sulting crystalline mass (35 mg, 96%) was identical with that of authentic **2**;[4] none of the 5′*R* isomer **1** was detected, even with the very high signal-to-noise ratio resulting from prolonged spectral accumulation.

**6,5′(*S*)-Cyclo-1-(*β*-D-xylofuranosyl)uracil (16) and 6,5′(*R*)-Cyclo-1-(*β*-D-xylofuranosyl)uracil (14).** Sodium cyanoborohydride (40 mg, 0.64 mmol) was added to a suspension of **11** (150 mg, 0.53 mmol) in a mixture of water, acetic acid, and methanol (1:1:1, 6 mL). The mixture was stirred and warmed briefly to ~40 °C to effect dissolution and then cooled to room temperature. The reduction was monitored by the disappearance of the 310-nm peak of **11** and the appearance of absorption at 268 nm, a process that was complete after ~3.5 h. The solution was deionized by passage through an excess of Dowex 50 ($H^+$), the eluate and washings were concentrated to dryness, and methanol was repeatedly evaporated from the residue. The NMR spectrum ($Me_2SO$-$d_6$) of the residue showed compounds **14**/**16** in a ratio of 1:5. Pure **14** (80 mg) was obtained by crystallization of the residue from hot 80% ethanol: mp 246–248 °C; UV $\lambda_{max}$ ($H_2O$) 268 nm, $\lambda_{min}$ 233 nm; $\lambda_{max}$ (pH 9) 266 nm, $\lambda_{min}$ 241 nm.

Anal. Calcd for $C_9H_{10}N_2O_6$ (mol wt 242.19): C, 44.63; H, 4.16; N, 11.57. Found: C, 44.56; H, 4.14; N, 11.47.

A further sample of **14** (30 mg) and pure **16** (10 mg) was obtained by fractionation of the residue by preparative TLC ($CH_2Cl_2$/MeOH, 8:1; triple development). Compound **16** crystallized from aqueous ethanol: mp 250–253 °C dec, darkens and shrinks above 230 °C; UV $\lambda_{max}$ ($H_2O$) 271 nm, $\lambda_{min}$ 237 nm; $\lambda_{max}$ (pH 10) 270 nm, $\lambda_{min}$ 245 nm.

Anal. Calcd for $C_9H_{10}N_2O_6$ (mol wt 242.19): C, 44.63; H, 4.16; N, 11.57. Found: C, 44.86; H, 4.14; N, 11.36.

**6,5′(*S*)-Cyclo-3′,5′-*O*-isopropylidine-1-*β*-D-xylofuranosyl)uracil (15).** A suspension of **16** (54 mg, 0.22 mmol) in acetone (3 mL) containing 15 mg of *p*-toluenesulfonic acid monohydrate and 0.1 mL of 2,2-dimethoxypropane was stirred rapidly at room temperature. The slow dissolution of **16** (~1 h) was followed by the appearance of crystalline **15**. After 3 h, the crystals (27 mg) were removed and washed with cold acetone. The filtrate was diluted with 0.1 mL of water, solid sodium bicarbonate was added, and the mixture was filtered. The filtrate was evaporated to dryness, and a solution of the residue in methanol was applied to a preparative TLC plate. After development (EtOAc), the appropriate zone was removed, the silica was extracted with ethyl acetate, and the filtrate was concentrated to dryness. Crystallization from 90% acetone afforded 20 mg (total yield 75%) of **15**: mp 265–266 °C, UV $\lambda_{max}$ ($H_2O$) 269.5 nm, $\lambda_{min}$ 233 nm; $\lambda_{max}$ (pH 10) 270 nm, $\lambda_{min}$ 243 nm.

Anal. Calcd for $C_{12}H_{14}N_2O_6$ (mol wt 282.25): C, 51.07; H, 5.00; N, 9.93. Found: C, 51.24; H, 5.05; N, 9.89.

**Registry No.**—**1**, 59728-02-8; **2**, 59686-60-1; **12**, 59686-58-7; acetic acid, 64-19-7; diazomethane, 334-88-3; methyl iodide, 74-88-4; phenylhydrazide, 100-63-0; 2,2-dimethoxypropane, 77-76-9.

## References and Notes

(1) This investigation was supported by funds from the American Cancer Society (Grant CH-38) and from the National Institute of Health, U.S. Public Health Service (Grant No. 17085, for NMR studies).

(2) This paper is the second in a series entitled Conformationally Restricted Analogues of Pyrimidine Nucleosides. For Part 1, see ref 4.

(3) Reviews that stress the relationship between nucleoside–nucleotide conformation and biological activity include the following: (a) D. C. Ward and E. Reich, *Annu. Rep. Med. Chem.*, 272 (1969); (b) W. Saenger, *Angew. Chem., Int. Ed. Engl.*, **12,** 591 (1973). For examples of the use of conformationally restricted nucleotides to investigate enzyme specificity see the following: (a) A. Hampton, P. J. Harper, and T. Sakai, *Biochemistry,* **11,** 4965 (1972); (b) A. Matsuda, M. Tezuka, and T. Ueda, *Nucleic Acids Res., Spec. Publ.,* **No. 2,** S 13 (1976); (c) J. Zemlicka, *J. Am. Chem. Soc.,* **97,** 5896 (1975).

(4) B. A. Otter, E. A. Falco, and J. J. Fox, *J. Org. Chem.,* **41,** 3133 (1976).

(5) The synthesis of 6,5′(*S*)- and 6,5′(*R*)-cyclocytidine will be reported in a subsequent paper.

(6) J. R. Parikh and W. von E. Doering, *J. Am. Chem. Soc.,* **89,** 5505 (1967).

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(8) R. Youssefyeh, D. Tegg, J. P. H. Verheyden, G. H. Jones, and J. G. Moffatt, *Tetrahedron Lett.,* 435 (1977). See also D. L. Leland and M. P. Kotick, *Carbohydr. Res.,* **38,** C9 (1974).

(9) It is not clear whether the C-3′ epimerization precedes or follows hydroxymethylation at C-4′ because the stability of uridine 5′-aldehyde alone in base was not reported. In either case, four initial products are possible since C-4′ can also epimerize, but this number is reduced to two (C-3′ epimers) because the subsequent Cannizzaro reaction removes the C-4′ asymmetry.

