Synthesis and Physical Properties of Barrelene, a Unique Möbius-like Molecule

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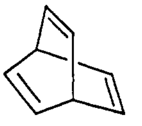
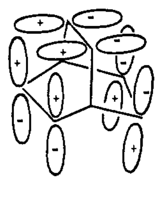
Abstract: A practical synthesis of bicyclo[2.2.2]-2,5,7-octatriene (barrelene) was devised. This procedure and a subsequent variation began with a large-scale synthesis of α-pyrone and a generally useful "double Diels–Alder reaction." The infrared and ultraviolet spectra of barrelene are reported. Also, the nmr spectrum is analyzed as an $AA'B_3B_3'$ system by use of the ^{13}C satellite spectrum and a calculation of the theoretical spectrum. The details of the molecular orbital calculations reported earlier are given. The Hückel energy was found to be independent of precise transannular overlap, despite electron delocalization, affording a unique example of delocalization without the usually attendant delocalization stabilization. The molecule represents the first hydrocarbon having a sign discontinuity in its basis set of atomic orbitals and in all MO's and is a Möbius-like system.

The presently described research had its beginning a number of years ago and has been the object of intensive effort in our laboratories. We now report in detail the synthetic aspects and initial phases of these studies.

It was first noted by Hine[1] in 1955 that the then unknown bicyclo[2.2.2]-2,5,7-octatriene (**1**) contained six π electrons in a cyclic, although nonplanar, arrangement and thus might be aromatic in accordance with the familiar $4n + 2$ rule derived from MO theory by Hückel to explain the stability of aromatic molecules. Hine noted, however, that the requirement of like algebraic sign of overlapping lobes of the p orbitals could not be satisfied in this molecule.



1a



1b

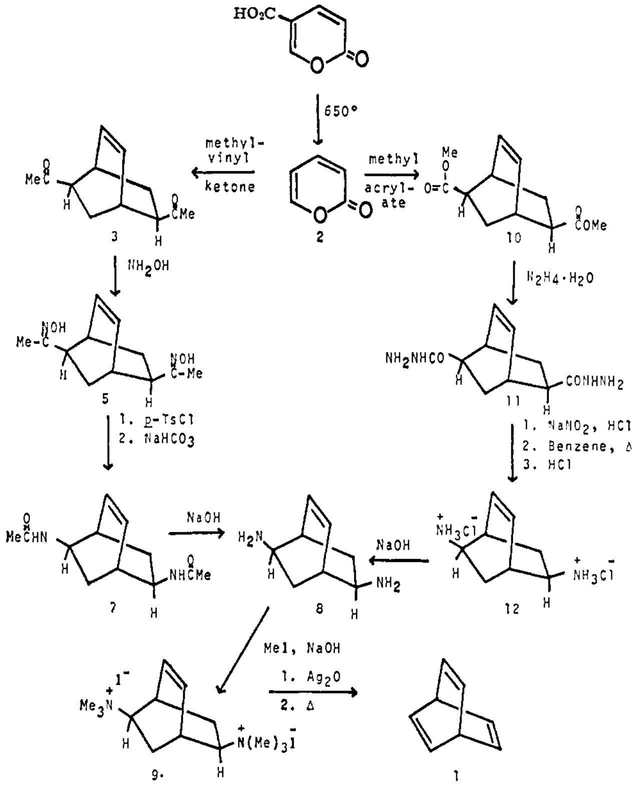
1c

Consequently there was considerable interest in achieving a synthesis of this compound. This was culminated by the report of Zimmerman and Paufler in 1960 of the first synthesis of this system, and the trivial name barrelene was proposed because of the barrel-shaped array of molecular orbitals (note **1c**).[2] The initial synthesis described in our preliminary communication,[2] with improvements and variations, is now given in detail, together with a discussion of the electronic structure of the system.

Synthesis

The original procedure for the preparation of barrelene is outlined in Chart I. The development of a large-scale, efficient preparation of α-pyrone (**2**) was a necessary starting point for this synthesis, since previously only small-scale pyrolysis of heavy metal salts of coumalic acid[3] and a semimicro-scale decarboxylation of α-pyrone-6-carboxylic acid using copper[4] had afforded α-pyrone. Our method[5] involves the decarboxylation of coumalic acid by passage *in vacuo* over fine copper turnings at 650° and affords large amounts of **2**. In large-scale runs, 100 g hr^{-1} rates were attainable in yields of 60–65%. Much higher yields (>90%) could be obtained on a smaller scale using especially pure coumalic acid.

Chart I. Synthesis of Bicyclo[2.2.2]-2,5,7-octatriene



The α-pyrone (**2**) was treated with methyl vinyl ketone in a decarboxylative double Diels–Alder addition

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(1) J. Hine, J. A. Brown, L. H. Zaldow, W. R. Gardner, and M. Hine, *J. Amer. Chem. Soc.*, 77, 594 (1955).

(2) H. E. Zimmerman and R. M. Paufler, *ibid.*, **82**, 1514 (1960).

(3) H. von Pechmann, *Ann.*, 264, 272 (1891).

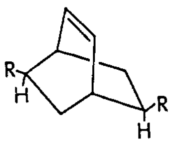
(4) J. Fried and R. C. Elderfield, *J. Org. Chem.*, **6**, 566 (1941).

(5) The presently reported procedure is a modification of the method we described earlier.[6]

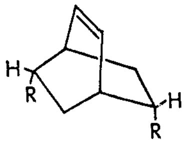
(6) H. E. Zimmerman, G. L. Grunewald, and R. M. Paufler, *Org. Syn.*, **46**, 101 (1966).

to afford an oily mixture of 5,7-diacetylbicyclo[2.2.2]-2-octene (**3**), 5,8-diacetylbicyclo[2.2.2]-2-octene (**4**), and other isomers.

From this mixture a crystalline isomer, mp 90–91°, was obtained in 18% yield. The nmr spectrum of the crystalline isomer showed the vinyl protons as a symmetrical pair of doublets attributed to an A_2X_2 system,[7] with equivalent vinyl hydrogens, and was compatible with structures **3a** and **3b** out of the six isomers possible. It was found that base-catalyzed epimerization of the oily mixture of diketones led to two stable isomers, one of which was the mp 90–91° crystalline isomer. It was further shown that the solid diketone isomer was unchanged under the alkaline epimerization conditions. This observation supports structure **3a**, in which the acetyl groups are *endo* to the unsaturated bridge, since this should be the more stable configuration.[8]



3a



3b

The diketone **3** was converted to the corresponding dioxime with hydroxylamine in 97% yield. The dioxime **5** was converted to the ditosylate **6**. This, in turn, was subjected to a solvolytic Beckmann rearrangement under alkaline conditions, to give a 52% yield of diamide **7**. The diamide **7** could be obtained directly from dioxime **5**, using benzenesulfonyl chloride–sodium hydroxide, but with lower yields.

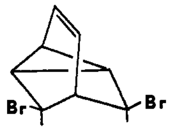
Alkaline hydrolysis of the diamide **7** gave the diamine **8**, and quaternization with methyl iodide and sodium hydroxide afforded the 5,7-bis(trimethylammonium)-bicyclo[2.2.2]-2-octene diiodide (**9**) in 62% yield from diamide **7**. This compound underwent a double Hofmann elimination to afford benzene as a minor component and barrelene (**1**) in 75% yield.

A convenient alternative (note Chart I) to the original synthesis utilized a Curtius conversion in place of the Beckmann rearrangement to replace the carbon substituents by amino groups.[10] Here methyl acrylate was employed as the dienophile and gave a similar double Diels–Alder addition. A crystalline product (26% yield) was obtained, whose structure was taken to be that of 5,7-*endo*,*endo*-dicarbomethoxybicyclo-[2.2.2]-2-octene (**10**), due to the similarity of its nmr spectrum to that of **3**. The diester **10** was smoothly converted to the dihydrazide **11** (98%). This compound underwent a double Curtius rearrangement under anhydrous conditions with acid work-up, to afford the dihydrochloride (**12**) of the already known diamine **8** (70%). The identity of **8** from this route established the 5,7 structure and *endo*,*endo* stereochemistry. While the second synthesis improved the yield only *ca.* twofold, this route proved especially convenient in facility of operation.

In both reaction schemes it was possible to complete the total synthesis using the mixture of noncrystalline diketones or diesters formed in the initial Diels–Alder additions. No crystalline products were then obtained throughout the series of reactions. However, since the final Hofmann elimination afforded a product mixture containing over 50% benzene, the use of these several isomers was not practical, and only the crystalline Diels–Alder adducts were used in subsequent work.

