(1) NEW METHODS OF APPROACH TO THE BICYCLO[5:3:0]DECANE SYSTEM.

(2) ATTEMPTED SYNTHESIS OF THE INDACENES.

A THESIS SUBMITTED FOR THE DEGREE OF Ph.D.

by

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A C K N O W L E D G M E N T S.

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C O N T E N T S.

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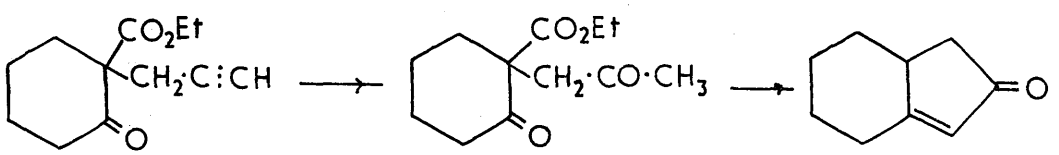
S U M M A R Y.

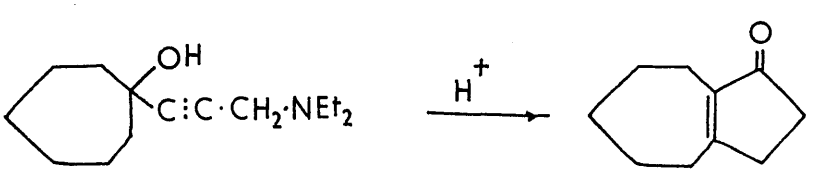
PART I.

NEW METHODS OF APPROACH TO THE BICYCLO[5:3:0]DECANE SYSTEM.

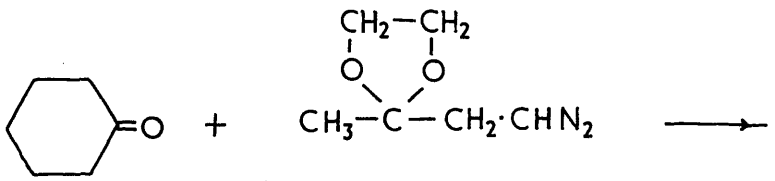
A. Condensation of propargyl bromide with 2-ethoxycarbonylcycloalkanones furnishes products which, by hydration and subsequent ring closure, give bicyclic compounds with a five-membered ring fused to the ring of the starting material. e.g.

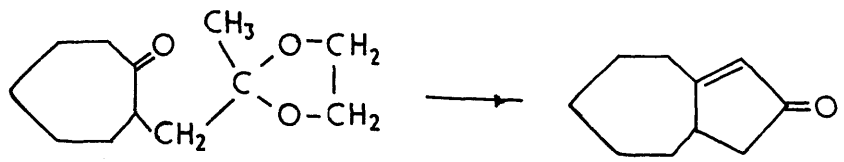


B. Condensation of cycloheptanone with readily available acetylenic Mannich bases gives products which may be converted directly to bicyclo[5:3:0]decane derivatives by heating with formic acid - phosphoric acid e.g.



C. Substituted cyclohexanones are subjected to ring expansion with a diazo-compound of such a nature that the resulting cycloheptanone possesses a side chain capable of condensing with the ring carbonyl group to yield bicyclo[5:3:0] decane derivatives directly e.g.





PART II.

ATTEMPTED SYNTHESIS OF THE INDACENES.

Attempted syntheses of the postulated quasi-aromatic hydrocarbons, symmetrical and assymmetrical indacenes have been investigated which involve dehydrogenation of the relevant hydroindacenes. The

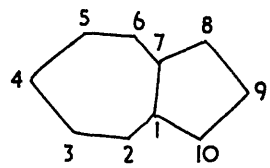
structure assigned to a supposed derivative of s-indacene reported in the literature has been shown to be erroneous.

PART I.

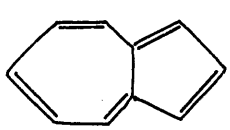
NEW METHODS OF APPROACH TO THE BICYCLO[5:3:0]DECANE SYSTEM.

NEW METHODS OF APPROACH TO THE BICYCLO [5:3:0] DECANE SYSTEM.

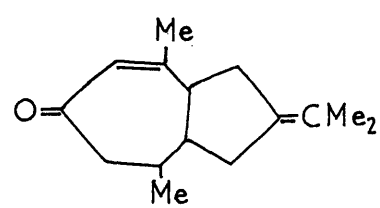
(a) Historical.



Interest in compounds containing the bicyclo [5:3:0] decane system stems from two sources. In the first place they may be readily dehydrogenated to give derivatives of the non-benzenoid aromatic system, Azulene[1], and hitherto most of the synthetic work in the field has been accomplished with this end in view. A less investigated aspect of this system relates to the synthesis of the naturally occurring sesquiterpenoid members of the group i.e. guaiol, partheniol and the α- and β- vetivones. This latter study is more complex because of the added stereochemical considerations.



Azulene



Vetivone

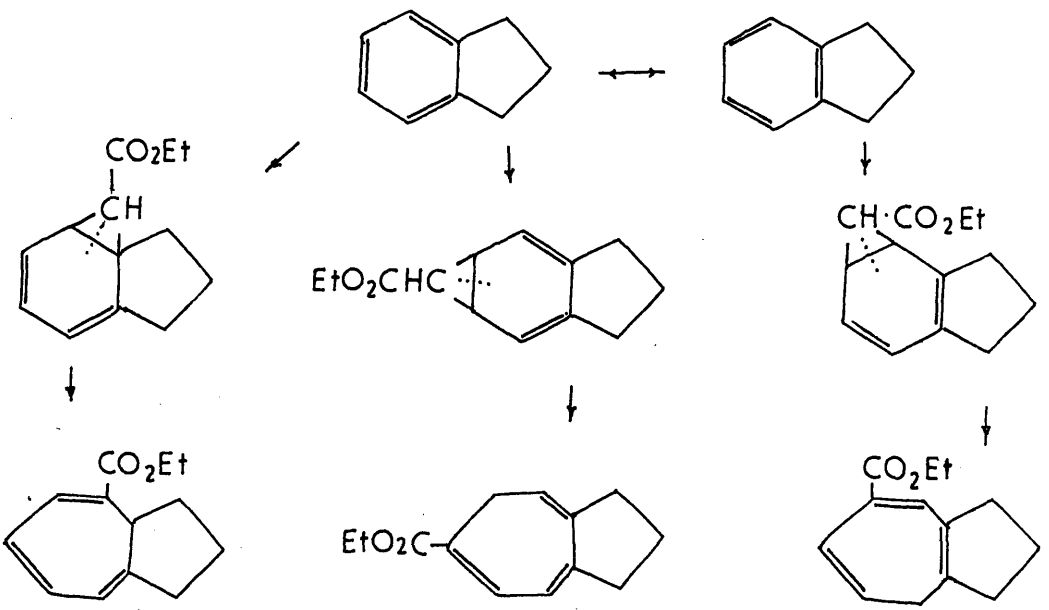
The methods hitherto employed for the preparation of bicyclo [5:3:0] decanes fall into the following classes.

A - RING EXPANSION METHOD.

Application of the ring expansion principle to aromatic and alicyclic compounds is by far the most widely used method for preparation of the bicyclo [5:3:0] decane nucleus.

1 - Buchner Type.

This procedure was discovered by Buchner[2] and was first applied to the synthesis of the bicyclo [5:3:0] decanes by Plattner[3]. In the simplest case, the action of diazoacetic ester on indane at elevated temperatures involved addition to the benzenoid ring and subsequent enlargement to the seven-membered ring.

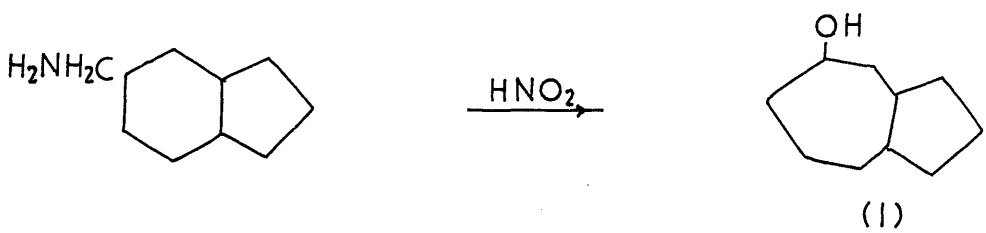


As is seen, the method gives rise to three position isomers, although this drawback becomes less serious if the ethoxycarbonyl group is to be eliminated at a later stage. The products from this process have always been dehydrogenated further to azulenes and the procedure has rarely been used to prepare the bicyclo [5:3:0] decanes themselves.

In a recent modification diazomethane has been used for the photochemical ring expansion of indane, thus leading to a convenient synthesis of azulene itself[4].

2 - Demjanow Type.

Related to the diazoacetic ester procedure is the Demjanow ring expansion method[5], first applied to bicyclo [5:3:0] decane synthesis by Arnold[6] and later by Plattner and coworkers[7]. In a typical case, treatment of 5-aminomethylhydrindane with nitrous acid furnished bicyclo [5:3:0] decan-3-ol (I).

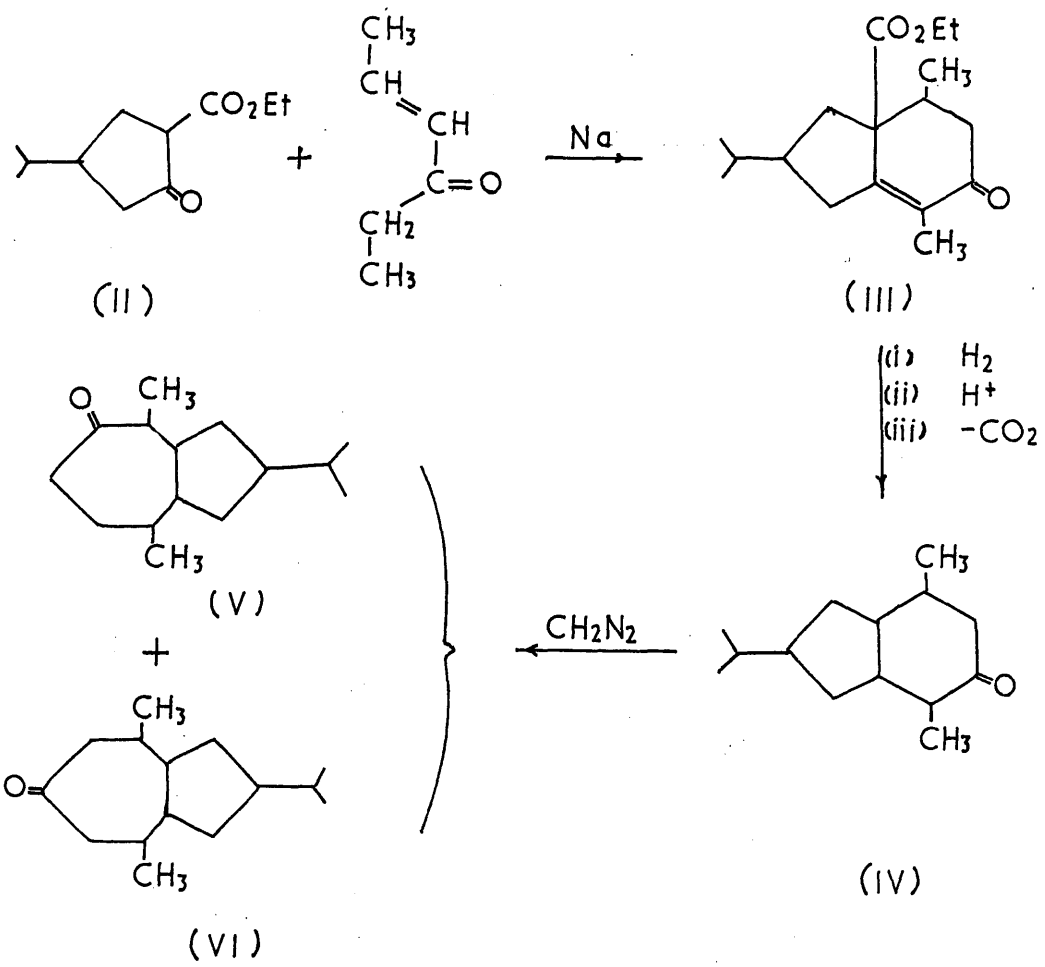


(I)

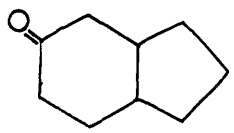
3- Diazomethane Ring Expansion of Ketones.

The application of the diazomethane ring expansion of ketones, a process introduced by Meerwein[8], to the

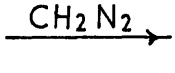
synthesis of bicyclo [5:3:0] decanes was introduced by Coats and Cook[9]. They condensed ethyl 4-isopropylcyclopentanone-2-carboxylate (II) with hex-2-en-4-one in presence of metallic sodium to give the bicyclic compound (III). After reduction, hydrolysis and decarboxylation of (III), the resultant bicyclic ketone (IV) was treated with diazomethane to give a mixture of the two ketones (V) and (VI) containing the vetivone carbon skeleton. However, the yields in this synthesis were very poor.

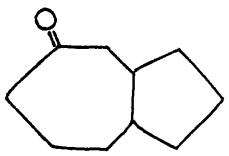


Using this method Arnold[6] obtained two ketones of structure (VII), both of which led to the same azulene.



5-Hydrindone



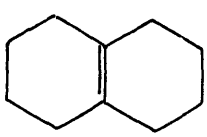


(VII)

He assumed therefore, that the two ketones were cis-trans isomers. Plattner[7] confirmed this view by separating the semicarbazones and isolating the pure cis- and trans- bicyclo [5:3:0] decan-3-ones.

B - FROM CYCLODECANE-1:6-DIONE

This route was adopted for the first total azulene synthesis by Pfau and Plattner[10]. In this procedure, 9-decalol is dehydrated to 9:10-octalin (VIII) which is then ozonised to give cyclodecane-1:6-dione (IX). This diketone undergoes an internal aldol condensation in the presence of sodium carbonate to give bicyclo [5:3:0] dec-1(7)-en-2-one (X).



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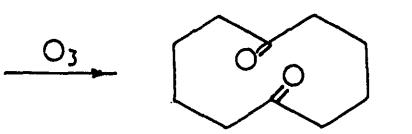

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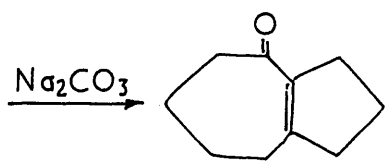
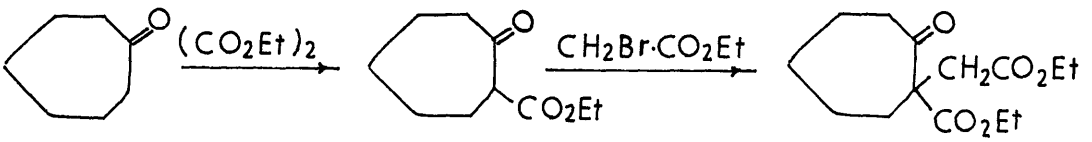


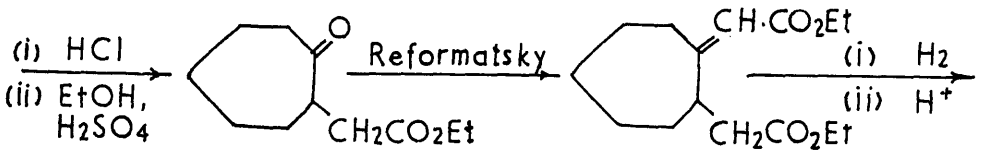
(X)

C - FROM CYCLOHEPTANONE.

Another method of approach to the bicyclo [5:3:0] decane system entails the elaboration of the five-membered ring on to a preformed seven-membered ring system. This procedure is well suited to the preparation of 8- and 9-substituted bicyclo [5:3:0] decanes. Thus Plattner, Furst, and Jirasek[11] used the following procedure for the preparation of 9-alkyl substituted bicyclo [5:3:0] decanes. Ethyl cycloheptanone-2-carboxylate (XI), was condensed with ethyl bromoacetate and the product was subjected to hydrolysis and decarboxylation to give ethyl cycloheptanone-2-acetate (XII). Subjection of this compound to a Reformatsky reaction followed by hydrogenation and hydrolysis gave cycloheptane-1:2-diacetic acid (XIII), which was then cyclised via its barium salt to give bicyclo [5:3:0] decan-9-one (XIV). The 9-alkyl substituent was finally introduced by interaction with a Grignard reagent and dehydration of the carbinol produced.



(XI)



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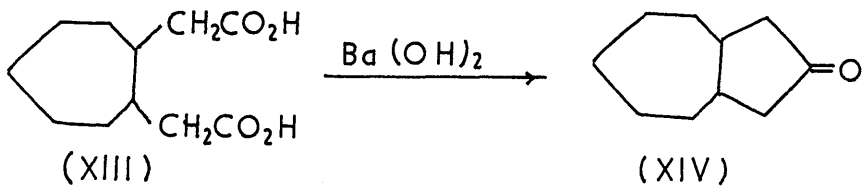
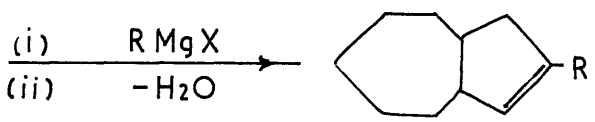
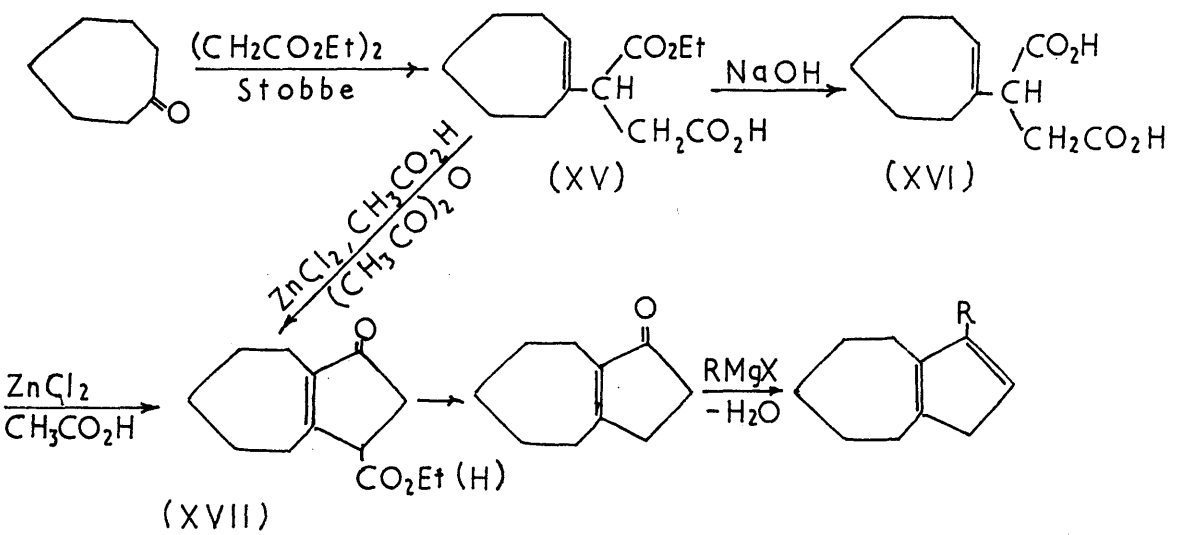


(XIII) (XIV)



For the preparation of 8-substituted compounds, Plattner and Buchi[12] applied a modified Stobbe condensation as follows

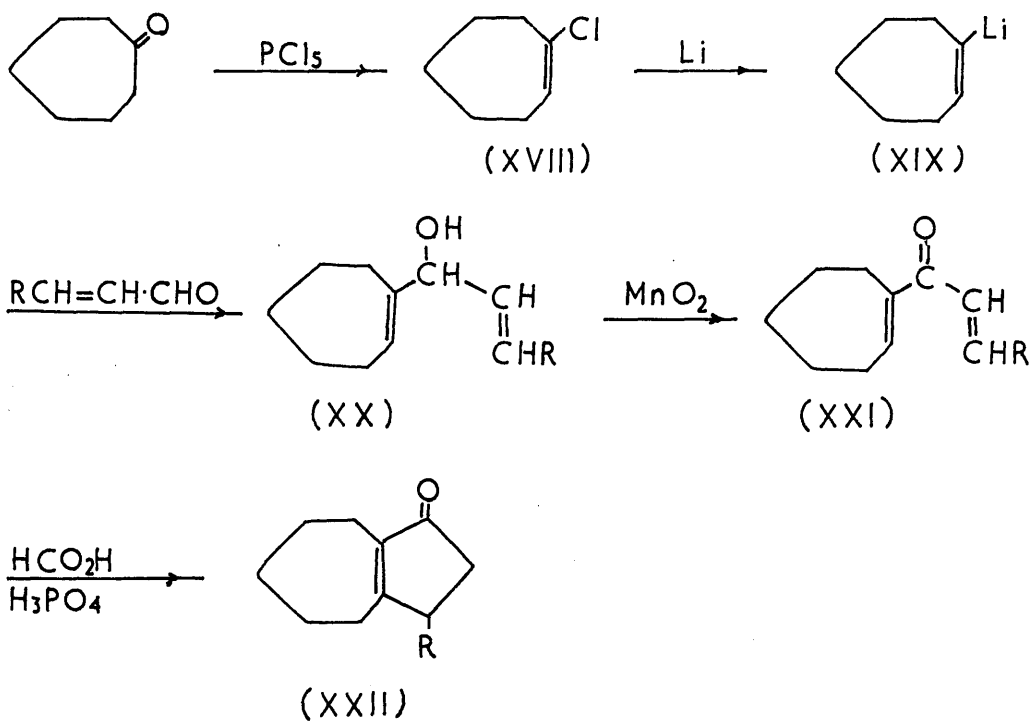


(XV) (XVI) (XVII)

It will be seen that either the initial half ester (XV) or the hydrolysed product (XVI) can be cyclised to the keto acid (XVII).