(10) Carbonyl hydration, and its effect on the UV spectrum, may be a common feature of 6-acylpyrimidines. Thus orotaldehyde (uracil 6-carboxaldehyde) absorbs in water (pH 1) at 261 nm ($\epsilon$ 8200), but it also shows a small shoulder at 300 nm ($\epsilon$ 700). On the basis of the above results, the 261-nm peak represents hydrated orotaldehyde, and the 300-nm peak can be attributed to the anhydrous form. In dioxane, orotaldehyde absorbs only at 300 nm. The literature value [K.-Y. Zee-Cheng and C. C. Cheng, *J. Heterocycl. Chem.,* **4,** 163 (1967)] for orotaldehyde is $\lambda_{max}$ (pH 1–7) 261 nm ($\epsilon$ 13 300), with no mention of 200-nm absorption. We could not reproduce the $\epsilon$ 13 300 value, but we feel that our figure of $\epsilon$ 8200 is more in line with the value reported by the same authors for thymine 6-carboxaldehyde ($\epsilon$ 7800). In MeSO-$d_6$, anhydrous orotaldehyde shows NMR signals at $\delta$ 9.56 (s, CHO) and 6.28 (dd, H-5, $J_{N_3H,5} = J_{N_1H,5} = 1.8$ Hz). In $D_2O$, the anhydrous form [$\delta$ 9.60 (s, CHO), $\delta$ 6.49 (s, H-5)] and the hydrated form [$\delta$ 5.92 (d, H-5, $J_{allylic} = 1$ Hz), $\delta$ 5.75 (d $CH(OD)_2$)] are present in a ratio of ~1:15.

(11) B. F. Borch, M. D. Bernstein, and H. D. Durst, *J. Am. Chem. Soc.,* **93,** 2897 (1971).

(12) H. O. House, "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, New York, N.Y., 1972, pp 58–59.

(13) All of the compounds described can be named as substituted 6,9-epoxypyrimido[1,6-*a*]azepines, but for ease of comparison with ordinary nucleosides we prefer the trivial 6,5′-cyclonucleoside designations used herein.

(14) The melting point depends on the rate of heating. Examination of the UV spectrum of the resolidified melt shows that partial rearrangement to xylo isomer **11** occurs. Similarly, *aged* solutions of **9** in $Me_2SO$-$d_6$–$D_2O$ rearrange to **11** on heating. In both cases, the reaction is probably catalyzed by alkali leached from the glass.

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# A Serendipitous Synthesis of 1,2,5,6-Tetramethyl-3,4,7,8-tetramethylenetricyclo[3.3.0.$0^{2,6}$]octane

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The title compound (**5**) can be prepared by photosensitized dimerization of 1,2-dimethyl-3,4-dimethylenecyclobutene (**1**) to *anti*-1,2,5,6-tetramethyl-3,4,7,8-tetramethylenetricyclo[4.2.0.$0^{2,6}$]octane (**2**), followed by flow system pyrolysis of **2** at 380 °C. At lower temperatures an intermediate, 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenecycloocta-1,5-diene (**3**), can be isolated. On direct or sensitized photolysis of **3**, **5** is also obtained. The photochemistry of **2** has been explored, and its fragmentation to **1** on direct irradiation is discussed. The photosensitized dimerization of **1** to **2** is also discussed and interpreted in favor of a frontier orbital model for predicting the products of such reactions.

As an intermediate in a proposed synthesis, we required 1,2:5,6-bis(ethano)cyclooctatetraene (**4**, R = H) or a simple derivative thereof. Attempts to convert 1,2:5,6-bis(ethano)cycloocta-1,5-diene[2] to the tetraene proved fruitless, and so we investigated the route to **4**, R = $CH_3$, shown in Scheme I. Our synthesis began with the photochemical dimerization of

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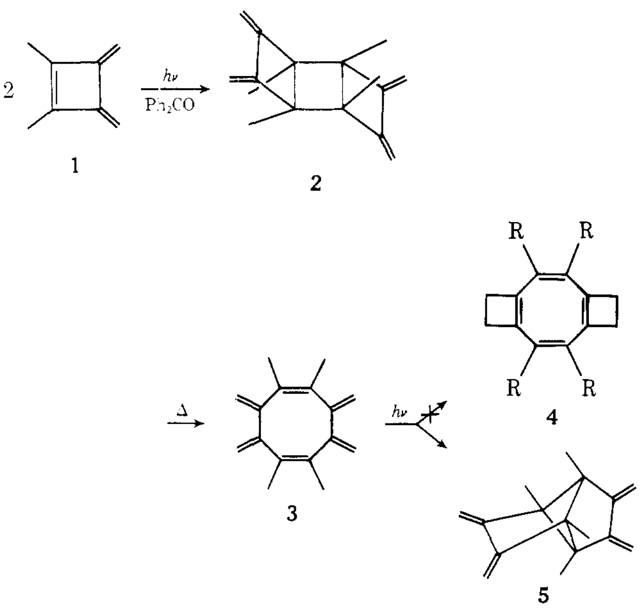
Scheme I

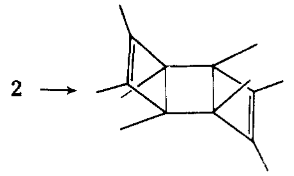


1,2-dimethyl-3,4-dimethylenecyclobutene (1).[3] Although this step and the next—the thermal cleavage of the photodimer (2) to 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenecycloocta-1,5-diene (3)—both proceeded successfully,[4] photolysis of 3 gave, instead of 4, 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenetricyclo[3.3.0.0$^{2,6}$]octane (5). While the failure of the last step precluded the utilization of Scheme I for the preparation of 4, this route did afford a serendipitous synthesis of 5, a compound whose chemistry[5] was to provide the key to understanding the chemical consequences of orbital interactions in compounds containing unsaturatively 1,3-bridged cyclobutane rings.[6] We report herein details of this synthesis of 5 and discuss the thermal and photochemical behavior of the intermediates.

