Synthesis of trisubstituted olefins by RCM using an O-Si-C tether
Application to the total synthesis of dolabelide C

Stéphane Wittmann (MSc)

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

School of Chemistry
College of Science & Engineering
University of Glasgow

September 2015

Table of Contents

Acknowledgements

Firstly, I would like to deeply thank my PhD supervisor Dr. Joëlle Prunet for giving me the opportunity to work in her group. I would like to thank her for her help during the PhD and for giving me great autonomy in the realisation of the project. I really appreciated that project and I hope dolabelide C will soon be synthesised thanks to Alex and Alex Jr. !!

I would like to give big thanks also to all the past and present members of the Prunet group: Aurélien Letort for all the fun times in the lab during these three and a half years, Michael Mathieson for the good times spent at the beginning of the PhD, Alexandre Audic (Phillibert) for all the interesting discussions we had and for continuing the project, Stephen Morrison (Momo) for being always nice and full of interesting informations, Andres Garzon for sharing the fumehood with me for nine months and teaching me spanish, Amaia Altuna (Senorita burrita), Toni Wilkes (Twilkes), Alan Jeuken (The Joker), Marion, Alice, Quentin, Tim, Lampros (l'homme-flèche), Laurie, Roddie (DK), David, Andrew, Thomas (Wee Tam), Gillian, Alys, Pauline and Chiara. Good luck also to the new student, Alex Jr, for continuing the project.

Thanks to Dr David France for all his good advices and to all the members of the France group: Lewis and Craig for all the crazy times in the lab, David (DP), Jo and Pooja. Thanks to all the other members of the Raphael Lab: Tom Cogswell (Tomcat) for all the good times and for his funny accent, Alan Sewell (Big Al) for all the good chats, Liam and Sean for making the lab livelier, Ezequiel for all the good chats about music, Mhairi for always being in a good mood, Hugh (the HughMan) for his great beard, the two Ric(c)ardos and Alejandro (Tocayo). Thanks to all the members of the Henderson Lab: Filo for being crazy, but full of good advices, Aurélien Jr. and Ludo, Michael Popadynec (MickeyP, Popadom), Chao, Verena, Laëtitia, Kirsten and Michael Sparenberg. Thanks to all the members of the Loudon Lab: Ewen, Masha for all the Russian lessons, Carlos, Filip, Alex Harkiss and all the other members. Thanks also to my flatmate and past member of the Cooke group, Luis Serrano, for all the good times spent in the flat during almost three years; and thanks to all the members of the Spanish crew, in particular Irene and the two Marcs.

I would like to thank all the members of staff that have been of great help during these three and a half years, especially Ted, Bruce, Karen, Ali, Jim and Harry.

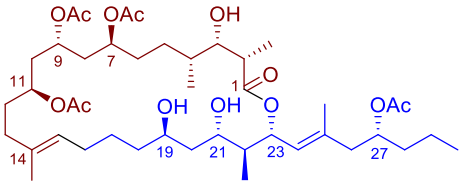
My gratitute goes also to the University of Glasgow for funding.

Finally, I would like to thank my family and friends: my parents, Jeannine and Jean-François, my aunts, Cécile and Pascale and my two best friends, Romain and Xavier. You were all of great support during all these years.

Author's Declaration

This thesis represents the original work of Stéphane Wittmann unless otherwise explicitly stated and referenced in the text. The research was carried out at the University of Glasgow in the Raphael Laboratory under the supervision of Dr Joëlle Prunet during the period from the 3rd of October 2011 to the 31st of March 2015.

Abstract



Dolabelide C

Dolabelide C is a macrolide, part of the dolablide family, isolated in 1997 from the Japanese sea hare, *Dolabella auricularia*. Dolabelide C contains a polyhydroxylated macrocycle structure with eleven stereogenic centers and two trisubstituted olefins. It exhibits cytotoxicity against cervical cancer HeLa-S_3 cells. Dolabelide C and the other members of the dolabelide family have been the object of several studies in several groups.

The approach envisaged in the Prunet group towards the synthesis of dolabelide C consists in disconnecting the molecule into two fragments of similar lengths, the C1-15 and the C16-30 fragments. Previously within the group, both fragments had been successfully synthesised. However, new routes have been envisaged in order to improve these syntheses.

For the synthesis of the C16-30 fragment, the fragment had been previously synthesised by cross metathesis, but this reaction led to an *E*/*Z* ratio to 4:1 at best. The new route consists in employing a temporary silicon-tethered ring-closing metathesis reaction in order to obtain a single isomer. This method was investigated on model substrates and was then employed for the synthesis of the C16-30 fragment of dolabelide C.

Finally, the use of a new route for the synthesis of the C1-15 fragment is discussed. The C1-15 fragment had been synthesised previously using a Mukaiyama aldol as the key step. However, as the ketone is not present in the natural product, several steps were required in order to remove it. The use of a cross metathesis between two fragments was investigated for the synthesis of this fragment in a more concise manner.

Abbreviations

(+)-DAIB: (2*R*)-(+)-3-exo-(dimethylamino)isoborneol
(−)-DAIB: (2*S*)-(−)-3-exo-(dimethylamino)isoborneol
(*R*,*R*)-**[Co]**: (*R*,*R*) -(−)-*N*,*N*'-*bis*(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane diaminocobalt(III) acetate
(*R*,*R*)-BDPP: (2*R*,4*R*)-(+)-2,4-*bis*(diphenylphosphino)pentane
(*R*,*R*)-**[Ti]**: cyclopentadienyl[(*4R*,*trans*)-2,2-dimethyl-*a*,*a*,*a*',*a*'-tetraphenyl-1,3-dioxolane-4,5-dimethanolato-*O*,*O*']titanium chloride
(*S*,*S*)-**[Co]**: (*S*,*S*) -(+)-*N*,*N*'-*bis*(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane diaminocobalt(III) acetate
(*S*,*S*)-**[Ti]**: cyclopentadienyl[(*4S*,*trans*)-2,2-dimethyl-*a*,*a*,*a*',*a*'-tetraphenyl-1,3-dioxolane-4,5-dimethanolato-*O*,*O*']titanium chloride
Δ: reflux
Ac: acetyl
AIBN: azobisisobutyronitrile
Aq.: aqueous
Ar: aryl
BINAP: 2,2'-*bis*(diphenylphosphino)-1,1'-binaphthyl
Bn: benzyl
4-BQ: 4-benzoquinone
brsm: based on recovered starting materials
n-Bu: *n*-butyl
Cat.: catalytic
c-Hexyl/Cy: cyclohexyl
CM: cross metathesis
Cp: cyclopentadienyl
CSA: camphorsulfonic acid
d: day
DCE: 1,2-dichloroethane
DCM: dichloromethane
DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DIBAL-H: diisobutylaluminium hydride
DIPEA: *N*-diisopropylethylamine
DMAP: dimethylaminopyridine
DMF: dimethylformamide
DMI: 1,3-dimethyl-2-imidazolidinone
DMP/DMPI: Dess-Martin periodinane
DMPU: 1,3-dimethyltetrahydropyrimidin-2(1*H*)-one
DMSO: dimethylsulfoxide
dr: diastereomeric ratio
ee: enantiomeric excess
eq./equiv: equivalent
Et: ethyl
h: hour
HMDS: hexamethyldisilazide
HMPA: hexamethylphosphoramide
HWE: Horner–Wadsworth–Emmons
IBX: 2-iodoxybenzoic acid
IC_{50}: half maximal inhibitory concentration
Im: imidazole
Ipc: isopinocampheyl

i-Pr:	isopropyl
L_n:	ligands
LDA:	lithium diisopropylamide
M:	molar
m-CPBA:	*m*-chloroperbenzoic acid
Me:	methyl
Mes:	mesityl (2,4,6-trimethylphenyl)
min:	minute
MOM:	methoxymethyl
MS:	molecular sieves
MW:	molecular weight
NIS:	*N*-iodosuccinimide
NMO:	*N*-methylmorpholine *N*-oxide
NMR:	nuclear magnetic resonance
Np:	2-naphthyl
n-Pr:	*n*-propyl
P:	protecting group
Ph:	phenyl
Pin:	pinacol
PMB:	*p*-methoxybenzyl
PMP:	*p*-methoxyphenyl
PPTS:	pyridinium *p*-toluenesulfonate
quant.:	quantitative
R:	alkyl or aryl group
RCM:	ring-closing metathesis
RDS:	rate-determining step
rt:	room temperature
TBAF:	tetrabutylammonium fluoride
TBAI:	tetrabutylammonium iodide
TBDPS:	*tert*-butyldiphenylsilyl
TBS:	*tert*-butyldimethylsilyl
t-Bu:	*tert*-butyl
TEA:	triethylamine
TES:	triethylsilyl
Tf:	triflyl (trifluoromethanesulfonyl)
THF:	tetrahydrofuran
TIPS:	triisopropylsilyl
TLC:	thin-layer chromatography
TMS:	trimethylsilyl
Tol:	4-methylphenyl
TS:	transition state

Chapter 1: Introduction

1.1 - Presentation of dolabelides

A twenty-year pursuit of the cell growth inhibitory and antineoplasic constituents of the Western Indian Ocean (Mauritius) sea hare ***Dolabella auricularia*** (Figure 1) has resulted in the discovery of fifteen structurally unique peptide, cyclopeptide, depsipeptide, and cyclodepsipeptide-type substances designated as dolastatins 1-15.[1]

Figure 1: *Dolabella auricularia*[2]

Among the dolastatins, **10** and **15** have displayed strong potency in experimental antineoplasic and tubulin assembly systems (Figure 2).

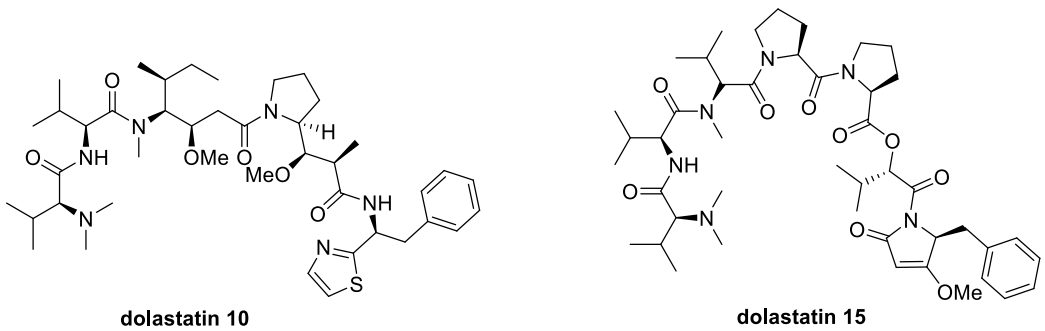


Figure 2: Dolastatins 10 and 15

Following the discovery of the dolastatins, novel compounds named dolabelides were isolated.

The dolabelide family is a family of four macrolides named dolabelides A to D. Dolabelides A and B are 22-membered macrolides isolated and characterised in 1995 by Yamada from the Japanese sea hare, *Dolabella auricularia*.[3]

---

[1] Pettit, G. R.; Kamano, Y.; Herald, C. L.; Fujii, Y.; Kizu, H.; Boyd, R. R.; Boettner, F. E.; Doubek, D. L.; Schmidt, J. M.; Chapuis, J.-C.; Michel, C. *Tetrahedron* **1993**, *49*, 9151.
[2] http://www.gastropods.com/8/Shell_29538.shtml.
[3] Ojika, M.; Nagoya, T.; Yamada, K. *Tetrahedron Lett.* **1995**, *36*, 7491.

Dolabelides C and D are 24-membered macrolides isolated and characterised in 1997 by Yamada from the same source as dolabelides A and B.[4] The structures of the dolabelide macrolides are presented in the following figure (Figure 3):

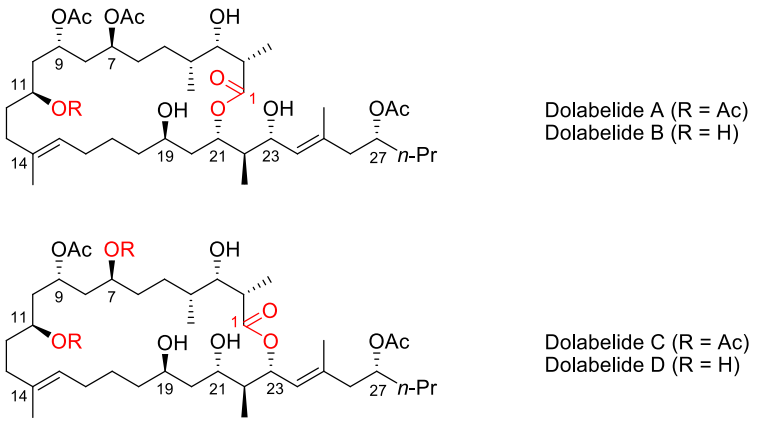


Figure 3: The dolabelide family

Dolabelides A, B, C and D exhibited cytotoxicity against cervical cancer HeLa-S_3 cells with IC_{50} values of 6.3, 1.3, 1.9 and 1.5 µg/mL, respectively. However, the quantity available of the dolabelides is very low. For example, only 99 mg of dolabelide C can be isolated from 138 kg (wet weight) of ***Dolabella auricularia***.

Moreover, the polyhydroxylated macrocycle structure of the dolabelides can let us hope for not only an antitumoral activity, but also an antibiotic activity.
Common features among the dolabelide family are:

- Eleven stereogenic centers, eight of which bear an oxygenated function and three methyl groups.
- Two *E*-configured trisubstituted olefins.
- A lactone group

Other structural features possessed by this family of macrolactones include 1,3-*anti*-diol fragments found at C7/C9 and C19/C21, along with an accompanying 1,3-*syn*-diol at C9/C11 and polypropionate fragments at C1/C4 and C21/C23.

The stereochemical complexity and biological profile of this class of compounds has attracted synthetic interest from several groups. In 2006, the first total synthesis of dolabelide D was reported by Leighton and co-workers[5] and in 2011, the first total synthesis of dolabelide C was reported by Hanson and co-workers.[6] Genêt, Phansavath and co-workers also worked on the synthesis of the C1-13 fragment of dolabelides[7] and on the C15-30 subunit of dolabelide A.[8] Keck and co-workers reported the synthesis of the C1-13 subunit of dolabelide B in 2005.[9]

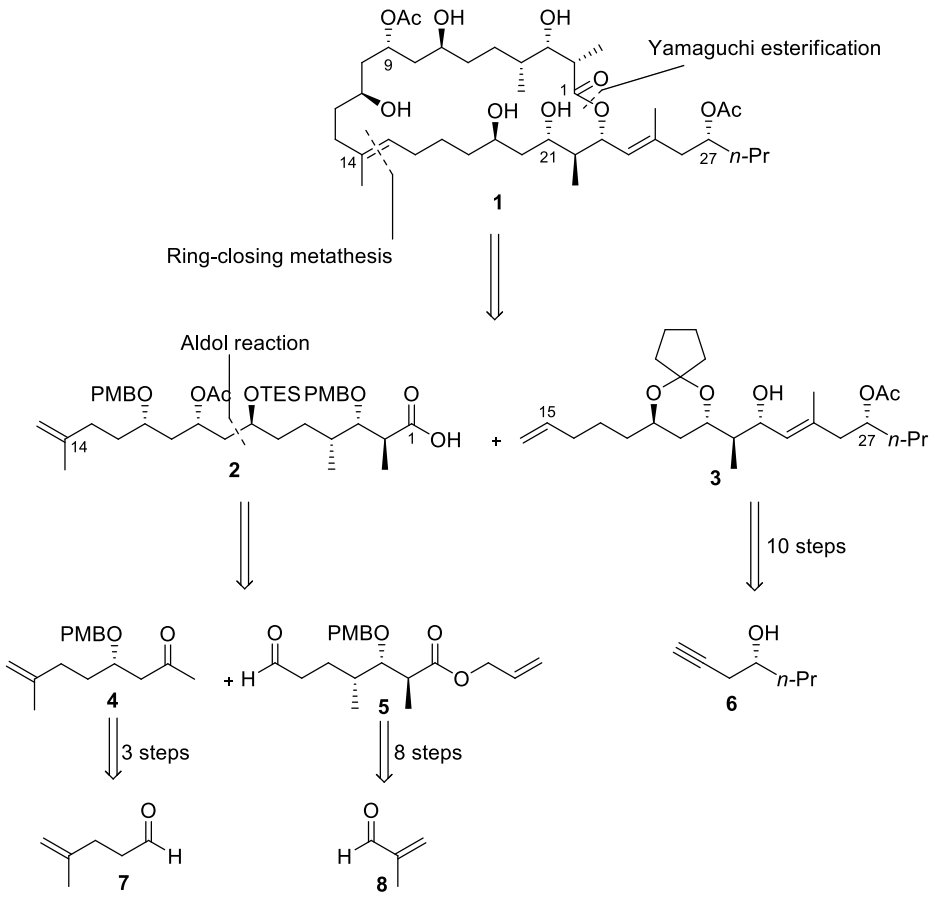
---

[4] Suenaga, K.; Nagoya, T.; Shibata, T.; Kigoshi, H.; Yamada, K. *J. Nat. Prod.* **1997**, *60*, 155.
[5] Park, P. K.; O'Malley, S. J.; Schmidt, D. R.; Leighton, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 2796.
[6] (a) Waetzig, J. D.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 109; (b) Whitehead, A.; Waetzig, J. D.; Thomas, C. D.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 1421; (c) Hanson, P. R.; Chegondi, R.; Nguyen, J.; Thomas, C. D.; Waetzig, J. D.; Whitehead, A. *J. Org. Chem.* **2011**, *76*, 4358.
[7] Le Roux, R.; Desroy, N.; Phansavath, P.; Genêt, J.-P. *Synlett* **2005**, 429.
[8] (a) Desroy, N.; Le Roux, R.; Phansavath, P.; Chiummiento, L.; Bonini, C.; Genêt, J.-P. *Tetrahedron Lett.* **2003**, *44*, 1763; (b) Roche, C.; Desroy, N.; Haddad, M.; Phansavath, P.; Genêt, J.-P. *Org. Lett.* **2008**, *10*, 3911.
[9] Keck, G. E.; McLaws, M. D. *Tetrahedron Lett.* **2005**, *46*, 4911.

1.2 - Previous syntheses of dolabelides

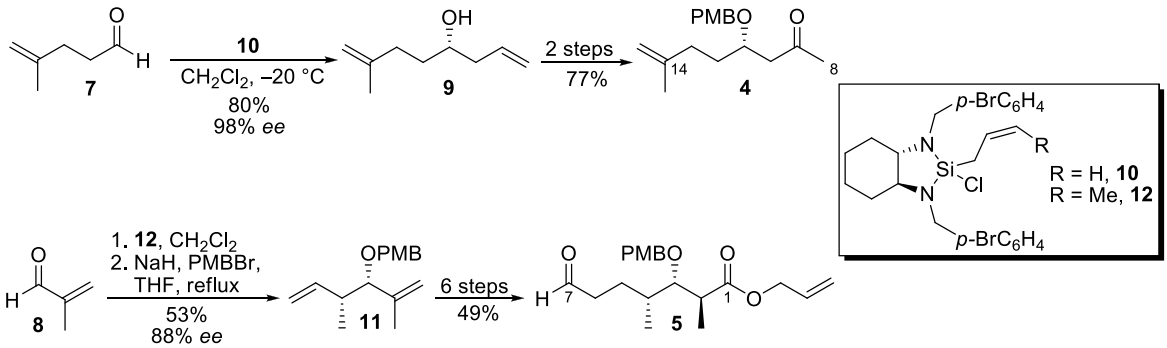
1.2.1 - Leighton synthesis of dolabelide D5

The Leighton synthesis of dolabelide D is based on the coupling of two fragments using macrolactonisation and ring-closing metathesis.
The retrosynthesis of dolabelide D is presented in the following scheme (Scheme 1):



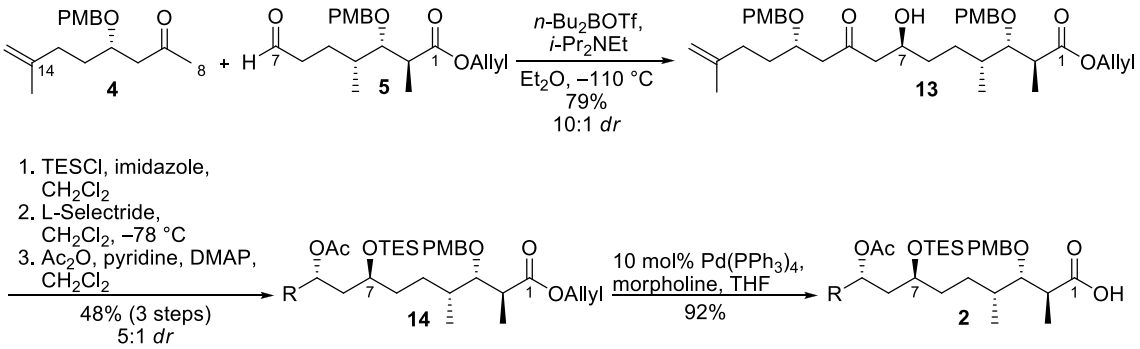
Scheme 1: Retrosynthesis of Leighton's dolabelide D synthesis

The key steps in the synthesis of the C1-14 fragment are the allylation and crotylation reactions using the reagents **10** and **12** developed in the Leighton group (Scheme 2).



Scheme 2: Synthesis of the C1-14 fragment

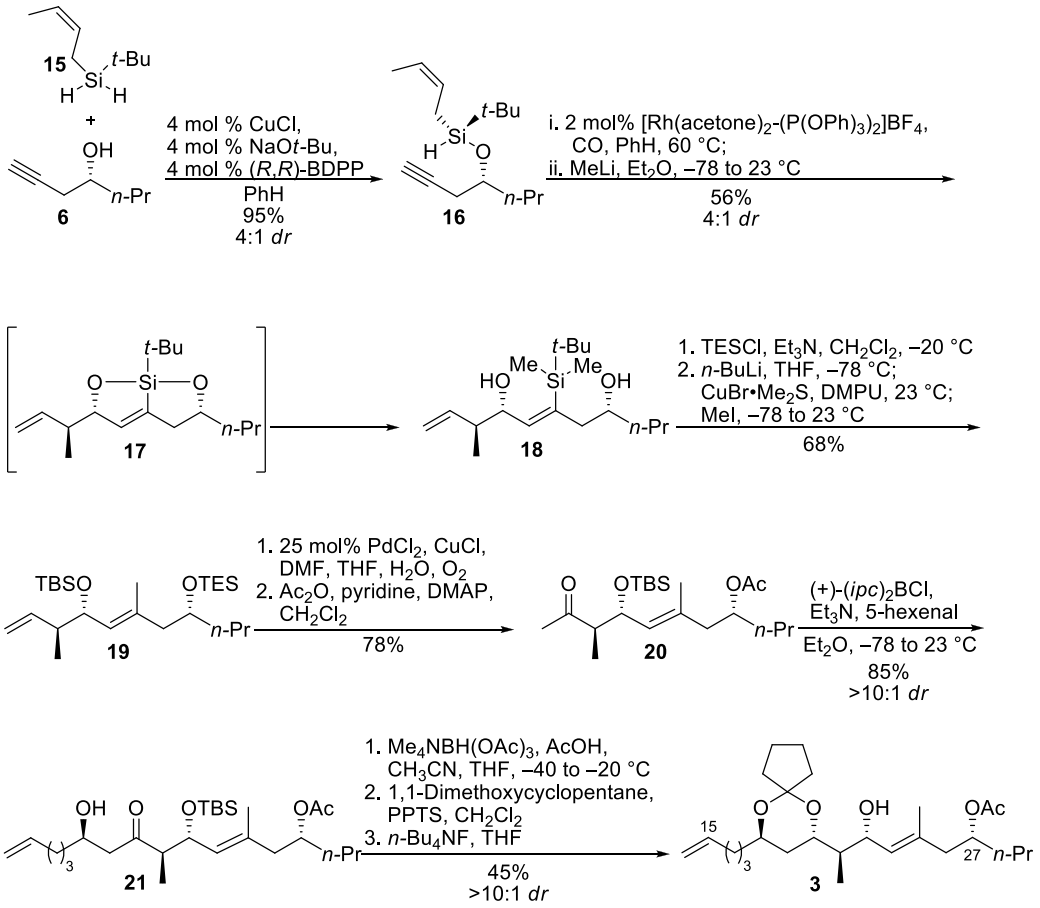
The completion of the synthesis of the C1-14 fragment is shown in the following scheme (Scheme 3):



Scheme 3: Completion of the synthesis of the C1-14 fragment

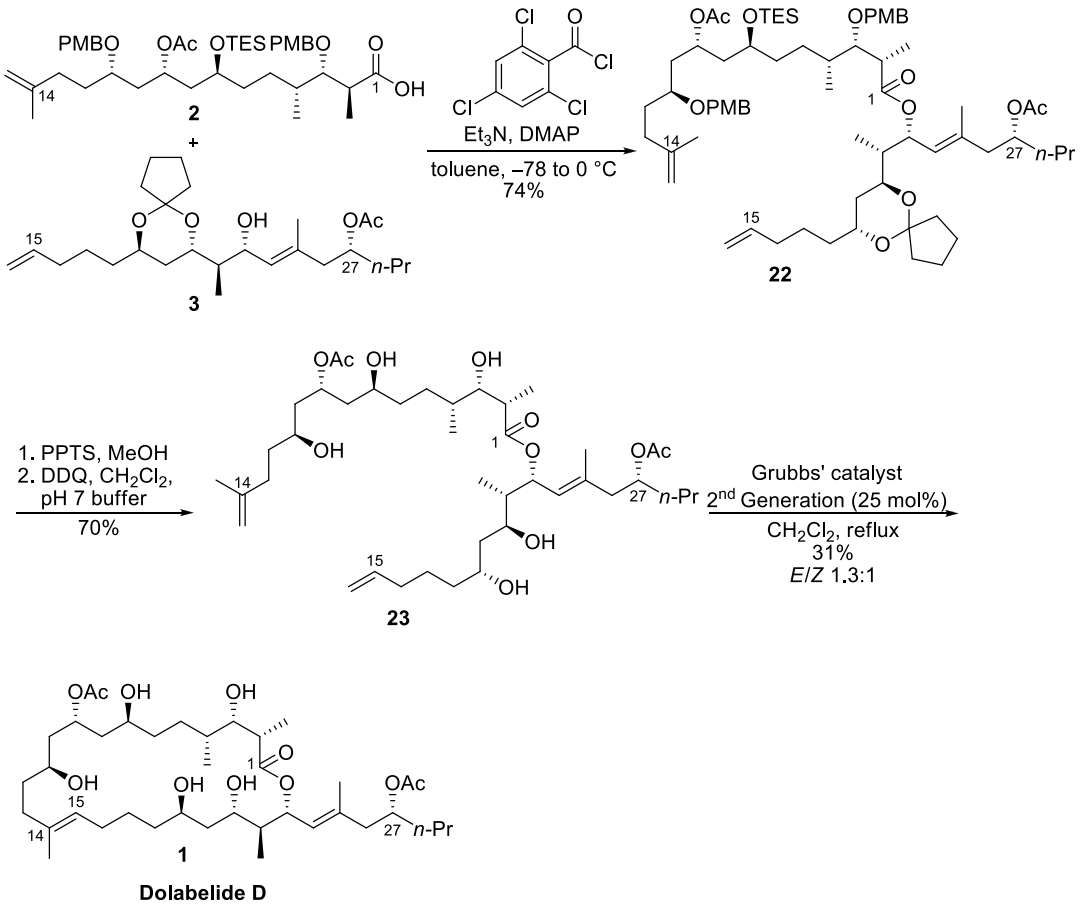
The two fragments are coupled using a 1,5-*anti* selective aldol reaction with a diastereomeric ratio of 10:1. The completion of the synthesis was done using the following sequence of steps: protection of the alcohol as a TES ether, diastereoselective reduction of the ketone with L-selectride, protection of the alcohol as an acetate and deprotection of the allyl ester to lead to the carboxylic acid. The C1-14 fragment is formed in thirteen steps in 9% yield for the longest chain.

The synthesis of the C15-30 fragment (Scheme 4) commenced with a catalytic asymmetric silane alcoholysis, developed in the Leighton group, with alcohol **6** and *tert*-butyl-*cis*-crotylsilane **15** to provide **16** as the major component of a 4:1 mixture of diastereomers in 95% yield. Rhodium-catalysed tandem silylformylation-crotylsilylation proceeded stereospecifically to provide, after quenching with methyllithium, a 4:1 mixture of diastereomers favouring 1,5-*syn*-diol **18** in 56% yield. Selective protection of the less hindered alcohol as its triethylsilyl (TES) ether, followed by treatment of the other alcohol with *n*-BuLi and then CuBr·Me_2S and DMPU, initiated a Brook-like 1,4-carbon (sp^2) to oxygen silane migration, and the resulting vinylcopper species was then alkylated with MeI to provide **19** in 68% yield. A Wacker oxidation gave the ketone from the alkene and removed the triethylsilyl ether group at the same time; the alcohol was then protected as an acetate in 78% yield for the two steps. Asymmetric Paterson aldol coupling with 5-hexenal then gave aldol **21** in 85% yield and with >10:1 diastereoselectivity. *Anti* diastereoselective (>10:1 *dr*) ß-hydroxyketone reduction, followed by protection of the 1,3-*anti*-diol as a cyclopentylidene ketal and deprotection of the *tert*-butylydimethylsilyl ether with tetrabutylammonium fluoride gave the C15-30 fragment in 45% yield for the three steps. The C15-30 fragment was obtained in ten steps and 11% overall yield.



Scheme 4: synthesis of the C15-30 fragment

Coupling of the two fragments using Yamaguchi esterification gave the corresponding ester in 74% yield. Cleavage of the cyclopentylidene ketal using pyridinium *p*-toluenesulfonate and the *p*-methoxybenzyl ether and the triethylsilyl ether using DDQ gave the polyol **23** in 70% yield. Final cyclisation using ring-closing metathesis occurred with a low selectivity (*E*/*Z* ratio of 1.3:1) and gave dolabelide D in a 31% isolated yield (Scheme 5).

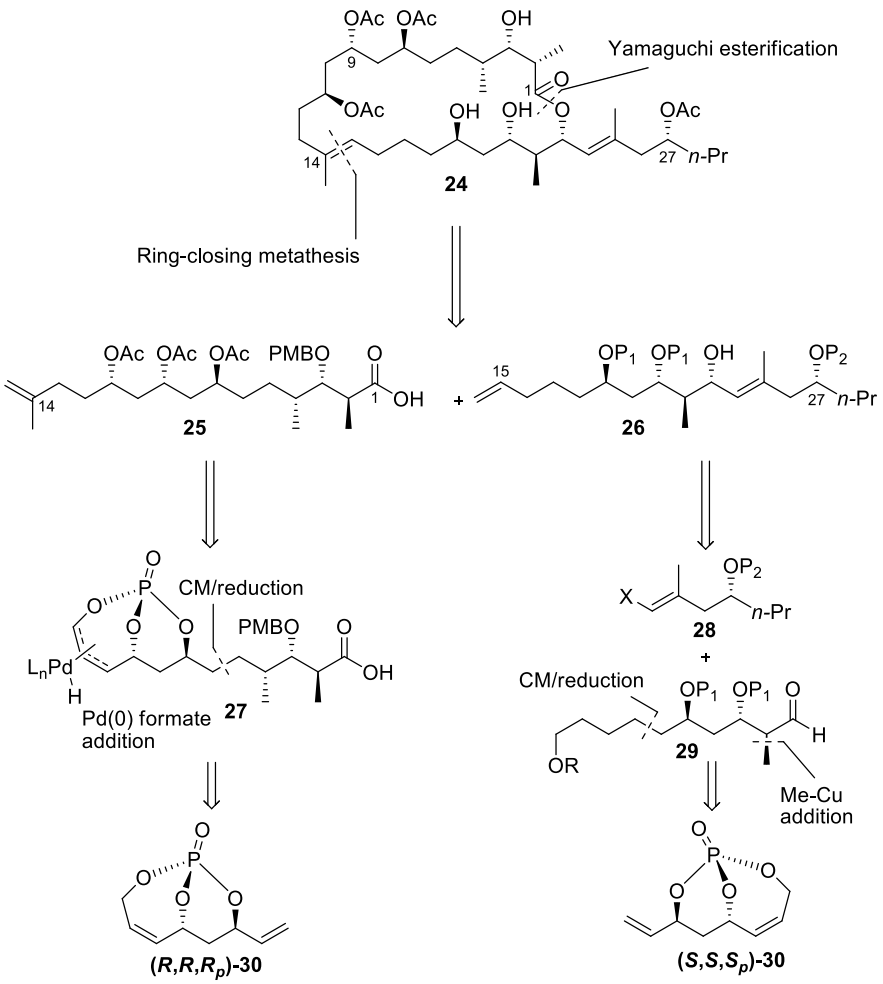


Scheme 5: Coupling of the two fragments to form dolabelide D

The synthesis of dolabelide D was achieved by Leighton group in seventeen steps and 1.4% yield for the longest linear sequence.

1.2.2 - Hanson's synthesis of dolabelide C6

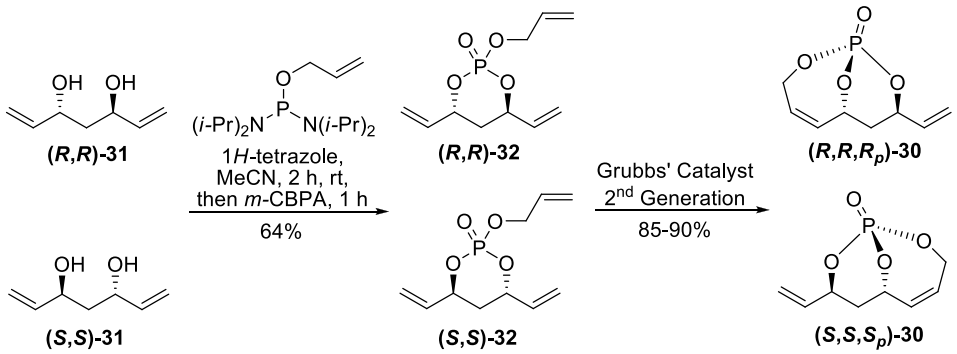
The Hanson synthesis of dolabelide C is based, as the Leighton synthesis, on the coupling of two fragments with an esterification reaction and cyclisation using a ring-closing metathesis reaction. The synthesis of the two separated fragments is based on the use of a phosphate-tether mediated approach (Scheme 6).



Scheme 6: Hanson's Retrosynthesis of dolabelide C

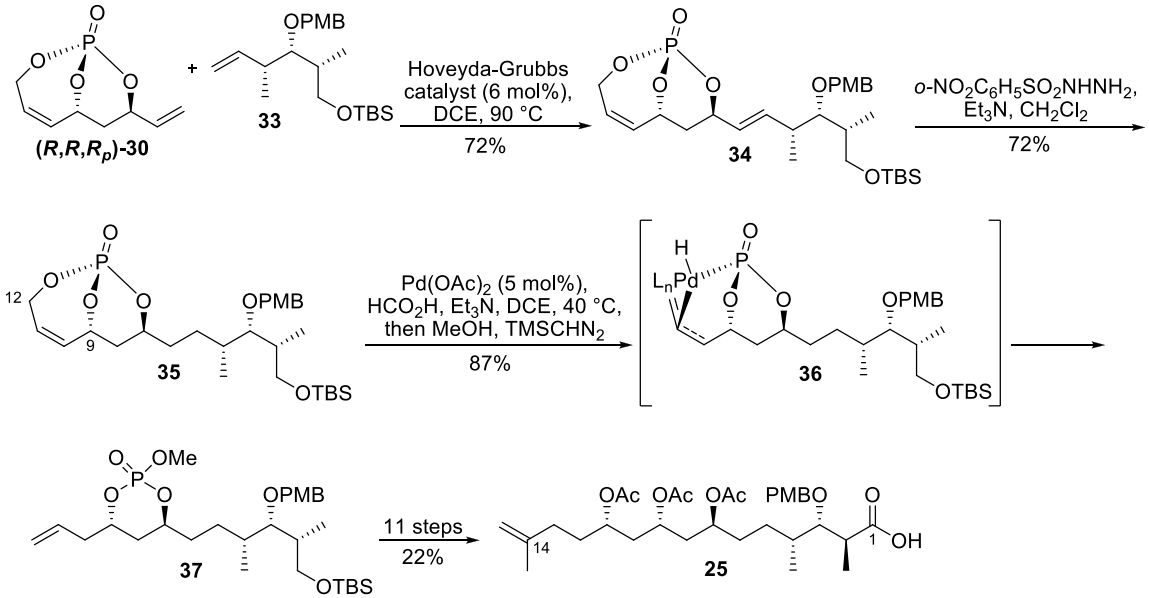
The enantiomeric phosphate triester building blocks **(*R*,*R*,*R*$_P$)-30** and **(*S*,*S*,*S*$_P$)-30** (Scheme 7) were assembled *via* a phosphate tether/RCM desymmetrisation approach.[10] The phosphate tether was obtained through a one-step coupling/oxidation sequence from commercially available allyl tetraisopropylphosphorodiamidite and *anti*-diol **31** to yield the pseudo-C_2-symmetric triene **32**. Desymmetrisation by ring-closing metathesis (RCM) using second-generation Grubbs' catalyst afforded *P*-chiral bicyclo[4.3.1]phosphate **30** and is based on the premise that only the terminal olefin *cis* to the phosphate-tethered olefin reacts to generate **30** possessing two sterically differentiated olefins.

[10] (a) Burke, S. D.; Muller, N.; Beaudry, C. M. *Org. Lett.* **1999**, *1*, 1827. (b) Burke, S. D.; Voight, E. A. *Org. Lett.* **2001**, *3*, 237. (c) Lambert, W. T.; Burke, S. D. *Org. Lett.* **2003**, *5*, 515. For desymmetrization of a C_2-symmetric diol using the Prins cyclisation, see: (d) Rychnovsky, S. D.; Yang, G.; Hu, Y.; Khire, U. R. *J. Org. Chem.* **1997**, *62*, 3022.



Scheme 7: Synthesis of the phosphate triester building blocks **30**

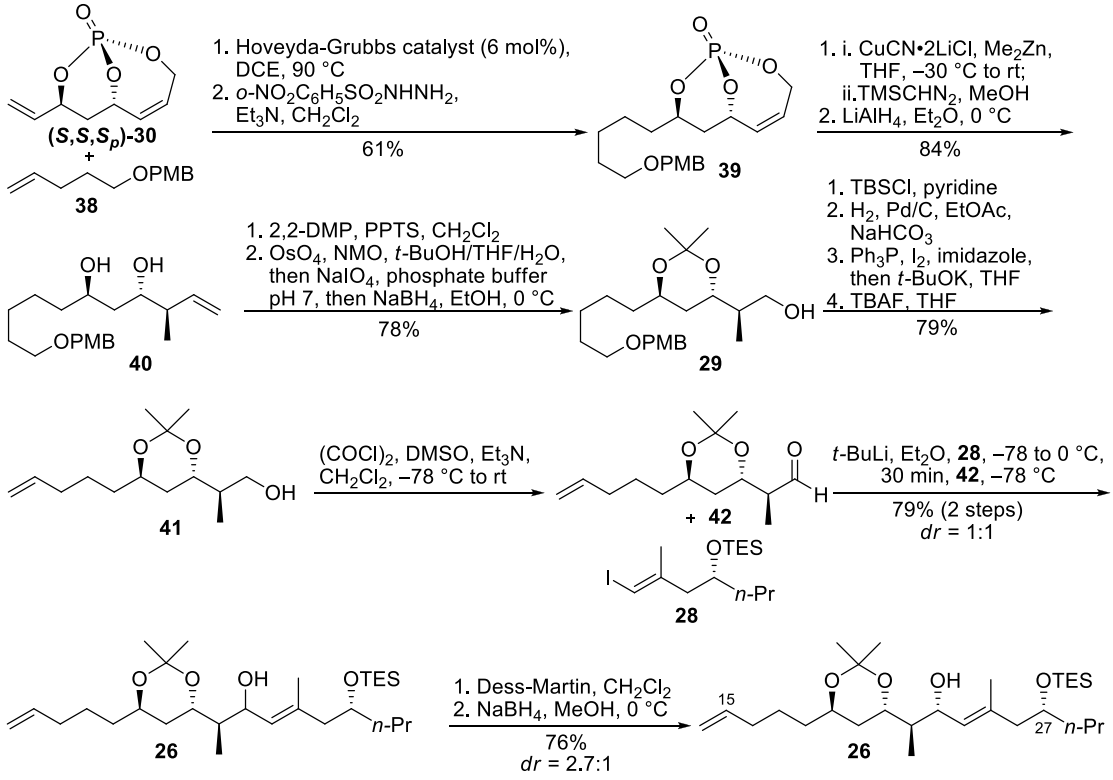
The synthesis of the C1-14 fragment (Scheme 8) commenced by the coupling of **(*R*,*R*,*R*$_P$)-30** with compound **33** using cross-metathesis, followed by regioselective hydrogenation of the formed double bond using diimide reduction (generated *in situ* from *o*-nitrobenzenesulfonyl hydrazine), which gave compound **35** in 52% yield for the two steps. Compound **37** is obtained through Pd-catalysed formate reduction, followed by methylation of the phosphate intermediate, which gave the desired product in 87% yield. The regioselectivity of this step is due to the orthogonal orbital alignment within **35**, which allows for selective Pd(0)-catalyzed ionisation of C12 over the C9 allylic phosphate position. This ionisation allows Pd to deliver the hydride selectively at the internal C10 position to provide the desired terminal olefin. Additional steps allowed the synthesis of C1-14 in sixteen steps from diol **31** in 5.7% yield.



Scheme 8: Synthesis of the C1-14 fragment

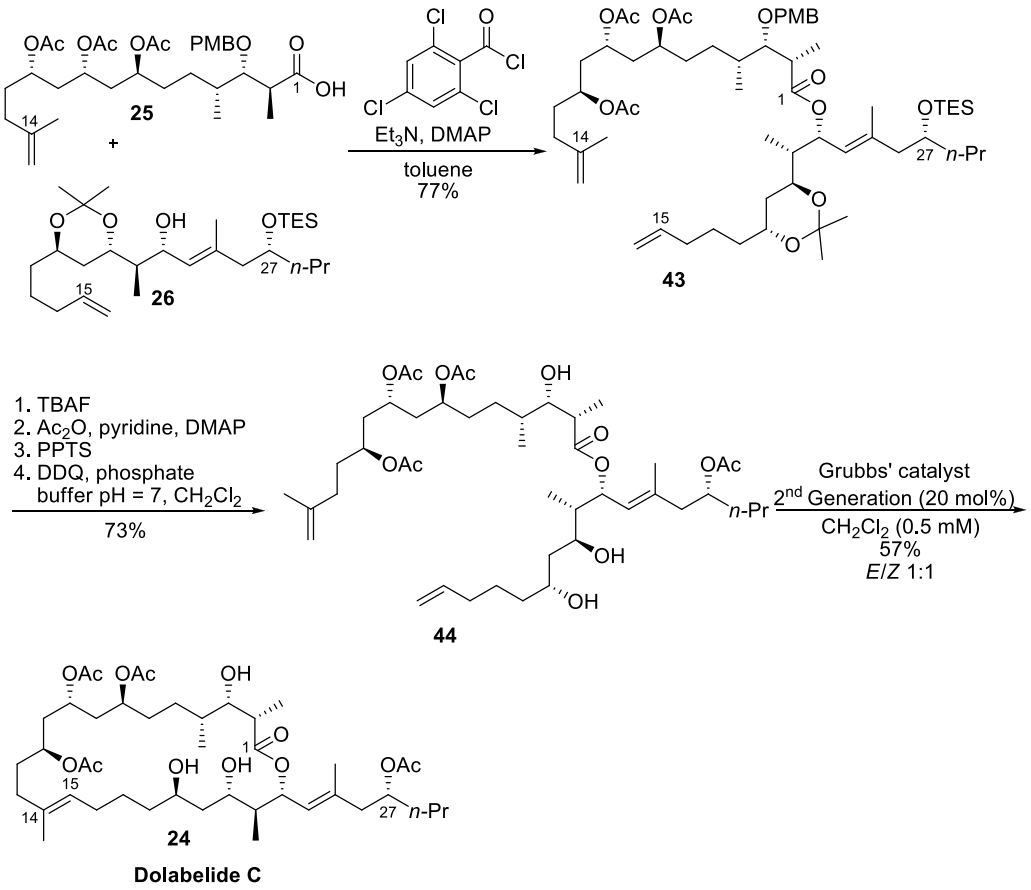
The synthesis of the C15-30 fragment (Scheme 9) commenced by the coupling of **(*S*,*S*,*S*$_P$)-30** with olefin **38** using cross metathesis, followed by regioselective hydrogenation of the formed double bond using diimide reduction (generated *in situ* from *o*-nitrobenzenesulfonyl hydrazine), which gave compound **39** in 61% yield for the two steps. Regio- and diastereoselective methyl cuprate addition to **39** and subsequent phosphate cleavage produced diol **40** in 84% yield. Protection of the 1,3-*anti*-diol as an acetonide, followed by conversion of the alkene into the primary alcohol, gave the alcohol **29** in 78% yield. Compound **41** was obtained in 79% yield through the following sequence of reactions: protection reaction of the alcohol as a *t*-butyldimethylsilyl ether, cleavage of the *p*-methoxybenzyl ether,

conversion of the alcohol into a terminal olefin through an iodination/elimination sequence and removal of the *t*-butyldimethylsilyl ether group. Swern oxidation, followed by addition of the lithiated C24-30 fragment to the formed aldehyde, gave the alcohol **26** in 79% yield with a diastereomeric ratio of 1:1. Separation of the two isomers with column chromatography, followed by recycling (oxidation/reduction) of the undesired diastereomer, gave the C15-30 fragment in 76% yield and with a diastereomeric ratio of 2.7:1. The synthesis of the C15-30 fragment was achieved in thirteen steps and in 14% yield.



Scheme 9: Synthesis of the C15-30 fragment

The synthesised fragments were coupled using Yamaguchi esterification to give the ester **43** in 77% yield (Scheme 10). The RCM precursor was obtained in 73% yield through the following sequence of reactions: cleavage of the triethylsilyl ether, acetylation of the alcohol, removal of the acetonide group and removal of the *p*-methoxybenzyl ether. Cyclisation of compound **44** using a ring-closing metathesis reaction occurred with low selectivity (*E*/*Z* ratio of 1:1) and gave dolabelide C in a 57% isolated yield.



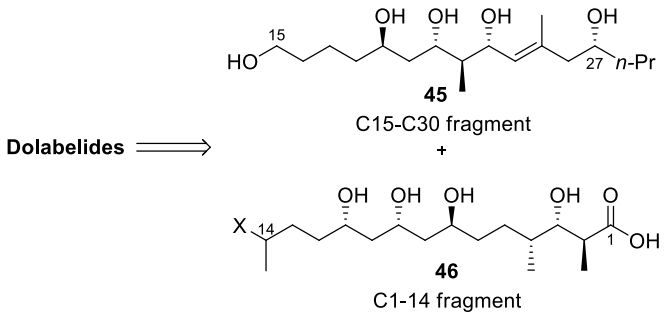
Scheme 10: Coupling of the two fragments to form dolabelide C

The synthesis of dolabelide C was achieved in twenty four steps and 1.2% yield from diol **31**.

1.2.3 - Genêt and Phansavath's synthesis of the C1-13 subunit of dolabelides7 and synthesis of the C15-30 subunit of dolabelide A8

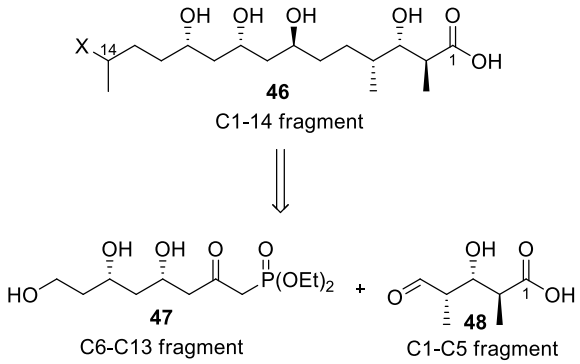
Genêt, Phansavath and co-workers developed methodology for the asymmetric reduction of ß-ketoesters and ß-hydroxyketones. They decided to make use of this methodology for the synthesis of the dolabelides.

Their retrosynthesis (Scheme 11) is based on the disconnection of dolabelides into two fragments. The envisaged disconnections are the C14-C15 bond, which is a trisubstituted alkene and the C1-C21 (or C1-23 bond), which corresponds to the macrolactone bond. They envisaged that the construction of the C14-15 bond could be achieved by either a ‘one-pot’ Julia olefination between an aldehyde at C15 and a sulfonyl benzothiazole at C14 or a Horner-Wadsworth-Emmons reaction between an aldehyde at C15 and a phosphonate at C14.



Scheme 11: Genêt's retrosynthesis of dolabelides

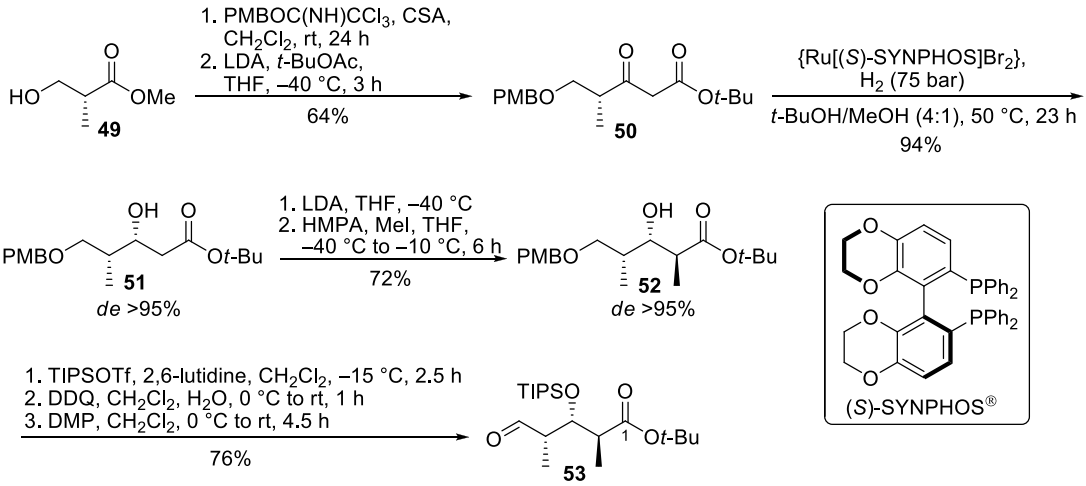
The retrosynthesis of the the C1-14 fragment is shown in the following scheme (Scheme 12):



Scheme 12: Retrosynthesis of the C1-14 fragment

It is based on the coupling of two fragments by a Horner-Wadsworth-Emmons reaction. A homologation reaction at the C13 carbon would then deliver either the sulfonyl benzothiazole or the phosphonate at C14.

The synthesis of the C1-5 fragment is shown in the following scheme (Scheme 13):

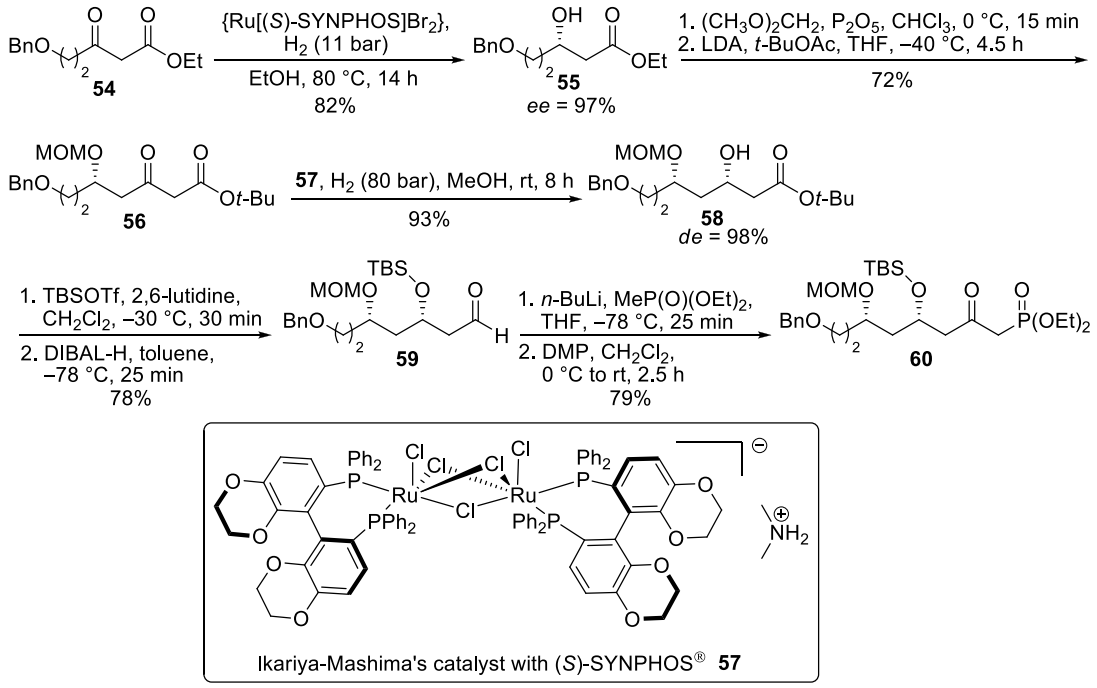


Scheme 13: Synthesis of the C1-5 fragment

From the commercially available Roche ester, protection of the alcohol as a PMB ether, followed by side-chain extension with lithio *tert*-butyl acetate, afforded the asymmetric hydrogenation precursor **50**. Asymmetric hydrogenation of **50** was performed using the chiral ruthenium complex {Ru[(S)-SYNPHOS]Br_2} and proceeded in 94% yield and with an excellent diastereoselectivity. A Frater diastereoselective methylation led then to the methylated product **52** in 72% yield

and with a diastereomeric excess superior to 95%. Finally, the completion of the C1-5 fragment was done in 76% yield using the following sequence: protection of the alcohol as a TIPS ether, PMB ether removal using DDQ and Dess-Martin oxidation. The C1-5 fragment **53** was thus synthesised in seven steps from Roche ester in 33% overall yield with excellent diasteroselectivity in the construction of the C2 and C3 stereocentres.

The synthesis of the ß-keto phosphonate partner (fragment C6-13) for the HWE reaction is detailed in the following scheme (Scheme 14):



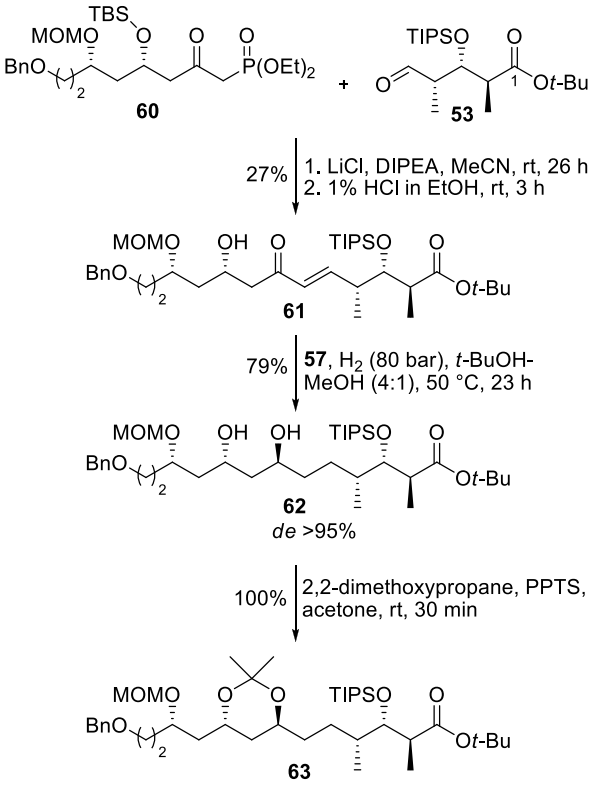
Scheme 14: Synthesis of the C6-13 fragment

The synthesis started with the ß-keto ester **54**, which can be easily synthesis in three steps from propan-1,3-diol.[11] Asymmetric hydrogenation of **54** with the chiral ruthenium complex {Ru[(*S*)-SYNPHOS]Br_2} proceeded in 82% yield with an excellent enantiomeric excess of 97%. Protection of the alcohol as a MOM ether, followed by side-chain extension with lithio *tert*-butyl acetate, gave the ß-keto ester **56** in 72% yield. The second stereocenter was then introduced with another asymmetric hydrogenation reaction. The catalyst used was the Ikariya-Mashima's catalyst[12] with their (*S*)-SYNPHOS ligand in order to avoid the deprotection of the secondary alcohol. This hydrogenation reaction proceeded smoothly in 93% yield and with an enantiomeric excess of 98%. The completion of the C6-13 fragment was achieved in four steps and 62% yield using the following sequence of steps: protection of the secondary alcohol as a TBS ether, ester to aldehyde reduction using DIBAL-H, addition of lithio diethyl methyl phosphonate and oxidation of the resulting ß-hydroxy phosphonate. The synthesis of C6-13 fragment was thus achieved in eight steps and 34% overall yield from ß-keto ester **54**.

[11] Paterson, I.; Smith, J. D.; Ward, R. A. *Tetrahedron* **1995**, *51*, 9413. Claffey, M. M.; Hayes, C. J.; Heathcock, C. H. *J. Org. Chem.* **1999**, *64*, 8267.

[12] Ikariya, T.; Ishii, Y.; Kawano, H.; Arai, T.; Saburi, M.; Yoshikawa, S.; Akutagawa, S. *J. Chem. Soc., Chem. Commun.* **1985**, 922. Ohta, T.; Tonomura, Y.; Nozaki, K.; Takaya, H.; Mashima, K. *Organometallics* **1996**, *15*, 1521. Mashima, K.; Nakamura, T.; Matsuo, Y.; Tani, K. J. *Organomet. Chem.* **2000**, *607*, 51.

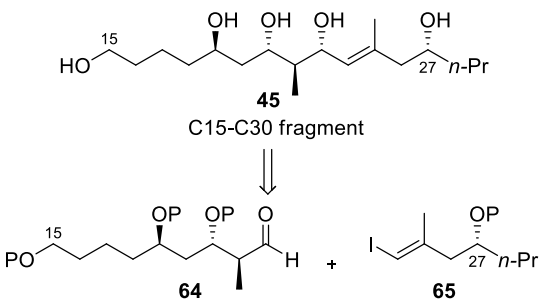
With the two fragments in hand, the HWE reaction and the completion of the C1-13 fragment were carried out (Scheme 15). The HWE reaction was performed using Masamune-Roush conditions, which are suitable in the presence of base-sensitive aldehydes like aldehyde **53**, and afforded stereoselectively the *E*-enone in 38% yield. After selective deprotection of the TBS ether, the asymmetric hydrogenation of the ß-hydroxy enone was performed in order to install the stereogenic center at C7 and to reduce the alkene. This reaction proceeded in 79% yield and with a diastereoselective excess superior to 95%. Finally, conversion of the diol into an acetonide afforded, in quantitative yield, the C1-13 fragment of dolabelides.



Scheme 15: Completion of the synthesis of the C1-13 fragment

This synthesis, achieved in fifteen steps and with an overall yield of 7%, makes use of the catalytic asymmetric hydrogenation reaction of ß-keto esters and a ß-hydroxy ketone, developed in the Genêt group, in order to install the hydroxyl groups at C3, C7, C9 and C11 stereocenters in an iterative manner.

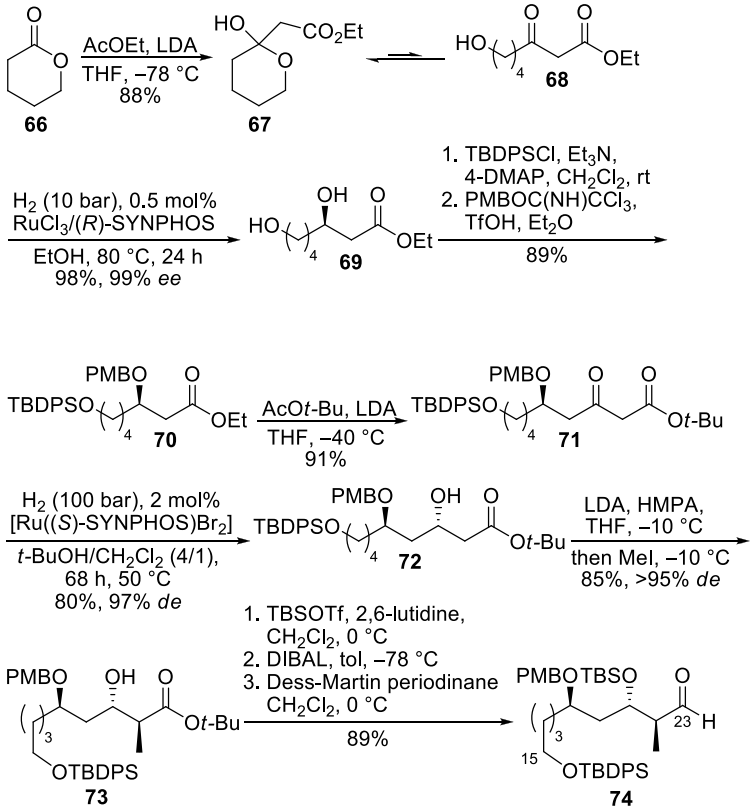
The retrosynthesis of the C15-30 fragment (Scheme 16) is based on the coupling of a vinyl iodide fragment with an aldehyde.



Scheme 16: Retrosynthesis of the C15-30 fragment

The key steps in the Genêt and Phansavath synthesis of the C15-30 subunit of dolabelide A are ruthenium SYNPHOS-catalysed asymmetric hydrogenation reactions to install the stereochemistry on the C19, C21 and C27 carbon atoms and a zirconium-promoted carboalumination reaction to form the C24-25 trisubstituted olefin.

The synthesis of the C15-23 fragment (Scheme 17) commenced with the addition of the enolate of ethyl acetate to the lactone **66**, which resulted in the formation of the cyclic hemiketal **67** in 88% yield. This compound is in equilibrium with the ß-keto ester **68**, which is suitable for ruthenium-mediated asymmetric hydrogenation of the ketone function. Reduction afforded the ß-hydroxy ester **69** in 98% yield and with an enantiomeric excess of 99%. Protection of the primary alcohol as a *t*-butyldiphenylsilyl ether, followed by protection of the remaining alcohol as a *p*-methoxybenzyl ether, gave the compound **70** in 89% yield. A chain extension with the enolate of *tert*-butyl acetate delivered the ß-keto ester **71** in 91% yield, which was then hydrogenated in an asymmetric fashion using ruthenium-SYNPHOS catalyst and gave compound **72** in 80% yield and with a diastereomeric excess of 97%. A diastereoselective Frater methylation using lithium diisopropylamide afforded compound **73** in 85% yield and with a diastereomeric excess over 95%. The fragment C15-23 was then obtained in 89% yield through the following sequence: protection of the remaining alcohol as a *t*-butyldimethylsilyl ether, reduction of the ester to the alcohol and oxidation of the alcohol to the corresponding aldehyde.

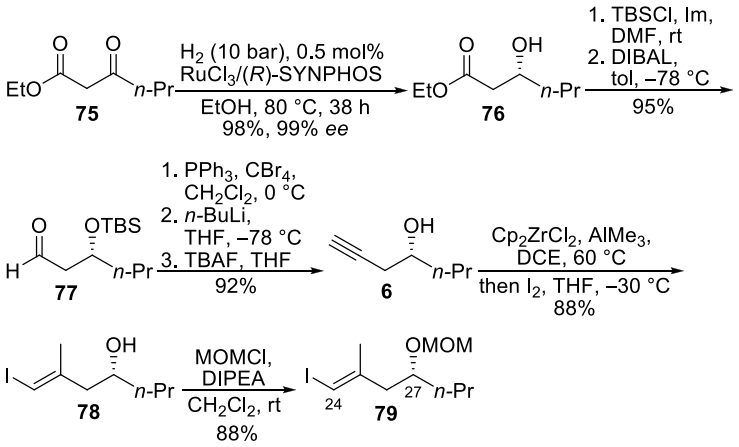


Scheme 17: Synthesis of the C15-23 fragment

The first fragment was obtained in ten steps with a yield of 42%.

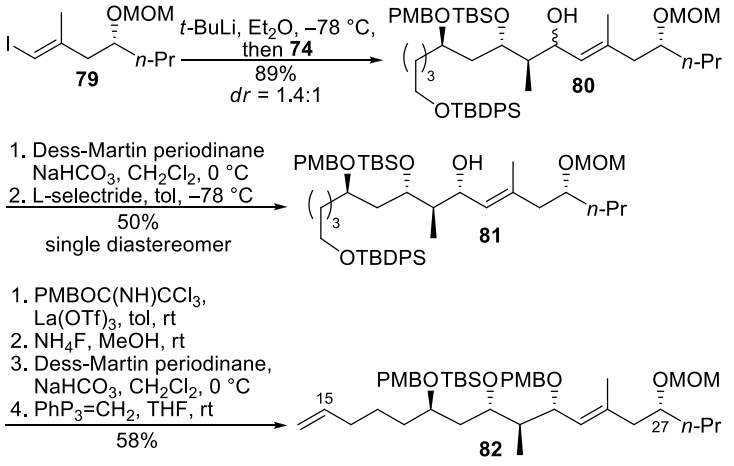
The synthesis of the C24-30 fragment (Scheme 18) started with the asymmetric hydrogenation of the commercially available ethyl 3-oxohexanoate **75** using the

same conditions as the hydrogenation of **68** and afforded the ß-hydroxy ester **76** in 98% yield and with an enantiomeric excess of 99%. Protection of the alcohol as a *t*-butyldimethylsilyl ether, followed by reduction of the ester to the aldehyde, gave compound **77** in 95% yield. Alkyne **6** was obtained in 92% yield *via* Corey-Fuchs reaction, followed by deprotection of the *t*-butyldimethylsilyl ether. The trisubstituted alkene **78** was obtained in 88% yield through a zirconium-promoted carboalumination reaction, followed by quenching with iodine. Subsequent protection of the alcohol as the methoxymethyl ether gave the C24-30 fragment in 88% yield. The synthesis of the C24-30 fragment was achieved in eight steps and in 66% yield.



Scheme 18: Synthesis of the C24-30 fragment

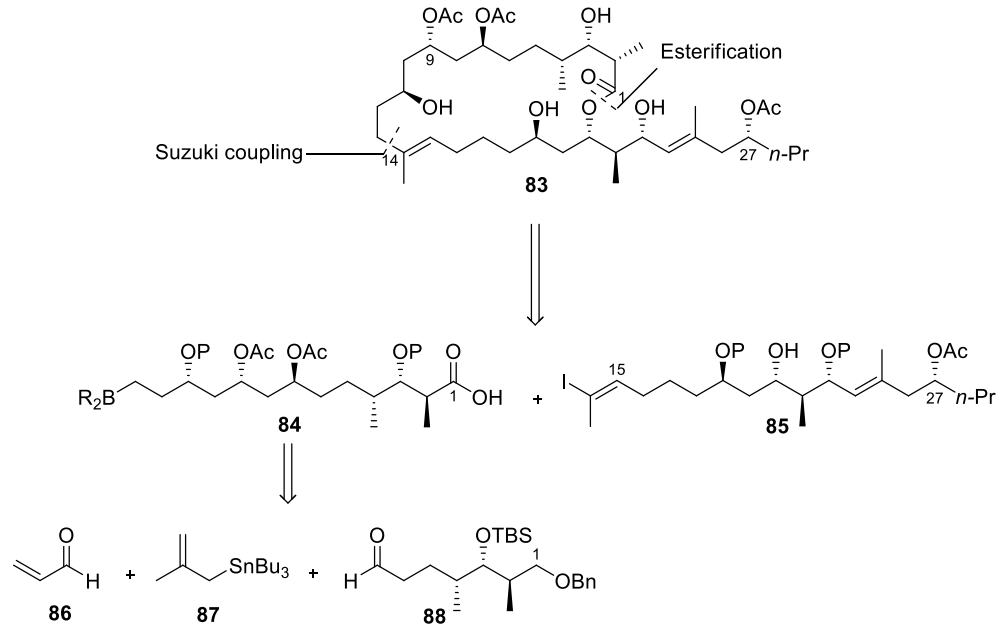
The C24-30 fragment was then converted into the corresponding organolithium reagent and coupled with the C15-23 fragment to give alcohol **80** in 89% yield with a diastereomeric ratio of 1.4:1 (Scheme 19). Subsequent oxidation/reduction reaction sequence gave the alcohol **81** as a single diastereomer in 50% yield (Scheme 19). The C15-30 fragment (Scheme 19) was then obtained in 58% yield through the following sequence of reactions: protection of the alcohol as a *p*-methoxybenzyl ether, removal of the *t*-butyldiphenylsilyl ether, oxidation of the alcohol to the corresponding ketone and Wittig olefination. The synthesis of the C15-30 subunit of dolabelide A was achieved by Genêt, Phansavath and co-workers in seventeen steps for the longest linear sequence and with an overall yield of 11%.



Scheme 19: Synthesis of the C15-30 fragment

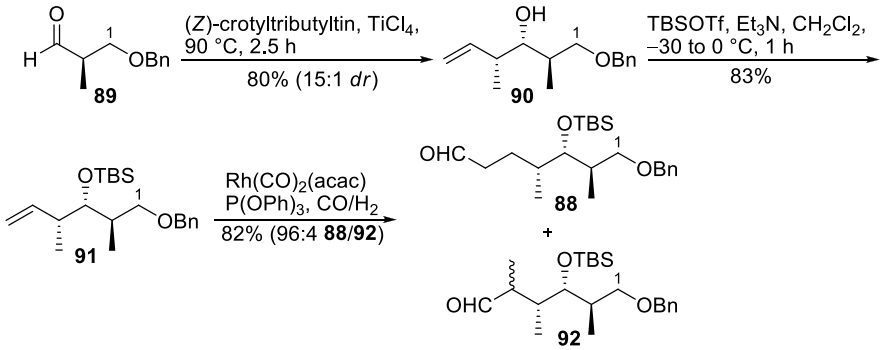
1.2.4 - Keck's synthesis of the C1-13 subunit of dolabelide B9

The retrosynthesis envisaged by Keck, shown in the following scheme (Scheme 20), is based on the disconnections at the macrolactone bond and at the C13-14 bond, which could then be connected *via* a Suzuki coupling. They then suggested that the C1-13 fragment could be constructed from aldehyde **88** and acrolein through a sequence of asymmetric allylation using a 2-substituted allylstannane reagent, aldol reaction with 1,5-induction, and 1,3-reduction.



Scheme 20: Keck's retrosynthesis of the C1-13 subunit of dolabelide B

The synthesis of the C1-7 fragment is shown in the following scheme (Scheme 21):

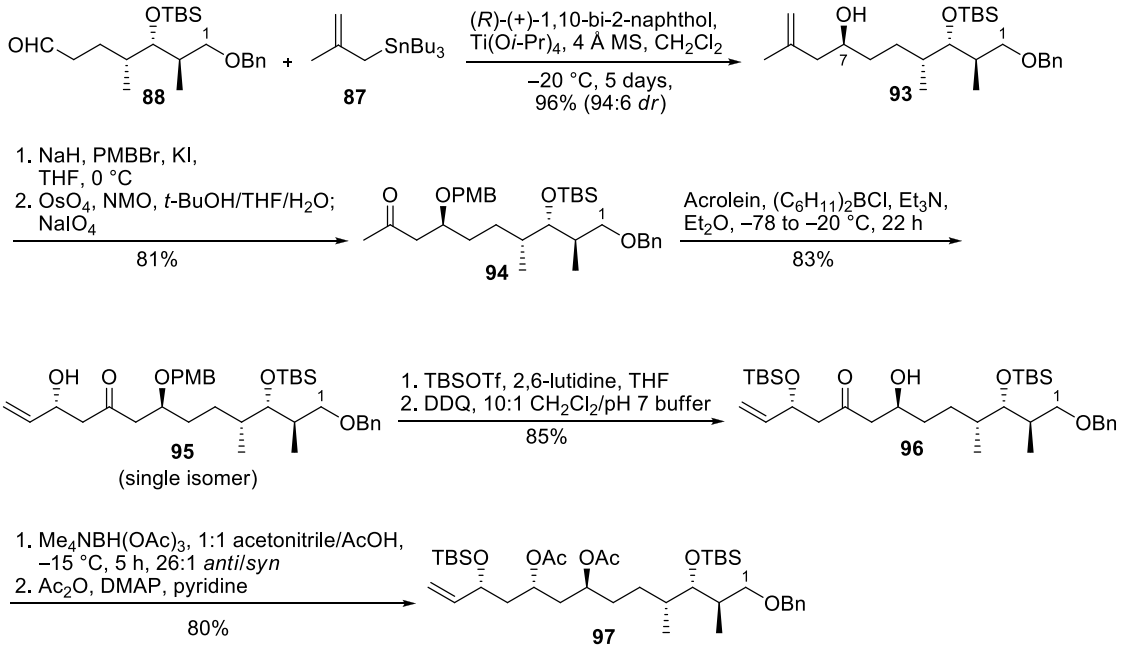


Scheme 21: Synthesis of the C1-7 fragment

This synthesis starts with a diastereoselective addition of a crotylstannane to aldehyde **89** in presence of titanium tetrachloride. This methodology, developed by Keck and co-workers, allows the installation of the stereochemistry on carbons C3 and C4. The desired isomer was formed in 80% yield and with 15:1 diastereomeric ratio. After protection of the alcohol as a silyl ether, the aldehyde was formed *via* an hydroformylation catalysed by rhodium. This method led almost exclusively to the desired aldehyde over the branched one due to the steric hindrance around the methyl substituent at C4. The aldehyde was then obtained in 82% yield and with a 96/4 ratio of isomers. This fragment is then obtained in three steps with a 54% yield.

For the completion of the synthesis (Scheme 22), Keck and co-workers decided to set the stereochemistry of the carbon atom at C7 using a chiral catalyst and to then use this new stereocenter to help install the stereochemistry at the carbon atoms C9 and C11.

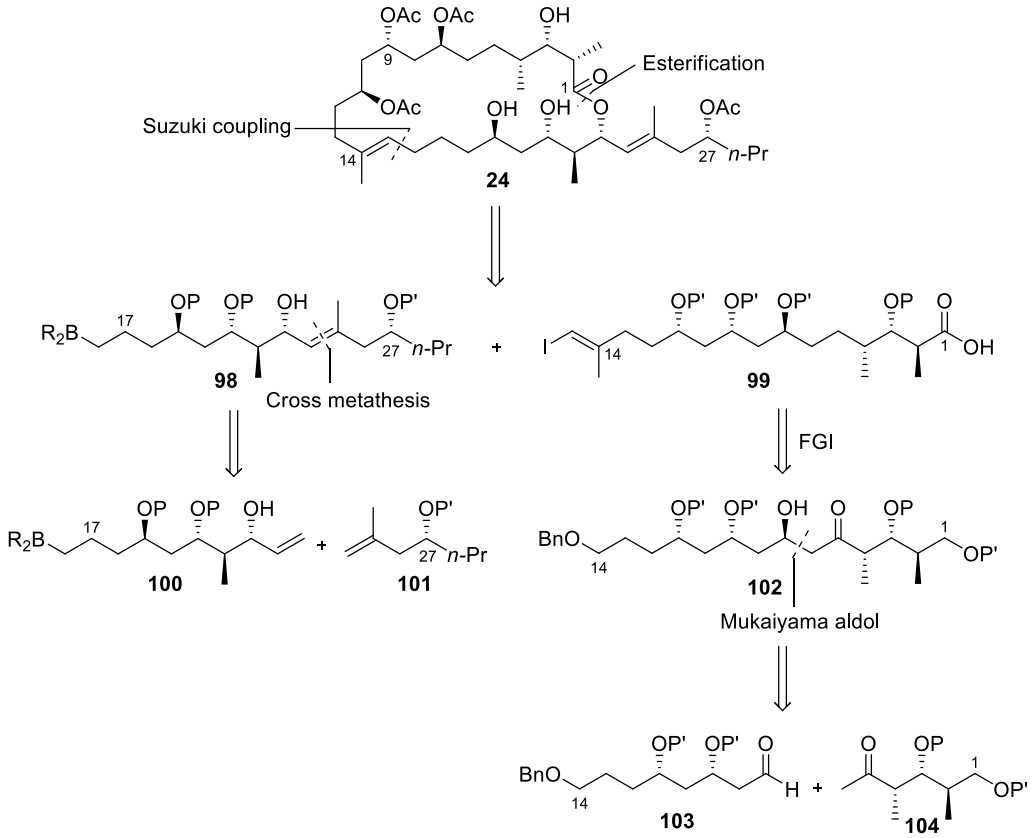
The stereochemistry at C7 was then introduced through a BITIP-catalysed methallylation, which gave the alcohol **93** in 96% yield and with a 94:6 diastereoselectivity. After protection of the alcohol as a PMB ether, followed by oxidative cleavage, the formed ketone was then reacted with acrolein *via* an aldol condensation using conditions developed by Paterson and co-workers. This reaction gave the 1,5-*anti*-diol **95** as a single isomer in 83% yield. After protection of the formed alcohol as a TBS ether, followed by removal of the PMB ether using DDQ, the ketone was reduced in a diastereoselective manner using tetramethylammonium triacetoxyborohydride. Subsequent protection of the 1,3 *anti* diol as an acetate led to the C1-13 fragment in eleven steps and 24% yield.



Scheme 22: Completion of the synthesis of the C1-13 fragment

1.3 - Previous work in the Prunet Group

The retrosynthesis of dolabelide C envisaged in the Prunet group is shown in the following scheme (Scheme 23):



Scheme 23: Retrosynthesis of dolabelide C

Disconnections at the macrolactone bond and at the C15-16 bond led to the fragments C1-15 and C16-30. The key steps for the syntheses of these two fragments are a Mukaiyama aldol and a cross metathesis.

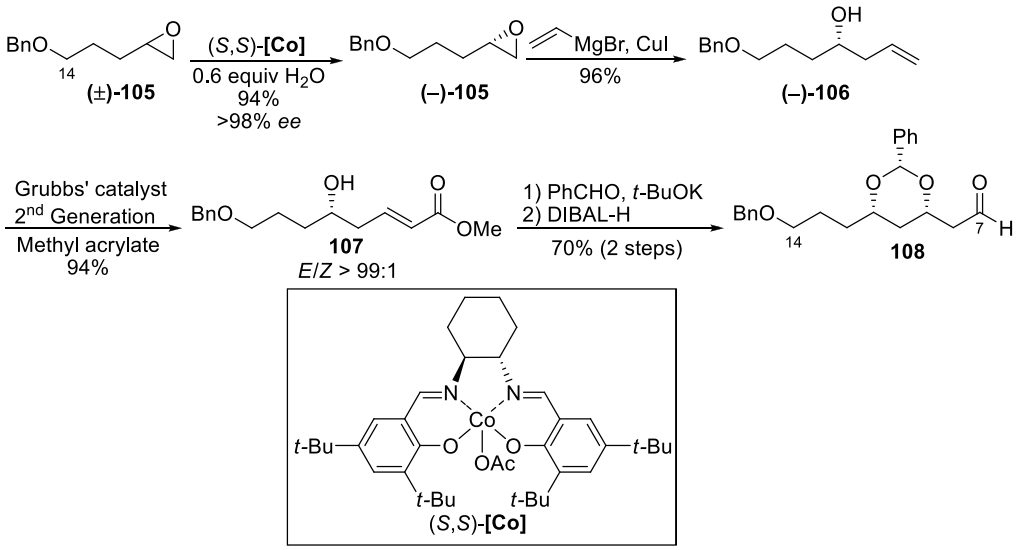
1.3.1 – Work on the C1-15 fragment

The C1-15 fragment was previously synthesised in the Prunet group by Aurélie Vincent in 17 steps and 11.4% yield.[13]
The key steps are:

- A Jacobsen kinetic resolution[14] to install the first stereocentre at C11
- A diastereoselective oxa-Michael addition[15] to install the C9 stereocentre *via* a benzylidene acetal
- A Mukaiyama aldol

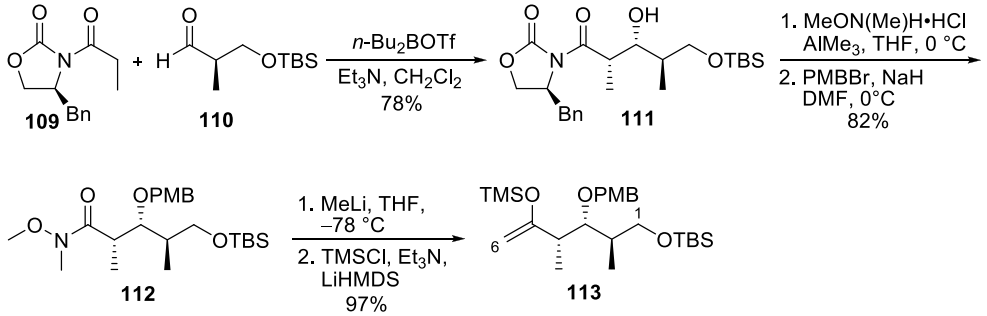
[13] Vincent, A.; Prunet, J. *Synlett* **2006**, 2269.
[14] (a) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307. (b) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (c) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (d) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421.
[15] Evans, D.A.; Gauchet-Prunet, J. A. *J. Org. Chem.* **1993**, *58*, 2446.

The syntheses of the two aldol partners are shown in schemes 24 and 25.
The synthesis of aldehyde **108** commenced by the Jacobsen kinetic resolution of racemic epoxide **(±)-105** and delivered enantiopure epoxide **(−)-105** in 94% yield and excellent enantioselectivity. Opening of the epoxide by a vinyl cuprate, followed by cross metathesis with methyl acrylate gave alcohol **107** in 90% yield over two steps. Finally, a diastereoselective oxa-Michael reaction, followed by reduction with DIBAL-H afforded aldehyde **108** in two steps and 70% yield.



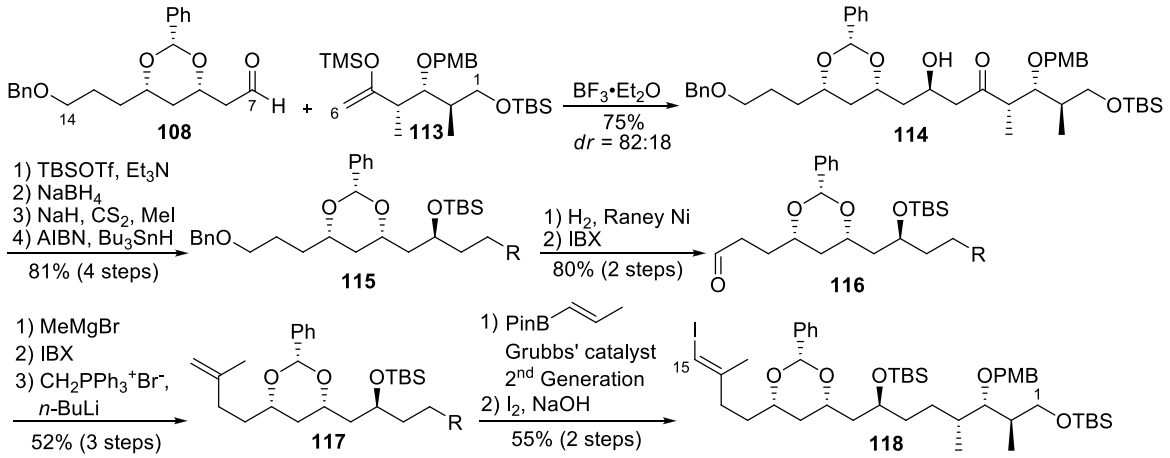
Scheme 24: Synthesis of aldehyde **108**

The synthesis of TMS-enol ether **113** started with an Evans aldol reaction between aldehyde **110**, obtained from Roche ester, and oxazolidinone **109**. Oxazolidinone **111** was obtained in 78% yield. Weinreb amide formation with *N*,*O*-dimethylhydroxylamine hydrochloride and trimethylaluminum, followed by protection of the secondary alcohol as a PMB ether gave Weinreb amide **112** in 82% yield. The synthesis was then completed by treatment with methyllithium to form the methyl ketone, followed by enol ether formation with trimethylsilylchloride, triethylamine and LiHMDS.



Scheme 25: Synthesis of enolate **113**

The completion of the synthesis of the C1-15 fragment is shown in the following scheme (Scheme 26):



Scheme 26: Synthesis of the C1-15 fragment

Mukaiyama aldol between aldehyde **108** and silyl enol ether **113** delivered the desired hydroxyketone in 93% yield as a 82:18 mixture of diastereomers, from which the major diastereomer was isolated in 75% yield. After protection of the secondary alcohol of **114** as a TBS ether, the ketone was removed using the following sequence of steps: reduction with sodium borohydride, conversion of the resulting alcohol into the corresponding xanthate and Barton-McCombie deoxygenation with AIBN and tributyltin hydride. Benzyl group removal by hydrogenation with Raney-Nickel catalyst, followed by IBX oxidation gave aldehyde **116** in 80% yield. The 1,1-disubstituted alkene moiety was then installed using the following sequence of steps: methylmagnesium bromide addition, IBX oxidation of the secondary alcohol to the ketone and Wittig olefination with methyltriphenylphosphonium bromide. Finally, cross metathesis with the required boronate, followed by boron-iodine exchange furnished the C1-15 fragment of dolabelide C in 55% yield after separation from the minor *Z* isomer.

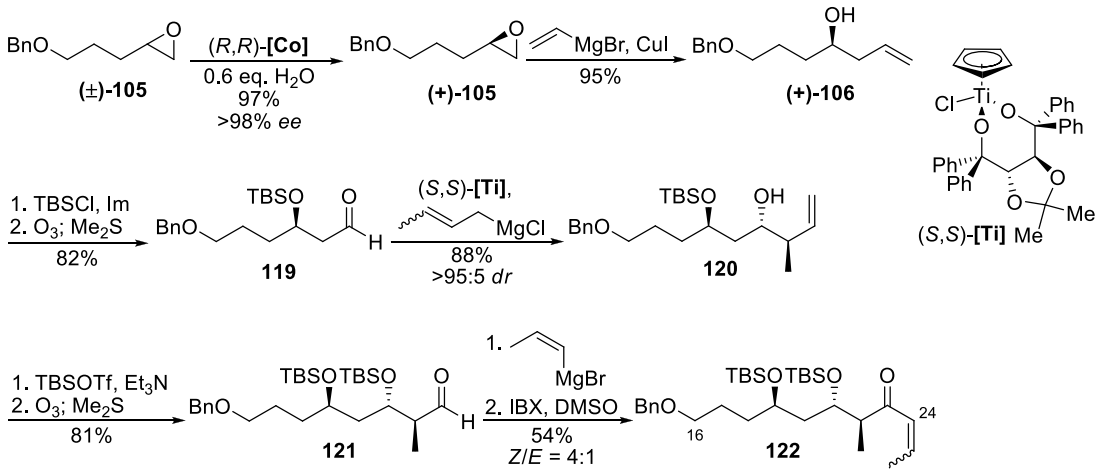
1.3.2 – Work on the C16-30 fragment

The C16-30 subunit of dolabelide C was previously synthesised in the Prunet group using cross-metathesis as the key step for the formation the trisubstituted alkene at the C24-25 position.[16] After examination of cross-metathesis reactions between allylic alcohol derivatives and enone derivatives, the propenyl ketone was found to be the more suitable functional group for the cross-metathesis reaction.

The synthesis of a C16-24 fragment (Scheme 27) containing a propenyl ketone was then performed. Jacobsen hydrolytic kinetic resolution of epoxide **(±)-105** using Jacobsen's salen (Co) catalyst ((*R*,*R*)-**[Co]**), followed by epoxide opening with a vinyl Grignard reagent gave the alcohol **(+)-105** in 92% yield for two steps and with an enantiomeric excess superior to 98%. A protection reaction of the alcohol as a *t*-butyldimethylsilyl ether, followed by reductive ozonolysis reaction gave the aldehyde **119** in 82% yield. The stereochemistry present on the C21 and C22 carbon atoms was installed *via* a Duthaler crotylation[17] using the complex (*S*,*S*)-**[Ti]** and the alcohol **120** was produced in 88% yield and a diastereomeric ratio superior to 95:5. The same sequence of deprotection and reductive ozonolysis as used previously gave the corresponding aldehyde **121** in 81% yield. Final Grignard

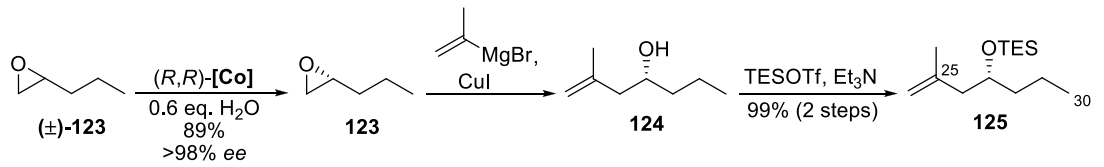
[16] Braun, M.-G.; Vincent, A.; Boumediene, M.; Prunet, J. *J. Org. Chem.* **2011**, *76*, 4921.
[17] Hafner, A.; Duthaler, R. O.; Marti, R.; Rhis, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321.

addition, followed by an oxidation reaction, delivered the CM precursor **122** in 54% yield and an *E*/*Z* ratio of 1:4. The C16-24 fragment was obtained in nine steps in 29% yield.