Recently Braude and Forbes[13] have developed a five stage process for the conversion of cycloheptanone imto bicyclo [5:3:0] dec-1(7)-en-8-one as follows.

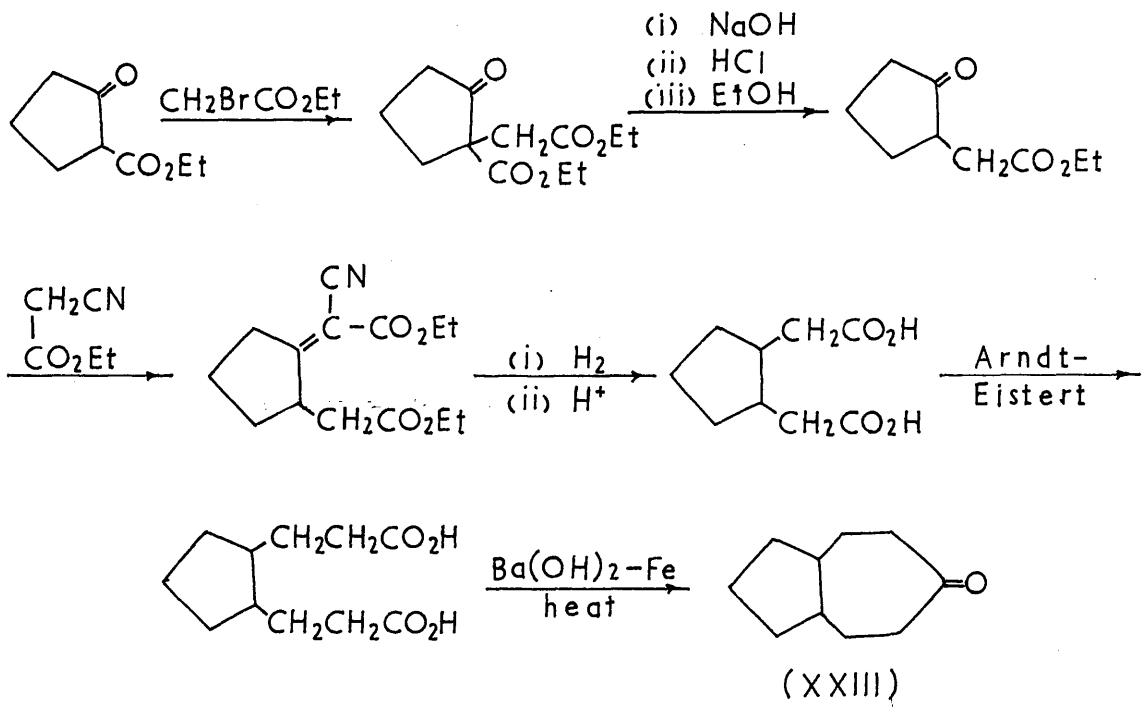
1 - Chlorocycloheptene (XVIII), prepared by treating cycloheptanone with phosphorus pentachloride, was converted into 1-cycloheptenyl lithium (XIX) by reaction with lithium metal in ether suspension. The lithium alkenyl then underwent the usual addition reaction with acraldehyde or crotonaldehyde, to give the dialkenyl carbinol (XX). Oxidation of the latter with manganese dioxide in petrol suspension afforded the dialkenyl ketone (XXI). Treatment of this ketone with a hot mixture of formic and phosphoric acids resulted in cyclisation to the bicyclo [5:3:0] dec-1(7)-en-8-one (XXII).



D - FROM CYCLOPENTANONE.

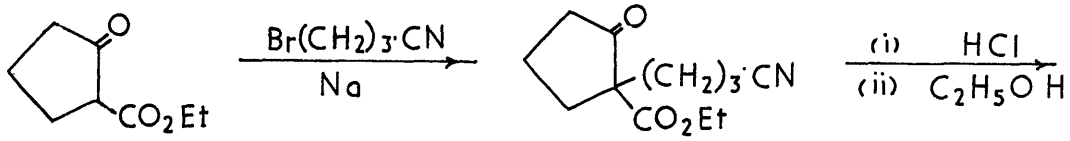
This procedure has been found to be well suited for the synthesis of 3- and 4- substituted bicyclo [5:3:0] decanes, and it is potentially adaptable to the preparation of 2-substituted derivatives. The 4-alkyl substituents are usually inaccessible by any other route.

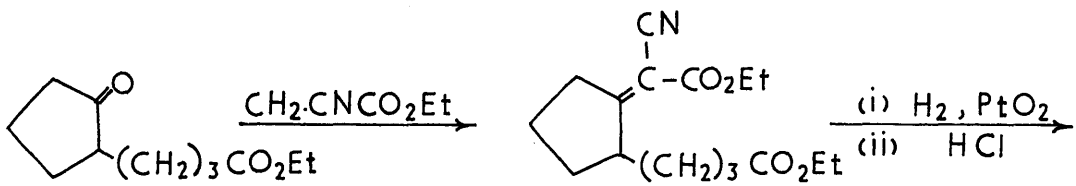
Sorm and Fajkes[14], and Plattner and Studer[15] independently synthesised bicyclo [5:3:0] decan-4-one (XXIII) from ethyl cyclopentanonecarboxylate by a substantially identical method in the following manner.

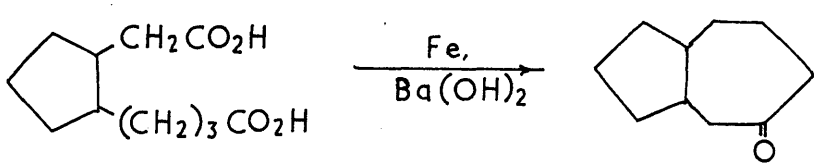


(XXIII)

bicyclo [5:3:0] Decan-3-one (XXIV) has also been synthesised from ethyl cyclopentanonecarboxylate by a related procedure[16] as follows.



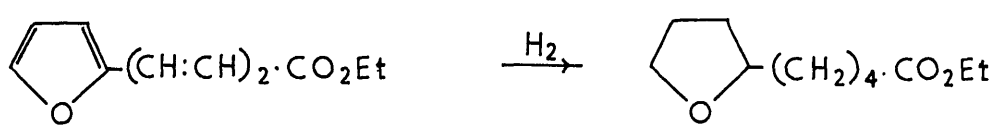


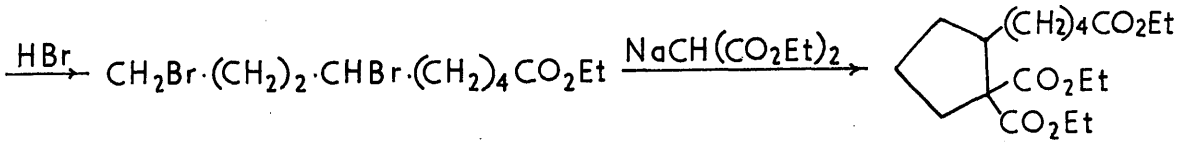


(XXIV)

E - FROM FURFURAL

The following ingenious method of preparing bicyclo [5:3:0] decan-2-one (XXV) has recently been described by Pommer[17]; this approach needs neither a cycloheptane nor a cyclopentane as an initial building unit but employs the readily available furfural as starting material.

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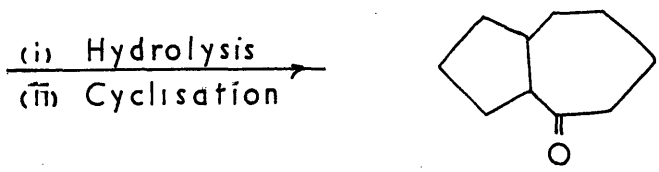
CH2Br·(CH2)2·CHBr·(CH2)4CO2Et
NaCH(CO2Et)2
(CH2)4CO2Et
CO2Et
CO2Et


(i) Hydrolysis
(ii) Cyclisation
O

(XXV)

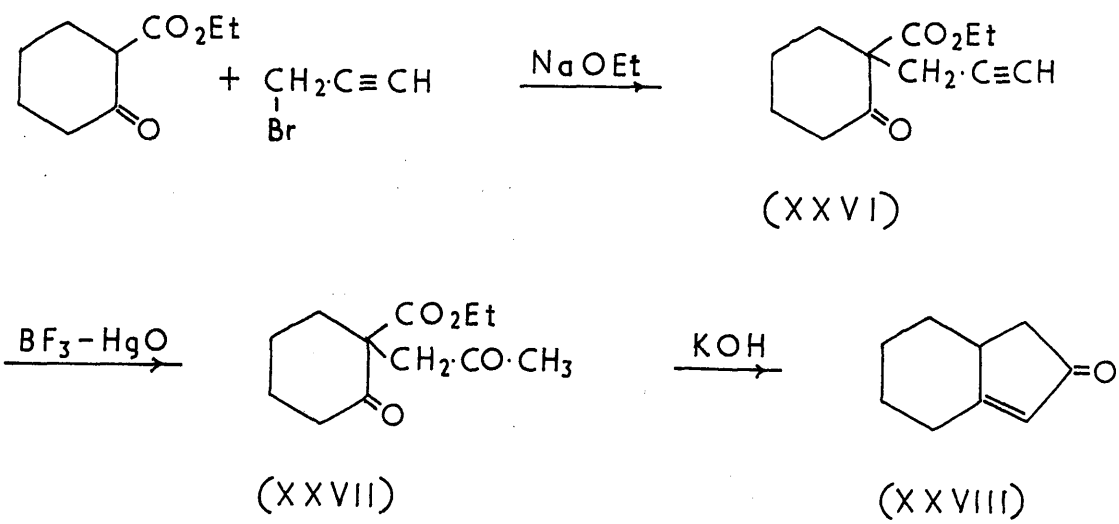
(b) Theoretical.

As may be seen from the previous section many of the synthetic methods leading to bicyclo [5:3:0] decanes are long and tedious and the overall yields are frequently very low. The main aim of this work has been to devise methods which eliminate these disadvantages.

A - The Propargyl Bromide Approach.

This approach utilises the ready hydration of a triple bond to the corresponding ketone to build the five-membered ring on to a preformed cyclic ketone.

As a pilot experiment for this reaction, the synthesis of bicyclo [4:3:0] non-6-en-8-one (XXVIII) was carried out from the readily available ethyl cyclohexanonecarboxylate as follows.



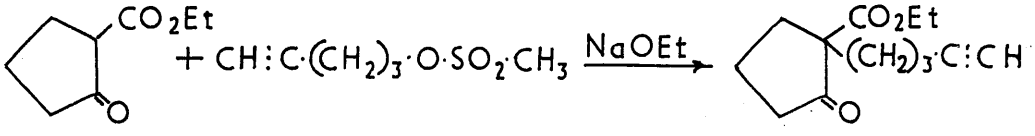
Reaction of the sodio-derivative of ethyl cyclohexanone-carboxylate with propargyl bromide in alcohol gave a good yield of the expected alkylation product (XXVI) which with methanolic boron trifluoride in the presence of mercuric oxide[18] yielded the hydration product (XXVII). Attempts to prepare (XXVII) directly from ethyl cyclohexanonecarboxylate and chloroacetone were unsuccessful under a variety of conditions, very small yields of impure products being obtained. When the diketone (XXVII) was heated with dilute potassium hydroxide solution in an atmosphere of nitrogen, an intramolecular aldol-type condensation took place with concomitant hydrolysis and decarboxylation to furnish finally the hitherto unknown bicyclic ketone (XXVIII).

Although this synthesis involved only a few steps and the over-all yield was quite high, it was not considered very satisfactory for the preparation of bicyclo [5:3:0] dec-1(10)-en-9-one as the starting material in this case, ethyl cycloheptanonecarboxylate, is not readily available. The process has, however, recently been successfully applied to this case elsewhere[19].

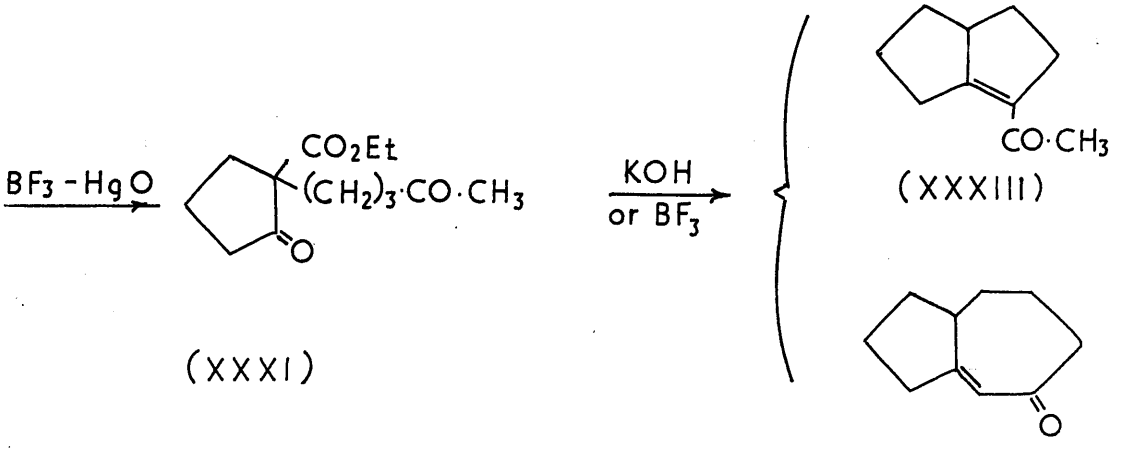
With the above successful reaction as precedent, an allied synthesis was attempted which involved the formation of a seven-membered ring on a preformed five-membered ring, starting from the readily available

ethyl cyclopentanonecarboxylate as follows.

Pent-1-yn-5-yl methanesulphonate (XXIX), prepared from pent-1-yn-5-ol and methanesulphonyl chloride in pyridine, was condensed with the sodio-derivative of ethyl cyclopentanonecarboxylate in alcohol to give a good yield of the ester (XXX); the yield was improved by carrying out the condensation in xylene. On treatment of this ester (XXX) with methanolic boron trifluoride in the presence of mercuric oxide[18], the hydration product (XXXI) was produced.



(XXIX) (XXX)

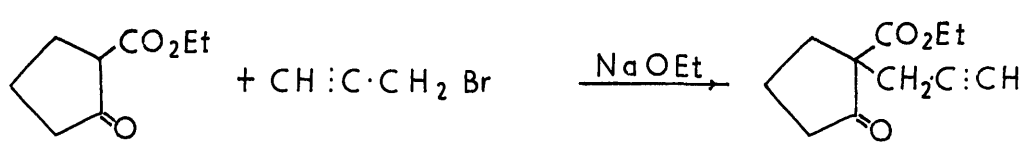


(XXXI) (XXXIII)

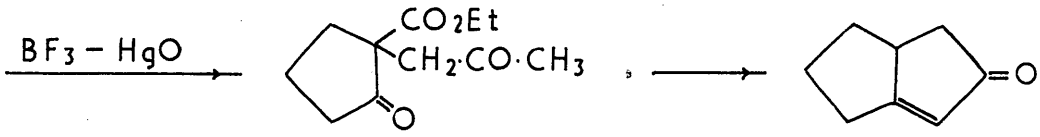
(XXXII)

It was expected that on treatment of the diketone (XXXI) with dilute potassium hydroxide solution, an intramolecular aldol-type condensation similar to that described above will take place with concomitant hydrolysis and decarboxylation of the ester grouping to furnish either (XXXII) or (XXXIII), or, a mixture of both. However, treatment of the diketone (XXXI) with dilute potassium hydroxide solution in an atmosphere of nitrogen gave a very small amount of a complex mixture containing ketonic material which gave a pale yellow 2:4-dinitrophenyl-hydrazone, thus showing the absence of the α:β-unsaturated ketonic group present in both of the expected compounds (XXXII) and (XXXIII). It is possible that under the condition of the cyclisation fission of the five-membered ring occurred, a reaction which has been noted before.

The same difficulty was encountered when the propargyl bromide procedure was applied to ethyl cyclopentanonecarboxylate in the hope of preparing a pentalane derivative (XXXVI)



(XXXIV)

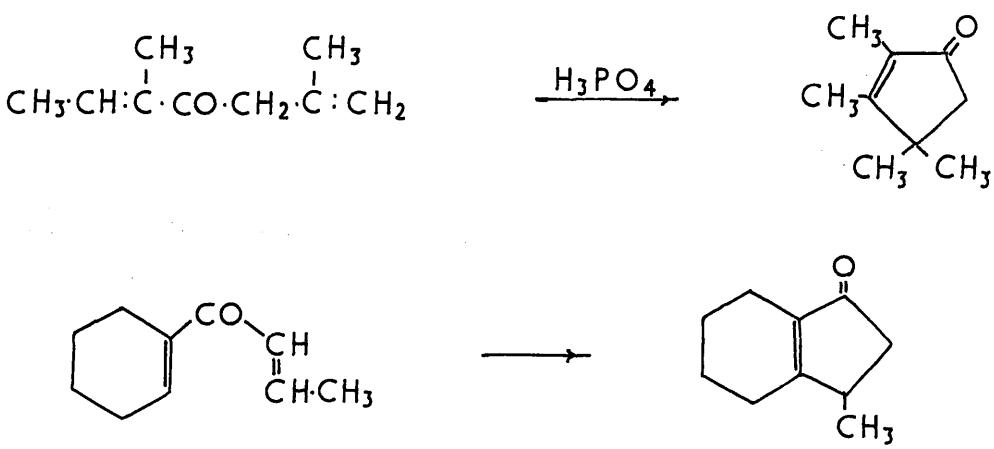


(XXXV) (XXXVI)

In this case, propargyl bromide reacted with the sodio-derivative of ethyl cyclopentanonecarboxylate to give the expected product (XXXIV). The diketone (XXXV) was obtained via the hydration of the acetylenic ketoester (XXXIV) by the method described above[18]; in this case the diketone (XXXV) was found to be preparable, although in smaller yield, by the direct interaction of chloroacetone with the sodio-derivative of ethyl cyclopentanonecarboxylate. However, treatment of this diketone (XXXV) with a variety of reagents such as sodium ethoxide in alcohol, potassium tert.-butoxide in tert.-butanol and dilute aqueous potassium hydroxide failed to furnish the required bicyclo [3:3:0] oct-1-en-3-one (XXXVI).

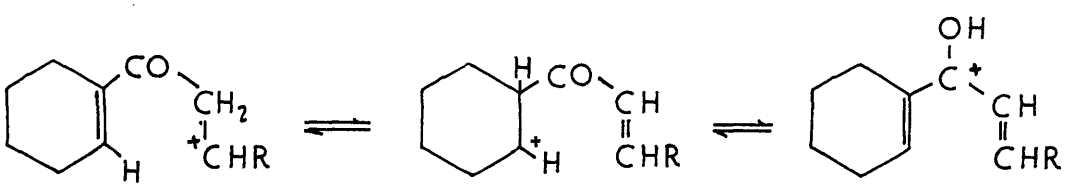
B - The Mannich Base Approach.

The acid induced cyclisation of a wide variety of vinyl allyl and divinyl ketones to substituted cyclopentenones, has been described recently in a series of memoirs by Nazarov and co-workers[20], the most general procedure involving treatment with a hot mixture of phosphoric and formic acids, e.g.

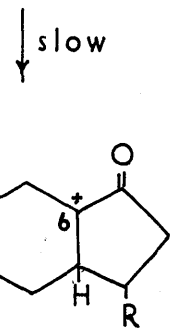


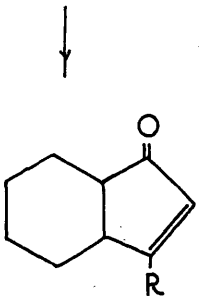
The mechanism of the Nazarov reaction has been discussed by Braude and Coles[21] with particular reference to the bicyclic examples of the type (XXXVIII). They defined the prime function of the acid medium in these reactions as that of a proton-donor; the ethylenic compound, acting as a weak base, is converted into a carbonium ion by reversible addition of one or more protons. The subsequent steps of the reaction consist

of the formation of the new carbon-carbon link accompanied by the transference of the positive charge to $C_{(6)}$ and the reversible loss of a proton from the new ion (XXXVIIIa).

