) ν 2982 (m), 1743 (s, CO carbonate), 1370 (s), 1274 (s), 1254 (s), 1161 (s) cm^{-1}; MS (EI, 150 °C) *m*/*z* (%) 235 (M^+, 2), 179 (M^+-$(CH_3)_2C{=}CH_2$, 80), 134 (50), 118 (90), 57 (100); HRMS (EI) 235.1211 [$C_{13}H_{17}NO_3$ (M^+) requires 235.1208]. Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 65.91; H, 7.29; N, 5.87.



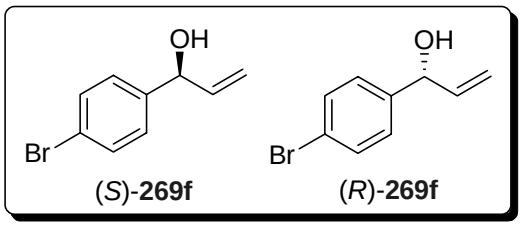
(*R*)-1-Phenylprop-2-en-1-ol (*R*)-(269a); (*S*)-1-Phenylprop-2-en-1-ol (*S*)-(269a) . Novozyme® 435 (1 g) was added to a mixture of 1-phenylprop-2-en-1-ol (5.02 g, 37.4 mmol), isoprenyl acetate (14.78 g, 147.6 mmol), and activated 4Å molecular sieves powder (5.0 g) in dry toluene (300 mL) and the resulting suspension was stirred at 40 °C for 16 h. The suspension was then cooled to ambient temperature, filtered, and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5) gave corresponding acetate (*R*)-**270a** as a colourless liquid (3.104 g), followed by (*S*)-**269a** (2.247 g, 45%, >99% ee (Chiral GC)) as a colourless liquid. The acetate (*R*)-**270a** (2.910 g, 16.51 mmol) was placed in a 25 mL flask and cooled to 0 °C. A solution of KOH (1.085 g, 19.27 mmol) in water (1.0 mL) was added dropwise, the cooling bath was removed, and the solution was heated at 60 °C for 2 h. The mixture was then cooled to ambient temperature, water (40 mL) was added, the product was extracted with ethyl acetate (3 × 50 mL), and the organic solution was dried (Na_2SO_4), and evaporated to furnish (*R*)-**269a** as a colourless liquid (2.195 g, 43%, >99% ee (Chiral GC)). The combined yield of both enantiomers was 88% and the chemical purity >99% (GC). Chiral GC (Supelco β-DEX 120 column, oven 110 °C isothermal) t_R = 23.75 min ((*R*)-**269a**), t_R = 25.07 min ((*S*)-**269a**).



(*S*)-**269c** (*R*)-**269c**

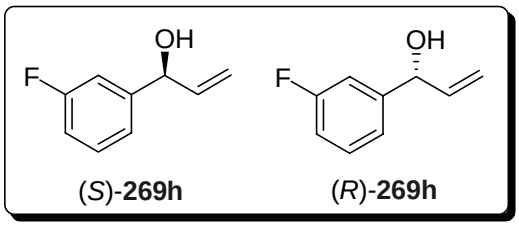
(*R*)-1-(3',4'-Dimethoxyphenyl)prop-2-en-1-ol (*R*)-(269c) and (*S*)-1-(3',4'-Dimethoxyphenyl)prop-2-en-1-ol (*S*)-(269c). Vinylmagnesium bromide (122 mL, 122 mmol, 1.0M solution in THF) was added slowly to a cold (-83 °C) solution of 3,4-dimethoxybenzaldehyde (20.02 g, 120.5 mmol) in THF (100 mL). The reaction mixture was stirred for an additional 2 h (while the cooling bath was allowed to warm up to 0 °C), quenched with saturated aqueous solution of ammonium chloride (50 mL), diluted with ethyl acetate (400 mL), washed with brine (3 × 100 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave crude (±)-**269c** as a yellow oil (22.46 g, 96%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.12 (d, J_{HH} = 3.2 Hz, 1H, OH), 3.86 (s, 3H, CH_3O), 3.87 (s, 3H, CH_3O), 5.12-5.14 (m, 1H, 1-H), 5.18 (ddd, $^3J_{3\text{-Ha},2\text{-H}}$ = 10.3 Hz, $^4J_{3\text{-Ha},1\text{-H}}$ = 1.4 Hz, $^2J_{3\text{-Ha},3\text{-Hb}}$ = 1.4 Hz, 1H, 3-Ha), 5.33 (ddd, $^3J_{3\text{-Hb},2\text{-H}}$ = 17.1 Hz, $^4J_{3\text{-Hb},1\text{-H}}$ = 1.5 Hz, $^2J_{3\text{-Hb},3\text{-Ha}}$ = 1.4 Hz, 1H, 3-Hb), 6.03 (ddd, $^3J_{2\text{-H},3\text{-Hb}}$ = 17.1 Hz, $^3J_{2\text{-H},3\text{-Ha}}$ = 10.3 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 5.9 Hz, 1H, 2-H), 6.82 (d, $^3J_{5'\text{-H},6'\text{-H}}$ = 8.1 Hz, 1H, 5'-H), 6.89 (dd, $^3J_{6'\text{-H},5'\text{-H}}$ = 8.1 Hz, $^4J_{6'\text{-H},2'\text{-H}}$ = 1.9 Hz, 1H, 6'-H), 6.90 (d, $^4J_{2'\text{-H},6'\text{-H}}$ = 1.9 Hz, 1H, 2'-H).

Novozyme® 435 (2 g) was added to a mixture of a crude (±)-**269c** (14.86 g, 76.5 mmol), isoprenyl acetate (35 mL, 317 mmol), and activated 4Å molecular sieves powder (10 g) in dry toluene (650 mL) and the resulting suspension was stirred at 40 °C for 18 h. The suspension was then cooled to ambient temperature, filtered, and evaporated. Gradient chromatography of the residue on a column of silica gel (8 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20 to 62:38) gave the corresponding acetate (*R*)-**270c** as a colourless liquid (8.28 g), followed by (*S*)-**269c** (3.27 g, 22%) as a colourless liquid. The acetate (*R*)-**270c** (8.28 g, 35.0 mmol) was placed in a 100 mL flask and cooled to 0 °C and a solution of KOH (2.26 g, 40.3 mmol) in MeOH (3.0 mL) was added dropwise. The cooling bath was removed and the solution was heated at 50 °C for 2 h. The mixture was then cooled to ambient temperature, brine (50 mL) was added, and the resulting solution was extracted with ethyl acetate (3 × 80 mL), dried (Na_2SO_4), and filtered. Evaporation of the filtrate furnished (*R*)-**269c** as a colourless liquid (6.72 g, 45%). The combined yield of both enantiomers was 67%. (*R*)-**269c**: $[\alpha]_D$ +10.8 (*c* 3.69, PhH). (*S*)-**269c**: $[\alpha]_D$ -10.8 (*c* 2.78, PhH).

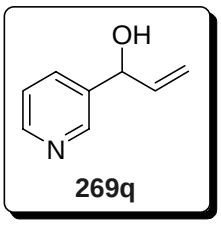


(*R*)-1-(4'-Bromophenyl)prop-2-en-1-ol (*R*)-(269f) and (*S*)-1-(4'-Bromophenyl)prop-2-en-1-ol (*S*)-(269f). Vinylmagnesium bromide (105 mL, 105 mmol, 1.0M solution in THF) was added slowly to a cold (-83 °C) solution of 4-bromobenzaldehyde (18.54 g, 100.2 mmol) in THF (100 mL). The reaction mixture was stirred for an additional 2 h (while the cooling bath was allowed to warm up to 0 °C), the reaction was quenched with saturated aqueous solution of ammonium chloride (50 mL), diluted with ethyl acetate (400 mL), washed with brine (3 × 100 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave crude (±)-**269f** as a yellow oil (20.43 g, 95%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.36 (d, J_{HH} = 3.1 Hz, 1H, OH), 5.12-5.13 (m, 1H, 1-H), 5.20 (ddd, $^3J_{3\text{-Ha},2\text{-H}}$ = 10.3 Hz, $^4J_{3\text{-Ha},1\text{-H}}$ = 1.3 Hz, $^2J_{3\text{-Ha},3\text{-Hb}}$ = 1.3 Hz, 1H, 3-Ha), 5.32 (ddd, $^3J_{3\text{-Hb},2\text{-H}}$ = 17.1 Hz, $^4J_{3\text{-Hb},1\text{-H}}$ = 1.3 Hz, $^2J_{3\text{-Hb},3\text{-Ha}}$ = 1.3 Hz, 1H, 3-Hb), 5.97 (ddd, $^3J_{2\text{-H},3\text{-Hb}}$ = 17.1 Hz, $^3J_{2\text{-H},3\text{-Ha}}$ = 10.3 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 6.1 Hz, 1H, 2-H), 7.22 (d, $^3J_{HH}$ = 8.5 Hz, 2H, 2'-H, and 6'-H), 7.47 (d, $^3J_{HH}$ = 8.5 Hz, 2H, 3'-H, and 5'-H).

Novozyme® 435 (2 g) was added to a mixture of a crude (±)-**269f** (14.98 g, 70.3 mmol), isoprenyl acetate (35 mL, 317 mmol), and activated 4Å molecular sieves powder (10 g) in dry toluene (650 mL) and the resulting suspension was stirred at 40 °C for 18 h. The resulting suspension was then cooled to ambient temperature, filtered, and evaporated. Gradient chromatography of the residue on a column of silica gel (8 × 10 cm) with a mixture of hexanes and ethyl acetate (98:2 to 94:6) gave corresponding acetate (*R*)-**270f** as a colourless liquid (8.16 g), followed by (*S*)-**269f** (3.28 g, 22%) as a colourless liquid. The acetate (*R*)-**270f** (7.47 g, 29.3 mmol) was placed in a 100 mL flask and cooled to 0 °C and a solution of KOH (1.89 g, 33.7 mmol) in MeOH (2.0 mL) was added dropwise. The cooling bath was removed and the solution was heated at 50 °C for 2 h. The mixture was then cooled to ambient temperature, brine (50 mL) was added, and the resulting solution was extracted with ethyl acetate (3 × 80 mL), dried (Na_2SO_4), and filtered. Evaporation of the filtrate furnished (*R*)-**269f** as a colourless liquid (6.24 g, 41%). The combined yield of both enantiomers was 63%. (*R*)-**269f**: $[\alpha]_D$ -12.2 (*c* 3.69, PhH). (*S*)-**269f**: $[\alpha]_D$ +11.59 (*c* 3.28, PhH).



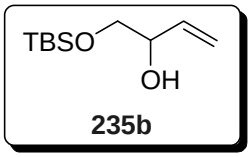
(*R*)-1-(3'-Fluorophenyl)prop-2-en-1-ol (*R*)-(269h) and (*S*)-1-(3'-Fluorophenyl)prop-2-en-1-ol (*S*)-(269h). Vinylmagnesium bromide (85 mL, 85 mmol, 1.0M solution in THF) was added slowly to a cold (-83 °C) solution of 3-fluorobenzaldehyde (9.85 g, 79.4 mmol) in THF (100 mL). The reaction mixture was stirred for an additional 2 h (while the cooling bath was allowed to warm up to 0 °C), the reaction was quenched with saturated aqueous solution of ammonium chloride (50 mL), diluted with ethyl acetate (400 mL), washed with brine (3 × 100 mL), and dried (Na_2SO_4). Evaporation of the organic phase gave crude (±)-**269h** as a yellow oil (11.93 g, 98%). Novozyme® 435 (2 g) was added to a mixture of a crude (±)-**269h** (11.52 g, 75.7 mmol), isoprenyl acetate (35 mL, 317 mmol), and activated 4Å molecular sieves powder (10 g) in dry toluene (650 mL) and the resulting suspension was stirred at 40 °C for 20 h. The suspension was then cooled to ambient temperature, filtered, and evaporated. Gradient chromatography of the residue on a column of silica gel (8 × 10 cm) with a mixture of hexanes and ethyl acetate (98:2 to 96:4) gave the corresponding acetate (*R*)-**270h** as a colourless liquid (6.42 g, 80%), followed by (*S*)-**269h** (4.57 g, 40%) as a colourless liquid. The acetate (*R*)-**270h** (6.41 g, 33.0 mmol) was placed in a 100 mL flask and cooled to 0 °C and a solution of KOH (2.13 g, 38.0 mmol) in MeOH (3.0 mL) was added dropwise. The cooling bath was removed and the solution was heated at 50 °C for 2 h. The mixture was then cooled to ambient temperature, brine (50 mL) was added, and the resulting solution was extracted with ethyl acetate (3 × 80 mL), dried (Na_2SO_4), and filtered. Evaporation of the filtrate furnished (*R*)-**269h** as a colourless liquid (4.76 g, 41%). The combined yield of both enantiomers was 81%. (*R*)-**269h**: $[\alpha]_D$ -12.25 (*c* 4.57, PhH). Anal. Calcd. for C_9H_9FO: C, 71.04; H, 5.96. Found: C, 70.98; H, 6.01. (*S*)-**269h**: $[\alpha]_D$ +13.13 (*c* 4.53, PhH). Anal. Calcd. for C_9H_9FO: C, 71.04; H, 5.96. Found: C, 70.78; H, 5.91.



269q

(±)-1-(Pyrid-3'-yl)prop-2-en-1-ol (±)-(269q). A solution of vinylmagnesium bromide (43 mL, 43 mmol, 1.0M in THF) was added slowly to a solution of pyridine-3-carboxaldehyde (4.50 g, 42.0 mmol) in THF (80 mL) at 0 °C. The resulting solution was stirred at room temperature overnight, then quenched with saturated aqueous solution of NH_4Cl, diluted with Et_2O (100 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 15 cm) with ethyl acetate gave (±)-**269q** as a yellow oil (1.82 g, 32%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 5.15 (dt, $^3J_{cis\text{-}3\text{-}H,2\text{-}H}$ = 10.2 Hz, $^2J_{3\text{-}H,3\text{-}H}$ = 1.3 Hz, 1H, 3-H), 5.17 (d, $^3J_{1\text{-}H,2\text{-}H}$ = 6.2 Hz, 1H, H-1), 5.29 (dt, $^3J_{trans\text{-}3\text{-}H,2\text{-}H}$ = 17.1 Hz, $^2J_{3\text{-}H,3\text{-}H}$ = 1.3 Hz, 1H, 3-H), 5.67 (bs, 1H, OH), 5.96 (ddd, $^3J_{2\text{-}H,trans\text{-}3\text{-}H}$ = 17.1 Hz, $^3J_{2\text{-}H,cis\text{-}3\text{-}H}$ = 10.2 Hz, $^3J_{2\text{-}H,1\text{-}H}$ = 6.2 Hz, 1H, 2-H), 7.21 (ddd, $^3J_{5'\text{-}H,4'\text{-}H}$ = 7.9 Hz, $^3J_{5'\text{-}H,6'\text{-}H}$ = 4.9 Hz, J_{HH} = 0.8 Hz, 1H, 5'-H), 7.69 (dddd,$^3J_{4'\text{-}H,5'\text{-}H}$ = 7.9 Hz, $^4J_{4'\text{-}H,2'\text{-}H}$ = 2.2 Hz, $^4J_{4'\text{-}H,6'\text{-}H}$ = 1.7 Hz, J_{HH} = 0.6 Hz, 1H, 4'-H), 8.30 (dd, $^3J_{6'\text{-}H,5'\text{-}H}$ = 4.9 Hz, $^4J_{6'\text{-}H,4'\text{-}H}$ = 1.7 Hz, 1H, 6'-H), 8.41 (d, $^4J_{2'\text{-}H,4'\text{-}H}$ = 2.2 Hz, 1H, 2'-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 72.44 (CH), 115.52 (CH_2), 123.43 (CH), 134.46 (CH), 138.86 (C), 139.82 (CH), 147.59 (CH), 147.91 (CH); MS (CI) *m*/*z* (%) 136 ($M+H^+$, 100), 118 (15); HRMS (CI) 136.0760 [$C_8H_{10}ON$ ($M+H^+$) requires 136.0762]. Anal. Calcd. for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.53; H, 6.73; N, 10.26.

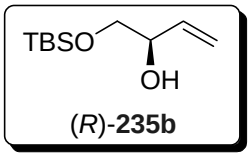
6.5. Synthesis of Protected Butenediols and Their Carbonates



235b

(±)-1-(*tert*-Butyldimethylsilyloxy)but-3-en-2-ol (±)-(235b). A solution of *tert*-butyl(chloro)dimethylsilane (4.600 g, 30.52 mmol) in THF (20 mL) was added slowly to a solution of butene-1,2-diol (±)-**235a** (2.721 g, 30.87 mmol) and DMAP (400 mg, 3.27 mmol) in a mixture of Et_3N (15 mL) and THF (60 mL) at 0 °C and the mixture was stirred overnight at 20 °C. The reaction was then quenched with water, diluted with Et_2O (200 mL), three times washed with brine, dried (Na_3SO_4), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl

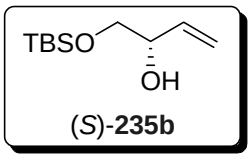
acetate (98:2) gave the butenol (±)-**235b** as a yellowish liquid (5.081 g, 81%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.07 (s, 6H, CH_3), 0.90 (s, 9H, *t*-Bu), 2.60 (d, $^3J_{OH,2\text{-}CH}$ = 3.4 Hz, 1H, OH), 3.44 (dd, $^2J_{1\text{-}Ha,1\text{-}Hb}$ = 10.0 Hz, $^3J_{1\text{-}Ha,2\text{-}H}$ = 7.6Hz, 1H, 1-Ha), 3.64 (dd, $^2J_{1\text{-}Hb,1\text{-}Ha}$ = 10.0 Hz, $^3J_{1\text{-}Hb,2\text{-}H}$ = 3.8 Hz, 1H, 1-Hb), 4.15 (m, 1H, 2-H), 5.17 (ddd, $^3J_{4\text{-}Ha,3\text{-}H}$ = 10.6 Hz, $^2J_{4\text{-}Ha,4\text{-}Hb}$ = 1.5 Hz, $^4J_{4\text{-}Ha,2\text{-}H}$ = 1.4 Hz, 1H, 4-Ha), 5.33 (ddd, $^3J_{4\text{-}Hb,3\text{-}H}$ = 17.3 Hz, $^4J_{4\text{-}Hb,2\text{-}H}$ = 1.6 Hz, $^2J_{4\text{-}Hb,4\text{-}Ha}$ = 1.5 Hz, 1H, 4-Hb), 5.80 (ddd, $^3J_{3\text{-}H,4\text{-}Hb}$ = 17.3 Hz, $^3J_{3\text{-}H,4\text{-}Ha}$ = 10.6 Hz, $^3J_{3\text{-}H,2\text{-}H}$ = 5.7 Hz, 1H, 3-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ -5.42 (CH_3), -5.39 (CH_3), 18.27 ($C(CH_3)_3$), 25.83 ($C(CH_3)_3$), 66.94 (CH_2-1), 72.96 (CH-2), 116.36 (CH_2-4), 136.67 (CH-3). Anal. Calcd. for $C_{10}H_{22}O_2Si$: C, 59.35; H, 10.96. Found: C, 59.36; H, 11.07.



(*R*)-**235b**

(*R*)-1-(*tert*-Butyldimethylsilyloxy)but-3-en-2-ol (*R*)-(235b). A solution of *tert*-butylchlorodimethylsilane (4.34 g, 28.8 mmol) in THF (20 mL) was added slowly to a cold solution (0 °C) of diol (*R*)-**235a** (2.53 g, 28.6 mmol) in a mixture of THF (60 mL), Et_3N (15 mL, 107 mmol), and DMAP (376 mg, 3.07 mmol). The cooling bath was then removed and the solution was stirred overnight. The reaction was quenched with water (20 mL), diluted with ether (100 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with hexanes (200 mL), followed by elution with a mixture of hexanes and ethyl acetate (98:2) gave (*R*)-**235b** as a colourless oil (3.83 g, 66%) with chemical purity >99% (GC) and >99% ee (chiral GC): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.05 (s, 6H, CH_3), 0.88 (s, 9H, *t*-Bu), 2.65 (d, $^3J_{2\text{-}OH,2\text{-}H}$ = 3.6 Hz, 1H, 2-OH), 3.43 (dd, $^2J_{1\text{-}Ha,1\text{-}Hb}$ = 9.9 Hz, $^3J_{1\text{-}Ha,2\text{-}H}$ = 7.6 Hz, 1H, 1-Ha), 3.62 (dd, $^2J_{1\text{-}Hb,1\text{-}Ha}$ = 9.9 Hz, $^3J_{1\text{-}Hb,2\text{-}H}$ = 3.8 Hz, 1H, 1-Hb), 4.10-4.15 (m, 1H, 2-H), 5.15 (dd, $^3J_{4\text{-}Ha,3\text{-}H}$ = 10.6 Hz, $^2J_{4\text{-}Ha,4\text{-}Hb}$ = 1.2 Hz, 1H, 4-Ha), 5.31 (dd, $^3J_{4\text{-}Hb,3\text{-}H}$ = 17.3 Hz, $^2J_{4\text{-}Hb,4\text{-}Ha}$ = 1.2 Hz, 1H, 4-Hb), 5.78 (ddd, $^3J_{3\text{-}H,4\text{-}Hb}$ = 17.3 Hz, $^3J_{3\text{-}H,4\text{-}Ha}$ = 10.6 Hz, $^3J_{3\text{-}H,2\text{-}H}$ = 5.7 Hz, 1H, 3-H). Anal. Calcd. for $C_{10}H_{22}O_2Si$: C, 59.35; H, 10.96. Found: C, 59.21; H, 11.13. Chiral GC showed >99% ee (Supelco β-DEX 120 column, oven 70 °C for 5 min then gradient 1 °C.min^{-1} to 105 °C) t_R = 31.48 min ((*S*)-**235b**), t_R = 32.68 min ((*R*)-**235b**).

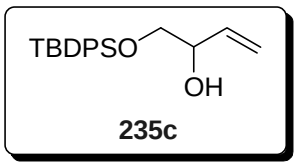
Fraction distillation of the crude product obtained by the above procedure (131 mmol scale) gave (*R*)-**235b** as a colourless liquid (21.35 g, 80%): bp 43-45 °C at 270 Pa.



(*S*)-**235b**

(*S*)-1-(*tert*-Butyldimethylsilyloxy)but-3-en-2-ol (*S*)-(235b). A solution of *tert*-butyl(chloro)dimethylsilane (9.26 g, 61.5 mmol) in THF (40 mL) was added slowly to a cold solution (0 °C) of diol (*S*)-**235a** (5.28 g, 59.9 mmol) in a mixture of THF (120 mL), Et_3N (30 mL, 215 mmol), and DMAP (640 mg, 5.23 mmol). The cooling bath was removed and the solution was stirred overnight. The reaction was quenched with water (20 mL), diluted with ether (200 mL), washed with brine (3 × 80 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with hexanes (200 mL), followed by elution with a mixture of hexanes and ethyl acetate (98:2) gave (*S*)-**235b** as a colourless oil (9.29 g, 76%) with chemical purity >99% (GC) and >99% ee (chiral GC): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.05 (s, 6H, CH_3), 0.88 (s, 9H, *t*-Bu), 2.65 (d, $^3J_{2\text{-OH},2\text{-H}}$ = 3.6 Hz, 1H, 2-OH), 3.43 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 9.9 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 7.6 Hz, 1H, 1-Ha), 3.62 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 9.9 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 3.8 Hz, 1H, 1-Hb), 4.10-4.15 (m, 1H, 2-H), 5.15 (dd, $^3J_{4\text{-Ha},3\text{-H}}$ = 10.6 Hz, $^2J_{4\text{-Ha},4\text{-Hb}}$ = 1.2 Hz, 1H, 4-Ha), 5.31 (dd, $^3J_{4\text{-Hb},3\text{-H}}$ = 17.3 Hz, $^2J_{4\text{-Hb},4\text{-Ha}}$ = 1.2 Hz, 1H, 4-Hb), 5.78 (ddd, $^3J_{3\text{-H},4\text{-Hb}}$ = 17.3 Hz, $^3J_{3\text{-H},4\text{-Ha}}$ = 10.6 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 5.7 Hz, 1H, 3-H). Anal. Calcd. for $C_{10}H_{22}O_2Si$: C, 59.35; H, 10.96. Found: C, 59.13; H, 11.13. Chiral GC showed >99% ee (Supelco β-DEX 120 column, oven 70 °C for 5 min then gradient 1 °C.min^{-1} to 105 °C) t_R = 31.48 min ((*S*)-**235b**), t_R = 32.68 min ((*R*)-**235b**).

Fraction distillation of the crude product obtained by the above procedure (156 mmol scale) gave (*S*)-**235b** as a colourless liquid (25.16 g, 80%): bp 46-48 °C at 300 Pa.

