Bredt's Rule. III. The Synthesis and Chemistry of Bicyclo[3.3.1]non-1-ene[1-3]

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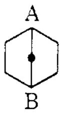
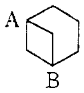
Abstract: A rational criterion for the assessment of the limits of Bredt's rule is presented. It is postulated that the strain energies of bridgehead alkenes can be reasonably related to the strain energies of *trans*-cycloalkenes. Bicyclo[3.3.1]non-1-ene (**13**) is synthesized to test the validity of the postulate. Electrophilic and nucleophilic additions and cycloaddition reactions of the alkene **13** with 1,3-diphenylisobenzofuran, cyclohexadiene, and diazomethane are described. The diazomethane adduct **33** is utilized in a synthesis of tricyclo[4.3.1.$0^{1,3}$]decane (**34**). Reaction of the alkene with *m*-chloroperbenzoic acid produces the epoxide, 2-oxatricyclo[4.3.1.$0^{1,3}$]decane (**28**).

Bredt's rule is a qualitative generalization which describes the reluctance of bridged bicyclic systems to allow the placement of double bonds at their bridgeheads. The familiar rule was developed over a period of more than twenty years due primarily to the work of Bredt and coworkers.[4,5] A typical statement of the rule was made by Bredt:[4] "On the basis of our conceptions of the positions of atoms in space, in the systems of the pinane and camphane series, as well as similarly constituted compounds, a carbon double bond cannot occur at the branching positions A and B of the carbon bridge (bridgeheads)."





The rule is amply supported[5] by numerous examples of alcohols which fail to dehydrate, β-keto acids which fail to decarboxylate, diacids which refuse to form anhydrides, alkyl halides which refuse to eliminate hydrogen halide, and, more recently, ketones which do not exchange their α-hydrogen atoms. Bredt frequently referred to the use of molecular models in his discussions of bridgehead alkenes, and it is clear that he recognized that a bridgehead double bond is under strain which tends to distort the substituents of the double bond away from the favored planar geometry. In modern terms we recognize that this torsional strain acts to twist the p_z orbitals of the doubly bonded carbon atoms away from the geometry required for maximum π overlap.

Over the years organic chemists have come to regard the existence of a double bond in an isolable compound or a reaction intermediate as a "violation" of Bredt's rule. However, since Bredt clearly did not intend that the rule should apply to larger ring systems, it seems inappropriate to regard the existence of bridgehead double bonds in such systems as violations. In fairness to Bredt we prefer to speak of such ring systems as being outside the limits of applicability of the rule.

In the late 1940's Prelog[5a,b] and coworkers demonstrated that larger bicyclic ring systems can accommodate bridgehead double bonds. On the basis of their research, it was concluded that bicyclic ring systems in the [*n*.3.1] series with $n = 5$ can have a bridgehead double bond and that the bicyclo[4.3.1]decyl and smaller ring systems cannot. It must be emphasized, however, that all of the compounds studied by Prelog were formed under equilibrating conditions. Thus, this research does not constitute a rigorous test of the possibility of actually preparing bridgehead alkenes, but demonstrates that the bridgehead alkenes actually prepared are more stable than the nonbridgehead alkenes with which they are isomeric.

Fawcett,[5a] in reviewing the literature through 1950, made the first serious attempt to define the limits of Bredt's rule in quantitative terms. Fawcett defined the *S* number as the sum of the number of atoms in the bridges of a bicyclic system. Thus, bicyclo[3.3.1]nonane has an *S* number of 7. On the basis of information available to him, Fawcett made the tentative proposal that bridged bicyclic ring systems with $S = 9$ are large enough to permit isolation of bridgehead alkenes and that transient reaction intermediates with bridgehead double bonds should be possible for $S = 7$. At the time of Fawcett's proposal it was recognized that the stability of a bridgehead double bond depends on which branch of a bicyclic system contains it. For example, the [3.3.1] acid **1** which has its keto group in the small bridge resists decarboxylation when heated alone or with quinoline at 240°.[6] In contrast, Meerwein's acid **2** loses 4 mol of carbon dioxide when heated with water in an autoclave at 220° for 1 hr.[7] Finally, the adamantane derivative **3** which is a homolog of Meerwein's acid is reported to be extremely resistant to decarboxylation.[8] These anomalies are not adequately

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[1] This work was supported by the Petroleum Research Fund, administered by the American Chemical Society, and by the Faculty Research Fund of the Horace H. Rackham School of Graduate Studies of the University of Michigan.

[2] Previous paper in the series: J. R. Wiseman, H. Chan, and C. J. Ahola, *J. Amer. Chem. Soc.*, **91**, 2812 (1969).

[3] A preliminary account of a portion of this work has appeared as a communication: J. R. Wiseman, *ibid.*, **89**, 5966 (1967).

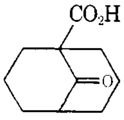
[4] J. Bredt, H. Thouet, and J. Schmit, *Ann.*, **437**, 1 (1924), and references therein.

[5] For reviews and discussions see (a) F. S. Fawcett, *Chem. Rev.*, **47**, 219 (1950); (b) V. Prelog, *J. Chem. Soc.*, 420 (1950); (c) R. C. Fort, Jr., and P. von R. Schleyer, *Advan. Alicyclic Chem.*, **1**, 364–370 (1966); (d) H. H. Wasserman in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley & Sons, Inc., New York, N. Y., 1956, pp 351–354; (e) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 298–302.

[6] A. C. Cope and M. E. Synerholm, *J. Amer. Chem. Soc.*, **72**, 5228 1950). Referred to in ref 5a, p 245.

[7] H. Meerwein, F. Kiel, G. Klosgen, and E. Schoch, *J. Prakt. Chem.*, **104**, 163, 166 (1922).

[8] O. Bottger, *Ber.*, **70B**, 314 (1937).



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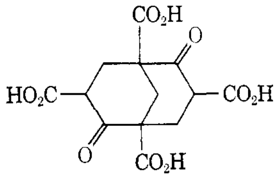

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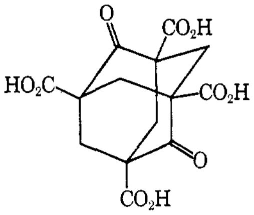

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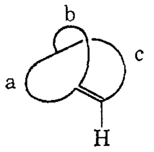
explained by Fawcett's proposal, and since 1950 other inconsistencies have appeared.

