SMALL RING CARBOCYCLIC STUDIES

A Thesis presented by

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ABSTRACT

The chemistry of tricyclo$[1.1.0.0^{2,4}]$butane (tetrahedrane) and bicyclo[1.1.0]butanes is reviewed in some detail.

The photolysis of pyridazine under varied conditions is reported. The synthesis and photochemical behaviour of 8-phenyl-1,6,8-triazabicyclo[4.3.0]nona-2,4-diene-7,9-dione and the attempted synthesis of 1,4-diphthalimidobuta-1,3-diene is described.

The attempted synthesis of bicyclobutanes from cyclobutanes <u>via</u> extrusion reactions is discussed.

The stereochemistry of 1-methyl-3-phenylbicyclo[1.1.0]butane-2,4-dicarboxylic acid is determined and the feasibility of this compound as a precursor for a tetrahedrane is investigated. The attempted synthesis of bicyclobutanes which have functionality that would render them potential precursors for a tetrahedrane is also described.

To Jane

ACKNOWLEDGEMENTS

I thank Professor D. H. R. Barton, F.R.S., for the opportunity to participate in research at Imperial College. I also wish to thank both Professor D. H. R. Barton and Dr. P. D. Magnus for their enthusiasm and guidance throughout the course of this work.

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The friendship of my many colleagues in the Chemistry Department will always be appreciated.

Finally, I wish to thank my mother and father whose constant help and encouragement throughout my education has enabled me to write this thesis.

Peter R. Reucroft,

September 1970 Whiffen Laboratory.

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To travel hopefully is a better thing than to arrive, and the true success is to labour.

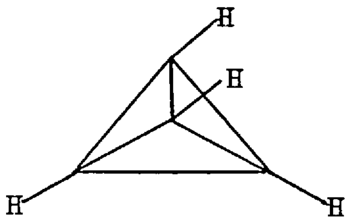
R. L. STEVENSON

Virginibus Puerisque. vi. El Dorado

REVIEW

Introduction

Polycyclic compounds composed of a number of fused small rings have been known for some time but in recent years there has been a resurgence of interest in such compounds. Most groups of these have become accessible to the organic chemist and are both theoretically and preparatively interesting. The strain inherent in small ring compounds causes them to exhibit unusual and frequently unexpected properties, both of a chemical and theoretical nature. Of special interest is tricyclo[1.1.0.0^{2,4}]butane (1), commonly called tetrahedrane, which is one of the most highly condensed compounds composed of carbon-carbon single bonds. It is the simplest compound possessing a cage structure.



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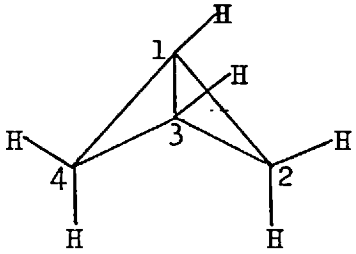

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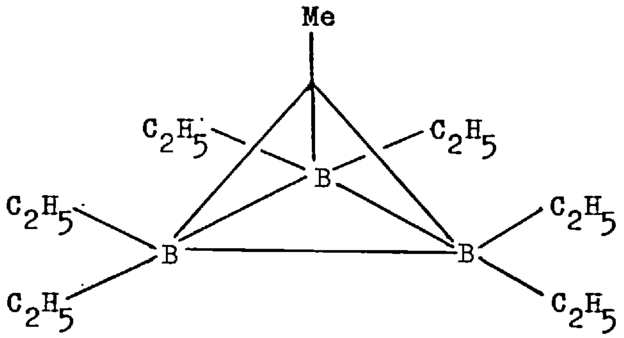
As the attempted synthesis of tetrahedrane forms a major part of this thesis, the molecule will be examined in detail in this review.

Bicyclo[1.1.0]butane (2) bears an obvious structural similarity to tetrahedrane and because of the fact that substituted bicyclobutanes were utilised in the synthetic work described in this thesis, the chemistry of bicyclobutanes will be reviewed with particular emphasis on those aspects of their chemistry which render them potential precursors to substituted tetrahedranes.

Tetrahedrane

The most highly fused system comprising only small-membered rings is the tetrahedron (1),[1] but the only example of this structural type that has been synthesised consists of three boron atoms and one carbon atom at the apices of the tetrahedron i.e. the carborane (3).[2] The tetrahedron consisting of four carbon atoms



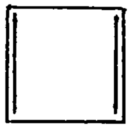
(3)

is a cyclobutadiene isomer,[3] but it may be thought of as being formed from two molecules of acetylene[4] or by interlinking of opposite corners of a four-membered ring.

At the present time, however, this parent tetrahedron has not been synthesised although there is evidence for its transient existence as a reaction intermediate,[5] and mass spectral studies have suggested structures of tetrahedral symmetry for some fragmentations.[6]

Stability

The unstable character of the cyclobutadiene molecule (4) has led to the suggestion[1] that a tetrahedral isomer (1),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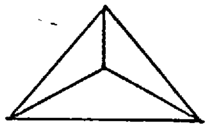
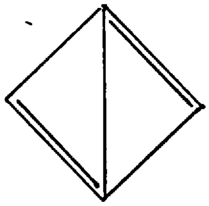

(1)

differing from the former system by a non-planar distortion, might possess greater stability. Such a structure, with its six equivalent carbon-carbon single bonds, would possess a closed-shell electronic configuration in contrast to cyclobutadiene, although its greater strain energy might nullify this advantage. The molecule P_4, which has the same number of bonding electrons as tetrahedrane, is known to possess tetrahedral geometry, but the failure to find similar stable structures for N_4 could indicate that such an arrangement is less probable for first-row elements.

Baird and Dewar[7] have carried out a series of self-consistent field molecular orbital (SCF MO) calculations on small ring systems. For such species the quantity known as the strain energy, i.e. the difference in energy between the compound and the value that would be expected for a strain-free analogue, is an important parameter. The results for tetrahedrane and bicyclobutadiene (5) (another theoretical molecule) in particular were noted - the



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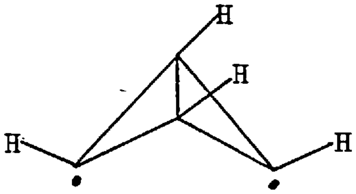
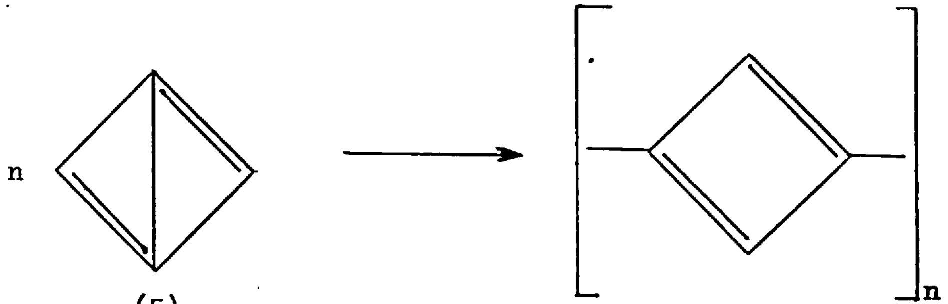


(6)

former was predicted to have an extremely large strain energy, greater by 83 kcal mol^{-1} than that of bicyclobutane. Since this value approximates to the bond energy of a carbon-carbon single bond, the conversion of tetrahedrane to the bicyclobutane diradical (6) should be essentially thermoneutral. If these calculations are correct, then tetrahedrane cannot exist as a stable entity at ambient temperatures but might conceivably be stable if formed in a matrix at low temperature, for example by photochemical production.

Calculations[7] suggest, however, that bicyclo[1.1.0]butadiene (5) should be thermally stable but extremely reactive, and polymerisation to polycyclobutadiene was predicted to be exothermic, i.e.



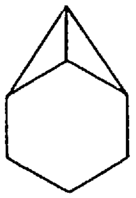
(5)

Unfortunately, as bicyclobutadiene (5) is unknown chemically, the prediction remains untested.

More recently the geometry of tetrahedrane and its stability relative to (a) cyclobutadiene and (b) two acetylene molecules has been investigated by ab initio self-consistent field molecular orbital and configuration interaction (CI) calculations.[8] It should be noted that the single determinantal wave function of the SCF method gave a better representation of the tetrahedrane ground state - a classical closed-shell species - than that of cyclobutadiene, with its partially filled valence shell. Configuration interaction (i.e. use of a multideterminantal wave function) was introduced into the calculations to increase the flexibility of the molecular wave functions employed thereby removing most of the bias towards tetrahedrane obtained from the simple SCF treatment. The CI calculations showed tetrahedrane to be considerably less stable than cyclobutadiene. A figure of 70.3 kcal mol^{-1} was deduced - a value which is in reasonable agreement with the estimate of 84.2 kcal mol^{-1} made by Baird and Dewar.[7]

The calculations necessary to compare the relative stabilities of C_4H_4 isomers and two acetylene molecules are rather complex and of necessity only upper and lower limits were determined. For tetrahedrane the energy difference was placed between 70 and 100 kcal mol^{-1} in favour of two acetylene molecules.

It is relevant to mention here the correlation between ^{13}C-H spin-spin coupling constants and internuclear angles for cyclic molecules. In general, the spin-spin coupling constant is a function of the internuclear angle such that the greater the strain involved, the greater is the coupling constant. It has been calculated[9] that tetrahedrane should have a J_{C-H} of about 225 Hz, i.e. a value lower than that of acetylene - 251 Hz - but higher than that of tricyclo$[4.1.0.0^{2,7}]$heptane (7)[10] - 200 Hz - or 1,5-diphenyltricyclo$[2.1.1.0^{4,5}]$pentan-3-one (8)[11] - 190 Hz.



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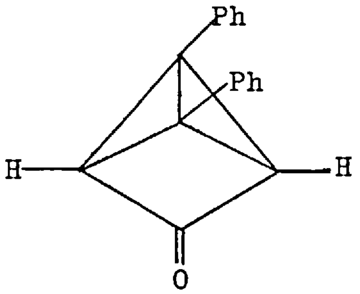

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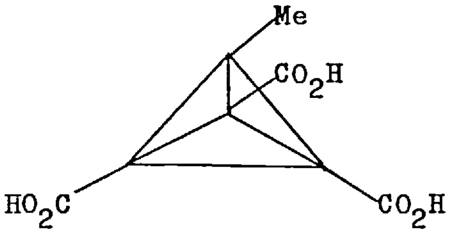
In conclusion, it seems clear that semi-empirical methods can give a reasonable idea of the amount of strain energy associated with cyclic systems when used to compare the relative stabilities of molecules of approximately the same size. Thus it seems quite certain that cyclobutadiene is substantially more stable than tetrahedrane and both isomers are unstable relative to two acetylene molecules.

Synthesis

Beesley and Thorpe[12] were the first to claim the synthesis of a tetrahedrane derivative, viz., 1-methyltricyclo$[1.1.0.0^{2,4}]$butane-2,3,4-tricarboxylic acid (9), but since their preparation was found to be unreproducible[13] the status of their work is uncertain and their claim, together with another for the preparation of the cellulose ester of (9),[14] must be discounted.



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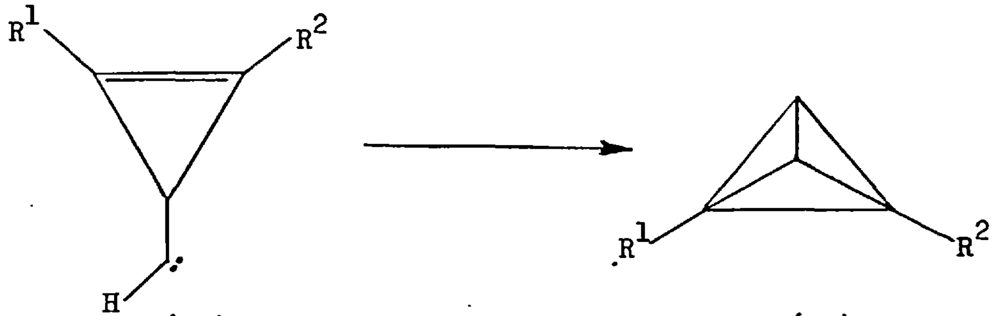
Conceptually, a simple route to a tetrahedrane structure is the intramolecular addition of a carbene to a cyclopropene double bond, viz.,



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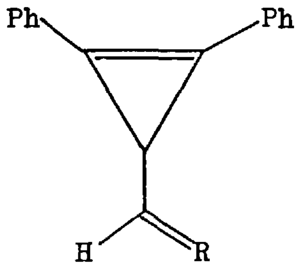
Such an approach was indeed examined and the synthesis of diphenyltetrahedrane (11; $R^1 = R^2 = Ph$) by low temperature photolysis of the sodium salt of (Δ^2-2,3-diphenylcyclopropenyl)-carboxaldehyde tosylhydrazone (12; R = $\left[N{-}N^{-}{-}SO_2C_7H_7\right]Na^{+}$) was



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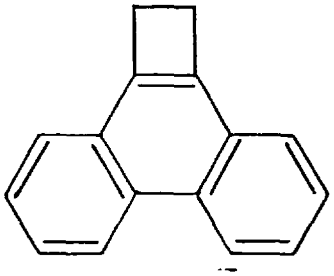
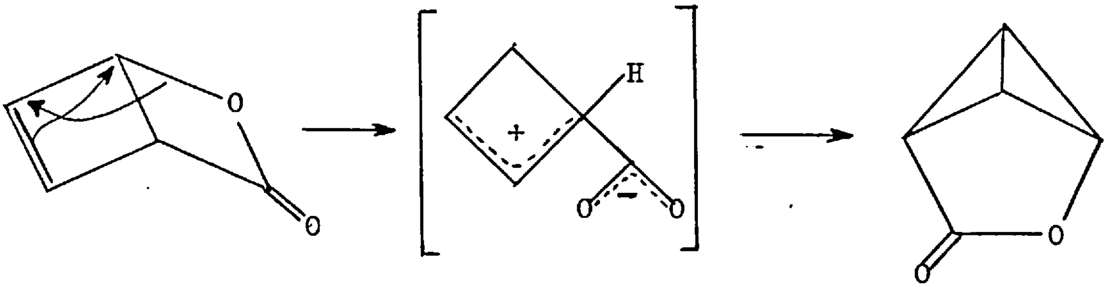


(13)

reported.[15] However, this work was later retracted by its authors[16] in favour of the alternative formulation (13) for the product hydrocarbon.

The cyclopropenyl carbene (10; $R^1 = R^2 = Ph$) has also been approached <u>via</u> (Δ^2-2,3-diphenylcyclopropenyl)diazomethane (12; R = N_2)[17] but the thermal and photochemical decomposition of this compound yielded neither an isolable tetrahedrane nor the dimeric compounds conceivably derived from it. Isolated instead were nitrogen (60-90% yield), diphenylacetylene (10-40% yield), benzoic acid, and some polymeric material. The diphenylacetylene probably originated in the step in which nitrogen was lost from the diazo-compound and tetrahedrane may have given rise to the polymers. Attempts to trap the reaction intermediates with cyclohexene or butadiene were unsuccessful as were experiments designed for isolation of volatile compounds from reaction mixtures which had been hydrogenated immediately after decomposition of the diazo-compound.

Bicyclo[2.2.0]pyran-2-one (14) was synthesised by Corey and Pirkle[18] as a possible precursor to cyclobutadiene. However, when



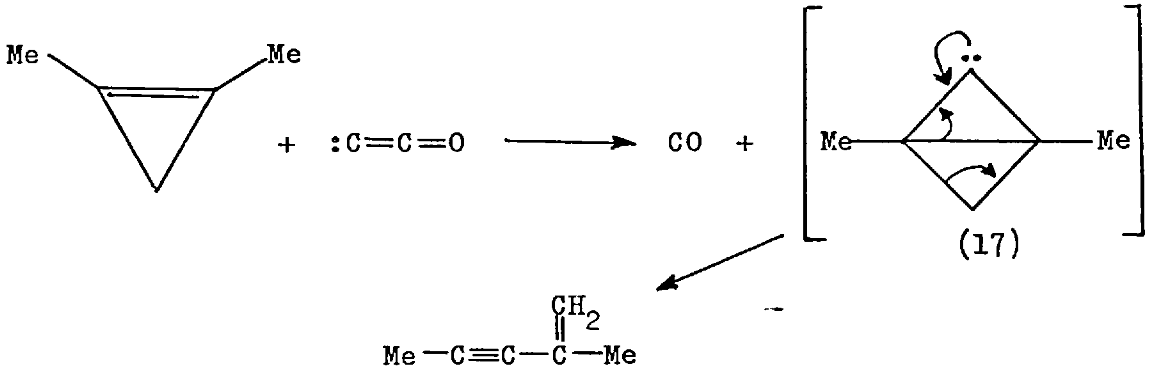
(14) (15) (16)

(14) was dissolved in aprotic solvents such as acetonitrile or dichloromethane it underwent a rearrangement to the tricyclic product (16). A reasonable intermediate for this rearrangement might be the dipolar ion (15) which could well exist as an intramolecular ion-pair in the comparatively non-polar solvents which suffice for this rearrangement.

By analogy with (14), (16) could give tetrahedrane by the elimination of the elements of carbon dioxide with the simultaneous formation of a new carbon-carbon single bond. The authors did not report any experimental attempts to effect this elimination but presumably they must have considered such a possibility.

More recently, approaches to tetrahedrane have been devised which involve the intermediacy of bicyclic carbenes. Photolysis of carbon suboxide in 1,2-dimethylcyclopropene[19] gave 2-methylpent-1-ene-3-yne (18). The intermediate (17) could, in principle,

$$C_3O_2 \xrightarrow{h\nu} CO + :C{=}C{=}O$$

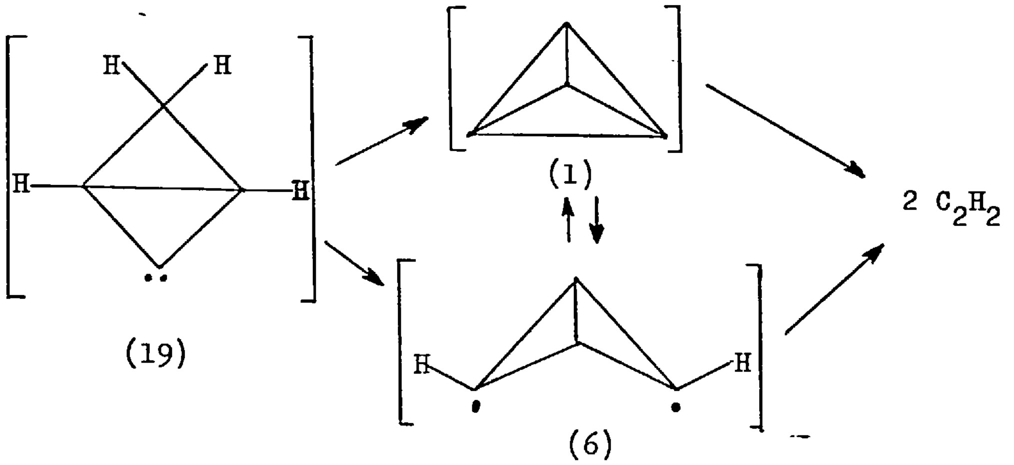


(17)

(18)

undergo intramolecular insertion to give dimethyltetrahedrane. However, a carbenoid rearrangement to the vinylacetylene derivative (18) seemed to be preferred. A number of factors may have favoured this route over intramolecular insertion, in particular, the lack of adequate de-excitation of the excited intermediate (17). Conceivably, a liquid or solid phase experiment could alter the product spectrum.

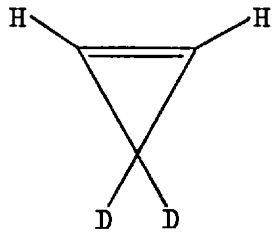
The reactions of atomic carbon and carbonylcarbene with cyclopropene[20] were quite similar to the above process, but the products in the first case were acetylene, vinylacetylene, and diacetylene, and in the second, acetylene and vinylacetylene. With carbonylcarbene, the singlet species shows a preference of 10^4 for insertion into normal C=C bonds compared with C—H bonds, thus it seems quite probable that acetylene and vinylacetylene were formed from an intermediate such as (19). This species could decompose



to acetylene by either or both of the two pathways shown, i.e. tetrahedrane was a plausible intermediate in these systems. Use of orbital symmetry arguments[21] was judged to indicate that direct decomposition of (1) to acetylene was forbidden (the greater thermodynamic stability of acetylene is, of course, irrelevant to such arguments) but that decomposition via (6) was allowed.[20] It should be noted that the merit of such interpretations for these systems is unclear because of the variety of excited states that may.

be accessible at the available internal energies of the intermediates.

The studies of Shevlin and Wolf[5] provide the most convincing evidence for the occurrence, albeit transient, of tetrahedrane. These authors investigated the gas phase photolysis of carbon suboxide in the presence of cyclopropene and isolated acetylene and vinylacetylene. The bicyclic carbene (19) was proposed as an intermediate which could give tetrahedrane. In order to determine if the acetylene produced was formed from the decomposition of tetrahedrane, the photolysis was carried out with a specifically labelled precursor (20) which, according to the above proposition,



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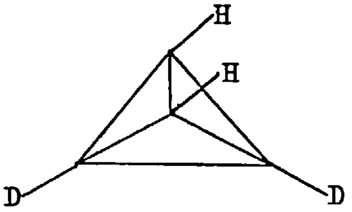
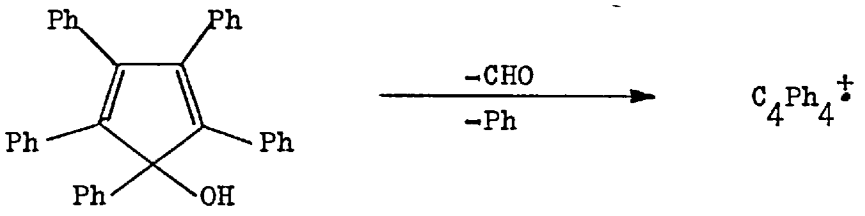


(21)

would give rise to (21). The product acetylenes - C_2H_2, C_2HD, and C_2D_2 - were analysed by mass spectrometry and their ratio compared with that calculated assuming the intermediacy of tetrahedrane. The theoretical and experimental values were extremely close indicating that tetrahedrane is indeed an intermediate in the reaction. To further substantiate this conclusion, 2-^{14}C-carbon suboxide was photolysed with the labelled cyclopropene (20) and the distribution of radioactivity among the three product acetylenes determined. Once again the experimental values corresponded extremely well with the calculated ones. These results indicated that tetrahedrane had a finite lifetime at room temperature.

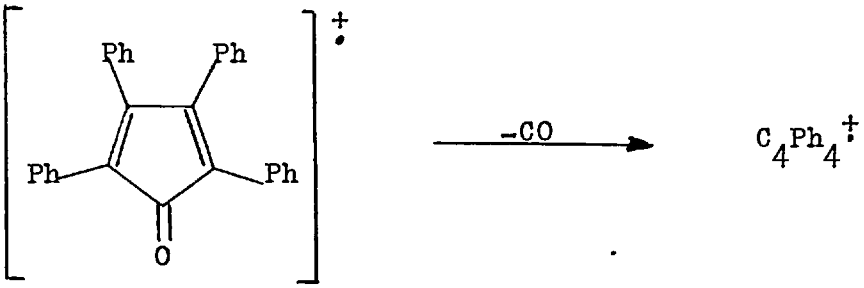
The mass spectral fragmentation pattern of certain cyclic dienes has been rationalised by the postulated intermediacy of a 'tetrahedron-like' radical-cation. A major route proposed for the decomposition of pentaphenylcyclopentadienol (22)[6] was the stepwise



(22)

loss of the elements of aryl and CHO to give a C_4Ph_4 ion. Labelling experiments (utilising p-fluorophenyl groups) suggested a tetrahedral symmetry for this species at some point before its further fragmentation. Although the mode of formation seems unlikely the observation of this species could infer that the tetraphenyltetrahedrane radical-cation might possess unusual stability in mass spectral decompositions especially if the observations below are considered.

This labelling method has also been applied to the following systems which gave a tetrahedral C_4Ph_4 ion by fragmentation of the molecular ion :-



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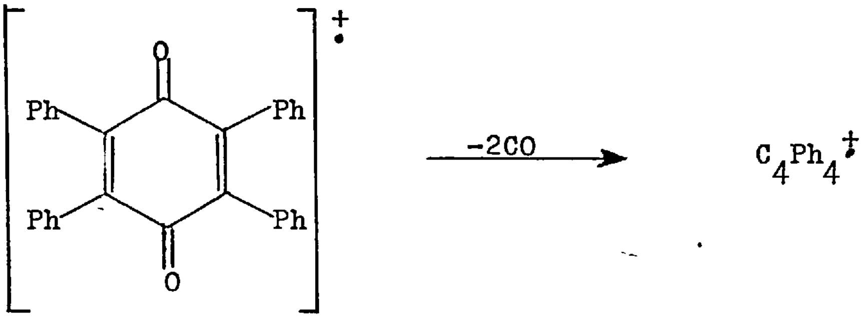

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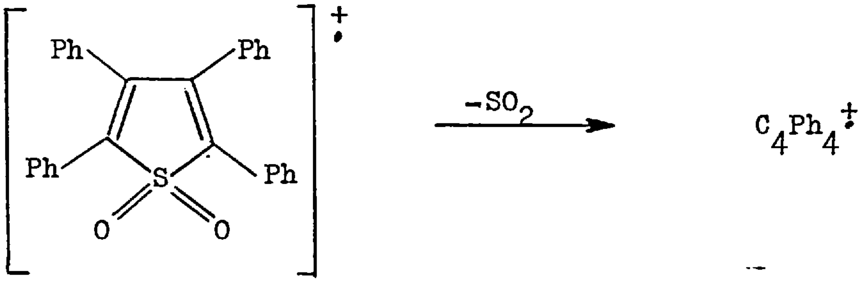

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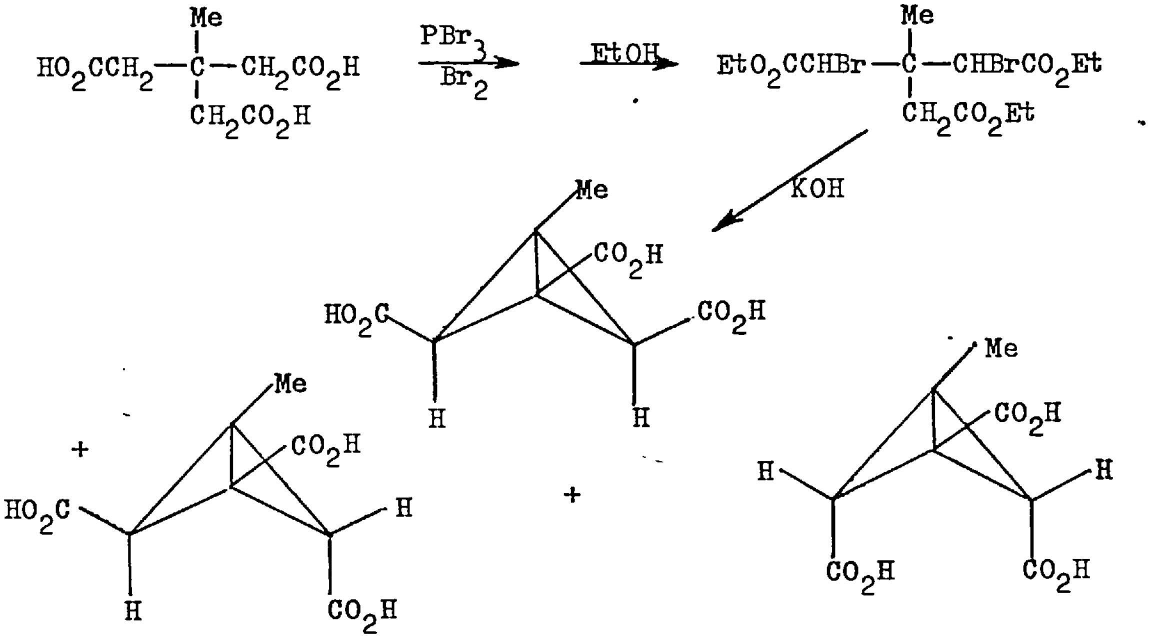
Bicyclo[1.1.0]butanes

Small ring bicyclic compounds have been known for a relatively short time. The first authentic bicyclo[1.1.0]butane derivative was reported in 1959 but since then their chemistry has been extensively explored.