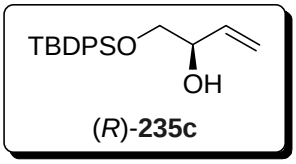


235c

(±)-1-(*tert*-Butyldiphenylsilyloxy)but-3-en-2-ol (±)- (235c).[223]

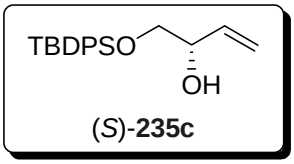
tert-Butyl(chloro)diphenylsilane (16.0 g, 58.2 mmol) was added slowly to a cold (0 °C) solution of diol (±)-**235a** (5.0 g, 56.8 mmol), Et_3N (20 mL) and DMAP (488 mg, 4.00 mmol) in THF (100 mL). The reaction mixture was stirred at room temperature for 24 h and then quenched with saturated aqueous NaCl (50 mL), extracted with AcOEt (3 × 150 mL), dried ($MgSO_4$), and evaporated. Chromatography on a column of silica gel (8 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5) gave (±)-**235c** as a colourless oil (17.68 g, 95%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.14 (s, 9H, *t*-Bu), 2.73 (d,

$^{3}J_{2\text{-OH},2\text{-H}}$ = 3.9 Hz, 1H, 2-OH), 3.62 (dd, $^{2}J_{1\text{-Ha},1\text{-Hb}}$ = 10.2 Hz, $^{3}J_{1\text{-Ha},2\text{-H}}$ = 7.4 Hz, 1H, 1-Ha), 3.76 (dd, $^{2}J_{1\text{-Hb},1\text{-Ha}}$ = 10.2 Hz, $^{3}J_{1\text{-Hb},2\text{-H}}$ = 3.9 Hz, 1H, 1-Hb), 4.27-4.32 (m, 1H, 2-H), 5.21 (ddd, $^{3}J_{4\text{-Ha},3\text{-H}}$ = 10.6 Hz, $^{2}J_{4\text{-Ha},4\text{-Hb}}$ = 1.5 Hz, $^{4}J_{4\text{-Ha},2\text{-H}}$ = 1.5 Hz, 1H, 4-Ha), 5.37 (ddd, $^{3}J_{4\text{-Hb},3\text{-H}}$ = 17.3 Hz, $^{2}J_{4\text{-Hb},4\text{-Ha}}$ = 1.5 Hz, $^{4}J_{4\text{-Hb},2\text{-H}}$ = 1.5 Hz,1H, 4-Hb), 5.89 (ddd, $^{3}J_{3\text{-H},4\text{-Hb}}$ = 17.3 Hz, $^{3}J_{3\text{-H},4\text{-Ha}}$ = 10.6 Hz, $^{3}J_{3\text{-H},2\text{-H}}$ = 5.6 Hz, 1H, 3-H), 7.40-7.48 (m, 6H, H-arom), 7.72-7.74 (m, 4H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ 19.21 ($C(CH_3)_3$), 26.80 ($C(CH_3)_3$), 67.63 (CH_2-1), 72.96 (CH-2), 116.41 (CH_2-4), 127.73 (CH-arom), 129.78 (CH-arom), 132.98 (CH-arom), 135.48 (C-arom), 136.59 (CH-3); consistent with the literature data.[223]



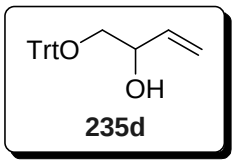
(*R*)-**235c**

(*R*)-1-(*tert*-Butyldiphenylsilyloxy)but-3-en-2-ol (*R*)-(235c).
tert-Butyl(chloro)diphenylsilane (7.60 g, 27.7 mmol) was added slowly to a cold (0 °C) solution of diol (*R*)-**235a** (2.18 g, 24.7 mmol), Et_3N (10 mL) and DMAP (288 mg, 2.36 mmol) in THF (40 mL). The reaction mixture was stirred at room temperature for 24 h and then quenched with saturated aqueous NaCl (50 mL), extracted with AcOEt (3 × 150 mL), dried ($MgSO_4$), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5) gave (*R*)-**235c** as a colourless oil (7.06 g, 88%). $[\alpha]_D$ +5.2 (*c* 0.9, $CHCl_3$). Anal. Calcd. for $C_{20}H_{26}O_2Si$: C, 73.57; H, 8.03. Found: C, 73.49; H, 8.13.



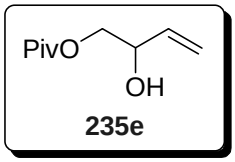
(*S*)-**235c**

(*S*)-1-(*tert*-Butyldiphenylsilyloxy)but-3-en-2-ol (*S*)-(235c).[223]
tert-Butyl(chloro)diphenylsilane (7.50 g, 27.3 mmol) was added slowly to a cold (0 °C) solution of diol (*S*)-**235a** (2.20 g, 25.0 mmol), Et_3N (10 mL) and DMAP (300 mg, 2.46 mmol) in THF (50 mL). The reaction mixture was stirred at room temperature for 24 h and then quenched with saturated aqueous NaCl (50 mL), extracted with AcOEt (3 × 150 mL), dried ($MgSO_4$), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5) gave (*S*)-**235c** as a colourless oil (7.02 g, 86%). $[\alpha]_D$ -4.9 (*c* 1.2, $CHCl_3$). Anal. Calcd. for $C_{20}H_{26}O_2Si$: C, 73.57; H, 8.03. Found: C, 73.31; H, 8.39. Consistent with the literature data.[223]



235d

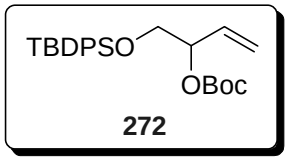
(±)-1-(Trityloxy)but-3-en-2-ol (235d).[224] A solution of chloro(triphenyl)methane (5.90 g, 21.2 mmol) in dichloromethane (10 mL) was slowly added to a cold (0 °C) solution of diol (±)-**235a** (1.76 g, 20.0 mmol), Et_3N (10 mL) and DMAP (100 mg, 0.82 mmol) in dichloromethane (20 mL). The reaction mixture was stirred at room temperature for 24 h and then quenched with saturated aqueous NaCl (20 mL), extracted with ethyl acetate (3 × 100 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5) gave (±)-**235d** as a colourless oil (5.82 g, 88%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.44 (d, $^3J_{2\text{-OH},2\text{-H}}$ = 3.9 Hz, 1H, 2-OH), 3.14 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 9.4 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 7.5 Hz, 1H, 1-Ha), 3.24 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 9.4 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 3.7 Hz, 1H, 1-Hb), 4.27-4.33 (m, 1H, 2-H), 5.18 (ddd, $^3J_{4\text{-Ha},3\text{-H}}$ = 10.6 Hz, $^2J_{4\text{-Ha},4\text{-Hb}}$ = 1.4 Hz, $^4J_{4\text{-Ha},2\text{-H}}$ = 1.4 Hz, 1H, 4-Ha), 5.32 (ddd, $^3J_{4\text{-Hb},3\text{-H}}$ = 17.2 Hz, $^2J_{4\text{-Hb},4\text{-Ha}}$ = 1.4 Hz, $^4J_{4\text{-Hb},2\text{-H}}$ = 1.4 Hz, 1H, 4-Hb), 5.83 (ddd, $^3J_{3\text{-H},4\text{-Hb}}$ = 17.2 Hz, $^3J_{3\text{-H},4\text{-Ha}}$ = 10.6 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 5.7 Hz, 1H, 3-H), 7.25-7.29 (m, 3H, H-arom), 7.31-7.35 (m, 6H, H-arom), 7.44-7.48 (m, 6H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ 67.37 (CH_2-1), 71.98 (CH-2), 86.72 (*C*Ph_3), 116.33 (CH_2-4), 127.10 (CH-arom), 127.85 (CH-arom), 128.61 (CH-arom), 136.92 (CH-3), 143.71 (C-arom); MS (EI) *m*/*z* (%) 330 (1, M^+) 243 (100, Trt), 228 (15), 215 (15), 183 (22), 165 (90), 105 (40), 77 (25). Anal. Calcd. for $C_{23}H_{22}O_2$: C,83.60; H, 6.71. Found: C, 81.43; H, 6.58. Consistent with the literature data.[224]



235e

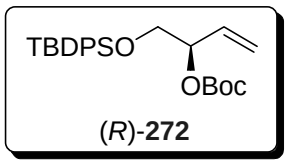
(±)-2-Hydroxybut-3-enyl Pivalate (235e).[223] Pivaloylchloride (2.40 g, 19.9 mmol) was slowly added to a cold (0 °C) solution of diol (±)-**235a** (1.78 g, 20.2 mmol), Et_3N (10 mL) and DMAP (100 mg, 0.82 mmol) in dichloromethane (20 mL) and the reaction mixture was stirred at room temperature for 24 h, and then quenched with saturated aqueous NaCl (50 mL), extracted with ethyl acetate (3 × 100 mL), dried (Na_2SO_4), and evaporated. Gradient chromatography on a column of silica gel (5 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5 to 80:20) gave (±)-**235e** as a colourless oil (1.81 g, 53%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.13 (s, 9H, *t*-Bu), 2.94 (s, 1H, 2-OH), 3.99 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 11.4 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 6.6 Hz, 1H, 1-Ha), 4.04 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 11.4 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 4.3 Hz, 1H,

1-Hb), 4.26-4.31 (m, 1H, 2-H), 5.14 (ddd, $^{3}J_{4\text{-Ha},3\text{-H}}$ = 10.6 Hz, $^{2}J_{4\text{-Ha},4\text{-Hb}}$ = 1.4 Hz, $^{4}J_{4\text{-Ha},2\text{-H}}$ = 1.4 Hz, 1H, 4-Ha), 5.29 (ddd, $^{3}J_{4\text{-Hb},3\text{-H}}$ = 17.2 Hz, $^{2}J_{4\text{-Hb},4\text{-Ha}}$ = 1.4 Hz, $^{4}J_{4\text{-Hb},2\text{-H}}$ = 1.4 Hz,1H, 4-Hb), 5.78 (ddd, $^{3}J_{3\text{-H},4\text{-Hb}}$ = 17.2 Hz, $^{3}J_{3\text{-H},4\text{-Ha}}$ = 10.6 Hz, $^{3}J_{3\text{-H},2\text{-H}}$ = 5.6 Hz, 1H, 3-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ 26.97 (C(CH$_3$)$_3$), 38.64 (C(CH$_3$)$_3$), 67.34 (CH$_2$-1), 70.74 (CH-2), 116.56 (CH$_2$-4), 136.36 (CH-3), 178.58 (CO carbonyl); MS (CI) *m*/*z* (%) 173 (98, M+H$^+$), 155 (100, M$^+$-OH), 103 (22, M$^+$-*t*Bu-H$_2$O); HRMS (CI) 173.1180 [$C_9H_{17}O_3$ (M+H$^+$) requires 173.1178]; consistent with the literature data.[223]



272

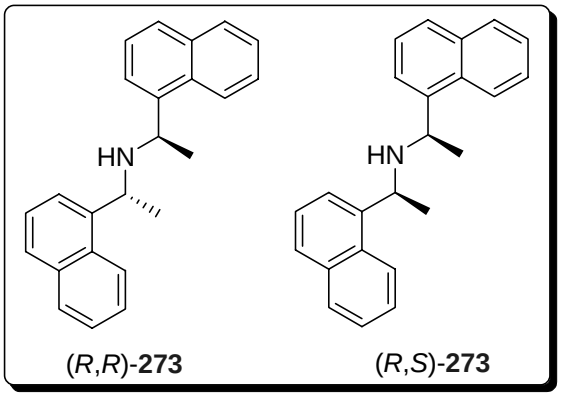
(±)-*tert*-Butyl 1-(*tert*-Butyldiphenylsilyloxy)but-3-en-2-yl Carbonate (±)-(272). A solution of *n*-butyllithium (5.0 mL, 2.0M in pentane) was added slowly to a solution of silylated diol (±)-**235c** (3.260 g, 9.98 mmol) in THF (10 mL) at 0 °C. The resulting solution was stirred at 0 °C for 20 min and than transfered, at room temperature, (*via* canula), to a solution of Boc anhydride (2.45 g, 11.2 mmol) in THF (30 mL), and stirred at room temperature overnight. The reaction was quenched with brine (20 mL), diluted with ethyl acetate (100 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated. Chromatography on a column of silica gel (5 × 15 cm) with a mixture of hexanes and ethyl acetate (95:5) gave (±)-**272** as a yellowish oil (4.03 g, 94%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.06 (s, 9H, *t*-Bu), 1.51 (s, 9H, *t*-Bu), 3.70 (dd, $^{2}J_{1\text{-H},1\text{-H}}$ = 10.9 Hz, $^{3}J_{1\text{-H},2\text{-H}}$ = 4.5 Hz, 1H, 1-H), 3.77 (dd, $^{2}J_{1\text{-H},1\text{-H}}$ = 10.9 Hz, $^{3}J_{1\text{-H},2\text{-H}}$ = 7.3 Hz, 1H, 1-H), 5.23 (dt, $^{3}J_{\text{cis-4-H},3\text{-H}}$ = 10.7 Hz, $^{2}J_{4\text{-H},4\text{-H}}$ = 1.2 Hz, 1H, 4-H), 5.26 (m, 1H, 2-H), 5.34 (dt, $^{3}J_{\textit{trans}\text{-4-H},3\text{-H}}$ = 17.3 Hz, $^{2}J_{4\text{-H},4\text{-H}}$ = 1.2 Hz, 1H, 4-H), 5.81 (ddd, $^{3}J_{3\text{-H},\textit{trans}\text{-4-H}}$ = 17.1 Hz, $^{3}J_{3\text{-H},\textit{cis}\text{-4-H}}$ = 10.6 Hz, $^{3}J_{3\text{-H},2\text{-H}}$ = 6.4 Hz, 1H, 3-H), 7.37-7.46 (m, 6H, H-arom), 7.68-7.72 (m, 4H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 19.20 (C(CH$_3$)$_3$), 26.71 (C(CH$_3$)$_3$), 27.81 (C(CH$_3$)$_3$), 65.41 (CH$_2$-1), 77.90 (CH-2), 81.89 (C(CH$_3$)$_3$), 118.22 (CH$_2$-4), 127.64 (CH-arom), 129.65 (CH-arom), 133.20 (CH-3), 133.29 (C-arom), 135.60 (CH-arom), 152.95 (CO carbonate); IR (neat) ν 2932 (m), 2858 (m), 1743 (s, CO carbonate), 1428 (m), 1368 (m), 1276 (s), 1254 (s), 1165 (s), 1113 (s), 702 (s) cm^{-1}; MS (CI-NH$_3$) *m*/*z* (%) 444 (M+NH$_4^+$, 100), 388 ([M+NH$_4^+$]-C$_4$H$_8$, 15), 371 (5), 326 (5), 309 (MH$^+$-C$_4$H$_8$-CO$_2$-H$_2$O, 20), 216 (8). Anal. Calcd. for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.31; H, 8.12.



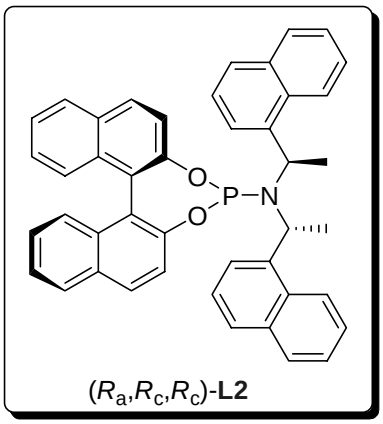
(*R*)-**272**

(*R*)-*tert*-Butyl 1-(*tert*-Butyldiphenylsilyloxy)but-3-en-2-yl Carbonate (*R*)-(272). A solution of *n*-butyllithium (2.5 mL, 2.0M in pentane) was added slowly to a solution of silylated diol (*R*)-**235c** (1.630 g, 4.99 mmol) in THF (10 mL) at 0 °C. The resulting solution was stirred at 0 °C for 20 min and than transferred, at room temperature, (*via* canula) to a solution of Boc anhydride (1.230 g, 5.63 mmol) in THF (20 mL) and the mixture was stirred at room temperature overnight. The reaction was quenched with brine, diluted with ethyl acetate (100 mL), washed with brine (3 × 50 mL), dried (Na_2SO_4) and evaporated. Chromatography on a column of silica gel (5 × 15 cm) with a mixture of hexanes and ethyl acetate (95:5) gave (*R*)-**272** as a yellowish oil (2.02 g, 95%): $[\alpha]_D$ +17.0 (*c* 1.7, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.06 (s, 9H, *t*-Bu), 1.51 (s, 9H, *t*-Bu), 3.70 (dd, $^2J_{1\text{-H},1\text{-H}}$ = 10.9 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 4.5 Hz, 1H, 1-H), 3.77 (dd, $^2J_{1\text{-H},1\text{-H}}$ = 10.9 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 7.3 Hz, 1H, 1-H), 5.23 (dt, $^3J_{cis\text{-4-H},3\text{-H}}$ = 10.7 Hz, $^2J_{4\text{-H},4\text{-H}}$ = 1.2 Hz, 1H, 4-H), 5.26 (m, 1H, 2-H), 5.34 (dt, $^3J_{trans\text{-4-H},3\text{-H}}$ = 17.3 Hz, $^2J_{4\text{-H},4\text{-H}}$ = 1.2 Hz, 1H, 4-H), 5.81 (ddd, $^3J_{3\text{-H},trans\text{-4-H}}$ = 17.1 Hz, $^3J_{3\text{-H},cis\text{-4-H}}$ = 10.6 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 6.4 Hz, 1H, 3-H), 7.37-7.46 (m, 6H, H-arom), 7.68-7.72 (m, 4H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 19.20 ($C(CH_3)_3$), 26.71 ($C(CH_3)_3$), 27.81 ($C(CH_3)_3$), 65.41 (CH_2-1), 77.90 (CH-2), 81.89 ($C(CH_3)_3$), 118.22 (CH_2-4), 127.64 (CH-arom), 129.65 (CH-arom), 133.20 (CH-3), 133.29 (C-arom), 135.60 (CH-arom), 152.95 (CO carbonate). Anal. Calcd. for $C_{25}H_{34}O_4Si$: C, 70.38; H, 8.03. Found: C, 70.15; H, 8.10.

6.6. Synthesis of Ligands for the Asymmetric Allylic Substitution

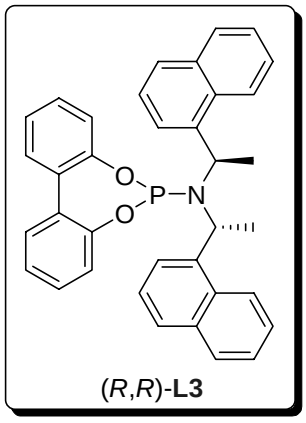


(*R*,*S*)-Bis[1-(1-naphthyl)ethyl]amine (*R*,*S*)-(273), and (*R*,*R*)-Bis[1-(1-naphthyl)ethyl]amine (*R*,*R*)-(273).[225] A mixture of (*R*)-(+)-(1-naphthyl)ethylamine (1.71 g, 10.0 mmol), 1-acetylnaphthalene (1.70 g, 10.0 mmol), dry sodium hydrogencarbonate (4.20 g, 50.0 mmol), 4 Å sieves (7.0 g) in benzene (5 mL) was heated at 80 °C for 20 h. The mixture was then filtered and the filtrate was evaporated. The crude imine thus obtained was stirred with sodium borohydride (1.52 g, 40.0 mmol) in THF (30 mL) at room temperature for 24 h. The reaction was quenched with 6M HCl, neutralised with saturated aqueous sodium carbonate, extracted with dichloromethane (3 × 50 mL), dried, and evaporated. Chromatography on a column of silica gel (20 × 5 cm) with a mixture of hexanes and ethyl acetate (90:10) gave (*R*,*R*)-**273** (480 mg, 15%) as the lipophilic component, followed by a mixture of (*R*,*R*)- and (*R*,*S*)-diastereoisomers (857 mg, 26%), and finally by (*R*,*S*)-**273** (241 mg, 8%) as a colourless oil: (*R*,*R*)-**273**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.46 (d, $^{3}J_{HH}$ = 6.7 Hz, 6H, CH_3), 1.93 (brs, 1H, NH), 4.51 (q, $^{3}J_{HH}$ = 6.7 Hz, 2H, CH), 7.22 (ddd, J_{HH} = 8.3 Hz, J_{HH} = 6.8 Hz, J_{HH} = 1.4 Hz, 2H, CH-arom), 7.42 (ddd, J_{HH} = 8.0 Hz, J_{HH} = 6.8 Hz, J_{HH} = 1.1 Hz, 2H, CH-arom), 7.55 (t, J_{HH} = 7.6 Hz, 2H, CH-arom), 7.75 – 7.82 (m, 6H, H-arom), 7.87 (dd, J_{HH} = 8.3 Hz, J_{HH} = 1.4 Hz, , 2H, CH-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 24.5, 51.2, 122.6, 123.1, 125.2, 125.4, 125.6, 127.1, 128.7, 131.4, 133.9, 141.9; consistent with the literature data.[225] (*R*,*S*)-**273**:[225] ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.53 (d, J_{HH} = 6.6 Hz, 6H, CH_3), 1.79 (brs, 1H, NH), 4.76 (q, J_{HH} = 6.6 Hz, 2H, CH), 7.41 – 7.50 (m, 6H), 7.64 (dd, J_{HH} = 7.2 Hz, J_{HH} = 1.0 Hz, 2H, CH-arom), 7.77 (d, J_{HH} = 8.2 Hz, 2H, CH-arom); 7.88 (dd, J_{HH} = 7.8 Hz, J_{HH} = 1.7 Hz, 2H, CH-arom); 8.03 (d, J_{HH} = 8.4 Hz, 2H, CH-arom); consistent with the literature data.[225]



(R_a,R_c,R_c)-**L2**

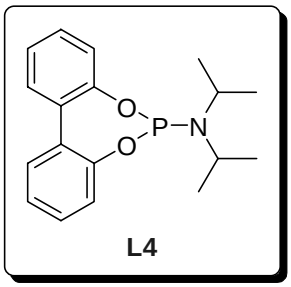
***O,O'*-(*R*)-(1,1'-Dinaphtyl-2,2'-diyl)-*N,N*-di-(*R,R*)-1-naphtylethylphosphoramidite (R_a,R_c,R_c)-(L2).**[217] A solution of amine (*R*,*R*)-**273** (357 mg, 1.10 mmol) in THF (2 mL) was added slowly to a mixture of Et_3N (1.45 g, 14.3 mmol) and PBr_3 (375 mg, 1.40 mmol) in THF (2 mL) at 0 °C and the resulting mixture was stirred at room temperature for 3 h. The mixture was than cooled to 0 °C and a solution of (*R*)-BINOL (320 mg, 1.10 mmol) in THF (1 mL) was added, and the mixture was stirred at room temperature overnight. The reaction was than diluted with toluene (20 mL), passed through a short path of alumina (3 × 5 cm) and evaporated. Chromatography on a column of alumina (5 × 5 cm) with toluene gave (R_a,R_c,R_c)-**L2** as a white foam (285 mg, 39%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.46 (d, J_{HH} = 6.7 Hz, 6H, CH_3), 5.56 (m, 2H, CH-arom); 6.73 (t, J_{HH} = 7.7 Hz, 2H, CH); 7.15-8.05 (m, 24H, CH-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 21.46 (CH_3), 29.70 (CH_3), 49.57 (CH), 49.64 (CH), 121.81, 122.22, 122.77, 123.15, 124.27, 124.32, 124.41, 124.54, 124.82, 124.90, 125.30, 126.13, 126.15, 126.91, 127.18, 127.21, 128.23, 128.37, 129.73, and 130.50 (CH-arom), 131.51, 132.90, 133.08, 138.31, 149.53, 150.40, 150.39, and 150.46 (C-arom); consistent with the literature data.[217]



(*R*,*R*)-**L3**

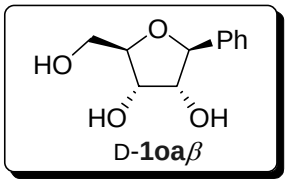
***O,O'*-(1,1'-Diphenyl-2,2'-diyl)-*N,N*-di-(*R,R*)-1-naphthylethylphosphoramidite (*R,R*)-(L3).**[226] A solution of amine (*R*,*R*)-**273** (126 mg, 0.39 mmol) in THF (1 mL) was added slowly to a mixture of Et_3N (1.0 g, 7 mmol) and PBr_3 (120 mg, 0.44 mmol) in THF (1 mL) at 0 °C and the resulting mixture was stirred at room temperature for 3 h. The

mixture was than cooled to 0 °C and a solution of biphenol **277** (80 mg, 0.43 mmol) in THF (1 mL) was added, and the mixture was stirred at room temperature overnight. The reaction was than diluted with toluene (10 mL), passed through a short path of alumina (3 × 5 cm), and evaporated. Chromatography on a column of alumina (5 × 5 cm) with toluene gave (*R*,*R*)-**L3** as a white foam (159 mg, 34%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.54 (d, J_{HH} = 7.7 Hz, 6H, CH_3), 5.64 (p, J_{HH} = 7.3 Hz, 2H, CH), 7.00 (d, J_{HH} = 7.7Hz, 2H, H-arom), 7.01-7.19 (m, 4H, H-arom), 7.37 (ddd, J_{HH} = 8.3 Hz, J_{HH} = 6.8 Hz, J_{HH} = 1.4, 2H, H-arom), 7.43-7.46 (m, 4H, H-arom), 7.61 (dd, J_{HH} = 7.6 Hz, J_{HH} = 7.4 Hz, 2H, H-arom), 7.73 (d, J_{HH} = 8.5 Hz, 2H, H-arom), 7.82 (d, J_{HH} = 8.2 Hz, 2H, H-arom), 7.87 (d, J_{HH} = 7.4 Hz, 2H, H-arom), 8.02 (d, J_{HH} = 7.2 Hz, 2H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 23.2 (CH_3), 23.3 (CH_3), 51.9 (CH), 52.0 (CH), 122.0, 122.9, 123.6, 124.2, 125.4, 125.5, 125.8, 127.4, 128.8, 128.9, 129.7 (CH-arom), 130.2, 130.5, 133.9, 142.0, 151.5, and 151.6 (C-arom); consistent with the literature data.[226]