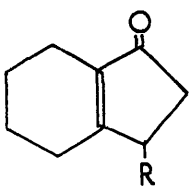


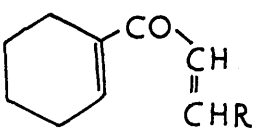
(XXXVIIa) (XXXVIIb) (XXXVIIc)





(XXXVIIIa) (XXXIX)



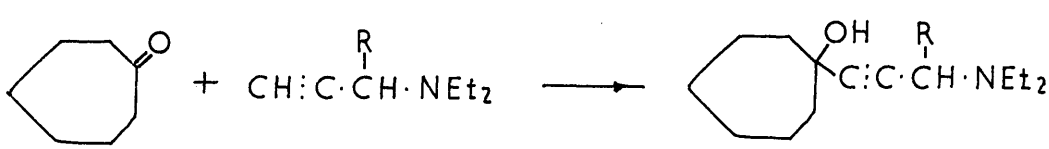


(XXXVIII) (XXXVII)

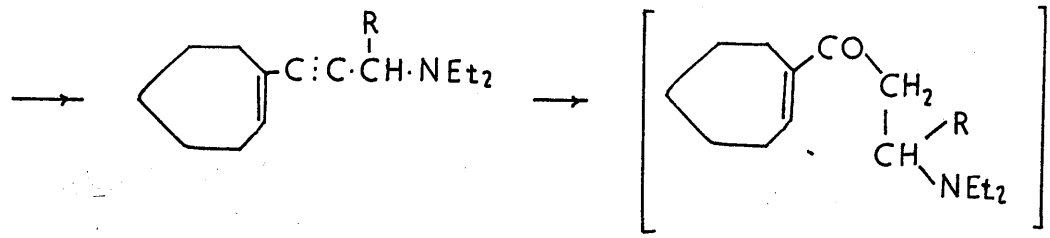
Cyclisation of (XXXVIIb) would lead to the ketone (XXXIX); since none of the latter is detected, the rate of cyclisation of (XXXVIIa) must either be faster than that of (XXXVIIb), or, as appears more likely, the equilibrium proportion of (XXXVIIa) must be considerably higher than that of (XXXVIIb).

The wide applicability of the reaction suggested its extension to compounds of the bicyclo [5:3:0] decane system. This approach has indeed already been envisaged by Braude and Forbes[13] in their method already described on p. 8 whereby cycloheptanone was converted into bicyclo [5:3:0] dec-1(7)-en-8-one in five stages. While presenting several novel features, the route involved is rather lengthy and is not readily adaptable to large-scale working.

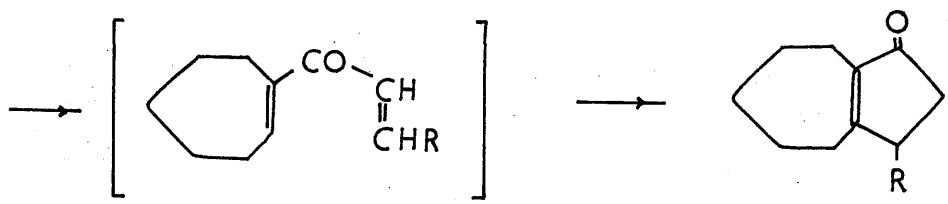
A new approach was suggested by the recent availability of acetylenic amines of the general type (XL) which are obtainable by subjecting acetylene to the Mannich reaction[22]. By their use a convenient two-stage conversion of cycloheptanone into bicyclo [5:3:0] dec-1(7)-en-8-one (XLV; R = H) has been achieved.



(XL) (XLI)



(XLII) (XLIII)

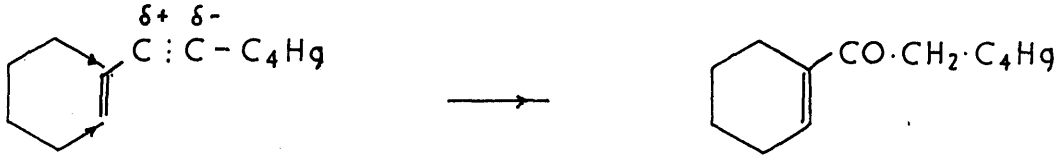


(XLIV) (XLV)

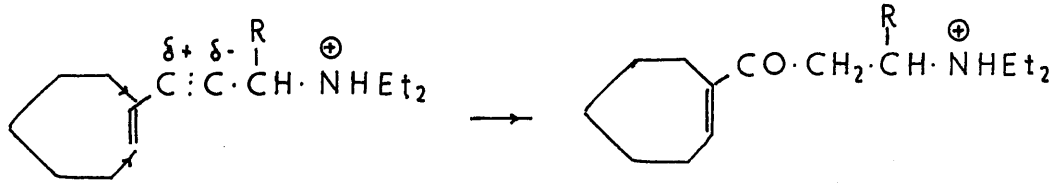
A condensation in liquid ammonia between cycloheptanone and the lithium salt of 3-diethylaminoprop-1-yne(XL; R = H) (prepared in situ by treating 2-bromo-3-diethylaminoprop-1-ene with two mols. of lithamide) gave the corresponding acetylenic carbinol (XLI; R = H). Heating this compound

with phosphoric acid - formic acid yielded mainly the dehydration product, the enyne (XLII; R = H) together with a small amount of the cyclised product (XLV; R = H). When the process was repeated in the presence of a small quantity of mercuric acetate, conversion to bicyclo [5:3:0] dec-1(7)-en-8-one (XLV; R = H) ensued in moderate yield. The identity of the material was confirmed by a mixed melting point of its semicarbazone with an authentic specimen.

The rationale of this novel cyclisation may be envisaged as follows. The initial formation of the dehydration product (XLII; R = H) is followed by the hydration of the triple bond to form the unsaturated diethylaminoketone (XLIII; R = H). The mode of addition leading to this vinyl ketone rather than to the isomeric allyl ketone may be confidently predicted from the results of Hamlet, Henbest, and Jones[18] on the hydration of substituted vinylacetylenes.



(XLVI) (XLVIa)



(XLIIa) (XLIIIa)

Thus in the case of the vinylacetylene (XLVI) these workers found that the hydration yielded the conjugated ketone (XLVIa) rather than the alternative isomer. In the case of (XLIIa) this mode of hydration would be favoured even more because of the electron attracting properties of the nearby tertiary ammonium cation formed in the acid medium.

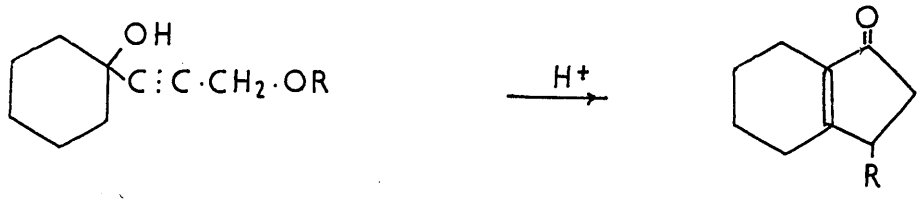
The hydration product (XLIII) is seen to be a β-diethylaminoketone and the elimination of diethylamine from this product to form the divinyl ketone (XLIV) is a reaction for which many precedents are available[23]. Finally, cyclisation of (XLIV) by the mechanism already described (p. 18) leads to the bicyclo [5:3:0] decanone (XLV; R = H).

In support of this mechanism, it was found that the postulated intermediate, the ethylenic-acetylenic amine (XLII), underwent cyclisation to (XLV) under the

same conditions. The other hypothetical intermediate, the diethylaminoketone (XLIII) was not readily available, but the six membered ring analogue of (XLIII) (readily prepared by a Mannich reaction on 1-acetylcyclohex-1-ene[24]) was found to undergo ready cyclisation to the six-membered analogue of (XLV) under the same conditions.

Extension of the synthesis to the homologous 3-diethylaminobut-1-yne (XL; R = CH_3) gave the corresponding acetylenic alcohol (XLI; R = CH_3). The presence of the methyl group in this compound greatly facilitated its cyclisation to (XLV; R = CH_3), the conversion proceeding smoothly in the absence of mercuric salt.

The attractiveness of this procedure from the preparative point of view is further enhanced by the ease of separation of the neutral product from any unchanged basic intermediates.

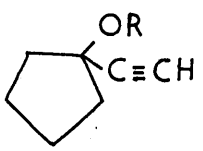


(XLVII) (XLVIII)

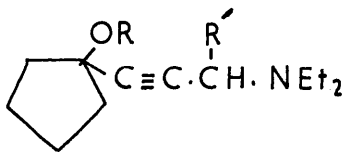
Application of the procedures to cyclohexanone yielded bicyclo [4:3:0] non-1(6)-ene-7-one (XLVIII; R = H) and its 9-methyl homologue (XLVIII; R = CH_3). The former compound was also obtained by the cyclisation of 1-(3′-hydroxyprop-1′-ynyl) cyclohexan-1-ol (XLVII; R = H), prepared from cyclohexanone and propargyl alcohol[25]; in this case elimination of water occurs instead of elimination of diethylamine. In an attempt to increase the overall yield of the above cyclisation, cyclohexanone was condensed with 2-prop-2′-yne-1′-yloxytetrahydropyran[26] to give 1-(3′-tetrahydropyranyl-2-oxyprop-1′-ynyl) cyclohexan-1-ol (XLVII; R = 2-tetrahydropyranyl). The condensation was carried out both via the Grignard complex and by means of lithamide in liquid ammonia; the latter process gave a superior yield. Cyclisation of (XLVII; R = 2-tetrahydropyranyl) with formic-phosphoric acid mixture gave (XLVIII; R = H) in higher yield.

An attempt was also made to apply the process to the production of pentalane derivatives. Reaction of both the Grignard complex of 3-diethylaminobut-1-yne (XL; R = CH_3), and the lithium salt of 3-diethylaminoprop-1-yne (XL; R = H) with cyclopentanone gave disappointing

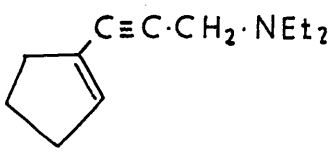
yields, much cyclopentylidenecyclopentanone being produced in both cases. The expected products, 1-(3′-diethylaminobut-1′-ynyl) cyclopentan-1-ol (L; R = H; R′= CH_3) and 1-(3′-diethylaminoprop-1′-ynyl) cyclopentan-1-ol (L; R = R′= H) respectively, were obtained in a very poor yield; both were unstable, quickly darkened in colour and resinified on standing.



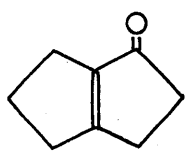
(XLIX)



(L)



(LI)

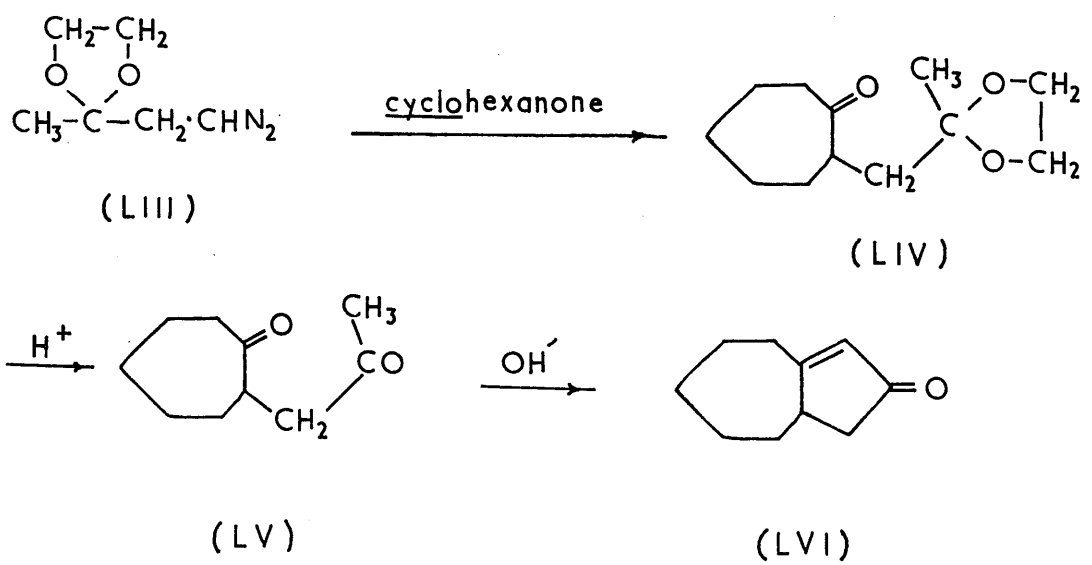


(LII)

As there were indications that this instability derived from the presence of a free hydroxyl group in these compounds a route was devised to (L; R = $CO.CH_3$; R′= H) in which this grouping was protected as its acetate. Thus interaction of 1-acetoxy-1-ethynylcyclopentane (XLIX) with diethylamine and paraformaldehyde[27] gave the required ester. Subjection of this compound to the cyclisation procedure did furnish the expected bicyclo [3:3:0]oct-1(5)-en-6-one (Lll), but much tar was simultaneously produced and the yield was correspondingly low. The main product was the intermediate vinylacetylene 1-(3′-diethylaminoprop-1′-ynyl) cyclopent-1-ene (Ll).

C- The 1-Diazo-3:3-(ethylenedioxy) butane Approach

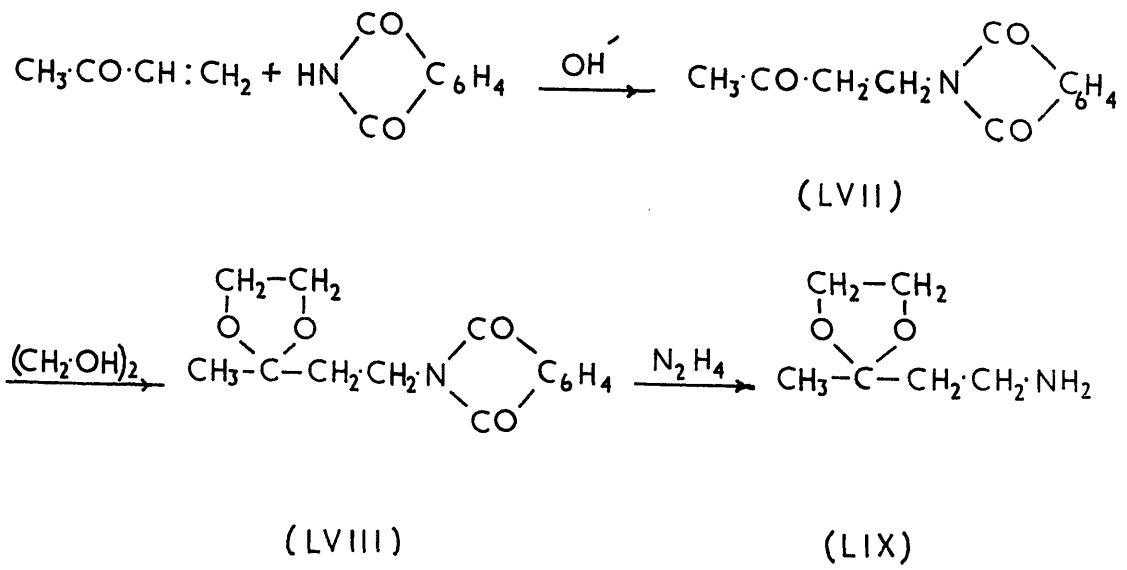
Most of the useful methods of synthesis of the bicyclo [5:3:0] decane carbon skeleton start from cycloheptanone. This ketone is itself not a readily available material and, when homologous cycloheptanones have to be prepared, the procedure becomes very tedious. A method was therefore envisaged by which the readily available cyclohexanones would be subjected to ring expansion by a diazo-compound of such a nature that the resulting cycloheptanone would possess a side-chain capable of condensing with the ring carbonyl group to yield the bicyclo [5:3:0] decane skeleton directly. Thus the older method of cycloheptanone formation followed by elaboration of the five-membered ring would be telescoped into one reaction.

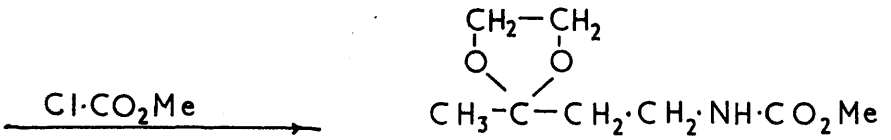


(LIII) (LIV) (LV) (LVI)

The substituted diazo-compound chosen for this purpose was 1-diazo-3:3-(ethylenedioxy) butane (LIII) which contains a potential carbonyl group. It would be reasonable to assume that ring expansion of cyclohexanone with this reagent should lead to the 2-substituted cycloheptanone (LIV), whence, by obvious procedures of acid hydrolysis and subsequent base-catalysed internal condensation bicyclo [5:3:0] dec-7-en-9-one (LVI) should result.

The first task was to prepare the urethane (LX) nitrosation of which would lead to the required diazo-compound (LIII). Initially this was achieved by the following route.





(LX)

The starting material, methyl vinyl ketone was treated with phthalimide in ethyl acetate solution in the presence of benzyl trimethylammonium hydroxide (Triton B) to give a good yield of the addition product (LVII). When this phthalimidoketone was condensed with ethylene glycol in the presence of a catalytic amount of toluene-p-sulphonic acid, it furnished the corresponding ethylene ketal (LVIII). Reaction of (LVIII) with hydrazine hydrate in aqueous solution removed the protecting phthalyl group and afforded the free ketal-amine (LIX) which was then condensed with methyl chloroformate in alkaline medium to give the desired urethane (LX).

Although the yields in this reaction sequence were good the process suffered from two drawbacks.

In the first place supplies of anhydrous methyl vinyl ketone were difficult to procure, and, even when available, the ketone polymerised very readily. Secondly the intermediate ketal-amine (LIX) was very soluble in water and its isolation in good yield involved a continuous extraction with ether of three days' duration. The process was obviously not suitable for large-scale working. An attempt to remove this second difficulty by addition of urethane itself to methyl vinyl ketone failed completely.

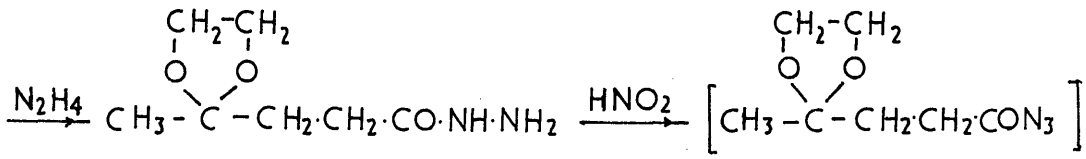
An alternative synthesis was therefore evolved which completely eliminated all the above difficulties.

$$CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CO_2Et \xrightarrow[H^+]{(CH_2\cdot OH)_2}$$

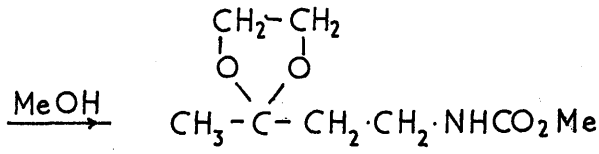
(LXI)

$$CH_3\text{-}C(O\text{-}CH_2\text{-}CH_2\text{-}O)\text{-}CH_2\cdot CH_2\cdot CO_2Et \longrightarrow$$

(LXII)



(LXIII)



(LX)

The starting material in this case was the readily available ethyl laevulinate (LXI) which was firstly converted into its ethylene ketal (LXII) by the usual process. Treatment of this ketal-ester with hydrazine then furnished the corresponding ketal-hydrazide (LXIII) which, when subjected to the Curtius degradation in the presence of methanol, yielded the urethane (LX) identical with the product prepared by the first route. No

difficulty was experienced in carrying through this sequence of reactions on a large scale involving 250g. of the ketal hydrazide (LXIII).