Addition of Bromine to Barrelene. In carbon tetrachloride, barrelene took up 1 mol of bromine to give a mixture of products. Silica gel chromatography afforded an oil and a solid melting at 133.5–134.5°; both compounds analyzed for $C_8H_8Br_2$, indicating the addition of 1 mol of bromine.

The nmr spectrum of the solid dibromide is consistent with structure **13**. The spectrum shows five markedly different kinds of protons which are given the following assignments: τ 3.92, vinyl proton adjacent to bromine atoms; 4.46, vinyl; 5.83, methines bearing the bromine atoms; 6.91, bridgehead; and 8.00, assigned to the three cyclopropyl hydrogens. The nmr of the oily isomer offered suggestive but less than firm evidence for structure **14**.



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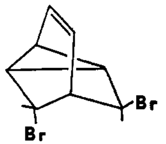

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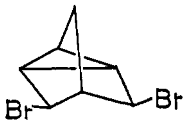
The reaction is analogous to the known bromination of bicyclo[2.2.1]-2,5-heptadiene[11,12] and bicyclo-[2.2.2]-2,5-octadiene, from which two saturated products were obtained in each case. Bicyclo[2.2.1]-2,5-heptadiene is known[11,12] to give *exo*,*exo*-3,5-dibromotricyclene (**15**) and *endo*,*exo*-3,5-dibromotricyclene (**16**). Similarly, bicyclo[2.2.2]-2,5-octadiene gives[13] *exo*,*exo*-3,5-dibromohomotricyclene (**17**) and *endo*,*exo*-3,5-dibromohomotricyclene (**18**).



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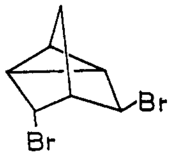

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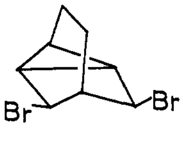

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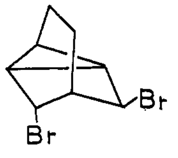

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Hydrogenation of Barrelene. In addition to the analytical and spectral data, the structure of **1** was demonstrated by its catalytic hydrogenation to the known bicyclo[2.2.2]octane. Hydrogenation of barrel-

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(7) J. A. Pople, W. G. Schnieder, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 140.

(8) It is known, for example,[9] that equilibration of 5-carbomethoxy-bicyclo[2.2.2]-2-octene with potassium methoxide gives a value of 0.45 for the ratio of *exo* to *endo* isomer at 100° (*exo* and *endo* to the unsaturated bridge). A similar ratio (0.42) was obtained for the 5-nitro compounds.

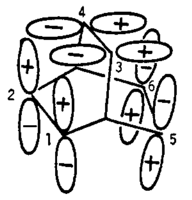
(9) R. J. Ouellette and G. E. Booth, *J. Org. Chem.*, **30**, 423 (1965).

(10) We acknowledge helpful suggestions by Dr. G. Schröder which led to our trying this route.

(11) L. Schmerling, J. P. Luvisi, and R. W. Welch, *J. Amer. Chem. Soc.*, **78**, 2819 (1956).

(12) S. Winstein and M. Shatavsky, *Chem. Ind.* (London), 56 (1956).

(13) C. A. Grob and J. Hostynek, *Helv. Chim. Acta*, **46**, 1676 (1963).



1d

Figure 1. A convenient basis set of AO's for the MO treatment of barrelene. (Note: numbering of orbitals does not conform to IUPAC number of carbon skeleton.)

$$\psi_6 = (1/\sqrt{6})(\chi_1 - \chi_2 + \chi_3 - \chi_4 + \chi_5 - \chi_6) \qquad A_1''$$

$$\begin{aligned}\psi_5 &= (1/2\sqrt{3})(\chi_1 - \chi_2 + \chi_5 - \chi_6) - (1/\sqrt{3})(\chi_3 - \chi_4) \\ \psi_4 &= (1/2)(\chi_1 - \chi_2 - \chi_5 + \chi_6)\end{aligned} \qquad E''$$

$$\psi_3 = (1/\sqrt{6})(\chi_1 + \chi_2 + \chi_3 + \chi_4 + \chi_5 + \chi_6) \qquad A_2'$$

$$\begin{aligned}\psi_2 &= (1/2\sqrt{3})(\chi_1 + \chi_2 + \chi_5 + \chi_6) - (1\sqrt{3})(\chi_3 + \chi_4) \\ \psi_1 &= (1/2)(\chi_1 + \chi_2 - \chi_5 - \chi_6)\end{aligned} \qquad E'$$

Figure 2. Molecular orbitals of barrelene.

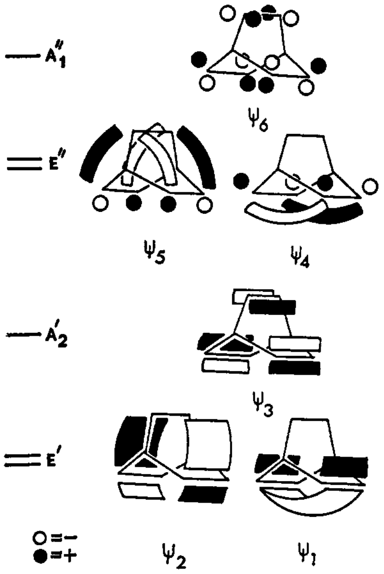


Figure 3. Pictorial representation of the molecular orbitals of barrelene.

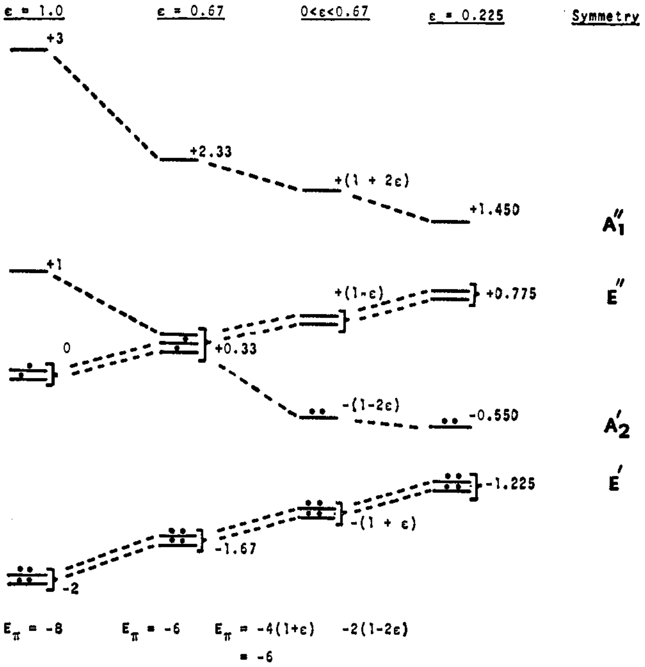


Figure 4. Molecular orbital energies of barrelene. (Note that $\epsilon = \beta_{26}/\beta_{12}$ and energy is in units of $|\beta|$.)

ene in ethanol using platinum oxide proceeded normally with constant uptake of 3 mol. The single product had a melting point and an infrared spectrum which were identical with those reported[1,14] for bicyclo[2.2.2]-octane. Subsequently Turner[15] has obtained a 93.8 kcal/mol value for the total heat of hydrogenation and a 37.6 kcal/mol value for the first double bond. This suggested about 10 kcal/mol destabilization due to angular strain.

Molecular Orbital Considerations. As has been noted earlier, barrelene is a unique molecule, in which it is not possible to select a set of p orbitals such that there will be no overlap between lobes of different sign. It is of interest to consider the effect this has on the molecular orbital treatment of the molecule and on its stability.

An arbitrary, but convenient, basis set of atomic orbitals[16] is selected as shown in Figure 1. This set has the advantage that all transannular overlap integrals are identical (and positive). The transannular overlap is found to be 0.225 of the normal ethylenic p-p overlap (note section on Calculations), but for generality we will take this transannular overlap as a variable positive parameter ϵ, where $\epsilon = 1$ in the event that overlap is as favorable as in ethylene and $\epsilon = 0$ for no overlap.