We propose a more fundamental criterion for the qualitative evaluation of the strain of bicyclic bridgehead alkenes. This criterion also allows one to predict which branches of a bicyclic ring system can contain a bridgehead double bond. Formula **4** represents a bridged bicyclic ring system comprised of three branches, with a double bond in branch a terminating at the bridgehead. The three branches of the ring system comprise three rings (ab, ac, and bc). The double bond is exocyclic to ring ab, but endocyclic in rings ac and bc. Since the double bond is at the branching point of the two rings, it must be substituted *cis* in one ring and *trans* in the other. In structure **4** the double bond is drawn *trans* in ring ac. Thus, we believe that the strain of bridgehead alkenes is closely related to the strain of *trans*-cycloalkenes. Ordinarily, a bridgehead double bond will be more stable when it is *trans* in the larger of the two rings in which it is endocyclic.



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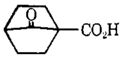
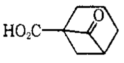
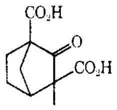
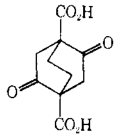
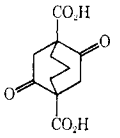
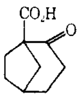
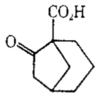
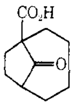
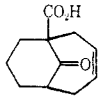
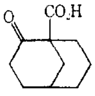
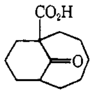
trans-Cyclooctene has been known for many years as an unstable but isolable compound,[9] whereas *trans*-cycloheptene has been prepared only as a transient reactive species.[10] A similar situation exists for *trans*-2-cyclooctenone[11] and *trans*-2-cycloheptenone.[12] By analogy, a bicyclic bridgehead alkene should be isolable when the larger of the two rings containing the double bond is at least eight-membered, and certain bicyclic compounds may possibly be isolable with the double bond *trans* in a seven-membered ring. Similarly, transient reaction intermediates should be possible when the larger ring containing the double bond is at least seven-membered. Decarboxylation studies of bicyclic β-keto acids provide qualitative support for this view.

Table I lists a few of the known keto acids showing the qualitative correlation of ease of decarboxylation with the size of the larger ring which would contain the double bond of the intermediate enol.

Table I. Thermal Decarboxylation of Bicyclic β-Keto Acids

Compound	Decarboxylation temp, °C	Enol ring size[a]	Orbital angle,[b] deg	Ref
	Not at 500	5	90	*h*
	350[c]	6	90	*i*
	Not at 310	6	90	*j*
	280[d]	6	*Ca.* 90	*k*
1	Not at 240	6	90	
3	Not at 346	6	90	*m*
	240	7	80	*n*
5 	260	7	50	*o*
6 	320	7	60	*o*
	220	7	65	*p*
	240	7	65	*q*
7 	145	8	30	*o*
2	220[e] 110[f]	8	30	*r*
	132[g]	8	30	*s*

[a] The larger of the two rings including the keto function of the keto acid. [b] See ref 13b. The orbital angles are approximate in several cases due to flexibility of the ring system. [c] With rearrangement. [d] Reported to lose one carboxyl group in low yield at 280° (see footnote *k*). [e] Heating with water for 1 hr in an autoclave at 220°. [f] By hydrolysis of the corresponding tetraester in a boiling mixture of concentrated hydrochloric acid, water, and acetic acid containing cuprous chloride.[7] [g] Keto acids with ring sizes larger than eight atoms decarboxylate readily below 100°. [h] C. F. H. Allen, G. A. Reynolds, S. K. Webster, and J. L. R. Williams, *J. Org. Chem.*, **27**, 1447 (1962). [i] S. Beckman and O. S. Ling, *Ber.*, **94**, 1899 (1961). [j] O. Aschan, *Ann.*, **410**, 243 (1915). [k] P. C. Guha, *Ber.*, **72B**, 1359 (1939). [l] See ref 6. [m] See ref 8. [n] G. Wood and E. P. Woo, *Can. J. Chem.*, **46**, 3713 (1968). [o] See ref 13. [p] C. J. Ahola, unpublished results, this laboratory. [q] R. D. Sands, *J. Org. Chem.*, **29**, 2488 (1964). [r] See ref 7. [s] E. W. Warnhoff, C. M. Wong, and W. T. Tai, *J. Org. Chem.*, **32**, 2664 (1967).

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(9) K. Ziegler and H. Wilms, *Naturwissenschaften*, **34**, 157 (1948); *Ann.*, **567**, 1 (1950).

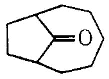
(10) E. J. Corey, F. A. Carey, and R. A. E. Winter, *J. Amer. Chem. Soc.*, **87**, 934 (1965).

(11) P. E. Eaton and K. Lin, *ibid.*, **86**, 2087 (1964).

(12) E. J. Corey, M. Tada, R. LaMahieu, and L. Libit, *ibid.*, **87**, 2051 (1965); P. E. Eaton and K. Lin, *ibid.*, **87**, 2052 (1965).

On the basis of their investigations with three of the keto acids in Table I, compounds **5**, **6**, and **7**, Ferris and Miller[13] have proposed that these keto acids decarboxylate *via* an ionic transition state. These workers determined the temperature required for *complete* decarboxylation of the keto acid in 0.5 hr. Using molecular models they measured the angle which the bond between the bridgehead and the carboxyl carbon makes with the p orbital of the carbonyl carbon. They plotted the decarboxylation temperature against the cosine of the measured angle and obtained a straight line for the three compounds investigated. We have also listed the orbital angle for the compounds in Table I. As may be seen from Table I, the correlation with ring size is adequate to explain the data. We do not feel that the evidence of Ferris and Miller requires an unusual transition state for any of these keto acids.

The data available for the exchange of the α hydrogens of bicyclic ketones also support our arguments concerning ring size.[14-16] For example, the hydrogens of the ketone **8** were completely exchanged in 1 hr by treatment with sodium methoxide in methanol-O-*d* at room temperature.[14,15] Ketone **9** was unchanged by these conditions, but after heating of the solution to reflux for 48 hr, the ketone was 41% undeuterated, 47% monodeuterated, and 13% dideuterated.[15] Similarly, bicyclo[3.3.1]nonan-2-one (**10**) was found to exchange up to three hydrogen atoms for deuterium when heated at 95° for several days in deuterium oxide containing 0.1 *M* NaOD. In discussing this result Schaefer and Lark pointed out that the intermediate enolate anion should be more stable in the chair–boat conformation **11** than in the chair–chair conformation **12**. In support of this view, they cited the fact that the Meerwein acid **2**, which can adopt the chair–boat conformation, decarboxylates readily while the adamantanoid acid **3** resists all attempts at decarboxylation. We prefer to interpret these results in the light of our arguments presented above. The two conformations of the enolate anion are actually geometric isomers. In conformation **11** the double bond is *trans* in the eight-membered ring and *cis* in the six-membered ring, whereas the double bond in conformation **12** is substituted *cis* in the eight-membered ring and *trans* in the six-membered ring. The analogy with the acids **2** and **3** is not valid, since the addition of the methylene bridge to **2** in transforming it into **3** closes an additional six-membered ring. Thus, decarboxylation of **3** would require an enol substituted *trans* in a six-membered ring.



