Synthesis of the Benzotricyclo[3.2.0.0^{2,7}]heptene Ring System via the Intramolecular [2 + 2]-Cycloaddition Reaction of Some Cyclopropene Derivatives

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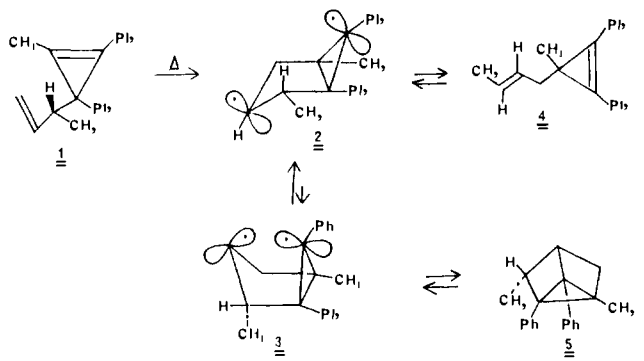
Abstract: The photo and thermal reactions of a number of 1,2-diphenyl-3-methyl-3-(*o*-vinylphenyl)-substituted cyclopropenes have been studied. The thermolysis of these systems gave substituted benzotricyclo[3.2.0.0^{2,7}]heptenes in good yield by means of a novel intramolecular [2 + 2] cycloaddition. The sensitized di-π-methane photorearrangement of several substituted benzonorbornenes was used to independently synthesize the thermal cycloadducts. The observed regiospecificity of the rearrangement is understandable in terms of formation of the most stable diradical intermediate. In contrast to the thermal results, the photosensitized irradiation afforded a mixture of two products. In addition to the [2 + 2] cycloadduct, a new compound was isolated whose formation involves attack of the ortho position of the triplet state on the terminal vinyl carbon followed by diradical coupling and subsequent rearomatization. Thermolysis or sensitized photolysis of several unsymmetrically substituted 1,3-diphenyl-2-methyl-2-(*o*-vinylphenyl)cyclopropenes afforded related cycloadducts. With these systems, the [2 + 2]-cycloaddition reaction is highly regiospecific and involves bonding from the cyclopropene carbon bearing the methyl group onto the terminal vinyl carbon. The silver ion and singlet excited-state behavior of several substituted cyclopropenes was also studied, and the results obtained were compared to the reactions which occur on thermolysis or sensitized photolysis.

Cycloaddition reactions have figured prominently in both synthetic and mechanistic organic chemistry.[1-5] Current understanding of the underlying principles in this area has grown from a fruitful interplay between theory and experiment.[6] During the past decade there has been remarkable interest in the development of intramolecular cycloaddition processes.[7,8] Internal cycloadditions have been found to offer a powerful solution to many problems in complex natural product synthesis.[9] Converting olefin geometry into the stereochemistry of saturated carbon combined with forming two rings simultaneously from acyclic precursors accounts for the popularity of this approach. Diels-Alder reactions,[9] dipolar cycloadditions,[10] and photochemical cyclobutane formation,[11,12] when performed intramolecularly, often display exceptional regio- and stereochemical control. Our research group has been involved over the past few years in a program of synthesizing unusual polycyclic ring systems which uses the intramolecular [2 + 2] cycloaddition of alkenes as the primary strategy.[13-16] Cycloaddition across the double bond of a highly strained alkene such as cyclopropene proceeds quite readily since it reduces ring strain by 26 kcal/mol.[17,18] We report here the results of our studies with cyclopropene derivatives containing π-unsaturation which show that the internal cycloaddition reaction is a particularly attractive route for the synthesis of some unusual tricyclic ring compounds.[19]

Results

We had previously reported that the thermolysis of 3-allyl-substituted cyclopropenes results in a novel intramolecular [2 + 2] cycloaddition.[20] For example, heating a sample of cyclopropene **1** results in both a Cope rearrangement and tricyclo[2.2.0.0^{2,6}]hexane formation. The mechanism which has been proposed to account for the stereochemical results encountered on thermolysis of **1** involves the formation of a biradical intermediate (**2**) in a conformation which is analogous to the chair conformation of cyclohexane. Subsequent fragmentation of this species affords the Cope rearrangement product **4**. Ring inversion of the initially formed chair intermediate **2** generates the boat diradical **3** which cyclizes to the tricyclo[2.2.0.0^{2,6}]hexane ring system. Tricyclohexane **5** was also formed from the thermolysis of cyclopropene **4** via intermediates **2** and **3**. The overall inversion of stereochemistry in the thermal [2 + 2]-cycloaddition reaction of **4** can be attributed to the fact that the thermal reaction proceeds through a four-center, chairlike conformation. The ring flip of the initially formed chair intermediate **2** to the boat diradical **3** is the major factor responsible for the overall inversion of stereochemistry of the thermal cycloaddition.

As an extension of our studies dealing with intramolecular cycloaddition reactions of cyclopropene derivatives, we have examined the thermal and photochemical behavior of several 3-(*o*-vinylphenyl)-substituted cyclopropenes. Thermolysis of 1,2-diphenyl-3-methyl-3-(*o*-vinylphenyl)cyclopropene (**6**) at 175 °C



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(1) Kloetzel, M. C. *Org. React. (N.Y.)* **1948**, *4*, 1.
(2) Wasserman, A. "Diels-Alder Reactions"; Elsevier: New York, 1965.
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(4) Huisgen, R.; Grashey, R.; Sauer, J. "Chemistry of Alkenes"; Patai, S., Ed.; Interscience: New York, 1964; pp 878-928.
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(10) Padwa, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 123.
(11) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135.
(12) Baldwin, S. W. *Org. Photochem.* **1981**, *5*, 123.
(13) Padwa, A.; Blacklock, T. J. *J. Am. Chem. Soc.* **1979**, *101*, 3390.
(14) Padwa, A. *Acc. Chem. Res.* **1979**, *12*, 310.
(15) Padwa, A. *Org. Photochem.* **1979**, *4*, 261.
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(19) For a preliminary report, see: Padwa, A.; Rieker, W. F. *J. Org. Chem.* **1979**, *44*, 3275.
(20) Padwa, A.; Blacklock, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 5648.

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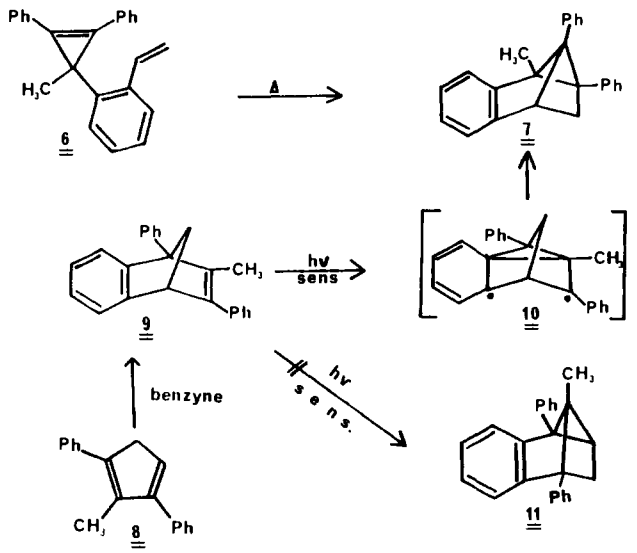
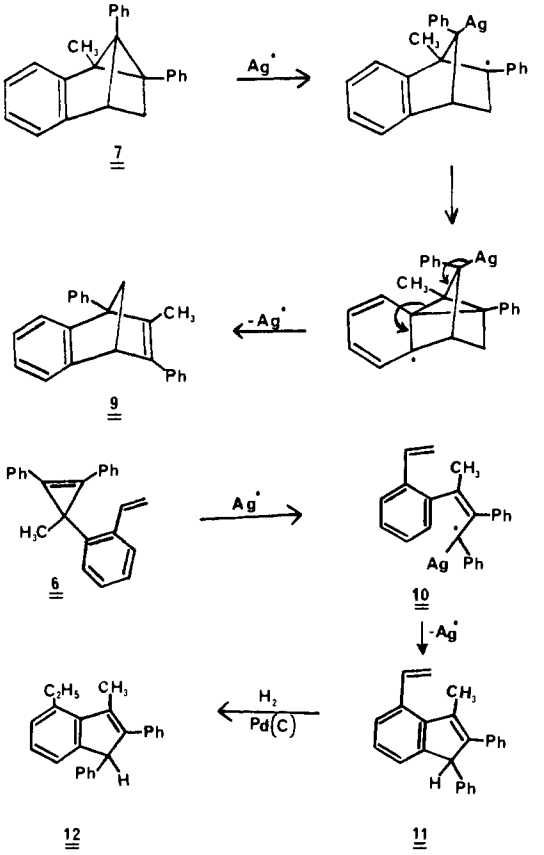