Syntheses

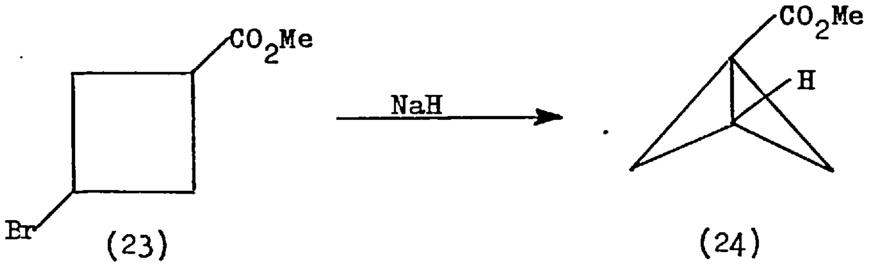
A number of syntheses of bicyclobutanes appeared in the older literature;[25] that of Beesley and Thorpe[12] merits some consideration. Their reaction scheme was as follows:-



Despite the detailed experimental directions provided, it has not been possible to reproduce their work.[13] Interestingly, the procedure which succeeded in producing the first bicyclobutane was similar to that reported by Beesley and Thorpe. Perhaps ring closure might have been effected if a milder reagent had been tried. The other bicyclobutane preparations mentioned have been proved incorrect and revised structures have been proposed.[26]

The first authentic bicyclobutane derivative was prepared by base-catalysed cyclisation of methyl 3-bromocyclobutanecarboxylate (23).[27] The optimum yield of methyl bicyclobutane-1-carboxylate (24) (77%) was obtained using sodium hydride as the base. The reaction proceeded equally well for 3-alkyl-3-halocyclobutanes, e.g., methyl

3-bromo-3-methylcyclobutanecarboxylate (25) gave methyl 3-methyl-



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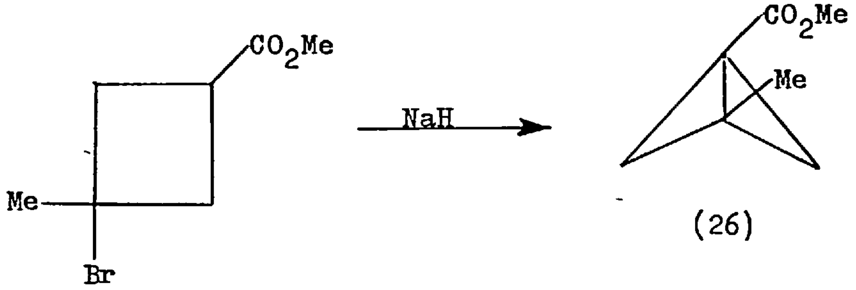


(25) (26)

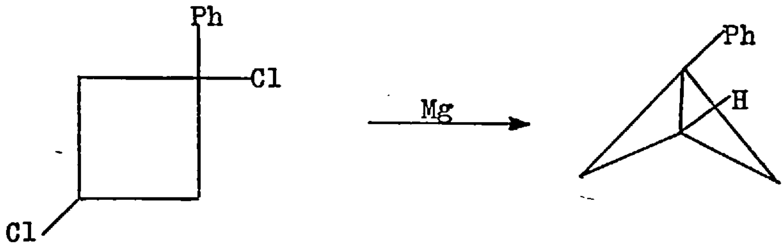
bicyclobutane-1-carboxylate(26) (90% yield).[28] Analogous reactions occurred when the ester group was replaced by a nitrile function.[29]

The principle synthetic routes to bicyclobutanes can be conveniently sub-divided into the following groups:- transannular elimination reactions, electrochemical processes, intermolecular carbene additions, intramolecular carbene reactions, and intramolecular photolytic reactions.

Transannular Elimination Reactions

In this type of reaction a new transverse carbon-carbon bond is formed in an existing ring by elimination of HX or X_2, where X is a good leaving group (halide, tosyl, *etc*.). Strong bases and alkali metals are generally used to effect these transformations.

The first bicyclobutane synthesis[27] - mentioned previously - falls into this category. Other syntheses are similar in principle and differ only in functionality of substrate and reagent used. A complete list of these examples is irrelevant to the present review; the following cases are representative of the principle:-



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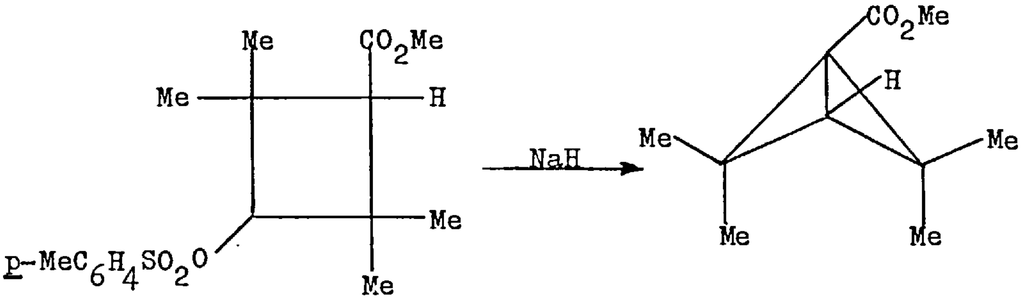

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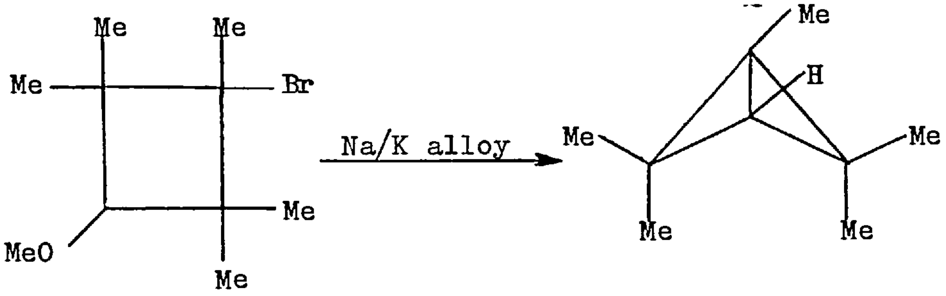

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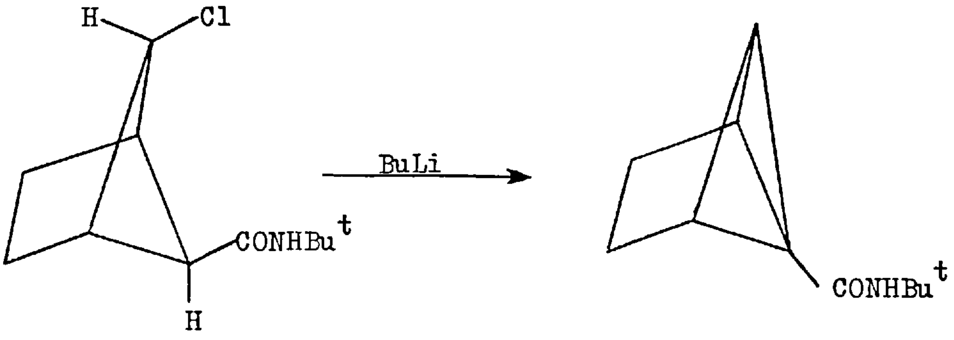


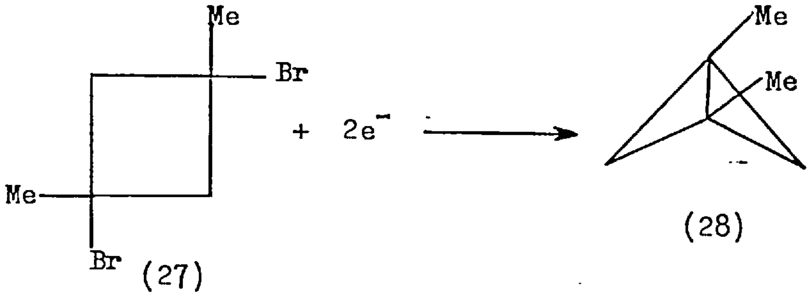
(ref. 33)

This last reaction is similar to the base-catalysed cyclisations of 3-halocyclobutane esters; however, the chlorine atom is not correctly oriented for a conventional S_N2 reaction.

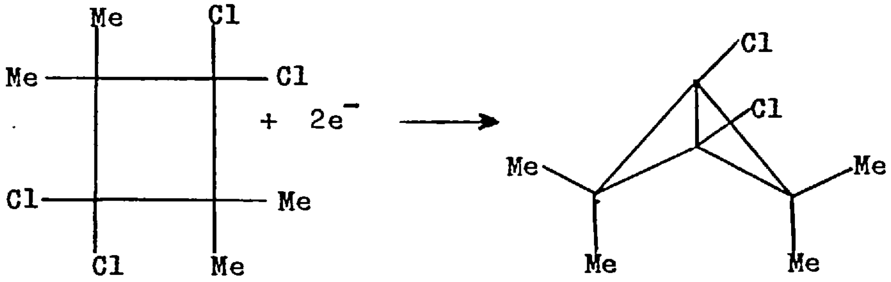
Electrochemical Processes

Electrolytic coupling of two carbon atoms to form a new carbon-carbon single bond has not found wide application in small ring chemistry, possibly due to some of the practical difficulties involved or to the paucity of work in this field.

1,3-Dimethylbicyclobutane (28) has been synthesised by electrolysis of a solution of 1,3-dibromo-1,3-dimethylcyclobutane (27).[34]



The reaction was extended to the synthesis of bicyclobutanes (*e.g.* 30) from cyclobutanes (*e.g.* 29) containing more than two halogen atoms,[34] *viz.*;



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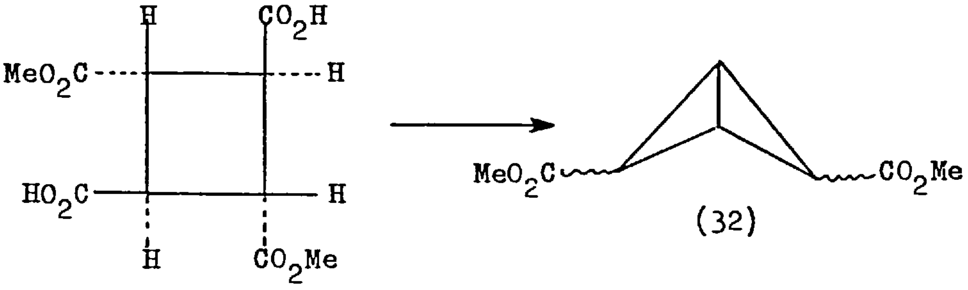
Electrolytic decarboxylation was used by Vellturo[35] in a synthesis of dimethyl bicyclobutane-2,4-dicarboxylate (32) from the diacid-diester (31) (10% yield).

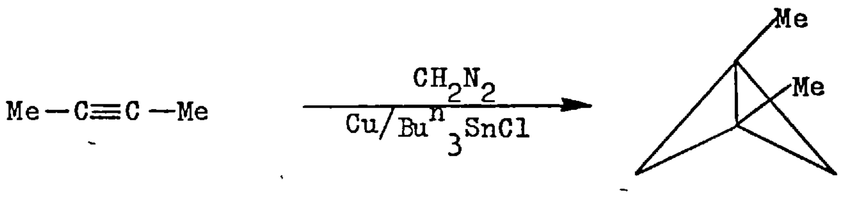


(31) (32)

Unfortunately, as the bicyclobutane diester (32) could not be hydrolysed to the diacid, the crucial transannular bond formation could not be tested on this potential precursor of tetrahedrane.

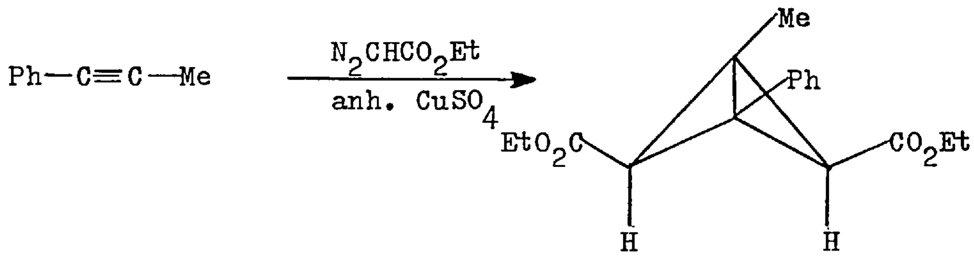
Intermolecular Carbene Additions

The reaction of carbenes with olefinic double bonds to yield cyclopropanes is well documented. Less well-known is the reaction between carbenes and acetylenes to yield cyclopropenes and/or bicyclobutanes. Unfortunately, the latter has very limited use. The reaction does not proceed at all, or only with difficulty, when the substituents on the acetylenic bond are sterically large, *e.g.*, phenyl, and the yields are poor. Nevertheless, the method provides a direct route to simple substituted bicyclobutanes. The examples below are representative:-

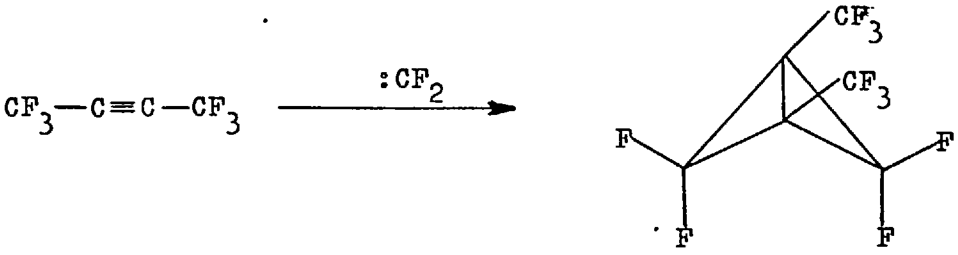


(ref. 36)

(Note that neither photolytic nor copper-catalysed reaction of diazomethane with the acetylene led to any bicyclobutane - modification of the copper-catalysed reaction by addition of tri-n-butyl tin chloride was essential)



(ref. 37)



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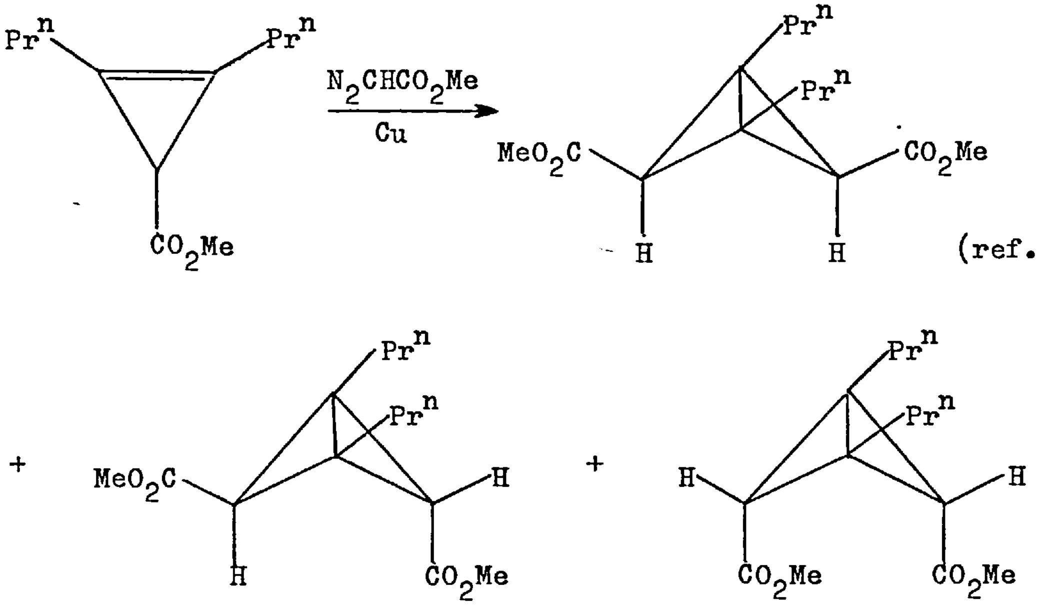
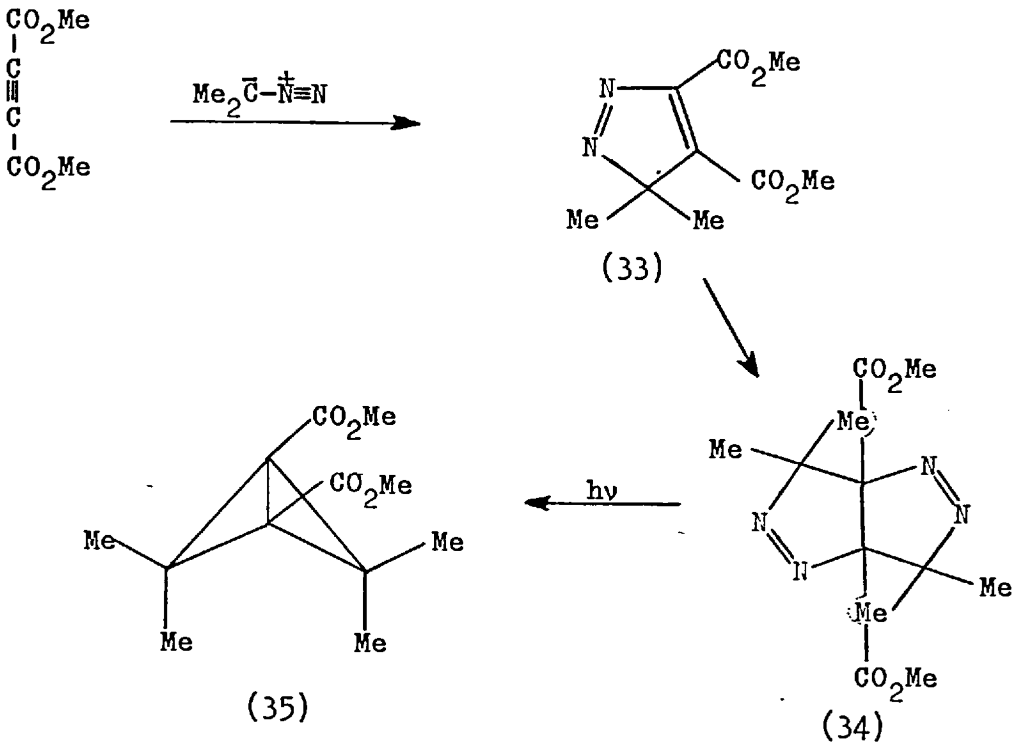


(ref. 39)

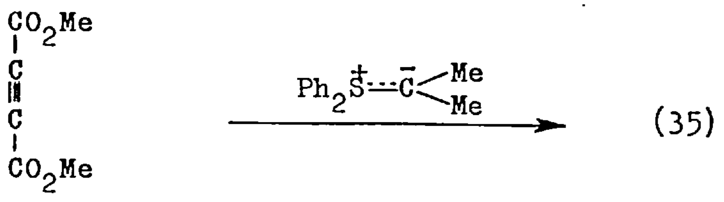
This last reaction is unique in that it is the only one which gave rise to all three possible isomeric bicyclobutanes - exo,exo-, exo,endo-, and endo,endo-. Generally, only the exo,exo- isomer is isolated.

It is convenient to include in this section two reactions which are not strictly carbene additions but which involve double-additions to acetylenes. In the first, a 1,3-dipolar addition to a triple bond gave initially the pyrazole (33).[40]



Further treatment of this gave the bicyclic derivative (34), which yielded the bicyclobutane (35) on photolysis.

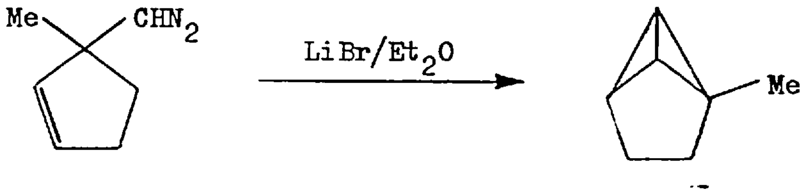
The second reaction involved the use of diphenylsulphonium isopropylide on an acetylene[41] to give the bicyclobutane (35) in low



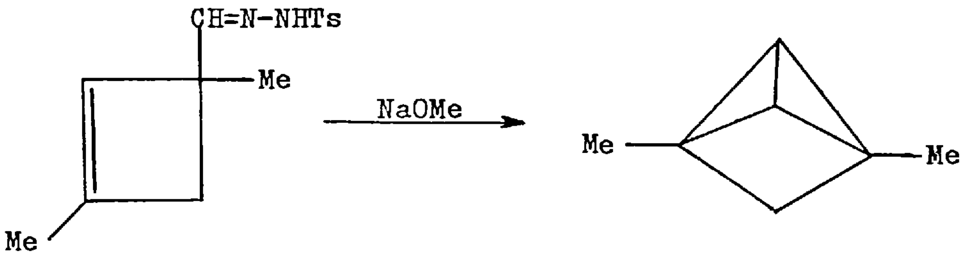
yield (16%)

Intramolecular Carbene Reactions

In the absence of other substrates, carbenes can undergo intramolecular C=C addition or intramolecular C—H insertion reactions to give highly strained systems. This method is of particular use for the preparation of bicyclobutanes and there are many examples in the literature. Generally, an inorganic catalyst or light is used to decompose a diazo-compound producing a carbene intermediate which then reacts further. A complete list of reactions is not required for the present survey. The examples shown below are representative both of the different types of product and of the reaction conditions necessary.



(ref. 42)



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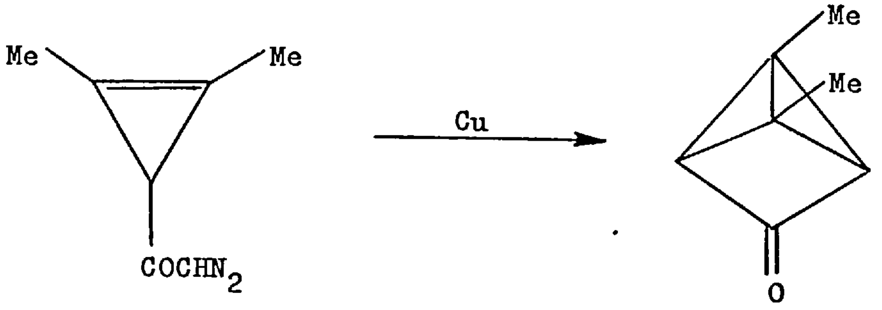

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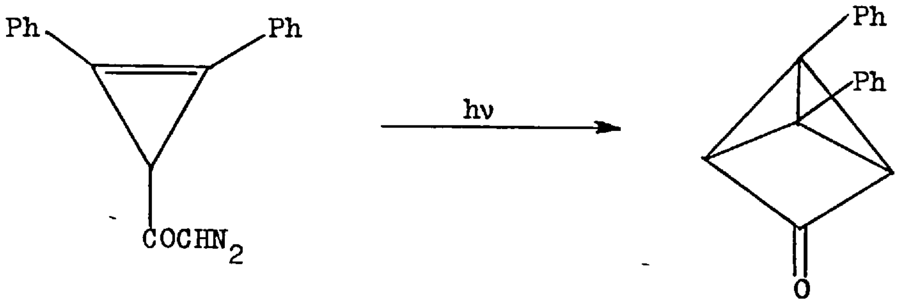
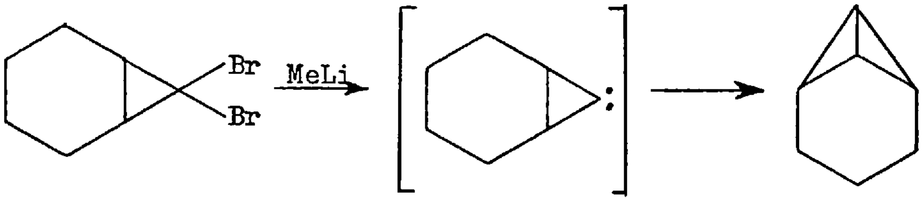


(ref. 11)



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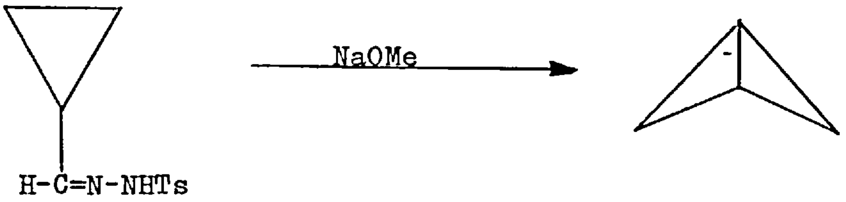
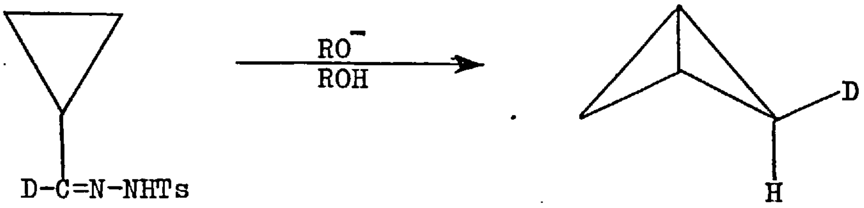


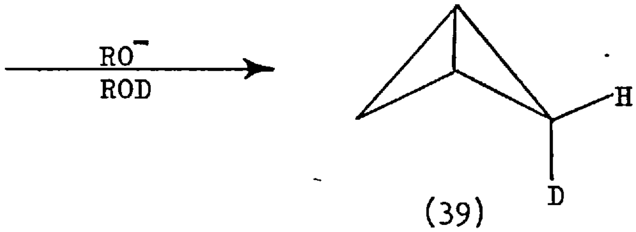
(36)

(ref. 45)

The formation of bicyclobutane from cyclopropanecarboxaldehyde tosylhydrazone (36) has been studied in detail. The tosylhydrazone was decomposed by base in an aprotic solvent to give cyclobutene but if a proton source, such as ethylene glycol, was present, bicyclobutane was the major and cyclobutene the minor product.[45] Cyclopropane-d-carboxaldehyde tosylhydrazone (37) reacted to give almost exclusively 2-exo-d_1-bicyclobutane (38).[46] When the unlabelled



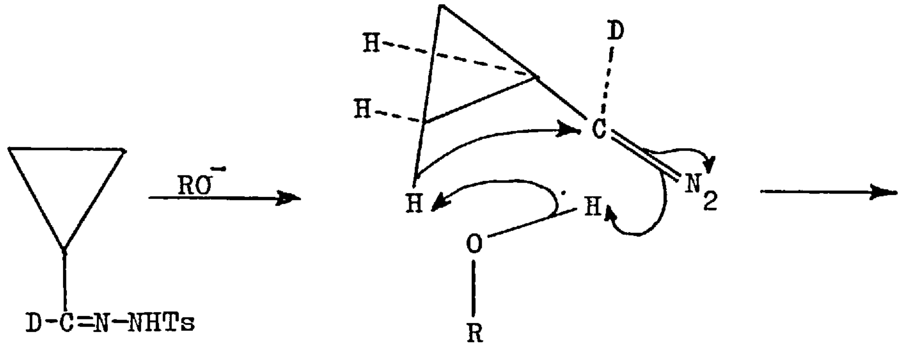
(37) (38)



(36) (39)

tosylhydrazone anion was allowed to decompose in d_2-ethylene glycol, the isotopic label was found in the endo-position of bicyclobutane (39).[47]

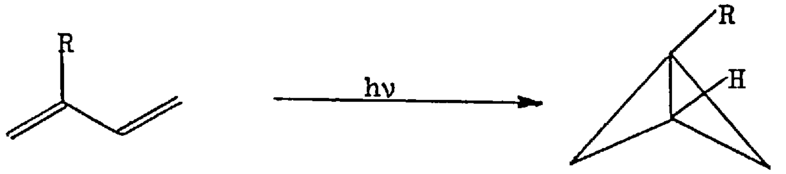
A simple three-step process can be envisaged for this reaction. Diazomethylcyclopropane would be formed first and protonated with loss of nitrogen to give the cyclopropyl carbonium ion. This could then bridge with de-protonation to give bicyclobutane. This process does not account for the stereochemical result, however, for if the cyclopropyl carbonium ion were an intermediate the two methylene hydrogens would be equivalent and the products from both reactions would have the deuterium distributed equally between the exo- and endo-positions. It is known that the protonation step is rate controlling as a solvent kinetic isotope effect of k_H/k_D = ca. 4 was observed;[46] thus a possible mechanism is:-



(37) (38)

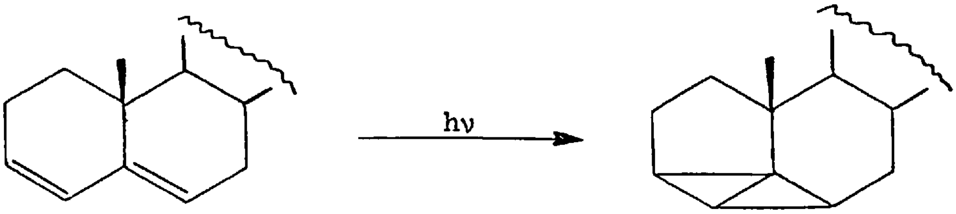
Intramolecular Photolytic Reactions

Olefinic systems can isomerise on absorption of light. Thus if two double bonds are in sufficiently close proximity they can interact to produce a bicyclobutane. Essentially, this reaction involves the photochemical reversal of the thermal decomposition of bicyclobutane and three examples will illustrate the method:-

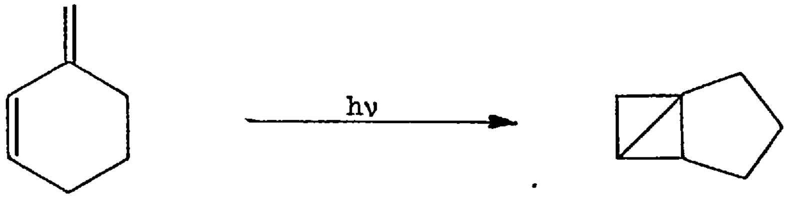


(R = H or CN)

(ref. 48)

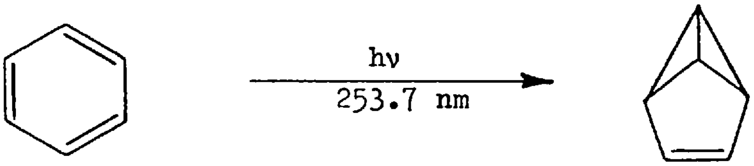


(ref. 49)



(ref. 50)

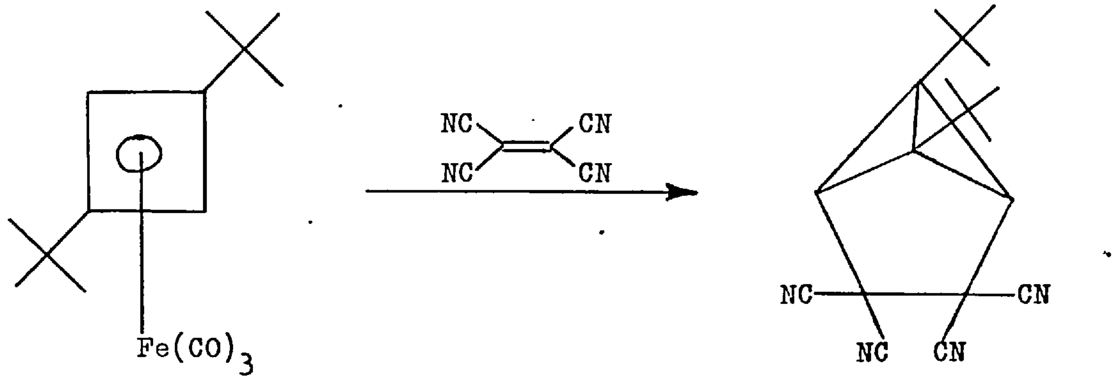
Also worthy of note in this section is the photoisomerisation of benzene to give benzvalene (40), a very unstable bicyclobutane



(40)

derivative.[51] Substituted benzenes give rise to substituted benzvalenes.[52]

A further reaction which, although it does not involve the <u>photochemical</u> rearrangement of bonds, nevertheless involves some bond rearrangement can be mentioned here. Decomposition of the iron tricarbonyl complex of 1,3-di-t-butylcyclobutadiene (41) in the presence of tetracyanoethylene afforded the dihydrobenzvalene derivative (42) in high yield.[53] The appearance of (42) was readily explicable in terms of orbital symmetry arguments provided that (41) possessed a singlet ground state. In its simplest form the reaction is a $\left[{}_{\pi}2_{s} + {}_{\pi}2_{a} + {}_{\pi}2_{a}\right]$ cycloaddition which is an allowed process



(41) (42)

according to the Woodward-Hoffmann rules.[21]

Properties

The nature of the bonding in three-membered rings has been considered by a number of authors.[54,55] Coulson and Moffitt[54] noted that although lines drawn to connect the carbon atoms of three-membered rings would intersect at angles of 60°, the orbitals of carbon could not readily be distorted from the tetrahedral (sp^3) angle of 109.5° to this small value. The smallest theoretically possible angle between orbitals of carbon is 90°, i.e. the angle between pure p-orbitals. Even if pure p-orbitals were involved in the carbon-carbon bonding of such systems, the centres of density of the bonding electron clouds would lie outside of straight lines connecting the carbon atoms. Thus it is obvious that the overlapping orbitals which form the carbon-carbon bonds in these strained systems are not linearly oriented.