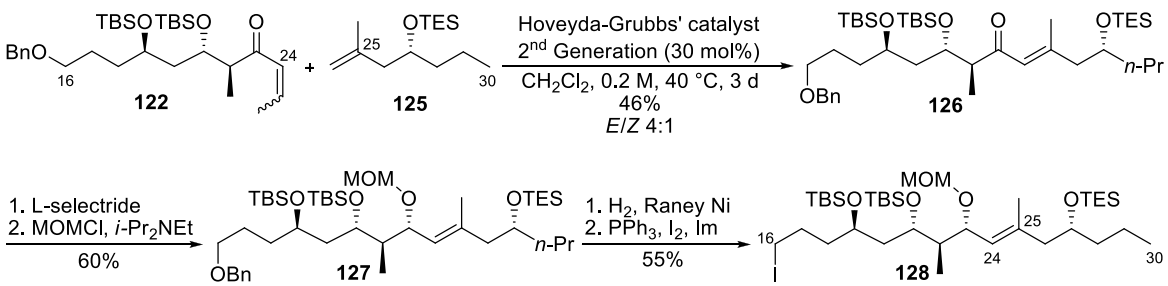
Scheme 27: Synthesis of the C16-24 fragment

Jacobsen hydrolytic kinetic resolution of epoxide **(±)-123**, followed by epoxide opening with a Grignard reagent and protection of the formed alcohol as a triethylsilyl ether gave the second fragment in three steps in 88% yield and with an enantiomeric excess of 98% (Scheme 28).



Scheme 28: Synthesis of the C25-30 fragment

Coupling of the two fragments through a cross-metathesis reaction using second-generation Hoveyda-Grubbs' catalyst afforded the trisubstituted olefin **126** as a 4:1 mixture of *E*/*Z* isomers, from which the major isomer was isolated in 46% yield (Scheme 29). The C16-30 subunit of dolabelide C (Scheme 29) was then obtained in 33% yield *via* the following reaction sequence: diastereoselective reduction using L-selectride, protection of the formed alcohol as a methoxymethyl ether, removal of the benzyl ether and conversion of the alcohol to the iodide using the Garregg reaction.



Scheme 29: Synthesis of the C16-30 subunit of dolabelide C

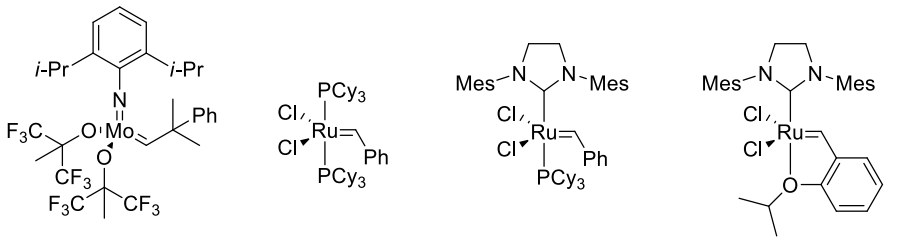
The synthesis of the C16-30 subunit of dolabelide C was achieved in fourteen steps with a yield of 4.4%.

1.4 - Previous work on the use of silicon tether in RCM

The advantages of intramolecular transformations as opposed to intermolecular transformations are well known. The use of a temporary tether was thus developed in order to transform an intermolecular reaction into an intramolecular reaction and use the advantages of the intramolecular transformations. Tethering two partners decrease the entropic demand of the reaction, which results in a more facile reaction and allows the use of milder reaction conditions.[18]

Optimal tethers must be easily introduced and removed and should display a good stability toward the reaction conditions. Commonly used elements for tethers are silicon, phosphorus, sulfur, boron, zinc, aluminum and magnesium. The silicon tether is one of the most commonly used due to its easy access, its stability and its ease of removal. Additionally, silyl groups readily undergo refunctionalisation to give a series of synthetically useful intermediates through protodesilylation, oxidation, silane-group transfer, or transmetallation.[18]

Since its development and through the discovery of new catalysts, olefin metathesis has become a powerful tool in organic synthesis. Metathesis catalysts exhibit high activity, high thermal stability and excellent functional-group compatibility. Commonly used catalysts are shown in the following figure (Figure 4):



129 Schrock's catalyst

130 Grubbs' I catalyst

131 Grubbs' II catalyst

132 Hoveyda-Grubbs' II catalyst

Figure 4: Common metathesis catalysts

A limitation found in the use of ring-closing metathesis is the inability to control the *E*/*Z* geometry in the case of medium and large rings. The use of a temporary tether for ring-closing metathesis allows the formation of *Z*-olefin in most medium rings by adding a ring strain. Furthermore, increasing the size of geminal alkyl substitution on silicon leads to bond angle distortion in which the angle between the substituents containing reactive alkenes decreases. This phenomenon, also known as the Thorpe-Ingold effect, greatly facilitates the cyclization of tethered alkenes.[18]

The use of a temporary silicon tether for ring-closing metathesis has then become the subject of several studies and is now a powerful tool in organic synthesis. Two types of silicon tethers are commonly used: the O-Si-O tether and the O-Si-C tether.

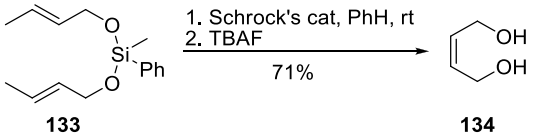
[18] (a) Čusak, A. *Chem. Eur. J.* **2012**, *18*, 5800; (b) P. A. Evans, *Metathesis in Natural Product Synthesis:Strategies, Substrates and Catalysis* (Eds.: J. Cossy, S. Arseniyadis, C. Meyer), Wiley-VCH, Weinheim, **2010**, pp. 225 –259.

1.4.1 - The O-Si-O tether

a. Symmetrical silaketals

The temporary silicon-tethered ring-closing metathesis (TST-RCM) sequence was initially described by Grubbs and Fu,[19] as a method for the construction of achiral 1,4- diols.

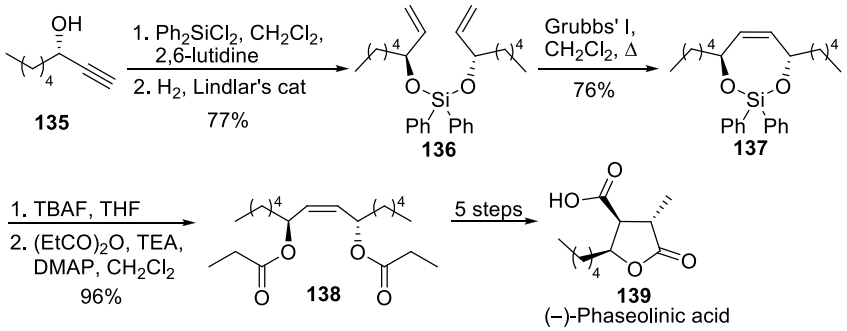
The synthesis of (*Z*)-but-2-ene-1,4-diol using a TST-RCM sequence is shown in the following scheme (Scheme 30):



Scheme 30: Synthesis of (*Z*)-but-2-ene-1,4-diol using a TST-RCM sequence

Due to the sensitivity of the cyclic silaketal, after RCM using Schrock's catalyst, the crude material was treated directly with TBAF in order to remove the tether and to afford the diol. Symmetrical silaketals can be easily accessed by silylation of the hydroxyl group with the appropriate tethering agent bearing the reactive dichlorosilane functionality.

An example of the use of a symmetrical silaketal in the synthesis of a natural product is described in the following scheme (Scheme 31):



Scheme 31: Synthesis of (−)-phaseolinic acid

In their synthesis of (−)-phaseolinic acid, Garcia and co-workers[20] used a TST-RCM sequence. Treatment of propargylic alcohol **135** with dichlorodiphenylsilane, followed by partial hydrogenation of the alkyne to give the alkene, gave the RCM precursor **136**. RCM proceeded smoothly in 76% yield with first-generation Grubbs' catalyst. Subsequent removal of the tether with TBAF gave the symmetrical 1,4-diol. Another six steps were required to synthesise (−)-phaseolinic acid.

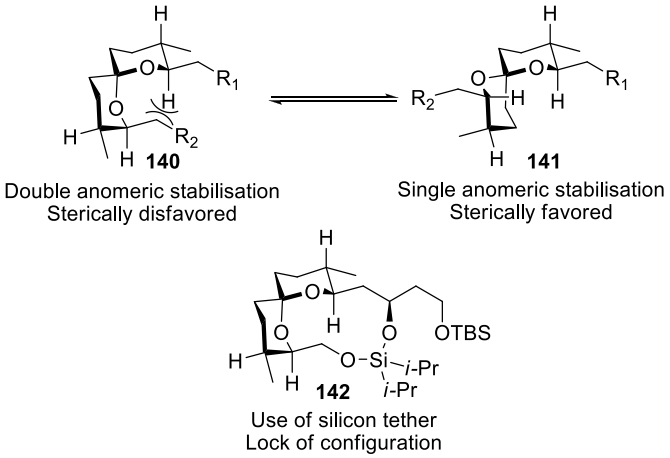
[19] Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426.
[20] Amador, M.; Ariza, X.; Garcia, J.; Ortiz, J. *J. Org. Chem.* **2004**, *69*, 8172.

b. Unsymmetrical silaketals

The preparation of unsymmetrical silaketals is often hindered by the formation of symmetrical silaketals. A usual method to synthesise these silaketals is to use an excess of dichlorosilane. However, this excess might be difficult to remove, especially in the case of heavier silanes. Several approaches have been reported in order to synthesise these compounds in the most elegant manner.[21,22,23]

1,2-Disubstituted alkenes

In their synthesis of spirofungin A, Kozmin and Marjanovic[24] used a TST-RCM sequence in an interesting way. The spiroketal present in spirofungin A can be obtained through spiroketalisation. However, the spontaneous spiroketalisation leads to an equilibrium between two forms (Scheme 32). The desired spiroketal **140** is favored by a double anomeric stabilisation, but is sterically disfavored. On the other hand, the other spiroketal **141** shows a single anomeric stabilisation, but is sterically favored. Kozmin and Marjanovic decided to make use of the silicon tether in order to lock the configuration into the desired one.

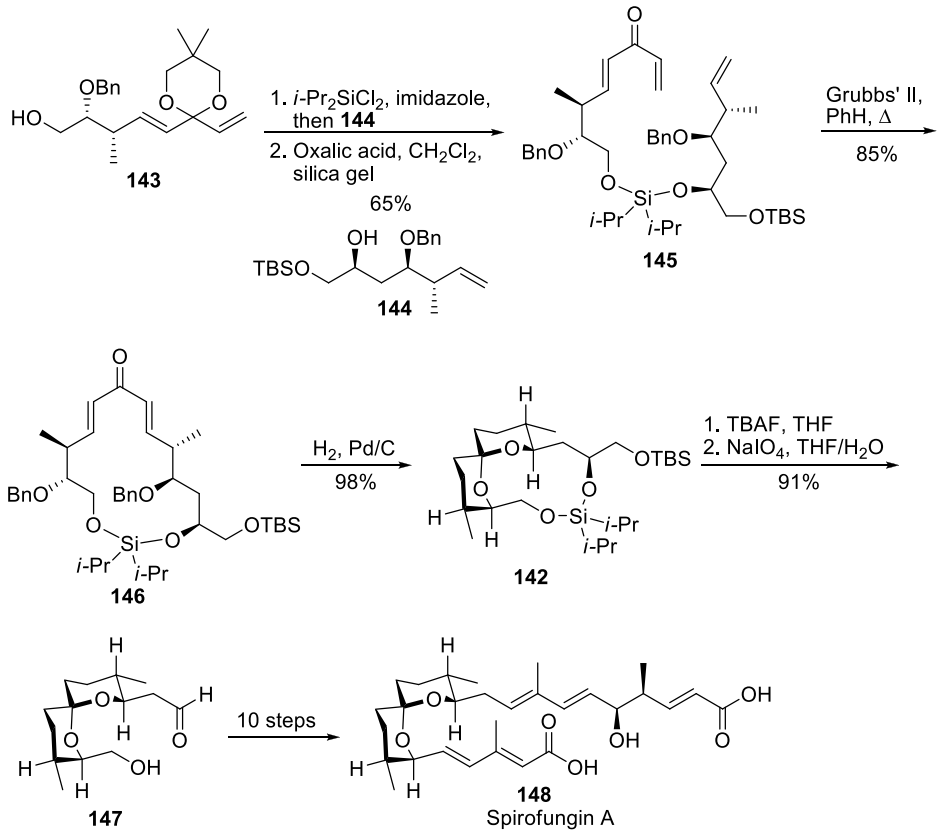


Scheme 32: Use of silicon tether to lock configuration during spiroketalisation

Treatment of primary alcohol **143** with diisopropyldichlorosilane and imidazole, followed by addition of alcohol **144** led to the silaketal intermediate (Scheme 33). Subsequent removal of the 1,4-dioxane afforded the RCM precursor **145**. RCM using second-generation Grubbs' catalyst delivered the 15-membered cycle in 85% yield. Hydrogenation of the double bonds and removal of the benzyl ethers using H_2 and Pd/C, followed by spontaneous spiroketalisation led to the desired spiroketal **142** in 98% yield. Silyl deprotection using TBAF, followed by glycol cleavage gave hydroxy aldehyde **147**. The total synthesis of spirofungin A was then completed in ten further steps.

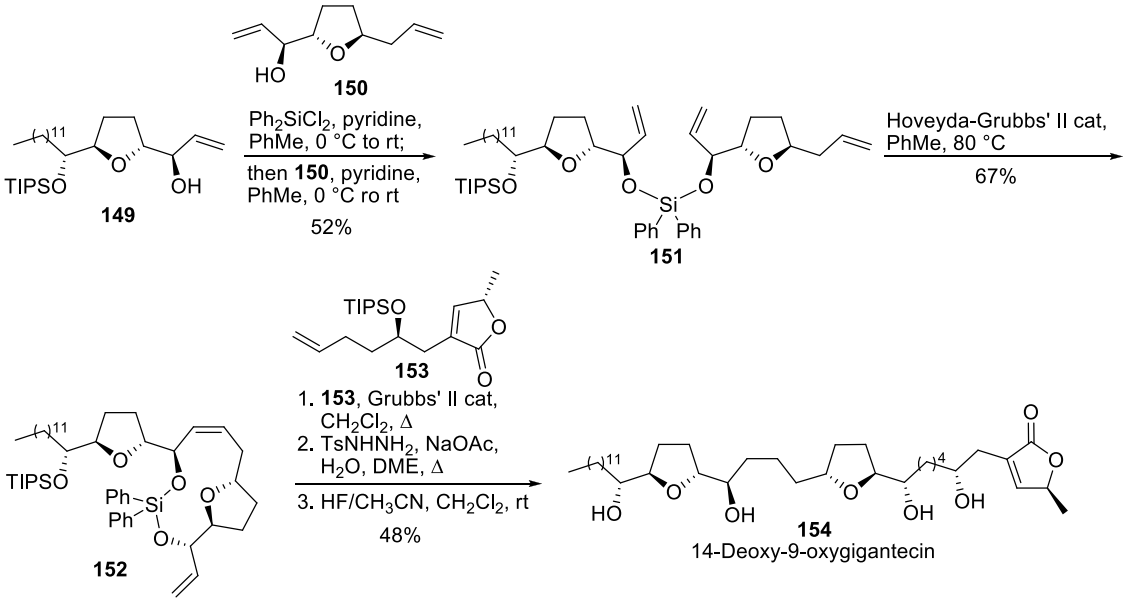
---

[21] Petit, M.; Chouraqui, G.; Aubert, C.; Malacria, M. *Org. Lett.* **2003**, *5*, 2037.
[22] Cordier, C.; Morton, D.; Leach, S.; Woodhall, T.; O'Leary-Steele, C.; Warriner, S.; Nelson, A. *Org. Biomol. Chem.* **2008**, *6*, 1734.
[23] Matsui, R.; Seto, K.; Fujita, K.; Suzuki, T.; Nakazaki, A.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2010**, *49*, 10068.
[24] Marjanovic, J.; Kozmin, S. A. *Angew. Chem.* **2007**, *119*, 9010 ; *Angew. Chem. Int. Ed.* **2007**, *46*, 8854.



Scheme 33: Synthesis of spirofungin A

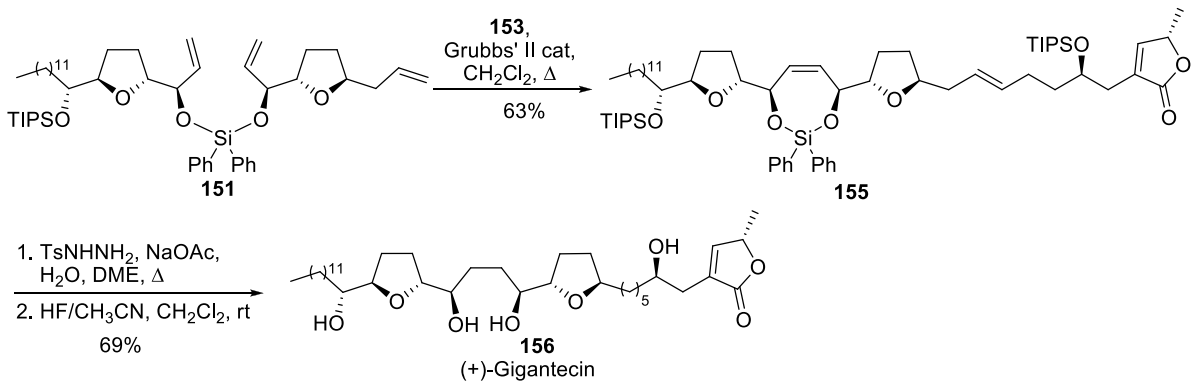
En route to the synthesis of (+)-gigantecin, Hoye and co-workers[25] synthesised silaketal **151** by coupling diphenyldichlorosilane with alcohols **149** and **150** (Scheme 34). However, treatment of **151** with second-generation Hoveyda-grubbs' catalyst led to the unexpected eleven-membered ring silaketal **152** rather than the desired seven-membered ring. Cross metathesis with fragment **153**, followed by diimide reduction and silyl deprotection gave 14-deoxy-9-oxygigantecin.



Scheme 34: Synthesis of 14-deoxy-9-oxygigantecin

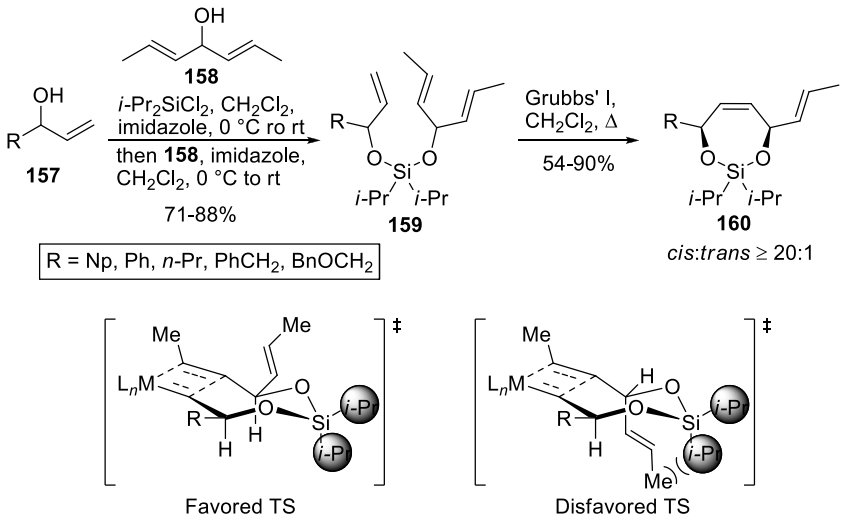
[25] Hoye, T. R.; Eklov, B. M.; Jeon, J.; Khoroosi, M. *Org. Lett.* **2006**, *8*, 3383.

In order to synthesise (+)-gigantecin, they decided to reverse the order of the two metathesis reactions. Treatment of silaketal **151** with second-generation Grubbs' catalyst in the presence of fragment **153** led to cross metathesis and ring-closing metathesis and the desired seven-membered ring silaketal **155** was obtained in 63% (Scheme 35). Subsequent diimide reduction and global silyl deprotection afforded (+)-gigantecin in 69% yield.



Scheme 35: Synthesis of (+)-gigantecin

Evans and co-workers[26] reported the use of a TST-RCM sequence in order to induce a long-range asymmetry (Scheme 36). Ring-closing metathesis of silaketal **159** using first-generation Grubbs' catalyst afforded the seven-membered ring silaketal with a good 1,4-diastereocontrol. They reported the use of first-generation Grubbs' catalyst generated better results over second-generation Grubbs' catalyst and Schrock's catalyst. This stereoinduction is based on the interaction between the isopropyl group on the silicon tether and the substituent with the pseudo-axial position on the forming ring. In the transition state leading to the *cis* product, both hydrogens are in pseudo-axial position and the steric clash is minimised. On the other transition state, there is a steric clash between the isopropyl group and the propenyl substituent.

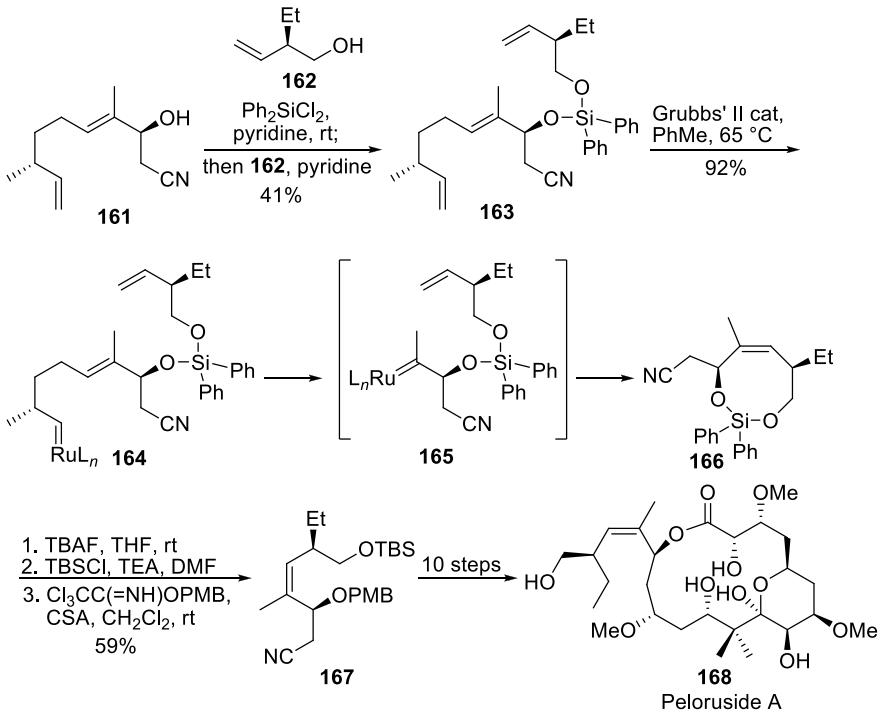


Scheme 36: Long-range asymmetric induction

[26] Evans, P. A.; Cui, J.; Buffone, G. P. *Angew. Chem.* **2003**, *115*, 1776; *Angew. Chem. Int. Ed.* **2003**, *42*, 1734.

Trisubstituted alkenes

Hoye and co-workers[27] reported the use of a temporary silicon-tethered relay ring-closing metathesis in their synthesis of peloruside A (Scheme 37). After synthesising silaketal **163** by coupling alcohols **161** and **162** with diphenyldichlorosilane, treatment of the RRCM precursor with second-generation Grubbs' catalyst led the ruthenium to attach onto the most hindered alkene by releasing methylcyclohexene and then led to the desired cyclised silaketal. Subsequent removal of the tether, followed by TBS and PMB protection of the hydroxyl groups gave compound **167**. An additional ten steps were required to synthesise peloruside A from intermediate **167**.

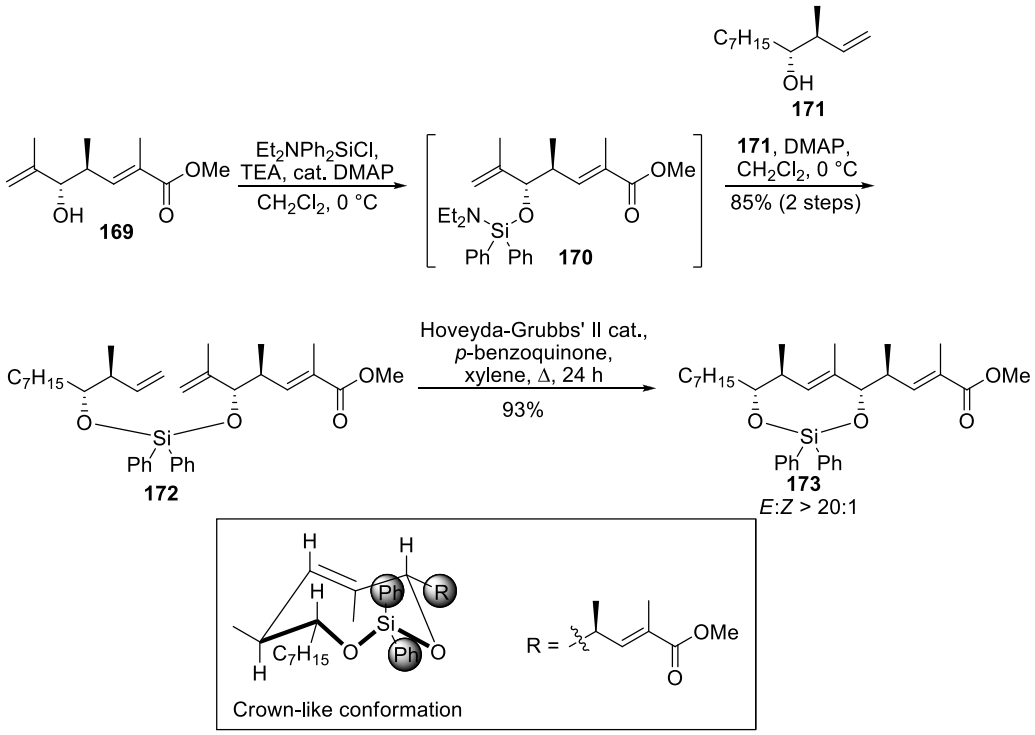


Scheme 37: Synthesis of peloruside A

Kobayashi and co-workers used a TST-RCM in order to synthesise natural products containing a a pent-2-ene-1,5-diol moiety.[23] They first decided to try this methodology with a model system (Scheme 38). Treatment of alcohol **169** with *N*,*N*-diethylaminochlorodiphenylsilane in the presence of TEA and catalytic amount of 4-dimethylaminopyridine, followed by addition of alcohol **171** led to the formation of the silaketal **172** in 85% yield. The silaketal **172** was then subjected to ring-closing metathesis with second-generation Hoveyda-Grubbs' catalyst in xylene in the presence of *p*-benzoquinone and cyclic silaketal **173** was obtained in 93% yield and with almost exclusively the *E*-olefin geometry.

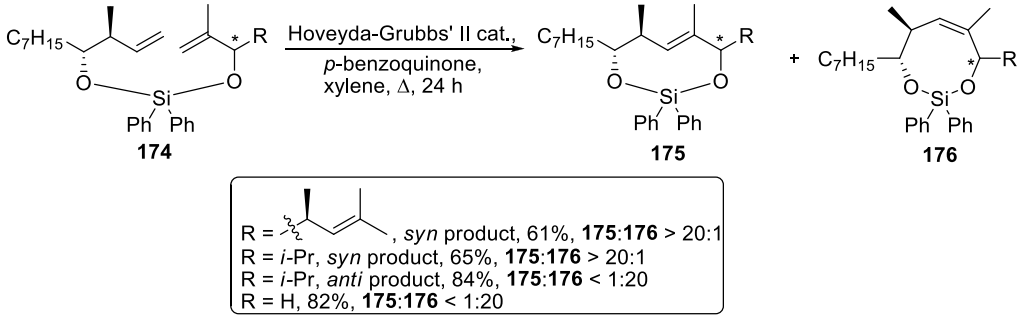
NOE experiments revealed that the silacycle existed in a crown-like conformation in which all the sterically demanding substituents were in pseudo-equatorial positions (Scheme 38).

[27] Hoye, T. R.; Jeon, J.; Kopel, L. C.; Ryba, T. D.; Tennakoon, M. A.; Wang, Y. *Angew. Chem.* **2010**, *122*, 6287; *Angew. Chem. Int. Ed.* **2010**, *49*, 6151



Scheme 38: Use of a TST-RCM sequence for the formation a pent-2-ene-1,5-diol moiety

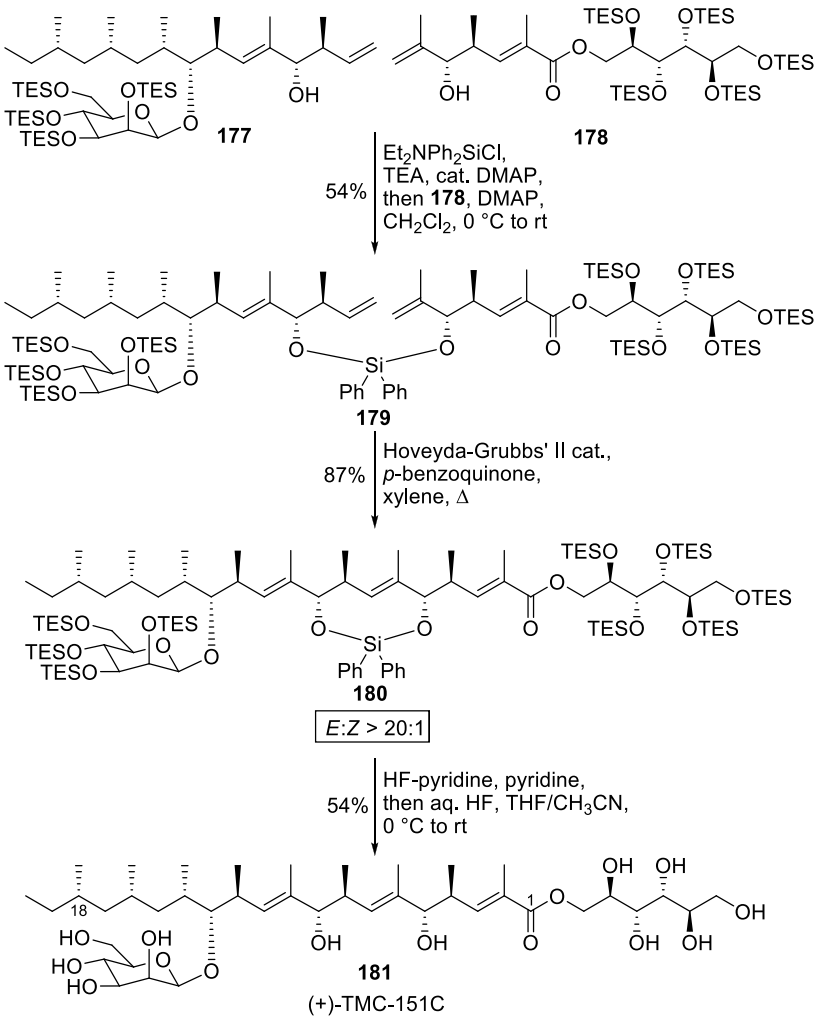
While investigating the scope of this methodology,[23] they discovered that sterically similar products gave a similar outcome (Scheme 39). However, when the two hydroxyl groups were in an *anti* relationship or when the steric bulk was reduced, the *Z*-olefin product was obtained.



Scheme 39: Scope investigation

They then applied this methodology to the total synthesis of (+)-TMC-151C[28] (Scheme 40). After coupling the two alcohol fragments **177** and **178** with *N*,*N*-diethylaminochlorodiphenylsilane in order to install the silicon tether, subjection of the silaketal to ring-closing metathesis led to the desired *E*-olefin product in 87% yield. Finally, global silyl deprotection afforded (+)-TMC-151C in 54% yield.

[28] Matsui, R.; Seto, K.; Sato, Y.; Suzuki, T.; Nakazaki, A.; Kobayashi, S. *Angew. Chem.* **2011**, *123*, 706; *Angew. Chem. Int. Ed.* **2011**, *50*, 680



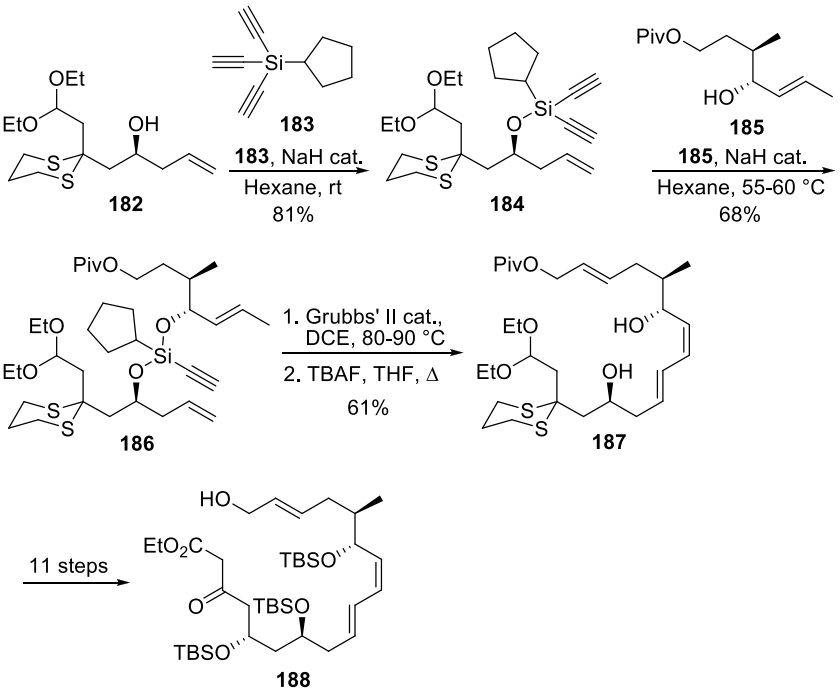
Scheme 40: Synthesis of (+)-TMC-151C

Tandem enyne RCM

Enyne metathesis is an important reaction that allows to install a new 1,3-diene functionality in to the molecule. When combined with ring-closing metathesis or cross metathesis it allows the formation of new acyclic or cyclic frameworks. However, enyne metathesis suffers from a lack of regio- and stereocontrol. The use of a temporary silicon tether could thus be applied to enyne metathesis in order to offer a new reactivity and help improve the regio- and stereocontrol.

Lee and Mukherjee reported the use of a temporary silicon tether tandem enyne RCM in their formal synthesis of (−)-cochleamycin A[29] (Scheme 41). The tandem enyne RCM precursor **186** was synthesised by two consecutive base-induced alkynylsilane alcoholysis reaction. Tandem enyne RCM, followed by silyl deprotection delivered the desired product containing the *E*,*Z*-1,3-diene moiety in 61% yield. An additional eleven steps were required in order to complete the formal synthesis of (−)-cochleamycin A.

[29] Mukherjee, S.; Lee, D. *Org. Lett.* **2009**, *11*, 2916



Scheme 41: Formal synthesis of (−)-cochleamycin A

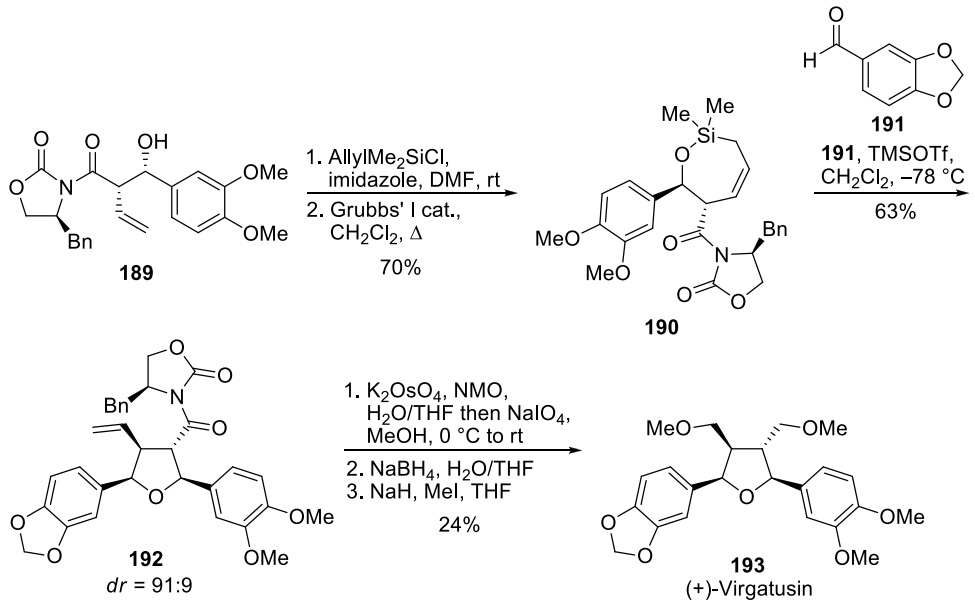
1.4.2 - The O-Si-C tether

The use of an alkylsilane as a tether is interesting, because the product can then be further functionalised. Functionalisation by protodesilylation or oxidation are common examples. A few examples of the use of an O-Si-C tether in organic synthesis will be shown here.

a. 1,2-Disubstituted alkenes

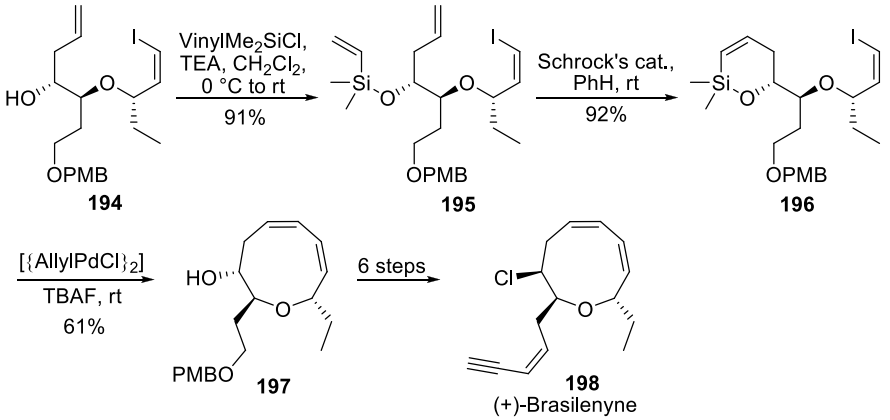
Marsden and co-workers used a TST-RCM/Hosomi-Sakurai reaction strategy in their total synthesis of (+)-virgatusin (Scheme 42).[30] Coupling of alcohol **189** with allyldimethylchlorosilane, followed by RCM gave the desired silacycle **190** in 70% yield. Treatment of the silacycle with trimethylsilyltriflate in the presence of aldehyde **191** led to the key Hosomi-Sakurai type condensation reaction in 63% yield with good stereocontrol. The synthesis of (+)-virgatusin was then completed in three steps and 24% yield using the following sequence of steps: Lemieux-Johnson oxidation of the alkene, reduction of both the aldehyde and the oxazolidinone auxiliary with sodium borhydride, and Williamson etherification with iodomethane.

[30] Akindele, T.; Marsden, S. P.; Cumming, J. G. *Org. Lett.* **2005**, *7*, 3685.



Scheme 42: Synthesis of (+)-virgatusin

Denmark and Yang developed a TST-RCM/silicon-assisted intramolecular palladium-catalysed cross-coupling and applied this strategy to the synthesis of (+)-brasilenyne (Scheme 43).[31] Silylation of alcohol **194** with vinyldimethylchlorosilane, followed by ring-closing metathesis with Schrock's catalyst gave the 6-membered silacycle **196** in 84% yield over two steps. The formation of the nine-membered cyclic ether **197** was accomplished in 61% yield using a palladium-catalysed intramolecular cross-coupling with TBAF as an activator of the silane. The synthesis of (+)-brasilenyne was completed in an additional six steps.

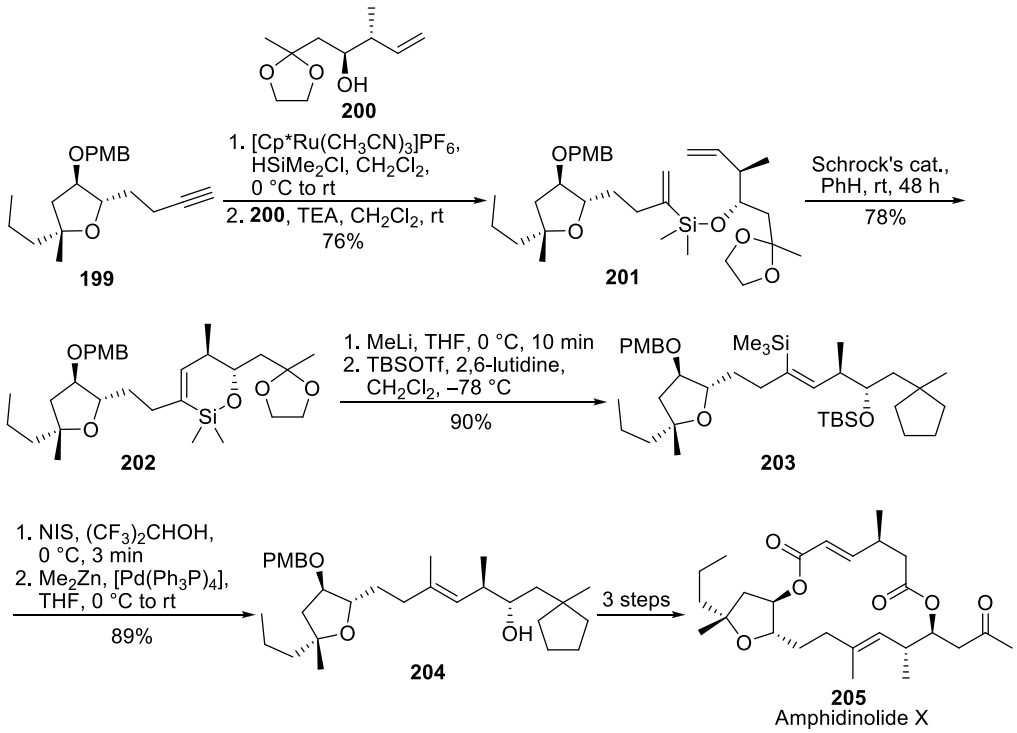


Scheme 43: Synthesis of (+)-Brasilenyne

[31] (a) Denmark, S. E.; Yang, S. M. *J. Am. Chem. Soc.* **2002**, *124*, 15196; (b) Denmark, S. E.; Yang, S. M. *J. Am. Chem. Soc.* **2004**, *126*, 12432.

b. Trisubstituted alkenes

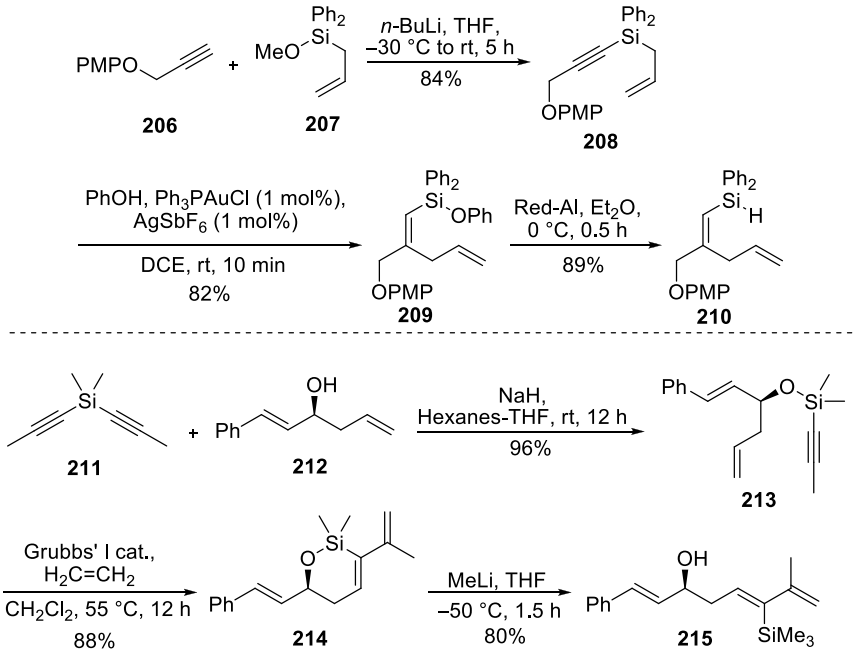
Vilarrasa and co-workers decided to use the TST-RCM reaction strategy in their total synthesis of amphidinolide X in order to form a trisubstituted alkene (Scheme 44).[32] The hydrosilylation of the alkyne **199** with dimethylchlorosilane using Trost's catalyst gave the chlorosilane, which was coupled *in situ* with alcohol **200** in order to form the O-Si-C tether in 76% yield. Vinylsilane **201** was then subjected to RCM with Schrock's catalyst and the six-membered silacycle was obtained in 78% yield. Treatment of the silacycle with methyllithium induced the opening of the cycle and the alcohol product was then protected as a TBS ether using TBS triflate. The trimethylsilyl group was then converted into a methyl group in two steps and 89% yield by idodesilylation with NIS and methylation with dimethylzinc following Negishi's protocol. Completion of the total synthesis of amphidinolide X was performed in an additional three steps.



Scheme 44: Synthesis of amphidinolide X

Lee and Volchkov reported, in their total synthesis of (−)-amphidinolide V,[33] the use of an interesting silane dehydrogenative coupling in order to install the silicon tether as well as an 1,3-allylic transposition of an eight-membered ring silacycle into a six-membered ring silacycle using rhenium oxide. The syntheses of the two partners for the silane dehydrogenative coupling are shown in the following scheme (Scheme 45):

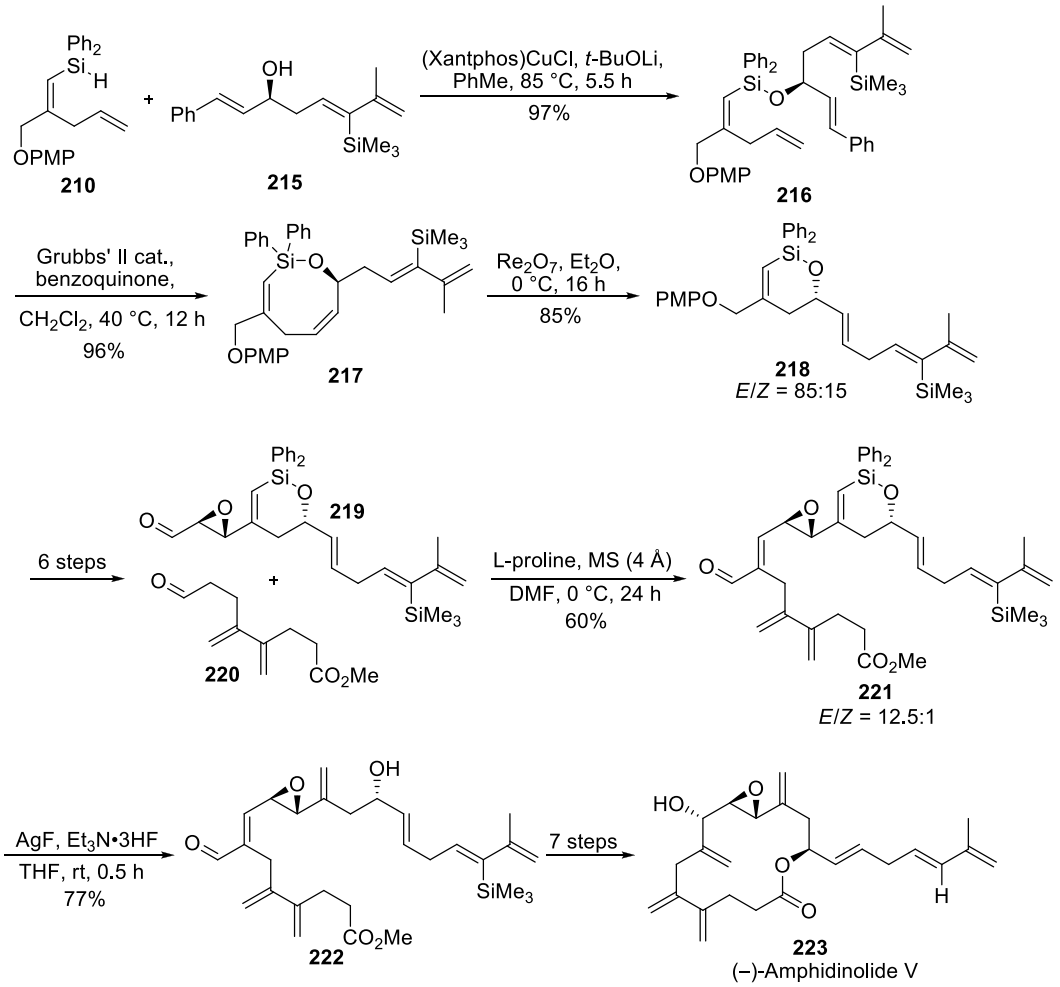
[32] Rodríguez-Escrich, C.; Urpí, F.; Vilarrasa, J. *Org. Lett.* **2008**, *10*, 5191.
[33] Volchkov, I.; Lee, D. *J. Am. Chem. Soc.* **2013**, *135*, 5324.



Scheme 45: Syntheses of silane **210** and alcohol **215**

Silane **210** was synthesised in three steps and and 61% yield from alkyne **206** and silane **207**. The synthesis commenced with the addition of the lithiated alkyne **206** onto the methoxysilane **207** to deliver the alkynylsilane **208** in 84% yield. Gold-catalysed intramolecular allylation of **208** in the presence of phenol gave phenoxysilane **209** in 82% yield. Reduction of **209** with Red-Al afforded the silane partner **210** in 89% yield. The alcohol partner was synthesised in three steps and 68% yield from alcohol **212** and silane **211**. After formation of oxysilane **213** by silane alcoholysis, Lee and Volchkov used a TST-enyne RCM, followed by methyllithium cleavage to obtain alcohol **215**.

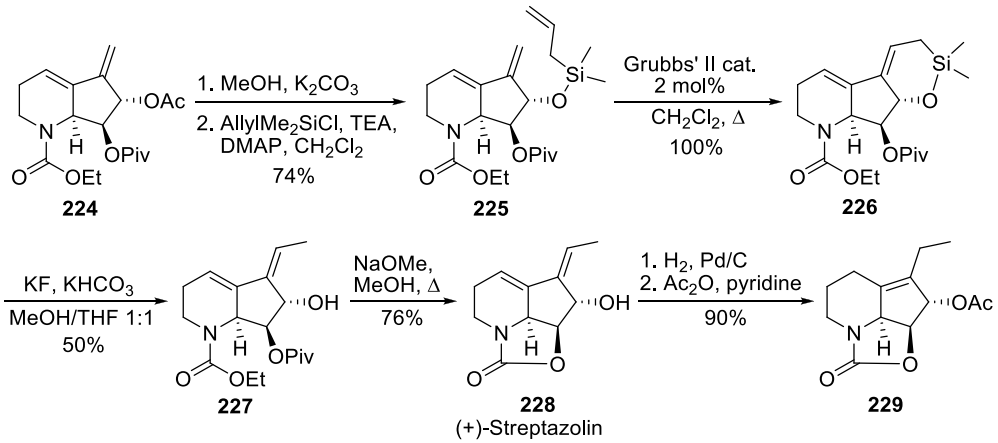
The two partners were then coupled in excellent yield using (xantphos)copper chloride as a catalyst and lithium *tert*-butoxide (Scheme 46). Oxysilane **216** was then subjected to ring-closing metathesis using second-generation Grubbs' catalyst in the presence of *p*-benzoquinone and the eight-membered silacycle was obtained in 96% yield. 1,3-Allylic transposition with rhenium oxide delivered silacycle **218** in 85% yield and with a diastereomeric ratio of 85:15. Compound **218** was then converted into aldehyde **219** in six further steps, which was coupled with aldehyde **220** by an organocatalytic aldol condensation reaction. The diphenylsilyl group was then selectively removed using silver fluoride and $Et_3N{\cdot}3HF$ in 77% yield. A further seven steps were needed in order to complete the synthesis of (−)-amphidinolide V.



Scheme 46: Completion of the synthesis of (−)-amphidinolide V

There are few examples of the use of tethered RCM reactions to synthesise trisubstituted olefins containing a motif similar to the one found in dolabelide C. Miller and Li decided to use a TST-RCM strategy to install selectively the *Z*-olefin present in (+)-straptazolin (Scheme 47).[34] Deacetylation of intermediate **224**, followed by coupling with allyldimethychlorosilane gave the RCM precursor **225** in 74% yield. Ring-closing metathesis afforded the silacycle in quantitative yield. The next step, however, proved problematic. After optimisation, protodesilylation using potassium fluoride and potassium bicarbonate gave the desired allylic alcohol **227** in 50% yield. The synthesis of (+)-streptazolin was then completed by removal of pivaloate group followed by concomitant urethane formation in 76% yield. Due to the partial decomposition upon the isolation, (+)-streptazolin was then converted to the more stable acetate **229** in two steps.

[34] Li, F.; Miller, M. J. *J. Org. Chem.* **2006**, *71*, 5221.

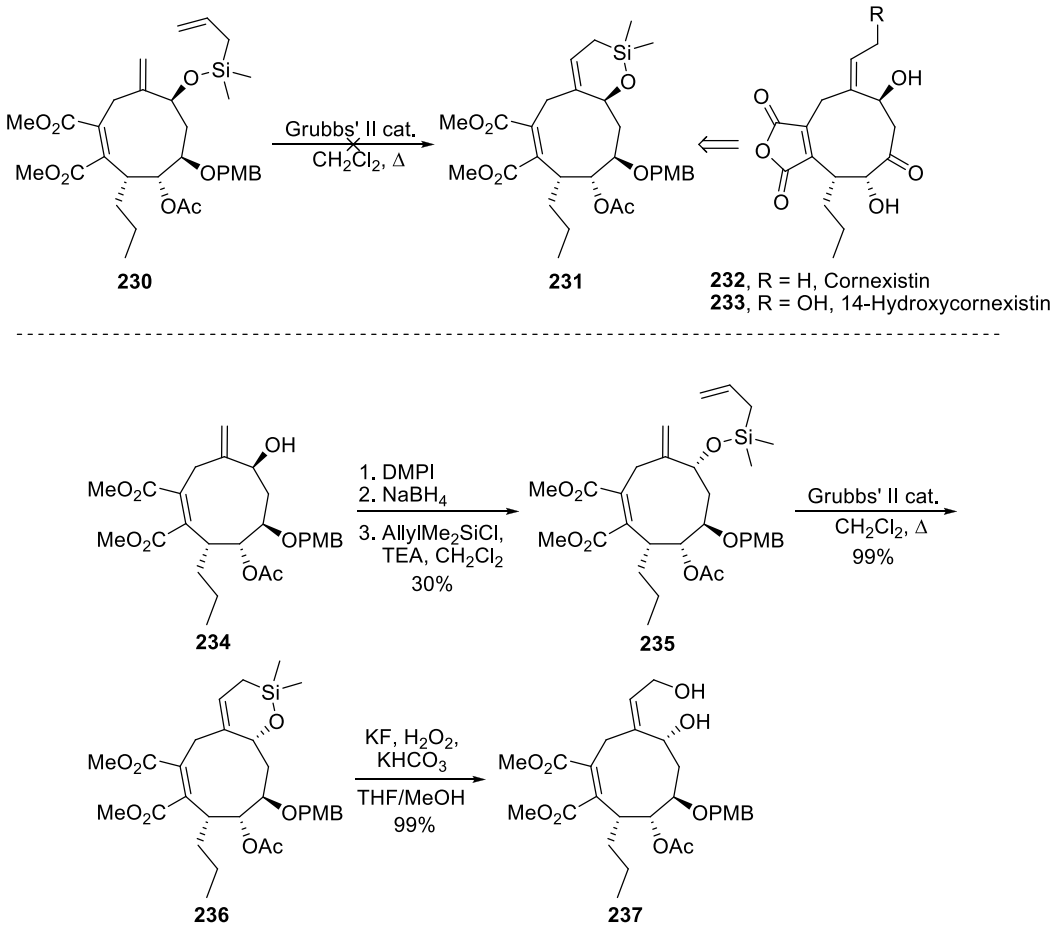


Scheme 47: Synthesis of (+)-streptazolin

Similarly to the work done by Miller and Li, Taylor and co-workers decided to use a TST-RCM to control the geometry of the allylic alcohol present in cornexistin and its analog 14-hydroxycornexistin (Scheme 48).[35] Toward this end, oxysilane **230** was subjected to ring-closing metathesis. However, only dimeric products were obtained, regardless of the catalyst employed. It was proposed that substrate **230** was conformationally mismatched for the RCM reaction.

They then decided to invert the stereochemistry of the allylic alcohol and synthesised in three steps and 30% yield a new oxysilane **235**. In this case, treatment of substrate **235** with second-generation Grubbs' catalyst gave the desired silacycle in quantitative yield. Subsequent Tamao-Fleming reaction delivered a late-stage intermediate toward the synthesis of 14-hydroxycornexistin in quantitative yield.

[35] Tung, J. C.; Chen, W.; Noll, B. C.; Taylor, R. E.; Fields, S. C.; Dent, W. H. III.; Green, F. R. *Synthesis* **2007**, 2388.



Scheme 48: Synthesis of 14-hydroxycornexistin precursor

c. Asymmetric ring-closing metathesis

Alkene metathesis is now a commonly used method in organic synthesis, and studies are now being done in order to render this reaction asymmetric. These studies are also being expanded to the use of chiral metathesis complexes in the TST-RCM reactions.

Schrock and co-workers examined the efficiencies of catalysts **238**-**242** (Figure 5) for the enantioselective formation of silacycles.[36]

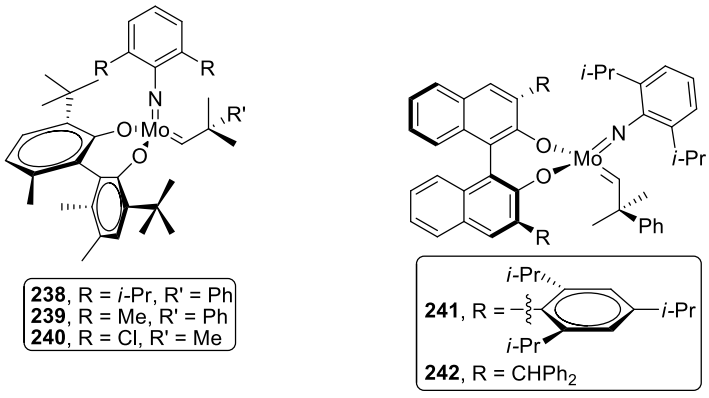
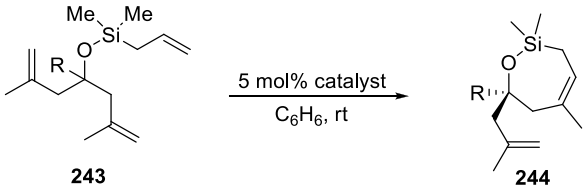


Figure 5: Chiral catalysts for metathesis

[36] Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 8251.

Binol complexes seem to be typically more effective in the asymmetric synthesis of six-membered ring silacycles. However, it is often difficult to predict which class of catalyst will be the best choice.[36]

They then expanded the scope to the synthesis of seven-membered ring silacycle.[37] Substrates **243** were then synthesised. These substrates would deliver, by ARCM, tertiary seven-membered ring siloxanes, which could then be easily functionalised to deliver tertiary alcohols of high optical purity, compounds that are often difficult to prepare by any other method. The results obtained are summarised in the following table (Table 1):

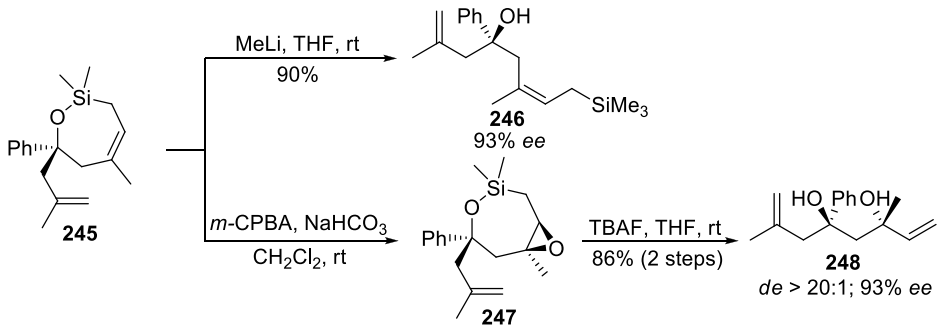


Entry	R	Catalyst	Conv (%); yield (%)	*ee* (%)
1	Ph	**238**	> 98; 92	93
2	*p*-BrPh	**240**	> 98; 98	94
3	Cy	**238**	> 98; 91	83
4	*i*-Pr	**238**	> 98; 92	90
5	*n*-Bu	**239**	> 98; 87	66
6	Me	**242**	> 98; 90	47

Table 1: Syntheses of seven-membered ring silacycles by TST-ARCM

Substrates containing an aromatic group or an isopropyl group were obtained in good yield and with good enantiomeric excesses. A more bulky cyclohexyl group gave a slightly lower enantiomeric excess. However, with sterically less bulky substrates, the reaction proceeded with an erosion of enantioselectivity.

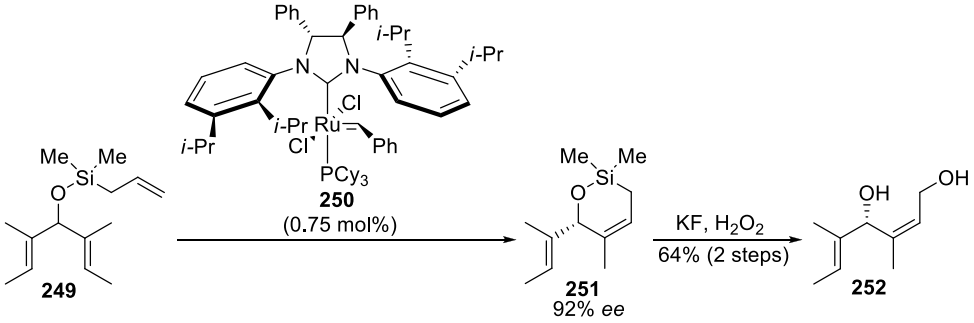
Hoveyda and co-workers then described the functionalisation of silacycle **245** (Scheme 49). Treatment with methyllithium gave tertiary alcohol **246** in good yield and good enantioselectivity. Epoxidation, followed by tether removal, led to the formation of diol **248** in good yield and excellent diastereocontrol and enantioselectivity.



Scheme 49: Functionalisation of silacycle **245**

[37] Kiely, A. F.; Jernelius, J. A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 2868.

Funk reported the use of a chiral version of the second-generation Grubbs' catalyst to synthesise a substrate containing a similar motif to the one present in dolabelide C (Scheme 50).[38]



Scheme 50: Synthesis of diol **252** by TST-ARCM

Treatment of oxysilane **249** with catalyst **250** delivered the six-membered silacycle **251** with good enantioselectivity. Subsequent Tamao-Fleming oxidation gave the diol **252** in 64% yield over two steps.

1.5 - Presentation of Project

As presented in the introduction, dolabelide C possesses a trisubstituted olefin, which is highlighted in red in Figure 6. This type of olefin can be obtained through cross metathesis, but the *E*/*Z* ratios vary from 2.3:1 to 4:1.

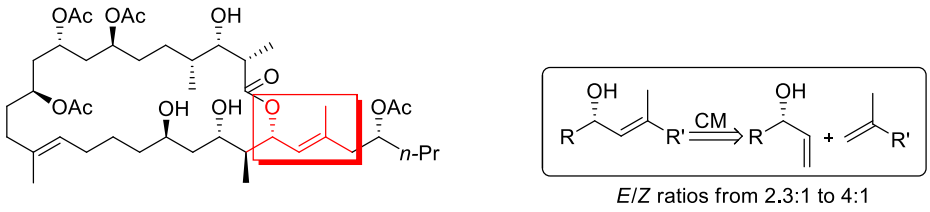
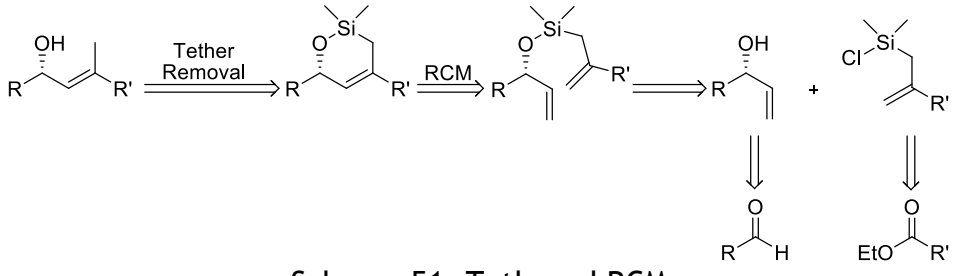


Figure 6: Olefin at C24-25 of dolabelide C

The first objective of this project is to develop a new diastereoselective access to this type of trisubstituted olefin by employing a ring-closing metathesis reaction (RCM) on a substrate where two olefinic fragments have been linked by a silicon tether (Scheme 51).

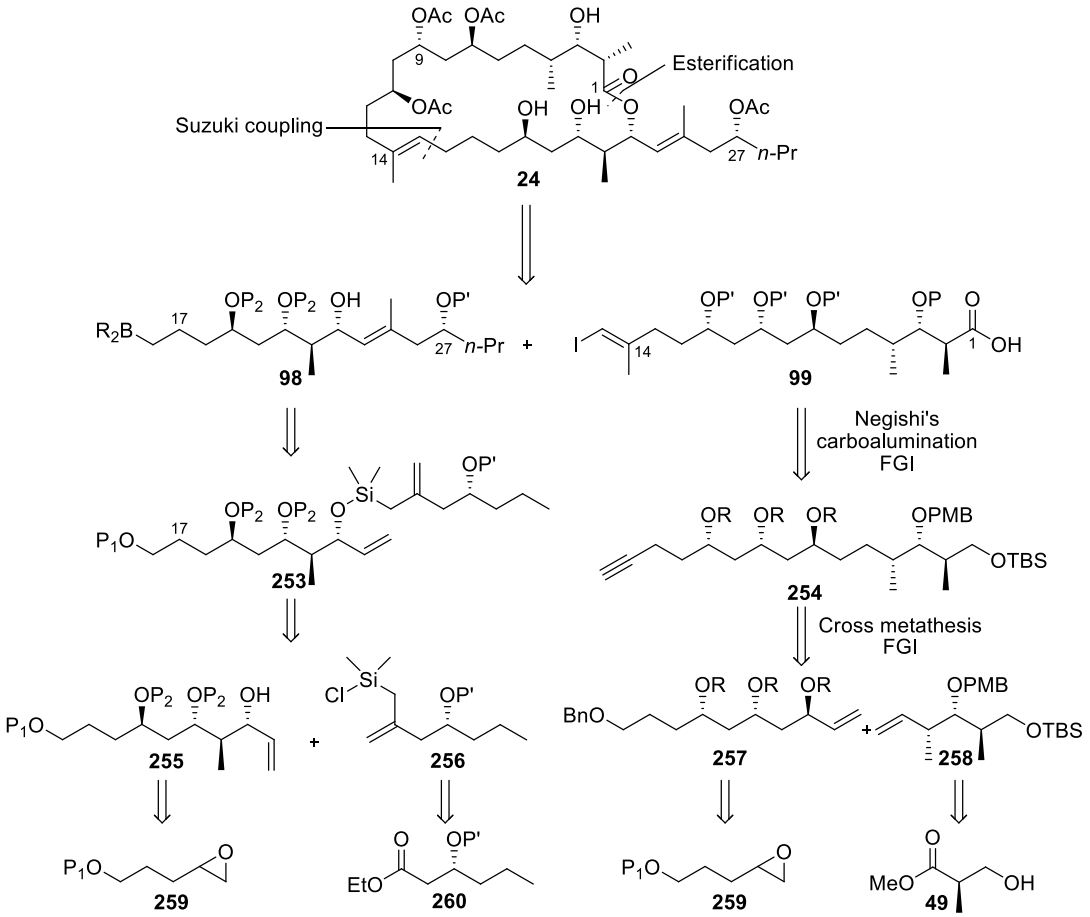


Scheme 51: Tethered RCM

The methodology will first be tried on racemic model compounds to validate the method and will then be used for the synthesis of dolabelide C.

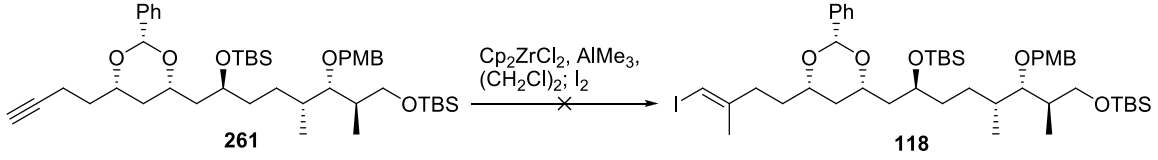
[38] Funk, T. W. *Org. Lett.* **2009**, *11*, 4998.

The revised retrosynthesis of dolabelide C is presented in the following scheme (Scheme 52):



Scheme 52: Retrosynthesis of fragment C15-30 using tethered RCM

The main disconnections are the same as for the previously envisaged synthesis discussed in the introduction, but other routes are envisaged for the syntheses of both fragments C1-15 and C16-30. The fragment C16-30 could be obtained using the proposed methodology by coupling alcohol **255** with silane **256**, which could be obtained from epoxide **259** and ester **260**, respectively. A second part of this project is to optimise the synthesis of the C1-15 fragment. Indeed, the Mukaiyama aldol reaction (see Scheme 26) employed before is a high yielding method. However, as the ketone is not present in the natural product, several steps are required in order to remove it. Moreover, a Negishi carboalumination reaction was tried on substrate **261** (Scheme 53), but it only led to decomposition. This might be due to the fact that the benzylidene acetal is incompatible with the reaction conditions.



Scheme 53: Negishi's carboalumination on substrate **261**

The new synthesis would involve cross metathesis between the two fragments **257** and **258** and the Negishi carboalumination reaction would be tried on a substrate containing various protecting groups rather than the benzylidene acetal.

Chapter 2: Synthesis of trisubstituted alkenes by RCM using an O-Si-C tether

As was presented in the introduction, we were interested in developing new methodology to synthesise a trisubstituted alkene flanked with an allylic alcohol *via* a ring-closing metathesis reaction using an O-Si-C tether for this purpose.

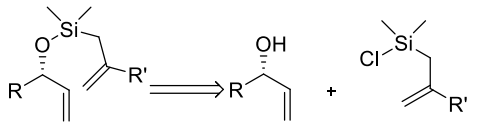
In order to explore the reaction, we first decided to work on model substrates. In a first part, the synthesis of the substrates and the different trials performed to install the silicon tether will be discussed.

In a second part, the ring-closing metathesis reaction and the different trials performed for the removal of the silicon tether will be presented.

Finally, the newly developed methodology will be applied to the synthesis of the C16-30 fragment of dolabelide C.

2.1 - Previous work in the group

The first method envisaged for the formation of the silicon tether was to synthesise a chlorosilane derivative and to then couple it with an allylic alcohol (Scheme 54).

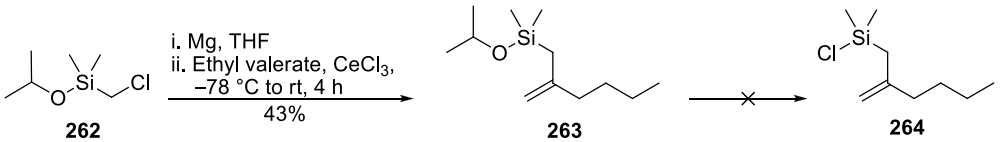


Scheme 54: Retrosynthesis envisaged for the silicon tether formation

Previous work was also done in the Prunet group by Mehdi Boumediene on the synthesis of a model system of the trisubstituted olefin at C24-25 *via* ring-closing metathesis using an oxygen-silicon-carbon tether link.[39]

In the study performed in the Prunet group by Mehdi Boumediene, several methods for the synthesis of a chlorodimethyl(2-alkylallyl)silane compound were tried.

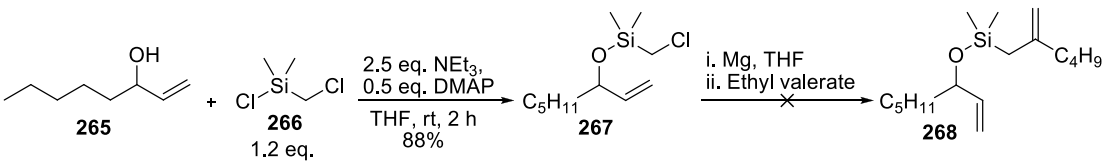
The first method was to synthesise the alkoxysilane **263** and convert it to the corresponding chlorosilane. The alkoxysilane **263** was synthesised *via* a Peterson olefination reaction between ethyl valerate and the isopropoxysilane **262** in 43% yield (Scheme 55). Several conditions were screened to convert the alkoxysilane into the chlorosilane, but the chlorosilane could not be obtained.



Scheme 55: First method

[39] Boumediene, M., *Master thesis*, *Ecole Polytechnique* **2007**

The second method was to form the silicon-oxygen link first, then perform the Peterson olefination reaction. The allylic alcohol **265** was thus reacted with chloro(chloromethyl)dimethylsilane **266** to form the protected alcohol **267** in 88% yield (Scheme 56). However, the Peterson olefination of this compound with ethyl valerate did not lead to the desired product.

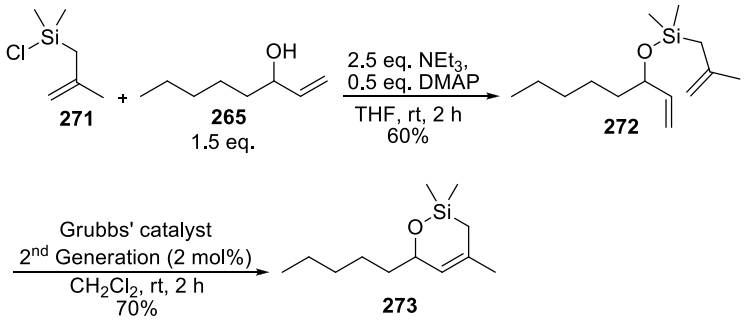


Scheme 56: Second method

The last method tried by Mehdi Boumediene was to form the chlorodimethyl(2-alkylallyl)silane compound via a Grignard addition.[40] Reaction of the Grignard reagent formed from the chloride compound **270** with dichlorodimethylsilane gave the desired product **271** in 22% yield (Scheme 57). The yield is quite low, because double addition of the Grignard reagent to the dichlorosilane probably happens as a side reaction (literature yield = 35%).

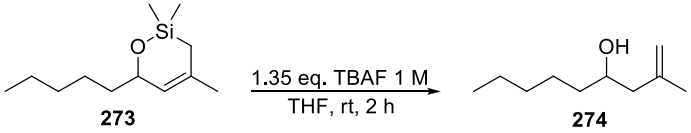
Scheme 57: Third method

The chlorosilane compound **271** was then reacted with the allylic alcohol **265** to form the silyl ether **272** in 60% yield (Scheme 58). The cyclisation reaction was then successfully achieved in 70% yield using ring-closing metathesis (Scheme 58).



Scheme 58: Tethered RCM

However, cleavage of the oxygen-silicon-carbon tether using a 1 M tetrabutylammonium fluoride solution in tetrahydrofuran led to isomerisation of the double bond to form a terminal alkene (Scheme 59).



Scheme 59: Cleavage trial

[40] Fürstner, A.; Voigtländer, D. *Synthesis* **2000**, 7, 959.

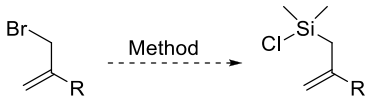
It was therefore important to find better conditions for the formation of the allylchlorosilane and for the cleavage of the silicon tether.

2.2 - Formation of the silicon tether

2.2.1- Substrate synthesis using previous route

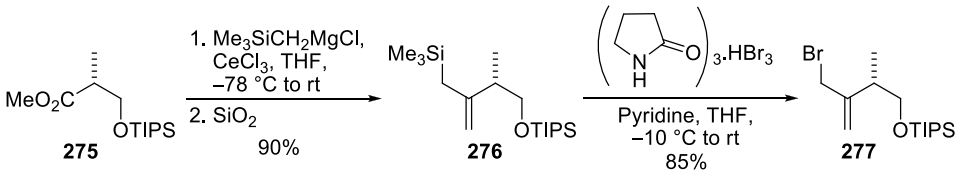
a. Synthesis of allyl bromides

Seeing as the synthesis of chlorosilane **271** from allyl chloride **270** had been partially successful, we decided to explore further the synthesis of a chlorosilane from an allyl halide substrate and to see if we could find a more efficient route (Scheme 60).



Scheme 60: Synthesis of chlorosilane from allyl bromide compound

We first decided to synthesise several bromide substrates. For this, we chose to use a method employed by Clark and co-workers in their synthesis of the tricyclic core of Neoliacinic Acid (Scheme 61).[41] This method consists in synthesising the bromide compound by Peterson olefination[42] from an ester, followed by bromination[43] with pyrrolidone hydrotribromide.



Scheme 61: Synthesis of allyl bromide **277** by Clark and co-workers

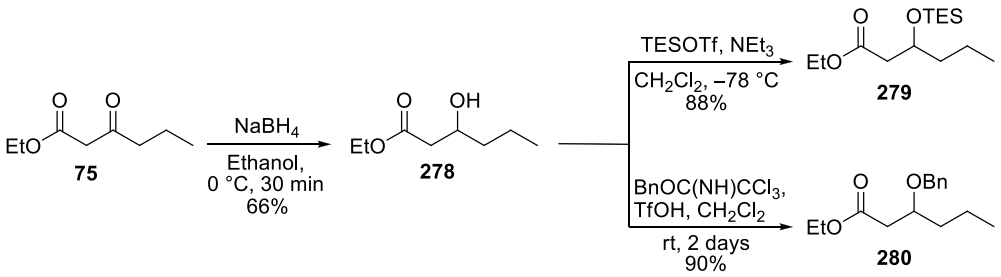
Esters **279** and **280** were then synthesised in two steps from commercially available ethyl 3-oxohexanoate (Scheme 62). We decided to start from ethyl 3-oxohexanoate, because it would lead to a silane containing the same motif as the silane required for the synthesis of dolabelide C, making them relevant model substrates.

---

[41] Clark, J. S.; Baxter, C. A.; Dossetter, A. G.; Poigny, S.; Castro, J. L.; Whittingham, W. G. *J. Org. Chem.* **2008**, *73*, 1040.

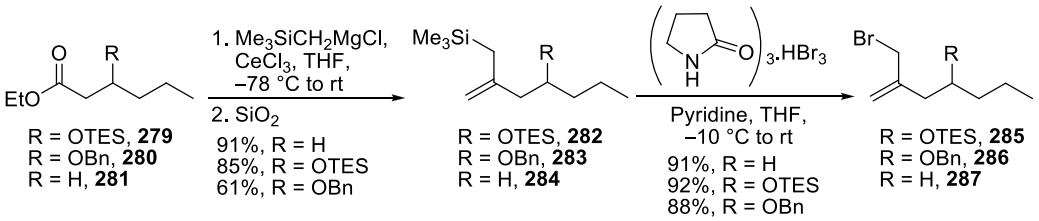
[42] (a) Narayanan, B. A.; Bunnelle, W. H. *Tetrahedron Lett.* **1987**, *28*, 6261. (b) Lee, T. V.; Channon, J. A.; Cregg, C.; Porter, J. R.; Roden, F. S.; Yeoh, H. T.-L. *Tetrahedron* **1989**, *45*, 5877. (c) Mickleson, T. J.; Koviach, J. L.; Forsyth, C. J. *J. Org. Chem.* **1996**, *61*, 9617.

[43] (a) Grafstein, D. *J. Am. Chem. Soc.* **1955**, *77*, 6650. (b) Awang, D. V. C.; Wolfe, S. *Can. J. Chem.* **1969**, *47*, 706.



Scheme 62: Syntheses of esters **279** and **280**

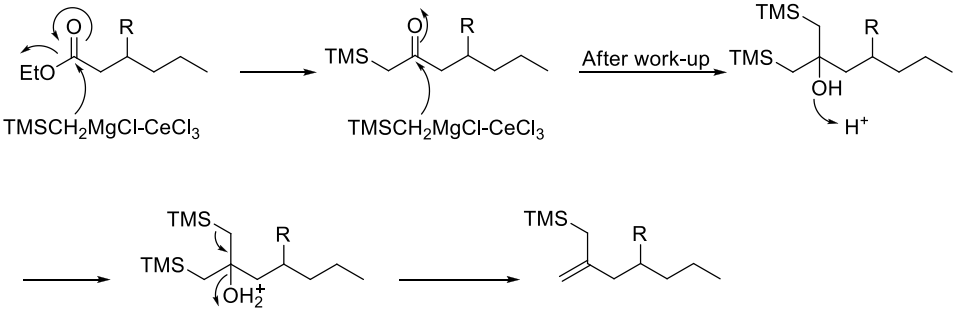
With these two esters in hand, along with commercially available ethyl caproate, allyl bromides **285**-**287** were synthesised by Peterson olefination, followed by bromination (Scheme 63).



Scheme 63: Syntheses of bromides **285**-**287**

In the first step, a Peterson olefination reaction was used to synthesise an allylic silane. The Peterson olefination reaction is commonly used to synthesise alkenes from aldehydes or ketones. When an ester is used, an allylic silane is obtained.

The mechanism of this reaction is presented in the following scheme (Scheme 64):



Scheme 64: Mechanism of the Peterson olefination

There is a double addition of the organocerium reagent to the ester. Subsequent elimination leads to the allyl silane.

The use of cerium chloride allows the formation of an organocerium reagent, which is more nucleophilic than the Grignard reagent alone. In the case the organocerium reagent is prepared *via* a Grignard reagent, the reagent formed is an ate complex of the form "R-MgX·$CeCl_3$", whereas if it is prepared from an organolithium reagent, it is believed to form something similar to a 'true' organocerium structure, "R-$CeCl_2$".[44] As organocerium reagents are relatively non-basic, they tolerate the use of alcohols, amines and enolisable protons.[44,45]

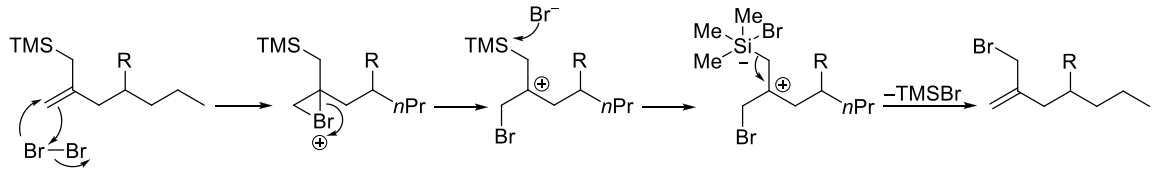
Cerium chloride is very hygroscopic and rapidly absorbs water to form a hydrate. Practically, cerium chloride can be bought anhydrous and needs to be handled

[44] Liu, H.-J.; Shia, K.-S.; Shang, X.; Zhu, B.-Y. *Tetrahedron* **1999**, *55*, 3803.
[45] Imamoto, T.; Suguira, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233.

under argon or nitrogen atmosphere, or it can be bought in its heptahydrate form and needs to be dried at 120 to 160 °C for several hours in order to be fully dried and ready to use.

For the last elimination step to occur, treatment of the crude intermediate with silica gel is needed. In the case of R = H, the elimination can occur during column chromatography. However, when R ≠ H, treatment of the intermediate with silica in dichloromethane while stirring for one day is required.

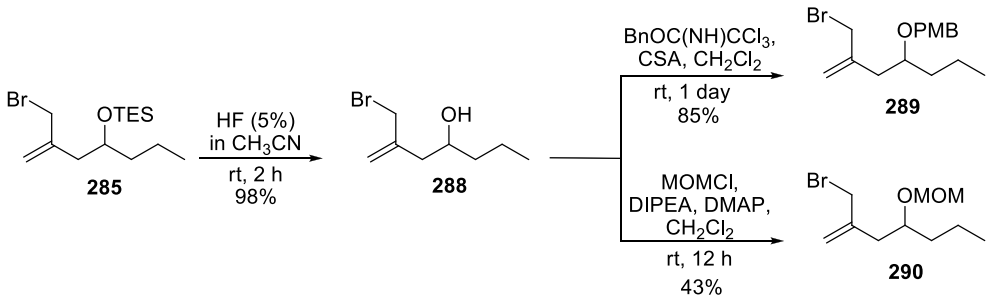
The bromination step is performed using pyrrolidone hydrotribromide as a brominating agent. Pyrrolidone hydrotribromide is a source of Br_3^-. It is much less electrophilic and less reactive toward aromatic rings and double bonds than bromine. This is due to the fact that Br_3^- is in equilibrium with bromine and bromide and can furnish a low concentration of bromine when dissolved in a solvent. Anhydrous tetrahydrofuran contributes to the selectivity of the reagent because of the stability of Br_3^- in this solvent. The mechanism of the reaction is presented in the following scheme (Scheme 65):



Scheme 65: Mechanism of the bromination reaction

Bromine addition to the double bond leads to a carbocation. Attack of the bromide anion to the silicon atom gives the silicate, which affords the desired allylic bromide by elimination.

From bromide **285**, two additional substrates were synthesised. After silyl deprotection using HF (5%) in acetonitrile, PMB- and MOM-protected compounds **289** and **290** were synthesised (Scheme 66).

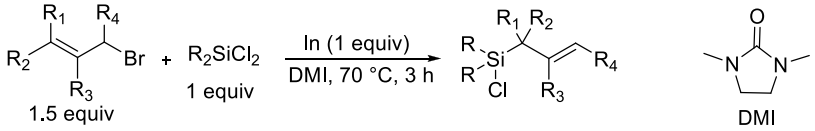


Scheme 66: Syntheses of bromides **289** and **290**

b. Synthesis of allylchlorosilanes

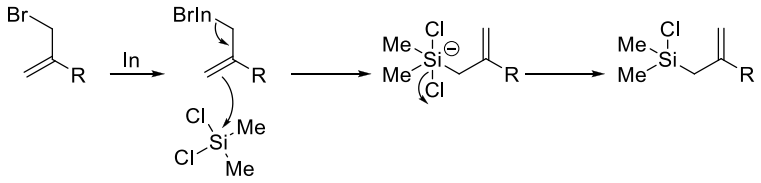
Use of indium

The first method envisaged for the synthesis of the allylchlorosilane involved the use of indium[46] (Scheme 67).



Scheme 67: Synthesis of chlorosilanes using indium

The use of indium allows the formation of an allylindium bromide species similar to a Grignard reagent. The use of a Grignard reagent often leads to diallylation of the chlorosilane, but with an allyl indium reagent, monoallylation can be achieved depending on the ratio indium/dichlorosilane/allyl bromide. The mechanism of this reaction is shown in the following scheme (Scheme 68):



Scheme 68: Mechanism of the reaction with indium

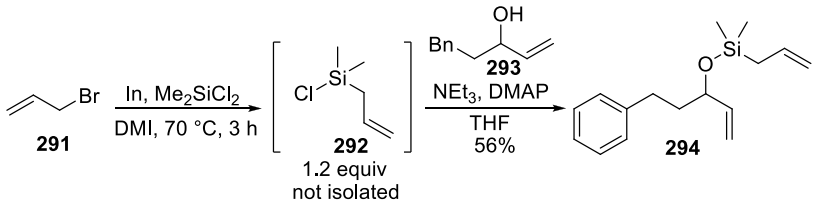
After insertion of indium, there is a γ-attack of the allylindium species to the chlorosilane leading to the formation of the allylchlorosilane.

The solvent used, DMI, is rather unusual. DMI is a polar, aprotic organic solvent close to 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) and has a boiling point of 225 °C. Its excellent solvating ability for both inorganic and organic compounds makes DMI a good solvent for the formation of organometallic reagents.

We first decided to try this method with commercially available allyl bromide. A typical procedure involves the addition of the chlorosilane to a solution of the allylindium species in DMI at 70 °C. After three hours, the mixture is filtered and the chlorosilane is isolated by distillation.

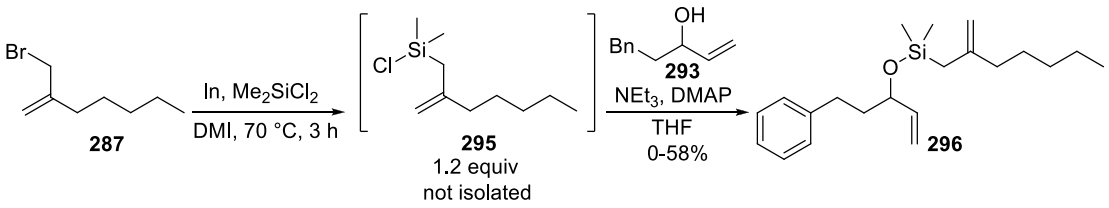
However, although allylchlorosilane **292** (Scheme 69) could not be isolated using conditions described in the literature, the use of the reaction mixture for the coupling[47] of chlorosilane **292** with the allylic alcohol **293** (synthesised in one step from hydrocinnamaldehyde) led to the desired product (Scheme 69).

[46] Li, Z.; Yang, C.; Zheng, H.; Qiu, H.; Lai, G. *J. Organomet. Chem.* **2008**, *693*, 3771.
[47] Fujiwara, T.; Yanai, K.; Shimane, K.; Takamori, M.; Takeda, T. *Eur. J. Org. Chem.* **2001**, 155.