The nitrosation of the urethane (LX) proceeded normally to give the corresponding N-nitrosourethane. The normal procedure of ring expansion involves treatment of a methanolic solution of a cyclohexanone containing suspended potassium carbonate with the relevant N-nitrosourethane; the corresponding diazo-compound is thus generated *in situ* and reacts as soon as it is formed with the ketone. Application of this procedure to cyclohexanone and the above N-nitrosourethane unexpectedly failed completely even when a wide variety of experimental conditions were used. Although the theoretical volume of nitrogen was evolved, only unchanged cyclohexanone could be isolated. It was then found that the diazo-compound was reacting with the methanol as soon as it was formed; thus the theoretical volume of nitrogen was collected when the N-nitrosourethane was treated with methanol and potassium carbonate alone. This annoying complication was soon eliminated when it was found that ethanol was not attacked by the diazo-compound; this seems to be one of the few clear-cut cases where the slightly greater acidity

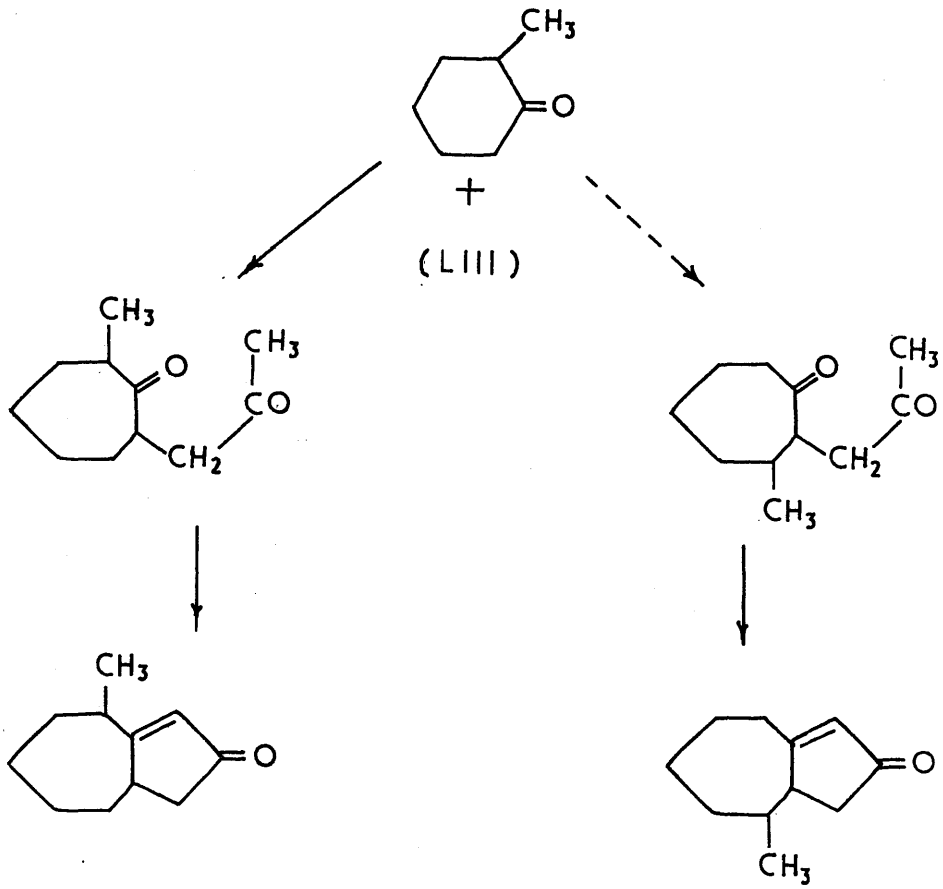
of methanol as compared to ethanol makes itself manifest. ($K_{methanol}$ 2 x 10^{-7}; $K_{ethanol}$ 1.5 x 10^{-9} at 25°)

Ring expansion of cyclohexanone using potassium carbonate in ethanol proceeded smoothly to give the expected substituted cycloheptanone (LIV), acid hydrolysis of which furnished 2-acetonylcycloheptan-1-one (LV). Base-catalysed internal aldol condensation of this diketone then furnished the required bicyclo [5:3:0] dec-7-en-9-one (LVI). On a preparative scale the isolation of the pure intermediates (LIV) and (LV) is unnecessary; the overall yield of (LVI) from the N-nitrosourethane was 30% and the process proved very reproducible.

Attention was then turned to the preparation of homologues. Application of the method to 4-methyl- and 4-isopropylcyclohexanones furnished 4-methyl- and 4- isopropyl bicyclo [5:3:0] dec-7-en-9-ones respectively. In these cases the steric relation between the 4-substituent and the ring junction at $C_{(1)}$ could theoretically be cis or trans but only one product was isolated from these reactions. The primary ring-expanded product (analogous to LIV) possesses a carbonyl group adjacent to the newly-introduced side chain and the

enolisation of this group would provide a ready means for this molecule to assume its most stable configuration; by plausible analogy with 1:4-disubstituted cyclohexanones this is almost certainly the trans-isomer.

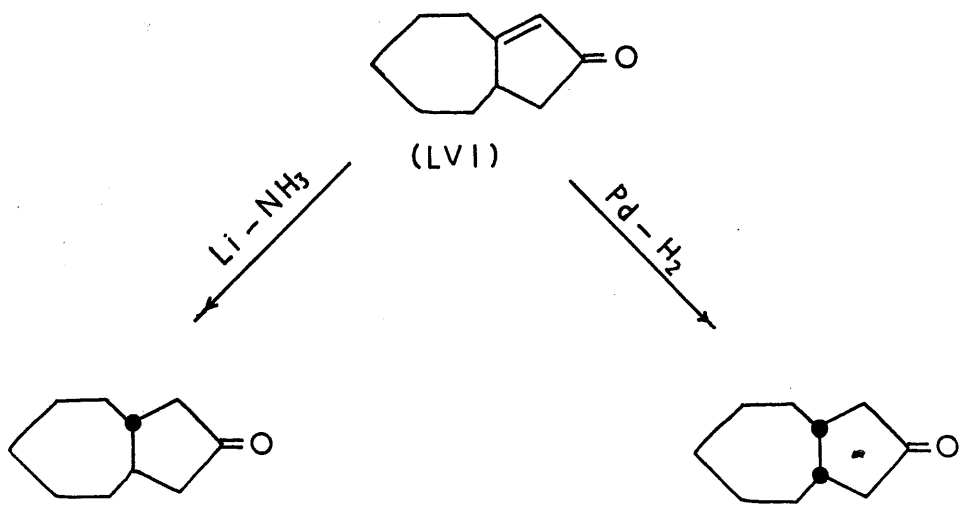
Application of this ring expansion procedure to 2-methyl-cyclohexanone could theoretically proceed to give two position isomers (LXIV) and (LXV).



(LXIV) (LXV)

In practice, the procedure applied to this ketone gave a very meagre yield of bicyclic ketone which seemed to be homogeneous as it furnished only one 2:4-dinitrophenylhydrazone. It is likely that the product possessed structure (LXIV) as the intermediate monocyclic diketone would involve less steric interference between the methyl and the acetonyl groups than would be the case in the intermediate for (LXV).

Application of the process to 2:6-dimethylcyclohexanone did not proceed smoothly and no isolatable product was encountered.

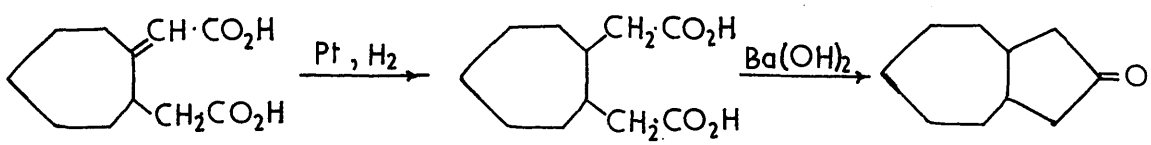


(LVI)

(LXVI)

(LXVII)

The availability of bicyclo [5:3:0]dec-7-en-9-one (LVI) by the above process suggested its conversion to the corresponding cis and trans saturated ketones by stereospecific reduction of the double bond. Catalytic hydrogenation of (LVI) furnished cis-bicyclo [5:3:0] decan-9-one (LXVII) characterised as the semicarbazone (m.p. 198-199°) and the 2:4-dinitrophenylhydrazone (m.p. 125-126°); similarly, reduction with lithium in liquid ammonia produced trans-bicyclo [5:3:0] decan-9-one (LXVI), semicarbazone (m.p. 221-223°) and 2:4-dinitrophenylhydrazone (m.p. 138°). The melting point of the latter semicarbazone agrees with that (m.p. 222-223°) recorded for a bicyclo [5:3:0] decan-9-one of unknown steric configuration[11] prepared by the cyclisation of a cycloheptane-1:2-diacetic acid (LXIX) which was in turn procured by the catalytic hydrogenation of the corresponding unsaturated acid (LXVIII).



(LXVIII) (LXIX)

It is highly probable that the reduction product (LXIX) consisted largely of the trans-isomer by analogy with results obtained for the corresponding cyclohexane derivative[40]. The cyclisation would then furnish the trans bicyclo-ketone, a conclusion in full agreement with the results described above.

E X P E R I M E N T A L

A.

bicyclo [4:3:0] Non-6-en-8-one.

Ethyl 2-Keto-1-propargylcyclohexane-1-carboxylate.

Ethyl 2-ketocyclohexane-1-carboxylate (12.5g.) was added to a solution of sodium ethoxide prepared from sodium (1.7 g.) in absolute ethyl alcohol (300 c.c.) and the mixture heated under reflux for half an hour. Propargyl bromide (10 g.) was then added to the boiling solution during one hour and heating was continued for another two hours. Most of the alcohol was removed on the steam bath, water (200 c.c.) was added to the residue and the product extracted with benzene (3 x 70 c.c.). Evaporation and distillation gave ethyl 2-keto-1-propargylcyclohexane-1-carboxylate (12 g.; 83%), b.p. 154°/12 mm., n_D^{19} 1.4590. In spite of the sharp boiling point, a satisfactory carbon analysis for this compound could not be obtained. The semicarbazone crystallised from aqueous alcohol in colourless needles m.p. 144°.

(Found : N, 15.7 . $C_{13}H_{19}O_3N_3$

requires : N, 15.8 %).

Ethyl 1-Acetonyl-2-keto-cyclohexane-1-carboxylate.

Ethyl2-keto-1-propargylcyclohexane-1-carnoxylate (7.3 g.) in methanol (15 c.c.) was added slowly to a catalyst solution prepared by warming together red mercuric oxide (0.5 g.), boron trifluoride - ether complex (0.2 c.c.), trichloroacetic acid (10 mg.), and methanol (1 c.c.). After the initial exothermic reaction was over, the mixture was shaken at room temperature for two hours and then poured into dilute sulphuric acid. After extraction with ether (3 x 50 c.c.) the combined ether extracts were shaken with dilute sulphuric acid then with water, dried (Na_2SO_4) and finally evaporated. Distillation gave ethyl 1-acetonyl-2-ketocyclohexane-1-carboxylate (6 g.; 75%) as a pale yellow oil, b. p. 144°/1mm., n_D^{19} 1.4504. In spite of the sharp boiling point of the product described above, a satisfactory carbon analysis for it could not be obtained. The semicarbazone crystallised from aqueous alcohol in plates m.p. 214°

(Found : N, 24.9 . $C_{14}H_{24}O_4N_6$

requires : N, 24.8 %).

Attempts to prepare the foregoing ester directly from ethyl 2-ketocyclohexane-1-carboxylate and chloroacetone were unsuccessful under a variety of conditions, very small yields of impure products being obtained.

Cyclisation

Ethyl 1-acetonyl-2-ketocyclohexane-1-carboxylate (3 g.) and aqueous potassium hydroxide solution (5%; 150 c.c.) were heated under reflux for six hours under nitrogen. After being cooled, the mixture was acidified with dilute sulphuric acid and the product extracted with ether (3 x 50 c.c.). Evaporation and distillation gave bicyclo [4:3:0] non-6-en-8-one (1.3 g.; 73%) as a colourless oil, b.p. 88°/4mm., n_D^{19} 1.5190.

(Found : C, 79.1 ; H, 8.9 . $C_9H_{12}O$

requires : C, 79.4 ; H, 8.8 %).

Light absorption in ethanol; λ max. 2280A° (ε = 16,500) and 2860A° (ε = 140) [Acheson and Robinson[28], record λ max. 2250A° (ε = 18,150) for 3-methylcyclopent-2-enone]. The 2:4-dinitrophenylhydrazone formed red

needles from alcohol m.p. 200°.

(Found : C, 57.0 ; H, 4.9 ; N, 18.1 . $C_{15}H_{16}O_4N_4$

requires : C, 56.9 ; H, 5.1 ; N, 17.7%).

Light absorption in ethanol λ max. 2580A° (ε = 19,000) and 3900A° (ε = 26,500). The semicarbazone crystallised from aqueous alcohol in leaflets m.p.224°.

(Found : N, 21.5 . $C_{10}H_{15}ON_3$

requires : N, 21.7 %).

Attempt Preparation of bicyclo [5:3:0] Dec-6-en-5-one.

Pent-1-yn-5-yl methanesulphonate.

In a three-necked flask fitted with a mechanical stirrer, a dropping funnel and a calcium chloride tube a mixture of pent-1-yn-5-ol (55g.) and dry pyridine (80 c.c.) was introduced and the flask cooled in ice-cold water. Methane sulphonyl chloride (100g.) was then added from the dropping funnel at such a rate that temperature of the reaction mixture did not rise above 25-30°. After the addition was complete, the stirring was continued for a further three hours. Decomposition with ice-cold water, extraction with ether and distillation gave pent-1-yn-5-yl methane-sulphonate (90g. ; 85%) as a colourless oil, b.p. 138°/9mm., n_D^{16} 1.4574.
(Found : C, 44.4 ; H, 5.96 . $C_6H_{10}O_3S$
requires : C, 44.4 ; H, 6.17 %).

Ethyl 2-Keto-1-(pent-1'-yn-5'yl) cyclopentane-1-carboxylate.

a) Ethyl 2-ketocyclopentane-1-carboxylate (20g.) was added to a solution of sodium ethoxide (from sodium, 3g.)

in absolute alcohol (200 c.c.) and the mixture was heated under reflux for half an hour. Sodium iodide (1g.) was then added followed by pent-1-yn-5-yl methanesulphonate (23g.) which was added over a period of one and a half hours while the mixture was being heated under reflux; heating was then continued for a further two hours. After removal of the alcohol, water was added and the reaction mixture was extracted with ether. Evaporation and distillation gave ethyl 2-keto-1-(pent-1′-yn-5′-yl) cyclopentane-1-carboxylate (17g. ; 60%) as a colourless oil b.p. 150°/9mm., n_D^{18} 1.4538.

In spite of the sharp boiling point of this product, no accurate analytical figures could be obtained.

(Found : C, 68.8 ; H, 8.5 . $C_{13}H_{18}O_3$

requires : C, 70.2 ; H, 8.1 %).

The semicarbazone crystallised from aqueous alcohol in colourless prisms m.p. 145°

(Found : C, 60.6 ; H, 7.6 ; N, 14.4 . $C_{14}H_{21}O_3N_3$

requires : C, 60.2 ; H, 7.5 ; N, 15.0 %).

b) Metallic sodium (2.3 g.) was atomised in dry xylene (200 c.c.) and ethyl 2-ketocyclopentane-1-carboxylate

(15.6g.) was then added during half an hour while the mixture was being stirred and heated under reflux. After a further half an hour's heating, pent-1-yn-5-yl methanesulphonate (16.2g.) was added and heating and stirring continued for a further 4 hours. Removal of the solvent under reduced pressure, addition of water and extraction with ether followed by distillation gave ethyl 2-keto-1-(pent-1'-yn-5'-yl) cyclopentane-1-carboxylate (18g. ; 81%) b.p. 118°/1mm., n_D^{19} 1.4532.

Ethyl 2-Keto-1-(pentan-2'-one-5'-yl)cyclopentane-1-carboxylate

A solution of the foregoing ester (17g.) in methanol (32 c.c.) was added slowly to a catalyst solution prepared by warming together red mercuric oxide (1.2g.), boron trifluoride - ether complex (0.4c.c.), trichloroacetic acid (20mg.), and methanol (3 c.c.). After the initial exothermic reaction was over, the mixture was shaken at room temperature for two hours and then poured into dilute sulphuric acid. After extraction with ether, the combined ether extracts were shaken with dilute sulphuric acid followed by water, dried (Na_2SO_4) and finally evaporated. Distillation gave ethyl 2-keto-1-(pentan-2'-one-

5'-yl) cyclopentane-1-carboxylate (15g. ; 83%) as a colourless oil, b.p. 122°/0.2 mm., n_D^{21} 1.4540.

(Found : C,63.6 ; H, 8.45 . $C_{13}H_{20}O_4$
requires : C,64.1 ; H, 8.3 %).

Attempted Cyclisation:

a) The foregoing ester (3g.) was heated under reflux with a 5% solution of aqueous potassium hydroxide (200 c.c.) for six hours under an atmosphere of nitrogen. After being cooled, the mixture was acidified with dilute sulphuric acid and the product extracted with ether. Evaporation and distillation gave a colourless oil (0.5g.), b.p. 86-118°/4mm. The substance afforded a light yellow 2:4-dinitrophenylhydrazone which could not be crystallised satisfactorily.

b) The above ester (1g.) was heated under reflux with boron trifluoride - ether complex (3 c.c.) for three hours; the colour of the mixture changed to light brown-red. Decomposition with potassium acetate and ice and extraction with ether gave pale yellow oil (0.1g.) which was converted into a bright-red 2:4-

dinitrophenylhydrazone. Repeated chromatography of this derivative afforded no pure compound.

Attempt Preparation of bicyclo[3:3:0]oct-1-en-3-one.

Ethyl 2-Keto-1-propargylcyclopentane-1-carboxylate.

To a solution of sodium ethoxide (from sodium, 2.3g) in absolute alcohol (100 c.c.) was added ethyl 2-ketocyclopentane-1-carboxylate (16g.) and the mixture was heated under reflux for half an hour. Propargyl bromide (12g.) was then added over a period of one hour and the heating was continued for a further two hours. Removal of the solvent, addition of water and extraction with ether followed by distillation gave ethyl 2-keto-1-propargylcyclopentane-1-carboxylate (12g. ; 60%) as a colourless oil, b.p. 125°/10mm., n_D^{17} 1.4630.

In spite of the sharp boiling point of the product no accurate analytical figures could be obtained.

(Found : C, 66.4 ; H, 7.8 . $C_{11}H_{14}O_3$

requires : C, 68.0 ; H, 7.2 %).

The semicarbazone crystallised from aqueous alcohol in colourless needles m.p. 126°.

(Found : N, 16.3 . $C_{12}H_{17}O_3N_3$

requires : N, 16.7 %).

Ethyl 1-Acetonyl-2-ketocyclopentane-1-carboxylate.

a) The foregoing ester (10g.) in methanol (30 c.c.) was added slowly to a catalyst solution prepared by warming together red mercuric oxide (0.9g.), boron trifluoride - ether complex (0.3 c.c.), trichloroacetic acid (10 mg.) and methanol (2 c.c.). After shaking for two hours at room temperature the mixture was poured into dilute sulphuric acid and extracted with ether. Distillation gave ethyl 1-acetonyl-2-keto-cyclopentane-1-carboxylate (7.7 g.; 70%) as a colourless oil b.p. 150°/10 mm., n_D^{14} 1.4610.

b) Ethyl 2-Ketocyclopentane-1-carboxylate (20g.) was added to a solution of sodium ethoxide (from sodium 3.6g.) in absolute alcohol (100 c.c.) and the mixture heated under reflux for half an hour. Monochloroacetone (18g.) was then added during one hour and heating was continued for a further two hours. Removal of the solvent and extraction with ether followed by distillation gave ethyl 1-acetonyl-2-ketocyclopentane-1-carboxylate (8g. ; 30%), b.p. 137°/6mm., n_D^{17} 1.4593.

In spite of the sharp boiling points of both the products obtained from either 'a' or 'b' no accurate analytical figures were obtained.

(Found : C, 60.8 ; H, 7.3 . $C_{11}H_{16}O_4$

requires : C, 62.2 ; H, 7.5 %).

The highly insoluble semicarbazone (probably the bis-semicarbazone) was difficult to purify. Crystallisation from acetic acid gave a product melting over the range 237-248°, but the analytical figures were not satisfactory.

(Found : C, 43.2 ; H, 6.69 ; N, 22.46 . $C_{13}H_{22}O_4N_6$

requires : C, 47.8 ; H, 6.7 ; N, 25.7 %).

Attempted Cyclisation:

a) The foregoing ester (2g.) was added to a solution of potassium tertiary butoxide (from potassium, 0.5g.) in tertiary butanol (30 c.c.) and the mixture heated under reflux for two hours on the steam bath; the colour of the solution turned rapidly to brownish-red and an oil separated. The mixture was set aside for 30 hours. Most of the solvent was then removed under reduced pressure and dilute sulphuric acid was added. After extraction with ether and evaporation, the starting ester (1.8g.) was recovered unchanged.

b) The ester (2g.) was added to a 3% solution of sodium methoxide in absolute methyl alcohol (100 c.c.) and dry ethyl acetate (30g.) was added. After standing for two days the reaction mixture was thrown into dilute sulphuric acid and the product isolated with ether. The initial ester (1.7g.) was recovered unchanged.

c) The ester (1g.) was heated under reflux with a 2% solution of aqueous potassium hydroxide (60 c.c.) for twenty minutes; the colour of the mixture changed from light yellow to orange-red. Cooling and acidification yielded a trace of a brown resinous material. Extraction with ether again gave the starting ester (0.85g.) unchanged.

Repetition of the experiment with a 5% solution of aqueous potassium hydroxide and heating for five hours gave tars and no αβ-unsaturated ketone could be detected.

B.

bicyclo [4:3:0] Non-1(6)-en-7-one.

1-(3'-Diethylaminoprop-1'-ynyl) cyclohexan-1-ol.

To a solution of lithamide (formed from lithium, 2.2g., by the catalytic action of ferric nitrate) in liquid ammonia (400c.c.) was added 2-bromo-3-diethylamino-prop-1-ene (30g.) and the contents of the flask were stirred for four hours. A solution of cyclohexanone (14g.) in an equal volume of ether was then added dropwise over thirty minutes and the stirring continued for a further four hours. After the addition of powdered ammonium chloride (10g.), the ammonia was allowed to evaporate overnight, the residue treated with excess 2N-sulphuric acid and then extracted with ether to remove non-basic materials. The ethereal extract was washed, dried and evaporated. Distillation gave unchanged cyclohexanone (6g.). The acid aqueous layer was then basified with concentrated ammonia solution and extracted with ether (3 x 100 c.c.). The combined ether extracts were then washed with water, dried and evaporated.