## Results and Discussion

It was with some trepidation that we carried out the photosensitized dimerization of 1, since there are a total of nine products that might be reasonably expected to result from this reaction. Indeed, in the sensitized irradiation of 1,2-dimethylenecyclobutane three of the four possible dimers are obtained as primary photoproducts and the fourth is formed as the result of a Cope rearrangement of one of these, when purification of the dimer mixture by GLC is attempted.[2] However, the HOMO and, since 1 is an AH,[7] the LUMO of 1 both have coefficients of the largest magnitude at C-1 and C-2. Thus, it seemed reasonable to expect that upon sensitized photolysis of 1 the excitation would be localized principally at these atoms of the ring, rather than in the exocyclic double bonds. Moreover, frontier molecular orbital theory predicts ground state 1 to be most readily attacked at these ring carbons, again because both the HOMO and LUMO have coefficients of the largest magnitude at these atoms.[8] Therefore, there was some reason to hope that the photodimerization of 1 might be regioselective and lead principally to 2 or to its syn stereoisomer.

In the event, when 1 was irradiated through Pyrex in a benzene solution, containing sufficient benzophenone to absorb 99% of the light, a single dimeric product was obtained after chromatography of the crude photolysate over alumina. The $^1$H NMR spectrum of the crystalline product showed four equivalent methyl groups and four equivalent vinyl groups, thus indicating the gross structure 2 for the dimer. The stereochemistry was established as anti by reduction of the dimer to *anti*-octamethyltricyclo[4.2.0.0$^{2,5}$]octadiene (6), a reaction which could be carried out either by hydrogenation over a 5% Pd/C catalyst[9] or with lithium in ammonia–tetrahydrofuran–*tert*-butyl alcohol. The melting point (125 °C) of the reduction product was in good agreement with that (127 °C) reported for the *anti*-octamethyltricyclooctadiene (6)[10a] but not with that (196 °C) of the syn isomer.[10b] The $^1$H NMR spectrum of the reduction product in $CDCl_3$ showed two singlets of equal area at $\delta$ 0.91 and 1.56, in excellent agreement with the spectrum of an authentic sample of 6,[10c] but different from that of the syn compound ($\delta$ 0.99 and 1.49), which we prepared by the literature procedure[10b] for comparison.



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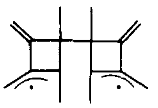
The structure of the photodimer (2) formed on sensitized irradiation of 1 is of some theoretical interest, for despite the steric hindrance afforded by the methyl groups attached to the endocyclic double bond of 1, the gross structure of 2 is in accord with the prediction based on analysis of the frontier MO's of 1. Usually, however, the products of sensitized photodimerization reactions are rationalized by the principle of formation of the most stable diradical intermediate.[11] For instance, in the sensitized photodimerization of dienes the most stable diradical is that which results from bonding between the terminal atoms of the excited triplet and the ground state diene. However, the formation of the same diradical is predicted by frontier orbital analysis, since the HOMO and LUMO of a diene have their largest coefficients at the terminal atoms. Although frontier orbital analysis and the principle of formation of the most stable diradical make the same prediction regarding the intermediate initially created by the sensitized photolysis of dienes (and, more generally, of linearly conjugated polyenes), these two models differ in their prediction of the diradical involved in the photosensitized dimerization of 1. As noted above, frontier orbital analysis predicts 7 to be the diradical intermediate in this reaction, while the more stable diradical is 8.[12] Thus, this reaction offers a test of the two different models, and from the product (2) actually obtained, it is apparent that the frontier MO model is the one that provides the correct prediction.



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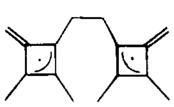

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While the frontier orbital model does correctly predict the regiochemistry of the dimer (2) formed from 1, it fails to anticipate the observed stereochemistry. Secondary orbital interactions should give rise to formation of the syn rather than the anti dimer, for maximum overlap of the lower and upper of the two singly occupied MO's in the excited molecule of 1 with, respectively, the HOMO and LUMO of the ground-state molecule, should favor a geometry leading to dimer with syn stereochemistry.[8] Presumably steric effects are responsible for formation of the anti dimer (2), and assuming that frontier orbital analysis provides the correct explanation of the dimer's regiochemistry, one concludes that secondary orbital interactions must be of lesser importance than such steric effects in the transition state for the photosensitized dimerization of 1.

Although the formation of 2 in this reaction was of theoretical interest for the reasons outlined above, the practical

**(b) At 380 °C to 1,2,5,6-Tetramethyl-3,4,7,8-tetramethylenetricyclo[3.3.0.0$^{2,6}$]octane (5).** A sample of **2** was pyrolyzed as described above, except that the temperature of the column was 380 °C. The NMR spectrum of the residue after solvent evaporation showed, in addition to a small amount of unresolved absorption in the aliphatic region, $\delta$ 0.70 (s, 12 H), 4.83 (s, 4 H), 5.48 (s, 4 H).

**(c) At 300 °C to a Mixture of 3 and 5.** A sample of **2** was pyrolyzed at 300 °C as described above. The NMR of the crude pyrolysate showed it to consist of an approximately 1:1 mixture of **3** and **5**. The products were separated by preparative GLC on a 0.375 in. × 10 ft column of 20% Carbowax 20 M on Chromosorb W. At 170 °C and a flow rate of 180 mL/min two peaks appeared with retention times of 10 and 17 min. These were collected and their NMR spectra were recorded. From the spectra the crystalline material with the shorter retention time was identified as **5** and the oily compound with the longer retention time as **3**. (Compound **5** appeared to polymerize at about 100 °C, so a melting point could not be determined). The UV spectrum (hexane) of **3** showed a single broad absorption with $\lambda_{max}$ 240 nm (log $\epsilon$ 4.1), while that of **5** showed fine structure with $\lambda_{max}$ 241 nm (log $\epsilon$ 4.0), 248 nm (log $\epsilon$ 4.1), and 259 nm (log $\epsilon$ 3.9). Exact masses calcd for $C_{16}H_{20}$: 212.1565. Found: 212.1586 for **3** and 212.1630 for **5**.

**(d) By Injection into a GLC Instrument.** Pure samples of **3** or **5** could be obtained by injection of **2** into a GLC instrument. At a column temperature of 160 °C **3** was the product collected. However, at 210 °C **5** was the principal product. The Carbowax column described above was used for preparing **3** in this way, while the SE-30 column was used for **5**.

**Pyrolysis of 3 to 5.** A sample of **3**, prepared by pyrolysis of **2** at 240 °C, was repyrolyzed in the flow system at 380 °C. The product was identified by NMR as **5**.

**Photolysis of 3 to 5. (a) Direct.** To a quartz NMR tube was added a solution of 20 $\mu$L of **3** in 0.5 mL of hexane. After degassing for 0.75 h, as described above, the solution was irradiated with a 450-W Hanovia high-pressure lamp for 0.5 h. Evaporation of the solvent left a slightly off-white crystalline solid, which was identified by NMR as **5**.