for 4 h gave a quantitative yield of benzotricycloheptene **7**: NMR ($CDCl_3$, 100 MHz) δ 1.40 (s, 3 H), 1.41 (d, 1 H, J = 9.0 Hz), 2.99 (dd, 1 H, J = 9.0 and 8.0 Hz), 3.69 (d, 1 H, J = 8.0 Hz), 7.42–7.03 (m, 14 H); ^{13}C NMR ($CDCl_3$, ppm) 12.4 (q), 38.1 (t), 42.5 (s), 44.3 (s), 45.9 (d), 68.3 (s), 120–129 (m), 136 (s), 139 (s), 144 (s), and 148 (s). The identity of structure **7** was based on its spectroscopic and analytical properties and was further confirmed by comparison with an independently synthesized sample. The reported sensitized photorearrangement of benzonorbornadienes to benzotricyclo[3.2.0.0^{2,7}]heptenes[21,22] suggested a similar approach for the synthesis of **7**. The preparation of benzonorbornadiene **9** was achieved in high yield by treating 2-methyl-1,3-diphenyl-1,3-cyclopentadiene (**8**)[23] with benzyne. A dilute solution of **9** in benzene was photolyzed in the presence of acetophenone to give **7** as the exclusive photoproduct (98%). No signs of the isomeric benzotricyclic hydrocarbon **11** could be detected in the crude photolysate. The observed regiospecificity of the di-π-methane photorearrangement of **9** is expected on the basis of formation of the most stable diradical intermediate.[24,25]

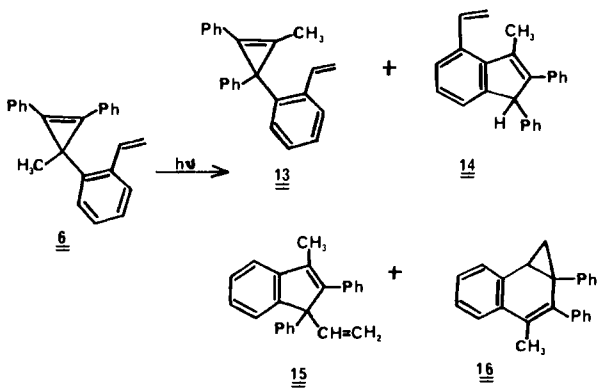
During the course of our studies with benzotricycloheptene **7**, we found that this substrate rapidly rearranged to benzonorbornadiene **9** when treated with 3 mol % of silver perchlorate in benzene at room temperature. This transformation formally corresponds to a silver-induced di-π-methane retrorearrangement. Interestingly, Paquette and Zon have reported that the parent benzotricycloheptene ring is unreactive toward catalytic amounts of silver perchlorate in benzene.[26] The rearrangement of **7** to **9** probably involves addition of silver ion across the 1,7-σ bond. This generates a stable carbonium ion which can be attacked by the π electrons of the neighboring aromatic ring. A subsequent reductive elimination of the metal ion would yield the observed product. The ready reactivity of **7** and the inertness of the parent benzotricycloheptane system is readily understandable in terms of relative carbonium ion stabilities.

In dramatic contrast with the thermal results, exposure of dilute benzene solutions of **6** to catalytic amounts of silver perchlorate



at room temperature resulted in the formation of indene **11** in quantitative yield. The structure of **11** was established by catalytic reduction to **12**, which in turn was compared with an authentic sample.[27] In line with earlier evidence for the intermediacy of a metal-bonded carbonium ion–metal-complexed carbene hybrid intermediate in the transition metal promoted rearrangement of strained ring systems,[28–30] it is tempting to suggest the involvement of a related species in the silver-induced rearrangement of the above system. Thus, we propose that silver ion behaves as a very specific Lewis acid which attacks the cyclopropene ring to yield argentocarbonium ion **10**. This species readily undergoes an electrocyclization followed by loss of silver ion to give the observed indene skeleton.

We have also studied the photochemical behavior of cyclopropene **6**. Direct irradiation of **6** in benzene with Pyrex-filtered light afforded a mixture of four compounds. These structures were assigned as 1,3-diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (**13**, 21%), 1,2-diphenyl-3-methyl-4-vinylindene (**14**, 16%), 1,2-



diphenyl-1-vinyl-3-methylindene (**15**, 16%), and 1,2-dihydro-4-

(21) Edman, J. P. *J. Am. Chem. Soc.* **1966**, *88*, 3454; **1969**, *91*, 7103.
(22) Tufariello, J. J.; Rowe, D. W. *J. Org. Chem.* **1971**, *36*, 2057.
(23) Padwa, A.; Blacklock, T. J.; Getman, D.; Hatanaka, N.; Loza, R. *J. Org. Chem.* **1978**, *43*, 1481.
(24) Hixson, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973**, *73*, 531.
(25) (a) Paquette, L. A.; Cottrell, D. M.; Snow, R. A.; Gifkins, K. B.; Clardy, J. *J. Am. Chem. Soc.* **1975**, *97*, 3275. (b) Santiago, C.; Houk, K. N.; Snow, R. A.; Paquette, L. A. *Ibid.* **1976**, *98*, 7443. (c) Paquette, L. A.; Cottrell, D. M.; Snow, R. A. *Ibid.* **1977**, *99*, 3723. (d) Snow, R. A.; Cottrell, D. M.; Paquette, L. A. *Ibid.* **1977**, *99*, 3734. (e) Paquette, L. A.; Ku, A. Y.; Santiago, C.; Rozeboom, M. D.; Houk, K. N. *Ibid.* **1979**, *101*, 5972. (f) Ku, A. Y.; Paquette, L. A.; Rozeboom, M. D.; Houk, K. N. *Ibid.* **1979**, *101*, 5981. (g) Paquette, L. A.; Bay, E.; Ku, A. Y.; Rondan, N. G.; Houk, K. N. *J. Org. Chem.* **1982**, *47*, 422.
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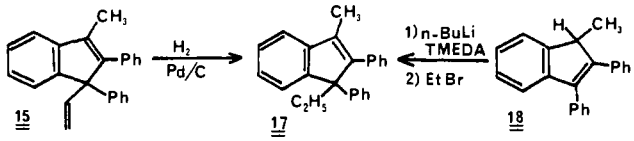
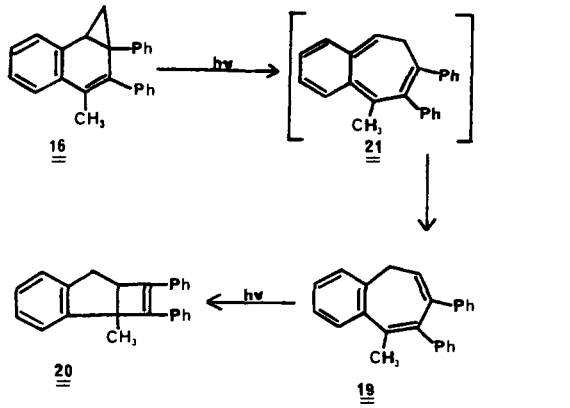
(29) Paquette, L. A. *Acc. Chem. Res.* **1971**, *4*, 280.
(30) Padwa, A.; Blacklock, T. J.; Loza, R. *J. Org. Chem.* **1982**, *47*, 3712.

methyl-2,3-diphenylcyclopropa[*a*]naphthalene (**16**, 41%). Structures **13** and **14** were verified by comparison with independently synthesized samples. The structure of **15** was established by catalytic reduction to **17**, which in turn was independently



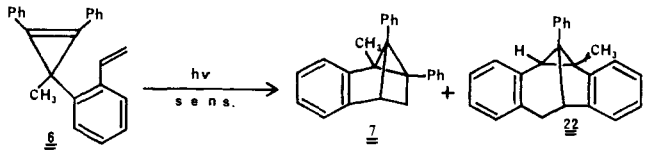
synthesized by treating 1-methyl-2,3-diphenylindene (**18**) with *n*-butyllithium followed by alkylation with ethyl bromide. The identity of **16** was determined by its straightforward spectral characteristics [NMR ($CDCl_3$, 90 MHz) δ 0.61 (dd, 1 H, J = 5.5 and 3.5 Hz), 1.98 (s, 3 H), 2.19 (dd, 1 H, J = 9.6 and 3.5 Hz), 2.53 (dd, 1 H, J = 9.6 and 5.5 Hz), 6.94–7.56 (m, 14 H)].