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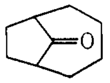

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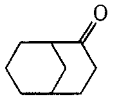

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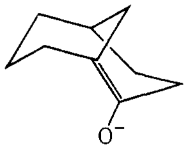

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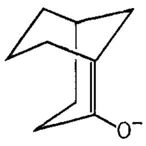

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Synthesis of Bicyclo[3.3.1]non-1-ene. When this work was initiated there was no known bridgehead alkene in which both rings containing the double bond were smaller than nine membered.[17] Thus we decided to test the above postulate concerning isolable compounds by attempting the synthesis of bicyclo[3.3.1]non-1-ene (**13**).[21] This compound may be formally derived from *trans*-cyclooctene by placing a methano bridge between the 1 and 5 positions, and models indicate that this bridge does not appreciably increase the strain over that of *trans*-cyclooctene.[22]

In considering methods for the synthesis of the alkene **13** we felt that it would be absolutely necessary to avoid acidic conditions in order to preclude electrophilic addition to the double bond or isomerization of the double bond to another location. The simplest approach seemed to be an elimination reaction from an appropriately bridgehead-substituted bicyclononane. Since the first synthesis of *trans*-cyclooctene by Willstatter[23] (first recognized as such by Ziegler and Wilms[9]) utilized the Hofmann elimination, we decided to use this method for the final reaction of our synthetic sequence.

The synthesis was accomplished with standard synthetic reactions starting with 1-ethoxycarbonylbicyclo[3.3.1]nonan-9-one (**14**).[24] The carbonyl group of **14** was removed by conversion to the ethylenedithioketal **15**, followed by desulfurization with Raney nickel. The ester **16**, obtained in 96% yield, was hydrolyzed to the corresponding acid **17**, which was in turn converted to the bridgehead amine **18** by the Curtius procedure. Methylation of the primary amine **18** by the Clark–Eschweiler technique gave the tertiary amine **19** in 99% yield, and the tertiary amine was converted to the methiodide **20** in 98% yield. The quaternary ammonium iodide was converted to the corresponding hydroxide **21** by treatment with an aqueous suspension of silver oxide.

Pyrolysis of the quaternary ammonium hydroxide produced the bridgehead alkene **13** in 35% yield after purification by preparative vpc. Approximately 5% of the tertiary amine **19** was also produced in the pyrolysis.

The structure of the alkene **13** is based on its spectra and on chemical degradation. The formula is established as C_9H_{14} by the mass spectrum and elemental analysis. The spectra are in accord with the assigned structure and, with the exception of the ultraviolet spectrum, are not unusual (see Experimental Section).

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[13] (a) J. P. Ferris and N. C. Miller, *J. Amer. Chem. Soc.*, **85**, 1325 (1963); (b) *ibid.*, **88**, 3522 (1966).

[14] C. D. Gutsche and T. D. Smith, *ibid.*, **82**, 4067 (1960).

[15] Reported in K. Biemann, "Mass Spectrometry, Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 246–247.

[16] J. P. Schaefer and J. C. Lark, *J. Org. Chem.*, **30**, 1337 (1965).

[17] At that time bicyclo[4.4.1]undec-1-ene[18] (ten-membered ring) and bicyclo[4.3.1]dec-1-ene[19] (nine-membered ring) were known. All of the bridgehead alkenes prepared by Prelog and coworkers[5b] had their double bonds endocyclic in rings of at least ten atoms. Since completion of this work additional examples of alkenes in eight-membered rings have been provided in the syntheses of dehydrodianthracene[20] and two bridgehead alkenes in the [4.2.1] ring system.[2]

[18] T. Westman, Ph.D. Dissertation, University of California, 1962.

[19] F. T. Bond, Ph.D. Dissertation, University of California, 1962.

[20] N. M. Weinshenker and F. D. Greene, *J. Amer. Chem. Soc.*, **90**, 506 (1968).

[21] Bicyclo[3.3.1]non-1-ene has also been synthesized by J. A. Marshall and H. Faubl (*ibid.*, **89**, 5965 (1967)), using a completely different synthetic scheme.

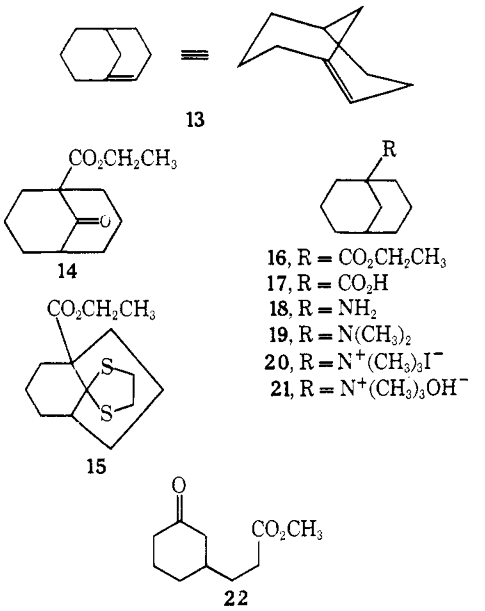
[22] P. M. Lesko and R. B. Turner have determined the strain energy of **13** (*ca.* 12 kcal/mol) to be somewhat higher than that of *trans*-cyclooctene (9.2 kcal/mol) and *cis*-di-*t*-butylethylene (9.3 kcal/mol), *ibid.*, **90**, 6888 (1968).

[23] R. Willstatter and E. Waser, *Ber.*, **43**, 1176 (1910).

[24] E. W. Colvin and W. Parker, *J. Chem. Soc.*, 5764 (1965).