L4

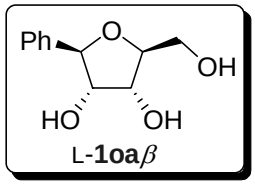
***O,O'*-(1,1'-Diphenyl-2,2'-diyl)-*N,N*-diisopropylphosphoramidite (L4).**[220] A solution of *i*-Pr_2NH (1.010 g, 9.98 mmol) in THF (10 mL) was added slowly to a mixture of Et_3N (7.26 g, 71.7 mmol) and PBr_3 (2.85 g, 10.5 mmol) in THF (40 mL) at 0 °C and the resulting mixture was stirred at room temperature for 3 h. The mixture was then cooled to 0 °C and a solution of biphenol **277** (1.86 g, 10.0 mmol) in THF (10 mL) was added. This mixture was stirred at room temperature overnight, then diluted with toluene (20 mL) and passed through a short path of alumina (3 × 5 cm), and evaporated. Chromatography on a column of alumina (5 × 5 cm) with toluene gave **L4** as a white foam (1.51 g, 48%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.27 (d, J = 6.8 Hz, 12H, CH_3), 3.50-3.63 (m, 2H, CH), 7.21-7.28 (m, 4H, CH-arom), 7.37 (ddd, J_{HH} = 7.7 Hz, J_{HH} = 7.6 Hz, J_{HH} = 1.5 Hz, 2H, CH-arom), 7.50 (dd, J_{HH} = 7.7 Hz, J_{HH} = 1.5 Hz, 2H, CH-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 24.0(CH_3), 44.5 (C), 44.6 (C), 122.1, 124.1, 128.9, 129.6 (CH-arom), 130.8, and 151.9 (C-arom); MS (CI) 316 (100, $M+H^+$), 247 (8), 187 (10, $Ph(OH)\text{-}Ph(OH)^+$); HRMS (CI) 316.1468 [$C_{18}H_{23}NO_2P$ ($M+H^+$) requires 316.1466]; Anal. Calcd for $C_{18}H_{22}NO_2P$: C, 68.56; H, 7.03; N, 4.43. Found: C, 68.33; H, 7.16; N, 4.38; consistent with the literature data.[220]



D-**1oa*β***

1'-Deoxy-1'-phenyl-*β*-D-ribofuranose (D-1oa*β*).[144b]

Complex $Et_3N.3HF$ (75 μL, 0.46 mmol) was added to a solution of silane D-**232ba*β*** (76 mg, 0.23 mmol) in THF (5 mL), the reaction mixture was stirred at 20 °C overnight, and then evaporated. Flash chromatography on a column of silica gel (3 × 10 cm) with ethyl acetate gave D-**1oa*β*** (36 mg, 75%) as a white crystalline solid: mp 112 °C (ethyl acetate), (lit.[144b] mp 121-122 °C); $[\alpha]_D$ -24.8 (*c* 0.44, MeOH); ^{1}H-NMR (400.1 MHz, CD_3OD) δ 3.73 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 12.1 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.8 Hz, 1H, 5'-Ha), 3.79 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 12.1 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.9 Hz, 1H, 5'-Hb), 3.88 (dd, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.4 Hz, $^3J_{2'\text{-H},3'\text{-H}}$ = 5.8 Hz, 1H, 2'-H), 3.95 (ddd, $^3J_{4'\text{-H},3'\text{-H}}$ = 4.8 Hz, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.8 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.9 Hz, 1H, 4'-H), 4.03 (dd, $^3J_{3'\text{-H},2'\text{-H}}$ = 5.8 Hz, $^3J_{3'\text{-H},4'\text{-H}}$ = 4.8 Hz, 1H, 3'-H), 4.69 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.4 Hz, 1H, 1'-H), 5.28 (s, 3H, OH), 7.22-7.32 (m, 3H, H-arom), 7.36-7.39 (m, 2H, H-arom); ^{13}C-NMR (100.6 MHz, CD_3OD) δ 62.66 (CH_2-5'), 71.48 (CH-3'), 77.42 (CH-2'), 84.78 (CH-4'), 84.81 (CH-1'), 126.33, 128.07, and 128.57 (CH-arom), 140.03 (C-arom); MS (CI) *m*/*z* (%) 211 ([M+H$^+$], 25), 193 ([M+H$^+$]-H_2O, 100); HRMS (CI) 211.0973 [$C_{11}H_{15}O_4$ (M+H$^+$) requires 211.0970]; consistent with the literature data.[144b]

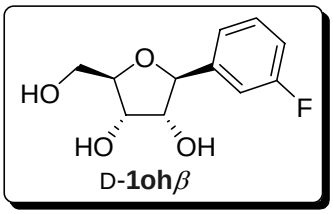


L-**1oa*β***

1'-Deoxy-1'-phenyl-*β*-L-ribofuranose (L-1oa*β*).[144b]

Complex $Et_3N.3HF$ (0.2 mL, 1.2 mmol) was added to a solution of silane L-**232ba*β*** (77 mg, 0.24 mmol) in THF (5 mL), the reaction mixture was stirred at 20 °C overnight, and then evaporated. Flash chromatography on a column of silica gel (3 × 10 cm) with ethyl acetate gave L-**1oa*β*** (36 mg, 72%) as a white crystalline solid: mp 112-113 °C (ethyl acetate), (lit.[144b] mp 121-122 °C); $[\alpha]_D$ +25.0 (*c* 0.48, MeOH); ^{1}H-NMR (400.1 MHz, CD_3OD) δ 3.73 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 12.1 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.8 Hz, 1H, 5'-Ha), 3.79 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 12.1 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.9 Hz, 1H, 5'-Hb), 3.88 (dd, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.4 Hz, $^3J_{2'\text{-H},3'\text{-H}}$ = 5.8 Hz, 1H, 2'-H), 3.95 (ddd, $^3J_{4'\text{-H},3'\text{-H}}$ = 4.8 Hz, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.8 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.9 Hz, 1H, 4'-H), 4.03 (dd, $^3J_{3'\text{-H},2'\text{-H}}$ = 5.8 Hz, $^3J_{3'\text{-H},4'\text{-H}}$ = 4.8 Hz, 1H, 3'-H), 4.69 (d, $^3J_{1'\text{-H},2'\text{-H}}$ =

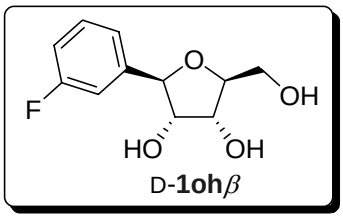
6.4 Hz, 1H, 1'-H), 5.28 (s, 3H, OH), 7.22-7.32 (m, 3H, H-arom), 7.36-7.39 (m, 2H, H-arom); ^{13}C-NMR (100.6 MHz, CD_3OD) δ 62.66 (CH_2-5'), 71.48 (CH-3'), 77.42 (CH-2'), 84.78 (CH-4'), 84.81 (CH-1'), 126.33, 128.07, and 128.57 (CH-arom), 140.03 (C-arom); MS (CI) *m/z* (%) 211 ([M+H$^+$], 80), 193 ([M+H$^+$]-H_2O, 100); HRMS (CI) 211.0972 [$C_{11}H_{15}O_4$ (M+H$^+$) requires 211.0970]; consistent with the literature data.[144b]



D-**1oh*β***

1'-Deoxy-1'-(3-fluorophenyl)-*β*-D-ribofuranose (D-1oh*β*).

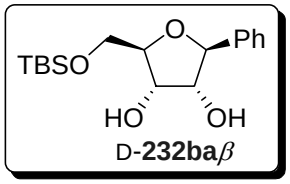
Complex $Et_3N.3HF$ (0.25 mL, 1.5 mmol) was added to a solution of silane D-**232bh*β*** (118 mg, 0.34 mmol) in THF (4 mL) and the reaction mixture was stirred at 20 °C overnight, and then evaporated. Flash chromatography on a column of silica gel (3 × 10 cm) with ethyl acetate gave D-**1oh*β*** (50 mg, 65%) as a white solid: mp 92-93 °C (ethyl acetate); $[\alpha]_D$ -31.6 (*c* 0.35, MeOH); ^{1}H-NMR (400.1 MHz, CD_3OD) δ 3.32-3.33 (bs, 3H, OH), 3.74 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.9 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.7 Hz, 1H, 5'-Ha), 3.81 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.9 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.7 Hz, 1H, 5'-Hb), 3.85 (dd, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.8 Hz, $^3J_{2'\text{-H},3'\text{-H}}$ = 5.7 Hz, 1H, 2'-H), 4.00 (ddd, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.7 Hz, $^3J_{4'\text{-H},3'\text{-H}}$ = 4.2 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.7 Hz, 1H, 4'-H), 4.05 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 5.7 Hz, $^3J_{3'\text{-H},4'\text{-H}}$ = 4.2 Hz, $^4J_{3'\text{-H},1'\text{-H}}$ = 0.5 Hz, 1H, 3'-H), 4.73 (dd, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.8 Hz, $^4J_{1'\text{-H},3'\text{-H}}$ = 0.5 Hz, 1H, 1'-H), 6.99 (dddd, $^3J_{4\text{-H,F}}$ = 9.0 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 7.9 Hz, J_{HH} = 2.7 Hz, J_{HH} = 1.0 Hz, 1H, 4-H), 7.21-7.26 (m, 1H, 2-H, and 6-H), 7.33 (ddd, $^3J_{5\text{-H},6\text{-H}}$ = 8.0 Hz, $^3J_{5\text{-H},4\text{-H}}$ = 7.9 Hz, $^4J_{5\text{-H,F}}$ = 6.0 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 63.35 (CH_2-5'), 72.59 (CH-3'), 78.87 (CH-2'), 84.50 (d, $^4J_{CF}$ = 1.6 Hz, CH-1'), 86.20 (CH-4'), 113.66 (d, $^2J_{CF}$ = 22.4 Hz, CH-2), 115.09 (d, $^2J_{CF}$ = 21.5 Hz, CH-4), 122.77 (d, $^4J_{CF}$ = 2.7 Hz, CH-6), 130.73 (d, $^3J_{CF}$ = 8.3 Hz, CH-5), 142.95 (d, $^3J_{CF}$ = 6.8 Hz, C-1), 164.34 (d, $^1J_{CF}$ = 244.3 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.83; MS (CI) *m/z* (%) 229 ([M+H$^+$], 55), 211 ([M+H$^+$]-H_2O, 100); HRMS (CI) 229.0878 [$C_{11}H_{14}FO_4$ (M+H$^+$) requires 229.0876]. Anal. Calcd. for $C_{11}H_{13}FO_4$: C, 57.89; H, 5.74. Found: C, 57.61; H, 5.75.



D-**1oh**β

1'-Deoxy-1'-(3-fluorophenyl)-β-L-ribofuranose (L-1ohβ).

Complex $Et_3N.3HF$ (1.5 mL, 9.2 mmol) was added to a solution of silane L-**232bh**β (666 mg, 1.94 mmol) in THF (15 mL) and the reaction mixture was stirred at 20 °C overnight, and then evaporated. Flash chromatography on a column of silica gel (3 × 10 cm) with ethyl acetate gave L-**1oh**β (276 mg, 62%) as a white solid: mp 92-93 °C (ethyl acetate); $[\alpha]_D$ +27.1 (*c* 0.48, MeOH); ^{1}H-NMR (400.1 MHz, CD_3OD) δ 3.32-3.33 (bs, 3H, OH), 3.74 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.9 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.7 Hz, 1H, 5'-Ha), 3.81 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.9 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.7 Hz, 1H, 5'-Hb), 3.85 (dd, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.8 Hz, $^3J_{2'\text{-H},3'\text{-H}}$ = 5.7 Hz, 1H, 2'-H), 4.00 (ddd, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.7 Hz, $^3J_{4'\text{-H},3'\text{-H}}$ = 4.2 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.7 Hz, 1H, 4'-H), 4.05 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 5.7 Hz, $^3J_{3'\text{-H},4'\text{-H}}$ = 4.2 Hz, $^4J_{3'\text{-H},1'\text{-H}}$ = 0.5 Hz, 1H, 3'-H), 4.73 (dd, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.8 Hz, $^4J_{1'\text{-H},3'\text{-H}}$ = 0.5 Hz, 1H, 1'-H), 6.99 (dddd, $^3J_{4\text{-H,F}}$ = 9.0 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 7.9 Hz, J_{HH} = 2.7 Hz, J_{HH} = 1.0 Hz, 1H, 4-H), 7.21-7.26 (m, 1H, 2-H, and 6-H), 7.33 (ddd, $^3J_{5\text{-H},6\text{-H}}$ = 8.0 Hz, $^3J_{5\text{-H},4\text{-H}}$ = 7.9 Hz, $^4J_{5\text{-H,F}}$ = 6.0 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 63.35 (CH_2-5'), 72.59 (CH-3'), 78.87 (CH-2'), 84.50 (d, $^4J_{CF}$ = 1.6 Hz, CH-1'), 86.20 (CH-4'), 113.66 (d, $^2J_{CF}$ = 22.4 Hz, CH-2), 115.09 (d, $^2J_{CF}$ = 21.5 Hz, CH-4), 122.77 (d, $^4J_{CF}$ = 2.7 Hz, CH-6), 130.73 (d, $^3J_{CF}$ = 8.3 Hz, CH-5), 142.95 (d, $^3J_{CF}$ = 6.8 Hz, C-1), 164.34 (d, $^1J_{CF}$ = 244.3 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.83; IR (NaCl, neat) ν 3376 (s, OH), 2932 (s), 2883 (s), 2501 (s), 1615 (s), 1591 (s), 1488 (s), 1450 (s) cm^{-1}; MS (CI) *m*/*z* (%) 229 ([M+H$^+$], 50), 211 ([M+H$^+$]-H_2O, 100); HRMS (CI) 229.0875 [$C_{11}H_{14}FO_4$ (M+H$^+$) requires 229.0876].

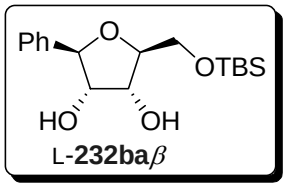


D-**232ba**β

5'-*O*-(*tert*-Butyldimethylsilyl)-1'-phenyl-β-D-ribofuranose (D-232baβ).

Grubbs 1st generation catalyst **C1** (42.4 mg, 0.051 mmol) was added to a solution of silane (2*S*,1'*R*)-**234ba** (328 mg, 1.03 mmol) in dichloromethane (20 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h, and then evaporated. The resulting residue was dissolved in a mixture of ethyl acetate (5 mL) and acetonitrile (5 mL), cooled to 0 °C, and a cold (0 °C) solution of $RuCl_3 \cdot H_2O$ (30 mg, 0.12 mmol), and $NaIO_4$ (357 mg, 1.67 mmol) in water (4 mL) was added in one portion. After 15 s, the reaction was

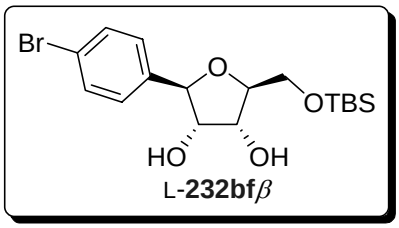
quenched with a 50% aqueous solution of $Na_2S_2O_3$ (10 mL). The aqueous layer was separated, and extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried (Na_2SO_4) and evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) to afford silane D-**232ba**β as a colourless oil (83 mg, 24%): $[\alpha]_D$ -10.2 (*c* 0.74, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.10 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.92 (s, 9H, *t*-Bu), 3.28 (bs, 2H, OH), 3.85 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.8 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.3 Hz, 1H, 5'-Ha), 3.89 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.8 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.4 Hz, 1H, 5'-Hb), 4.00 (dd, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.4 Hz, $^3J_{2'\text{-H},3'\text{-H}}$ = 5.5 Hz, 1H, 2'-H), 4.06 (dd, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.3 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.4 Hz, 1H, 4'-H), 4.21 (dd, $^3J_{3'\text{-H},2'\text{-H}}$ = 5.5 Hz, J_{HH} = 4.0 Hz, 1H, 3'-H), 4.76 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.4 Hz, 1H, 1'-H), 7.28-7.37 (m, 3H, H-arom), 7.42-7.44 (m, 2H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.53 (CH_3), -5.40 (CH_3), 18.31 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 63.71 (CH_2-5'), 72.75 (CH-3'), 77.97 (CH-2'), 84.15 (CH-4'), 84.33 (CH-1'), 126.05, 127.82, and 128.35 (CH-arom), 140.02 (C-arom); IR (NaCl, neat) ν 3421, 2929 (s), 2858 (s), 2360 (s), 1255 (s) cm^{-1}; MS (CI) *m*/*z* (%) 325 ([M+H$^+$], 100); HRMS (CI) 325.1837 [$C_{17}H_{29}O_4Si$ (M+H$^+$) requires 325.1835].



L-**232ba**β

5'-*O*-(*tert*-Butyldimethylsilyl)-1'-deoxy-1'-phenyl-β-L-ribofuranose (L-232baβ).
Silane L-**233ba**β (337 mg, 1.16 mmol) was dissolved in a mixture of ethyl acetate (5 mL) and acetonitrile (5 mL), cooled to 0 °C, and a cold (0 °C) solution of $RuCl_3 \cdot H_2O$ (30 mg, 0.12 mmol), and $NaIO_4$ (400 mg, 1.87 mmol) in water (5 mL) was added in one portion. After 15 s, the reaction was quenched with 50% aqueous solution of $Na_2S_2O_3$ (15 mL). The aqueous layer was separated, and extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried (Na_2SO_4), evaporated, and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) to afford starting silane L-**233ba**β (232 mg, 69% of starting mass), followed by diol L-**232ba**β (colourless oil, 103 mg, 27%, 87% based on recovered silane): $[\alpha]_D$ +10.8 (*c* 0.37, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.10 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.92 (s, 9H, *t*-Bu), 3.28 (bs, 2H, OH), 3.85 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.8 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.3 Hz, 1H, 5'-Ha), 3.89 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.8 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.4 Hz, 1H, 5'-Hb), 4.00 (dd, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.4 Hz, $^3J_{2'\text{-H},3'\text{-H}}$ = 5.5 Hz, 1H, 2'-H), 4.06 (dd, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.3 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.4 Hz, 1H, 4'-H), 4.21 (dd, $^3J_{3'\text{-H},2'\text{-H}}$ = 5.5 Hz, J_{HH} = 4.0 Hz, 1H, 3'-H), 4.76 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.4 Hz, 1H, 1'-H), 7.28-7.37 (m, 3H, H-arom), 7.42-7.44 (m, 2H, H-arom); ^{13}C-NMR (100.6 MHz,

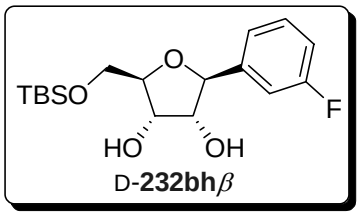
$CDCl_3$) δ -5.53 (CH_3), -5.40 (CH_3), 18.31 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 63.71 (CH_2-5'), 72.75 (CH-3'), 77.97 (CH-2'), 84.15 (CH-4'), 84.33 (CH-1'), 126.05, 127.82, and 128.35 (CH-arom), 140.02 (C-arom); IR (NaCl, neat) ν 3421, 2929 (s), 2858 (s), 2360 (s), 1255 (s) cm^{-1}; MS (CI) *m*/*z* (%) 325 ([M+H^+], 100); HRMS (CI) 325.1836 [$C_{17}H_{29}O_4Si$ (M+H^+) requires 325.1835].



L-**232bf*β***

5'-*O*-(*tert*-Butyldimethylsilyl)-1'-(4-bromophenyl)-1'-deoxy-*β*-L-ribofuranose (L-232bf*β*).

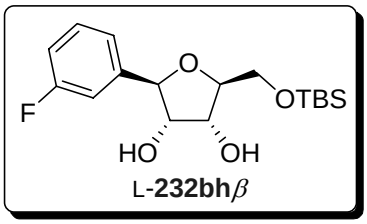
Grubbs 1st generation catalyst **C1** (72.0 mg, 0.087 mmol) was added to a solution of silane (2*R*,1'*S*)-**234bf** (2.483 g, 6.25 mmol) in dichloromethane (60 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h, and then evaporated. The resulting residue was dissolved in a mixture of ethyl acetate (30 mL) and acetonitrile (30 mL), cooled to 0 °C, and intensively stirred with mechanical overhead stirrer. A cold (0 °C) solution of $RuCl_3 \cdot H_2O$ (166 mg, 0.67 mmol), and $NaIO_4$ (1.656 g, 7.74 mmol) in water (25 mL) was added in one portion. After 15 s, the reaction was quenched with a 50% aqueous solution of $Na_2S_2O_3$ (50 mL). The aqueous layer was separated, and extracted with dichloromethane (3 × 300 mL). The combined organic phase was dried (Na_2SO_4) and evaporated. Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) gave diol L-**232bf*β*** (colourless oil, 786 mg, 31%): $[\alpha]_D$ -35.1 (*c* 0.74, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.04 (s, 3H, CH_3), 0.05 (s, 3H, CH_3), 0.90 (s, 9H, *t*-Bu), 2.57 (bs, 2H, OH), 3.55-3.76 (m, 4H), 4.54-4.56 (m, 1H), 7.34 (d, $^3J_{2\text{-H},3\text{-H}}$ = 8.4 Hz, 2H, 2-H, and 6-H), 7.50 (d, $^3J_{3\text{-H},2\text{-H}}$ = 8.4 Hz, 2H, 3-H, and 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.42 (CH_3), -5.40 (CH_3), 18.30 ($C(CH_3)_3$), 25.84 ($C(CH_3)_3$), 65.97 (CH_2-5'), 73.10 (CH-3'), 74.26 (CH-2'), 79.34 (CH-1'), 79.72 (CH-4'), 120.14 (C-4), 129.22 (CH-2, and CH-6), 131.62 (CH-3, and CH-5), 137.36 (C-1); IR (NaCl, neat) ν 3420 (s, OH), 2954 (s), 2928 (s), 2857 (s), 1255 (s) cm^{-1}; MS (CI) *m*/*z* (%) 403/405 ([M+H^+], 100); HRMS (CI) 403.0916/405.0774 [$C_{17}H_{28}BrO_4Si$ (M+H^+) requires 403.0940/405.0922].



D-**232bh*β***

5'-*O*-(*tert*-Butyldimethylsilyl)-1'-deoxy-1'-(3-fluorophenyl)-*β*-D-ribofuranose (D-232bh*β*).

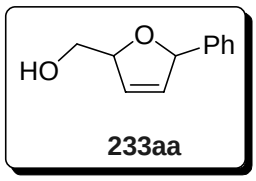
Silane D-**233bh*β*** (313 mg, 1.01 mmol) was dissolved in a mixture of ethyl acetate (5 mL) and acetonitrile (5 mL), cooled to 0 °C, and a cold (0 °C) solution of $RuCl_3 \cdot H_2O$ (30 mg, 0.12 mmol), and $NaIO_4$ (320 mg, 1.50 mmol) in water (4 mL) was added in one portion. After 45 s, the reaction was quenched with a 50% aqueous solution of $Na_2S_2O_3$ (15 mL). The aqueous layer was separated, and extracted with ethyl acetate (3 × 50 mL). The combined organic phase was dried (Na_2SO_4), evaporated, and chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) to afford diol D-**232bh*β*** as a colourless oil (211 mg, 61%): $[\alpha]_D$ -16.7 (*c* 1.20, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.10 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.91 (s, 9H, *t*-Bu), 2.56 (bs, 2H, OH), 3.86 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.8 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.0 Hz, 1H, 5'-Ha), 3.89 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.8 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.2 Hz, 1H, 5'-Hb), 3.97-4.01 (m, 1H, 2'-H), 4.08 (dd, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.0 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.2 Hz, 1H, 4'-H), 4.22-4.25 (m, 1H, 3'-H), 4.76 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.5 Hz, 1H, 1'-H), 6.97 (dddd, $^3J_{4\text{-H,F}}$ = 8.4 Hz, J_{HH} = 8.3 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 4-H), 7.11-7.16 (m, 1H, 2-H), 7.18-7.21 (m, 1H, 6-H), 7.27-7.33 (m, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.56 (CH_3), -5.43 (CH_3), 18.30 ($C(CH_3)_3$), 25.88 ($C(CH_3)_3$), 63.64 (CH_2-5'), 72.83 (CH-3'), 78.05 (CH-2'), 83.60 (d, $^4J_{CF}$ = 1.9 Hz, CH-1'), 84.38 (CH-4'), 112.83 (d, $^2J_{CF}$ = 22.3 Hz, CH-2), 114.64 (d, $^2J_{CF}$ = 21.2 Hz, CH-4), 121.58 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 129.83 (d, $^3J_{CF}$ = 8.2 Hz, CH-5), 143.90 (d, $^3J_{CF}$ = 6.6 Hz, C-1), 162.97 (d, $^1J_{CF}$ = 246.7 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.59; IR (NaCl, neat) ν 3398 (s, OH), 2929 (s), 2858 (s), 1617 (s), 1592 (s) cm^{-1}; MS (CI) *m*/*z* (%) 343 ([M+H$^+$], 100); HRMS (CI) 343.1740 [$C_{17}H_{28}FO_4Si$ (M+H$^+$) requires 343.1741]. Anal. Calcd. for $C_{17}H_{27}FO_4Si$: C, 59.62; H, 7.95. Found: C, 59.47; H, 8.06.