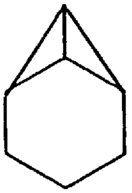
The maximum possible overlap of these orbitals is achieved by:-

(1) shortening of the carbon-carbon bond distance from the normal value of 1.540 Å to 1.497 Å in bicyclobutane (and to 1.524 Å in cyclopropane),

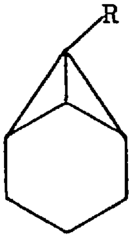
(2) reduction of the tetrahedral valence angle (to 105° according to calculations[54]). This is made possible by partial changes in the state of hybridisation - the ring bonds assume greater *p*-character, and the exocyclic bonds consequently acquire additional *s*-character,

(3) delocalisation of electrons as a result of the higher *p*-character of the ring bonds. Stabilisation of the entire bond system results and also a ring current in the plane of the three carbon atoms.

Most of the important properties of bicyclobutanes result from this maximisation of orbital overlap. For example, since the position of maximum probability for an *s*-electron lies closer to the nucleus than that of a *p*-electron, the acidity of protons increases with increasing *s*-character of the C-H bond. The large 1*s* - 2*s* bond index for the bridgehead protons coupled with the calculated low electron density[56] provides a rationale for the acidity of these protons of bicyclobutane. Thus the protons on the bridgehead carbon atoms of tricyclo$[4.1.0.0^{2,7}]$heptane (7) were exchanged for deuterium with t-BuOD in the presence of t-BuOK.[10] Moreover, treatment of (7) with butyl lithium gave the lithio-derivative (43; R = Li) which could be carboxylated with CO_2, methylated with methyl iodide, or deuterated. Repetition of the metalation-alkylation sequence converted the monomethyl derivative (43; R = Me) to the dimethyl derivative (44).



(7)



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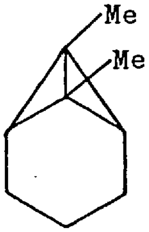
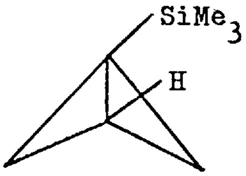


(44)

Similarly, bicyclobutane has been silylated (see (45)) by treatment[57] of the lithio-derivative with trimethylsilyl chloride.



(45)

The complete set of structural parameters of bicyclobutane[58] (obtained from microwave spectra) showed that all carbon-carbon bonds in bicyclobutane were of equal length within experimental and theoretical error. However, application of the CNDO (complete neglect of differential overlap) method to the electronic structure of bicyclobutane[56] suggested that its central bond had considerably greater p-character than the carbon-carbon bonds of cyclopropane. Also, the qualitative results of Pomerantz and Abrahamson[59] indicated that the π-character, although delocalised, was particularly manifest in the bridgehead bond and there is chemical evidence for multiple bond character at this site.[28]

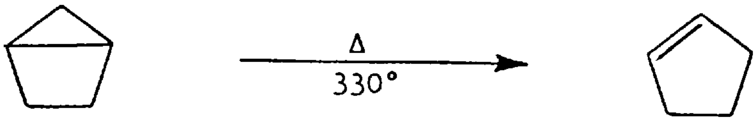
The π-character of the bridgehead bond is clearly revealed by the u.v. spectrum of methyl 3-methylbicyclobutane-1-carboxylate (26). The trace bears a strong resemblance to that of an αβ-unsaturated ester.[28] Furthermore, bridgehead substituted diphenyl derivatives have spectra suggesting conjugative interaction between the two phenyl groups.[60]

The strain inherent in a bicyclobutane ring causes this system to have unique properties and any increase of this strain, such as may be brought about by incorporation into a polycyclic molecule, will result in a magnification of these properties. Thus any bent bonds in highly strained polycyclic molecules will have unusual reactivity. This, with the π-character of the bridgehead bond noted above, leads to a rationalisation of the chemistry of bicyclobutanes.

Reactions

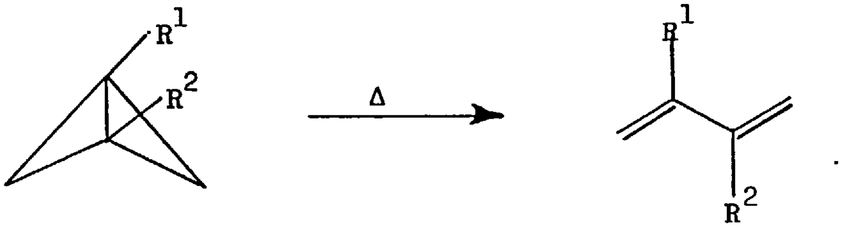
Pyrolysis

By analogy with the thermal isomerisation of bicyclo[2.1.0]pentane (46) to cyclopentene (47),[61] bicyclobutanes would be expected to undergo thermal isomerisation to cyclobutenes and perhaps



(46) (47)

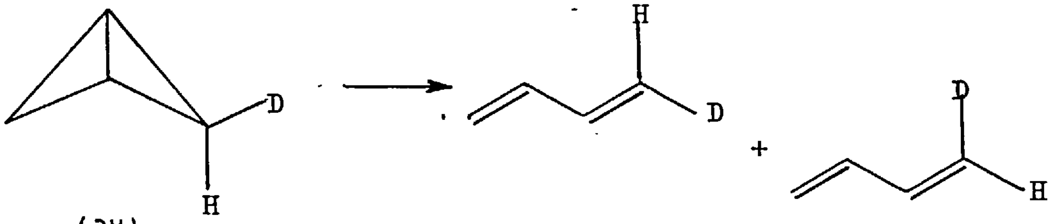
subsequently to form butadiene derivatives. However, this assumption is incorrect as in all examples studied the cyclobutene has never been isolated, only the butadiene. Since 1,3-disubstituted bicyclobutanes (48) always give 2,3-disubstituted butadienes (49),[29,36,38,40] a cyclobutene intermediate is not possible and the



(48) (49)

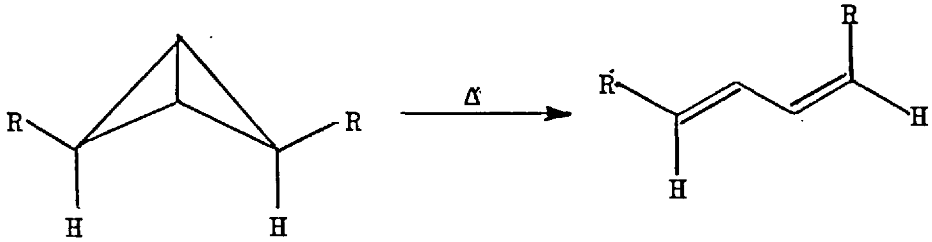
rearrangement must proceed with preservation of the bridgehead bond. That the bridgehead bond remains intact during this isomerisation is compelling evidence to support the calculations of Pomerantz and Abrahamson.[59] These indicated that the bridgehead bond should be the strongest and thermal lability should reside in the peripheral bonds.

When 2-exo-d_1-bicyclobutane (38) was pyrolysed, the butadiene



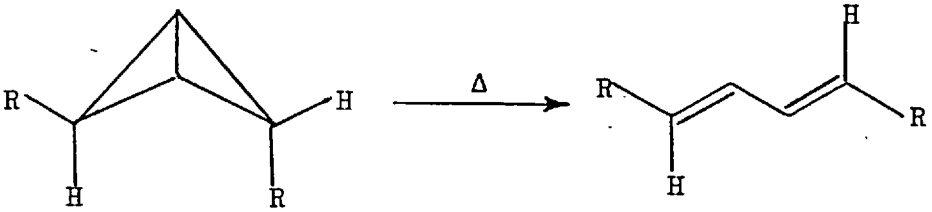
(38)

formed had the deuterium distributed between the cis- and trans-positions.[46] It was concluded that the reaction probably involved a synchronous cleavage of both carbon-carbon bonds, but no reference was made to orbital symmetry rules. These predict[21] that a conrotatory-disrotatory mode of methylene rotation is thermally allowed. This corresponds to the process shown,



(50)

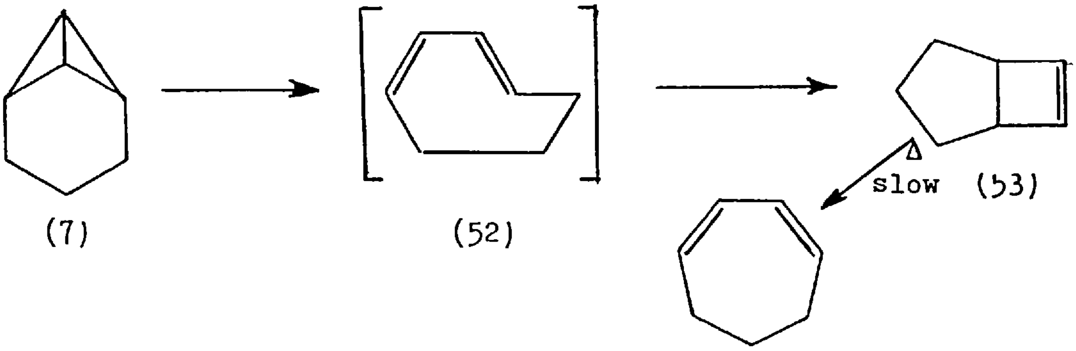
and



(51)

and agrees with the experimental observations of Closs and Pfeffer[62] who found that diene formation from <u>exo</u>,<u>exo</u>- and <u>exo</u>,<u>endo</u>-2,4-dimethylbicyclobutane (50; R = Me and 51; R = Me respectively) was stereoselective (93.2 and 95% respectively).

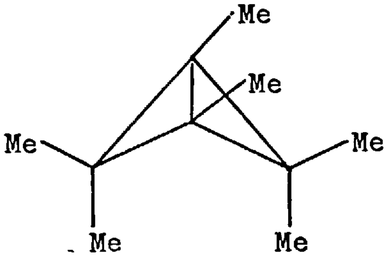
Also, the rearrangement of tricyclo$[4.1.0.0^{2,7}]$heptane (7) gave



(7) (52) (53) (54)

bicyclo[3.2.0]hept-6-ene (53) rather than cis,cis-1,3-cycloheptadiene (54)[63] and the probable intermediate, cis,trans-1,3-cycloheptadiene (52) corresponds to the concerted type of process described above.

The isomerisation of hexamethylbicyclobutane (55)[64] appears to



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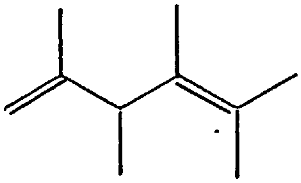
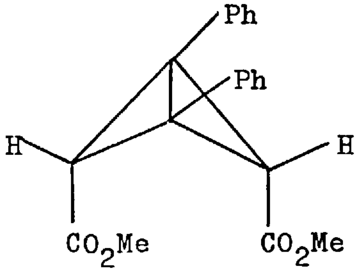


(56)

be an exception to this. This compound isomerised to 2,3,4,5-tetramethylhexa-1,4-diene (56) during attempted purification by g.l.c. However, as this was not a true thermal isomerisation, it is possible that the column material was implicated in the process.

In contrast, under mild thermolysis conditions, the bridgehead bond can be broken. Woodward,[60] and others,[65] showed that endo,endo-dimethyl 1,3-diphenylbicyclobutane-2,4-dicarboxylate (57) was the



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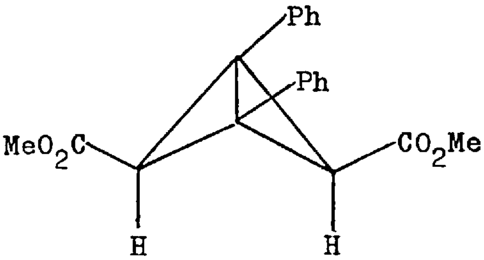


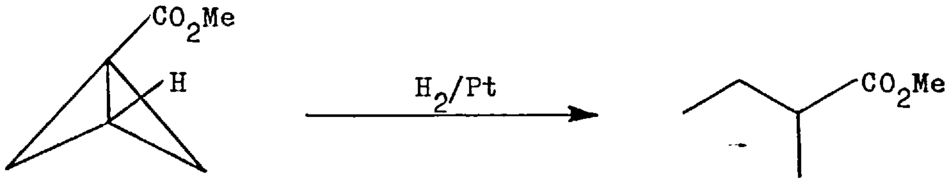
(58)

product of the thermal isomerisation of the *exo*,*exo*-isomer (58). The thermal interconversion of (57) and (58) is accomplished by breaking the 1,3-bond as in the well-studied isomerisations of bicyclo[2.1.0]pentanes.[66] The greater crowding of the ester groups in the *endo*,*endo*-isomer (57) should have decreased its stability relative to that of the *exo*,*exo*-isomer (58); however, the former was slightly more stable.

Hydrogenation

Catalytic reduction of bicyclobutanes is generally characterised by the uptake of two moles of hydrogen, but the mode of cleavage is variable. Two principle patterns are evident, namely:-

(1) cleavage of the central and one other cyclopropyl bond, *e.g.*,



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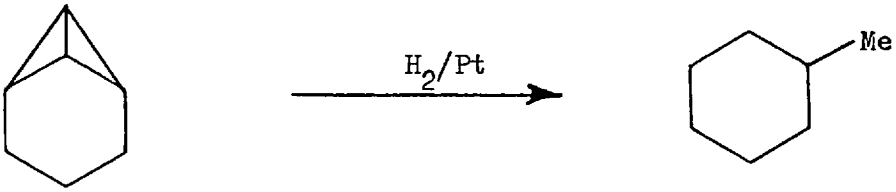

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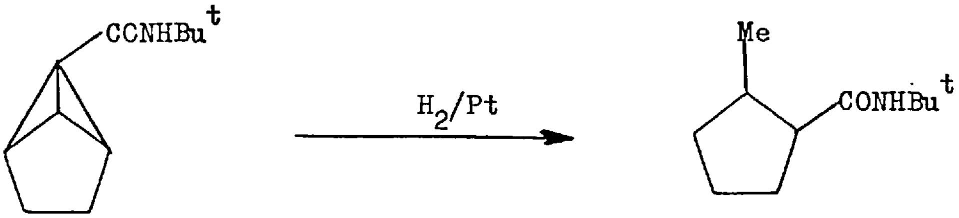
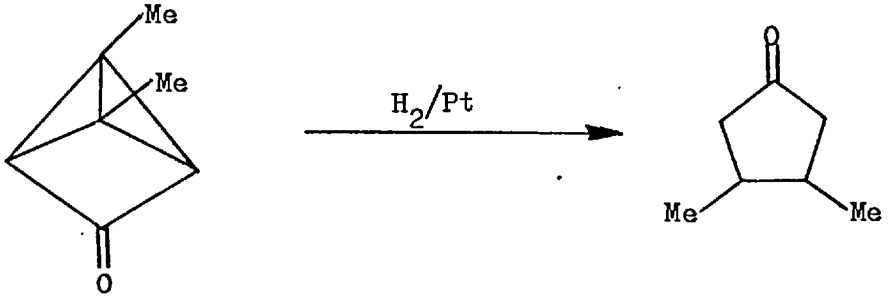


(ref. 33)

(2) cleavage of two cyclopropyl bonds but not the central bond, *e.g.*,



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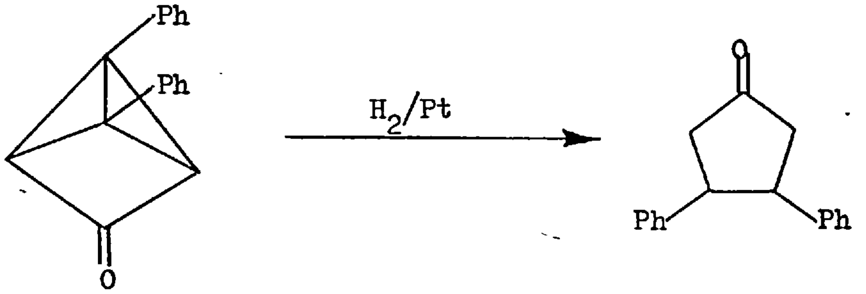
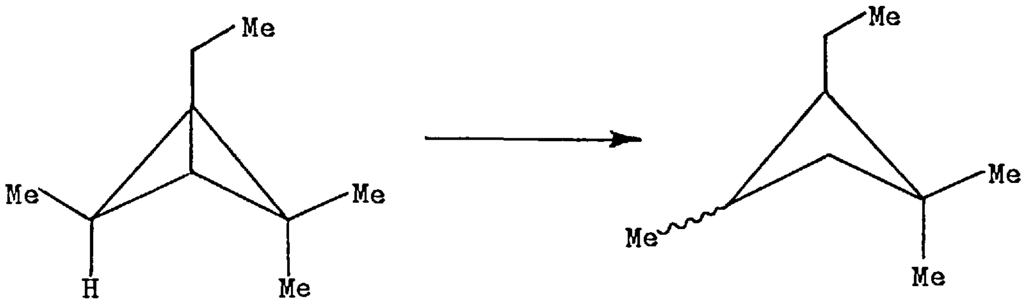
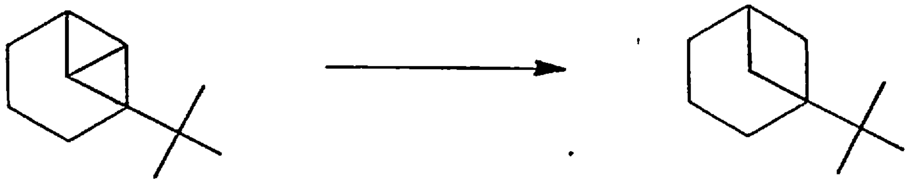


(ref. 11)

A third pattern has been reported[36,67] which involved 1,3-reduction *i.e.* uptake of one mole of hydrogen only, but in both cases the cyclobutane was isolated as a minor product. Recently, however, the quantitative reduction of a large number of bicyclobutanes, of varied structure, to the corresponding cyclobutanes has been reported.[68] The reagent used was lithium in refluxing ethylamine or ethylenediamine. The following examples typify the results:-

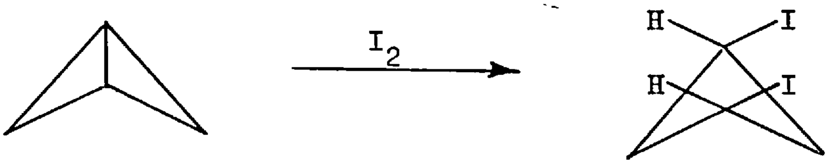


(78% *trans*; 22% *cis*)



Reaction with Electrophiles

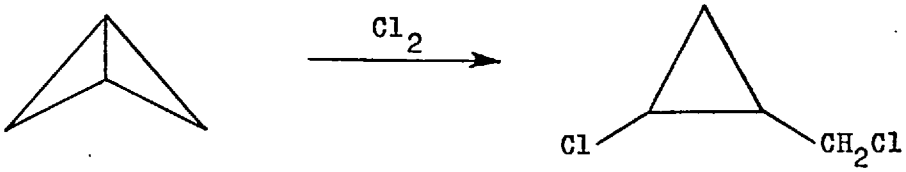
Treatment of bicyclobutane with iodine led predominantly to cis-1,3-di-iodocyclobutane (59)[28] and a corresponding reaction



(59)

occurred with 1,3-dimethylbicyclobutane.[36] Interestingly, the latter di-iodide could be converted back to the bicyclobutane by reaction with lithium aluminium hydride. The cis-stereochemistry of the di-iodides suggests that the addition occurred via a four-centre activated complex.

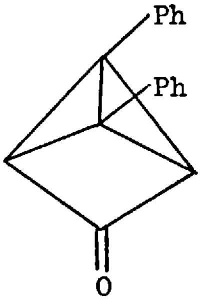
Addition of bromine to bicyclobutane gave a mixture of cis- and trans-1,3-dibromocyclobutanes (44% and 19% yield respectively) and a bromocyclopropane derivative.[28] Addition of chlorine, however, (carried out in the gaseous phase rather than in solution) did not result in addition across the bridgehead bond. In this case, the product appeared to be 2-chlorocyclopropylmethyl chloride (60).[28]



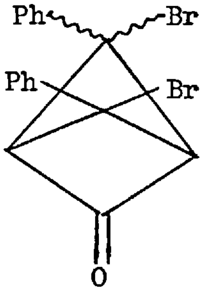
(60)

Thus iodine and chlorine gave two very different types of product whereas bromine was intermediate, giving a mixture of both types. No explanation for this can be determined from the available data.

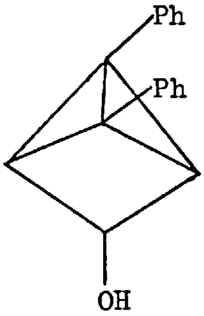
Similar halogenation reactions occur with more highly strained bicyclobutanes. For example, bromination[69] of 1,5-diphenyltricyclo-$[2.1.0.0^{4,5}]$pentan-3-one (8) gave the unstable dibromide (61) which,



(8)



(61)

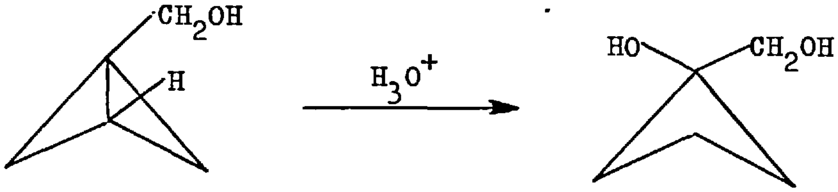


(62)

on treatment with lithium aluminium hydride, yielded the tricyclo-$[2.1.0.0^{4,5}]$pentane system (i.e. 62) once more.

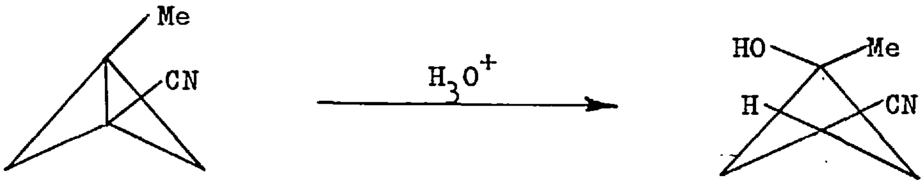
The majority of bicyclobutanes undergo hydration in dilute acid solution. Cyclobutanol (55%) and cyclopropylcarbinol (45%)[28] were formed from the parent hydrocarbon. The reaction probably proceeded *via* a bicyclobutonium ion.

Bicyclobutane-1-carbinol (63) reacted almost instantaneously in



(63) (64)

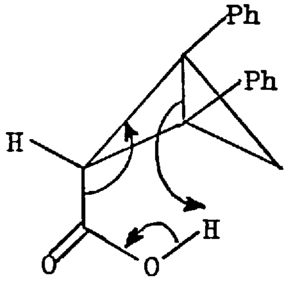
dilute acid (pH 4) and afforded 1-hydroxycyclobutanecarbinol (64).[28] Thus the addition followed the Markownikoff rule. 3-Methylbicyclobutane-1-nitrile (65) also reacted in a similar manner[29] but in this



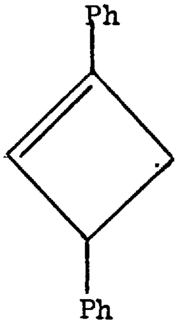
(65)

case only one isomer was obtained which appeared to correspond to the *cis*-addition of water. The reaction probably involved initial protonation at C-1 on the side opposite the nitrile group, followed by hydration of the carbonium ion thus formed at C-3.

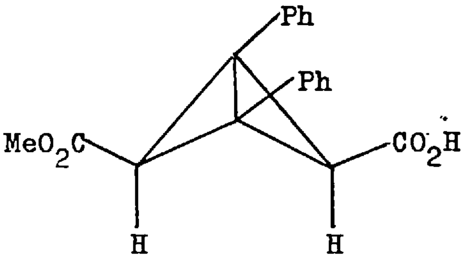
The direction of protonation can be deduced from the observation by Masamune[69] that the bicyclobutane carboxylic acid (66) underwent facile decarboxylation at 85° to give the cyclobutene (67), whereas



(66)



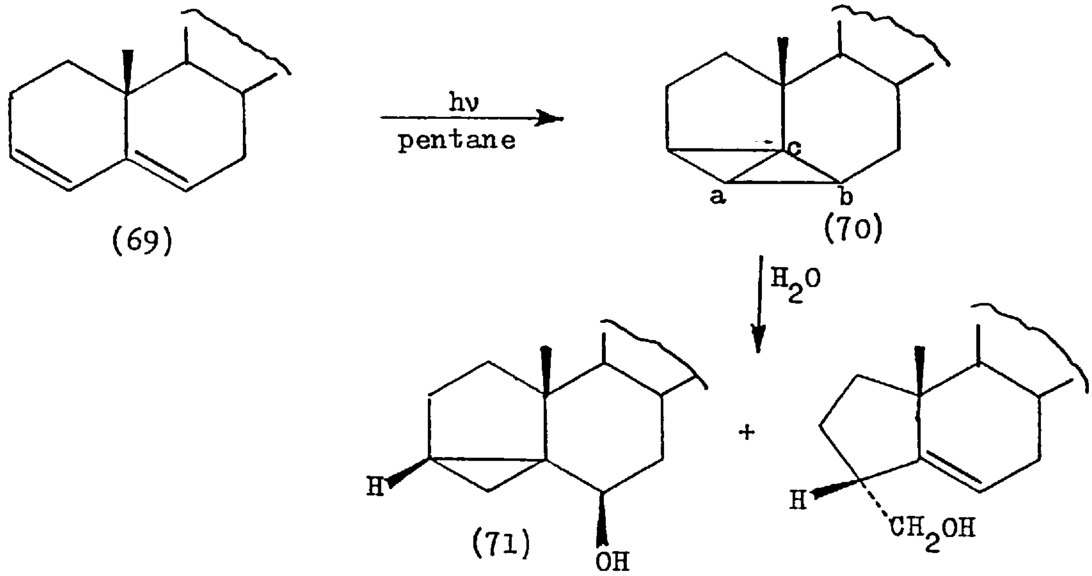
(67)



(68)

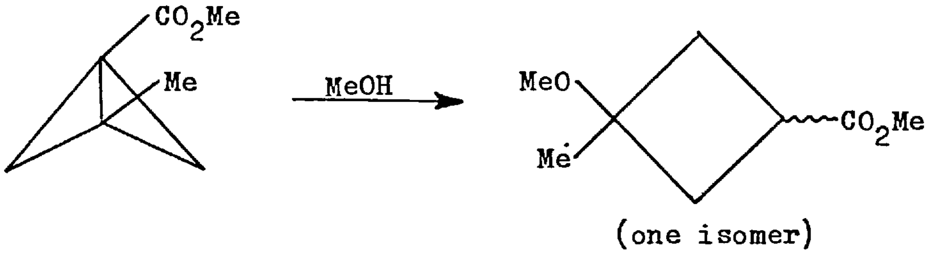
the acid (68) was stable at 200°. Only the former could involve intramolecular protonation at C-1 on the side opposite the phenyl group.

Dauben's group[49] has examined the hydration of the bicyclobutane (70), which is obtained by photolysis of 3,5-cholestadiene (69), and



found the major product to be the cyclopropylcarbinol (71).