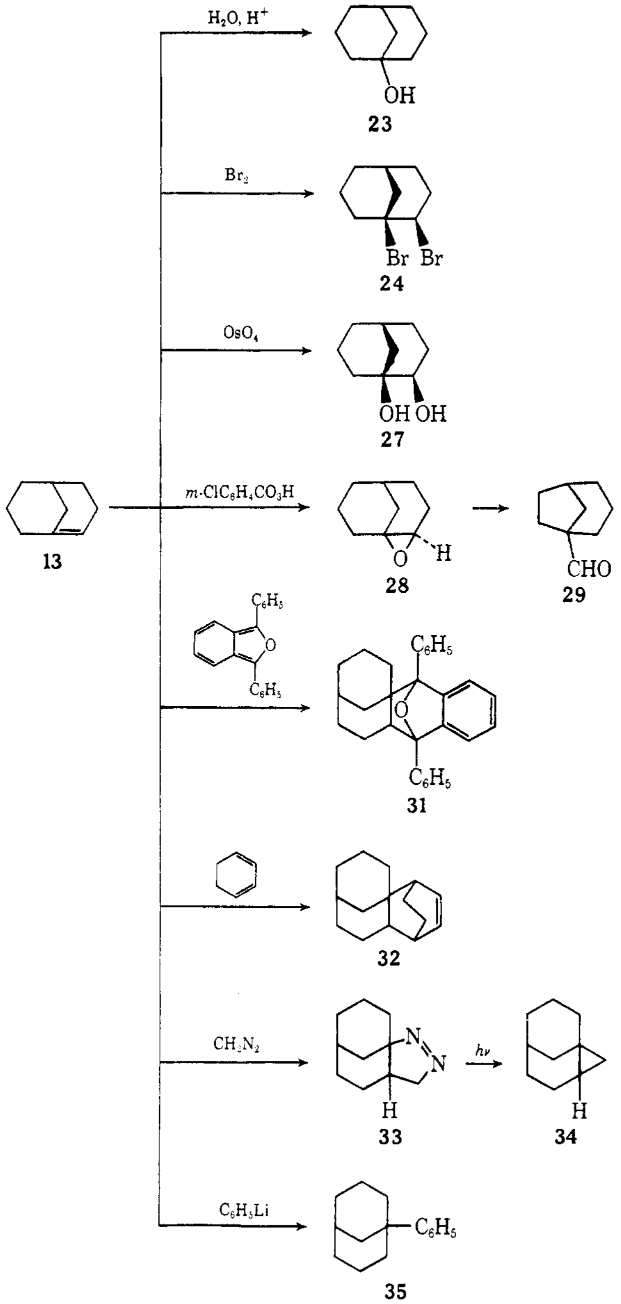
Oxidation of **13** with potassium permanganate and sodium periodate followed by methylation with diazomethane produced the keto ester **22**, identical with a sample synthesized from *m*-hydroxycinnamic acid. Acid-catalyzed hydration of **13** with a dilute solution of perchloric acid in aqueous acetone produced bicyclo[3.3.1]nonan-1-ol (**23**) as the only volatile product. These experiments leave little doubt concerning the identity of the product of the Hofmann elimination.

Chart I

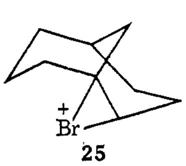


Chemistry of Bicyclo[3.3.1]non-1-ene. The bridgehead alkene **13** is clearly a highly strained and reactive compound. Thus it is of interest to explore the behavior of this compound toward various reagents.[25] The reactions of **13** are depicted in Chart II. The facile hydration of the double bond of **13** formed a part of the proof of structure of the compound. Marshall and Faubl[21] have described the addition of acetic acid to **13** and Lesko and Turner[22] have used this reaction in a calorimetric determination of the strain energy of **13**.

Chart II



Bicyclo[3.3.1]non-1-ene (**13**) reacts with bromine in carbon tetrachloride to give a crystalline dibromide **24** which results from *syn* addition of bromine. The nmr spectrum of **24** shows a single proton on a carbon atom bearing bromine. This hydrogen atom gives rise to a rather sharp peak (width at half-height, 7.5 Hz) and is assigned the *endo* (equatorial) configuration. Thus, the bromine atom at C-2 must be *exo* (axial). The bridgehead bromine atom must be equatorial; thus, the two bromine atoms are *cis* with respect to the six-membered ring. Since the double bond of **13** is *cis* in the six-membered ring, the addition of bromine is *syn*. The bromonium ion **25**, if it is formed at all, should be highly strained since it must retain a portion of the strain of the alkene. This ion contains a *trans*-fused bicyclo[6.1.0] ring system with an additional methylene bridge. Carbon atoms 1 and 2 of **25** are protected from backside attack by bromide ion. Furthermore, backside attack at the bridgehead would give rise to a *trans*-fused bicyclo[3.3.1]nonane. The ion **25** can open to **26**, thus relieving its strain, and attack of bromide ion on **26** produces the dibromide **24**. The reaction may, of course, involve only the intermediate **26**.[25a]



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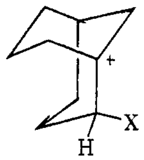

26, X = Br
30, X = OH

The alkene reacts with oximium tetroxide to give the diol **27** which provides additional support for the structural assignment of the dibromide **25**. The

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(25) J. A. Marshall and H. Faubl have also observed some of the reactions we report. We thank Professor Marshall for communicating his results to us prior to publication.

(25a) Note Added in Proof. Reaction of the dibromide **24** with sodium in *t*-butyl alcohol and tetrahydrofuran produces the alkene **13** along with bicyclo[3.3.1]nonane in a 9:1 ratio. This experiment verifies the structure of dibromide **24** and provides an additional synthesis of alkene **13**.

nmr spectra of the diol and the dibromide are very similar, differing only in the chemical shift of the hydrogens at C-2 and in the resonance due to the hydroxylic protons of **27**.

The alkene **13** enters into an exothermic reaction with *m*-chloroperbenzoic acid producing the expected epoxide **28**. When purification of the epoxide was attempted by vapor phase chromatography on an old column, the compound rearranged exclusively to the aldehyde **29**. This rearrangement is probably caused by traces of acid on the vpc column and most likely proceeds through the ion **30**, which rearranges by migration of C-3 to C-1. Migration of the hydrogen atom attached to C-2 is precluded by the geometry of **30**, which places the bond to the hydrogen atom orthogonal to the p_z orbital at C-1.

Cycloaddition reactions of **13** proceed rapidly. Thus, the yellow color of 1,3-diphenylisobenzofuran is observed to disappear within minutes after the addition of the alkene **13**, and the adduct **31** is produced in high yield.