Cyclopropa[*a*]naphthalene **16** was found to undergo a novel



rearrangement on further irradiation. Thus, photolysis of a benzene solution of **16** through a Pyrex filter for 3 h produced 1-methyl-6,7-diphenyl-2,3-benzobicyclo[3.2.0]hepta-2,6-diene (**20**) in 42% yield. The identity of **20** was determined by its straightforward spectral properties [NMR ($CDCl_3$, 90 MHz) δ 1.66 (s, 3 H), 3.02 (d, 1 H, J = 3.5 Hz), 3.11 (d, 1 H, J = 8.6 Hz), 3.52 (dd, 1 H, J = 8.6 and 3.5 Hz), 7.05–7.56 (m, 14 H)]. The mass spectrum of **20** shows the facile loss of diphenylacetylene while the UV spectrum has absorptions at 291 and 277 nm which are consistent with the 1,2-diphenylcyclobutene chromophore.[31] The other compound isolated from the crude photolysate was assigned as 9-methyl-7,8-diphenyl-5*H*-benzocycloheptene (**19**, 52%) on the basis of its spectral properties (see Experimental Section). Consideration of the product distribution as a function of time showed an initial buildup of **19** followed by a decrease in amount. Evidence that **19** is an intermediate in the formation of **20** was obtained by the finding that the photolysis of a pure sample of **19** gave **20** in high yield. The formation of **19** from **16** can readily be accounted for in terms of an electrocyclic ring opening followed by a subsequent 1,7-hydrogen shift. The isolation of a benzocycloheptene from the irradiation of a benzobicyclo[4.1.0]heptene has ample precedent in the literature.[32-35] Electrocyclic ring closure of **19** accounts for the formation of structure **20**.

In contrast to the direct photolysis, the sensitized irradiation of **6** (thioxanthone) produced a mixture of benzotricycloheptene



(31) White, E. H.; Anhalt, J. P. *Tetrahedron Lett.* **1965**, 3937.
(32) Burdett, K. A.; Shenton, F. L.; Yates, D. H.; Swenton, J. S. *Tetrahedron* **1974**, *30*, 2057.
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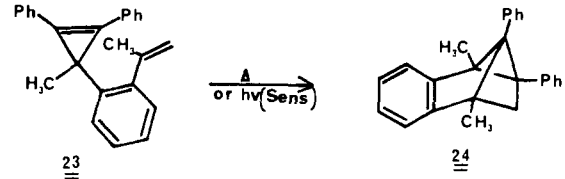
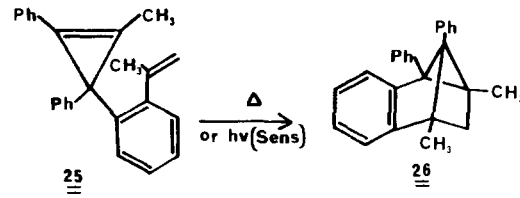
7 (63%) and 4b,4c,9b,9c-tetrahydro-9c-methyl-4c-phenyl-5*H*-benzo[*b*]cyclopropa[*lm*]fluorene (**22**, 35%). The structure of **22** was assigned on the basis of its NMR spectrum which showed signals at δ 1.43 (s, 3 H), 2.61 (s, 1 H), 2.73 (dd, 1 H, J = 15.3 and 3.3 Hz), 3.31 (dd, 1 H, J = 15.3 and 3.3 Hz), 3.87 (t, 1 H, J = 3.3 Hz), and 6.88–7.40 (m, 13 H).

1,2-Diphenyl-3-methyl-3-(*o*-2-propenylphenyl)cyclopropene (**23**) represents a system in which the products of the thermolysis



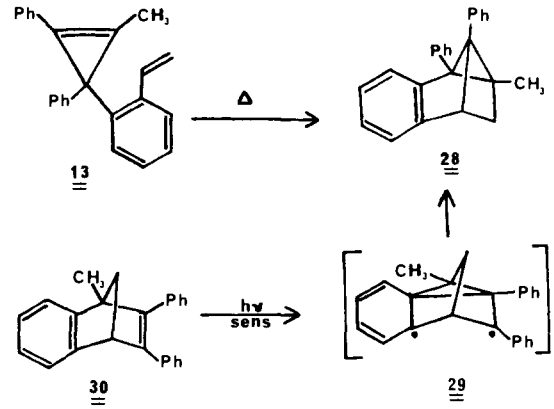
and triplet-sensitized photolysis were found to be identical. Thus, heating a sample of **23** at 160 °C gave cycloadduct **24** in 96% isolated yield. The triplet-sensitized irradiation of **23** also afforded **24** as the exclusive cycloadduct. This result may be most simply interpreted on the basis of an unusually easy [2 + 2] cycloaddition between the double bond and the cyclopropene ring.

The thermal and photosensitized behavior of the closely related unsymmetrical isomer **25** was also investigated. Upon heating



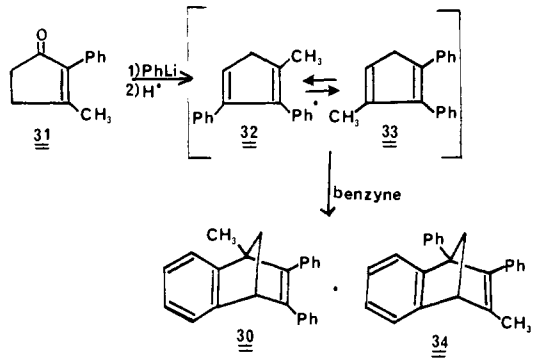
at 160 °C for 15 min, **25** was quantitatively converted into benzotricycloheptene **26**. The triplet-sensitized photolysis of **25** also afforded **26** in 94% yield.

Further examples which would support the generality of the intramolecular [2 + 2] cycloaddition of cyclopropenes bearing π unsaturation were sought. With this in mind, we investigated the thermal chemistry of 1,3-diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (**13**) in order to probe the regiospecificity



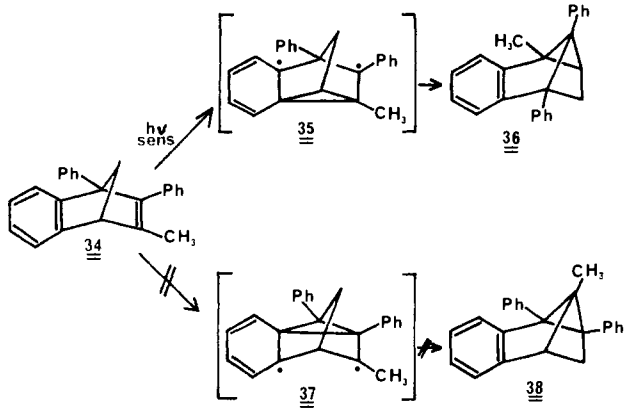
of the internal cycloaddition. Upon heating at 175 °C for 45 min, **13** was converted into a single product in quantitative yield. The structure of the product (**28**) was assigned on the basis of its spectral properties (see Experimental Section) and was further verified by comparison with an independently synthesized sample obtained from the sensitized photolysis of benzonorbornene **30**. The preparation of benzonorbornadiene **30** was achieved by the addition of phenyllithium to 2-phenyl-3-methylcyclopent-2-enone (**31**) followed by an acid-induced dehydration to give a mixture of 1-methyl-2,3-diphenyl-1,3-cyclopentadiene (**32**) and 1,2-diphenyl-3-methyl-1,3-cyclopentadiene (**33**) in a 1:3 ratio. These two cyclopentadienes could not be separated from each other. This is not unreasonable since McLean[36-38] and others[39,40] have shown

(36) McLean, S.; Haynes, P. *Tetrahedron Lett.* **1964**, 2385; *Tetrahedron* **1965**, *21*, 2329.