Distillation of the residue gave 1-(3′-diethylaminoprop-1′-ynyl)cyclohexan-1-ol (13 g. ; 75% based on reacted ketone) as an almost colourless viscous oil, b.p. 84°/0.2mm., n_D^{19} 1.4959.

(Found : N, 7.0 . $C_{13}H_{23}ON$ requires : N, 6.7 %).

Cyclisation:

1-(3′- Diethylaminoprop-1′-ynyl)cyclohexan-1-ol (4g.) was heated under reflux for six hours with a mixture of formic acid (10g.) and phosphoric acid (3g.). After being cooled, the reaction mixture was diluted with water and extracted twice with 100c.c. of ether. Washing of the ethereal extract with dilute sodium carbonate solution, drying (Na_2SO_4) and distillation gave a very small amount of a ketonic material which gave a dark red 2:4-dinitrophenylhydrazone.

On neutralisation of the acid aqueous layer with concentrated ammonia solution an oil was separated which was extracted with ether (3 x 60 c.c.). Washing, drying and evaporation of the combined ether extracts followed by distillation of the residue gave 1-(3′-diethyl-

aminoprop-1'-ynyl)cyclohex-1-ene (3.4g. ; 90%) as an almost colourless oil, b.p. 78°/0.2 mm., n_D^{18} 1.5001; light absorption in ethanol λ max., 2300A° (ε = 9500). (Found : N, 6.7 . $C_{13}H_{21}N$ requires : N, 7.3 %).

1-(3'-Diethylaminoprop-1'-ynyl)cyclohex-1-ene (3g.) was reheated under reflux with a mixture of formic acid (10g.) and phosphoric acid (2.5g.) containing mercuric acetate (0.5g.) for five hours. Dilution with water, extraction with ether and distillation gave bicyclo [4:3:0]non-1(6)-en-7-one (1g. ; 48%) as a colourless oil, b.p. 154°/16mm., n_D^{16} 1.5022. The 2:4-dinitrophenylhydrazone had m.p. 238° undepressed when admixed with an authentic sample (Mathieson[29], gave m.p. 238° for this derivative).

In another experiment, 1-(3'-diethylamino-prop-1'-ynyl)-cyclohexan-1-ol (4g.) was heated under reflux for four hours with formic acid (10g.) and phosphoric acid (3g.); mercuric acetate (0.5g.) was then added and the heating continued for a further four hours. After being cooled,

the reaction mixture was diluted with water and extracted with ether. Distillation gave bicyclo[4:3:0]non-1(6)-en-7-one (1.3g. ; 50%), b.p. 142°/10mm., n_D^{18} 1.5010.

1-(3'-Hydroxyprop-1'-ynyl)cyclohexan-1-ol.

This was prepared by a modification of the published procedure as follows[25].

To a solution of ethylmagnesium bromide prepared from ethyl bromide (46g.) and magnesium (10g.) in dry ether (120 c.c.), propargyl alcohol (100%; 10g.) in dry benzene (80 c.c.) was added during half an hour. Ether was then distilled off while another 80 c.c. of dry benzene were added from the dropping funnel. After heating under reflux and stirring for one hour, cyclohexanone (22g.) in dry benzene (50 c.c.) was added during one hour and the reaction mixture was stirred and heated for a further three hours. After the addition of ice and dilute hydrochloric acid, the excess acid was neutralised, the aqueous layer saturated with solid sodium chloride and the whole then extracted continuously with ether. Distillation gave 1-(3'-hydroxyprop-1'-ynyl)-cyclohexan-1-ol (14g. ; 54%) as an almost colourless viscous oil b.p. 110°/0.2mm.

Cyclisation:

When the foregoing glycol (5g.) was heated under reflux for four hours with formic acid (10g.) and phosphoric acid (2g.) and the product worked up as usual, the same bicyclo [4:3:0]non-1(6)-en-7-one mentioned above (2.2g. ; 50%) b.p. 144°/10mm., n_D^{17} 1.5017 was isolated.

1-(3'-Tetrahydropyranyl-2-oxyprop-1'-ynyl)cyclohexan-1-ol.

(i) To a solution of ethylmagnesium bromide prepared from ethyl bromide (22g.) and magnesium (4.8g.) in ether (100 c.c.), 2-prop-2'-yn-1'-yloxytetrahydropyran (20g.) in dry benzene (100 c.c.) was added during half an hour. Dry benzene (100 c.c.) was then added while the ether was being distilled off and the reaction mixture heated under reflux and stirred for two hours. cycloHexanone (19 g.) in dry benzene (50 - 70 c.c.) was added during one hour whereby most of the solid complex was dissolved and the solution became clear. Heating and stirring was continued for a further three hours and the reaction mixture then left overnight. Decomposition with ammonium chloride and extraction with benzene followed by distillation gave 1-(3'-tetrahydropyranyl-2-oxyprop-1'-ynyl)cyclohexan-1-ol (19 g.; 58%) as a light yellow oil b.p. 106°/0.2mm., which showed signs of decomposition at

the boiling point.

(ii) To a solution of lithamide prepared from lithium (0.7g.) in liquid ammonia (400 c.c.), 2-prop-2′-yn-1′-yloxytetrahydropyran (14g.) was added during half an hour and the reaction mixture stirred for three hours. cycloHexanone (10g.) in an equal volume of dry ether was then added and the stirring continued for a further four hours. After decomposition with solid ammonium chloride (10g.) and evaporation of ammonia overnight, 1-(3′-tetrahydropyranyl-2-oxyprop-1′-ynyl) cyclohexan-1-ol was isolated as a pale yellow oil (18g. ; 75%). The undistilled product was used direct for cyclisation.

Hydrolysis:

The foregoing tetrahydropyran adduct (10g.) was treated with 10% methyl alcoholic sulphuric acid (100 c.c.) at room temperature then left overnight. The reaction mixture was then diluted with water (300 c.c.) and extracted with ether (3 x 60 c.c.). Distillation gave 1-(3′-hydroxyprop-1′-ynyl)cyclohexan-1-ol (2.5g. ; 40%), b.p. 122°/0.4mm., 108-110°/0.2mm.

Cyclisation:

When 1-(3'-tetrahydropyrano-2-oxyprop-1'-ynyl)cyclohexan-1-ol (6g.) was heated under reflux for five hours with a mixture of formic acid (15g.) and phosphoric acid (3.5g.) and worked up in the usual manner, it afforded bicyclo [4:3:0]non-1(6)-en-7-one (1.9 g. ; 55%), b.p. 143°/10mm., n_D^{18} 1.5012.

Cyclisation of β-N-Morpholinoethylcyclohex-1-enyl Ketone Hydrochloride.

When a mixture of β-N-morpholinoethylcyclohex-1-enyl ketone hydrochloride[24] (1g.), formic acid (3g.) and phosphoric acid (1g.) was heated under reflux for four hours, then worked up as in the above cognate preparation, it gave a small yield of bicyclo [4:3:0]non-1(6)-en-7one, identified as its 2:4-dinitrophenylhydrazone (m.p. and mixed m.p.).

9-Methylbicyclo[4:3:0]Non-1(6)-en-7-one

1-(3'-Diethylaminobut-1'-ynyl)cyclohexan-1-ól.

a) To a solution of ethylmagnesium bromide prepared from ethyl bromide (30g.) and magnesium (6g.) in dry ether (150 c.c.), 3-diethylaminobut-1-yne (30g.) in dry benzene (200 c.c.) was added slowly during half an hour; the reaction mixture was then warmed gradually until the evolution of ethane had ceased and the last traces of ether were removed. cycloHexanone (25g.) in dry benzene (100 c.c.) was added during half an hour and the mixture stirred and heated under reflux for a further three hours. After decomposition with ammonium chloride solution, the product was extracted with ether and the combined ether extracts were washed, dried and evaporated. Distillation gave 1-(3'-diethylaminobut-1'-ynyl)cyclohexan-1-ol (20g.; 36%) as an almost colourless viscous oil, b.p. 100°/0.6mm., n_D^{21} 1.4910.

(Found : N, 5.85 . $C_{14}H_{25}ON$

requires : N, 6.2 %).

b) 3-Diethylaminobut-1-yne (25g.) was added to a solution of lithamide prepared from lithium (1.5g.) in liquid ammonia (400 c.c.) over a period of twenty minutes. After one hour's stirring a solution of cyclohexanone (20g.) in an equal volume of dry ether was added during one hour. The crystalline lithium salt of the acetylenic amine changed slowly into a dark viscous oil after stirring for four hours at the end of which solid ammonium chloride was added (15g.) and the ammonia was allowed to evaporate. Extraction with ether followed by distillation gave 1-(3'-diethyl-aminobut-1'-ynyl) cyclohexan-1-ol (25g. : 57%), b.p. 92°/0.4mm., n_D^{20} 1.4916.

Cyclisation:

The foregoing acetylenic alcohol (4g.) was heated for two and a half hours with a mixture of formic acid (10g.) and phosphoric acid (3g.) at about 110°C. A thin top layer of yellow oil slowly formed. After dilution with water and extraction twice with 100c.c. of ether, the combined ether extracts were washed with dilute sodium carbonate solution, dried (Na_2SO_4) then evaporated. Distillation gave 9-methyl bicyclo [4:3:0] non-1(6)-en-7-one (1.4g. ; 51%) as a colourless liquid, b.p. 135°/16mm.,

n_D^{19} 1.5116. The 2:4-dinitrophenylhydrazone formed red needles from alcohol - ethyl acetate mixture and had m.p. 242° undepressed when admixed with an authentic sample. (Hamlet, Henbest, and Jones[18] gave n_D^{15} 1.5135 ; 2:4-dinitrophenylhydrazone m.p. 246°).

bicyclo [5:3:0]Dec-1(7)-en-8-one.

1-(3'-Diethylaminoprop-1'-ynyl)cycloheptan-1-ol.

To a solution of lithamide prepared from lithium (2.2g.) in liquid ammonia (500 c.c.) was added 2-bromo-3-diethylaminoprop-1-ene (30g.) and the mixture stirred for four hours. A solution of cycloheptanone (11.2g.) in dry ether (15 c.c.) was then added over thirty minutes and the stirring continued for a further four hours. After the introduction of powdered ammonium chloride (10g.), the ammonia was allowed to evaporate overnight and the residue treated with excess 2N-sulphuric acid and ether to remove the unreacted ketone. The aqueous layer was further extracted with ether and the combined ether extracts were washed, dried and evaporated. Distillation gave unchanged cycloheptanone (4.2g.). The acidic aqueous layer was then made alkaline with concentrated ammonia and extracted with ether (3 x 100 c.c.); the combined ether extracts were washed, dried and evaporated. Distillation of the residue gave 1-(3'-diethylaminoprop-1'-ynyl) cycloheptan-1-ol (9.9g; 72% based on reacted ketone) as an almost colourless viscous oil, b.p.

102°/0.3mm., n_D^{19} 1.4985.

(Found : N, 6.4 . $C_{14}H_{25}ON$

requires: N, 6.3 %).

Cyclisation:

A mixture of 1-(3'-diethylaminoprop-1'-ynyl) cycloheptan-1-ol (4.4g.), formic acid (12g.) and phosphoric acid (3.5g.) was heated under reflux for six hours. After being cooled and diluted with water, the reaction mixture was extracted several times with ether. The combined ether extracts were washed thoroughly with dilute sodium carbonate solution, then with water and finally dried. Distillation gave bicyclo [5:3:0]dec-1(7)-en-8-one (0.25g. ; 8%) as a colourless liquid b.p. 73°/0.2mm., n_D^{18} 1.5241. The semicarbazone crystallised from dilute alcohol in colourless needles and had m.p. 236° undepressed when admixed with an authentic sample (Cook, Philip, and Somerville[30], recorded b.p. 58-60°/0.1mm., $n_D^{11.5}$ 1.5275, semicarbazone m.p. 235-236° for this ketone). The 2:4-dinitrophenylhydrazone, after purification by chromoatography (benzene - alumina) and crystallisation from alcohol - ethyl acetate, formed red needles m.p. 230°.

(Found : C, 58.2 ; H, 5.2 ; N, 17.1 . $C_{16}H_{18}O_4N_4$
requires : C, 58.1 ; H, 5.4 ; N, 16.95 %).

Neutralisation of the acidic aqueous layer with concentrated ammonia furnished an oil which was extracted with ether. Evaporation of the ether extract and distillation of the residue gave 1-(3'-diethylaminoprop-1'-ynyl)cyclohept-1-ene (3.2g. ; 80%) as an almost colourless oil b.p. 88°/0.2mm., n_D^{17} 1.5088.
(Found : N, 6.7 . $C_{14}H_{23}N$
requires : N, 6.8 %).

When this amine (2.4g.) was heated under reflux with a mixture of formic acid (12g.), phosphoric acid (3.5g.) and mercuric acetate (0.5g.) for six hours and worked up in the usual manner, the same bicyclo[5:3:0]dec-1(7)-en-8one (0.7g.; 41%) b.p. 72-74°/0.2mm., n_D^{17} 1.5247, was obtained.

Subjection of 1-(3'-diethylaminoprop-1'-ynyl) cycloheptan-1-ol (1.3g.) to a hot mixture of formic and phosphoric acids (10g. and 2g. respectively) for a period of four hours, then addition of mercuric acetate (0.5g.)

and further heating under reflux for another four hours gave the same bicyclo [5:3:0]dec-1-(7)-en-8-one (0.3g.; 38%) b.p. 62°/0.1mm., n_D^{18} 1.5243.

10-Methylbicyclo[5:3:0]Dec-1(7)-en-8-one

1-(3'-Diethylaminobut-1'-ynyl)cycloheptan-1-ol.

a) 3-Diethylaminobut-1-yne (15g.) in dry benzene (150 c.c.) was added to an ethereal solution of ethylmagnesium bromide [prepared from magnesium (2.4g.) and ethyl bromide (11g.)] and the mixture gradually warmed during the addition to distil off the ether; heating was continued until the evolution of ethane had ceased. A solution of cycloheptanone (11.2g.) in dry benzene (100 c.c.) was then added during one hour and the reaction mixture stirred and heated under reflux for four hours. After decomposition with ammonium chloride, extraction with ether and distillation, 1-(3'-diethylaminobut-1'-ynyl) cyclo-heptan-1-ol (9g. ; 38%) was obtained as an almost colourless viscous oil, b.p. 104°/0.5 mm., n_D^{15} 1.4962

(Found : N, 6.1 , $C_{15}H_{27}ON$

requires : N, 5.9 %).

A very small amount of cycloheptamone was recovered.

b) To a solution of lithamide (from lithium, 1.7g.) in liquid ammonia (400 c.c.) was added 3-diethyl-aminobut-1-yne (28 g.) and the reaction mixture stirred for one hour. cycloHeptanone (20g.) in an equal volume of dry ether was then run in during one hour and the stirring continued for a further four hours. After addition of powdered ammonium chloride (12g.), ammonia was allowed to evaporate, the residue treated with excess 2N- sulphuric acid and then extracted with ether to remove the non-basic constituents. Evaporation of the ether and distillation of the residue gave cycloheptanone (11.5g.). The acidic aqueous layer was then basified with concentrated ammonia and the separated oil taken up in ether. The combined ether extracts were washed, dried and evaporated. Distillation gave the same 1-(3'-diethylaminobut-1'-ynyl)cycloheptan-1-ol (13.5g. ; 80% based on reacted ketone), b.p. 107-108°/0.6 mm., n_D^{17} 1.4951.

Cyclisation:

1-(3'-Diethylaminobut-1'-ynyl)cycloheptan-1-ol (5g.) was heated under reflux with a mixture of formic acid (12g.) and phosphoric acid (3.5g.) for four hours. The reaction mixture was then diluted with water and extracted

several times with ether. The combined ether extracts were washed with dilute sodium carbonate solution, dried (Na_2SO_4) and evaporated. Distillation gave 10-methyl-bicyclo [5:3:0] dec-1(7)-en-8-one (1.2g.; 35%) as a colourless liquid b.p. 140°/15mm., n_D^{20} 1.5138. The 2:4-dinitrophenylhydrazone crystallised from ethyl acetate - alcohol mixture in red needles m.p. 236° undepressed on admixture with an authentic sample (Braude and Forbes[13], recorded n_D^{23} 1.5118, 2:4-dinitrophenylhydrazone m.p. 236°). The semicarbazone crystallised from alcohol in colourless needles m.p. 216°.

(Found : N, 18.65 . $C_{12}H_{19}ON_3$

requires : N, 19.0 %).

bicyclo [3:3:0]Oct-1(5)-en-4-one.

1-(3'-Diethylaminobut-1-'-ynyl)cyclopentan-1-ol.

To a solution of ethylmagnesium bromide [prepared from magnesium (6g.) and ethyl bromide (30g.)] in dry ether (100 c.c.), was added 3-diethylaminobut-1-yne (30g.) in dry ether (100 c.c.) and the mixture gently warmed until the evolution of ethane had ceased. A solution of cyclopentanone (22g.) in dry ether (80 c.c.) was then added during one hour and the stirring and heating continued for a further three hours. Decomposition with 2N-sulphuric acid, extraction with ether and distillation gave cyclopentylidenecyclopentanone (18 g.) b.p. 112°/10mm. The semicarbazone crystallised from alcohol in prisms m.p. 225°.

(Found : C, 63.9; H, 8.4; N,20.4. Calculated for $C_{11}H_{17}ON_3$: C, 63.7; H, 8.2; N, 20.2%).

The 2:4-dinitrophenylhydrazone formed red needles from alcohol - ethyl acetate m.p. 228°

(Found : C, 58.4; H, 5.7; N, 16.8 . Calculated for $C_{16}H_{18}O_4N_4$: C,58.1; H, 5.4; N, 16.9%).

When the acid aqueous layer was basified with concentrated ammonia, extracted with ether then followed by distillation, an almost colourless viscous oil [presumably 1-(3'-diethylaminobut-1'-ynyl)cyclopentan-1-ol] (2g.; 3.8%), b.p. 92°/0.4mm., n_D^{18} 1.4950, was obtained. This liquid was unstable and darkened quickly and consequently no accurate analytical figures were obtainable.

1-(3'-Diethylaminoprop-1'-ynyl)cyclopentan-1-ol.

2-Bromo-3-diethylaminoprop-1-ene (30g.) was added to a solution of lithamide prepared from lithium (2.2g.) in liquid ammonia (400 c.c.) and the mixture stirred for four hours. A solution of cyclopentanone (13g.) in an equal volume of ether was then added during two hours and the stirring was continued for another three hours. After the addition of ammonium chloride (10g.), the ammonia was allowed to evaporate overnight and the residue treated with 2N-sulphuric acid. Extraction with ether and distillation gave a large amount of the self condensation product of cyclopentanone mentioned above. However, basification of the acid aqueous layer with

concentrated ammonia solution, extraction with ether and distillation gave an almost colourless oil (4g.; 13.7%) b.p. 84°/0.4 mm., n_D^{17} 1.4992. This substance, possibly 1-(3'-diethyl-aminoprop-1'-ynyl)cyclopentan-1-ol, was extremely unstable and darkened in colour even in a sealed tube and consequently no correct analytical figures could be obtained.

1-Acetoxy-1-ethynylcyclopentane.

A mixture of 1-ethynylcyclopentan-1-ol (8g.) and acetic anhydride (15 c.c.) was heated under reflux for two hours. After being cooled, the reaction mixture was thrown into water and neutralised with dilute sodium hydroxide solution. Extraction with ether and distillation gave 1-acetoxy-1-ethynylcyclopentane (9.5g. ; 86%) as a colourless liquid with a smell resembling that of turpentine, b.p. 68°/15mm., n_D^{16} 1.4595.

(Found : C, 70.75 ; H, 7.2 . $C_9H_{12}O_2$

requires: C,71.0 ; H, 7.8 %).

1-Acetoxy-1-(3'-Diethylaminoprop-1'-ynyl) cyclopentane.

A mixture of 1-acetoxy-1-ethynylcyclopentane (8.5g.), diethylamine (4 g.), paraformaldehyde (2.2g.) and pure dioxan (10 c.c.) was heated under reflux on the steam bath for three hours and then left overnight at room temperature. The reaction mixture was treated with dilute hydrochloric acid and the neutral constituents removed by extraction with ether. Basification of the aqueous layer with dilute sodium hydroxide solution in the cold, extraction with ether and distillation gave 1-acetoxy-1-(3'-diethylaminoprop-1'-ynyl)cyclopentane (11g.; 83%) as a colourless oil b.p. 76°/0.2mm., n_D^{18} 1.4722

(Found : N, 5.75 . $C_{14}H_{23}O_2N$

requires : N, 5.9 %).