L-**232bh*β***

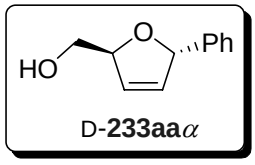
5'-*O*-(*tert*-Butyldimethylsilyl)-1'-deoxy-1'-(3-fluorophenyl)-*β*-L-ribofuranose (L-232bh*β*).

Grubbs 1st generation catalyst **C1** (71.0 mg, 0.090 mmol) was added to a solution of silane (2*R*,1'*S*)-**234bh** (1.951 g, 5.80 mmol) in dichloromethane (50 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h, and then evaporated. The resulting residue was dissolved in a mixture of ethyl acetate (25 mL) and acetonitrile (25 mL), cooled to 0 °C, and intensively stirred with mechanical overhead stirrer. A cold (0 °C) solution of $RuCl_3 \cdot H_2O$ (140 mg, 0.60 mmol), and $NaIO_4$ (1.430 g, 6.69 mmol) in water (20 mL) was added in one portion. After 15 s, the reaction was quenched with a 50% aqueous solution of $Na_2S_2O_3$ (50 mL), the aqueous layer was separated, and extracted with ethyl acetate (3 × 250 mL). The combined organic phase was dried (Na_2SO_4), evaporated, and chromatographed on a column of silica gel (3 cm × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) to afford diol L-**232bh*β*** as a colourless oil (667 mg, 34%): $[\alpha]_D$ -15.7 (*c* 1.15, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.10 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.91 (s, 9H, *t*-Bu), 2.56 (bs, 2H, OH), 3.86 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.8 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 4.0 Hz, 1H, 5'-Ha), 3.89 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.8 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.2 Hz, 1H, 5'-Hb), 3.97-4.01 (m, 1H, 2'-H), 4.08 (dd, $^3J_{4'\text{-H},5'\text{-Ha}}$ = 4.0 Hz, $^3J_{4'\text{-H},5'\text{-Hb}}$ = 3.2 Hz, 1H, 4'-H), 4.22-4.25 (m, 1H, 3'-H), 4.76 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.5 Hz, 1H, 1'-H), 6.97 (dddd, $^3J_{4\text{-H,F}}$ = 8.4 Hz, J_{HH} = 8.3 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 4-H), 7.11-7.16 (m, 1H, 2-H), 7.18-7.21 (m, 1H, 6-H), 7.27-7.33 (m, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.56 (CH_3), -5.43 (CH_3), 18.30 ($C(CH_3)_3$), 25.88 ($C(CH_3)_3$), 63.64 (CH_2-5'), 72.83 (CH-3'), 78.05 (CH-2'), 83.60 (d, $^4J_{CF}$ = 1.9 Hz, CH-1'), 84.38 (CH-4'), 112.83 (d, $^2J_{CF}$ = 22.3 Hz, CH-2), 114.64 (d, $^2J_{CF}$ = 21.2 Hz, CH-4), 121.58 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 129.83 (d, $^3J_{CF}$ = 8.2 Hz, CH-5), 143.90 (d, $^3J_{CF}$ = 6.6 Hz, C-1), 162.97 (d, $^1J_{CF}$ = 246.7 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ -113.59; IR (NaCl, neat) ν 3398 (s, OH), 2929 (s), 2858 (s), 1617 (s), 1592 (s) cm^{-1}; MS (CI) *m*/*z* (%) 343 ([M+H$^+$], 100); HRMS (CI) 343.1740 [$C_{17}H_{28}FO_4Si$ (M+H$^+$) requires 343.1741]. Anal. Calcd. for $C_{17}H_{27}FO_4Si$: C, 59.62; H, 7.95. Found: C, 59.47; H, 8.06.



233aa

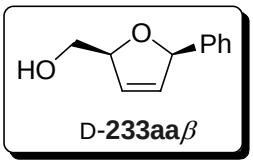
2',3'-Didehydro-1',2',3'-trideoxy-1'-phenyl-*α*/*β*-D/L-ribofuranose (233aa). A solution of TBAF (0.5 mL, 0.5 mmol, 1.0M solution in THF) was added to a solution of the protected dihydrofuran **233ca** (60 mg, 0.15 mmol) in THF (2 mL). The mixture was stirred at room temperature until no more starting material was detected by TLC. The reaction was quenched with brine and extracted with $CHCl_3$. Chromatography on a column of neutral alumina (3 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5 to 67:33) gave **233aa** as a colourless oil (14 mg, 53%): ^{1}H-NMR (400.1 MHz, $CDCl_3$, mixture of diastereoisomers in a 1:2.6 ratio, the minor diastereoisomer is marked with * where possible) δ 3.58-4.15 (m, 2H, C*H*$_2$); 4.18-4.24 and 5.00*-5.04* (m, 1H, CH_2C*H*), 5.06*-5.07* and 5.15-5.19 (m, 1H, PhC*H*), 5.81-6.16 (m, 2H, C*H*=C*H*), 7.30-7.39 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 68.0 and 70.8 (*C*H_2), 75.2 and 76.8 (CH_2*C*H), 87.3 and 88.1 (Ph*C*H), 126.4 and 126.5 and 132.4 and 133.4 (*C*H=*C*H), 127.2, 127.7, 128.0, 128.2, 128.5, 128.6; MS (CI) *m*/*z* (%) 177 ([M+H$^+$], 80), 159 ([M+H$^+$]-H_2O, 100); HRMS (CI) 177.0915 [$C_{11}H_{13}O_2$ (M+H$^+$) requires 177.0916].



D-**233aa***α*

2',3'-Didehydro-1',2',3'-trideoxy-1'-phenyl-*α*-D-ribofuranose (D-233aa*α*).
Complex $Et_3N.3HF$ (1.0 mL, 6.1 mmol) was added to a solution of silane D-**233ba***α* (441 mg, 1.52 mmol) in THF (10 mL) and the reaction mixture was stirred at 20 °C overnight and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5 to 67:33) gave D-**233aa***α* (176 mg, 66%) as a colourless oil: $[\alpha]_D$ -332.4 (*c* 1.71, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.42 (s, 1H, OH), 3.59 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.7 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.2 Hz, 1H, 5'-Ha), 3.74 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.7 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.2 Hz, 1H, 5'-Hb), 5.10 (m, 1H, 4'-H), 5.81 (ddd, $^4J_{1'\text{-H},4'\text{-H}}$ = 5.7 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.6 Hz, 1H, 1'-H), 5.85 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.6 Hz, 1H, 3'-H), 5.95 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.6 Hz, 1H, 2'-H), 7.24-7.33 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.95 (CH_2-5'), 87.37 (CH-4'), 87.99 (CH-1'), 126.28 (CH-arom), 126.51 (CH-3'), 127.99, and 128.48 (CH-arom), 132.16 (CH-2'), 141.27 (C-arom); IR (NaCl, neat) ν 3406 (s, OH), 2868 (s), 1493 (m), 1454 (m), 1065 (s) cm^{-1}; MS (CI) *m*/*z* (%) 177 ([M+H$^+$], 95), 159

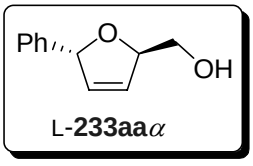
([M+H$^+$]-H_2O, 100); HRMS (CI) 177.0917 [$C_{11}H_{13}O_2$ (M+H$^+$) requires 177.0916]. Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.82; H, 6.96.



D-**233aa**β

2',3'-Didehydro-1',2',3'-trideoxy-1'-phenyl-β-L-ribofuranose (D-233aaβ).

Complex $Et_3N.3HF$ (0.4 mL, 2.5 mmol) was added to a solution of silane D-**233ba**β (203 mg, 0.70 mmol) in THF (5 mL). Reaction mixture was stirred at 20 °C overnight and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20 to 60:40) gave D-**233aa**β (84 mg, 68%) as a colourless oil: $[\alpha]_D$ +77.5 (*c* 1.28, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.96 (t, $^3J_{5\text{-OH},5\text{-H}}$ = 6.0 Hz, 1H, 5-OH), 3.67 (ddd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 11.6 Hz, $^3J_{5\text{-Ha},5\text{-OH}}$ = 6.1 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.2 Hz, 1H, 5-Ha), 3.78 (ddd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 11.6 Hz, $^3J_{5\text{-Hb},5\text{-OH}}$ = 5.9 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 3.3 Hz, 1H, 5-Hb), 5.00-5.03 (m, 1H, 4-H), 5.80-5.82 (m, 1H, 1-H), 5.94 (ddd, $^3J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, J_{HH} = 2.4 Hz, J_{HH} = 1.4 Hz, 1H, 3-H), 6.00 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 2-H), 7.29-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.99 (CH_2-5), 87.19 (CH-4), 87.85 (CH-1), 126.95 (CH-arom), 127.65 (CH-3), 128.13 (CH-arom), 128.58 (CH-arom), 131.48 (CH-2), 141.05 (C-arom); IR (NaCl, neat) ν 3365 (m, OH), 2929 (m), 2858 (m), 2360 (s), 1454 (m) cm^{-1}; MS (CI) *m*/*z* (%) 177 ([M+H$^+$], 80), 159 ([M+H$^+$]-H_2O, 100); HRMS (CI) 177.0918 [$C_{11}H_{13}O_2$ (M+H$^+$) requires 177.0916].

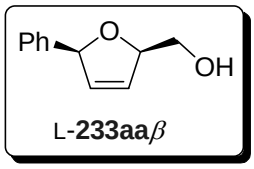


L-**233aa**α

2',3'-Didehydro-1',2',3'-trideoxy-1'-phenyl-α-L-ribofuranose (L-233aaα).

Complex $Et_3N.3HF$ (0.8 mL, 4.9 mmol) was added to a solution of silane L-**233ba**α (463 mg, 1.59 mmol) in THF (10 mL) and the reaction mixture was stirred at 20 °C overnight and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (95:5 to 67:33) gave L-**233aa**α (199 mg, 71%) as a colourless oil: $[\alpha]_D$ +334.6 (*c* 1.79, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.42 (s, 1H, OH), 3.59 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.7 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.2 Hz, 1H, 5'-Ha), 3.74 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.7 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.2 Hz, 1H, 5'-Hb), 5.10 (m, 1H, 4'-H), 5.81 (ddd, $^4J_{1'\text{-H},4'\text{-H}}$ = 5.7 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.6 Hz, 1H, 1'-H), 5.85 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.6 Hz, 1H, 3'-H), 5.95 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.6 Hz, 1H, 2'-H), 7.24-7.33 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.95

(CH_2-5'), 87.37 (CH-4'), 87.99 (CH-1'), 126.28 (CH-arom), 126.51 (CH-3'), 127.99, and 128.48 (CH-arom), 132.16 (CH-2'), 141.27 (C-arom); IR (NaCl, neat) ν 3406 (s, OH), 2868 (s), 1493 (m), 1454 (m), 1065 (s) cm^{-1}; MS (CI) *m*/*z* (%) 177 ([M+H^+], 95), 159 ([M+H^+]-H_2O, 100); HRMS (CI) 177.0918 [$C_{11}H_{13}O_2$ (M+H^+) requires 177.0916]. Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.73; H, 6.95.

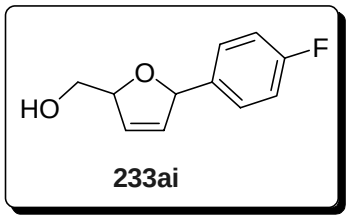


L-**233aa**β

2',3'-Didehydro-1',2',3'-trideoxy-1'-phenyl-β-L-ribofuranose (L-233aaβ).
Complex $Et_3N.3HF$ (0.5 mL, 3.0 mmol) was added to a solution of silane L-**233ba**β (254 mg, 0.87 mmol) in THF (5 mL). Reaction mixture was stirred at 20 °C overnight and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20 to 60:40) gave L-**233aa**β (82 mg, 54%) as a colourless oil: $[\alpha]_D$ -78.8 (*c* 1.32, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.96 (t, $^3J_{5\text{-OH},5\text{-H}}$ = 6.0 Hz, 1H, 5-OH), 3.67 (ddd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 11.6 Hz, $^3J_{5\text{-Ha},5\text{-OH}}$ = 6.1 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.2 Hz, 1H, 5-Ha), 3.78 (ddd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 11.6 Hz, $^3J_{5\text{-Hb},5\text{-OH}}$ = 5.9 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 3.3 Hz, 1H, 5-Hb), 5.00-5.03 (m, 1H, 4-H), 5.80-5.82 (m, 1H, 1-H), 5.94 (ddd, $^3J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, J_{HH} = 2.4 Hz, J_{HH} = 1.4 Hz, 1H, 3-H), 6.00 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 2-H), 7.29-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.99 (CH_2-5), 87.19 (CH-4), 87.85 (CH-1), 126.95 (CH-arom), 127.65 (CH-3), 128.13 (CH-arom), 128.58 (CH-arom), 131.48 (CH-2), 141.05 (C-arom); IR (NaCl, neat) ν 3365 (m, OH), 2929 (m), 2858 (m), 2360 (s), 1454 (m) cm^{-1}; MS (CI) *m*/*z* (%) 177 ([M+H^+], 80), 159 ([M+H^+]-H_2O, 100); HRMS (CI) 177.0918 [$C_{11}H_{13}O_2$ (M+H^+) requires 177.0916]. Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.59; H, 6.82.

via three-step procedure: *n*-Butyllithium (0.5 mL, 1.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (211 mg, 1.02 mmol) in THF (1 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* a cannula) to a suspension of copper(I) iodide (200 mg, 1.05 mmol) in THF (2 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C and a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (9.7 mg, 0.014 mmol) in THF (1 mL) and allylcarbonate (*S*)-**267a** (170 mg, 0.72 mmol, neat) were added, consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of

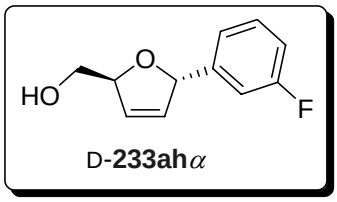
silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*,1'*S*)-**234ba** as a colourless oil (182 mg, 79%, as a single diastereoisomer). Silane (2*R*,1'*S*)-**234ba** was dissolved in CH_2Cl_2 (10 mL), Grubbs 1st generation catalyst **C1** (10.1 mg, 0.012 mmol) was added under a stream of argon atmosphere and the mixture was stirred at 40 °C for 5 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to afford silane L-**233ba***β* as a colourless oil (146 mg, 88%). Silane L-**233ba***β* was dissolved in THF (4.5 mL), complex $Et_3N.3HF$ (150 μL, 0.92 mmol) was added, the reaction mixture was stirred overnight at 20 °C, and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (90:10 to 67:33) gave L-**233aa***β* (47 mg, 53%, 37% from (*R*)-**235b** over 3 steps) as a colourless oil: $[\alpha]_D$ -78.3 (*c* 1.24, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.96 (t, $^3J_{5\text{-OH},5\text{-H}}$ = 6.0 Hz, 1H, 5-OH), 3.67 (ddd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 11.6 Hz, $^3J_{5\text{-Ha},5\text{-OH}}$ = 6.1 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.2 Hz, 1H, 5-Ha), 3.78 (ddd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 11.6 Hz, $^3J_{5\text{-Hb},5\text{-OH}}$ = 5.9 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 3.3 Hz, 1H, 5-Hb), 5.00-5.03 (m, 1H, 4-H), 5.80-5.82 (m, 1H, 1-H), 5.94 (ddd, $^3J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, J_{HH} = 2.4 Hz, J_{HH} = 1.4 Hz, 1H, 3-H), 6.00 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 2-H), 7.29-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.99 (CH_2-5), 87.19 (CH-4), 87.85 (CH-1), 126.95 (CH-arom), 127.65 (CH-3), 128.13 (CH-arom), 128.58 (CH-arom), 131.48 (CH-2), 141.05 (C-arom); MS (EI) *m*/*z* (%) 176 ([M^+], 10), 145 (100), 127 (50), 117 (95), 115 (95); HRMS (EI) 176.0842 [$C_{11}H_{12}O_2$ (M^+) requires 176.0837]. Chiral GC (Supelco β-DEX 120 column, oven 135 °C isothermal, *t* = 42.79 min) showed >99% de, >99% ee (t_R = 42.48 min (L-**233aa***β*), t_R = 44.27 min (D-**233aa***β*), t_R = 51.25 (L-**233aa***α*), t_R = 54.79 (D-**233aa***α*)).[227]



233ai

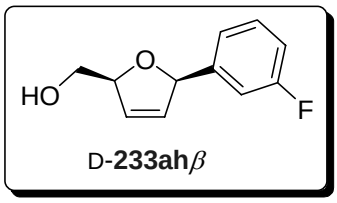
2',3'-Didehydro-1',2',3'-trideoxy-1'-(4-fluorophenyl)-*α*/*β*-D/L-ribofuranose (233ai). Complex $Et_3N.3HF$ (90 μL, 0.55 mmol) was added to a solution of silane **233ci** (108 mg, 0.25 mmol) in THF (4 mL) and the mixture was stirred at room temperature for 16 h. The resulting solution was evaporated (40 °C) and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to

remove the non-polar compounds, followed by elution with a mixture of hexanes and ethyl acetate (67:33) that gave the D4 ribofuranose **233ai** as a colourless oil (23 mg, 48%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.83 (t, $^{3}J_{HH}$ = 6.4 Hz, 1H, OH), 3.67 (ddd, $^{2}J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.4 Hz, J_{HH} = 6.0 Hz, J_{HH} = 4.9 Hz, 1H, 1-Ha), 3.79 (ddd, $^{2}J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.4 Hz, J_{HH} = 5.7 Hz, J_{HH} = 3.1 Hz, 1H, 1-Hb), 4.98-5.02 (m, 1H, 4'-H), 5.77-5.78 (m, 1H, 1'-H), 5.95 (d, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 6.7 Hz, 1H, 2'-H), 5.97 (d, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 6.7 Hz, 1H, 3'-H), 7.05 (t, $^{3}J_{3\text{-H},2\text{-H}}$ = 8.7 Hz, $^{3}J_{3\text{-H,F}}$ = 8.7 Hz, 2H, 3-H), 7.33 (dd, $^{3}J_{2\text{-H},3\text{-H}}$ = 8.7 Hz, $^{4}J_{2\text{-H,F}}$ = 5.4 Hz, 2H, 2-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.95 (CH_2-5'), 87.14 (CH-1'), 87.21 (CH-4'), 115.50 (d, $^{2}J_{CF}$ = 21.5 Hz, CH-3), 128.02 (CH-2'), 128.82 (d, $^{3}J_{CF}$ = 8.3 Hz, CH-2), 131.48 (CH-3'), 137.02 (d, $^{4}J_{CF}$ = 3.1 Hz, C-1), 162.63 (d, $^{1}J_{CF}$ = 246.5 Hz, C-4); MS (CI, 150 °C) *m/z* (%) 195 (M^+, 60), 177 (M^+-H_2O, 100); HRMS (CI) 195.0822 [$C_{11}H_{12}FO_2$ (M^+) requires 195.0821].



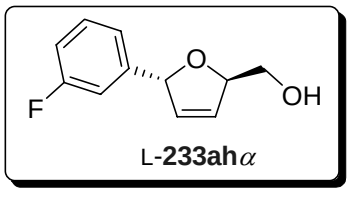
D-**233ah**α

2',3'-Didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-α-D-ribofuranose (D-233ahα). Complex $Et_3N.3HF$ (0.4 mL, 2.3 mmol) was added to a solution of silane D-**233bh**α (178 mg, 0.57 mmol) in THF (5 mL) and the reaction mixture was stirred at 20 °C overnight, and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (67:33 to 60:40) gave D-**233ah**α (97 mg, 88%) as a colourless oil: $[\alpha]_D$ -236.8 (*c* 1.90, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.05 (bs, 1H, OH), 3.65 (dd, $^{2}J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.7 Hz, $^{3}J_{5'\text{-Ha},4'\text{-H}}$ = 5.2 Hz, 1H, 5'-Ha), 3.81 (dd, $^{2}J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.7 Hz, $^{3}J_{5'\text{-Hb},4'\text{-H}}$ = 3.2 Hz, 1H, 5'-Hb), 5.14-5.18 (m, 1H, 4'-H), 5.85 (ddd, $^{3}J_{1'\text{-H,F}}$ = 5.8 Hz, J_{HH} = 2.1 Hz, J_{HH} = 2.1 Hz, 1H, 1'-H), 5.92 (ddd, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.5 Hz, 1H, 2'-H), 6.00 (ddd, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.6 Hz, 1H, 3'-H), 6.95-7.13 (m, 3H, 2-H, 4-H, and 6-H), 7.31 (ddd, $^{3}J_{HH}$ = 7.9 Hz, $^{3}J_{HH}$ = 7.7 Hz, $^{4}J_{5\text{-H,F}}$ = 5.8 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.95 (CH_2-5'), 87.35 (d, $^{4}J_{CF}$ = 1.8 Hz, CH-1'), 87.53 (CH-4'), 113.12 (d, $^{2}J_{CF}$ = 21.9 Hz, CH-2), 114.71 (d, $^{2}J_{CF}$ = 21.3 Hz, CH-4), 121.78 (d, $^{4}J_{CF}$ = 2.9 Hz, CH-6), 126.90 (CH-2'), 130.07 (d, $^{3}J_{CF}$ = 8.1 Hz, CH-5), 131.84 (CH-3'), 144.06 (d, $^{3}J_{CF}$ = 6.4 Hz, C-1), 163.00 (d, $^{1}J_{CF}$ = 246.3 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.28; IR (NaCl, neat) ν 3405 (s, OH), 2928 (m), 2874 (m), 1615 (s), 1592 (s), 1488 (s), 1449 (s), 1264 (s) cm^{-1}; MS (CI) *m/z* (%) 195 ([M+H^+], 15), 177 ([M+H^+]-H_2O, 100); HRMS (CI) 195.0816 [$C_{11}H_{12}FO_2$ (M+H^+) requires 195.0821].



D-**233ah**β

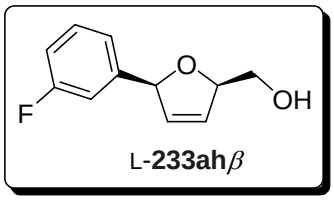
2',3'-Didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-β-D-ribofuranose (D-233ahβ). Complex $Et_3N.3HF$ (1.0 mL, 6.0 mmol) was added to a solution of silane D-**233bh**β (459 mg, 1.49 mmol) in THF (10 mL) and the reaction mixture was stirred at 20 °C overnight, and then evaporated. Flash chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) gave D-**233ah**β (176 mg, 61%) as a colourless oil: $[\alpha]_D$ +64.2 (*c* 1.90, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.19 (bs, 1H, OH), 3.66 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.8 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.2 Hz, 1H, 5'-Ha), 3.78 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.8 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.4 Hz, 1H, 5'-Hb), 4.98-5.02 (m, 1H, 4'-H), 5.78 (d, $^3J_{1'\text{-H,F}}$ = 5.9 Hz, 1H, 1'-H), 5.93 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.1 Hz, J_{HH} = 1.1 Hz, 1H, 2'-H), 5.96 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.1 Hz, J_{HH} = 1.2 Hz, 1H, 3'-H), 6.99 (dddd, $^3J_{4\text{-H,F}}$ = 8.4 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 8.0 Hz, $^4J_{4\text{-H},2\text{-H}}$ = 2.6 Hz, $^4J_{4\text{-H},6\text{-H}}$ = 1.0 Hz, 1H, 4-H), 7.07 (ddd, $^3J_{2\text{-H,F}}$ = 9.7 Hz, $^4J_{2\text{-H},4\text{-H}}$ = 2.6 Hz, $^4J_{2\text{-H},6\text{-H}}$ = 1.6 Hz, 1H, 2-H), 7.12 (dddd, $^3J_{6\text{-H},5\text{-H}}$ = 7.7 Hz, $^4J_{6\text{-H},2\text{-H}}$ = 1.6 Hz, $^4J_{6\text{-H},4\text{-H}}$ = 1.0 Hz, $^5J_{6\text{-H,F}}$ = 0.5 Hz, 1H, 6-H), 7.32 (ddd, $^3J_{5\text{-H},4\text{-H}}$ = 8.0 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 7.7 Hz, $^4J_{5\text{-H,F}}$ = 5.8 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 65.02 (CH_2-5'), 87.18 (d, $^4J_{CF}$ = 1.8 Hz, CH-1'), 87.37 (CH-4'), 113.75 (d, $^2J_{CF}$ = 21.8 Hz, CH-2), 114.98 (d, $^2J_{CF}$ = 21.2 Hz, CH-4), 122.38 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 127.89 (CH-2'), 130.13 (d, $^3J_{CF}$ = 8.1 Hz, CH-5), 131.17 (CH-3'), 143.78 (d, $^3J_{CF}$ = 6.5 Hz, C-1), 162.95 (d, $^1J_{CF}$ = 246.5 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.06; IR (NaCl, neat) ν 3406 (s, OH), 2929 (m), 2870 (m), 1615 (s), 1592 (s), 1488 (s), 1449 (s), 1263 (s) cm^{-1}; MS (CI) *m*/*z* (%) 195 ([M+H$^+$], 30), 177 ([M+H$^+$]-H_2O, 100); HRMS (CI) 195.0819 [$C_{11}H_{12}FO_2$ (M+H$^+$) requires 195.0821]. Anal. Calcd. for $C_{11}H_{11}FO_2$: C, 68.03; H, 5.71. Found: C, 68.23; H, 5.72.