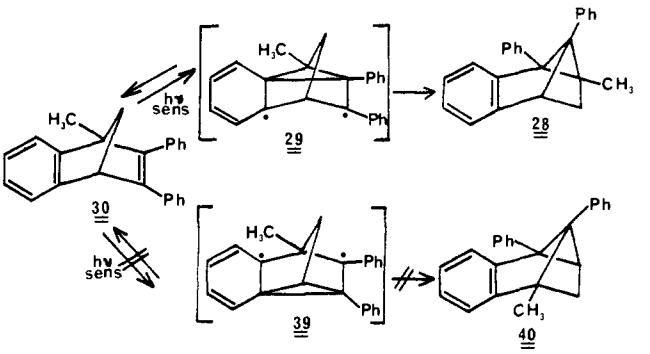
that equilibration of 1,3-cyclopentadienes can be established through a purely thermal 1,5 migration of a hydrogen atom. This process is so facile that in certain systems it takes place at an appreciable rate in solution even at room temperature.[37] This is presumably the case with cyclopentadienes **32** and **33**. Treatment of this mixture with benzyne afforded a 1:3 mixture of benzonorborenes **30** and **34** which could be separated by silica gel chromatography.

The regiochemistry associated with the di-π-methane photorearrangement of the above benzonorbornenes deserves some comment. Di-π-methane photorearrangements have long been considered to proceed in stepwise fashion via a pair of biradical intermediates.[24] When benzovinyl bridging is involved, the conversion to product has been formulated as the result of initial bond making to generate a cyclopropane moiety followed by cleavage of an alternate three-membered ring bond. Paquette and coworkers have studied the effect of substituent groups on the regioselectivity of the di-π-methane rearrangement of benzonorbornenes and found that bridgehead substituents can markedly influence the product distribution.[25] The level of stabilization available to the di-π-methane intermediate usually dominates the product-forming step.[25] Thus, the formation of benzotricycloheptene **7** from the sensitized irradiation of **9** is to be expected on the basis of the most stable diradical intermediate. The photosensitized conversion of **34** into **36** is also consistent with

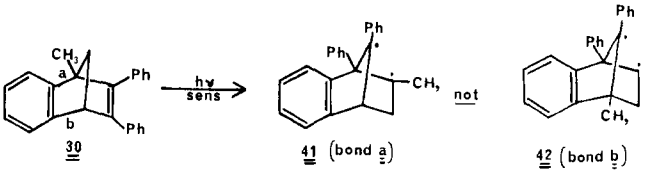


this principle. It is clear that with these systems the initial bonding step controls the regiochemistry of the rearrangement.

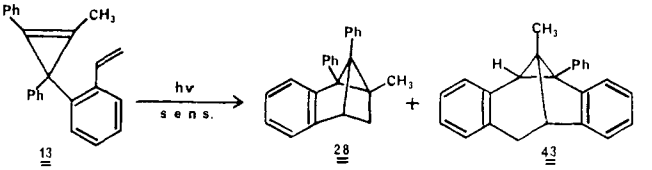
The regioselectivity encountered with benzonorbornene **30** is somewhat more difficult to rationalize. The presence of phenyl substituents on both positions of the double bond could lead to two different π–π bridging intermediates (**29** or **39**) and therefore produce two different benzotricycloheptenes (**28** or **40**). In fact, only a single regioisomer is produced (i.e., **28**). A reasonable explanation to account for this result is that the regiochemistry of the reaction is controlled by the direction of cleavage of the



initially produced diradical intermediate.[24] Bond fragmentation of **29** would afford a more stable tertiary and benzylic diradical. Bond cleavage of **39**, on the other hand, would lead to a less stable secondary and benzylic diradical. This explanation is reasonable provided the initial π–π bridging step is reversible. Another alternative explanation is a direct light-induced 1,2-aryl shift which would generate the immediate precursor (i.e., **41**) of benzotricycloheptene **28** directly.

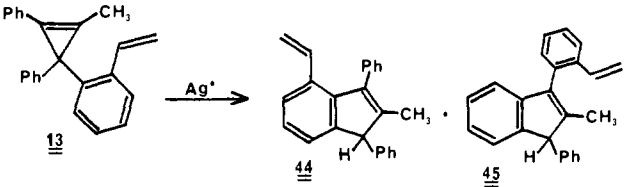


The photosensitized reaction of cyclopropene (**13**) was also studied in order to assess the triplet-induced behavior of this system. In contrast to the thermal results, the thioxanthone-sensitized irradiation of **13** gave rise to a mixture of **28** (46%)



and **43** (35%) [NMR ($CDCl_3$, 100 MHz) δ 1.43 (s, 3 H, 2.61 (s, 1 H), 2.73 (dd, 1 H, J = 15.3 and 3.3 Hz), 3.31 (dd, 1 H, J = 15.3, 3.3 Hz), 3.87 (t, 1 H, J = 3.3 Hz), 6.88–7.40 (m, 13 H)]. As was the case with thermolysis, the [2 + 2]-intramolecular cycloaddition reaction is highly regiospecific and involves initial bonding from the cyclopropene carbon bearing the methyl group onto the terminal vinyl carbon.

Attention was next turned to the silver ion induced reaction of the unsymmetrically substituted system **13** so as to contrast its behavior with that encountered on thermolysis and sensitized photolysis. When **13** was treated with silver perchlorate in benzene



a mixture of indens [**44** (64%) and **45** (36%)] was obtained. The structures of these materials were easily assigned on the basis of their characteristic NMR spectra. Both products are derived from the exclusive cleavage of the cyclopropene bond attached to the phenyl group. There were no detectable quantities of products derived from cleavage of the alternate σ bond. The initially formed argentocarbonium ion apparently undergoes electrocyclization across both the phenyl and *o*-vinylphenyl groups followed by silver ion loss to give the observed indenes.

Examination of the reaction kinetics of the thermolysis of the above systems was carried out in order to derive additional mechanistic information concerning the intramolecular [2 +

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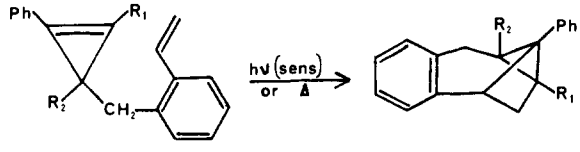
Table I. First-Order Rate Constants and Arrhenius Parameters for the Intramolecular [2 + 2]-Cycloaddition Reaction[a-f]

cyclopropene	temp, °C	$k \times 10^6$ s^{-1}	E_a	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	$\Delta S^{\ddagger}$
6	94	0.23				
6	103	0.55	27.1	26.5	33.0	−21.6
6	114	1.62				
13	94	0.14				
13	103	0.32	27.2	26.6	33.3	−22.6
13	114	0.96				
23	94	2.21				
23	103	4.86	24.0	23.4	31.1	−25.8
23	114	12.2				
25	94	1.38				
25	103	2.98	23.3	22.7	31.2	−28.5
25	114	7.29				

[a] Energy units are kcal/mol. [b] Error limits in the reported rate constants are generally ±3%. [c] Arrhenius parameters were determined by plotting log k vs. $1/T$; the slope of the line is $-E_a/2.303R$. [d] $\Delta S^{\ddagger} = 4.576(\log A - 13.23)$ at 25 °C. [e] $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$. [f] $\Delta H^{\ddagger} = E_a - RT$.