Solution of the sixth-order secular determinant (eq 1) may be accomplished by appropriate addition and subtraction of rows and columns.[17] Alternatively, a resort to group theory using D_{3h} symmetry affords the same results. See Figures 2–4.

$$\begin{array}{c|cccccc|}
 & \chi_1 & \chi_2 & \chi_3 & \chi_4 & \chi_5 & \chi_6 \\
\chi_1 & X & 1 & -\epsilon & 0 & -\epsilon & 0 \\
\chi_2 & 1 & X & 0 & -\epsilon & 0 & -\epsilon \\
\chi_3 & -\epsilon & 0 & X & 1 & -\epsilon & 0 \\
\chi_4 & 0 & -\epsilon & 1 & X & 0 & -\epsilon \\
\chi_5 & -\epsilon & 0 & -\epsilon & 0 & X & 1 \\
\chi_6 & 0 & -\epsilon & 0 & -\epsilon & 1 & X
\end{array} = 0 \qquad (1)$$

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(14) R. Seka and O. Tramposch, *Ber.*, 75B, 1379 (1942).

(15) R. B. Turner, *J. Amer. Chem. Soc.*, 86, 3586 (1964).

(16) A basis set, of course, is an arbitrarily selected definitional set of orbitals to be used in a quantum mechanical "mixing" process and should not be confused with the molecular orbitals resulting from the mixing process (*i.e.*, from solution of the secular determinant).

(17) A convenient device in solving secular determinants is addition and subtraction of rows and columns, including the headings giving the basis set. The addition–subtraction is carried out following the symmetry of the molecule, and the resulting secular determinant is then in terms of the new basis orbitals heading the rows and columns. This convenient trick seems not to have been previously published. In the present instance, addition and subtraction of rows (and then columns) 1 and 2, 3 and 4, and 5 and 6 lead to two third-order determinants. One contains interaction elements between the symmetric MO's (χ_1 + χ_2), ($\chi_3 + \chi_4$), and ($\chi_5 + \chi_6$); the other derives from the antisymmetric MO's ($\chi_1 - \chi_2$), ($\chi_3 - \chi_4$), and ($\chi_5 - \chi_6$). Each of these may be further simplified by addition–subtraction with the use of the second plane of symmetry. The latter plane of symmetry (through the bridgehead atoms) could be used initially. Then second- and fourth-order determinants result. The six molecular orbitals obtained are depicted in LCAO MO form in Figure 2 and also are given pictorially in Figure 3. The energies are given generally and for specific values in Figure 4.

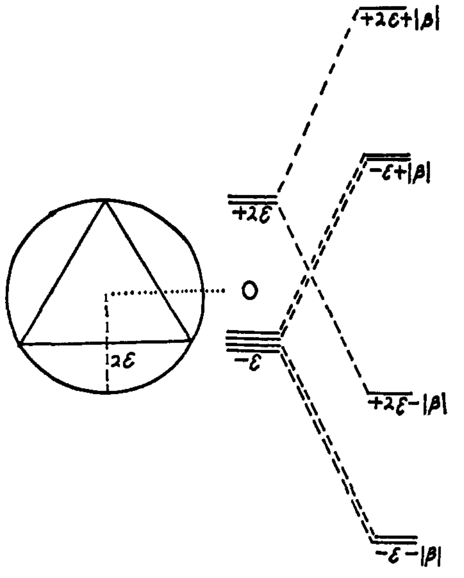

Figure 5. Use of the Möbius circle mnemonic to derive the MO's of barrelene.

obtained from solution of the secular determinantal equation.

Configuration Interaction Calculations. It was of interest to carry out configuration interaction calculations on barrelene, using the procedure described by us earlier.[19] The method used linear combinations of Slater determinants of the correct form to be singlet and triplet eigenfunctions. All possible singly excited configurations plus the ground state were allowed to interact. Interestingly, the relative magnitude of the repulsion integrals γ_{26} and γ_{25} was found to control the separation between S_1 and S_2 excited states while the magnitude of the resonance integrals β_{23}, β_{26}, β_{25}, when kept constant relative to one another, controlled the vertical positioning of the excited states. These resonance and repulsion integrals are linear combinations of integrals of the types π–π, σ–σ, and also the π–σ and (perpendicular) π–π' types.[20] The last two are nonzero only for the repulsion integrals. The linear combination in each case was determined by analytic solid geometry. The basic integrals were obtained as indicated in the Experimental Section.

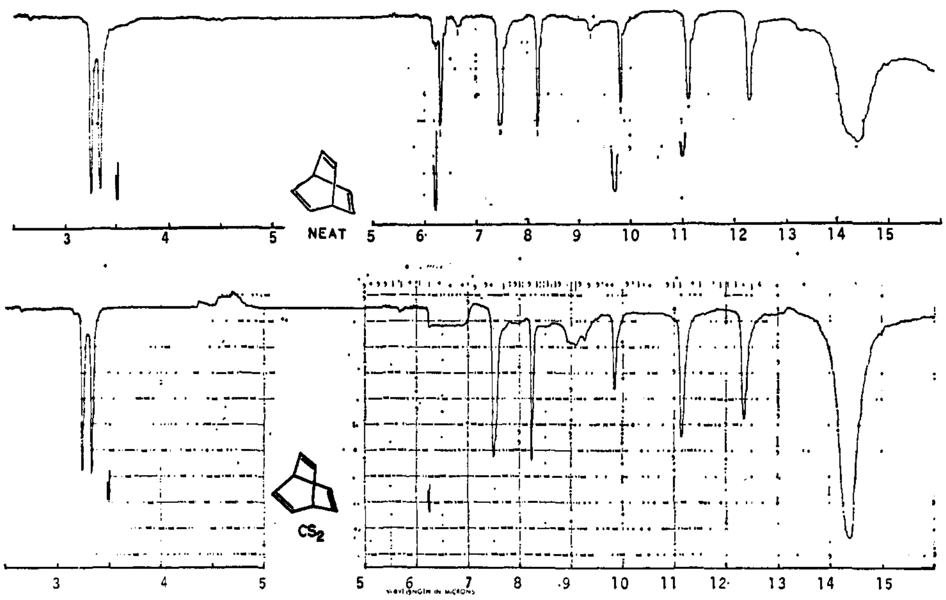

Figure 6. (a, top) Infrared spectrum of barrelene (neat). (b, bottom) Infrared spectrum of barrelene in CS_2.

There is another aspect of interest to the electronics of barrelene. Since barrelene has an odd number of sign changes between orbitals in "proceeding around the barrel," this molecule represents an example of a Möbius system.[18] For such systems there is a convenient device for obtaining the exact molecular orbital energies, and this is applicable to barrelene. Here one draws a circle of radius 2ϵ and inscribes an equilateral triangle with one side down; the triangle is used with the two triangular arrays of p orbitals in mind (*i.e.*, orbitals χ_1, χ_3, χ_5 and also χ_2, χ_4, and χ_6). Prior to interaction of the two sets of orbitals, we obtain (see Figure 5) MO's at $+2\epsilon$ and $-\epsilon$. However, ethylenic mixing of the orbitals of the two faces leads to splitting by $\pm 1|\beta|$ to give the six final MO energies (see Figure 5 again). We note that the result is identical with that

The energies derived with reasonable integrals, obtained as above, were all modestly close to the values of S_1 and S_2 measured by ultraviolet absorption. The predicted energies as a function of integral choice are given in Table I along with the experimental values. It can be seen that the best fit was obtained with the integrals $\beta_{23} = 2.11$, $\beta_{26} = 0.4638$, $\beta_{25} = 0.3592$, $\gamma_{23} = 7.45$, and $\gamma_{25} = 1.525$ eV.

Several investigators have also calculated the excited-state energies of barrelene; a summary of their values is given in Table II. Infrared spectra of barrelene are given in Figure 6.

Nuclear Magnetic Resonance Spectrum of Barrelene. The 60-Mc nmr spectrum of a neat sample of barrelene is reproduced in Figure 7. The top part of the figure

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(18) (a) H. E. Zimmerman, *J. Amer. Chem. Soc.*, **88**, 1564 (1966); (b) H. E. Zimmerman, *Science*, **153**, 837 (1966).

(19) H. E. Zimmerman, R. W. Binkley, J. J. McCullough, and G. A. Zimmerman, *J. Amer. Chem. Soc.*, **89**, 6589 (1967).

(20) π–π' integral represents the repulsion between electrons in two p orbitals perpendicular to one another and to an interatomic axis.