**(b) Sensitized.** To a Pyrex NMR tube was added a solution of 20 $\mu$L of **3** and 5 mg of benzophenone in 0.5 mL of benzene. After degassing for 1 h, the solution was irradiated through a Pyrex filter with a 450-W Hanovia high-pressure lamp. After 0.5 h the NMR spectrum showed clean and total conversion to **5**.

**Reduction of 5 with Lithium in Ammonia–Tetrahydrofuran-*tert*-Butyl Alcohol.** The reduction of 26 mg of **5** was carried out essentially as described above for **2**, except that the reaction was quenched by adding saturated ammonium chloride solution until the blue color was discharged before allowing the reaction mixture to warm. The product isolated was a colorless oil whose NMR spectrum ($CDCl_3$) showed a well resolved but complex series of sharp absorptions $\delta$ 0.8–1.2, a broad singlet with some fine structure $\delta$ 1.6, and a broad unresolved absorption $\delta$ 2.2–2.6. Integration gave the relative areas as 6:6:1. The mass spectrum of the product showed the molecular ion at $M^+/e$ 218, confirming the addition of three moles of hydrogen. Analytical GLC on a 0.25 in. × 10 ft column of 5% Carbowax 20 M at 100 °C and a flow rate of 60 mL/min showed three peaks with retention times 10.5, 13.6, and 15.7 min and relative areas of approximately 1:2:1.

**Reduction of Octamethylsemibullvalene (10).** A 40-mg sample of **10**[27a] prepared by the literature procedure[38] was reduced under the same conditions as **5**. The NMR and the mass spectrum of the product and its GLC trace were all superimposable upon those obtained from the product of the reduction of **5**.

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**Registry No.**—**1**, 25467-12-3; **2**, 34101-24-1; **3**, 33507-29-8; **5**, 34106-16-6; **6**, 20380-33-0; 3,4-dichlorotetramethylcyclobutene, 1194-30-5.

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(3) R. Criegee, *Angew. Chem., Int. Ed. Engl.*, **1**, 519 (1962).

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(8) W. C. Herndon, *Top. Curr. Chem.*, **46,** 141 (1974).

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(10) (a) R. Criegee, G. Schroder, G. Maier, and H. G. Fischer, *Chem. Ber.*, **93,** 1553 (1960); (b) R. Criegee and G. Louis, *ibid.*, **90,** 417 (1957). (c) We wish to thank Professor G. Schröder for locating a sample of **6** and Professor R. Askani for sending us its NMR spectrum.

(11) See, for example, N. Turro, "Molecular Photochemistry", W. A. Benjamin, New York, N.Y., 1967, p 216.

(12) The Hückel energy of the 2-vinylallyl radical is $-0.37\beta$ greater than that of the cyclobutadienylcarbinyl radical. The $\pi$ system of the former molecule can be viewed as resulting from the union of a vinyl group to C-2 of an allyl radical, while that of the latter comes from union at C-1 and C-3 of the allyl radical. The same perturbation argument that explains why union of a lone carbon at C-2 of allyl (leading to trimethylenemethane) is less favorable than union at C-1 and C-3 (leading to cyclobutadiene)[13] rationalizes this energy difference.

(13) W. T. Borden and E. R. Davidson, *J. Am. Chem. Soc.*, **99,** 4587 (1977).

(14) H.-D. Martin and E. Eisenmann, *Tetrahedron Lett.*, 661 (1975), and references therein.

(15) Sensitized photolysis of **2** did not lead to detectable cleavage but only to its slow disappearance to products that, while uncharacterized, might reasonably be expected[2,11] to be dimers of **2.**

(16) R. Gleiter, E. Heilbronner, M. Hekman, and H.-D. Martin, *Chem. Ber.*, **106,** 28 (1973).

(17) This is one of the degenerate pair of HOMO's of the cyclobutane ring; J. S. Wright and L. Salem, *J. Am. Chem. Soc.*, **94,** 322 (1972).

(18) The localized transition dipoles cancel, because the transition is antisymmetric with respect to the $C_2$ axis present in **2.**

(19) Not only does this singlet state involve an excitation from the HOMO of **2** to the LUMO, but also the localized transition dipoles interact in an electrostatically favorable head-to-tail fashion,[18] thus giving this excited singlet a relatively low Coulombic repulsion energy. See ref 7, pp 144–147, for a discussion.

(20) (a) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8,** 781 (1969). (b) Such photochemical retrograde cycloadditions upon irradiation of dienes are by no means unknown, but usually they involve excitation of a cyclohexadiene moiety with concomitant extrusion of a molecule of benzene. See, for example, ref 21.

(21) G. Schröder, *Chem. Ber.*, **97,** 3140 (1964).

(22) J. A. Elix, M. V. Sargent, and F. Sondheimer, *J. Am. Chem. Soc.*, **92,** 969 (1970).

(23) R. Srinivassan, *J. Am. Chem. Soc.*, **85,** 819 (1963); R. Srinivassan, *ibid.*, **86,** 3318 (1964).

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(25) A. Suzuki and M. Itoh, *Tetrahedron Lett.*, 1003 (1967).

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(27) (a) R. Criegee and R. Askani, *Angew. Chem., Int. Ed. Engl.*, **7,** 537 (1968); (b) H. E. Zimmerman and H. Iwamura, *J. Am. Chem. Soc.*, **92,** 2015 (1970); (c) L. A. Paquette, R. K. Russell, and R. E. Wingard, Jr., *Tetrahedron Lett.*, 7113 (1973).

(28) Paquette and his co-workers have found that the parent semibullvalene is converted to cyclooctatetraene on pyrolysis.[27c] Pyrolysis of cyclooctatetraene gives dihydropentalene, whose formation has been rationalized by a mechanism involving the same type of biradical intermediate; M. Jones, Jr., and L. O. Schwab, *J. Am. Chem. Soc.*, **90,** 6549 (1968).

(29) The thermal interconversions could proceed by an allowed, concerted, ${}_{\pi}2_a + {}_{\pi}4_a$ reaction.[20a] Mechanistic variants for the photochemical transformations are also possible. For a review and discussion of $(CH)_8$ chemistry see L. T. Scott and M. Jones, Jr., *Chem. Rev.*, **72,** 181 (1972).