2]-cycloaddition process. Rates of rearrangement were effected in ampules sealed under vacuum. A trace of pyridine was added to inhibit acid-catalyzed ring opening. The cycloaddition was followed by HPLC and good first-order dependence of the rate data was obtained, indicating that the reaction is a true unimolecular process. Rate constants for conversion of the cyclopropene to the benzotricycloheptene were measured at three temperatures over a 20-deg range. The activation parameters were determined by least-squares analysis and are given in Table I. The rates and the corresponding Arrhenius parameters are essentially identical with those determined for the Cope rearrangement of 1,2-diphenyl-3-allyl and 1,3-diphenyl-2-allylcyclopropene.[41] The difference in the rate of cycloaddition of the symmetrical (i.e., **6** and **23**) and unsymmetrical (**13** and **25**) substituted cyclopropenes is negligible. This would tend to suggest that destruction of conjugation of the phenyl substituents does not play an important role in the overall cycloaddition. From Table I it is seen that the cycloaddition of the 3-(*o*-2-propenylphenyl) system (i.e., **23** and **25**) proceeds at a rate approximately 10 times faster than the *o*-vinylphenyl-substituted system. While this rate difference is small, it is significant that the 2-propenylphenyl-substituted system is reacting at a faster rate than the *o*-vinylphenyl-substituted one. This is perfectly consistent with a stepwise process proceeding through a diradical intermediate.

With these results in hand we decided to investigate the chemistry of a 3-(*o*-vinylbenzyl)-substituted cyclopropene in order to probe the effect of chain length on the [2 + 2]-cycloaddition reaction. Upon heating at 175 °C, **46** is converted into a single

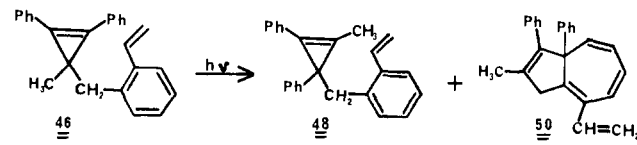


46: R_1=Ph; R_2=CH_3
48; R_1=CH_3; R_2=Ph

47; R_1=Ph; R_2=CH_3
49; R_1=CH_3; R_2=Ph

product in quantitative yield whose structure is assigned as cycloadduct **47** on the basis of its spectral properties. The triplet sensitized irradiation of **46** also gave **47** as the exclusive cycloadduct. Tricyclohexane **49** was formed in high yield from the closely related unsymmetrical cyclopropene **48** upon thermolysis or sensitized photolysis.

In contrast to the results outlined above, the direct irradiation of **46** produced a mixture of **48** and dihydroazulene **50**. The structure of **50** was assigned primarily on the basis of its NMR spectrum which showed a singlet at δ 1.65 (3 H), doublets at 3.44 (1 H, J = 18.0 Hz), 3.78 (1 H, J = 18.0 Hz), 5.13 (1 H, J =

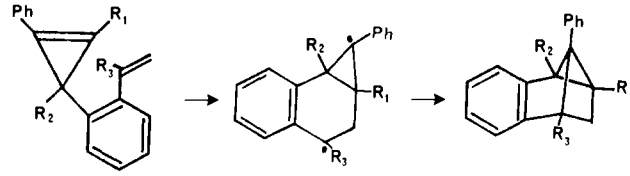


46 **48** **50**

11.0 Hz), and 5.28 (1 H, J = 18.0 Hz), multiplets at 5.60 (1 H) and 6.30 (5 H), a doublet of doublets at 6.65 (1 H, J = 18.0 and 11.0 Hz), and a multiplet at 6.8–7.3 (8 H).

Discussion

The thermal [2 + 2] cycloaddition of untwisted ethylenes to form cyclobutanes is a rare phenomenon.[42-47] The constraints imposed upon such reactions by orbital symmetry factors make them of more than usual mechanistic interest.[48] In cyclopropene, the torsional angle is close to zero and p–p overlap should not be significantly different from that of a normal olefin. Thus, the likelihood of cyclopropene to undergo [2 + 2] cycloaddition should primarily be due to relief of angle bending rather than torsional strain. The intramolecular [2 + 2] cycloaddition encountered on thermolysis of a series of *o*-vinylphenyl-substituted cyclopropenes is unique in that the other reported examples of thermal olefin cycloadditions either occur in compounds in which the double bond is subjected to severe torsional strain[49-54] or else involve reactants that bear substituents capable of stabilizing diradical or dipolar intermediates.[55-57] The results obtained on thermolysis of the above systems may be most simply interpreted on the basis of an unusually easy bond formation between the double bond and the cyclopropene ring to produce a diradical intermediate which collapses to the observed cycloadduct. This interpretation is



perfectly consistent with the kinetic results whereby the rate of cycloaddition is accelerated by the presence of a methyl group on the neighboring π bond (i.e., $R_3 = CH_3$). The driving force for the thermal reactions is undoubtedly associated with the considerable relief of bond angle strain of the cyclopropene ring. It would seem as though the strain energy present in the benzotricycloheptene skeleton is less than that present in the cyclopropene ring.[58] It should also be pointed out that in the case of the unsymmetrically substituted cyclopropene system (i.e., $R_1 = CH_3$; R_2 = Ph), there is a distinct preference for that product arising from bonding between the terminal olefinic carbon and

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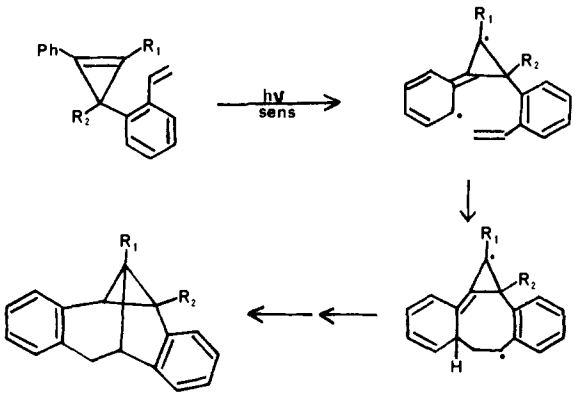
the cyclopropene carbon bearing the methyl group. This is undoubtedly related to the fact that $\pi-\pi$ bridging will give the most stable biradical and thus lead to the preferential formation of benzotricycloheptenes **26** and **28**.

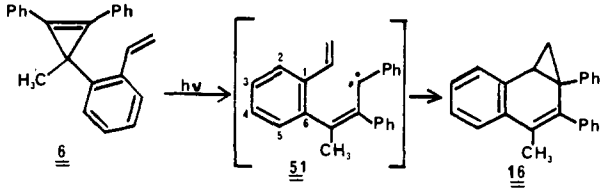
As was pointed out earlier, the triplet-sensitized behavior of the 3-(*o*-vinylphenyl)-substituted cyclopropene system produced a mixture of tricyclic compounds (**7** and **22** or **28** and **43**). While



22; R_1=Ph; R_2=CH_3
43; R_1=CH_3; R_2=Ph

the formation of **7** (or **28**) is uneventful, the formation of **22** (or **43**) involves a more complicated process. This reaction may be pictured as proceeding by attack of the ortho position of the triplet state of **6** (or **13**) on the terminal vinyl carbon followed by diradical coupling and a subsequent rearomatization. Examination of molecular models indicate that the geometry for such a process is quite favorable. Formation of benzotricyclononane **22** (or **43**) from the photosensitized reaction is probably related to the fact that the triplet state of **6** (or **13**) possesses a significant amount of radical character on the ortho position of the aromatic ring. This is not the case in the thermal reaction of these compounds.