Cyclisation:

1-Acetoxy-1-(3'-diethylaminoprop-1'-ynyl)cyclopentane (8 g.) was heated under reflux for five hours with formic acid (15g.) and phosphoric acid (3g.); the reaction mixture rapidly darkened. After being cooled, the

mixture was diluted with water then extracted with ether (4 x 50 c.c.); the combined ether extracts were washed with dilute sodium carbonate solution and water, dried and evaporated. Distillation gave bicyclo [3:3:0]oct-1(5)-en-4-one (0.3g.; 7%) b.p. 122°/15mm., n_D^{21} 1.5226 (Cope and Schmitz[31] give n_D^{25} 1.5202). The semicarbazone of this product melted unsharply at ca. 205° (Cope and Schmitz[31] give m.p. 230 - 232.2°) even after repeated crystallisation; this suggests contamination of the product with the uncyclised divinyl ketone. The 2:4-dinitrophenylhydrazone was readily purified by chromatography (benzene - alumina) and crystallised from alcohol - ethyl acetate in red needles m.p. 196°; light absorption in ethanol λ max., 3800A° (ε = 27,500) and 2550A° (ε = 16,500).

(Found : N, 18.75 . $C_{14}H_{14}O_4N_4$ requires : N, 18.5 %) .

Neutralisation of the acid aqueous layer with concentrated ammonia solution gave an oil which was extracted with ether. Evaporation and distillation gave 1-(3'-diethylaminoprop-1'-ynyl)cyclopent-1-ene (5 g. ; 87%) as an almost colourless oil b.p. 57°/0.2 mm., n_D^{16} 1.4995.

The product was very sensitive to light and decomposes quickly in air; good analytical figures were only obtainable when the analysis was carried out immediately after distillation.

(Found : N, 7.95 . $C_{12}H_{19}N$

requires : N, 7.9 %).

When a mixture of 1-(3'-diethylaminoprop-1'-ynyl) cyclopent-1-ene (5g.), formic acid (10g.), phosphoric acid (3 g.) and mercuric acetate (0.5g.) was heated under reflux for four hours, then worked up as in the above cognate preparation, it gave the same bicyclo [3:3:0]oct-1(5)-en-4-one(0.2g.; 6%), b.p. 128°/16 mm., n_D^{20} 1.5230.

C.

bicyclo[5:3:0]Dec-7-en-9-one.

3-Keto-1-phthalimidobutane.

A mixture of phthalimide (18g.), freshly distilled anhydrous methyl vinyl ketone (8.7g.) and benzyltrimethylammonium hydroxide (3 c.c.) in ethyl acetate (70 c.c.) was heated and stirred at 60°C for half an hour; no apparent change was observed and the phthalimide remained suspended in solution. When the temperature of the mixture was raised to the boiling point of the solvent, the suspension disappeared and the solution became clear after ten minutes; stirring and heating was continued for a further 20 minutes. Evaporation to dryness under reduced pressure gave 3-keto-1-phthalimidobutane as a colourless solid (24g.; 90%) which crystallised from alcohol in colourless rhombs m.p. 112°. The product was practically insoluble in ether and moderately soluble in hot water.

(Found : C, 66.3 ; H, 5.26 ; N, 6.7 . $C_{12}H_{11}O_3N$ requires : C, 66.3 ; H, 5.06 ; N, 6.4%).

The 2:4-dinitrophenylhydrazone crystallised from alcohol-ethylacetate mixture in light orange prisms m.p. 176°.

(Found : C, 54.63 ; H, 3.3 ; N, 17.78 . $C_{18}H_{15}O_6N_5$ requires : C, 54.15 ; H, 3.7 ; N, 17.63%).

3:3-(Ethylenedioxy)-1-Phthalimidobutane.

3-Keto-1-phthalimidobutane (15g.), ethylene glycol (6.5g.) and toluene-p-sulphonic acid (0.2g.) in dry benzene (300 c.c.) were heated under reflux for three hours in an apparatus equipped for automatic water separation. After being cooled, the benzene solution was washed with dilute sodium carbonate solution followed by water, dried and the solvent distilled off. The solid residue, 3:3-(ethylenedioxy)-1-phthalimidobutane (15g.; 83%), crystallised from alcohol in colourless prisms m.p. 122°. The mixed m.p. with the starting material was 100-105°.

(Found : C, 64.8 ; H, 5.7 ; N, 5.2 . $C_{14}H_{15}O_4N$ requires : C, 64.7 ; H, 5.7 ; N, 5.3%).

Treatment of the ketal with warm 2:4-dinitrophenylhydrazine reagent gave the same 2:4-dinitrophenylhydrazone described above.

3:3-(Ethylenedioxy) butylamine.

The foregoing phthalimido-compound (15g.) and hydrazine hydrate (100% ; 3g.) in water (250 c.c.) were heated under reflux until all the solid had dissolved (40-50 minutes). To the cooled mixture, dilute sodium hydroxide solution was added and the aqueous solution extracted continuously with ether for two days. Evaporation and distillation gave 3:3-(ethylenedioxy) butylamine (5.6 g. ; 78.5%) as a colourless oil, b.p. 121-2°/100mm., n_D^{22} 1.4460.

The product was characterised by its 2:4-dinitrophenyl derivative, which crystallised from alcohol in light yellow prisms, m.p. 116-118°.

(Found : C, 48.67 ; H, 5.23 ; N, 14.22 . $C_{12}H_{15}O_6N_3$ requires : C, 48.67 ; H, 4.7 ; N, 14.1%).

N-(Methoxycarbonyl)-3:3-(ethylenedioxy) butylamine.

3:3-(Ethylenedioxy) butylamine (1.3g.) was dissolved in ether (15 c.c.) and the solution cooled to 0°C; methyl chloroformate (1g.), and a solution of dilute sodium hydroxide (0.4g.) in water (4 c.c.) were then added dropwise from separate dropping funnels with

continuous shaking. After 10-15 minutes, the ethereal layer was separated and the aqueous layer was extracted twice with 10 c.c. of ether. The combined ether solutions were then dried over anhydrous potassium carbonate and evaporated. Distillation gave N-(methoxycarbonyl)-3:3-(ethylenedioxy) butylamine (1.6 g.; 84%) as a colourless viscous water-soluble oil, b.p. 148-150/16mm., n_D^{22} 1.4538.

(Found : C, 49.87 ; H, 7.50 ; N, 7.48 . $C_8H_{15}O_4N$
requires : C, 50.2 ; H, 7.9 ; N, 7.4 %).

The corresponding 2:4-dinitrophenylhydrazone crystallised from methanol in light yellow silky needles m.p. 121°.

(Found : C, 44.5 ; H, 4.82 ; N, 21.64 . $C_{12}H_{15}O_6N_5$
requires : C, 44.3 ; H, 4.61 ; N, 21.53%).

Attempted Direct Preparation of N-(Ethoxycarbonyl)-3-ketobutylamine.

A mixture of urethane (8.9g.), freshly distilled methyl vinyl ketone (7g.), in ethyl acetate (50 c.c.) was stirred and heated gradually until the temperature of the solution reached 60°C. Benzyltrimethylammonium hydroxide (3 c.c.) was added and the stirring was continued while the temperature of the solution was kept at 60°C. for

20 minutes. Evaporation of the solvent under reduced pressure gave a colourless gum (8.5g.) which solidified on cooling and was proved to be the unchanged urethane (m.p. and mixed m.p.).

Repetition of the experiment with stirring and heating under reflux for 40 minutes afforded only the unchanged urethane.

4:4-(Ethylenedioxy) pentanoic hydrazide.

A mixture of ethyl 4:4-(ethylenedioxy) pentanoate (100g.) and hydrazine hydrate (100% ; 35g.) was heated under reflux for four hours; the solution became homogeneous after 45 minutes. Distillation gave 4:4-(ethylenedioxy) pentanoic hydrazide (80g.; 87%) as a colourless viscous oil, b.p. 142°/0.4mm., which solidified on cooling to a mass of prisms m.p. ca. 34°. The substance was extremely hygroscopic.

(Found : C, 46.65 ; H, 7.7 ; N, 16.30 . $C_7H_{14}O_3N_2$ requires : C, 48.2 ; H, 8.0 ; N, 16.09%).

The corresponding methylbenzylidene - derivative (prepared from the hydrazide by heating with acetophenone) crystallised from alcohol in colourless needles m.p. 98 - 100°.

(Found : C, 65.36 ; H, 6.70 ; N, 10.34 . $C_{15}H_{20}O_3N_2$
requires : C, 65.2 ; H, 7.2 ; N, 10.14%).

N-(Methoxycarbonyl)-3:3-(ethylenedioxy) butylamine.

A mixture of the foregoing hydrazide (60g.) and sodium nitrite (60g.), in water (150 c.c.) was covered with ether (120 c.c.) and cooled to -5°C. An ice-cold solution of concentrated sulphuric acid (33 g.) in water (120 c.c.) was then added with occasional shaking, at such a rate that the temperature of the mixture remained between -5° and 0°C. When the addition was complete, the ether layer was decanted and the aqueous layer washed twice with fresh ether. The combined ether extracts were dried over anhydrous sodium sulphate at 0°C.; after the drying agent had been filtered off, methanol (100 c.c.) was added and the ether distilled off. The resulting alcoholic solution was then heated under reflux for two hours. Removal of the solvent and distillation gave N-(methoxycarbonyl)-3:3-(ethylenedioxy) butylamine (33g. ; 50.7%) as a colourless viscous water-soluble oil, b.p. 142°/12mm., 98-100°/0.4mm., n_D^{23} 1.4530, n_D^{18} 1.4555. It was shown to be identical

with the substance prepared above by m.p. and mixed m.p. of its 2:4-dinitrophenylhydrazone.

N-Nitroso-N-(methoxycarbonyl)-3:3-(ethylenedioxy) butylamine.

A mixture of N-(methoxycarbonyl)-3:3-(ethylenedioxy) butylamine (10g.), sodium nitrite (60g.), crushed ice (10g.) and water (80 c.c.) were covered with ether (30 c.c.) and cooled to 0°. A cold solution of concentrated nitric acid (20 c.c.) in water (30 c.c.) was then added slowly from a dropping funnel, the end of which was dipped in the aqueous layer. The solution was shaken occasionally and the temperature was kept below 5°. After the addition was complete, the top ether layer which acquired a deep bluish-green colour was separated and the aqueous layer washed twice with fresh ether. The combined ether solutions were washed with cold concentrated potassium bicarbonate solution and dried over anhydrous sodium sulphate at 0°. Evaporation of the ether at room temperature under reduced pressure gave a pink coloured viscous oil (10g.) which decomposed on attempted distillation; this product was used as such for the ring expansion experiments.

2(2':2'. Ethylene-dioxypropyl) cycloheptan -1-one.

The foregoing N-nitroso-compound (10g.) was added dropwise to a stirred mixture of cyclohexanone (6g.), absolute alcohol (20 c.c.) and freshly ignited potassium carbonate (3g.), at such a rate that the temperature of the reaction mixture did not rise over 28°. The colour of the mixture changed gradually to orange and 900 c.c. of nitrogen were collected after five hours (theoretical: 1030 c.c.). After removal of the potassium carbonate by filtration, the alcohol was distilled off and water added. Extraction with ether and distillation gave the following fractions.

a) b.p. 40-80°/16mm. (3.4g.)

b) b.p. 82-86°/0.2 mm. (6g.)

Fraction 'b' was yellow in colour and gave a positive Lassaigne test for nitrogen. When this liquid was taken up in a small volume of ether and shaken up several times with water then distilled, it gave a colourless oil (4.8g.; 48%) which gave a negative Lassaigne test for nitrogen, b.p. 94°/0.3mm., $n_D^{20.5}$ 1.4747. In spite of the sharp boiling point of this product no satisfactory analytical figures were obtained.

2-Acetonylcycloheptan-1-one.

A solution of the foregoing material (4g.) in alcohol (20 c.c.) was treated with an aqueous 5% solution of sulphuric acid (5 c.c.) then set aside overnight. Dilution with water and extraction with ether followed by distillation gave 2-acetonylcycloheptan-1-one (2.5g. ; 80%) as a colourless oil, b.p. 128°/12mm., n_D^{19} 1.4700.
(Found : C, 69.72 ; H, 9.03 . $C_{10}H_{16}O_2$
requires : C, 71.4 ; H, 9.5 %).

bicyclo [5:3:0]Dec-7-en-9-one.

A mixture of 2-acetonylcycloheptan-1-one (2g.), an aqueous 5% solution of potassium hydroxide (150 c.c.) and ethyl alcohol (10 c.c.) was heated under reflux for three hours. At the end of this period, the reaction mixture was steam distilled and the distillate extracted with ether. Evaporation and distillation gave bicyclo [5:3:0]dec-7-en-9-one (1.3g. ; 72%) as a colourless oil, b.p. 118-120°/16mm., n_D^{19} 1.5212.
(Found : C, 79.6 ; H, 8.9 . $C_{10}H_{14}O$
requires : C, 80.0 ; H, 9.3%).

Light absorption in ethanol λ max., 2890 Å (ε = 186) and 2330 Å (ε = 12,590).

The 2:4-dinitrophenylhydrazone crystallised from alcohol-ethyl acetate in red needles m.p. 184°-185° (LLoyd and Rowe[19] give b.p. 94°/2mm., 2:4 dinitrophenylhydrazone m.p. 185° for this ketone).

(Found : C, 59.31 ; H, 5.51 ; N, 17.1 . $C_{16}H_{18}O_4N_4$
requires : C, 58.1 ; H, 5.45 ; N, 16.96%).

Light absorption in ethanol λ max., 3880 Å (ε = 26,730).

The semicarbazone crystallised from alcohol in plates m.p. 220-222°.

(Found : N, 20.0 . $C_{11}H_{17}O N_3$
requires : N, 20.2%).

General Ring Expansion and Cyclisation Procedure.

It is not necessary for the preparation of the bicyclic ketones to isolate any of the intermediates. The preparation may thus be modified as follows.

The N-nitroso-compound (10g.) was added from a dropping funnel to a stirred mixture of the ketone (5-7g.), absolute alcohol (20 c.c.) and anhydrous potassium carbonate (2-4g.), at such a rate that the temperature of the reaction mixture remained between 20-30°. Between 800-1000 c.c. of nitrogen were collected after five hours.

On removal of the potassium carbonate by filtration, the mixture was treated with an aqueous 5% solution of sulphuric acid (10 c.c.) then left overnight. After addition of water, the solution was saturated with ammonium sulphate and extracted with ether. The product was given a rough distillation to remove unchanged ketone, then treated with alkali. After steam distillation, the final product was isolated with ether and distilled.

4-Isopropylbicyclo [5:3:0]dec-7-en-9-one.

Ring expansion of 4-isopropylcyclohexanone and cyclisation of the intermediate diketone with alkali furnished 4-isopropylbicyclo [5:3:0]dec-7-en-9-one (28%) as a colourless oil, b.p. 136-139°/18mm., n_D^{21} 1.5085.

The 2:4-dinitrophenylhydrazone crystallised from alcohol-ethyl acetate in red needles m.p. 142-144°. On being chromatographed on a long alumina column, only one band was observed; the melting point of the product after elution and crystallisation was the same. (Found : C, 61.44 ; H, 6.58 ; N, 14.90 . $C_{19}H_{22}O_4N_4$ requires : C, 61.28 ; H, 6.45 ; N, 15.0%).

Light absorption in ethanol λ max., 3880 Å (ε = 29,000).

4-Methylbicyclo [5:3:0]dec-7-en-9-one.

Expansion of 4-methylcyclohexanone and cyclisation of the intermediate diketone as described above gave 4-methylbicyclo[5:3:0]dec-7-en-9-one (32%) as a colourless oil b.p. 124°/16mm.

(Found : C, 80.4 ; H, 9.4 . $C_{11}H_{16}O$

requires : C, 80.4 ; H, 9.7%).

The 2:4-dinitrophenylhydrazone crystallised from alcohol-ethyl acetate in red needles m.p. 155-157°. On being chromatographed on a long alumina column, only one band was observed and the melting point of the product was the same.

(Found : C, 59.10 ; H, 6.11 ; N, 16.29 . $C_{17}H_{20}O_4N_4$

requires : C, 59.30 ; H, 5.81 ; N, 16.27%).

Light absorption in ethanol λ max., 3880Å

(ε = 28,900).

The semicarbazone crystallised from ethanol in plates m.p. 222-224°.

(Found : N, 18.85 . $C_{12}H_{19}ON_3$

requires : N, 19.00%).

6-Methylbicyclo[5:3:0]dec-7-en-9-one.

Ring expansion of 2-methylcyclohexanone and cyclisation of the intermediate diketone as in the above cognate reaction furnished a small amount of a ketonic material which gave a red 2:4-dinitrophenylhydrazone. This latter was chromatographed (benzene-alumina); only one band was observed and the product after elution crystallised from alcohol - ethyl acetate in red needles m.p. 128-130°.

(Found : C, 59.51 ; H, 6.06 ; N, 16.20 . $C_{17}H_{20}O_4N_4$ requires : C, 59.30 ; H, 5.81 ; N, 16.2 %).

Light absorption in ethanol λ max., 3880Å (ε = 27,900).

Attempt Preparation of 2:6-Dimethylbicyclo[5:3:0]dec-7-en-9-one

Ring expansion of 2:6-dimethylcyclohexanone and cyclisation of the product with alkali gave only tars; most of the 2:6-dimethylcyclohexanone was recovered unchanged.

Reduction of bicyclo[5:3:0]Dec-7-en-9-one.

Catalytic Hydrogenation.

bicyclo[5:3:0]Dec-7-en-9-one (90 mg.) in methanol (30 c.c.) was subjected to hydrogenation in presence of palladium charcoal (5% ; 5 mg); 14.5 c.c. of hydrogen (theoretical for one double bond, 14.3 c.c.) were absorbed after 15 minutes at 21°/760mm. After being filtered, the alcoholic solution was treated with methyl alcoholic solution of semicarbazide acetate and the resultant semicarbazone crystallised from methanol in colourless needles m.p. 198-199°. Heating this semicarbazone with an alcoholic solution of 2:4-dinitrophenylhydrazine sulphate gave the corresponding 2:4-dinitrophenylhydrazone which crystallised from alcohol in orange-yellow needles m.p. 125-126°.
(Found : C, 58.12; H, 6.24 ; N, 17.0 . $C_{16}H_{20}O_4N_4$
requires : C, 57.83; H, 6.0 ; N, 16.86%).

Lithium and Liquid Ammonia Reduction:

bicyclo [5:3:0]Dec-7-en-9-one (150 mg.) in ether (5 c.c.) was added to a solution of lithium (100 mg.)

in liquid ammonia (50 c.c.). After half an hour's standing, ammonium chloride was added and the ammonia was left to evaporate. Extraction with ether gave an oil which was converted directly to the semicarbazone which crystallised from ethanol in colourless plates m.p. 221-223° (Plattner, Furst and Jirasek[11] gave m.p. 222-223° for the semicarbazone of their ketone).

Transformation of the semicarbazone to the corresponding 2:4-dinitrophenylhydrazone by the method described above gave the latter derivative which crystallised from ethanol in two polymorphic forms; red sheaves of needles were obtained on slow crystallisation and yellow plates were formed by rapid cooling of the solution. Both the red and the yellow modifications partially melted at 129-130° then rapidly resolidified to a mass of yellow needles which melted sharply at 138°. (Found : C, 58.3 ; H, 5.98 ; N, 17.0. $C_{16}H_{20}O_4N_4$ requires : C, 57.8 ; H, 6.0 ; N, 16.86%).

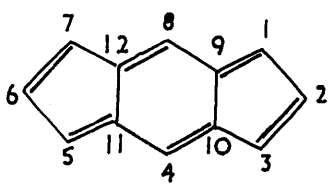
PART II.

ATTEMPTED SYNTHESIS OF THE INDACENES.

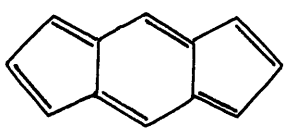
ATTEMPTED SYNTHESIS OF THE INDACENES.

(a) Historical and Theoretical

Hitherto the azulene system is the sole example of a structure possessing aromatic properties which contains a five-membered ring functioning as an integral part of the resonating nucleus. However, many such systems can be envisaged on paper. Among these are the two closely related structures symmetrical (s) and asymmetrical (as) indacene.