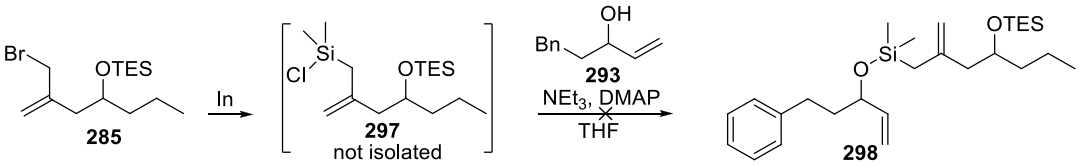
Scheme 69: Coupling of chlorosilane **292** and alcohol **293**

Allylchlorosilane **295** also could not be isolated using literature conditions, but the use of the reaction mixture for the coupling of allylchlorosilane **295** with the allylic alcohol **293** led to the desired product (Scheme 70). However, this reaction was not reproducible.



Scheme 70: Formation and coupling of allylchlorosilane **295** with alcohol **293**

This method was also tried on the TES-protected substrate **285** without success (Scheme 71). Indium reagents appear to be really sensitive toward steric hindrance[48] and seemed not suitable for more highly functionalised substrates. It was thus necessary to find a more reliable method for the synthesis of the chlorosilane.



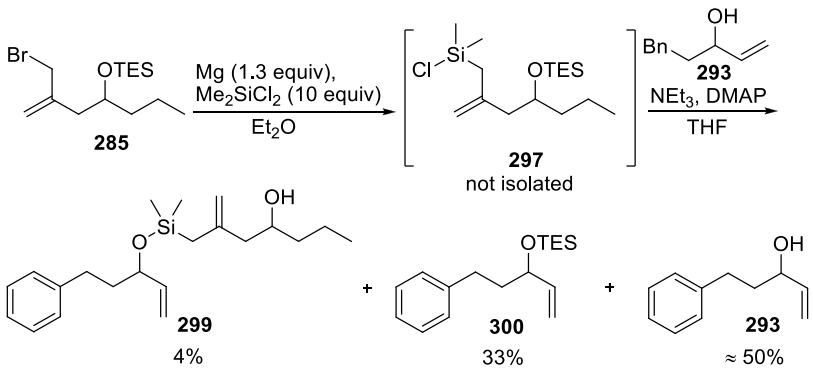
Scheme 71: Coupling with indium on substrate **282**

Use of magnesium

In the preliminary work done by Mehdi Boumediene, the use of magnesium allowed the formation of the desired chlorosilane in low yield. Seeing as the use of indium did not allow the formation of the silicon tether for our substrates, we then decided to investigate further the use of magnesium.

Forming the Grignard reagent and reacting it with 10 equivalents of dichlorodimethylsilane (to avoid diaddition) was tried and the reaction mixture was then added to a solution of alcohol **293**, along with triethylamine and DMAP (Scheme 72).

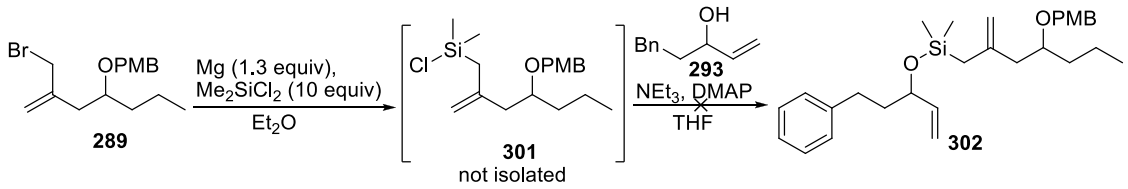
[48] Legros, J.; Meyer, F.; Coliboeuf, M.; Crousse, B.; Bonnet-Delpon, D.; Bégué, J.-P. *J. Org. Chem.* **2003**, *68*, 6444.



Scheme 72: Trial with magnesium on substrate **285**

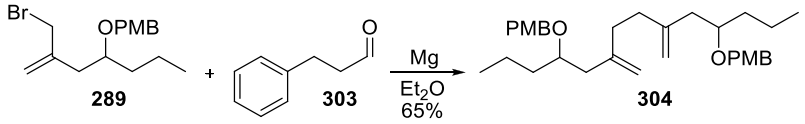
A small amount of the unprotected desired product **299** was obtained, along with the TES-protected alcohol **300** and unreacted alcohol **293**.

Treatment of PMB-protected substrate with magnesium and dimethyldichlorosilane was then tried in order to avoid the deprotection observed with the TES-protected substrate. However, none of the desired product was observed (Scheme 73).



Scheme 73: Trial with magnesium on substrate **289**

Reaction of the Grignard reagent with an aldehyde was then tried to verify if the Grignard reagent was forming. However, no addition product was observed and the Würtz coupling product **304** was obtained in 65% yield instead (Scheme 74).



Scheme 74: Coupling of Grignard reagent with an aldehyde

As a way to avoid Würtz coupling could not easily be found, the use of magnesium was not investigated further.

Use of zinc

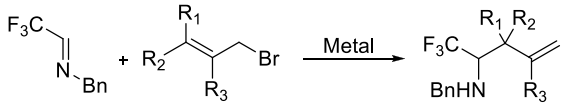
We then decided to investigate the use of zinc for the formation of the chlorosilane.

There are examples in the literature of addition of allylzinc reagents to aldehydes or imines.[48,49] It is also known that indium gives poor results when increasing steric hindrance and that zinc gives better results than magnesium and indium.

Bégué and co-workers[48] showed indeed that magnesium, indium and zinc give good results for the addition of an allylic bromide to an imine (Table 2). However, when

[49] Zhang, Y.; Jia, X.; Wang, J.-X. *Eur. J. Org. Chem.* **2009**, 2983.

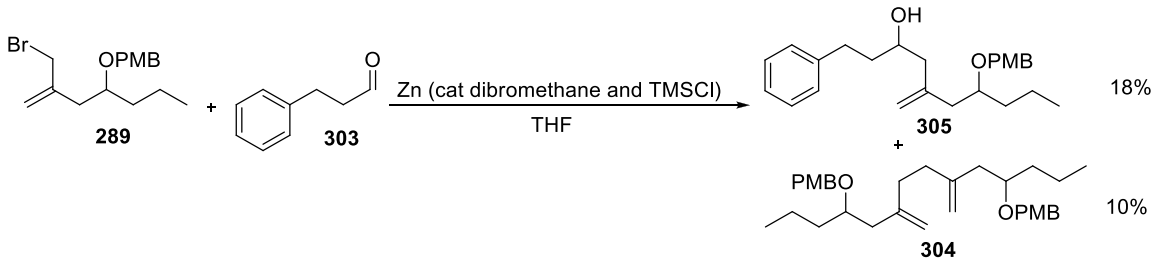
the steric hindrance is increased, only zinc produces good results. In the last entry, we can see that with a bromide substrate similar to ours, they get a good result.



Substrate	Metal	Time (h)	Yield (%)
$R_1 = R_2 = R_3 = H$	Mg (in Et_2O)	0.75	75
	In (in DMF)	1	96
	Zn (in DMF)	0.75	95
$R_1 = R_2 = Me$, $R_3 = H$	Mg (in Et_2O)	1	20
	In (in DMF)	24	Traces
	Zn (in DMF)	1	97
$R_1 = R_2 = H$, $R_3 = Me$	Zn (in DMF)	0.75	75

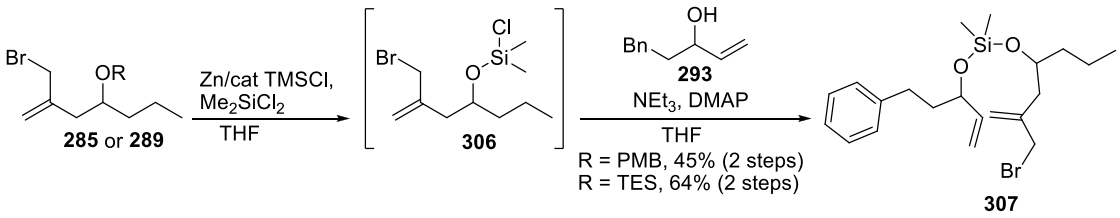
Table 2: Use of metals for the addition of allyl bromides to imines

Addition of an allylzinc reagent to dihydrocinnamaldehyde was then tried as a model reaction and the addition product was obtained in 18% yield, along with 10% of Würtz coupling product (Scheme 75).



Scheme 75: Coupling of zinc reagent with dihydrocinnamaldehyde

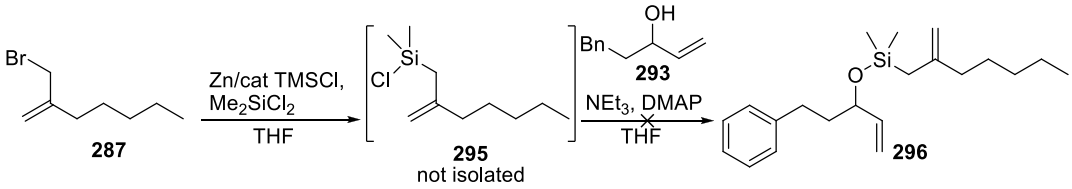
Reaction of the allylzinc species with dichlorodimethylsilane, followed by addition of the reaction mixture to a solution containing alcohol **293**, triethylamine and DMAP was then performed for both PMB and TES-protected substrates (Scheme 76).



Scheme 76: Trial with to form the silicon tether

Reactions of both substrates afforded the same product, which at first seemed to be the unprotected product **299** (see Scheme 72 for structure). However, the chemical shift of the CH_2, which was supposed to be linked to silicon, was too high and the peaks in the mass spectrum indicated that the product **307** was formed. Under the reaction conditions, the protecting group was cleaved, which led to the oxygen-silicon-oxygen tether product.

The same conditions were also tried on substrate **287**, but only the starting alcohol was recovered, which is in correlation with the fact that an alcohol was needed in order to form the oxygen-silicon-oxygen tether (Scheme 77).

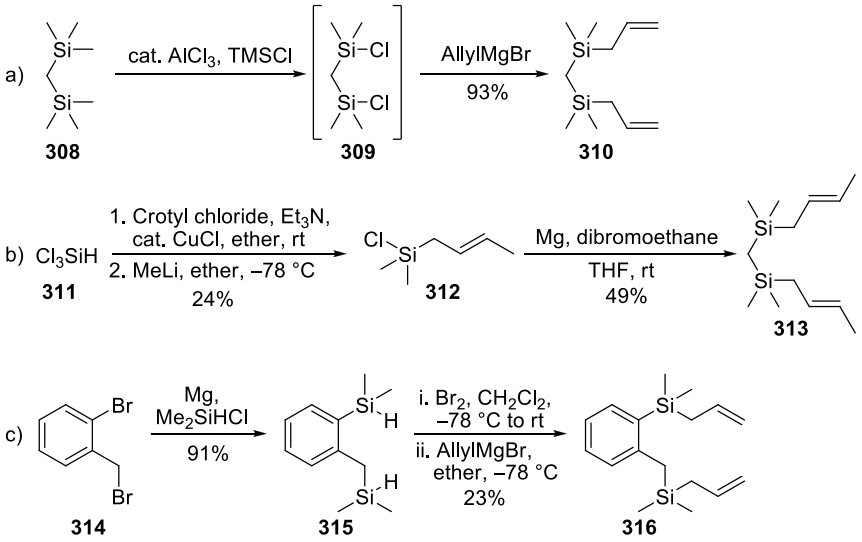


Scheme 77: Trial with zinc on substrate **287**

2.2.2 - Substrate synthesis using chlorination of hydrosilanes

The synthesis of the chlorosilane from the allyl bromide compound was problematic, and so we decided to look for other methods to form the silicon tether.

Shibato and co-workers[50] have reported various methods to synthesise chlorosilanes (Scheme 78).

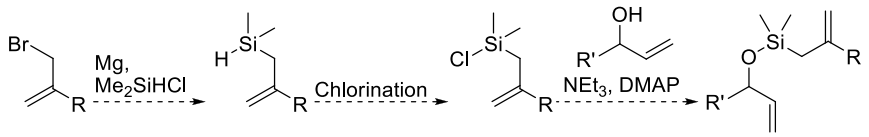


Scheme 78: Methods for the synthesis of chlorosilanes

In the first method, the chlorosilane is synthesised by aluminum chloride catalysed chlorination of the silane with chlorotrimethylsilane. This method was not investigated due to use of a strong Lewis acid, which might not be suitable for more sensitive substrate. In the second method, a cuprous chloride-catalysed condensation of trichlorosilane with (*E*)-crotyl chloride, followed by subsequent treatment with methyllithium was employed to synthesise the chlorosilane. This method required sensitive chlorosilanes to be isolated and carried through two steps. This method was also not investigated. The last method, however, seemed interesting, because it involved the synthesis of a hydrosilane, followed by bromination.

[50] Shibato, A.; Itagaki, Y.; Tayama, E.; Hokke, Y.; Asao, N.; Maruoka, K. *Tetrahedron* **2000**, *56*, 5373.

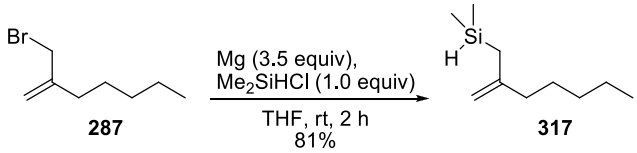
Hydrosilanes are more stable than chlorosilanes and can be purified using column chromatography. Examples of the synthesis of silanes[50,51] from alkyl bromides using magnesium are reported in the literature. The reaction also allows the use of one equivalent of chlorodimethylsilane, because there is no risk of diaddition.
We wanted, however, to avoid the use of bromine. It was then found in the literature that there are several methods for the chlorination of silanes.[52,53,54] The new envisaged method is shown in the following scheme (Scheme 79):



Scheme 79: Formation of silicon-tether *via* chlorination of hydrosilanes

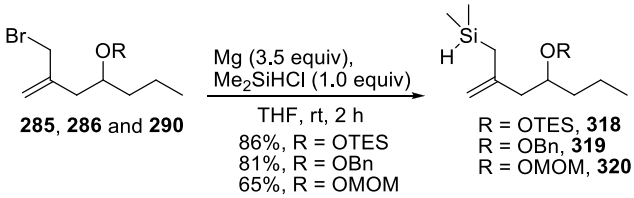
a. Synthesis of hydrosilanes

Formation of the hydrosilane from bromide compound **287** was attempted. However, a mixture of the desired product and the Würtz coupling product was obtained; the compounds were inseparable by column chromatography. After optimisation, it was found that slow addition of a solution of the allylic bromide to a solution of 3.5 equivalents of magnesium and one equivalent of chlorodimethylsilane allowed formation of the Würtz coupling product to be reduced to 9%. Silane **317** was then synthesised in 81% yield (Scheme 80).



Scheme 80: Synthesis of hydrosilane **316**

Applying the same conditions to substrates **285**, **286** and **290** allowed the formation of hydrosilanes **318**-**320** in good yields with no trace of by-products (Scheme 81).



Scheme 81: Synthesis of hydrosilanes **318-320**

[51] Robertson, J.; Hall, M. J.; Stafford, P. M.; Green, S. P. *Org. Biomol. Chem.* **2003**, *1*, 3758.
[52] Kunai, A.; Ohshita, J. *J. Organomet. Chem.* **2003**, *686*, 3.
[53] Savela, R.; Zawartka, W.; Leino, R. *Organometallics* **2012**, *31*, 3199.
[54] Pongkittiphan, P.; Theodorakis, E. A.; Chavasiri, W. *Tetrahedron Lett.* **2009**, *50*, 5080.

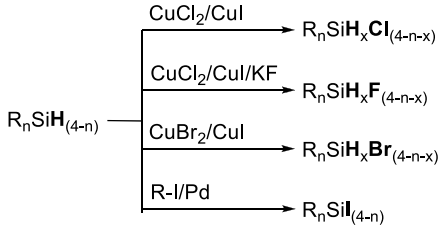
b. Chlorination of hydrosilanes

Several methods of chlorination of hydrosilanes are reported in the literature. Three methods were tried:

- Use of copper(II) chloride and copper(I) iodide.[52]
- Use of iron(III) chloride and acetyl chloride.[53]
- Use of palladium dichloride and hexachloroethane.[54]

Use of $CuCl_2$, CuI[52]

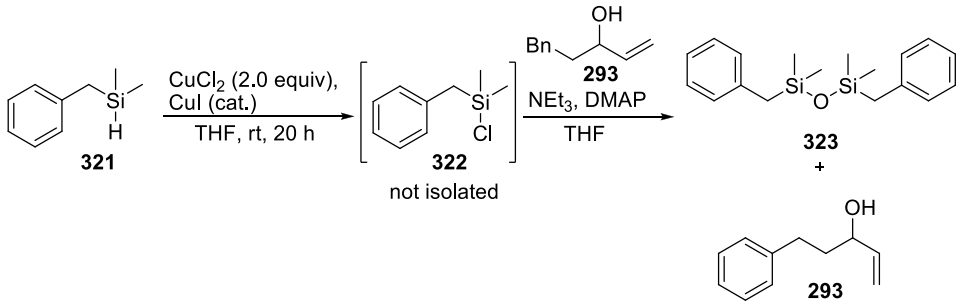
Ohshita and Kunai reported the synthesis of halosilanes from hydrosilanes (Scheme 82).



Scheme 82: Syntheses of halosilanes

The chlorination and bromination reactions involved oxidative halogenation of the hydrosilyl bond with copper(II) chloride or bromide in presence of a catalytic amount of copper iodide. This method allows the replacement of only one hydrogen by a halogen atom. Chlorosilanes can also be converted into fluorosilanes by treatment with potassium fluoride. The formation of iodosilanes, on the other hand, can be accomplished by Pd-catalysed hydrogen-iodine exchange. In this case, all hydrogen atoms are replaced by iodine atoms.

We thus decided to investigate the use of copper(II) chloride/copper iodide for the chlorination of silanes. Chlorination of benzyldimethylsilane using copper(II) chloride and copper(I) iodide was tried as a model reaction. Copper chloride and copper iodide were pre-dried at 100 °C under vacuum overnight and the reaction was carried out in THF at room temperature for 20 h. The chloride **322** was not isolated but was treated with the alcohol **293** to form the silicon tether directly. However, the desired product was not obtained. Only the alcohol **293** was recovered, along with the siloxane **323** (Scheme 83).



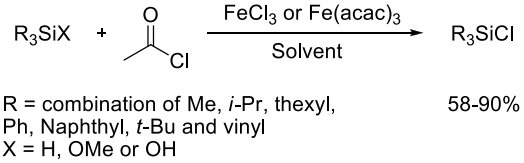
Scheme 83: Chlorination of hydrosilane **321** using copper dichloride and copper iodide

These results mean that the chlorosilane is formed, but under these conditions it cannot be isolated and only the siloxane is obtained. Schlenk filtration was also tried, but this only led to the formation of the siloxane **323**.

The detailed mechanism of this chlorination reaction is not clear. However, the facts that a trace amount of copper iodide catalyses the present reaction and two equivalents of copper chloride is necessary to replace one Si-H by Si-Cl suggests that a certain reactive species such as CuICl or CuI_2 might be formed and plays a role in the present reaction.

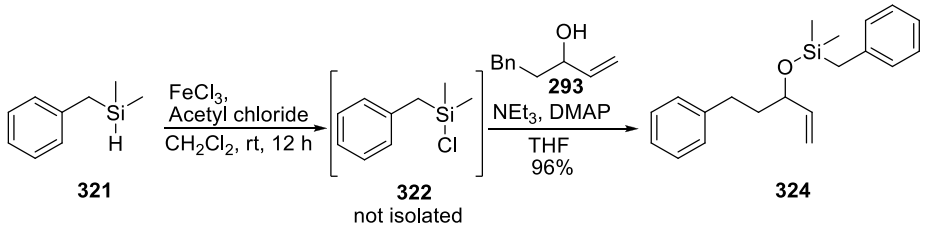
Use of $FeCl_3$ and acetyl chloride[53]

Leino and co-workers reported the iron-catalysed chlorination of silanes with iron(III) chloride and acetyl chloride (Scheme 84).



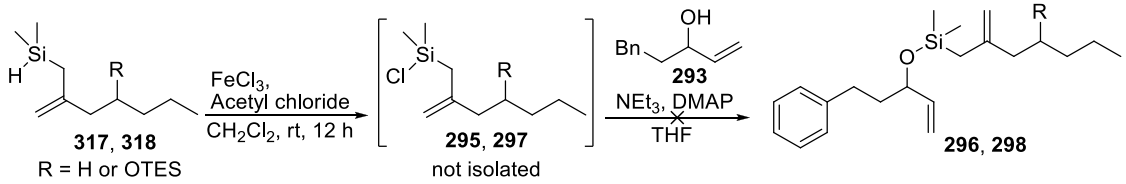
Scheme 84: Iron-catalysed chlorination of silanes

This method works on a large variety of silanes and involves the use of the common and cheap iron(III) chloride as a catalyst and acetyl chloride as a chlorine donor. Chlorination of benzyldimethylsilane using iron(III) chloride and acetyl chloride was tried as a model reaction. Reaction of benzyldimethylsilane in the presence of iron chloride and acetyl chloride in dichloromethane at room temperature for 12 h, followed by addition of the reaction mixture to a solution of alcohol **293**, triethylamine and DMAP, led to the desired product **324** in 96% yield (Scheme 85).



Scheme 85: Chlorination using iron chloride and acetyl chloride on compound **321**

The same conditions were tried on silanes **317** and **318**, but the desired products were not obtained (Scheme 86).

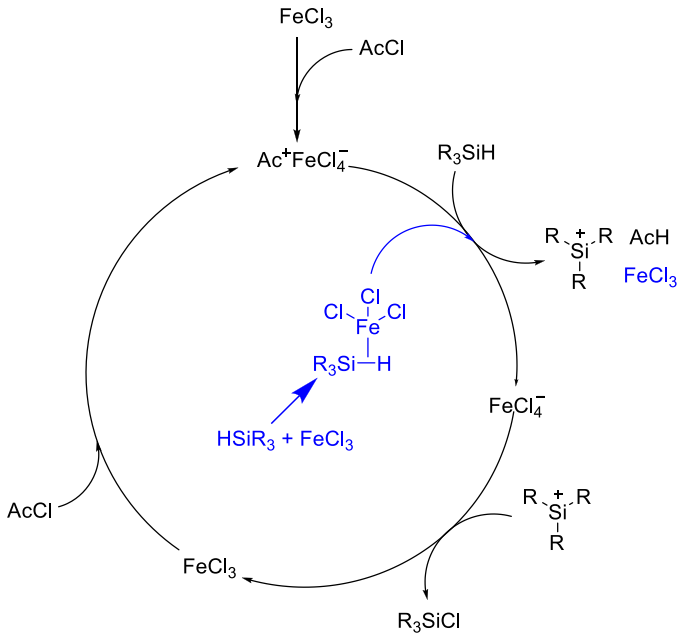


Scheme 86: Chlorination using iron chloride on substrates **317** and **318**

In the case of silane **318**, the TES-protected alcohol **300** (see Scheme 72 for structure) was obtained in 92% yield. These results might be due to the hydrochloric acid derived from acetyl chloride, which could cleave the TES-

protecting group. Cleavage of the silicon-alkyl bonds were also observed by Leino and co-workers under some reaction conditions.

The mechanism of this reaction is presented in the following scheme (Scheme 87):



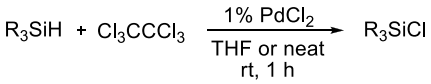
Scheme 87: Mechanism of the chlorination using iron chloride

The first step is the dissociation of the chlorine to form an acylium ion and [$FeCl_4^-$]. The next step is a nucleophilic attack of the silyl hydride to the acyl cation to form a silyl cation. This silyl cation is then chlorinated by [$FeCl_4^-$] and the iron(III) catalyst is regenerated. An alternative pathway is shown in blue. It involves the formation of an η^2-$HSiR_3$ Fe(IV) complex, which then releases the silyl cation.

Use of palladium dichloride and hexachloroethane[54]

The final method envisaged is the chlorination of hydrosilanes using palladium dichloride and a chlorinating agent.

Chavasiri and co-workers reported the Pd-catalysed chlorination of hydrosilanes with palladium chloride as catalyst and hexachloroethane as chlorinating agent (Scheme 88).

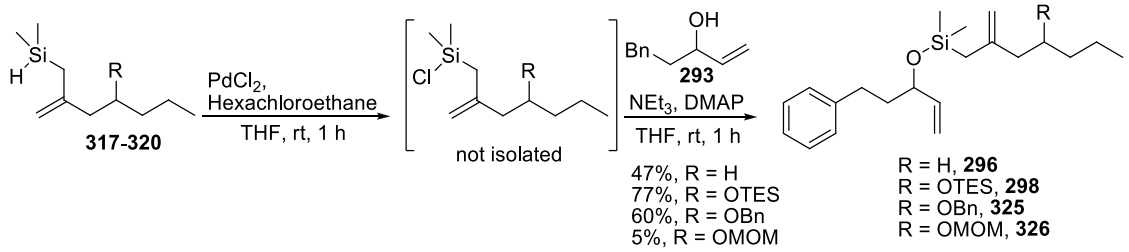


Scheme 88: Pd-catalysed chlorination of hydrosilanes

The advantages of this method are the following: low catalyst loading, low quantity of chlorinating agent required (0.25-0.50 equiv), low quantity of solvent required and short reaction time.

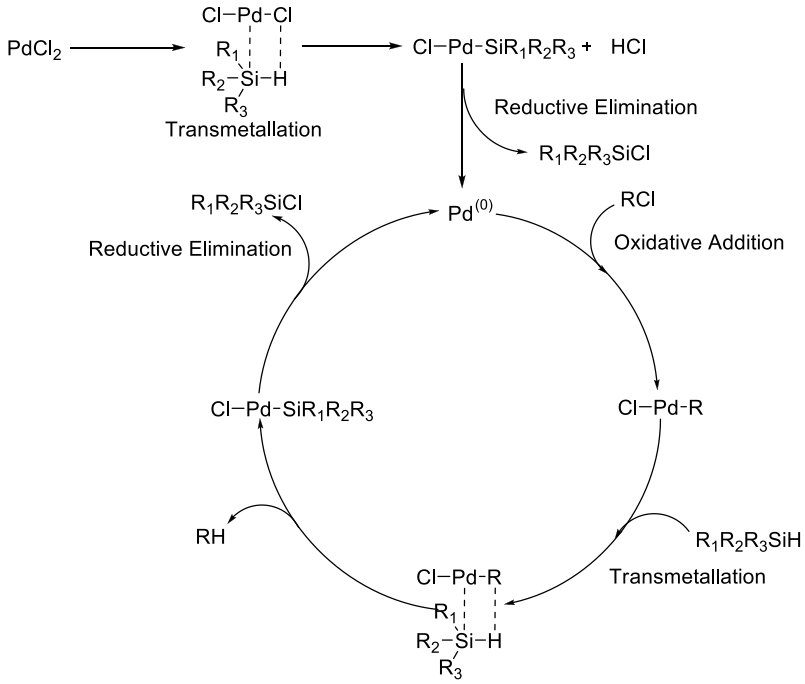
Treatment of silanes **317**-**320** with palladium dichloride and hexachloroethane in THF at room temperature for one hour, followed by addition of the reaction mixture to a solution of alcohol **293**, triethylamine and DMAP led to the desired alkoxysilanes in good yields (Scheme 89). Only substrate **320** gave a poor yield.

The MOM protecting group might have been too sensitive for the reaction conditions.



Scheme 89: Pd-catalysed chlorination and coupling on substrates **317-320**

The mechanism of the palladium-catalysed chlorination of silane is shown in the following scheme (Scheme 90):



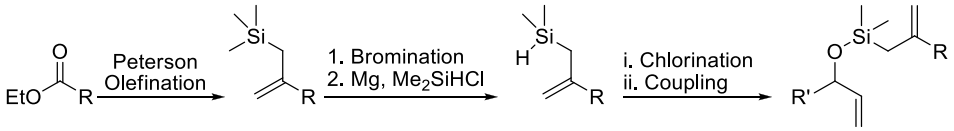
Scheme 90: Mechanism of the chlorination using palladium dichloride

The first step is a transmetallation of the hydrosilane with the palladium(II) chloride, forming the silylpalladium species and releasing HCl. Reductive elimination leads to the formation of the desired chlorosilane and Pd(0). Oxidative addition of the chlorinating agent leads to a palladium(II) species, which can again undergo a transmetallation with the silane. Further reductive elimination leads to the desired chlorosilane and Pd(0) is regenerated.

2.2.3 - Substrate synthesis involving a new Peterson reaction

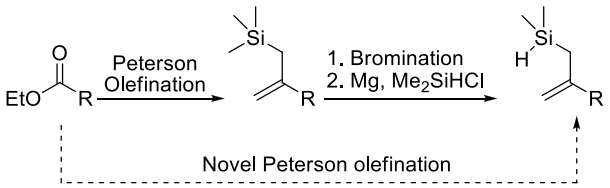
a. New Peterson olefination

An efficient method has been found to form the desired alkoxysilanes. This method is summarised in the following scheme (Scheme 91):



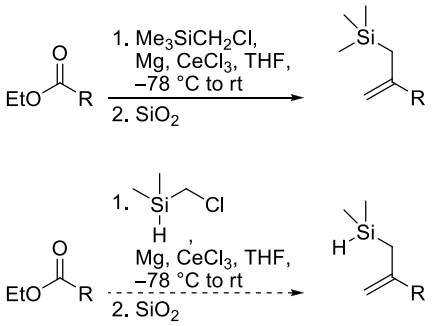
Scheme 91: Formation of silicon tether from esters

However, three steps are required to synthesise the hydrosilane from the ester. Moreover, an alkylsilane is formed by Peterson and that silane is then converted to a hydrosilane *via* a bromide derivative. We were thus interested to investigate the synthesis of the desired hydrosilane in one step by a novel Peterson olefination (Scheme 92).



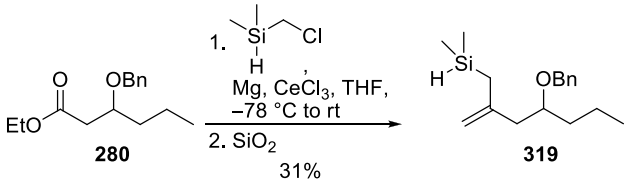
Scheme 92: New Peterson olefination

This novel Peterson olefination reaction would require the use of chloromethyldimethylsilane, which is commercially available from Sigma-Aldrich (Scheme 93).



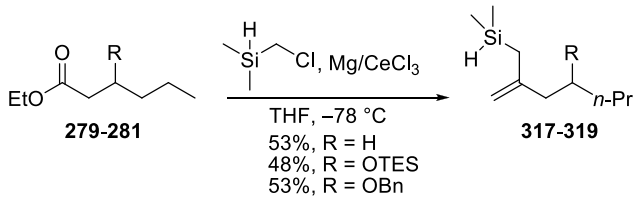
Scheme 93: Peterson olefination with chloromethyldimethylsilane

We decided to try the same conditions as previously used for Peterson olefination. A first try was performed on small scale on substrate **280** (Scheme 94).



Scheme 94: First trial of new Peterson olefination

To our delight, hydrosilane **319** was obtained. However, the yield was low. Due to formation of the Grignard being difficult on small scale, we decided to apply these same conditions on larger scale on substrates **279**-**281** (Scheme 95).



Scheme 95: Synthesis of silanes **317**-**319**

We were pleased to see that silanes **317**-**319** were obtained in acceptable yields. The only by-product observed was the unreacted intermediate **327** (Figure 7).

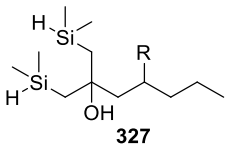
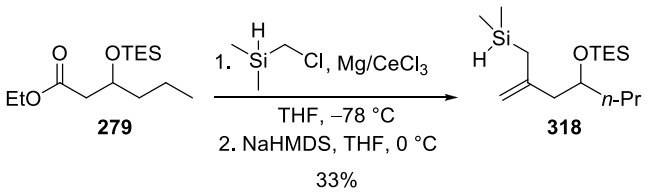


Figure 7: Intermediate **327**

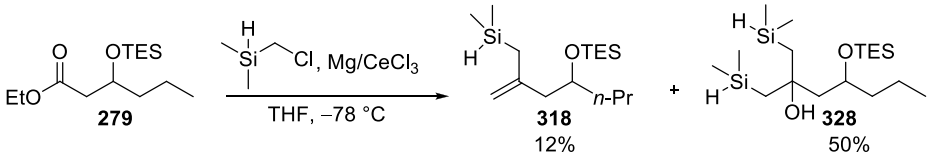
In the case of R = H, the moderate yield was attributed to the fact that this compound might be slightly volatile, because no by-products were observed. When R ≠ H, the moderate yield was due to the elimination process being incomplete. We then decided to try different methods for the elimination. First, we treated the crude mixture of silane **318** and the intermediate with NaHMDS (Scheme 96).



Scheme 96: Treatment with NaHMDS

No intermediate was observed after elimination. However, the desired product was only obtained in low yield. The use of NaHMDS seemed to generate unknown impurities as the crude mixture was very messy by NMR and TLC.

We decided then to separate the product and the intermediate after the first step and then try other conditions for the elimination on the intermediate. Treatment of ester **279** with the organocerium reagent, followed by work up and purification by column chromatography gave hydrosilane **318** in 12% yield and intermediate **328** in 50% yield (Scheme 97).

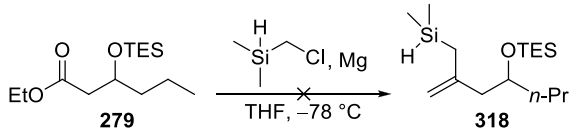


Scheme 97: Separation of product and intermediate

The moderate total yield of 62% was due to the addition of the organocerium reagent being incomplete. Organocerium reagents being very sensitive to

moisture, the conversion on the first step is really dependant of the dryness of all the reagents.

It is to be noted that without cerium, only the starting material is recovered (Scheme 98).



Scheme 98: Trial without cerium

With the isolated intermediate in hand, other conditions for the elimination reaction were explored (Table 3).

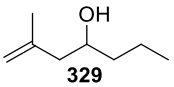
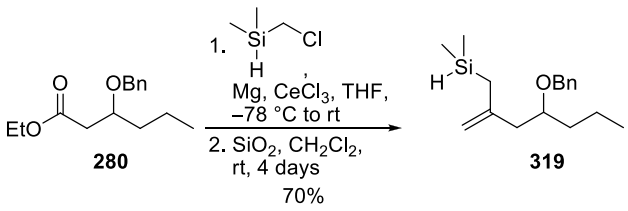
Conditions	Results
NaH, THF, rt, overnight	Messy mixture of starting material, product and impurities
$BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C, 1 h	 **329** 40%
SiO_2, CH_2Cl_2, rt, overnight	Full conversion to product

Table 3: Elimination trials

First, treatment with sodium hydride overnight was performed. A messy mixture of starting material, product and unknown impurities was obtained. The use of sodium hydride was not explored further.

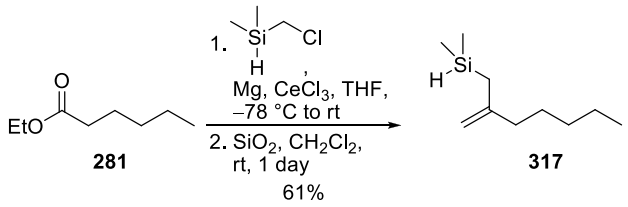
Intermediate **328** was then reacted with boron trifluoride etherate. The formation of the alkene was observed, but all the silyl bonds had been cleaved and compound **329** was obtained in 40% yield. These conditions were too harsh for substrates bearing a silyl group. Finally, the previously used conditions, which involved stirring the intermediate in dichloromethane with silica gel, were found to be the most efficient as overnight treatment with silica led to complete conversion into the desired silane. Each substrate was found to require a different time when stirring with silica gel. Moreover, when the elimination process with silica was complete, the hydrosilanes were found to be suitable for use without further purification.

Treatment of substrate **280** with the standard conditions for the first step, followed by stirring with silica over a period of four days led to complete conversion to the desired hydrosilane with an improved yield of 70% (Scheme 99).



Scheme 99: Stirring for four days for the elimination

Similarly, hydrosilane **317** was obtained in 61% yield by stirring with silica over one day (Scheme 100).



Scheme 100: Improved yield for silane **316**

In conclusion, hydrosilanes were successfully synthesised in one step by Peterson olefination. To our knowledge, it is the first exemple of the use of a Peterson olefination to synthesise hydrosilanes. The scope of this reaction will be explored further in the future.

b. Silane dehydrogenative coupling

The silicon tether was successfully installed using the Pd-catalysed chlorination of silane as the key step. We wanted, however, to improve the methodology even further by using a copper-catalysed silane dehydrogenative coupling to form the oxysilane. This coupling (described in the introduction) was used by Lee and co-workers in their synthesis of (−)-amphidinolide V and it allows the formation of the oxysilane in one step and good yield from the hydrosilane.

Various transition metal complexes have been reported as catalysts for silane dehydrogenative coupling. However, due to low activity, many catalysts are applicable to just a limited range of substrates. Some possess alkene hydrosilylation, hydrogenation, and isomerisation properties, which limit the scope to saturated alcohols. Reported catalysts include $RhCl(PPh_3)_3$,[55] $Rh_2(OCOC_4F_7)_4$,[56] $RuCl_2$(*p*-cymene)$_2$,[57] $Ru_3(CO)_{12}$[58] and $[(Ph_3P)CuH]_6$.[59]

Sawamura and co-workers reported the use of a copper-xantphos catalyst (Figure 8) as a very efficient catalyst for dehydrogenative silylation.[60]

---

[55] Ojima, I.; Kogure, T.; Nihonyanagi, M.; Kono, H.; Inaba, S. *Chem. Lett.* **1973**, 501.
[56] Doyle, M. P.; High, K. G.; Bagheri, V.; Pieters, R. J.; Lewis, P. J.; Pearson, M. M. *J. Org. Chem.* **1990**, *55*, 6082.
[57] Miller, R. L.; Maifeld, S. V.; Lee, D. *Org. Lett.* **2004**, *6*, 2773.
[58] Funatsu, A.; Kubota, T.; Endo, M. (Shin-Etsu Chemical Industry Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP2001-114788, 2001.
[59] (a) Lorenz, C.; Schubert, U. *Chem. Ber.* **1995**, *128*, 1267. (b) Mahoney, W. S.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 8818.
[60] Ito, H.; Watanabe, A.; Sawamura, M. *Org. Lett.* **2005**, *7*, 1869.

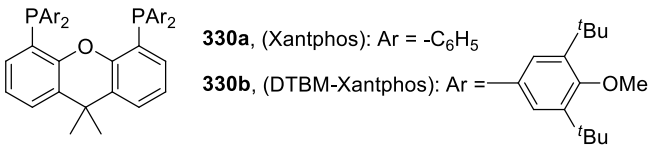
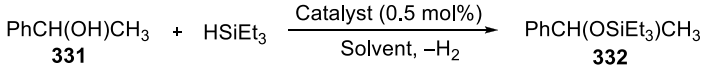


Figure 8: Copper-xantphos catalysts

Their comparative study between various catalysts for the silylation of alcohol **330** with triethylsilane is shown in the following table (Table 4):

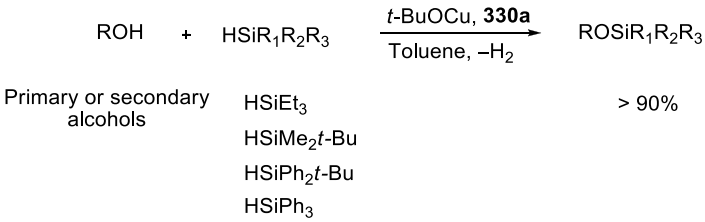


Entry	Catalyst	Solvent	Temp (˚C)	Time (h)	Yield (%)
1	*t*-BuOCu, **330a**	Toluene	24	1	99
2	$[(Ph_3P)CuH]_6$	Toluene	23	2	Trace
3	*t*-BuOCu, PPh_3	Toluene	24	2	1
4	*t*-BuOCu, dppe	Toluene	23	2	2
5	*t*-BuOCu, dppp	Toluene	22	2	34
6	*t*-BuOCu, dppf	Toluene	23	2	12
7	*t*-BuOCu, (*R*)-BINAP	Toluene	23	2	5
8	$RhCl(PPh_3)_3$	Toluene	22	2	Trace
9	$Rh_2(OCOC_4F_7)_4$	CH_2Cl_2	23	2	3
10	$RuCl_2$(*p*-cymene)$_2$	neat	25	2	6
11	$Ru_3(CO)_{12}$	neat	26	2	Trace

Table 4: Comparative study of catalysts

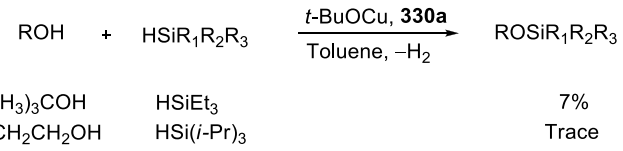
They found that the copper complex generated in situ by mixing *t*-BuOCu and xantphos resulted in really high activity in a short period of time. Almost no product was observed when using the commonly used $[(Ph_3P)CuH]_6$ catalyst. Replacing the ligand (entries 3-7) resulted in drastic loss of activity. Other previously reported catalysts (entries 8-11) also gave poor results under the same conditions.

This method gives good results with primary and secondary alcohols with various silanes (Scheme 101).



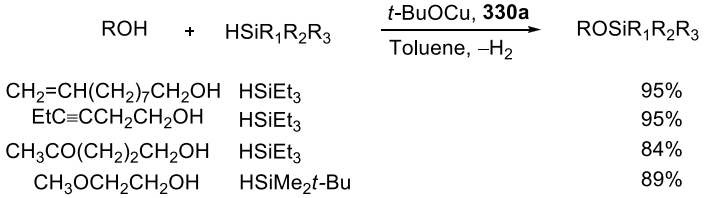
Scheme 101: Coupling with primary and secondary alcohols

The two limitations reported are that only traces of products were observed when using a tertiary alcohol or a bulkier silane (Scheme 102).



Scheme 102: Coupling with a tertiary alcohol and a bulky silane

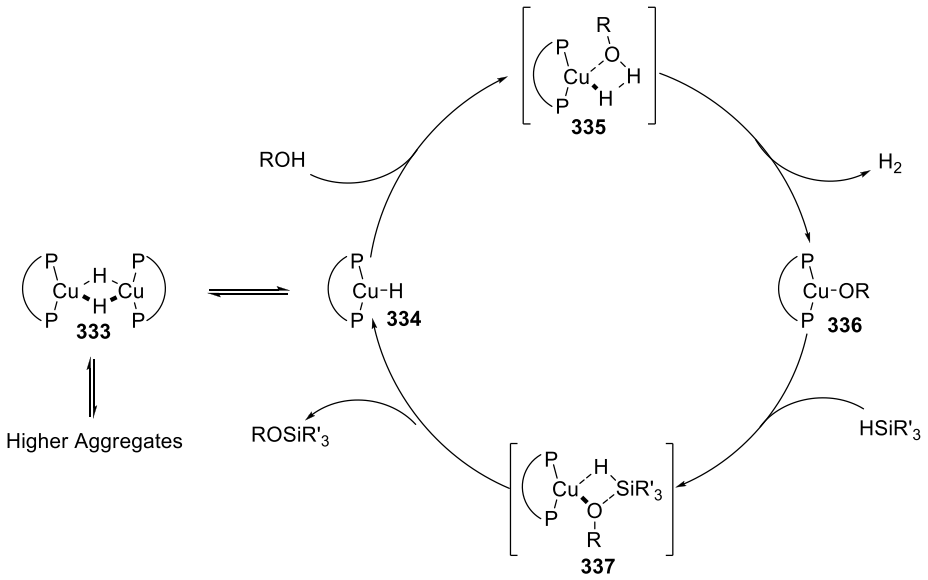
Good results were obtained with substrates containing an alkene or an alkyne. Moreover, no carbonyl hydrosilylation was observed and an alkoxy group, which is a potential coordination site for the metal center, showed no influence over the reactivity (Scheme 103).



Scheme 103: Coupling with alcohols containing other functional groups

This method also allows the selective silylation of a primary alcohol over a secondary alcohol even with rather small silyl groups such as $PhMe_2Si$ and Et_3Si groups.

The mechanism of this reaction is shown in the following scheme (Scheme 104):



Scheme 104: Mechanism of the reaction

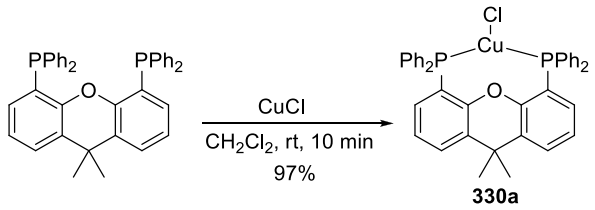
Mixing *t*-BuOCu, the phosphine and the hydrosilane leads to the formation of the copper(I) hydride, which is the active species. This species is in equilibrium with the dimer **333** and higher aggregates. The copper hydride then reacts with the alcohol through σ-bond metathesis forming the alkoxycopper **336** and releasing hydrogen. A second σ-bond metathesis with the hydrosilane produces the desired alkoxysilane and the copper hydride active species is regenerated.

The high efficiency of the xantphos ligand over other phosphines might be explained by the large P-Cu-P bite angle expected for xantphos, which could

exhibit an effect on the rate of the σ-bond metathesis between the copper hydride **334** and the alcohol.

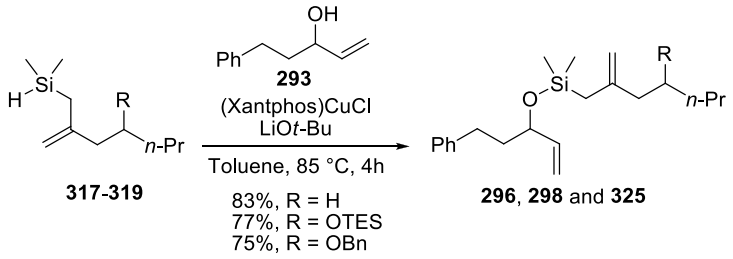
An asymmetric version of this reaction was also reported by Leighton and co-workers in their synthesis of dolabelide D, as detailed in the introduction (see Scheme 4).

The conditions we decided to use were the modified Sawamura conditions used by Lee and Volchkov in their total synthesis of amphidinolide V due to the similarity of the substrates used. In this modified version, (xantphos)CuCl is prepared and can be stored. Treatment *in situ* with lithium *tert*-butoxide gives the (xantphos)CuO*t*-Bu species, which then reacts with the silane to form the active copper hydride species. (xantphos)CuCl can be easily prepared by treating copper(I) chloride with xantphos (Scheme 105).



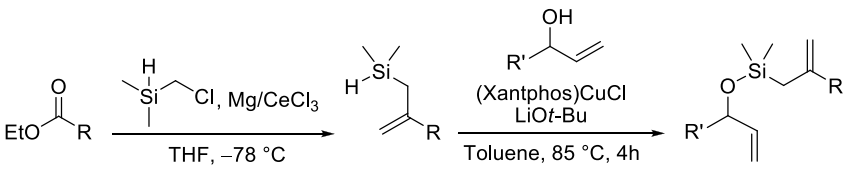
Scheme 105: Preparation of **330a**

With the pre-catalyst in hand, we decided to try this method on substrates **317**-**319**. To our delight, alkoxysilanes **296**, **298** and **325** were obtained in high yields using this one-step method (Scheme 106).



Scheme 106: Coupling on silanes **317**-**319**

In conclusion, new methodology was developed to synthesise alkoxyallylsilanes in two steps from the corresponding esters (Scheme 107).



Scheme 107: New methodology for the synthesis of alkoxyallylsilanes

2.3 - Ring-closing metathesis and tether cleavage

2.3.1 - Ring-closing metathesis

Now that the silicon tether link was formed, the ring closing metathesis could be tried on different substrates.

As already discussed in the introduction, olefin metathesis represents a powerful tool for the formation of carbon-carbon bonds. Ring-closing and ring-opening metathesis as well as cross metathesis were the subject of numerous studies.[61] Several catalysts have been developed such as molybdenum-based Shrock's catalyst,[62] as well as more stable ruthenium-based Grubbs'[63] and Hoveyda-Grubbs'[64] catalysts (Figure 9).

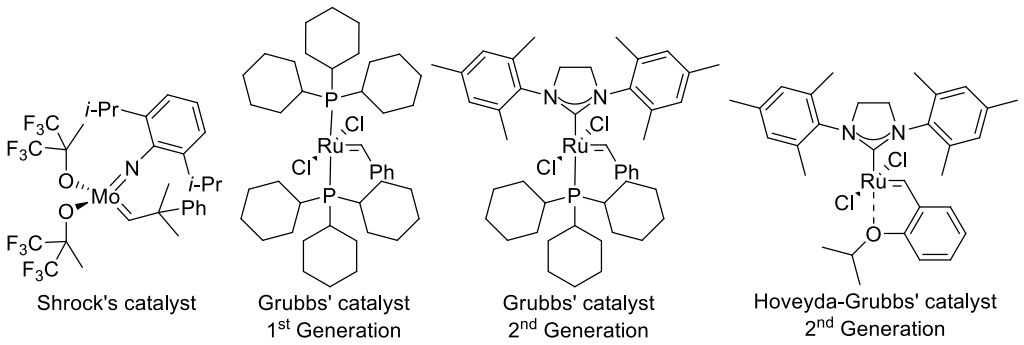


Figure 9: Metathesis' catalysts

Several variants of these catalysts have been developed, in particular chiral versions[65] (Figure 10).

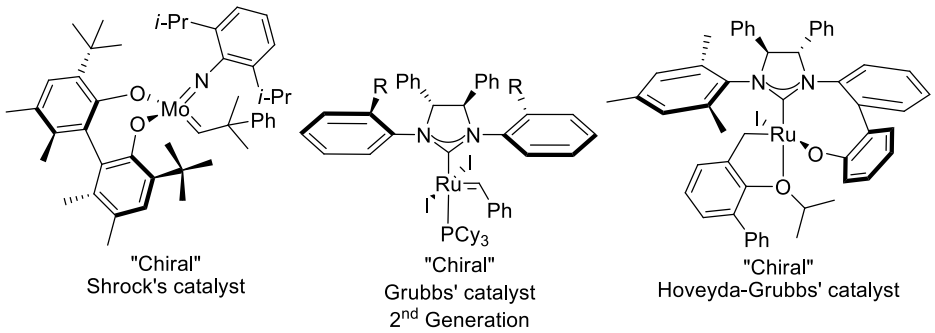


Figure 10: Chiral metathesis catalysts

---

[61] For reviews on olefin metathesis see: (a) Fürstner, A. *Angew. Chem.* **2000**, *112*, 3140; *Angew. Chem. Int. Ed.* **2000**, *39*, 3012. (b) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem.* **2005**, *117*, 4564; *Angew. Chem. Int. Ed.* **2005**, *44*, 4490 (c) Prunet, J.; Grimaud, L. *Metathesis in Natural Product Synthesis*; Cossy, J.; Arseniyadis, S.; Meyer, C.; Eds.; Wiley: New York, 2010. (d) Prunet, J. *Eur. J. Org. Chem.* **2011**, 3634.

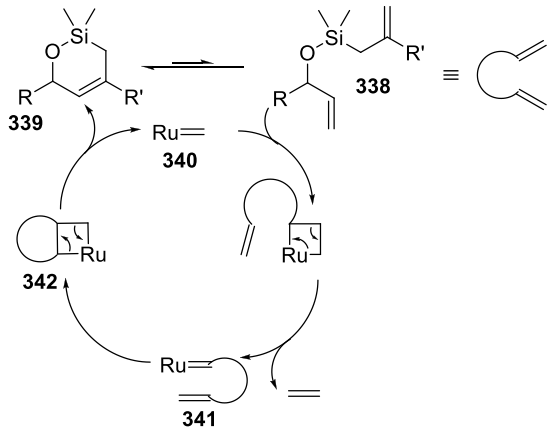
[62] (a) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875. (b) Bazan, G.C.; Khosravi, E.; Schrock, R.R.; Feast, W.J.; Gibson, V.C.; O'Regan, M.B.; Thomas, J.K.; Davis, W.M. *J. Am. Chem. Soc.* **1990**, *112*, 8378. (c) Bazan, G. C.; Oskam, J. H.; Cho, H.-N.; Park, L. Y.; Schrock, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 6899.

[63] (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew.Chem. Int. Ed. Engl.* **1995**, *34*, 2039. (b) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org.Lett.* **1999**, *1*, 953.

[64] Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.

[65] Hoveyda, H. A.; Zhugrakin, A. R. *Nature* **2007**, *450*, 243.

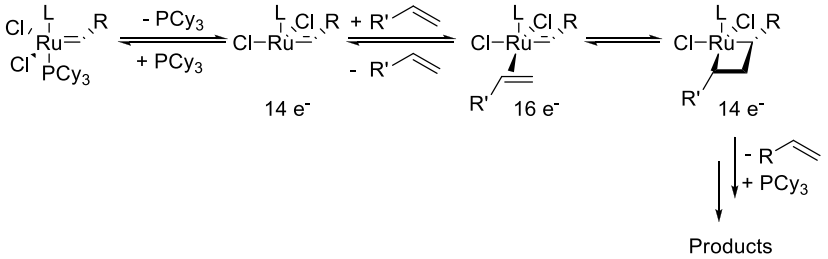
The mechanism of the metathesis reaction is shown in the following scheme (Scheme 108):



Scheme 108: Mechanism of the metathesis reaction

This reaction involves the ruthenium alkylidene **340**, which is formed from the catalyst after the first catalytic cycle. This ruthenium alkylidene undergoes the sequence of cycloaddition/cycloreversion with one of the terminal alkenes of compound **338**, which leads to the formation of the carbene **341**. After cycloaddition with the other terminal alkene, the ruthenacyclobutane **342** is obtained. A final cycloreversion reaction leads to the desired compound **339** and regenerates the ruthenium methylidene catalyst.

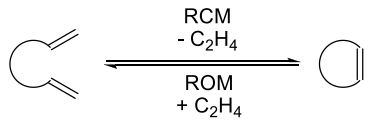
In the case of the catalysts based on ruthenium, the first step of the mechanism is the dissociation of the phosphine ligand, which generates a 14-electron carbene species (Scheme 109). This species coordinates to the olefin and leads through cycloaddition/cycloreversion to the ruthenium alkylidene.



Scheme 109: First step of the mechanism with ruthenium based catalysts

Since all the steps are in equilibrium, a mixture of olefins is obtained. It is then necessary to shift the equilibrium in the desired direction. In the case of the ring-closing metathesis, the forward process is entropically driven because RCM cuts one substrate molecule into two products. In this case, ethene is formed, which is volatile and the equilibrium will then be pushed toward the formation of the cycloalkene.

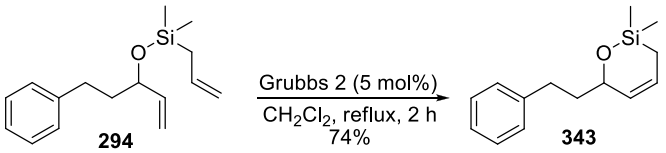
Depending on the desired reaction, the equilibrium can be pushed towards product formation by running the reaction under ethene or under a light vacuum (Scheme 110).



Scheme 110: Driving force of the reaction

In the case of the RCM, ethene is released. Running the reaction under vacuum can drive the reaction towards the formation of the cycloalkene. On the other hand, ring-opening metathesis (ROM) needs a flow of ethene to go in the forward direction.

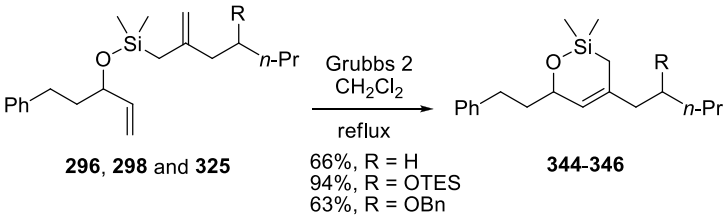
The metathesis reaction was first performed in dichloromethane with 5 mol% of second-generation Grubbs' catalyst on substrate **294** (Scheme 111).[66]



Scheme 111: RCM on substrate **294**

The cyclised product was obtained in 74% yield for substrate **294**. For compound **294**, the metathesis was also tried using first-generation Grubbs' catalyst and the reaction proceeds in 72% yield.

The RCM was then performed on substrates **296**, **298** and **325** and cyclised alkenes **344**-**346** were afforded in good yields (Scheme 112).



Scheme 112: Metathesis on substrates **296**, **298** and **325**

In the cases of R = H and OTES, the reaction was run with 5 mol% of catalyst during two and three hours respectively. In the case of R = OBn, the reaction had to be run during six hours with an addition of 2.5 mol% of catalyst every two hours.

For the substrates with a 1,1-disubstituted alkene, treatment with first-generation Grubbs' catalyst did not lead to the formation of the desired cycloalkene in satisfactory yield.

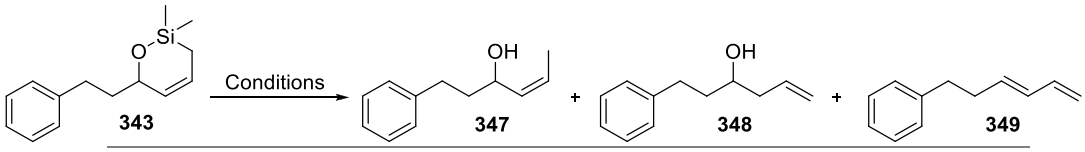
[66] Meyer, C.; Cossy, J. *Tetrahedron Lett.* **1997**, *38*, 4757.

2.3.2 - Tether cleavage trials

With the cyclised products in hand, we could work on the final step of the methodology, which is the tether cleavage by protodesilylation.

Very few examples of cleavage of a similar tether by protodesilylation have been reported in the literature. The closest example, already discussed in the introduction, has been reported by Li and Miller and a mix of potassium fluoride and potassium bicarbonate was used for this reaction (see Scheme 47).

We first decided to screen these reaction conditions, along with other conditions, on substrate **343**. The results are shown in the following table (Table 5):



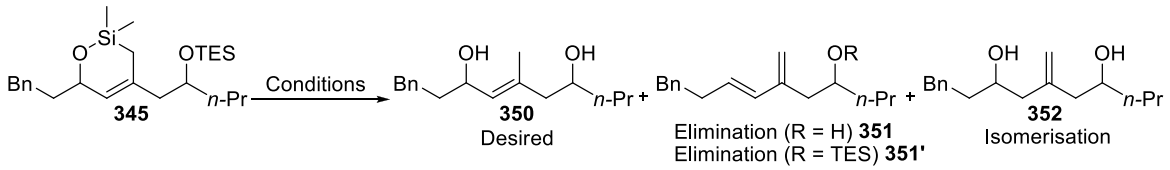
Conditions	Yield 347	Recovered 343	Yield 348	Yield 349
KF (4 equiv), $KHCO_3$ (4 equiv), MeOH/THF 1:1 0 °C, 30 min, rt, 2 h	/	100%	/	/
KF (10 equiv), $KHCO_3$ (10 equiv), MeOH/THF 1:1 0 °C, 30 min, rt, one day	/	100%	/	/
TBAF (6 equiv), DMF, 65 °C, 3h	/	/	26%	30%
TBAF (6 equiv), DMF, rt, 1 h	/	/	/	100%[a]
HF (5%) in CH_3CN (22 equiv), 1h at rt	/	/	/	100%[a]

[a] conversion

Table 5: Tether cleavage trials on **343**

The conditions reported by Li and Miller only led to recovery of the starting material in this case. Unfortunately, treatment with TBAF or HF led to eliminated product **349** and isomerised product **348**.

At this point, we hoped that the substrates containing the trisubstituted alkene would show a different reactivity profile and so we decided to screen various conditions on substrate **345**. The results are presented in the following table (Table 6):



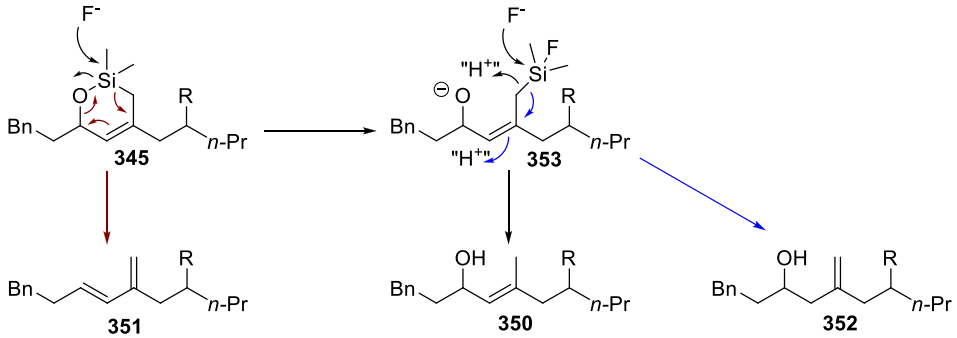
Conditions	Yield 350	Recovered 345	Yield 351	Yield 351'	Yield 352
KF, $KHCO_3$, MeOH/THF 1:1	16%	41%	/	/	/
HF (5%) in CH_3CN	/	/	60%	/	/
TBAF (2 equiv), THF	/	/	100%[a]	/	/
TBAF (2 equiv), THF, −30 °C to −10 °C	/	/	/	/	100%[a]
KF/18-crown-6, DMF	/	/	100%[a]	/	/
CsF, CH_3CN	/	100%	/	/	/
$Sc(OTf)_3$, toluene	/	/	/	100%[a]	/
CsF, DMSO, 90 °C	/	/	100%[a]	/	/
KHF_2 (3 equiv), DMF	/	Mixture[b]	/	/	/

[a] conversion. [b] Mixture of **345** and **351**

Table 6: Cleavage trials on substrate **345**

In this case, the conditions reported by Li and Miller allowed the formation of the desired product, but in very low yield. However, this reaction was not reproducible and all the attempts to improve the yield were unsuccessful. Treatment of compound **345** with various fluoride sources led to either the formation of the eliminated product or the isomerised product. Treatment with the Lewis acid scandium triflate led to the eliminated product in which the TES ether had not been cleaved.

Three different mechanisms seem to be in competition for this reaction (Scheme 113).



Scheme 113: Proposed mechanisms for the cleavage

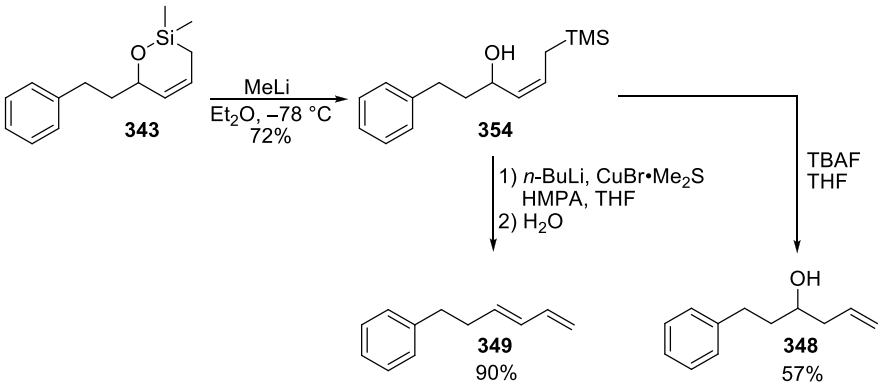
The attack of the fluoride anion might either trigger the elimination, which leads to compound **351**, or lead to the formation of intermediate **353**. From this intermediate, either direct protodesilylation or prime protonation can happen, forming the desired product and the isomerised product respectively.

We decided, at this point, to perform cleavage in two steps by opening of the silicon tether, followed by silyl cleavage in order to potentially avoid the elimination.

2.3.3 - Opening of the tether and other tether cleavage trials

Leighton and co-workers reported, in their total synthesis of dolabelide D, the opening of a silicon tether with methyllithium (see Scheme 4). Subsequent Brook-like rearrangement allowed the conversion of the silyl group into a methyl group.

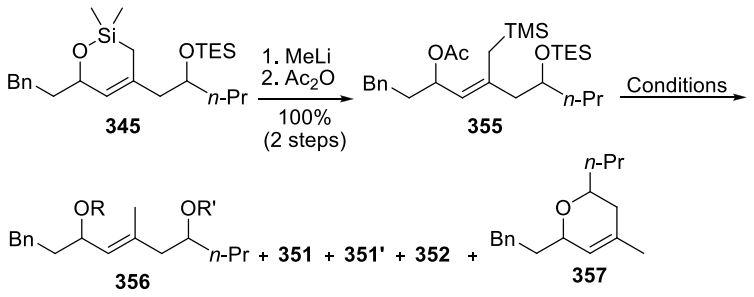
We first decided to try to open the silicon tether on substrate **343**, followed by the use of two different methods for the removal of the TMS group (Scheme 114).



Scheme 114: Tether removal trials on substrate **343**

Addition of methyllithium to **343** led to the allylic trimethylsilane **354** in 72% yield. A Brook-like rearrangement was then attempted using butyllithium, copper bromide and HMPA in THF, followed by hydrolysis. However, this only led to the elimination product **349** in 90% yield. Treatment of compound **354** with TBAF led to the isomerised product **348** in 57% yield.

We then envisaged protecting the secondary alcohol and then exploring several conditions for the cleavage of the silyl group. Methyllithium opening of substrate **345**, followed by protection of the alcohol as an acetate afforded the allylsilane in quantitative yield (Table 7). The different conditions used for the silyl group cleavage are reported in the following table (Table 7):



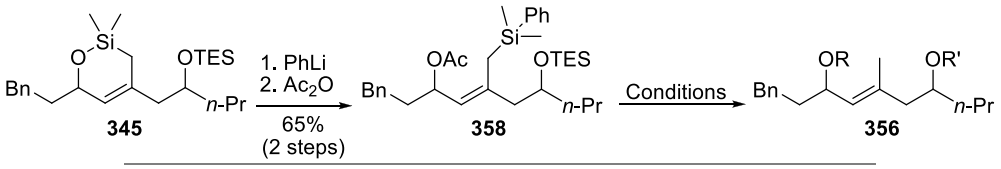
Conditions	Yield 356	Recovered 355	Yield 351	Yield 357
KF, $KHCO_3$, MeOH, THF	/	100%	/	/
KF (2 eq), 18-crown-6 (2 eq), DMF	/	/	Mixture[a]	/
TBAF (3 equiv), 0 °C	/	/	Mixture[a]	/
HF (5%) in CH_3CN (1 eq)	/	/	Mixture[b]	/
KF (2 eq), 18-crown-6 (0.5 eq), DMF	/	100%	/	/
$Sc(OTf)_3$, toluene	/	/	/	80%
$BF_3{\cdot}OEt_2$, −78 °C	/	/	Mixture[a]	/
KF, $KHCO_3$, MeOH, THF, 50 °C	/	/	100%[c]	/
AgF (3 eq), CH_3CN	/	/	100%[c]	/

[a] mixture of **351** and **351'**. [b] very messy mixture of different products. [c] conversion

Table 7: Cleavage trials on **355**

The conditions reported by Li and Miller led to no reaction. Treatment with various fluoride sources mainly led to elimination. Treatment with boron trifluoride etherate also led to elimination. When substrate **355** was subjected to treatment with scandium triflate, the unexpected cyclised product **357** was obtained.

Similarly, opening with phenyllithium instead of methyllithium, followed by protection of the alcohol as an acetate was carried out and substrate **358** was obtained in 65% yield (Table 8). We wanted to see if the substituents on the silyl group might influence the outcome of the cleavage. For this substrate, a few conditions were explored (Table 8):



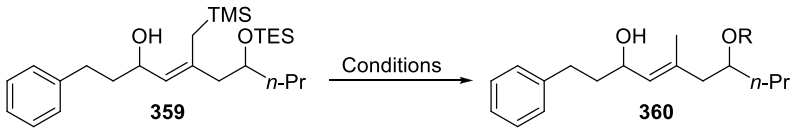
Conditions	Yield 356	Recovered 358	Yield 351
KF, $KHCO_3$ (15 eq), MeOH, THF, 1 day	/	40%[a]	35%
TBAF (3 eq), CuI (3 eq), THF, 1 h	/	Mixture[b]	/
CsF, DMSO, 90 °C, 5 h	/	/	100%[c]
KHF_2 (3 eq), DMF, 5 h	/	Mixture[b]	

[a] along with 15% of starting material without TES. [b] mixture of **358** and **351**. [c] conversion

Table 8: Cleavage trials on **358**

However, elimination was again the main product obtained with various fluoride sources.

Finally, having synthesised substrate **359** containing the unprotected alcohol, we decided to try some conditions also on that substrate. The results obtained are presented in the following table (Table 9):

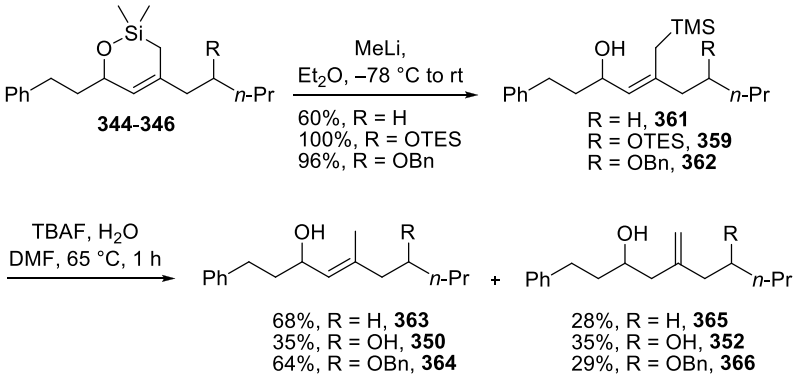


Conditions	Yield 350	Recovered 359	Yield 351	Yield 351'	Yield 352
TBAF (3 equiv), −10 °C	/	100%	/	/	/
$BF_3{\cdot}OEt_2$, −78 °C	/	/	/	100%[a]	/
$Sc(OTf)_3$, toluene	/	/	/	100%[a]	/
TBAF (6 equiv), DMF, 65 °C, 5 h	**25%**	/	27%	/	17%

[a] conversion

Table 9: Cleavage trials on **359**

Subjection of substrate **359** to Lewis acids led to elimination. However, when compound **359** was reacted with TBAF at −10 °C, no reaction was observed. TBAF usually led to quick formation of the eliminated product in the other cases, so we then decided to use stronger conditions. Running the reaction in DMF at 65 °C led to a mixture of the desired product, elimination product and isomerised product. At this point, we decided to add water in order to help the protodesilylation. The two-step procedure was performed on substrates **344**-**346** (Scheme 115).



Scheme 115: Two steps removal of tether on **344**-**346**

We were pleased to see that in the three cases, elimination was not observed and a 2:1 mixture of desired product to isomerised product was obtained. Only in the case of R = OTES, was a different ratio obtained. This might be due to the cleavage of the TES group being in competition with the cleavage of the allylsilane and influencing the outcome of the reaction. The geometry of the double has been assigned using nOe experiment (Figure 11).

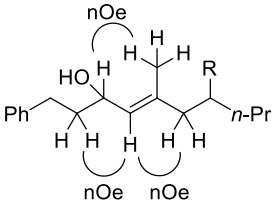


Figure 11: Determination of the geometry of the double bond by nOe experiment

Under the basic conditions created by TBAF, the alkoxide is formed, which disfavours the elimination. There still is competition between the formation of the desired product and the isomerised product, with the direct protodesilylation being favoured.

2.4 - Application of the methodology to the synthesis of an enantiomerically enriched substrate and synthesis of the C16-30 fragment of dolabelide C

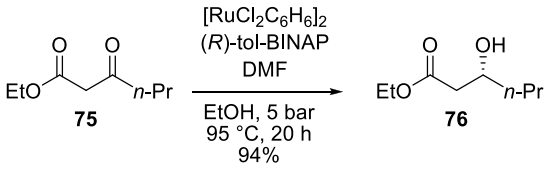
2.4.1 - Synthesis of an enantioenriched alkoxysilane

a. Synthesis of an enantioenriched silane and an enantioenriched alcohol

We decided, before applying the methodology to the synthesis of the C16-30 fragment of dolabelide C, to use it to couple an enantioenriched silane with an enantioenriched alcohol.

For this, we envisaged the synthesis of an enantioenriched silane, which could be used also for the synthesis of the C16-30 fragment of dolabelide C. We decided to synthesise an enantioenriched version of substrate **319** (see Scheme 81 for structure). Enantioselective synthesis was achieved by employing the asymmetric

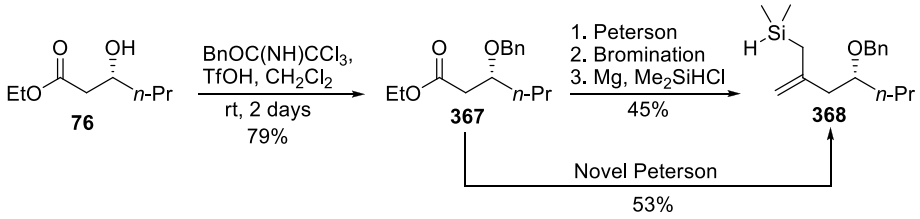
hydrogenation reaction developed by Noyori on ethyl 3-oxohexanoate.[67] Benzeneruthenium(II) chloride dimer, along with BINAP ligand allow the asymmetric reduction of ß-ketoesters to ß-hydroxyesters with enantiomeric excesses of over 98%.[68] Treatment of ethyl 3-oxohexanoate with the ruthenium catalyst, prepared in situ with benzeneruthenium(II) chloride dimer and (*R*)-tol-BINAP, allowed the formation of the desired ß-hydroxyester in 94% yield (Scheme 116).



Scheme 116: Noyori's asymmetric hydrogenation reaction

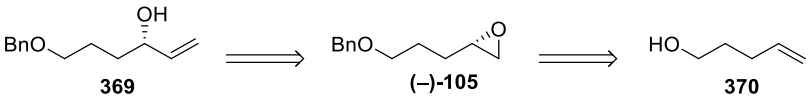
The optical rotation data matched that reported in the literature.

Having the enantioenriched ß-hydroxyester in hand, completion of the synthesis of the hydrosilane was achieved following the previously developed procedure. The silane can be obtained in four steps and 36% yield following the Peterson/bromination/Grignard addition sequence or in two steps and 42% yield employing the novel Peterson olefination method (Scheme 117).



Scheme 117: Synthesis of enantioenriched silane **368**

For the synthesis of the enantioenriched alcohol, we decided to form the allylic alcohol by opening an epoxide with a sulfur ylide (Scheme 118). We chose this method because **(−)-105** will be needed later on for the synthesis of the C1-15 fragment of dolabelide C and had already been synthesised by Aurélie Vincent. This epoxide can be obtained from commercially available 4-penten-1-ol.

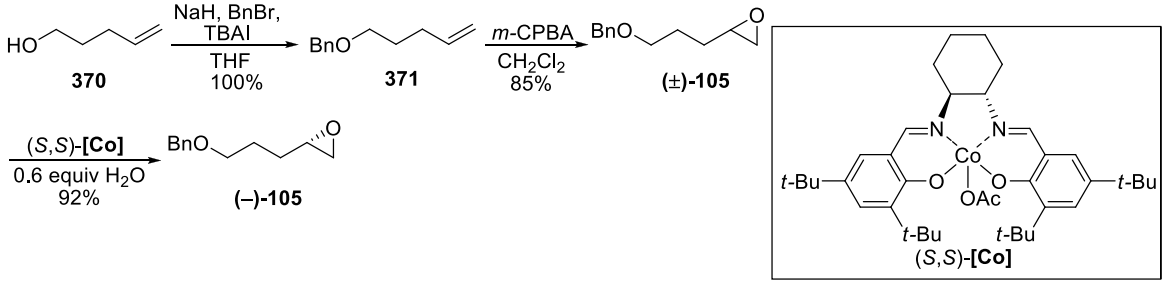


Scheme 118: Retrosynthesis of alcohol **375**

The synthesis of epoxide **(−)-105** is shown in the following scheme (Scheme 119):

[67] For review on asymmetric catalysis developed by Noyori and co-workers, see: Noyori, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 2008.

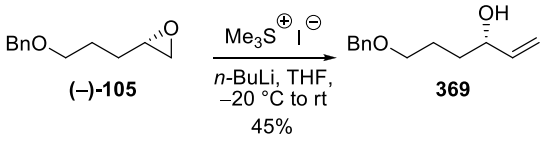
[68] Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856; Kitamura, M.; Tokunaga, M.; Ohkuma, T.; Noyori, R. *Org. Synth.* **1992**, *71*, 1; Noyori, R.; Kitamura, M.; Ohkuma, T. *Proc. Natl. Acad. Sci.* **2004**, *101*, 5356.



Scheme 119: Synthesis of epoxide **(–)-105**

Racemic epoxide **105** is obtained by benzylation of alcohol **370**, followed by epoxidation of the resulting benzyl ether **371** with *m*-CPBA. Epoxide **105** was then subjected to a Jacobsen kinetic resolution reaction[69] to afford the desired enantioenriched epoxide in 92% yield.

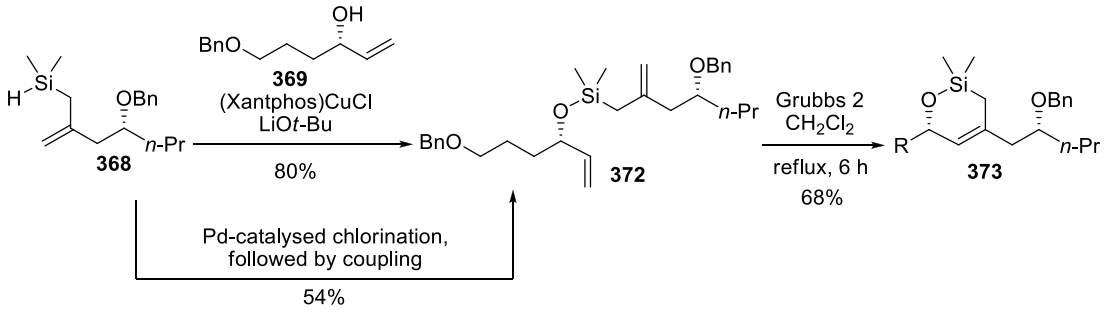
Finally, treatment of the enantioenriched epoxide with trimethylsulfonium iodide and *n*-butyllithium afforded allylic alcohol **369** in 45% yield (Scheme 120).



Scheme 120: Synthesis of alcohol **369** from **(–)-105**

b. Coupling, RCM and tether cleavage

With the two enantioenriched substrates in hand, coupling and RCM reactions were carried out (Scheme 121).

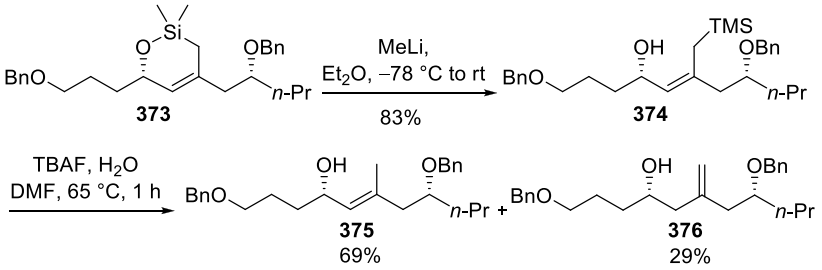


Scheme 121: Synthesis of substrate **373**

Using either the silane dehydrogenative coupling or the Pd-catalysed chlorination, followed by coupling, the oxysilane **372** was obtained in 80% and 54% yields, respectively. Subjection of diene **372** to RCM gave the desired silacycle in 68% yield.
Finally, the two-step procedure for the removal of the silicon tether led to the formation of the desired allylic alcohol **375** in 57% yield over two steps, along with the homoallylic alcohol **376** in 24% yield (Scheme 122).

---

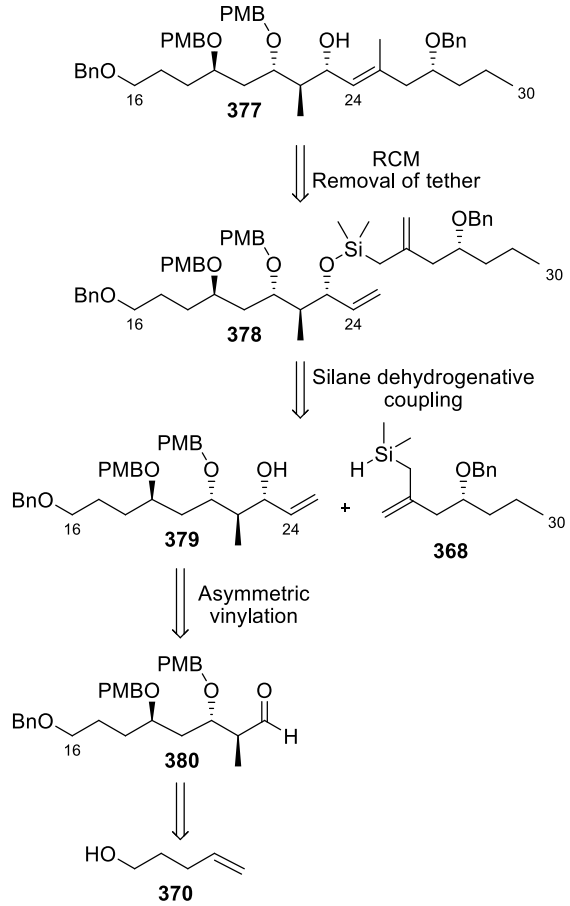
[69] (a) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307. (b) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (c) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (d) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421. (e) Nielsen, L. P. C.; Stevenson, C. P.; Blackmond, D. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 1360.



Scheme 122: Completion of the synthesis of **375**

2.4.2 - Application to the synthesis of the C16-30 fragment of dolabelide C

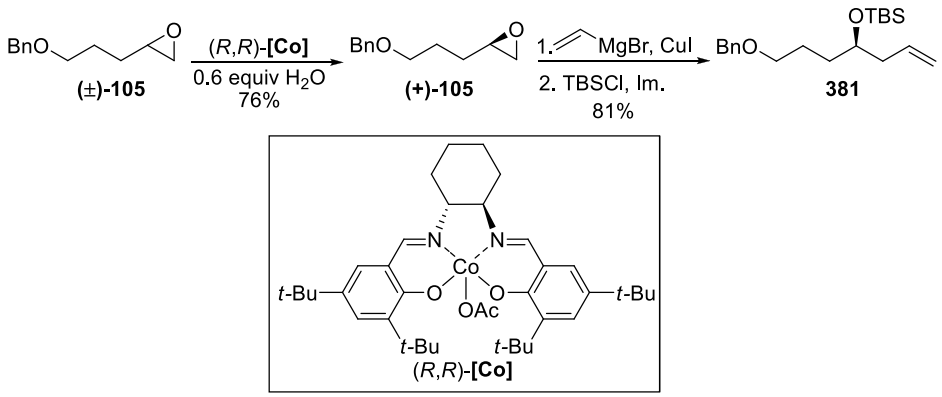
With the methodology successfully employed for the synthesis of the alcohol **375**, the application of the methodology to the synthesis of the C16-30 fragment of dolabelide C was undertaken. The retrosynthesis envisaged for the C16-30 fragment is shown in the following scheme (Scheme 123):



Scheme 123: Retrosynthesis of the C16-30 fragment

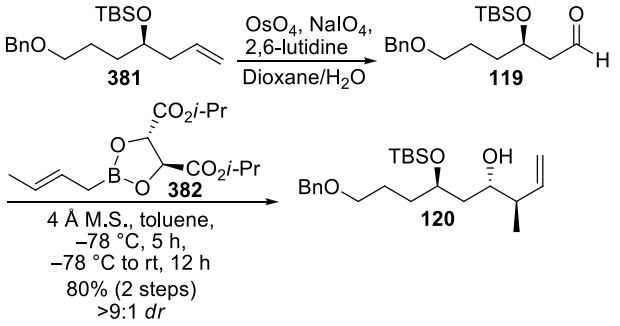
The C16-30 fragment could be obtained using the novel methodology by coupling the alcohol **379** with the hydrosilane **368**, followed by ring-closing metathesis and removal of the tether. Hydrosilane **368** had been prepared already. Alcohol **379** could be synthesised by an asymmetric vinylation reaction from aldehyde **380**, which had been synthesised in the Prunet group from 4-penten-1-ol.

The synthesis of substrate **381** was carried out following the procedure previously developed in the group for the synthesis of the C16-30 fragment,[16] using the following sequence of steps: Jacobsen kinetic resolution, cuprate opening of the epoxide and protection of the alcohol as a silyl ether (Scheme 124).



Scheme 124: Synthesis of substrate **381**

For the following two steps, we decided to use the improved procedure for oxidative cleavage of olefins developed by Jin and co-workers,[70] followed by Roush crotylboration[71] for their ease of use instead of ozonolysis and Duthaler crotylation[72] (Scheme 125). Substrate **120** was obtained in 80% yield and with a diastereomeric ratio of greater than 9:1 using this method, as opposed to a 79% yield and a diastereomeric ratio of greater than 95:5 for the ozonolysis/Duthaler crotylation sequence.



Scheme 125: Synthesis of alcohol **120**

The improved procedure for the oxidative cleavage of olefins developed by Jin and co-workers involves the use of 2,6-lutidine as an additive to increase the yield of the reaction. They found that 2,6-lutidine helps to suppress the formation of α-hydroxy ketone side products. It accelerates the rate of the reaction and can also be used as a weak base to neutralise the acid generated in the reaction and so prevent the cleavage of acid-labile protecting groups.

[70] Yu, W.; Mei, Y.; Kang, Y.; Hua, Z.; Jin, Z. *Org. Lett.* **2004**, *6*, 3217.
[71] Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.
[72] Hafner, A.; Duthaler, R. O.; Marti, R.; Rhis, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321.

There exist several reagents for the asymmetric crotylation of aldehydes, using different metals.[73]

The most commonly used are the following ones:

- The ones derived from boron such as Brown crotylboranes[74] and Roush crotylboronates[71]
- The crotyltitanates studied by Hoppe[75] and Duthaler[72]
- The crotylstannanes developed by Keck[76]
- The crotylsilanes developed by Leighton[77] and Panek[78]

These reagents can be regrouped in three types (Table 10).[73]

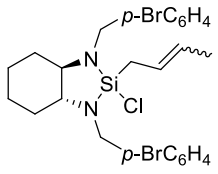
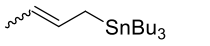
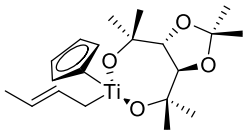
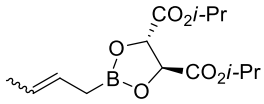
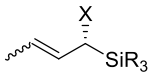
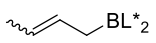
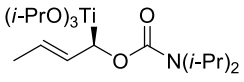
Type I reagents	Type II reagents	Type III reagents
 Leighton crotylsilanes	 Keck crotylstannanes	 Duthaler crotyltitanates
 Roush crotylboronates	 Panek crotylsilanes	
 Brown crotylboranes		
 Hoppe crotyltitanates		

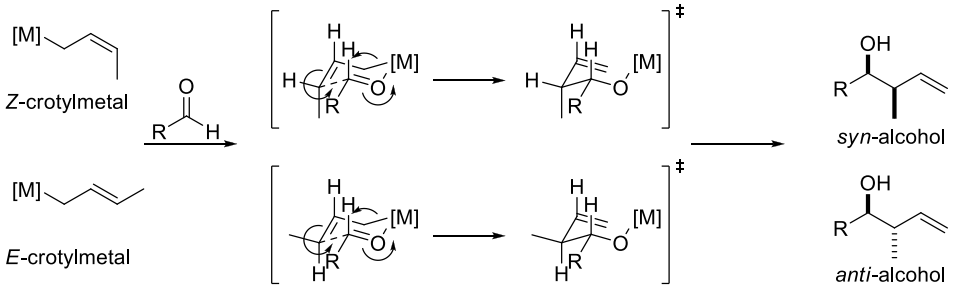
Table 10: Reagents for asymmetric crotylation

The characteristics of the different types of reagents are summarised below:

Type I

- *Syn*/*anti* ratio of products reflects the *Z*/*E* ratio of crotylmetal reagent
- Reaction takes place *via* a closed chair-like transition state (Scheme 126)

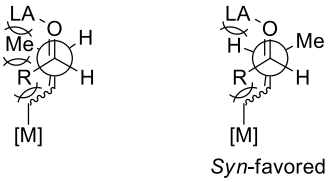
[73] Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH : Weinheim 2000, chapitre 10; Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH : Weinheim 2000, chapitre 11.
[74] Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1989**, *54*, 1570.
[75] Hoppe, D.; Zschage, O. *Angew. Chem. Int. Ed.* **1989**, *28*, 69.
[76] Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889.
[77] Burns, N. Z.; Hackman, B. M.; Ng, P. Y.; Powelson, I.A.; Leighton, J. L. *Angew. Chem. Int. Ed. Engl.* **2006**, *45*, 3811.
[78] Masse, C. E.; Panek, J. S. Chem. Rev. 1995, 95, 1293-1316; Hu, T.; Takenaka, N.; Panek, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 12806.