Table I. Barrelene Excited-State Energies from Configuration Interaction Calculations as a Function of Integrals

α_{22}, eV	−11.1600	−11.1600	−11.1600	−11.1600	−11.1600	−11.1600	−11.1600	−11.1600	−11.1600
β_{23}, eV	−2.90	−2.90	−2.90	−2.40	−2.40	−2.40	−2.11	−2.11	−2.11
β_{26}, eV	0.6432	0.6432	0.6432	0.5276	0.5276	0.5276	0.4638	0.4638	0.4638
β_{25}, eV	0.4936	0.4936	0.4936	0.4087	0.4087	0.4087	0.3592	0.3592	0.3592
γ_{22}, eV	10.5300	10.5300	10.5300	10.5300	10.5300	10.5300	10.5300	10.5300	10.5300
γ_{23}, eV	7.4500	7.4500	7.4500	7.4500	7.4500	7.4500	7.4500	7.4500	7.4500
γ_{26}, eV	3.4000	3.4000	1.7290	3.4000	3.4000	1.7290	3.4000	3.4000	1.7290
γ_{25}, eV	2.7640	1.5250	1.5250	2.7640	1.5250	1.5250	2.7640	1.5250	1.5250
S_1, eV	5.7780	4.8422	6.4013	5.0640	4.0452	5.6370	4.6259	3.5621	5.1709
nm	214	256	194	245	306	220	268	349	240
S_2, eV	7.4716	8.9073	7.1834	6.7678	8.2456	6.3602	6.3519	7.8626	5.8693
nm	166	139	173	183	150	195	195	158	211
Experimental									
S_1, eV	5.1900								
nm	239								
S_2, eV	5.9600								
nm	208								

is a 500-Hz scan downfield from tetramethylsilane; the middle two parts of the figure are expanded portions of the vinyl and bridgehead protons of barrelene; the bottom part of the figure shows the downfield vinyl pattern of the carbon-13 spectrum.

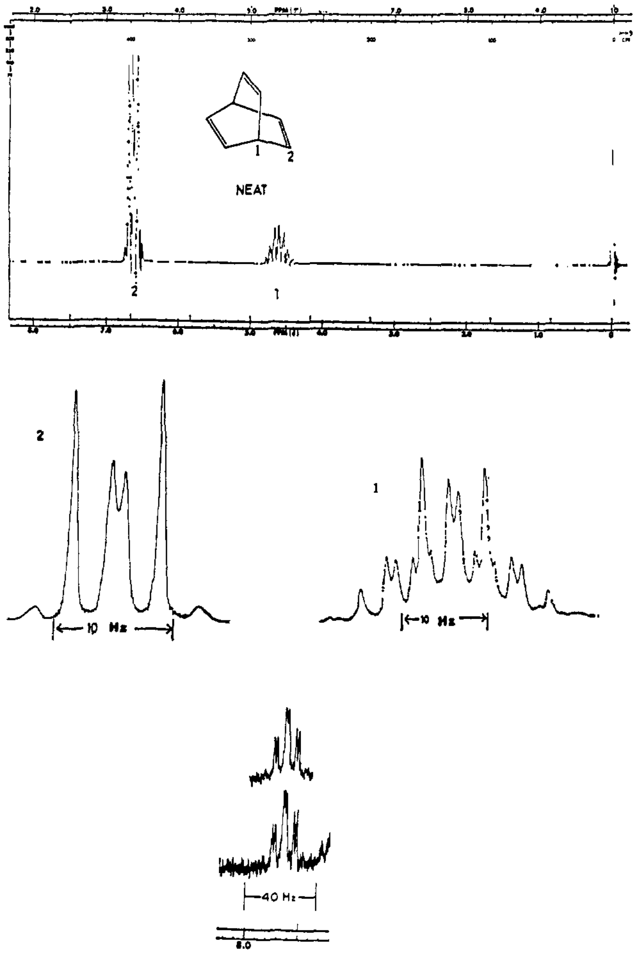

Figure 7. (top) Normal scan of barrelene, nmr spectrum; (middle) expanded; (bottom) C-13 satellite spectrum.

Table II. Calculated Transition Energies for Barrelene

Investigators	Transition energies eV	nm
Wilcox,	5.77	215
Winstein, and	6.75	184
McMillan[a]	6.82	182
Giacometti	5.23	237
and Rigatti[b]	6.96	178
Paldus and Koutecky[c]	5.19	239
	5.98	207
Allinger and Miller[d]	5.79	214
	6.40	194
This work	5.17	241
	5.87	207
Observed	5.19	239
	5.96	208

[a] C. F. Wilcox, Jr., S. Winstein, and W. G. McMillan, *J. Amer. Chem. Soc.*, **82**, 5450 (1960). [b] G. Giacometti and G. Rigatti, *Ric. Sci.*, **30**, 1061 (1960). [c] J. Paldus and J. Koutecky, *Collect. Czech. Chem. Commun.*, **27**, 2139 (1962). [d] N. L. Allinger and M. A. Miller, *J. Amer. Chem. Soc.*, **86**, 2811 (1964).

A first-order treatment of the bridgehead hydrogens of barrelene, using $J_{12} = 4.20$ Hz and $J_{13} = 3.10$ Hz as measured from the vinyl pattern, affords the expression $\nu = 91.1 \pm nJ_{12} \pm mJ_{13}$ Hz (with n and $m = 0.5$ and 1.5). This naive interpretation was reported earlier[2] and is in excellent agreement with the observed lines. However, symmetry and accidental equivalence may lead to a "deceptively simple"[21] spectrum. In barrelene protons 2 and 3 are magnetically equivalent, and although they are strongly coupled (*vide infra*), this coupling is not apparent from inspection of the ordinary proton spectrum.[22]

The correct coupling constants were obtained by examination of the vinyl ^{13}C side bands due to ^{13}C–H spin–spin interaction. The satellites appear symmetrically displaced about the signal of the proton to which the ^{13}C is bonded and can be analyzed with a first-order treatment[23] (see Figure 8). The downfield ^{13}C pattern for the vinyl hydrogens of barrelene was determined on a neat sample and is shown in Figure 7c; the upfield pattern was also obtained but with lower resolution. Both were eight-line patterns.

With values of J_{12}, J_{13}, and J_{23} available it was possible to determine the theoretical nmr spectrum using a

[21] R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **39**, 216 (1961).

[22] A. Abragam, "Principles of Nuclear Magnetism," Oxford University Press, Oxford, England, 1961, p 480.

[23] J. B. Strothers, *Quart. Rev.* (London), 144 (1965).

variation of the Frequint IV program of Bothner-By,[24] modified to deal with eight-spin systems. The theoretical spectrum is given in Table III along with the experimental results. It is seen that the fit is excellent both in line position and intensity. The coupling constants for barrelene are given in Table IV along with those of norbornadiene and norbornene for comparison.

Table III. Nuclear Magnetic Resonance Spectral Data for Barrelene

Obsd spectrum: Chemical shift, Hz	Obsd spectrum: Rel intens	Calcd spectrum: Chemical shift, Hz	Calcd spectrum: Rel intens
265.2	0.16	265.1	0.15
268.2	0.42	268.1	0.32
269.2	0.42	269.3	0.37
271.2	0.42	271.2	0.31
272.3	0.58	272.3	0.94
273.4	0.42	273.3	0.37
274.4	0.16	274.5	0.11
275.4	1.00	275.3	0.97
276.6	1.00	276.4	1.00
277.6	0.16	277.6	0.12
278.6	0.42	278.4	0.37
279.7	0.58	279.4	0.53
280.8	0.42	280.5	0.34
282.7	0.42	282.6	0.43
284.0	0.42	283.5	0.45
287.0	0.16	286.5	0.21
391.4	0.32	391.2	0.46
394.3	6.50	394.6	6.07
397.5	3.95	297.5	5.52
398.6	3.95	398.6	5.42
401.6	6.50	401.6	5.46
404.9	0.32	404.9	0.39

Table IV. Coupling Constants for Barrelene, Norbornadiene, and Norbornene (All Values Are ±0.10 Hz)

	J_{12}	J_{13}	J_{23}
Barrelene	5.50	1.60	6.30
Norbornadiene	2.70	0.95	5.05
Norbornene	2.95	0.55	5.80

s Character of C–H Bonds of Barrelene. It was possible to obtain one further result from the ^{13}C satellite spectrum of barrelene. Both the upfield and downfield ^{13}C patterns of the bridgehead hydrogens were very complex and poorly resolved, but the coupling constant between ^{13}C and the bridgehead proton was easily obtained. The $J_{^{13}C-H}$ values for barrelene are given in Table V with literature values for norbornadiene and norbornene. By use of the relationship $\rho_{C-H} = 0.20J_{^{13}C-H}$ derived by Muller and Pritchard[25] for nonionic bonds, we obtained the per cent s character of the C–H bonds of barrelene directly from the ^{13}C–H coupling constants. The values are given in Table VI, along with those of norbornadiene and norbornene.