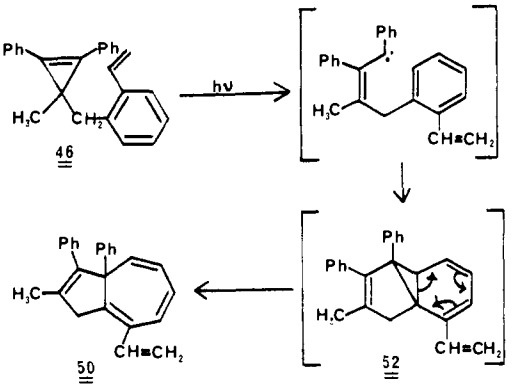
The most reasonable explanation to account for the products obtained on direct irradiation involves a sequence consisting of ring opening of the cyclopropene ring to a vinylcarbene intermediate. Singlet states of cyclopropenes are known to produce vinylcarbene intermediates which can cyclize back to the cyclopropene or undergo reactions characteristic of singlet methylene.[59,60] These include intramolecular hydrogen transfer,[61] insertion in a C–H bond,[62] alkyl group migration,[63] electrocyclization,[23,64] and cycloaddition to π bonds.[65] Thus, the formation of cyclopropa[*a*]naphthalene **16** from the irradiation of



6 **51** **16**

6 can be rationalized in terms of intramolecular addition of the carbene carbon onto the neighboring double bond. It would seem as though the ring opening of the singlet state of the cyclopropene is faster than addition to the neighboring π bond. In fact, recent MO calculations suggest that the singlet excited state of cyclopropenes can readily open in an unactivated process to relieve the strain energy present in the ring.[66] The calculations also indicate that triplet states of cyclopropenes have a large barrier (13 kcal/mol) for ring opening. This would account for the difference in the photochemical behavior of the two excited states.

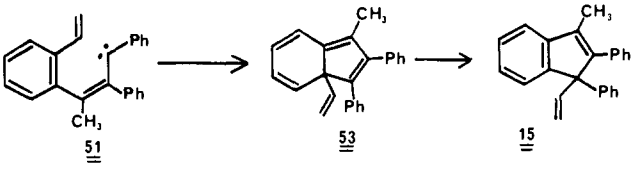
The formation of dihydroazulene **50** from the direct irradiation



46 **52** **50**

of **46** is also consistent with a vinylcarbene intermediate which attacks the π electrons of the adjacent aromatic ring to give **52** as a transient species. This reactive norcaradiene can rapidly be converted to dihydroazulene via an electrocyclic ring-opening reaction. The formation of dihydroazulene **50** by the addition of the vinylcarbene onto the neighboring aromatic ring has good precedent in the literature.[67,68] In fact, this type of reaction has been used as a key step in a general azulene synthesis.[69]

The mechanism by which **6** is converted into indenes **14** and **15** also requires some comment. These products can be rationalized in terms of vinylcarbene **51**. Aside from adding to the



51 **53** **15**

neighboring double bond, **51** can cyclize onto the ortho positions of the aromatic ring. While the formation of **14** is uneventful,[23] the isolation of **15** represents a more complicated process. This reaction may be pictured as proceeding by cyclization of **51** onto the carbon bearing the vinyl group so as to generate isoindene **53**. A subsequent 1,5 vinyl shift accounts for the formation of **15**. The last step of this sequence is not unreasonable since there are several reports in the literature which proceed via a 1,5 sigmatropic vinyl shift.[70,71]

One final point worth mentioning deals with the photorearrangement of **6** to **13**. A limited number of examples exist where the electronically excited singlet state of the cyclopropene retains the three-membered ring.[65] In these special cases, the photoreaction observed corresponds to a 1,2-substituent shift.[65] We propose a mechanism for the conversion of **6** into **13** which involves $\pi-\pi^*$ bridging of the excited cyclopropene to give diradical **54** which subsequently cleaves to produce the rearranged cyclopropene. The bridging and cleavage steps are closely related to that suggested by Zimmerman and Hovey to rationalize the rearrangement of **55** to **57**.[72] The fact that a similar rearrangement does not take place with 1,2,3-triphenyl-3-methylcyclopropene is understandable since the *o*-vinyl moiety appears to be necessary to stabilize the initially formed diradical intermediate. Cyclopropene **46** also gives a 1,2-rearranged product (**48**) on direct irradiation. In this case it would seem that side-chain fragmen-

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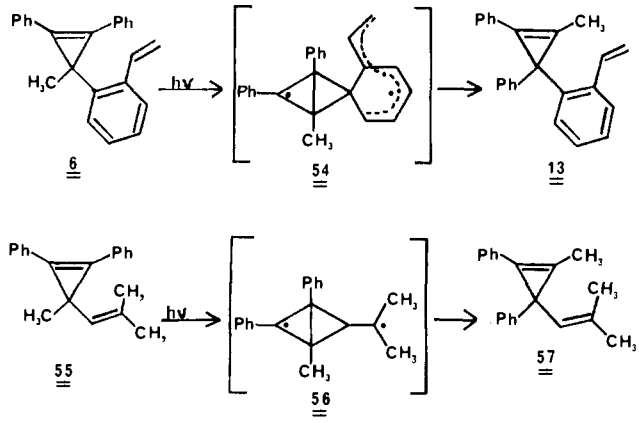

tation can compete with ring opening to the vinylcarbene. The initially produced cyclopropenyl–*o*-vinylbenzyl radical pair undergoes a subsequent recombination to give the observed product. The role of radical-pair recombination with a series of 3-allyl-substituted cyclopropenes is well established and provides good analogy for this suggestion.[65]

In conclusion, the results of our work dealing with the intramolecular [2 + 2] cycloaddition of cyclopropene derivatives provide an attractive approach for the synthesis of some novel strained carbocycles. The facility of the [2 + 2] cycloaddition is undoubtedly associated with the considerable relief of bond angle strain of the cyclopropene ring. Further studies on the scope of the internal [2 + 2]-cycloaddition reaction are in progress and will be reported in due course.

Experimental Section[73]

Preparation of 1,2-Diphenyl-3-methyl- (6) and 1,3-Diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (13). To a stirred suspension of activated magnesium prepared according to the method of Rieke[74] in 150 mL of refluxing tetrahydrofuran was added 6.0 g of *o*-bromovinylbenzene. The mixture was allowed to reflux for 40 min and the Grignard solution was then added to a stirred slurry containing 1.6 g of diphenylmethylcyclopropenylium perchlorate[23] in 100 mL of anhydrous tetrahydrofuran at −78 °C under a nitrogen atmosphere. The mixture was allowed to warm to 5 °C overnight. After the mixture was quenched with a saturated ammonium chloride solution, the organic layer was taken up in ether, washed 3 times with water, and dried over magnesium sulfate. Removal of the solvent under reduced pressure left a light yellow oil which was chromatographed on a 100 × 1.5 cm silica gel column, using a 9% benzene–hexane mixture as the eluent. The first component isolated from the column contained 1.05 g (64%) of 1,2-diphenyl-3-methyl-3-(*o*-vinylphenyl)cyclopropene (6): mp 68–69 °C; IR (KBr) 3030, 1800, 1630, 1590, 1490, 1470, 1435, 1410, 1380, 1070, 1045, 1030, 1110, 1000, 910, 835, 775, 760, 750, 735, 730, 680 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.86 (s, 3 H), 5.32 (dd, 1 H, J = 10.9, 1.4 Hz), 5.56 (dd, 1 H, J = 17.4, 1.4 Hz), 7.08–7.81 (m, 15 H); UV (95% ethanol) 317, 227 nm (ϵ 22 500, 30 000); mass spectrum, m/e 308 (M^+, base), 294, 293, 220, 215, 205, 202.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.43; H, 6.61.

The second component isolated from the column contained 0.106 g (7%) of 1,3-diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (**13**): mp 111–112 °C; IR (KBr) 2985, 1845, 1625, 1590, 1480, 1435, 1380, 1120, 1070, 990, 980, 900, 790, 775, 760, 750, 710, 795, 790 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 2.44 (s, 3 H), 5.10 (dd, 1 H, J = 17.5, 1.4 Hz), 6.86–7.64 (m, 15 H); UV (95% ethanol) 256 nm (ϵ 22 100); mass spectrum, m/e 308 (M^+, base), 293, 215.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.47; H, 6.39.