Scheme 126: Transition states for type I

Type II

- *Syn*-selective products are generated regardless of geometry of crotylmetal reagent
- Undergo Lewis acid catalysis
- Reaction occurs *via* open transition state (antiperiplanar TS proposed by Yamamoto[79])(Scheme 127)

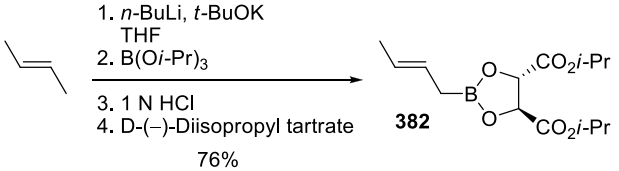


Scheme 127: Transition states for type II

Type III

- *Anti*-selective products are generated regardless of geometry of crotylmetal reagent
- Crotylmetal reagent is generated *in situ* and equilibration gives more stable *E*-isomer
- Reaction occurs *via* closed chair-like transition state

We decided to use the Roush crotylboronate reagent as it is relatively easy to make and easy to use. The synthesis of the crotylboronate is shown in the following scheme (Scheme 128):



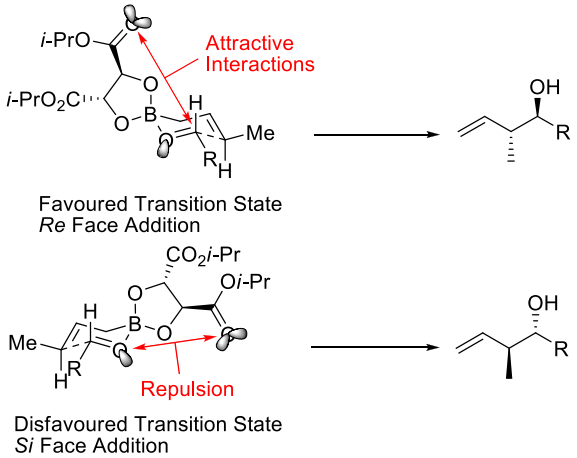
Scheme 128: Synthesis of compound **382**

The crotylboronate **382** was synthesised from *trans*-2-butene in 76% yield. Deprotonation of *trans*-2-butene using Schlosser base,[80] followed by addition of

[79] Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **2005**, *102*, 7107.
[80] Schlosser, M.; Desponds, O.; Lehman, R.; Moret, E.; Rauchschwalbe, G. *Tetrahedron* **1993**, *49*, 10175.

triisopropyl borate and hydrolysis of the resulting boronate led to the boronic acid. Treatment of the boronic acid with D-(−)-diisopropyl tartrate, which was synthesised from D-(−)-tartaric acid, led to crotylboronate **382**.

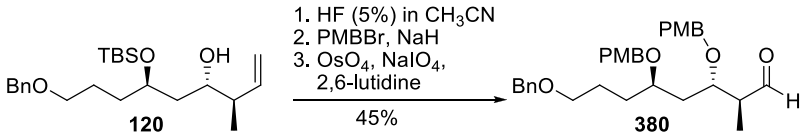
The selectivity of the crotylboration reaction is explained in the following scheme (Scheme 129):[81]



Scheme 129: Selectivity of the crotylboration reaction

In the *Re* face addition, there is an attractive interaction between the lone pair of the oxygen atom of the ester carbonyl and the carbon atom of the aldehyde. In the *Si* face addition, there is a repulsion between the lone pair of the oxygen atom of the ester carbonyl and the lone pair of the oxygen atom of the aldehyde.

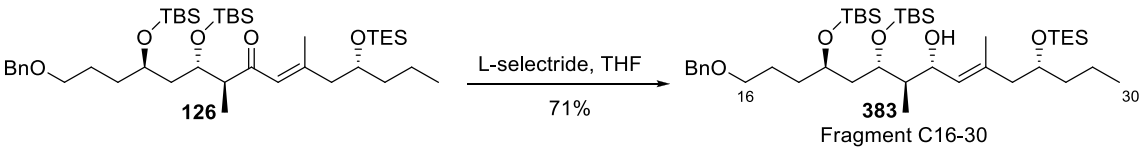
Aldehyde **380** was then synthesised in three steps with a 45% yield using the following sequence of steps: silyl cleavage with a 5% solution of hydrofluoric acid in acetonitrile, protection of the alcohols as PMB ethers and oxidative cleavage of the olefin (Scheme 130).



Scheme 130: Synthesis of aldehyde **380**

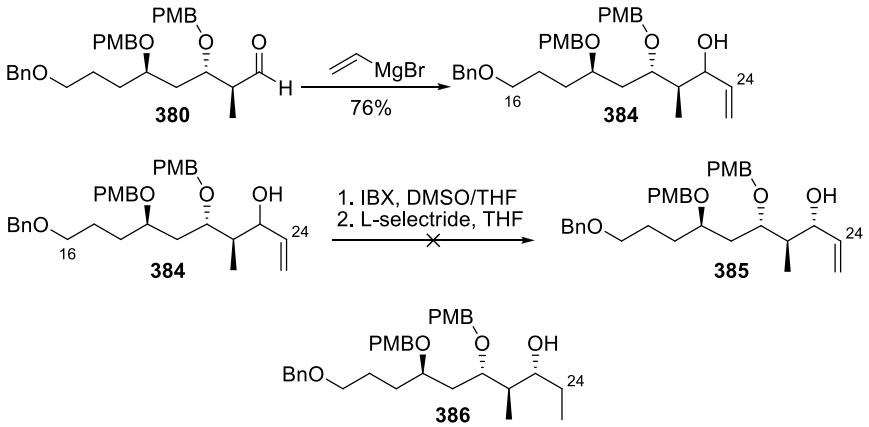
We envisaged for the next step to install the stereochemistry at carbon C23 *via* an enantioselective vinylation. Several groups reported the enantioselective addition of vinyl reagents to aldehydes.[82,83,84,85] However due to a lack of time, we decided to try a three-step sequence to synthesise the allylic alcohol with the right stereochemistry: addition of vinylmagnesium bromide to obtain a mixture of diastereomers, oxidation of the allylic alcohol to the enone and diastereoselective reduction with L-selectride.
The previous synthesis of the C16-30 fragment in the group involved the diastereoselective reduction of an enone at a late stage (Scheme 131).

[81] Roush, W. R.; Haltermann, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294.
[82] Lumbroso, A.; Cooke, M. L.; Breit, B. *Angew. Chem. Int. Ed.* **2013**, *52*, 1890.
[83] Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1988**, *29*, 5645.
[84] Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1991**, *32*, 5777.
[85] Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593.



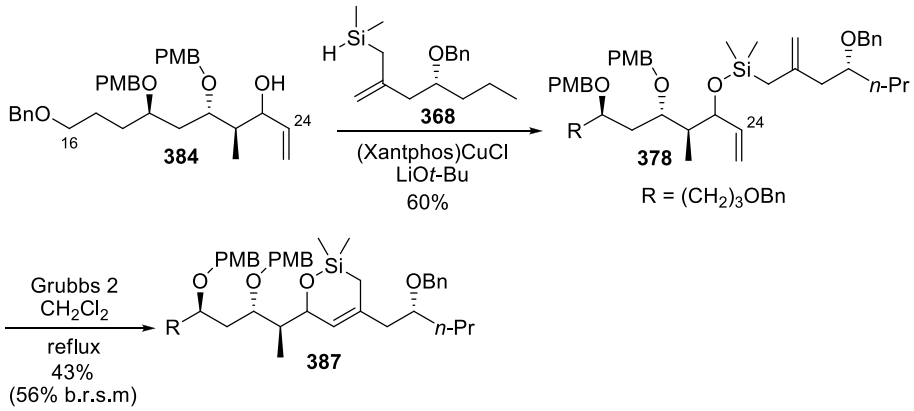
Scheme 131: Diastereoselective reduction of enone **126**

Addition of vinylmagnesium bromide to aldehyde **380** gave the allylic alcohol **384** in 76% yield as a 1:1 mixture of diastereomers (Scheme 132). The alcohol was then subjected to the same conditions that had been used by Marie-Gabrielle Braun. However, the desired product was not obtained, but alcohol **386** was isolated as the only product (Scheme 132). In this case, the olefin being less hindered led to the alkene being reduced along with the ketone.



Scheme 132: Formation of allylic alcohol **384**

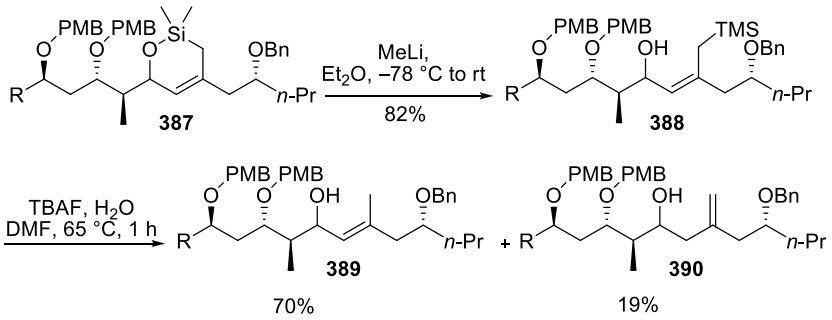
We then decided to use this method at a late stage in the synthesis as previously described. Alcohol **384** was subjected to silane dehydrogenative coupling with hydrosilane **368**, followed by RCM of **378** using the Grubbs second-generation catalyst (Scheme 133).



Scheme 133: Synthesis of silacycle **387**

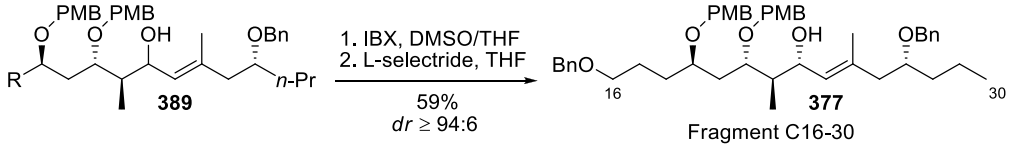
Oxysilane **378** was obtained in 60% yield. The allylic alcohol partner being more hindered than the model substrates used before, this substrate might require an increased reaction time in order to obtain a better yield. Similarly, probably due to the steric hindrance around the alcohol, the ring-closing metathesis only afforded the desired product in 43% yield even when using 18 mol% of catalyst and running the reaction for three days.

The two-step procedure for the tether cleavage afforded alcohol **389** in 57% yield, along with isomerised product **390** in 16% yield (Scheme 134). These results match the results obtained on model substrates.



Scheme 134: Tether cleavage on substrate **387**

Finally, oxidation of **389** with IBX, followed by diastereoselective reduction using L-selectride afforded the C16-30 fragment of dolabelide C in 59% yield with a diastereomeric ratio of greater than 94:6 (Scheme 135).

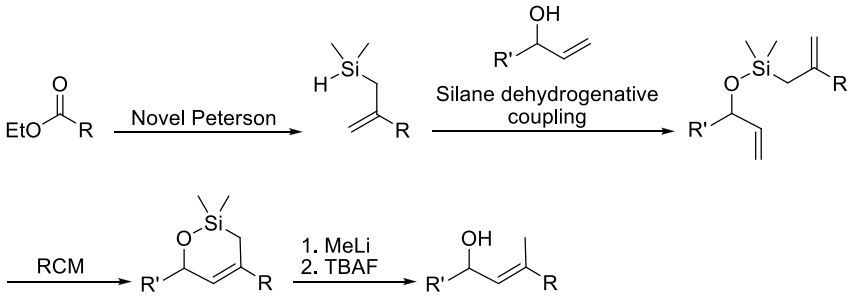


Scheme 135: Completion of the synthesis of the C16-30 fragment of dolabelide C

The C16-30 fragment of dolabelide C was obtained from 4-penten-1-ol in seventeen steps and 1.3% overall yield for the longest linear sequence.

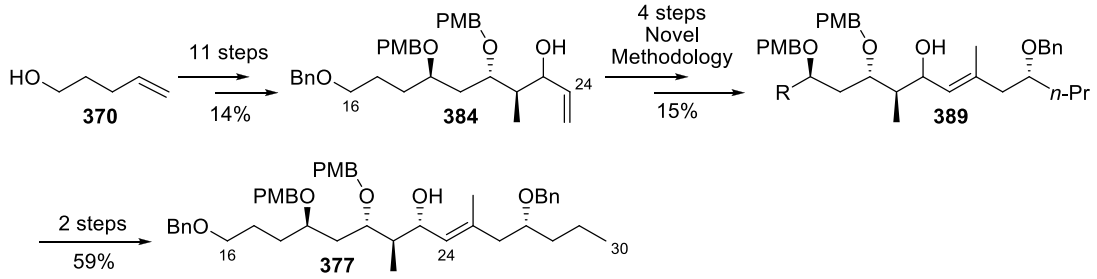
2.5 - Conclusions

New methodology has been developed in order to synthesise trisubstituted alkenes flanked with an allylic alcohol (Scheme 136). This method involves a temporary silicon tether ring-closing metathesis reaction and makes use of a novel Peterson olefination reaction and a silane dehydrogenative coupling to install the silicon tether.



Scheme 136: Newly developed methodology

This methodology has been applied successfully to the synthesis of the C16-30 fragment of dolabelide C (Scheme 147).

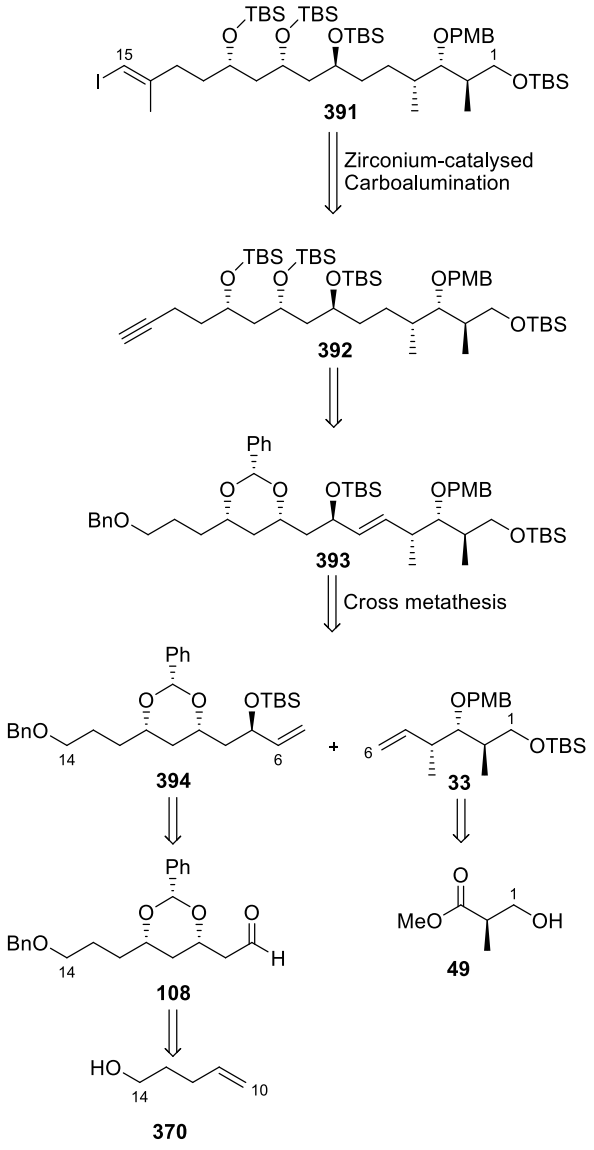


Scheme 137: Application of the methodology to the synthesis of the C16-30 fragment

Chapter 3: Synthesis of the C1-15 fragment of dolabelide C

As discussed in the introduction, the C1-15 fragment of dolabelide C was previously synthesised in the Prunet group by Aurélie Vincent using a Mukaiyama aldol reaction as the key step. However, the additional steps required to remove the ketone at C5 by reduction followed by Barton-McCombie deoxygenation make the route lengthy and inefficient. Moreover, as the Negishi carboalumination previously envisaged to form the product **118** was leading to decomposition, the sequence used to form **118** from **117** is also quite long in terms of steps (see scheme 26).

A new route is thus envisaged for the synthesis of the C1-15 fragment. The key steps would be a cross metathesis and a zirconium-catalysed carboalumination. The retrosynthesis is showed in the following scheme (Scheme 138):



Scheme 138: Retrosynthesis of the C1-15 fragment

The failure of the previously attempted carboalumination reaction is thought to be due to the low stability of the benzylidene acetal under the reaction

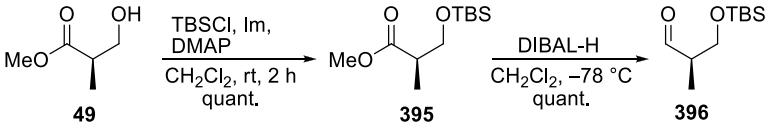
conditions. Thus, the use of different protecting groups such as silyl ethers is considered. In the newly envisaged synthesis, the Negishi carboalumination reaction would thus be attempted on substrate **392**, which could be obtained from alkene **393**. This alkene could come from a cross metathesis reaction between the fragments **394** and **33**. Alkene **394** could be synthesised by an asymmetric vinylation from aldehyde **108**, which has been previously synthesised in the Prunet group from 4-penten-1-ol. Alkene **33** could be synthesised from (*R*)-(−)-Roche ester.

We will first discuss the syntheses of the two fragments **394** and **33**. The results obtained for the coupling of these two fragments by cross metathesis will then be presented. Finally, the completion of the synthesis will be detailed.

3.1 - Synthesis of the C1-5 fragment

The synthesis of the C1-5 fragment **33** is known;[6(a)] it can be obtained by subjecting the aldehyde derived from the Roche ester to an asymmetric crotylation.

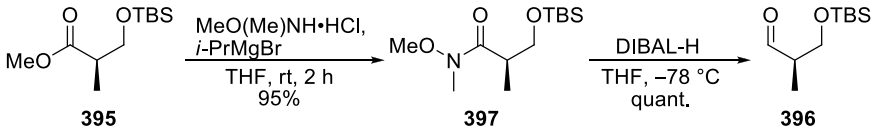
Aldehyde **396** was synthesised quantitatively in two steps from the Roche ester by protection of the alcohol as a TBS ether, followed by DIBAL-H reduction of the ester **395** (Scheme 139). This aldehyde is sensitive to silica gel and so the crude product was carried out to the next step without further purification.



49 **395** **396**

Scheme 139: Synthesis of aldehyde **396**

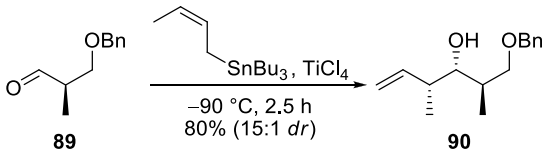
However, the reduction of the ester was not reproducibly high yielding. We decided to go through a two-step procedure *via* a Weinreb amide to synthesise the aldehyde **396** from the ester **395**. Treatment of the ester **395** with *N*,*O*-dimethylhydroxylamine hydrochloride and isopropylmagnesium bromide gave the Weinreb amide **397** in 95% yield (Scheme 140). DIBAL-H reduction of the Weinreb amide gave the desired aldehyde in reproducibly high yields.



395 **397** **396**

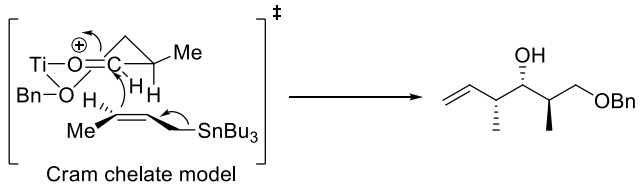
Scheme 140: Synthesis of aldehyde **408** *via* Weinreb amide

For the completion of the synthesis of this fragment, we first decided to perform diastereoselective crotylation by relying on substrate control. In his synthesis of the C1-13 subunit of dolabelide B, Keck and co-workers synthesised a similar substrate by diastereoselective addition of crotylstannane on to aldehyde (Scheme 141).



Scheme 141: Diastereoselective addition of crotylstannane on aldehyde **89**

The explanation for the selectivity of the reaction is shown in the following scheme (Scheme 142):

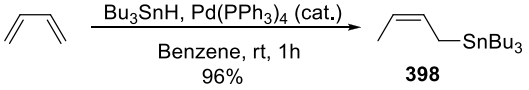


Scheme 142: Mechanism of the addition of crotylstannane on aldehyde **89**

The reaction goes through a Cram chelate transition state and the addition of the crotylstannane occurs from the opposite face of the carbonyl group that is not blocked by the methyl group. In this case, the protecting group of the alcohol being a benzyl group, the chelation is possible. In our case, however, the chelation is more difficult due to the presence of the silyl protecting group.

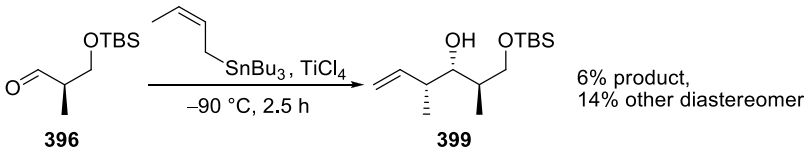
We decided to try this method with different Lewis acids to see if it would be possible to get a good selectivity.

First, *cis*-crotylstannane **398** was synthesised in 96% yield through Pd-catalysed hydrostannation of 1,3-butadiene[86] (Scheme 143).



Scheme 143: Synthesis of crotylstannane **398**

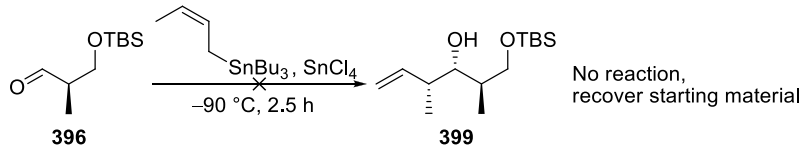
With the stannane in hand, we decided to try first the reaction with titanium tetrachloride as a Lewis acid promoter (Scheme 144).



Scheme 144: Use of titanium tetrachloride

The reaction was very low yielding and and led to poor selectivity.

We then tried to use tin tetrachloride as a Lewis acid (Scheme 145).



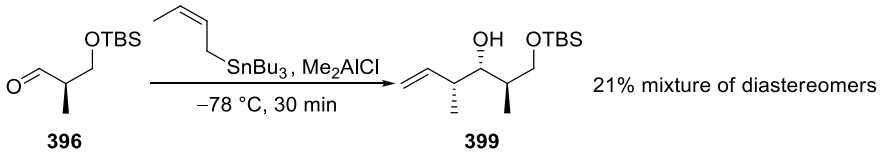
Scheme 145: Use of tin tetrachloride

[86] Miyake, H.; Yamamura, K. *Chem. Lett.* **1992**, 507.

In this case, no reaction was observed and only the starting material was recovered.

Finally, we decided to try using dimethylaluminum chloride as a Lewis acid. It has been shown that this reagent allows chelation even in the presence of silyl groups and good selectivity has been reported, especially when used to promote the Mukaiyama aldol reaction.[87] Two equivalents of this reagent are required as Me_2Al^+ and $Me_2AlCl_2^-$ are formed from comproportionation of Me_2AlCl. Me_2Al^+ is the species acting as the strong Lewis acid.

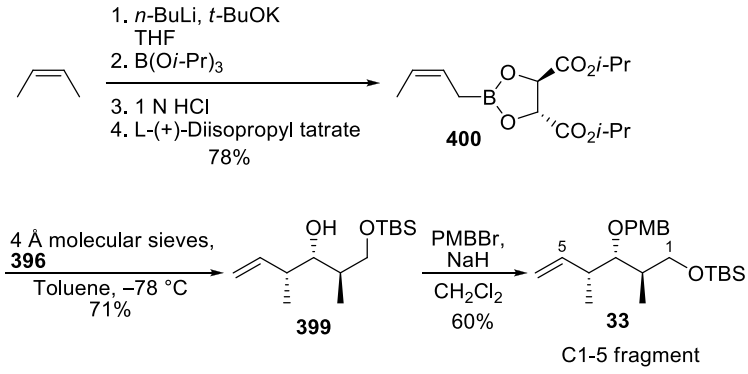
However, even when using that reagent, no selectivity was observed and the reaction was very low yielding (Scheme 146).



Scheme 146: Use of dimethylaluminum chloride

We then decided to employ the Roush crotylboration reaction to install the two remaining stereocentres because this method had already been used for the synthesis of the C16-30 fragment of dolabelide C.

The crotylboronate needed for the synthesis was obtained from *cis*-butene and L-(+)-diisopropyl tartrate using the same method as before (Scheme 147). Treatment of aldehyde **396** with the chiral crotylboronate using the same procedure as before afforded the desired alcohol in 71% yield. Subsequent protection of the alcohol as a PMB ether delivered the C1-5 fragment in 60% yield (Scheme 147).



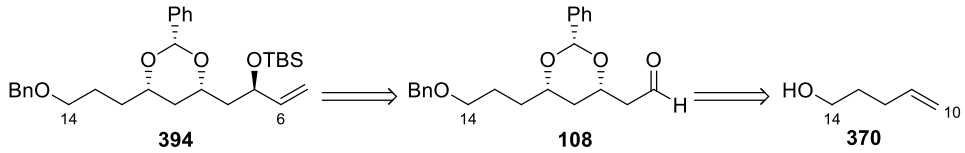
Scheme 147: Synthesis of fragment C1-5

The C1-5 fragment was synthesised in five steps and 40% yield from Roche ester using the above method.

[87] Evans, D. A.; Allison, B. D.; Yang, M. G.; Masse, C. E. *J. Am. Chem. Soc.* **2001**, *123*, 10840.

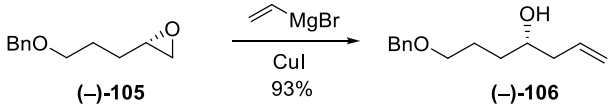
3.2 - Synthesis of the C6-15 fragment

The second fragment can be obtained from aldehyde **108**, which has already been synthesised by Aurélie Vincent starting from 4-penten-1-ol (Scheme 148).



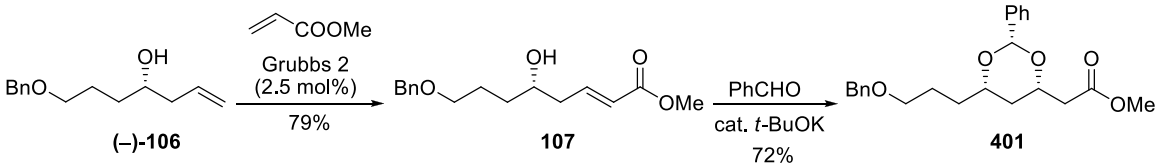
Scheme 148: Retrosynthesis of fragment C6-15

Alcohol **(−)-106** can be synthesised from epoxide **105** (Scheme 149), the synthesis of which was presented before (see Scheme 119).



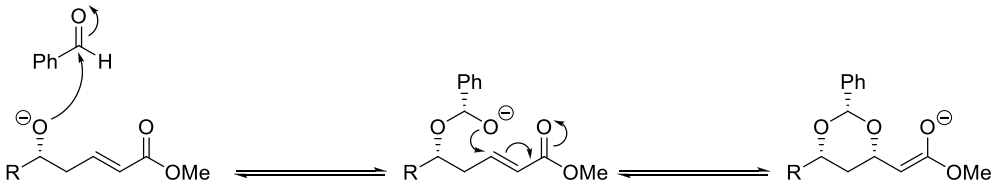
Scheme 149: Synthesis of alcohol **(−)-106**

Alcohol **(−)-106** was then reacted with methyl acrylate *via* a cross metathesis reaction leading to alcohol **107** in 79% yield (Scheme 150). Treatment of this alcohol with benzaldehyde in the presence of a catalytic amount of potassium *tert*-butoxide led to benzylidene acetal **401** in 72% *via* a diastereoselective oxa-Michael reaction.[88]



Scheme 150: Synthesis of ester **401**

The mechanism of the Michael addition is shown in the following scheme (Scheme 151).



Scheme 151: Mechanism of the Michael addition

The hemiacetal formed in the first step adds in a reversible way to the Michael acceptor to form the enolate. This reaction leads predominantly to the 1,3-*syn* diol in which all the substituents are in the equatorial position (Figure 12). This is due to the fact that the reaction is under thermodynamic control and *anti* benzylidene acetal that is formed can isomerise *via* a retro-Michael addition to form the most stable *syn* isomer.

[88] Evans, D.A.; Gauchet-Prunet, J. A. *J. Org. Chem.* **1993**, *58*, 2446.

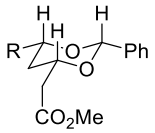
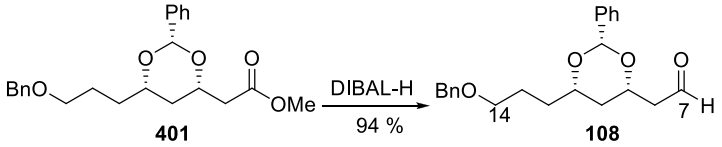


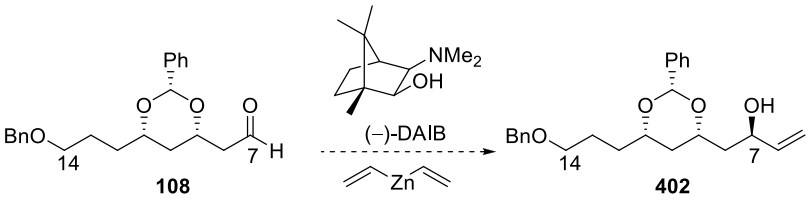
Figure 12: Chair conformation with substituents in equatorial position

Finally, DIBAL-H reduction gave aldehyde **108** in 94% yield (Scheme 152).



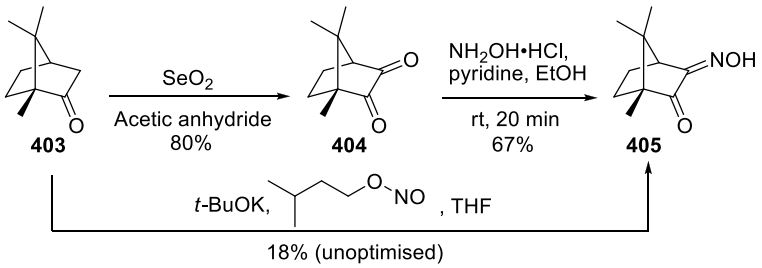
Scheme 152: Synthesis of aldehyde **108**

With the aldehyde in hand, a method to install the stereocentre at C7 was needed. As discussed in chapter II, enantioselective vinylation of aldehyde was envisaged as a way of introducing this stereocentre with C-C bond formation (Scheme 153).



Scheme 153: Enantioselective vinylation

For this, (−)-DAIB ligand was required. The synthesis of this ligand from (+)-camphor has been reported in the literature.[89] Oxime **405** can be synthesised in two steps and 54% yield by oxidation of (+)-camphor with selenium dioxide, followed by oxime formation with hydroxylamine hydrochloride and pyridine (Scheme 154). Alternatively, as the use of selenium dioxide is not ideal on large scale, this oxime can be synthesised directly by treatment of (+)-camphor with isopentyl nitrite and potassium *tert*-butoxide.[90]



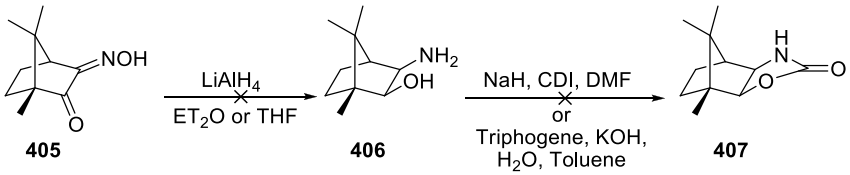
Scheme 154: Synthesis of oxime **405**

With the oxime in hand, the next steps involved reduction of the ketone and the oxime to yield an aminoalcohol, followed by protection as a cyclic carbamate. However, the reduction was really messy and none of the desired product was obtained using various conditions (Scheme 155). Attempts at protecting the aminoalcohol as a carbamate were tried on the crude product, but the desired product was not obtained.

---

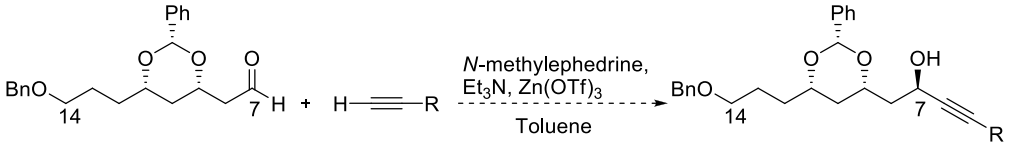
[89] (a) White, J. D.; Wardrop, D. J.; Sundermann, K. F. *Org. Synth.* **2002**, *79*, 125. (b) White, J. D.; Wardrop, D. J.; Sundermann, K. F. *Org. Synth.* **2002**, *79*, 130.

[90] Bosiak, M. J.; Krzemiński, M. P.; Jaisankar, P.; Zaidlewicz, M. *Tetrahedron: Asymmetry* **2008**, *19*, 956.



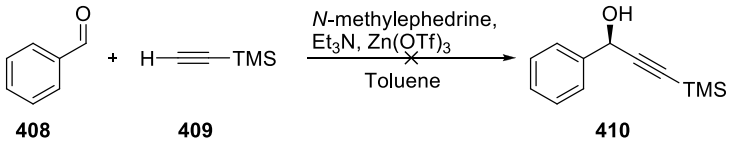
Scheme 155: Synthesis of substrate **407**

Because the synthesis of (−)-DAIB proved problematic, we decided to use a different method, involving enantioselective alkynylation of aldehydes developed by Carreira and co-workers[91] (Scheme 156).



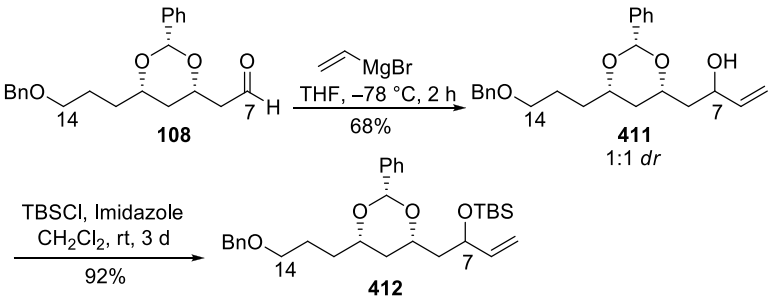
Scheme 156: Enantioselective alkynylation of aldehydes

We decided to test the standard procedure by reaction of benzaldehyde with TMS-protected acetylene (Scheme 157). However, after several attempts, no reaction was observed and only the starting materials were recovered.



Scheme 157: Trial on benzaldehyde

At this point, we decided to synthesise the allylic alcohol by addition of vinylmagnesium bromide and continue the synthesis with a mixture of diastereomers as a model substrate. Treatment of aldehyde **108** with vinylmagnesium bromide, followed by protection of the alcohol as a TBS ether afforded the C6-15 fragment in 63% yield over two steps (Scheme 158).



Scheme 158: Synthesis of substrate **412**

This fragment was synthesised in nine steps and 24% yield.

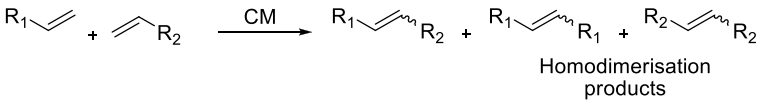
[91] Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806.

3.3 - Coupling of the two fragments by cross metathesis

The metathesis reaction was presented in the previous chapter with particular focus on ring-closing metathesis. In this part, we are going to discuss more about cross metathesis and the results obtained for the cross metathesis reaction between the two fragments C1-5 and C6-14 will be presented.

3.3.1 - Background on cross metathesis

As opposed to ring-closing metathesis, where the reaction leads mainly to one product, homodimerisation products can be observed in the case of the cross metathesis (Scheme 159).



Scheme 159: Cross metathesis

Grubbs and co-workers established an empirical model to predict the selectivity of the cross metathesis reaction.[92] The olefins are grouped into four different types depending on their abilities to homodimerise (Table 11). This classification depends of the catalyst used; the profile presented below is for the most commonly used second-generation Grubbs' catalyst.

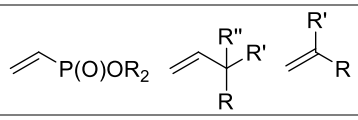
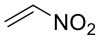
Type I	Fast homodimerisation Homodimer consumable	ex:  R = OH, X, Ph, alkyl, SiR'_2, NR'_2...
Type II	Slow homodimerisation Homodimer rarely consumable	ex:  R = COOR', CHO, COR', $CONR'_2$, CH(OH)R'...
Type III	No homodimerisation	ex: 
Type IV	Spectators to CM	ex: 

Table 11: Classification of olefins

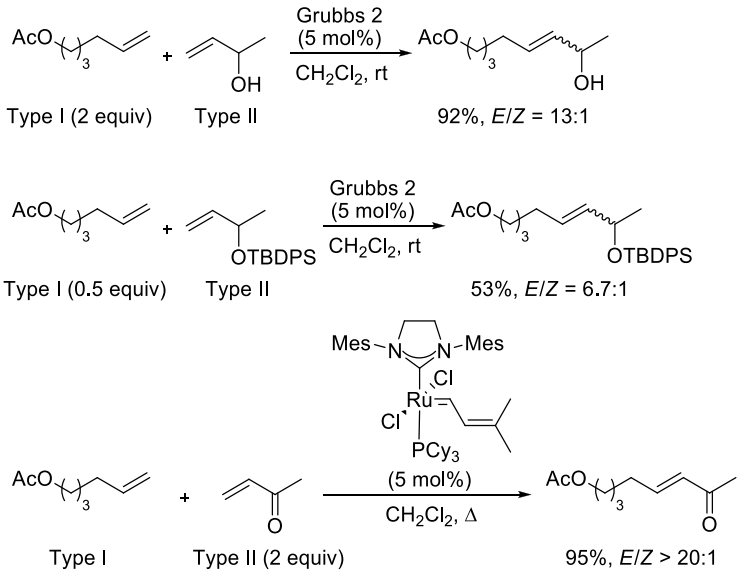
Electron-rich olefins and less hindered olefins are part of the first type. Electron-poor olefins and more hindered olefins belong to Type II-III.

In order to obtain good selectivity, it is important to minimise the formation of the homodimers, either by preventing initial formation of these homodimers or by using olefins which lead to homodimers that are active towards metathesis.

Moreover, cross metathesis generally leads to the *trans* olefin, which is the more thermodynamically favoured. In the case of trisubstituted olefins, it is more difficult to predict the outcome of the reaction. When olefins of different types are reacted together, good chemo- and stereoselectivities are usually observed. Some examples are presented below. For example, reactions between a type I olefin and a type II olefin usually give good yields and good selectivities (Scheme

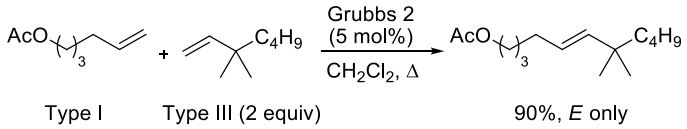
[92] Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360.

160). Unprotected allylic alcohols have been shown to give better results than protected alcohols.[92] Enones also seem to give slightly better results than allylic alcohols.[93]



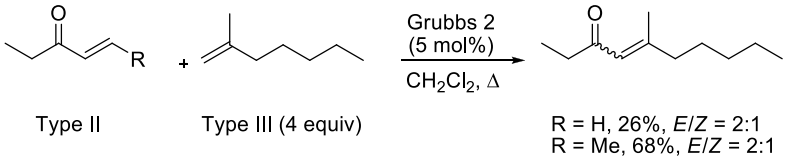
Scheme 160: Cross metathesis between type I and II olefins

Reactions between a type I olefin and a type III olefin give good selectivities in favour of the cross-coupled product (Scheme 161).[92] A type III olefin does not homodimerise, so by using an excess of this olefin only the desired product is obtained. Moreover, due to the steric bulk being important, only the *trans* isomer is obtained.



Scheme 161: Cross metathesis between type I and III olefins

Reactions between a type II olefin and a type III olefin usually give lower yields due to the lower reactivities of the two olefins. The use of an excess of type III allows the yield to be improved because the homodimerisation of the type II olefin is minimised. In the following example (Scheme 162),[92] this goal is achieved by the use of a more hindered type II olefin. As discussed before, the *E*/*Z* selectivity is lower for the formation of a trisubstituted olefin.



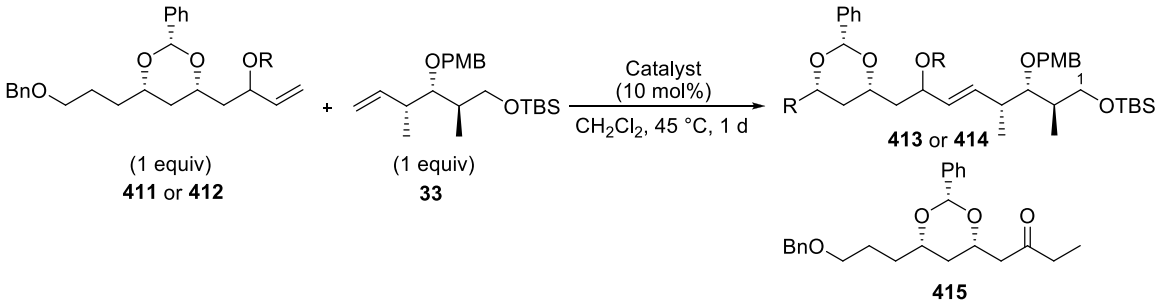
Scheme 162: Cross metathesis between type II and III olefins

[93] Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783.

3.3.2 - Cross metathesis between the two fragments

a. Preliminary results

Having synthesised the TBS protected substrate **412** and the unprotected substrate **411**, we decided to try the cross metathesis on both substrates. Second-generation Grubbs' catalyst and second-generation Hoveyda-Grubbs' catalyst were chosen as catalysts as they are the most commonly used ones in the literature. As both substrates are type II olefins and are both valuable fragments, we decided to use one equivalent of each partner. Several trials were undertaken using 10 mol% of catalyst and the reactions were performed in dichloromethane at reflux for one day. The results are shown in the following table (Table 12):



R group	Catalyst	Concentration (mol/L)	Yield 413 or 414	Recovered 412	Recovered 33	Yield 415
-TBS	Grubbs 2	0.14	17%	50%	30%	/
-TBS	Hoveyda-Grubbs 2	0.11	/	100%	100%	/
-H	Grubbs 2	0.14	40%	/	/	
-H	Hoveyda-Grubbs 2	0.17	50%	/	25%	25%
-H	Hoveyda-Grubbs 2	0.5	45%	/	25%	25%

Table 12: Cross metathesis trials on substrates **411** and **412**

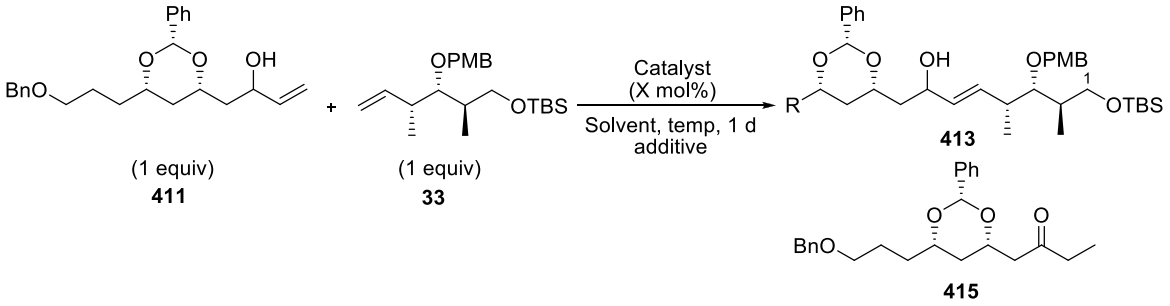
As was already reported in the literature, the substrate with an alcohol protected as a silyl ether gave lower reactivities. When using the second-generation Grubbs catalyst, a 17% yield of the desired product was obtained, along with large amounts of unreacted starting materials. In the presence of second-generation Hoveyda-Grubbs' catalyst, no reaction was observed. With the unprotected substrate, better results were obtained. The second-generation Hoveyda-Grubbs catalyst seemed to give a slightly better result as it has often been shown in the literature. However, when using the unprotected allylic alcohol, the main by-product was the isomerised product **415**. The isomerisation of alkenes and allylic alcohols with ruthenium-based catalysts is known in the literature.[94,95] Finally, increasing the concentration gave similar results using the second-generation Hoveyda-Grubbs catalyst. In each case, the substrates being relatively bulky type II olefins, no homodimerisation or very small amounts of homodimers were

[94] McGrath, D. V.; Grubbs, R. H. *Organometallics* **1994**, *13*, 224.
[95] Gurjar, M. K.; Yakambram, P. *Tetrahedron Lett.* **2001**, *42*, 3633.

observed. In the case of the allylic alcohol **411**, homodimerisation was probably slower than cross metathesis and isomerisation.

b. Further trials to optimise the metathesis reaction

Having established that the unprotected allylic alcohol gave better results and that the second-generation Hoveyda-Grubbs catalyst seemed to be the best catalyst, we decided to change other variables like solvent, temperature or the presence of an additive. The results are shown in the following table (Table 13):

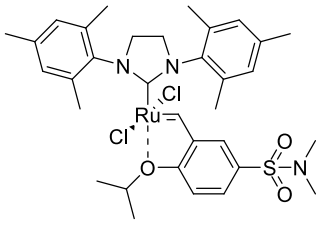


Catalyst	X	Solvent	Temp	Additive	Yield 413	Recovered 33	Yield 415
Hoveyda-Grubbs 2	10	CH_2Cl_2	45 °C	/	25%	40%	20%
Zhan 1B	10	CH_2Cl_2	45 °C	/	50%[a]	25%	25%
Hoveyda-Grubbs 2	10	1,2-DCE	85 °C	/	18%	40%	42%
Hoveyda-Grubbs 2	10	CH_2Cl_2	45 °C	4-BQ	26%	30%	16%
Hoveyda-Grubbs 2	5	CH_2Cl_2	45 °C	/	3[b]	1	1

[a] addition dropwise of **411**. [b] NMR ratio

Table 13: Further trials

First, dropwise addition of **411** in order to potentially avoid the isomerisation led to a lower yield. The use of the Zhan 1B catalyst (Figure 12) gave the same result as the best result obtained with second-generation Hoveyda-Grubbs catalyst.



Zhan 1B catalyst

Figure 12: Zhan 1B catalyst

This catalyst can show better results in certain cases due to the electron-withdrawing group in *para* position to the alkoxy group. This can result in a faster initiation due to the faster dissociation between the ether ligand and the ruthenium.

Running the reaction at a higher temperature in 1,2-dichloroethane gave a lower yield and seemed to increase the amount of isomerised product formed. The use of 1,4-benzoquinone as an additive, which has been shown to minimise isomerisation in certain cases,[96] did not give better results in our case. Finally, the use of only 5 mol% of catalyst resulted in a slightly better conversion to the desired product as judged from the crude NMR spectrum. A higher amount of catalyst might favour the isomerisation.

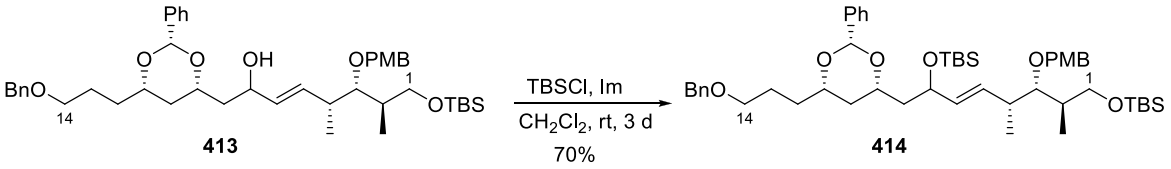
In conclusion, it seemed difficult to improve the yield of the cross metathesis reaction to greater than 50-60%. However, an advanced model intermediate in the synthesis of the C1-15 fragment of dolabelide C has successfully been obtained by cross metathesis.

3.4 - End of the synthesis

Having successfully synthesised substrate **413**, we could carry on with the completion of the synthesis on the model fragment. The final steps would involve the hydrogenation of the double bond and the removal of the benzyl and the benzylidene acetal groups, followed by conversion of the primary alcohol into an alkyne in order to attempt the zirconium-catalysed carboalumination reaction.

3.4.1 - Hydrogenation of the double bond and removal of protecting groups

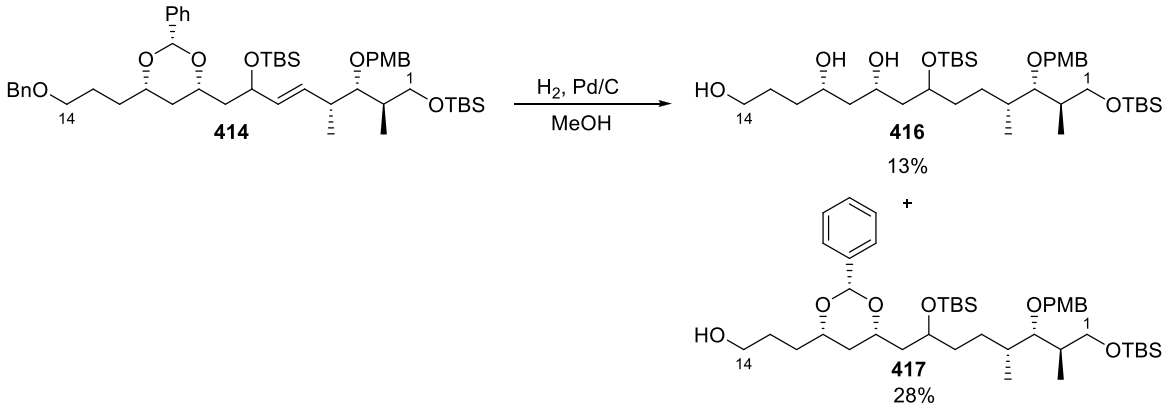
Firstly, the secondary alcohol was protected as a silyl ether in 70% yield (Scheme 163).



Scheme 163: Synthesis of substrate **414**

The hydrogenation trials could then be performed on substrate **414**. Treatment with hydrogen in the presence of palladium on carbon as a catalyst was performed and a mixture of desired product and benzylidene-acetal protected substrate was obtained (Scheme 164).

[96] Hong, S. H.; Sander, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160.

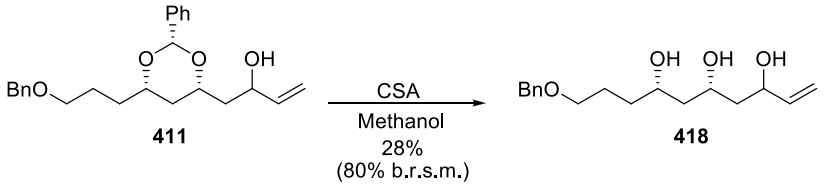


Scheme 164: Hydrogenation on substrate **414**

After other trials, it appeared that it would be difficult to remove the benzylidene acetal group without partially or totally removing the PMB group. We then decided to try removing the benzylidene acetal group before performing the cross metathesis reaction.

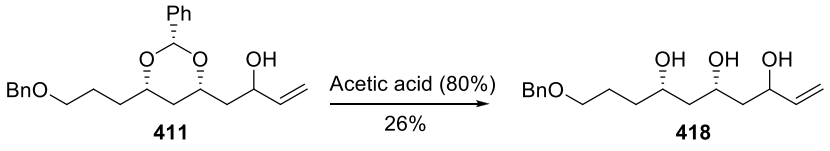
3.4.2 - Deprotection of the benzylidene acetal before metathesis

Common methods to remove a benzylidene acetal group involve hydrogenation or the use of an acid. The use of hydrogenation before the cross metathesis was not an option, and so we decided to use an acid for the removal of the benzylidene acetal group. Treatment with camphorsulfonic acid (CSA) was performed and the desired product was obtained in 28% yield (Scheme 165).



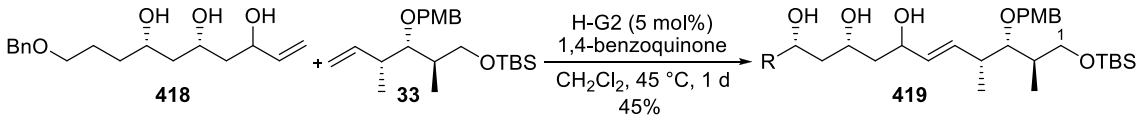
Scheme 165: Removal of benzylidene acetal with CSA

Although, the desired product was formed, the reaction was quite slow and a lot of starting material was recovered. We then decided to try a different acid like acetic acid (Scheme 166). However, a similar yield was obtained.



Scheme 166: Removal of benzylidene acetal with acetic acid

At this point, we decided to carry on with the synthesis and the cross metathesis reaction was performed with substrate **418** (Scheme 167).



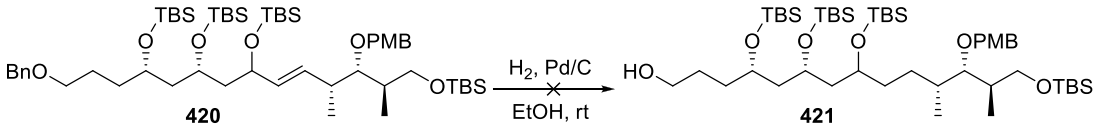
Scheme 167: Cross metathesis with **418**

The desired product was obtained in 45% yield, along some unreacted alkene **33** and other unknown by-products. Protection of the triol as the tris-silyl ether **420** was then carried out delivering the desired product in 50% yield (Scheme 168).

Scheme 168: Protection of the triol as a tris-TBS ether

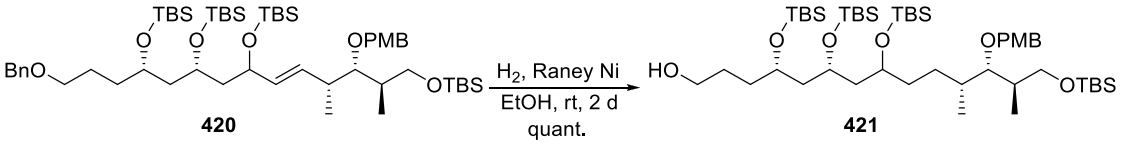
3.4.3 - Hydrogenation of the new substrate

With substrate **420** in hand, we could perform the hydrogenation in order to remove the benzyl group and reduce the double bond. We first tried to perform the hydrogenation reaction using palladium on carbon as the catalyst; however, it appeared again difficult to get a complete conversion without removal of the PMB group (Scheme 169).



Scheme 169: Hydrogenation with Pd/C

We then chose to use Raney nickel as the catalyst, as it was known to be less active and to allow selective hydrogenation of benzyl groups and alkenes in the presence of a PMB ether. We were pleased to see that the desired product was afforded quantitatively in the presence of Raney nickel (Scheme 170).



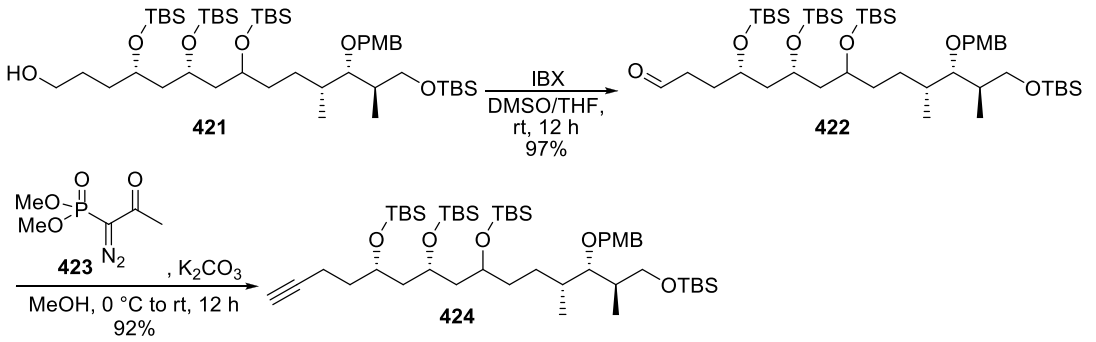
Scheme 170: Hydrogenation with Ni Raney

3.4.4 - Ohira-Bestmann reaction and zirconium-catalysed carboalumination

With alcohol **421** in hand, formation of the alkyne could be performed. We decided to install the alkyne by oxidation with IBX, followed by an Ohira-Bestmann reaction.[97,98] After oxidation of alcohol **421** to aldehyde **422** with IBX in 97% yield, treatment of the resulting aldehyde with phosphonate **423** and potassium carbonate gave alkyne **424** in 92% (Scheme 171).

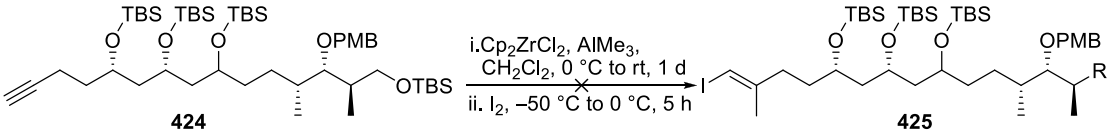
[97] Ohira, S. *Synth. Commun.* **1989**, *19*, 561; Müller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521.

[98] Seyferth, D.; Marmor, R. S.; Hibert, P. *J. Org. Chem.* **1971**, *36*, 1379; Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1979**, *44*, 4997; Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1982**, *47*, 1837.



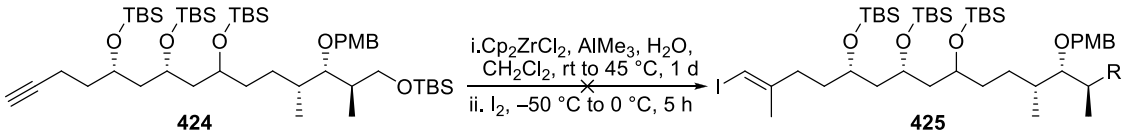
Scheme 171: Synthesis of alkyne **424**

To install the vinyl iodide moiety in the molecule, we decided to use the zirconium-catalysed carboalumination reaction developed by Negishi.[99] Treatment of alkyne **424** with bis(cyclopentadienyl) zirconium(IV) dichloride and trimethylaluminum in dichloromethane at room temperature for one day, followed by addition of iodine only led to the recovery of starting material (Scheme 172).



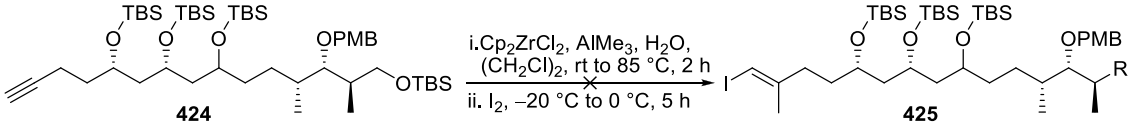
Scheme 172: First trial

We then tried the addition of water in order to form the alkenylalane species, which has been shown to improve the formation process by Wipf and co-workers.[100] However, even after heating at reflux in dichloromethane, only the starting material was recovered (Scheme 173).



Scheme 173: Trial with water

Finally, we decided to try increasing the number of equivalents of Cp_2ZrCl_2, trimethylaluminum and water to 0.6, 16 and 8 as opposed to 0.3, 3 and 1.5 used previously. The solvent was also changed to 1,2-dichloroethane in order to increase the reflux temperature to 85 °C. However, the desired product was not obtained and the starting material was not recovered (Scheme 174).



Scheme 174: Increase of equivalents and use of 1,2-dichloroethane

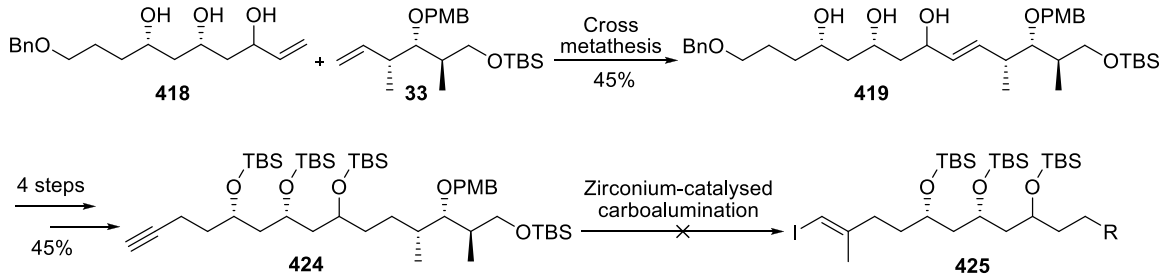
[99] Van Horn, D. E.; Negishi, E.-i. *J. Am. Chem. Soc.* **1978**, *100*, 2252; Yoshida, T.; Negishi, E.-i. *J. Am. Chem. Soc.* **1981**, *103*, 4985; Negishi, E.-i.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639; Negishi, E.-i.; Kondakov, D. Y.; Choueiry, D.; Kasai, K.; Takahashi, T. *J. Am. Chem. Soc.* **1996**, *118*, 9577.

[100] Wipf, P.; Lim, S. *Angew. Chem. Int. Ed.* **1993**, *32*, 1068.

As all these reactions have been performed on small scale, it would be interesting to try these conditions again on larger scale.

3.5 - Conclusions

A late-stage model intermediate in the synthesis of the C1-15 fragment of dolabelide C has successfully been synthesised using cross metathesis as the key step (Scheme 175). However, the final fragment could not be obtained using the zirconium-catalysed carboalumination developed by Negishi (Scheme 175).

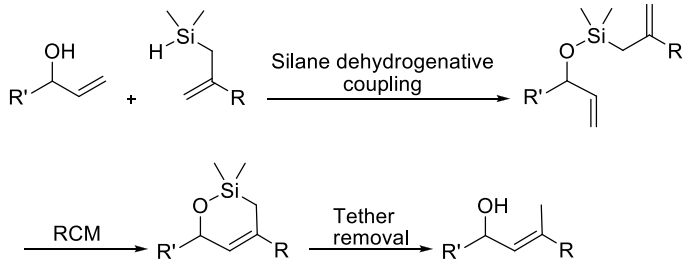


Scheme 175: Synthesis of **424** with cross metathesis of the key step and zirconium-catalysed carboalumination on **424**

Conclusions and perspectives

Synthesis of trisubstituted alkenes by RCM using an O-Si-C tether

A new methodology has been developed for the synthesis of trisubstituted alkenes by employing a ring-closing metathesis with a temporary silicon tether (Scheme 176).



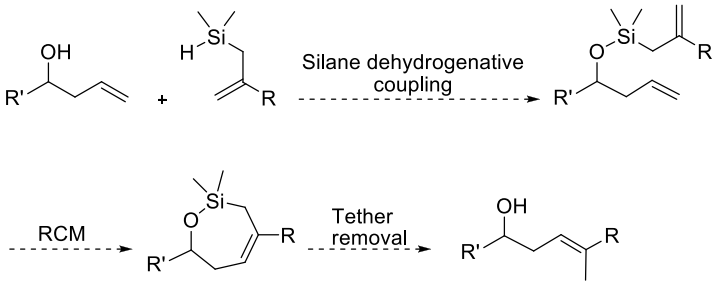
Scheme 176: New methodology

In the process of developing this methodology, a new way of synthesising allylhydrosilane has been discovered in which a novel Peterson olefination reaction is used (Scheme 177).

Scheme 177: Novel Peterson olefination

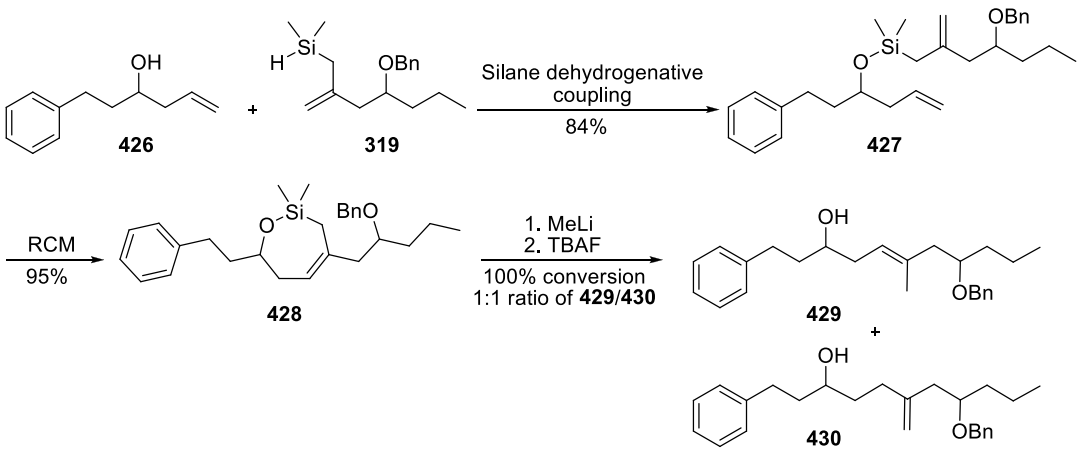
This methodology has then been successfully applied to the synthesis of the C16-30 fragment of dolabelide C (see Scheme 137).

Ongoing work in the Prunet group, carried out by Alexandre Audic, is being undertaken to expand this methodology to the synthesis of a seven-membered ring silacycle (Scheme 178).



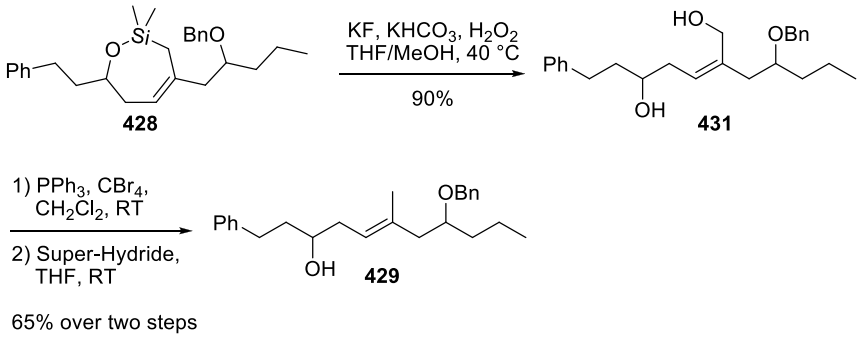
Scheme 178: Synthesis of seven-membered ring silacycle

It has been shown that the methodology gives good results for the synthesis of the seven-membered ring silacycle (Scheme 179). However, the previously developed two-step procedure for the tether removal gave an inseparable 1:1 mixture of isomers (Scheme 179).



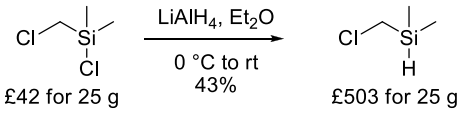
Scheme 179: Synthesis of alcohol **429** using the new methodology

A new procedure has then been developed by Alexandre Audic for the tether removal. This method involves a Tamao-Fleming oxidation, followed by bromination and reduction (Scheme 180).



Scheme 180: New procedure for the tether removal

Moreover, regarding the novel Peterson olefination, a new procedure has been found for the synthesis of the chloromethyldimethylsilane starting material (Scheme 181). It allows the preparation of a large quantity of chloromethyldimethylsilane for a greatly decreased cost, making this methodology more interesting for synthetic chemistry.

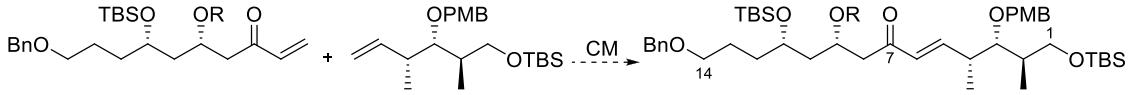


(Slow addition of SM on LAH)
Reaction on 15 g scale

Scheme 181: New synthesis of chloromethyldimethylsilane

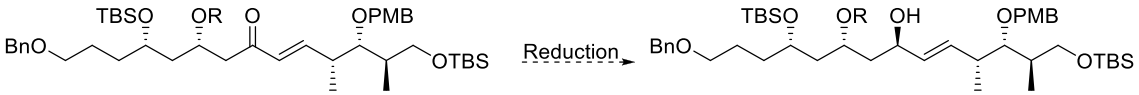
Synthesis of the C1-15 fragment of dolabelide C

A model for the late-stage intermediate in the synthesis of the C1-15 fragment of dolabelide C has been synthesised using cross metathesis as the key step (see Scheme 175). Future work involve the use of an enone for the cross metathesis in order to prevent isomerisation happening in the case of the allylic alcohol (Scheme 182).



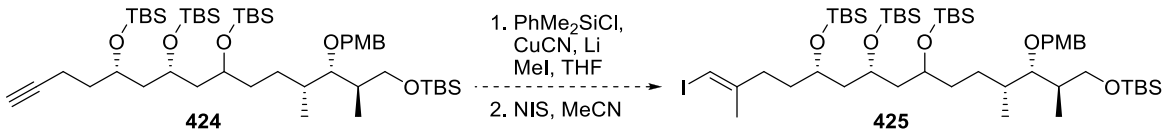
Scheme 182: Cross metathesis with an enone

The desired stereochemistry at C-7 could then be installed using CBS reduction or an Evans-Tishchenko reaction (Scheme 183).



Scheme 183: Installation of the stereochemistry at C-7

Finally, the Negishi carboalumination reaction would have to be performed on a larger scale. Other methods, like a silylcupration, could also be tried in order to form the desired vinylsilane (Scheme 184).



Scheme 184: Synthesis of **425** by silylcupration

Experimental

General Experimental

Apparatus:

NMR spectra were recorded using a Bruker DPX-400 spectrometer (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) and a Bruker DPX-500 spectrometer (^{1}H NMR: 500 MHz, ^{13}C NMR: 125 MHz). Deuterated chloroform ($CDCl_3$) was used as the solvent for both ^{1}H and ^{13}C NMR, with residual solvent peak δ7.27 being used for calibration of ^{1}H NMR, and $CDCl_3$ peak at δ77.0 for ^{13}C. Chemical shifts (δ) are expressed in parts per million (ppm) and coupling constants (*J*) are expressed in Hertz (Hz). Signal splitting patterns are described as: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), sextet (sext), septet (sept), octet (oct), nonet (non), multiplet (m), broad doublet (br d), or any combination of the above. Assignements were obtained using COSY, DEPT and HSQC when necessary.
IR spectra were recorded using a Golden Gate™ attachment, utilising a type IIa diamond as a single reflection element, allowing for direct reading of powder or oil samples.
High resolution mass spectra were recorded under CI, EI or ESI conditions by the University of Glasgow analytical service.
Optical rotations were determined as solutions irradiating with the sodium D line (λ = 589 nm) using an AA series Automatic polarimeter. $[\alpha]_D$ values are given in units 10^{-1} degcm^{2}g^{-1}.

Chromatography:

Flash chromatography was executed under forced flow conditions, using the indicated solvent system and EMD Guduran silica gel 60 as solid support. Thin layer chromatography (TLC) was carried out on Merck silica gel 60 covered aluminum sheets, and monitored by UV-light or by staining with a solution of anisaldehyde or potassium permanganate.

Solvents and reagents:

Reaction solvents were collected from an in-house solvent purification system (THF, CH_2Cl_2, Et_2O, CH_3CN). Chlorodimethylsilane, dichlorodimethylsilane and triethylamine were distilled over CaH_2. Dry ethanol, dry methanol and dry DMF were used from commercial bottles. Chromatography solvents were HPLC grade solvents, stored in Winchester bottles. All reagents were used directly from supplier.

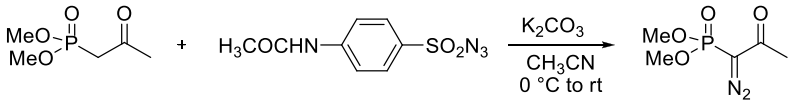
General conditions:

Air or moisture sensitive reactions were carried out in pre-dried glassware; either overnight in an oven (125 °C) or by flame drying *in vacuo*. Argon was used to create an inert atmosphere.

Preparation of PMBBr[101]

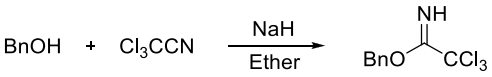
A solution of PMB-OH (2.5 g) in diethyl ether (10 mL) was shaken with HBr (47% sol in water, 5 mL) in a separatory funnel. The organic phase was then washed with 20 mL of a saturated aqueous NaBr solution, dried over K_2CO_3, filtered and concentrated *in vacuo*.

Preparation of Dimethyl-1-diazo-2-oxopropylphosphonate



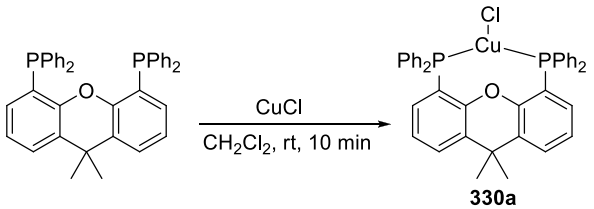
A solution of dimethyl (2-oxopropyl)-phosphonate (547 µL, 4 mmol) and *p*-acetamidobenzenesulfonyl azide[102] (1.06 g, 4.4 mmol, 1.1 equiv) in acetonitrile (20 mL) at 0 °C was treated with potassium carbonate (665 mg, 4.8 mmol, 1.2 equiv) and stirred for 2 hours. It was then filtered (removal of potassium carbonate) and concentrated *in vacuo*. After dilution in chloroform and stirring for 30 min, the solution was filtered (removal of *N*-(4-sulfamoylphenyl)-acetamide) and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 80:20) to afford dimethyl (1-diazo-2-oxopropyl)-phosphonate.

Preparation of 2,2,2-Trichloroacetimidate[103]



Sodium hydride (60% dispersion in mineral oil, 60 mg, 1.5 mmol, 0.15 equiv) was suspended in ether (2 mL) and a solution of benzyl alcohol (1.04 mL, 10 mmol) in ether (2 mL) was added dropwise. After stirring 20 min, the solution was cooled to 0 °C and freshly distilled trichloroacetonitrile (1 mL, 10 mmol) was added dropwise during 10 min. The solution was allowed to warm to 20°C over 1 hour, concentrated to a syrup, treated with 5 mL of pentane containing 0.6 mL of methanol, shaken vigorously and filtered. The filtrate and pentane washings were concentrated. This sequence was repeated twice to remove a precipitate. The resultant benzyl 2,2,2-trichloroacetimidate was concentrated *in vacuo* and used directly.

Preparation of (xantphos)CuCl[33]



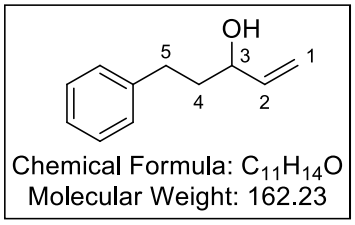
330a

To a stirred solution of xantphos (600 mg, 1.04 mmol) in dichloromethane (11 mL) was added copper (I) chloride (113 mg, 1.14 mmol, 1.10 equiv) and the reaction

[101] Ruder, S. M.; Ronald, R. C. *Tetrahedron Lett.* **1987**, *28*, 135.
[102] Davies, H. M. L.; Cantrell, W. R.; Romines, K. R.; Baum, J. S. *Org. Synth*. **1992**, *70*, 93.
[103] Wessel, H.-P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. I* **1985**, 2247.

was stirred at room temperature for 10 min. The solvent was then removed by distillation under argon and the precipitated solid was triturated in dry and degassed acetonitrile (4 mL). The suspension was vigorously stirred for 4 h and filtered under argon atmosphere. The wet cake was washed with acetonitrile (3 × 6 mL) and dried under vacuum to afford an off-white powder (682 mg, 97%).

5-Phenylpent-1-en-3-ol 293[104]



Chemical Formula: $C_{11}H_{14}O$
Molecular Weight: 162.23

A vinylmagnesium bromide solution (0.7 M in THF, 40 mL, 28 mmol, 2.5 equiv) was added dropwise to a stirred solution of hydrocinnamaldehyde (1.53 g, 11.4 mmol) in THF (100 mL) at −78 °C under argon. The mixture was stirred for 2 h at −78 °C under argon. The reaction was quenched with a saturated aqueous solution of ammonium chloride (100 mL) and extracted with ether (3 × 80 mL). The ether extracts were combined and washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo* to deliver a yellow oil. Purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave the alcohol **293** (1.47 g, 80%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, ***H***-Ar), 7.22-7.17 (m, 3H, ***H***-Ar), 5.91 (ddd, *J* = 16.9, 10.4, 6.2 Hz, 1H, C***H***-2), 5.25 (dd, *J* = 16.9, 1.4 Hz, 1H, C***H***-1$_{trans}$), 5.14 (dd, *J* = 10.4, 1.4 Hz, 1H, C***H***-1$_{cis}$), 4.14 (m, 1H, C***H***-3), 2.80-2.65 (m, 2H, C***H***-5), 1.90-1.83 (m, 2H, C***H***-4), 1.51 (broad s, 1H, C3-***OH***).

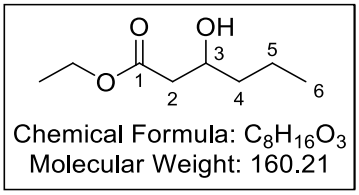
^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8 (C-Ar), 141.0 (C-2), 128.4 (C-Ar), 128.4 (C-Ar), 125.8 (C-Ar), 114.9 (C-1), 72.4 (C-3), 38.5 (C-4), 31.6 (C-5).

IR (neat, cm^{-1}) 3350, 3063, 3026, 2925, 2861, 1603, 1497, 1454, 1118.

HRMS (EI, *m*/*z*) calcd for $(C_{11}H_{14}O)^+$ 162.1045, found 162.1043.

[104] Grünanger, C. U.; Breit B. *Angew. Chem. Int. Ed.* **2010**, *49*, 967.

Ethyl 3-Hydroxyhexanoate 278[105]



Chemical Formula: $C_8H_{16}O_3$
Molecular Weight: 160.21

Sodium borohydride (2.39 g, 62.6 mmol, 1.00 equiv) was added to a stirred solution of ethyl 3-oxohexanoate (10.0 mL, 62.6 mmol) in ethanol (125 mL) at 0 °C under argon. The reaction mixture was stirred for 30 min at 0 °C. The reaction mixture was then quenched with a 1 M aqueous solution of hydrochloric acid (100 mL) and extracted with ethyl acetate (3 × 80 mL). The combined organic layers were then washed with brine (2 × 150 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver a clear oil. Purification by column chromatography on silica gel (petroleum ether-ether 7/3) gave the product **278** (6.66 g, 66%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (q, *J* = 7.1 Hz, 2H, C***H*****$_2$**-ethyl ester), 4.01 (m, 1H, C***H***-3), 2.92 (broad s, 1H, C3-***OH***), 2.50 (dd, *J* = 16.4, 3.1 Hz, 1H, C***H***-2), 2.39 (dd, *J* = 16.4, 9.0 Hz, 1H, C***H***-2), 1.57-1.35 (m, 4H, C***H***-4, C***H***-5), 1.28 (t, *J* = 7.1 Hz, 3H, C***H*****$_3$**-ethyl ester), 0.93 (t, *J* = 7.1 Hz, 3H, C***H***-6).

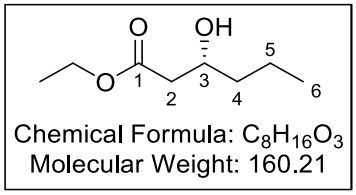
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1 (C-1), 67.7 (C-3), 60.6 (***C***H_2-ethyl ester), 41.3 (C-2), 38.6 (C-4), 18.6 (C-5), 14.1 (C-6 or ***C***H_3-ethyl ester), 13.9 (C-6 or ***C***H_3-ethyl ester).

IR (neat, cm^{-1}) 3480, 2960, 2934, 2874, 1733, 1373, 1260, 1166, 1097, 1017.

HRMS (EI, *m*/*z*) calcd for $(C_8H_{17}O_3)^+$ 161.1178, found 161.1180.

[105] Mori, K.; Takaishi, H. *Tetrahedron* **1989**, *45*, 1639.

Ethyl (*R*)-3-Hydroxyhexanoate 76[106]



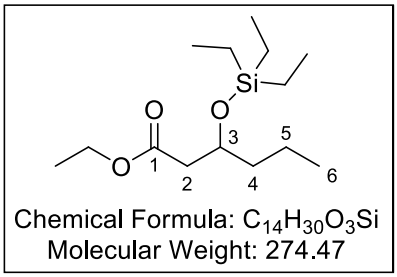
Chemical Formula: $C_8H_{16}O_3$
Molecular Weight: 160.21

To a stirred solution of benzeneruthenium (II) chloride dimer (130 mg, 0.260 mmol, 0.005 equiv) in degassed dry DMF (8 mL) was added (*R*)-Tol-BINAP (350 mg, 0.516 mmol, 0.01 equiv). The solution was stirred at 110 °C for 20 min. The solvent was then removed by distillation and the residue was dried *in vacuo* for 30 min. Ethyl 3-oxohexanoate (8.0 g, 51 mmol) and degassed dry ethanol (30 mL) were added. The flask containing the solution was then placed in an autoclave and the reaction mixture was stirred at 95 °C and under 5 bars of hydrogen for 20 h. Concentration *in vacuo* of the solution, followed by purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave the product **76** (7.6 g, 94%) as a light brown oil.

$[\alpha]^{25}_D$ = −30.0° (*c* 1.0, $CHCl_3$) (*Lit.*: $[\alpha]^{25}_D$ = −30.8° (*c* 1.0, $CHCl_3$))[106]

[106] Ramos, A. S.; Ribeiro, J. B.; Lopes, R. O.; Leite, S. G. F.; de Souza, R. O. M. A. *Tetrahedron Lett.* **2011**, *52*, 6127.

Ethyl 3-(Triethylsilyloxy)hexanoate 279



Chemical Formula: $C_{14}H_{30}O_3Si$
Molecular Weight: 274.47

Triethylsilyl triflate (0.21 mL, 0.94 mmol, 1.5 equiv) was added dropwise to a stirred solution of alcohol **278** (0.10 g, 0.62 mmol) and triethylamine (0.21 mL, 1.6 mmol, 2.5 equiv) in dichloromethane (1 mL) at −78 °C under argon. The reaction was stirred for 1 h at −78 °C. The reaction mixture was then quenched with a saturated aqueous sodium hydrogen carbonate solution (3 mL) and extracted with ethyl acetate (3 × 3 mL). The combined organic extracts were washed with brine (10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo* to deliver a clear oil. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ethyl acetate 96/4) gave the product **279** (0.15 g, 88%) as a clear oil.

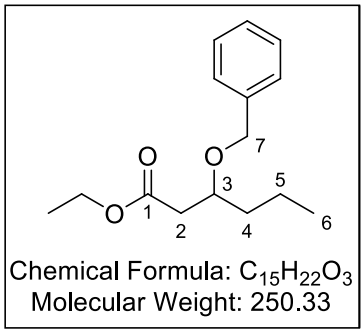
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (m, 1H, C***H***-3), 4.12 (q, *J* = 7.1 Hz, 2H, C***H*****$_2$**-ethyl ester), 2.43 (m, 2H, C***H***-2), 1.51-1.42 (m, 2H, C***H***-4), 1.40-1.30 (m, 2H, C***H***-5), 1.26 (t, *J* = 7.1 Hz, 3H, C***H*****$_3$**-ethyl ester), 0.95 (t, *J* = 7.9 Hz, 9H, C***H*****$_3$**-TES group), 0.91 (t, *J* = 7.1 Hz, 3H, C***H***-6), 0.59 (q, *J* = 7.9 Hz, 6H, C***H*****$_2$**-TES group).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9 (C-1), 69.2 (C-3), 60.3 (***C***H_2-ethyl ester), 42.9 (C-2), 40.0 (C-4), 18.4 (C-5), 14.2 (C-6 or ***C***H_3-ethyl ester), 14.1 (C-6 or ***C***H_3-ethyl ester), 6.8 (***C***H_3-TES), 4.9 (***C***H_2-TES).

IR (neat, cm^{-1}) 2957, 2938, 2913, 2877, 1737, 1460, 1375, 1310, 1237, 1177, 1087, 1040, 1004.

HRMS (EI, *m*/*z*) calcd for $(C_{14}H_{31}O_3Si)^+$ 275.2042, found 275.2039.

Ethyl 3-(benzyloxy)hexanoate 280



Chemical Formula: $C_{15}H_{22}O_3$
Molecular Weight: 250.33

To a stirred solution of ß-hydroxyester **278** (1.45 g, 9.05 mmol) and benzyl trichloroacetimidate (6.86 g, 27.2 mmol, 3.00 equiv) in dichloromethane (20 mL) was added slowly triflic acid (0.1 mL, 1 mmol, 0.1 equiv). The solution was stirred 2 days at room temperature and was then quenched by addition of a saturated aqueous solution of sodium bicarbonate (20 mL). The mixture was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 96/4) gave the benzylated alcohol **280** (2.04 g, 90%) as a pale yellow oil.

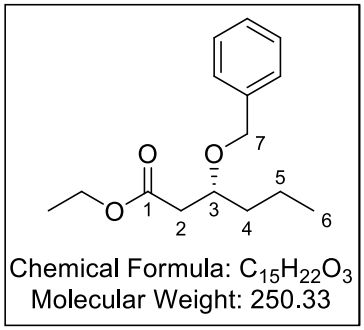
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H, ***H***-Ar), 4.59 (d, *J* = 11.4 Hz, 1H, C***H***-7), 4.54 (d, *J* = 11.4 Hz, 1H, C***H***-7), 4.16 (q, *J* = 7.2 Hz, 2H, C***H*****$_2$**-ethyl ester), 4.15 (q, *J* = 7.2 Hz, 2H, C***H*****$_2$**-ethyl ester), 3.92 (app tt, *J* = 7.1, 5.4 Hz, 1H, C***H***-3), 2.63 (dd, *J* = 15.0, 7.1 Hz, 1H, C***H***-2), 2.48 (dd, *J* = 15.0, 5.4 Hz, 1H, C***H***-2), 1.68-1.39 (m, 4H, C***H***-4, C***H***-5), 1.26 (t, *J* = 7.2 Hz, 3H, C***H*****$_3$**-ethyl ester), 0.94 (t, *J* = 7.2 Hz, 3H, C***H***-6).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.8 (C-1), 138.6 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.5 (C-Ar), 76.0 (C-3), 71.5 (C-7), 60.4 (***C***H_2-ethyl ester), 40.0 (C-2), 36.7 (C-4), 18.4 (C-5), 14.2 (C-6 or ***C***H_3-ethyl ester), 14.1 (C-6 or ***C***H_3-ethyl ester).

IR (neat, cm^{-1}) 2959, 2934, 2872, 1732, 1467, 1454, 1369, 1308, 1230, 1179, 1092, 1067, 1028.

HRMS (CI, *m*/*z*) calcd for $(C_{15}H_{23}O_3)^+$ 251.1647, found 251.1650.

Ethyl (*R*)-3-(Benzyloxy)hexanoate 367

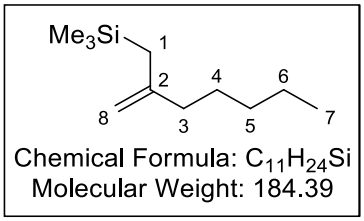


Chemical Formula: $C_{15}H_{22}O_3$
Molecular Weight: 250.33

Benzylated alcohol **367** was obtained according to the previous procedure from the corresponding ß-hydroxyester **76.**
Scale: 47.1 mmol
Yield: 79%

$[\alpha]^{25}_D = -4.0^\circ$ (*c* 1.0, $CHCl_3$)

Trimethyl(2-methyleneheptyl)silane 284



Chemical Formula: $C_{11}H_{24}Si$
Molecular Weight: 184.39

Cerium(III) chloride heptahydrate (27.8 g, 74.5 mmol, 3.50 equiv) was added to a 500 mL three-necked round-bottomed flask and dried under vacuum at 120 °C for 2 h, 140 °C for 2 h and then at 160 °C for 2 h. The flask was allowed to cool down and was purged with argon for 10 min, and dry THF (200 mL) was added. The mixture was stirred for 20 h at room temperature under argon to give the cerium(III) chloride-THF complex as a white precipitate.
A trimethylsilylmethylmagnesium chloride solution (1.30 M in THF, 57.0 mL, 74.5 mmol, 3.50 equiv) was added dropwise at −78 °C under argon. The gray suspension was stirred for 30 min, and then ethyl caproate (3.07 g, 21.3 mmol) in dry THF (15 mL) was added at −78 °C. The reaction was stirred at −78 °C for 2 h, the flask was then removed from the cold bath, and the mixture was stirred at room temperature for 15 h. The reaction mixture was cooled to 0 °C, a saturated aqueous solution of ammonium chloride (200 mL) was added at 0 °C, and the mixture was stirred for 20 min. Water was added, and the mixture was extracted with ether (3 × 150 mL). The combined ether extracts were washed with water and brine (2 × 300 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil. The oil was then stirred overnight with silica in dichloromethane. Filtration, followed by concentration *in vacuo* gave the allylic silane **284** (3.59 g, 91%) as a clear oil.

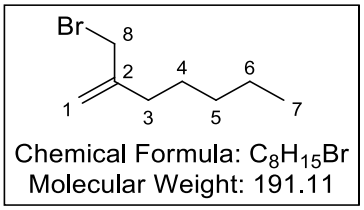
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (s, 1H, C***H***-8), 4.49 (s, 1H, C***H***-8), 1.94 (t, *J* = 7.6 Hz, 2H, C***H***-3), 1.52 (s, 2H, C***H***-1), 1.46-1.39 (m, 2H, C***H***-4), 1.35-1.22 (m, 4H, C***H***-5, C***H***-6), 0.89 (t, *J* = 7.0 Hz, 3H, C***H***-7), 0.01 (s, 9H, -Si(C***H*****$_3$**$)_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0 (C-2), 106.6 (C-8), 38.2 (C-3), 31.7 (C-1), 27.5 (C-4 or C-5), 26.8 (C-4 or C-5), 22.6 (C-6), 14.1 (C-7), −1.3 (-Si(***C***$H_3)_3$).