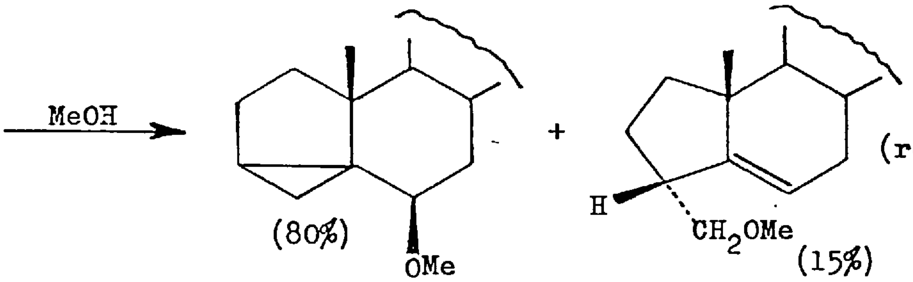
Addition of alcohols across a bicyclobutane carbon-carbon bond takes place readily, as indicated by the following examples:-



(ref. 28)

and

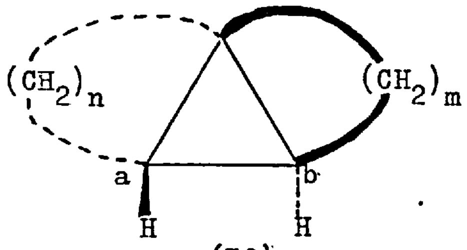
(70)



(ref. 49)

The reactivity of a series of bicyclobutanes towards methanol has been determined and it was found that the relative rates could be related to the strain energies of the substrates.[50] A mechanism involving a bicyclobutonium ion has been proposed.[70] Similar results have been reported for the acid-catalysed addition of methanol to bicyclobutanes.[71]

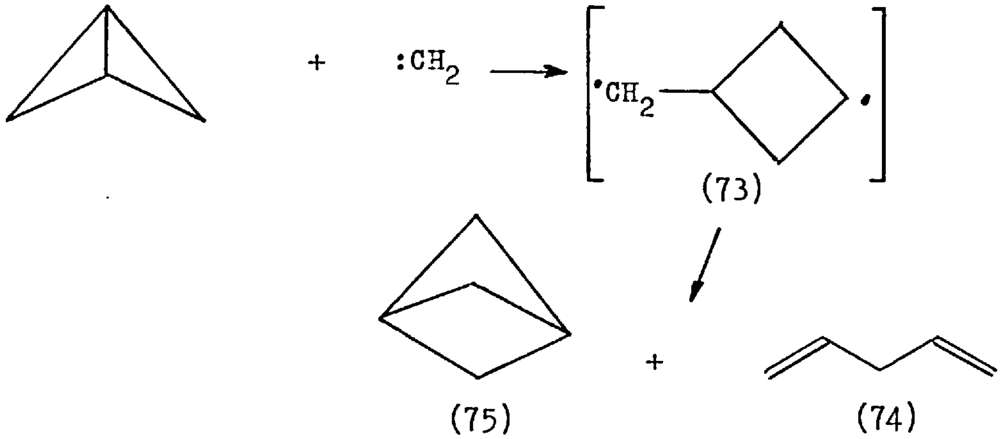
The central bond a-c of (70) might have been expected to have the greatest reactivity but it has been noted[72] that in a system such as (72) i.e. a di-cis-fused cyclopropane, a 'twisting' or 'torquing' of the cyclopropyl moiety by the two cis-fused rings should occur. This would result in an opposing horizontal displacement of the orbitals forming the a-b bond when n and m are sufficiently small.



(72)

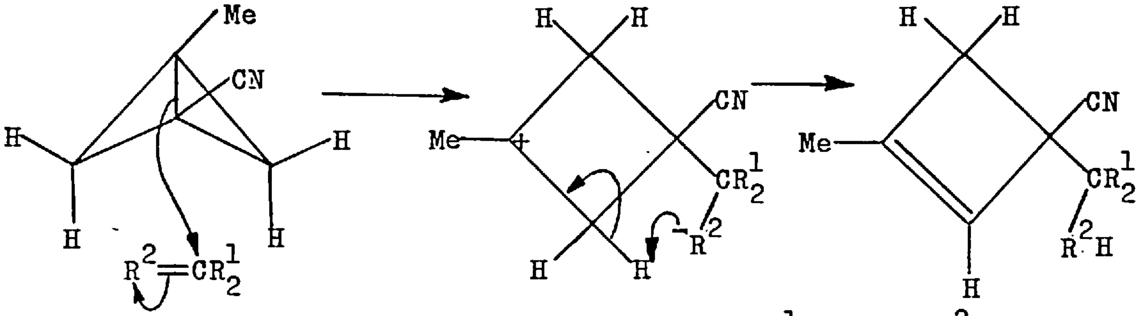
Consequently the 'twisted' a–b bond of (70) should have less orbital overlap than the a–c bond, and therefore should have greater reactivity. Confirmation of this hypothesis was provided by the above reactions of (70) and also by its reactions with other electrophiles such as ketones, phosgene, halogens, and tetracyanoethylene, which yielded derivatives of A-norcholest-5-ene.[73]

The usual high reactivity of the bridgehead bond is again demonstrated in the reaction of bicyclobutanes with carbenes. Treatment of bicyclobutane with methylene, generated photochemically at -50°, led to isolation of 1,4-pentadiene (74) as the major product



and bicyclo[1.1.1]pentane (75) in trace amounts.[28] A two-step mechanism involving the diradical intermediate (73) accommodates these observations.

As expected, bicyclobutanes react with electron-deficient multiple bonds giving substituted cyclobutenes.[29,34] The general reaction is:-



$R^1 = CF_3$; $R^2 = O$

$R^1 = CF_2Cl$; $R^2 = O$

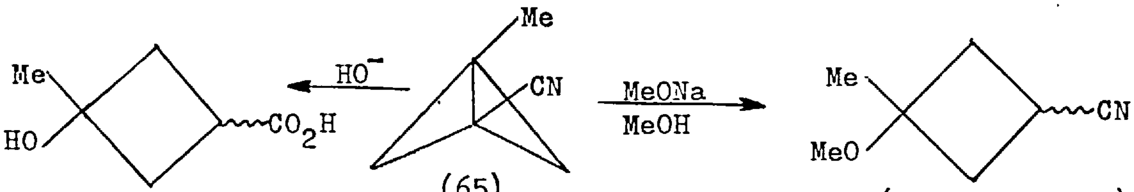
$R^1 = CF_3$; $R^2 = C(CN)_2$

Introduction of two methyl groups at C-2, i.e. one endo-methyl group, completely suppressed the reaction with hexafluoroacetone.[29]

Reaction with Nucleophiles

Addition of water[29] to the bridgehead bond can be achieved not only under the acidic conditions mentioned previously but also under basic conditions.

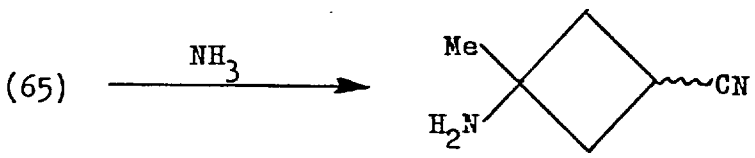
The same is true of the addition of methanol,[29] e.g.,



(65)

(cis and trans)

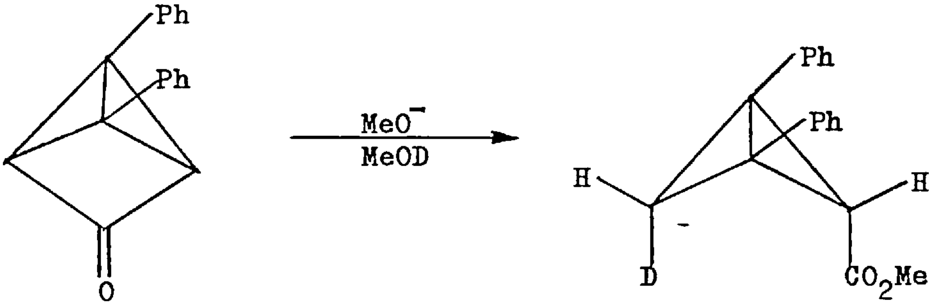
Nucleophiles also reacted spontaneously with 3-methylbicyclobutane-1-nitrile (65) without a catalyst. Typical of these reactions is that with ammonia which occurred at 100° affording a single isomer of



(76)

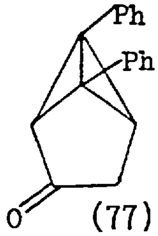
3-amino-3-methylcyclobutanenitrile (76).[29]

Masamune[69] has found that 1,5-diphenyltricyclo$[2.1.0.0^{4,5}]$pentan-3-one (8) readily underwent reaction with methoxide resulting in



(8)

cleavage of the acyl-carbon bond. The reaction proceeded with retention of configuration. No ring opening occurred with the homologue, 1,6-diphenyltricyclo$[3.1.0.0^{5,6}]$hexan-3-one (77) under

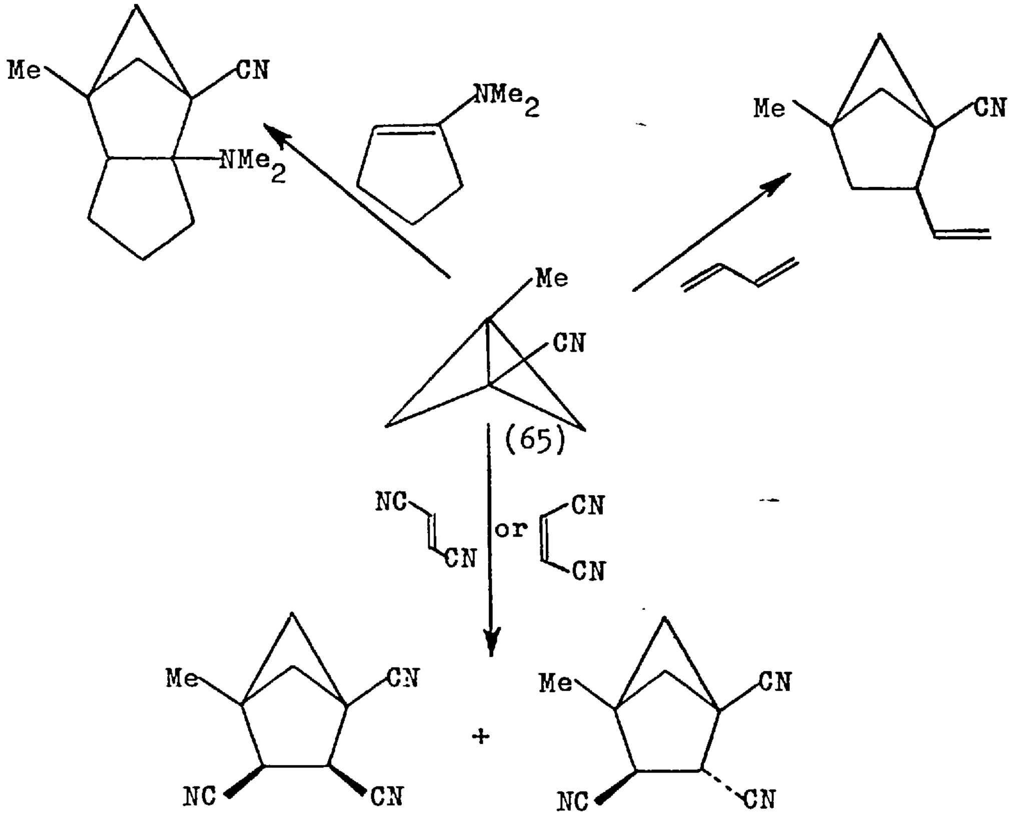


(77)

similar conditions.[74]

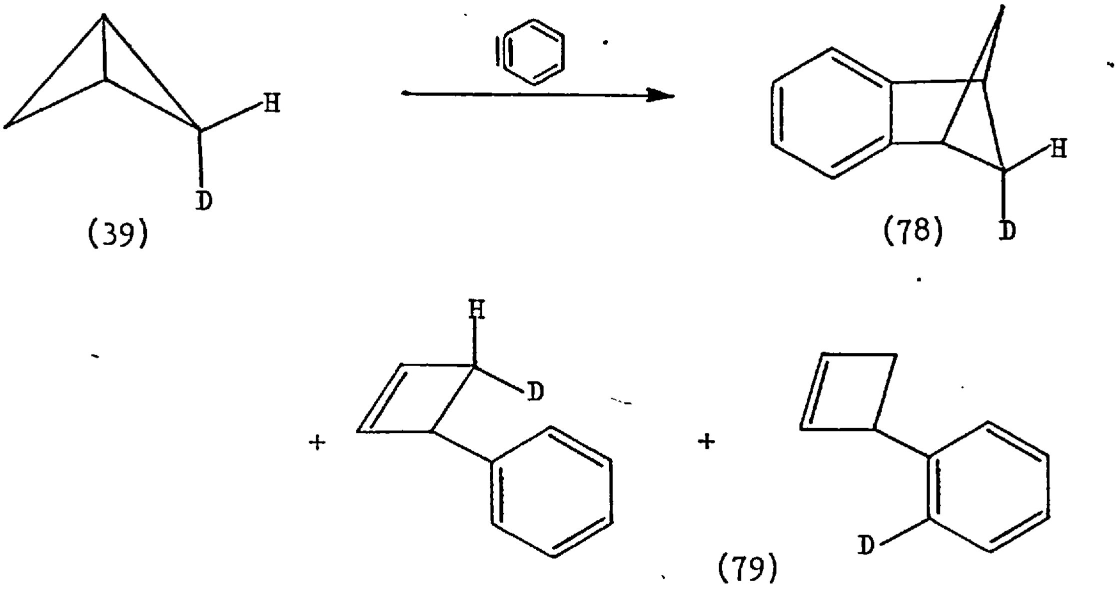
Cycloaddition reactions

Attempts to add one-atom fragments across the bridgehead bond have not generally proved successful, however, addition of two-atom fragments, in a cycloaddition process, occurs readily, especially with 3-methylbicyclobutane-1-nitrile (65).[75] Typical examples are:-

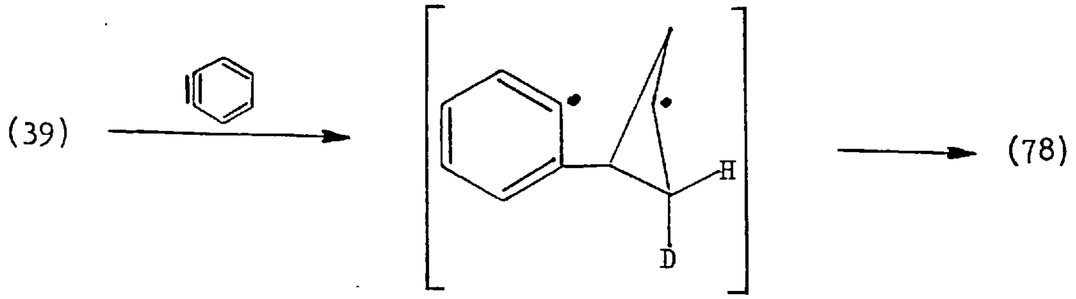


Analogous reactions occurred with acrylonitrile, ethylene, styrene, and p-methoxystyrene.[75] In all cases derivatives of 4-methylbicyclo[2.1.1]hexanenitrile were produced. Since both fumaronitrile and maleonitrile gave a mixture of cis- and trans-dinitriles the reaction probably proceeds in two steps *via* a diradical intermediate.

The reaction of bicyclobutane with benzyne gave two products, formed by a cycloaddition and an ene reaction,[76] *viz.*,

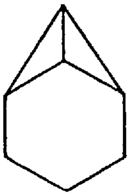


The mechanism was deduced by a labelling experiment.[77] Treatment of *endo*-d$_1$-bicyclobutane (39) with benzyne produced benzobicyclo[2.1.1]-hex-2-ene (78) with deuterium exclusively in the *endo*-position. The ene reaction product (79) had half the deuterium *cis* to the phenyl group and half in the phenyl group. These results were consistent with backside (*i.e.* *endo*-) attack of benzyne on bicyclobutane *via* a diradical intermediate as shown:-

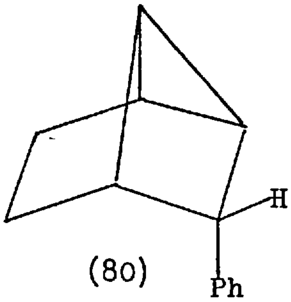


A corollary to this mechanism is that substitution of methyl groups for hydrogens at C-1 and C-3 should inhibit the cycloaddition reaction as a result of steric compression. This expectation was realised, for 1,3-dimethylbicyclobutane did not give a cycloadduct with benzyne.[77]

The ene reaction should not occur with a bridged bicyclobutane such as tricyclo[$4.1.0.0^{2,7}$]heptane (7) as this would require the formation of a double bond at the bridgehead of a bicyclo[3.1.1]-heptane.[78] Thus (7), on treatment with benzyne gave the single product 2-phenyltricyclo[$4.1.0.0^{3,7}$]heptane (80).[79] The stereochemistry of the phenyl group in the product required that benzyne attacked from the same side as the trimethylene bridge <u>i.e.</u>, backside attack as with bicyclobutane. A diradical mechanism was proposed as there is definitive evidence for the formation of diradical intermediates in the addition of carbon-carbon multiple bonds to bicyclo[2.1.0]pentane[80] which provide ample precedent for the above reaction.



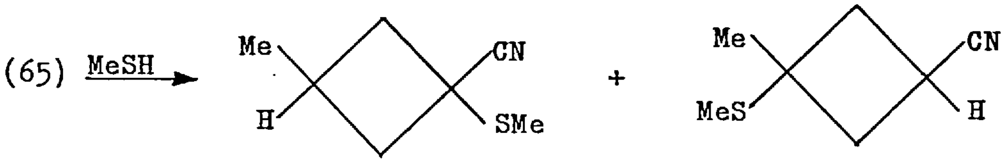
(7)



(80)

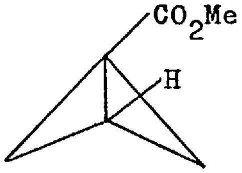
Radical Reactions

Thiols added to 3-methylbicyclobutane-1-nitrile (65) in a radical chain process.[28] In the case of methane thiol, thermal activation at 100° or u.v. irradiation at 8° led to a mixture of substituted cyclobutenes as shown.

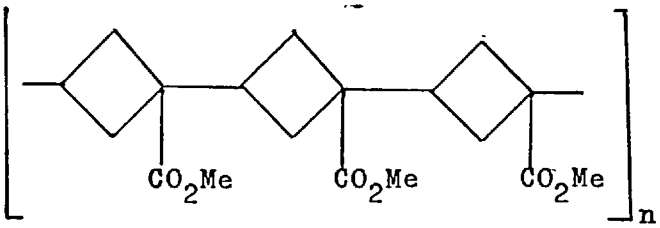


(cis and trans) (cis and trans)

Some substituted bicyclobutanes polymerise in the absence of free radical inhibitors. Polymerisation of methyl bicyclobutane-1-carboxylate (24) occurred readily giving material which resembled a polyacrylate.[28] N.m.r. studies indicated the structure to be (81).



(24)



(81)

Similar results were recorded for bicyclobutane-1-nitrile.[81]

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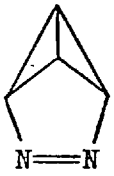
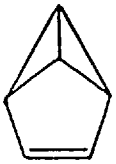
DISCUSSION

Photolysis of Pyridazine

One of the difficulties to be expected in a synthesis of tetrahedrane which utilises, as a precursor, some derivative of bicyclo[1.1.0]butane, is that of forming the final carbon-carbon bond between C-2 and C-4. Conceptually, one possibility is the thermal or photochemical extrusion of some fragment linking C-2 and C-4 in a bicyclobutane. An obvious example is the azo-compound (1).



(1)

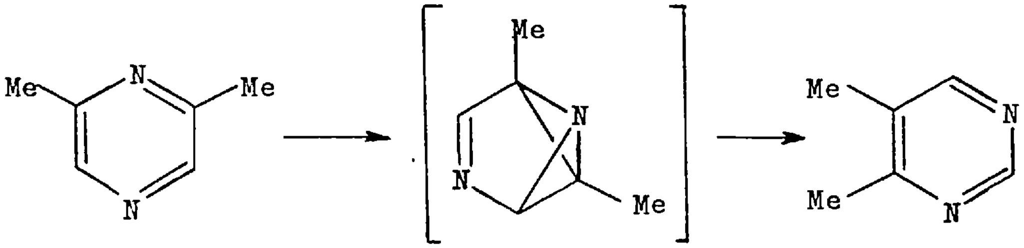


(2)

(3)

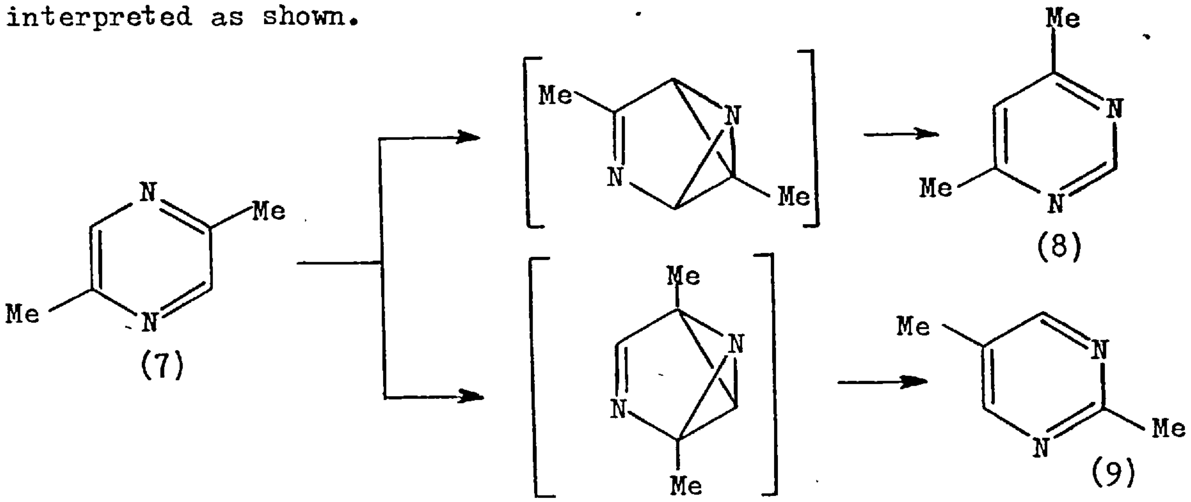
Benzene, when photolysed in the liquid phase at 254 nm gave a number of isomeric photoproducts, one of which was the tricyclic isomer, benzvalene (2).[1] By analogy with this isomerisation, it is conceivable that the aromatic heterocycle, pyridazine (3), could give rise to an isomeric photoproduct which contains the two nitrogen atoms in the desired positions i.e.(1).

Indeed, there is a precedent for such a reaction in the published photochemistry of methylpyrazines.[2] Benzvalene-type intermediates

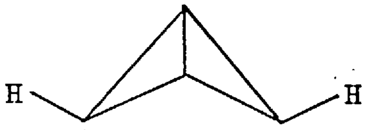


(4) (5) (6)

have been postulated. For example, photolysis of 2,6-dimethylpyrazine (4) gave 4,5-dimethylpyrimidine (6) presumably <u>via</u> the diazabenzvalene (5). Similarly, photolysis of 2,5-dimethylpyrazine (7) gave a mixture of the pyrimidines (8) and (9) whose origin is interpreted as shown.



The diazabenzvalene (1) would be expected, on the basis of the known behaviour of diaza-compounds,[3] to lose nitrogen readily producing the diradical (10), or even directly tetrahedrane.

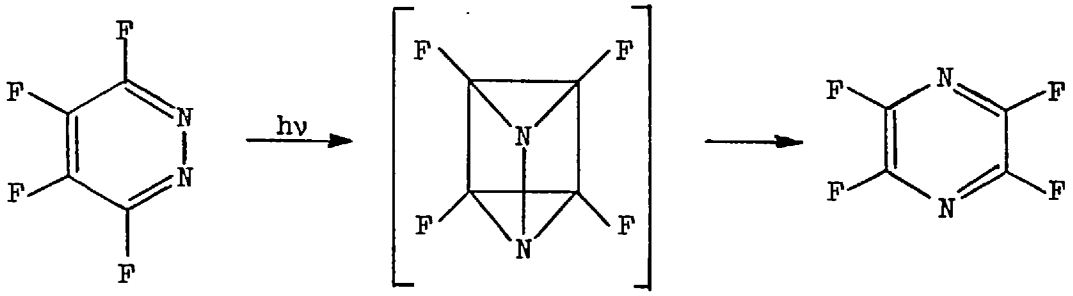


(10)

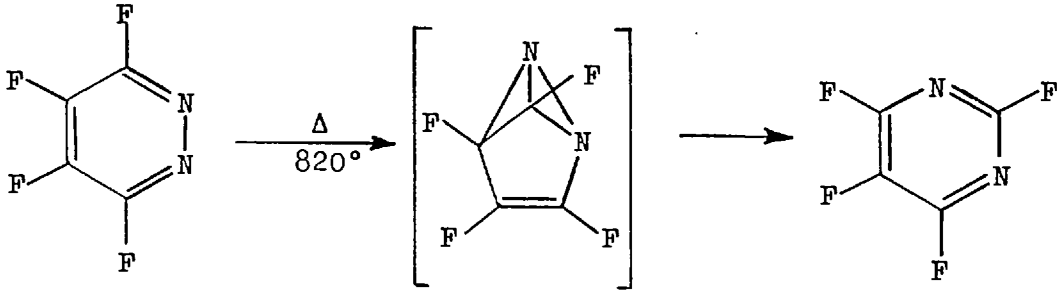
In initial experiments pyridazine was photolysed with a low pressure mercury lamp in anhydrous ether at room temperature. During 48 hours' irradiation there was little change in the u.v. spectrum of aliquots of the reaction mixture and distillation of the total photolysate gave only starting material and a dark brown tar. Use of different solvents led to the same result and even irradiation of neat pyridazine produced no material with the requisite high field signals in its n.m.r. spectrum.

Finally, neat pyridazine (as a moving thin film) was photolysed in quartz apparatus with a low pressure mercury lamp. The system was flushed with dry, oxygen-free nitrogen such that any volatile substances formed would immediately be swept into a trap cooled in liquid nitrogen. In using this technique, the photolysis was monitored by n.m.r. examination of both the photolysate and the contents of the trap. However, no isomerisation was observed and no volatile materials were detected during a continuous reaction period of 3 days.

Subsequent to this work, the isomerisation of perfluoropyridazines to perfluoropyrimidines and perfluoropyrazines was reported.[4] The intermediacy of both benzvalene- and prismane-type derivatives was proposed, viz.,



and

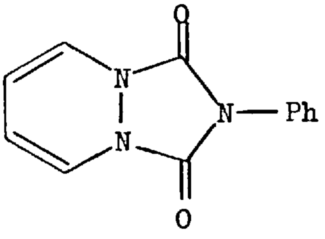


Interestingly, it is the perfluoro valence isomers of hexamethylbenzene which are reported to be the most stable.[5] It appears that the fluoro-substituents confer some degree of stability to the valence isomers permitting their isolation in a pure state. In this respect, perhaps the photolysis of hexa(trifluoromethyl)pyridazine might be more encouraging, but it should be noted that rearrangement of the diazabenzvalene and diazaprismane derivatives mentioned above was preferential to elimination of nitrogen.

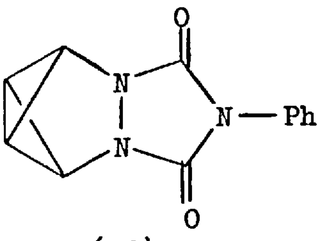
Diene Photolysis

Although the photolytic rearrangement of trans-1,3-dienes to bicyclobutanes is known,[6,7] analogous rearrangement of cis-1,3-dienes is unknown except in the rather special case of benzene.[1] (Formally the photochemical isomerisation of benzene to benzvalene involves the 'criss-cross' rearrangement of two of its three 'double bonds'.)

The diene judged suitable for this study was (11). It was



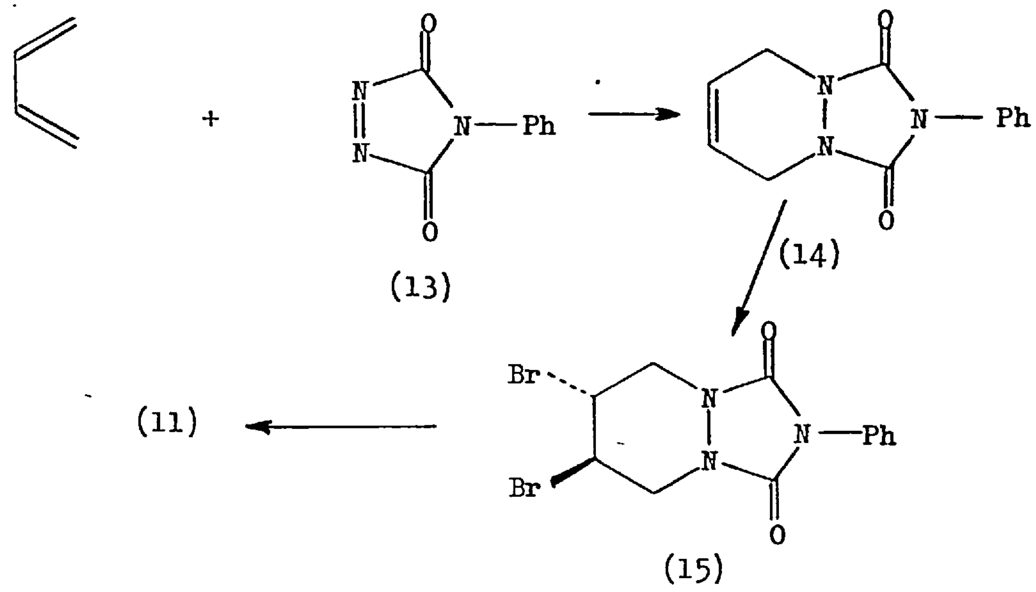
(11)



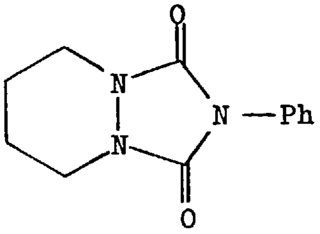
(12)

thought that this diene, on photolysis, might yield the bicyclobutane derivative (12) from which the 2,4-bridge would be removable by known methods.[8] Scheme A outlines the steps involved in the synthesis of (11).

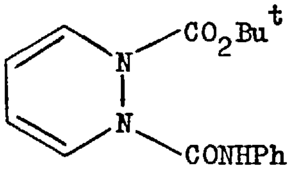
Scheme A



Treatment of butadiene with 4-phenyl-1,2,4-triazolin-3,5-dione (13),[9] generated in situ from 4-phenylurazole, in acetone at -50° gave the adduct (14)[10] in quantitative yield. Attempts at allylic bromination of (14) met with no success, neither did treatment of (14) with mercuric acetate in an effort to promote direct dehydrogenation.[11] However, the desired transformation was effected by use of bromine in chloroform (14→15) followed by dehydrobromination with potassium t-butoxide in anhydrous ether (15→11). The n.m.r. spectrum of (11) clearly showed the presence of four vinylic protons (as two two-proton multiplets at 3.08 τ and 4.62 τ). The proof of the structure follows from its spectral properties and its quantitative hydrogenation to the saturated compound (16) (2.18 mol H_2 uptake/mol (11)), identical in all respects with an authentic sample prepared by hydrogenation of (14).