(I a)



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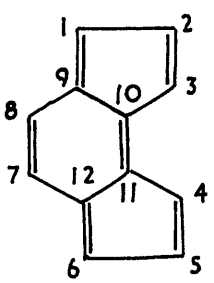

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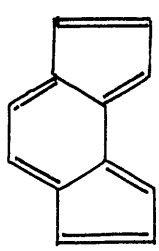
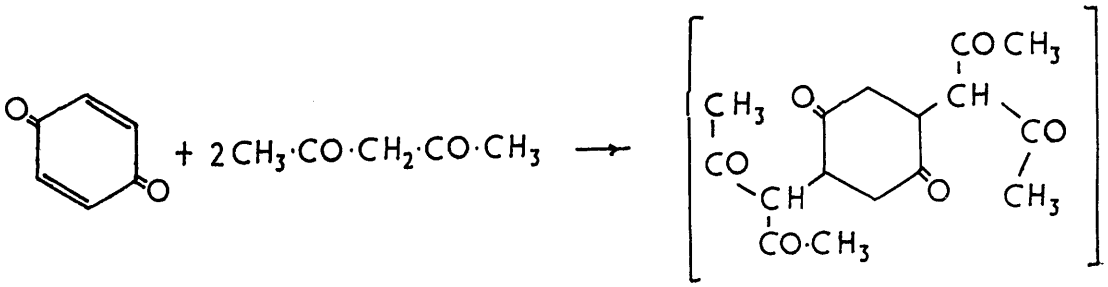


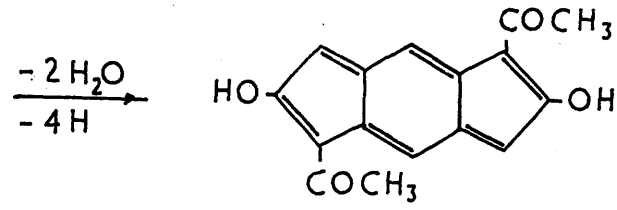
(II b)

Recently, Brown[32] has concluded from molecular orbital calculations that there is no theoretical barrier to the existence of these two compounds. His deductions also predicted that s-indacene should be the more stable, a result which is also explicable on the basis of resonance concepts; thus the two most stable contributing forms of s-indacene (Ia) and (Ib) are equivalent, whereas the corresponding structures for as-indacene (IIa) and (IIb) are non-equivalent.

In 1927 Ionescu[33] reported the isolation of a dark green, highly insoluble, high melting compound (A) from the product of the interaction of benzoquinone and acetylacetone in pyridine. On the basis of analytical figures (on the alcohol-washed crude product!) he concluded that the compound (A) was 1:5-diacetyl-2:6-dihydroxy s-indacene (IV); his mechanism of formation of this product involved a double Michael addition of the acetylacetone to the double bonds of the benzoquinone followed by



(III)

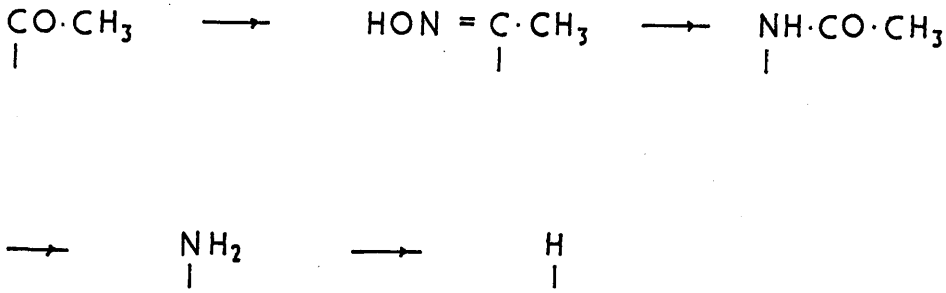


(IV)

dehydration of the dienol form of the intermediate (III) and subsequent dehydrogenation to the s-indacene (IV).

From the point of view of an investigation of synthetic routes to s-indacene, compound (A) is obviously an attractive starting material and it was decided to accept tentatively Ionescu's structure as a working hypothesis. Compound (A) was prepared according to Ionescu's directions, although the reaction was found to be temperamental, and his description of its physical properties was confirmed. Attempts were then started to "strip" the nucleus of its substituent groupings in order to obtain the basic s-indacene structure. Manipulation of the compound proved very difficult because of its

total insolubility in nearly all organic solvents but its slight solubility in hot pyridine suggested the possibility of removing the acetyl groups by means of a Beckmann rearrangement of the oxime followed by hydrolysis and deamination.



Treatment of (A) with hydroxylamine hydrochloride in hot pyridine furnished a dark red crystalline compound which decomposed without melting. Analysis did not agree with that expected from either a monoxime or a dioxime of structure (IV) but corresponded with the empirical formula $C_{11}H_8N_2O_2$. Beckmann rearrangement of this product gave a trace of amorphous material which could not be satisfactorily purified. This route was therefore not further investigated.

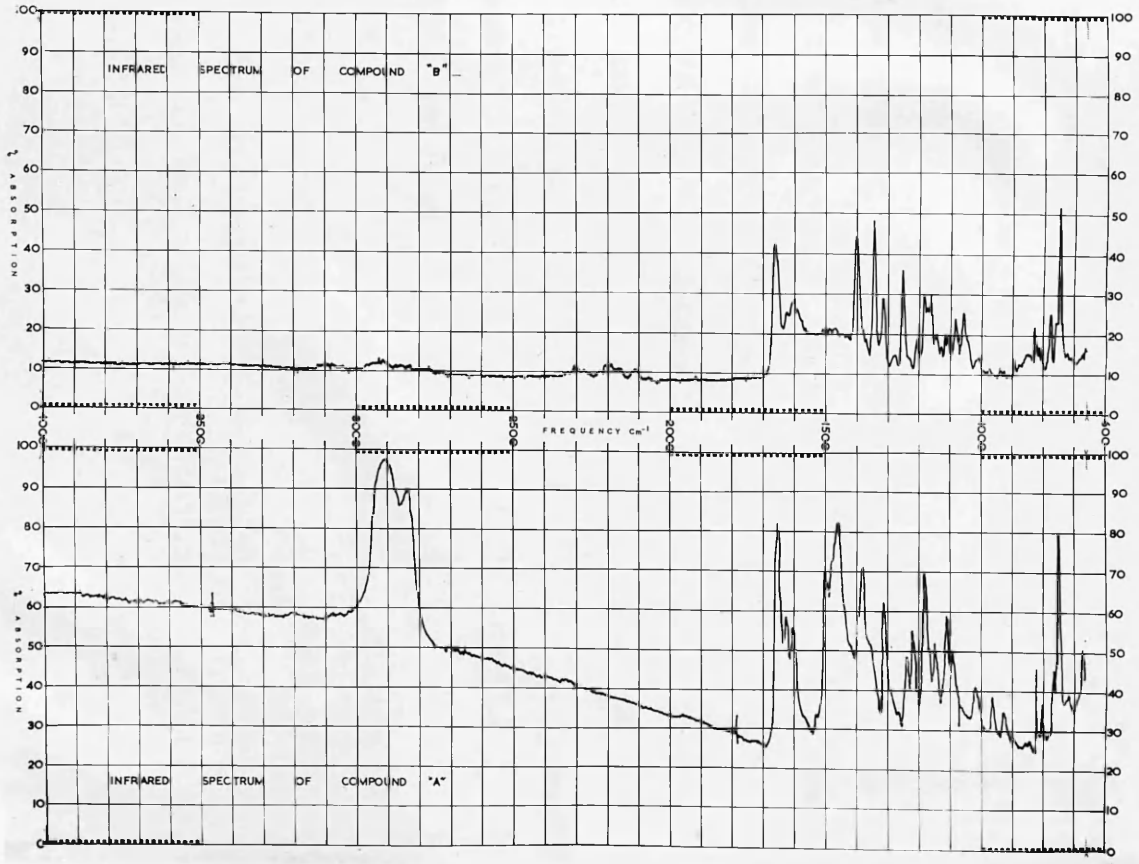
Drastic zinc dust reduction of compound (A) was then attempted in order to try and remove all the oxygen functions of the compound simultaneously. Fusion of (A) with a mixture of zinc chloride, sodium chloride and zinc dust gave a dark violet crystalline compound (B) which was moderately soluble in organic solvents to give solutions with a bright red fluorescence. The analytical figures of this substance corresponded to no feasible formula involving carbon, hydrogen and oxygen only.

The comparative solubility of compound (A) in phosphoric acid suggested the employment of this acid as solvent for a milder zinc dust reduction. The product in this case seemed identical with compound (B) obtained as above by the zinc melt method and possessed an identical analysis.

At this point it was decided to attempt a rigorous purification of compound (A) before embarking on further degradations. This process was greatly facilitated by the discovery that part of the product sublimed in high vacuum leaving a black non-volatile residue, thus demonstrating conclusively the heterogeneity of Ionescu's material. This volatile component (which was highly

crystalline) could also be extracted by high boiling solvents such as diethyl phthalate and diethyl malonate to leave the same black amorphous residual material. Surprisingly, the volatile and non-volatile substances gave almost identical carbon and hydrogen figures which were very close to those required for the postulated s-indacene structure (IV). At this point a sodium fusion test for nitrogen was carried out and was found to be strongly positive both for the volatile and non-volatile components. Recalculation of the analytical figures on this basis gave the empirical formula $C_{11}H_7NO_2$ and this was confirmed by nitrogen analysis; the molecular formulae for the two components are obviously different multiples of this basic formula. On this basis the product of oximation is a monoxime, $C_{11}H_8N_2O_2$, agreeing with the analysis found. Both the zinc melt and zinc-phosphoric acid reduction products now agree with the formula C_9H_5NO in which one acetyl group has been replaced with hydrogen.

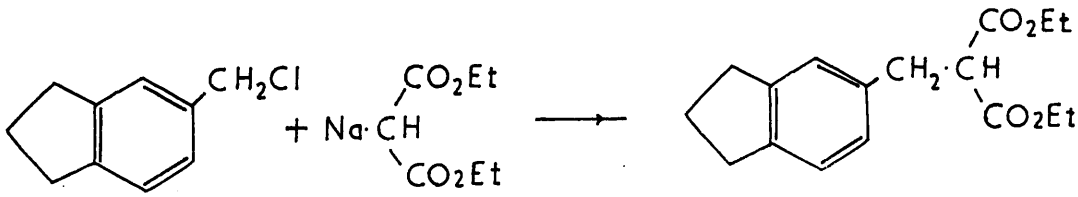
$$(C_9H_4NO)\cdot\overset{\overset{NOH}{\|}}{C}\cdot CH_3 \longleftarrow (C_9H_4NO)\cdot CO\cdot CH_3 \longrightarrow (C_9H_4NO)H$$

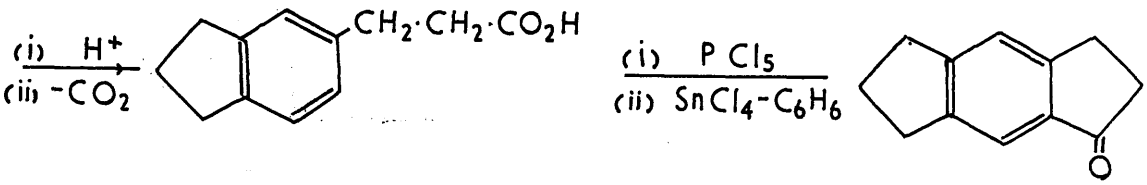

INFRARED SPECTRUM OF COMPOUND "B"
INFRARED SPECTRUM OF COMPOUND "A"
% ABSORPTION
FREQUENCY Cm⁻¹
4000
3500
3000
2500
2000
1500
1000
500
100
90
80
70
60
50
40
30
20
10
0

The infra-red spectra of the volatile component of (A) (Nujol mull) and of the reduction product (B) (in carbon disulphide) were too complex to afford any useful information although both showed a strong αβ-unsaturated carbonyl band at 1660cm.$^{-1}$ and an intense band at 750cm^{-1} possibly attributable to a disubstituted benzene nucleus.

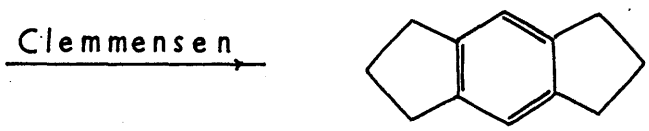
The building up of products of empirical formula $C_{11}H_7NO_2$ from the units benzoquinone, acetylacetone and pyridine is not at all an obvious process. The unravelling of the constitution of these products, although of great potential interest, was obviously a long term project and, since they were fairly certainly not indacenes, it was decided to abandon further investigation on them.

An obvious route to the indacenes involves the dehydrogenation of the requisite hydroaromatic carbon skeleton. The synthesis of a ketone of this type (V) has been recently reported by the following route from indane[34].





(V)

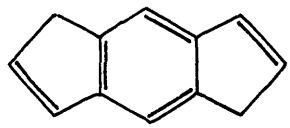


(VI)

Clemmensen reduction of this ketone gave the parent compound trivially named s-hydrindacene (VI).

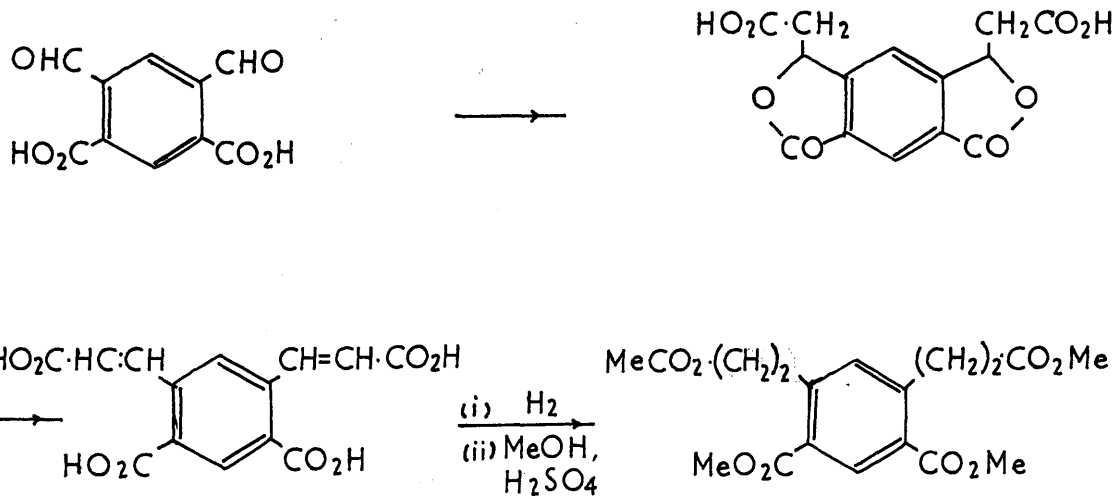
For the purpose of conversion to s-indacene it was deemed desirable to start from a hydrindacene containing a substituent in both five-membered rings which could be readily converted into a double bond

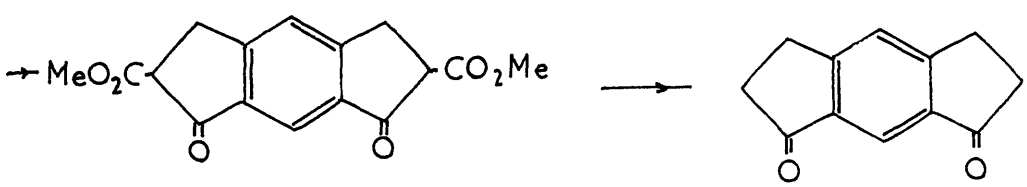
to give a compound of type (VII); this needs only a loss of two hydrogen atoms to be converted into s-indacene.



(VII)

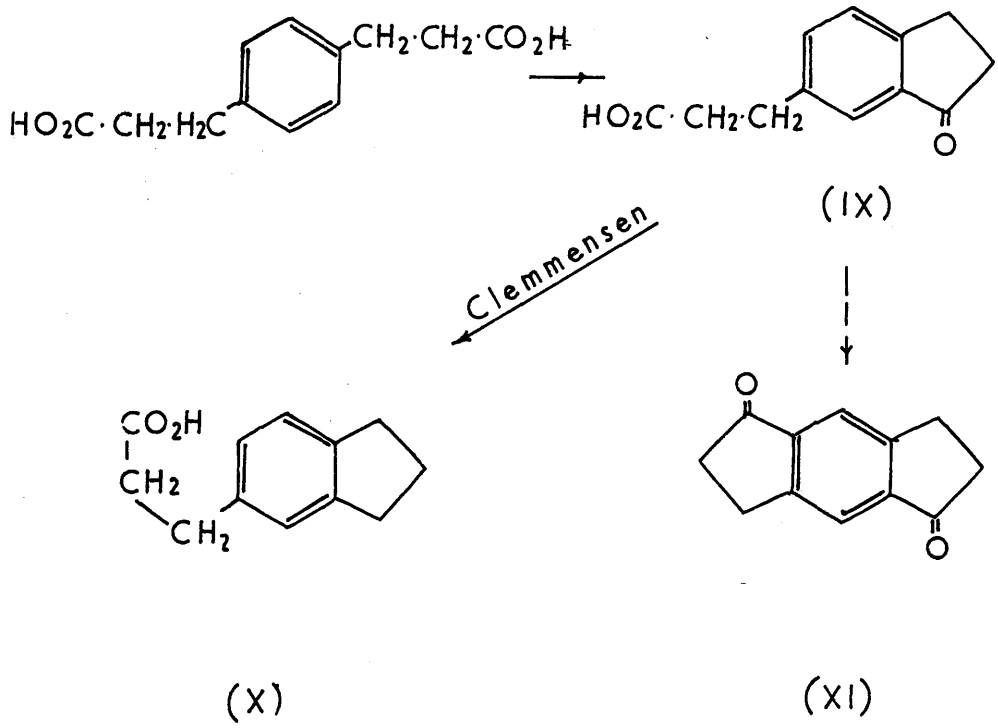
The only doubly-substituted hydrindacene of this type recorded (VIII) has been reported by Ruggli[35] who employed the following route.





(VIII)

As is seen the route is very tedious and uses a comparatively inaccessible starting material. In order to procure a similar type of compound more easily the following route was investigated.

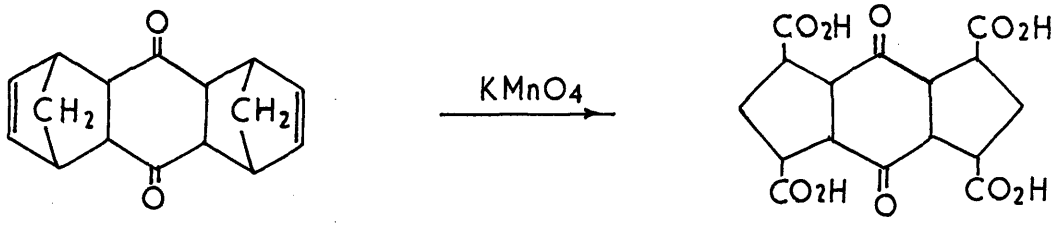


(X) (XI)

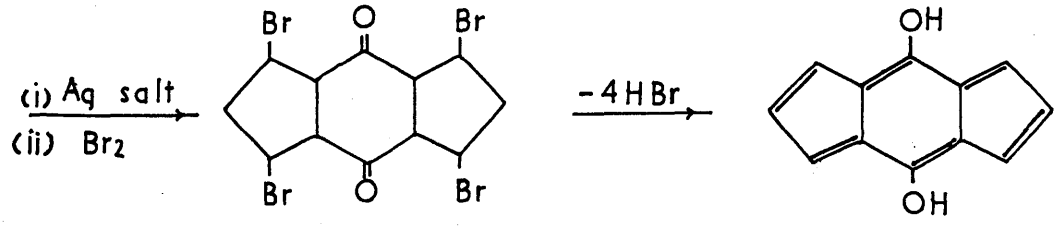
The readily available p-phenylenedipropionic acid was heated with polyphosphoric acid in an attempt to close both five-membered rings to give the diketohydrindacene (XI). The sole product however, was the indanone (IX)

only one such cyclisation having occurred. The constitution of the compound was confirmed by Clemmensen reduction to the known indanepropionic acid (X). All attempts to achieve the further cyclisation of the indanone (IX) were unsuccessful; this is no doubt due to the deactivating effect of the neighbouring electron-attracting carbonyl group on the benzene nucleus.

Another possible route to s-indacene was then tried using the readily prepared adduct of benzoquinone with two molecules of cyclopentadiene[36].



(XII) (XIII)

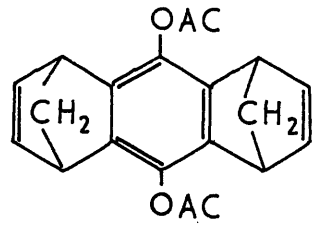


(XIV) (XV)

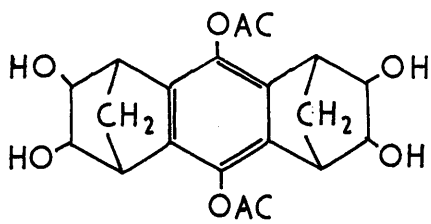
Oxidative fission of the double bonds of the adduct (XII) should yield the tetracarboxylic acid (XIII), Hunsdiecker degradation of which should furnish the corresponding tetrabromide (XIV). Removal of four molecules of hydrogen bromide from this compound should theoretically produce compound (XV), a dihydroxy-s-indacene.

All attempts at direct oxidation of the adduct (XII) with potassium permanganate, sodium permanganate / carbon dioxide, and nitric acid failed as the molecule seemed to undergo complete degradation. As this was thought to be due to the comparatively labile central cyclohexane-1:4-dione ring, this portion of the molecule was aromatised with palladised charcoal in acetic anhydride to the corresponding diacetate (XVI).