IR (neat, cm^{-1}) 2956, 2929, 2861, 1633, 1467, 1418, 1248, 1157.

HRMS (CI, *m*/*z*) calcd for $(C_{11}H_{25}Si)^+$ 185.1726, found 185.1722.

2-(Bromomethyl)hept-1-ene 287[107]



Chemical Formula: $C_8H_{15}Br$
Molecular Weight: 191.11

General procedure for bromination

Pyrrolidone hydrotribromide (4.1 g, 7.8 mmol, 1.0 equiv) was added to a stirred solution of the allylic silane **284** (1.44 g, 7.82 mmol) and pyridine (4.1 mL, 51 mmol, 6.5 equiv) in dry THF (322 mL) at −10 °C under argon. The mixture was stirred for 2 h and allowed to warm to room temperature during this period. A saturated aqueous solution of sodium thiosulfate (250 mL) was added and the resulting mixture was stirred for 5 min. The mixture was extracted with ether (3 × 200 mL). The ether extracts were combined and washed with a saturated aqueous solution of copper sulfate (2 × 300 mL) and brine (2 × 300 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver a yellow oil. Purification by column chromatography on silica gel (petroleum ether-ether 99/1) gave the bromide **287** (1.36 g, 91%) as a clear oil.

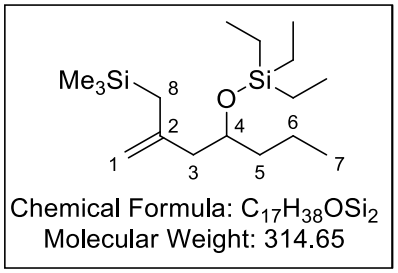
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 (s, 1H, C***H***-1), 4.96 (s, 1H, C***H***-1), 3.97 (s, 2H, C***H***-8), 2.21 (t, *J* = 7.6 Hz, 2H, C***H***-3), 1.51-1.43 (m, 2H, C***H***-4), 1.38-1.25 (m, 4H, C***H***-5, C***H***-6), 0.90 (t, *J* = 7.0 Hz, 3H, C***H***-7).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7 (C-2), 114.8 (C-1), 36.9 (C-8), 33.3 (C-3), 31.4 (C-4 or C-5), 27.0 (C-4 or C-5), 22.5 (C-6), 14.0 (C-7).

IR (neat, cm^{-1}) 2957, 2928, 2859, 1640, 1467, 1437, 1249, 1208.

[107] Overman, L. E.; Lesuisse, D. *Tetrahedron Lett.* **1985**, *26*, 4167.

Triethyl(2-((trimethylsilyl)methyl)hept-1-en-4-yloxy)silane 282



The crude silane **282** was obtained from the corresponding ester **279** according to the procedure described above for silane **284**. The crude oil was purified by column chromatography on silica gel (petroleum ether-ether 98/2) and the resulting oil was stirred overnight with silica in dichloromethane. The mixture was then filtered and concentrated *in vacuo* to give the allylic silane **282** as a clear oil.
Scale: 18.0 mmol
Yield: 85%

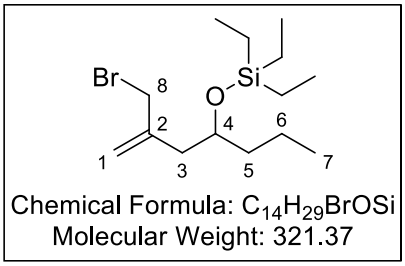
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (m, 1H, C***H***-1), 4.56 (m, 1H, C***H***-1), 3.80 (m, 1H, C***H***-4), 2.15 (ddd, *J* = 13.6, 5.8, 0.8 Hz, 1H, C***H***-3), 2.07 (ddd, *J* = 13.6, 7.1, 0.5 Hz, 1H, C***H***-3), 1.53 (s, 2H, C***H***-8), 1.51-1.26 (m, 4H, C***H***-5, C***H***-6), 0.97 (t, *J* = 8.1 Hz, 9H, C***H***$_3$-TES group), 0.91 (t, *J* = 7.1 Hz, 3H, C***H***-7), 0.61 (q, *J* = 7.8 Hz, 6H, C***H***$_2$-TES group), 0.03 (s, 9H, -Si(C***H***$_3$)$_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5 (C-2), 109.6 (C-1), 71.2 (C-4), 46.6 (C-3), 39.3 (C-5), 27.1 (C-8), 18.6 (C-6), 14.3 (C-7), 7.0 (***C***H$_3$-TES group), 5.1 (***C***H$_2$-TES group), −1.4 (-Si(***C***H$_3$)$_3$).

IR (neat, cm^{-1}) 2955, 2910, 2876, 1634, 1458, 1416, 1248, 1099, 1074, 1040, 1005.

HRMS (ESI, *m*/*z*) calcd for $(C_{17}H_{38}OSi_2Na)^+$ 337.2353, found 337.2327.

(2-(Bromomethyl)hept-1-en-4-yloxy)triethylsilane 285



Chemical Formula: $C_{14}H_{29}BrOSi$
Molecular Weight: 321.37

Bromide **285** was obtained according to the general procedure for bromination described above from the corresponding allylic silane **282**.
Scale: 7.95 mmol
Yield: 92%

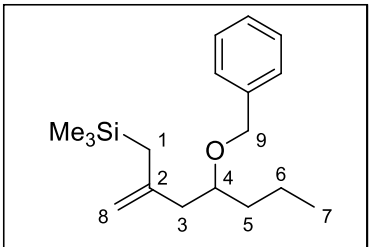
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (m, 1H, C***H***-1), 5.00 (m, 1H, C***H***-1), 4.06 (dd, *J* = 10.0, 0.5 Hz, 1H, C***H***-8), 4.00 (dd, *J* = 10.0, 0.8 Hz, 1H, C***H***-8), 3.84 (app quint, *J* = 6.1 Hz, 1H, C***H***-4), 2.41 (ddd, *J* = 14.0, 5.8, 0.8 Hz, 1H, C***H***-3), 2.34 (ddd, *J* = 14.0, 6.1, 0.8 Hz, 1H, C***H***-3), 1.46-1.26 (m, 4H, C***H***-5, C***H***-6), 0.97 (t, *J* = 8.0 Hz, 9H, C***H***$_3$-TES group), 0.91 (t, *J* = 7.1 Hz, 3H, C***H***-7), 0.61 (q, *J* = 8.0 Hz, 6H, C***H***$_2$-TES group).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0 (C-2), 117.7 (C-1), 70.9 (C-4), 41.0 (C-3), 39.3 (C-5), 37.4 (C-8), 18.6 (C-6), 14.2 (C-7), 6.9 (***C***H_3-TES group), 5.1 (***C***H_2-TES group).

IR (neat, cm^{-1}) 2957, 2936, 2913, 2876, 1458, 1414, 1377, 1238, 1209, 1105, 1074, 1040, 1005.

HRMS (CI, *m*/*z*) calcd for $(C_{14}H_{30}{}^{79}BrOSi)^+$ 321.1249, found 321.1248.

(4-(Benzyloxy)-2-methyleneheptyl)trimethylsilane 283



Chemical Formula: $C_{18}H_{30}OSi$
Molecular Weight: 290.52

Cerium(III) chloride heptahydrate (21.3 g, 57.1 mmol, 3.50 equiv) was dried under vacuum at 120 °C for 2 h, 140 °C for 2 h and then at 160 °C for 2 h. The flask was allowed to cool down to room temperature and was purged with argon for 10 min, and dry THF (190 mL) was added. The mixture was stirred for 20 h at room temperature under argon to give the cerium(III) chloride-THF complex as a white precipitate.
To a stirred solution of magnesium (1.4 g, 57 mmol, 3.5 equiv) and 1,2-dibromoethane (3 drops) in THF (48 mL) at 65 °C was added slowly a solution of chloromethyltrimethylsilane (8.0 mL, 58 mmol, 3.5 equiv) in THF (12 mL). The solution was then stirred for 2 h at room temperature.
The above solution was then added dropwise (over 1 h) at −78 °C to the cerium. The gray suspension was stirred for 30 min, and then ester **280** (4.09 g, 16.3 mmol) in dry THF (20 mL) was added at −78 °C. The reaction was stirred at −78 °C for 2 h, the flask was then removed from the cold bath, and the mixture was stirred at room temperature for 15 h. A saturated aqueous solution of ammonium chloride (200 mL) was added at 0 °C, and the mixture was stirred for 20 min. Water was added, and the mixture was extracted with diethyl ether (3 × 200 mL). The combined ether extracts were washed with water and brine (2 × 300 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil. The oil was stirred one day with silica gel in dichloromethane. The mixture was then filtered and concentrated *in vacuo* and the resulting crude oil was purified by column chromatography on silica gel (petroleum ether-ether 98/2) to give the allylic silane **283** (2.90 g, 61%) as a clear oil.

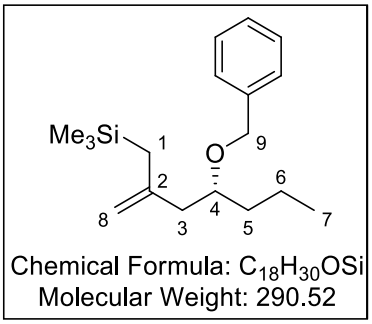
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H, ***H***-Ar), 4.68-4.67 (m, 1H, C***H***-8), 4.62-4.61 (m, 1H, C***H***-8), 4.58 (d, *J* = 11.5 Hz, 1H, C***H***-9), 4.51 (d, *J* = 11.5 Hz, 1H, C***H***-9), 3.58-3.52 (m, 1H, C***H***-4), 2.34 (dd, *J* = 14.0, 6.2 Hz, 1H, C***H***-3), 2.10 (dd, *J* = 14.0, 6.5 Hz, 1H, C***H***-3), 1.56 (d, *J* = 2.5 Hz, 2H, C***H***-1), 1.54-1.47 (m, 3H, C***H***-5, C***H***-6), 1.41-1.33 (m, 1H, C***H***-6), 0.91 (t, *J* = 7.1 Hz, 3H, C***H***-7), 0.04 (s, 9H, -Si(C***H₃***)$_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7 (C-2), 139.0 (C-Ar), 128.3 (C-Ar), 127.8 (C-Ar), 127.4 (C-Ar), 109.6 (C-8), 77.8 (C-4), 71.1 (C-9), 43.1 (C-3), 36.5 (C-5), 27.1 (C-1), 18.7 (C-6), 14.2 (C-7), −1.3 (-Si(***C***H$_3$)$_3$).

IR (neat, cm^{-1}) 2957, 2934, 2872, 1497, 1454, 1248, 1090, 1069, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{18}H_{30}OSiNa)^+$ 313.1958, found 313.1949.

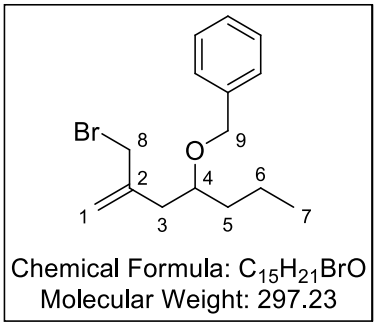
(*R*)-(4-(Benzyloxy)-2-methyleneheptyl)trimethylsilane 432



The crude silane **432** was obtained from the corresponding ester **367** according to the procedure described above for silane **283**. The crude oil obtained after stirring one day with silica gel, followed by filtration and concentration *in vacuo*, was used for the next step without further purification.
Scale: 20.0 mmol
Yield: quant.

$[\alpha]^{25}_{D}$ = +13.6° (*c* 1.0, $CHCl_3$)

(((2-(Bromomethyl)hept-1-en-4-yl)oxy)methyl)benzene 286



Chemical Formula: $C_{15}H_{21}BrO$
Molecular Weight: 297.23

Bromide **286** was obtained according to the general procedure for bromination described above from the corresponding allylic silane **283**. (Purification by column chromatography on silica gel (petroleum ether-ether 98/2)).
Scale: 10.0 mmol
Yield: 88%

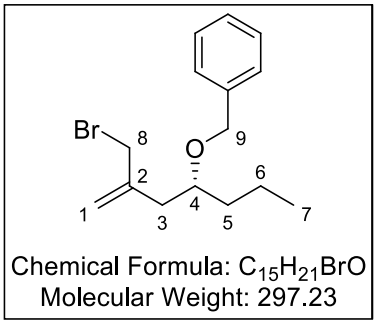
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H, ***H***-Ar), 5.26 (s, 1H, C***H***-1), 5.05 (s, 1H, C***H***-1), 4.58 (d, *J* = 11.5 Hz, 1H, C***H***-9), 4.55 (d, *J* = 11.5 Hz, 1H, C***H***-9), 4.04 (d, *J* = 10.1 Hz, 1H, C***H***-8), 3.99 (d, *J* = 10.1 Hz, 1H, C***H***-8), 3.60 (app quint, *J* = 5.8 Hz, 1H, C***H***-4), 2.52 (dd, *J* = 14.7, 5.6 Hz, 1H, C***H***-3), 2.47 (dd, *J* = 14.7, 6.6 Hz, 1H, C***H***-3), 1.63-1.34 (m, 4H, C***H***-5, C***H***-6), 0.93 (t, *J* = 7.3 Hz, 3H, C***H***-7).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9 (C-2), 138.7 (C-Ar), 128.3 (C-Ar), 127.8 (C-Ar), 127.5 (C-Ar), 117.6 (C-1), 77.2 (C-4), 70.9 (C-9), 37.7 (C-3), 37.3 (C-8), 36.1 (C-5), 18.6 (C-6), 14.2 (C-7).

IR (neat, cm^{-1}) 2957, 2932, 2870, 1497, 1454, 1352, 1209, 1067, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{15}H_{21}O^{79}BrNa)^+$ 319.0668, found 319.0660.

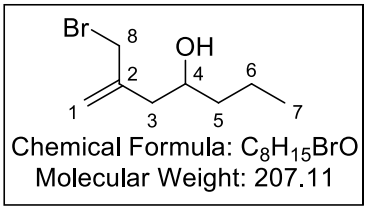
(*R*)-((2-(Bromomethyl)hept-1-en-4-yloxy)methyl)benzene 433



Bromide **433** was obtained according to the general procedure for bromination described above from the corresponding allylic silane **432**. (Purification by column chromatography on silica gel (petroleum ether-ether 97/3)).
Scale: 20.0 mmol
Yield: 71%

$[\alpha]^{25}_{D}$ = +12.4° (*c* 1.0, $CHCl_3$)

2-(Bromomethyl)hept-1-en-4-ol 288



Chemical Formula: $C_8H_{15}BrO$
Molecular Weight: 207.11

A solution of bromide **285** (0.99 g, 3.1 mmol) in 5/95 HF/CH_3CN (20 mL) was stirred for 2 h at room temperature. A saturated aqueous solution of calcium chloride (40 mL) was added to the reaction mixture. The mixture was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate (20 mL), brine (50 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the alcohol **288** as a clear oil (0.63 g, 98%), which was used without further purification.

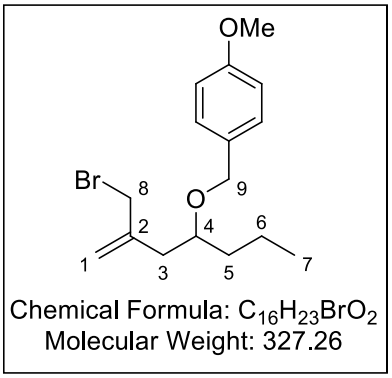
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31 (m, 1H, C***H***-1), 5.09 (app q, *J* = 1.3 Hz, 1H, C***H***-1), 4.05 (dd, *J* = 10.1, 0.7 Hz, 1H, C***H***-8), 4.02 (dd, *J* = 10.1, 0.5 Hz, 1H, C***H***-8), 3.83 (m, 1H, C***H***-4), 2.50 (ddd, *J* = 14.5, 3.5, 1.0 Hz, 1H, C***H***-3), 2.24 (ddd, *J* = 14.5, 9.3, 0.8 Hz, 1H, C***H***-3), 1.52-1.38 (m, 4H, C***H***-5, C***H***-6), 0.96 (t, *J* = 7.2 Hz, 3H, C***H***-7).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7 (C-2), 118.0 (C-1), 69.3 (C-4), 41.8 (C-3), 39.5 (C-5), 36.6 (C-8), 18.9 (C-6), 14.0 (C-7).

IR (neat, cm^{-1}) 3364, 2957, 2932, 2872, 1638, 1379, 1209, 1121, 1070, 1018.

HRMS (CI, *m*/*z*) calcd for $(C_8H_{16}{}^{79}BrO)^+$ 207.0385, found 207.0384.

1-((2-(Bromomethyl)hept-1-en-4-yloxy)methyl)-4-methoxybenzene 289



To a stirred solution of sodium hydride (48.0 mg, 1.14 mmol, 0.300 equiv) in diethyl ether (2 mL) was added dropwise a solution of 4-methoxybenzyl alcohol (1.10 g, 7.56 mmol, 2.00 equiv) in diethyl ether (2 mL). The mixture was stirred for 20 min at room temperature. Freshly distilled trichloroacetonitrile (0.800 mL, 7.56 mmol, 2.00 equiv) was then added dropwise at 0 °C and the resulting mixture was stirred for 1 h and the temperature was allowed to warm up during this period. The solution was then concentrated *in vacuo* and the crude oil was washed with a solution of pentane (5 mL) and methanol (0.6 mL), filtered and concentrated *in vacuo*. This process washing/filtration/concentration was repeated three times to give 4-methoxybenzyl trichloroacetimidate (1.9 g, 89%) as a clear oil.
To a stirred solution of alcohol **288** (717 mg, 3.46 mmol) in dichloromethane (7.5 mL) was added the previously formed 4-methoxybenzyl trichloroacetimidate in dichloromethane (0.5 mL), followed by camphorsulfonic acid (81 mg, 0.35 mmol, 0.10 equiv). The mixture was then stirred for one day at room temperature. A saturated aqueous solution of sodium bicarbonate (15 mL) was then added. The mixture was extracted with diethyl ether (3 × 10mL) and the combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography (dry column) on silica gel (petroleum ether-ether 9/1) gave the protected alcohol **289** (962 mg, 85%) as a clear oil.

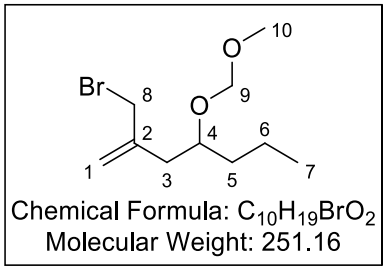
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.5 Hz, 2H, ***H***-Ar), 6.88 (d, *J* = 8.5 Hz, 2H, ***H***-Ar), 5.25 (m, 1H, C***H***-1), 5.03 (m, 1H, C***H***-1), 4.50 (d, *J* = 11.1 Hz, 1H, C***H***-9), 4.47 (d, *J* = 11.1 Hz, 1H, C***H***-9), 4.03 (d, *J* = 10.0 Hz, 1H, C***H***-8), 3.99 (d, *J* = 10.0 Hz, 1H, C***H***-8), 3.81 (s, 3H, C***H***$_3$-PMB), 3.57 (m, 1H, C***H***-4), 2.49 (dd, *J* = 14.9, 6.4 Hz, 1H, C***H***-3), 2.45 (dd, *J* = 14.9, 6.4 Hz, 1H, C***H***-3), 1.56-1.31 (m, 4H, C***H***-5, C***H***-6), 0.92 (t, *J* = 7.2 Hz, 3H, C***H***-7).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C-Ar), 142.9 (C-2), 130.8 (C-Ar), 129.4 (C-Ar), 117.6 (C-1), 113.7 (C-Ar), 76.8 (C-4), 70.5 (C-9), 55.3 (***C***H_3-PMB), 37.7 (C-3), 37.4 (C-8), 36.1 (C-5), 18.7 (C-6), 14.1 (C-7).

IR (neat, cm^{-1}) 2955, 2934, 2870, 1613, 1512, 1464, 1302, 1244, 1209, 1173, 1034.

HRMS (ESI, *m*/*z*) calcd for $(C_{16}H_{23}{}^{79}BrO_2Na)^+$ 349.0774, found 349.0764.

2-(Bromomethyl)-4-(methoxymethoxy)hept-1-ene 290



Chemical Formula: $C_{10}H_{19}BrO_2$
Molecular Weight: 251.16

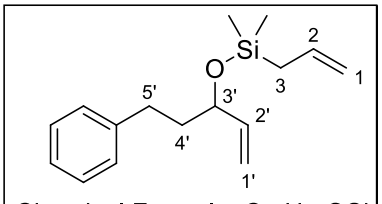
To a stirred solution of alcohol **288** (461 mg, 2.23 mmol) in dichloromethane (3 mL) at 0 °C were added methoxymethyl chloride (0.29 mL, 3.5 mmol, 1.5 equiv), diisopropylethylamine (0.60 mL, 3.5 mmol, 1.5 equiv) and DMAP (4 mg, 0.03 mmol, 1.5 mol%). The solution was stirred overnight at room temperature and was then quenched by addition of a saturated aqueous solution of ammonium chloride (3 mL). The mixture was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 95/5) gave allyl bromide **290** (241 mg, 43%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22 (d, 1H, *J* = 1.1 Hz, C***H***-1), 5.05 (d, 1H, *J* = 1.1 Hz, C***H***-1), 4.67 (d, 1H, *J* = 7.1 Hz, C***H***-9), 4.65 (d, 1H, *J* = 7.1 Hz, C***H***-9), 4.16 (dd, 1H, *J* = 11.8, 1.0 Hz, C***H***-8), 4.08 (dd, 1H, *J* = 11.8, 0.9 Hz, C***H***-8), 3.78-3.72 (m, 1H, C***H***-4), 3.37 (s, 3H, C***H***-10), 2.44 (ddd, 1H, *J* = 14.5, 5.5, 1.0 Hz, C***H***-3), 2.37 (ddd, 1H, *J* = 14.5, 6.8, 0.9 Hz, C***H***-3), 1.56-1.31 (m, 4H, C***H***-5, C***H***-6), 0.93 (t, 3H, *J* = 7.2 Hz, C***H***-7).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.4 (C-2), 117.0 (C-1), 95.3 (C-9), 75.3 (C-4), 55.6 (C-10), 48.4 (C-8), 38.1 (C-3), 36.6 (C-5), 18.6 (C-6), 14.1 (C-7).

IR (neat, cm^{-1}) 2959, 2932, 2874, 1441, 1260, 1148, 1096, 1036.

Allyldimethyl(5-phenylpent-1-en-3-yloxy)silane 294



Chemical Formula: $C_{16}H_{24}OSi$
Molecular Weight: 260.45

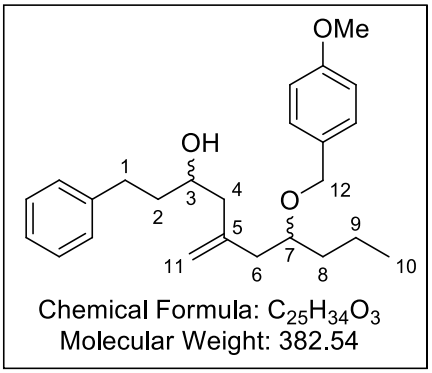
Allyl bromide (0.70 g, 5.8 mmol, 1.8 equiv) was added to a stirred solution of indium (0.44 g, 3.8 mmol, 1.2 equiv) in DMI (7.5 mL) at room temperature under argon. The mixture was stirred for 2 h at room temperature under argon. Dichlorodimethylsilane (0.48 g, 3.8 mmol, 1.2 equiv) was added to the mixture and the reaction was stirred for 3 h at 70 °C under argon.
The mixture was allowed to cool down and was added dropwise to a stirred solution of **293** (0.50 g, 3.1 mmol), triethylamine (0.78 g, 7.7 mmol, 2.5 equiv) and DMAP (0.19 g, 1.5 mmol, 0.50 equiv) in THF (10 mL) at 0 °C under argon. The reaction mixture was stirred overnight at room temperature under argon. The reaction mixture was then quenched with a saturated aqueous solution of sodium hydrogen carbonate (10 mL) and extracted with ether (3 × 10 mL). The ether extracts were combined and washed with brine (2 × 20 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to deliver a yellow oil. Purification by column chromatography on silica gel (petroleum ether-ether 99/1) gave the product **294** (0.29 g, 56%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H, ***H***-Ar), 7.20-7.16 (m, 3H, ***H***-Ar), 5.89-5.74 (m, 2H, C***H***-2, C***H***-2'), 5.18 (ddd, *J* = 17.1, 1.5, 1.4 Hz, 1H, C***H***-1'$_{trans}$), 5.08 (ddd, *J* = 10.4, 1.5, 1.3 Hz, 1H, C***H***-1'$_{cis}$), 4.92-4.84 (m, 2H, C***H***-1), 4.14 (m, 1H, C***H***-3'), 2.73-2.57 (m, 2H, C***H***-5'), 1.89-1.74 (m, 2H, C***H***-4'), 1.63 (d, *J* = 8.1 Hz, 2H, C***H***-3), 0.125 (s, 3H, -Si(C***H***$_3$)$_{2-}$), 0.121 (s, 3H, -Si(C***H***$_3$)$_{2-}$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2 (C-Ar), 141.2 (C-2'), 134.2 (C-2), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 114.3 (C-1'), 113.6 (C-1), 73.5 (C-3'), 39.5 (C-4'), 31.6 (C-5'), 25.0 (C-3), −1.7 (-Si(***C***H$_3$)$_2$), −1.9 (-Si(***C***H$_3$)$_2$).

IR (neat, cm^{-1}) 3078, 3027, 2949, 2915, 2860, 1631, 1605, 1497, 1454, 1422, 1252, 1083, 1030.

7-(4-Methoxybenzyloxy)-5-methylene-1-phenyldecan-3-ol 305



Zinc dust (24 mg, 0.37 mmol, 1.2 equiv) was heated to 70 °C. 1,2-Dibromoethane (3.0 µL, 0.040 mmol, 0.12 equiv) and THF (0.1 mL) were then added and the mixture was stirred at 70 °C for 10 min. The reaction mixture was allowed to cool down. Chlorotrimethylsilane (3.0 µL, 0.025 mmol, 0.080 equiv) and THF (0.1 mL) were then added and the mixture was stirred for another 10 min. A solution of bromide **289** (100 mg, 0.310 mmol) in THF (0.2 mL) was then added and the reaction mixture was stirred at room temperature for 5-10 min. The solution was then concentrated *in vacuo* and hydrocinnamaldehyde (0.030 mL, 0.25 mmol, 0.80 equiv) was added, and the reaction was stirred in open air for 2 h. A saturated aqueous solution of ammonium chloride (5 mL) was added and the mixture was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 95/5) gave alcohol **305** (17 mg, 18%) as a clear oil and as a 1:1 mixture of diastereomers.

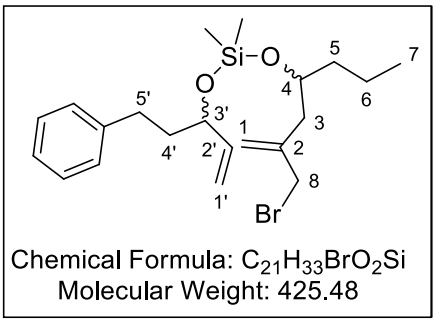
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.18 (m, 7H, ***H***-Ar), 6.87 (d, *J* = 8.6 Hz, 2H, ***H***-Ar (PMB)), 4.93 (m, 2H, C***H***-11), 4.47-4.40 (m, 2H, C***H***-12), 3.80 (s, 3H, C***H***$_3$-PMB group), 3.72 (m, 1H, C***H***-3), 3.53 (m, 1H, C***H***-7), 2.83-2.76 (m, 1H, C***H***-1), 2.70-2.63 (m, 1H, C***H***-1), 2.38-2.09 (m, 4H, C***H***-4, C***H***-6), 1.76 (m, 2H, C***H***-2), 1.58-1.33 (m, 4H, C***H***-8, C***H***-9), 0.92 (t, *J* = 7.1 Hz, 1.5H, C***H***-10), 0.91 (t, *J* = 7.3 Hz, 1.5 H, C***H***-10).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C-Ar), 144.3 (C-5), 143.8 (C-5), 142.2 (C-Ar), 142.2 (C-Ar), 130.7 (C-Ar), 130.6 (C-Ar), 129.4 (C-Ar), 129.4 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 115.2 (C-11), 115.1 (C-11), 113.7 (C-Ar), 77.6 (C-7), 77.1 (C-7), 70.6 (C-12), 70.4 (C-12), 68.6 (C-3), 68.2 (C-3), 55.2 (***C***H$_3$-PMB), 45.1 (C-4), 45.0 (C-4), 40.5 (C-6), 40.1 (C-6), 38.8 (C-2), 38.8 (C-2), 36.1 (C-8), 36.0 (C-8), 32.1 (C-1), 18.6 (C-9), 18.5 (C-9), 14.3 (C-10).

IR (neat, cm^{-1}) 3428, 3026, 2955, 2932, 2868, 1730, 1612, 1512, 1454, 1246, 1173, 1032.

HRMS (EI, *m*/*z*) calcd for $(C_{25}H_{34}O_3)^+$ 382.2508, found 382.2513.

(2-(Bromomethyl)hept-1-en-4-yloxy)dimethyl(5-phenylpent-1-en-3-yloxy)silane 307



Chemical Formula: $C_{21}H_{33}BrO_2Si$
Molecular Weight: 425.48

Zinc dust (24 mg, 0.37 mmol, 1.2 equiv) was heated to 70 °C. Chlorotrimethylsilane (0.4 µL, 0.003 mmol, 0.01 equiv) and THF (0.25 mL) were then added and the mixture was stirred at 70 °C for 15 min. The mixture was allowed to cool down and a solution of bromide **285** or **289** (99.6 mg for **285**, 101 mg for **289**, 0.310 mmol) in THF (0.25 mL) was added dropwise. The solution was stirred for 5 min at room temperature. The solution was then added dropwise to a stirred solution of freshly distilled dichlorodimethylsilane (0.37 mL, 3.1 mmol, 10 equiv) in THF (0.25 mL) at room temperature. The reaction mixture was stirred for 30 min at room temperature. The solution was concentrated *in vacuo* using a trap-to-trap distillation and the obtained oil was dried under vacuum pump for 30 min.
A solution of the previous oil in THF (0.5 mL) was then added dropwise to a stirred solution of alcohol **293** (42 mg, 0.26 mmol, 0.83 equiv), triethylamine (0.090 mL, 0.65 mmol, 2.1 equiv) and DMAP (16 mg, 0.13 mmol, 0.42 equiv) in THF (1 mL) at 0 °C. The reaction mixture was stirred overnight at room temperature. A saturated aqueous solution of sodium bicarbonate (5 mL) was added and the mixture was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 99/1) gave the dioxasilocine **307** (71 mg, 64% for **285**; 50 mg, 45% for **289**) as a clear oil and as a 1:1 mixture of diastereomers.

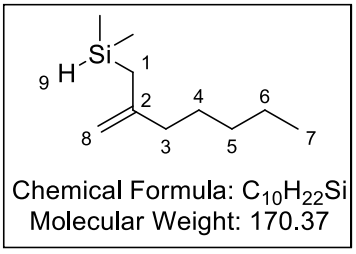
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H, ***H***-Ar), 7.20-7.17 (m, 3H, ***H***-Ar), 5.86 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1H, C***H***-2'), 5.24 (s, 1H, C***H***-1), 5.19 (dt, *J* = 17.0, 1.3 Hz, 1H, C***H***-1'$_{trans}$), 5.1 (dt, *J* = 10.4, 1.1 Hz, 1H, C***H***-1'$_{cis}$), 5.00 (s, 1H, C***H***-1), 4.27 (app q, *J* = 6.2 Hz, 1H, C***H***-3'), 4.08 (dd, *J* = 10.0, 1.7 Hz, 1H, C***H***-8), 3.99 (d, *J* = 10.0 Hz, 1H, C***H***-8), 3.99 (m, 1H, C***H***-4), 2.72-2.61 (m, 2H, C***H***-5'), 2.45 (d, *J* = 14.3, 5.6 Hz, 1H, C***H***-3), 2.36 (ddd, *J* = 14.0, 6.6, 2.4 Hz, 1H, C***H***-3), 1.92-1.79 (m, 2H, C***H***-4'), 1.49-1.28 (m, 4H, C***H***-5, C***H***-6), 0.91 (t, *J* = 7.1 Hz, 3H, C***H***-7), 0.13 (s, 6H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9 (C-2), 142.1 (C-Ar), 140.8 (C-2'), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 117.8 (C-1), 114.5 (C-1'), 73.2 (C-3'), 70.9 (C-4), 40.9 (C-3), 39.4 (C-5 or C-4'), 39.2 (C-5 or C-4'), 37.5 (C-8), 31.4 (C-5'), 18.7 (C-6), 14.1 (C-7), −1.3 (-Si(***C***H$_3$)$_2$-), −1.4 (-Si(***C***H$_3$)$_2$-), −1.5 (-Si(***C***H$_3$)$_2$-), −1.7 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2961, 2938, 2870, 1456, 1258, 1078, 1041.

HRMS (ESI, *m*/*z*) calcd for ($C_{21}H_{33}{}^{79}BrO_2SiNa$)$^+$ 447.1325, found 447.1307.

Dimethyl(2-methyleneheptyl)silane 317



Chemical Formula: $C_{10}H_{22}Si$
Molecular Weight: 170.37

Method 1:

To a stirred solution of magnesium (150 mg, 6.22 mmol, 3.30 equiv) and chlorodimethylsilane (0.210 mL, 1.86 mmol, 1.00 equiv) in THF (1 mL) was added dropwise (over 1 h) at room temperature a solution of bromide **287** (355 mg, 1.86 mmol) in THF (1.8 mL). The reaction mixture was stirred at room temperature for 2 h. A saturated aqueous solution of ammonium chloride (5 mL) was then added and the mixture was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver silane **317** (257 mg, 81%) as a clear oil.

Method 2:

Cerium(III) chloride heptahydrate (10.1 g, 27.1 mmol, 5.00 equiv) was dried under vacuum at 120 °C for 2 h, 140 °C for 2 h and then at 160 °C for 2 h. The flask was allowed to cool down to room temperature and was purged with argon for 10 min, and dry THF (97 mL) was added. The mixture was stirred for 20 h at room temperature under argon to give the cerium(III) chloride-THF complex as a white precipitate.
To a stirred solution of magnesium (600 mg, 27.1 mmol, 5.00 equiv) and 1,2-dibromoethane (3 drops) in THF (24 mL) at 65 °C was added slowly a solution of chloromethyldimethylsilane (3.30 mL, 27.1 mmol, 5.00 equiv) in THF (6 mL). The solution was then stirred for 2 h at room temperature.
The above solution was then added dropwise (over 1 h) at −78 °C to the cerium. The gray suspension was stirred for 30 min, and then ethyl caproate (0.90 mL, 5.4 mmol) in dry THF (9.9 mL) was added at −78 °C. The reaction was stirred at −78 °C for 2 h, the flask was then removed from the cold bath, and the mixture was stirred at room temperature for 15 h. A saturated aqueous solution of ammonium chloride (130 mL) was added at 0 °C, and the mixture was stirred for 20 min. Water was added, and the mixture was extracted with diethyl ether (3 × 100 mL). The combined ether extracts were washed with water and brine (2 × 200 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil. The oil was stirred for one day with silica gel in dichloromethane. The mixture was then filtered and concentrated *in vacuo* to deliver silane **317** (563 mg, 61%) as a clear oil.

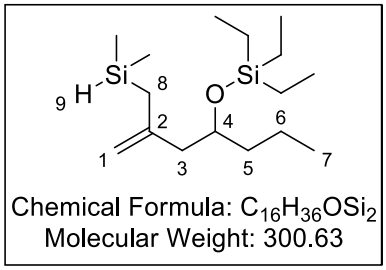
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (m, 1H, C***H***-8), 4.56 (m, 1H, C***H***-8), 3.91 (non, *J* = 3.5 Hz, 1H, Si-***H***), 1.99 (t, *J* = 7.6 Hz, 2H, C***H***-3), 1.60 (dd, *J* = 3.5, 1.0 Hz, 2H, C***H***-1), 1.48-1.41 (m, 2H, C***H***-4), 1.35-1.25 (m, 4H, C***H***-5, C***H***-6), 0.90 (t, *J* = 7.1 Hz, 3H, C***H***-7), 0.10 (d, *J* = 3.5 Hz, 6H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6 (C-2), 107.2 (C-8), 37.8 (C-3), 31.6 (C-4 or C-5), 27.4 (C-4 or C-5), 24.3 (C-1 or C-6), 22.6 (C-1 or C-6), 14.1 (C-7), −4.3 (-Si(***C***$H_3)_2$-).

IR (neat, cm^{-1}) 2955, 2926, 2859, 1730, 1647, 1458, 1248.

HRMS (EI, *m*/*z*) calcd for $C_{10}H_{22}Si$ 170.1491, found 170.1487.

(2-((Dimethylsilyl)methyl)hept-1-en-4-yloxy)triethylsilane 318



Chemical Formula: $C_{16}H_{36}OSi_2$
Molecular Weight: 300.63

Method 1:

Hydrosilane **318** was obtained from the corresponding bromide **285** according to the procedure (method 1) described above for hydrosilane **317**. In this case, the reaction time was increased to 5 h. (Purification by column chromatography on silica gel (petroleum ether)).
Scale: 3.11 mmol
Yield: 86%

Method 2:

Hydrosilane **318** was obtained from the corresponding ester **279** according to the procedure (method 2) described above for hydrosilane **317**. (Purification by column chromatography on silica gel (petroleum ether-ether 99/1)).
Scale: 5.87 mmol
Yield: 48%

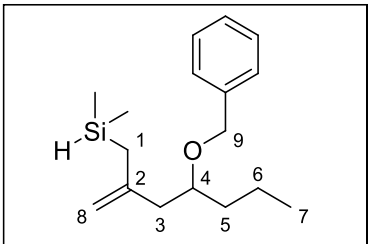
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (s, 1H, C***H***-1), 4.63 (s, 1H, C***H***-1), 3.93 (non, *J* = 3.6 Hz, 1H, Si-***H***), 3.82 (m, 1H, C***H***-4), 2.20 (dd, *J* = 13.8, 5.7 Hz, 1H, C***H***-3), 2.12 (dd, *J* = 13.8, 7.1 Hz, 1H, C***H***-3), 1.62 (dd, *J* = 14.0, 3.3 Hz, 1H, C***H***-8), 1.59 (dd, *J* = 14.0, 3.3 Hz, 1H, C***H***-8), 1.52-1.27 (m, 4H, C***H***-5, C***H***-6), 0.97 (t, *J* = 8.0 Hz, 9H, C***H***$_3$-TES group), 0.91 (t, *J* = 6.9 Hz, 3H, C***H***-7), 0.61 (q, *J* = 8.0 Hz, 6H, C***H***$_2$-TES group), 0.11 (d, *J* = 3.6 Hz, 3H, -Si(C***H***$_3$)$_2$-), 0.10 (d, *J* = 3.6 Hz, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2 (C-2), 110.3 (C-1), 71.0 (C-4), 46.2 (C-3), 39.3 (C-5), 24.7 (C-8), 18.6 (C-6), 14.2 (C-7), 7.0 (***C***H$_3$-TES group), 5.1 (***C***H$_2$-TES group), −4.4 (-Si(***C***H$_3$)$_2$-), −4.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2957, 2936, 2911, 2876, 2118, 1634, 1458, 1414, 1377, 1250, 1124, 1099, 1074, 1040, 1005.

HRMS (EI, *m*/*z*) calcd for $(C_{16}H_{36}OSi_2)^+$ 300.2305, found 300.2292.

(4-(Benzyloxy)-2-methyleneheptyl)dimethylsilane 319



Chemical Formula: $C_{17}H_{28}OSi$
Molecular Weight: 276.49

Method 1:

Hydrosilane **319** was obtained from the corresponding bromide **286** according to the procedure (method 1) described above for hydrosilane **317**. In this case, the reaction time was increased to 5 h. (Purification by column chromatography on silica gel (petroleum ether-ether 97/3)).
Scale: 8.71 mmol
Yield: 81%

Method 2:

Hydrosilane **319** was obtained from the corresponding ester **280** according to the procedure (method 2) described above for hydrosilane **317**. (Equivalents of cerium(III) chloride heptahydrate, magnesium and chloromethyldimethylsilane increased to 5).
Scale: 3.28 mmol
Yield: 70%

Work up and purification:

A 10% aqueous solution of acetic acid (40 mL) was added and the mixture was extracted with diethyl ether (3 × 50 mL). The combined ether extracts were washed with a saturated aqueous solution of sodium bicarbonate (2 × 50 mL) and brine (50 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil. The resulting oil was stirred one day with silica gel in dichloromethane. The mixture was then filtered and concentrated *in vacuo*, followed by purification by column chromatography on silica gel (petroleum ether-ether 98/2) to give the hydrosilane **319** (363 mg, 40%) and the intermediate **326** (347 mg, 30%) as clear oils. The intermediate was stirred another 3 days with silica in dichloromethane and after filtration and concentration *in vacuo*, the hydrosilane **319** (285 mg, quant.) was obtained as a clear oil. (70% combined yield).

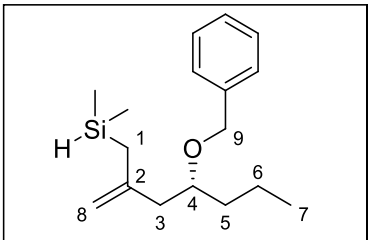
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 5H, ***H***-Ar), 4.70 (m, 1H, C***H***-8), 4.67 (m, 1H, C***H***-8), 4.58 (d, *J* = 11.6 Hz, 1H, C***H***-9), 4.50 (d, *J* = 11.6 Hz, 1H, C***H***-9), 3.94 (non, *J* = 3.6 Hz, 1H, Si-***H***), 3.56 (m, 1H, C***H***-4), 2.38 (ddd, *J* = 14.1, 6.1, 0.8 Hz, 1H, C***H***-3), 2.15 (ddd, *J* = 14.1, 6.6, 0.9 Hz, 1H, C***H***-3), 1.63 (m, 2H, C***H***-1), 1.54-1.32 (m, 4H, C***H***-5, C***H***-6), 0.91 (t, *J* = 7.1 Hz, 3H, C***H***-7), 0.11 (d, *J* = 3.6 Hz, 3H, -Si(C***H***$_3$)$_2$-), 0.10 (d, *J* = 3.6 Hz, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3 (C-2), 139.0 (C-Ar), 128.3 (C-Ar), 127.8 (C-Ar), 127.4 (C-Ar), 110.3 (C-8), 77.6 (C-4), 71.0 (C-9), 42.7 (C-3), 36.4 (C-5), 24.6 (C-1), 18.7 (C-6), 14.2 (C-7), −4.4 (-Si(***C***H_3)$_2$-).

IR (neat, cm^{-1}) 2957, 2932, 2872, 2114, 1634, 1497, 1454, 1248, 1092, 1067, 1028, 885, 839, 733, 696.

HRMS (ESI, *m*/*z*) calcd for $(C_{17}H_{28}OSiNa)^+$ 299.1802, found 299.1793.

(*R*)-(4-(Benzyloxy)-2-methyleneheptyl)dimethylsilane 368



Chemical Formula: $C_{17}H_{28}OSi$
Molecular Weight: 276.49

Method 1:

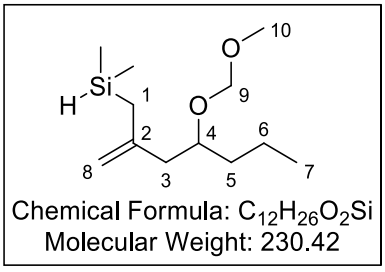
Hydrosilane **368** was obtained from the corresponding bromide **433** according to the procedure (method 1) described above for hydrosilane **317**. In this case, the reaction time was increased to 5 h. (Purification by column chromatography on silica gel (petroleum ether-ether 97/3)).
Scale: 14.3 mmol
Yield: 64%

Method 2:

Hydrosilane **368** was obtained from the corresponding ester **367** according to the procedure (method 2) described above for hydrosilane **317**. (Purification by column chromatography on silica gel (petroleum ether-ether 95/5)).
Scale: 8.55 mmol
Yield: 53%

$[\alpha]^{25}_{D}$ = +15.2° (*c* 1.0, $CHCl_3$)

(4-(Methoxymethoxy)-2-methyleneheptyl)dimethylsilane 320



Hydrosilane **320** was obtained from the corresponding bromide **290** according to the procedure (method 1) described above for hydrosilane **317**. In this case, the reaction time was increased to 5 h. (Purification by column chromatography on silica gel (petroleum ether-ether 99/1, then 98/2)).
Scale: 0.70 mmol
Yield: 65%

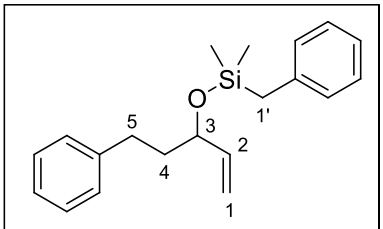
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.70-4.69 (m, 1H, C***H***-8), 4.68 (d, 1H, *J* = 7.0 Hz, C***H***-9), 4.66-4.65 (m, 1H, C***H***-8), 4.64 (d, 1H, *J* = 7.0 Hz, C***H***-9), 3.93 (non, 1H, *J* = 3.5 Hz, -Si***H***-), 3.76-3.71 (m, 1H, C***H***-4), 3.38 (s, 3H, C***H***-10), 2.29 (ddd, 1H, *J* = 14.0, 6.5, 0.9 Hz, C***H***-3), 2.13 (ddd, 1H, *J* = 14.0, 6.5, 0.9 Hz, C***H***-3), 1.67-1.60 (m, 2H, C***H***-1), 1.54-1.32 (m, 4H, C***H***-5, C***H***-6), 0.93 (t, 3H, *J* = 7.1 Hz, C***H***-7), 0.11 (s, 3H, -Si(C***H₃***)$_2$-), 0.11 (s, 3H, -Si(C***H₃***)$_2$-).

^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0 (C-2), 110.5 (C-8), 95.3 (C-9), 75.5 (C-4), 55.5 (C-10), 43.3 (C-3), 36.8 (C-5), 24.3 (C-1), 18.6 (C-6), 14.2 (C-7), −4.3 (-Si(***C***H$_3$)$_2$-), −4.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2957, 2932, 2876, 2114, 1634, 1250, 1152, 1099, 1038.

HRMS (ESI, *m*/*z*) calcd for $(C_{12}H_{26}O_2SiNa)^+$ 253.1600, found 253.1583.

Benzyldimethyl(5-phenylpent-1-en-3-yloxy)silane 324



Chemical Formula: $C_{20}H_{26}OSi$
Molecular Weight: 310.51

To a stirred solution of benzyldimethysilane (100 mg, 0.670 mmol, 1.20 equiv) in dichloromethane (1.1 mL) was added iron (III) chloride (2.2 mg, 0.013, 2.4 mol%) and acetyl chloride (0.070 mL, 1.0 mmol, 1.8 equiv). The reaction mixture was stirred overnight at room temperature.
The reaction mixture was then added to a stirred solution of alcohol **293** (91 mg, 0.56 mmol), triethylamine (0.20 mL, 1.4 mmol, 2.5 equiv) and DMAP (34 mg, 0.28 mmol, 0.50 equiv) in THF (2 mL) at 0 °C. The reaction mixture was stirred overnight at room temperature. A saturated aqueous solution of sodium bicarbonate (5 mL) was added and the mixture was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 99/1) gave the silane **324** (167 mg, 96%) as a clear oil.

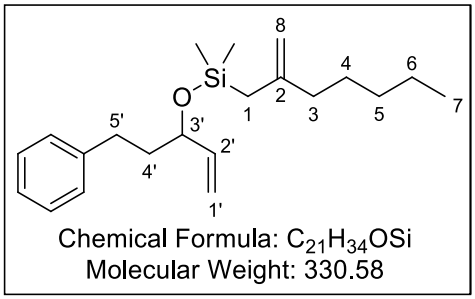
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, ***H***-Ar), 7.24-7.16 (m, 5H, ***H***-Ar), 7.11-7.06 (m, 3H, ***H***-Ar), 5.85 (ddd, *J* = 17.0, 10.2, 6.3 Hz, 1H, C***H***-2), 5.16 (dt, *J* = 17.0, 1.5 Hz, 1H, C***H***-1$_{trans}$), 5.09 (dt, *J* = 10.2, 1.3 Hz, 1H, C***H***-1$_{cis}$), 4.13 (m, 1H, C***H***-3), 2.70-2.55 (m, 2H, C***H***-5), 2.23 (d, *J* = 13.6 Hz, 1H, C***H***-1'), 2.18 (d, *J* = 13.9 Hz, 1H, C***H***-1'), 1.89-1.74 (m, 2H, C***H***-4), 0.09 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.09 (s, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2 (C-Ar), 141.1 (C-2), 139.1 (C-Ar), 128.4 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 125.7 (C-Ar), 124.1 (C-Ar), 114.4 (C-1), 73.6 (C-3), 39.4 (C-4), 31.5 (C-5), 27.2 (C-1'), −1.5 (-Si(***C***H$_3$)$_2$-), −1.9 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 3057, 3030, 2951, 2859, 1495, 1452, 1252, 1209, 1155, 1084, 1055.

HRMS (ESI, *m*/*z*) calcd for $(C_{20}H_{26}OSiNa)^+$ 333.1645, found 333.1634.

Dimethyl(2-methyleneheptyl)(5-phenylpent-1-en-3-yloxy)silane 296



Chemical Formula: $C_{21}H_{34}OSi$
Molecular Weight: 330.58

Method 1:

General procedure

To a stirred solution of silane **317** (36 mg, 0.21 mmol, 1.2 equiv) in THF (0.05 mL) were added palladium dichloride (0.40 mg, 0.0020 mmol, 1.2 mol%) and hexachloroethane (25 mg, 0.10 mmol, 0.60 equiv). The reaction mixture was stirred for 1 h at room temperature.
The reaction mixture was then added to a stirred solution of alcohol **293** (28 mg, 0.18 mmol), triethylamine (0.060 mL, 0.44 mmol, 2.5 equiv) and DMAP (11 mg, 0.090 mmol, 0.50 equiv) in THF (0.4 mL) at 0 °C. The reaction mixture was stirred for 1 h at room temperature. A saturated aqueous solution of sodium bicarbonate (3 mL) was added and the mixture was extracted with ether (3 × 3 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 99.5/0.5) gave the silane **296** (27 mg, 47%) as a clear oil.

Method 2:

General procedure

To a stirred solution of alcohol **293** (280 mg, 1.73 mmol), silane **317** (324 mg, 1.90 mmol, 1.10 equiv) and xantphos copper chloride (59 mg, 0.086 mmol, 0.050 equiv) in toluene (50 mL) at 85 °C was added lithium *tert*-butoxide (2.2 M in THF, 0.55 mL, 1.2 mmol, 0.70 equiv) in toluene (14 mL) *via* syringe pump over 4 h. The solution was stirred another 30 min at 85 °C and was monitored by TLC. After cooling it down to room temperature, the reaction was quenched by addition of a saturated aqueous solution of ammonium chloride (60 mL). The mixture was extracted with diethyl ether (3 × 50 mL) and the combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 99/1) gave the oxysilane **296** (475 mg, 83%) as a clear oil.

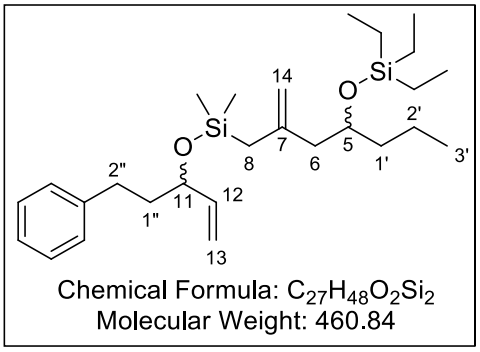
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, ***H***-Ar), 7.20-7.17 (m, 3H, ***H***-Ar), 5.85 (ddd, *J* = 17.0, 10.3, 6.3 Hz, 1H, C***H***-2'), 5.18 (dt, *J* = 17.0, 1.6 Hz, 1H, C***H***-1'$_{trans}$), 5.09 (dt, *J* = 10.3, 1.7 Hz, 1H, C***H***-1'$_{cis}$), 4.63 (m, 1H, C***H***-8), 4.58 (m, 1H, C***H***-8), 4.14 (m, 1H, C***H***-3'), 2.73-2.58 (m, 2H, C***H***-5'), 2.00 (t, *J* = 7.7 Hz, 2H, C***H***-3), 1.89-1.76 (m, 2H, C***H***-4'), 1.64 (s, 2H, C***H***-1), 1.44 (m, 2H, C***H***-4), 1.36-1.25 (m, 4H, C***H***-5, C***H***-6), 0.90 (t, *J* = 7.0 Hz, 3H, C***H***-7), 0.14 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.13 (s, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9 (C-2), 142.2 (C-Ar), 141.2 (C-2'), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 114.3 (C-1'), 107.6 (C-8), 73.6 (C-3'), 39.5 (C-4'), 38.2 (C-3), 31.7 (C-5' or C-5), 31.6 (C-5' or C-5), 27.5 (C-4 or C-1), 27.1 (C-4 or C-1), 22.6 (C-6), 14.1 (C-7), −1.1 (-Si(***C***H_3)$_2$-), −1.4 (-Si(***C***H_3)$_2$-).

IR (neat, cm^{-1}) 3030, 2957, 2930, 2859, 1636, 1456, 1249, 1082, 1030.

HRMS (CI, *m*/*z*) calcd for $(C_{21}H_{35}OSi)^+$ 331.2457, found 331.2453.

3,3-Diethyl-9,9-dimethyl-7-methylene-11-phenethyl-5-propyl-4,10-dioxa-3,9-disilatridec-12-ene 298



Method 1:

Silane **298** was obtained from the corresponding silane **318** and alcohol **293** according to the general procedure (method 1) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ether 99.5/0.5)).
Scale: 1.38 mmol
Yield: 45% (1:1 mixture of diastereomers)

Method 2:

Silane **298** was obtained from the corresponding silane **318** and alcohol **293** according to the general procedure (method 2) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ether 99/1)).
Scale: 0.49 mmol
Yield: 77% (1:1 mixture of diastereomers)

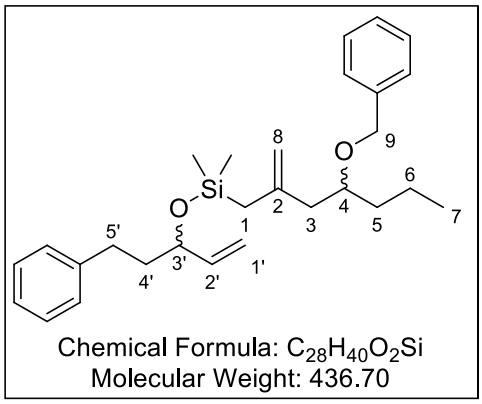
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, ***H***-Ar), 7.20-7.17 (m, 3H, ***H***-Ar), 5.85 (ddd, *J* = 16.9, 10.4, 6.3 Hz, 1H, C***H***-12), 5.18 (dt, *J* = 16.9, 1.5 Hz, 1H, C***H***-13$_{trans}$), 5.09 (dt, *J* = 10.4, 1.3 Hz, 1H, C***H***-13$_{cis}$), 4.66 (s, 1H, C***H***-14), 4.65 (s, 1H, C***H***-14), 4.14 (app q, *J* = 6.1 Hz, 1H, C***H***-11), 3.81 (m, 1H, C***H***-5), 2.73-2.58 (m, 2H, C***H***-2"), 2.23-2.10 (m, 2H, C***H***-6), 1.89-1.76 (m, 2H, C***H***-1"), 1.65 (m, 2H, C***H***-8), 1.52-1.27 (m, 4H, C***H***-1', C***H***-2'), 0.97 (t, *J* = 8.0 Hz, 9H, C***H***$_3$-TES group), 0.90 (t, *J* = 6.8 Hz, 3H, C***H***-3'), 0.61 (q, *J* = 8.0 Hz, 6H, C***H***$_2$-TES group), 0.14 (m, 6H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4 (C-7), 142.2 (C-Ar), 141.2 (C-12), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 114.3 (C-13), 110.7 (C-14), 73.6 (C-11), 71.1 (C-5), 46.6 (C-6), 39.5 (C-1' or C-1"), 39.4 (C-1' or C-1"), 31.6 (C-2"), 27.4 (C-8), 18.6 (C-2'), 14.2 (C-3'), 7.0 (***C***H$_3$-TES group), 5.1 (***C***H$_2$-TES group), −1.1 (-Si(***C***H$_3$)$_2$-), −1.1 (-Si(***C***H$_3$)$_2$-), −1.4 (-Si(***C***H$_3$)$_2$-), −1.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 3028, 2955, 2933, 2876, 1634, 1456, 1249, 1074, 1040.

HRMS (ESI, *m*/*z*) calcd for $(C_{27}H_{48}O_2Si_2Na)^+$ 483.3085, found 483.3076.

(4-(Benzyloxy)-2-methyleneheptyl)dimethyl((5-phenylpent-1-en-3-yl)oxy)silane 325



Method 1:

Silane **325** was obtained from the corresponding silane **319** and alcohol **293** according to the general procedure (method 1) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ether 99/1)).
Scale: 7.06 mmol
Yield: 60% (1:1 mixture of diastereomers)

Method 2:

Silane **325** was obtained from the corresponding silane **319** and alcohol **293** according to the general procedure (method 2) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ether 99/1)).
Scale: 0.74 mmol
Yield: 75% (1:1 mixture of diastereomers)

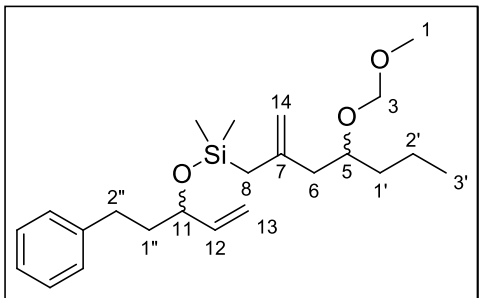
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.26 (m, 7H, ***H***-Ar), 7.21-7.18 (m, 3H, ***H***-Ar), 5.86 (dddd, 1H, *J* = 17.0, 10.4, 6.4, 1.7 Hz, C***H***-2'), 5.19 (ddt, 1H, *J* = 17.0, 2.9, 1.6 Hz, C***H***-1'*trans*), 5.1 (d, 1H, *J* = 10.4 Hz, C***H***-1'*cis*), 4.74 (m, 1H, C***H***-8), 4.7 (s, 1H, C***H***-8), 4.6 (d, 1H, *J* = 11.5 Hz, C***H***-9), 4.52 (d, 1H, *J* = 11.5 Hz, C***H***-9), 4.15 (app q, 1H, *J* = 6.4 Hz, C***H***-3'), 3.59 (app quint, 1H, *J* = 5.9 Hz, C***H***-4), 2.67 (m, 2H, C***H***-5'), 2.43 (m, 1H, C***H***-3), 2.19 (m, 1H, C***H***-3), 1.91-1.76 (m, 2H, C***H***-4'), 1.69 (m, 2H, C***H***-1), 1.57-1.34 (m, 4H, C***H***-5, C***H***-6), 0.93 (t, 3H, *J* = 6.7 Hz, C***H***-7), 0.17 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.16 (s, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6 (C-Ar), 142.1 (C-2), 141.2 (C-2'), 139.0 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.8 (C-Ar), 127.4 (C-Ar), 125.7 (C-Ar), 114.4 (C-1'), 110.6 (C-8), 77.6 (C-9), 73.6 (C-3'), 71.0 (C-4), 43.1 (C-3), 39.5 (C-5 or C-4'), 36.4 (C-5 or C-4'), 31.6 (C-5'), 27.3 (C-1), 18.7 (C-6), 14.2 (C-7), −1.1 (-Si(***C***H$_3$)$_2$-), −1.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2957, 2932, 2870, 1497, 1454, 1350, 1250, 1067, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{28}H_{40}O_2SiNa)^+$ 459.2690, found 459.2679.

9,9-Dimethyl-7-methylene-11-phenethyl-5-propyl-2,4,10-trioxa-9-silatridec-12-ene 326



Chemical Formula: $C_{23}H_{38}O_3Si$
Molecular Weight: 390.63

Silane **326** was obtained from the corresponding silane **320** and alcohol **293** according to the general procedure (method 1) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ether 99/1)).
Scale: 0.30 mmol
Yield: 5% (1:1 mixture of diastereomers)

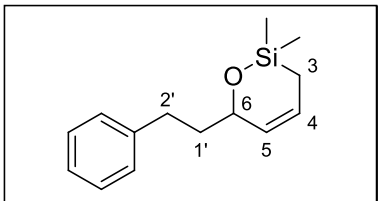
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.17 (m, 5H, ***H***-Ar), 5.84 (ddd, 1H, *J* = 17.1, 10.3, 6.4 Hz, C***H***-12), 5.17 (dt, 1H, *J* = 17.1, 1.5 Hz, C***H***-13$_{trans}$), 5.09 (dt, 1H, *J* = 10.3, 1.5 Hz, C***H***-13$_{cis}$), 4.71-4.70 (m, 1H, C***H***-14), 4.68 (d, 0.5H, *J* = 7.0 Hz, C***H***-3), 4.68 (d, 0.5H, *J* = 7.0 Hz, C***H***-3), 4.68-4.67 (m, 1H, C***H***-14), 4.63 (d, 1H, *J* = 7.0 Hz, C***H***-3), 4.16-4.11 (m, 1H, C***H***-11), 3.77-3.71 (m, 1H, C***H***-5), 3.38 (s, 3H, C***H***-1), 2.72-2.58 (m, 2H, C***H***-2"), 2.34-2.27 (m, 1H, C***H***-6), 2.19-2.13 (m, 1H, C***H***-6), 1.89-1.75 (m, 2H, C***H***-1"), 1.71-1.63 (m, 2H, C***H***-8), 1.54-1.30 (m, 4H, C***H***-1', C***H***-2'), 0.92 (t, 3H, *J* = 7.1 Hz, C***H***-3'), 0.15 (s, 1.5H, -Si(C***H$_3$***)$_2$-), 0.15 (s, 1.5H, -Si(C***H$_3$***)$_2$-), 0.14 (s, 1.5H, -Si(C***H$_3$***)$_2$-), 0.13 (s, 1.5H, -Si(C***H$_3$***)$_2$-).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3 (C-7), 142.2 (C-Ar), 141.2 (C-12), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 114.4 (C-13), 110.9 (C-14), 95.4 (C-3), 75.6 (C-5), 73.6 (C-11), 55.5 (C-1), 43.7 (C-6), 39.5 (C-1"), 36.9 (C-1'), 31.6 (C-2"), 27.1 (C-8), 18.6 (C-2'), 14.2 (C-3'), −1.1 (-Si(***C***H$_3$)$_2$-), −1.1 (-Si(***C***H$_3$)$_2$-), −1.3 (-Si(***C***H$_3$)$_2$-), −1.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2957, 2931, 2874, 1455, 1252, 1152, 1093, 1039.

HRMS (ESI, *m*/*z*) calcd for $(C_{23}H_{38}O_3SiNa)^+$ 413.2482, found 413.2481.

2,2-Dimethyl-6-phenethyl-3,6-dihydro-2*H*-1,2-oxasiline 343



Chemical Formula: $C_{14}H_{20}OSi$
Molecular Weight: 232.39

To a solution of silane **294** (0.15 g, 0.58 mmol) in dichloromethane (11 mL) was added second-generation Grubbs' catalyst (25 mg, 0.030 mmol, 5.0 mol %) under argon. The solution was stirred at 45 °C (reflux) for 2 h and monitored by TLC. The reaction mixture was then concentrated *in vacuo*. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ether 98/2) gave the product **343** (99 mg, 74%) as a clear oil.

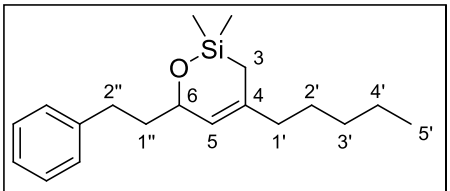
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.25 (m, 2H, ***H***-Ar), 7.22-7.15 (m, 3H, ***H***-Ar), 5.88 (m, 1H, C***H***-5), 5.57 (dq, *J* = 10.8, 2.2 Hz, 1H, C***H***-4), 4.42 (m, 1H, C***H***-6), 2.81-2.66 (m, 2H, C***H***-2'), 1.91-1.75 (m, 2H, C***H***-1'), 1.25 (m, 2H, C***H***-3), 0.21 (s, 3H, -Si(C***H*****$_3$**$)_{2\text{-}}$), 0.18 (s, 3H, -Si(C***H*****$_3$**$)_{2\text{-}}$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5 (C-Ar), 132.4 (C-5), 128.5 (C-Ar), 128.3 (C-Ar), 125.6 (C-Ar), 124.2 (C-4), 71.4 (C-6), 39.9 (C-2'), 31.3 (C-1'), 12.2 (C-3), 0.4 (-Si(***C***$H_3)_{2\text{-}}$), −0.7 (-Si(***C***$H_3)_{2\text{-}}$).

IR (neat, cm^{-1}) 3026, 2958, 2936, 2877, 1642, 1604, 1497, 1454, 1257, 1030.

HRMS (EI, *m*/*z*) calcd for $(C_{14}H_{20}OSi)^+$ 232.1283, found 232.1280.

2,2-Dimethyl-4-pentyl-6-phenethyl-3,6-dihydro-2*H*-1,2-oxasiline 344



Chemical Formula: $C_{19}H_{30}OSi$
Molecular Weight: 302.53

To a solution of compound **296** (19 mg, 0.058 mmol) in dichloromethane (1.5 mL) was added second-generation Grubbs' catalyst (2.5 mg, 0.0029 mmol, 5.0 mol %) under argon. The solution was stirred for 2 h at 45 °C (reflux). Another 5.0 mol% of second-generation Grubbs' catalyst were added and the solution was stirred for 2 h at 45 °C. The reaction mixture was then concentrated *in vacuo*. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ether 96/4) gave the product **344** (11 mg, 63%) as a clear oil.

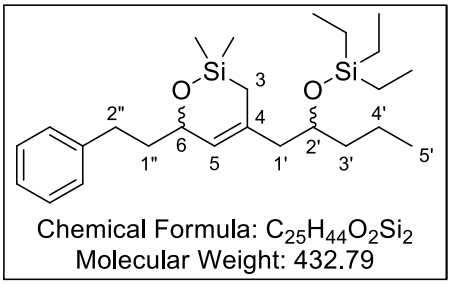
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H, ***H***-Ar), 7.23-7.16 (m, 3H, ***H***-Ar), 5.34 (m, 1H, C***H***-5), 4.40 (m, 1H, C***H***-6), 2.80-2.66 (m, 2H, C***H***-2"), 2.02 (t, *J* = 7.3 Hz, 2H, C***H***-1'), 1.91-1.75 (m, 2H, C***H***-1"), 1.42 (quint, *J* = 7.1 Hz, 2H, C***H***-2'), 1.36-1.24 (m, 5H, C***H***-3, C***H***-3', C***H***-4'), 1.13 (d, *J* = 17.2 Hz, 1H, C***H***-3), 0.90 (t, *J* = 6.8 Hz, 3H, C***H***-5'), 0.20 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.16 (s, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7 (C-4), 136.4 (C-Ar), 128.5 (C-Ar), 128.2 (C-Ar), 125.7 (C-Ar or C-5), 125.6 (C-Ar or C-5), 71.4 (C-6), 41.5 (C-1'), 40.2 (C-1"), 31.4 (C-3' or C-2"), 31.3 (C-3' or C-2"), 27.1 (C-2'), 22.6 (C-4'), 15.6 (C-3), 14.1 (C-5'), 0.2 (-Si(***C***H$_3$)$_2$-), −0.8 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 3026, 2955, 2926, 2859, 1603, 1497, 1454, 1250, 1215, 1096, 1074, 1030.

HRMS (ESI, *m*/*z*) calcd for $(C_{19}H_{30}OSiNa)^+$ 325.1958, found 325.1949.

2,2-Dimethyl-6-phenethyl-4-(2-(triethylsilyloxy)pentyl)-3,6-dihydro-2*H*-1,2-oxasiline 345



Chemical Formula: $C_{25}H_{44}O_2Si_2$
Molecular Weight: 432.79

Silacycle **345** was obtained from the corresponding silane **298** according to the procedure described above for silacycle **343**. In this case, the reaction time was increased to 3 h. (Purification by column chromatography on silica gel (petroleum ether-ether 95/5)).
Scale: 4.80 mmol
Yield: 94% (1:1 mixture of diastereomers)

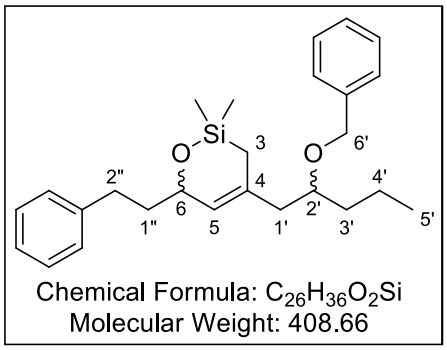
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H, ***H***-Ar), 7.22-7.16 (m, 3H, ***H***-Ar), 5.39-5.21 (m, 1H, C***H***-5), 4.42-4.13 (m, 1H, C***H***-6), 3.87-3.63 (m, 1H, C***H***-2'), 2.84-2.63 (m, 2H, C***H***-2"), 2.27-2.12 (m, 2H, C***H***-1'), 1.92-1.77 (m, 2H, C***H***-1"), 1.50-1.11 (m, 6H, C***H***-3, C***H***-3', C***H***-4'), 0.98 (m, 9H, C***H***$_3$-TES group), 0.90 (m, 3H, C***H***-5'), 0.65-0.49 (m, 6H, C***H***$_2$-TES group), 0.23-0.07 (m, 6H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6 (C-Ar), 142.5 (C-Ar), 133.3 (C-4), 133.2 (C-4), 128.6 (C-Ar or C-5), 128.5 (C-Ar or C-5), 128.5 (C-Ar or C-5), 128.5 (C-Ar or C-5), 128.4 (C-Ar or C-5), 128.3 (C-Ar or C-5), 128.2 (C-Ar or C-5), 125.6 (C-Ar), 71.4 (C-6), 70.4 (C-2'), 70.2 (C-2'), 50.3 (C-1'), 50.1 (C-1'), 40.1 (C-1"), 40.0 (C-1"), 39.0 (C-3'), 39.0 (C-3'), 31.5 (C-7), 31.4 (C-2"), 18.6 (C-3 or C-4'), 18.5 (C-3 or C-4'), 16.4 (C-3 or C-4'), 16.3 (C-3 or C-4'), 14.3 (C-5'), 14.2 (C-5'), 7.0 (***C***H$_3$-TES group), 7.0 (***C***H$_3$-TES group), 6.9 (***C***H$_3$-TES group), 6.8 (***C***H$_3$-TES group), 6.3 (***C***H$_3$-TES group), 5.2 (***C***H$_2$-TES group), 5.1 (***C***H$_2$-TES group), 0.3 (-Si(***C***H$_3$)$_2$-), −0.7 (-Si(***C***H$_3$)$_2$-), −0.7 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 3026, 2955, 2910, 2876, 1724, 1603, 1497, 1454, 1412, 1248, 1069, 1032, 1006.

HRMS (CI, *m*/*z*) calcd for $(C_{25}H_{45}O_2Si_2)^+$ 433.2958, found 433.2953.

4-(2-(Benzyloxy)pentyl)-2,2-dimethyl-6-phenethyl-3,6-dihydro-2*H*-1,2-oxasiline 346



Chemical Formula: $C_{26}H_{36}O_2Si$
Molecular Weight: 408.66

To a solution of compound **325** (240 mg, 0.550 mmol) in dichloromethane (13 mL) was added second-generation Grubbs' catalyst (12 mg, 0.014 mmol, 2.5 mol%) under argon. The reaction was stirred for 2 h at 45 °C (reflux) and was monitored by TLC. The sequence addition/stirring was repeated once. The reaction mixture was then concentrated *in vacuo*. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ether 96/4) gave the product **346** (142 mg, 63%) as a clear oil and as a 1:1 mixture of diastereomers.

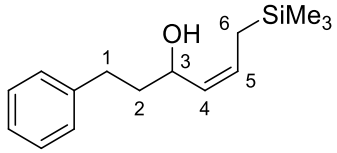
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.09 (m, 10H, ***H***-Ar), 5.46-5.39 (m, 1H, C***H***-5), 4.58-4.47 (m, 2H, C***H***-6'), 4.44-4.34 (m, 1H, C***H***-6), 3.60-3.50 (m, 1H, C***H***-2'), 2.81-2.64 (m, 2H, C***H***-2"), 2.40 (dd, 1H, *J* = 13.5, 6.4 Hz, C***H***-1'), 2.17 (dd, 1H, *J* = 13.5, 6.3 Hz, C***H***-1'), 1.91-1.74 (m, 2H, C***H***-1"), 1.55-1.07 (m, 6H, C***H***-3, C***H***-3', C***H***-4'), 0.92 (t, 3H, *J* = 7.1 Hz, C***H***-5'), 0.21 (s, 1.5H, -Si(C***H₃***)$_2$-), 0.19 (s, 1.5H, -Si(C***H₃***)$_2$-), 0.17 (s, 1.5H, -Si(C***H₃***)$_2$-), 0.16 (s, 1.5H, -Si(C***H₃***)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.5 (C-Ar), 138.9 (C-4), 133.1 (C-Ar), 128.8 (C-Ar), 128.5 (C-Ar), 128.4 (C-5), 128.3 (C-Ar), 128.2 (C-Ar), 127.7 (C-Ar), 127.7 (C-Ar), 127.4 (C-Ar), 125.6 (C-Ar), 76.9 (C-2'), 71.5 (C-6), 71.4 (C-6), 70.9 (C-6'), 46.6 (C-1'), 40.0 (C-1"), 36.3 (C-3'), 31.4 (C-2"), 31.4 (C-2"), 18.7 (C-4'), 18.6 (C-4'), 16.2 (C-3), 14.2 (C-5'), 0.3 (-Si(***C***H$_3$)$_2$-), 0.2 (-Si(***C***H$_3$)$_2$-), −0.7 (-Si(***C***H$_3$)$_2$-), −0.8 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2957, 2930, 2870, 1497, 1454, 1346, 1250, 1094, 1069, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{26}H_{36}O_2SiNa)^+$ 431.2377, found 431.2362.

(*Z*)-1-Phenyl-6-(trimethylsilyl)hex-4-en-3-ol 354[108]



Chemical Formula: $C_{15}H_{24}OSi$
Molecular Weight: 248.44

General procedure

To a stirred solution of oxysilane **343** (185 mg, 0.810 mmol) in diethyl ether (30 mL) at −78 °C was added dropwise methyllithium (1.6 M solution in diethyl ether, 1.5 mL, 2.4 mmol, 3.0 equiv). The reaction was stirred 1 h at −78 °C and was allowed to warm up to room temperature for 1 h. The mixture was quenched by addition of a saturated aqueous solution of ammonium chloride (50 mL) and was extracted with diethyl ether (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 8/2) gave allylic alcohol **354** (145 mg, 72%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, ***H***-Ar), 7.23-7.17 (m, 3H, ***H***-Ar), 5.59-5.52 (m, 1H, C***H***-5), 5.40-5.35 (m, 1H, C***H***-4), 4.41 (m, 1H, C***H***-3), 2.80-2.64 (m, 2H, C***H***-1), 1.92 (dddd, *J* = 13.4, 9.9, 7.5, 5.7 Hz, 1H, C***H***-2), 1.77 (dddd, *J* = 13.4, 10.1, 6.4, 5.4 Hz, 1H, C***H***-2), 1.58-1.47 (m, 2H, C***H***-6), 1.3 (d, *J* = 3.6 Hz, 1H, C3-***OH***), 0.02 (s, 9H, -Si(C***H₃***)$_3$).

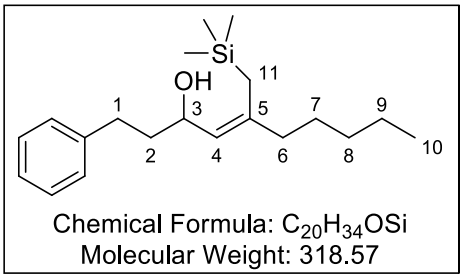
^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (C-Ar), 130.1 (C-4), 129.0 (C-5), 128.4 (C-Ar), 128.3 (C-Ar), 125.8 (C-Ar), 66.8 (C-3), 39.1 (C-2), 31.8 (C-1), 19.2 (C-6), −1.9 (-Si(***C***H$_3$)$_3$).

IR (neat, cm^{-1}) 3354, 3026, 2953, 2928, 1647, 1603, 1497, 1454, 1420, 1248, 1148, 1030.

HRMS (CI, *m*/*z*) calcd for $(C_{15}H_{23}Si)^+$ 231.1569, found 231.1570.

[108] Angoh, A. G.; Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1984**, 534.

(*Z*)-1-Phenyl-5-((trimethylsilyl)methyl)dec-4-en-3-ol 361



Chemical Formula: $C_{20}H_{34}OSi$
Molecular Weight: 318.57

Allylic alcohol **361** was obtained from the corresponding silacycle **344** according to the general procedure described above for allylic alcohol **354**. (Purification by column chromatography on silica gel (petroleum ether-ether 9/1)).
Scale: 0.66 mmol
Yield: 60%

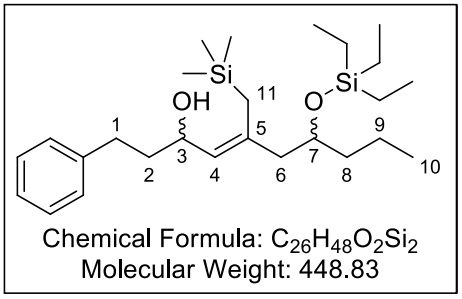
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.16 (m, 5H, ***H***-Ar), 5.12 (d, 1H, *J* = 8.9 Hz, C***H***-4), 4.31-4.22 (m, 1H, C***H***-3), 2.76 (ddd, 1H, *J* = 14.0, 10.1, 5.5 Hz, C***H***-1), 2.66 (ddd, 1H, *J* = 14.0, 9.8, 6.5 Hz, C***H***-1), 1.96-1.85 (m, 3H, C***H***-2, C***H***-6), 1.78-1.70 (m, 1H, C***H***-2), 1.58 (d, 1H, *J* = 13.5 Hz, C***H***-11), 1.53 (dd, 1H, *J* = 13.5, 0.8 Hz, C***H***-11), 1.42 (quint, 2H, *J* = 8.0 Hz, C***H***-7), 1.36-1.23 (m, 4H, C***H***-8, C***H***-9), 1.21 (d, 1H, *J* = 3.5 Hz, C3-***OH***), 0.90 (t, 3H, *J* = 7.1 Hz, C***H***-10), 0.01 (s, 9H, -Si(C***H*****$_3$**$)_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2 (C-Ar), 141.9 (C-5), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 124.5 (C-4), 68.1 (C-3), 39.4 (C-2), 39.0 (C-6), 32.0 (C-1), 31.6 (C-8), 27.8 (C-7), 22.6 (C-9), 21.8 (C-11), 14.1 (C-10), 0.8 (-Si(***C***$H_3)_3$).

IR (neat, cm^{-1}) 3360, 2953, 2928, 2858, 1497, 1454, 1248, 1157, 1030.

HRMS (ESI, *m*/*z*) calcd for $(C_{20}H_{34}OSiNa)^+$ 341.2271, found 341.2258.

(*Z*)-1-Phenyl-7-(triethylsilyloxy)-5-((trimethylsilyl)methyl)dec-4-en-3-ol 359



Chemical Formula: $C_{26}H_{48}O_2Si_2$
Molecular Weight: 448.83

Crude allylic alcohol **359** was obtained from the corresponding silacycle **345** according to the general procedure described above for allylic alcohol **354**. (Purification by filtration through a silica plug)).
Scale: 0.81 mmol
Yield: quant. (1:1 mixture of diastereomers)

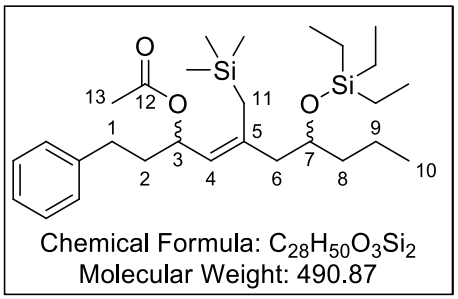
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.17 (m, 5H, ***H***-Ar), 5.15 (d, 1H, *J* = 8.9 Hz, C***H***-4), 4.28-4.21 (m, 1H, C***H***-3), 3.82-3.77 (m, 1H, C***H***-7), 2.82-2.64 (m, 2H, C***H***-1), 2.18-2.10 (m, 1H, C***H***-6), 2.08-2.01 (m, 1H, C***H***-6), 1.93-1.84 (m, 1H, C***H***-2), 1.79-1.70 (m, 1H, C***H***-2), 1.65 (d, 0.5H, *J* = 13.4 Hz, C***H***-11), 1.57-1.51 (m, 1H, C***H***-11), 1.56 (d, 0.5H, *J* = 13.4 Hz, C***H***-11), 1.51-1.27 (m, 4H, C***H***-8, C***H***-9), 1.20 (d, 0.5H, *J* = 3.6 Hz, C3-***OH***), 1.19 (d, 0.5H, *J* = 3.7 Hz, C3-***OH***), 0.97 (t, 4.5H, *J* = 7.9 Hz, -Si(CH_2C***H_3***$)_3$), 0.97 (t, 4.5H, *J* = 7.9 Hz, -Si(CH_2C***H_3***$)_3$), 0.90 (t, 3H, *J* = 6.8 Hz, C***H***-10), 0.61 (q, 6H, *J* = 7.9 Hz, -Si(C***H_2***$CH_3)_3$), 0.02 (s, 4.5H, -Si(C***H_3***$)_3$), 0.01 (s, 4.5H, -Si(C***H_3***$)_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2 (C-Ar), 138.9 (C-5), 138.5 (C-5), 128.4 (C-Ar), 128.3 (C-Ar), 127.3 (C-4), 127.0 (C-4), 125.74 (C-Ar), 71.7 (C-7), 71.2 (C-7), 68.0 (C-3), 67.9 (C-3), 47.2 (C-6), 46.9 (C-6), 39.3 (C-2 or C-8), 39.2 (C-2 or C-8), 31.9 (C-1), 31.9 (C-1), 22.8 (C-11), 22.3 (C-11), 18.6 (C-9), 18.4 (C-9), 14.3 (C-10), 14.3 (C-10), 6.98 (-Si(CH_2***C***$H_3)_3$), 5.15 (-Si(***C***$H_2CH_3)_3$), −0.8 (-Si(***C***$H_3)_3$), −0.8 (-Si(***C***$H_3)_3$).

IR (neat, cm^{-1}) 3421, 2955, 2935, 2876, 1496, 1456, 1415, 1249, 1156, 1124, 1101, 1039, 1006.

HRMS (ESI, *m*/*z*) calcd for $(C_{26}H_{48}O_2Si_2Na)^+$ 471.3085, found 471.3095.

(*Z*)-1-Phenyl-7-(triethylsilyloxy)-5-((trimethylsilyl)methyl)dec-4-en-3-yl acetate 355



Chemical Formula: $C_{28}H_{50}O_3Si_2$
Molecular Weight: 490.87

To a stirred solution of alcohol **359** (47 mg, 0.11 mmol) in dichloromethane (1 mL) were added triethylamine (0.022 mL, 0.16 mol, 1.5 equiv), acetic anhydride (12 µL, 0.13 mmol, 1.2 equiv) and DMAP (1.3 mg, 0.010 mmol, 0.10 equiv). The solution was stirred overnight at room temperature and was then quenched by addition of a saturated aqueous solution of sodium bicarbonate (1 mL). The mixture was extracted with diethyl ether (3 × 2 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude compound **355** (50 mg, quant.) was used without further purification (1:1 mixture of diastereomers).

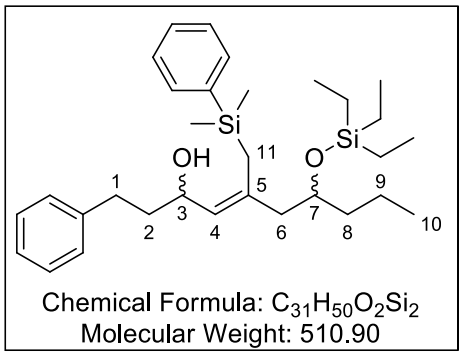
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.17 (m, 5H, ***H***-Ar), 5.51-5.45 (m, 1H, C***H***-3), 5.13 (d, 0.5H, *J* = 9.4 Hz, C***H***-4), 5.09 (d, 0.5H, *J* = 9.4 Hz, C***H***-4), 3.84-3.77 (m, 1H, C***H***-7), 2.71-2.57 (m, 2H, C***H***-1), 2.20-2.11 (m, 1H, C***H***-6), 2.08-1.97 (m, 2H, C***H***-2, C***H***-6), 2.02 (s, 3H, C***H***-13), 1.91 (d, 0.5H, *J* = 13.5 Hz, C***H***-11), 1.85-1.78 (m, 1H, C***H***-2), 1.75 (d, 0.5H, *J* = 13.5 Hz, C***H***-11), 1.57 (d, 0.5H, *J* = 13.5 Hz, C***H***-11), 1.52 (d, 0.5H, *J* = 13.5 Hz, C***H***-11), 1.47-1.25 (m, 4H, C***H***-8, C***H***-9), 0.96 (t, 9H, *J* = 7.9 Hz, -Si(CH_2C***H*****$_3$**$)_3$), 0.92-0.87 (m, 3H, C***H***-10), 0.60 (q, 6H, *J* = 7.9 Hz, -Si(C***H*****$_2$**$CH_3)_3$), 0.02 (s, 4.5H, -Si(C***H*****$_3$**$)_3$), 0.01 (s, 4.5H, -Si(C***H*****$_3$**$)_3$).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5 (C-12), 141.6 (C-Ar), 141.3 (C-5), 140.9 (C-5), 128.4 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 125.8 (C-Ar), 122.6 (C-4), 122.4 (C-4), 71.4 (C-7), 71.2 (C-7), 71.2 (C-3), 71.1 (C-3), 47.1 (C-6), 47.1 (C-6), 39.4 (C-8), 39.1 (C-8), 37.0 (C-2), 36.9 (C-2), 31.8 (C-1), 31.6 (C-1), 22.9 (C-11), 22.6 (C-11), 21.3 (C-13), 21.2 (C-13), 18.4 (C-9), 14.3 (C-10), 7.0 (-Si(CH_2***C***$H_3)_3$), 5.1 (-Si(***C***$H_2CH_3)_3$), −0.8 (-Si(***C***$H_3)_3$), −0.8 (-Si(***C***$H_3)_3$).

IR (neat, cm^{-1}) 2956, 2937, 2875, 1733, 1497, 1456, 1369, 1237, 1158, 1124, 1071, 1039, 1015.

HRMS (ESI, *m*/*z*) calcd for $(C_{28}H_{50}O_3Si_2Na)^+$ 513.3191, found 513.3166.

(*Z*)-5-((Dimethyl(phenyl)silyl)methyl)-1-phenyl-7-(triethylsilyloxy)dec-4-en-3-ol 434



To a stirred solution of oxysilane **345** (50 mg, 0.12 mmol) in diethyl ether (5 mL) at −78 °C was added dropwise phenyllithium (2.0 M solution in dibutyl ether, 0.35 mL, 0.34 mmol, 3.0 equiv). The reaction was stirred 2 h at −78 °C and was allowed to warm up to room temperature for 1 h. The mixture was quenched by addition of a saturated aqueous solution of ammonium chloride (5 mL) and was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 9/1) gave alcohol **434** (42 mg, 68%) as a clear oil and as a 1:1 mixture of diastereomers.

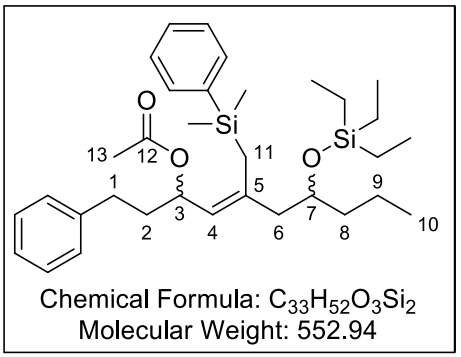
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.14 (m, 10H, ***H***-Ar), 5.05 (d, 1H, *J* = 9.0 Hz, C***H***-4), 3.95-3.86 (m, 1H, C***H***-3), 3.77-3.71 (m, 1H, C***H***-7), 2.68-2.48 (m, 2H, C***H***-1), 2.13-1.95 (m, 2H, C***H***-6), 1.81-1.62 (m, 3H, C***H***-2, C***H***-11), 1.60-1.50 (m, 1H, C***H***-2), 1.44-1.19 (m, 4H, C***H***-8, C***H***-9), 0.95 (t, 4.5H, *J* = 7.9 Hz, -Si($CH_2C\boldsymbol{H_3}$)$_3$), 0.94 (t, 4.5H, *J* = 7.9 Hz, -Si($CH_2C\boldsymbol{H_3}$)$_3$), 0.87 (t, 1.5H, *J* = 7.0 Hz, C***H***-10), 0.86 (t, 1.5H, *J* = 6.9 Hz, C***H***-10), 0.57 (q, 3H, *J* = 7.9 Hz, -Si($C\boldsymbol{H_2}CH_3$)$_3$), 0.56 (q, 3H, *J* = 7.9 Hz, -Si($C\boldsymbol{H_2}CH_3$)$_3$), 0.33 (s, 1.5H, -Si($C\boldsymbol{H_3}$)$_2$Ph), 0.32 (s, 1.5H, -Si($C\boldsymbol{H_3}$)$_2$Ph), 0.29 (s, 1.5H, -Si($C\boldsymbol{H_3}$)$_2$Ph), 0.28 (s, 1.5H, -Si($C\boldsymbol{H_3}$)$_2$Ph).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.2 (C-Ar), 137.3 (C-5), 133.7 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.1 (C-4), 127.9 (C-Ar), 125.7 (C-Ar), 71.8 (C-7), 71.3 (C-7), 67.8 (C-3), 47.2 (C-6), 46.7 (C-6), 39.3 (C-8), 39.2 (C-8), 38.7 (C-2), 31.7 (C-1), 31.7), 22.6 (C-11), 22.1 (C-11), 18.6 (C-9), 18.3 (C-9), 14.2 (C-10), 7.0 (-Si($CH_2\boldsymbol{C}H_3$)$_3$), 5.1 (-Si($\boldsymbol{C}H_2CH_3$)$_3$), −2.3 (-Si($\boldsymbol{C}H_3$)$_2$Ph), −2.5 (-Si($\boldsymbol{C}H_3$)$_2$Ph), −2.5 (-Si($\boldsymbol{C}H_3$)$_2$Ph), −2.6 (-Si($\boldsymbol{C}H_3$)$_2$Ph).