L-**233ah**α

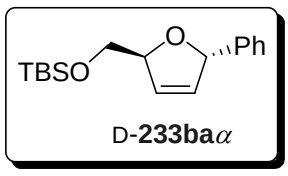
2',3'-Didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-α-L-ribofuranose (L-233ahα). Complex $Et_3N.3HF$ (1.0 mL, 6.0 mmol) was added to a solution of silane L-**233bh**α (455 mg, 1.48 mmol) in THF (10 mL) and the reaction mixture was stirred at 20 °C overnight, and then evaporated. Gradient chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (75:25 to 60:40) gave L-**233ah**α

(218 mg, 76%) as a colourless oil: $[\alpha]_D$ +288.2 (*c* 2.04, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 2.05 (bs, 1H, OH), 3.65 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 11.7 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.2 Hz, 1H, 5'-Ha), 3.81 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 11.7 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 3.2 Hz, 1H, 5'-Hb), 5.14-5.18 (m, 1H, 4'-H), 5.85 (ddd, $^3J_{1'\text{-H,F}}$ = 5.8 Hz, J_{HH} = 2.1 Hz, J_{HH} = 2.1 Hz, 1H, 1'-H), 5.92 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.5 Hz, 1H, 2'-H), 6.00 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.6 Hz, 1H, 3'-H), 6.95-7.13 (m, 3H, 2-H, 4-H, and 6-H), 7.31 (ddd, $^3J_{HH}$ = 7.9 Hz, $^3J_{HH}$ = 7.7 Hz, $^4J_{5\text{-H,F}}$ = 5.8 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 64.95 (CH_2-5'), 87.35 (d, $^4J_{CF}$ = 1.8 Hz, CH-1'), 87.53 (CH-4'), 113.12 (d, $^2J_{CF}$ = 21.9 Hz, CH-2), 114.71 (d, $^2J_{CF}$ = 21.3 Hz, CH-4), 121.78 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 126.90 (CH-2'), 130.07 (d, $^3J_{CF}$ = 8.1 Hz, CH-5), 131.84 (CH-3'), 144.06 (d, $^3J_{CF}$ = 6.4 Hz, C-1), 163.00 (d, $^1J_{CF}$ = 246.3 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.28; IR (NaCl, neat) ν 3405 (s, OH), 2928 (m), 2874 (m), 1615 (s), 1592 (s), 1488 (s), 1449 (s), 1264 (s) cm^{-1}; MS (CI) *m*/*z* (%) 195 ([M+H$^+$], 40), 177 ([M+H$^+$]-H_2O, 100); HRMS (CI) 195.0824 [$C_{11}H_{12}FO_2$ (M+H$^+$) requires 195.0821].



L-**233ah**β

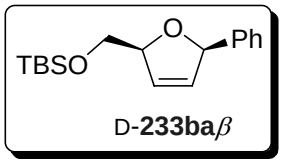
2',3'-Didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-β-L-ribofuranose (L-233ahβ). Complex $Et_3N.3HF$ (0.2 mL, 1.3 mmol) was added to a solution of silane L-**233bh**β (100 mg, 0.32 mmol) in THF (5 mL) and the reaction mixture was stirred at 20 °C overnight, and then evaporated. Flash chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (80:20) gave L-**233ah**β (42 mg, 67%) as a colourless oil: $[\alpha]_D$ -63.4 (*c* 1.90, $CHCl_3$); HRMS (CI) 195.0820 [$C_{11}H_{12}FO_2$ (M+H$^+$) requires 195.0821]. Anal. Calcd. for $C_{11}H_{11}FO_2$: C, 68.03; H, 5.71. Found: C, 68.19; H, 5.77.



D-**233ba**α

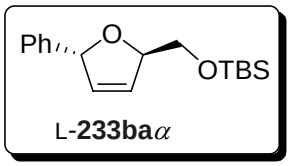
5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-2',3'-dideoxy-1'-phenyl-α-D-ribofuranose (D-233baα). Grubbs 1st generation catalyst **C1** (6.9 mg, 0.008 mmol) was added to a solution of silane (2*S*,1'*S*)-**234ba** (266 mg, 0.83 mmol) in dichloromethane (10 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 5 h. The resulting solution was evaporated and the residue was chromatographed on a column

of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane D-**233ba**α as a colourless oil (136 mg, 56%): $[\alpha]_D$ -69.6 (*c* 1.02, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.06 (s, 3H, CH_3), 0.07 (s, 3H, CH_3), 0.90 (s, 9H, *t*-Bu), 3.66 (dd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 10.3 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.7 Hz, 1H, 5-Ha), 3.77 (dd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 10.3 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 4.6 Hz, 1H, 5-Hb), 5.02-5.07 (m, 1H, 4-H), 5.78-5.80 (m, 1H, 1-H), 5.92 (ddd, $^3J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, J_{HH} = 2.1 Hz, J_{HH} = 1.4 Hz, 1H, 3-H), 5.97 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 2-H), 7.22-7.36 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.33 (CH_3), -5.28 (CH_3), 18.37 ($C(CH_3)_3$), 25.93 ($C(CH_3)_3$), 66.03 (CH_2-5), 87.24 (CH-4), 88.04 (CH-1), 126.40, and 127.75 (CH-arom), 128.13 (CH-2), 128.44 (CH-arom), 131.28 (CH-3), 141.85 (C-arom); IR (NaCl, neat) ν 3380 (s), 2954 (s), 2930 (s), 2858 (s), 1725 (m), 1257 (s), 1113 (m), 836 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 291 ([M+H$^+$], 70), 149 (100); HRMS (CI) 291.1776 [$C_{17}H_{27}O_2Si$ (M+H$^+$) requires 291.1780].



D-**233ba**β

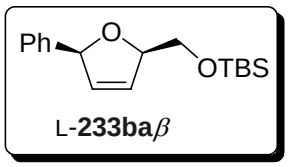
5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-2',3'-dideoxy-1'-phenyl-β-D-ribofuranose (D-233baβ). Grubbs 1st generation catalyst **C1** (12.5 mg, 0.015 mmol) was added to a solution of silane (2*S*,1'*R*)-**234ba** (483 mg, 1.52 mmol) in dichloromethane (20 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 5 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane D-**233ba**β as a colourless oil (441 mg, 78%): $[\alpha]_D$ -35.5 (*c* 1.24, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 6H, CH_3), 0.93 (s, 9H, *t*-Bu), 3.73 (dd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 10.3 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.9 Hz, 1H, 5-Ha), 3.85 (dd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 10.3 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 4.8 Hz, 1H, 5-Hb), 4.96 (ddddd, $^3J_{4\text{-H},5\text{-Ha}}$ = 5.9 Hz, $^3J_{4\text{-H},5\text{-Hb}}$ = 4.8 Hz, $^4J_{4\text{-H},1\text{-H}}$ = 4.0 Hz, $^3J_{4\text{-H},3\text{-H}}$ = 2.1 Hz, $^4J_{4\text{-H},2\text{-H}}$ = 1.4 Hz, 1H, 4-H), 5.80 (ddd, $^4J_{1\text{-H},4\text{-H}}$ = 4.0 Hz, $^3J_{1\text{-H},2\text{-H}}$ = 2.4 Hz, $^4J_{1\text{-H},3\text{-H}}$ = 1.6 Hz, 1H, 1-H), 5.92 (ddd, $^3J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, $^3J_{3\text{-H},4\text{-H}}$ = 2.1 Hz, $^4J_{3\text{-H},1\text{-H}}$ = 1.6 Hz, 1H, 3-H), 6.02 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, $^3J_{2\text{-H},1\text{-H}}$ = 2.4 Hz, $^4J_{2\text{-H},4\text{-H}}$ = 1.4 Hz, 1H, 2-H), 7.27-7.40 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.38 (CH_3), 18.37 ($C(CH_3)_3$), 25.89 ($C(CH_3)_3$), 66.42 (CH_2-5), 87.15 (CH-4), 87.95 (CH-1), 126.84, 127.77, and 128.27 (CH-arom), 128.33 (CH-2), 130.99 (CH-3), 141.65 (C-arom); IR (NaCl, $CHCl_3$) ν 3371 (s), 2954 (s), 2930 (s), 2858 (s), 1726 (m), 1257 (s), 1113 (s), 836 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 305 (100), 291 ([M$^+$], 50); HRMS (CI) 291.1778 [$C_{17}H_{27}O_2Si$ (M$^+$) requires 291.1780].



L-**233ba**α

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-2',3'-dideoxy-1'-phenyl-α-L-ribofuranose (L-233baα).

Grubbs 1st generation catalyst **C1** (55.0 mg, 0.067 mmol) was added to a solution of silane (2*R*,1'*R*)-**234ba** (1.226 g, 3.85 mmol) in dichloromethane (40 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to afford silane L-**233ba**α as a colourless oil (1.019 g, 91%): $[\alpha]_D$ +202.6 (*c* 1.90, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.06 (s, 3H, CH_3), 0.07 (s, 3H, CH_3), 0.90 (s, 9H, *t*-Bu), 3.66 (dd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 10.3 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.7 Hz, 1H, 5-Ha), 3.77 (dd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 10.3 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 4.6 Hz, 1H, 5-Hb), 5.02-5.07 (m, 1H, 4-H), 5.78-5.80 (m, 1H, 1-H), 5.92 (ddd, $^3J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, J_{HH} = 2.1 Hz, J_{HH} = 1.4 Hz, 1H, 3-H), 5.97 (ddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.5 Hz, 1H, 2-H), 7.22-7.36 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.33 (CH_3), -5.28 (CH_3), 18.37 ($C(CH_3)_3$), 25.93 ($C(CH_3)_3$), 66.03 (CH_2-5), 87.24 (CH-4), 88.04 (CH-1), 126.40, and 127.75 (CH-arom), 128.13 (CH-2), 128.44 (CH-arom), 131.28 (CH-3), 141.85 (C-arom); IR (NaCl, neat) ν 3373 (s), 2931 (s), 2858 (s), 1730 (m), 1467 (m), 1257 (s), 1113 (s), 837 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 291 ([M+H$^+$], 100); HRMS (CI) 291.1779 [$C_{17}H_{27}O_2Si$ (M+H$^+$) requires 291.1780].

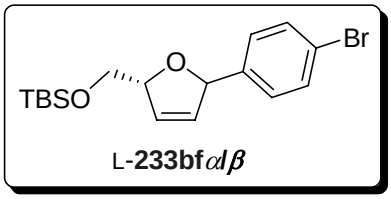


L-**233ba**β

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-2',3'-dideoxy-1'-phenyl-β-L-ribofuranose (L-233baβ).

Grubbs 1st generation catalyst **C1** (34.1 mg, 0.041 mmol) was added to a solution of silane (2*R*,1'*S*)-**234ba** (1.129 g, 3.54 mmol) in dichloromethane (40 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to give silane L-**233ba**β as a colourless oil (880 mg, 86%): $[\alpha]_D$ -24.6 (*c* 1.83, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 6H, CH_3), 0.93 (s, 9H, *t*-Bu), 3.73 (dd, $^2J_{5\text{-Ha},5\text{-Hb}}$ = 10.3 Hz, $^3J_{5\text{-Ha},4\text{-H}}$ = 5.9 Hz, 1H, 5-Ha), 3.85 (dd, $^2J_{5\text{-Hb},5\text{-Ha}}$ = 10.3 Hz, $^3J_{5\text{-Hb},4\text{-H}}$ = 4.8 Hz, 1H, 5-Hb), 4.96 (ddddd, $^3J_{4\text{-H},5\text{-Ha}}$

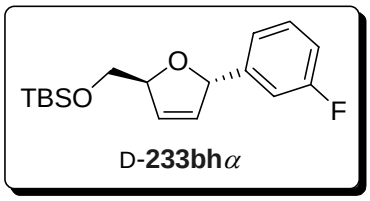
= 5.9 Hz, $^{3}J_{4\text{-H},5\text{-Hb}}$ = 4.8 Hz, $^{4}J_{4\text{-H},1\text{-H}}$ = 4.0 Hz, $^{3}J_{4\text{-H},3\text{-H}}$ = 2.1 Hz, $^{4}J_{4\text{-H},2\text{-H}}$ = 1.4 Hz, 1H, 4-H), 5.80 (ddd, $^{4}J_{1\text{-H},4\text{-H}}$ = 4.0 Hz, $^{3}J_{1\text{-H},2\text{-H}}$ = 2.4 Hz, $^{4}J_{1\text{-H},3\text{-H}}$ = 1.6 Hz, 1H, 1-H), 5.92 (ddd, $^{3}J_{3\text{-H},2\text{-H}}$ = 6.1 Hz, $^{3}J_{3\text{-H},4\text{-H}}$ = 2.1 Hz, $^{4}J_{3\text{-H},1\text{-H}}$ = 1.6 Hz, 1H, 3-H), 6.02 (ddd, $^{3}J_{2\text{-H},3\text{-H}}$ = 6.1 Hz, $^{3}J_{2\text{-H},1\text{-H}}$ = 2.4 Hz, $^{4}J_{2\text{-H},4\text{-H}}$ = 1.4 Hz, 1H, 2-H), 7.27-7.40 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.38 (CH_3), 18.37 ($C(CH_3)_3$), 25.89 ($C(CH_3)_3$), 66.42 (CH_2-5), 87.15 (CH-4), 87.95 (CH-1), 126.84, 127.77, and 128.27 (CH-arom), 128.33 (CH-2), 130.99 (CH-3), 141.65 (C-arom); IR (NaCl, neat) ν 3375 (s), 2954 (s), 2931 (s), 2858 (s), 1468 (m), 1255 (s), 1103 (s), 839 (s) cm^{-1}; MS (CI) *m*/*z* (%) 291 ([M+H$^+$], 100); HRMS (CI) 291.1760 [$C_{17}H_{27}O_2Si$ (M+H$^+$) requires 291.1780].



L-**233bf***α*/*β*

1'-(4-Bromophenyl)-5'-*O*-(*tert*-butyldimethylsilyl)-2',3'-didehydro-2',3'-dideoxy-*α*/*β*-L-ribofuranose (L-233bf*α*/*β*). Grubbs 1st generation catalyst **C1** (20.0 mg, 0.024 mmol) was added to a solution of silane (2*R*)-**234bf** (967 mg, 2.43 mmol) in dichloromethane (20 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 5 h. The resulting solution was evaporated. Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane L-**233bf***α*/*β* as a colourless oil (755 mg, 84%); mixture of diastereoisomers **A**, **B**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.01 (s, 6H, CH_3), 0.02 (s, 6H, CH_3), 0.84 (s, 9H, *t*-Bu), 0.85 (s, 9H, *t*-Bu), 3.62 (dd, $^{2}J_{5'\text{A-Ha},5'\text{A-Hb}}$ = 10.4 Hz, $^{3}J_{5'\text{A-Ha},4'\text{A-H}}$ = 5.5 Hz, 1H, 5'A-Ha), 3.65 (dd, $^{2}J_{5'\text{B-Ha},5'\text{B-Hb}}$ = 10.5 Hz, $^{3}J_{5'\text{B-Ha},4'\text{B-H}}$ = 5.4 Hz, 1H, 5'B-Ha), 3.71 (dd, $^{2}J_{5'\text{A-Hb},5'\text{A-Ha}}$ = 10.4 Hz, $^{3}J_{5'\text{A-Hb},4'\text{A-H}}$ = 4.5 Hz, 1H, 5'A-Hb), 3.75 (dd, $^{2}J_{5'\text{B-Hb},5'\text{B-Ha}}$ = 10.4 Hz, $^{3}J_{5'\text{B-Hb},4'\text{B-H}}$ = 4.6 Hz, 1H, 5'B-Hb), 4.85-4.89 (m, 1H, 4'A-H or 4'B-H), 4.97-5.02 (m, 1H, 4'B-H or 4'A-H), 5.65-5.67 (m, 1H, 1'A-H or 1'B-H), 5.69-5.71 (m, 1H, 1'B-H or 1'A-H), 5.80 (ddd, $^{3}J_{HH}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.6 Hz, 1H, 3'A-H or 3'B-H), 5.84 (ddd, $^{3}J_{HH}$ = 6.1 Hz, J_{HH} = 2.1 Hz, J_{HH} = 1.5 Hz, 1H, 3'B-H or 3'A-H), 5.91-5.94 (m, 2H, 2'A-H, and 2'B-H), 7.12 (d, $^{3}J_{2\text{-H},3\text{-H}}$ = 8.4 Hz, 2H, 2A-H or 2B-H), 7.21 (d, $^{3}J_{2\text{-H},3\text{-H}}$ = 8.4 Hz, 2H, 2B-H or 2A-H), 7.39 (d, $^{3}J_{3\text{-H},2\text{-H}}$ = 8.4 Hz, 2H, 3A-H or 3B-H), 7.40 (d, $^{3}J_{3\text{-H},2\text{-H}}$ = 8.4 Hz, 2H, 3B-H or 3A-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.37 (CH_3), -5.34 (CH_3), -5.32 (CH_3), -5.30 (CH_3), 18.36 ($C(CH_3)_3$), 18.40 ($C(CH_3)_3$), 25.91 ($C(CH_3)_3$), 65.88, and 66.16 (CH_2-1), 87.25, 87.35, 87.36, and 87.37 (CH-1', and CH-4'), 121.56, and 121.65 (C-4), 128.10, and 128.41 (CH-2' or CH-3'), 128.59, and 128.65 (CH-2), 130.71, and 130.90 (CH-3' or CH-2'), 131.37, and 131.52 (CH-3), 140.88, and 140.93 (C-1); MS (CI) *m*/*z* (%)

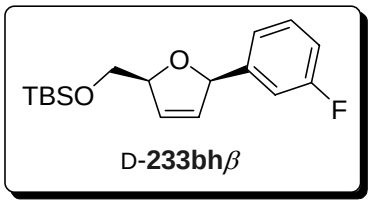
369/371 ([M^+], 100), 353/355 (10), 311/313 (30), 237/239 (20), 195/197 (20); HRMS (CI) 369.0882/371.0878 [$C_{17}H_{26}BrO_2Si$ (M^+) requires 369.0885/371.0867].



D-**233bh**α

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-α-D-ribofuranose (D-233bhα).

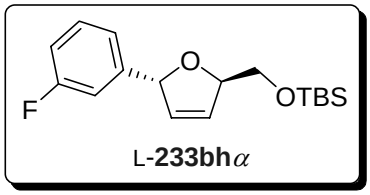
Grubbs 1st generation catalyst **C1** (12.0 mg, 0.014 mmol) was added to a solution of silane (2*S*,1'*S*)-**234bh** (329 mg, 0.97 mmol) in dichloromethane (8 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to afford silane D-**233bh**α as a colourless oil (285 mg, 95%): $[\alpha]_D$ -154.4 (*c* 1.80, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 3H, CH_3), 0.10 (s, 3H, CH_3), 0.93 (s, 9H, *t*-Bu), 3.70 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.4 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.5 Hz, 1H, 5'-Ha), 3.80 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.4 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 4.6 Hz, 1H, 5'-Hb), 5.05-5.11 (m, 1H, 4'-H), 5.81-5.82 (m, 1H, 1'-H), 5.93 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.0 Hz, J_{HH} = 1.6 Hz, 1H, 3'-H), 6.01 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.5 Hz, 1H, 2'-H), 6.96 (dddd, $^3J_{4\text{-H,F}}$ = 9.5 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 8.5 Hz, $^4J_{4\text{-H},2\text{-H}}$ = 2.6 Hz, $^4J_{4\text{-H},6\text{-H}}$ = 1.0 Hz, 1H, 4-H), 7.03 (ddd, $^3J_{2\text{-H,F}}$ = 9.7 Hz, $^4J_{2\text{-H},4\text{-H}}$ = 2.6 Hz, $^4J_{2\text{-H},6\text{-H}}$ = 1.6 Hz, 1H, 2-H), 7.07-7.10 (m, 1H, 6-H), 7.30 (ddd, $^3J_{5\text{-H},4\text{-H}}$ = 8.5 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 7.7 Hz, $^4J_{5\text{-H,F}}$ = 5.8 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.34 (CH_3), -5.30 (CH_3), 18.37 ($C(CH_3)_3$), 25.92 ($C(CH_3)_3$), 65.91 (CH_2-5'), 87.36 (d, $^4J_{CF}$ = 1.8 Hz, CH-1'), 87.45 (CH-4'), 113.21 (d, $^2J_{CF}$ = 21.8 Hz, CH-2), 114.55 (d, $^2J_{CF}$ = 21.3 Hz, CH-4), 121.84 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 128.47 (CH-2'), 129.93 (d, $^3J_{CF}$ = 8.1 Hz, CH-5), 130.87 (CH-3'), 144.69 (d, $^3J_{CF}$ = 6.5 Hz, C-1), 163.04 (d, $^1J_{CF}$ = 246.1 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.55; IR (NaCl, neat) ν 2955 (s), 2930 (s), 2858 (s), 1730 (m), 1593 (s), 1258 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 309 ([M+H^+], 100); HRMS (CI) 309.1687 [$C_{17}H_{26}FO_2Si$ (M+H^+) requires 309.1686].



D-**233bh**β

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-β-D-ribofuranose (D-233bhβ).

Grubbs 1st generation catalyst **C1** (40.1 mg, 0.049 mmol) was added to a solution of silane (2*S*,1'*R*)-**234bh** (1.346 g, 4.00 mmol) in dichloromethane (50 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to give silane D-**233bh**β as a colourless oil (1.185 g, 96%): $[\alpha]_D$ +8.0 (*c* 2.63, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 6H, CH_3), 0.93 (s, 9H, *t*-Bu), 3.71 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.5 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.5 Hz, 1H, 5'-Ha), 3.77 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.5 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 4.9 Hz, 1H, 5'-Hb), 4.89-4.95 (m, 1H, 4'-H), 5.73-5.75 (m, 1H, 1'-H), 5.94 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 1.8 Hz, J_{HH} = 1.2 Hz, 1H, 3'-H), 5.97 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.1 Hz, 1H, 2'-H), 6.98-7.11 (m, 3H, 2-H, 4-H, and 6-H), 7.30-7.32 (m, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.36 (CH_3), 18.35 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 62.97 (CH_2-5'), 87.19 (d, $^4J_{CF}$ = 1.8 Hz, CH-1'), 87.29 (CH-4'), 113.84 (d, $^2J_{CF}$ = 21.7 Hz, CH-2), 114.82 (d, $^2J_{CF}$ = 21.2 Hz, CH-4), 122.44 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 129.47 (CH-2'), 129.99 (d, $^3J_{CF}$ = 8.1 Hz, CH-5), 130.20 (CH-3'), 144.41 (d, $^3J_{CF}$ = 6.6 Hz, C-1), 162.99 (d, $^1J_{CF}$ = 246.3 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.33; IR (NaCl, neat) ν 2954 (s), 2931 (s), 2858 (s), 1742 (m), 1592 (m), 1258 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 309 ([M+H$^+$], 100); HRMS (CI) 309.1687 [$C_{17}H_{26}FO_2Si$ (M+H$^+$) requires 309.1686].

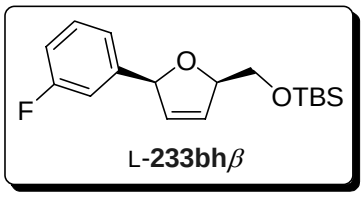


L-**233bh**α

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-α-L-ribofuranose (L-233bhα).