Table V. $J_{^{13}C-H}$ for Barrelene, Norbornadiene, and Norbornene

	$J_{^{13}C-H}$, Hz: Barrelene	Norbornadiene	Norbornene
Olefinic positions	176 ± 1	172 ± 1[a]	166 ± 1[a]
Bridgehead positions	140 ± 1	146 ± 1[b]	142 ± 1[b]

[a] P. Laszlo and P. von R. Schleyer, *J. Amer. Chem. Soc.*, **86**, 1171 (1964). [b] K. Tori, R. Muneyuki, and H. Tanida, *Can. J. Chem.*, **41**, 3142 (1963).

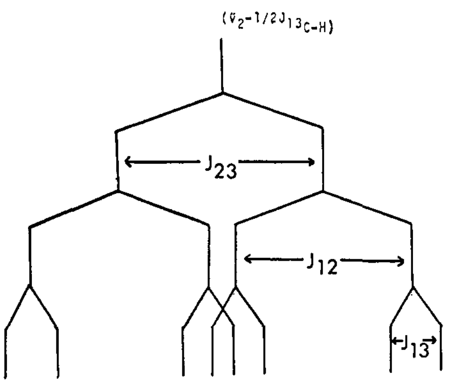

Figure 8. First-order treatment of the downfield ^{13}C vinyl pattern for barrelene: J_{12} = 5.50, J_{23} = 6.30, and J_{13} = 160 Hz.

Table VI. Per Cent s Character of C–H Bonds of Barrelene, Norbornadiene, and Norbornene

	% s character: Olefinic C–H bond	% s character: Bridgehead C–H bond
Barrelene	35	28
Norbornadiene	34	29
Norbornene	33	28

Experimental Section[26]

Coumalic Acid. This was prepared by the method of Wiley and Smith,[27] except that very thorough washing with large volumes (1 l./100 g) of ice water was necessary. The tan solid, mp 186–205° (57% after drying for 3 days at 50°), could be used directly for large-scale preparative runs without crystallization.

α-Pyrone. The following is an improved modification[28] of the procedure we reported earlier.[29] In a typical preparative run 1060 g (7.58 mol) of finely powdered, crude coumalic acid was placed in a 30 × 10 cm cylindrical flask, attached vertically to a constricted tube fitted with a four-bladed paddlewheel powder-stopcock, and fitted directly onto a 55 × 3 cm Vycor tube passing through a vertical high-temperature oven (Lindberg Model CF-IR high-temperature combustion furnace) with a 22-cm heating zone. The Vycor tube was loosely packed with *ca.* 15 g of Baker Light Copper (CP) turnings in the hot zone and with a *ca.* 25-mm layer of 6-mm Berl saddles held just above the hot zone by a copper wire spiral. The Vycor tube was attached vertically to a 1-l. ice-cooled flask by an adapter with vacuum takeoff and also bearing a 2-l. flask serving as a gas-surge resorvoir. Following the ice trap were two Dry Ice traps and a large-volume vacuum pump. The system was evacuated and the oven maintained at 650–675°; the coumalic acid was dropped directly onto the Berl

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[24] (a) A. A. Bothner-By and C. Naar-Colin, *J. Amer. Chem. Soc.*, **83**, 231 (1961). We thank Professor Bothner-By for supplying the original Frequint IV program. (b) The modification involved replacement of the relatively slow Jacobi diagonalization routine by a Householder–Wilkinson process, dimensioning the program to handle eight-spin systems and necessary changes to decrease computer storage requirements.

[25] N. Muller and D. E. Pritchard, *J. Chem. Phys.*, **31**, 1471 (1959).

[26] All melting points were taken on a hot-stage apparatus calibrated with known samples.

[27] R. Wiley and N. Smith, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1963, p 201.

[28] We acknowledge helpful suggestions by Dr. W. Roth which led us to use a vertical arrangement.

[29] H. E. Zimmerman, G. L. Grunewald, and R. M. Paufler, *Org. Syn.*, **46**, 101 (1966).

saddles at such a rate as to keep the pressure below 10 mm. The deep yellow α-pyrone was collected in the ice trap and distilled (bp 83° (2.6 mm)) to afford 465 g (4.844 mol) of colorless α-pyrone (63.9%).

Diels–Alder Reaction of α-Pyrone and Methyl Vinyl Ketone. A stirred solution of 162 g (1.686 mol) of α-pyrone and 486 g of (6.93 mol) of methyl vinyl ketone was heated at reflux for 69.5 hr at which time the internal temperature had risen to 157°. Distillation of the yellow product at *ca.* 15 mm afforded a small amount of low-boiling material. Further distillation at 0.07 mm gave: fraction 1, 116 g of colorless oil, bp 25–90°; 2, 27 g of yellow oil, bp 112°; 3, 213 g of light yellow oil, bp 121°; 4, 158 g of light yellow oil, bp 124°. All four fractions were seeded with the solid isomer from an earlier run and were kept at 5° for 4 days. The 5,7-*endo,endo*-diacetylbicyclo[2.2.2]-2-octene which had crystallized out of fractions 3 and 4 was filtered and recrystallized from benzene–hexane, to afford 60.5 g (0.315 mol, 18.8%), mp 85–87°. A sample was recrystallized to mp 90–91° (lit.[2] 85–86°); nmr (CCl_4) τ 3.96 (symmetrical quartet, 2 H, =CH), 7.03 (m, 2 H, bridgeheads), 7.41 (septet, 2 H, -C*H*COCH$_3$), 7.97 (s, 6 H, -COCH$_3$), 8.23 (broad d, 2 H, 2 H of CH$_2$'s), and 8.37 (t, 2 H, 2 H of CH$_2$'s).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.95; H, 8.31.

To 7.0 ml of a solution of 0.40 g of 2,4-dinitrophenylhydrazine and 1.0 ml of 6 *N* hydrochloric acid in 40 ml of methanol was added 0.13 g of 5,7-*endo,endo*-diacetylbicyclo[2.2.2]-2-octene, mp 85–87°. The resulting solid recrystallized from chloroform–hexane yielded 0.36 g of bis-3,4-dinitrophenylhydrazone, mp 238–239°.

Anal. Calcd for $C_{24}H_{24}N_8O_8$: C, 52.17; H, 4.35; N, 20.29. Found: C, 51.85; H, 4.38; N, 20.46.

Epimerization of Diacetylbicyclo[2.2.2]-2-octene Isomers. A solution of 50.0 g of the residual oil from which 5,7-*endo,endo*-diacetylbicyclo[2.2.2]-2-octene had crystallized was treated with sodium methoxide solution prepared from 700 ml of methanol and 1.5 g of freshly cut sodium. The mixture was stirred for 4.5 hr, neutralized to pH 6 with 5% hydrochloric acid, added to 250 ml of saturated sodium chloride solution, and ether extracted. The dried extracts were concentrated *in vacuo* to give 22.5 g of brown oil.

A 5.25-g sample of this oil was distilled on a spinning-band column (0.05 mm): fraction 1, 1.147 g, bp 102.5°; 2, 1.040 g, bp 102.5–103.2°; 3, 0.780 g, bp 103.2°; 4, 0.768 g, bp 104°; 5, 0.389 g, bp 106–111°; and 6, 0.226 g, bp 111.5–113°. Fractions 5 and 6 gave crystals which were shown to be 5,7-*endo,endo*-diacetylbicyclo[2.2.2]-2-octene by melting point, ir spectra, and formation of dioxime identical with authentic material. Fractions 1 and 2 consisted of one compound whose ir and nmr showed it to be a different diacetylbicyclo[2.2.2]-2-octene isomer. Fractions 3 and 4 were a mixture of the two isomers; nmr of fraction 1 (CCl_4) τ 3.80 (further split quintet, 2 H, =CH), 6.7–7.7 (m, 4 H, bridgeheads and CHCOCH$_3$), 7.83 (s, 3 H, COCH$_3$), 7.99 (s, 3 H, COCH$_3$), 8.15–8.75 (m, 4 H, CH$_2$).

Dioxime of 5,7-*endo,endo*-Diacetylbicyclo[2.2.2]-2-octene. A mixture of 15.0 g (0.078 mol) of 5,7-*endo,endo*-diacetylbicyclo-[2.2.2]-2-octene, mp 88–89°, 12.0 g (0.17 mol) of hydroxylamine hydrochloride, and 12.0 g (0.113 mol) of anhydrous sodium carbonate in 400 ml of 47% aqueous ethanol was refluxed for 30 min. The dioxime was precipitated with 250 ml of water and cooling to 0°; filtration and thorough washing with ice water afforded 17.0 g (98%) of 5,7-*endo,endo*-diacetylbicyclo[2.2.2]-2-octene dioxime, mp 232.5–233.5° (lit.[2] 229–230°).