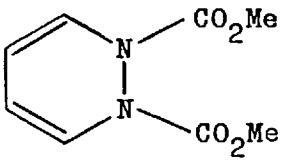
(16)



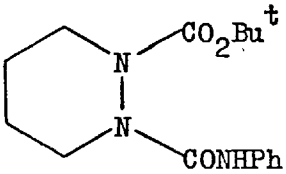
(17)

Conditions necessary for the dehydrobromination of (15) were established only with difficulty. Various methods were tried but all were found to be inferior to that involving potassium t-butoxide in ether. Potassium carbonate in tetrahydrofuran and pyridine alone both produced very little reaction, whereas potassium t-butoxide in tetrahydrofuran or t-butanol caused extensive decomposition, as did sodium hydride in benzene.

It was determined that optimum conditions for the dehydrobromination required high-dilution techniques. If concentrated solutions were used then, although the bicyclic diene (11) was present, the 1,2-dihydropyridazine (17) was isolated as the major product in some 50% yield. The n.m.r. spectrum of the latter indicated the presence of a t-butyl group bonded to oxygen (nine-proton singlet at 8.05 τ): the remainder of the spectrum was rather complex, but consistent with the proposed structure. Further evidence for this structure came from the u.v. spectrum which exhibited an absorption at 298 nm (ε 4,600) which compares extremely well with the value of 296 nm (ε 2,900) reported for dimethyl 1,2-dihydropyridazine-1,2-dicarboxylate (18).[12] Chemical evidence for



(18)



(19)

structure (17) was provided by quantitative hydrogenation to (19) (2.01 mol H_2 uptake/mol (17)) and its conversion, in 27% yield, to the bicyclic diene (11) upon treatment with sodium hydride in refluxing benzene. No attempt was made to maximise the yield for this reaction.

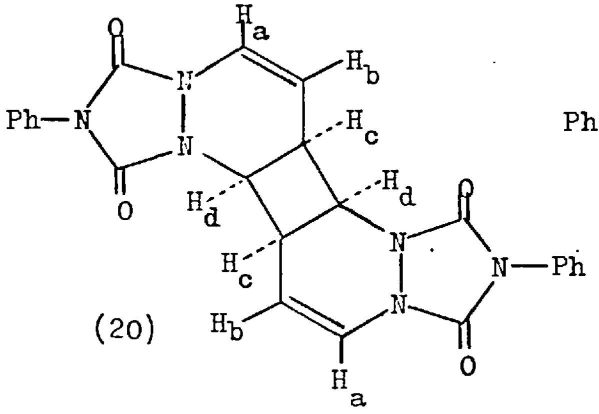
For the crucial photolysis, the bicyclic diene (11) was dissolved in anhydrous ether and irradiated with a low pressure mercury lamp. However, only brown oils were isolated from such experiments and the i.r. spectra of the crude products indicated (by the absence of absorptions at <u>ca</u>. 1760 cm^{-1}) that the imide ring was no longer intact. Consequently, the 368 nm absorption of the diene was irradiated by means of a tungsten lamp. Irradiation of a dilute benzene solution of (11) with a 750 W tungsten lamp for a period of <u>ca</u>. 40 hours produced virtually complete photolysis.[†]

[†] Cleaner photolyses were obtained with benzene rather than ethereal solutions of the diene.

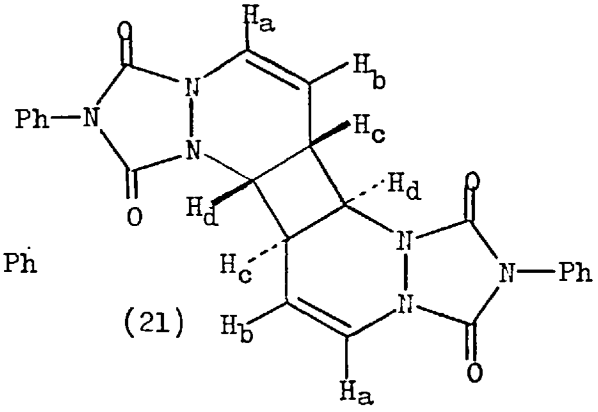
Examination of the crude photolysis product by t.l.c. showed the presence of two closely running components. Multiple elution preparative layer chromatography served to separate these products and their spectroscopic properties were investigated.

The n.m.r. spectrum of the faster-running material (isolated in 28% yield) was rather complex but showed the presence of a low field vinylic proton at 3.09 τ (double doublet), another vinylic proton at 4.99 τ (double doublet), a one-proton triplet at 5.27 τ, and a one-proton multiplet at 6.15-6.40 τ. The aromatic protons occurred at 2.4-2.8 τ. Decoupling experiments indicated that the proton at 3.09 τ was coupled to the one at 4.99 τ (J = 8.5 Hz) and to the proton at 6.15-6.40 τ (J = 1.5 Hz). The proton at 4.99 τ was also coupled to the signal at 6.15-6.40 τ (J = 4.0 Hz) as was the triplet at 5.27 τ (J = 8.0 Hz).

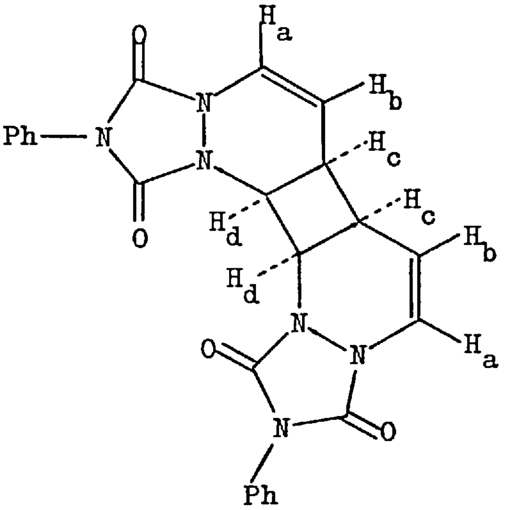
With this evidence, together with the i.r. spectrum which indicated the presence of the imide ring through peaks at 1765 and 1720 cm^{-1}, it is impossible to conceive a monomeric formulation for the photoproduct. The data is, however, consistent with a dimeric structure. The four possible dimers are:-



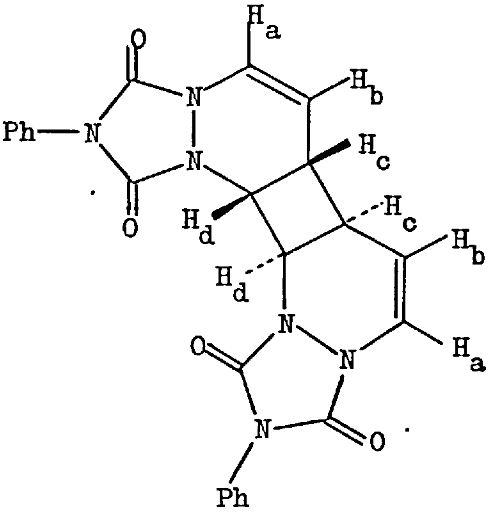
(20)



(21)



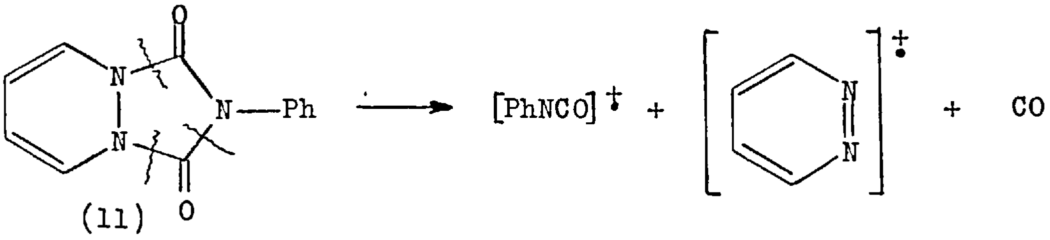
(22)



(23)

With all of these dimers, the signals at 3.09 τ and 4.99 τ can be readily assigned to protons H_a and H_b respectively. The complex signal at 6.15-6.40 τ must be ascribed to proton H_c as this is the only proton in all of these formulations which can couple to the other three. This leaves the triplet at 5.27 τ as the signal due to H_d. The fact that this signal is a triplet is completely in accord with structure (20) as H_d is adjacent to two chemically and magnetically equivalent protons (H_c). A triplet could possibly arise from H_d of (22), but only if the two H_d protons were chemically equivalent but not magnetically equivalent, and only if the coupling constants between $H_d—H_c$ and $H_d—H_d$ were fortuitously identical. Structures (21) and (23) can be eliminated as neither would produce a triplet for H_d. The differing dihedral angles between the protons in the $H_d—H_c$ interactions would produce differing coupling constants, thus leading to a distorted triplet or a double doublet for H_d. Consequently, the *trans*-*syn*-dimer (20) is favoured.

The photodimer (20) was unstable and could not be isolated in a pure crystalline state. An analytically determined molecular weight measurement gave a value of 542 (calculated for a dimeric structure - 454). This large discrepancy is no doubt due to decomposition of the dimer when in solution. No molecular ion was observed in the mass spectrum of (20) but the appearance of a peak at m/e 227 (corresponding to the bicyclic diene (11)) a short time after injection of (20) into the mass spectrometer supported the dimeric structure. Such a dimer could readily yield the diene (11) on pyrolysis. The ion of highest m/e observed in the mass spectrum was at m/e 438. It is interesting to note that the significant peaks in this region of the spectrum were at m/e 438, 410, 382, 354, and at m/e 424, 396, 368, *i.e.*, two series of peaks with a difference of 28 mass units between each member of each series. This would correspond to loss of carbon monoxide. In agreement with this observation was the fact that the diene (11) underwent mass spectral fragmentation to give ions corresponding to phenylisocyanate, pyridazine, and carbon monoxide, *i.e.*,



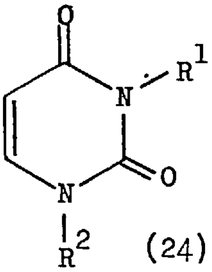
(11)

The second, slower-running photoproduct also had a complex n.m.r. spectrum. A one-proton doublet was observed at 3.06 τ ($J = 8.5$ Hz) together with multiplets at 4.8-5.3 τ (two protons) and 6.6-6.9 τ (one proton). Decoupling experiments furnished the following information:- irradiation of the one-proton multiplet at *ca.* 6.7 τ collapsed the two-proton multiplet to a doublet at 4.95 τ ($J = 8.5$ Hz) and a singlet at 5.04 τ. Irradiation at *ca.* 5 τ collapsed the doublet at 3.06 τ to a sharp singlet. This information, taken together with i.r. absorption bands at 1765 and 1720 cm^{-1}, again indicates a dimeric structure.

The downfield shift of proton H_d from 5.27 τ to 5.04 τ is indicative of some deshielding influence from a group such as the imide carbonyl. Conversely, the upfield shift of the allylic proton from 6.15-6.40 τ to 6.6-6.9 τ can be accounted for by the removal of a deshielding influence, *e.g.*, a carbonyl group. If the *cis*-*syn*-dimer (22) and the *cis*-*anti*-dimer (23) are considered then it is seen that the imide carbonyl group can deshield proton H_d in both dimers whereas the allylic proton (H_c) is now no longer in the sphere of influence of this group.

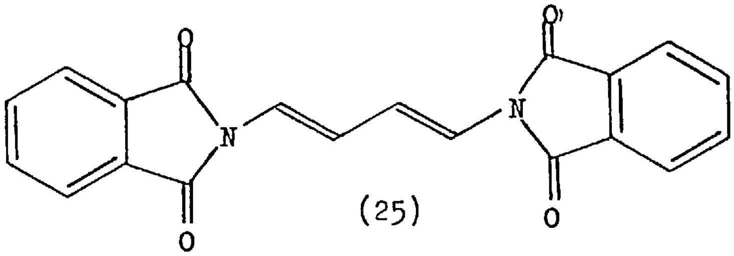
In this case, the spectroscopic evidence does not allow a differentiation between structures (22) and (23); possibly the *syn*-dimer (22) is favoured because of its greater symmetry, but the *anti*-dimer (23) cannot definitely be eliminated.

One of the most extensively studied photodimerisations in the field of heterocyclic chemistry is that of the pyrimidine bases, *e.g.*, (24)[13] and these studies provide a precedent for the above dimerisation.



(24)

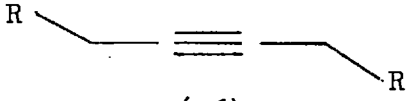
By analogy with the photochemical isomerisation of butadiene to bicyclobutane,[6] it is possible that the diene (25) might give a



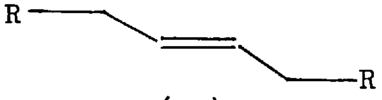
(25)

2,4-disubstituted bicyclobutane on photolysis. Such a compound should be useful as a precursor to tetrahedrane if the nitrogen functions at the 2,4-positions could be oxidatively coupled, and then eliminated with concomitant formation of a new carbon-carbon bond. The synthesis of (25) was therefore attempted.

But-2-yne-1,4-diol (26; R = OH) on treatment with thionyl chloride in pyridine gave 1,4-dichlorobut-2-yne (26; R = Cl)[14] which



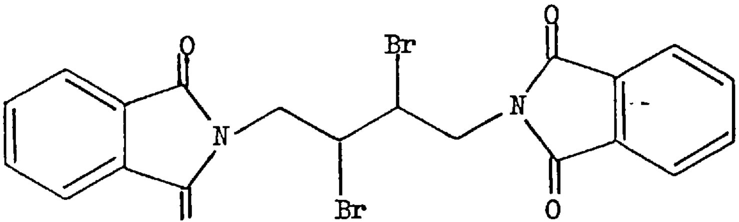
(26)



(27)

was then treated with potassium phthalimide in dimethylformamide to yield 1,4-diphthalimidobut-2-yne (26; R = phthalimido).[15] Attempts to rearrange this acetylene directly to the 1,3-diene (25) <u>via</u> the corresponding allene were unsuccessful. Treatment of (26; R = phthalimido) with sodamide in tetrahydrofuran produced no observable reaction whereas treatment with potassium t-butoxide in t-butanol caused extensive degradation. I.r. measurements showed that the imide system had been destroyed.

The corresponding olefin, 1,4-diphthalimidobut-2-ene (27; R = phthalimido) was prepared in quantitative yield by modification of a literature method[16] which utilised 1,4-dichlorobut-2-ene (27; R = Cl) and potassium phthalimide. Treatment of the olefin with an excess of bromine in chloroform gave the dibromide (28) in 88% yield. However, all attempts to dehydrobrominate this compound to the diene (25) were unsuccessful. Reaction with potassium t-butoxide in either t-butanol or ether led to very polar material, and no products could be isolated by simple solvent extraction procedures. Attempts to effect the allylic bromination of (27; R = phthalimido) were also unsuccessful.

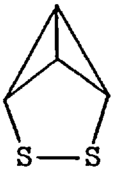


(28)

At this stage alternative approaches to tetrahedrane were conceived, and the previous route was not pursued further.

Studies in the Cyclobutane Series

Extrusion of sulphur from a synthon such as (29) with concomitant formation of a bond between the carbon atoms previously joined to sulphur constitutes, in principle, another route to tetrahedrane. A corollary to this idea is the possibility that a cyclobutane-1,3-dithiol (30), on oxidation to the disulphide followed by sulphur extrusion,[17] could lead to a bicyclobutane.



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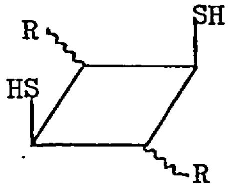
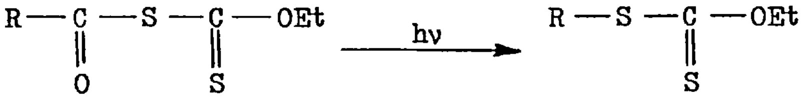


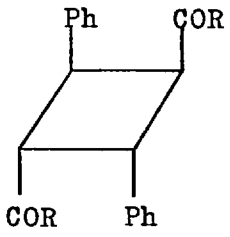
(30)

It is known [18] that photolysis of acyl xanthates gives alkyl xanthates, viz.,



$$R-\underset{\underset{O}{\|}}{C}-S-\underset{\underset{S}{\|}}{C}-OEt \xrightarrow{h\nu} R-S-\underset{\underset{S}{\|}}{C}-OEt$$

Such alkyl xanthates could act as precursors of the corresponding thiols, so the synthesis of a suitable acyl xanthate was undertaken. Accordingly, α-trans-cinnamic acid was photolysed, in the solid state, for a period of eight days to give α-truxillic acid (31; R = OH)[19] in 26% yield. Treatment of the acid with thionyl chloride furnished the di-acyl chloride (31; R = Cl) which gave the di-acyl


(31)

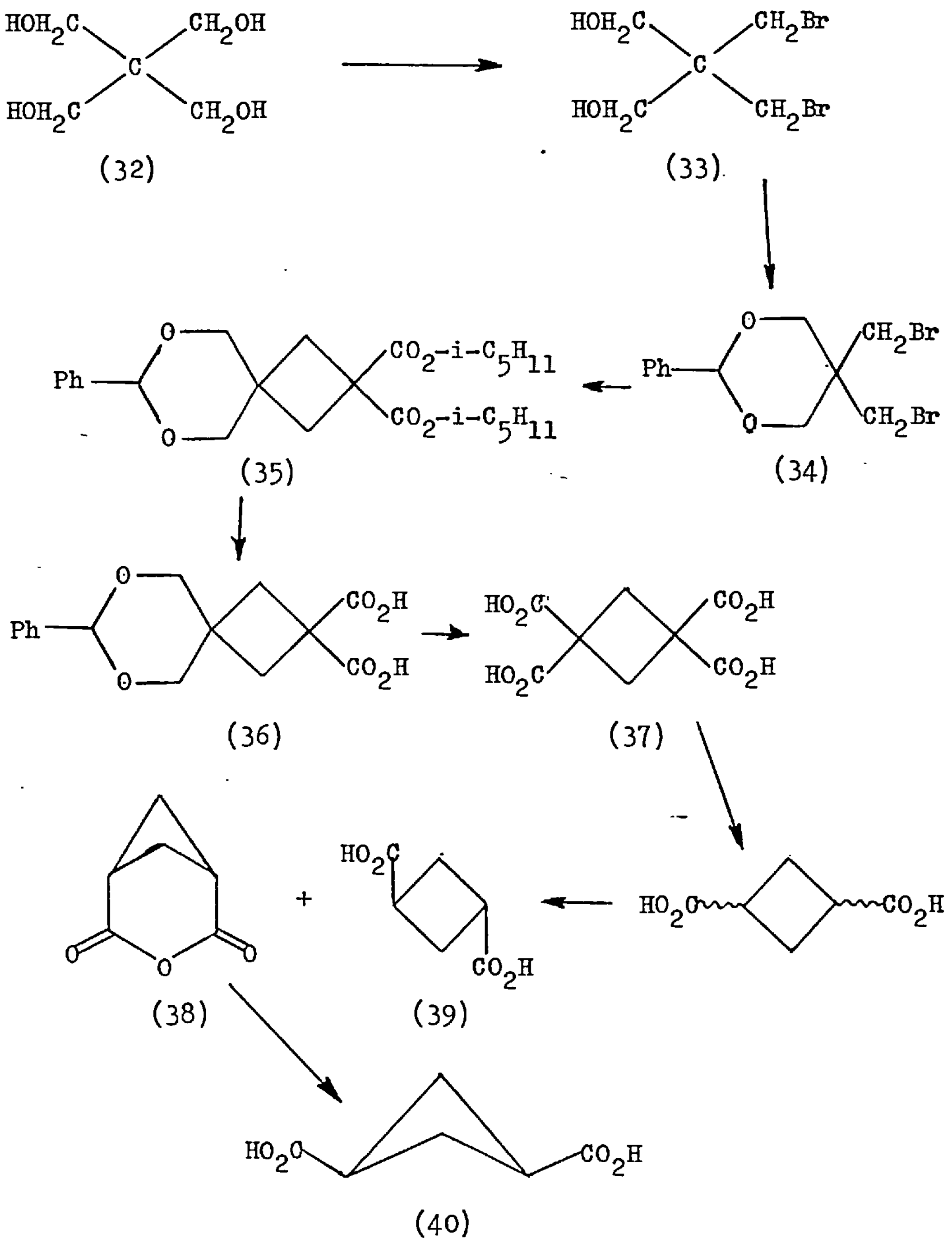
xanthate (31; R = SCSOEt) with potassium O-ethyl xanthate. The n.m.r. spectrum of (31; R = SCSOEt) was entirely compatible with the formulation shown and was similar, in appropriate respects, to the spectrum of the parent di-acyl chloride (31; R = Cl). The u.v. spectrum of the dixanthate exhibited peaks at 282 and 393 nm (ε 19,000 and 126); the parameters of the longer wavelength band being closely similar to published data for the dixanthate of glutaric acid (385 nm (ε 99)).

Photolysis of (31; R = SCSOEt) in benzene solution with a medium pressure mercury lamp resulted in its decomposition. Although some products were isolated by preparative layer chromatography, none corresponded to the required compound.

The preparation of a cis-di-acyl xanthate was next attempted. For this purpose the synthesis of cis-cyclobutane-1,3-dicarboxylic acid[20] was undertaken. The route is outlined in Scheme B.

Pentaerythritol (32) with dry hydrobromic acid in acetic acid gave the dibromo-derivative (33) which was converted to the acetal (34) with benzaldehyde. Treatment of this acetal with di-ethyl sodio-

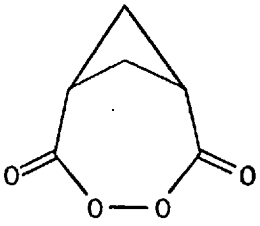
Scheme B


HOH$_2$C
CH$_2$OH
HOH$_2$C
CH$_2$OH
(32)
HOH$_2$C
CH$_2$Br
HOH$_2$C
CH$_2$Br
(33)
Ph
CH$_2$Br
CH$_2$Br
(34)
Ph
CO$_2$-i-C$_5$H$_{11}$
CO$_2$-i-C$_5$H$_{11}$
(35)
Ph
CO$_2$H
CO$_2$H
(36)
HO$_2$C
HO$_2$C
CO$_2$H
CO$_2$H
(37)
HO$_2$C
CO$_2$H
(38)
HO$_2$C
CO$_2$H
(39)
HO$_2$C
CO$_2$H
(40)

malonate gave (35) which on saponification yielded the dicarboxylic acid (36). Hydrolysis and oxidation of (36) led to the tetra-acid (37) which was in turn decarboxylated to a mixture of *cis*- and *trans*-cyclobutane-1,3-dicarboxylic acids. Treatment of this mixture of acids with acetyl chloride converted the *cis*-isomer to the anhydride (38), without affecting the *trans*-isomer (39). Sublimation separated the *cis*-anhydride from the *trans*-di-acid and hydrolysis gave the required *cis*-di-acid (40).

Treatment of the *cis*-di-acid (40) with oxalyl chloride under mild conditions gave a mixture of starting material and *cis*-anhydride (38); no acid chloride was detected. However, the use of phosphorus pentachloride gave the di-acyl chloride of (40), but attempts to make the derived di-acyl xanthate were unsuccessful. Attempts to convert the *cis*-di-acid (40) to the corresponding *cis*-diamine (and then oxidatively couple the two nitrogen functions) by means of the Schmidt reaction[21] were unsuccessful.

At this stage it was recognised that the cyclic peroxide (41)



(41)

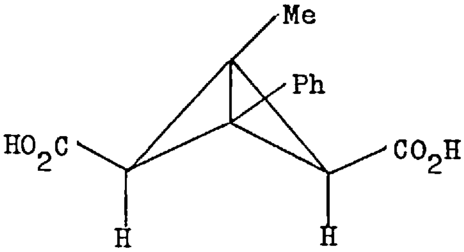
might lose two molecules of carbon dioxide with the simultaneous formation of a new carbon-carbon single bond. The synthesis of (41) was therefore attempted.

Treatment of (38) either with aqueous sodium peroxide solution or with 50% hydrogen peroxide solution resulted in no observable reaction.

As subsequent approaches to a tetrahedrane derivative involved the direct use of bicyclobutanes, these model studies were not pursued further.

Studies in the Bicyclobutane Series

The structural similarity of bicyclobutane and tetrahedrane has been mentioned previously (see Review) and it was decided, therefore, to use a bicyclobutane derivative as a precursor for a tetrahedrane. The compound chosen for study was the known 1-methyl-3-phenylbicyclobutane-2,4-dicarboxylic acid (42)[22] which was prepared by copper sulphate-catalysed addition of ethyl diazoacetate



(42)

to 1-phenylpropyne followed by hydrolysis to the di-acid.

The stereochemistry of this compound was unknown at the time the present work was undertaken. When first reported,[22] the stereochemistry of (42) was assumed to be that shown, but no proof was available. A definite assignment was clearly desirable before any chemical modifications were attempted. Consequently, a proof of stereochemistry was sought.

The use of dissociation constant measurements in the elucidation of molecular structure has been known for some time,[23] and was particularly emphasised by Barton[24] in the field of diterpene resin acids. This method is applicable to the present case.

Thermodynamic dissociation constants (K_1 and K_2) of a dibasic acid H_2A are defined by:-

$$K_1 = \frac{[H]^+[HA]^- f_1}{[H_2A] f_o} \qquad \text{and} \qquad K_2 = \frac{[H]^+[A]^= f_2}{[HA]^- f_1}$$

where $[H]^+$ signifies the activity of hydrogen ions, and f_o, f_1, and f_2 are activity coefficients of the species H_2A, HA^-, and $A^=$ respectively.

In a solution of total acid concentration 'a' (moles)

$$a = [H_2A] + [HA]^- + [A]^=$$

and when a strong monoacidic base, which may be taken as completely dissociated, has been added to give a molar concentration 'b', electrical neutrality requires that:-

$$b + [H]^+ = [HA]^- + 2[A]^= + [OH]^-$$

Defining α, β, and γ as

$$\alpha = b + [H]^+ - [OH]^- = [HA]^- + 2[A]^=$$
$$\beta = a - b - [H]^+ + [OH]^- = [H_2A] - [A]^=$$
$$\gamma = 2a - b - [H]^+ + [OH]^- = 2[H_2A] + [HA]^-$$

it can readily be shown that

$$\frac{([H]^+)^2\alpha f_2}{\gamma f_o} = K_1\left[\frac{[H]^+\beta f_2}{\gamma f_1}\right] + K_1K_2 \quad \ldots (1)$$

f_o is unlikely to differ appreciably from unity when the ionic strength (I) is less than 0.01. In general, f_1 and f_2 are not known; in very dilute solution they will not be much less than unity and can be estimated by the Debye-Huckel limiting law, i.e.,

$$\log f_1 = -0.5\sqrt{I} \quad \text{and} \quad \log f_2 = -2.0\sqrt{I}$$

The ionic strength can be estimated by successive approximations if necessary, but in the very dilute solutions (generally less than 0.001 M) used in this work, may be taken without serious error as $(b + [H]^+)$ when $b < a$ and as $(2b - a)$ when $b > a$.

Equation (1) may be plotted as a linear function giving values for K_1 and K_2.

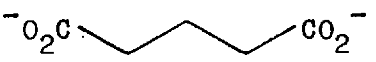
In the present case, linear plots were obtained for the titration of (42) against 0.02 N sodium hydroxide solution both in 50% methanol/water and in aqueous solution. The titration in 50% methanol/water gave $pK_1 = 7.20$ and $pK_2 = 8.43$. However, to compare these results with published results for other dicarboxylic acids, it was more convenient to carry out the titration in aqueous solution. Compound (42) was not readily soluble in cold water,† and it was

---

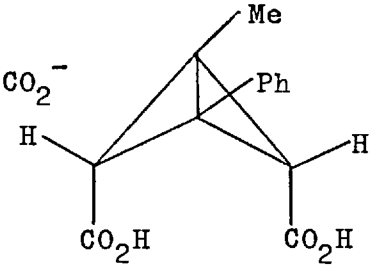
† The di-acid was dissolved by hot water, but heating the solutions resulted in 'leaching' of the glass beaker thus causing unwanted pH changes.

necessary to add two equivalents of sodium hydroxide to an aqueous suspension of the di-acid. The disodium salt thus obtained was titrated against 0.02 N hydrochloric acid. This back-titration gave $pK_1 = 6.16$ and $pK_2 = 7.12$.

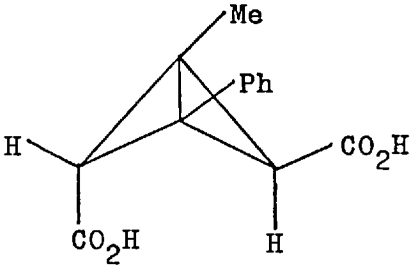
The difference between pK_1 and pK_2 (0.96) compares very favourably with the corresponding figure (1.07) for glutaric acid,[25] which has the same number of carbon atoms between the two carboxy-groups as (42). When the two carboxy-groups of glutaric acid are both ionised, the conformation adopted is that shown in (43). The similarity of the values of ΔpK of (42) and glutaric acid lead to the conclusion that the two ionised carboxy-groups of (42) are in an analogous environment to that depicted in (43), i.e., as far away from one another as possible (see (42)).