Thermolysis of 1,2-Diphenyl-3-methyl-3-(*o*-vinylphenyl)cyclopropene (6). A solution containing 77.0 mg of 6 in 0.5 mL of a pyridine–benzene (1:4) mixture was heated in a sealed tube at 175 °C for 4 h. The solvent was removed under reduced pressure to leave behind a light yellow oil which was chromatographed on a 3.0 × 0.5 cm silica gel column, using hexane as the eluent. The white solid obtained (73.8 mg, 96%) was identified as (1α,1aβ,6α,6aβ)-1,1a,6,6a-tetrahydro-1a-methyl-1,6a-diphenyl-1,6-methanocycloprop[*a*]indene (**7**) on the basis of its spectroscopic properties: mp 86–87 °C; IR (KBr) 3010, 2900, 1605, 1495, 1465, 1440, 1380, 1240, 1210, 1180, 1155, 1125, 1075, 1030, 1020, 985, 915, 845, 755, 700 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.40 (s, 3 H), 1.41 (d, 1 H, J = 9.0 Hz), 2.99 (dd, 1 H, J = 9.0, 8.0 Hz), 3.69 (d, 1 H, J = 8.0 Hz), 7.03–7.42 (m, 14 H); ^{13}C NMR (20 MHz, $CDCl_3$) 12.4 (q, J = 127 Hz), 38.1 (t, J = 140 Hz), 42.5 (s), 44.3 (s), 45.9 (d, J = 151 Hz), 68.3 (s), 119.7–129.3 (m), 135.9 (s), 138.8 (s), 144.5 (s), 148.4 (s); UV (95% ethanol) shoulder 223 nm (ϵ 22 700); mass spectrum, m/e 308 (M^+, base), 294, 293, 231, 216, 215, 203, 192, 115, 103, 91, 77.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.40; H, 6.58.

Independent Synthesis of (1α,1aβ,6α,6aβ)-1,1a,6,6a-Tetrahydro-1a-methyl-1,6a-diphenyl-1,6-methanocycloprop[*a*]indene (7). A solution containing 0.65 g of isopentyl nitrite in 100 mL of methylene chloride was heated at reflux. To this solution was added 0.68 g of anthranilic acid and 1.15 g of 2-methyl-1,3-diphenyl-1,3-cyclopentadiene[23] (**8**) in 100 mL of acetone over a 30-min period. The resulting solution was heated at reflux for an additional 8 h and was allowed to stir overnight. A saturated solution of sodium bicarbonate was added and the mixture was extracted with methylene chloride. The methylene chloride was dried over magnesium sulfate and the solvent was removed under reduced pressure. The resulting black oil that was obtained was chromatographed on a 25 × 5 cm silica gel column, using hexane as the eluent. The first component isolated from the column contained 0.81 g (53%) of a white crystalline solid which was identified as 1,4-dihydro-2-methyl-1,3-diphenyl-1,4-methanonaphthalene (**9**) on the basis of its spectral properties: mp 122–123 °C; IR (KBr) 3030, 2975, 1630, 1610, 1495, 1455, 1445, 1385, 1190, 1160, 1125, 1095, 1060, 1040, 1015, 970, 960, 925, 915, 885, 780, 770, 755, 740, 705 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.83 (s, 3 H), 2.57 (dd, 1 H, J = 7.1, 1.6 Hz), 2.78 (dd, 1 H, J = 7.1, 1.6 Hz), 4.14 (t, 1 H, J = 1.6 Hz), 6.94–7.65 (m, 14 H); UV (cyclohexane) 277, 237 nm (ϵ 8900, 16 400); mass spectrum, m/e 308 (M^+, base), 293, 215, 192, 191, 115, 91.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.42; H, 6.57.

A solution containing 158 mg of **9** and 2.5 g of acetophenone in 250 mL of anhydrous benzene was irradiated for 12 h under an argon atmosphere with a 550-W Hanovia mercury arc lamp equipped with a Pyrex filter sleeve. The solvent was removed under a reduced pressure and the resulting yellow oil was chromatographed on a 60 × 1.5 cm silica gel column, using hexane as the eluent. The first component isolated from the column contained 155 mg (98%) of a white crystalline solid which was identical in every detail with (1α,1aβ,6α,6aβ)-1,1a,6,6a-tetrahydro-1a-methyl-1,6a-diphenyl-1,6-methanocycloprop[*a*]indene (**7**) obtained from the thermolysis of 1,2-diphenyl-3-methyl-3-(*o*-vinylphenyl)cyclopropene (6).

Thermolysis of 1,3-Diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (13). A solution containing 80.0 mg of **13** in 0.5 mL of a 20% pyridine–benzene mixture was heated in a sealed tube at 175 °C for 45 min. The solvent was removed under reduced pressure to leave behind a light yellow solid which was chromatographed on a 4 × 1.5 cm silica gel column, using hexane as the eluent. The resulting white crystalline solid isolated (79.8 mg, 99%) was assigned as (1α,1aβ,6α,6aβ)-1,1a,6,6a-tetrahydro-1-methyl-1a,6a-diphenyl-1,6-methanocycloprop[*a*]indene (**28**) on the basis of its spectroscopic properties: mp 154–155 °C; IR (KBr) 2900, 1605, 1500, 1465, 1445, 1380, 1220, 1080, 1045, 1020, 950, 790, 760, 755, 735, 715, 700 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.41 (d, 1 H, J = 8.9 Hz), 1.61 (s, 3 H), 2.76 (dd, 1 H, J = 8.9, 7.6 Hz), 3.78 (d, 1 H, J = 7.6 Hz), 6.63–7.29 (m, 14 H); UV (95% ethanol) 249 nm (ϵ 13 300); mass spectrum, m/e 308 (M^+, base), 293, 229, 216, 215, 130.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.33; H, 6.62.

Independent Synthesis of (1α,1aβ,6α,6aβ)-1,1a,6,6a-Tetrahydro-1-methyl-1a,6a-diphenyl-1,6-methanocycloprop[*a*]indene (28). To a solution containing 2.88 g of 2-phenyl-3-methylcyclopent-2-enone[23] (**31**) in 125 mL of anhydrous ether was added 40 mL of a 1.0 M phenyllithium solution at 0 °C. After stirring at 0 °C for 1 h, the solution was poured into water and extracted with ether. The ether layer was washed with water and dried over magnesium sulfate. Removal of the solvent left a clear oil which was dissolved in 160 mL of ethanol containing 17 mL of acetic acid. The solution was stirred for 4 h and was then poured onto ice water. The mixture was extracted with ether, washed with a 5% sodium bicarbonate solution and water, and dried over magnesium sulfate. Removal of the solvent left 2.5 g of a clear oil whose NMR spec-

(73) All melting points and boiling points are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Atlanta, GA. The infrared absorption spectra were determined on a Perkin-Elmer 467 infrared spectrophotometer. The ultraviolet absorption spectra were measured with a Cary Model 14 recording spectrophotometer, using 1-cm matched cells. The proton magnetic resonance spectra were determined at 90 MHz, using a Varian EM-390 spectrometer. Mass spectra were determined with a Finnegan 4000 mass spectrometer at an ionizing voltage of 70 eV.

(74) Rieke, R. D.; Bales, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 1775.

trum indicated it to be a 1:3 mixture of 1,2-diphenyl-3-methyl- (**32**) and 1-methyl-2,3-diphenyl-1,3-cyclopentadiene (**33**). The mixture of isomeric cyclopentadienes could not be separated by extensive column chromatography and was used directly in the next reaction without further purification.