5,7-*endo,endo*-Diacetylbicyclo[2.2.2]-2-octene Dioxime Di-*p*-toluenesulfonate. To a solution of 10.0 g (0.25 mol) of sodium hydroxide and 12.5 (0.0564 mol) of 5,7-*endo,endo*-diacetylbicyclo-[2.2.2]-2-octene dioxime, mp 230°, in 200 ml of water and 150 ml of acetone at 5° was added 22.0 g (0.109 mol) of *p*-toluenesulfonyl chloride in 50 ml of acetone with stirring. Ten minutes later 400 ml of ice–water was added and the mixture stirred for 30 min. Filtration afforded 25.0 g (83.8%) of di-*p*-toluenesulfonate, mp 139–140°. Recrystallization from acetone–water gave mp 143–144°.

Anal. Calcd for $C_{26}H_{30}O_6N_2S_2$: C, 58.95; H, 5.64; N, 5.36. Found: C, 58.14; H, 5.62; N, 5.28.

Beckmann Rearrangement of 5,7-*endo,endo*-Diacetylbicyclo-[2.2.2]-2-octene Dioxime Di-*p*-toluenesulfonate. A solution of 24.5 g (0.462 mol) of the di-*p*-toluenesulfonate, mp 144°, and 25.0 g (0.298 mol) of sodium bicarbonate in 500 ml of water and 500 ml of dioxane (Spectral Grade) was refluxed for 2 hr. The mixture was concentrated *in vacuo* and the residue exhaustively extracted with hot chloroform. Concentration afforded 5.2 g of oily solid, which was washed with acetone and recrystallized from absolute ethanol, to give 3.3 g (27.8%) of 5,7-*endo,endo*-diacetamidobicyclo-[2.2.2]-2-octene, mp 260–261°. Better yields were obtainable by avoiding isolation of the intermediate unstable ditosylate.

Anal. Calcd for $C_{12}H_{18}N_2O_2$: C, 64.91; H, 8.10; N, 12.61. Found: C, 64.69; H, 7.98; N, 12.41.

5,7-*endo,endo*-Diacetamidobicyclo[2.2.2]-2-octene. A solution of 50.0 g (0.225 mol) of 5,7-*endo,endo*-diacetylbicyclo[2.2.2]-2-octene dioxime, mp 230–232°, and 40.0 g (1.0 mol) of sodium hydroxide in 500 ml of acetone and 700 ml of water was cooled to 5°, and 88.0 g (0.46 mol) of *p*-toluenesulfonyl chloride in 250 ml of acetone was added over 30–60 min to keep the temperature below 10°. After an additional 10 min, 1.5 l. of ice–water was added, the mixture stirred for 45 min, and the di-*p*-tosylate filtered, washed with cold water, and added while still damp to 1.3 l. of dioxane, 1.3 l. of water, and 104 g of sodium bicarbonate. The mixture was refluxed for 1.5 hr, cooled, neutralized with 5% hydrochloric acid, and concentrated *in vacuo* below 40°. The residue was exhaustively extracted with hot chloroform; concentration afforded an oily solid, which was washed with acetone and sublimed *in vacuo*, to yield 26.1 g (52.2%) of 5,7-*endo,endo*-diacetamidobicyclo[2.2.2]-2-octene, mp 256–262°. The compound was recrystallized from 95% ethanol–acetone to mp 268–269° (lit.[2] 260–261°).

Beckmann Rearrangement Using Benzenesulfonyl Chloride.[30] A solution of 2.00 g (0.008 mol) of 5,7-*endo,endo*-diacetylbicyclo-[2.2.2]-2-octene dioxime, 3.34 g (0.0189 mol) of benzenesulfonyl chloride, and 1.4 g of sodium hydroxide in 10 ml of water and 40 ml of acetone was refluxed for 4.25 hr. The solution was neutralized with 5% hydrochloric acid and concentrated *in vacuo* at 30°. The residue was exhaustively extracted with hot chloroform. The chloroform was removed by distillation and the residue washed with acetone, to give 0.50 g (25%) of 5,7-*endo,endo*-diacetamidobicyclo[2.2.2]-2-octene, mp 235–242°.

5,7-*endo,endo*-Diaminobicyclo[2.2.2]-2-octene. A suspension of 10.0 g (0.045 mol) of 5,7-*endo,endo*-diacetamidobicyclo[2.2.2]-2-octene, mp 256–262°, in 435 g of 33% sodium hydroxide solution was stirred and refluxed under nitrogen for 69 hr. The solution was ether extracted and dried, and the ether carefully removed by distillation with a Vigreux column, leaving 6.0 g (97%) of 5,7-*endo,endo*-diaminobicyclo[2.2.2]-2-octene, which was used immediately for the next step; nmr ($CDCl_3$) τ 3.70 (quartet, 2 H, CH=), 7.07 (doublet of triplets, 2 H, C*H*NH$_2$), 7.53 (m, 2 H, bridgehead), 8.06 (m, 2 H, *exo*-H of CH$_2$'s), 8.88 (s, 4 H, NH$_2$), and 9.14 (doublet of triplets, 2 H, *endo*-H of CH$_2$'s).

Quaternization of 5,7-*endo,endo*-Diaminobicyclo[2.2.2]-2-octene. A solution of 6.0 g (0.043 mol) of 5,7-*endo,endo*-diaminobicyclo-[2.2.2]-2-octene in 250 ml of anhydrous methanol was refluxed with protection from carbon dioxide by a sodium hydroxide tube. Then 186 g (1.31 mol) of methyl iodide and 7.2 g (0.18 mol) of sodium hydroxide pellets were added in portions over 3.0 hr. The mixture was concentrated *in vacuo* and the residue (44 g) chromatographed on a 4.0 × 90 cm silica gel (Davidson 60–200 mesh) column slurry packed with 1:1 benzene–methanol. The mixture was applied to the column in *ca.* 3 ml of water and 50 ml of methanol. The sodium iodide was eluted with 4.5 l. of 1:1 benzene–methanol, and 5,7-bis(trimethylammonium)bicyclo[2.2.2]-2-octene diiodide subsequently was eluted with 5 l. of methanol. The compound could be recrystallized from methanol and did not melt below 350°.

Anal. Calcd for $C_{14}H_{28}N_2I_2$: C, 35.18; H, 5.85; N, 5.85. Found: C, 34.95; H, 5.73; N, 5.68.

Bicyclo[2.2.2]-2,5,7-octatriene. Freshly prepared silver oxide, formed by mixing aqueous solutions of 21.0 g (0.123 mol) of silver nitrate and 5.5 g (0.137 mol) of sodium hydroxide, was filtered, thoroughly washed with water, and transferred with 25 ml of water to a stirred solution of 12.50 g (0.0262 mol) of 5,7-*endo,endo*-bis(trimethylammonium)bicyclo[2.2.2]-2-octene diiodide in 75 ml of water. The flask was stoppered with a sodium hydroxide carbon dioxide exclusion tube and heated for 30 min at 50°, after which the mixture was filtered and the solid residue washed with water. The combined aqueous solution was concentrated *in vacuo* at 30° to *ca.* 10 ml followed by heating with stirring at *ca.* 20 mm in a flask connected to two Dry Ice traps in series. When water distillation was completed, the temperature was slowly raised to 120° (0.5 mm) and material collected in the

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(30) R. F. Brown, N. M. van Gulick, and G. H. Schmid, *J. Amer. Chem. Soc.*, 77, 1094 (1955).

Dry Ice traps. The products were ether extracted, dried, and concentrated to *ca.* 5 ml with a 25 cm × 15 mm Helipak column. Preparative vpc on a 200 × 2.5 cm column packed with 15% Apiezon L on Chromosorb P (acid washed, 60–80 mesh) at 100° and 20 psi of helium afforded 2.064 g (76%) of bicyclo[2.2.2]-2,5,7-octatriene and 58 mg of benzene (identified by vpc retention time and ir spectral comparison with an authentic sample). The retention times for benzene and barrelene were 3.25 and 9.9 min. On a 200 × 0.65 cm analytical column packed with 15% Ucon oil LB 550X on Chromosorb P at 76° and 20 psi of helium retention times were 6 and 27 min, respectively. Spectral data for bicyclo-[2.2.2]-2,5,7-octatriene were: ir (neat) 3.26, 3.35, 6.21, 6.35, 7.50, 8.23, 9.22, 9.81, 11.12, 12.35, and 14.38 μ; nmr (neat) τ 3.37 (sextet, 6 H, CH=), 5.40 (m, 2 H, bridgehead); uv max (ethanol) 208 (ϵ 1120) and 239 nm (ϵ 320).