(43)



(44)



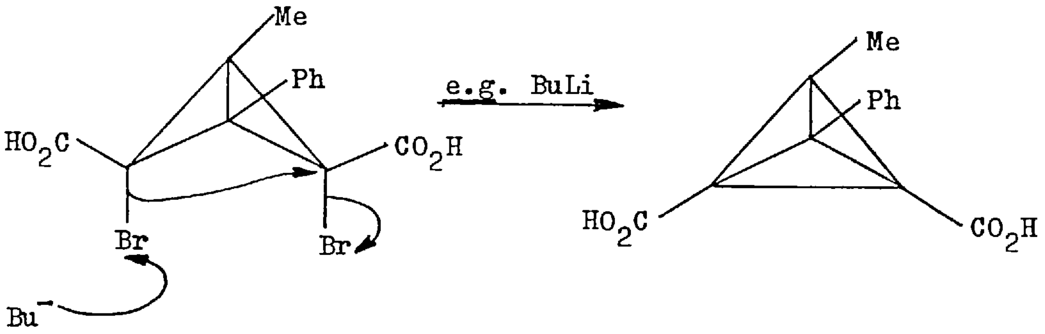
(45)

The shape of the titration curve is also significant - only one endpoint was observed. This fact indicates the presence of two ionised carboxy-groups not interacting with one another. A configuration such as (44) can be eliminated because if one carboxy-group were ionised, the negative charge would effect the pK_a of the second carboxy-group, probably leading to the observation of two end-points on the titration curve, and most certainly leading to a larger difference between pK_1 and pK_2.

The exo,endo-isomer (45) can also be eliminated by the appearance of a sharp two-proton singlet at 8.47 τ in the n.m.r. spectrum of the di-acid, and a sharp two-proton singlet at 8.37 τ in the spectrum of its dimethyl ester; both signals correspond to the ring protons. Isomer (45) has two non-equivalent ring protons and would exhibit two singlets.

The stereochemistry of (42) is, therefore, defined by the exo, exo-arrangement shown.

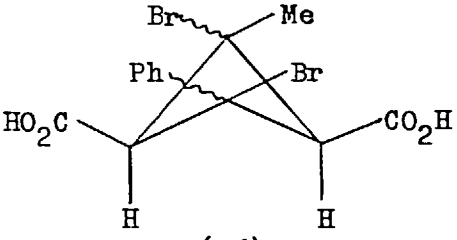
If the ring protons of (42) were to be replaced by bromine atoms, then it is conceivable that the following process might lead to a tetrahedrane, even though the stereochemistry of the bromine atoms would not be ideal for an elimination reaction.[26]



Replacement of the ring protons was therefore attempted. Treatment of (42) with phosphorus and bromine[27] and with phosphorus trichloride and bromine[28] both led to extensive degradation (n.m.r.

evidence).

As the introduction of bromine into (42) by replacement of hydrogen atoms was unsuccessful, it was decided to attempt to replace the carboxy-groups by halogen. For this purpose, the modified[29] Hunsdiecker[30] reaction was examined. Treatment of a suspension of (42) and red mercuric oxide in dry carbon tetrachloride with one equivalent of bromine led to a complex mixture of products. The n.m.r. spectrum exhibited no absorptions in the region expected for the ring protons (ca. 8.5 τ), but peaks at ca. 5.7 τ and ca. 7.5 τ (in the ratio 2:3) suggested that bromine might have added to the bridgehead bond. Indeed, when mercuric oxide was omitted from the reaction, the sole product was the unstable cyclobutane dibromide (46).



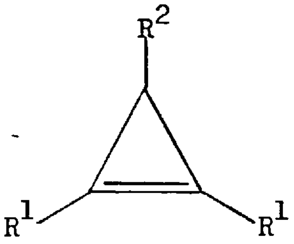
(46)

The correctness of this assignment was indicated by the n.m.r. spectrum which showed singlet absorptions at 5.67 τ (two protons) and 7.42 τ (three protons) attributable to the cyclobutane ring protons and methyl group respectively. The phenyl group appeared as a composite of two- and three-proton multiplets (at 1.95-2.20 τ and 2.50-2.75 τ respectively) and the exchangeable acid protons were at -0.63 τ (two-proton broad singlet). Confirmatory evidence came from the mass spectrum which, although it did not exhibit a molecular ion, had structurally significant peaks at m/e 311 and 313 (M^+ - Br), 293 and 295 (corresponding to loss of a bromine atom and the elements of water - indicating the <u>cis</u>-relation of the carboxy-groups), and 230 (loss of two molecules of HBr to give a cyclobutadiene radical-cation).

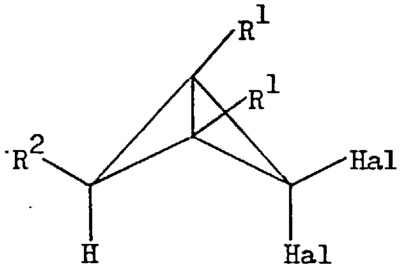
Attempts were next made to replace the carboxy-groups by iodine. Having first established that iodine did not add to the bridgehead bond of (42), this compound was irradiated with a tungsten lamp as a suspension in refluxing carbon tetrachloride together with lead tetra-acetate, and the mixture treated with iodine. This technique[31] is known to work well for a number of acids, but in the present case t.l.c. indicated a complex mixture. Preparative layer chromatography served to separate some of these components but mass spectral examination of the isolated materials showed them to have very high molecular weights (strong ions observed up to m/e 690). These substances are most probably decomposition or polymerisation products and were not investigated further. The fact that some decarboxylation was indeed taking place was revealed when the exit gases were passed through a trap at -80° and then into saturated aqueous barium hydroxide solution. The yield of barium carbonate corresponded to 58% of the theoretical.

Decarboxylation of (42) with lead tetra-acetate alone was also unsuccessful as was attempted pyrolytic decarboxylation. Extensive decomposition occurred in the former, and unchanged starting material was recovered from the latter.

Another approach to the synthesis of a halobicyclobutane that was considered was the generation of such a species from a cyclopropene. Thus the addition of a dihalocarbene to a cyclopropene (e.g., (47)) should lead to a 2,2-dihalobicyclobutane such as (48).

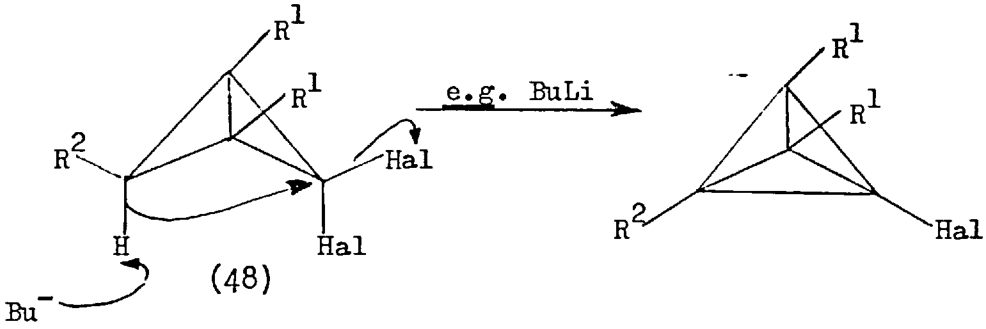


(47)



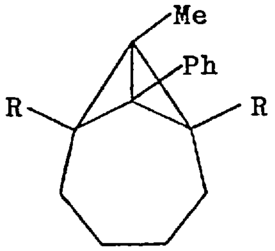
(48)

Suitable choice of R^2 so as to make the α-proton acidic opens up the possibility of dehydrohalogenation of (48), i.e.,



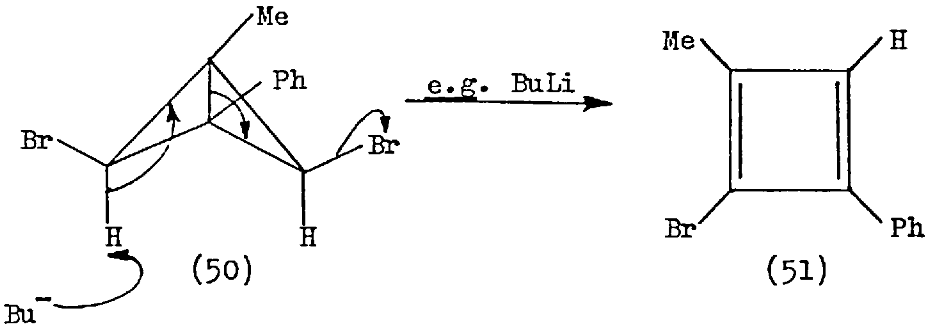
Accordingly, 1,2-diphenylcycloprop-1-ene-3-carboxylic acid (47; R^1 = Ph, R^2 = CO_2H) was synthesised by treatment of diphenylacetylene with ethyl diazo-acetate in the presence of anhydrous copper sulphate.[32] Attempts to add either dichlorocarbene or dibromocarbene to the acid (47; R^1 =Ph, R^2 = CO_2H) or to its methyl ester (47; R^1 = Ph, R^2 = CO_2Me) were unsuccessful. Treatment of these cyclopropenes with sodium trichloro-acetate, phenyl (trichloromethyl)mercury[33] (sources of dichlorocarbene), or potassium t-butoxide/bromoform (a source of dibromocarbene) led to recovery of starting material - no addition products were observed.

As attempts to decarboxylate the bicyclobutane di-acid (42) were unsuccessful, the preparation of the acid (49; R = CO_2H) was considered in the expectation that the tertiary nature of the carboxy-groups might render them removable under milder conditions than those required for a secondary acid such as (42). Moreover,



(49)

if bromodecarboxylation of (42) had given the dibromide (50), then subsequent dehydrobromination could have given the cyclobutadiene (51)

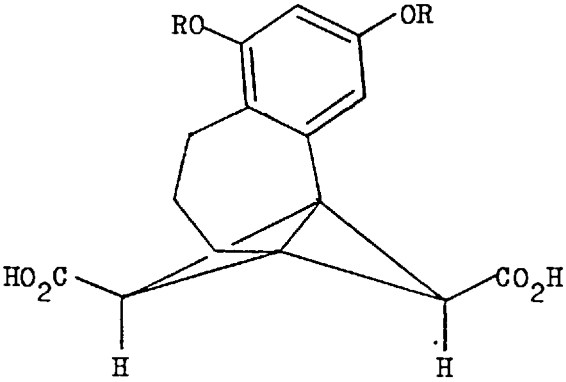


(50) (51)

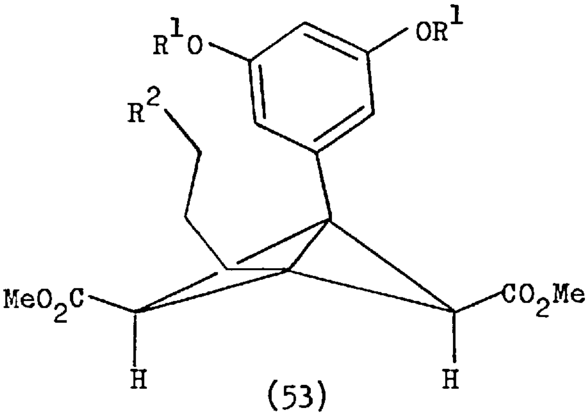
rather than the corresponding tetrahedrane. The proposed use of the tricyclic di-acid (49; R = CO_2H) as the precursor of the corresponding dibromide (49; R = Br) would circumvent this difficulty as dehydrobromination to a cyclobutadiene would be impossible without gross violation of Bredt's rule.

Treatment of a benzene solution of the dimethyl ester of (42) with sodium hydride in the presence of 1,4-dibromobutane resulted in no observable reaction. Use of the benzene-soluble sodium salt of hexamethyldisilazane[34] and 1,4-dibromobutane, however, resulted in the immediate consumption of starting material giving very polar products. The only isolable materials were dark-brown tars. The same result was obtained when the reaction was repeated in the presence of the more reactive dibromide, xylylene dibromide. This approach was not pursued further.

The prevention of cyclobutadiene formation from a dibromide such as (50) can be accomplished by formation of a ring across the 1,3-positions of a bicyclobutane instead of across the 2,4-positions, as in (49). The tricyclo-compound (52) fulfils this condition. It was



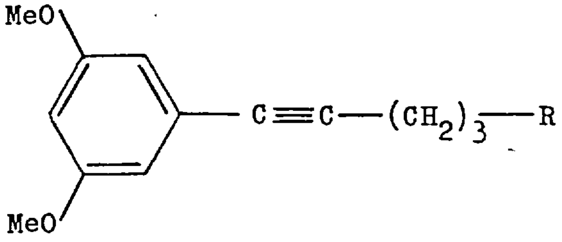
(52)



(53)

thought that the substituted bicyclobutane (53; R^1 = Me, R^2 = Br) would be a suitable precursor of (52; R = Me) as cyclisation should be induced by mild Lewis acids, or in the case of (53; R^1 = H, R^2 = Br) by base to give (52; R = H). Accordingly, the synthesis of (53; R^1 = Me, R^2 = Br) was undertaken.

The initial synthetic objective was the acetylene (54) where



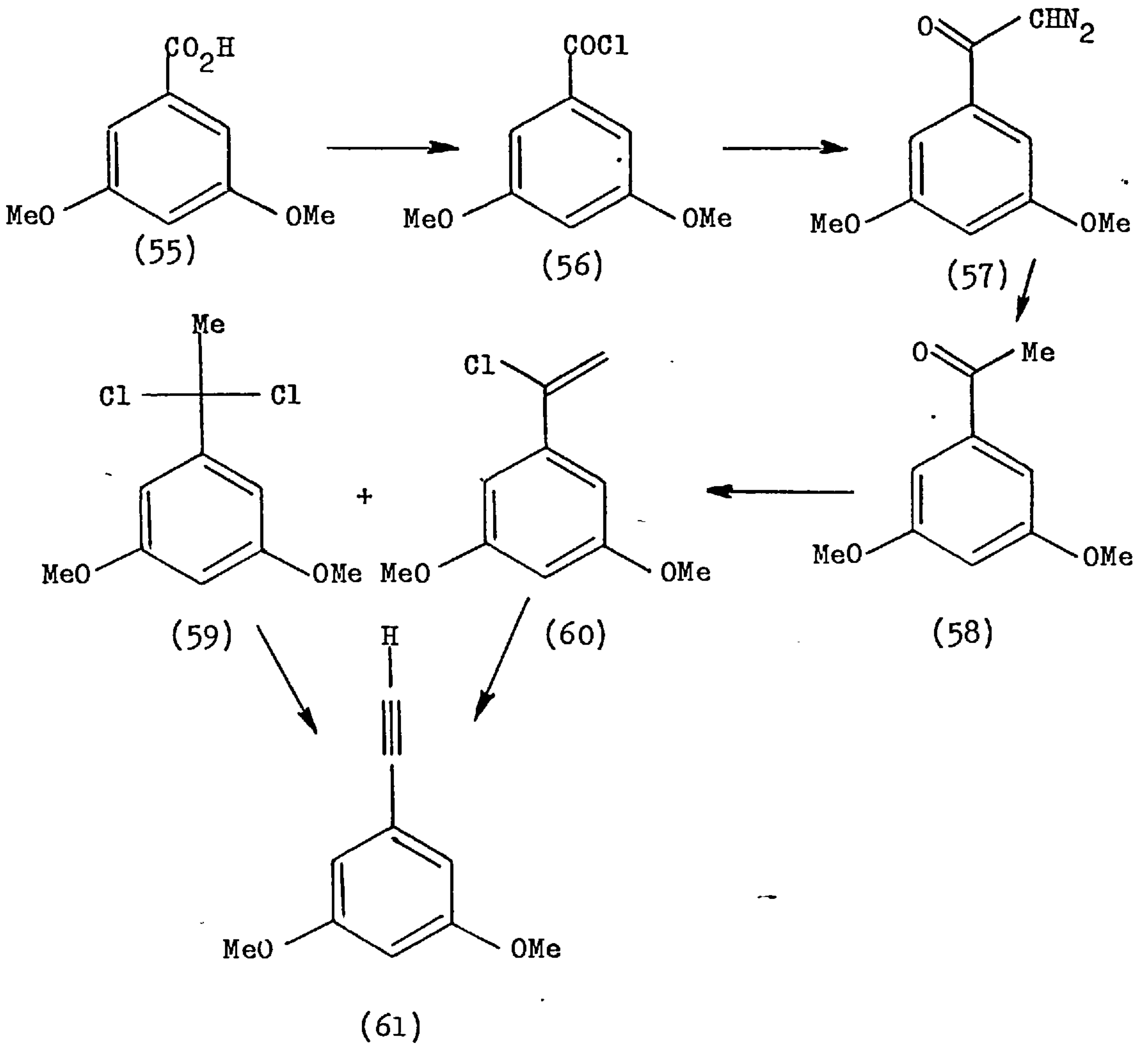
(54)

R = bromine, or some group which could be replaced by bromine after the proposed double addition of ethyl diazo-acetate to (54). Scheme C outlines the synthetic steps involved.

Treatment of 3,5-dimethoxybenzoic acid (55) with thionyl chloride gave the acid chloride (56) which furnished the crystalline diazo-ketone (57) with diazomethane. This diazo-ketone was decomposed with hydriodic acid to yield 3,5-dimethoxyacetophenone (58).[35]† Phosphorus pentachloride converted the acetophenone into a mixture of the dichloride (59) and the α-chlorostyrene (60), and

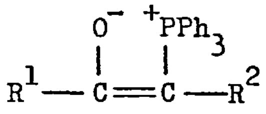
[†Treatment of the acid chloride (56) with dimethylcadmium gave the acetophenone (58),[36] but in lower yield than the procedure described above.]

Scheme C



this mixture, without separation, gave the required acetylene (61) on treatment with ethanolic potassium hydroxide. Attempts to alkylate the acetylene were unsuccessful. As a more elegant synthesis of the acetylene (54) was conceived, this approach was put aside.

It has been shown[37] that pyrolysis of β-ketoalkylidene triphenylphosphoranes (62) constitutes a general synthesis of acetylenes (63)



$$R^1-\overset{O^-}{\overset{|}{C}}=\overset{^+PPh_3}{\overset{|}{C}}-R^2$$

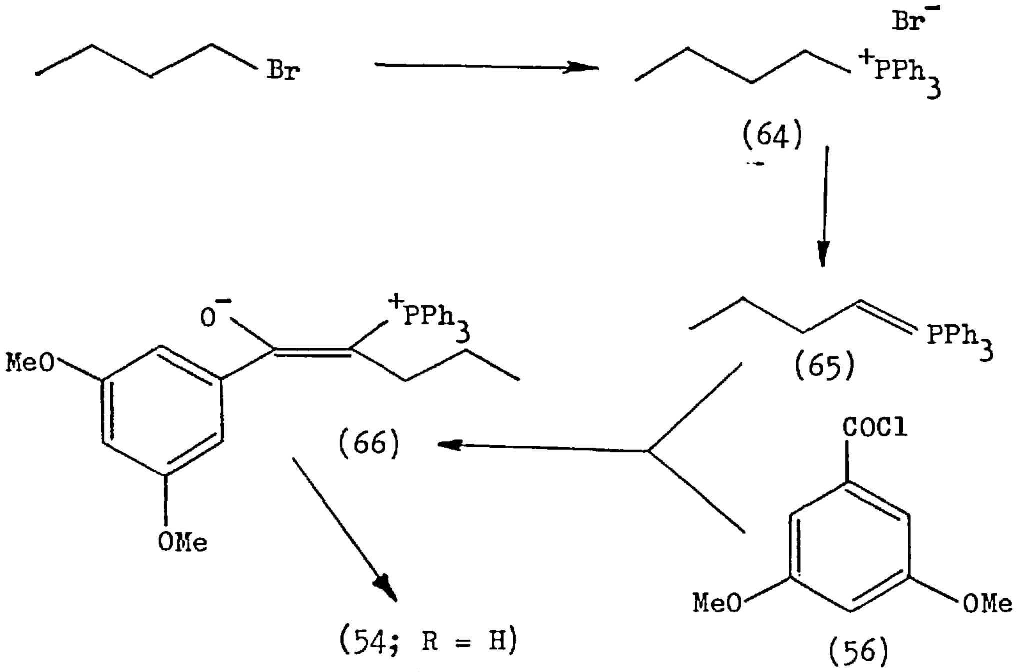
(62)

$$R^1-C\equiv C-R^2$$

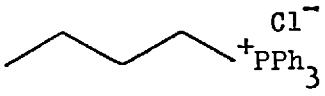
(63)

<u>provided</u> that (a) neither R^1 nor R^2 is hydrogen and (b) R^1 or R^2 is a phenyl or carbonyl group. This method can be applied to the synthesis of the acetylene (54). The tetrahydropyranyloxy group was selected as R, but since the synthetic scheme had only been applied to simple acetylenes[37] the feasibility of the route was tested by the synthesis of the acetylene (54; R = H). The approach is outlined in Scheme D.

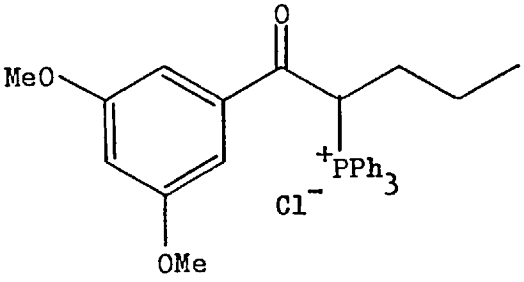
Scheme D



The action of butyl lithium on n-butyltriphenylphosphonium bromide (64) gave the corresponding ylid (65) which was treated with 0.5 equivalents of 3,5-dimethoxybenzoyl chloride in ether. The two products from this reaction should have been the phosphorane (66) and the phosphonium chloride (67), but only extremely hygroscopic solids were obtained which corresponded to neither of the expected products (n.m.r. evidence). The phosphorane (66) was generated, however, by addition of the ylid (65) to an ethereal solution of one equivalent of the acid chloride (56) (56 → 68) followed by treatment with base below 10°. When the phosphorane (66) was pyrolysed at 270–280° for a period of 20 minutes (lower temperatures led to incomplete pyrolysis) a mixture of products was obtained. Chromatography followed by distillation gave the analytically pure acetylene (54; R = H) in 26% yield.



(67)

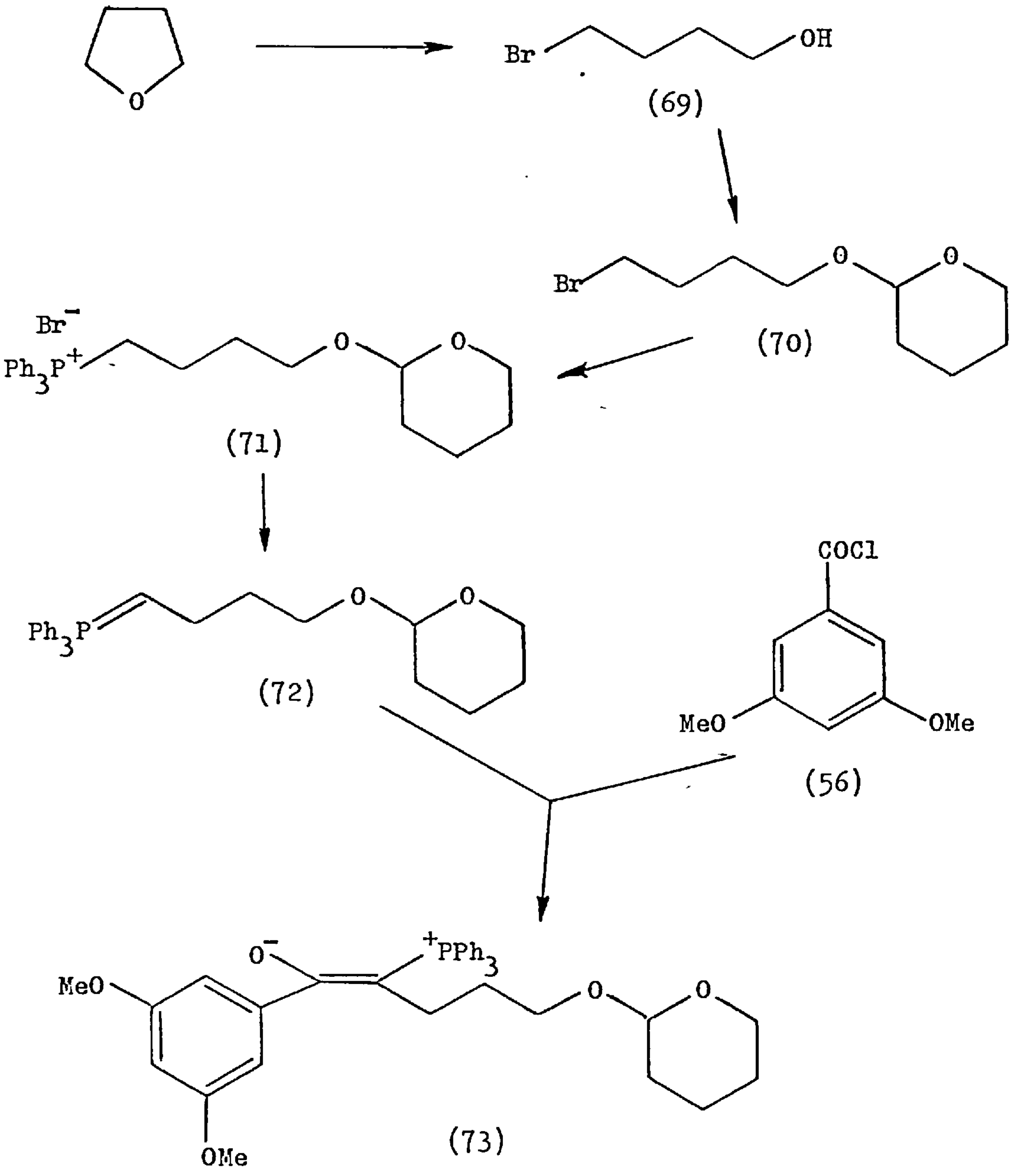


(68)

With the feasibility of the reaction established attention was next focussed on the synthesis (shown in Sheme E) of the protected acetylene (54; R = OTHP).

Treatment of tetrahydofuran with hydrogen bromide gave the bromohydrin (69) which was converted to the protected derivative (70)

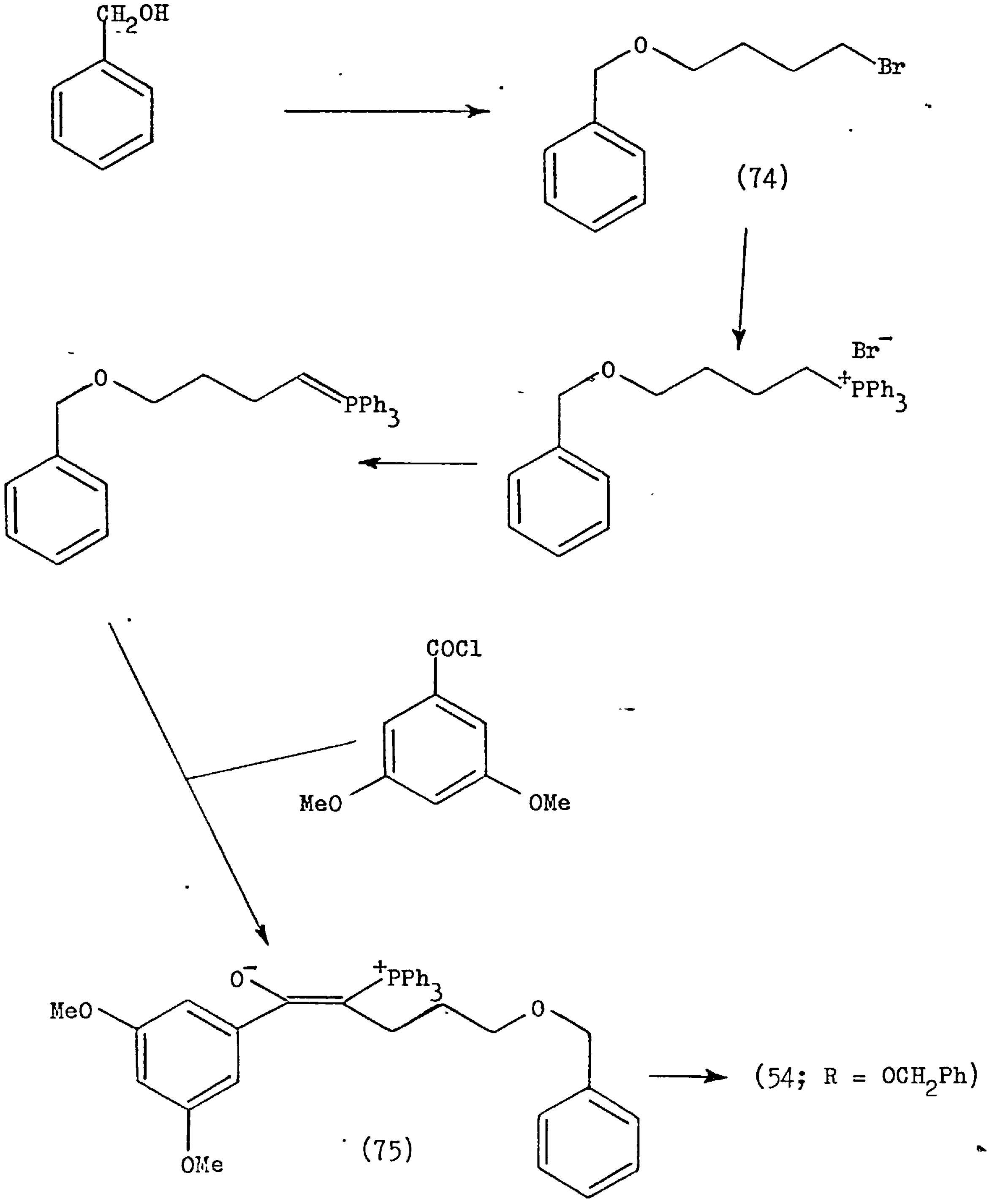
Scheme E


O
Br
OH
(69)
Br
O
O
(70)
Br⁻
Ph₃P⁺
O
O
(71)
Ph₃P
O
O
(72)
COCl
MeO
OMe
(56)
O⁻
⁺PPh₃
MeO
OMe
O
O
(73)

with dihydropyran in benzene. Conversion to the phosphonium bromide (71) proceeded smoothly and the derived ylid (72) was treated immediately with one equivalent of 3,5-dimethoxybenzoyl chloride (56) to give a small amount of a brown oil. The n.m.r. of this oil was rather complex (the presence of phosphorus in a molecule causes extensive line broadening) but was consistent with the expected constitution (73). Pyrolysis of the phosphorane did not lead to any acetylenic product. The mixture was complex and n.m.r. measurements indicated that the tetrahydropyranyl moiety had not survived the high temperature used. Consequently an alternative protecting group was tried and the synthesis of the acetylene (54; R = OCH_2Ph) was undertaken. Scheme F indicates the steps involved.