Less reactive dienes also form Diels–Alder adducts with **13**. Thus, cyclohexadiene forms the adduct **32** when heated in benzene solution with alkene **13**. Because of the complexity of nmr resonance due to the vinyl hydrogens of **32**, we believe that it is a mixture of *endo* and *exo* isomers, although separation of the isomers could not be effected by vpc. The reaction between **13** and cyclohexadiene proceeds slowly at room temperature, being approximately 2% complete after 48 hr.

The cycloaddition of diazomethane to **13** also proceeds quickly leading to the adduct **33**. The assignment of the orientation of the diazomethane moiety in **33** is based on the nmr spectrum which shows two protons at *ca.* τ 4.0. Photolysis of **33** causes the elimination of nitrogen with formation of the tricyclic hydrocarbon **34**. The hydrocarbon **34** may be regarded as a *trans*-bicyclo[6.1.0]nonane with an additional methylene bridge spanning the larger ring. As such, it must retain a portion of the strain energy of the alkene **13**. The bromonium ion **25** and the epoxide **28** also have this feature.

Nucleophilic addition to **13** is effected by phenyllithium, leading to 1-phenylbicyclo[3.3.1]nonane (**35**). The position of attachment of the phenyl group is assigned on the basis of the nmr spectrum which shows no resonance which may be assigned to a benzylic proton. Thus, the phenyl group adds to the bridgehead of **13**, producing the more stable secondary carbanion.

The most noticeable characteristic of the alkene **13** is its powerful odor which is detectable in extremely low concentrations. The alkene **13** is thermally stable in the absence of acids and can be passed through a gas chromatography column at temperatures to 170°. A sample stored at room temperature in a sealed tube has remained liquid for 2 years. Very recently, however, we have noticed some evidence of minute crystals on the walls of the tube. When the alkene **13** is exposed to the atmosphere it forms a white solid. Care must be taken to exclude oxygen during preparation of samples for infrared spectra. Otherwise, additional peaks appear in the spectrum at 1720, 2670, and 2820 cm^{-1} indicating that oxygen cleaves the double bond.

Experimental Section[26]

1-Ethoxycarbonylbicyclo[3.3.1]nonan-9-one (14). 1-Ethoxycarbonylbicyclo[3.3.1]nonen-9-one (59.9 g, 0.283 mol, a mixture of Δ^2 and Δ^3 isomers prepared by the procedure of Colvin and Parker[24]) was hydrogenated in ethanol solution using 1.0 g of 5% palladium on carbon. After 4.5 hr the theoretical amount of hydrogen was absorbed. The catalyst was removed by filtration and the ethanol removed on a rotary evaporator. The residue (58.1 g, 98%) crystallized; mp 43.5–45° (lit. 26–32°[24]), $\gamma_{\max}$ 1730, 1725 cm^{-1}.

EthyleneDithioketal of 1-Ethoxycarbonylbicyclo[3.3.1]nonan-9-one (15). Dry hydrogen chloride gas was passed over the surface of a solution of 37.75 g (0.176 mol) of the keto ester **14** and 95 ml (0.89 mol) of 1,2-ethanedithiol in 75 ml of chloroform. Cloudiness developed immediately and in a few minutes droplets of water could be seen. After 4 hr no starting **14** remained. The reaction mixture was distilled at 20 mm at temperatures up to 150° until no more material distilled. The residue, 50.8 g (99%) was pure by vpc; $\gamma_{\max}$ 1725 cm^{-1}. On standing several months the dithioketal crystallized. Recrystallization from ethanol gave material of melting point 51–52°.

Anal. Calcd for $C_{12}H_{22}S_2O_2$: C, 58.69; H, 7.74. Found: C, 58.89; H, 7.66.

1-Ethoxycarbonylbicyclo[3.3.1]nonane (16). The procedure of Djirassi, Halpern, Pettit, and Thomas was followed.[27] A solution of 47.7 g (0.166 mol) of the thioketal **15** was added to a stirred suspension of W-2 Raney nickel in ethanol (prepared from 600 g of nickel–aluminum alloy[28]). The mixture was slowly warmed to reflux, and heating was continued for 12 hr. The Raney nickel was removed by filtration and washed on the filter with ethanol. The combined ethanol solutions were distilled yielding 35.0 g (80%) of the ester **16**, $\gamma_{\max}$ 1725 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.60; H, 10.26.

In another experiment an overall 98% yield of **16** was obtained based on the starting keto ester **14**.

Bicyclo[3.3.1]nonane-1-carboxylic Acid (17). 1-Ethoxycarbonylbicyclo[3.3.1]nonane (**16**) (16.99 g, 0.0866 mol) was heated overnight on a steam bath with 300 ml of 10% sodium hydroxide. The clear solution was cooled and acidified with concentrated hydrochloric acid. The acid was collected on a filter, washed with water, and dried: yield 14.35 g (98.7%), mp 95.5–97.0°. Recrystallization from ethanol gave needles, mp 98–99°, $\gamma_{\max}$ 3600–2500 broad, 1700 cm^{-1}.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.48; H, 9.71.

1-Aminobicyclononane (18). The procedure of Smith was followed.[29] A solution of 12.62 g (0.075 mol) of the acid **17** and 15 ml (0.21 mol) of thionyl chloride was heated on a steam bath for 2 hr. The solvent and excess thionyl chloride were removed on a rotary evaporator. The acid chloride ($\gamma_{\max}$ 1780 cm^{-1}) was dissolved in 20 ml of dry acetone and added dropwise to a stirred saturated solution of sodium azide (31.48 g) in water. The solution was stirred overnight, and in the morning the mixture was transferred to a separatory funnel and extracted with methylene chloride. The methylene chloride extract was dried over sodium sulfate and filtered and the solvent was removed on a rotary evaporator ($\gamma_{\max}$ 2125, 1700 cm^{-1}). The residue was dissolved in benzene and heated under reflux overnight. In the morning the benzene was removed on the rotary evaporator, and the residue ($\gamma_{\max}$ 2250 cm^{-1}) was stirred with 300 ml of 12% hydrochloric acid. Evolution of carbon dioxide ceased after 45 min, and the reaction mixture was heated on a steam bath for an additional 12 hr. The solution was made basic by the addition of potassium hydroxide pellets and the amine was extracted with methylene chloride. The methylene chloride

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(26) Melting points were determined on a Thomas–Hoover capillary melting point apparatus. Nmr spectra were determined in carbon tetrachloride solution with tetramethylsilane as standard, on a Varian A-60 instrument. C_{13}-H coupling constant data were obtained on a Varian HR-100, using a time-averaging computer. Ir spectra were measured on a Model 237 Perkin-Elmer spectrophotometer in carbon tetrachloride. The uv spectrum of **13** was determined on a Model 14 spectrophotometer under a nitrogen atmosphere; other uv spectra were determined on a Perkin-Elmer Model 202 UV spectrophotometer. Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(27) C. Djerassi, O. Halpern, G. R. Pettit, and G. H. Thomas, *J. Org. Chem.*, **24**, 1 (1959).