(30) J. Meinwald, D. Schmidt, and H. Tsuruta, *J. Am. Chem. Soc.*, **91,** 5877 (1969); H. E. Zimmerman, J. D. Robbins, and J. Schantl, *ibid.*, **91,** 5878 (1969). Alternatively, the reaction can be described as a forbidden ${}_{\pi}2_s + {}_{\sigma}2_s$ process.

(31) On irradiation, tricyclo[3.3.0.0$^{2,6}$]octadiene gives a mixture of semibullvalene and cyclooctatetraene; J. Meinwald and H. Tsuruta, *J. Am. Chem. Soc.*, **92,** 2579 (1970). Although the former product could originate from the same biradical, a concerted, photochemically allowed, 1,3 sigmatropic shift would also account for the formation of semibullvalene. A similarly allowed reaction of the ${}_{\pi}2_s + {}_{\sigma}2_s + {}_{\pi}2_s + {}_{\sigma}2_s$ type rationalizes the formation of the latter product.

(32) R. Srinivasan and A. Levi, *J. Am. Chem. Soc.*, **86,** 3756 (1964).

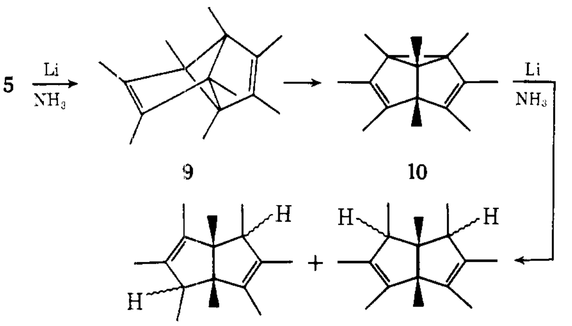
(33) Perhaps less likely, but nevertheless possible, is that the octamethyltricyclooctadiene (**9**) undergoes reduction with concomitant cleavage of the cyclobutane ring, so that rearrangement of **9** to octamethylsemibullvalene **10** is not involved.

(34) J. E. Baldwin and A. H. Andrist, *J. Am. Chem. Soc.*, **93,** 3289 (1971); M. J. Goldstein and R. Hoffmann, *ibid.*, **93,** 6193 (1971).

(35) This procedure is essentially that of R. Stafford, Ph.D. Thesis, Harvard

however, was only the first of several apparently anomalous aspects of the chemistry of **5** that we encountered.[5]

The rearrangement of tricyclo[3.3.0.0$^{2,6}$]octa-3,7-diene to semibullvalene suggested a chemical method for proving the structure of **5**. Conversion of the exocyclic methylene groups of **5** into endocyclic double bonds should trigger rearrangement to a derivative of semibullvalene. Therefore, we investigated the reduction of **5**. Hydrogenation of **5** over a Pd/C catalyst, unlike the case in the reduction of **2**, proceeded 1,2 instead of 1,4. Consequently, **5** was reduced using lithium in a mixture of tetrahydrofuran, ammonia, and *tert*-butyl alcohol at −30 °C. The material isolated was not, however, octamethylsemibullvalene (**10**) but a mixture of octamethylbicyclo[3.3.0]octadienes, apparently resulting from a further two-electron reduction of **10**. This result might have been anticipated, since Schröder has reported the analogous reduction of bullvalene under similar conditions.[21] Indeed, when octamethylsemibullvalene (**10**) was itself subjected to the conditions of the reaction, the crude product mixture showed the identical $^1$H NMR spectrum and GLC trace as the mixture of products obtained from reduction of **5**. It seems plausible, therefore, that under the reaction conditions **5** is, in fact, reduced to octamethyltricyclo[3.3.0.0$^{2,6}$]octa-3,7-diene (**9**), which rearranges to **10**, and that **10** then undergoes a further two-electron reduction to give the observed products. If this is actually the course taken by the reaction,[33] it indicates that **9** rearranges at a somewhat lower temperature (−30 °C) than the parent tricyclo[3.3.0.0$^{2,6}$]octa-3,7-diene, which apparently can be distilled at 0 °C.[30]



Another obvious method for converting the exocyclic methylenes of **5** into endocyclic double bonds is a Diels–Alder cycloaddition reaction. Besides providing further chemical proof of the structure of **5**, such a reaction labels the positions of the endocyclic double bonds present in the tricyclooctadiene that is expected to be formed initially. This labeling allowed a test of a proposed explanation for the rapid rearrangement of tricyclo[3.3.0.0$^{2,6}$]octa-3,7-dienes, involving a symmetry-allowed $_\sigma2_s + _\sigma2_a$ pathway from them to semibullvalenes.[34] The results of our studies of the cycloaddition reactions of **5** and the conclusions drawn from them are contained in the accompanying paper.[5]

## Experimental Section

**1,2-Dimethyl-3,4-dimethylenecyclobutene (1).**[35] To a 100-mL round bottom flask equipped with a magnetic stirrer and reflux condenser was added 17.9 g of 3,4-dichlorotetramethylcyclobutene[36] and 38 g of quinoline. The mixture was heated at 120 °C under nitrogen for 0.5 h until two layers separated. Upon cooling, the lower layer solidified. The upper layer was decanted, water was added to the lower layer, and the resulting solution was extracted with hexane. The hexane extracts and the upper layer were combined and distilled under aspirator pressure. A colorless liquid, boiling at 35–40 °C, was collected and amounted to 6.2 g (60% yield). its NMR spectrum (CDCl$_3$) showed: δ 1.85 (s, 6 H), 4.44 (s, 2 H), 4.53 (s, 2 H); UV (hexane) $\lambda_{max}$ 245 nm (log ε 3.8). Exact mass calcd for $C_8H_{10}$: 106.0783. Found: 106.0800.