IR (neat, cm^{-1}) 3428, 2955, 2934, 2874, 1497, 1456, 1427, 1248, 1113, 1038, 1007.

HRMS (CI, *m*/*z*) calcd for $(C_{31}H_{49}OSi_2)^+$ 493.3322, found 493.3321.

(*Z*)-5-((Dimethyl(phenyl)silyl)methyl)-1-phenyl-7-(triethylsilyloxy)dec-4-en-3-yl acetate 358



Chemical Formula: $C_{33}H_{52}O_3Si_2$
Molecular Weight: 552.94

Compound **358** was obtained from the corresponding allylic alcohol **434** according to the procedure described above for compound **355**.
Scale: 0.078 mmol
Yield: quant. (1:1 mixture of diastereomers)

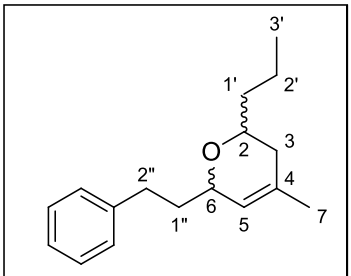
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.49 (m, 2H, ***H***-Ar), 7.37-7.33 (m, 3H, ***H***-Ar), 7.29-7.26 (m, 2H, ***H***-Ar), 7.20-7.12 (m, 3H, ***H***-Ar), 5.44-5.34 (m, 1H, C***H***-3), 5.11 (d, 0.5H, *J* = 9.4 Hz, C***H***-4), 5.07 (d, 0.5H, *J* = 9.5 Hz, C***H***-4), 3.76-3.68 (m, 1H, C***H***-7), 2.59-2.41 (m, 2H, C***H***-1), 2.21 (d, 0.5H, *J* = 13.6 Hz, C***H***-11), 2.08-1.82 (m, 3H, C***H***-2, C***H***-6), 2.07 (d, 0.5H, *J* = 13.6 Hz, C***H***-11), 2.00 (s, 1.5H, C***H***-13), 1.99 (s, 1.5H, C***H***-13), 1.73 (d, 0.5H, *J* = 13.6 Hz, C***H***-11), 1.70 (d, 0.5H, *J* = 13.6 Hz, C***H***-11), 1.66-1.54 (m, 1H, C***H***-2), 1.38-1.18 (m, 4H, C***H***-8, C***H***-9), 0.93 (t, 4.5H, *J* = 7.9 Hz, -Si($CH_2C\boldsymbol{H_3}$)$_3$), 0.93 (t, 4.5H, *J* = 7.9 Hz, -Si($CH_2C\boldsymbol{H_3}$)$_3$), 0.87-0.83 (m, 3H, C***H***-10), 0.57-0.51 (m, 6H, -Si($C\boldsymbol{H_2}CH_3$)$_3$), 0.30 (s, 1.5H, -Si($\boldsymbol{C}H_3$)$_2$Ph), 0.29 (s, 1.5H, -Si($\boldsymbol{C}H_3$)$_2$Ph), 0.29 (s, 1.5H, -Si($\boldsymbol{C}H_3$)$_2$Ph), 0.29 (s, 1.5H, -Si($\boldsymbol{C}H_3$)$_2$Ph).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4 (C-12), 141.7 (C-5 or C-Ar), 140.6 (C-5 or C-Ar), 140.2 (C-5 or C-Ar), 133.6 (C-Ar), 129.1 (C-4), 128.3 (C-Ar), 127.8 (C-Ar), 125.8 (C-Ar), 123.3 (C-Ar), 123.2 (C-Ar), 71.3 (C-3 or C-7), 71.1 (C-3 or C-7), 71.0 (C-3 or C-7), 47.1 (C-6), 46.9 (C-6), 39.5 (C-8), 39.1 (C-8), 36.8 (C-2), 36.6 (C-2), 31.7 (C-1), 31.6 (C-1), 22.4 (C-11), 22.2 (C-11), 21.2 (C-13), 18.4 (C-9), 14.3 (C-10), 6.9 (-Si($CH_2\boldsymbol{C}H_3$)$_3$), 5.1 (-Si($\boldsymbol{C}H_2CH_3$)$_3$), −2.2 (-Si($\boldsymbol{C}H_3$)$_2$Ph), −2.5 (-Si($\boldsymbol{C}H_3$)$_2$Ph), −2.7 (-Si($\boldsymbol{C}H_3$)$_2$Ph).

IR (neat, cm^{-1}) 2957, 2876, 1732, 1456, 1369, 1238, 1113, 1015.

HRMS (ESI, *m*/*z*) calcd for $(C_{33}H_{52}O_3Si_2Na)^+$ 575.3353, found 575.2962.

4-Methyl-6-phenethyl-2-propyl-3,6-dihydro-2*H*-pyran 357



Chemical Formula: $C_{17}H_{24}O$
Molecular Weight: 244.37

To a stirred solution of allylic silane **355** (25 mg, 0.051 mmol) in toluene (2 mL) was added scandium triflate (25 mg, 0.051 mmol, 1.0 equiv). The mixture was stirred at room temperature for 1 h and was then quenched by addition of water. The solution was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude NMR showed a mixture of diastereomers in a 1:1 ratio. Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 95/5) gave the cyclic ether **357** (diastereomer 1: 5 mg, 40%; diastereomer 2: 5 mg, 40%) as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.16 (m, 5H, ***H***-Ar), 5.31 (s, 1H, C***H***-5), 4.04-3.97 (m, 1H, C***H***-6), 3.52-3.46 (m, 1H, C***H***-2), 2.83-2.70 (m, 2H, C***H***-2"), 1.97-1.89 (m, 1H, C***H***-3), 1.86-1.74 (m, 3H, C***H***-3, C***H***-1"), 1.69 (s, 3H, C***H***-7), 1.65-1.39 (m, 4H, C***H***-1', C***H***-2'), 0.96 (t, 3H, *J* = 7.1 Hz, C***H***-3').

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5 (C-Ar), 132.7 (C-4), 128.6 (C-Ar), 128.2 (C-Ar), 125.6 (C-Ar), 124.0 (C-5), 73.8 (C-6), 73.7 (C-2), 38.2 (C-1'), 37.5 (C-1"), 36.3 (C-3), 31.5 (C-2"), 23.0 (C-7), 18.8 (C-2'), 14.1 (C-3').

IR (neat, cm^{-1}) 2957, 2928, 2872, 1497, 1454, 1379, 1130, 1101, 1078, 1030.

HRMS (CI, *m*/*z*) calcd for $(C_{17}H_{25}O)^+$ 245.1905, found 245.1898.

Other diastereomer:

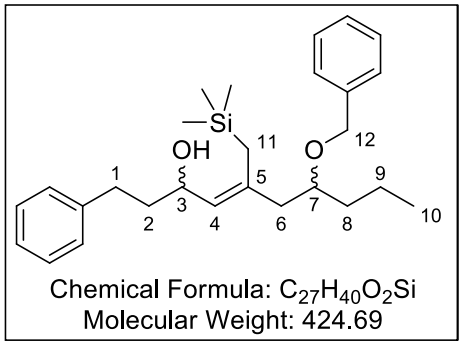
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.17 (m, 5H, ***H***-Ar), 5.40-5.37 (m, 1H, C***H***-5), 4.17-4.10 (m, 1H, C***H***-6), 3.69 (tt, 1H, *J* = 8.2, 4.3 Hz, C***H***-2), 2.83 (ddd, 1H, *J* = 13.8, 10.2, 4.9 Hz, C***H***-2"), 2.69 (ddd, 1H, *J* = 13.8, 9.9, 6.9 Hz, C***H***-2"), 1.96-1.82 (m, 3H, C***H***-3, C***H***-1"), 1.74-1.67 (m, 1H, C***H***-1"), 1.70 (s, 3H, C***H***-7), 1.61-1.53 (m, 2H, C***H***-1', C***H***-2'), 1.48-1.39 (m, 2H, C***H***-1', C***H***-2'), 0.97 (t, 3H, *J* = 7.1 Hz, C***H***-3').

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.4 (C-Ar), 131.8 (C-4), 128.5 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 123.2 (C-5), 71.9 (C-6), 67.3 (C-2), 37.7 (C-1'), 35.8 (C-3, C-1"), 32.4 (C-2"), 23.2 (C-7), 19.1 (C-2'), 14.1 (C-3').

IR (neat, cm^{-1}) 2957, 2928, 2872, 1497, 1454, 1379, 1130, 1101, 1078, 1030.

HRMS (CI, *m*/*z*) calcd for $(C_{17}H_{25}O)^+$ 245.1905, found 245.1898.

(Z)-7-(Benzyloxy)-1-phenyl-5-((trimethylsilyl)methyl)dec-4-en-3-ol 362



Allylic alcohol **362** was obtained from the corresponding silacycle **346** according to the general procedure described above for allylic alcohol **354**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 8/2))
Scale: 0.46 mmol
Yield: 96% (1:1 mixture of diastereomers)

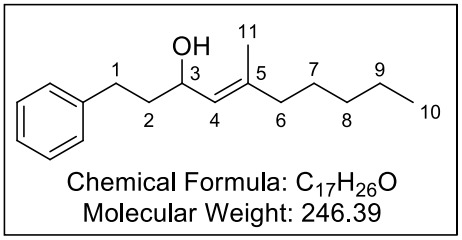
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.10 (m, 10H, ***H***-Ar), 5.20 (dd, 1H, *J* = 8.9, 3.2 Hz, C***H***-4), 4.53 (m, 2H, C***H***-12), 4.25 (m, 1H, C***H***-3), 3.53 (m, 1H, C***H***-7), 2.78-2.63 (m, 2H, C***H***-1), 2.29 (dd, 1H, *J* = 13.7, 6.7 Hz, C***H***-6), 2.09 (m, 1H, C***H***-6), 1.88 (m, 1H, C***H***-2), 1.73 (m, 1H, C***H***-2), 1.65-1.34 (m, 6H, C***H***-8, C***H***-9, C***H***-11), 0.91 (m, 3H, C***H***-10), 0.02 (s, 9H, -Si(C***H*****$_3$**$)_3$).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (C-Ar), 138.9 (C-Ar or C-5), 138.5 (C-Ar or C-5), 128.4 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.5 (C-Ar), 127.3 (C-4), 125.7 (C-Ar), 78.0 (C-7), 71.0 (C-12), 68.0 (C-3), 44.0 (C-6), 39.3 (C-2), 36.4 (C-8), 31.9 (C-1), 22.2 (C-11), 18.5 (C-9), 14.2 (C-10), 0.81 (-Si(***C***$H_3)_3$).

IR (neat, cm^{-1}) 3437, 2955, 2929, 1495, 1454, 1248, 1059, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{27}H_{40}O_2SiNa)^+$ 447.2690, found 447.2680.

(*E*)-5-Methyl-1-phenyldec-4-en-3-ol 363



Chemical Formula: $C_{17}H_{26}O$
Molecular Weight: 246.39

General procedure

To a stirred solution of allylic silane **361** (118 mg, 0.370 mmol) in DMF (8 mL) were added water (40 µL, 2.2 mmol, 6.0 equiv) and tetrabutylammonium fluoride (1.0 M solution in THF, 2.22 mL, 2.22 mmol, 6.00 equiv). The solution was stirred at 65 °C for 1 h and was then quenched by addition of a saturated aqueous solution of ammonium chloride (5 mL). The mixture was then extracted with diethyl ether (3 × 5 mL) and the combined organic layers were washed with brine (3 × 10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 9/1, then 8/2) gave alcohol **363** (62 mg, 68%) as a clear oil and alcohol **365** (26 mg, 28%) as a clear oil.

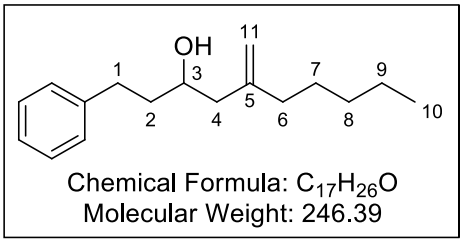
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.17 (m, 5H, ***H***-Ar), 5.23 (dq, 1H, *J* = 8.7, 1.3 Hz, C***H***-4), 4.40 (dtd, 1H, *J* = 8.7, 6.7, 3.5 Hz, C***H***-3), 2.74-2.62 (m, 2H, C***H***-1), 2.01 (t, 2H, *J* = 7.8 Hz, C***H***-6), 1.94 (ddt, 1H, *J* = 13.3, 9.5, 6.7 Hz, C***H***-2), 1.77 (ddt, 1H, *J* = 13.3, 9.5, 6.7 Hz, C***H***-2), 1.65 (d, 3H, *J* = 1.3 Hz, C***H***-11), 1.47-1.39 (m, 2H, C***H***-7), 1.36-1.23 (m, 5H, C3-***OH***, C***H***-8, C***H***-9), 0.90 (t, 3H, *J* = 7.1 Hz, C***H***-10).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.1 (C-Ar), 139.5 (C-5), 128.4 (C-Ar), 128.3 (C-Ar), 127.4 (C-4), 125.7 (C-Ar), 68.1 (C-3), 39.5 (C-6), 39.2 (C-2), 31.8 (C-1), 31.5 (C-8), 27.4 (C-7), 22.5 (C-9), 16.5 (C-11), 14.0 (C-10).

IR (neat, cm^{-1}) 3320, 2955, 2926, 2857, 1495, 1454, 1030.

HRMS (CI, *m*/*z*) calcd for $(C_{17}H_{25})^+$ 229.1956, found 229.1958.

5-Methylene-1-phenyldecan-3-ol 365



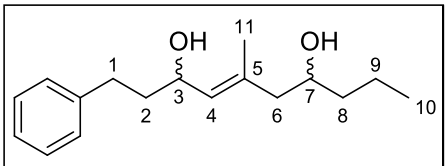
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.17 (m, 5H, ***H***-Ar), 4.92-4.89 (m, 1H, C***H***-11), 4.84 (s, 1H, C***H***-11), 3.74 (dtt, 1H, *J* = 9.3, 6.1, 3.3 Hz, C***H***-3), 2.90-2.79 (m, 1H, C***H***-1), 2.71 (dt, 1H, *J* = 13.8, 8.1 Hz, C***H***-1), 2.28 (dd, 1H, *J* = 13.7, 3.3 Hz, C***H***-4), 2.11 (dd, 1H, *J* = 13.7, 9.3 Hz, C***H***-4), 2.01 (t, 2H, *J* = 7.7 Hz, C***H***-6), 1.83-1.76 (m, 2H, C***H***-2), 1.50-1.22 (m, 6H, C***H***-7, C***H***-8, C***H***-9), 0.90 (t, 3H, *J* = 7.0 Hz, C***H***-10).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.8 (C-5), 142.2 (C-Ar), 128.4 (C-Ar), 128.4 (C-Ar), 125.8 (C-Ar), 112.3 (C-11), 68.1 (C-3), 44.6 (C-4), 38.8 (C-2), 35.8 (C-6), 32.1 (C-1), 31.5 (C-8), 27.4 (C-7), 22.5 (C-9), 14.0 (C-10).

IR (neat, cm^{-1}) 3360, 2928, 2859, 1643, 1454, 1051.

HRMS (CI, *m*/*z*) calcd for $(C_{17}H_{25})^+$ 229.1956, found 229.1959.

(*E*)-5-Methyl-1-phenyldec-4-ene-3,7-diol 350



Chemical Formula: $C_{17}H_{26}O_2$
Molecular Weight: 262.39

Method 1:

To a stirred solution of compound **345** (10 mg, 0.023 mmol) in MeOH/THF (0.5 mL/0.5 mL) was added at 0 °C potassium bicarbonate (10 mg, 0.099 mmol, 4.3 equiv) and potassium fluoride (6.0 mg, 0.099 mmol, 4.3 equiv). The reaction mixture was stirred for 30 min at 0 °C and 1 h 30 at room temperature. Potassium bicarbonate (20 mg, 0.20 mmol, 8.6 equiv) and potassium fluoride (9.0 mg, 0.15 mmol, 6.5 equiv) were added to the reaction mixture and the solution was stirred overnight at room temperature. Water (5 mL) was then added and the mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ether 9/1, 7/3, 4/6, then 2/8) gave the product **350** (1.0 mg, 16%, 57% brsm) as a clear oil and as a 1:1 mixture of diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2H, ***H***-Ar), 7.22-7.17 (m, 3H, ***H***-Ar), 5.51-5.44 (m, 1H, C***H***-4), 4.40-4.27 (m, 1H, C***H***-3), 3.80-3.69 (m, 1H, C***H***-7), 2.78-2.63 (m, 2H, C***H***-1), 2.51-2.16 (m, 1H, C***H***-6), 1.99-1.90 (m, 2H, C***H***-2, C***H***-6), 1.85-1.76 (m, 4H, C***H***-2, C***H***-11), 1.53-1.30 (m, 4H, C***H***-8, C***H***-9), 0.98-0.93 (m, 3H, C***H***-10).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (C-Ar), 137.5 (C-5), 131.5 (C-4), 128.4 (C-Ar), 128.3 (C-Ar), 125.7 (C-Ar), 68.5 (C-7), 66.4 (C-3), 40.4 (C-6 or C-8), 40.2 (C-6 or C-8), 38.6 (C-2), 32.0 (C-1), 23.6 (C-11), 18.9 (C-9), 14.0 (C-10).

IR (neat, cm^{-1}) 3323, 3026, 2955, 2928, 2858, 1728, 1665, 1603, 1497, 1454, 1377, 1121, 1051, 1007.

HRMS (CI, *m*/*z*) calcd for $(C_{17}H_{25}O)^+$ 245.1905, found 245.1902.

Method 2:

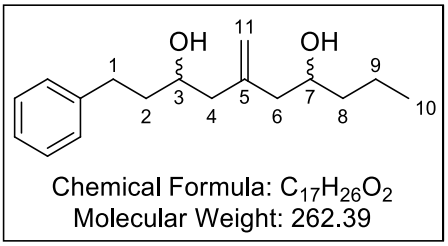
Allylic alcohol **350** and alcohol **352** were obtained from the corresponding allylic alcohol **359** according to the general procedure described above for allylic alcohol **363**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 4/6)).
Scale: 0.080 mmol
Yield: 35% for **350** and 35% for **352** (1:1 mixtures of diastereomers)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H, ***H***-Ar), 7.22-7.17 (m, 3H, ***H***-Ar), 5.34 (dq, 1H, *J* = 8.7, 1.0 Hz, C***H***-4), 4.45-4.39 (m, 1H, C***H***-3), 3.77-3.70 (m, 1H, C***H***-7), 2.76-2.63 (m, 2H, C***H***-1), 2.22 (dd, 1H, *J* = 13.6, 3.2 Hz, C***H***-6), 2.07 (ddd, 1H, *J* = 13.6, 9.2, 0.6 Hz, C***H***-6), 1.95 (ddt, 1H, *J* = 13.5, 9.3, 6.7 Hz, C***H***-2), 1.83-1.74 (m,

1H, C***H***-2), 1.70 (d, 3H, *J* = 1.0 Hz, C***H***-11), 1.54-1.35 (m, 4H, C***H***-8, C***H***-9), 0.95 (t, 3H, *J* = 7.1 Hz, C**H**-10).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7 (C-Ar), 136.0 (C-5), 131.1 (C-4), 128.4 (C-Ar), 128.4 (C-Ar), 125.9 (C-Ar), 68.6 (C-7), 67.9 (C-3), 47.9 (C-6), 39.4 (C-8), 39.2 (C-2), 31.8 (C-1), 18.9 (C-9), 16.8 (C-11), 14.1 (C-10).

5-Methylene-1-phenyldecane-3,7-diol 352



Chemical Formula: $C_{17}H_{26}O_2$
Molecular Weight: 262.39

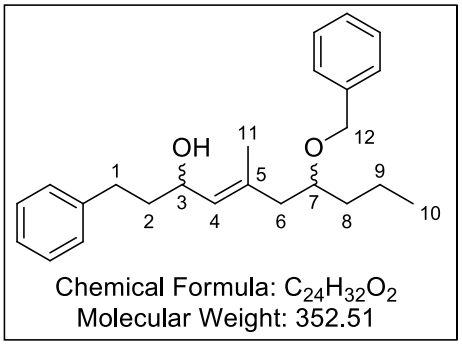
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.18 (m, 5H, ***H***-Ar), 5.02 (s, 1H, C***H***-11), 4.99 (s, 1H, C***H***-11), 3.83-3.73 (m, 2H, C***H***-3, C***H***-7), 2.86-2.80 (m, 1H, C***H***-1), 2.75-2.68 (m, 1H, C***H***-1), 2.34-2.04 (m, 4H, C***H***-4, C***H***-6), 2.02 (br s, 2H, C3-***OH***, C7-***OH***), 1.85-1.78 (m, 2H, C***H***-2), 1.52-1.35 (m, 4H, C***H***-8, C***H***-9), 0.97-0.93 (m, 3H, C***H***-10).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.1 (C-5), 143.8 (C-5), 142.0 (C-Ar), 128.4 (C-Ar), 125.8 (C-Ar), 115.7 (C-11), 115.3 (C-11), 69.8 (C-3 or C-7), 69.3 (C-3 or C-7), 69.1 (C-3 or C-7), 68.5 (C-3 or C-7), 44.7 (C-4 or C-6), 44.5 (C-4 or C-6), 44.0 (C-4 or C-6), 43.8 (C-4 or C-6), 39.5 (C-8), 39.5 (C-8), 38.9 (C-2), 38.9 (C-2), 32.1 (C-1), 32.1 (C-1), 18.9 (C-9), 18.8 (C-9), 14.1 (C-10), 14.0 (C-10).

IR (neat, cm^{-1}) 3314, 2957, 2930, 2871, 1496, 1454, 1074, 1030.

HRMS (ESI, *m*/*z*) calcd for $(C_{17}H_{26}O_2Na)^+$ 285.1825, found 285.1814.

(*E*)-7-(Benzyloxy)-5-methyl-1-phenyldec-4-en-3-ol 364



Allylic alcohol **364** and alcohol **366** were obtained from the corresponding allylic alcohol **362** according to the general procedure described above for allylic alcohol **363**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 7/3))
Scale: 0.12 mmol
Yield: 64% for **364** and 29% for **366** (1:1 mixtures of diastereomers)

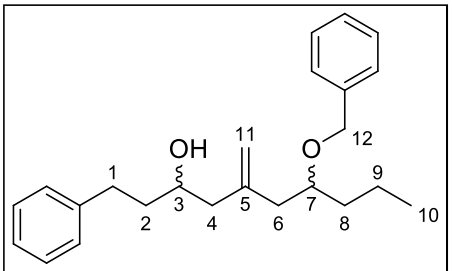
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.06 (m, 10H, ***H***-Ar), 5.22 (dq, 1H, *J* = 8.5, 1.2 Hz, C***H***-4), 4.45 (s, 2H, C***H***-12), 4.31 (dt, 1H, *J* = 8.5, 6.6 Hz, C***H***-3), 3.51-3.45 (m, 1H, C***H***-7), 2.66-2.53 (m, 2H, C***H***-1), 2.28 (dd, 1H, *J* = 13.4, 6.8 Hz, C***H***-6), 2.10 (dd, 1H, *J* = 13.4, 6.3 Hz, C***H***-6), 1.85 (ddt, 1H, *J* = 13.4, 9.5, 6.6 Hz, C***H***-2), 1.68 (ddt, 1H, *J* = 13.4, 9.7, 6.6 Hz, C***H***-2), 1.59 (d, 3H, *J* = 1.2 Hz, C***H***-11), 1.52-1.17 (m, 4H, C***H***-8, C***H***-9), 0.84 (t, 3H, *J* = 7.0 Hz, C***H***-10).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0 (C-Ar), 138.9 (C-5), 136.2 (C-Ar), 130.3 (C-4), 128.4 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.5 (C-Ar), 125.8 (C-Ar), 77.2 (C-7), 70.9 (C-12), 68.0 (C-3), 44.5 (C-6), 39.1 (C-2), 36.2 (C-8), 31.8 (C-1), 18.5 (C-9), 17.1 (C-11), 14.2 (C-10).

IR (neat, cm^{-1}) 3387, 2955, 2930, 2870, 1495, 1454, 1350, 1059, 1028.

HRMS (EI, *m*/*z*) calcd for $(C_{24}H_{32}O_2)^+$ 352.2402, found 352.2399.

7-(Benzyloxy)-5-methylene-1-phenyldecan-3-ol 366



Chemical Formula: $C_{24}H_{32}O_2$
Molecular Weight: 352.51

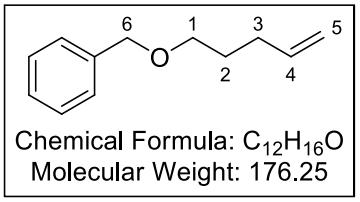
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.10 (m, 10H, ***H***-Ar), 4.97-4.91 (m, 2H, C***H***-11), 4.54-4.44 (m, 2H, C***H***-12), 3.77-3.65 (m, 1H, C***H***-3), 3.59-3.49 (m, 1H, C***H***-7), 2.84-2.74 (m, 1H, C***H***-1), 2.71-2.61 (m, 1H, C***H***-1), 2.40-2.01 (m, 4H, C***H***-4, C***H***-6), 1.83-1.69 (m, 2H, C***H***-2), 1.57-1.25 (m, 4H, C***H***-8, C***H***-9), 0.94-0.89 (m, 3H, C***H***-10).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2 (C-5 or C-Ar), 143.8 (C-5 or C-Ar), 142.2 (C-5 or C-Ar), 128.7 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 127.8 (C-Ar), 127.5 (C-Ar), 125.8 (C-Ar), 115.1 (C-11), 78.0 (C-7), 77.5 (C-7), 71.0 (C-12), 70.8 (C-12), 68.6 (C-3), 68.2 (C-3), 45.0 (C-4), 40.5 (C-6), 40.2 (C-6), 38.8 (C-2), 38.7 (C-2), 36.1 (C-8), 36.0 (C-8), 32.1 (C-1), 18.6 (C-9), 18.4 (C-9), 14.2 (C-10).

IR (neat, cm^{-1}) 3431, 2955, 2930, 2870, 1495, 1454, 1348, 1063, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{24}H_{32}O_2Na)^+$ 375.2295, found 375.2281.

((Pent-4-enyloxy)methyl)benzene 371[109]



Chemical Formula: $C_{12}H_{16}O$
Molecular Weight: 176.25

Tetrabutylammonium iodide (0.43 g, 1.2 mmol, 0.010 equiv) was added to a stirred suspension of NaH (60% dispersion in mineral oil, 8.80 g, 221 mmol, 1.90 equiv) in THF (70 mL). After cooling to 0 °C, a solution of 4-penten-1-ol (10.0 g, 116 mmol) in THF (50 mL) was added dropwise and the mixture was stirred at room temperature for 30 min. Benzyl bromide (22.0 mL, 186 mmol, 1.60 equiv) was added at 0 °C and the reaction mixture was stirred at room temperature for 5 h. The reaction was quenched by careful addition of crushed ice and the solution was extracted with ether (3 × 100 mL). The combined organic layers were washed with brine (200 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (petroleum ether-ether 96/4, 9/1, 8/2, then 7/3) to afford the protected alcohol **371** (20.5 g, quant.) as a clear oil.

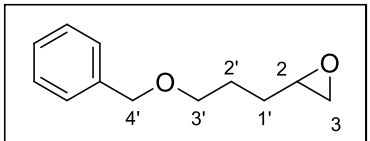
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H, ***H***-Ar), 5.83 (ddt, *J* = 17.1, 10.3, 6.7 Hz, 1H, C***H***-4), 5.03 (dq, *J* = 17.1, 1.8 Hz, 1H, C***H***-5$_{trans}$), 4.97 (ddt, *J* = 10.3, 2.1, 1.2 Hz, 1H, C***H***-5$_{cis}$), 4.52 (s, 2H, C***H***-6), 3.50 (t, *J* = 6.6 Hz, 2H, C***H***-1), 2.16 (qt, *J* = 7.1, 1.3 Hz, 2H, C***H***-3), 1.73 (app quint, *J* = 6.6 Hz, 2H, C***H***-2).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6 (C-Ar), 138.3 (C-4), 128.3 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 114.7 (C-5), 72.9 (C-6), 69.7 (C-1), 30.3 (C-3), 28.9 (C-2).

HRMS (CI, *m*/*z*) calcd for $(C_{12}H_{17}O)^+$ 177.1279, found 177.1284.

[109] Srihari, P.; Kumaraswamy, B.; Somaiah, R.; Yadav, J. S. *Synthesis* **2010**, 1039.

2-(3-(Benzyloxy)propyl)oxirane (±)-105[109]



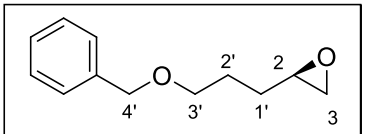
Chemical Formula: $C_{12}H_{16}O_2$
Molecular Weight: 192.25

To a stirred solution of alkene **371** (2.5 g, 14 mmol) in dichloromethane (60 mL) was added *m*-CPBA (5.0 g, 20 mmol, 1.4 equiv). The reaction mixture was stirred overnight at room temperature. The mixture was then filtered and dichloromethane (20 mL) was added. The solution was washed with a saturated aqueous solution of sodium thiosulfate (2 × 60 mL), a saturated aqueous solution of sodium bicarbonate (60 mL), brine, dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 4/6) gave the epoxide **(±)-105** (2.3 g, 85%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H, ***H***-Ar), 4.52 (s, 2H, C***H***-4'), 3.58-3.48 (m, 2H, C***H***-3'), 2.97-2.93 (m, 1H, C***H***-2), 2.76 (ddd, *J* = 5.0, 4.0, 0.4 Hz, 1H, C***H***-3), 2.48 (dd, *J* = 5.0, 2.7 Hz, 1H, C***H***-3), 1.86-1.58 (m, 4H, C***H***-1', C***H***-2').

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (C-Ar), 128.3 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 72.9 (C-4'), 69.7 (C-3'), 52.1 (C-2), 47.1 (C-3'), 29.3 (C-1'), 26.1 (C-2').

(*R*)-2-(3-(Benzyloxy)propyl)oxirane (+)-105[16]



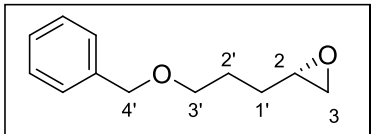
Chemical Formula: $C_{12}H_{16}O_2$
Molecular Weight: 192.25

Reference procedure[16]

To a stirred solution of (*R*,*R*)-Jacobsen's catalyst (21 mg, 0.034 mmol, 0.50 mol%) in toluene (0.08 mL) was added acetic acid (0.0080 mL, 0.14 mmol, 0.020 equiv) and the reaction was stirred for 1 h open to air at room temperature. The mixture was then concentrated *in vacuo* and put under high vacuum for 30 min. Epoxide **(±)-105** (1.35 g, 7.00 mmol) was then added in one portion at room temperature followed by dropwise addition (over 5-10 min) of water (0.070 mL, 3.9 mmol, 0.57 equiv) at 0 °C. The mixture was then stirred for one day at room temperature. Purification by column chromatography on silica gel (petroleum ether-ether 8/2) gave the epoxide **(+)-105** (514 mg, 76%) as a yellow oil.

$[\alpha]^{25}_D$ = +9.3° (*c* 1.0, $CHCl_3$) (*Lit.*: $[\alpha]^{25}_D$ = +8.7° (*c* 1.1, $CHCl_3$))[16]

(*S*)-2-(3-(Benzyloxy)propyl)oxirane (−)-105[110]



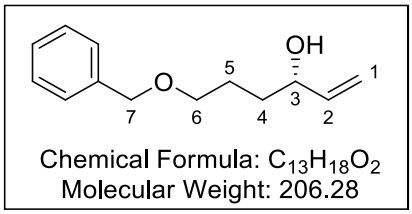
Chemical Formula: $C_{12}H_{16}O_2$
Molecular Weight: 192.25

Epoxide **(−)-105** was obtained from the corresponding epoxide **(±)-105** using the (*S*,*S*)-Jacobsen's catalyst according to the procedure described above for epoxide **(+)-105**.
Scale: 60.4 mmol
Yield: 92%

[α]$^{25}_D$ = −8.3° (*c* 2.1, $CHCl_3$) (*Lit.*: [α]$^{20}_D$ = −7.4° (*c* 2.08, $CHCl_3$))[110]

[110] Kühnert, S. V.; Maier, M. E. *Org. Lett.* **2002**, *4*, 643.

(*S*)-6-(Benzyloxy)hex-1-en-3-ol 369[111]



Chemical Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28

Reference procedure[111]

To a sirred solution of trimethylsulfonium iodide (6.4 g, 31 mmol, 3.0 equiv) in THF (24 mL) at −20 °C was added dropwise *n*-butyllithium (2.1 M solution in hexane, 14.8 mL, 31.2 mmol, 3.00 equiv) over 20 min. The solution was stirred 30 min at −20 °C and epoxide **(−)-105** (2.0 g, 10 mmol), dissolved in THF (12 mL), and was then added slowly at −20 ° C. The reaction was allowed to warm up to room temperature for 1 h and was stirred another 2 h at room temperature. The mixture was then quenched by addition of water (25 mL) and was extracted with ethyl acetate (3 × 25 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave alcohol **369** (968 mg, 45%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H, ***H***-Ar), 5.88 (ddd, 1H, *J* = 17.2, 10.4, 5.9 Hz, C***H***-2), 5.23 (dt, 1H, *J* = 17.2, 1.5 Hz, C***H***-1$_{trans}$), 5.10 (dt, 1H, *J* = 10.4, 1.5 Hz, C***H***-1$_{cis}$), 4.53 (s, 2H, C***H***-7), 4.17-4.10 (m, 1H, C***H***-3), 3.52 (t, 2H, *J* = 5.9 Hz, C***H***-6), 2.33 (br s, 1H, C3-***OH***), 1.77-1.57 (m, 4H, C***H***-4, C***H***-5).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1 (C-2), 138.2 (C-Ar), 128.4 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 114.4 (C-1), 73.0 (C-7), 72.7 (C-3), 70.3 (C-6), 34.3 (C-4), 25.8 (C-5).

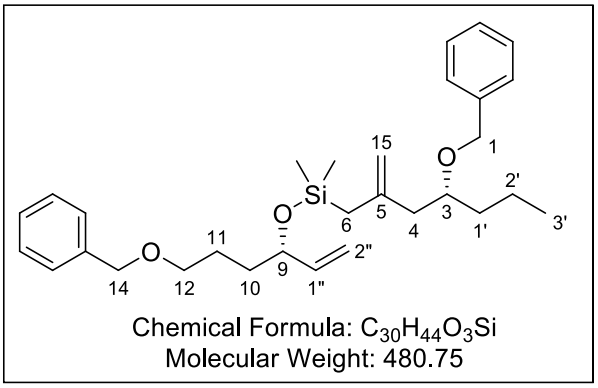
IR (neat, cm^{-1}) 3399, 2924, 2857, 1497, 1454, 1362, 1096, 1074, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{13}H_{18}O_2Na)^+$ 229.1199, found 229.1200.

$[\alpha]^{25}_D$ = +1.2° (*c* 1.0, $CHCl_3$) (*Lit.*: $[\alpha]^{25}_D$ = +2.5° (*c* 1.0, $CHCl_3$))[112]

[111] Kuilya, T. K.; Chatterjee, S.; Goswami, R. K. *Tetrahedron* **2014**, *70*, 2905.
[112] Venkatesham, A.; Nagaiah, K. *Tetrahedron: Asymmetry* **2012**, *23*, 1186.

(3*R*,9*S*)-7,7-Dimethyl-5-methylene-1,14-diphenyl-3-propyl-9-vinyl-2,8,13-trioxa-7-silatetradecane 372



Chemical Formula: $C_{30}H_{44}O_3Si$
Molecular Weight: 480.75

Method 1:

Silane **372** was obtained from the corresponding silane **368** and alcohol **369** according to the general procedure (method 1) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 96/4)).
Scale: 4.65 mmol
Yield: 54%

Method 2:

Silane **372** was obtained from the corresponding silane **368** and alcohol **369** according to the general procedure (method 2) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 95/5)).
Scale: 1.96 mmol
Yield: 80%

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.25 (m, 10H, ***H***-Ar), 5.80 (ddd, 1H, *J* = 17.0, 10.4, 6.3 Hz, C***H***-1"), 5.14 (dt, 1H, *J* = 17.0, 1.5 Hz, C***H***-2"$_{trans}$), 5.04 (ddd, 1H, *J* = 10.4, 1.5, 0.9 Hz, C***H***-2"$_{cis}$), 4.72-4.70 (m, 1H, C***H***-15), 4.68-4.66 (m, 1H, C***H***-15), 4.58 (d, 1H, *J* = 11.5 Hz, C***H***-1), 4.50 (s, 2H, C***H***-14), 4.50 (d, 1H, *J* = 11.5 Hz, C***H***-1), 4.13-4.07 (m, 1H, C***H***-9), 3.56 (app quint, 1H, *J* = 6.0 Hz, C***H***-3), 3.50-3.44 (m, 2H, C***H***-12), 2.38 (ddd, 1H, *J* = 14.0, 6.3, 0.6 Hz, C***H***-4), 2.16 (ddd, 1H, *J* = 14.0, 6.3, 0.6 Hz, C***H***-4), 1.72-1.32 (m, 10H, C***H***-10, C***H***-11, C***H***-1', C***H***-2', C***H***-6), 0.91 (t, 3H, *J* = 7.1 Hz, C***H***-3'), 0.14 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.13 (s, 3H, -Si(C***H***$_3$)$_2$-).

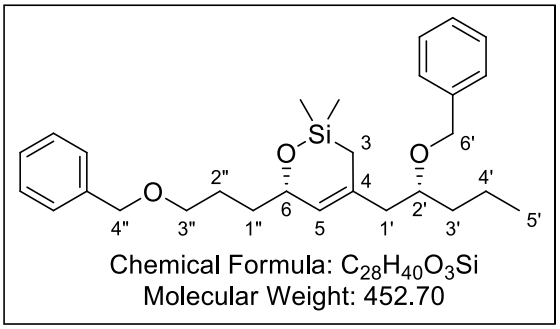
^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6 (C-Ar), 141.3 (C-1"), 139.1 (C-5 or C-Ar), 138.6 (C-5 or C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.8 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 114.1 (C-2"), 110.6 (C-15), 77.6 (C-3), 73.9 (C-9), 72.8 (C-14), 71.0 (C-1), 70.3 (C-12), 43.1 (C-4), 36.4 (C-1'), 34.5 (C-10), 27.3 (C-6), 25.7 (C-11), 18.7 (C-2'), 14.2 (C-3'), 1.2 (-Si(***C***H$_3$)$_2$-), −1.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2955, 2932, 2861, 1634, 1467, 1454, 1360, 1250, 1092, 1067, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{30}H_{44}O_3SiNa)^+$ 503.2952, found 503.2935.

[α]$^{24}_D$ = +12.4° (*c* 1.0, $CHCl_3$)

(*S*)-4-((*R*)-2-(Benzyloxy)pentyl)-6-(3-(benzyloxy)propyl)-2,2-dimethyl-3,6-dihydro-2*H*-1,2-oxasiline 373



Chemical Formula: $C_{28}H_{40}O_3Si$
Molecular Weight: 452.70

To a solution of compound **372** (300 mg, 0.624 mmol) in dichloromethane (15 mL) was added second-generation Grubbs' catalyst (14 mg, 0.016 mmol, 2.5 mol%) under argon. The reaction was stirred for 2 h at 45 °C (reflux) and was monitored by TLC. The sequence addition/stirring was repeated twice. The reaction mixture was then concentrated *in vacuo*. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ether 9/1) gave the product **373** (193 mg, 68%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H, ***H***-Ar), 5.43-5.40 (m, 1H, C***H***-5), 4.57 (d, 1H, *J* = 11.5 Hz, C***H***-6'), 4.51 (d, 1H, *J* = 11.5 Hz, C***H***-6'), 4.51 (s, 2H, C***H***-4"), 4.43-4.36 (m, 1H, C***H***-6), 3.60-3.54 (m, 1H, C***H***-2'), 3.50 (td, 2H, *J* = 6.5, 1.0 Hz, C***H***-3"), 2.39 (dd, 1H, *J* = 13.6, 6.3 Hz, C***H***-1'), 2.16 (dd, 1H, *J* = 13.6, 6.3 Hz, C***H***-1'), 1.82-1.62 (m, 3H, C***H***-1", C***H***-2"), 1.60-1.33 (m, 5H, C***H***-3', C***H***-4', C***H***-1"), 1.27 (d, 1H, *J* = 16.9 Hz, C***H***-3), 1.11 (dd, 1H, *J* = 16.9, 1.2 Hz, C***H***-3), 0.92 (t, 3H, *J* = 7.0 Hz, C***H***-5'), 0.17 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.13 (s, 3H, -Si(C***H***$_3$)$_2$-).

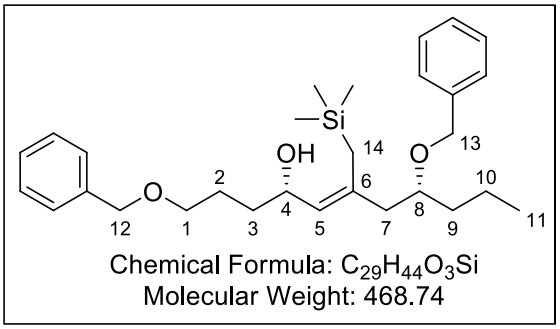
^{13}C NMR (126 MHz, $CDCl_3$) δ 139.0 (C-4 or C-Ar), 138.74 (C-4 or C-Ar), 133.0 (C-4 or C-Ar), 128.6 (C-5), 128.3 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.4 (C-Ar), 127.4 (C-Ar), 77.0 (C-2'), 72.8 (C-4"), 71.9 (C-6), 70.8 (C-6'), 70.5 (C-3"), 46.6 (C-1'), 36.3 (C-3'), 34.9 (C-1"), 25.4 (C-2"), 18.6 (C-4'), 16.2 (C-3), 14.2 (C-5'), 0.2 (-Si(***C***H$_3$)$_2$-), −0.8 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2955, 2926, 2855, 1497, 1454, 1360, 1250, 1096, 1069, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{28}H_{40}O_3SiNa)^+$ 475.2639, found 475.2621.

[α]$^{26}_D$ = +23.6° (*c* 1.0, $CHCl_3$)

(4*S*,8*R*,*Z*)-1,8-*Bis*(benzyloxy)-6-((trimethylsilyl)methyl)undec-5-en-4-ol 374



Allylic alcohol **374** was obtained from the corresponding silacycle **373** according to the general procedure described above for allylic alcohol **354**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 7/3)).
Scale: 0.32 mmol
Yield: 83%

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H, ***H***-Ar), 5.16 (d, 1H, *J* = 8.8 Hz, C***H***-5), 4.56-4.49 (m, 4H, C***H***-12, C***H***-13), 4.31-4.21 (m, 1H, C***H***-4), 3.58-3.48 (m, 1H, C***H***-8), 3.51 (t, 2H, *J* = 6.2 Hz, C***H***-1), 2.30 (ddd, 1H, *J* = 13.7, 6.6, 0.6 Hz, C***H***-7), 2.09 (dd, 1H, *J* = 13.7, 6.4 Hz, C***H***-7), 1.78-1.28 (m, 10H, C***H***-2, C***H***-3, C***H***-9, C***H***-10, C***H***-14), 0.92 (t, 3H, *J* = 7.0 Hz, C***H***-11), 0.06 (s, 9H, -Si(C***H***$_3$)$_3$).

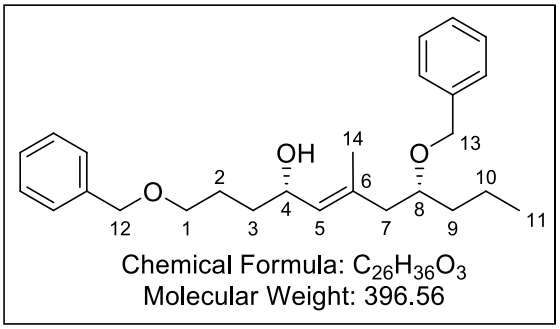
^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9 (C-6 or C-Ar), 138.4 (C-6 or C-Ar), 138.1 (C-6 or C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.5 (C-5 or C-Ar), 127.4 (C-5 or C-Ar), 77.9 (C-8), 72.9 (C-12 or C-13), 71.0 (C-12 or C-13), 70.4 (C-1), 68.4 (C-4), 43.9 (C-7), 36.4 (C-9), 34.7 (C-3), 26.0 (C-2), 22.2 (C-14), 18.5 (C-10), 14.2 (C-11), −0.7 (-Si(***C***H$_3$)$_3$).

IR (neat, cm^{-1}) 3451, 2955, 2932, 2868, 1454, 1360, 1248, 1094, 1071, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{29}H_{44}O_3SiNa)^+$ 491.2952, found 491.2929.

[α]$^{28}_D$ = −14.4° (*c* 1.0, $CHCl_3$)

(4*S*,8*R*,*E*)-1,8-*Bis*(benzyloxy)-6-methylundec-5-en-4-ol 375



Allylic alcohol **375** and alcohol **376** were obtained from the corresponding allylic alcohol **374** according to the general procedure described above for allylic alcohol **363**. (Purification by column chromatography on silica gel (petroleum ether-ethyl acetate 6/4)).
Scale: 0.23 mmol
Yield: 69% for **375** and 29% for **376**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 10H, ***H***-Ar), 5.26 (dq, 1H, *J* = 8.7, 1.2 Hz, C***H***-5), 4.52 (s, 2H, C***H***-12), 4.52 (s, 2H, C***H***-13), 4.42-4.33 (m, 1H, C***H***-4), 3.57-3.47 (m, 1H, C***H***-8), 3.51 (t, 2H, *J* = 6.1 Hz, C***H***-1), 2.35 (dd, 1H, *J* = 13.7, 6.4 Hz, C***H***-7), 2.15 (dd, 1H, *J* = 13.7, 6.4 Hz, C***H***-7), 1.80 (d, 1H, *J* = 3.0 Hz, C4-***OH***), 1.71-1.27 (m, 8H, C***H***-2, C***H***-3, C***H***-9, C***H***-10), 1.69 (d, 3H, *J* = 1.2 Hz, C***H***-14), 0.91 (t, 3H, *J* = 7.0 Hz, C***H***-11).

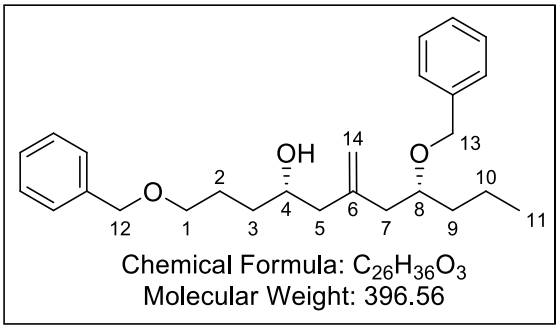
^{13}C NMR (126 MHz, $CDCl_3$) δ 138.9 (C-6 or C-Ar), 138.4 (C-6 or C-Ar), 135.6 (C-6 or C-Ar), 130.5 (C-5), 128.4 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.4 (C-Ar), 77.3 (C-8), 73.0 (C-12 or C-13), 70.9 (C-12 or C-13), 70.4 (C-1), 68.3 (C-4), 44.4 (C-7), 36.2 (C-9), 34.7 (C-3), 25.9 (C-2), 18.5 (C-10), 17.1 (C-14), 14.2 (C-11).

IR (neat, cm^{-1}) 3423, 2956, 2930, 2869, 1453, 1362, 1091, 1066, 1028.

HRMS (CI, *m*/*z*) calcd for $(C_{26}H_{37}O_3)^+$ 397.2743, found 397.2740.

$[\alpha]^{26}_D$ = −2.4° (*c* 1.0, $CHCl_3$)

(4*S*,8*R*)-1,8-*Bis*(benzyloxy)-6-methyleneundecan-4-ol 376



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.25 (m, 10H, ***H***-Ar), 4.95 (s, 1H, C***H***-14), 4.92 (s, 1H, C***H***-14), 4.52 (s, 2H, C***H***-12), 4.52 (s, 2H, C***H***-13), 3.75-3.70 (m, 1H, C***H***-4), 3.58-3.53 (m, 1H, C***H***-8), 3.51 (td, 2H, *J* = 6.2, 1.4 Hz, C***H***-1), 2.44 (d, 1H, *J* = 2.7 Hz, C4-***OH***), 2.39 (dd, 1H, *J* = 14.0, 6.7 Hz, C***H***-7), 2.24 (dd, 1H, *J* = 13.9, 4.4 Hz, C***H***-5), 2.22 (dd, 1H, *J* = 14.0, 5.7 Hz, C***H***-7), 2.12 (dd, 1H, *J* = 13.9, 9.1 Hz, C***H***-5), 1.79-1.33 (m, 8H, C***H***-2, C***H***-3, C***H***-9, C***H***-10), 0.91 (t, 3H, *J* = 7.2 Hz, C***H***-11).

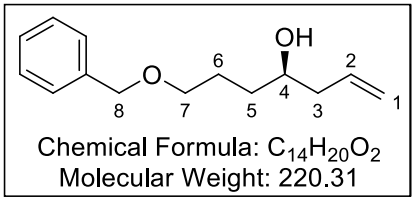
^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3 (C-6), 138.7 (C-Ar), 138.4 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 127.87 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 114.7 (C-14), 77.9 (C-8), 72.3 (C-12 or C-13), 71.0 (C-12 or C-13), 70.5 (C-1), 69.2 (C-4), 44.9 (C-5), 40.7 (C-7), 36.1 (C-9), 34.2 (C-3), 26.2 (C-2), 18.5 (C-10), 14.2 (C-11).

IR (neat, cm^{-1}) 3427, 2955, 2931, 2869, 1453, 1362, 1092, 1066, 1028.

HRMS (CI, *m*/*z*) calcd for $(C_{26}H_{37}O_3)^+$ 397.2743, found 397.2746.

[α]$^{26}_D$ = −6.8° (*c* 1.0, $CHCl_3$)

(*R*)-7-(Benzyloxy)hept-1-en-4-ol (+)-106[16]



Chemical Formula: $C_{14}H_{20}O_2$
Molecular Weight: 220.31

Reference procedure[16]

To a stirred suspension of copper (I) iodide (223 mg, 1.17 mmol, 0.500 equiv) in THF (9 mL) was added vinylmagnesium bromide (0.7 M THF solution, 17 mL, 12 mmol, 5.0 equiv) dropwise at −30 °C. After 30 min, epoxide **(+)-105** (450 mg, 2.30 mmol) in THF (3 mL) was slowly added to the mixture at −30 °C. After stirring at −30 °C for 2 h, the reaction was quenched with a saturated aqueous solution of ammonium chloride (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 8/2) gave the homoallylic alcohol **(+)-106** (421 mg, 83%) as a clear oil.

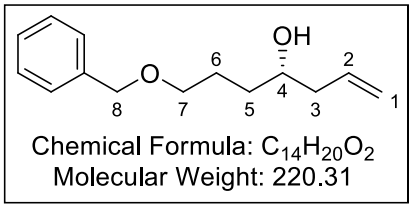
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H, ***H***-Ar), 5.90-5.79 (m, 1H, C***H***-2), 5.12 (br d, *J* = 16.2 Hz, 1H, C***H***-1$_{trans}$), 5.12 (br d, *J* = 11.3 Hz, 1H, C***H***-1$_{cis}$), 4.53 (s, 2H, C***H***-8), 3.68 (app tq, *J* = 8.0, 4.0 Hz, 1H, C***H***-4), 3.53 (t, *J* = 5.9 Hz, 2H, C***H***-7), 2.34 (d, *J* = 4.0 Hz, 1H, C4-***OH***), 2.33-2.26 (m, 1H, C***H***-3), 2.23-2.16 (m, 1H, C***H***-3), 1.80-1.72 (m, 2H, C***H***-6), 1.71-1.62 (m, 1H, C***H***-5), 1.56-1.47 (m, 1H, C***H***-5).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2 (C-Ar), 135.0 (C-2), 128.4 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 117.8 (C1), 73.0 (C-8), 70.6 (C-4), 70.4 (C-7), 41.9 (C-3), 34.0 (C-5), 26.2 (C-6).

MS (CI) 221 $(C_{14}H_{31}O_2)^+$.

$[\alpha]^{25}_D$ = +7.7° (*c* 1.0, $CHCl_3$) (*Lit.*: $[\alpha]^{25}_D$ = +6.8° (*c* 1.0, $CHCl_3$))[16]

(*S*)-7-(Benzyloxy)hept-1-en-4-ol (−)-106[113]

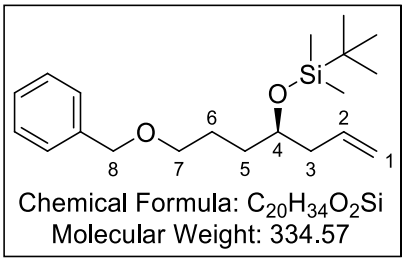


Allylic alcohol **(−)-106** was obtained from the corresponding epoxide **(−)-105** according to the procedure described above for allylic alcohol **(+)-106**.
Scale: 12.8 mmol
Yield: 93%

[α]$^{26}_D$ = −8.4° (*c* 2.1, $CHCl_3$) (*Lit.*: $[\alpha]^{22}_D$ = −8.8° (*c* 1.16, $CHCl_3$))[113]

[113] Packard, G. K.; Hu, Y.; Vescovi, A.; Rychnovsky, S. D. *Angew. Chem. Int. Ed.* **2004**, *43*, 2822.

(*R*)-(7-(Benzyloxy)hept-1-en-4-yloxy)(*tert*-butyl)dimethylsilane 381[16]



Chemical Formula: $C_{20}H_{34}O_2Si$
Molecular Weight: 334.57

To a stirred solution of the alcohol **(+)-106** (2.0 g, 9.1 mmol) in dichloromethane (90 mL) was added imidazole (1.8 g, 27 mmol, 3.0 equiv) and TBSCl (2.7 g, 18 mmol, 2.0 equiv) at 0 °C. After stirring at room temperature for three days, the reaction was quenched with a saturated aqueous solution of ammonium chloride and extracted with diethyl ether (3 × 100 mL). The combined organic layers were washed with brine (200 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 98/2) gave the protected alcohol **381** (3.0 g, 97%) as a clear oil.

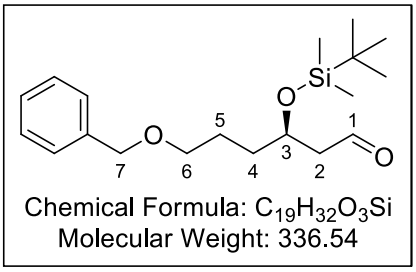
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5H, ***H***-Ar), 5.81 (ddt, *J* = 16.7, 10.6, 7.1 Hz, 1H, C***H***-2), 5.04 (br d, *J* = 16.7 Hz, 1H, C***H***-1$_{trans}$), 5.03 (br d, *J* = 10.6 Hz, 1H, C***H***-1$_{cis}$), 4.51 (s, 2H, C***H***-8), 3.72 (quint, *J* = 6.1 Hz, 1H, C***H***-4), 3.47 (t, *J* = 6.6 Hz, 2H, C***H***-7), 2.22 (app td, *J* = 6.1, 1.1 Hz, 2H, C***H***-3), 1.75-1.42 (m, 4H, C***H***-5, C***H***-6), 0.89 (s, 9H, -SiC(C***H***$_3$)$_3$-), 0.05 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.04 (s, 3H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 (C-Ar), 135.2 (C-2), 128.4 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 116.8 (C-1), 72.8 (C-8), 71.8 (C-4), 70.6 (C-7), 42.0 (C-3), 33.2 (C-5), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.6 (C-6), 18.1 (-Si***C***(CH$_3$)$_3$-), −4.4 (-Si(C***H***$_3$)$_2$-), −4.5 (-Si(C***H***$_3$)$_2$-).

HRMS (CI, *m*/*z*) calcd for $(C_{20}H_{35}O_2Si)^+$ 335.2406, found 335.2418.

[α]$^{25}_D$ = +13.7° (*c* 1.0, $CHCl_3$) (*Lit.*: [α]$^{25}_D$ = +13.6° (*c* 1.0, $CHCl_3$))[16]

(*R*)-6-(Benzyloxy)-3-(*tert*-butyldimethylsilyloxy)hexanal 119[16]



Chemical Formula: $C_{19}H_{32}O_3Si$
Molecular Weight: 336.54

To a stirred solution of alkene **381** (1.61 g, 4.81 mmol) and 2,6-lutidine (1.13 mL, 9.75 mmol, 2.00 equiv) in a mixture of dioxane (37 mL) and water (11.3 mL) was added osmium tetroxide (2.5 wt% in ^{t}BuOH, 0.96 mL, 0.097 mmol, 0.020 equiv), followed by sodium periodate (4.14 g, 19.5 mmol, 4.00 equiv). The mixture was stirred for 3 h and monitored by TLC. The reaction was quenched by addition of a saturated aqueous solution of sodium sulfite (25 mL), followed by stirring for 10 min. The solution was extracted with dichloromethane (3 × 30 mL) and the combined organic layers were washed with brine (60 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Filtration through a plug of silica gel gave the aldehyde **119** (1.87 g), which was used for the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (t, 1H, *J* = 2.5 Hz, C***H***-1), 7.38-7.28 (m, 5H, ***H***-Ar), 4.51 (s, 2H, C***H***-7), 4.23 (quint, 1H, *J* = 5.6 Hz, C***H***-3), 3.48 (t, 2H, *J* = 6.0 Hz, C***H***-6), 2.54 (ddd, 2H, *J* = 5.6, 2.5, 1.2 Hz, C***H***-2), 1.72-1.60 (m, 4H, C***H***-4, C***H***-5), 0.88 (s, 9H, -SiC(C***H***$_3$)$_3$-), 0.08 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.06 (s, 3H, -Si(C***H***$_3$)$_2$-).

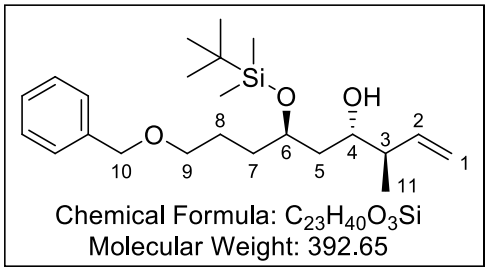
^{13}C NMR (126 MHz, $CDCl_3$) δ 202.1 (C-1), 138.51 (C-Ar), 128.4 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 72.9 (C-7), 70.1 (C-6), 68.0 (C-3), 50.8 (C-2), 34.4 (C-4), 25.8 (-SiC(***C***H$_3$)$_3$-), 25.4 (C-5), 18.0 (-Si***C***(CH$_3$)$_3$-), −4.4 (-Si(***C***H$_3$)$_2$-), −4.7 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2954, 2928, 2856, 1724, 1473, 1454, 1362, 1253, 1096, 1040.

HRMS (ESI, *m*/*z*) calcd for $(C_{19}H_{32}O_3SiNa)^+$ 359.2013, found 359.1992.

[α]$^{29}_D$ = −5.1° (*c* 1.5, $CHCl_3$) (*Lit.*: [α]$^{25}_D$ = −2.7° (*c* 1.5, $CHCl_3$))[16]

(3*R*,4*S*,6*R*)-9-(Benzyloxy)-6-(*tert*-butyldimethylsilyloxy)-3-methylnon-1-en-4-ol 120[16]



A suspension of 4 Å powdered molecular sieves (510 mg) in anhydrous toluene (5 mL) was treated with a solution of (*S*,*S*)-diisopropyl (*E*)-crotylboronate **382** (814 mg, 2.72 mmol, 1.80 equiv) in toluene (5 mL) at room temperature. After 30 min, the reaction mixture was cooled to −78 °C and treated dropwise (over 40 min) with a solution of aldehyde **119** (510 mg, 1.51 mmol) in anhydrous toluene (2 mL). The solution was stirred at −78 °C for 5 h and was allowed to warm up to room temperature overnight. A 1 N aqueous solution of sodium hydroxide (2 mL) was added at 0 °C to hydrolyse D-(−)-diisopropyl tartrate and the resulting mixture was stirred at room temperatrue for 3 h. The mixture was extracted with diethyl ether (3 × 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 85/15) gave alcohol **120** (474 mg, 80%) as a clear oil and as a 9:1 mixture of diastereomers.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H, ***H***-Ar), 5.82 (ddd, 1H, *J* = 16.6, 11.2, 7.8 Hz, C***H***-2), 5.10-5.03 (m, 2H, C***H***-1), 4.51 (s, 2H, C***H***-10), 4.05-4.00 (m, 1H, C***H***-6), 3.81 (ddt, 1H, *J* = 10.0, 5.1, 2.2 Hz, C***H***-4), 3.48 (t, 2H, *J* = 6.1 Hz, C***H***-9), 3.11 (d, 1H, *J* = 2.2 Hz, C4-***OH***), 2.17 (app sxt, 1H, *J* = 6.8 Hz, C***H***-3), 1.70-1.50 (m, 6H, C***H***-5, C***H***-7, C***H***-8), 1.04 (d, 3H, *J* = 6.8 Hz, C***H***-11), 0.90 (s, 9H, -SiC(C***H***$_3$)$_3$-), 0.10 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.08 (s, 3H, -Si(C***H***$_3$)$_2$-).

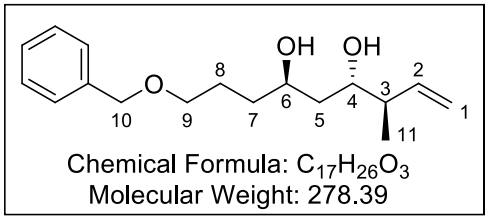
^{13}C NMR (126 MHz, $CDCl_3$) δ 140.7 (C-2), 138.6 (C-Ar), 128.3 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 115.2 (C-1), 72.9 (C-10), 71.3 (C-4), 71.2 (C-6), 70.4 (C-9), 44.1 (C-3), 38.7 (C-5), 33.0 (C-7), 26.0 (C-8), 25.8 (-SiC(***C***H$_3$)$_3$-), 18.0 (-Si***C***(CH$_3$)$_3$-), 15.7 (C-11), −4.5 (-Si(***C***H$_3$)$_2$-), −4.7 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 3486, 2954, 2929, 2856, 1472, 1454, 1362, 1255, 1097, 1074, 1004.

HRMS (ESI, *m*/*z*) calcd for $(C_{23}H_{40}O_3SiNa)^+$ 415.2639, found 415.2630.

[α]$^{29}_D$ = −12.8° (*c* 1.0, $CHCl_3$) (*Lit.*: [α]$^{25}_D$ = −1.0° (*c* 1.0, $CHCl_3$))[16]

(3*R*,4*S*,6*R*)-9-(Benzyloxy)-3-methylnon-1-ene-4,6-diol 435

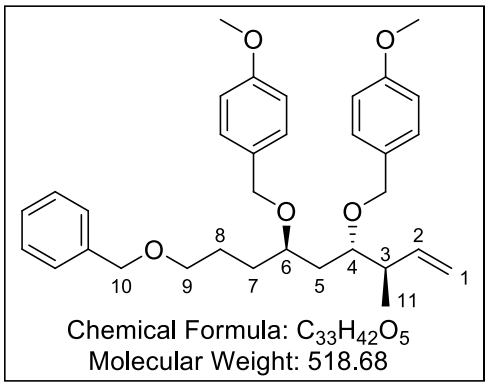


Protected alcohol **120** (450 mg, 1.15 mmol) was dissolved in a 5/95 solution of hydrofluoric acid/acetonitrile (25 mL) and was stirred for 3 h at room temperature. The solution was then quenched by addition of a saturated aqueous solution of calcium chloride (20 mL). The mixture was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate (20 mL), washed with brine (20 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Filtration through a plug of silica gel gave the desired diol **435** (300 mg) as a clear oil, which was used for the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H, ***H***-Ar), 5.80-5.73 (m, 1H, C***H***-2), 5.14-5.10 (m, 2H, C***H***-1), 4.53 (s, 2H, C***H***-10), 3.98-3.92 (m, 1H, C***H***-6), 3.76-3.72 (m, 1H, C***H***-4), 3.56-3.51 (m, 2H, C***H***-9), 3.28 (d, 1H, *J* = 4.0 Hz, C6-***OH***), 2.45 (d, 1H, *J* = 3.3 Hz, C4-***OH***), 2.29-2.20 (m, 1H, C***H***-3), 1.80-1.71 (m, 2H, C***H***-8), 1.66-1.56 (m, 4H, C***H***-5, C***H***-7), 1.02 (d, 3H, *J* = 6.8 Hz, C***H***-11).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.6 (C-2), 138.4 (C-Ar), 128.4 (C-Ar), 127.7 (C-Ar) ,127.7 (C-Ar), 116.3 (C-1), 73.1 (C-10), 71.9 (C-4), 70.6 (C-9), 69.0 (C-6), 44.4 (C-3), 39.6 (C-5), 34.8 (C-7), 26.5 (C-8), 16.1 (C-11).

4,4'-((3*R*,4*S*,6*R*)-9-(Benzyloxy)-3-methylnon-1-ene-4,6-diyl)*bis*(oxy)*bis*(methylene)*bis*(methoxybenzene) 436[16]



To a stirred solution of diol **435** (295 mg, 1.06 mmol) in DMF (4 mL) at 0 °C was added PMBBr (767 mg, 3.82 mmol, 3.60 equiv) in DMF (3 mL), followed by NaH (60% dispersion in mineral oil, 145 mg, 3.60 mmol, 3.40 equiv). The solution was allowed to warm up to room temperature overnight and was monitored by TLC. PMBBr (1.0 g, 5.0 mmol, 4.7 equiv) in DMF (3 mL), followed by NaH (60% dispersion in mineral oil, 200 mg, 4.96 mmol, 4.70 equiv) were added and the solution was stirred for another 5 h. The reaction was then quenched by addition of water. The mixture was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with brine (25 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 9/1, then 8/2) gave the protected alcohol **436** (430 mg, 72% (2 steps)) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H, ***H***-Ar), 7.24-7.21 (m, 4H, ***H***-Ar (PMB)), 6.87-6.84 (m, 4H, ***H***-Ar (PMB)), 5.82 (ddd, 1H, *J* = 16.8, 10.9, 6.8 Hz, C***H***-2), 5.09-5.03 (m, 2H, C***H***-1), 4.52-4.42 (m, 3H, C***H*****$_2$**-PMB), 4.51 (s, 2H, C***H***-10), 4.26 (d, 1H, *J* = 11.1Hz, C***H*****$_2$**-PMB), 3.79 (s, 3H, C***H*****$_3$**-PMB), 3.79 (s, 3H, C***H*****$_3$**-PMB), 3.65-3.59 (m, 2H, C***H***-4, C***H***-6), 3.48 (t, 2H, *J* = 6.2 Hz, C***H***-9), 2.63-2.55 (m, 1H, C***H***-3), 1.70-1.51 (m, 6H, C***H***-5, C***H***-7, C***H***-8), 1.03 (d, 3H, *J* = 6.9 Hz, C***H***-11).

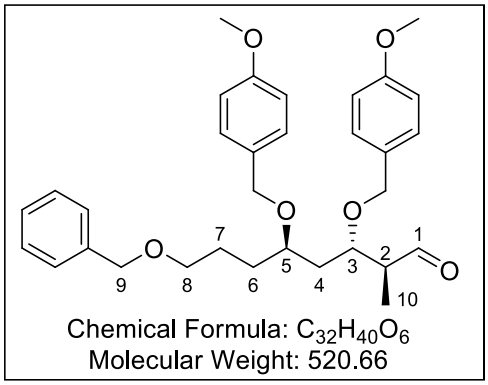
^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0 (C-Ar), 140.7 (C-2), 138.6 (C-Ar), 131.1 (C-Ar), 131.1 (C-Ar), 129.3 (C-Ar), 128.3 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 114.6 (C-1), 113.7 (C-Ar), 78.8 (C-4 or C-6), 75.1 (C-4 or C-6), 72.8 (C-10), 71.3 (***C***H_2-PMB), 70.5 (C-9), 70.2 (***C***H_2-PMB), 55.2 (***C***H_3-PMB), 40.0 (C-3), 36.0 (C-5), 30.5 (C-7), 25.2 (C-8), 13.7 (C-11).

IR (neat, cm^{-1}) 2949, 2859, 1612, 1512, 1454, 1244, 1173, 1069, 1034.

HRMS (ESI, *m*/*z*) calcd for $(C_{33}H_{42}O_5Na)^+$ 541.2924, found 541.2907.

[α]$^{25}_D$ = −39.6° (*c* 1.0, $CHCl_3$)

(2*S*,3*S*,5*R*)-8-(Benzyloxy)-3,5-*bis*(4-methoxybenzyloxy)-2-methyloctanal 380

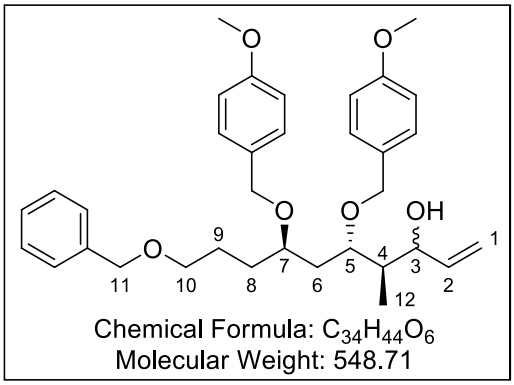


Aldehyde **380** was obtained from the corresponding alkene **436** according to the procedure described above for aldehyde **119**. The crude aldehyde was used for the next step without further purification.
Scale: 2.17 mmol
Yield: quant.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (d, 1H, *J* = 1.7 Hz, C***H***-1), 7.37-7.27 (m, 5H, ***H***-Ar), 7.23 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 7.18 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 6.86 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 6.85 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 4.51 (s, 2H, C***H***-9), 4.51-4.48 (m, 1H, C***H$_2$***-PMB), 4.43 (d, 1H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.30 (d, 1H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.26 (d, 1H, *J* = 11.2 Hz, C***H$_2$***-PMB), 4.01 (ddd, 1H, *J* = 9.4, 4.7, 2.8 Hz, C***H***-3), 3.79 (s, 6H, C***H$_3$***-PMB), 3.69-3.62 (m, 1H, C***H***-5), 3.51-3.44 (m, 2H, C***H***-8), 2.78-2.69 (m, 1H, C***H***-2), 1.73-1.51 (m, 6H, C***H***-4, C***H***-6, C***H***-7), 1.10 (d, 3H, *J* = 7.0 Hz, C***H***-10).

^{13}C NMR (126 MHz, $CDCl_3$) δ 203.9 (C-1), 159.3 (C-Ar), 159.2 (C-Ar), 138.6 (C-Ar), 130.9 (C-Ar), 130.3 (C-Ar), 129.3 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 113.8 (C-Ar), 113.8 (C-Ar), 75.8 (C3), 74.7 (C5), 72.9 (C-9), 71.7 (***C***H$_2$-PMB), 70.4 (C-8), 70.1 (***C***H$_2$-PMB), 55.3 (***C***H$_3$-PMB), 49.9 (C-2), 37.5 (C-4), 30.3 (C-6), 25.8 (C-7), 9.2 (C-10).

(4*R*,5*S*,7*R*)-10-(Benzyloxy)-5,7-*bis*(4-methoxybenzyloxy)-4-methyldec-1-en-3-ol 384



To a stirred solution of aldehyde **380** (1.13 g, 2.17 mmol) in THF (28 mL) was added dropwise vinylmagnesium bromide (0.7 M solution in THF, 10.9 mL, 7.60 mmol, 3.50 equiv) at −78 °C. The solution was stirred at −78 °C for 2 h and was then quenched by addition of a saturated aqueous solution of ammonium chloride (20 mL). The mixture was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave the allylic alcohol **384** (600 mg, 50% (2 steps)) as a pale yellow oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

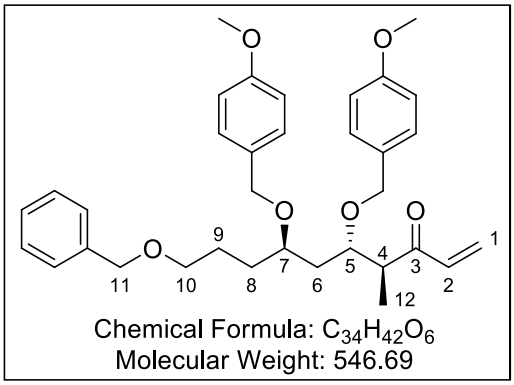
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H, ***H***-Ar), 7.24-7.18 (m, 4H, ***H***-Ar (PMB)), 6.88-6.83 (m, 4H, ***H***-Ar (PMB)), 5.91-5.77 (m, 1H, C***H***-2), 5.28-5.12 (m, 2H, C***H***-1), 4.51 (s, 2H, C***H***-11), 4.50-4.20 (m, 4.5H, C***H***-3, C***H*****$_2$**-PMB), 3.93-3.86 (m, 0.5H, C***H***-3), 3.79 (s, 1.5H, C***H*****$_3$**-PMB), 3.79 (s, 1.5H, C***H*****$_3$**-PMB), 3.78 (s, 1.5H, C***H*****$_3$**-PMB), 3.78 (s, 1.5H, C***H*****$_3$**-PMB), 3.70-3.66 (m, 1H, C***H***-5 or 7), 3.63-3.56 (m, 1H, C***H***-5 or 7), 3.51-3.46 (m, 2H, C***H***-10), 3.02 (d, 0.5H, *J* = 3.1 Hz, C3-***OH***), 2.58 (d, 0.5H, *J* = 3.3 Hz, C3-***OH***), 2.02-1.51 (m, 7H, C***H***-4, C***H***-6, C***H***-8, C***H***-9), 0.97 (d, 1.5H, *J* = 7.1 Hz, C***H***-12), 0.83 (d, 1.5H, *J* = 7.0 Hz, C***H***-12).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3 (C-Ar), 139.8 (C-Ar), 139.7 (C-2), 130.8 (C-Ar), 130.4 (C-Ar), 129.5 (C-Ar), 129.4 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 115.9 (C-1), 114.5 (C-1), 113.8 (C-Ar), 113.8 (C-Ar), 80.3 (C5 or C7), 77.2 (C-3), 75.9, 75.7, 75.3 (C5 or C7), 72.9 (C-11), 72.6 (C-3), 70.9 (***C***H_2-PMB), 70.4 (C-10), 70.1 (***C***H_2-PMB), 55.3 (***C***H_3-PMB), 41.7 (C-4), 40.7 (C-4), 37.9 (C-6), 30.4 (C-8), 25.1 (C-9), 11.1 (C-12), 11.0 (C-12).

IR (neat, cm^{-1}) 3433, 2936, 2859, 1612, 1512, 1454, 1302, 1246, 1173, 1065, 1032.

HRMS (ESI, *m*/*z*) calcd for $(C_{34}H_{44}O_6Na)^+$ 571.3036, found 571.3079.

(4*S*,5*S*,7*R*)-10-(Benzyloxy)-5,7-*bis*(4-methoxybenzyloxy)-4-methyldec-1-en-3-one 437



To a stirred solution of alcohol **384** (580 mg, 1.06 mmol) in DMSO (40 mL) and THF (20 mL) was added 2-iodoxybenzoic acid (1.04 g, 3.70 mmol, 3.50 equiv) at room temperature. After the solution had been stirred overnight, water (50 mL) was added and the solution was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave the enone **437** (438 mg, 76%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H, ***H***-Ar), 7.21 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 7.15 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 6.87-6.81 (m, 4H, ***H***-Ar (PMB)), 6.45 (dd, 1H, *J* = 17.4, 10.5 Hz, C***H***-2), 6.24 (dd, 1H, *J* = 17.4, 1.3 Hz, C***H***-1$_{trans}$), 5.74 (dd, 1H, *J* = 10.5, 1.3 Hz, C***H***-1$_{cis}$), 4.50 (s, 2H, C***H***-11), 4.47 (d, 1H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.42 (d, 1H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.25 (d, 2H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.00-3.94 (m, 1H, C***H***-5), 3.79 (s, 3H, C***H$_3$***-PMB), 3.78 (s, 3H, C***H$_3$***-PMB), 3.68-3.61 (m, 1H, C***H***-7), 3.49-3.44 (m, 2H, C***H***-10), 3.18 (app quint, 1H, *J* = 6.8 Hz, C***H***-4), 1.71-1.54 (m, 6H, C***H***-6, C***H***-8, C***H***-9), 1.08 (d, 3H, *J* = 6.8 Hz, C***H***-12).

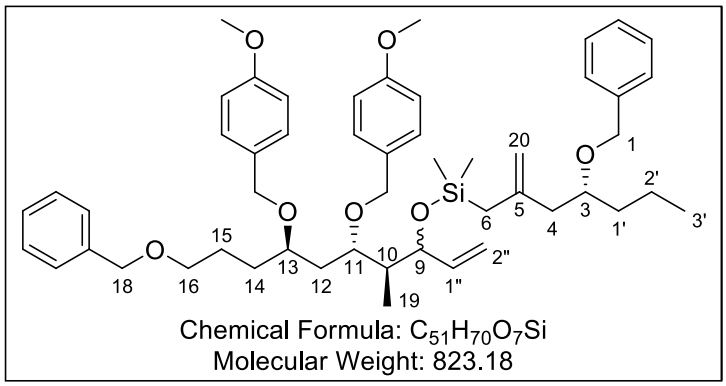
^{13}C NMR (126 MHz, $CDCl_3$) δ 202.2 (C-3), 159.2 (C-Ar), 159.1 (C-Ar), 138.7 (C-Ar), 135.8 (C-2), 131.1 (C-Ar), 130.6 (C-Ar), 129.4 (C-Ar), 129.2 (C-Ar), 128.3 (C-Ar), 128.0 (C-1), 127.6 (C-Ar), 127.5 (C-Ar), 113.8 (C-Ar), 113.7 (C-Ar), 77.0 (C-5), 74.8 (C-7), 72.8 (C-11), 72.0 (***C***H$_2$-PMB), 70.4 (C-10), 69.9 (***C***H$_2$-PMB), 55.3 (***C***H$_3$-PMB), 47.5 (C-4), 37.0 (C-6), 30.4 (C-8), 25.2 (C-9), 11.1 (C-12).

IR (neat, cm^{-1}) 2936, 2861, 1695, 1674, 1611, 1512, 1454, 1302, 1246, 1173, 1067, 1030.

HRMS (ESI, *m*/*z*) calcd for $(C_{34}H_{42}O_6Na)^+$ 569.2874, found 569.2852.

[α]$^{23}_D$ = −25.2° (*c* 1.0, $CHCl_3$)

(3*R*,10*S*,11*S*,13*R*)-11,13-*Bis*(4-methoxybenzyloxy)-7,7,10-trimethyl-5-methylene-1,18-diphenyl-3-propyl-9-vinyl-2,8,17-trioxa-7-silaoctadecane 378



Silane **378** was obtained from the corresponding silane **368** and alcohol **384** according to the general procedure (method 2) described above for silane **296**. (Purification by column chromatography on silica gel (petroleum ether-ether 8/2)).
Scale: 0.56 mmol
Yield: 60% (1:1 mixture of diastereomers)

(Datas recorded on the mixture of diastereomers)

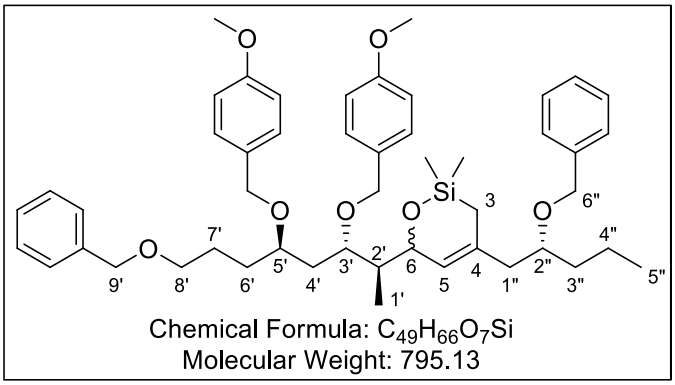
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 10H, ***H***-Ar), 7.23-7.16 (m, 4H, ***H***-Ar (PMB)), 6.85-6.81 (m, 4H, ***H***-Ar (PMB)), 5.77 (ddd, 1H, *J* = 17.3, 10.3, 7.1 Hz, C***H***-1"), 5.17-5.04 (m, 2H, C***H***-2"), 4.72-4.63 (m, 2H, C***H***-20), 4.58-4.54 (m, 1H, C***H***-1), 4.50 (s, 2H, C***H***-18), 4.49-4.39 (m, 3H, C***H***-1, C***H$_2$***-PMB), 4.24 (d, 1H, *J* = 11.2 Hz, C***H$_2$***-PMB), 4.20 (d, 1H, *J* = 11.2 Hz, C***H$_2$***-PMB), 3.98 (t, 1H, *J* = 7.3 Hz, C***H***-9), 3.92-3.86 (m, 1H, C***H***-11), 3.77 (s, 3H, C***H$_3$***-PMB), 3.76 (s, 3H, C***H$_3$***-PMB), 3.71-3.62 (m, 1H, C***H***-13), 3.59-3.51 (m, 1H, C***H***-3), 3.49-3.45 (m, 2H, C***H***-16), 2.41-2.31 (m, 1H, C***H***-4), 2.17-2.09 (m, 1H, C***H***-4), 2.04-1.96 (m, 1H, C***H***-10), 1.72-1.59 (m, 7H, C***H***-6, C***H***-12, C***H***-14, C***H***-15), 1.52-1.30 (m, 5H, C***H***-12, C***H***-1', C***H***-2'), 0.94-0.88 (m, 3H, C***H***-3'), 0.79 (d, 3H, *J* = 7.1 Hz, C***H***-19), 0.10 (s, 3H, -Si(C***H$_3$***)$_2$-), 0.10 (s, 3H, -Si(C***H$_3$***)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9 (C-Ar), 143.6 (C-5), 140.2 (C-1"), 139.0 (C-Ar), 138.7 (C-Ar), 131.3 (C-Ar), 129.4 (C-Ar), 129.2 (C-Ar), 129.2 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 127.3 (C-Ar), 115.7 (C-2"), 113.7 (C-Ar), 113.6 (C-Ar), 110.6 (C-20), 77.6 (C-3), 76.2 (C-9), 75.6 (C-11), 75.0 (C-13), 72.8 (C-18), 71.0 (C-1), 70.6 (C-16), 70.4 (***C***H$_2$-PMB), 70.3 (***C***H$_2$-PMB), 55.2 (***C***H$_3$-PMB), 43.2 (C-4), 41.1 (C-10), 36.4 (C-1'), 35.4 (C-12), 30.7 (C-14), 27.5 (C-6), 25.1 (C-15), 18.7 (C-2'), 14.2 (C-3'), 10.3 (C-19), −1.1 (-Si(***C***H$_3$)$_2$-), −1.2 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2955, 2934, 2866, 1612, 1512, 1454, 1246, 1063, 1036.

HRMS (ESI, *m*/*z*) calcd for $(C_{51}H_{70}O_7SiNa)^+$ 845.4783, found 845.4746.

6-((2*S*,3*S*,5*R*)-8-(Benzyloxy)-3,5-*bis*(4-methoxybenzyloxy)octan-2-yl)-4-((*R*)-2-(benzyloxy)pentyl)-2,2-dimethyl-3,6-dihydro-2*H*-1,2-oxasiline 387



To a solution of compound **378** (261 mg, 0.320 mmol) in dichloromethane (9 mL) was added second-generation Grubbs' catalyst (8 mg, 0.008 mmol, 3 mol%) under argon. The reaction was stirred for 2 h at 45 °C (reflux) and was monitored by TLC. The sequence addition/stirring was repeated once. Another 6 mol% of catalyst was added and the reaction was stirred for three days. A final 6 mol% of catalyst was added and the reaction was stirred for one more day. The reaction mixture was then concentrated *in vacuo*. Purification of the crude compound by column chromatography on silica gel (petroleum ether-ether 8/2) gave the product **387** (107 mg, 43%) as a clear oil.

(Datas recorded on the mixture of diastereomers)

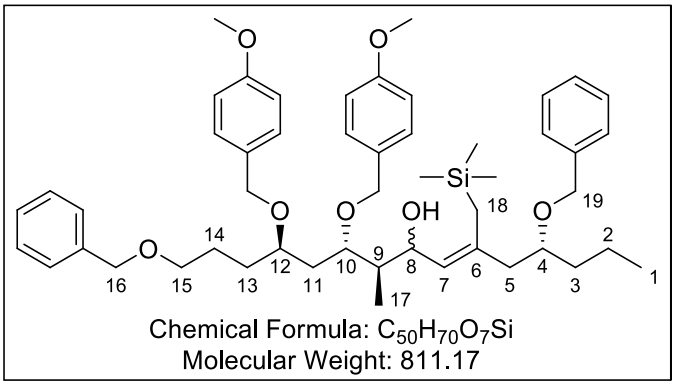
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.18 (m, 14H, ***H***-Ar), 6.86-6.80 (m, 4H, ***H***-Ar (PMB)), 5.52 (br s, 0.5H, C***H***-5), 5.34 (br s, 0.5H, C***H***-5), 4.69-4.65 (m, 0.5H, C***H***-6), 4.58-4.47 (m, 5H, C***H***-9', C***H***-6", C***H$_2$***-PMB), 4.44-4.40 (m, 1H, C***H$_2$***-PMB), 4.32-4.28 (m, 1H, C***H$_2$***-PMB), 4.26-4.24 (m, 0.5H, C***H***-6), 4.23-4.18 (m, 1H, C***H$_2$***-PMB), 3.99-3.95 (m, 0.5H, C***H***-3'), 3.80-3.75 (m, 6H, C***H$_3$***-PMB), 3.72-3.46 (m, 4.5H, C***H***-3', C***H***-5', C***H***-8', C***H***-2"), 2.42-2.38 (m, 1H, C***H***-1"), 2.20-2.14 (m, 1H, C***H***-1"), 2.08-1.99 (m, 0.5H, C***H***-2'), 1.76-1.06 (m, 12.5H, C***H***-3, C***H***-2', C***H***-4', C***H***-6', C***H***-7', C***H***-3", C***H***-4"), 0.96-0.81 (m, 6H, C***H***-1', C***H***-5"), 0.18-0.08 (4 s, 6H, -Si(C***H$_3$***)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9 (C-Ar), 139.0 (C-4 or C-Ar), 138.7 (C-4 or C-Ar), 129.4 (C-Ar), 129.2 (C-Ar), 129.1 (C-Ar), 128.6 (C-5), 128.3 (C-Ar), 128.3 (C-Ar), 127.8 (C-5), 127.6 (C-Ar), 127.6 (C-Ar), 127.4 (C-Ar), 113.7 (C-Ar), 113.6 (C-Ar), 77.2 (C-3' or C-5' or C-2"), 77.1 (C-3' or C-5' or C-2"), 75.9 (C-3'), 75.4 (C-3' or C-5' or C-2"), 73.9 (C-6), 72.8 (***C***H$_2$-Ar), 72.3 (C-6), 72.2 (***C***H$_2$-Ar), 70.8 (C-8' or ***C***H$_2$-Ar), 70.6 (C-8' or ***C***H$_2$-Ar), 69.9 (***C***H$_2$-Ar), 55.2 (***C***H$_3$-PMB), 46.7 (C-1"), 43.9 (C-2'), 42.1 (C-2'), 36.2 (C-4'), 30.9 (C-6'), 29.7 (C-3"), 25.4 (C-7'), 23.8 (C-3), 18.7 (C-4"), 14.2 (C-5"), 10.5 (C-1'), 9.6 (C-1'), 0.2 (-Si(***C***H$_3$)$_2$-), 0.0 (-Si(***C***H$_3$)$_2$-), −0.4 (-Si(***C***H$_3$)$_2$-), −0.8 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2955, 2929, 2861, 1612, 1513, 1454, 1361, 1246, 1172, 1067, 1036.

HRMS (ESI, *m*/*z*) calcd for $(C_{49}H_{66}O_7SiNa)^+$ 817.4470, found 817.4418.