(28) R. Mozingo, *Org. Syn.*, **3**, 181 (1955).

(29) P. A. S. Smith, *Org. Reactions*, **3**, 387 (1946).

extract was dried over sodium sulfate, filtered, and distilled. The residue was sublimed (50 mm, 80°) to give 7.63 g (74%) of the amine **18**, mp 115–117°. A sample of the amine purified by vpc melted at 119–120°: γ_{max} 3450–3300(w), 1125, and 1110 cm^{-1}.

Anal. Calcd for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.42; H, 12.29; N, 10.00.

1-Dimethylaminobicyclo[3.3.1]nonane (19). The procedure of Meinwald and Kaplan[30] was followed. 1-Aminobicyclo[3.3.1.]-nonane (**18**) (5.992 g, 0.0436 mol) was dissolved in 30 ml of 37% aqueous formaldehyde and 30 ml of formic acid. The solution was heated on a steam bath for 40 hr, with an additional 30 ml of formaldehyde solution added after 27 hr. The solution was cooled, poured into 50 ml of water, and made basic with sodium hydroxide. The tertiary amine was extracted with ether and the extract was dried over sodium sulfate and then filtered. The ether was removed by distillation, finally at reduced pressure. The residue, 7.296 g (99%) showed a single peak on vpc analysis (with shorter reaction times the secondary amine was also formed). An analytical sample was prepared by preparative vpc: nmr τ 7.88 (6 H), 8.0–8.7 (15 H).

Anal. Calcd for $C_{11}H_{21}N$: C, 78.98; H, 12.65; N, 8.37. Found: C, 78.84; H, 12.67; N, 8.30.

Trimethylbicyclo[3.3.1]non-1-ylammonium Iodide (20). Methyl iodide (11.4 g, 0.08 mol) was added to a solution of 5.187 g (0.031 mol) of the 1-dimethylaminobicyclo[3.3.1]nonane (**19**) in 100 ml of ether. Cloudiness developed immediately. After 48 hr the crystals were collected by filtration: yield 9.35 g (98%), mp 259–262° dec. An analytical sample was purified by recrystallization from acetone–ether, mp 255–256° dec.

Anal. Calcd for $C_{12}H_{24}NI$: C, 46.61; H, 7.82. Found: C, 46.73; H, 7.76.

Bicyclo[3.3.1]non-1-ene (13). The procedure is a modification of that of Meinwald and Kaplan.[30] Silver oxide (2.5 g, 10 mmol) was added to a solution of 1.000 g (3.24 mmol) of the quaternary ammonium iodide **20** in 20 ml of water. After 1 hr the solution was filtered and the volume reduced to about 3 ml on a rotary evaporator. The solution was then transferred to a small long-necked flask and the remaining water removed under vacuum. The flask was heated to 140° for 20 min during which time the pyrolysate distilled and was collected in a trap at −70°. The contents of the trap were dissolved in pentane. The pentane solution was washed with water and saturated sodium chloride solution, dried over sodium sulfate, and distilled at atmospheric pressure until about 1 ml remained. The pure alkene, 137 mg (35%), was isolated by: vpc;[31] ir γ_{max} 3050, 2960, 2940, 2870, 1620, 1475, and 1455 cm^{-1}; uv λ_{max} (pentane) 206 nm (ϵ 7500); *m/e* 122; nmr τ 4.38 (t, $J = 7$ Hz, 1 H), 7.25–7.61 (broad, 1 H), 7.61–9.2 (12 H); $J_{^{13}C-H}$ for the vinylic proton was found to be 156.2 Hz.

Anal. Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.55; H, 11.62.

Hydration of Bicyclo[3.3.1]non-1-ene (13). A 30-mg (0.25 mmol) sample of the alkene **13** was dissolved in 6 ml of 80% aqueous acetone and 1 drop of 70% perchloric acid was added. After 2 hr the reaction mixture was diluted with water and extracted with pentane. The pentane solution was washed with 5% sodium bicarbonate solution, dried over sodium sulfate, filtered, and concentrated by distillation. Analysis of the residue by vpc[31] showed no starting alkene and a single volatile product. This product was collected by preparative vpc and was identical in all respects with bicyclo[3.3.1]nonan-1-ol (**23**).[32]

1,2-Dibromobicyclo[3.3.1]nonane (24). A solution of 122 mg (1.0 mmol) of bicyclo[3.3.1]non-1-ene (**13**) in 25 ml of CCl_4 was added to a solution of 502 mg (3.24 mmol) of bromine in 25 ml of CCl_4. Concentration of the solution and distillation at 160° (0.5 mm) afforded 155 mg (55%) of the dibromide **24**, mp 36–37°; nmr, (CCl_4) τ 5.40 (1 H, broad singlet, width at half-height 7.5 Hz), 6.9–8.80 (complex, 13 H).

Anal. Calcd for $C_9H_{14}Br_2$: C, 38.32; H, 5.00; Br, 56.68. Found: C, 38.30; H, 4.80.

Bicyclo[3.3.1]nonane-1,2-diol (27). The procedure of Gunstone was followed.[33] A solution of 241 mg (1.98 mmol) of **13** in dry ether was added to a solution of 500 mg (2.0 mmol) of osmium tetroxide and 0.35 ml of pyridine in dry ether at 0°. Brown crystals formed immediately, and after 2 hr at 0° the crystals were filtered, washed with ether, and dried in air. A solution of 1.0 g of mannitol in 10 ml of 10% aqueous potassium hydroxide was added, and a clear solution was obtained in 2 hr. After 18 hr, this solution was extracted with methylene chloride (4 × 30 ml), and the combined extracts were dried (Na_2SO_4) and concentrated. The white crystalline diol **27** was purified by preparative vpc, 110 mg (35%), mp 219–221°; ir γ_{max} 3425 cm^{-1}; nmr τ 6.50 (1 H, broad singlet, width at half-height 6.5 Hz), 6.77 (2 H, s), 7.30–9.05 (complex, 13 H).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.06; H, 10.21.