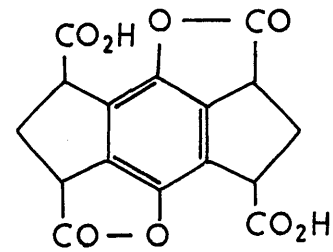
(XVI)



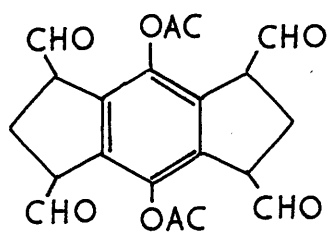
(XVI)



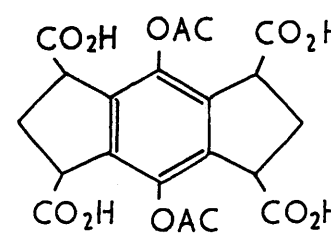
(XVIII)



(XVII)



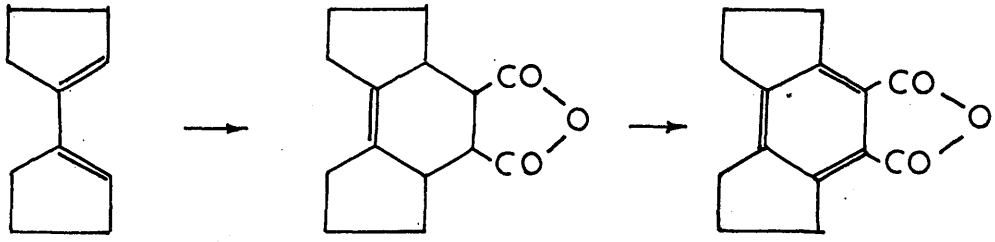
(XIX)



(XX)

Direct oxidation of this derivative with sodium permanganate buffered by carbon dioxide gave, in one case, a small yield of an acidic material with an analysis compatible with the dilactonic structure (XVII) but the process was not reproducible.

An indirect method of oxidation was then tried on the aromatised compound (XVI). The double bonds were hydroxylated by osmium tetroxide - hydrogen peroxide to yield the amorphous tetrol (XVIII). Glycol fission with sodium bismuthate[37] yielded a solution which gave the aldehydic reactions that would be expected from the product (XIX). Isolation of this tetra-aldehyde proved impossible, however, and the whole reaction mixture was then oxidised with silver oxide in order to obtain the tetra-acid (XX). Attempts to isolate the extremely water-soluble product by estrification gave only tars.



(XXI) (XXII) (XXIII)

In an attempt to procure a derivative of as-indacene, dicyclopentenyl (XXI) was condensed with maleic anhydride to give the adduct[38] (XXII). Dehydrogenation of this compound affected only the six-membered ring to yield the benzenoid derivative (XXIII). More drastic dehydrogenation led only to decomposition products. An attempt to brominate the five-membered rings in (XXIII) was made using carbon tetrabromide, a reagent specific for substituting carbon atoms adjacent to a benzene ring[39]. Only tarry products were obtained, however.

E X P E R I M E N T A L

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INTERACTION BETWEEN BENZOQUINONE AND ACETYLACETONE IN PYRIDINE.

Benzoquinone (20g.; 2 mols.) was dissolved in dry pyridine (25 c.c.) and acetylacetone (10g.; 1 mol.) was added in small portions with cooling and shaking. After the addition of half of the acetylacetone, the colour of the pyridine solution changed to dark brownish-red and most of the benzoquinone dissolved with much evolution of heat. Finally, after the addition was complete, the solution became viscous and acquired a dark brownish-violet colour. After being cooled at 0°C. for one day, the reaction mixture was diluted with alcohol (70-80 c.c.) and the solution was filtered. The resulting solid was washed several times with cold then with boiling alcohol.

The product (1 g.), consisted of dark green needles which did not melt up to 360°, and was practically insoluble in most of the organic solvents. However, it was sparingly soluble in hot pyridine, nitrobenzene, ethyl phthalate and ethyl malonate to give an intense violet solution. Crystallisation from the latter two solvents gave minute dark green needles; the violet colour of

the hot solution faded on cooling and standing for some time. An insoluble residue remained after continual extraction of the crude material with these solvents. The substance dissolved in concentrated sulphuric acid and phosphoric acid with a dark green colour and was reprecipitated unchanged on dilution with water. Sublimation at 320°/0.2mm., furnished dark green needles together with a considerable non-volatile black residue (ca. 50%). The green sublimate (A) showed all the properties described above and on resublimation no residue was left. Both the sublimed compound and the black residue gave a strongly positive Lassaigne test for nitrogen.

[Found : C, 71.62; H, 4.41 ; N, 7.80 (crude material)
C, 71.19; H, 3.85 ; N, 7.28 (sublimed material)
$C_{11} H_7 O_2 N$
requires : C, 71.3 ; H, 3.7 ; N, 7.5
Ionescu's postulated structure $C_{16}H_{12}O_4$
requires : C, 71.6 ; H, 4.48 %]

The black residue was complately insoluble in hot pyridine, nitrobenzene, ethyl phthalate etc.; it was soluble in concentrated sulphuric acid and phosphoric acid and was reprecipitated on dilution with water. Analysis of the crude green material before sublimation was almost

the same as after sublimation; a fact which suggests that the black residue may possibly possess a structure allied to that of the green sublimate but differs in the number of structural units per molecule.

Attempted Reduction of the Green Compound (A).

(i) Catalytic Hydrogenation:

The green material (0.5g.) in hot pyridine (25 c.c.) was subjected to hydrogenation in presence of platinum oxide; a very small volume of hydrogen was absorbed over a period of three hours and finally absorption stopped completely. The substance was recovered unchanged.

(ii) Hydrosulphite Reduction:

The green substance (50 mg.) was added to a mixture of dilute sodium hydroxide and sodium hydrosulphite solution. After being warmed, the material changed colour gradually to dark blue. The resulting dark blue solid did not melt up to 360°; it was sparingly soluble in ethyl malonate with a faint blue-green colour and a bright green fluorescence.

(iii)Huang Minlon Reduction:

A mixture of the green material (0.5g.), triethylene glycol (10 c.c.), solid sodium hydroxide (1.6g.) and 95% hydrazine hydrate solution (2 c.c.) was heated under reflux for one hour. The condenser was then removed and the temperature was raised to 200°. After being cooled, the reaction mixture was poured into water. A trace of a brown amorphous precipitate was collected on a filter; the filtrate had a bluish-violet colour. On evaporation of the filtrate under reduced pressure, tars were obtained.

(iv) Zinc Melt Reduction:

The green material (4g.) was ground with zinc dust (4.8g.) then sodium chloride (4.8g.) was introduced and the whole mixture finely ground together. This mixture was transferred to a 250 c.c. conical flask, mixed with freshly-fused, pulverised zinc chloride (28g.) and about 8-10 drops of water were added. The reaction mixture was heated gradually up to 300° with continuous stirring. At this point, frothing took place and the temperature was kept at 300° for 5 minutes. After being cooled, the reaction mixture was boiled with water (200c.c.) and

then extracted continuously with benzene. The benzene extract acquired a dark red-violet colour with a blue fluorescence. After being dried and concentrated, the benzene solution was chromatographed over alumina using benzene as a developing solvent; a deep blue band was obtained which on elution gave a dark violet solid (0.2 g.). Recrystallisation from benzene-light petroleum (b.p. 40-60°) (1:1) gave dark violet silky needles which did not melt up to 360°.

The product was soluble in most organic solvents; it dissolved in concentrated phosphoric acid and reprecipitated on dilution with water.

(Found : C, 75.5 ; H, 3.9 ; N, 9.6 . C_9H_5NO requires : C, 75.5 ; H, 3.8 ; N, 9.7%).

(V) Zinc and Phosphoric Acid Reduction:

The green material (1g.) was dissolved in concentrated phosphoric acid (100 c.c.) then small pieces of granulated zinc metal were added and the solution was heated at 120° for six hours with the frequent addition of fresh pieces of zinc. At the end of this period, the solution was clear and had a light blue-green colour.

Cooling and dilution with water (300 c.c.) furnished a dark blue solid which was extracted continuously with ether; the ether extract acquired a dark blue colour with a bright red fluorescence. Evaporation of the ether solution gave a dark violet solid which was sublimed at 200°/0.2mm., and was identical in properties and analysis with the violet compound obtained from the zinc melt experiment described above.

(Found : C, 75.33 ; H, 3.33 ; N, 10.0 . C_9H_5NO
requires : C, 75.5 ; H, 3.8 ; N, 9.7%).

Attempted Oxidation of the Green Compound (A).

(i) Potassium Permanganate Oxidation:

A suspension of the green material (0.1g.) in boiling acetone (50 c.c.) was treated with a hot 5% solution of potassium permanganate in acetone until the colour of the permanganate persisted. Sulphur dioxide gas was then passed into the solution and the precipitated salts were filtered and washed thoroughly with hot acetone. The combined acetone solutions were then evaporated to dryness; no residue was obtained. The inorganic salts were dissolved in a very small amount of water, acidified

with dilute sulphuric acid and extracted with ether. Evaporation of the ether extract gave no residue.

When the experiment was repeated with potassium permanganate in acetic acid, similar results were obtained.

(ii) Persulphuric Acid Oxidation:

A suspension of the green material (0.5g.) in hot glacial acetic acid (150 c.c.) was treated with concentrated sulphuric acid (1 c.c.) and potassium persulphate (4g.) and the reaction mixture heated under reflux for three hours. The colour of the mixture at the beginning was dark green with a faint violet fluorescence which changed slowly to brown-red and finally to yellowish-brown. Most of the acetic acid was removed under reduced pressure, water was added and the aqueous solution extracted continuously with ether. Evaporation of the ether extract gave no residue.

(iii) Performic Acid Oxidation:

The green material (0.1g.) was added to a mixture of formic acid (30 c.c.) and hydrogen peroxide (3 c.c.). After being heated for about twenty minutes, the reaction

mixture was diluted with water; the substance was recovered unchanged.

(iv) Concentrated Nitric Acid Oxidation:

The green material (0.5g.) was covered with concentrated nitric acid (3-4 c.c.); a vigorous reaction started after a few seconds. After the reaction subsided, the reaction mixture was heated for about three minutes then poured into water and cooled. The brown-red precipitate (60 mg.) was filtered off; it did not melt up to 360°. It was soluble in dilute sodium bicarbonate solution with effervescence and was precipitated on addition of dilute nitric acid. Addition of an aqueous solution of barium nitrate to a methyl alcoholic solution of the product gave a buff precipitate which might have been the corresponding barium salt. No satisfactory method of purifying the compound could be found.

Action of Bromine:

Addition of bromine to a hot solution of the green material in acetic acid gave a brown colour which changed

quickly to violet-brown. Evaporation of the solvent gave a trace of a brown-violet solid which did not melt up to 350°.

Oximation of the Green Compound (A).

The green compound (0.5g.) and hydroxylamine hydrochloride (0.5g.; 4 moles) in dry pyridine (30 c.c.) were heated at 100° for three hours; the colour of the reaction mixture changed from green to dark violet-red. After removal of pyridine under reduced pressure, the residue was extracted with chloroform; the chloroform solution was washed several times with water, dried and distilled. The residual dark red solid (0.1g.) crystallised from dilute pyridine in dark red prisms which did not melt up to 350°. The substance decomposed violently when heated over a direct flame and was soluble in dilute sodium hydroxide solution with red colour. The solution in alcohol showed a bright crimson fluorescence.

(Found : C, 63.93 ; H, 4.30 ; N, 14.46 .

$C_{11}H_8O_2N_2$ (monoxime)

requires : C, 66.0 ; H, 4.0 ; N, 14.0 %).

Attempted Beckmann Rearrangement of the Oxime:

The oxime (0.3g.) was treated with 85% sulphuric acid (6 c.c.) and the mixture heated for few seconds on the flame. After being cooled and diluted with water (75 c.c.), the reaction mixture was heated under reflux for five hours then filtered. The filtrate was made neutral with dilute sodium hydroxide solution and the precipitated solid was collected on a filter. The product was blue-black in colour and did not melt up to 350°. Its solution in alcohol showed a bright blue fluorescence.

(Found : C, 50.4 ; H, 4.5 ; N, 3.4 . $C_{18}H_{19}O N_4$
requires : C, 50.8 ; H, 4.4 ; N, 3.2%).

Attempted Acetylation and Benzoylation of the Green Compound (A).

The green substance (A) was recovered unchanged after being heated under reflux with acetic anhydride for two hours. It was also recovered unchanged after treatment with excess benzoyl chloride in pyridine.

Dicyclopentadienequinone (XII).

This was prepared according to the directions of Albrecht[36].

Attempt Degradative Oxidation of (XII).

(i) Potassium Permanganate:

A solution of potassium permanganate (0.5g.) in acetone (15 c.c.) was added to a solution of dicyclopentadiene-quinone (0.2g.) in acetone (10 c.c.) and the mixture was heated under reflux for half an hour. Sulphur dioxide was passed into the solution, the precipitated salts were collected on a filter and washed several times with acetone. When the filtrate and the washings were combined and evaporated no solid residue was obtained. Dissolution of the precipitated salts in water and subsequent acidification yielded no identifiable product.

(ii) Sodium Permanganate-Carbon Dioxide:

Dicyclopentadienequinone (1g.) was dissolved in benzene (6 c.c.) and water (40 c.c.) was added. A

steady stream of carbon dioxide was passed into the stirred mixture while a 15% solution of sodium permanganate (30 c.c.) was added at such a rate that the temperature of the mixture remained below 30°. When the addition was complete, sulphur dioxide was passed in; the resulting clear solution was acidified with dilute sulphuric acid and extracted with ether (3 x 50 c.c.). The combined ether extracts were dried, then evaporated. No crystalline material was obtained.

(iii) Nitric Acid (50%):

Dicyclopentadienequinone (1g.) was covered with 50% (V/V) nitric acid (6 c.c.). The reaction mixture became warm and a vigorous reaction took place. The material seemed to be completely oxidised.

(iv) Glycol Formation (Hydroxylation):

To a solution of dicyclopentadienequinone (1g.) in tertiary butanol (10 c.c.) was added a 10% solution of hydrogen peroxide in tertiary butanol (5.c.c.) followed by two drops of a solution of osmium tetroxide in tertiary butanol. The mixture was warmed on the steam

bath for few seconds whereby most of the dicyclopentadienequinone dissolved and the resulting solution kept at 0° overnight. Removal of the solvent under reduced pressure gave a colourless amorphous solid which was soluble in water and in alcohol but could not be crystallised. The product melted over a very wide range.

The Diacetate (XVI).

Dicyclopentadienequinone (5g.), palladised charcoal (0.2g.; 10%) and acetic anhydride (80 c.c.) were heated under reflux for two hours. After being filtered, the solution was diluted with water and cooled; the precipitated solid (2.8g.) crystallised from ethyl acetate in leaflets m.p. 235°.

Degradative Oxidation of (XVI).

(i) Potassium Permanganate:

To a warm solution of (XVI) (0.2g.) in acetone (10 c.c.) was added a 5% solution of potassium permanganate in acetone (10 c.c.) and the mixture warmed on the steam bath for 20 minutes. Sulphur dioxide was passed into the cooled solution and the precipitated salts filtered and washed with hot acetone. On evaporation of the

combined acetone solutions a trace of an acidic material was obtained.

(ii) Sodium Permanganate - Carbon Dioxide:

A solution of (XVI) (3g.) in benzene (20 c.c.) was poured into a 500 c.c. flask containing water (150 c.c.) and a steady stream of carbon dioxide was passed in. A 15% solution of sodium permanganate was added with vigorous stirring at such a rate that the temperature of the reaction mixture remained below 50°. When the reaction was complete (persistance of the permanganate colour), a stream of sulphur dioxide was passed into the mixture and the clear solution was acidified with dilute sulphuric acid. Extraction with ether (4 x 50 c.c.) and evaporation gave a buff coloured solid (0.1g.) which crystallised from ethyl acetate in prisms m.p. 130°. The substance was soluble in dilute sodium carbonate solution and was precipitated on acidification.

(Found : C, 59.2 ; H, 4.68 . $C_{16}H_{10}O_8$

requires : C, 58.2 ; H, 3.05%).

Repetition of the experiment under the same conditions could not reproduce the above result.

Hydroxylation of (XVI) to Glycol (XVIII).

The diacetate (XVI) (1g.) was covered with a 10% solution of hydrogen peroxide in tertiary butanol (7 c.c.); two drops of osmium tetroxide in tertiary butanol were then added and the reaction mixture warmed for a few seconds. The solution was then cooled and left at room temperature overnight. Evaporation of the solvent under reduced pressure produced an almost colourless amorphous solid (0.6 g.). The product was soluble in water and in alcohol but could not be crystallised. It melted over a wide range at about 200°.

Attempted Fission of Glycol (XVIII).

A mixture of the foregoing glycol (1g.), Analar sodium bismuthate (1g.), phosphoric acid (2.5 c.c.) and water (15 c.c.) was shaken in a stoppered bottle until the bismuth compound was completely reduced (disappearance of the orange-yellow colour). The bismuth phosphate was removed by filtration and the aqueous solution extracted several times with ether. Evaporation of the combined ether extracts gave no residue and it seemed that the

resultant aldehyde remained in the aqueous solution. This latter was then shaken with silver oxide for one hour then set aside overnight. Extraction with ether again afforded no product. The aqueous layer was evaporated almost to dryness under reduced pressure; a 3% solution of sulphuric acid in methanol (20 c.c.) was added to the residue and the mixture heated under reflux for one hour. At the end of this period, the sulphuric acid was neutralised with sodium methoxide and the precipitated sodium sulphate filtered off. Evaporation of the solvent gave a tarry residue.

Indan-1-one-6-propionic acid (IX)

In a flask protected from moisture, phosphorus pentoxide (50g.) was dissolved in syrupy phosphoric acid (34 c.c.) by swirling and heating on the steam bath for half an hour. p-Phenylenedipropionic acid (1g.) was then added and the contents of the flask were heated at 100° for four hours, then at 130° for one hour ; the solution became clear and acquired a brownish-red colour. After being cooled, the reaction mixture was poured on to ice, diluted with water and extracted several times with benzene. The combined benzene extracts were washed well with water, dried then concentrated. Addition of light petroleum (b.p. 40-60°) gave yellowish crystals (0.6g.). Boiling with charcoal in benzene gave a colourless product which crystallised from benzene - light petroleum (b.p. 40-60°) (3:1) in colourless prisms m.p. 148°.

(Found : C, 70.27 ; H, 5.36 . $C_{12}H_{12}O_3$

requires : C, 70.5 ; H, 5.8 %).

The 2:4-dinitrophenylhydrazone crystallised from alcohol in bright red needles m.p. 214°.

(Found : C, 56.53 ; H, 4.52 ; N, 14.44 . $C_{18}H_{16}O_6N_4$

requires : C, 56.2 ; H, 4.16 ; N, 14.5 %).

Attempted Cyclisation of Indan-1-one-6-propionic Acid.

Indan-1-one-6-propionic acid (0.4g.) was covered with fluorosulphonic acid (5 c.c.) and the mixture heated under reflux for three hours. The cooled reaction mixture was treated with crushed ice, diluted with water and extracted several times with ether. The combined ether extracts were shaken twice with dilute sodium hydroxide solution then with water, dried and finally evaporated. No residue was left. Acidification of the basic extract with dilute sulphuric acid followed by extraction with ether and evaporation gave unchanged indan-1-one-6-propionic acid (0.35g.) (m.p. and mixed m.p.).

Indane-5-propionic Acid.

A mixture of amalgamated zinc (10g.), water (7c.c.), concentrated hydrochloric acid (14 c.c.), acetic acid (4 c.c.), toluene (8 c.c.) and indan-1-one-6-propionic acid (0.5g.) was refluxed for 36 hours during which time an additional 12 c.c. of concentrated hydrochloric acid was added. Extraction with ether and evaporation of the solvent gave indane-5-propionic acid (0.3g.), which crystallised from aqueous acetic acid in colourless needles m.p. 84-86° (Arnold and Barnes[34] give m.p. 85-86°).

3:4:5:6-Dicyclopentenophthalic Anhydride.

1:2:3:6-Tetrahydro-3:4:5:6-dicyclopentenophthalic anhydride[38] (0.5g.) and palladised charcoal (20%) in mesitylene (20 c.c.) were heated under reflux for twenty hours. After removal of palladium charcoal by filtration; the solvent was evaporated under reduced pressure; the solid residue crystallised from alcohol (charcoal) in colourless prisms m.p. 262°.

The product was soluble in dilute sodium hydroxide solution after prolonged boiling, thus confirming the presence of the anhydride group.

(Found : C, 73.7 ; H, 5.07 . $C_{14}H_{12}O_3$

requires: C, 73.68; H, 5.2 %).

Attempted further dehydrogenation of 3:4:5:6-dicyclopentenophthalic anhydride with selenium at 360° for six hours, left most of the material unchanged.

1:2:3:6-Tetrahydro-3:4:5:6-dicyclopentenophthalic anhydride was also subjected to dehydrogenation with selenium at 360° for five hours. A small amount of 3:4:5:6-dicyclopentenophthalic anhydride was obtained (m.p. and mixed m.p.).

Attempted Bromination With Carbon Tetrabromide.

3:4:5:6-Dicyclopentenophthalic anhydride (0.1g.) and carbon tetrabromide (0.6g.) in carbon tetrachloride (6 c.c.) were heated in a sealed tube at 120-150° for four hours. (c.f. Hunter and Edgar[39]). The product was an intractable tar and no crystalline material could be obtained.

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