Grubbs 1st generation catalyst **C1** (20.0 mg, 0.024 mmol) was added to a solution of silane (2*R*,1'*R*)-**234bh** (650 mg, 1.93 mmol) in dichloromethane (15 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to give silane L-**233bh**α as a

colourless oil (580 mg, 97%): $[\alpha]_D$ +147.1 (*c* 2.40, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 3H, CH_3), 0.10 (s, 3H, CH_3), 0.93 (s, 9H, *t*-Bu), 3.70 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.4 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.5 Hz, 1H, 5'-Ha), 3.80 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.4 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 4.6 Hz, 1H, 5'-Hb), 5.05-5.11 (m, 1H, 4'-H), 5.81-5.82 (m, 1H, 1'-H), 5.93 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.0 Hz, J_{HH} = 1.6 Hz, 1H, 3'-H), 6.01 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.3 Hz, J_{HH} = 1.5 Hz, 1H, 2'-H), 6.96 (dddd, $^3J_{4\text{-H,F}}$ = 9.5 Hz, $^3J_{4\text{-H},5\text{-H}}$ = 8.5 Hz, $^4J_{4\text{-H},2\text{-H}}$ = 2.6 Hz, $^4J_{4\text{-H},6\text{-H}}$ = 1.0 Hz, 1H, 4-H), 7.03 (ddd, $^3J_{2\text{-H,F}}$ = 9.7 Hz, $^4J_{2\text{-H},4\text{-H}}$ = 2.6 Hz, $^4J_{2\text{-H},6\text{-H}}$ = 1.6 Hz, 1H, 2-H), 7.07-7.10 (m, 1H, 6-H), 7.30 (ddd, $^3J_{5\text{-H},4\text{-H}}$ = 8.5 Hz, $^3J_{5\text{-H},6\text{-H}}$ = 7.7 Hz, $^4J_{5\text{-H,F}}$ = 5.8 Hz, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.34 (CH_3), -5.30 (CH_3), 18.37 ($C(CH_3)_3$), 25.92 ($C(CH_3)_3$), 65.91 (CH_2-5'), 87.36 (d, $^4J_{CF}$ = 1.8 Hz, CH-1'), 87.45 (CH-4'), 113.21 (d, $^2J_{CF}$ = 21.8 Hz, CH-2), 114.55 (d, $^2J_{CF}$ = 21.3 Hz, CH-4), 121.84 (d, $^4J_{CF}$ = 2.9 Hz, CH-6), 128.47 (CH-2'), 129.93 (d, $^3J_{CF}$ = 8.1 Hz, CH-5), 130.87 (CH-3'), 144.69 (d, $^3J_{CF}$ = 6.5 Hz, C-1), 163.04 (d, $^1J_{CF}$ = 246.1 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.55; IR (NaCl, neat) ν 2955 (s), 2930 (s), 2858 (s), 1730 (m), 1593 (s), 1258 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 309 ([M+H$^+$], 100); HRMS (CI) 309.1682 [$C_{17}H_{26}FO_2Si$ (M+H$^+$) requires 309.1686].

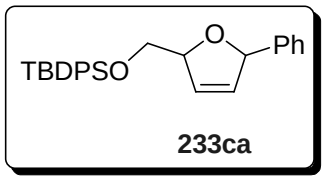


L-**233bh*β***

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-didehydro-1',2',3'-trideoxy-1'-(3-fluorophenyl)-*β*-L-ribofuranose (L-233bh*β*).

Grubbs 1st generation catalyst **C1** (27.1 mg, 0.033 mmol) was added to a solution of silane (2*R*,1'*S*)-**234bh** (1.088 g, 3.23 mmol) in dichloromethane (15 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 3 h. The solution was evaporated and chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (99:1) to afford silane L-**233bh*β*** as a colourless oil (946 mg, 95%): $[\alpha]_D$ -7.7 (*c* 1.14, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 6H, CH_3), 0.93 (s, 9H, *t*-Bu), 3.71 (dd, $^2J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.5 Hz, $^3J_{5'\text{-Ha},4'\text{-H}}$ = 5.5 Hz, 1H, 5'-Ha), 3.77 (dd, $^2J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.5 Hz, $^3J_{5'\text{-Hb},4'\text{-H}}$ = 4.9 Hz, 1H, 5'-Hb), 4.89-4.95 (m, 1H, 4'-H), 5.73-5.75 (m, 1H, 1'-H), 5.94 (ddd, $^3J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, J_{HH} = 1.8 Hz, J_{HH} = 1.2 Hz, 1H, 3'-H), 5.97 (ddd, $^3J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, J_{HH} = 2.2 Hz, J_{HH} = 1.1 Hz, 1H, 2'-H), 6.98-7.11 (m, 3H, 2-H, 4-H, and 6-H), 7.30-7.32 (m, 1H, 5-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.36 (CH_3), 18.35 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 62.97 (CH_2-5'), 87.19 (d, $^4J_{CF}$ = 1.8 Hz, CH-1'), 87.29 (CH-4'), 113.84 (d, $^2J_{CF}$ = 21.7 Hz, CH-2), 114.82 (d, $^2J_{CF}$ = 21.2 Hz, CH-4), 122.44 (d, $^4J_{CF}$ = 2.9 Hz,

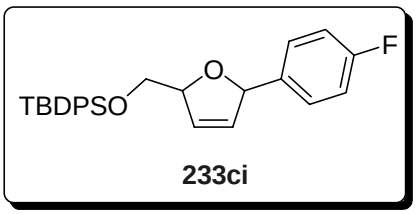
CH-6), 129.47 (CH-2'), 129.99 (d, $^3J_{CF}$ = 8.1 Hz, CH-5), 130.20 (CH-3'), 144.41 (d, $^3J_{CF}$ = 6.6 Hz, C-1), 162.99 (d, $^1J_{CF}$ = 246.3 Hz, CF-3); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.33; IR (NaCl, neat) ν 2954 (s), 2931 (s), 2858 (s), 1742 (m), 1592 (m), 1258 (s) cm^{-1};[228] MS (CI) *m*/*z* (%) 309 ([M+H$^+$], 100); HRMS (CI) 309.1687 [$C_{17}H_{26}FO_2Si$ (M+H$^+$) requires 309.1686].



233ca

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-1',2',3'-trideoxy-1'-phenyl-*α*/*β*-D/L-ribofuranose (233ca).

A solution of the 2nd generation Grubbs catalyst **C2** (20.0 mg, 0.024 mmol) in degassed dichloromethane (1 mL) was added to a solution of the diene **234ca** (224 mg, 0.53 mmol) in degassed dichloromethane (5 mL) and the mixture was stirred at room temperature overnight. The solvent was then evaporated and the residue was chromatographed on a column of neutral alumina (3 × 5 cm) with a mixture of hexanes and Et_2O (95:5) to give **233ca** as a colourless oil (217 mg, 99%): ^{1}H-NMR (400.1 MHz, $CDCl_3$, mixture of diasteroisomers in a 1:1.30 ratio, minor diastereoisomer is marked with * where possible) δ 1.07* and 1.09 (s, 9H, *t*-Bu), 3.59* (dd, *J* = 8.2 and 10.9 Hz, 1H, aC*H*$_2$), 3.65 (dd, *J* = 3.6 and 11.6Hz, 1H, aC*H*$_2$), 3.84* (dd, *J* = 4.0 and 11.6Hz, 1H, bC*H*$_2$), 3.92 (dd, *J* = 5.4 and 10.9Hz, 1H, bC*H*$_2$), 4.15-4.18 and 4.41*-4.46* (m, 1H, CH_2CH), 5.00-5.02 and 5.06*-5.08* (m, 1H, PhC*H*), 5.78-6.02 (m, 2H, C*H*=C*H*), 7.29-7.46 and 7.67-7.32 (m, 15H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 26.9 and 30.3 (*t*-Bu), 63.6 and 64.1 (CH_2CH), 68.4 and 68.5 (CH_2), 75.6 and 76.4 (PhCH), 127.3 and 131.2 and 127.9 and 130.2 (CH=CH), 127.6, 127.7, 128.4, 133.7, 133.9, 134.0, 135.7, 135.8, 140.4; HRMS (CI-NH_3, 100 °C) 432.2360 [$C_{27}H_{34}NO_2Si$ (M+NH_4^+) requires 432.2359].

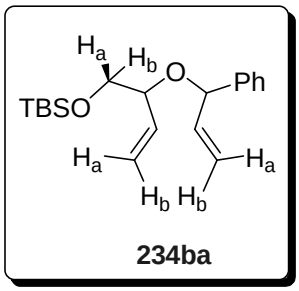


233ci

5'-*O*-(*tert*-Butyldiphenylsilyl)-2',3'-didehydro-1',2',3'-trideoxy-1'-(4-fluorophenyl)-*α*/*β*-D/L-ribofuranose (233ci).

Benzylidene-bis(tricyclohexylphosphine)dichlororuthenium (**C1**; Grubbs 1st generation catalyst; 73.4 mg, 0.089 mmol) was added to a solution of silane **234ci** (278 mg,

0.60 mmol) in dichloromethane (15 mL) under a stream of argon atmosphere and the mixture was stirred at 40 °C for 5 h. The resulting solution was evaporated and the residue was chromatographed on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) to afford silane **233ci** as a colourless oil (108 mg, 41%): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.09 (s, 9H, *t*-Bu), 3.80 (dd, $^{2}J_{5'\text{-Ha},5'\text{-Hb}}$ = 10.6 Hz, $^{3}J_{5'\text{-Ha},4'\text{-H}}$ = 5.2 Hz, 1H, 5'-Ha), 3.85 (dd, $^{2}J_{5'\text{-Hb},5'\text{-Ha}}$ = 10.6 Hz, $^{3}J_{5'\text{-Hb},4'\text{-H}}$ = 4.9 Hz, 1H, 5'-Hb), 5.01 (dddd, $^{3}J_{4'\text{-H},5'\text{-Ha}}$ = 5.2 Hz, $^{3}J_{4'\text{-H},5'\text{-Hb}}$ = 4.9 Hz, $^{4}J_{4'\text{-H},2'\text{-H}}$ = 2.4 Hz, $^{3}J_{4'\text{-H},3'\text{-H}}$ = 1.4 Hz, 1H, 4'-H), 5.77-5.79 (m, 1H, 1'-H), 5.89 (ddd, $^{3}J_{2'\text{-H},3'\text{-H}}$ = 6.1 Hz, $^{4}J_{2'\text{-H},4'\text{-H}}$ = 2.4 Hz, $^{3}J_{2'\text{-H},1'\text{-H}}$ = 1.5 Hz, 1H, 2'-H), 6.03 (ddd, $^{3}J_{3'\text{-H},2'\text{-H}}$ = 6.1 Hz, $^{4}J_{3'\text{-H},1'\text{-H}}$ = 2.4 Hz, $^{3}J_{3'\text{-H},4'\text{-H}}$ = 1.4 Hz, 1H, 3'-H), 6.95 (t, $^{3}J_{HH}$ = 8.8 Hz, $^{3}J_{HF}$ = 8.8 Hz, 2H, 3-H), 7.30-7.47 (m, 8H, H-arom), 7.67-7.71 (m, 4H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 19.26 ($C(CH_3)_3$), 26.85 ($C(CH_3)_3$), 66.93 (CH_2-5'), 87.15 (CH-4'), 87.32 (CH-1'), 115.11 (d, $^{2}J_{CF}$ = 21.5 Hz, CH-3), 127.65 (CH-arom), 128.52 (CH-3'), 128.68 (d, $^{3}J_{CF}$ = 8.2 Hz, CH-2), 129.64 and 129.67 (CH-arom), 131.06 (CH-2'), 133.25 and 133.51 (C-arom), 135.59 and 135.66 (CH-arom), 137.49 (d, $^{4}J_{CF}$ = 3.1 Hz, C-1), 162.43 (d, $^{1}J_{CF}$ = 245.6 Hz, C-4); MS (CI, 150 °C) *m*/*z* (%) 433 (M^+, 3), 375 (10), 355 (100), 257 (10); HRMS (CI) 433.2000 [$C_{27}H_{30}FO_2Si$ (M^+) requires 433.1999].

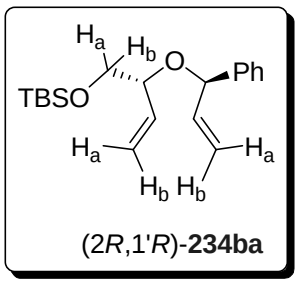


234ba

***tert*-Butyl(dimethyl)(2-(1'-(phenyl)allyloxy)but-3-enyloxy)silane (234ba).**

n-Butyllithium (0.5 mL, 1.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (±)-**235b** (206 mg, 1.00 mmol) in THF (1 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (200 mg, 1.05 mmol) in THF (2 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (7.8 mg, 0.011 mmol) and $(t\text{-BuO})_2PN(i\text{Pr})_2$ (6.0 mg, 0.021 mmol) in THF (1 mL) and allylcarbonate (±)-**267a** (124 mg, 0.53 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes

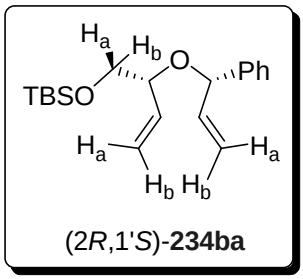
and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane **234ba** as colourless oil (142 mg, 84%, an equimolar mixture of diastereoisomers **A**, **B**): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.03 (s, 6H, CH_3), 0.08 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.89 (s, 9H, *t*-Bu), 0.92 (s, 9H, *t*-Bu), 3.57 (dd, $^{2}J_{1A\text{-}Ha,1A\text{-}Hb}$ = 10.5 Hz, $^{3}J_{1A\text{-}Ha,2A\text{-}H}$ = 5.3 Hz, 1H, 1A-Ha), 3.63 (dd, $^{2}J_{1B\text{-}Ha,1B\text{-}Hb}$ = 10.5 Hz, $^{3}J_{1B\text{-}Ha,2B\text{-}H}$ = 5.3 Hz, 1H, 1B-Ha), 3.70 (dd, $^{2}J_{1A\text{-}Hb,1A\text{-}Ha}$ = 10.5 Hz, $^{3}J_{1A\text{-}Hb,2A\text{-}H}$ = 6.6 Hz, 1H, 1A-Hb), 3.76 (dd, $^{2}J_{1B\text{-}Hb,1B\text{-}Ha}$ = 10.5 Hz, $^{3}J_{1B\text{-}Hb,2B\text{-}H}$ = 6.6 Hz, 1H, 1B-Hb), 3.83 (ddddd, $^{3}J_{2\text{-}H,3\text{-}H}$ = 6.9 Hz, $^{3}J_{2\text{-}H,1\text{-}Hb}$ = 6.6 Hz, $^{3}J_{2\text{-}H,1\text{-}Ha}$ = 5.3 Hz, $^{4}J_{2\text{-}H,4\text{-}Ha}$ = 1.0 Hz, $^{4}J_{2\text{-}H,4\text{-}Hb}$ = 1.0 Hz, 1H, 2A-H or 2B-H), 4.06 (ddddd, $^{3}J_{2\text{-}H,3\text{-}H}$ = 6.9 Hz, $^{3}J_{2\text{-}H,1\text{-}Hb}$ = 6.6 Hz, $^{3}J_{2\text{-}H,1\text{-}Ha}$ = 5.3 Hz, $^{4}J_{2\text{-}H,4\text{-}Ha}$ = 1.0 Hz, $^{4}J_{2\text{-}H,4\text{-}Hb}$ = 1.0 Hz, 1H, 2B-H or 2A-H), 4.95 (d, $^{3}J_{1'\text{-}H,2'\text{-}H}$ = 7.2 Hz, 1H, 1'A-H or 1'B-H), 4.95 (d, $^{3}J_{1'\text{-}H,2'\text{-}H}$ = 6.1 Hz, 1H, 1'B-H or 1'A-H), 5.10-5.34 (m, 8H, 4A-H, 3'A-H, 4B-H, and 3'B-H), 5.74 (ddd, $^{3}J_{3\text{-}H,4\text{-}Ha}$ = 17.3 Hz, $^{3}J_{3\text{-}H,4\text{-}Hb}$ = 10.4 Hz, $^{3}J_{3\text{-}H,2\text{-}H}$ = 6.9 Hz, 1H, 3A-H or 3B-H), 5.77 (ddd, $^{3}J_{3\text{-}H,4\text{-}Ha}$ = 16.2 Hz, $^{3}J_{3\text{-}H,4\text{-}Hb}$ = 11.5 Hz, $^{3}J_{3\text{-}H,2\text{-}H}$ = 6.9 Hz, 1H, 3B-H or 3A-H), 5.90 (ddd, $^{3}J_{2'\text{-}H,3'\text{-}Ha}$ = 17.3 Hz, $^{3}J_{2'\text{-}H,3'\text{-}Hb}$ = 10.2 Hz, $^{3}J_{2'\text{-}H,1'\text{-}H}$ = 7.2 Hz, 1H, 2'A-H or 2'B-H), 5.98 (ddd, $^{3}J_{2'\text{-}H,3'\text{-}Ha}$ = 17.2 Hz, $^{3}J_{2'\text{-}H,3'\text{-}Hb}$ = 10.3 Hz, $^{3}J_{2'\text{-}H,1'\text{-}H}$ = 6.1 Hz, 1H, 2'B-H or 2'A-H), 7.23-7.38 (m, 10H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.37 (CH_3), -5.31 (CH_3), -5.28 (CH_3), -5.18 (CH_3), 18.35 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 66.24, and 66.29 (CH_2-1), 78.52, and 78.75 (CH-2), 79.90, and 80.26 (CH-1'), 115.29, 116.68, 117.85, and 118.09 (CH_2-4, and CH_2-3'), 126.73, 127.19, 127.34, 127.51, 128.25, and 128.35 (CH-arom), 136.14, and 136.27 (CH-3), 138.78, and 139.49 (CH-2'), 140.99, and 141.52 (C-arom); IR (NaCl, neat) ν 2956 (s), 2929 (s), 2857 (s), 1472 (m), 1257 (s), 1087 (s), 838 (s) cm^{-1}; MS (CI-NH_3, 160 °C) *m*/*z* (%) 336 ([M+NH_4^+], 30), 117 (100); HRMS (CI-NH_3, 100 °C) 336.2357 [$C_{19}H_{34}NO_2Si$ (M+NH_4^+) requires 336.2359]. Anal. Calcd. for $C_{19}H_{30}O_2Si$: C, 71.64; H, 9.49. Found: C, 71.26; H, 9.57.



(2*R*,1'*R*)-**234ba**

(2*R*,1'*R*)-*tert*-Butyl(dimethyl)(2-(1'-(phenyl)allyloxy)but-3-enyloxy)silane (2*R*,1'*R*)-(234ba). *n*-Butyllithium (3.0 mL, 6.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (1.236 g, 6.11 mmol) in THF (7 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated

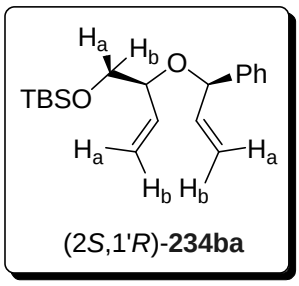
was transferred (*via* cannula) to a suspension of copper(I) iodide (1.200 g, 6.30 mmol) in THF (12 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (40.4 mg, 0.060 mmol) in THF (5.0 mL) and allylcarbonate (*R*)-**267a** (1.226 g, 5.23 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*,1'*R*)-**234ba** as colourless oil (1.388 g, 83%, as a single diastereoisomer): $[\alpha]_D$ -10.2 (*c* 3.73, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.08 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.92 (s, 9H, *t*-Bu), 3.63 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 5.3 Hz, 1H, 1-Ha), 3.76 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.6 Hz, 1H, 1-Hb), 4.06 (ddddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.9 Hz, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.6 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 5.3 Hz, $^4J_{2\text{-H},4\text{-Ha}}$ = 0.9 Hz, $^4J_{2\text{-H},4\text{-Hb}}$ = 0.9 Hz, 1H, 2-H), 4.95 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 7.3 Hz, 1H, 1'-H), 5.20-5.35 (m, 4H, 4-Ha, 4-Hb, 3'-Ha, and 3'-Hb), 5.74 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 17.3 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 10.4 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 6.9 Hz, 1H, 3-H), 5.90 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.3 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.2 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 7.3 Hz, 1H, 2'-H), 7.23-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.31 (CH_3), -5.18 (CH_3), 18.35 ($C(CH_3)_3$), 25.91 ($C(CH_3)_3$), 66.29 (CH_2-1), 78.75 (CH-2), 80.26 (CH-1'), 116.68, 117.84 (CH_2-4, and CH_2-3'), 126.73, 127.34, and 128.25 (CH-arom), 136.28 (CH-3), 138.79 (CH-2'), 141.53 (C-arom); IR (NaCl, neat) ν 2955 (s), 2928 (s), 2857 (s), 1471 (m), 1255 (s), 1128 (s), 1086 (s) cm^{-1}; MS (CI-iso, 150 °C) *m/z* (%) 319 ([M+H$^+$], 5), 117 (100); HRMS (CI) 319.2091 [$C_{19}H_{31}O_2Si$ (M+H$^+$) requires 319.2093]. Anal. Calcd. for $C_{19}H_{30}O_2Si$: C, 71.64; H, 9.49. Found: C, 71.45; H, 9.54.



(2*R*,1'*S*)-**234ba**

(2*R*,1'*S*)-*tert*-Butyl(dimethyl)(2-(1'-(phenyl)allyloxy)but-3-enyloxy)silane (2*R*,1'*S*)-(234ba). *n*-Buthyllithium (3.1 mL, 6.2 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (1.252 g, 6.19 mmol) in THF (6 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (1.200 g, 6.30 mmol) in

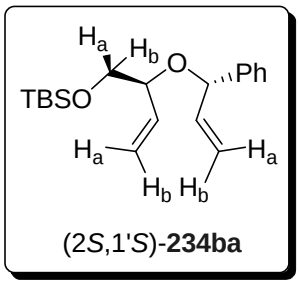
THF (12 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (40.0 mg, 0.060 mmol) in THF (12.0 mL) and allylcarbonate (*S*)-**267a** (1.180 g, 5.04 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*,1'*S*)-**234ba** as colourless oil (1.232 g, 77%, as a single diastereoisomer): $[\alpha]_D$ -23.3 (*c* 2.62, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.04 (s, 6H, CH_3), 0.89 (s, 9H, *t*-Bu), 3.58 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 5.3 Hz, 1H, 1-Ha), 3.71 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.6 Hz, 1H, 1-Hb), 3.84 (ddddd, $^3J_{2\text{-H},3\text{-H}}$ = 7.0 Hz, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.6 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 5.3 Hz, $^4J_{2\text{-H},4\text{-Ha}}$ = 0.8 Hz, $^4J_{2\text{-H},4\text{-Hb}}$ = 0.8 Hz, 1H, 2-H), 4.96 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.1 Hz, 1H, 1'-H), 5.12-5.28 (m, 4H, 4-H, and 3'-H), 5.78 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 16.2 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 11.4 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 7.0 Hz, 1H, 3-H), 5.98 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.1 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.4 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.1 Hz, 1H, 2'-H), 7.25-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.37 (CH_3), -5.28 (CH_3), 18.34 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 66.24 (CH_2-1), 78.52 (CH-2), 79.89 (CH-1'), 115.26, and 118.07 (CH_2-4, and CH_2-3'), 127.19, 127.50, and 128.34 (CH-arom), 136.14 (CH-3), 139.49 (CH-2'), 140.99 (C-arom); IR (NaCl, neat) ν 2955 (s), 2928 (s), 2857 (s), 1471 (m), 1255 (s), 1121 (s), 1083 (s), 838 (s) cm^{-1}; MS (CI-Iso, 150 °C) *m*/*z* (%) 319 ([$M+H^+$], 3), 185 (10), 117 (100); HRMS (CI) 319.2092 [$C_{19}H_{31}O_2Si$ ($M+H^+$) requires 319.2093]. Anal. Calcd. for $C_{19}H_{30}O_2Si$: C, 71.64; H, 9.49. Found: C, 71.45; H, 9.57.