2-Oxatricyclo[4.3.1.0^{1,3}]decane (28). The procedure of Hibbert and Burt[34] was followed. To a solution of the alkene **13** (137 mg, 1.13 mmol) in chloroform, was added a solution of 225 mg (1.25 mmol) of *m*-chloroperbenzoic acid in 30 ml of chloroform cooled to 0° by an ice bath. When the reaction is carried out without external cooling, considerable exothermicity is observed. After 20 hr the solution was washed with 5% sodium hydroxide (4 × 50 ml) and saturated sodium chloride solution and dried (Na_2SO_4). Concentration of the solution and distillation at 150° (1 mm) afforded 50 mg (32%) of the epoxide **28**: ir γ_{max} 3010, 2950, 2880, 1015, 910, 885, and 865 cm^{-1}; nmr τ 7.32 (1 H, t, $J = 6$ Hz), 7.5–9.2 (13 H).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.02; H, 10.16.

During attempted analysis of the epoxide **28** by vpc, it was found to rearrange completely to the aldehyde **29**: ir γ_{max} 1725, 2820, and 2700 cm^{-1}; nmr 0.6 (1 H, s), 7.62 (1 H, broad), 7.8–8.9 (12 H, complex).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.84; H, 10.01.

Diels–Alder Adduct of Bicyclo[3.3.1]non-1-ene and 1,3-Diphenylisobenzofuran (31). A solution of 122 mg (1.0 mmol) of bicyclo-[3.3.1]non-1-ene (**13**) in 10 ml of benzene was added to a solution of 1.00 g (3.70 mmol) of 1,3-diphenylisobenzofuran in 40 ml of benzene at room temperature. During the addition, occasional decoloration was observed. After 4 hr the excess 1,3-diphenylisobenzofuran was destroyed by reaction with maleic anhydride. The benzene was removed and the residue was boiled with alcoholic potassium hydroxide to hydrolyze the maleic anhydride adduct. The neutral materials from this reaction were separated by preparative thin-layer chromatography on silica gel affording 320 mg (84%) of the adduct **31**, mp 179–180°: nmr τ 2.7–3.2 (complex), 7.8–9.5 (complex); integration of the nmr spectrum shows equal numbers of aliphatic and aromatic protons.

Anal. Calcd for $C_{29}H_{28}O$: C, 88.73; H, 7.19. Found: C, 88.76; H, 7.06.

Diels–Alder Adduct of Bicyclo[3.3.1]non-1-ene and 1,3-Cyclohexadiene (32). A solution of 122 mg (1.00 mmol) of **13** in 8 ml of pentane was combined with a solution of 0.78 g (9.72 mmol) of 1,3-cyclohexadiene at room temperature. After 48 hr, analysis by vpc indicated 2% of the adduct had formed. The solution was sealed in a Carius tube and heated to 110° for 42 hr. After removal of the solvent, the adduct, 150 mg (74%), was isolated by: preparative vpc; ir γ_{max} 1620 and 3060 cm^{-1}; nmr τ 3.61–3.42 (2 H, complex), 7.55–9.56 (20 H, complex).

Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 88.86; H, 10.93.

2,3-Diazatricyclo[6.3.1.0^{1,5}]dodec-2-ene (33). A solution of diazomethane in ether (prepared from 2.0 g of N-nitroso-N-methylurea[35]) was added to a solution of **13** in 50 ml of ether cooled to 0°. Occasional disappearance of the yellow color of diazomethane was noted during the early stages of the addition. After 15 hr at 0°, the solvent was removed, and the white crystalline residue sublimed at 75° (20 mm) to give 180 mg (99%) of pyrazoline **33**, mp 84–85°; ir γ_{max} 1555 cm^{-1}; uv $\lambda^{pentane}_{max}$ 327 nm (ϵ 302); nmr τ 5.80 (1 H, $J_{ab} = 17.5$ Hz, $J_{ax} = 3$ Hz), 6.25 (1 H, $J_{ab} = 17.5$ Hz, $J_{ax} = 2$ Hz).

Anal. Calcd for $C_{10}H_{16}N_2$: C, 73.13; H, 9.82; N, 17.06. Found: C, 73.19; H, 9.81; N, 17.18.

Tricyclo[4.3.1.0^{1,3}]decane (34). A solution of 140 mg (0.855 mmol) in **33** in 300 ml of purified pentane was photolyzed using a 450-W Hanovia lamp and a Pyrex filter. The absorption at 327 nm decreased to zero after 2 hr. The solvent was distilled and the hydrocarbon **34** was isolated by preparative vpc, 75 mg (65%); ir γ_{max} 3070, 3010, and 1030 cm^{-1}; nmr τ 7.6–8.8 (9 H), 8.8–9.2 (4 H), 9.2–9.9 (3 H); *m/e* 136, 45% of base peak.

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(30) J. Meinwald and B. E. Kaplan, *J. Amer. Chem. Soc*,. **89**, 2611 (1967).

(31) A 1.5 m × 0.635 cm column packed with 20% carbowax 20M and 10% KOH on 60–80 Chromosorb W was used for these separations.

(32) Kindly supplied by Professor William G. Dauben.

(33) F. D. Gunstone, *Advan. Org. Chem., Methods, Results*, **1**, 110 (1960).

(34) H. Hibbert and P. Burt, *Org. Syn. Coll.*, **1**, 494 (1944).

(35) F. Arndt, *ibid.*, **2**, 165 (1943).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.01; H, 11.72.

1-Phenylbicyclo[3.3.1]nonane (35). A solution of 122 mg (1.0 mmol) of **13** and 4 ml of phenyllithium (Foote Co., 1.91 *M* benzene–ether, 70:30) in 25 ml of pentane was refluxed for 60 hr. The disappearance of alkene was followed by vpc (20% carbowax–10% KOH on Chromosorb W, 5 ft × 1/4 in.). The mixture was hydrolyzed; the pentane layer was separated, dried (Na_2SO_4), and concentrated. Analysis by vpc showed five products; the first four were shown to be derived from hydrolysis of phenyllithium, the latter being 1-phenylbicyclo[3.3.1]nonane. Collection of **35** by preparative vpc afforded 65 mg (33%); nmr (CCl_4) τ 2.82 (5 H), 7.65–9.4 (15 H).