A ^{13}C nmr spectrum (neat) was obtained by high attenuation and very rapid sample spinning, using a Varian A-60A spectrometer. For the vinyl pattern, eight lines were observed, centered at ±88 Hz from the 398-Hz proton pattern, giving a value of $J_{^{13}C-H} = 176 \pm 1$ Hz. The bridgehead pattern was a complex multiplet, centered at ±70 Hz from the 276-Hz proton pattern, yielding a value of $J_{^{13}C-H} = 140 \pm 1$ Hz. First-order analysis of the downfield ^{13}C-vinyl pattern afforded: $J_{23} = 6.30 \pm 0.10$ Hz, $J_{12} = 5.50 \pm 0.10$ Hz, and $J_{13} = 1.60 \pm 0.10$ Hz.

Anal. Calcd for C_8H_8: C, 92.30; H, 7.70. Found: C, 92.60; H, 7.73.

Diels–Alder Addition of Methyl Acrylate to α-Pyrone. A solution of 235.6 g (2.45 mol) of freshly distilled α-pyrone, 453 g (5.39 mol) of methyl acrylate, and 5.0 g of hydroquinone was stirred and refluxed for 116 hr. At this time the temperature had risen from 92 to 178°, and the mixture was deep yellow. Distillation afforded a small amount of material boiling below 90° (1 mm), and 475 g of colorless oil was collected at 106° (0.2 mm). Crystals formed in the oil immediately, and the 5,7-*endo,endo*-dicarbomethoxybicyclo[2.2.2]-2-octene was collected and crystallized from ether–hexane, to give 146.5 g (0.653 mol, 26.7%), mp 93.5–94°. The spectral data were: ir (KBr) 3.26, 3.36, 3.39, 3.46, 5.80, 6.94, 7.25, 7.35, 7.59, 8.00, 8.30, 9.40, 11.15, 13.05, and 14.30 μ; nmr ($CDCl_3$) τ 3.82 (m, 2 H, CH=), 6.38 (s, 6 H, CO_2CH_3), 7.00 (m, 2 H, bridgehead), 7.40 (triplet of doublets, 2 H, $CHCO_2CH_3$), 8.25 (m, 4 H, CH_2).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.27; H, 7.00.

5,7-*endo,endo*-Dicarbomethoxybicyclo[2.2.2]-2-octene Dihydrazide. To a stirred solution of 6.673 g (0.0298 mol) of 5,7-*endo,endo*-dicarbomethoxybicyclo[2.2.2]-2-octene in 20 ml of absolute ethanol was added 6.0 ml of 99–100% hydrazine hydrate. After 30 min at room temperature the solution was refluxed for 10 hr and concentrated *in vacuo*, to give 6.50 g of 5,7-*endo,endo*-dicarbomethoxybicyclo[2.2.2]-2-octene dihydrazide, mp 202–206° (97.4%). The product was recrystallized with 95% ethanol to mp 229.5–230.5°. The spectral data were: ir (KBr) 3.03, 3.27, 3.41, 6.10, 6.28, 6.61, 6.93, 7.26, 7.50, 7.85, 7.97, 9.04, and 14.07 μ.

Anal. Calcd for $C_{10}H_{16}N_4O_2$: C, 53.56; H, 7.22; N, 24.98. Found: C, 53.70; H, 7.34; N, 24.60.

5,7-*endo,endo*-Diaminobicyclo[2.2.2]-2-octene Dihydrochloride.[31] To a solution of 20.0 g (0.0892 mol) of 5,7-*endo,endo*-dicarbomethoxybicyclo[2.2.2]-2-octene dihydrazide, 3.4 ml (0.190 mol) of 6 *N* hydrochloric acid, 440 ml of water, and 550 ml of ether cooled to 0°, a solution of 12.30 g (0.1784 mol) of sodium nitrite in 110 ml of water was added at a rate to keep the temperature below 5°. After 5 min the solution of the diazide was separated, the aqueous layer washed with ether and the combined ethereal solution washed with 150 ml of saturated sodium bicarbonate solution, then with 250 ml of water, and dried at 0°. The ether solution was added to 1 l. of dry benzene and the ether removed by distillation under dry nitrogen. After addition of 40 g of molecular sieve (Linde, Type 4A, activated at 400°), the benzene solution was refluxed with stirring for 16 hr. The mixture was filtered directly into 500 ml of rapidly stirred, concentrated hydrochloric acid and diluted with 500 ml of water. Concentration of the aqueous layer afforded 26 g (69.7%) of 5,7-*endo,endo*-diaminobicyclo-[2.2.2]-2-octene dihydrochloride which could be used directly or recrystallized from methanol–isopropyl alcohol. The dihydrochloride did not melt below 320°; nmr (D_2O) τ 3.60 (quartet, 2 H, CH=), 6.54 (m, 2 H, $CHNH_3Cl$), 7.11 (m, 2 H, bridgehead), 7.88 (octet, 2 H, *exo*-H of CH_2's), and 8.81 (doublet of triplets, 2 H, *endo*-H of CH_2's).

Quaternization of 5,7-*endo,endo*-Diaminobicyclo[2.2.2]-2-octene formed *in situ*. A solution of 10.0 g (0.48 mol) of 5,7-*endo,endo*-diaminobicyclo[2.2.2]-2-octene dihydrochloride and 9.2 g of sodium hydroxide in 22 ml of water was stirred under nitrogen. An nmr sample was taken of the colorless oil, and it was identical with that of 5,7-*endo,endo*-diaminobicyclo[2.2.2]-2-octene obtained from the original synthesis, thus confirming the stereochemistry of this synthetic variation. When the mixture became clear, 250 ml of methanol was added. The solution was refluxed and 186 g (1.31 mol) of methyl iodide was added over 3 hr. The mixture was refluxed for 6 additional hr, cooled, and concentrated *in vacuo*. The residue was chromatographed on a 4.0 × 90 cm silica gel (Davidson 60–200 mesh) column slurry packed with 1:1 benzene–methanol. The mixture was applied to the column in 60 ml of methanol. The sodium iodide was eluted with 4.5 l. of 1:1 benzene–methanol, and subsequent elution with 5 l. of methanol afforded 7.72 g (0.0161 mol, 33.8%) of 5,7-bis(trimethylammonium)-bicyclo[2.2.2]-2-octene diiodide.

Bromination of Bicyclo[2.2.2]2,5,7-octatriene. In 5.0 ml of carbon tetrachloride, 0.118 g (13 mmol) of bicyclo[2.2.2]-2,5,7-octatriene was titrated with 1.410 ml of 0.001285 *M* bromine in carbon tetrachloride with no evidence of HBr being given off. Concentration *in vacuo* gave 0.298 g (95.5%) of residue, which was chromatographed on a 2.5 cm × 45 mm column slurry packed with silica gel and hexane. Elution with 100-ml fractions gave the following: fractions 1–4, hexane, nil; 5–10, 5% benzene in hexane, 60 mg of an oil; 11–14, 10% benzene in hexane, 188 mg of solid, mp 132–133°; 15–18, methanol, 50 mg of unidentifiable material. The 5,8-*exo,exo*-dibromotricyclo[2.2.2.0^{6,7}]-2-octene was recrystallized from benzene–methanol to mp 133.5–134.5°; nmr (CS_2) τ 3.92 (m, 1 H, CH=), 4.41 (m, 1 H, CH=), 5.83 (d, 2 H, HCBr), 6.91 (m, 1 H, bridgehead), and 8.00 (m, 3 H, cyclopropyl).

Anal. Calcd for $C_8H_8Br_2$: C, 36.42; H, 3.04. Found: C, 36.34; H, 2.93.

For the oil from fractions 5–10 nmr (CS_2) τ 3.69 (broad m, 2 H, CH=), 5.25 (m, 1 H, HCBr), 6.47 (s, 1 H, HCBr), 7.23 (m, 1 H, bridgehead), and 8.08 (m, 3 H, cyclopropyl).

Anal. Calcd for $C_8H_8Br_2$: C, 36.42; H, 3.04. Found: C, 36.63; H, 2.95.