(2S,1'*R*)-**234ba**

(2*S*,1'*R*)-*tert*-Butyl(dimethyl)(2-(1'-(phenyl)allyloxy)but-3-enyloxy)silane (2*S*,1'*R*)-(234ba). *n*-Buthyllithium (3.0 mL, 6.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*S*)-**235b** (1.236 g, 6.11 mmol) in THF (6 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (1.200 g, 6.30 mmol) in THF (12 mL) at room temperature. The mixture turned light yellow and was then stirred

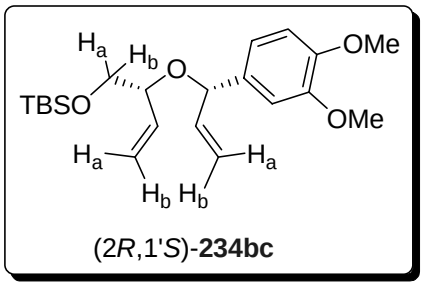
for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (40.0 mg, 0.060 mmol) in THF (3.5 mL) and allylcarbonate (*R*)-**267a** (1.133 g, 4.84 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*S*,1'*R*)-**234ba** as colourless oil (1.263 g, 82%, as a single diastereoisomer): $[\alpha]_D$ +25.3 (*c* 1.11, MeOH); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.04 (s, 6H, CH_3), 0.89 (s, 9H, *t*-Bu), 3.58 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 5.3 Hz, 1H, 1-Ha), 3.71 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.6 Hz, 1H, 1-Hb), 3.84 (ddddd, $^3J_{2\text{-H},3\text{-H}}$ = 7.0 Hz, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.6 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 5.3 Hz, $^4J_{2\text{-H},4\text{-Ha}}$ = 0.8 Hz, $^4J_{2\text{-H},4\text{-Hb}}$ = 0.8 Hz, 1H, 2-H), 4.96 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.1 Hz, 1H, 1'-H), 5.12-5.28 (m, 4H, 4-H, and 3'-H), 5.78 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 16.2 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 11.4 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 7.0 Hz, 1H, 3-H), 5.98 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.1 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.4 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.1 Hz, 1H, 2'-H), 7.25-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.37 (CH_3), -5.28 (CH_3), 18.34 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 66.24 (CH_2-1), 78.52 (CH-2), 79.89 (CH-1'), 115.26, and 118.07 (CH_2-4, and CH_2-3'), 127.19, 127.50, and 128.34 (CH-arom), 136.14 (CH-3), 139.49 (CH-2'), 140.99 (C-arom); IR (NaCl, neat) ν 2955 (s), 2928 (s), 2857 (s), 1471 (m), 1255 (s), 1121 (s), 1083 (s), 838 (s) cm^{-1}; MS (CI-NH_3, 150 °C) *m*/*z* (%) 336 ([M+NH_4^+], 100), 134 (90), 117 (60). Anal. Calcd. for $C_{19}H_{30}O_2Si$: C, 71.64; H, 9.49. Found: C, 71.80; H, 9.52.



(2*S*,1'*S*)-**234ba**

(2*S*,1'*S*)-*tert*-Butyl(dimethyl)(2-(1'-(phenyl)allyloxy)but-3-enyloxy)silane (2*S*,1'*S*)-(234ba). *n*-Butyllithium (1.4 mL, 2.8 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*S*)-**235b** (556 mg, 2.74 mmol) in THF (3 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (600 mg, 3.15 mmol) in THF (6 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (18.0 mg, 0.027 mmol) in THF (1.5 mL) and allylcarbonate (*S*)-**267a**

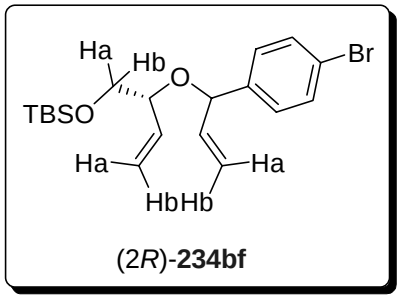
(436 mg, 1.86 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*S*,1'*S*)-**234ba** as a colourless oil (468 mg, 79%, as a single diastereoisomer): $[\alpha]_D$ +11.5 (*c* 0.78, MeOH); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.08 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.92 (s, 9H, *t*-Bu), 3.63 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 5.3 Hz, 1H, 1-Ha), 3.76 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.6 Hz, 1H, 1-Hb), 4.06 (ddddd, $^3J_{2\text{-H},3\text{-H}}$ = 6.9 Hz, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.6 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 5.3 Hz, $^4J_{2\text{-H},4\text{-Ha}}$ = 0.9 Hz, $^4J_{2\text{-H},4\text{-Hb}}$ = 0.9 Hz, 1H, 2-H), 4.95 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 7.3 Hz, 1H, 1'-H), 5.20-5.35 (m, 4H, 4-Ha, 4-Hb, 3'-Ha, and 3'-Hb), 5.74 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 17.3 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 10.4 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 6.9 Hz, 1H, 3-H), 5.90 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.3 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.2 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 7.3 Hz, 1H, 2'-H), 7.23-7.38 (m, 5H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.31 (CH_3), -5.18 (CH_3), 18.35 ($C(CH_3)_3$), 25.91 ($C(CH_3)_3$), 66.29 (CH_2-1), 78.75 (CH-2), 80.26 (CH-1'), 116.68, 117.84 (CH_2-4, and CH_2-3'), 126.73, 127.34, and 128.25 (CH-arom), 136.28 (CH-3), 138.79 (CH-2'), 141.53 (C-arom); IR (NaCl, neat) ν 2955 (s), 2928 (s), 2857 (s), 1471 (m), 1255 (s), 1128 (s), 1086 (s) cm^{-1}; MS (CI-NH_3, 150 °C) *m/z* (%) 336 ([M+NH_4^+], 95), 117 (100). Anal. Calcd. for $C_{19}H_{30}O_2Si$: C, 71.64; H, 9.49. Found: C, 71.75; H, 9.57.



(2*R*,1'*S*)-**234bc**

(2*R*,1'*S*)-*tert*-Butyl(dimethyl)(2-(1'-(3'',4''-dimethoxyphenyl)allyloxy)but-3-enyloxy) silane (2*R*,1'*S*)-(234bc). *n*-Butyllithium (5.0 mL, 10.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (2.022 g, 9.99 mmol) in THF (8 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (2.000 g, 10.50 mmol) in THF (20 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (62.4 mg, 0.093 mmol) in THF (5.0 mL) and allylcarbonate (*S*)-**267c** (2.511 g, 8.53 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst

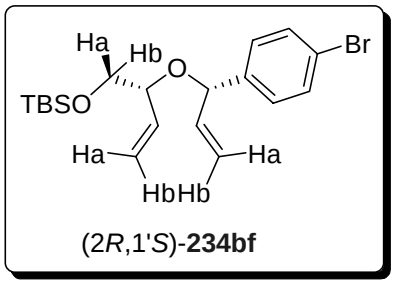
was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (67:33). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98:2) gave silane (2*R*,1'*S*)-**234bc** as colourless oil (2.267 g, 70%): $[\alpha]_D$ -20.4 (*c* 2.30, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ -0.04 (s, 3H, CH_3), -0.01 (s, 3H, CH_3), 0.84 (s, 9H, *t*-Bu), 3.54 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.4 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 5.6 Hz, 1H, 1-Ha), 3.66 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.4 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.3 Hz, 1H, 1-Hb), 3.77-3.82 (m, 1H, 2-H), 3.84 (s, 3H, CH_3O), 3.85 (s, 3H, CH_3O), 4.87 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 5.9 Hz, J_{HH} = 1.3 Hz, J_{HH} = 1.3 Hz, 1H, 1'-H), 5.08 (ddd, $^3J_{3'\text{-Hb},2'\text{-H}}$ = 10.4 Hz, J_{HH} = 1.7 Hz, J_{HH} = 1.3 Hz, 1H, 3'-Hb), 5.16-5.24 (m, 3H, 3'-Ha, 4-Ha, and 4-Hb), 5.75 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 16.3 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 11.4 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 7.0 Hz, 1H, 3-H), 5.95 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.2 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.4 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 5.9 Hz, 1H, 2'-H), 6.80 (d, $^3J_{5''\text{-H},6''\text{-H}}$ = 8.0 Hz, 1H, 5''-H), 6.84 (d, $^4J_{2''\text{-H},6''\text{-H}}$ = 1.8 Hz, 1H, 2''-H), 6.86 (ddd, $^3J_{6''\text{-H},5''\text{-H}}$ = 8.0 Hz, $^4J_{6''\text{-H},2''\text{-H}}$ = 1.8 Hz, J_{HH} = 0.4 Hz, 1H, 6''-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.47 (CH_3), -5.40 (CH_3), 18.22 ($C(CH_3)_3$), 25.76 ($C(CH_3)_3$), 55.65, and 55.68 (2 × CH_3O), 66.17 (CH_2-1), 78.08 (CH-2), 79.53 (CH-1'), 109.99 (CH-2''), 110.70 (CH-5''), 114.90 (CH_2-3'), 117.85 (CH_2-4), 119.56 (CH-6''), 133.36 (C-1''), 136.21 (CH-3), 139.38 (CH-2'), 148.35, and 148.91 (C-3'', and C-4''); IR (NaCl, neat) ν 2955 (s), 2928 (s), 2858 (s), 1614 (m), 1256 (s) cm^{-1}; MS (EI) *m*/*z* (%) 378 ([M^+], 80), 321 (100), 265 (90), 246 (60); HRMS (CI) 378.2225 [$C_{21}H_{34}O_4Si$ (M^+) requires 378.2226].



(2*R*)-**234bf**

(2*R*)-(2-(1'-(4''-Bromophenyl)allyloxy)but-3-enyloxy)(*tert*-butyl)dimethylsilane (2*R*)-(234bf). *n*-Butyllithium (3.0 mL, 6.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (1.227 mg, 6.06 mmol) in THF (6 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (1.200 g, 6.30 mmol) in THF (12 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (36.8 mg, 0.055 mmol) in THF (6 mL) and allylcarbonate (±)-**267f** (1.533 g, 4.89 mmol, neat) were added consecutively. The cooling bath was then removed and the

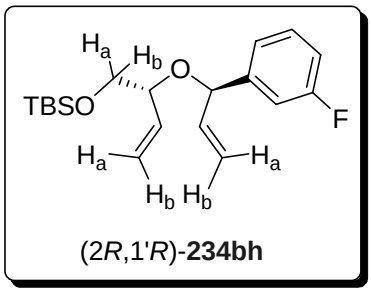
reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*)-**234bf** as yellowish oil (1.464 g, 75%, equimolar mixture of diastereoisomers **A**, **B**): ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.09 (s, 6H, CH_3), 0.12 (s, 3H, CH_3), 0.13 (s, 3H, CH_3), 0.94 (s, 9H, *t*-Bu), 0.96 (s, 9H, *t*-Bu), 3.62 (dd, $^{2}J_{1A\text{-}Ha,1A\text{-}Hb}$ = 10.5 Hz, $^{3}J_{1A\text{-}Ha,2A\text{-}H}$ = 4.9 Hz, 1H, 1A-Ha), 3.68 (dd, $^{2}J_{1B\text{-}Ha,1B\text{-}Hb}$ = 10.6 Hz, $^{3}J_{1B\text{-}Ha,2B\text{-}H}$ = 5.1 Hz, 1H, 1B-Ha), 3.73 (dd, $^{2}J_{1A\text{-}Hb,1A\text{-}Ha}$ = 10.5 Hz, $^{3}J_{1A\text{-}Hb,2A\text{-}H}$ = 6.9 Hz, 1H, 1A-Hb), 3.79 (dd, $^{2}J_{1B\text{-}Hb,1B\text{-}Ha}$ = 10.6 Hz, $^{3}J_{1B\text{-}Hb,2B\text{-}H}$ = 6.7 Hz, 1H, 1B-Hb), 3.85 (ddddd, $^{3}J_{2A\text{-}H,3A\text{-}H}$ = 7.0 Hz, $^{3}J_{2A\text{-}H,1A\text{-}Hb}$ = 6.9 Hz, $^{3}J_{2A\text{-}H,1A\text{-}Ha}$ = 4.9 Hz, $^{4}J_{2A\text{-}H,4A\text{-}Ha}$ = 1.0 Hz, $^{4}J_{2A\text{-}H,4A\text{-}Hb}$ = 1.0 Hz, 1H, 2A-H), 4.08 (ddddd, $^{3}J_{2B\text{-}H,3B\text{-}H}$ = 7.0 Hz, $^{3}J_{2B\text{-}H,1B\text{-}Hb}$ = 6.7 Hz, $^{3}J_{2B\text{-}H,1B\text{-}Ha}$ = 5.1 Hz, $^{4}J_{2B\text{-}H,4B\text{-}Ha}$ = 0.9 Hz, $^{4}J_{2B\text{-}H,4B\text{-}Hb}$ = 0.9 Hz, 1H, 2B-H), 4.95 (d, $^{3}J_{1'\text{-}H,2'\text{-}H}$ = 7.2 Hz, 1H, 1'A-H or 1'B-H), 4.97 (d, $^{3}J_{1'\text{-}H,2'\text{-}H}$ = 6.1 Hz, 1H, 1'B-H or 1'A-H), 5.17-5.39 (m, 8H, 4A-H, 3'A-H, 4B-H, and 3'B-H), 5.76 (ddd, $^{3}J_{3\text{-}H,4\text{-}Ha}$ = 17.4 Hz, $^{3}J_{3\text{-}H,4\text{-}Hb}$ = 10.4 Hz, $^{3}J_{3\text{-}H,2\text{-}H}$ = 7.0 Hz, 1H, 3A-H or 3B-H), 5.79 (ddd, $^{3}J_{3\text{-}H,4\text{-}Ha}$ = 17.1 Hz, $^{3}J_{3\text{-}H,4\text{-}Hb}$ = 10.6 Hz, $^{3}J_{3\text{-}H,2\text{-}H}$ = 7.0 Hz, 1H, 3B-H or 3A-H), 5.88 (ddd, $^{3}J_{2'\text{-}H,3'\text{-}Ha}$ = 17.4 Hz, $^{3}J_{2'\text{-}H,3'\text{-}Hb}$ = 10.2 Hz, $^{3}J_{2'\text{-}H,1'\text{-}H}$ = 7.2 Hz, 1H, 2'A-H or 2'B-H), 5.97 (ddd, $^{3}J_{2'\text{-}H,3'\text{-}Ha}$ = 17.1 Hz, $^{3}J_{2'\text{-}H,3'\text{-}Hb}$ = 10.4 Hz, $^{3}J_{2'\text{-}H,1'\text{-}H}$ = 6.1 Hz, 1H, 2'B-H or 2'A-H), 7.29 (d, $^{3}J_{2''\text{-}H,3''\text{-}H}$ = 8.4 Hz, 2H, 2''A-H or 2''B-H), 7.30 (d, $^{3}J_{2''\text{-}H,3''\text{-}H}$ = 8.4 Hz, 2H, 2''B-H or 2''A-H), 7.50 (d, $^{3}J_{3''\text{-}H,2''\text{-}H}$ = 8.4 Hz, 2H, 3''A-H or 3''B-H), 7.51 (d, $^{3}J_{3''\text{-}H,2''\text{-}H}$ = 8.4 Hz, 2H, 3''B-H or 3''A-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.38 (CH_3), -5.31 (CH_3), -5.27 (CH_3), -5.19 (CH_3), 18.34 ($C(CH_3)_3$), 19.40 ($C(CH_3)_3$), 25.89 ($C(CH_3)_3$), 66.24, and 66.28 (CH_2-1), 78.81, and 78.91 (CH-2), 79.23, and 79.57 (CH-1'), 115.71, 117.17, 118.05, and 118.28 (CH_2-4, and CH_2-3'), 121.17, and 121.34 (C-4''), 128.45, and 128.92 (CH-2''), 131.30, and 131.45 (CH-3''), 135.80, and 135.99 (CH-3), 138.30, and 139.00 (CH-2'), 140.09, and 140.61 (C-1''); MS (CI-NH_3, 150 °C) *m*/*z* (%) 781 ([$2M^+$], 1), 608/610/612 (10), 580/581 (10), 414/416 (10), 212/214 (30), 195/197 (100). Anal. Calcd. for $C_{19}H_{23}BrO_2Si$: C, 57.42; H, 7.35. Found: C, 57.37; H, 7.30.



(2*R*,1'*S*)-**234bf**

(2*R*,1'*S*)-(2-(1'-(4''-Bromophenyl)allyloxy)but-3-enyloxy)(*tert*-butyl)dimethylsilane (2*R*,1'*S*)-(234bf). *n*-Butyllithium (5.0 mL, 10.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (2.022 g, 9.99 mmol) in THF (8 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (2.000 g, 10.50 mmol) in THF (20 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (62.4 mg, 0.093 mmol) in THF (5 mL) and allylcarbonate (*S*)-**267f** (2.527 g, 8.07 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*,1'*S*)-**234bf** as yellowish oil (2.724 g, 85%): $[\alpha]_D$ -18.8 (*c* 2.02, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.11 (s, 6H, CH_3), 0.95 (s, 9H, *t*-Bu), 3.63 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 4.9 Hz, 1H, 1-Ha), 3.73 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.9 Hz, 1H, 1-Hb), 3.85 (ddddd, $^3J_{2\text{-H},3\text{-H}}$ = 7.0 Hz, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.9 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 4.9 Hz, $^4J_{2\text{-H},4\text{-Ha}}$ = 1.0 Hz, $^4J_{2\text{-H},4\text{-Hb}}$ = 1.0 Hz, 1H, 2-H), 4.97 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.1 Hz, $^4J_{1'\text{-H},3'\text{-Ha}}$ = 1.2 Hz, $^4J_{1'\text{-H},3'\text{-Hb}}$ = 1.2 Hz, 1H, 1'-H), 5.19 (ddd, $^3J_{3'\text{-Hb},2'\text{-H}}$ = 10.3 Hz, J_{HH} = 1.7 Hz, $^4J_{3'\text{-Hb},1'\text{-H}}$ = 1.2 Hz, 1H, 3'-Hb), 5.24-5.34 (m, 3H, 3'-Ha, 4-Ha, and 4-Hb), 5.79 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 16.9 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 10.8 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 7.0 Hz, 1H, 3-H), 5.97 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.2 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.3 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 6.1 Hz, 1H, 2'-H), 7.30 (d, $^3J_{2''\text{-H},3''\text{-H}}$ = 8.2 Hz, 2H, 2''-H, and 6''-H), 7.52 (d, $^3J_{3''\text{-H},2''\text{-H}}$ = 8.2 Hz, 2H, 3''-H, and 5''-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.38 (CH_3), -5.27 (CH_3), 18.33 ($C(CH_3)_3$), 25.88 ($C(CH_3)_3$), 66.24 (CH_2-1), 78.80 (CH-2), 79.23 (CH-1'), 115.65 (CH_2-3'), 118.28 (CH_2-4), 121.34 (C-4''), 128.90 (CH-2'', and CH-6''), 131.44 (CH-3'', and CH-5''), 135.80 (CH-3), 139.01 (CH-2'), 140.09 (C-1''); IR (NaCl, neat) ν 3446 (s), 2954 (s), 2928 (s), 2857 (s), 1487 (m), 1472 (m), 1255 (s), 1121 (s), 1073 (s) cm^{-1}; MS (CI) *m*/*z* (%) 397/399 ([M+H$^+$], 10), 369

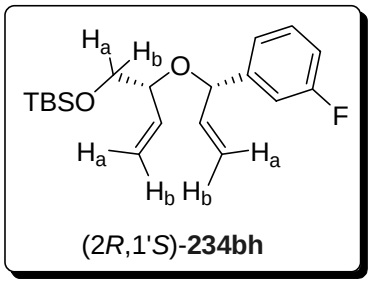
(30), 195/197 (100); HRMS (CI) 397.1156/399.1200 [$C_{19}H_{30}BrO_2Si$ ($M+H^+$) requires 397.1198/399.1180].



(2*R*,1'*R*)-**234bh**

(2*R*,1'*R*)-*tert*-Butyl(dimethyl)(2-(1'-(3''-fluorophenyl)allyloxy)but-3-enyloxy)silane (2*R*,1'*R*)-(234bh). *n*-Butyllithium (3.0 mL, 6.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (1.209 g, 5.97 mmol) in THF (5 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (1.200 g, 6.30 mmol) in THF (12 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (44.1 mg, 0.065 mmol) in THF (5.0 mL) and allylcarbonate (*R*)-**267h** (1.208 g, 4.79 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*,1'*R*)-**234bh** as colourless oil (1.161 g, 72%): $[\alpha]_D$ -14.7 (*c* 1.84, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.10 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.94 (s, 9H, *t*-Bu), 3.66 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 5.1 Hz, 1H, 1-Ha), 3.78 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.6 Hz, 1H, 1-Hb), 4.07 (ddddd, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.6 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 6.2 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 5.1 Hz, $^4J_{2\text{-H},4\text{-Ha}}$ = 1.2 Hz, $^4J_{2\text{-H},4\text{-Hb}}$ = 1.0 Hz, 1H, 2-H), 4.96 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 7.3 Hz, 1H, 1'-H), 5.25 (ddd, $^3J_{4\text{-Hb},3\text{-H}}$ = 10.4 Hz, $^2J_{4\text{-Hb},4\text{-Ha}}$ = 1.9 Hz, $^4J_{4\text{-Hb},2\text{-H}}$ = 1.0 Hz, 1H, 4-Hb), 5.28 (ddd, $^3J_{3'\text{-Hb},2'\text{-H}}$ = 10.2 Hz, $^3J_{3'\text{-Hb},3'\text{-Ha}}$ = 1.7 Hz, J_{HH} = 0.8 Hz, 1H, 3'-Hb), 5.29 (ddd, $^3J_{4\text{-Ha},3\text{-H}}$ = 17.4 Hz, $^3J_{4\text{-Ha},4\text{-Hb}}$ = 1.9 Hz, $^4J_{4\text{-Ha},2\text{-H}}$ = 1.2 Hz, 1H, 4-Ha), 5.35 (ddd, $^3J_{3'\text{-Ha},2'\text{-H}}$ = 17.4 Hz, $^3J_{3'\text{-Ha},3'\text{-Hb}}$ = 1.7 Hz, J_{HH} = 1.1 Hz, 1H, 3'-Ha), 5.75 (ddd, $^3J_{3\text{-H},4\text{-Ha}}$ = 17.4 Hz, $^3J_{3\text{-H},4\text{-Hb}}$ = 10.4 Hz, $^3J_{3\text{-H},2\text{-H}}$ = 6.2 Hz, 1H, 3-H), 5.88 (ddd, $^3J_{2'\text{-H},3'\text{-Ha}}$ = 17.4 Hz, $^3J_{2'\text{-H},3'\text{-Hb}}$ = 10.2 Hz, $^3J_{2'\text{-H},1'\text{-H}}$ = 7.3 Hz, 1H, 2'-H), 6.93-6.98 (m, 1H, 4''-H), 7.11-7.14 (m, 1H, 2''-H), 7.14-1.16 (m, 1H, 6''-H), 7.30 (ddd, J_{HH} = 8.1 Hz, J_{HH} = 8.1 Hz, $^4J_{5''\text{-H,F}}$ = 5.9 Hz, 1H, 5''-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.31 (CH_3), -5.19 (CH_3), 18.35 ($C(CH_3)_3$), 25.91 ($C(CH_3)_3$), 66.32 (CH_2-1), 78.98 (CH-2), 79.59 (d, $^4J_{CF}$ = 1.8 Hz,

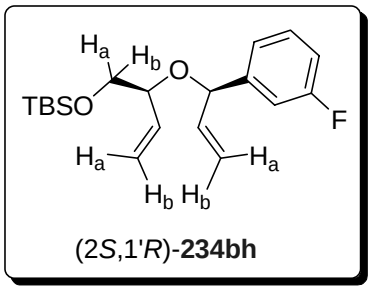
CH-1'), 113.62 (d, $^{2}J_{CF}$ = 22.1 Hz, CH-2''), 114.12 (d, $^{2}J_{CF}$ = 21.2 Hz, CH-4''), 117.23 (CH_2-3'), 118.04 (CH_2-4), 122.26 (d, $^{4}J_{CF}$ = 2.9 Hz, CH-6''), 129.64 (d, $^{3}J_{CF}$ = 8.2 Hz, CH-5''), 136.05 (CH-3), 138.31 (CH-2'), 144.31 (d, $^{3}J_{CF}$ = 6.9 Hz, C-1''), 162.89 (d, $^{1}J_{CF}$ = 245.5 Hz, CF-3''); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.78; IR (NaCl, neat) ν 2958 (s), 2931 (s), 2858 (s), 2360 (s), 1593 (m), 1253 (s), 1128 (s) cm^{-1}; MS (CI) *m*/*z* (%) 337 ([M+H$^+$], 10), 135 (100); HRMS (CI) 337.1998 [$C_{19}H_{30}FO_2Si$ (M+H$^+$) requires 337.1999]. Anal. Calcd. for $C_{19}H_{29}FO_2Si$: C, 67.81; H, 8.69. Found: C, 67.71; H, 8.55.