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.74; H, 10.17.

Ethyl Cyclohexanol-3-propionate. 3-Hydroxycinnamic acid[36] (82 g, 0.5 mol) was hydrogenated in ethanol using ruthenium oxide as a catalyst.[37] The catalyst was removed by filtration and the crude product isolated by evaporation of the ethanol. Distillation of the crude product gave 75 g (75%) of ethyl cyclohexanol-3-propionate, bp 145–148° (2.75 mm); ir γ_{max} 3650, 3600–3200 broad, 1735 cm^{-1}; nmr τ 6.01 (2 H, q, J = 7), 6.5–7.0 (1 H, broad), 7.37 (1 H, s), 7.8 (t, J = 7, overlapping other resonance), 7.6–9.0 (16 H), 8.8 (t, J = 7).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.86; H, 10.16.

Ethyl Cyclohexanone-3-propionate. A solution of 20 g (0.10 mol) of ethyl cyclohexanol-3-propionate in 100 ml of reagent grade acetone was cooled to 0°. A solution of 113 g of CrO_3, 115 ml of H_2SO_4, and 500 ml of water (Jones Reagent) was added with stirring until the solution remained orange-brown in color (35 ml). Ethyl cyclohexanone-3-propionate was isolated in 76% yield (15.0 g); ir γ_{max} 1720, 1740 cm^{-1}; nmr τ 5.95 (2 H, q, J = 7), 7.5–8.6 (13 H, complex), 8.76 (3 H, t, J = 7).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15; O, 24.21. Found: C, 66.69; H, 9.15.

Methyl Cyclohexanone-3-propionate (22). To 1.0 g (0.005 mol) of ethyl cyclohexanone-3-propionate was added 25 ml of methanol and a catalytic amount of hydrochloric acid. The solution was refluxed for 2 hr, cooled, and the solvent removed on a rotary evaporator. The residue was dissolved in ether, washed with 5% sodium bicarbonate solution, and dried (Na_2SO_4). Removal of solvent gave 0.80 g (89%) of the crude keto methyl ester. Purification of a small sample was effected by preparative vpc: ir γ_{max} 1720, 1745 cm^{-1}; nmr τ 6.58 (3 H, s), 7.6–9.16 (13 H, complex).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75; O, 26.05. Found: C, 65.29; H, 8.77.

Oxidation of Bicyclo[3.3.1]non-1-ene. The method is that of von Rudloff.[38] A solution of 122 mg (1.0 mmol) of **13** in 10 ml of pentane was stirred overnight at room temperature with a solution of 3.2 g of sodium periodate, 0.15 g of potassium permanganate, and 5.0 g of potassium carbonate in 65 ml of water. The acidic product of this reaction was isolated and treated with a solution of diazomethane in ether. The solvent was removed, and vpc analysis of the residue showed that the major product was methyl cyclohexanone-3-propionate **22**. A sample purified by vpc gave an infrared spectrum identical with that synthesized above.

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[36] Obtained from Hi Laboratories, Whitmore Lake, Mich. This compound apparently contained sufficient mineral acid to cause esterification during the catalytic hydrogenation.

[37] The hydrogenation was done by J. Hudson.

[38] E. von Rudloff, *Can. J. Chem.*, **34**, 1413 (1956).

The Synthesis and Cycloaddition Reactions of 7,8-Dimethylene-1,3,5-cyclooctatrienes. The Synthesis of Dicyclooctatetraeno[1,2:4,5]benzene[1]

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Contribution from the University Chemical Laboratory, Cambridge, England.

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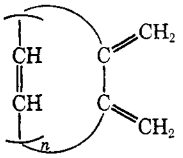
Abstract: 7,8-Dimethylene-1,3,5-cyclooctatriene (**4**) has been synthesized from 1,2-bis(hydroxymethyl)cyclooctatetraene (**6**), by conversion to 1,2-bis(bromomethyl)cyclooctatetraene (**7**) and subsequent zinc reduction. Treatment of **7** with potassium *t*-butoxide led to 7-methylene-8-bromomethylene-1,3,5-cyclooctatriene (**8**), while similar treatment of 1,2-bis(chloromethyl)cyclooctatetraene (**9**) gave 7-methylene-8-chloromethylene-1,3,5-cyclooctatriene (**10**). The exocyclic double bonds of **4**, **8**, and **10** proved to be the most reactive diene systems in thermal 1,4-cycloaddition reaction, and gave rise to fused cyclooctatetraene derivatives by addition to a variety of dienophiles. For instance, **4** and **8** have been converted to dicyclooctatetraeno[1,2:4,5]benzene (**27**). Although the possibility existed that **27** might represent a planar aromatic system, the spectral properties indicated that the eight-membered rings are nonplanar and do not possess delocalized π electrons.

Dimethylenecyclopolyenes of type **1** are an interesting class of compounds. The only representatives which had been studied when we commenced our work in this field were the first two members, 3,4-dimethylenecyclobutene (**2**)[3] and 5,6-dimethylene-1,3-cyclohexadiene (*o*-quinodimethane, *o*-xylylene) (**3**).[4,5]



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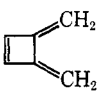

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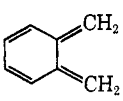

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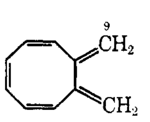

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[1] Unsaturated Eight-Membered Ring Compounds. VII. For Part VI, see J. A. Elix and M. V. Sargent, *J. Am. Chem. Soc.*, **91**, 4734 (1969).

[2] Author to whom inquiries should be addressed at the Chemistry Department, University College, London W.C.1, England.

[3] A. J. Blomquist and P. M. Maitlis, *Proc. Chem. Soc.*, 332 (1961); W. D. Huntsman and H. J. Wristers, *J. Am. Chem. Soc.*, **85**, 3308 (1963); **89**, 342 (1967); M. L. Heffernan and A. J. Jones, *Chem. Commun.*, 120 (1966); B. A. W. Coller, M. L. Heffernan, and A. J. Jones, *Aust. J. Chem.*, **21**, 1807 (1968).

[4] *Inter alia*, L. A. Errede, *J. Am. Chem. Soc.*, **83**, 949 (1961); K. Alder and M. Fremery, *Tetrahedron*, **14**, 190 (1961); D. A. Ben-Efraim and F. Sondheimer, *Tetrahedron Lett.*, 313 (1963); M. Avram, I. G.