***anti*-1,2,5,6-Tetramethyl-3,4,7,8-tetramethylenetricyclo[4.2.0.0$^{2,5}$]octane (2).** In 60 mL of benzene was dissolved 0.8 g of benzophenone, and the solution was degassed in a photolysis well by bubbling nitrogen slowly through it for 2 h. After addition of 2.0 g of **1**, degassing was continued for another 0.5 h. The solution was photolyzed through a Pyrex filter with a 450-W Hanovia high-pressure lamp for 4 h. Although monitoring the reaction by NMR showed some starting material was still present, longer irradiation led to loss of product and lower overall yields. Upon termination of the photolysis, the solvent was removed under reduced pressure and the residue chromatographed over 30 g of neutral alumina, using pentane to elute the column. The product was collected in the first 50–75 mL. Evaporation of the solvent gave 0.9 g of off-white cyrstalline material; NMR (CDCl$_3$) δ 1.05 (s, 12 H), 4.70 (s, 4 H), 5.27 (4 H); UV (hexane) $\lambda_{max}$ 243 nm (log ε 4.1). If the product was not stored under nitrogen at −78 °C, it decomposed, apparently to a polymer.[37] Polymerization also occurred rapidly when the crystals were heated to about 100 °C, so a melting point could not be obtained. Exact mass calcd for $C_{16}H_{20}$: 212.1565. Found: 212.1558.

**Reduction of 2 to *anti*-Octamethyltricyclo[4.2.0.0$^{2,5}$]octa-3,7-diene (6). (a) Catalytically.** A solution of 93 mg of **2** in 3 mL of ethyl acetate was hydrogenated at room temperature and atmospheric pressure over 14 mg of a 5% palladium on carbon catalyst. During the course of 0.75 h 2 mol equiv of hydrogen were taken up. Filtration and evaporation of the solvent left 90 mg of colorless crystalline material. The product, after purification by recrystallization from methanol and/or sublimation, had an NMR spectrum (CDCl$_3$) that consisted of two singlets of equal area at δ 0.91 and 1.56 (lit.[10c] δ 0.89 and 1.54). Material of the highest melting point was obtained by purifying the crude product by preparative GLC at 180 °C on a 0.375 in. × 10 ft column of 20% SE-30 on Chromosorb W. Only one major peak was observed with a retention time of 8.5 min at a flow rate of 180 mL/min. The crystals that were collected melted very sharply at 125 °C (lit.[10a] 127 °C).

**(b) With Lithium.** To a 250-mL flask, equipped with an actone–dry ice condenser and a magnetic stirrer, was added 100 mg of lithium pieces under a nitrogen atmosphere. The flask was cooled in an acetone–dry ice bath and 50 mL of ammonia was distilled through a KOH trap and condensed in the reaction flask. Then 25 mL of tetrahydrofuran (distilled from lithium aluminum hydride) and 10 mL of *tert*-butyl alcohol (distilled from sodium) were added by syringe. Finally, 55 mg of **2** in 2 mL of tetrahydrofuran was added by syringe to the refluxing, stirred, blue solution. After 2 h the cold bath was removed and after another 0.5 h the reaction was quenched by adding a saturated aqueous solution of ammonium chloride until the blue color was discharged. Water and ether were added to the flask, which was allowed to stand at room temperature and then at 60 °C for 1 h to complete the removal of the ammonia. Further ether was added, the two layers were separated, the aqueous phase was extracted with more ether, and the organic layers were combined, washed with water and brine, and dried over magnesium sulfate. Removal of the solvent on a rotary evaporator left an oily solid, which was recrystallized from methanol and sublimed at 5 × 10$^{-3}$ Torr at a bath temperature of 75 °C. The NMR spectrum of this material was identical with that prepared by catalytic reduction of **2**.

**Photolysis of 2. (a) Direct.** To a quartz NMR tube was added a solution of 20 mg of **2** in 0.5 mL of cyclohexane. The solution was degassed for 0.75 h by bubbling nitrogen slowly through it via a syringe needle that penetrated the septum with which the tube was capped. A shorter needle provided an outlet for the nitrogen. The needles were withdrawn and the NMR tube was irradiated with a 450-W Hanovia high-pressure lamp. After 1.5 h an NMR spectrum of the contents of the tube showed roughly 50% reversion of **2** to 1,2-dimethyl-3,4-dimethylenecyclobutene (**1**).

**(b) Sensitized.** To a Pyrex NMR tube was added a solution of 50 mg of **2** and 5 mg of benzophenone in 0.75 mL of benzene. After degassing, as described above, the tube was irradiated through a Pyrex filter with a 450-W Hanovia high-pressure lamp. A steady decrease in the concentration of **2** was observed by NMR with an attendant increase of a broad unresolved absorption in the aliphatic region. No trace of **1** was detectable. The disappearance of **2** was nearly complete after 1.5 h of irradiation.

**Pyrolysis of 2. (a) At 240 °C to 1,2,5,6-Tetramethyl-3,4,7,8-tetramethylenecycloocta-1,5-diene (3).** Using the flow system apparatus described previously,[2] 50 mg of **2**, dissolved in 0.5 mL of hexane, was added dropwise to the pyrolysis column, which was preheated to 240 °C. The nitrogen flow rate through the column was adjusted so that the residence time of the pyrolysate in the column was about 3 s. After the addition was complete, the column was washed with an additional 1.5 mL of hexane. The hexane solution was removed from the trap and evaporated. The NMR spectrum (CDCl$_3$) of the residue showed it to be pure **3**; δ 1.80 (s, 12 H), 4.80 (d, 4 H, *J* = 1.5 Hz), 5.10 (d, 4 H, *J* = 1.5 Hz).

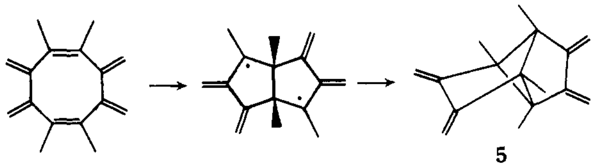
import of this result was that a convenient symthesis of **3** from **1** now seemed assured. Thermolysis of tricyclo[4.2.0.0$^{2,5}$]octane leads to 1,5-cyclooctadiene,[14] and by analogy there was little doubt that **2** would open to **3**. Indeed, on pyrolysis in a flow system at 240 °C the two required bonds were broken and **2** underwent smooth conversion to **3**. However, in contrast to the thermal reaction, direct photolysis of **2** led to cleavage of the two other allylic C–C bonds and the regeneration of **1**.[15]