The benzyl ether (74) was prepared by the action of the sodium salt of benzyl alcohol on 1,4-dibromobutane.[38] The preparation of the phosphorane (75) followed similar lines to those previously described for other phosphoranes. Pyrolysis of (75) at 280°/760 mmHg gave the desired acetylene (54; R = OCH_2Ph) which was isolated in 25% yield after chromatography and distillation. The n.m.r. spectrum of (54; R = OCH_2Ph) was fully consistent with the structure shown. The signals of the aromatic protons appeared as a five-proton singlet at 2.60 τ with a doublet (two protons) and distorted triplet (one proton) at 3.40 τ and 3.53 τ respectively. Singlets at 5.43 τ (two protons) and 6.23 τ (six protons) were attributable to the benzylic and methoxyl protons respectively and the aliphatic protons appeared as two two-

Scheme F


CH2OH
O
Br
(74)
Br⁻
⁺PPh3
O
PPh3
COCl
MeO
OMe
O⁻
⁺PPh3
MeO
O
OMe
(75)
(54; R = OCH2Ph)

proton triplets (6.35 τ, $-CH_2O-$, and 7.45 τ, $-C{\equiv}C-CH_2-$ respectively) and a quintet at 8.10 τ (two protons).

Unfortunately, the reaction of (54; R = OCH_2Ph) with ethyl diazo-acetate in the presence of anhydrous copper sulphate as a catalyst gave a complex mixture of products. Examination of the n.m.r. spectrum of the total reaction mixture established that no bicyclobutane had been formed as signals in the region 8.5 τ were definitely absent. Signals in this region were also absent from the crude mixture of acids obtained by hydrolysis of the reaction mixture. Similar results were obtained from copper sulphate-catalysed or light-initiated additions to the acetylene (54; R = H). It is possible that in the case of the copper sulphate-catalysed reactions, carbethoxycarbene might be inserting into the methoxylated aromatic nucleus rather than attacking the triple bond.[39]

At this stage, consideration of the low yield ($<10\%$) of the bicyclobutane (42) from the reaction of 1-phenylpropyne with ethyl diazo-acetate, and the anticipated lower yield of bicyclobutane from (54; R = OCH_2Ph), made development of an improved route to (42) imperative. It was thought that if conditions could be established for the synthesis of this compound in high yield from 1-phenylpropyne, then these same conditions could be applied to the reaction of (54; R = OCH_2Ph) with ethyl diazo-acetate. The expectation was that if a small quantity of a bicyclobutane was formed it could be detected.

The reported[22,40] intermolecular carbene additions leading to bicyclobutanes employ heterogeneous conditions, viz., copper sulphate or copper in cyclohexane. Although homogeneous metal-catalysed additions to olefins have been studied,[41,42] similar studies with acetylenes have not hitherto been reported. Consequently the homogeneous metal-catalysed addition of ethyl diazo-acetate to 1-phenylpropyne was examined.

The yield in this reaction was increased by the use of (trialkylphosphite)copper(I) halide catalysts.[43] Table I illustrates the results obtained with these soluble catalysts.

Table I

Catalyst	Temperature	Solvent	Yield (%)
$(EtO)_3P.CuCl$	80°	Cyclohexane	27
$(EtO)_3P.CuCl$	60°	Cyclohexane	28.5
$(EtO)_3P.CuCl$	40°	Cyclohexane	24
$(PhO)_3P.CuCl$	75°	Cyclohexane	37
$(PhO)_3P.CuCl$	60°	Cyclohexane	36
$(PhO)_3P.CuCl$	40°	Cyclohexane	32
$(EtO)_3P.CuI$	70°	Cyclohexane	25.5
$CuSO_4$	75°	Cyclohexane	10 - 20
$Cu(acac)_2$	75°	Cyclohexane	0
$Cu(acac)_2$	75°	Benzene	26

(Triphenylphosphite)cuprous chloride was found to give slightly higher yields than either (triethylphosphite)cuprous chloride or (triethylphosphite)cuprous iodide. Variation of temperature did not have any drastic effect on the reaction - the lower yield obtained from the experiments conducted at 40° was no doubt due to incomplete decomposition of ethyl diazo-acetate, which was still present in the reaction mixture four hours after completion of its dropwise addition to the acetylene. The optimum temperature was judged to be 70-80°; higher temperatures did not materially affect the yield. A ten-fold increase in the amount of catalyst was without significant effect.

The results with anhydrous copper sulphate were not reproducible - yields varied between 10 and 20%. Bis(acetylacetonate)copper(II) had no catalytic effect in cyclohexane at ca. 75° (probably due to its insolubility in this solvent) but did have some effect in benzene in which it is moderately soluble. Nevertheless, it was still not as efficient as (triphenylphosphite)cuprous chloride.

Having determined the most suitable catalyst, it then remained to attempt to improve the yield by variation of the solvent. Table II indicates the results of this study.

The maximum yield of bicyclobutane was obtained using cyclohexane as solvent, but this yield was not significantly different to that obtained without solvent. The lower yields with acetone, ethyl acetate, and tetrahydrofuran are probably due to hydrogen abstraction from these solvents by the copper carbenoid intermediate. The poor result with benzene is not unexpected for carbene insertion into the

Table II

Catalyst	Solvent	Yield (%)
$(PhO)_3P.CuCl$	No solvent	35
$(PhO)_3P.CuCl$	Cyclohexane	37
$(PhO)_3P.CuCl$	Acetone	30.5
$(PhO)_3P.CuCl$	Ethyl acetate	16.5
$(PhO)_3P.CuCl$	Tetrahydrofuran	26
$(PhO)_3P.CuCl$	Benzene	19.5
$(PhO)_3P.CuCl$	Nitrobenzene	21
$(PhO)_3P.CuCl$	Anisole	20

aromatic ring could be a significant competing reaction.

The results with nitrobenzene and anisole are surprising. The expectation was that nitrobenzene should give a higher yield than anisole, as the electron-donating group of the latter should render it more susceptible to attack by the carbene. However, the experiments revealed essentially no solvent difference between the two, although the yield (compared to cyclohexane) was lowered.

Unfortunately, when the acetylene (54; R = OCH_2Ph) was treated with ethyl diazo-acetate in the presence of (triphenylphosphite)cuprous chloride a complex mixture was obtained. The n.m.r. spectrum of the reaction mixture did not exhibit any singlet peaks in the region _ca._ 8.5 τ - the region in which the signal of the bicyclobutyl ring protons of the desired product (53; R^1 = Me, R^2 = OCH_2Ph) would be expected.

EXPERIMENTAL

General

Unless otherwise specified, the following data apply to experiments described in this section.

Melting points were taken on a Kofler block and are uncorrected. Infrared spectra were taken of chloroform solutions or nujol mulls with a Unicam SP 200 spectrometer. Ultraviolet spectra were recorded for ethanolic solutions with a Unicam SP 700 instrument. Mass spectra were taken with an A.E.I. MS 9 double focussing spectrometer: samples were introduced by direct probe insertion and an ionising potential of 70 eV was normally used. Nuclear magnetic resonance spectra refer to deuteriochloroform solutions with tetramethylsilane as internal standard, and were recorded with a Varian A-60 or, where indicated, a HA-100 instrument.

The following abbreviations refer to the n.m.r. data:- s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, qn = quintet, sx = sextuplet, bs = broad singlet, and m = multiplet.

Solids were dried _in vacuo_ at room temperature. Evaporation of all solvents was effected _in vacuo_ at the lowest feasible temperature. Column chromatography was on neutral alumina of Brockmann grade 3 or on acid-washed silica gel. Silica gel for t.l.c. and preparative layer chromatography was Merck material (GF_{254}). Alumina for t.l.c. and preparative layer chromatography was Merck aluminium oxide GF_{254}. Ether refers to diethyl ether and petroleum ether to the fraction of b.p. 60-80°.

Photolysis of Pyridazine (3)

Pyridazine (1.0 g), in a pyrex flask (500 ml) fitted with a quartz insert, was irradiated as a moving thin film with water cooling and under an atmosphere of nitrogen with a 40 W low pressure mercury vapour lamp (253.7 nm) for a period of 3 days. The exit gas was passed into a trap cooled in liquid nitrogen. Periodic examination (n.m.r.) of the contents of the trap indicated the absence of volatile material whereas similar examination of samples of the photolysate indicated only the presence of pyridazine (τ 1.10 (2H,t; J = 3.5 Hz) and 2.70 (2H,t; J = 3.5 Hz)). The photolysis was discontinued when general decomposition of the photolysate led to loss of resolution in the n.m.r. spectrum.

Diene Photolysis

4-Phenylurazole

4-Phenylurazole was prepared by the procedure of Zinner and Deucker[44] and had m.p. 205-207° (lit.[44] m.p. 203°); ν_{max} (nujol) 3150, 1775, and 1690 cm^{-1}.

8-Phenyl-1,6,8-triazabicyclo[4.3.0]non-3-ene-7,9-dione (14)

A stirred solution of 4-phenylurazole (15.0 g) in acetone (600 ml) was maintained at -50° and t-butyl hypochlorite (9.22 g) was added slowly. The resulting red solution was stirred at this temperature for a further period of 1 h and butadiene (16.0 g) was then introduced slowly. When the initial red colour had been discharged the cooling bath was removed and the solution left to come to room temperature. Evaporation of the solvent and crystallisation of the residue gave the adduct (14) (18.55 g, 96%), m.p. 161-162.5° (lit.[10] m.p. 157-159°); ν_{max} (nujol) 1770 and 1710 cm^{-1}; λ_{max} 212, 218, and 265 nm (ε 12,400, 13,000, and 1,600); τ 2.53 (5H,m), 4.07 (2H,bs), and 5.83 (4H,bs). (Found: C, 62.73; H, 4.74; N, 18.53. $C_{12}H_{11}N_3O_2$ requires C, 62.87; H, 4.84; N, 18.33%).

3,4-Dibromo-8-phenyl-1,6,8-triazabicyclo[4.3.0]nonane-7,9-dione (15)

A solution of the olefin (14) (6.76 g) in chloroform (100 ml) was treated dropwise, with stirring, with a solution of bromine (6.0 g) in chloroform (15 ml). Stirring at room temperature was continued overnight and the white crystalline dibromide was collected and washed with chloroform. The combined filtrates were washed with aqueous sodium thiosulphate solution and with water, dried (Na_2SO_4), and evaporated to dryness to yield a further crop of dibromide. All the solids were combined and crystallised from chloroform to give the product as fine needles (11.14 g, 97%), m.p. 258-260° (decomp.); ν_{max} (nujol) 1765 and 1710 cm^{-1}; λ_{max} 218 nm (ε 16,000); τ 2.53 (5H,s), 5.38 (2H,bs), and 5.68 (4H,d; J = 1 Hz). (Found: C, 36.91; H, 2.67; Br, 41.23; N, 10.77. $C_{12}H_{11}Br_2N_3O_2$ requires C, 37.05; H, 2.85; Br, 41.09; N, 10.80%).

8-Phenyl-1,6,8-triazabicyclo[4.3.0]nona-2,4-diene-7,9-dione (11)

Potassium t-butoxide (1.006 g) was added in portions to a stirred suspension of the dibromide (15) (442 mg) in anhydrous ether (400 ml; dried over sodium wire) maintained at 0°. The mixture was stirred for a further 15 min (0°) and then poured into water (100 ml). The organic layer was separated, combined with further ethereal extracts, washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue was crystallised from ethanol to afford yellow needles of the diene (112 mg, 44%), m.p. 206-208° (decomp.); ν_{max} (nujol) 1780, 1760, and 1695 cm^{-1}; λ_{max} 205, 227, 260 (shoulder), and 368 nm (ε 15,400, 15,200, 8,190, and 1,640); τ 2.59 (5H,s), 3.08 (2H,m), and 4.62 (2H,m). (Found: C, 63.38; H, 4.27; N, 18.29. $C_{12}H_9N_3O_2$ requires C, 63.43; H, 3.99; N, 18.49%).

8-Phenyl-1,6,8-triazabicyclo[4.3.0]nonane-7,9-dione (16)

A solution of the olefin (14) (485 mg) in ethanol (40 ml) was hydrogenated until no further uptake of hydrogen took place (1 atm; room temp.) over 10% palladium on carbon (22 mg). The mixture was filtered and the catalyst washed thoroughly with ethanol. The combined filtrates were evaporated to dryness and the residue crystallised from ethanol to give white needles of the saturated adduct (459 mg, 94%), m.p. 142-142.5°; ν_{max} (nujol) 1765 and 1705 cm^{-1}; λ_{max} 209 (shoulder) and 219 nm (ε 12,900 and 14,600); τ 2.57 (5H,m), 6.45 (4H,m), and 8.22 (4H,m). (Found: C, 62.49; H, 5.70; N, 18.35. $C_{12}H_{13}N_3O_2$ requires C, 62.32; H, 5.67; N, 18.18%).

Hydrogenation of 8-Phenyl-1,6,8-triazabicyclo[4.3.0]nona-2,4-diene-7,9-dione (11)

A solution of the diene (9.0 mg) in ethanol (5 ml) was hydrogenated until no further uptake of hydrogen took place (1 atm; room temp.) over 10% palladium on carbon (5 mg). The product was isolated in the manner described in the preceding hydrogenation experiment to give white needles of 8-phenyl-1,6,8-triazabicyclo[4.3.0]-nonane-7,9-dione (7.2 mg, 79%), m.p. 141-142°, identical (m.p., mixed m.p., i.r., and t.l.c. properties) with an authentic sample.

Butyl 2-(N-phenylcarboxamido)-1,2-dihydropyridazine-1-carboxylate (17)

Potassium t-butoxide (2.0 g) was added in portions to a stirred suspension of the dibromide (15) (785 mg) in anhydrous ether (200 ml; dried over sodium wire) maintained at 0°. The mixture was stirred for a further 25 min (0°) then poured into water. The organic layer was separated, combined with further ethereal extracts, washed with water, dried (Na_2SO_4), and evaporated to dryness to yield an off-white solid (434 mg). Crystallisation from ether gave the 1,2-dihydropyridazine (17) as white needles (275 mg, 45%), m.p. 144.5-145.5°; ν_{max} (nujol) 3250, 1740, 1665, and 1600 cm^{-1}; λ_{max} 205, 240, and 298 nm (ε 21,300, 16,200, and 4,600); τ 2.5-2.8 (5H,m), 2.8-3.1 (1H,bs) partially exchanged with D_2O, 2.96 (1H,m), 3.53 (1H,m), 4.25 (2H,m), and 8.50 (9H,s). (Found: C, 63.71; H, 6.44; N, 13.94. $C_{16}H_{19}N_3O_3$ requires C, 63.77; H, 6.36; N, 13.95%).

Hydrogenation of Butyl 2-(N-phenylcarboxamido)-1,2-dihydropyridazine-1-carboxylate (17)

A solution of the diene (17) (37.7 mg) in ethanol (10 ml) was hydrogenated until no further uptake of hydrogen took place (1 atm; room temp.) over 10% palladium on carbon (5.5 mg). The product was isolated as described for 8-phenyl-1,6,8-triazabicyclo[4.3.0]nonane-7,9-dione (16) to give the saturated derivative (19) (38.0 mg, 100%). Crystallisation from ethanol gave pure material m.p. 132.5-134°; ν_{max} (nujol) 3300, 1730 and 1665 cm^{-1}; τ 2.5-3.2 (5H,m), 5.5-6.2 (1H,bs), 6.8-7.8 (4H,m), 8.15-8.45 (4H,m), and 8.55 (9H,s). (Found: C, 63.17; H, 7.34; N, 13.87. $C_{16}H_{23}N_3O_3$ requires C, 62.93; H, 7.59; N, 13.76%).

Reaction of Butyl 2-(N-phenylcarboxamido)-1,2-dihydropyridazine-1-carboxylate with Sodium Hydride

Sodium hydride (6 mg; 50% dispersion in mineral oil) was added to a stirred refluxing solution of the dihydropyridazine (17) (25.8 mg) in anhydrous benzene (10 ml; dried over sodium wire). Stirring was continued at this temperature for a further 15 min and then the mixture was poured into water. The organic layer was separated, combined with further benzene extracts, washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue was applied to a preparative layer chromatography plate (alumina) and chromatographed using dichloromethane as eluent. Crystallisation from ethanol gave the bicyclic diene (11) (5.3 mg, 27%) identical (m.p., i.r., and t.l.c. properties) with an authentic sample.

Photolysis of 8-Phenyl-1,6,8-triazabicyclo[4.3.0]nona-2,4-diene-7,9-dione (11)

A solution of the diene (202 mg) in anhydrous benzene (120 ml; dried over sodium wire) was irradiated, with water cooling and under an atmosphere of nitrogen, with a 750 W tungsten lamp for 40 h (t.l.c. and u.v. control). The solution was evaporated to dryness to give an oil (180 mg). This oil was applied to preparative layer chromatography plates (silica) and chromatographed, with petroleum ether-dichloromethane (1:1 v/v) as eluent (multiple elution), to yield two components.

Faster running component (56 mg, 28%): ν_{max} (chloroform) 1765 and 1720 cm^{-1}; λ_{max} 199, 221, and 259 nm (ε 12,900, 7,800, and 10,000); τ (HA-100) 2.4-2.8 (5H,m), 3.09 (1H,dd; J = 8.5 Hz and 1.5 Hz), 4.99 (1H,dd; J = 8.5 Hz and 4.0 Hz), 5.27 (1H,t; J = 8.0 Hz), 6.15-6.40 (1H,m); mass spectrum: no M^+ but significant high mass peaks at m/e 438, 424, 410, 396, 382, 368, 354, and, a short time after injection into the spectrometer, 227.

Slower running component (30 mg, 15%): ν_{max} (chloroform) 1765 and 1720 cm^{-1}; λ_{max} 202, 218, 245, and 260 (shoulder) nm (ε 6,600, 6,200, 8,400, and 4,700); τ (HA-100) 2.3-2.9 (5H,m), 3.06 (1H,d; J = 8.5 Hz) 4.8-5.3 (2H,m), and 6.6-6.9 (1H,m).

1,4-Dichlorobut-2-yne (26; R = Cl)[14]

Thionyl chloride (43.6 ml, 71.5 g) was added slowly (over a period of 5 h) to a solution of but-2-yne-1,4-diol (21.5 g) in pyridine (35 ml) maintained at 10-20°. The cooling bath was then removed and the solution left to come to room temperature overnight. Ice-water was added to the mixture, the organic layer separated, and combined with further ethereal extracts. The combined extracts were washed with aqueous sodium bicarbonate solution and with water, dried (Na_2SO_4), and evaporated to dryness to give a brown oil. Distillation of this oil afforded 1,4-dichlorobut-2-yne (13.36 g, 44%), b.p. 69-70°/ 20 mmHg (lit.[14] b.p. 68-69°/17 mmHg).

1,4-Diphthalimidobut-2-yne (26; R = phthalimido)[15]

1,4-Dichlorobut-2-yne (8.00 g) was slowly added to a stirred solution of potassium phthalimide (24.32 g) in anhydrous dimethylformamide (102 ml; distilled from calcium hydride) heated on a steam bath. The suspension was stirred on the steam bath for a further 7 h, then removed and left to come to room temperature. Water (200 ml) was added and the precipitate collected, washed with water, and dried. Crystallisation from chloroform afforded pure 1,4-diphthalimidobut-2-yne (18.12 g, 81%), m.p. 281.5-283° (lit.[15] m.p. 281-282°); ν_{max} (nujol) 1770, 1720, and 1620 cm^{-1}.

Attempted rearrangement of 1,4-Diphthalimidobut-2-yne (26; R = phthalimido

(a) Sodamide (104 mg) was added in portions to a stirred solution of 1,4-diphthalimidobut-2-yne (172 mg) in anhydrous tetrahydrofuran

(50 ml; distilled from lithium aluminium hydride). No reaction was observed.

(b) 1,4-diphthalimidobut-2-yne (174 mg) was added in portions to a stirred solution of potassium t-butoxide (1.089 g) in t-butanol (25 ml) and the resulting suspension refluxed for 25 min during which time a yellow solution was obtained. This solution was poured into water and the mixture extracted with chloroform. The combined extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness. No product was obtained. The aqueous phase was then acidified with 6N hydrochloric acid and re-extracted with chloroform. The combined extracts were treated as described above to yield a solid (28 mg). The i.r. spectrum exhibited no absorption at ca. 1760 and 1720 cm^{-1} indicating that the imide system had been destroyed.

1,4-Diphthalimidobut-2-ene (27; R = phthalimido)[16]

1,4-Dichlorobut-2-ene (8.00 g) was slowly added to a stirred solution of potassium phthalimide (24.71 g) in anhydrous dimethylformamide (100 ml; distilled from calcium hydride) heated on a steam bath. The suspension was stirred on the steam bath overnight, then removed and left to come to room temperature. Water (200 ml) was added and the precipitate collected, washed with water, and dried to yield the diphthalimido derivative (22.50 g, 100%). Crystallisation from ethyl acetate gave white platelets, m.p. 229-230.5° (lit.[16] m.p. 230-231°); ν_{max} (nujol) 1760, 1710, and 1620 cm^{-1}.

2,3-Dibromo-1,4-diphthalimidobutane (28)

A solution of bromine (3.0 g, ca. 3 equiv.) in chloroform (5 ml) was slowly added to a stirred solution of 1,4-diphthalimidobut-2-ene (2.00 g) in chloroform (150 ml). After completion of the addition stirring was continued overnight at room temperature. The solution was washed with aqueous sodium thiosulphate solution and with water, dried (Na_2SO_4), and evaporated to dryness to yield the dibromide (2.56 g, 88%), m.p. 210.5-212.5°; ν_{max} (nujol) 1770 and 1720 cm^{-1}; τ 2.16 (8H,m), 5.68 (4H,bs), and 5.83 (2H,bs); mass spectrum, no M^+ but significant peaks at m/e 345, 284, 282, 215, 202, and 160 (base peak). $[(M^+ - HBr_2)$, 345.0867. $C_{20}H_{13}N_2O_4$ requires 345.0875)].

Attempts to Dehydrobrominate (28)

(a) The dibromide (28) (68 mg) was added in portions to a solution of potassium t-butoxide (336 mg) in t-butanol (20 ml; distilled from sodium) and the mixture stirred for a further 30 min after completion of the addition. All starting material was consumed (t.l.c. evidence). Water was added and the organic layer separated, combined with further chloroform extracts, washed with water, dried (Na_2SO_4), and evaporated to dryness. No residue was obtained. Acidification of the aqueous phase with 6N hydrochloric acid followed by extraction with chloroform again also gave no residue.

(b) The dibromide (28) (51 mg) was suspended in anhydrous ether (20 ml; dried over sodium wire) and potassium t-butoxide (125 mg) added in portions with stirring. Similar results to those recorded in (a) were observed on working up the reaction mixture.

Studies in the Cyclobutane Series

Truxillic Acid (31; R = OH)[19]

α-*Trans*-cinnamic acid (28 g) - prepared by evaporation of an ethereal solution of *trans*-cinnamic acid - was irradiated in a Rayonnet Photochemical Reactor with 16 11-in u.v. lamps (RPR - 350 nm) for a period of 8 days. The total product was placed in a soxhlet thimble and extracted overnight with refluxing ether. The residue in the thimble was crystallised from ethanol to give white needles of α-truxillic acid (7.26 g, 26%), m.p. 280-282° (lit.[45] m.p. 283-284°); ν_{max} (nujol) 3500-2500 and 1700 cm^{-1}; τ 2.62 (10H,m), 5.55 (2H,m), 6.02 (2H,m), and 0.25 (2H,bs) exchangeable with D_2O.

Truxillyl Chloride (31; R = Cl)

A suspension of truxillic acid (636 mg) in thionyl chloride (15 ml) was refluxed until dissolution was complete (*ca*. 4 h). Excess thionyl chloride was removed at the water pump to leave the acid chloride as a white solid (701 mg, 98%). Crystallisation from petroleum ether gave the pure material m.p. 126-127° (lit.[45] m.p. 127-128°); ν_{max} (nujol) 1775 cm^{-1}; τ 2.67 (10H,m) and 5.1-5.8 (4H,m).

Di-O-ethyl SS-truxillyl dixanthate (31; R = SCSOEt)

A solution of potassium O-ethyl xanthate (362 mg) in acetone (8 ml; Analar grade) was slowly added (over a period of 20 min) to a solution of truxillyl chloride (376 mg) in a mixture of acetone (14 ml; Analar grade) and dichloromethane (4 ml; dried by passage through a short column of alumina) maintained at ca. -35°. Stirring was continued at this temperature for a further 60 min after which time the cooling bath was removed and the mixture left to come to room temperature overnight. The solution was evaporated to dryness and the residue taken up in dichloromethane. This organic layer was washed with aqueous sodium bicarbonate solution and with water, dried (Na_2SO_4), and evaporated to dryness to give a yellow oil which crystallised on standing (490 mg, 86%). Crystallisation from benzene-petroleum ether gave m.p. 115-116°; ν_{max} (nujol) 1685 and 1260 cm^{-1}; λ_{max} 282 and 393 nm (ε 19,000 and 126); τ 2.72 (10H, s), 5.2-6.0 (4H, m), 5.48 (4H, q; J = 7 Hz), and 8.65 (6H, t; J = 7 Hz); mass spectrum, no M^+ but peaks at 383, 306, 278, 206, 176, 148. [(M^+ - SCSOEt), 383.0779. $C_{21}H_{19}O_3S_2$ requires 383.0776].

Photolysis of Di-O-ethyl SS-truxillyl dixanthate

A solution of the dixanthate (266 mg) in anhydrous benzene (75 ml; dried over sodium wire) was irradiated, with water cooling and under an atmosphere of nitrogen, with a 125 W medium pressure mercury vapour lamp for 75 min (t.l.c. and u.v. control). Evaporation of the solvent afforded a yellow oil (250 mg), ν_{max} (thin film) 1705 cm^{-1} (very broad). Preparative layer chromatography (silica) with dichloromethane as eluent gave two unstable oils, but the n.m.r. spectrum of each indicated that both were mixtures. These products were not investigated further.

Cis-cyclobutane-1,3-dicarboxylic Acid (40)[20]

Cis-cyclobutane-1,3-dicarboxylic acid was prepared from penta-erythritol (32) by a 7-stage literature procedure[20] and had m.p. 134.5-136° (lit.[20] m.p. 131-132°); ν_{max} (nujol) 3500-2500 and 1720 cm^{-1}.

Cis-cyclobutane-1,3-dicarboxylic Acid Chloride

(a) Oxalyl chloride (1.0 ml) was added slowly to a stirred suspension of *cis*-cyclobutane-1,3-dicarboxylic acid (197 mg) in anhydrous benzene (10 ml; dried over sodium wire) maintained at *ca*. 5°. Stirring was continued at this temperature for 1 h then the cooling bath was removed and the stirred mixture left to come to room temperature overnight. Evaporation of solvent at room temperature gave a white solid residue (163 mg), ν_{max} (nujol) 3500-2500, 1820, 1800, and 1720 cm^{-1}, *i.e.*, a mixture of the *cis*-dicarboxylic acid and the *cis*-anhydride (38).

(b) A mixture of the *cis*-anhydride (38) (313 mg) and phosphorus pentachloride (524 mg) was heated at 125° for a period of 15 min. Distillation of the mixture afforded phosphorus oxychloride followed by the *cis*-di-acyl chloride as a colourless fuming liquid

(373 mg, 83%), b.p. 70-71°/1 mmHg; ν_{max} (thin film) 1785 cm^{-1}; τ 6.35-6.90 (2H,m) and 7.05-7.60 (4H,m). (Found: C, 38.78; H, 3.44; Cl, 38.75. $C_6H_6Cl_2O_2$ requires C, 39.80; H, 3.34; Cl, 39.16%. Satisfactory carbon analysis could not be obtained for this unstable acid chloride).

Attempts to convert this di-acyl chloride to the dixanthate using potassium O-ethyl xanthate in acetone failed.

Attempted Synthesis of the Cyclic Peroxide (41)

(a) A solution of sodium peroxide (495 mg) in water (10 ml), maintained at ca. 0°, was slowly added to a solution of the cis-anhydride (38) (198 mg) in chloroform (10 ml) also maintained at ca. 0°. No reaction was observed. Increase of temperature was without effect.

(b) The cis-anhydride (38) (124 mg) was added in portions to aqueous hydrogen peroxide (5 ml; 50% w/v) maintained at 0°. No reaction was observed.

Studies in the Bicyclobutane Series

1-Phenylpropyne

1-Phenylpropyne was prepared according to the method of Hurd and Tockman[46] and had b.p. 82-83°/19 mmHg (lit.[46] b.p. 90°/20 mmHg).

Ethyl Diazo-acetate

A solution of ethyl glycinate hydrochloride (139.5 g) and sodium acetate (0.7 g) in water (275 ml) was cooled to *ca.* -15° and petroleum ether (b.p. 30-40°) (400 ml) was added. A mixture of 2N sulphuric acid (35 ml), sodium nitrite (110 g), and water (150 ml) was cooled to *ca.* 10° and added dropwise, with stirring, to the two-phase ethyl glycinate hydrochloride solution. The addition was made as rapidly as possible whilst keeping the temperature below 10°. Stirring was continued at 10° for a further 10 min then the yellow organic layer was separated, washed with aqueous sodium bicarbonate solution (until neutral) and with water, dried (Na_2SO_4), and evaporated to dryness. Distillation of the residue afforded ethyl diazo-acetate (65.64 g, 58%), b.p. 38-39°/10 mmHg (lit.[41] 34°/7.8 mmHg).