Hydrogenation of Bicyclo[2.2.2]-2,5,7-octatriene. A 0.125-g (12 mmol) sample of bicyclo[2.2.2]-2,5,7-octatriene was hydrogenated in 6.00 ml of absolute ethanol, using 0.0125 g of platinum dioxide catalyst. A total of 88.0 cm^3 (21°, 740 mm) of hydrogen was taken up at the constant rate of 3.2 cm^3 min^{-1} (92% of theory). The solution was filtered and treated with water to give 0.0877 g of precipitate, mp 166–167°. Preparative vpc gave 1 peak, and bicyclo[2.2.2]-octane was collected, mp 171–172° (lit.[15] 172°); ir (CS_2) 3.46, 3.53, 7.88, 10.10, 11.50, 12.19, and 12.50 μ.

Pyrolysis of Bicyclo[2.2.2]-2,5,7-octatriene. In a sealed Pyrex tube, 0.0952 g (0.915 mmol) of bicyclo[2.2.2]-2,5,7-octatriene was heated at 200° for 24 hr. The products were subjected to preparative vpc on a 200 × 2.5 cm column packed with tricresyl phosphate at 81° and gave 70 mg (71% recovery) of bicyclo[2.2.2]-2,5,7-octatriene and two very minor peaks, of which one showed the same retention time as benzene.

A 0.159-g sample of bicyclo[2.2.2]-2,5,7-octatriene was heated at 250° for 24 hr in a sealed Pyrex tube. The tube was broken and the gas produced collected in a liquid nitrogen trap. Analytical vpc on a 500 cm × 4 mm column packed with tricresyl phosphate at 24° showed acetylene, identified by the retention time of authentic material. Preparative vpc (tricresyl phosphate at 80°) on the liquid pyrolysis products gave one peak, and collection gave 0.101 g (89.3%) of benzene, which was identified by comparison of ir spectrum and vpc retention time with an authentic sample.

Configuration Interaction Calculations. By use of Prentiss–Hall Molecular Framework models, the relative positions and orientation of orbitals χ_2, χ_5, and χ_6 were measured. By use of solid analytic geometry, the following equations were derived.

$$\beta_{26} = {}^1/_4 H_{ab}(\sigma,\sigma) + {}^3/_4 H_{ab}/(\pi,\pi)$$

$$\beta_{25} = {}^1/_4 H_{ab}(\sigma,\sigma) + 0.559 H_{ab}(\pi,\pi)$$

$$\gamma_{26} = {}^1/_{16} G_{ab}(\sigma,\sigma) + {}^3/_8 G_{ab}/(\sigma,\pi) + {}^9/_{16} G_{ab}(\pi,\pi)$$

$$\gamma_{25} = {}^1/_{16} G_{ab}(\sigma,\sigma) + {}^3/_8 G_{ab}(\sigma,\pi) + 0.4374 G_{ab}(\pi,\pi) + {}^1/_{16} G_{ab}(\pi,\pi')$$

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[31] (a) P. A. S. Smith in "Organic Reactions," Vol. III, R. Adams, Ed., John Wiley & Sons, Inc., New York, N. Y., 1947, Chapter 9; (b) H. E. Zimmerman and M. D. Traxler, *J. Amer. Chem. Soc.*, 79, 1923 (1957).

The basic resonance integrals were taken in the ratio given by Kopineck's Tables.[32] For the repulsion integrals, both a point charge approximation[33] and the Kopineck values were tried.

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[32] V. H. J. Kopineck, *Z. Naturforsch.*, *A*, 5, 420 (1950).

[33] We find that the atomic positions are too close for the point charge approximation to give optimum results for repulsion integrals.

Pyrroles from Azaindoles. A Synthesis of Porphobilinogen and Related Pyrroles[1,2]

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Abstract: A new method for the synthesis of 2-aminomethyl-3-pyrroleacetic acids is described. The condensation of 2-methoxy- and 2-benzyloxy-4-methyl-5-nitropyridine with diethyl oxalate afforded the corresponding ethyl *o*-nitropyridinepyruvates, which on hydrogenation were transformed into the substituted ethyl 6-azaindole-2-carboxylates. Cleavage of the ethers and hydrogenation of the resulting pyrrolopyridones yielded the corresponding carboxypyrrole lactams which on decarboxylation and hydrolysis gave the 2-aminomethyl-3-pyrroleacetic acids. Substitution at the C-3 position of the 6-azaindole with a propionic acid and acetic acid side chain and repetition of the above sequence gave porphobilinogen and 2-aminomethyl-3,4-pyrrolediacetic acid.

In 1952, Westall[4] isolated from the urine of a porphyric patient a pyrrole which he called porphobilinogen and whose structure (XXVIII) was established by Cookson and Rimington.[5] This pyrrole proved to be the only direct biosynthetic precursor of uroporphyrinogen III in the common biosynthetic pathway to heme and chlorophylls. Its transformation into uroporphyrinogen III is an enzymic reaction whose mechanism is still not understood; its acid-catalyzed chemical polymerization results in a mixture of all four possible uroporphyrins[6] after oxidation. Important structural features of porphobilinogen are the 2-aminomethyl group which provides the *meso* carbons of the resulting porphyrinogens and the 3-acetic acid group which can influence the reactivity of the 2-aminomethyl group. The work now being reported was undertaken in order to develop a facile and practical synthesis of pyrroles containing these structural features.

Porphobilinogen (XXVIII) has been the subject of several syntheses in the past both to prove its structure[7,8] and to obtain it in preparative amounts.[9,10] All these syntheses made use of the classical Knorr synthesis of pyrroles and resulted in very poor over-all yields, the best of them[10] being around 1%. We sought a new synthetic procedure for this type of pyrrole and based our approach on the observation that porphobilinogen is easily and reversibly transformed into its lactam (XXV). The lactam may be considered as the α-piperidone form of a suitably substituted pyrrolo[2,3-*c*]pyridine (6-azaindole). The problem was to develop a good general synthesis for 5-substituted 6-azaindoles, which could then be transformed into α-pyridones and reduced to the corresponding α-piperidones.

Azaindoles form a relatively little studied heterocyclic system for which the best ring syntheses require such drastic reaction conditions that the synthesis of substituted azaindoles with sensitive groups cannot be achieved.[11] In the specific case of the synthesis of 6-azaindoles the literature presents very few examples. 2-Methyl-6-azaindole was prepared[11a,12] by a Madelung-type cyclization of acetyl- and diacetyl-3-amino-4-picoline which included an alkaline fusion at 300°. 6-Azaindole and 7-methyl-6-azaindole have been prepared[13] by a Pomerantz–Fritsch-type reaction on

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[1] A preliminary account of this work has been published: B. Frydman, M. E. Despuy, and H. Rapoport, *J. Am. Chem. Soc.*, 87, 3530 (1965).

[2] This research was supported in part by the Consejo Nacional de Investigaciones de la República Argentina and by the National Institutes of Health (Grants GM-11973 and AI-04888).

[3] Fellow of the Consejo Nacional de Investigaciones de la República Argentina, 1964–1966.

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[11] For a brief evaluation of various syntheses of azaindoles prior to 1960 see T. K. Adler and A. Albert, *J. Chem. Soc.*, 1794 (1960). Recent azaindole ring syntheses are (a) Madelung type: W. Hertz and D. R. K. Murty, *J. Org. Chem.*, 25, 2242 (1960); J. Reisch, *Ber.*, 97, 2717 (1964); A. Albert and R. E. Willette, *J. Chem. Soc.*, 4063 (1964); R. R. Lorenz, B. F. Tullar, C. F. Koelsch, and S. Archer, *J. Org. Chem.*, 30, 2531 (1965); (b) *via* hydrazones: G. E. Ficken and J. D. Kendall, *J. Chem. Soc.*, 3202 (1959); 584 (1961); A. H. Kelly, D. H. MacLeod, and J. Parrick, *Can. J. Chem.*, 43, 296 (1965); A. H. Kelly and J. Parrick, *ibid.*, 44, 2455 (1966); G. Tacconi and A. Perotti, *Ann. Chim.* (Rome), 55, 810, 1223 (1965); (c) *via* haloalkylpyridines: L. N. Yakhontov, M. Ya. Uritskaya, and M. V. Rubstov, *Zh. Obshch. Khim.*, 34, 1449, 1456 (1964); *Khim. Geterotsikl. Soedin., Akad. Nauk Latv. SSR*, 918 (1965); L. N. Yakhantov and M. V. Rubstov, *Zh. Obshch. Khim.*, 32, 432 (1962).

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