The different courses taken by the thermal and photochemical reactions of **2** are readily understood. In the thermal reaction it is the most strained and, consequently, the weakest allylic C–C bonds in **2** that are cleaved. However, in the photochemical reaction the allylic bonds that are broken are those whose orientation causes them to mix strongly with $\pi$ orbitals of the diene moieties. The analogous $\sigma$ bonds in both isomers of tricyclo[4.2.0.0$^{2,5}$]octa-3,7-diene interact strongly with the $\pi$ bonds, as revealed by the photoelectron spectra of these compounds.[16] The $\sigma$–$\pi$ interaction is sufficiently large that the "through-bond" mediated mixing between the double bonds is stronger than that "through space," even in the syn isomer.[16] It is to be expected, therefore, that considerable $\sigma$–$\pi$ mixing also exists in **2**. Specifically, the out-of-phase combination of localized bonding $\sigma$ orbitals[17] mixes strongly with the symmetric (with respect to the $C_2$ axis present in **2**) combination of diene HOMO's, and the in-phase combination of antibonding $\sigma$ orbitals mixes with the antisymmetric combination of the diene LUMO's. The MO's that result from the mixing are, respectively, the HOMO and the LUMO of **2**, each of which contains a substantial contribution from the appropriate combination of localized $\sigma$ MO's. Although the excitation of an electron from the HOMO to the LUMO of **2** represents a forbidden electronic transition,[18] the resulting excited singlet state is the one of lowest energy.[19] Therefore, it is not unlikely that, following an allowed transition, **2** would undergo electronic relaxation to this singlet state. Population of this state is tantamount to excitation of an electron from an MO with appreciable bonding $\sigma$ character to one with appreciable antibonding $\sigma$ character. Not only are the two ring bonds in **2** thus weakened, but also, the excitation, if viewed in the extreme as involving predominantly these localized $\sigma$ bonds, leaves populated just those orbitals required for a concerted and photochemically allowed $_\sigma2_s + {}_\sigma2_s$ retrograde cycloaddition.[20]

The photochemical cleavage of **2** to **1**, while of interest, especially as it contrasts with the thermal transformation of **2** to **3**, was certainly not synthetically useful and we did not investigate it further. Instead, we turned to the examination of the photochemistry of **3** in the hope that we could obtain **4** from **3** by direct irradiation. The desired closure is, of course, of the familiar butadiene → cyclobutene type, and precedent for the occurrence of this reaction in a molecule with some resemblance to **3** can be found in the photochemical transformation of 7,8-dimethylenecyclooctatriene to 1,2-ethanocyclooctatetraene.[22] On direct irradiation 1,2,5,6-tetramethylenecyclooctane also undergoes cyclobutene ring closure; however, transannular bond formation to give 2,6-dimethylene[3.3.2]propellane is competitive.[2] Transannular bond formation in **3**, particularly upon sensitization, which suppresses cyclobutene ring closure in tetramethylenecyclooctane,[2] therefore also seemed a likely photochemical event. Finally, photoinduced reaction of **3** at its internal double bonds too had precedent, not only in the photochemistry of 1,5-cyclooctadiene itself,[23] but also in that of 1,2:5,6-dibenzocyclooctatetraenes[24] and halogenated derivatives of dimethylenecyclooctatriene.[22]

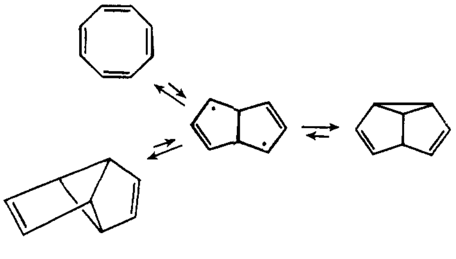
When the irradiation of **3**, either direct or sensitized, was actually carried out, the last of these pathways was the one followed. The only isolable product showed three $^1$H NMR signals at (CDCl$_3$) $\delta$ 0.70, 4.83, and 5.48 in the ratio 3:1:1, thus indicating that the molecule possessed four equivalent methyl and four equivalent methylene groups. The chemical shift of the methyl groups indicated that they were attached to saturated carbons, leading to the conclusion that the photoproduct was tricyclic. Thus, **5** and the syn isomer of **2** both provided reasonable structural assignments for the photoproduct. However, photochemical analogy[23,24] favored the former assignment, as did the occurrence of the methyl resonances in the photoproduct 0.35 ppm farther upfield than those in **2**, since magnetic shielding of equatorial methyl groups on puckered cyclobutane rings is a commonly observed phenomenon.[25] Further consideration of the syn isomer of **2** as the photoproduct was terminated by the discovery that, upon pyrolysis in a flow system at 380 °C or higher with a contact time of about 3 s, both **2** and **3** were converted to a single compound with the same $^1$H NMR spectrum as the photoproduct.

Scheme II



Although the finding that the photoproduct was also formed by pyrolysis of **3** eliminated on thermodynamic grounds the syn isomer of **2** as the molecule obtained from these reactions, the formation of **5** from **3** in the thermal rearrangement was, to say the least, surprising. The rearrangement of **3** to **5**, both photochemically and thermally, can be most easily rationalized, at least in a formal sense, in terms of the intermediacy of a biradical, as shown in Scheme II. A similar biradical intermediate has been suggested in the photochemical interconversion of cyclooctatetraene and semibullvalene[26] and in the thermal equilibration of substituted derivatives of these molecules.[27–29] The same biradical has also been postulated in the extraordinarily facile thermal transformation of bicyclo[3.3.0.0$^{2,6}$]octa-3,7-diene to semibullvalene.[30,31] These transformations are shown in Scheme III. The biradicals in the two schemes differ in that the double bonds that stabilize the biradical in Scheme III are endocyclic, so the formal shift of a double bond, necessary for the conversion of cyclooctatetraene and tricyclo[3.3.0.0$^{2,6}$]octa-3,7-diene into semibullvalene, can occur. In contrast, in the diradical in Scheme II the stabilizing double bonds are exocyclic and so, unlike the case in Scheme III, the exit to a semibullvalene derivative is blocked. A system similar to that portrayed in Scheme II has been investigated by Stiles and Burckhardt,[24] who explained the thermal and photochemical rearrangements of 1,2:5,6-dibenzocyclooctatetraenes by the intermediacy of tricyclic isomers analogous to **5**. However, Stiles and Burckhardt did not actually isolate the tricyclic isomers, a fact which is perhaps not surprising in view of the instability of tricyclo[3.3.0.0$^{2,6}$]octa-3,7-diene itself.[30] Thus, it seemed very strange, indeed, that we obtained **5** from pyrolysis of **3** at temperatures well above that at which tricyclo[3.3.0.0$^{2,6}$]octane undergoes *cleavage* to 1,5-cyclooctadiene.[32] This,

Scheme III



University, Camrbidge, Mass., 1971; and our product was indistinguishable from a sample prepared by him.