(4*R*,9*R*,10*S*,12*R*,*Z*)-4,15-*Bis*(benzyloxy)-10,12-*bis*(4-methoxybenzyloxy)-9-methyl-6-((trimethylsilyl)methyl)pentadec-6-en-8-ol 388



Allylic alcohol **388** was obtained from the corresponding silacycle **387** according to the general procedure described above for allylic alcohol **354**. (Purification by column chromatography on silica gel (petroleum ether-ether 7/3)).
Scale: 0.12 mmol
Yield: 82% (1:1 mixture of diastereomers)

(Datas recorded on the mixture of diastereomers)

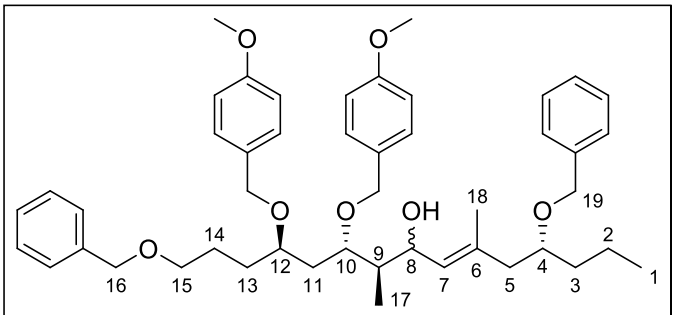
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.16 (m, 14H, ***H***-Ar), 6.87-6.80 (m, 4H, ***H***-Ar (PMB)), 5.25 (d, 0.5H, *J* = 8.3 Hz, C***H***-7), 5.15 (d, 0.5H, *J* = 9.0 Hz, C***H***-7), 4.58-4.43 (m, 6.5H, C***H***-8, C***H***-16, C***H***-19, C***H*****$_2$**-PMB), 4.36-4.21 (m, 2H, C***H*****$_2$**-PMB), 4.08-4.00 (m, 0.5H, C***H***-8), 3.96-3.92 (m, 0.5H, C***H***-10), 3.79-3.77 (m, 6H, C***H*****$_3$**-PMB), 3.69-3.45 (m, 4.5H, C***H***-4, C***H***-10, C***H***-12, C***H***-15), 2.63 (d, 0.5H, *J* = 2.7 Hz, C8-***OH***), 2.36-2.28 (m, 1H, C***H***-5), 2.13-2.03 (m, 1.5H, C***H***-5, C8-***OH***), 2.02-1.95 (m, 0.5H, C***H***-9), 1.80-1.24 (m, 12.5H, C***H***-2, C***H***-3, C***H***-9, C***H***-11, C***H***-13, C***H***-14, C***H***-18), 1.01 (d, 1.5H, *J* = 7.1 Hz, C***H***-17), 0.93-0.87 (m, 3H, C***H***-1), 0.78 (d, 1.5H, *J* = 7.0 Hz, C***H***-17) 0.06 (s, 4.5H, -Si(C***H*****$_3$**)$_3$-), 0.04 (s, 4.5H, -Si(C***H*****$_3$**)$_3$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1 (C-Ar), 159.1 (C-Ar), 159.1 (C-Ar), 138.8 (C-6 or C-Ar), 138.6 (C-6 or C-Ar), 130.9 (C-Ar), 130.7 (C-Ar), 129.4 (C-Ar), 129.4 (C-Ar), 129.3 (C-Ar), 129.2 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 126.7 (C-7), 125.8 (C-7), 113.8 (C-Ar), 113.8 (C-Ar), 113.7 (C-Ar), 113.7 (C-Ar), 80.6 (C-10), 78.1 (C-4), 76.8 (C-10), 75.8 (C-12), 75.4 (C-12), 72.9 (***C***H$_2$-Ar), 71.1 (***C***H$_2$-Ar), 71.0 (***C***H$_2$-Ar), 70.5 (C-8 or C-15 or ***C***H$_2$-Ar), 70.4 (C-8 or C-15 or ***C***H$_2$-Ar), 70.4 (C-8 or C-15 or ***C***H$_2$-Ar), 70.0 (C-8 or C-15 or ***C***H$_2$-Ar), 68.4 (C-8), 55.3 (***C***H$_3$-PMB), 44.1 (C-5), 42.5 (C-9), 41.4 (C-9), 38.4 (C-3), 36.2 (C-11), 35.8 (C-11), 30.7 (C-13), 30.3 (C-13), 25.3 (C-14), 22.3 (C-18), 18.7 (C-2), 18.4 (C-2), 14.2 (C-1), 11.0 (C-17), 10.7 (C-17), −0.6 (-Si(***C***H$_3$)$_3$-), −0.7 (-Si(***C***H$_3$)$_3$-).

IR (neat, cm^{-1}) 3470, 2953, 2934, 2869, 1612, 1513, 1454, 1246, 1172, 1065, 1036.

HRMS (ESI, *m*/*z*) calcd for ($C_{50}H_{70}O_7SiNa$)$^+$ 833.4783, found 833.4731.

(4*R*,9*R*,10*S*,12*R*,*E*)-4,15-*Bis*(benzyloxy)-10,12-*bis*(4-methoxybenzyloxy)-6,9-dimethylpentadec-6-en-8-ol 389



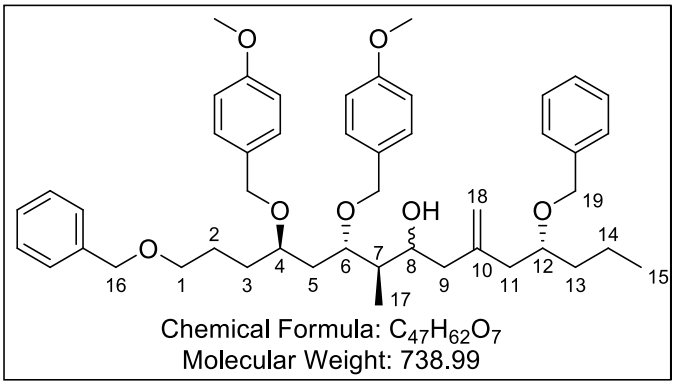
Allylic alcohol **389** and alcohol **390** were obtained from the corresponding allylic alcohol **388** according to the general procedure described above for allylic alcohol **363**. (Purification by column chromatography on silica gel (petroleum ether-ether 6/4)).
Scale: 0.091 mmol
Yield: 70% for **389** and 19% for **390** (1:1 mixtures of diastereomers)

(Datas recorded on the mixture of diastereomers)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.19 (m, 14H, ***H***-Ar), 6.85 (d, 4H, *J* = 8.3 Hz, ***H***-Ar (PMB)), 5.32 (d, 0.5H, *J* = 7.9 Hz, C***H***-7), 5.27 (d, 0.5H, *J* = 8.6 Hz, C***H***-7), 4.60 (dd, 0.5H, *J* = 8.1, 3.1 Hz, C***H***-8), 4.55 (d, 1H, *J* = 11.5 Hz, C***H***-19), 4.52 (s, 2H, C***H***-16), 4.51 (d, 1H, *J* = 11.5 Hz, C***H***-19), 4.48 (d, 0.5H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.47 (d, 0.5H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.47 (d, 0.5H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.43 (d, 0.5H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.35 (d, 0.5H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.28 (d, 0.5H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.23 (d, 0.5H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.21 (d, 0.5H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.15 (t, 0.5H, *J* = 8.9 Hz, C***H***-8), 3.96-3.93 (m, 1H, C***H***-10), 3.79 (s, 3H, C***H$_3$***-PMB), 3.77 (s, 3H, C***H$_3$***-PMB), 3.68-3.53 (m, 2H, C***H***-4, C***H***-12), 3.52-3.46 (m, 2H, C***H***-15), 2.39 (dd, 0.5H, *J* = 13.6, 5.9 Hz, C***H***-5), 2.32 (dd, 0.5H, *J* = 13.7, 6.3 Hz, C***H***-5), 2.19 (dd, 0.5H, *J* = 13.6, 6.8 Hz, C***H***-5), 2.15 (dd, 0.5H, *J* = 13.7, 6.3 Hz, C***H***-5), 2.04-1.97 (m, 1H, C***H***-9), 1.81-1.60 (m, 5H, C***H***-11, C***H***-13, C***H***-14), 1.69 (d, 1.5H, *J* = 1.2 Hz, C***H***-18), 1.65 (d, 1.5H, *J* = 1.2 Hz, C***H***-18), 1.58-1.45 (m, 4H, C***H***-2, C***H***-3, C***H***-11), 1.43-1.31 (m, 1H, C***H***-2), 1.02 (d, 1.5H, *J* = 7.0 Hz, C***H***-17), 0.91 (t, 3H, *J* = 7.2 Hz, C***H***-1), 0.76 (d, 1.5H, *J* = 7.0 Hz, C***H***-17).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1 (C-Ar), 159.1 (C-Ar), 138.9 (C-6 or C-Ar), 138.6 (C-6 or C-Ar), 136.1 (C-6 or C-Ar), 131.0 (C-Ar), 130.7 (C-Ar), 129.5 (C-7), 129.5 (C-Ar), 129.4 (C-Ar), 129.3 (C-Ar), 129.0 (C-7), 128.3 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 113.8 (C-Ar), 113.7 (C-Ar), 113.7 (C-Ar), 80.1 (C-4 or C-12), 77.2 (C-4), 76.6 (C-10), 75.6 (C-12), 72.8 (C-16), 72.5 (***C***H$_2$-PMB), 70.8 (C-19), 70.6 (***C***H$_2$-PMB), 70.4 (C-8), C-15), 70.1 (***C***H$_2$-PMB), 68.8 (C-8), 55.2 (***C***H$_3$-PMB), 55.2 (***C***H$_3$-PMB), 44.5 (C-5), 44.4 (C-5), 42.2 (C-9), 41.0 (C-9), 37.8, 36.1 (C-3), 35.7 (C-11), 30.5 (C-13), 25.2 (C-14), 18.4 (C-2), 17.4 (C-18), 14.2 (C-1), 11.2 (C-17), 10.5 (C-17).

(4*R*,6*S*,7*R*,12*R*)-1,12-*Bis*(benzyloxy)-4,6-*bis*(4-methoxybenzyloxy)-7-methyl-10-methylenepentadecan-8-ol 390



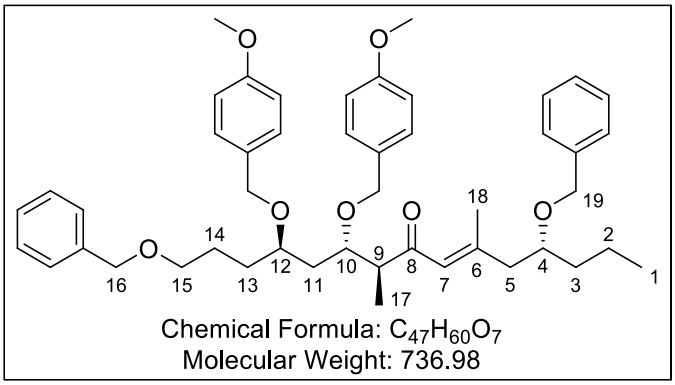
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.17 (m, 14H, ***H***-Ar), 6.86-6.82 (m, 4H, ***H***-Ar (PMB)), 4.97-4.91 (m, 2H, C***H***-18), 4.54-4.41 (m, 6H, C***H***-16, C***H***-19, C***H$_2$***-PMB), 4.33-4.17 (m, 2H, C***H$_2$***-PMB), 4.08-4.03 (m, 0.5H, C***H***-8), 4.00-3.96 (m, 0.5H, C***H***-6), 3.91-3.73 (m, 6H, C***H$_3$***-PMB), 3.69-3.51 (m, 3H, C***H***-4, C***H***-6, C***H***-8, C***H***-12), 3.50-3.45 (m, 2H, C***H***-1), 2.96 (br s, 0.5H, C8-***OH***), 2.48 (br s, 0.5H, C8-***OH***), 2.44-2.01 (m, 4H, C***H***-9, C***H***-11), 2.00-1.95 (m, 0.5H, C***H***-7), 1.77-1.24 (m, 10.5H, C***H***-2, C***H***-3, C***H***-5, C***H***-7, C***H***-13, C***H***-14), 1.00 (d, 1.5H, *J* = 7.0 Hz, C***H***-17), 0.93-0.88 (m, 3H, C***H***-15), 0.82 (d, 1.5H, *J* = 6.9 Hz, C***H***-17).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2 (C-Ar), 159.1 (C-Ar), 159.1 (C-Ar), 159.0 (C-Ar), 144.5 (C-10), 144.1 (C-10), 138 (C-Ar), 138.8 (C-Ar), 138.7 (C-Ar), 138.6 (C-Ar), 131.2 (C-Ar), 131.0 (C-Ar), 130.9 (C-Ar), 130.6 (C-Ar), 129.4 (C-Ar), 129.3 (C-Ar), 129.3 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 127.8 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 115.0 (C-18), 114.4 (C-18), 113.8 (C-Ar), 113.8 (C-Ar), 113.7 (C-Ar), 80.5 (C-6), 77.9 (C-12), 77.5 (C-12), 76.5 (C-6), 75.5 (C-4), 75.4 (C-4), 72.9 (***C***H$_2$-Ar), 72.8 (***C***H$_2$-Ar), 72.7 (***C***H$_2$-Ar), 71.0 (C-8), 70.9 (C-1), 70.6 (***C***H$_2$-Ar), 70.5 (***C***H$_2$-Ar), 70.4 (***C***H$_2$-Ar), 70.3 (***C***H$_2$-Ar), 70.1 (***C***H$_2$-Ar), 68.9 (C-8), 55.2 (***C***H$_3$-PMB), 42.7 (C-9 or C-11), 41.9 (C-9 or C-11), 40.7 (C-7), 40.6 (C-7), 40.5 (C-9 or C-11), 38.0 (C-5 or C-13), 36.2 (C-5 or C-13), 36.1 (C-5 or C-13), 36.0 (C-5 or C-13), 30.6 (C-3), 30.3 (C-3), 25.3 (C-2), 25.1 (C-2), 18.6 (C-14), 18.5 (C-14), 14.2 (C-15), 10.6 (C-17).

IR (neat, cm^{-1}) 3458, 2953, 2932, 2864, 1613, 1512, 1454, 1302, 1246, 1173, 1063, 1034.

HRMS (ESI, *m*/*z*) calcd for $(C_{47}H_{62}O_7Na)^+$ 761.4388, found 761.4360.

(4*R*,9*S*,10*S*,12*R*,*E*)-4,15-*Bis*(benzyloxy)-10,12-*bis*(4-methoxybenzyloxy)-6,9-dimethylpentadec-6-en-8-one 438



Enone **438** was obtained from the corresponding allylic alcohol **389** according to the procedure described above for enone **437**. (Purification by column chromatography on silica gel (petroleum ether-ether 7/3)).
Scale: 0.061 mmol
Yield: 89%

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.20 (m, 10H, ***H***-Ar), 7.16 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 7.12 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 6.80 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 6.77 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 6.12 (s, 1H, C***H***-7), 4.47-4.38 (m, 4H, C***H***-19, C***H$_2$***-PMB), 4.45 (s, 2H, C***H***-16), 4.20 (d, 1H, *J* = 10.9 Hz, C***H$_2$***-PMB), 4.19 (d, 1H, *J* = 11.2 Hz, C***H$_2$***-PMB), 3.94-3.91 (m, 1H, C***H***-10), 3.72 (s, 3H, C***H$_3$***-PMB), 3.72 (s, 3H, C***H$_3$***-PMB), 3.62-3.56 (m, 1H, C***H***-12), 3.54-3.49 (m, 1H, C***H***-4), 3.43-3.41 (m, 2H, C***H***-15), 2.86 (app quint, 1H, *J* = 6.7 Hz, C***H***-9), 2.38 (dd, 1H, *J* = 13.4, 6.4 Hz, C***H***-5), 2.16 (dd, 1H, *J* = 13.4, 6.2 Hz, C***H***-5), 2.08 (s, 3H, C***H***-18), 1.65-1.56 (m, 4H, C***H***-13, C***H***-14), 1.53-1.47 (m, 2H, C***H***-11), 1.45-1.38 (m, 3H, C***H***-2, C***H***-3), 1.35-1.26 (m, 1H, C***H***-2), 1.01 (d, 3H, *J* = 6.7 Hz, C***H***-17), 0.86 (t, 3H, *J* = 6.9 Hz, C***H***-1).

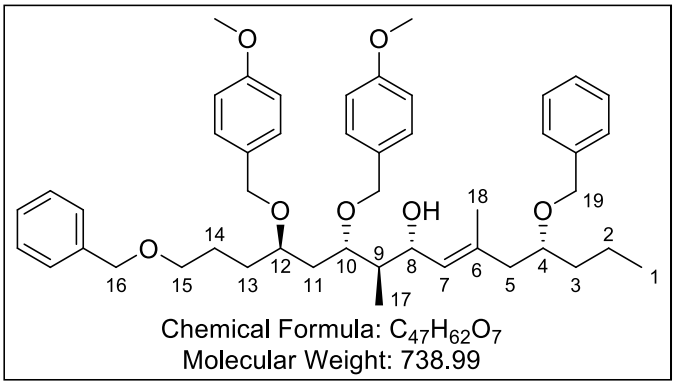
^{13}C NMR (126 MHz, $CDCl_3$) δ 202.4 (C-8), 159.1 (C-Ar), 159.0 (C-Ar), 156.0 (C-6), 138.6 (C-Ar), 138.5 (C-Ar), 131.1 (C-Ar), 130.7 (C-Ar), 129.3 (C-Ar), 129.1 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 125.3 (C-7), 113.7 (C-Ar), 77.1 (C-4), 76.6 (C-10), 74.8 (C-12), 72.8 (C-16), 71.6 (***C***H_2-PMB), 71.0 (C-19), 70.4 (C-15), 69.8 (***C***H_2-PMB), 55.2 (***C***H_3-PMB), 50.5 (C-9), 46.1 (C-5), 36.8 (C-11), 36.4 (C-3), 30.4 (C-13), 25.2 (C-14), 20.1 (C-18), 18.5 (C-2), 14.1 (C-1), 10.8 (C-17).

IR (neat, cm^{-1}) 2953, 2934, 2866, 1682, 1613, 1512, 1454, 1358, 1302, 1246, 1173, 1063, 1036.

HRMS (ESI, *m*/*z*) calcd for $(C_{47}H_{60}O_7Na)^+$ 759.4231, found 759.4194.

[α]$^{25}_D$ = +3.2° (*c* 1.0, $CHCl_3$)

(4*R*,8*R*,9*R*,10*S*,12*R*,*E*)-4,15-*Bis*(benzyloxy)-10,12-*bis*(4-methoxybenzyloxy)-6,9-dimethylpentadec-6-en-8-ol 377



To a solution of ketone **438** (38 mg, 0.052 mmol) in THF (2 mL), was added L-Selectride (1.0 M solution in THF, 0.090 mL, 0.090 mmol, 1.8 equiv). After stirring for 5 h at −78 °C, the reaction was quenched by successive addition of methanol (2 mL) and a saturated aqueous solution of ammonium chloride (2 mL). The aqueous phase was extracted with diethyl ether (3 × 4 mL) and the combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 5/5) gave allylic alcohol **377** (25 mg, 66%) as a clear oil and as a single diastereomer.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.26 (m, 10H, ***H***-Ar), 7.23 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 7.22 (d, 2H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 6.85 (d, 4H, *J* = 8.6 Hz, ***H***-Ar (PMB)), 5.27 (d, 1H, *J* = 8.9 Hz, C***H***-7), 4.55 (d, 1H, *J* = 11.5 Hz, C***H***-19), 4.52 (s, 2H, C***H***-16), 4.51 (d, 1H, *J* = 11.5 Hz, C***H***-19), 4.47 (d, 1H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.47 (d, 1H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.23 (d, 1H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.21 (d, 1H, *J* = 11.1 Hz, C***H$_2$***-PMB), 4.15 (app t, 1H, *J* = 8.9 Hz, C***H***-8), 3.96-3.93 (m, 1H, C***H***-10), 3.77 (s, 6H, C***H$_3$***-PMB), 3.65-3.53 (m, 2H, C***H***-4, C***H***-12), 3.49 (t, 2H, *J* = 5.0 Hz, C***H***-15), 2.39 (dd, 1H, *J* = 13.6, 5.9 Hz, C***H***-5), 2.19 (dd, 1H, *J* = 13.6, 6.8 Hz, C***H***-5), 2.05-1.96 (m, 1H, C***H***-9), 1.78-1.60 (m, 5H, C***H***-11, C***H***-13, C***H***-14), 1.69 (d, 3H, *J* = 1.2 Hz, C***H***-18), 1.58-1.45 (m, 4H, C***H***-2, C***H***-3, C***H***-11), 1.43-1.31 (m, 1H, C***H***-2), 0.90 (t, 3H, *J* = 6.9 Hz, C***H***-1), 0.75 (d, 3H, *J* = 7.0 Hz, C***H***-17).

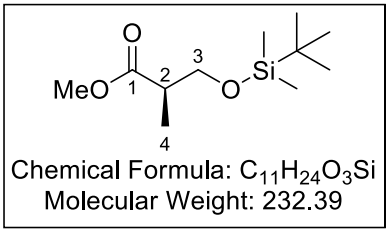
^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C-Ar), 159.1 (C-Ar), 138.9 (C-6 or C-Ar), 138.6 (C-6 or C-Ar), 136.1 (C-6 or C-Ar), 131.0 (C-Ar), 130.7 (C-Ar), 129.5 (C-7), 129.5 (C-Ar), 129.4 (C-Ar), 128.3 (C-Ar), 128.3 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 113.7 (C-Ar), 113.7 (C-Ar), 77.2 (C-4), 76.6 (C-10), 75.6 (C-12), 72.8 (C-16), 70.8 (C-19), 70.6 (***C***H_2-PMB), 70.4 (C-8, C-15), 55.2 (***C***H_3-PMB), 55.2 (***C***H_3-PMB), 44.5 (C-5), 41.0 (C-9), 36.1 (C-3), 35.7 (C-11), 30.5 (C-13), 25.2 (C-14), 18.4 (C-2), 17.4 (C-18), 14.2 (C-1), 10.5 (C-17).

IR (neat, cm^{-1}) 3441, 2932, 2862, 1612, 1512, 1458, 1358, 1304, 1242, 1034.

HRMS (ESI, *m*/*z*) calcd for $(C_{47}H_{62}O_7Na)^+$ 761.4388, found 761.4353.

[α]$^{23}_D$ = −35.2° (*c* 1.0, $CHCl_3$)

Methyl (*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpropanoate 395[114]



Chemical Formula: $C_{11}H_{24}O_3Si$
Molecular Weight: 232.39

A solution of *tert*-butyldimethylsilyl chloride (6.70 g, 44.0 mmol, 1.05 equiv) in dichloromethane (9.5 mL) was added dropwise to a solution of (*R*)-(−)-Roche ester (5.0 g, 42 mmol), imidazole (4.6 g, 68 mmol, 1.6 equiv) and DMAP (51 mg, 0.42 mmol, 1.0 mol%) in dichloromethane (47 mL) at 0 °C and the resulting white suspension stirred at room temperature overnight. Water (100 mL) was added to the reaction mixture, the layers were separated and the aqueous layer was extracted with dichloromethane (3 × 400 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 10/1) gave the protected alcohol **395** (9.75 g, quant.) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (dd, *J* = 9.7, 6.9 Hz, 1H, C***H***-3), 3.68 (s, 3H, C***H***$_3$-Methyl ester), 3.66 (dd, *J* = 9.9, 6.1 Hz, 1H, C***H***-3), 2.66 (m, 1H, C***H***-2), 1.14 (d, *J* = 7.1 Hz, 3H, C***H***-4), 0.88 (s, 9H, -SiC(C***H***$_3$)$_3$-), 0.05 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.04 (s, 3H, -Si(C***H***$_3$)$_2$-).

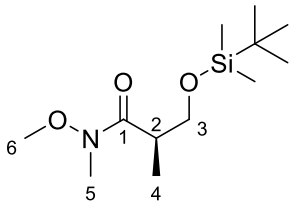
^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5 (C-1), 65.2 (C-3), 51.5 (***C***H$_3$-Methyl ester), 42.5 (C-2), 25.8 (-SiC(***C***H$_3$)$_3$-), 18.2 (-Si***C***(CH$_3$)$_3$-), 13.4 (C-4), -5.5 (-Si(***C***H$_3$)$_2$-).

HRMS (ESI, *m*/*z*) calcd for $(C_{11}H_{24}O_3SiNa)^+$ 255.1387, found 255.1380.

[α]$^{24}_D$ = −17.2° (*c* 1.0, $CHCl_3$) (*Lit.*: [α]$^{25}_D$ = −20.5° (*c* 1.0, $CHCl_3$))[114]

[114] Cooksey, J. P.; Ford, R.; Kocienski, P. J.; Pelotier, B.; Pons, J.-M. *Tetrahedron* **2010**, *66*, 6462.

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-*N*-methoxy-*N*,2-dimethylpropanamide 397[115]



Chemical Formula: $C_{12}H_{27}NO_3Si$
Molecular Weight: 261.43

To a stirred solution of ester **395** (13.5 g, 58.1 mmol) and *N*,*O*-dimethylhydroxylamine hydrochloride (8.49 g, 87.1 mmol, 1.50 equiv) in THF (160 mL) at −15 °C was added isopropylmagnesium bromide (3.0 M in 2-Me THF, 58.0 mL, 170 mmol, 3.00 equiv) dropwise over 20 min. The solution was stirred for 1.5 h at −15 °C. The reaction was quenched by addition of a saturated aqueous solution of ammonium chloride (100 mL) and extracted with diethyl ether (3 × 70 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Filtration through a plug of silica gel gave the desired Weinreb amide **397** (14.4 g, 95%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (dd, 1H, *J* = 9.5, 8.2 Hz, C***H***-3), 3.72 (s, 3H, C***H***-6), 3.54 (dd, 1H, *J* = 9.5, 6.1 Hz, C***H***-3), 3.23-3.12 (m, 1H, C***H***-2), 3.20 (s, 3H, C***H***-5), 1.08 (d, 3H, *J* = 6.9 Hz, C***H***-4), 0.88 (s, 9H, -SiC(C***H₃***)$_3$-), 0.05 (s, 3H, -Si(C***H₃***)$_2$-), 0.04 (s, 3H, -Si(C***H₃***)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1 (C-1), 65.7 (C-3), 61.5 (C-6), 38.1 (C-5), 32.0 (C-2), 25.8 (-SiC(***C***H$_3$)$_3$-), 18.2 (-Si***C***(CH$_3$)$_3$-), 13.4 (C-4), −5.5 (-Si(***C***H$_3$)$_2$-), −5.5 (-Si(***C***H$_3$)$_2$-).

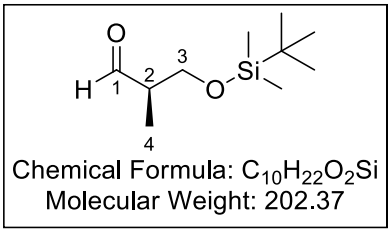
IR (neat, cm^{-1}) 2956, 2931, 2858, 1665, 1472, 1463, 1388, 1257, 1099.

HRMS (ESI, *m*/*z*) calcd for $(C_{12}H_{27}NO_3SiNa)^+$ 284.1652, found 284.1642.

[α]$^{25}_D$ = −20.0° (*c* 1.0, $CHCl_3$) (*Lit.*: [α]$^{20}_D$ = −17.1° (*c* 0.795, $CHCl_3$))[115]

[115] O'Sullivan, P. T.; Buhr, W.; Fuhry, M. A. M.; Harrison, J. R.; Davies, J. E.; Feeder, N.; Marshall, D. R.; Burton, J. W.; Holmes, A. B. *J. Am. Chem. Soc.* **2004**, *126*, 2194.

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpropanal 396[114]



Chemical Formula: $C_{10}H_{22}O_2Si$
Molecular Weight: 202.37

Method 1:

Diisobutylaluminium hydride (1.0 M solution in hexane, 4.5 mL, 4.5 mmol, 1.1 equiv) was added dropwise (over 1 h) to a solution of ester **395** (1.0 g, 4.3 mmol) in dichloromethane (20 mL) at −78 °C. The resulting colourless solution was stirred at −78 °C for 1 h and then warmed to −30 °C over 20 min. The reaction was quenched with a 10% aqueous solution of potassium sodium tartrate (50 mL) and the reaction mixture stirred vigorously for 2 h. The layers were separated and the aqueous layer was extracted with dichloromethane (2 × 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the aldehyde **396** (0.9 g, quant.) as a clear oil that was used without further purification.

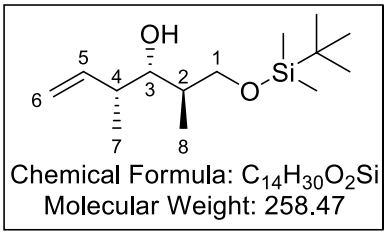
Method 2:

Diisobutylaluminium hydride (1.0 M solution in hexane, 82 mL, 82 mmol, 1.5 equiv) was added dropwise (over 20 min) to a solution of Weinreb amide **397** (14.3 g, 54.7 mmol) in THF (338 mL) at −78 °C. The solution was stirred at −78 °C for 1.5 h and was then quenched with a saturated aqueous solution of potassium sodium tartrate (250 mL). The reaction mixture was stirred vigorously for 4 h. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 200 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give the aldehyde **396** (12.0 g, quant.) as a clear oil that was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, *J* = 1.8 Hz, 1H, C***H***-1), 3.87 (dd, *J* = 10.1, 5.1 Hz, 1H, C***H***-3), 3.81 (dd, *J* = 10.1, 6.3 Hz, 1H, C***H***-3), 2.58-2.50 (m, 1H, C***H***-2), 1.10 (d, *J* = 7.1 Hz, 3H, C***H***-4), 0.88 (s, 9H, -SiC(C***H***$_3$)$_3$-), 0.06 (s, 6H, -Si(C***H***$_3$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 204.8 (C-1), 63.4 (C-3), 48.8 (C-2), 25.8 (-SiC(***C***H$_3$)$_3$-), 18.2 (-Si***C***(CH$_3$)$_3$-), 10.3 (C-4), −5.6 (-Si(***C***H$_3$)$_2$-).

(2*R*,3*S*,4*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylhex-5-en-3-ol 399[116]



n-Butyllithium (2.2 M solution in hexane, 38 mL, 84 mmol, 1.0 equiv) was added dropwise (over 2 h) to a mixture of *cis*-2-butene (7.8 mL, 89 mmol, 1.1 equiv) and potassium *tert*-butoxide (9.40 g, 83.9 mmol, 1.00 equiv) in THF (80 mL) at −78 °C. The resulting bright yellow solution was stirred at −50 °C for 20 min whereupon triisopropyl borate (19.4 mL, 83.9 mmol, 1.00 equiv) was added dropwise (over 1 h) to the reaction mixture at −78 °C. The resulting pale yellow solution was stirred at −78 °C for 15 min. The reaction mixture was then poured onto 1 M aqueous HCl solution (saturated with NaCl, 160 mL) and shaken vigorously. A solution of L-(+)-diisopropyl tartrate (20.7 g, 88.3 mmol, 1.05 equiv) in diethyl ether (30 mL) was added and the mixture shaken vigourously for 5 min. The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 80 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo* to give (*R,R*)-diisopropyl (*Z*)-crotylboronate **400** (19.5 g, 78%) as a colourless oil that was used without further purification.
A suspension of 4 Å powdered molecular sieves (143 mg) in anhydrous toluene (4 mL) was treated with a solution of (*R,R*)-diisopropyl (*Z*)-crotylboronate **400** (380 mg, 1.27 mmol, 1.80 equiv) in toluene (1 mL) at room temperature. After 30 min, the reaction mixture was cooled to −78 °C and treated dropwise (over 40 min) with a solution of aldehyde **396** (143 mg, 0.710 mmol) in anhydrous toluene (1 mL). The solution was stirred at −78 °C for 5 h and was allowed to warm up to room temperature for 1 h. A 1 N aqueous solution of sodium hydroxide (3 mL) was added at 0 °C to hydrolyse L-(+)-diisopropyl tatrate and the resulting mixture was stirred at room temperature for 2 h. The mixture was extracted with diethyl ether (3 × 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 96/4, then 9/1) gave alcohol **399** (130 mg, 71%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (ddd, *J* = 17.1, 10.4, 7.3 Hz, 1H, C***H***-5), 5.07 (dt, *J* = 17.1, 1.5 Hz, 1H, C***H***-6$_{trans}$), 5.04 (ddd, *J* = 10.4, 1.8, 1.0 Hz, 1H, C***H***-6$_{cis}$), 3.86 (dd, *J* = 9.8, 3.9 Hz, 1H, C***H***-1), 3.61 (d, *J* = 4.0 Hz, 1H, C3-***OH***), 3.61 (dd, *J* = 9.8, 6.3 Hz, 1H, C***H***-1), 3.42 (dt, *J* = 6.9, 4.6 Hz, 1H, C***H***-3), 2.39-2.31 (m, 1H, C***H***-4), 1.81 (app sextd, *J* = 6.9, 3.8 Hz, 1H, C***H***-2), 1.07 (d, *J* = 6.8 Hz, 3H, C***H***-7), 0.92 (d, *J* = 6.8 Hz, 3H, C***H***-8), 0.91 (s, 9H, -SiC(C***H***$_3$)$_3$-), 0.09 (s, 3H, -Si(C***H***$_3$)$_2$-), 0.09 (s, 3H, -Si(C***H***$_3$)$_2$-).

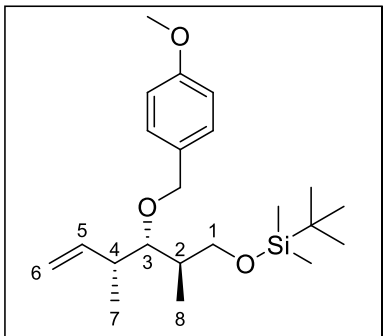
^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5 (C-5), 113.9 (C-6), 79.6 (C-3), 68.0 (C-1), 41.2 (C-4), 36.6 (C-2), 25.8 (-SiC(***C***H$_3$)$_3$-), 18.1 (-Si***C***(CH$_3$)$_3$-), 14.1 (C-8), 13.4 (C-7), −5.6 (-Si(***C***H$_3$)$_2$-), −5.7 (-Si(***C***H$_3$)$_2$-).

HRMS (ESI, *m/z*) calcd for $(C_{10}H_{22}O_2SiNa)^+$ 281.1907, found 281.1899.

[116] Matsumoto, K.; Kozmin, S. A. *Adv. Synth. Catal.* **2008**, *350*, 557.

[α]$^{26}_{D}$ = −8.0° (*c* 1.0, $CHCl_3$) (*Lit.*: [α]$^{26}_{D}$ = −6.8° (*c* 1.1, $CHCl_3$))[116]

tert-Butyl((2_R_,3_S_,4_R_)-3-(4-methoxybenzyloxy)-2,4-dimethylhex-5-enyloxy)dimethylsilane 33[6(a)]



Chemical Formula: $C_{22}H_{38}O_3Si$
Molecular Weight: 378.62

To a stirred solution of alcohol **399** (420 mg, 1.63 mmol) in DMF (4 mL) was added *p*-methoxybenzyl bromide (585 mg, 2.94 mmol, 1.80 equiv) in DMF (3 mL) at room temperature, followed by sodium hydride (60% dispersion in mineral oil, 112 mg, 2.75 mmol, 1.70 equiv) at 0 °C. The reaction was allowed to warm up to room temperature for 3 h. The solution was quenched by addition of water (5 mL) and was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (3 × 15 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 97/3, 95/5, then 9/1) gave alkene **33** (360 mg, 60%) as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, 2H, *J* = 8.7 Hz, ***H***-Ar), 6.87 (d, 2H, *J* = 8.7 Hz, ***H***-Ar), 5.94 (ddd, 1H, *J* = 17.5, 10.3, 7.5 Hz, C***H***-5), 5.08 (dt, 1H, *J* = 17.5, 1.6 Hz, C***H***-6$_{trans}$), 5.01 (ddd, 1H, *J* = 10.3, 1.6, 1.0 Hz, C***H***-6$_{cis}$), 4.51 (d, 1H, *J* = 10.7 Hz, C***H*$_2$**-PMB), 4.46 (d, 1H, *J* = 10.7 Hz, C***H*$_2$**-PMB), 3.81 (s, 3H, C***H*$_3$**-PMB), 3.67 (dd, 1H, *J* = 9.7, 3.9 Hz, C***H***-1), 3.63 (dd, 1H, *J* = 9.7, 6.0 Hz, C***H***-1), 3.29 (dd, 1H, *J* = 7.4, 4.4 Hz, C***H***-3), 2.48-2.42 (m, 1H, C***H***-4), 1.90-1.82 (m, 1H, C***H***-2), 1.05 (d, 3H, *J* = 6.8 Hz, C***H***-7), 0.96 (d, 3H, *J* = 6.9 Hz, C***H***-8), 0.91 (s, 9H, -SiC(C***H*$_3$**)$_3$-), 0.05 (s, 3H, -Si(C***H*$_3$**)$_2$-), 0.04 (s, 3H, -Si(C***H*$_3$**)$_2$-).

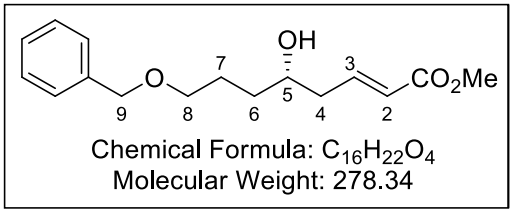
^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0 (C-Ar), 143.1 (C-5), 131.4 (C-Ar), 129.2 (C-Ar), 113.7 (C-Ar), 113.6 (C-6), 84.1 (C-3), 74.3 (***C***H$_2$-PMB), 64.8 (C-1), 55.3 (***C***H$_3$-PMB), 40.1 (C-4), 38.6 (C-2), 26.0 (-SiC(***C***H$_3$)$_3$-), 18.3 (-Si***C***(CH$_3$)$_3$-), 14.6 (C-8), 14.0 (C-7), −5.3 (-Si(***C***H$_3$)$_2$-), −5.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2957, 2930, 2857, 1614, 1514, 1462, 1248, 1086.

HRMS (ESI, *m*/*z*) calcd for $(C_{22}H_{38}O_3SiNa)^+$ 401.2482, found 401.2464.

[α]$^{23}_D$ = +20.8° (*c* 1.0, $CHCl_3$)

Methyl (*S*,*E*)-8-(Benzyloxy)-5-hydroxyoct-2-enoate 107[117]



Chemical Formula: $C_{16}H_{22}O_4$
Molecular Weight: 278.34

To a stirred solution of homoallylic alcohol **(−)-106** (1.15 g, 5.20 mmol) and methyl acrylate (1.5 mL, 16 mmol, 3.0 equiv) in dichloromethane (30 mL) was added second-generation Grubbs' catalyst (110 mg, 0.130 mmol, 2.50 mol%). The reaction mixture was stirred overnight at reflux. The mixture was then cooled to room temperature, concentrated *in vacuo* and directly purified by silica gel column chromatography (petroleum ether-ether 7/3) to afford exclusively the (*E*)-isomer **107** (1.37 g, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H, ***H***-Ar), 7.01 (dt, 1H, *J* = 15.5, 7.4 Hz, C***H***-3), 5.91 (dt, 1H, *J* = 15.5, 1.4 Hz, C***H***-2), 4.53 (s, 2H, C***H***-9), 3.81-3.74 (m, 1H, C***H***-5), 3.74 (s, 3H, -CO_2***Me***), 3.55-3.50 (m, 2H, C***H***-8), 2.78 (d, 1H, *J* = 4.1 Hz, C5-***OH***), 2.38 (ddd, 2H, *J* = 7.4, 6.3, 1.4 Hz, C***H***-4), 1.79-1.65 (m, 3H, C***H***-6, C***H***-7), 1.56-1.47 (m, 1H, C***H***-6).

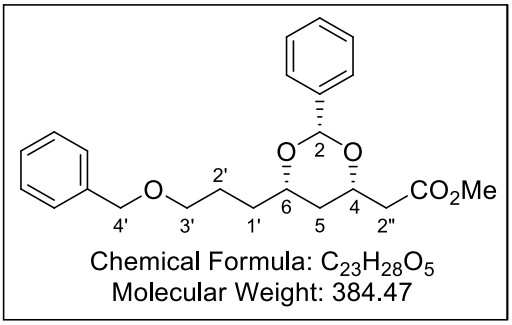
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8 (-***C***O_2Me), 145.8 (C-3), 137.9 (C-Ar), 128.4 (C-Ar), 127.7 (C-Ar), 123.2 (C-2), 73.1 (C-9), 70.3 (C-8), 70.3 (C-5), 51.4 (-CO_2***Me***), 40.2 (C-4), 34.7 (C-6), 26.3 (C-7).

HRMS (ESI, *m*/*z*) calcd for $(C_{16}H_{22}O_4Na)^+$ 301.1410, found 301.1404.

[α]$^{26}_D$ = −1.9° (*c* 2.1, $CHCl_3$) (*Lit.*: [α]$^{26}_D$ = −1.6° (*c* 0.76, CH_2Cl_2))[117]

[117] Fuwa, H.; Mizunuma, K.; Sasaki, M.; Suzuki, T.; Kubo, H. *Org. Biomol. Chem.* **2013**, *11*, 3442.

Methyl 2-((2*S*,4*S*,6*S*)-6-(3-(Benzyloxy)propyl)-2-phenyl-1,3-dioxan-4-yl)acetate 401[13]



Chemical Formula: $C_{23}H_{28}O_5$
Molecular Weight: 384.47

To a stirred solution of the homoallylic alcohol **107** (305 mg, 1.10 mmol) in THF (6.5 mL) at 0 °C was added freshly distilled benzaldehyde (0.14 mL, 1.2 mmol, 1.1 equiv), followed by *t*-BuOK (13 mg, 0.11 mmol, 0.10 equiv). The resulting solution was stirred for 15 min at 0 °C. This sequence (addition/stirring) was repeated twice. The reaction mixture was quenched with a saturated aqueous solution of ammonium chloride (6 mL). The aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 7/3) gave ester **401** (302 mg, 72%) as a clear oil.

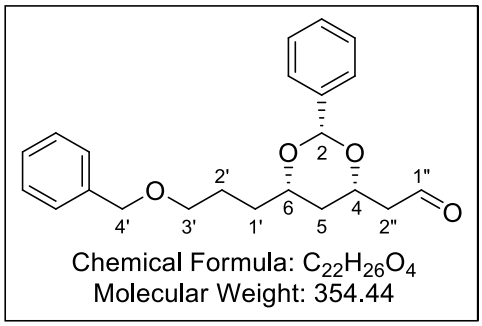
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.28 (m, 10H, ***H***-Ar), 5.55 (s, 1H, C***H***-2), 4.52 (s, 2H, C***H***-4'), 4.31 (dtd, 1H, *J* = 11.2, 6.7, 2.4 Hz, C***H***-4), 3.90-3.83 (m, 1H, C***H***-6), 3.72 (s, 3H, -CO_2***Me***), 3.57-3.48 (m, 2H, C***H***-3'), 2.75 (dd, 1H, *J* = 15.7, 6.7 Hz, C***H***-2"), 2.53 (dd, 1H, *J* = 15.7, 6.7 Hz, C***H***-2"), 1.91-1.65 (m, 5H, C***H***-5, C***H***-1', C***H***-2'), 1.45 (dt, 1H, *J* = 13.0, 11.2 Hz, C***H***-5).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2 (-***C***O_2Me), 138.5 (C-Ar), 138.5 (C-Ar), 128.6 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.0 (C-Ar), 100.5 (C-2), 76.3 (C-6), 73.1 (C-4), 72.9 (C-4'), 70.1 (C-3'), 51.7 (-CO_2***Me***), 40.8 (C-2"), 36.5 (C-5), 32.5 (C-1'), 25.4 (C-2').

HRMS (CI, *m*/*z*) calcd for $(C_{23}H_{29}O_5)^+$ 385.2015, found 385.2013.

[α]$^{28}_D$ = −6.6° (*c* 2.0, $CHCl_3$)

2-((2*S*,4*S*,6*S*)-6-(3-(Benzyloxy)propyl)-2-phenyl-1,3-dioxan-4-yl)acetaldehyde 108[13]



To a stirred solution of ester **401** (2.46 g, 6.40 mmol) in dichloromethane (20 mL) at −78 °C was added dropwise (over 30 min) diisobutylaluminum hydride (1.0 M solution in hexane, 9.0 mL, 9.0 mmol, 1.4 equiv). The reaction was stirred 1 h at −78 °C and was then quenched by addition of ethyl acetate (10 mL), diethyl ether (10 mL) and a saturated aqueous solution of Rochelle's salt (15 mL). The mixture was stirred 2 h at room temperature and was then extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine (60 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave aldehyde **108** (2.15 g, 95%) as a clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (t, 1H, *J* = 2.0 Hz, C***H***-1"), 7.49-7.28 (m, 10H, ***H***-Ar), 5.56 (s, 1H, C***H***-2), 4.52 (s, 2H, C***H***-4'), 4.40 (dddd, 1H, *J* = 11.2, 7.3, 5.0, 2.4 Hz, C***H***-4), 3.91-3.85 (m, 1H, C***H***-6), 3.57-3.47 (m, 2H, C***H***-3'), 2.82 (ddd, 1H, *J* = 16.9, 7.3, 2.0 Hz, C***H***-2"), 2.62 (ddd, 1H, *J* = 16.9, 5.0, 2.0 Hz, C***H***-2"), 1.90-1.65 (m, 5H, C***H***-5, C***H***-1', C***H***-2'), 1.49 (dt, 1H, *J* = 13.0, 11.2 Hz, C***H***-5).

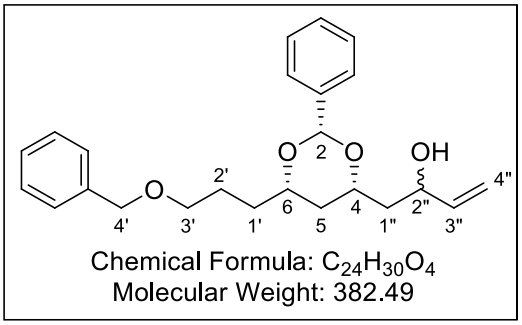
^{13}C NMR (126 MHz, $CDCl_3$) δ 200.4 (C-1"), 138.5 (C-Ar), 138.3 (C-Ar), 128.7 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.0 (C-Ar), 100.6 (C-2), 76.4 (C-6), 72.9 (C-4'), 71.8 (C-4), 70.0 (C-3'), 49.4 (C-2"), 36.6 (C-5), 32.4 (C-1'), 25.3 (C-2').

HRMS (ESI, *m*/*z*) calcd for $(C_{22}H_{26}O_4Na)^+$ 377.1723, found 377.1708.

$[\alpha]^{28}_D$ = −3.4° (*c* 2.0, $CHCl_3$) (*Lit.*: $[\alpha]^{26}_D$ = −6.0° (*c* 1.0, CH_2Cl_2))[118]

[118] Li, M.; O'Doherty, G. A. *Org. Lett.* **2006**, *8*, 6087.

1-((2*S*,4*R*,6*S*)-6-(3-(Benzyloxy)propyl)-2-phenyl-1,3-dioxan-4-yl)but-3-en-2-ol 411



Chemical Formula: $C_{24}H_{30}O_4$
Molecular Weight: 382.49

To a stirred solution of aldehyde **108** (2.14 g, 6.04 mmol) in THF (50 mL) at −78 °C was added dropwise vinylmagnesium bromide (0.7 M solution in THF, 26.0 mL, 18.1 mmol, 3.00 equiv). The reaction was stirred 2 h at −78 °C and monitored by TLC. The mixture was then quenched by addition of a saturated aqueous solution of ammonium chloride (50 mL) and was extracted with diethy ether (3 × 50 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on silica gel (petroleum ether-ether 6/4) gave allylic alcohol **411** (105 mg, 65%) as a yellow oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

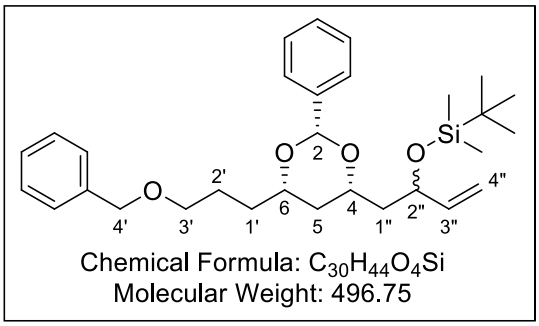
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.28 (m, 10H, ***H***-Ar), 5.97-5.85 (m, 1H, C***H***-3"), 5.55 (s, 0.5H, C***H***-2), 5.53 (s, 0.5H, C***H***-2), 5.33-5.27 (m, 1H, C***H***-4"), 5.16-5.11 (m, 1H, C***H***-4"), 4.52 (s, 2H, C***H***-4'), 4.52-4.41 (m, 1H, C***H***-2"), 4.20-4.07 (m, 1H, C***H***-4), 3.89-3.82 (m, 1H, C***H***-6), 3.57-3.49 (m, 2H, C***H***-3'), 2.93 (d, 0.5H, *J* = 1.8 Hz, C2"-***OH***), 2.44 (d, 0.5H, *J* = 5.2 Hz, C2"-***OH***), 1.94-1.44 (m, 8H, C***H***-5, C***H***-1', C***H***-2', C***H***-1").

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.8 (C-3"), 140.3 (C-3"), 138.5 (C-Ar), 138.3 (C-Ar), 128.7 (C-Ar), 128.6 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 128.2 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.0 (C-Ar), 126 (C-Ar), 114.6 (C-4"), 114.2 (C-4"), 100.6 (C-2), 100.5 (C-2), 76.6 (C-4 or C-6), 76.6 (C-4 or C-6), 76.6 (C-4 or C-6), 74.0 (C-4 or C-6), 72.9 (C-4'), 71.9 (C-2"), 70.1 (C-3'), 70.1 (C-3'), 69.4 (C-2"), 42.7 (C-1"), 42.1 (C-1"), 37.1 (C-5), 36.8 (C-5), 32.5 (C-1'), 32.5 (C-1'), 25.4 (C-2'), 25.4 (C-2').

IR (neat, cm^{-1}) 3436, 2944, 2915, 2854, 1453, 1342, 1096, 1027, 1015.

HRMS (ESI, *m*/*z*) calcd for $(C_{24}H_{30}O_4Na)^+$ 405.2036, found 405.2025.

(1-((2*S*,4*S*,6*S*)-6-(3-(Benzyloxy)propyl)-2-phenyl-1,3-dioxan-4-yl)but-3-en-2-yloxy)(*tert*-butyl)dimethylsilane 412



Chemical Formula: $C_{30}H_{44}O_4Si$
Molecular Weight: 496.75

To a stirred solution of allylic alcohol **411** (94 mg, 0.25 mmol) in dichloromethane (2.5 mL) were added imidazole (50 mg, 0.74, 3.0 equiv) and *tert*-butyldimethylsilyl chloride (74 mg, 0.49 mmol, 2.0 equiv). The solution was stirred for 3 days at room temperature and was then quenched by addition of a saturated aqueous solution of ammonium chloride (3 mL). The mixture was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 95/5) gave protected alcohol **412** (97 mg, 86%) as a clear oil.

(Datas recorded on the mixture of diastereomers)

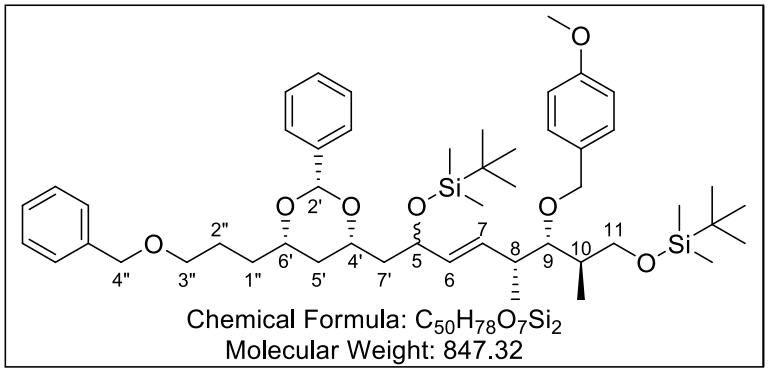
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.28 (m, 10H, ***H***-Ar), 5.89-5.80 (m, 1H, C***H***-3"), 5.49 (s, 0.5H, C***H***-2), 5.47 (s, 0.5H, C***H***-2), 5.21-5.17 (m, 1H, C***H***-4"), 5.09 (dt, 0.5H, *J* = 10.3, 1.1 Hz, C***H***-4"$_{cis}$), 5.02 (dt, 0.5H, *J* = 10.4, 1.2 Hz, C***H***-4"$_{cis}$), 4.52 (s, 2H, C***H***-4'), 4.48-4.44 (m, 0.5H, C***H***-2"), 4.40 (q, 0.5H, *J* = 6.3 Hz, C***H***-2"), 4.06-4.01 (m, 0.5H, C***H***-4), 3.89 (dddd, 0.5H, *J* = 10.5, 7.6, 5.1, 2.2 Hz, C***H***-4), 3.86-3.78 (m, 1H, C***H***-6), 3.57-3.48 (m, 2H, C***H***-3'), 2.00 (ddd, 0.5H, *J* = 13.6, 7.9, 5.6 Hz, C***H***-1"), 1.91-1.81 (m, 1H, C***H***-2'), 1.79-1.56 (m, 5.5H, C***H***-5, C***H***-1', C***H***-2', C***H***-1"), 1.48-1.39 (m, 1H, C***H***-5), 0.92 (s, 4.5H, -SiC(C***H$_3$***)$_3$-), 0.91 (s, 4.5H, -SiC(C***H$_3$***)$_3$-), 0.07 (s, 1.5H, -Si(C***H$_3$***)$_2$-), 0.07 (s, 1.5H, -Si(C***H$_3$***)$_2$-), 0.06 (s, 1.5H, -Si(C***H$_3$***)$_2$-), 0.04 (s, 1.5H, -Si(C***H$_3$***)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0 (C-3"), 141.0 (C-3"), 139.0 (C-Ar), 139.0 (C-Ar), 138.6 (C-Ar), 128.4 (C-Ar), 128.4 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 128.1 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.1 (C-Ar), 126.0 (C-Ar), 114.4 (C-4"), 113.5 (C-4"), 100.3 (C-2), 100.3 (C-2), 76.6 (C-6), 76.6 (C-6), 73.7 (C-4), 72.9 (C-4'), 72.9 (C-4'), 72.7 (C-4), 70.7 (C-2"), 70.2 (C-3'), 69.3 (C-2"), 44.7 (C-1"), 44.1 (C-1"), 37.4 (C-5), 37.2 (C-5), 32.6 (C-1'), 32.6 (C-1'), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.4 (C-2'), 25.4 (C-2'), 18.2 (-Si***C***(CH$_3$)$_3$-), −4.2 (-Si(***C***H$_3$)$_2$-), −4.3 (-Si(***C***H$_3$)$_2$-), -4.8 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2950, 2928, 2856, 1403, 1453, 1341, 1251, 1098, 1027.

HRMS (ESI, *m*/*z*) calcd for $(C_{30}H_{44}O_4SiNa)^+$ 519.2901, found 519.2887.

(8*R*,9*S*,10*R*,*E*)-5-(((2*S*,4*S*,6*S*)-6-(3-(Benzyloxy)propyl)-2-phenyl-1,3-dioxan-4-yl)methyl)-9-(4-methoxybenzyloxy)-2,2,3,3,8,10,13,13,14,14-decamethyl-4,12-dioxa-3,13-disilapentadec-6-ene 414



To a stirred solution of protected allylic alcohol **412** (50 mg, 0.10 mmol, 1.5 equiv) and alkene **33** (25 mg, 0.067 mmol) in dichloromethane (2 mL) was added second-generation Grubbs' catalyst (2.8 mg, 0.0033 mmol, 5.0 mol%). The solution was stirred at relfux for 2 h and monitored by TLC. Second-generation Grubbs' catalyst (4.6 mg, 0.0054 mmol, 8.0 mol%) was then added and the reaction was stirred one day at reflux. The solution was then concentrated *in vacuo* and the crude product was purified by column chromatography on silica gel (petroleum ether-ether 97/3, 9/5, then 9/1) to give the 1,2-disubstituted alkene **414** (17 mg, 30%) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

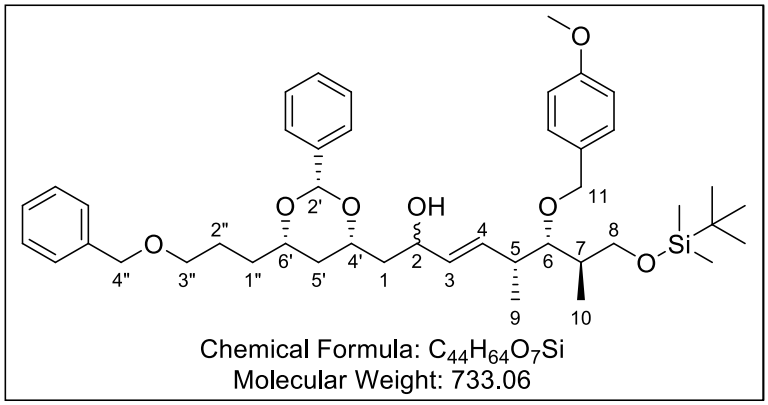
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.19 (m, 12H, ***H***-Ar), 6.88-6.81 (m, 2H, ***H***-Ar (PMB)), 5.72 (dd, 0.5H, *J* = 15.5, 7.7 Hz, C***H***-7), 5.65 (dd, 0.5H, *J* = 15.4, 8.2 Hz, C***H***-7), 5.52-5.46 (m, 1.5H, C***H***-6, C***H***-2'), 5.42 (s, 0.5H, C***H***-2'), 4.52 (s, 2H, C***H***-4"), 4.48 (d, 1H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.45 (d, 1H, *J* = 11.0 Hz, C***H$_2$***-PMB), 4.49-4.44 (m, 0.5H, C***H***-5), 4.37 (q, 0.5H, *J* = 7.0 Hz, C***H***-5), 4.05-4.00 (m, 0.5H, C***H***-6'), 3.91-3.85 (m, 0.5H, C***H***-4'), 3.84-3.72 (m, 1H, C***H***-4', C***H***-6'), 3.80 (s, 1.5H, C***H$_3$***-PMB), 3.78 (s, 1.5H, C***H$_3$***-PMB), 3.68-3.63 (m, 1H, C***H***-11), 3.59 (dd, 1H, *J* = 9.7, 6.4 Hz, C***H***-11), 3.56-3.48 (m, 2H, C***H***-3"), 3.25 (dd, 0.5H, *J* = 7.4, 4.2 Hz, C***H***-9), 3.22 (dd, 0.5H, *J* = 6.8, 4.9 Hz, C***H***-9), 2.49-2.40 (m, 1H, C***H***-8), 2.01 (ddd, 1H, *J* = 13.8, 7.7, 6.0 Hz, C***H***-7'), 1.91-1.80 (m, 2H, C***H***-10, C***H***-2"), 1.78-1.52 (m, 5H, C***H***-5', C***H***-7', C***H***-1", C***H***-2"), 1.46-1.35 (m, 1H, C***H***-5'), 1.05 (d, 1.5H, *J* = 6.8 Hz, C8-C***H$_3$***), 1.02 (d, 1.5H, *J* = 6.8 Hz, C8-C***H$_3$***), 0.95 (d, 1.5H, *J* = 6.9 Hz, C10-C***H$_3$***), 0.95 (d, 1.5H, *J* = 7.0 Hz, C10-C***H$_3$***), 0.92-0.90 (m, 18H, -SiC(C***H$_3$***)$_3$-), 0.07-0.03 (m, 12H, -Si(C***H$_3$***)$_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0 (C-Ar), 138.9 (C-Ar), 138.6 (C-Ar), 135.3 (C-7), 134.0 (C-7), 133.0 (C-6), 132.3 (C-6), 131.3 (C-Ar), 131.2 (C-Ar), 129.1 (C-Ar), 129.0 (C-Ar), 128.3 (C-Ar), 128.1 (C-Ar), 128.0 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.0 (C-Ar), 126.0 (C-Ar), 113.7 (C-Ar), 100.3 (C-2'), 84.8 (C-9), 84.2 (C-9), 76.6 (C-6'), 74.5 (***C***H$_2$-PMB), 73.8 (C-4'), 72.9 (C-4"), 70.5 (C-5), 70.2 (C-3"), 68.1 (C-5), 64.6 (C-11), 55.2 (***C***H$_3$-PMB), 45.0 (C-7'), 44.5 (C-7'), 39.3 (C-8), 38.7 (C-10), 37.4 (C-5'), 37.1 (C-5'), 32.6 (C-1"), 26.0 (-SiC(***C***H$_3$)$_3$-), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.5 (C-2"), 18.3 (-Si***C***(CH$_3$)$_3$-), 18.2 (-Si***C***(CH$_3$)$_3$-), 15.0 (C8-***C***H$_3$), 14.9 (C10-***C***H$_3$), 14.8 (C10-***C***H$_3$), 14.3 (C8-***C***H$_3$), −4.0 (-Si(***C***H$_3$)$_2$-), −4.7 (-Si(***C***H$_3$)$_2$-), −5.3 (-Si(***C***H$_3$)$_2$-), −5.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2954, 2929, 2856, 1514, 1457, 1249, 1087, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{50}H_{78}O_7Si_2Na)^+$ 869.5178, found 869.5177.

(5*R*,6*S*,7*R*,*E*)-1-((2*S*,4*R*,6*S*)-6-(3-(Benzyloxy)propyl)-2-phenyl-1,3-dioxan-4-yl)-8-(*tert*-butyldimethylsilyloxy)-6-(4-methoxybenzyloxy)-5,7-dimethyloct-3-en-2-ol 413



To a stirred solution of allylic alcohol **411** (50 mg, 0.13 mmol) and alkene **33** (49 mg, 0.13 mmol) in dichloromethane (2 mL) was added second-generation Hoveyda-Grubbs' catalyst (8.2 mg, 0.013 mmol, 10 mol%). The solution was stirred one day at reflux and monitored by TLC. The solution was then concentrated *in vacuo* and the crude product was purified by column chromatography on silica gel (petroleum ether-ether 95/5, 9/1, 8/2, 7/3, then 6/4) to give the 1,2-disubstituted alkene **413** (48 mg, 50%) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

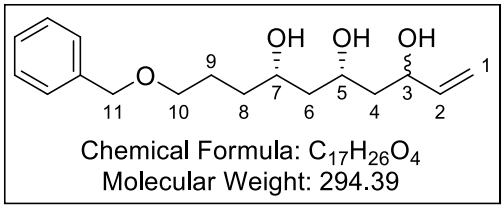
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49-7.45 (m, 3H, ***H***-Ar), 7.37-7.28 (m, 7H, ***H***-Ar), 7.24 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 6.86 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 5.77 (dd, 1H, *J* = 15.7, 8.2 Hz, C***H***-4), 5.56 (dd, 1H, *J* = 15.7, 6.2 Hz, C***H***-3), 5.51 (s, 1H, C***H***-2'), 4.52 (s, 2H, C***H***-11 or C***H***-4"), 4.47 (s, 2H, C***H***-11 or C***H***-4"), 4.45-4.38 (m, 1H, C***H***-2), 4.17-4.10 (m, 1H, C***H***-6'), 3.88-3.77 (m, 1H, C***H***-4'), 3.79 (s, 3H, C***H*****$_3$**-PMB), 3.68-3.63 (m, 2H, C***H***-8), 3.56-3.48 (m, 2H, C***H***-3"), 3.28 (dd, 1H, *J* = 7.5, 4.3 Hz, C***H***-6), 2.49-2.42 (m, 1H, C***H***-5), 2.28-2.24 (m, 1H, C2-***OH***), 1.90-1.80 (m, 3H, C***H***-1, C***H***-7, C***H***-2"), 1.78-1.63 (m, 4H, C***H***-1, C***H***-1", C***H***-2"), 1.56-1.38 (m, 2H, C***H***-5'), 1.04 (d, 3H, *J* = 6.8 Hz, C***H***-9), 0.95 (d, 3H, *J* = 6.9 Hz, C***H***-10), 0.91 (s, 9H, -SiC(C***H*****$_3$**$)_3$-), 0.05 (s, 3H, -Si(C***H*****$_3$**$)_2$-), 0.05 (s, 3H, -Si(C***H*****$_3$**$)_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0 (C-Ar), 138.6 (C-Ar), 138.5 (C-Ar), 135.3 (C-4), 131.6 (C-3), 131.3 (C-Ar), 129.2 (C-Ar), 128.6 (C-Ar), 128.3 (C-Ar), 128.2 (C-Ar), 127.6 (C-Ar), 127.5 (C-Ar), 126.0 (C-Ar), 113.7 (C-Ar), 100.5 (C-2'), 84.1 (C-6), 76.6 (C-6'), 74.3 (C-11 or C-4"), 74.0 (C-4'), 72.9 (C-11 or C-4"), 70.2 (C-3"), 69.2 (C-2), 64.7 (C-8), 55.3 (***C***H_3-PMB), 42.6 (C-1), 38.7 (C-5, C-7), 36.9 (C-5'), 32.5 (C-1"), 26.0 (-SiC(***C***$H_3)_3$-), 25.4 (C-2"), 18.3 (-Si***C***$(CH_3)_3$-), 14.7 (C-10), 14.3 (C-9), −5.3 (-Si(***C***$H_3)_2$-), −5.4 (-Si(***C***$H_3)_2$-).

IR (neat, cm^{-1}) 2932, 2855, 1458, 1358, 1250, 1080, 1026.

HRMS (ESI, *m*/*z*) calcd for $(C_{44}H_{64}O_7SiNa)^+$ 755.4314, found 755.4291.

(5*S*,7*S*)-10-(Benzyloxy)dec-1-ene-3,5,7-triol 418



Chemical Formula: $C_{17}H_{26}O_4$
Molecular Weight: 294.39

To a stirred solution of acetal **411** (1.73 g, 4.52 mmol) in methanol (40 mL) was added camphorsulfonic acid (1.05 g, 4.52 mmol, 1.00 equiv). The solution was stirred for three days at room temperature and monitored by TLC. More camphorsulfonic acid (0.53 g, 2.3 mmol, 0.50 equiv) was added and the solution was stirred for two more days. The reaction was then quenched with a saturated aqueous solution of sodium bicarbonate (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 5/5, then ether) gave the triol **418** (366 mg, 28% (80% b.r.s.m.)) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

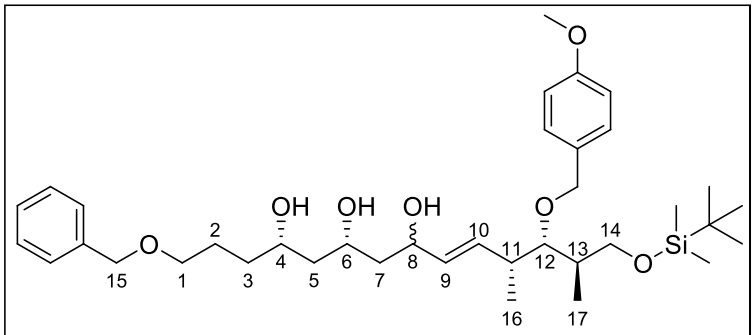
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H, ***H***-Ar), 5.97-5.85 (m, 1H, C***H***-2), 5.31 (dt, 0.5H, *J* = 17.2, 1.6 Hz, C***H***-1$_{trans}$), 5.25 (dt, 0.5H, *J* = 17.2, 1.5 Hz, C***H***-1$_{trans}$), 5.14 (dt, 0.5H, *J* = 10.5, 1.5 Hz, C***H***-1$_{cis}$), 5.10 (dt, 0.5H, *J* = 10.4, 1.4 Hz, C***H***-1$_{cis}$), 4.56-4.51 (m, 2H, C***H***-11), 4.50-4.38 (m, 1H, C***H***-3), 4.24-4.19 (m, 0.5H, C***H***-5), 4.16 (tt, 0.5H, *J* = 9.7, 2.6 Hz, C***H***-5), 4.08-4.04 (m, 1H, C5-***OH***), 3.94-3.86 (m, 1H, C***H***-7), 3.57-3.50 (m, 2H, C***H***-10), 3.47 (d, 0.5H, *J* = 1.6 Hz, C3-***OH***), 3.21 (d, 0.5H, *J* = 4.4 Hz, C3-***OH***), 1.83-1.49 (m, 8H, C***H***-4, C***H***-6, C***H***-8, C***H***-9).

^{13}C NMR (126 MHz, $CDCl_3$) δ 140.8 (C-2), 140.7 (C-2), 137.7 (C-Ar), 128.5 (C-Ar), 128.9 (C-Ar), 128.8 (C-Ar), 114.2 (C-1), 73.4 (C-3), 73.3 (C-5), 73.2 (C-11), 73.2 (C-11), 72.9 (C-7), 72.7 (C-7), 70.6 (C-10), 70.5 (C-3, C-5), 43.6 (C-4), 43.5 (C-3), 42.7 (C-6), 42.5 (C-6), 36.1 (C-8), 35.9 (C-8), 26.2 (C-9), 26.2 (C-9).

IR (neat, cm^{-1}) 3345, 2940, 2913, 2859, 1454, 1361, 1314, 1090, 1075, 1028.

HRMS (ESI, *m*/*z*) calcd for $(C_{17}H_{26}O_4Na)^+$ 317.1723, found 317.1715.

(4*S*,6*S*,11*R*,12*S*,13*R*,*E*)-1-(Benzyloxy)-14-(*tert*-butyldimethylsilyloxy)-12-(4-methoxybenzyloxy)-11,13-dimethyltetradec-9-ene-4,6,8-triol 419



To a stirred solution of allylic alcohol **418** (24 mg, 0.080 mmol), alkene **33** (31 mg, 0.080 mmol) and 1,4-benzoquinone (2.6 mg, 0.024 mmol, 0.30 equiv) in dichloromethane (2 mL) was added second-generation Hoveyda-Grubbs' catalyst (2.6 mg, 0.0041 mmol, 5.0 mol%). The solution was stirred one day at reflux and monitored by TLC. The solution was then concentrated *in vacuo* and the crude product was purified by column chromatography on silica gel (ether) to give the 1,2-disubstituted alkene **419** (19 mg, 45%) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

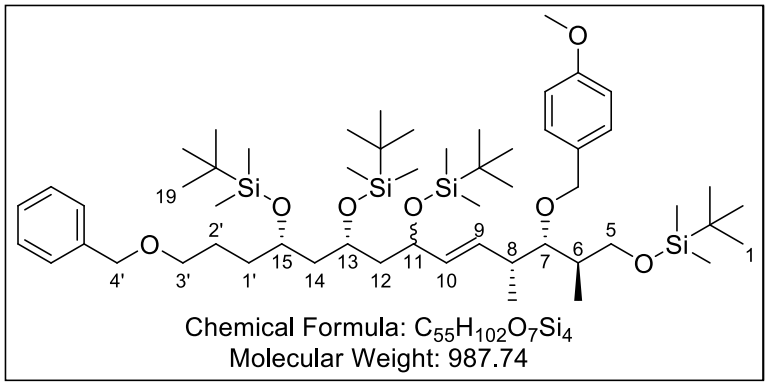
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 7H, ***H***-Ar), 6.87 (d, 2H, *J* = 8.5 Hz, ***H***-Ar (PMB)), 5.73 (dd, 1H, *J* = 15.6, 7.6 Hz, C***H***-10), 5.51 (dd, 1H, *J* = 15.6, 6.6 Hz, C***H***-9), 4.58-4.45 (m, 4H, C***H***-15, C$\boldsymbol{H_2}$-PMB), 4.40-4.32 (m, 1H, C***H***-8), 4.22-4.06 (m, 2H, C***H***-4 or C***H***-6, C-***OH***), 3.93-3.84 (m, 1H, C***H***-4 or C***H***-6), 3.80 (s, 3H, C$\boldsymbol{H_3}$-PMB), 3.68-3.63 (m, 2H, C***H***-14), 3.57-3.47 (m, 2H, C***H***-1), 3.26 (dd, 1H, *J* = 7.4, 4.5 Hz, C***H***-12), 3.14 (d, 0.5H, *J* = 1.3 Hz, C-***OH***), 2.97 (d, 0.5H, *J* = 3.9 Hz, C-***OH***), 2.49-2.38 (m, 1H, C***H***-11), 1.88-1.45 (m, 9H, C***H***-2, C***H***-3, C***H***-5, C***H***-7, C***H***-13), 1.04 (d, 3H, *J* = 6.8 Hz, C***H***-16), 0.95 (d, 3H, *J* = 6.9 Hz, C***H***-17), 0.91 (s, 9H, -SiC(C$\boldsymbol{H_3}$)$_3$-), 0.05 (s, 6H, -Si(C$\boldsymbol{H_3}$)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (C-Ar), 137.8 (C-Ar), 135.4 (C-10), 131.3 (C-9), 129.2 (C-Ar), 128.5 (C-Ar), 127.8 (C-Ar), 113.7 (C-Ar), 84.3 (C-12), 74.3 (C-15 or ***C***H$_2$-PMB), 73.4 (C-8), 73.3 (C-4 or C-6), 73.2 (C-15 or ***C***H$_2$-PMB), 72.6 (C-4 or C-6), 70.5 (C-1), 64.7 (C-14), 55.3 (***C***H$_3$-PMB), 43.6 (C-5, C-7), 38.6 (C-11, C-13), 35.9 (C-3), 26.1 (C-2), 26.0 (-SiC(***C***H$_3$)$_3$-), 18.3 (-Si***C***(CH$_3$)$_3$-), 14.7 (C-17), 14.3 (C-16), −5.3 (-Si(***C***H$_3$)$_2$-), −5.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 3364, 2930, 2857, 1612, 1514, 1454, 1248, 1084, 1036.

HRMS (ESI, *m*/*z*) calcd for $(C_{37}H_{60}O_7SiNa)^+$ 667.4001, found 667.3983.

(6*R*,7*S*,8*R*,13*S*,15*S*,*E*)-15-(3-(Benzyloxy)propyl)-11,13-*bis*(*tert*-butyldimethylsilyloxy)-7-(4-methoxybenzyloxy)-2,2,3,3,6,8,17,17,18,18-decamethyl-4,16-dioxa-3,17-disilanonadec-9-ene 420



To a stirred solution of the alcohol **419** (262 mg, 0.410 mmol) in dichloromethane (40 mL) was added imidazole (332 mg, 4.87 mmol, 12.0 equiv) and TBSCl (551 mg, 3.66 mmol, 9.00 equiv) at 0 °C. After stirring at room temperature for one day, the reaction was monitored by TLC and more imidazole (332 mg, 4.87 mmol, 12.0 equiv) and TBSCl (551 mg, 3.66 mmol, 9.00 equiv) were added. The reaction was then stirred for three days, followed by another addition of imidazole (332 mg, 4.87 mmol, 12.0 equiv) and TBSCl (551 mg, 3.66 mmol, 9.00 equiv). After another day of stirring, the reaction was quenched with a saturated aqueous solution of ammonium chloride and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (60 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 98/2) gave the protected alcohol **420** (146 mg, 36%) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

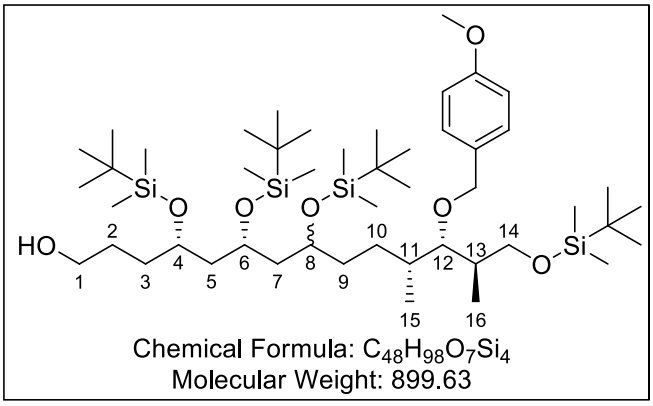
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 7H, ***H***-Ar), 6.87 (d, 2H, *J* = 8.7 Hz, ***H***-Ar (PMB)), 5.62 (dd, 1H, *J* = 15.7, 7.7 Hz, C***H***-9), 5.46 (dd, 1H, *J* = 15.7, 6.6 Hz, C***H***-10), 4.50 (s, 2H, C***H***-4'), 4.50-4.44 (m, 2H, C***H₂***-PMB), 4.18-4.11 (m, 1H, C***H***-11), 3.86-3.79 (m, 2H, C***H***-13, C***H***-15), 3.81 (s, 3H, C***H₃***-PMB), 3.66 (dd, 1H, *J* = 9.6, 4.0 Hz, C***H***-5), 3.58 (dd, 1H, *J* = 9.6, 6.4 Hz, C***H***-5), 3.46 (t, 2H, *J* = 6.6 Hz, C***H***-3'), 3.22 (dd, 1H, *J* = 6.7, 5.0 Hz, C***H***-7), 2.46-2.37 (m, 1H, C***H***-8), 1.89-1.81 (m, 1H, C***H***-6), 1.78-1.69 (m, 2H, C***H***-12, C***H***-2'), 1.68-1.52 (m, 5H, C***H***-12, C***H***-14, C***H***-1', C***H***-2'), 1.43-1.33 (m, 1H, C***H***-1'), 1.04 (d, 3H, *J* = 6.8 Hz, C8-C***H₃***), 0.95 (d, 3H, *J* = 7.0 Hz, C6-C***H₃***), 0.90 (s, 9H, -SiC(C***H₃***)$_3$-), 0.89 (s, 9H, -SiC(C***H₃***)$_3$-), 0.88 (s, 9H, -SiC(C***H₃***)$_3$-), 0.87 (s, 9H, -SiC(C***H₃***)$_3$-), 0.07-0.01 (m, 24H, -Si(C***H₃***)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (C-Ar), 138.7 (C-Ar), 134.3 (C-9), 132.9 (C-10), 131.3 (C-Ar), 129.1 (C-Ar), 128.3 (C-Ar), 127.5 (C-Ar), 127.4 (C-Ar), 113.7 (C-Ar), 84.8 (C-7), 74.4 (***C***H$_2$-PMB), 72.8 (C-4'), 70.9 (C-11), 70.8 (C-3'), 69.2 (C-13 or C-15), 66.9 (C-13 or C-15), 64.7 (C-5), 55.3 (***C***H$_3$-PMB), 47.3 (C-12), 45.6 (C-14), 39.0 (C-8), 38.7 (C-6), 33.5 (C-1'), 26.0 (-SiC(***C***H$_3$)$_3$-), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.6 (C-2'), 18.3 (-Si***C***(CH$_3$)$_3$-), 18.1 (-Si***C***(CH$_3$)$_3$-), 18.0 (-Si***C***(CH$_3$)$_3$-), 17.9 (-Si***C***(CH$_3$)$_3$-), 14.9 (C8-***C***H$_3$), 14.8 (C6-***C***H$_3$), −3.7 (-Si(***C***H$_3$)$_2$-), −4.1 (-Si(***C***H$_3$)$_2$-), −4.2 (-Si(***C***H$_3$)$_2$-), −4.3 (-Si(***C***H$_3$)$_2$-), −4.4 (-Si(***C***H$_3$)$_2$-), −4.6 (-Si(***C***H$_3$)$_2$-), −5.3 (-Si(***C***H$_3$)$_2$-), −5.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2953, 2928, 2857, 1514, 1462, 1360, 1248, 1078, 1040.

HRMS (ESI, *m*/*z*) calcd for $(C_{55}H_{102}O_7Si_4Na)^+$ 1009.6595, found 1009.6531.

(4*S*,6*R*,11*R*,12*S*,13*R*)-4,6,8,14-*Tetrakis*(*tert*-butyldimethylsilyloxy)-12-(4-methoxybenzyloxy)-11,13-dimethyltetradecan-1-ol 421



A solution of 2 mL of Raney nickel (W.R. Grace and Co. Raney® 2800, slurry, in H_2O, active catalyst) in water was transferred in a round-bottom flask under argon. The water was removed *via* syringe and ethanol (2 mL) was added. The solution was stirred for 2 min and the ethanol was then removed *via* syringe. This sequence of addition/stirring/removal was repeated three times. Ethanol (2 mL) was added, followed by benzyl ether **420** (77 mg, 0.078 mmol) dissolved in 1 mL of ethanol. The reaction was then purge with hydrogen and stirred for 2 days under 1 atmosphere of hydrogen, while being monitored by TLC. Filtration on celite gave the desired alcohol **421** (77 mg, quant.) as a clear oil (1:1 mixture of diastereomers), which was used for the next step without further purification.

(Datas recorded on the mixture of diastereomers)

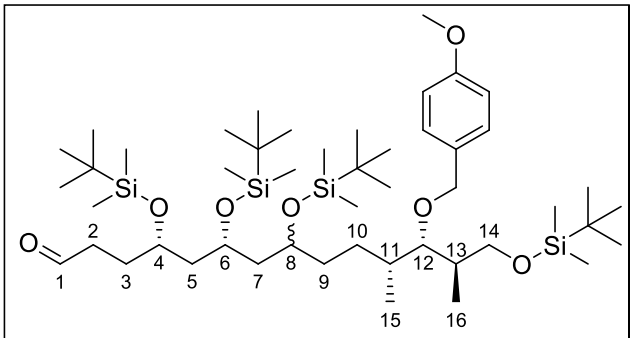
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, 2H, *J* = 8.6 Hz, ***H***-Ar), 6.87 (d, 2H, *J* = 8.6 Hz, ***H***-Ar), 4.51 (s, 2H, C***H*****$_2$**-PMB), 3.97-3.86 (m, 1H, C***H***-OTBS), 3.84-3.74 (m, 2H, C***H***-OTBS), 3.81 (s, 3H, C***H*****$_3$**-PMB), 3.74-3.57 (m, 4H, C***H***-1, C***H***-14), 3.27 (t, 0.5H, *J* = 8.4 Hz, C***H***-12), 3.27 (t, 0.5H, *J* = 8.4 Hz, C***H***-12), 1.86-1.78 (m, 1H, C***H***-13), 1.69-1.45 (m, 13H, C***H***-2, C***H***-3, C***H***-5, C***H***-7, C***H***-9, C***H***-10, C***H***-11), 0.92-0.89 (m, 42H, C***H***-15, C***H***-16, -SiC(C***H*****$_3$**$)_3$-), 0.09-0.03 (m, 24H, -Si(C***H*****$_3$**$)_2$-).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9 (C-Ar), 131.5 (C-Ar), 129.0 (C-Ar), 113.7 (C-Ar), 84.2 (C-12), 83.8 (C-12), 74.5 (***C***H_2-PMB), 70.2 (***C***H-OTBS), 69.7 (***C***H-OTBS), 69.2 (***C***H-OTBS), 67.6 (***C***H-OTBS), 67.1 (***C***H-OTBS), 65.0 (C-14), 63.2 (C-1), 55.2 (***C***H_3-PMB), 46.0 (C-5 or C-7), 45.1 (C-5 or C-7), 38.6 (C-13), 35.8 (C-3 or C-9), 35.7 (C-11), 33.4 (C-3 or C-9), 32.7 (C-3 or C-9), 30.6 (C-10), 29.7 (C-10), 28.2 (C-2), 26.0 (-SiC(***C***$H_3$$)_3$-), 25.9 (-SiC(***C***$H_3$$)_3$-), 25.9 (-SiC(***C***$H_3$$)_3$-), 25.9 (-SiC(***C***$H_3$$)_3$-), 18.3 (-Si***C***$(CH_3)_3$-), 18.1 (-Si***C***$(CH_3)_3$-), 18.0 (-Si***C***$(CH_3)_3$-), 17.9 (-Si***C***$(CH_3)_3$-), 14.7 (C-16), 13.3 (C-15), −3.7 (-Si(***C***$H_3$$)_2$-), −4.1 (-Si(***C***$H_3$$)_2$-), −4.2 (-Si(***C***$H_3$$)_2$-), −4.3 (-Si(***C***$H_3$$)_2$-), −4.4 (-Si(***C***$H_3$$)_2$-), −4.5 (-Si(***C***$H_3$$)_2$-), −5.3 (-Si(***C***$H_3$$)_2$-), −5.4 (-Si(***C***$H_3$$)_2$-).

IR (neat, cm^{-1}) 3414, 2953, 2928, 2857, 1514, 1462, 1250, 1040.

HRMS (ESI, *m*/*z*) calcd for $(C_{48}H_{98}O_7Si_4Na)^+$ 921.6287, found 921.6216.

(4*S*,6*R*,11*R*,12*S*,13*R*)-4,6,8,14-*Tetrakis*(*tert*-butyldimethylsilyloxy)-12-(4-methoxybenzyloxy)-11,13-dimethyltetradecanal 422



To a stirred solution of alcohol **421** (22 mg, 0.024 mmol) in DMSO (1 mL) and THF (1 mL) was added 2-iodoxybenzoic acid (14 mg, 0.049 mmol, 2.0 equiv) at room temperature. After the solution had been stirred overnight, water (5 mL) was added and the solution was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 95/5) gave the aldehyde **422** (21 mg, 97%) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

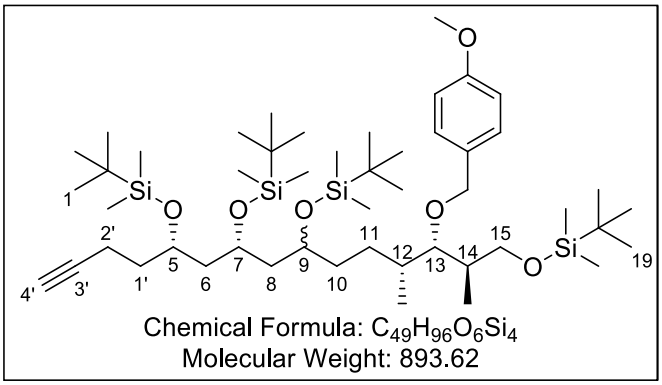
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81-9.77 (m, 1H, C***H***-1), 7.26 (d, 2H, *J* = 8.6 Hz, ***H***-Ar), 6.87 (d, 2H, *J* = 8.6 Hz, ***H***-Ar), 4.51 (s, 2H, C***H*****$_2$**-PMB), 3.95-3.87 (m, 1H, C***H***-OTBS), 3.86-3.68 (m, 3H, C***H***-OTBS, C***H***-14), 3.81 (s, 3H, C***H*****$_3$**-PMB), 3.66-3.61 (m, 1H, C***H***-14), 3.31-3.24 (m, 1H, C***H***-12), 2.53-2.42 (m, 2H, C***H***-2), 1.98-1.88 (m, 1H, C***H***-3), 1.86-1.76 (m, 1H, C***H***-13), 1.75-1.42 (m, 8H, C***H***-3, C***H***-5, C***H***-7, C***H***-9, C***H***-11), 1.32-1.13 (m, 2H, C***H***-10), 0.94-0.86 (m, 42H, C***H***-15, C***H***-16, -SiC(C***H*****$_3$**$)_3$-), 0.08-0.02 (m, 24H, -Si(C***H*****$_3$**$)_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4 (C-1), 159.0 (C-Ar), 131.5 (C-Ar), 129.0 (C-Ar), 113.7 (C-Ar), 84.1 (C-12), 83.8 (C-12), 74.5 (***C***H_2-PMB), 70.2 (***C***H-OTBS), 69.7 (***C***H-OTBS), 68.3 (***C***H-OTBS), 68.3 (***C***H-OTBS), 67.6 (***C***H-OTBS), 67.0 (***C***H-OTBS), 65.0 (C-14), 55.3 (***C***H_3-PMB), 45.9 (C-5 or C-7), 45.5 (C-5 or C-7), 45.2 (C-5 or C-7), 39.6 (C-2), 38.6 (C-13), 35.8 (C-9), 35.7 (C-11), 30.6 (C-10), 29.7 (C-3), 29.0 (C-3), 26.0 (-SiC(***C***$H_3$$)_3$-), 25.9 (-SiC(***C***$H_3$$)_3$-), 25.9 (-SiC(***C***$H_3$$)_3$-), 18.3 (-Si***C***$(CH_3)_3$-), 18.1 (-Si***C***$(CH_3)_3$-), 18.0 (-Si***C***$(CH_3)_3$-), 17.9 (-Si***C***$(CH_3)_3$-), 14.7 (C-16), 13.3 (C-15), −3.7 (-Si(***C***$H_3$$)_2$-), −4.1 (-Si(***C***$H_3$$)_2$-), −4.2 (-Si(***C***$H_3$$)_2$-), −4.3 (-Si(***C***$H_3$$)_2$-), −4.4 (-Si(***C***$H_3$$)_2$-), −4.6 (-Si(***C***$H_3$$)_2$-), −5.3 (-Si(***C***$H_3$$)_2$-), −5.4 (-Si(***C***$H_3$$)_2$-).

IR (neat, cm^{-1}) 2955, 2928, 2857, 1728, 1514, 1462, 1248, 1076, 1040.

HRMS (ESI, *m*/*z*) calcd for $(C_{48}H_{96}O_7Si_4Na)^+$ 919.6125, found 919.6073.