(2*R*,1'*S*)-**234bh**

(2*R*,1'*S*)-*tert*-Butyl(dimethyl)(2-(1'-(3''-fluorophenyl)allyloxy)but-3-enyloxy)silane (2*R*,1'*S*)-(234bh). *n*-Butyllithium (5.0 mL, 10.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*R*)-**235b** (2.024 g, 10.02 mmol) in THF (10 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (2.000 g, 10.50 mmol) in THF (20 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (65.0 mg, 0.092 mmol) in THF (5.0 mL) and allylcarbonate (*S*)-**267h** (2.005 g, 7.94 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*R*,1'*S*)-**234bh** as colourless oil (1.951 g, 73%): $[\alpha]_D$ -18.4 (*c* 1.96, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.06 (s, 6H, CH_3), 0.90 (s, 9H, *t*-Bu), 3.60 (dd, $^{2}J_{1\text{-Ha},1\text{-Hb}}$ = 10.6 Hz, $^{3}J_{1\text{-Ha},2\text{-H}}$ = 4.9 Hz, 1H, 1-Ha), 3.71 (dd, $^{2}J_{1\text{-Hb},1\text{-Ha}}$ = 10.6 Hz, $^{3}J_{1\text{-Hb},2\text{-H}}$ = 6.8 Hz, 1H, 1-Hb), 3.85 (ddddd, $^{3}J_{2\text{-H},3\text{-H}}$ = 7.0 Hz, $^{3}J_{2\text{-H},1\text{-Hb}}$ = 6.8 Hz, $^{3}J_{2\text{-H},1\text{-Ha}}$ = 4.9 Hz, J_{HH} = 1.0 Hz, J_{HH} = 1.0 Hz, 1H, 2-H), 4.96 (d, $^{3}J_{1'\text{-H},2'\text{-H}}$ = 6.1 Hz, 1H, 1'-H), 5.15 (ddd, J_{HH} = 10.4 Hz, J_{HH} = 1.4 Hz, J_{HH} = 1.4 Hz, 1H, 3'-Ha or 3'-Hb), 5.21-5.29 (m, 3H, 3'-Hb or 3'-Ha, 4-Ha, and 4-Hb), 5.76 (ddd, J_{HH} = 17.4 Hz, J_{HH} = 10.8 Hz, $^{3}J_{3\text{-H},2\text{-H}}$ = 7.0 Hz, 1H, 3-H), 5.94 (ddd, J_{HH} = 17.1 Hz, J_{HH} = 10.3 Hz, $^{3}J_{2'\text{-H},1'\text{-H}}$ = 6.1 Hz, 1H, 2'-H), 6.94-6.99 (m, 1H, 4''-H), 7.10-7.14 (m, 2H, 2''-H, and 6''-H), 7.27-7.32

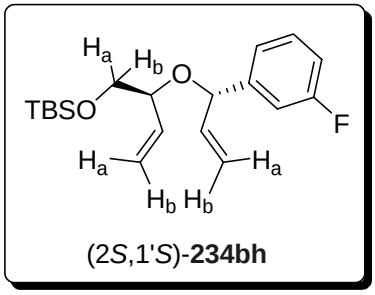
(m, 1H, 5''-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.39 (CH_3), -5.30 (CH_3), 18.36 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 66.32 (CH_2-1), 78.96 (CH-2), 78.38 (d, $^4J_{CF}$ = 1.7 Hz, CH-1'), 113.96 (d, $^2J_{CF}$ = 21.7 Hz, CH-2''), 114.36 (d, $^2J_{CF}$ = 21.3 Hz, CH-4''), 115.73 (CH_2-3'), 118.18 (CH_2-4), 122.73 (d, $^4J_{CF}$ = 2.8 Hz, CH-6''), 129.78 (d, $^3J_{CF}$ = 8.1 Hz, CH-5''), 136.90 (CH-3), 138.98 (CH-2'), 143.92 (d, $^3J_{CF}$ = 6.6 Hz, C-1''), 163.04 (d, $^1J_{CF}$ = 245.9 Hz, CF-3''); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.56; IR (NaCl, neat) ν 2955 (s), 2929 (s), 2858 (s), 1614 (m), 1592 (m), 1296 (s), 1126 (s), 1086 (s) cm^{-1}; MS (CI) *m*/*z* (%) 337 ([M+H$^+$], 5), 135 (100); HRMS (CI) 337.1997 [$C_{19}H_{30}FO_2Si$ (M+H$^+$) requires 337.1999]. Anal. Calcd. for $C_{19}H_{29}FO_2Si$: C, 67.81; H, 8.69. Found: C, 67.64; H, 8.80.



(2*S*,1'*R*)-**234bh**

(2*S*,1'*R*)-*tert*-Butyl(2-(1'-(3''-fluorophenyl)allyloxy)but-3-enyloxy)dimethylsilane (2*S*,1'*R*)-(234bh). *n*-Butyllithium (8.5 mL, 17.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*S*)-**235b** (3.440 g, 17.00 mmol) in THF (18 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (3.400 g, 17.85 mmol) in THF (35 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of [Ir(COD)Cl]$_2$ (107.9 mg, 0.161 mmol) in THF (5.0 mL) and allylcarbonate (*R*)-**267h** (3.605 g, 14.29 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*S*,1'*R*)-**234bh** as colourless oil (3.557 g, 74%): [α]$_D$ +18.3 (*c* 3.06, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.06 (s, 6H, CH_3), 0.90 (s, 9H, *t*-Bu), 3.60 (dd, $^2J_{1\text{-Ha},1\text{-Hb}}$ = 10.6 Hz, $^3J_{1\text{-Ha},2\text{-H}}$ = 4.9 Hz, 1H, 1-Ha), 3.71 (dd, $^2J_{1\text{-Hb},1\text{-Ha}}$ = 10.6 Hz, $^3J_{1\text{-Hb},2\text{-H}}$ = 6.8 Hz, 1H, 1-Hb), 3.85 (ddddd, $^3J_{2\text{-H},3\text{-H}}$ = 7.0 Hz, $^3J_{2\text{-H},1\text{-Hb}}$ = 6.8 Hz, $^3J_{2\text{-H},1\text{-Ha}}$ = 4.9 Hz, J_{HH} = 1.0 Hz, J_{HH} = 1.0 Hz, 1H, 2-H), 4.96 (d, $^3J_{1'\text{-H},2'\text{-H}}$ = 6.1 Hz, 1H, 1'-H), 5.15 (ddd, J_{HH} = 10.4 Hz, J_{HH} = 1.4 Hz, J_{HH} = 1.4 Hz, 1H, 3'-Ha or 3'-Hb), 5.21-5.29 (m, 3H, 3'-Hb or 3'-Ha, 4-Ha, and 4-Hb), 5.76 (ddd, J_{HH} = 17.4 Hz, J_{HH} = 10.8

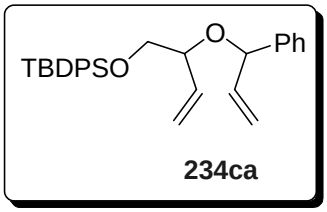
Hz, $^{3}J_{3\text{-H},2\text{-H}}$ = 7.0 Hz, 1H, 3-H), 5.94 (ddd, J_{HH} = 17.1 Hz, J_{HH} = 10.3 Hz, $^{3}J_{2'\text{-H},1'\text{-H}}$ = 6.1 Hz, 1H, 2'-H), 6.94-6.99 (m, 1H, 4''-H), 7.10-7.14 (m, 2H, 2''-H, and 6''-H), 7.27-7.32 (m, 1H, 5''-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.39 (CH_3), -5.30 (CH_3), 18.36 ($C(CH_3)_3$), 25.90 ($C(CH_3)_3$), 66.32 (CH_2-1), 78.96 (CH-2), 78.38 (d, $^{4}J_{CF}$ = 1.7 Hz, CH-1'), 113.96 (d, $^{2}J_{CF}$ = 21.7 Hz, CH-2''), 114.36 (d, $^{2}J_{CF}$ = 21.3 Hz, CH-4''), 115.73 (CH_2-3'), 118.18 (CH_2-4), 122.73 (d, $^{4}J_{CF}$ = 2.8 Hz, CH-6''), 129.78 (d, $^{3}J_{CF}$ = 8.1 Hz, CH-5''), 136.90 (CH-3), 138.98 (CH-2'), 143.92 (d, $^{3}J_{CF}$ = 6.6 Hz, C-1''), 163.04 (d, $^{1}J_{CF}$ = 245.9 Hz, CF-3''); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.56; IR (NaCl, neat) ν 2955 (s), 2929 (s), 2858 (s), 1614 (m), 1592 (m), 1296 (s), 1126 (s), 1086 (s) cm^{-1}; MS (CI) *m*/*z* (%) 337 ([M+H^{+}], 5), 135 (100); HRMS (CI) 337.1997 [$C_{19}H_{30}FO_2Si$ (M+H^{+}) requires 337.1999]. Anal. Calcd. for $C_{19}H_{29}FO_2Si$: C, 67.81; H, 8.69. Found: C, 67.55; H, 8.70.



(2*S*,1'*S*)-**234bh**

(2*S*,1'*S*)-*tert*-Butyl(dimethyl)(2-(1'-(3''-fluorophenyl)allyloxy)but-3-enyloxy)silane (2*S*,1'*S*)-(234bh). *n*-Butyllithium (4.0 mL, 8.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol (*S*)-**235b** (1.641 g, 8.11 mmol) in THF (8 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (1.600 g, 8.40 mmol) in THF (16 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (54.2 mg, 0.081 mmol) in THF (5.0 mL) and allylcarbonate (*S*)-**267h** (1.700 g, 6.73 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 20 h. The catalyst was precipitated by adding hexane (10 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane (2*S*,1'*S*)-**234bh** as colourless oil (1.765 g, 78%): $[\alpha]_D$ +15.2 (*c* 3.10, $CHCl_3$); ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 0.10 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.94 (s, 9H, *t*-Bu), 3.66 (dd, $^{2}J_{1\text{-Ha},1\text{-Hb}}$ = 10.5 Hz, $^{3}J_{1\text{-Ha},2\text{-H}}$ = 5.1 Hz, 1H, 1-Ha), 3.78 (dd, $^{2}J_{1\text{-Hb},1\text{-Ha}}$ = 10.5 Hz, $^{3}J_{1\text{-Hb},2\text{-H}}$ = 6.6 Hz, 1H, 1-Hb), 4.07 (ddddd, $^{3}J_{2\text{-H},1\text{-Hb}}$ = 6.6 Hz, $^{3}J_{2\text{-H},3\text{-H}}$ = 6.2 Hz, $^{3}J_{2\text{-H},1\text{-Ha}}$ = 5.1 Hz, $^{4}J_{2\text{-H},4\text{-Ha}}$ = 1.2 Hz, $^{4}J_{2\text{-H},4\text{-Hb}}$ = 1.0 Hz, 1H, 2-H), 4.96 (d, $^{3}J_{1'\text{-}}$

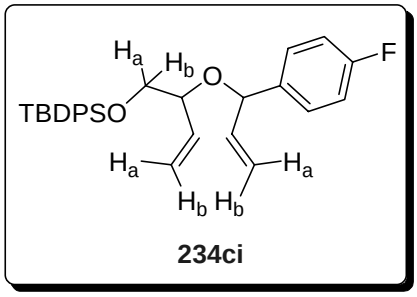
$_{H,2'\text{-}H}$ = 7.3 Hz, 1H, 1'-H), 5.25 (ddd, $^{3}J_{4\text{-}Hb,3\text{-}H}$ = 10.4 Hz, $^{2}J_{4\text{-}Hb,4\text{-}Ha}$ = 1.9 Hz, $^{4}J_{4\text{-}Hb,2\text{-}H}$ = 1.0 Hz, 1H, 4-Hb), 5.28 (ddd, $^{3}J_{3'\text{-}Hb,2'\text{-}H}$ = 10.2 Hz, $^{3}J_{3'\text{-}Hb,3'\text{-}Ha}$ = 1.7 Hz, J_{HH} = 0.8 Hz, 1H, 3'-Hb), 5.29 (ddd, $^{3}J_{4\text{-}Ha,3\text{-}H}$ = 17.4 Hz, $^{3}J_{4\text{-}Ha,4\text{-}Hb}$ = 1.9 Hz, $^{4}J_{4\text{-}Ha,2\text{-}H}$ = 1.2 Hz, 1H, 4-Ha), 5.35 (ddd, $^{3}J_{3'\text{-}Ha,2'\text{-}H}$ = 17.4 Hz, $^{3}J_{3'\text{-}Ha,3'\text{-}Hb}$ = 1.7 Hz, J_{HH} = 1.1 Hz, 1H, 3'-Ha), 5.75 (ddd, $^{3}J_{3\text{-}H,4\text{-}Ha}$ = 17.4 Hz, $^{3}J_{3\text{-}H,4\text{-}Hb}$ = 10.4 Hz, $^{3}J_{3\text{-}H,2\text{-}H}$ = 6.2 Hz, 1H, 3-H), 5.88 (ddd, $^{3}J_{2'\text{-}H,3'\text{-}Ha}$ = 17.4 Hz, $^{3}J_{2'\text{-}H,3'\text{-}Hb}$ = 10.2 Hz, $^{3}J_{2'\text{-}H,1'\text{-}H}$ = 7.3 Hz, 1H, 2'-H), 6.93-6.98 (m, 1H, 4''-H), 7.11-7.14 (m, 1H, 2''-H), 7.14-1.16 (m, 1H, 6''-H), 7.30 (ddd, J_{HH} = 8.1 Hz, J_{HH} = 8.1 Hz, $^{4}J_{5''\text{-}H,F}$ = 5.9 Hz, 1H, 5''-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ -5.31 (CH_3), -5.19 (CH_3), 18.35 ($C(CH_3)_3$), 25.91 ($C(CH_3)_3$), 66.32 (CH_2-1), 78.98 (CH-2), 79.59 (d, $^{4}J_{CF}$ = 1.8 Hz, CH-1'), 113.62 (d, $^{2}J_{CF}$ = 22.1 Hz, CH-2''), 114.12 (d, $^{2}J_{CF}$ = 21.2 Hz, CH-4''), 117.23 (CH_2-3'), 118.04 (CH_2-4), 122.26 (d, $^{4}J_{CF}$ = 2.9 Hz, CH-6''), 129.64 (d, $^{3}J_{CF}$ = 8.2 Hz, CH-5''), 136.05 (CH-3), 138.31 (CH-2'), 144.31 (d, $^{3}J_{CF}$ = 6.9 Hz, C-1''), 162.89 (d, $^{1}J_{CF}$ = 245.5 Hz, CF-3''); ^{19}F-NMR (376.5 MHz, $CDCl_3$) δ –113.78; IR (NaCl, neat) ν 2958 (s), 2931 (s), 2858 (s), 2360 (s), 1593 (m), 1253 (s), 1128 (s) cm^{-1}; MS (CI) *m*/*z* (%) 337 ([M+H$^+$], 10), 135 (100); HRMS (CI) 337.1998 [$C_{19}H_{30}FO_2Si$ (M+H$^+$) requires 337.1999]. Anal. Calcd. for $C_{19}H_{29}FO_2Si$: C, 67.81; H, 8.69. Found: C, 67.74; H, 8.79.



234ca

***tert*-Butyl(2-(1'-(phenyl)allyloxy)but-3-enyloxy)diphenylsilane (234ca).** *n*-Butyllithium (0.4 mL, 1.0 mmol, 2.5M solution in hexanes) was added slowly to a solution of protected butenediol (±)-**235c** (326 mg, 1.00 mmol) in THF (1 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (200 mg, 1.05 mmol) in THF (2 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of catalyst ($[Ir(COD)Cl]_2$ (14.0 mg, 0.020 mmol) and ligand (R_a,R_c,R_c)-**L2** (14.0 mg, 0.044 mmol) in THF (1 mL) and allylcarbonate (±)-**236a** (120 mg, 0.51 mmol, neat) were added respectively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and Et_2O (95:5) gave **234ca** as a colourless oil (198 mg, 93%): ^{1}H-NMR (400.1 MHz,

$CDCl_3$, a mixture of diastereoisomers in a 1:1.8 ratio, the minor diastereoisomer is marked with * where possible) δ 1.07* 1.10 (s, 9H, *t*-Bu), 3.28*-3.50* 3.62-3.86 (m, 2H, CH_2), 3.92*-3.97* 4.14-4.18 (m, 1H, CH_2CH), 4.98 (d, J_{HH} = 7.2 Hz, 0.6H, PhC*H*), 5.06* (d, J_{HH} = 7.5 Hz, 0.4H, PhC*H*), 5.11-5.36 (m, 4H, CH_2=CH), 5.72-5.80 and 5.77*-5.84* and 5.86-5.96 and 5.95*-6.04* (m, 2H, CH_2=C*H*), 7.22-7.47 and 7.66-7.76 (m, 15H, Ph); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 26.8 and 27.0 (*t*Bu), 66.8 (*C*H_2CH), 78.4 and 78.5 (CH_2*C*H), 79.7 and 80.2 (Ph*C*H), 115.1 and 116.6 and 117.9 and 118.1 (*C*H_2=CH), 126.7, 127.2, 127.6, 129.5, 129.6, 133.5, 133.6, 135.6, 135.7, 135.9, 136.0, 136.1, 141.0, 141.5. MS (CI-NH_3, 150 °C) *m*/*z* (%) 460 ([M+NH_4^+], 95), 444 (5), 364 (10), 252 (30), 193 (15), 52 (100); HRMS (CI-NH_3, 100 °C) 460.2670 [$C_{29}H_{38}NO_2Si$ (M+NH_4^+) requires 460.2672].

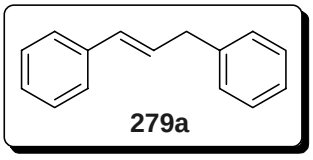


234ci

***tert*-Butyl(2-(1'-(4''-fluorophenyl)allyloxy)but-3-enyloxy)diphenylsilane (234ci).**

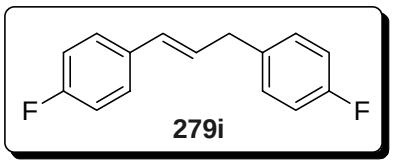
n-Butyllithium (1.2 mL, 3.0 mmol, 2.5M solution in hexanes) was added slowly to a solution of protected butenediol (±)-**235c** (986 mg, 3.02 mmol) in THF (3 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (600 mg, 3.15 mmol) in THF (6 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Ir(COD)Cl]_2$ (20.7 mg, 0.031 mmol) in THF (3 mL) and allylcarbonate (±)-**267i** (508 mg, 2.01 mmol, neat) were added consecutively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with a mixture of hexanes and ethyl acetate (98.5:1.5) gave silane **234ci** as a colourless oil (733 mg, 79%, mixture of diastereoisomers **A**, **B**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 1.06 (s, 9H, *t*-Bu), 1.09 (s, 9H, *t*-Bu), 3.63 (dd, $^2J_{1A\text{-}Ha,1A\text{-}Hb}$ = 10.5 Hz, $^3J_{1A\text{-}Ha,2A\text{-}H}$ = 4.7 Hz, 1H, 1A-Ha), 3.70 (dd, $^2J_{1B\text{-}Ha,1B\text{-}Hb}$ = 10.5 Hz, $^3J_{1B\text{-}Ha,2B\text{-}H}$ = 4.9 Hz, 1H, 1B-Ha), 3.76 (dd, $^2J_{1A\text{-}Hb,1A\text{-}Ha}$ = 10.5 Hz, $^3J_{1A\text{-}Hb,2A\text{-}H}$ = 6.8 Hz, 1H, 1A-Hb), 3.83 (dd, $^2J_{1B\text{-}Hb,1B\text{-}Ha}$ = 10.5 Hz, $^3J_{1B\text{-}Hb,2B\text{-}H}$ = 6.6 Hz, 1H, 1B-Hb), 3.89 (dddt, $^3J_{2A\text{-}H,1A\text{-}Hb}$ = 6.8 Hz,

$^{3}J_{2A\text{-}H,3A\text{-}H}$ = 5.7 Hz, $^{3}J_{2A\text{-}H,1A\text{-}Ha}$ = 4.7 Hz, $^{4}J_{2A\text{-}H,4A\text{-}H}$ = 1.0 Hz, 1H, 2A-H), 4.13 (dddt, $^{3}J_{2B\text{-}H,1B\text{-}Hb}$ = 6.6 Hz, $^{3}J_{2B\text{-}H,3B\text{-}H}$ = 5.9 Hz, $^{3}J_{2B\text{-}H,1B\text{-}Ha}$ = 4.9 Hz, $^{4}J_{2B\text{-}H,4B\text{-}H}$ = 1.1 Hz, 1H, 2B-H), 4.93-4.96 (m, 2H, 1'A-H, and 1'B-H), 5.12-5.34 (m, 8H, 3'A-H, 3'B-H, 4A-H, and 4B-H), 5.70-6.00 (m, 4H, 2'A-H, 2'B-H, 3A-H, and 3B-H), 6.98-7.05 (m, 4H, H-arom), 7.31-7.47 (m, 16H, H-arom), 7.65-7.76 (m, 8H, H-arom); HRMS (CI-NH_3, 100 °C) 478.2576 [$C_{29}H_{37}FNO_2Si$ ($M+NH_4^+$) requires 478.2578].



279a

(*E*)-Prop-1-ene-1,3-diyldibenzene (279a).[229] *n*-Butyllithium (0.5 mL, 1.0 mmol, 2.0M solution in pentane) was added slowly to a solution of protected butenediol **235c** (326 mg, 1.00 mmol) in THF (1 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (200 mg, 1.05 mmol) in THF (2 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $Rh(PPh)_3Cl$ (61.1 mg, 0.066 mmol) and $P(OMe)_3$ (25.0 mg, 0.201 mmol) in THF (1.0 mL) and allylcarbonate **267a** (136 mg, 0.58 mmol, neat) were added respectively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with hexanes gave **279a** as a colourless oil (26 mg, 46% of theory, 77% based on recovered carbonate). Subsequent elution with a mixture of hexanes and ethyl acetate (98.5:1.5) gave carbonate **267a** as a colourless oil (55 mg, 40% recovered). **279a**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 3.47 (d, $^{3}J_{3\text{-}H,2\text{-}H}$ = 6.6 Hz, 2H, 3-H), 6.28 (dt, $^{3}J_{2\text{-}H,1\text{-}H}$ = 15.8 Hz, $^{3}J_{2\text{-}H,3\text{-}H}$ = 6.6 Hz, 1H, 2-H), 6.38 (d, $^{3}J_{1\text{-}H,2\text{-}H}$ = 15.8 Hz, 1H, 1-H), 7.10-7.29 (m, 10H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 39.34 (CH_2-3), 126.10, 126.16, 127.08, 128.47, 128.48, and 128.65 (CH-arom), 129.20 (CH-2), 131.05 (CH-1), 137.45 (C-1'), 140.14 (C-1''); MS (EI) *m*/*z* (%) 194 (M^+, 40), 179 (15), 115 (20), 83 (100); HRMS (EI) 194.1094 [$C_{15}H_{14}$ (M^+) requires 194.1096]. Consistent with the literature data.[229]



279i

(*E*)-4,4'-(Prop-1-en-1,3-diyl)bis(fluorobenzen) (279i). *n*-Butyllithium (0.4 mL, 1.0 mmol, 2.5M solution in hexanes) was added slowly to a solution of protected butenediol **235c** (326 mg, 1.00 mmol) in THF (1 mL) and the mixture was stirred at 0 °C for 15 min. The lithium alkoxide thus generated was transferred (*via* cannula) to a suspension of copper(I) iodide (200 mg, 1.05 mmol) in THF (2 mL) at room temperature. The mixture turned light yellow and was then stirred for 30 min.[230] The resulting mixture was cooled to 0 °C, a cold (0 °C) solution of $[Rh(COD)Cl]_2$ (10.1 mg, 0.020 mmol) in THF (1.0 mL) and allylcarbonate **267i** (136 mg, 0.54 mmol, neat) were added respectively. The cooling bath was then removed and the reaction mixture was stirred at room temperature for 16 h. The catalyst was precipitated by adding hexane (5 mL) and the mixture was filtered through a pad of silica (3 × 3 cm) and the product was eluted with a mixture of hexanes and ethyl acetate (90:10). Chromatography on a column of silica gel (3 × 10 cm) with hexanes gave **279i** as colourless oil (27 mg, 43%). Subsequent elution with a mixture of hexanes and ethyl acetate (98.5:1.5) gave diallyl ether **234ci** as a colourless oil (78 mg, 31%). **279i**: ^{1}H-NMR (400.1 MHz, $CDCl_3$) δ 3.45 (d, $^3J_{3\text{-H},2\text{-H}}$ = 6.8 Hz, 2H, 3-H), 6.19 (dt, $^3J_{2\text{-H},1\text{-H}}$ = 15.7 Hz, $^3J_{2\text{-H},3\text{-H}}$ = 6.8 Hz, 1H, 2-H), 6.33 (d, $^3J_{1\text{-H},2\text{-H}}$ = 15.7 Hz, 1H, 1-H), 6.87-6.92 (m, 2H, H-arom), 7.12-7.25 (m, 6H, H-arom); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ 38.16 (CH_2-3), 114.76 (d, $^2J_{CF}$ = 21.7 Hz, CH-3''), 115.29 (d, $^2J_{CF}$ = 22.9 Hz, CH-3'), 126.31 (CH-2), 130.14 (d, $^3J_{CF}$ = 8.1 Hz, CH-2'), 130.31 (d, $^3J_{CF}$ = 8.2 Hz, CH-2''), 130.85 (CH-1), 133.68 (d, $^4J_{CF}$ = 1.1 Hz, C-1'), 136.83 (d, $^4J_{CF}$ = 3.1 Hz, C-1''), 160.27 (d, $^1J_{CF}$ = 249.2 Hz, CF-4'), 162.10 (d, $^1J_{CF}$ = 246.1 Hz, CF-4''); HRMS (EI) 230.0910 [$C_{15}H_{12}F_2$ (M^+) requires 230.0907].

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