(36) R. Criegee, *Org. Synth.*, **46**, 34 (1966).

(37) In previous work[2] we have observed that 1,2-dimethylenecyclobutane forms polymeric material, unless it is stored at low temperature under an inert atmosphere.

(38) R. Criegee, W. D. Wirth, W. Engel, and H.-A. Brune, *Chem. Ber.*, **96**, 2230 (1963).

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# Cycloaddition Reactions of 1,2,5,6-Tetramethyl-3,4,7,8-tetramethylenetricyclo[3.3.0.0$^{2,6}$]octane. Evidence for Chemical Consequences of Orbital Interactions in Molecules Containing Unsaturatively 1,3-Bridged Cyclobutane Rings

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*Received May 20, 1977*

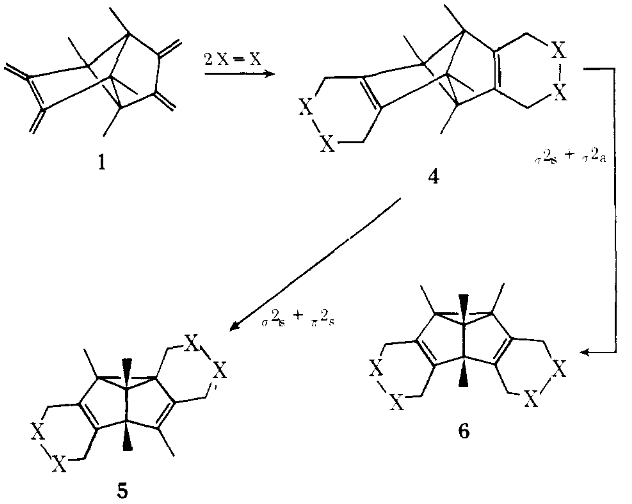
The title compound (1) reacts with tetracyanoethylene and *N*-phenyltriazolinedione to give rearranged adducts. Bond reorganization occurs after the first cycloaddition, and the structures of the products rule out a ${}_{\sigma}2_{s} + {}_{\sigma}2_{a}$ mechanism for rearrangement. With the latter dienophile an unrearranged monoadduct (**7b**) has been observed by NMR at low temperatures, and the activation parameters for its rearrangement to **8b** have been obtained. The energy of activation is consistent with that expected for a forbidden ${}_{\sigma}2_{s} + {}_{\pi}2_{s}$ process. The instability of molecules containing cyclobutane rings 1,3-bridged by ethylene, the contrasting thermal stability of **1**, and the reluctance of **1** to undergo Diels–Alder cycloaddition reactions are all rationalized by analysis of the interactions between the $\sigma$ orbitals of the cyclobutane ring and the $\pi$ orbitals of the unsaturated bridging groups. Calculations are reported that support this interpretation of the experimental results.

In the accompanying paper[2] we reported the transformation of 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenetricycloocta-1,5-diene into 1,2,5,6-tetramethyl-3,4,7,8-tetramethylenetricyclo[3.3.0.0$^{2,6}$]octane (**1**), either by direct or sensitized photolysis or by pyrolysis. That **1** is formed in the thermal reaction is really most surprising, since tricyclo[3.3.0.0$^{2,6}$]octa-3,7-diene (**2**) is a very unstable compound, undergoing rapid rearrangement to semibullvalene (**3**) at room temperature.[3] Indeed, the thermal rearrangement of **2** to **3** is so facile for a reaction that either involves a diradical intermediate[3] or proceeds by a forbidden but concerted ${}_{\sigma}2_{s} + {}_{\pi}2_{s}$ mechanism[4] that a novel, symmetry allowed, ${}_{\sigma}2_{s} + {}_{\sigma}2_{a}$ pathway was proposed for this transformation.[5]

The availability of **1** appeared to afford an excellent opportunity to test whether a ${}_{\sigma}2_{s} + {}_{\sigma}2_{a}$ pathway was, in fact, involved in the rearrangement of **2** to **3**. Diels–Alder cycloadditions of 2 mol of a dienophile to **1** would provide **4**, a derivative of **2** in which the positions of the double bonds are labeled by the six-membered rings. Rearrangement of **4** by a forbidden ${}_{\sigma}2_{s} + {}_{\pi}2_{s}$ pathway, whether concerted or involving a diradical as a discrete intermediate, requires the formal shift of a double bond and leads to **5**. In contrast, since the $\pi$ bonds are not involved in the ${}_{\sigma}2_{s} + {}_{\sigma}2_{a}$ mechanism, the labeling of the double bonds is different in the semibullvalene (**6**) that is the expected product if this pathway is utilized. Therefore, we undertook an investigation of the cycloaddition reactions of **1** in order to determine whether the semibullvalene formed had structure **5** or **6**.[6]

## Results

To our surprise, compound **1** proved to be a most unreactive diene. Using such dienophiles as dimethyl acetylenedicarboxylate, dicyanoacetylene, and diethyl azodicarboxylate, we were unable to obtain an adduct of **1**. Although **1** did react with tetracyanoethylene (TCNE) to give a bis adduct, even with this potent dienophile reaction was surprisingly slow, requiring 2.5 h in refluxing tetrahydrofuran for completion. For comparison, the reaction of TCNE with 1,2-dimethylenecyclobutane in THF is instantaneous at room temperature.



The $^1$H NMR spectrum of the TCNE bis adduct of **1** was entirely consistent with the formulation of its structure as **5** (X = $C(CN)_2$). Since **5** and **6** are both semibullvalenes, it was to be expected that both molecules would be rapidly fluxional at all but very low temperatures.[7] Whereas Cope rearrangement of **6** is not a degenerate process, the corresponding rearrangement of **5** is. Thus, on the NMR time scale **5**, because of its fluxionality, acquires an effective $C_2$ axis of symmetry, while **6** maintains only the plane of symmetry present in either of the nonequivalent divinylcyclopropane structures that can be written for it. Compounds **5** and **6** can, therefore, be most easily differentiated by the fact that the former should show only two types of methyl groups in its NMR spectrum, while the latter would be expected to exhibit three. At 100 MHz in acetone-$d_6$ the $^1$H NMR spectrum of the TCNE bis adduct of **1** showed only two methyl resonances, thus leading to the assignment of its structure as **5**.[2b]

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