(5*S*,7*R*,12*R*,13*S*,14*R*)-5-(But-3-ynyl)-7,9-*bis*(*tert*-butyldimethylsilyloxy)-13-(4-methoxybenzyloxy)-2,2,3,3,12,14,17,17,18,18-decamethyl-4,16-dioxa-3,17-disilanonadecane 424



To a stirred solution of dimethyl-1-diazo-2-oxopropylphosphonate (11 mg, 0.056 mmol, 2.0 equiv) and potassium carbonate (12 mg, 0.084 mmol, 3.0 equiv) in methanol (1 mL) was added aldehyde **422** (25 mg, 0.028 mmol) in methanol (1 mL) at 0 °C. The solution was stirred overnight at room temperature and was then quenched with water (3 mL) and with a saturated aqueous ammonium chloride solution (3 mL). The mixture was extracted with diethyl ether (3 × 5 mL) and the combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether-ether 97/3) gave the desired alkyne **424** (23 mg, 92%) as a clear oil and as a 1:1 mixture of diastereomers.

(Datas recorded on the mixture of diastereomers)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, 2H, *J* = 8.6 Hz, ***H***-Ar), 6.87 (d, 2H, *J* = 8.6 Hz, ***H***-Ar), 4.51 (s, 2H, C***H*****$_2$**-PMB), 3.97-3.88 (m, 1H, C***H***-OTBS), 3.85-3.78 (m, 1H, C***H***-OTBS), 3.81 (s, 3H, C***H*****$_3$**-PMB), 3.78-3.69 (m, 2H, C***H***-15, C***H***-OTBS), 3.66-3.61 (m, 1H, C***H***-15), 3.29-3.25 (m, 1H, C***H***-13), 2.28-2.22 (m, 2H, C***H***-2'), 1.93 (t, 1H, *J* = 2.5 Hz, C***H***-4'), 1.87-1.74 (m, 2H, C***H***-14, C***H***-1'), 1.71-1.46 (m, 10H, C***H***-6, C***H***-8, C***H***-10, C***H***-11, C***H***-12, C***H***-1'), 0.92-0.89 (m, 42H, C12-C***H*****$_3$**, C14-C***H*****$_3$**, -SiC(C***H*****$_3$**)$_3$-), 0.09-0.05 (m, 24H, -Si(C***H*****$_3$**)$_2$-).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (C-Ar), 131.5 (C-Ar), 129.0 (C-Ar), 113.7 (C-Ar), 84.6 (C-3'), 84.5 (C-3'), 84.1 (C-13), 83.8 (C-13), 74.5 (***C***H$_2$-PMB), 70.2 (***C***H-OTBS), 69.7 (***C***H-OTBS), 68.3 (C-4'), 68.0 (***C***H-OTBS), 67.5 (***C***H-OTBS), 67.0 (***C***H-OTBS), 65.0 (C-15), 55.3 (***C***H$_3$-PMB), 46.6 (C-6 or C-8), 46.0 (C-6 or C-8), 45.8 (C-6 or C-8), 45.5 (C-6 or C-8), 38.6 (C-14), 35.8 (C-10, C-1'), 35.7 (C-12), 30.6 (C-11), 26.0 (-SiC(***C***H$_3$)$_3$-), 25.9 (-SiC(***C***H$_3$)$_3$-), 25.9 (-SiC(***C***H$_3$)$_3$-), 18.3 (-Si***C***(CH$_3$)$_3$-), 18.1 (-Si***C***(CH$_3$)$_3$-), 18.0 (-Si***C***(CH$_3$)$_3$-), 17.9 (-Si***C***(CH$_3$)$_3$-), 14.7 (C14-***C***H$_3$), 14.4 (C-2'), 14.3 (C-2'), 13.4 (C12-***C***H$_3$), −3.8 (-Si(***C***H$_3$)$_2$-), −4.0 (-Si(***C***H$_3$)$_2$-), −4.1 (-Si(***C***H$_3$)$_2$-), −4.2 (-Si(***C***H$_3$)$_2$-), −4.2 (-Si(***C***H$_3$)$_2$-), −4.5 (-Si(***C***H$_3$)$_2$-), −4.6 (-Si(***C***H$_3$)$_2$-), −5.3 (-Si(***C***H$_3$)$_2$-), −5.4 (-Si(***C***H$_3$)$_2$-).

IR (neat, cm^{-1}) 2953, 2928, 2857, 1514, 1472, 1248, 1078, 1040.

HRMS (ESI, *m*/*z*) calcd for $(C_{49}H_{96}O_6Si_4Na)^+$ 915.6176, found 915.6106.

List of References

1. Pettit, G. R.; Kamano, Y.; Herald, C. L.; Fujii, Y.; Kizu, H.; Boyd, R. R.; Boettner, F. E.; Doubek, D. L.; Schmidt, J. M.; Chapuis, J.-C.; Michel, C. *Tetrahedron* **1993**, *49*, 9151.
2. http://www.gastropods.com/8/Shell_29538.shtml.
3. Ojika, M.; Nagoya, T.; Yamada, K. *Tetrahedron Lett.* **1995**, *36*, 7491.
4. Suenaga, K.; Nagoya, T.; Shibata, T.; Kigoshi, H.; Yamada, K. *J. Nat. Prod.* **1997**, *60*, 155.
5. Park, P. K.; O'Malley, S. J.; Schmidt, D. R.; Leighton, J. L. *J. Am. Chem. Soc.* **2006**, *128*, 2796.
6. (a) Waetzig, J. D.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 109; (b) Whitehead, A.; Waetzig, J. D.; Thomas, C. D.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 1421; (c) Hanson, P. R.; Chegondi, R.; Nguyen, J.; Thomas, C. D.; Waetzig, J. D.; Whitehead, A. *J. Org. Chem.* **2011**, *76*, 4358.
7. Le Roux, R.; Desroy, N.; Phansavath, P.; Genêt, J.-P. *Synlett* **2005**, 429.
8. (a) Desroy, N.; Le Roux, R.; Phansavath, P.; Chiummiento, L.; Bonini, C.; Genêt, J.-P. *Tetrahedron Lett.* **2003**, *44*, 1763; (b) Roche, C.; Desroy, N.; Haddad, M.; Phansavath, P.; Genêt, J.-P. *Org. Lett.* **2008**, *10*, 3911.
9. Keck, G. E.; McLaws, M. D. *Tetrahedron Lett.* **2005**, *46*, 4911.
10. (a) Burke, S. D.; Muller, N.; Beaudry, C. M. *Org. Lett.* **1999**, *1*, 1827. (b) Burke, S. D.; Voight, E. A. *Org. Lett.* **2001**, *3*, 237. (c) Lambert, W. T.; Burke, S. D. *Org. Lett.* **2003**, *5*, 515. For desymmetrization of a C_2-symmetric diol using the Prins cyclisation, see: (d) Rychnovsky, S. D.; Yang, G.; Hu, Y.; Khire, U. R. *J. Org. Chem.* **1997**, *62*, 3022.
11. Paterson, I.; Smith, J. D.; Ward, R. A. *Tetrahedron* **1995**, *51*, 9413. Claffey, M. M.; Hayes, C. J.; Heathcock, C. H. *J. Org. Chem.* **1999**, *64*, 8267.
12. Ikariya, T.; Ishii, Y.; Kawano, H.; Arai, T.; Saburi, M.; Yoshikawa, S.; Akutagawa, S. *J. Chem. Soc., Chem. Commun.* **1985**, 922. Ohta, T.; Tonomura, Y.; Nozaki, K.; Takaya, H.; Mashima, K. *Organometallics* **1996**, *15*, 1521. Mashima, K.; Nakamura, T.; Matsuo, Y.; Tani, K. J. *Organomet. Chem.* **2000**, *607*, 51.
13. Vincent, A.; Prunet, J. *Synlett* **2006**, 2269.
14. (a) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307. (b) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (c) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (d) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421.
15. Evans, D.A.; Gauchet-Prunet, J. A. *J. Org. Chem.* **1993**, *58*, 2446.
16. Braun, M.-G.; Vincent, A.; Boumediene, M.; Prunet, J. *J. Org. Chem.* **2011**, *76*, 4921.
17. Hafner, A.; Duthaler, R. O.; Marti, R.; Rhis, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321.
18. (a) Čusak, A. *Chem. Eur. J.* **2012**, *18*, 5800; (b) P. A. Evans, *Metathesis in Natural Product Synthesis:Strategies, Substrates and Catalysis* (Eds.: J. Cossy, S. Arseniyadis, C. Meyer), Wiley-VCH, Weinheim, **2010**, pp. 225 – 259.
19. Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426.
20. Amador, M.; Ariza, X.; Garcia, J.; Ortiz, J. *J. Org. Chem.* **2004**, *69*, 8172.
21. Petit, M.; Chouraqui, G.; Aubert, C.; Malacria, M. *Org. Lett.* **2003**, *5*, 2037.

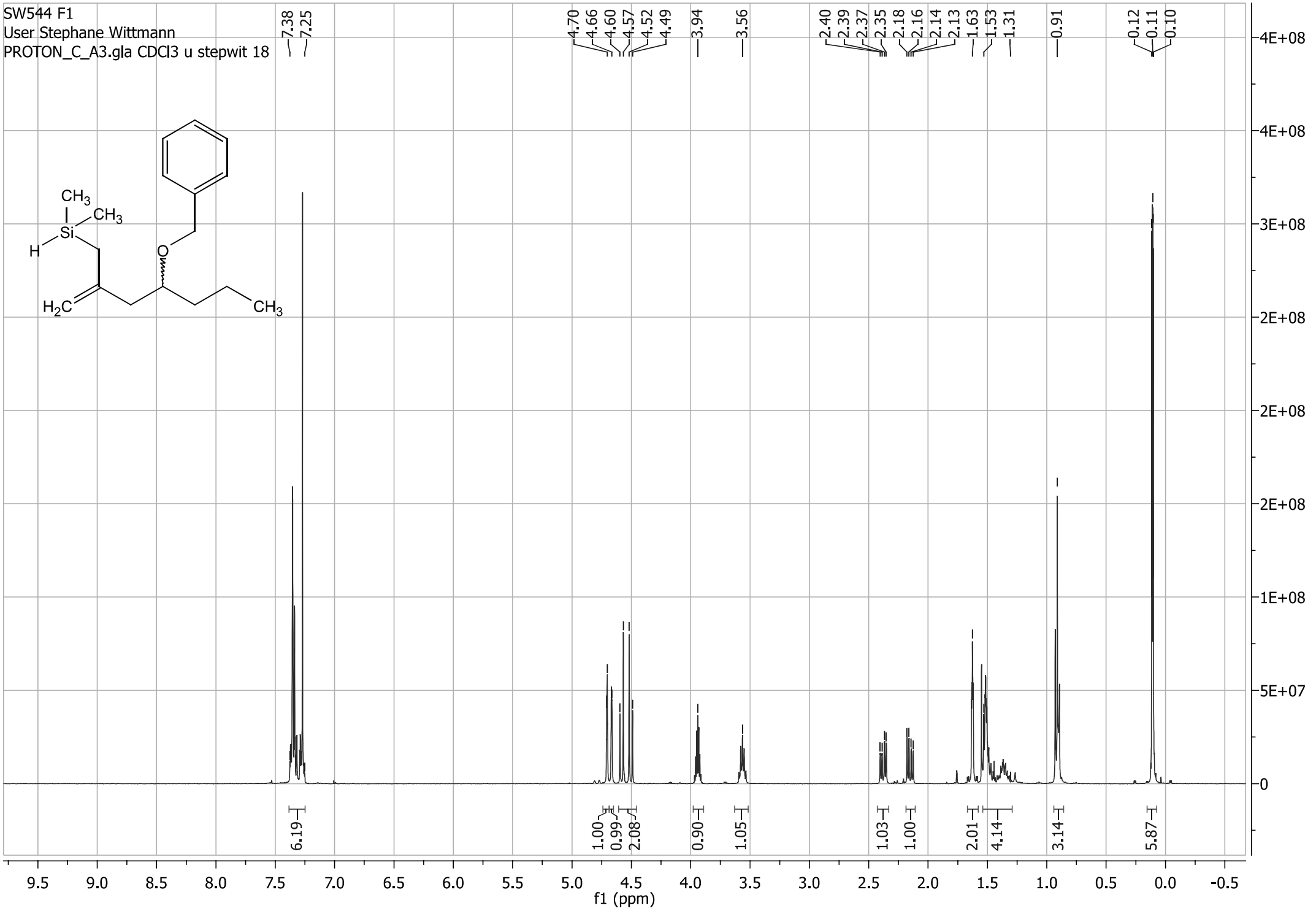
22. Cordier, C.; Morton, D.; Leach, S.; Woodhall, T.; O'Leary-Steele, C.; Warriner, S.; Nelson, A. *Org. Biomol. Chem.* **2008**, *6*, 1734.
23. Matsui, R.; Seto, K.; Fujita, K.; Suzuki, T.; Nakazaki, A.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2010**, *49*, 10068.
24. Marjanovic, J.; Kozmin, S. A. *Angew. Chem.* **2007**, *119*, 9010 ; *Angew. Chem. Int. Ed.* **2007**, *46*, 8854.
25. Hoye, T. R.; Eklov, B. M.; Jeon, J.; Khoroosi, M. *Org. Lett.* **2006**, *8*, 3383.
26. Evans, P. A.; Cui, J.; Buffone, G. P. *Angew. Chem.* **2003**, *115*, 1776; *Angew. Chem. Int. Ed.* **2003**, *42*, 1734.
27. Hoye, T. R.; Jeon, J.; Kopel, L. C.; Ryba, T. D.; Tennakoon, M. A.; Wang, Y. *Angew. Chem.* **2010**, *122*, 6287; *Angew. Chem. Int. Ed.* **2010**, *49*, 6151
28. Matsui, R.; Seto, K.; Sato, Y.; Suzuki, T.; Nakazaki, A.; Kobayashi, S. *Angew. Chem.* **2011**, *123*, 706; *Angew. Chem. Int. Ed.* **2011**, *50*, 680
29. Mukherjee, S.; Lee, D. *Org. Lett.* **2009**, *11*, 2916
30. Akindele, T.; Marsden, S. P.; Cumming, J. G. *Org. Lett.* **2005**, *7*, 3685.
31. (a) Denmark, S. E.; Yang, S. M. *J. Am. Chem. Soc.* **2002**, *124*, 15196; (b) Denmark, S. E.; Yang, S. M. *J. Am. Chem. Soc.* **2004**, *126*, 12432.
32. Rodríguez-Escrich, C.; Urpí, F.; Vilarrasa, J. *Org. Lett.* **2008**, *10*, 5191.
33. Volchkov, I.; Lee, D. *J. Am. Chem. Soc.* **2013**, *135*, 5324.
34. Li, F.; Miller, M. J. *J. Org. Chem.* **2006**, *71*, 5221.
35. Tung, J. C.; Chen, W.; Noll, B. C.; Taylor, R. E.; Fields, S. C.; Dent, W. H. III.; Green, F. R. *Synthesis* **2007**, 2388.
36. Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 8251.
37. Kiely, A. F.; Jernelius, J. A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 2868.
38. Funk, T. W. *Org. Lett.* **2009**, *11*, 4998.
39. Boumediene, M., *Master thesis*, *Ecole Polytechnique* **2007**
40. Fürstner, A.; Voigtländer, D. *Synthesis* **2000**, 7, 959.
41. Clark, J. S.; Baxter, C. A.; Dossetter, A. G.; Poigny, S.; Castro, J. L.; Whittingham, W. G. *J. Org. Chem.* **2008**, *73*, 1040.
42. (a) Narayanan, B. A.; Bunnelle, W. H. *Tetrahedron Lett.* **1987**, *28*, 6261. (b) Lee, T. V.; Channon, J. A.; Cregg, C.; Porter, J. R.; Roden, F. S.; Yeoh, H. T.-L. *Tetrahedron* **1989**, *45*, 5877. (c) Mickleson, T. J.; Koviach, J. L.; Forsyth, C. J. *J. Org. Chem.* **1996**, *61*, 9617.
43. (a) Grafstein, D. *J. Am. Chem. Soc.* **1955**, *77*, 6650. (b) Awang, D. V. C.; Wolfe, S. *Can. J. Chem.* **1969**, *47*, 706.
44. Liu, H.-J.; Shia, K.-S.; Shang, X.; Zhu, B.-Y. *Tetrahedron* **1999**, *55*, 3803.
45. Imamoto, T.; Suguira, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233.
46. Li, Z.; Yang, C.; Zheng, H.; Qiu, H.; Lai, G. *J. Organomet. Chem.* **2008**, *693*, 3771.
47. Fujiwara, T.; Yanai, K.; Shimane, K.; Takamori, M.; Takeda, T. *Eur. J. Org. Chem.* **2001**, 155.
48. Legros, J.; Meyer, F.; Coliboeuf, M.; Crousse, B.; Bonnet-Delpon, D.; Bégué, J.-P. *J. Org. Chem.* **2003**, *68*, 6444.
49. Zhang, Y.; Jia, X.; Wang, J.-X. *Eur. J. Org. Chem.* **2009**, 2983.
50. Shibato, A.; Itagaki, Y.; Tayama, E.; Hokke, Y.; Asao, N.; Maruoka, K. *Tetrahedron* **2000**, *56*, 5373.
51. Robertson, J.; Hall, M. J.; Stafford, P. M.; Green, S. P. *Org. Biomol. Chem.* **2003**, *1*, 3758.
52. Kunai, A.; Ohshita, J. *J. Organomet. Chem.* **2003**, *686*, 3.
53. Savela, R.; Zawartka, W.; Leino, R. *Organometallics* **2012**, *31*, 3199.

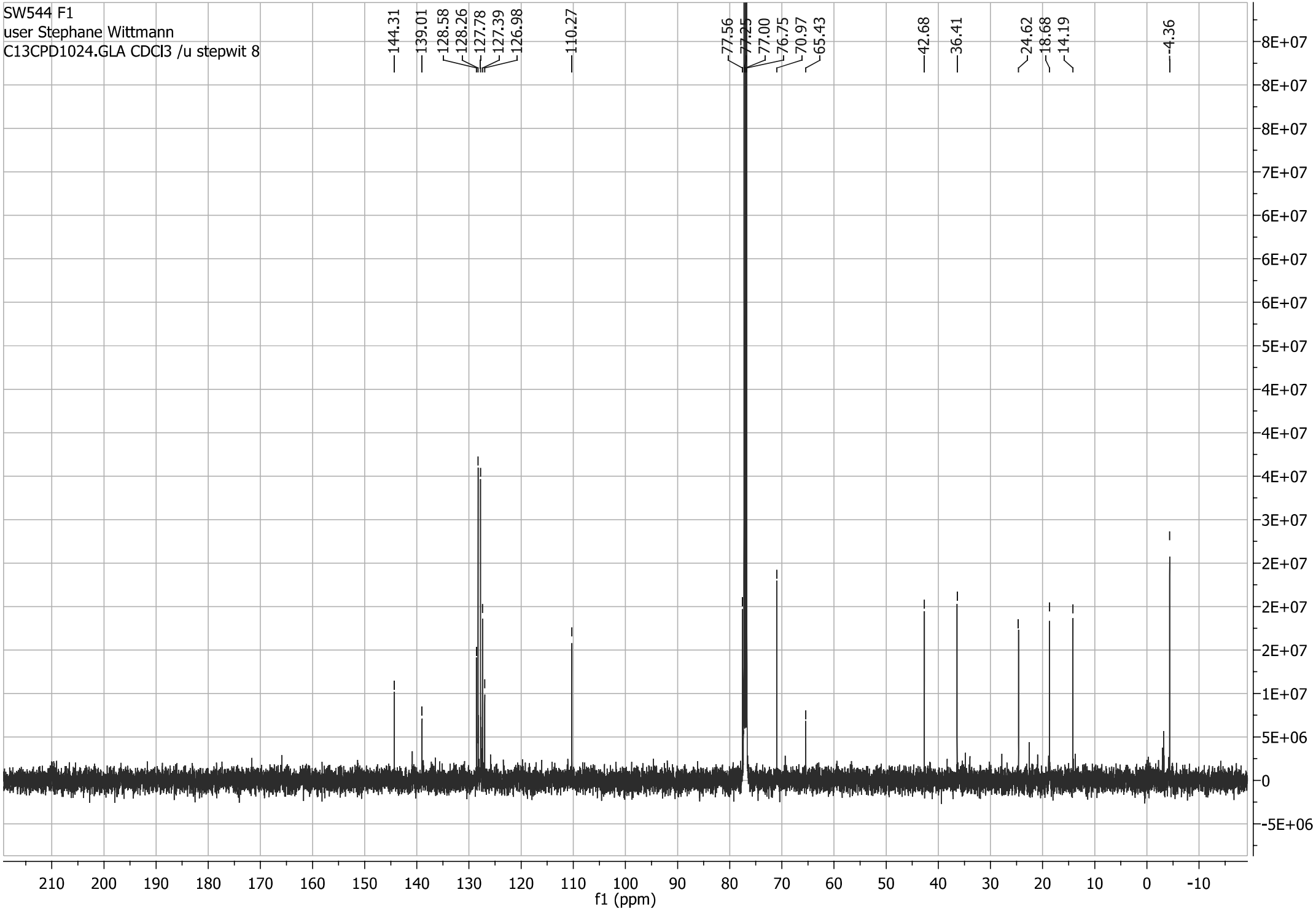
54. Pongkittiphan, P.; Theodorakis, E. A.; Chavasiri, W. *Tetrahedron Lett.* **2009**, *50*, 5080.
55. Ojima, I.; Kogure, T.; Nihonyanagi, M.; Kono, H.; Inaba, S. *Chem. Lett.* **1973**, 501.
56. Doyle, M. P.; High, K. G.; Bagheri, V.; Pieters, R. J.; Lewis, P. J.; Pearson, M. M. *J. Org. Chem.* **1990**, *55*, 6082.
57. Miller, R. L.; Maifeld, S. V.; Lee, D. *Org. Lett.* **2004**, *6*, 2773.
58. Funatsu, A.; Kubota, T.; Endo, M. (Shin-Etsu Chemical Industry Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP2001-114788, 2001.
59. (a) Lorenz, C.; Schubert, U. *Chem. Ber.* **1995**, *128*, 1267. (b) Mahoney, W. S.; Stryker, J. M. *J. Am. Chem. Soc.* **1989**, *111*, 8818.
60. Ito, H.; Watanabe, A.; Sawamura, M. *Org. Lett.* **2005**, *7*, 1869.
61. For reviews on olefin metathesis see: (a) Fürstner, A. *Angew. Chem.* **2000**, *112*, 3140; *Angew. Chem. Int. Ed.* **2000**, *39*, 3012. (b) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem.* **2005**, *117*, 4564; *Angew. Chem. Int. Ed.* **2005**, *44*, 4490 (c) Prunet, J.; Grimaud, L. *Metathesis in Natural Product Synthesis*; Cossy, J.; Arseniyadis, S.; Meyer, C.; Eds.; Wiley: New York, 2010. (d) Prunet, J. *Eur. J. Org. Chem.* **2011**, 3634.
62. (a) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875. (b) Bazan, G.C.; Khosravi, E.; Schrock, R.R.; Feast, W.J.; Gibson, V.C.; O'Regan, M.B.; Thomas, J.K.; Davis, W.M. *J. Am. Chem. Soc.* **1990**, *112*, 8378. (c) Bazan, G. C.; Oskam, J. H.; Cho, H.-N.; Park, L. Y.; Schrock, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 6899.
63. (a) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew.Chem. Int. Ed. Engl.* **1995**, *34*, 2039. (b) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org.Lett.* **1999**, *1*, 953.
64. Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.
65. Hoveyda, H. A.; Zhugrakin, A. R. *Nature* **2007**, *450*, 243.
66. Meyer, C.; Cossy, J. *Tetrahedron Lett.* **1997**, *38*, 4757.
67. For review on asymmetric catalysis developed by Noyori and co-workers, see: Noyori, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 2008.
68. Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856; Kitamura, M.; Tokunaga, M.; Ohkuma, T.; Noyori, R. *Org. Synth.* **1992**, *71*, 1; Noyori, R.; Kitamura, M.; Ohkuma, T. *Proc. Natl. Acad. Sci.* **2004**, *101*, 5356.
69. (a) Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307. (b) Martinez, L. E.; Leighton, J. L.; Carsten, D. H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5897. (c) Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936. (d) Jacobsen, E. N. *Acc. Chem. Res.* **2000**, *33*, 421. (e) Nielsen, L. P. C.; Stevenson, C. P.; Blackmond, D. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 1360.
70. Yu, W.; Mei, Y.; Kang, Y.; Hua, Z.; Jin, Z. *Org. Lett.* **2004**, *6*, 3217.
71. Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.
72. Hafner, A.; Duthaler, R. O.; Marti, R.; Rhis, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321.
73. Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH : Weinheim 2000, chapitre 10; Chemler, S. R.; Roush, W. R.

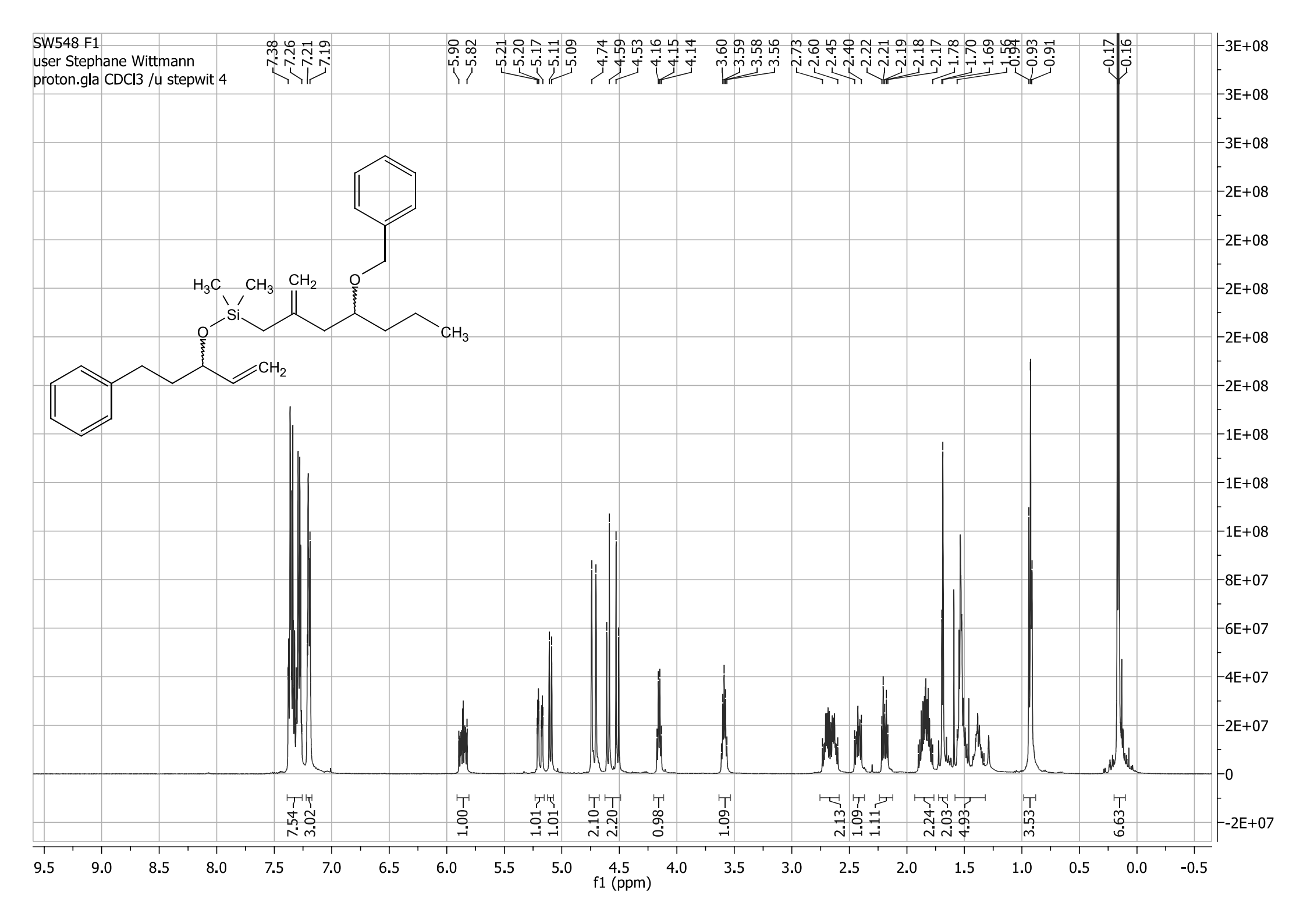
In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH : Weinheim 2000, chapitre 11.
74. Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1989**, *54*, 1570.
75. Hoppe, D.; Zschage, O. *Angew. Chem. Int. Ed.* **1989**, *28*, 69.
76. Keck, G. E.; Savin, K. A.; Cressman, E. N. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889.
77. Burns, N. Z.; Hackman, B. M.; Ng, P. Y.; Powelson, I.A.; Leighton, J. L. *Angew. Chem. Int. Ed. Engl.* **2006**, *45*, 3811.
78. Masse, C. E.; Panek, J. S. Chem. Rev. 1995, 95, 1293-1316; Hu, T.; Takenaka, N.; Panek, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 12806.
79. Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **2005**, *102*, 7107.
80. Schlosser, M.; Desponds, O.; Lehman, R.; Moret, E.; Rauchschwalbe, G. *Tetrahedron* **1993**, *49*, 10175.
81. Roush, W. R.; Haltermann, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294.
82. Lumbroso, A.; Cooke, M. L.; Breit, B. *Angew. Chem. Int. Ed.* **2013**, *52*, 1890.
83. Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1988**, *29*, 5645.
84. Oppolzer, W.; Radinov, R. N. *Tetrahedron Lett.* **1991**, *32*, 5777.
85. Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593.
86. Miyake, H.; Yamamura, K. *Chem. Lett.* **1992**, 507.
87. Evans, D. A.; Allison, B. D.; Yang, M. G.; Masse, C. E. *J. Am. Chem. Soc.* **2001**, *123*, 10840.
88. Evans, D.A.; Gauchet-Prunet, J. A. *J. Org. Chem.* **1993**, *58*, 2446.
89. (a) White, J. D.; Wardrop, D. J.; Sundermann, K. F. *Org. Synth.* **2002**, *79*, 125. (b) White, J. D.; Wardrop, D. J.; Sundermann, K. F. *Org. Synth.* **2002**, *79*, 130.
90. Bosiak, M. J.; Krzemiński, M. P.; Jaisankar, P.; Zaidlewicz, M. *Tetrahedron: Asymmetry* **2008**, *19*, 956.
91. Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806.
92. Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360.
93. Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783.
94. McGrath, D. V.; Grubbs, R. H. *Organometallics* **1994**, *13*, 224.
95. Gurjar, M. K.; Yakambram, P. *Tetrahedron Lett.* **2001**, *42*, 3633.
96. Hong, S. H.; Sander, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160.
97. Ohira, S. *Synth. Commun.* **1989**, *19*, 561; Müller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521.
98. Seyferth, D.; Marmor, R. S.; Hibert, P. *J. Org. Chem.* **1971**, *36*, 1379; Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1979**, *44*, 4997; Gilbert, J. C.; Weerasooriya, U. *J. Org. Chem.* **1982**, *47*, 1837.
99. Van Horn, D. E.; Negishi, E.-i. *J. Am. Chem. Soc.* **1978**, *100*, 2252; Yoshida, T.; Negishi, E.-i. *J. Am. Chem. Soc.* **1981**, *103*, 4985; Negishi, E.-i.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639; Negishi, E.-i.; Kondakov, D. Y.; Choueiry, D.; Kasai, K.; Takahashi, T. *J. Am. Chem. Soc.* **1996**, *118*, 9577.
100. Wipf, P.; Lim, S. *Angew. Chem. Int. Ed.* **1993**, *32*, 1068.
101. Ruder, S. M.; Ronald, R. C. *Tetrahedron Lett.* **1987**, *28*, 135.

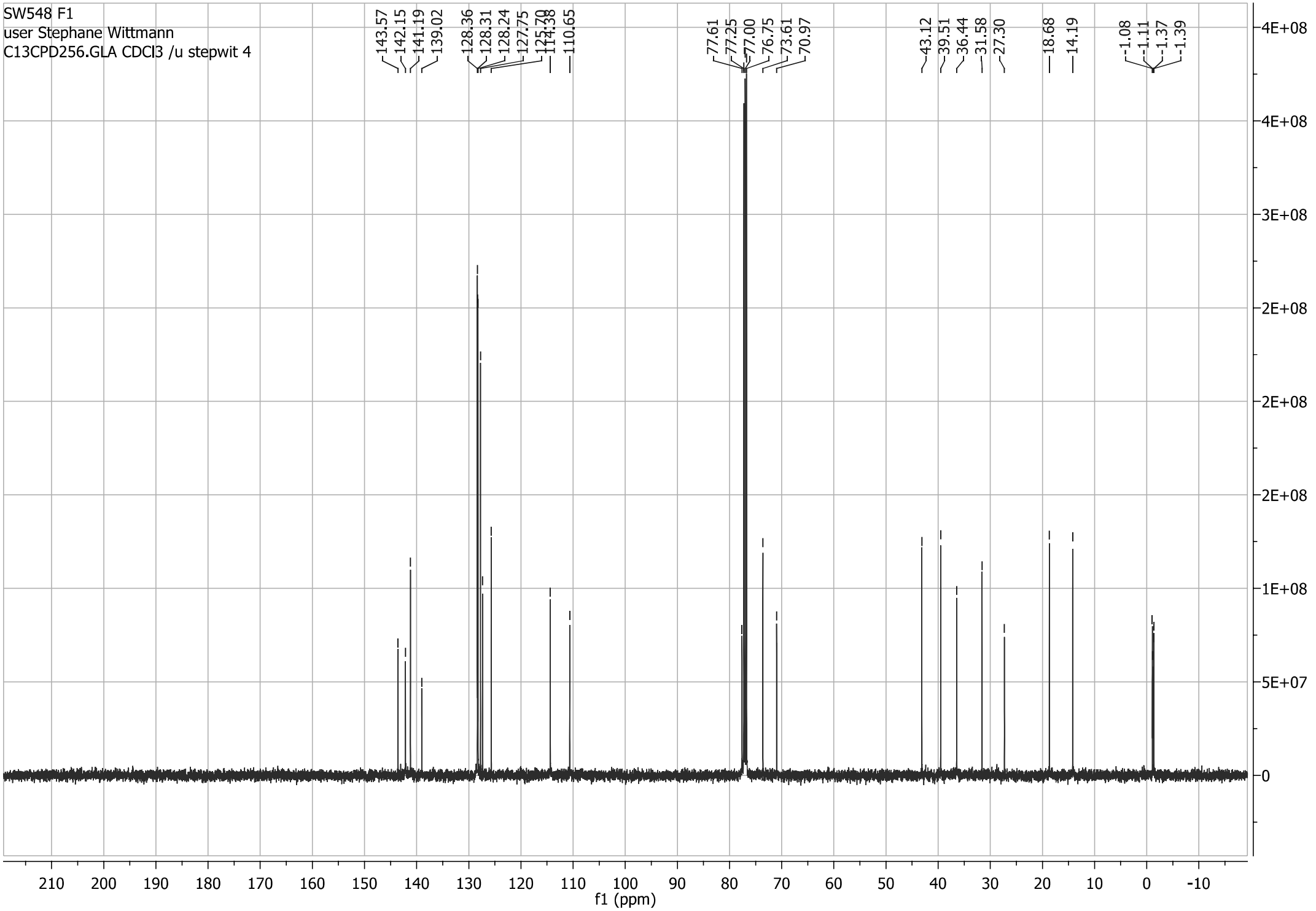
102. Davies, H. M. L.; Cantrell, W. R.; Romines, K. R.; Baum, J. S. *Org. Synth.* **1992**, *70*, 93.
103. Wessel, H.-P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. I* **1985**, 2247.
104. Grünanger, C. U.; Breit B. *Angew. Chem. Int. Ed.* **2010**, *49*, 967.
105. Mori, K.; Takaishi, H. *Tetrahedron* **1989**, *45*, 1639.
106. Ramos, A. S.; Ribeiro, J. B.; Lopes, R. O.; Leite, S. G. F.; de Souza, R. O. M. A. *Tetrahedron Lett.* **2011**, *52*, 6127.
107. Overman, L. E.; Lesuisse, D. *Tetrahedron Lett.* **1985**, *26*, 4167.
108. Angoh, A. G.; Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1984**, 534.
109. Srihari, P.; Kumaraswamy, B.; Somaiah, R.; Yadav, J. S. *Synthesis* **2010**, 1039.
110. Kühnert, S. V.; Maier, M. E. *Org. Lett.* **2002**, *4*, 643.
111. Kuilya, T. K.; Chatterjee, S.; Goswami, R. K. *Tetrahedron* **2014**, *70*, 2905.
112. Venkatesham, A.; Nagaiah, K. *Tetrahedron: Asymmetry* **2012**, *23*, 1186.
113. Packard, G. K.; Hu, Y.; Vescovi, A.; Rychnovsky, S. D. *Angew. Chem. Int. Ed.* **2004**, *43*, 2822.
114. Cooksey, J. P.; Ford, R.; Kocienski, P. J.; Pelotier, B.; Pons, J.-M. *Tetrahedron* **2010**, *66*, 6462.
115. O'Sullivan, P. T.; Buhr, W.; Fuhry, M. A. M.; Harrison, J. R.; Davies, J. E.; Feeder, N.; Marshall, D. R.; Burton, J. W.; Holmes, A. B. *J. Am. Chem. Soc.* **2004**, *126*, 2194.
116. Matsumoto, K.; Kozmin, S. A. *Adv. Synth. Catal.* **2008**, *350*, 557.
117. Fuwa, H.; Mizunuma, K.; Sasaki, M.; Suzuki, T.; Kubo, H. *Org. Biomol. Chem.* **2013**, *11*, 3442.
118. Li, M.; O'Doherty, G. A. *Org. Lett.* **2006**, *8*, 6087.

Appendices

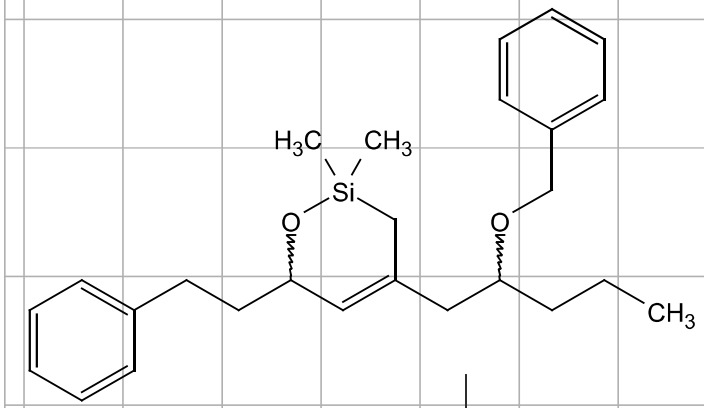

SW544 F1
User Stephane Wittmann
PROTON_C_A3.gla CDCl3 u stepwit 18
7.38
7.25
4.70
4.66
4.60
4.57
4.52
4.49
3.94
3.56
2.40
2.39
2.37
2.35
2.18
2.16
2.14
2.13
1.63
1.53
1.31
0.91
0.12
0.11
0.10
CH3
CH3
Si
H
O
H2C
CH3
6.19
1.00
0.99
2.08
0.90
1.05
1.03
1.00
2.01
4.14
3.14
5.87
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


SW544 F1
user Stephane Wittmann
C13CPD1024.GLA CDCl3 /u stepwit 8
144.31
139.01
128.58
128.26
127.78
127.39
126.98
110.27
77.56
77.25
77.00
76.75
70.97
65.43
42.68
36.41
24.62
18.68
14.19
-4.36
f1 (ppm)


SW548 F1
user Stephane Wittmann
proton.gla CDCl3 /u stepwit 4
7.38
7.26
7.21
7.19
5.90
5.82
5.21
5.20
5.17
5.11
5.09
4.74
4.59
4.53
4.16
4.15
4.14
3.60
3.59
3.58
3.56
2.73
2.60
2.45
2.40
2.22
2.21
2.19
2.18
2.17
1.78
1.70
1.69
1.56
0.94
0.93
0.91
0.17
0.16
H3C
CH3
CH2
O
Si
O
CH3
CH2
7.54
3.02
1.00
1.01
1.01
2.10
2.20
0.98
1.09
2.13
1.09
1.11
2.24
2.03
4.93
3.53
6.63
f1 (ppm)


SW548 F1
user Stephane Wittmann
C13CPD256.GLA CDCl3 /u stepwit 4
143.57
142.15
141.19
139.02
128.36
128.31
128.24
127.75
125.70
114.38
110.65
77.61
77.25
77.00
76.75
73.61
70.97
43.12
39.51
36.44
31.58
27.30
18.68
14.19
-1.08
-1.11
-1.37
-1.39
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

SW554 F4
user Stephane Wittmann
PROTON.GLA CDCl3 /u stepwit 43



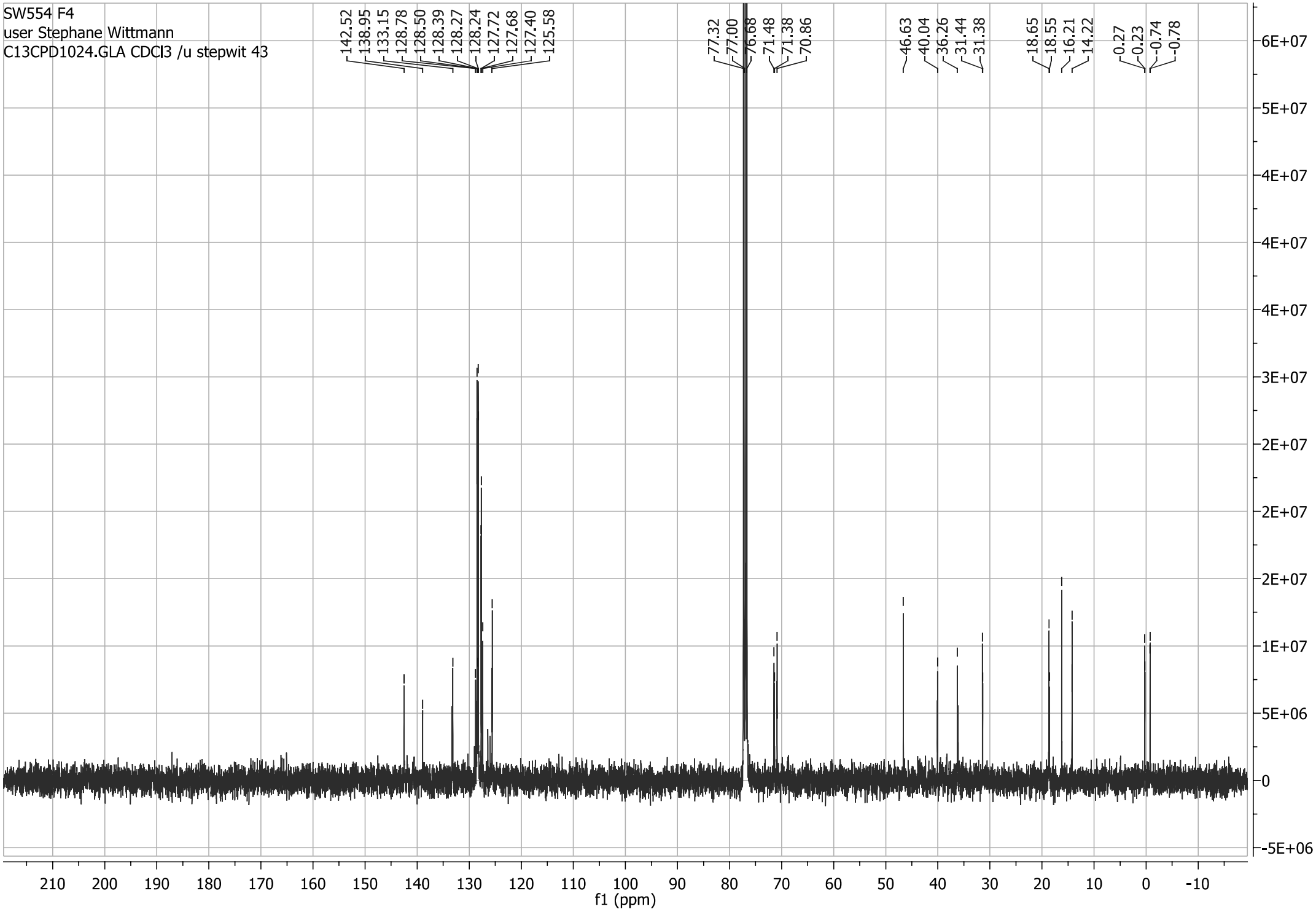
7.37 7.09 5.46 5.44 5.39 4.58 4.55 4.54 4.53 4.53 4.50 4.50 4.49 4.47 3.60 3.50 2.81 2.64 2.43 2.41 2.39 2.38 2.19 2.18 2.16 2.14 1.91 1.74 1.55 1.07 0.93 0.92 0.90 0.21 0.19 0.17 0.16

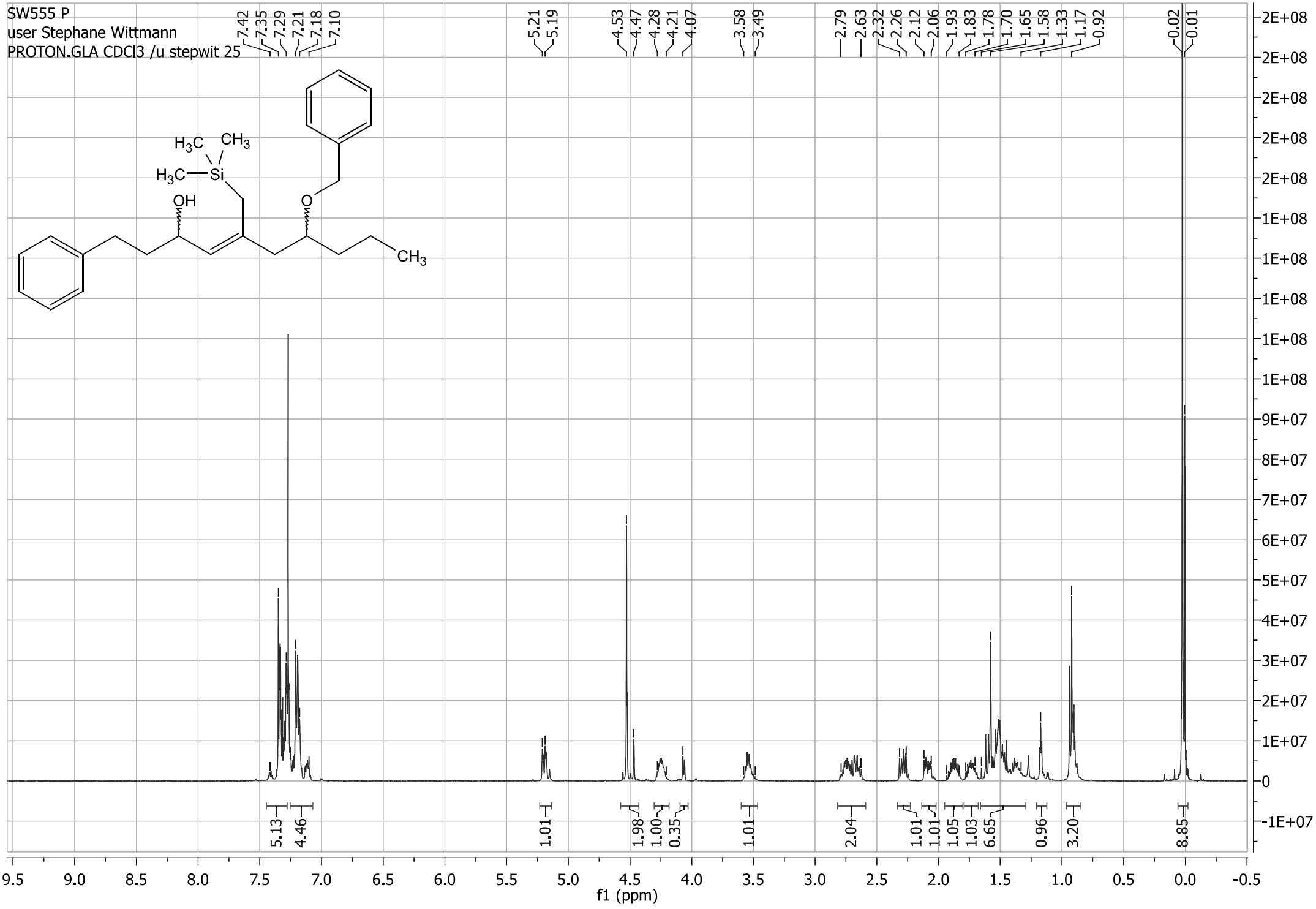
5.19 5.54 1.00 2.10 1.15 1.07 2.11 0.98 0.97 2.12 6.99 3.53 6.17

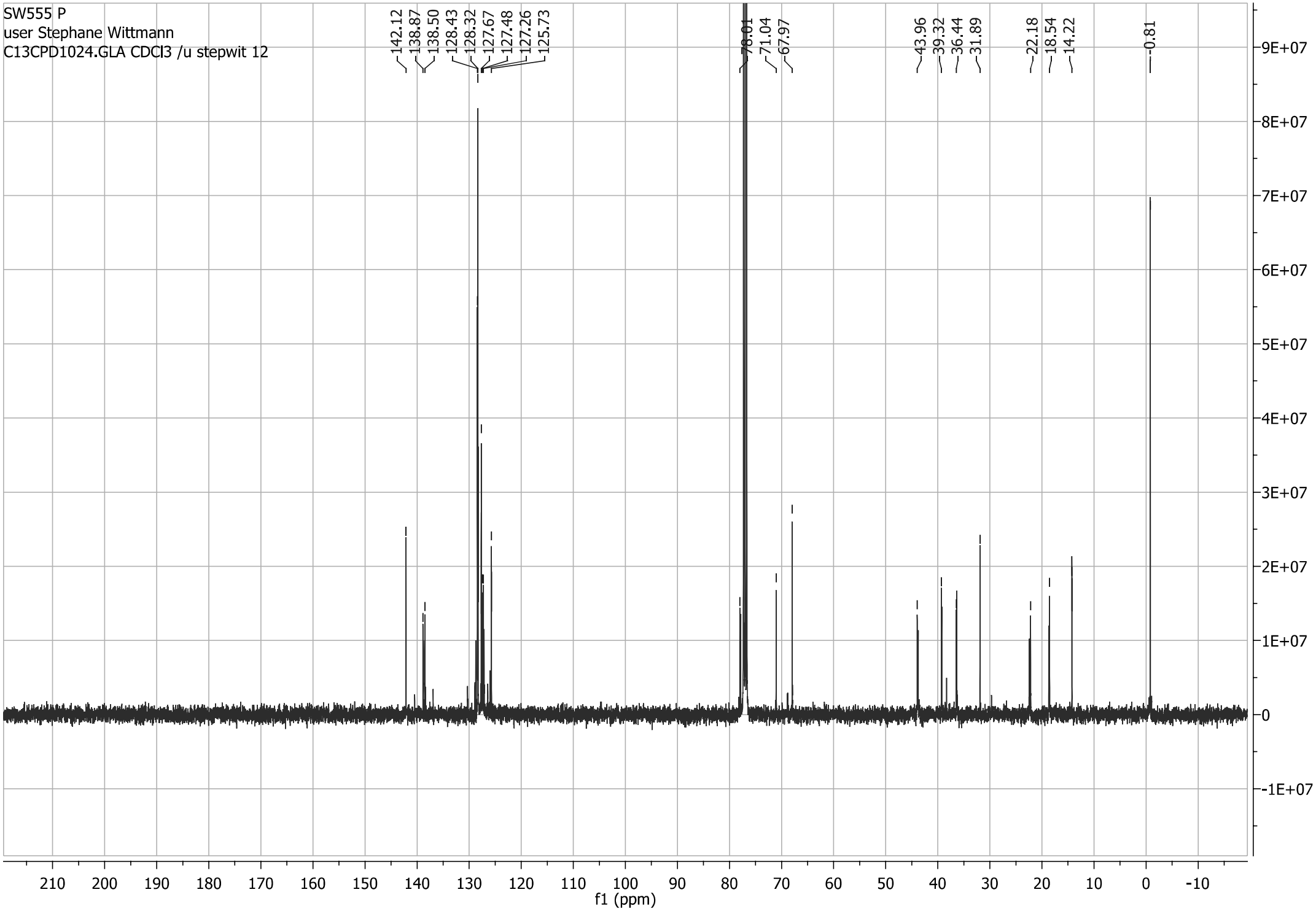
4E+08 4E+08 4E+08 3E+08 2E+08 2E+08 2E+08 1E+08 5E+07 0

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

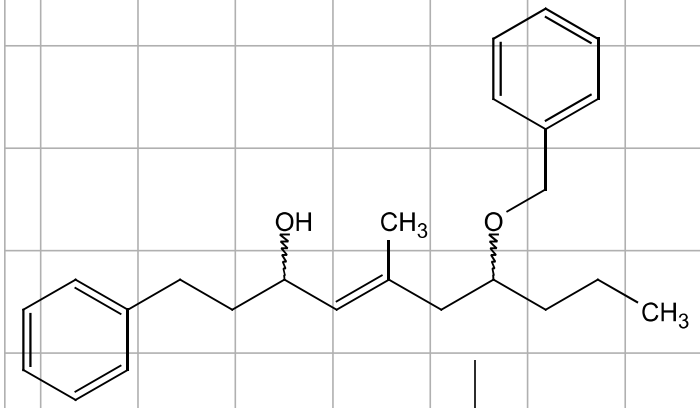
f1 (ppm)


SW554 F4
user Stephane Wittmann
C13CPD1024.GLA CDCl3 /u stepwit 43
142.52
138.95
133.15
128.78
128.50
128.39
128.27
128.24
127.72
127.68
127.40
125.58
77.32
77.00
76.68
71.48
71.38
70.86
46.63
40.04
36.26
31.44
31.38
18.65
18.55
16.21
14.22
0.27
0.23
-0.74
-0.78
6E+07
5E+07
4E+07
4E+07
4E+07
3E+07
2E+07
2E+07
2E+07
1E+07
5E+06
0
-5E+06
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


SW555 P
user Stephane Wittmann
PROTON.GLA CDCl3 /u stepwit 25
7.42
7.35
7.29
7.21
7.18
7.10
5.21
5.19
4.53
4.47
4.28
4.21
4.07
3.58
3.49
2.79
2.63
2.32
2.26
2.12
2.06
1.93
1.83
1.78
1.70
1.65
1.58
1.33
1.17
0.92
0.02
0.01
H3C
CH3
H3C
Si
OH
O
CH3
5.13
4.46
1.01
1.98
1.00
0.35
1.01
2.04
1.01
1.01
1.05
1.03
6.65
0.96
3.20
8.85
f1 (ppm)


SW555 P
user Stephane Wittmann
C13CPD1024.GLA CDCl3 /u stepwit 12
142.12
138.87
138.50
128.43
128.32
127.67
127.48
127.26
125.73
78.01
71.04
67.97
43.96
39.32
36.44
31.89
22.18
18.54
14.22
0.81
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
-1E+07
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

SW558 F3
user Stephane Wittmann
PROTON.GLA CDCl3 /u stepwit 58

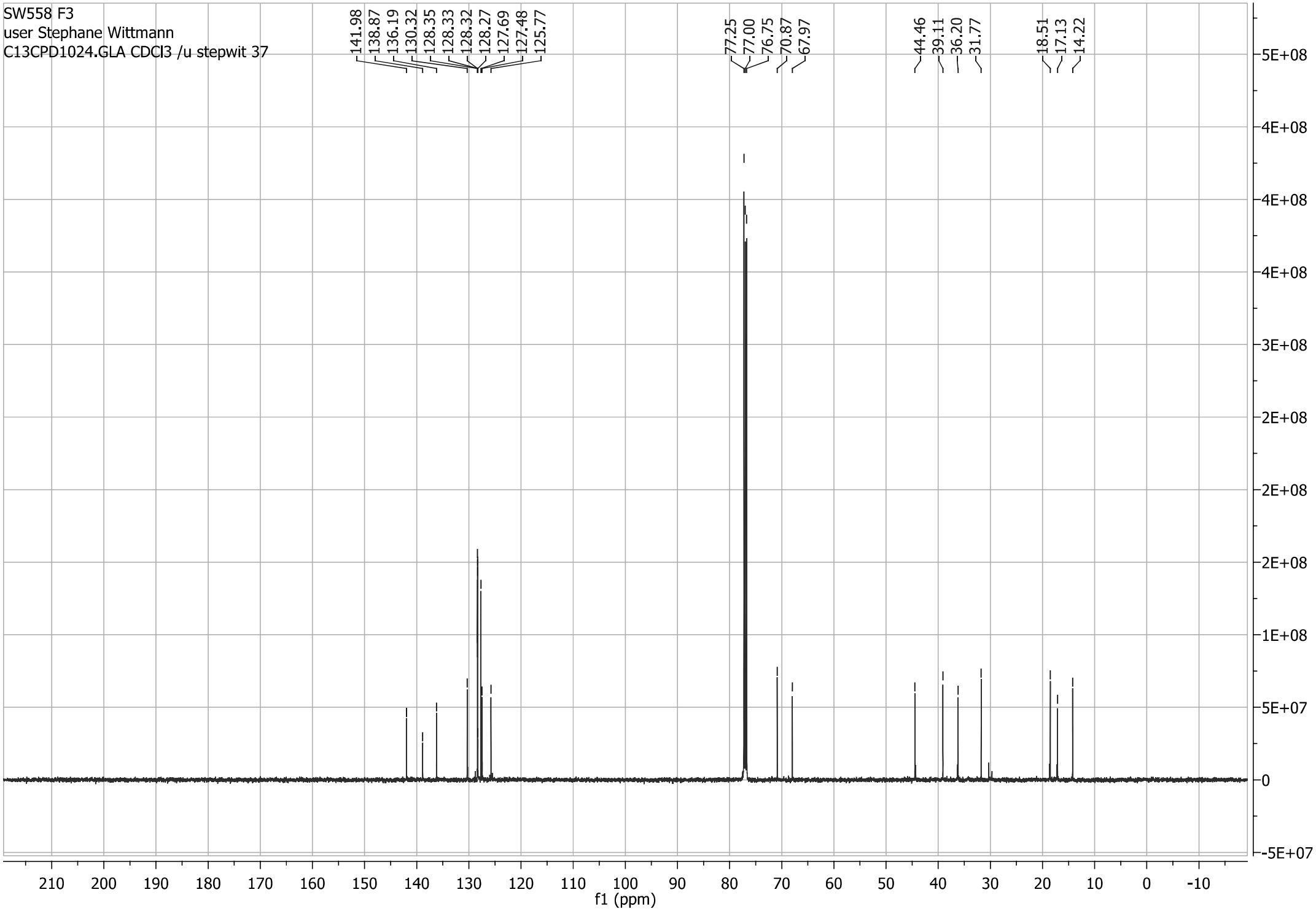


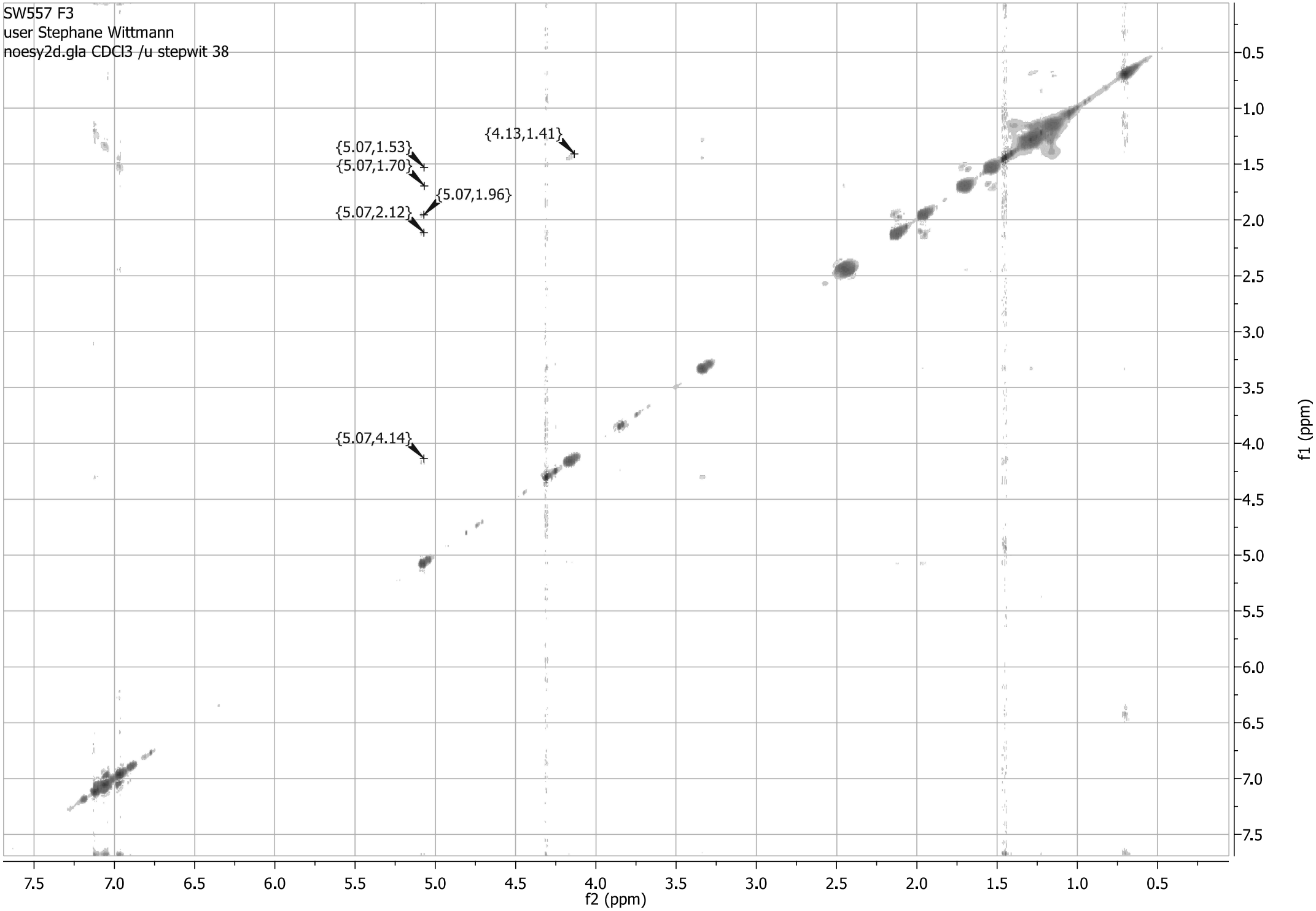
7.32 7.07 7.06 5.23 5.22 4.45 4.33 4.31 4.29 4.28 3.51 3.45 2.66 2.53 2.30 2.25 2.12 2.07 1.90 1.81 1.73 1.63 1.59 1.52 1.17 0.84

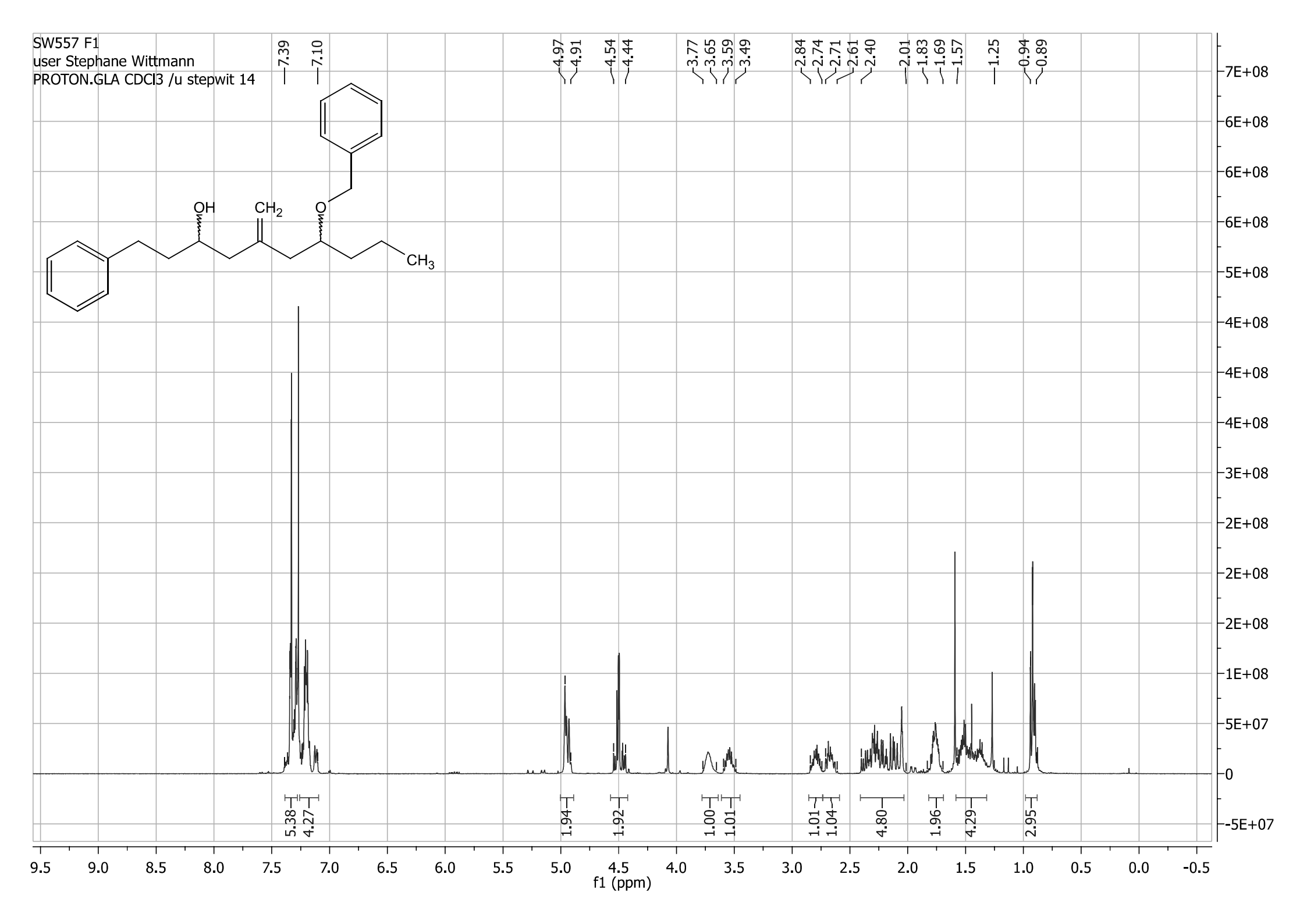
10.55 1.00 1.97 0.99 1.00 1.99 0.96 1.01 1.01 1.06 2.96 6.41 3.18

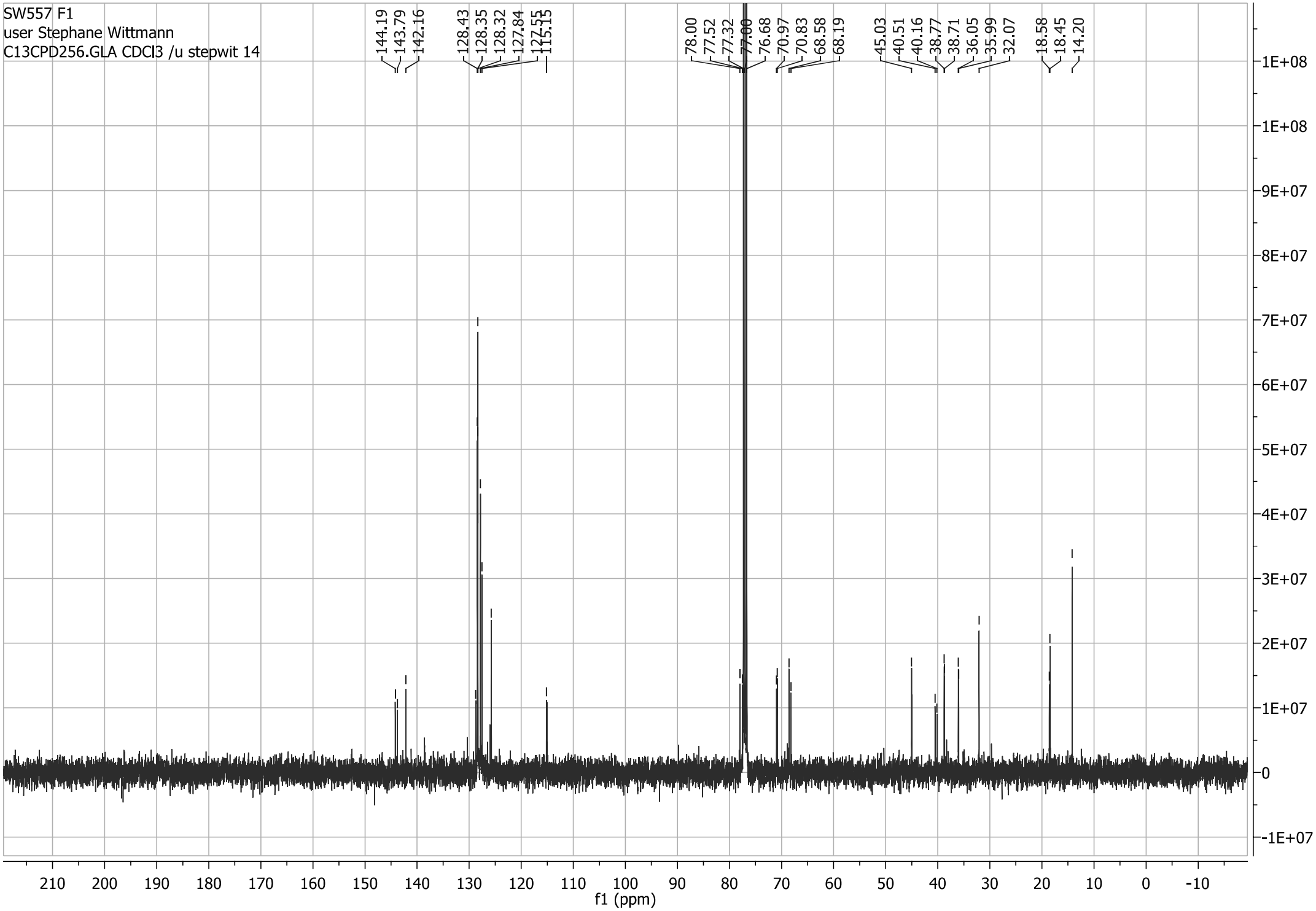
6E+08 6E+08 5E+08 4E+08 4E+08 4E+08 3E+08 2E+08 2E+08 2E+08 1E+08 5E+07 0 -5E+07

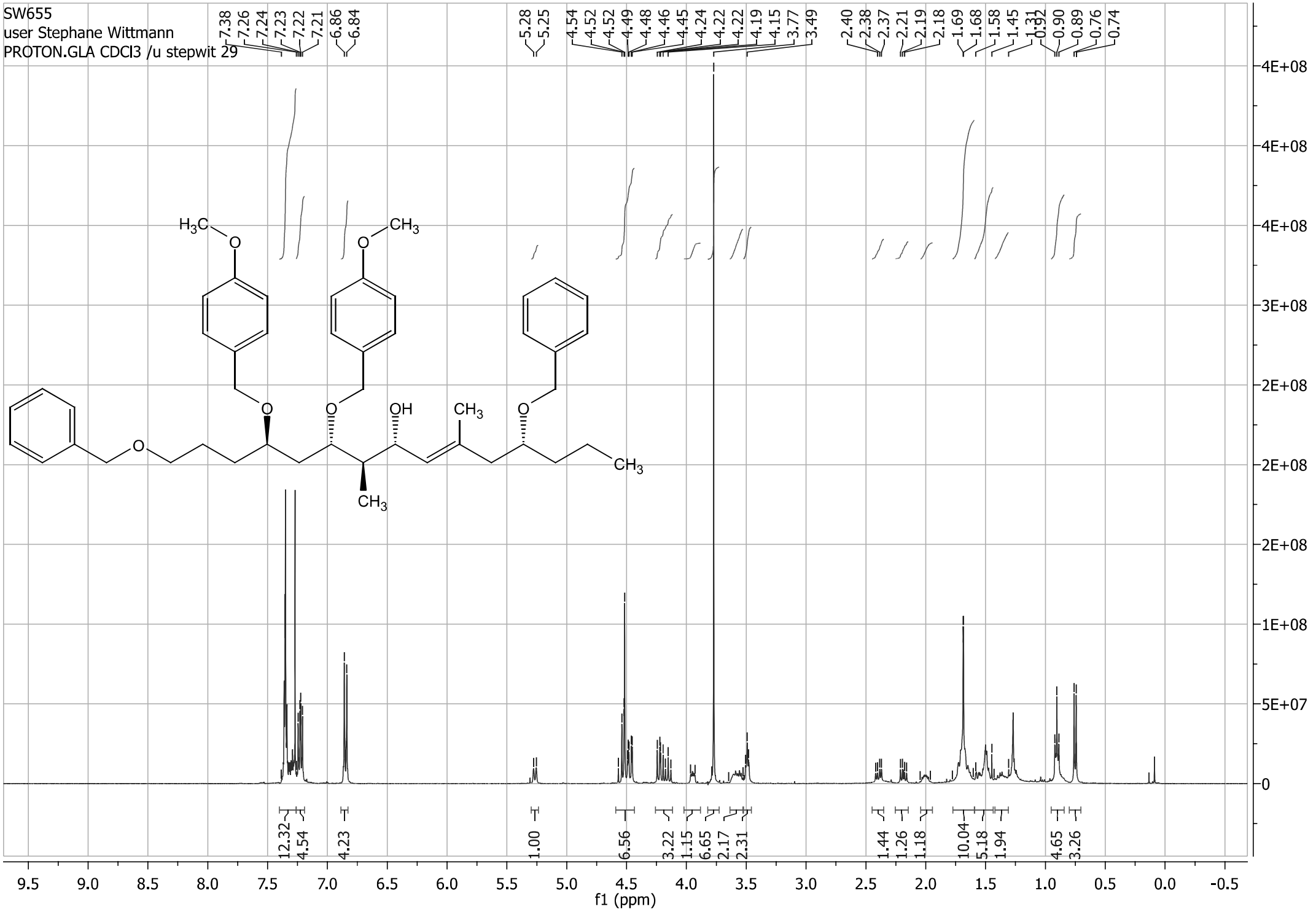
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

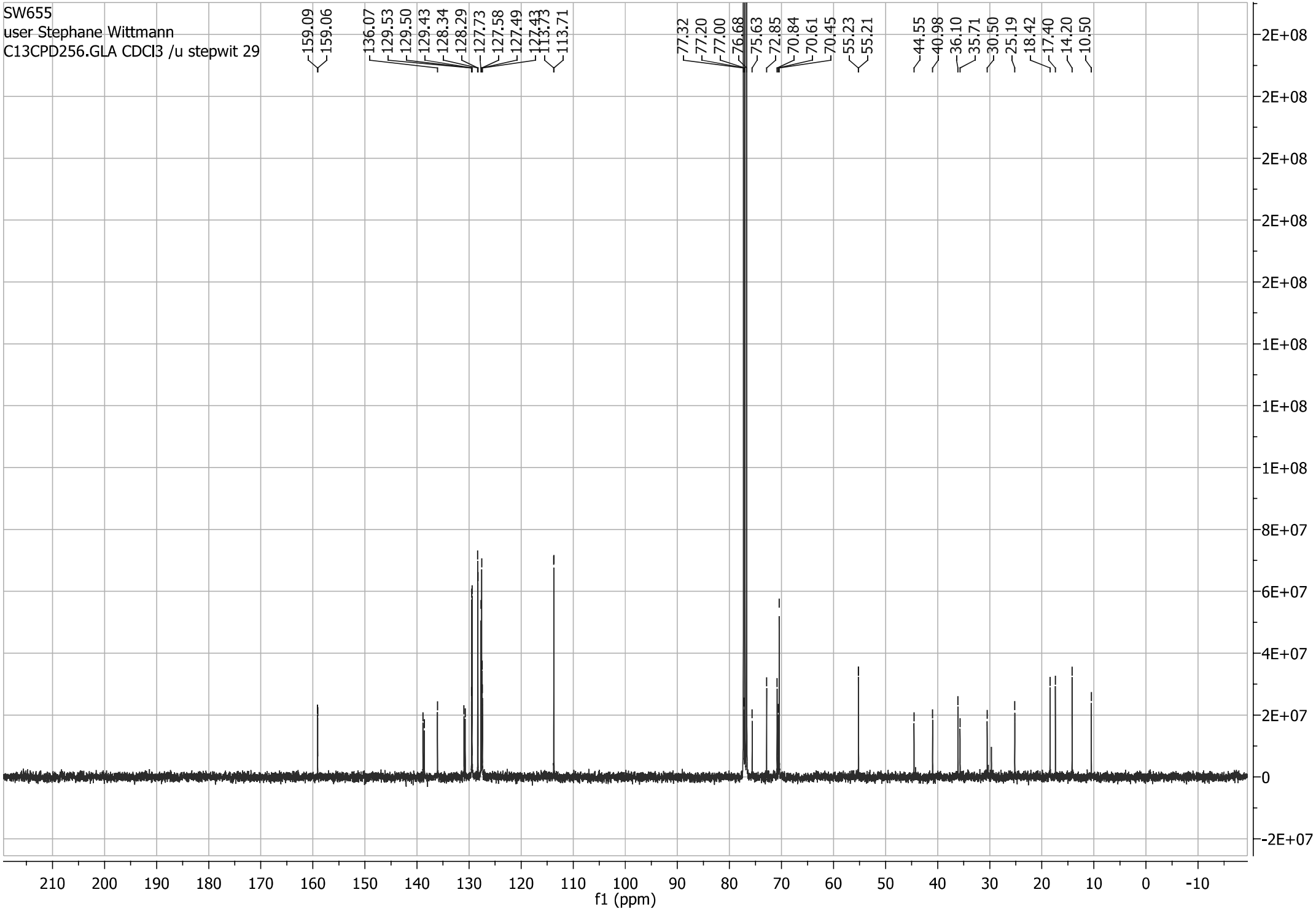

SW558 F3
user Stephane Wittmann
C13CPD1024.GLA CDCl3 /u stepwit 37
141.98
138.87
136.19
130.32
128.35
128.33
128.32
128.27
127.69
127.48
125.77
77.25
77.00
76.75
70.87
67.97
44.46
39.11
36.20
31.77
18.51
17.13
14.22
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

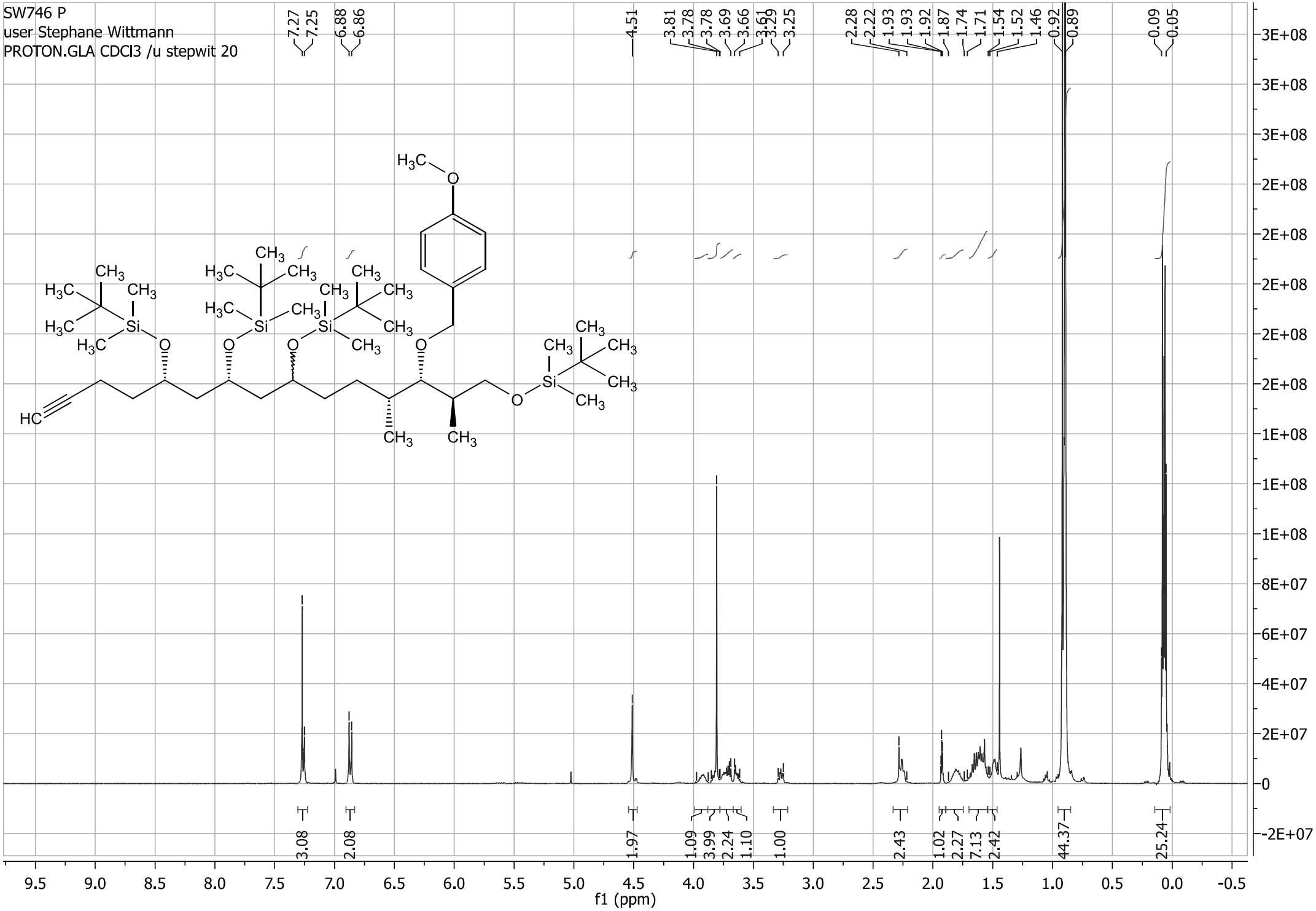

SW557 F3
user Stephane Wittmann
noesy2d.gla CDCl3 /u stepwit 38
{5.07,1.53}
{5.07,1.70}
{5.07,1.96}
{5.07,2.12}
{4.13,1.41}
{5.07,4.14}
f2 (ppm)
f1 (ppm)

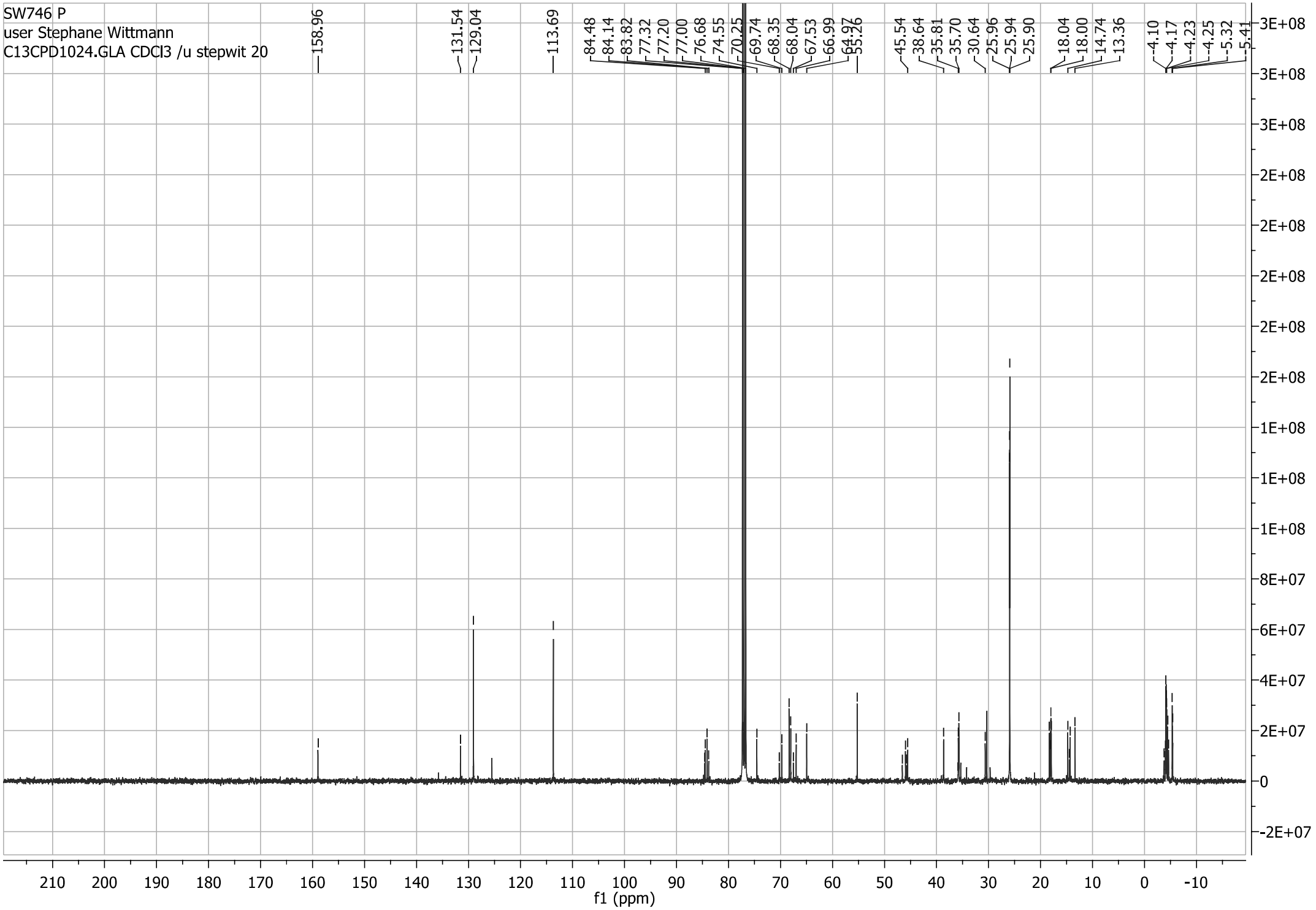

SW557 F1
user Stephane Wittmann
PROTON.GLA CDCl3 /u stepwit 14
7.39
7.10
4.97
4.91
4.54
4.44
3.77
3.65
3.59
3.49
2.84
2.74
2.71
2.61
2.40
2.01
1.83
1.69
1.57
1.25
0.94
0.89
OH
CH2
O
CH3
5.38
4.27
1.94
1.92
1.00
1.01
1.01
1.04
4.80
1.96
4.29
2.95
f1 (ppm)


SW557 F1
user Stephane Wittmann
C13CPD256.GLA CDCl3 /u stepwit 14
144.19
143.79
142.16
128.43
128.35
128.32
127.84
127.55
115.15
78.00
77.52
77.32
77.00
76.68
70.97
70.83
68.58
68.19
45.03
40.51
40.16
38.77
38.71
36.05
35.99
32.07
18.58
18.45
14.20
1E+08
1E+08
9E+07
8E+07
7E+07
6E+07
5E+07
4E+07
3E+07
2E+07
1E+07
0
-1E+07
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


SW655
user Stephane Wittmann
PROTON.GLA CDCl3 /u stepwit 29
7.38
7.26
7.24
7.23
7.22
7.21
6.86
6.84
5.28
5.25
4.54
4.52
4.52
4.49
4.48
4.46
4.45
4.24
4.22
4.22
4.19
4.15
3.77
3.49
2.40
2.38
2.37
2.21
2.19
2.18
1.69
1.68
1.58
1.45
1.31
0.92
0.90
0.89
0.76
0.74
H3C
O
CH3
O
O
O
OH
CH3
O
O
CH3
CH3
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
12.32
4.54
4.23
1.00
6.56
3.22
1.15
6.65
2.17
2.31
1.44
1.26
1.18
10.04
5.18
1.94
4.65
3.26
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


SW655
user Stephane Wittmann
C13CPD256.GLA CDCl3 /u stepwit 29
159.09
159.06
136.07
129.53
129.50
129.43
128.34
128.29
127.73
127.58
127.49
127.43
113.73
113.71
77.32
77.20
77.00
76.68
75.63
72.85
70.84
70.61
70.45
55.23
55.21
44.55
40.98
36.10
35.71
30.50
25.19
18.42
17.40
14.20
10.50
2E+08
2E+08
2E+08
2E+08
2E+08
1E+08
1E+08
1E+08
8E+07
6E+07
4E+07
2E+07
0
-2E+07
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


SW746 P
user Stephane Wittmann
PROTON.GLA CDCl3 /u stepwit 20
7.27
7.25
6.88
6.86
4.51
3.81
3.78
3.78
3.69
3.66
3.61
3.29
3.25
2.28
2.22
1.93
1.93
1.92
1.87
1.74
1.71
1.54
1.52
1.46
0.92
0.89
0.09
0.05
3.08
2.08
1.97
1.09
3.99
2.24
1.10
1.00
2.43
1.02
2.27
7.13
2.42
44.37
25.24
f1 (ppm)


SW746 P
user Stephane Wittmann
C13CPD1024.GLA CDCl3 /u stepwit 20
158.96
131.54
129.04
113.69
84.48
84.14
83.82
77.32
77.20
77.00
76.68
74.55
70.25
69.74
68.35
68.04
67.53
66.99
64.97
55.26
45.54
38.64
35.81
35.70
30.64
25.96
25.94
25.90
18.04
18.00
14.74
13.36
-4.10
-4.17
-4.23
-4.25
-5.32
-5.41
3E+08
3E+08
3E+08
2E+08
2E+08
2E+08
2E+08
2E+08
1E+08
1E+08
1E+08
8E+07
6E+07
4E+07
2E+07
0
-2E+07
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)