1-Methyl-3-phenylbicyclo[1.1.0]butane-2,4-dicarboxylic Acid (42)[22]

Ethyl diazo-acetate (55.44 g) was added very slowly (over a period of 7 h) to a stirred suspension of anhydrous copper sulphate (0.465 g) in a solution of 1-phenylpropyne (37.0 g) in cyclohexane (37 ml; distilled from sodium) maintained at *ca.* 80° under an atmosphere of nitrogen. As soon as the reaction commenced (*ca.* 2-3 min) the temperature was reduced to *ca.* 70°. After the completion of the addition the mixture was filtered (under nitrogen) and evaporated to dryness. Fractional distillation of the residue afforded a fraction (15.4 g) of b.p. 115-130°/0.1 mmHg).

A solution of this material (15.4 g) in 5% ethanolic potassium hydroxide solution (310 ml) was refluxed for 1 h and then evaporated to dryness. Water (75 ml) was added to the residue and the resulting aqueous solution extracted with ether. The aqueous layer was acidified with 6N sulphuric acid and again extracted with ether. The combined ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness to give a brown oil (9.72 g). Trituration of this oil with benzene afforded a white solid which was collected, washed with benzene, and dried. Crystallisation from aqueous ethanol gave the bicyclobutane dicarboxylic acid (4.0 g, 5.5%), m.p. 190-193° (lit.[22] m.p. 191-192.5°); ν_{max} (nujol) 3400-2500 and 1705 cm^{-1}; τ 2.35-2.90 (5H,m), 8.03 (3H,s), 8.47 (2H,s), and 0.53 (2H,bs) exchangeable with D_2O.

A solution of diazomethane in ether was added to a solution of the bicyclobutane dicarboxylic acid (50 mg) in ether (5 ml) until the yellow colouration persisted (excess diazomethane). The mixture was evaporated to dryness, the residue applied to a preparative layer chromatography plate (alumina), and chromatographed with dichloromethane as eluent. The dimethyl ester of (42) was obtained as a colourless liquid (44 mg, 79%); ν_{max} 1720 cm^{-1}; τ 2.4-2.9 (5H,m), 6.47 (6H,s), 8.05 (3H,s), and 8.37 (2H,s).

Titration of 1-Methyl-3-phenylbicyclo[1.1.0]butane-2,4-dicarboxylic Acid

0.0199N sodium hydroxide solution (2.473 ml, 2.000 equiv.) was added to a stirred suspension of the bicyclobutane dicarboxylic acid (5.70 mg) in water (37.5 ml). Stirring was continued until the pH of the mixture (measure by a pH meter) became steady (ca. 10 min) then the solution was titrated against 0.0200N hydrochloric acid. During the titration, monitored by a pH meter, the solution was stirred by passage of a stream of nitrogen previously saturated with water vapour. The pH scale was standardised by freshly made buffer solutions.

The thermodynamic dissociation constants were determined by Speakman's procedure,[25] giving the values $pK_1 = 6.16$ and $pK_2 = 7.12$.

Attempted Bromination of 1-Methyl-3-phenylbicyclo[1.1.0]butane-2,4-dicarboxylic Acid.

Bromine (1.0 g) was slowly added to a mixture of the bicyclobutane dicarboxylic acid (68 mg) and phosphorus (18 mg) at room temperature. The mixture was stirred for a further 5 h then evaporated to dryness and the residue taken up in ether. The organic layer was extracted with aqueous sodium bicarbonate solution, the combined bicarbonate extracts acidified with 6N sulphuric acid, and extracted with ether. The combined ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness to yield a brown gum (21 mg). T.l.c. and the n.m.r. spectrum both indicated this to be a complex mixture.

Similar results were obtained when the bicyclobutane (43 mg) was treated with bromine (1.0 g) and phosphorus trichloride (0.3 g).

Reaction of (42) with Mercuric Oxide and Bromine

A solution of bromine (6 mg) in anhydrous carbon tetrachloride (0.1 ml; distilled from phosphorus pentoxide) was added to a stirred suspension of the bicyclobutane carboxylic acid (42) (47 mg) and red mercuric oxide (85 mg) in refluxing anhydrous carbon tetrachloride (1.5 ml). The remainder of the bromine (58 mg) in carbon tetrachloride (1.0 ml) was added dropwise to the mixture 5 min after the initial addition. Refluxing was continued for 40 min and then the mixture was filtered, washed with aqueous sodium thiosulphate solution, 1% sodium hydroxide solution, water, dried (Na_2SO_4), and evaporated to dryness to give an oil (21 mg). T.l.c. examination showed many products formed.

1,3-Dibromo-1-methyl-3-phenylcyclobutane-2,4-dicarboxylic Acid

A solution of bromine (18.3 mg) in anhydrous carbon tetrachloride (0.32 ml; distilled from phosphorus pentoxide) was added in two portions to a suspension of the bicyclobutane dicarboxylic acid (42) (26.6 mg) in refluxing anhydrous carbon tetrachloride (4.5 ml). Refluxing was continued for 30 min then evaporation of solvent left a white residue. This residue was dissolved in ether, washed with aqueous sodium thiosulphate solution and with water, dried (Na_2SO_4), and evaporated to dryness to give the dibromide (40.1 mg, 89%), m.p. 210–212°; ν_{max} 3400–2500 and 1705 cm^{-1}; τ 1.95–2.20 (2H,m), 2.50–2.75 (3H,m), 5.67 (2H,s), 7.42 (3H,s), and –0.63 (2H,bs) exchangeable with D_2O; mass spectrum, no M^+ but significant peaks at m/e 313, 311, 295, 293, 230, 187, 186, 141, 102. (Found: C, 40.23; H, 3.20; Br, 40.72. $C_{13}H_{12}Br_2O_4$ requires C, 39.82; H, 3.08; Br, 40.77%).

Reaction of (42) with Lead Tetra-acetate and Iodine

(a) The bicyclobutane carboxylic acid (40.0 mg) and lead tetra-acetate (169 mg) were suspended in anhydrous carbon tetrachloride (1.0 ml; distilled from phosphorus pentoxide) and irradiated with a 300 W tungsten lamp, under an atmosphere of nitrogen, for a period of 5 min. A solution of iodine (96.5 mg) in carbon tetrachloride (2.0 ml) was then slowly added and irradiation and stirring continued for a further 8 h. The gas stream was passed through a trap at –80° and then into saturated aqueous barium hydroxide solution. The solution was filtered, washed with aqueous sodium thiosulphate solution, 1% sodium hydroxide solution, water, dried (Na_2SO_4), and evaporated to dryness to yield a yellow oil (23.2 mg), ν_{max} (thin film) 1735 cm^{-1}. Thin layer chromatographic examination of this oil revealed that many products had been formed. Examination of the mass spectra of the two faster running (t.l.c.) components showed strong ions as high as m/e 690 with no discernable fragmentation pattern. The yield of barium carbonate (gravimetric) was 39.1 mg (58% of 2 mol).

A solution of iodine (31.9 mg) in carbon tetrachloride (2.0 ml) was added slowly to a suspension of (42) (24.0 mg) in refluxing carbon tetrachloride (2.0 ml). Refluxing was continued overnight but no reaction was observed.

(b) Substitution of benzene as solvent had no effect on the reaction nor on the yield of barium carbonate. Variation of the intensity of the tungsten lamp also had no effect.

Attempted Decarboxylation of (42)

(a) Lead tetra-acetate (56.2 mg) was added in portions to a stirred solution of (42) (25.3 mg) in anhydrous dimethylsulphoxide (1.0 ml; redistilled) containing one drop of pyridine. Heating the solution at *ca.* 75° caused extensive decomposition (t.l.c. evidence)

(b) Pyrolysis of (42) at 150°/6×10^{-5} mmHg resulted in its sublimation and recovery.

Diphenylacetylene[47]

Diphenylacetylene was prepared from stilbene according to the procedure of Smith and Falkof[47] and had m.p. 60-61° (lit.[47] m.p. 60-61°).

1,2-Diphenylcycloprop-1-ene-3-carboxylic Acid (47; R^1 = Ph, R^2 = CO_2H)[32]

Ethyl diazo-acetate (4.3 g) was added slowly (over a period of 30 min) to a mixture of diphenylacetylene (13.3 g) and anhydrous copper sulphate (6.1 mg) maintained at *ca.* 125°. After the completion of the addition the mixture was left to come to room temperature and 10% methanolic sodium hydroxide solution (40 ml) was added. This mixture was refluxed for 1 h before dilution with water precipitated out diphenylacetylene which was collected and dried (9.88 g). The filtrate was concentrated to ca. 30 ml, acidified with 6N sulphuric acid, and the crude cyclopropene carboxylic acid collected and dried. Crystallisation from benzene gave the pure acid (2.94 g, 65% allowing for recovered diphenylacetylene), m.p. 207-210° (lit.[32] m.p. 210-211°); ν_{max} (nujol) 3200-2500 and 1690 cm^{-1}; τ 7.25 (1H, s), 2.1-2.9 (10H, m), and 0.42 (1H, bs) exchangeable with D_2O.

Attempted Addition of Dihalocarbenes to 1,2-Diphenylcycloprop-1-ene-3-carboxylic Acid (47; R^1 = Ph, R^2 = CO_2H)

(a) A mixture of the cyclopropene (99.7 mg) and sodium trichloroacetate (79.9 mg) in glyme (2.0 ml) was refluxed for 1 h. Starting material was recovered (73.2 mg, 73%).

(b) A mixture of the cyclopropene (101.7 mg) and phenyl(trichloromethyl)mercury[33] (345.1 mg) in benzene (1.5 ml) was refluxed for 24 h. No reaction was observed.

(c) Bromoform (0.1 ml, 290 mg) was added slowly to a solution of the cyclopropene (116.1 mg) in t-butanol (3.0 ml)/pentane (2.0 ml) containing potassium (50.7 mg). Starting material (83.8 mg, 72%) was recovered.

Similar results were obtained with dimethyl 1,2-diphenylcycloprop-

1-ene-3-carboxylate (47; R^1 = Ph, R^2 = CO_2Me)

Attempted Alkylation of Dimethyl 1-methyl-3-phenylbicyclo[1.1.0]-butane-2,4-dicarboxylate

(a) A solution of the bicyclobutane di-ester (35.9 mg) in anhydrous benzene (1.1 ml; dried over sodium wire) was added slowly to a stirred suspension of sodium hydride (15.9 mg; 50% dispersion in mineral oil) in benzene (1.0 ml). Stirring was continued for 1 h then 1,4-dibromobutane (35 mg) was added. No reaction was observed.

(b) A mixture of the bicyclobutane di-ester (51.2 mg) and the sodium salt of hexamethyldisilazane[34] (207.4 mg) in anhydrous benzene (3.0 ml), under an atmosphere of nitrogen, was refluxed for 5 min, then 1,4-dibromobutane (73 mg) was added in two portions. A complex tarry product was obtained.

(c) The sodium salt of hexamethyldisilazane (63.2 mg) was added in three portions to a mixture of the bicyclobutane di-ester (42.8 mg) and xylylene dibromide (46.1 mg) in anhydrous benzene (2.0 ml). A complex tarry product was obtained.

3,5-Dimethoxybenzoyl Chloride (56)

Thionyl chloride (82 g) was added slowly to a solution of 3,5-dimethoxybenzoic acid (100 g) in anhydrous benzene (450 ml; dried over sodium wire) containing dimethylformamide (0.1 ml) and the solution refluxed for 3 h. Evaporation of the solvent and distillation of the residue afforded the acid chloride (91.42 g, 83%), b.p. 124-125°/

2.0 mmHg (lit.[36] b.p. 136-138°/5 mmHg); ν_{max} (thin film) 1760 and 1600 cm^{-1}; τ 2.90 (2H,d; J = 2.2 Hz), 3.37 (1H,t; J = 2.2 Hz), and 6.18 (6H,s).

3,5-Dimethoxyacetophenone (58)

(a) A solution of 3,5-dimethoxybenzoyl chloride (18.0 g) in ether (200 ml) was added slowly to a stirred solution of diazomethane (from nitrosomethylurea (50 g)) in ether (450 ml). The mixture was stirred for a further 3 h at room temperature, then evaporated to dryness to give the yellow crystalline diazo-ketone (57) (m.p. 63-66°). This diazo-ketone was dissolved in chloroform (400 ml) and shaken vigorously with hydriodic acid (d 1.94; 50 ml) for 10 min. Water was added and the organic layer separated, washed with aqueous sodium thiosulphate solution, sodium hydroxide solution, water, dried (Na_2SO_4), and evaporated to dryness. Distillation of the residue gave 3,5-dimethoxyacetophenone (13.29 g, 82%), b.p. 122-123°/0.3 mmHg (lit.[35] b.p. 122°/0.5 mmHg); ν_{max} (thin film) 1685 and 1600 cm^{-1}; τ 2.88 (2H,d; J = 2.2 Hz), 3.33 (1H,t; J = 2.2 Hz), 6.17 (6H,s), and 7.45 (3H,s).

(b) Cadmium chloride (19.14 g) was added in portions to a solution of methyl magnesium bromide (from magnesium (4.6 g) and methyl bromide (18.5 g)) in anhydrous ether (70 ml; dried over sodium wire) to give a solution of dimethylcadmium. This solution was maintained at *ca.* 5° and a solution of 3,5-dimethoxybenzoyl chloride (20.0 g) in ether (30 ml) was added to it over a period of 30 min. The mixture was refluxed for 2 h, left to come to room temperature, and decomposed with 10% sulphuric acid (30 ml). The organic layer was washed with 10% sodium hydroxide solution and with water, dried (Na_2SO_4), and evaporated to dryness. Distillation of the residue gave the acetophenone (6.3 g, 35%) contaminated with a small amount of the acid chloride.

3,5-Dimethoxyphenylacetylene (61)

Phosphorus pentachloride (24.2 g) was added in portions to 3,5-dimethoxyacetophenone (20.7 g) maintained at ca. 35°. After the completion of the addition, the mixture was heated on a steam bath for 1 h. Phosphorus oxychloride was removed at the water-pump and the residue distilled to give a mixture of the dichloride (59) and the α-chlorostyrene (60) (16.0 g), b.p. 97-105°/0.03 mmHg; ν_{max} (thin film) 1600 cm^{-1}.

A suspension of potassium hydroxide (14.5 g) in ethanol (25 ml) was added to the mixture of (59) and (60) and the resulting suspension refluxed and stirred for a period of 6 h. The mixture was poured into water and extracted with benzene. The combined benzene extracts were dried (Na_2SO_4) and evaporated to dryness to give a brown oil (14.31 g). The total product was chromatographed on alumina (Grade 3) eluting with petroleum ether-benzene (4:1, v/v) to give the acetylene (2.43 g, 13%). Crystallisation from petroleum ether (b.p. 40-60°) gave the pure product m.p. 44-45°; ν_{max} (nujol) 3300, 2100, and 1600 cm^{-1}; λ_{max} 220, 244 (shoulder), 247

253, 294, and 301 nm (ε 15,500, 9,400, 10,000, 8,900, 2,350, and 2,350); τ 3.28 (2H,d; J = 2 Hz), 3.47 (1H,t; J = 2 Hz), 6.20 (6H,s), and 6.95 (1H,s). (Found: C, 73.88; H, 6.12. $C_{10}H_{10}O_2$ requires C, 74.05; H, 6.22%).

Treatment of the acetylene (515 mg) in ether (4 ml) with sodium (76 mg) in liquid ammonia (20 ml) followed by 1,3-dibromopropane (2.60 g, 4 equiv.) led to recovery of starting material.

n-Butyltriphenylphosphonium Bromide (64)

A solution of n-butyl bromide (13.7 g) and triphenylphosphine (26.2 g) in xylene (90 ml; distilled from sodium) was heated at 120° overnight. The precipitate was collected, washed with xylene, and dried to give the phosphonium salt (35.0 g, 88%), m.p. 235-236°; ν_{max} (nujol) 1595 and 1120 cm^{-1}; τ 2.0-2.4 (15H,m), 6.0-6.5 (2H,m), 8.60 (4H,m), and 9.07 (3H,t; J = 6 Hz).

1-(3,5-Dimethoxybenzoyl)-butylidenetriphenylphosphorane (66)

(a) A solution of butyl lithium (0.8 g) in anhydrous ether (9 ml; dried over sodium wire) was added slowly to a suspension of n-butyltriphenylphosphonium bromide (5.0 g) in ether (75 ml) under an atmosphere of nitrogen. The mixture was stirred for 1 h then a solution of 3,5-dimethoxybenzoyl chloride (1.25 g, 0.5 equiv.) in ether (20 ml) was added slowly. This suspension was stirred overnight at room temperature. Benzene (100 ml) was added and the precipitate collected. The filtrate was concentrated to yield an extremely hygroscopic solid which did not correspond to the expected phosphorane and was not investigated further.

(b) A solution of butyl lithium (2.4 g) in anhydrous ether (27 ml) was added slowly to a suspension of n-butyltriphenylphosphonium bromide (15 g) in ether (450 ml) under an atmosphere of nitrogen, and the mixture stirred at room temperature for 1 h. This red suspension was added slowly to a stirred solution of 3,5-dimethoxybenzoyl chloride (7.5 g) in ether (300 ml) and the resulting mixture stirred for a further 2 h. The suspension was extracted with 2N hydrochloric acid and the combined acid extracts made alkaline to phenolphthalein (at below 10°). This aqueous phase was extracted with benzene, the combined benzene extracts dried (Na_2SO_4), and evaporated to dryness to give the phosphorane as a brown gum (7.56 g, 42%); ν_{max} (thin film) 1600 and 1505 cm^{-1}; τ 2.2-2.9 (15H,m), 3.34 (2H,d; J = 2 Hz), 3.70 (1H,t; J = 2 Hz), 6.28 (6H,s), 7.6-8.5 (2H,m), 8.5-9.2 (2H,m), and 9.50 (3H,t; J = 6.5 Hz). This compound was not analysed.

1-(3,5-Dimethoxyphenyl)-pent-1-yne (54; R = H)

The phosphorane (66) (3.523 g) was pyrolysed at 270-280°/760 mmHg under an atmosphere of nitrogen for a period of 30 min. The residue was chromatographed on alumina (300 g; Grade 3) eluting with petroleum ether-benzene (9:1, v/v) to give the acetylene. Distillation afforded the pure product (384 mg, 26%), b.p. 81-82°/0.1 mmHg; ν_{max} (thin film) 2300 and 1600 cm^{-1}; λ_{max} 217, 246 (shoulder), 251, 256, 291, and 299 nm (ε 28,900, 13,300, 14,300, 14,000, 2,200, and 2,200); τ 3.48 (2H,d; J = 2 Hz), 3.67 (1H,t; J = 2 Hz), 6.27 (6H,s), 7.65 (2H,t; J = 6 Hz), 8.40 (2H,sx; J = 6 Hz), and 8.97 (3H,t; J = 6 Hz). (Found: C, 76.43; H, 7.87. $C_{13}H_{16}O_2$ requires C, 76.44; H, 7.90%).

4-Bromobutan-1-ol (69)

Hydrogen bromide gas was passed into anhydrous tetrahydrofuran (45 g; distilled from lithium aluminium hydride) maintained at *ca.* 10° until 1 equiv. of the gas had been absorbed (*ca.* 1 h). The mixture was then fractionally distilled to give the bromohydrin (16.3 g, 33% based on recovered tetrahydrofuran), b.p. 60-61°/1.5 mmHg (lit.[48] 63-65°/2 mmHg); ν_{max} (thin film) 3300 cm^{-1}; τ 6.17 (2H,t; J = 6 Hz), 6.53 (2H,t; J = 6 Hz), 7.9-8.4 (4H,m), and 6.4-6.7 (1H hidden by 6.53 τ triplet).

4-Bromobutan-1-ol Tetrahydropyranyl Ether (70)

Dihydropyran (9.8 g) was added slowly to a stirred solution of 4-bromobutan-1-ol (16.25 g) and *p*-toluene sulphonic acid (3 mg) in anhydrous benzene (20 ml; dried over sodium wire) and the solution was allowed to stand at room temperature overnight. Anhydrous potassium carbonate (1.0 g) was added and the suspension stirred for 1 h then filtered and evaporated to dryness. Distillation of the residue gave the tetrahydropyranyl ether as a colourless liquid (16.5 g, 65%), b.p. 86-88°/0.8 mmHg; ν_{max} (thin film) 2975 and 1045 cm^{-1}; τ 5.48 (1H,bs), 6.0-6.8 (6H,m), and 7.8-8.7 (10H,m); mass spectrum, M^{+} 238 and 236; significant peaks at m/e 137, 136, 135, and 134.

4-(Triphenylphosphonium bromide)-butan-1-ol Tetrahydropyranyl Ether (71)

A solution of the tetrahydropyranyl ether (70) (9.0 g) and triphenylphosphine (10.9 g) in xylene (20 ml; distilled from sodium) was heated at 110° for a period of 24 h. The precipitate was collected and dried to give the phosphonium bromide (14.29 g, 75%), m.p. 162-165°; ν_{max} (nujol) 1440 and 1120 cm^{-1}; τ 1.9-2.4 (15H,m), 5.6-6.6 (7H,m), and 7.8-8.6 (10H,m).

Reaction of the Ylid (72) with 3,5-Dimethoxybenzoyl Chloride

A solution of butyl lithium (0.39 g) in anhydrous ether (4 ml; dried over sodium wire) was slowly added to a suspension of the phosphonium bromide (71) (3.0 g) in ether (100 ml). Stirring was continued for a further 15 min then the resulting orange suspension was added slowly to a stirred solution of 3,5-dimethoxybenzoyl chloride (1.20 g) in ether (75 ml). The mixture was stirred for 3 h then worked up in the manner previously described for 1-(3,5-dimethoxybenzoyl)-butylidenetriphenylphosphorane (66) to give a yellow gum (272 mg, 8%); ν_{max} (thin film) 1600 cm^{-1}; τ 1.8-3.0 (15H,m), 3.30 (2H,m), 3.55 (1H,m), 5.5-7.0 (5H,m), 6.18 (6H,s), and 7.2-9.2 (10H,m). This compound was not analysed.

Pyrolysis of this gum at 270°/760 mmHg gave a complex mixture of products.

4-Benzyloxy-1-bromobutane (74)

(a) A mixture of 1,4-dibromobutane (30 g) and sodium hydride (6.0 mg; 50% dispersion in mineral oil) in anhydrous benzene (150 ml; dried over sodium wire) was refluxed during the slow addition of a solution of benzyl alcohol (10.8 g) in benzene (150 ml). The mixture was stirred and refluxed for a further period of 24 h, then left to come to room temperature. Water was added and the organic layer separated, combined with further benzene extracts, washed with water, dried (Na_2SO_4), and evaporated to dryness. Distillation of the residue gave the benzyl ether (16.21 g, 67%), b.p. 106-109°/0.4 mmHg (lit.[38] 103-105°/0.3 mmHg); ν_{max} (thin film) 1110, 750, and 710 cm^{-1}; τ 2.63 (5H, s), 5.50 (2H, s), 6.52 (2H, t; J = 6 Hz), 6.60 (2H, t; J = 6.5 Hz), and 7.8-8.4 (4H, m).

(b) A mixture of tetrahydrofuran (50 g; distilled from lithium aluminium hydride), benzyl bromide (57 g; redistilled), and freshly-fused zinc chloride (2.0 g) was stirred and refluxed for 24 h. The mixture was poured into water and extracted with ether. The combined ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness. Distillation of the residue afforded the benzyl ether (30.2 g, 37%), b.p. 109-116°/0.5 mmHg.

1-(Triphenylphosphonium bromide)-4-benzylbutane

A stirred solution of the benzyl ether (74) (20.02 g) and triphenylphosphine (23.0 g) in xylene (100 ml; distilled from sodium) was heated at 120° for a period of 24 h. The precipitate was collected and dried to give the phosphonium salt (32.67 g, 79%), m.p. 163-165°; ν_{max} (nujol) 1450 and 1125 cm^{-1}; τ 1.9-2.4 (15H,m), 2.70 (5H,s), 5.50 (2H,s), 6.0-6.6 (4H,m), and 7.85-8.30 (4H,m).

1-(3,5-Dimethoxybenzoyl)-4-benzyloxybutylidenetriphenylphosphorane (75)

A solution of methyl lithium (0.44 g) in anhydrous ether (8.3 ml) was added slowly to a suspension of the phosphonium bromide (10.0 g) in ether (300 ml) and the mixture stirred for a further 40 min. This orange suspension was added to a stirred solution of 3,5-dimethoxybenzoyl chloride (4.01 g) in ether (100 ml) and stirring continued for a further 2 h. The reaction was worked up in the manner previously described for 1-(3,5-dimethoxybenzoyl)-butylidenetriphenylphosphorane (66) to give a yellow gum (4.62 g, 40%); ν_{max} 1600 cm^{-1}; τ 2.0-2.9 (20H,m), 3.12 (2H,d; J = 2 Hz), 3.52 (1H,t; J = 2 Hz), 5.77 (2H,s), 6.22 (6H,s), 6.1-6.6 (2H,m), 6.92 (2H,t; J = 6.5 Hz), and 7.4-8.0 (2H,m). This compound was not analysed.

1-(3,5-Dimethoxyphenyl)-5-benzyloxypent-1-yne (54; R = OCH_2Ph)

The phosphorane (75) (224 mg) was pyrolysed at 280°/760 mmHg under an atmosphere of nitrogen for 35 min. Column chromatography of the residue on silica with benzene as the eluent gave the acetylene (29.5 mg, 25%). Distillation afforded the pure product b.p. 172°/0.02 mmHg; ν_{max} (thin film) 2260 and 1600 cm^{-1}; λ_{max} 213, 248 (shoulder), 251, 256, 291, and 299 nm (ε 47,000, 15,400, 16,000, 15,500, 2,500, and 2,500); τ 2.60 (5H,s), 3.40 (2H,d; J = 2 Hz), 3.53

(1H,t; J = 2 Hz), 5.43 (2H,s), 6.23 (6H,s), 6.35 (2H,t; J = 6 Hz), 7.45 (2H,t; J = 6 Hz), and 8.10 (2H,qn; J = 6 Hz); mass spectrum, M^+ 310 with significant peaks at m/e 222, 189, 165, and 91 base peak). (M^+ 310.1561. $C_{20}H_{22}O_3$ requires 310.1568).

Reaction of (54; R = OCH_2Ph) with Ethyl Diazo-acetate

A solution of ethyl diazo-acetate (683 mg) in cyclohexane (1.5 ml; distilled from sodium) was added slowly, over a period of 15 min, to a stirred suspension of anhydrous copper sulphate (2.2 mg) in a solution of the acetylene (54; R = OCH_2Ph) (103.6 mg) in cyclohexane (1.5 ml) maintained at *ca*. 80°. The mixture was stirred and heated for a further period of 1 h then left to come to room temperature and filtered. Evaporation of the solvent gave a brown oil (624 mg), ν_{max} (thin film) 1720 cm^{-1}. Thin layer chromatographic examination of the reaction mixture revealed that many products had been formed. The n.m.r. spectrum also indicated a mixture and did not exhibit any peaks in the region *ca*. 8.5 τ (*i.e.*, the expected region for bicyclobutyl ring protons in a system such as the present one).

A solution of the mixture (576 mg) in 5% ethanolic potassium hydroxide solution (100 ml) was left at room temperature for 2 h. The solution was evaporated to dryness and water added to the residue. This aqueous layer was extracted with ether, then acidified with 6N sulphuric acid and extracted again with ether. The combined ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness to give an almost black oil (158 mg). The n.m.r. spectrum again indicated a complex mixture.

Complex mixtures were also obtained from the copper sulphate-catalysed and light-initiated additions of ethyl diazo-acetate to the acetylene (54; R = H).

(Trialkyl- and Triarylphosphite)copper(I) Halides

The (trialkyl- and triarylphosphite)copper(I) halides were prepared[43] by mixing equimolar amounts of the appropriate phosphites and copper(I) halide salts in benzene. The reaction mixture was stirred until all the solid salt had dissolved, filtered, and evaporated to dryness to yield the complexes. Prepared in this way were:- (triethylphosphite)copper(I) chloride, colourless oil; (triphenylphosphite)copper(I) chloride, m.p. 87-89° (lit.[43] m.p. 88-89°); and (triethylphosphite)copper(I) iodide, m.p. 109-110° (lit.[43] m.p. 110-111°).

General Procedure for the 1-Phenylpropyne - Ethyl Diazo-acetate Reaction

A solution of 1-phenylpropyne (1.0 g) and the catalyst (*ca.* 10 mg) in the solvent (1.0 ml) was placed in a constant temperature bath at the appropriate temperature. Ethyl diazo-acetate (3.3 g, 1.5 equiv.) was added to this mixture very slowly (*ca.* 30-35 min). Stirring was continued for a further period of 1 h, then the mixture was heated so as to distil out any diethyl maleate (formed by dimerisation of the carbene), left to come to room temperature, dissolved in dichloromethane, and filtered through an alumina (Grade 3) column to remove polar material and catalyst. The solutions were evaporated to dryness and analysed by n.m.r. spectroscopy using p-chlorobenzaldehyde as an internal standard. Yields of bicyclobutane were calculated from the ratio of the integrals of the aldehydic proton of the standard and the bridgehead methyl group of the bicyclobutane (42). The reaction was always carried out under an atmosphere of nitrogen.

Reaction of (54; R = OCH_2Ph) with Ethyl Diazo-acetate in the Presence of (Triphenylphosphite)copper(I) Chloride

Ethyl diazo-acetate (0.5 g) was added very slowly to a stirred solution of the acetylene (54; R = OCH_2Ph) (60.3 mg) and (triphenylphosphite)copper(I) chloride (6.8 mg) in cyclohexane (0.5 ml; distilled from sodium) maintained at 80° under an atmosphere of nitrogen. Stirring and heating were continued for a further 20 min then the reaction mixture was worked up in an analogous manner to that described in the preceding general experiment to yield a dark brown oil (125.8 mg). The n.m.r. spectrum showed no singlet peaks in the region 8.5 τ - the region in which the bicyclobutyl ring protons would be expected.

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