A solution containing 2.22 g of isopentyl nitrite in 180 mL of methylene chloride was heated at reflux. To this solution was added a solution containing 2.30 g of anthranilic acid and 2.5 g of the crude 3:1 mixture of 3-methyl-1,2-diphenyl- (**33**) and 1-methyl-2,3-diphenyl-1,3-cyclopentadiene (**32**) in 180 mL of acetone over a 30-min period. The solution was allowed to reflux for 8 h and was then allowed to stir overnight. A saturated solution of sodium bicarbonate was added and the mixture was extracted with methylene chloride. The methylene chloride solution was dried over magnesium sulfate and the solvent was removed under reduced pressure. The resulting black oil was chromatographed on a 15 × 5 cm silica gel column, using hexane as the eluent. The first component isolated contained 1.47 g of a colorless oil which was shown to be a 2:1 mixture of isomers. These isomers could be fractionally crystallized apart, using a benzene–hexane mixture. The major fraction contained 871.7 mg (26%) of a white solid which was identified as 1,4-dihydro-3-methyl-1,2-diphenyl-1,4-methanonaphthalene (**34**) on the basis of its spectral properties: mp 137–138 °C; IR (KBr) 3010, 2880, 1620, 1485, 1435, 1375, 1250, 1190, 1040, 1005, 995, 940, 915, 905, 770, 755, 750, 690 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.87 (s, 3 H), 2.52 (dd, 1 H, J = 7.2, 1.2 Hz), 2.65 (dd, 1 H, J = 7.2, 1.4 Hz), 3.74 (b s, 1 H), 6.85–7.52 (m, 14 H); UV (95% ethanol) 272, shoulder 233 nm (ϵ 5300, 13 900); mass spectrum, m/e 308 (M$^+$), 293, 205, 192 (base), 191.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.31; H, 6.62.

The minor fraction contained 596 mg (18%) of a clear oil which could not be totally purified and consisted of 82% of 1,4-dihydro-1-methyl-2,3-diphenyl-1,4-methanonaphthalene (**30**) [NMR ($CDCl_3$, 100 MHz) δ 2.44 (s, 3 H), 2.28 (dd, 1 H, J = 7.0, 1.5 Hz), 2.55 (dd, 1 H, J = 7.0, 1.5 Hz), 4.21 (b s, 1 H), 6.81–7.36 (m, 14 H)] and 18% of 1,4-dihydro-3-methyl-1,2-diphenyl-1,4-methanonaphthalene (**34**).

A solution containing 165 mg of **34** and 2.5 g of acetophenone in 250 mL of anhydrous benzene was irradiated for 12 h under an argon atmosphere with a 550-W Hanovia mercury arc lamp equipped with a Pyrex filter sleeve. The solvent was removed under reduced pressure and the resulting yellow oil was chromatographed on a 60 × 1.5 cm silica gel column, using hexane as the eluent. The first component isolated from the column contained 121 mg (73%) of a white crystalline solid whose structure was assigned as (1α,1aβ,6α,6aβ)-1,1a,6,6a-tetrahydro-1a-methyl-6,6a-diphenyl-1,6-methanocycloprop[a]indene (**36**) on the basis of its spectral properties: mp 122–123 °C; IR (KBr) 2925, 2840, 1580, 1480, 1450, 1425, 1365, 1295, 1215, 1150, 1070, 1010, 980, 910, 865, 830, 770, 755, 750, 700, 695 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.33 (d, 1 H, J = 9.0 Hz), 1.44 (s, 3 H), 2.23 (d, 1 H, J = 3.6 Hz), 3.35 (dd, 1 H, J = 9.0, 3.6 Hz), 6.53–7.48 (m, 14 H); mass spectrum, m/e 308 (M$^+$, base), 294, 293, 217, 216, 215, 202.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.36; H, 6.62.

A solution containing 166 mg of a mixture of 1,4-dihydro-1-methyl-2,3-diphenyl-1,4-methanonaphthalene (**30**) (82%) and 1,4-dihydro-3-methyl-1,2-diphenyl-1,4-methanonaphthalene (**34**) (18%) and 3.5 g of acetophenone in 250 mL of anhydrous benzene was irradiated for 12 h under an argon atmosphere with a 550-W Hanovia mercury arc lamp equipped with a Pyrex filter sleeve. The solvent was removed under reduced pressure and the resulting yellow oil was chromatographed on a 60 × 1.5 cm silica gel column, using hexane as the eluent. The major component isolated from the column contained 55 mg (33%) of a white crystalline solid whose structure was identical with the thermal product obtained from the thermolysis of 2-methyl-1,3-diphenyl-3-(*o*-vinylphenyl)cyclopropene (**13**).

Irradiation of 1,2-Diphenyl-3-methyl-3-(*o*-vinylphenyl)cyclopropene (6) in Benzene. A solution containing 500 mg of 6 in 500 mL of anhydrous benzene was irradiated for 2.5 h under an argon atmosphere with a 550-W Hanovia mercury arc lamp equipped with a Pyrex filter sleeve. The solvent was removed under reduced pressure and the resulting yellow oil was chromatographed on a 150 × 1.5 cm silica gel column, using a 9% benzene–hexane mixture as the eluent. The first fraction isolated from the column contained 81 mg of 3-methyl-1-vinyl-1,2-diphenylindene (**15**), mp 77–78 °C; IR (KBr) 3060, 3025, 2975, 2910, 1620, 1590, 1480, 1460, 1440, 1400, 1375, 1020, 995, 920, 740, 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.07 (s, 3 H), 4.96–5.22 (m, 2 H), 6.32 (dd, 1 H, J = 17.3 and 10.0 Hz), 6.90–7.47 (m, 14 H); UV (95% ethanol) 288 and 222 nm (shoulder) (ϵ 14 900 and 20 500); mass spectrum, m/e 308 (M$^+$), 293, 215 (base), 100, 91.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.21; H, 6.60.

The structure of this material was established by catalytic reduction to 1,2-diphenyl-1-ethyl-3-methylindene (**17**). A suspension containing 31 mg of **15** and 5 mg of 5% palladium on charcoal in 25 mL of ethanol was hydrogenated in a Paar shaker for 2 h at 15 psi. The reaction mixture was filtered and the solvent was removed under reduced pressure. The resulting white crystalline solid (30 mg, 99%) obtained was identified as 1,2-diphenyl-1-ethyl-3-methylindene (**17**) on the basis of its spectral properties and by comparison with an independently synthesized sample: mp 84–85 °C; IR (KBr) 3075, 3050, 2980, 2940, 2925, 2860, 1590, 1485, 1460, 1450, 1440, 1375, 1100, 1025, 1005, 785, 775, 745, 730, 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 0.46 (t, 3 H, J = 6.1 Hz), 1.87–2.62 (m, 2 H), 2.18 (s, 3 H), 6.74–7.44 (m, 14 H); UV (95% ethanol) 290, shoulder 222 nm (ϵ 2260, 5190), mass spectrum, m/e 310 (M$^+$), 295, 283, 282, 281 (base), 265, 205, 204, 203, 202, 105, 91, 77.

Anal. Calcd for $C_{24}H_{22}$: C, 92.86; H, 7.14. Found: C, 92.82; H, 7.18.

An authentic sample of the above indene was prepared by treating 1-methyl-2,3-diphenylindene with *n*-butyllithium in hexane at −78 °C in the presence of tetramethylethylenediamine with ethyl bromide. Workup followed by chromatogrphic separation afforded a 64% yield of 1-methyl-1-ethyl-2,3-diphenylindene and 36% of 1,2-diphenyl-1-ethyl-3-methylindene (**17**) which was identical with the sample obtained from the catalytic hydrogenation of **15**.

The second fraction isolated from the crude photolysis mixture derived from the photolysis of 6 contained 207 mg of a white crystalline solid, mp 105–106 °C, whose structure was assigned as 1,2-dihydro-4-methyl-2,3-diphenylcyclopropa[a]naphthalene (**16**) on the basis of its spectral properties: IR (KBr) 3010, 1605, 1490, 1445, 1383, 1120, 1090, 1055, 1045, 1010, 985, 964, 935, 805, 780, 765, 745, 700 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 0.61 (dd, 1 H, J = 5.5, 3.5 Hz), 1.98 (s, 3 H), 2.19 (dd, 1 H, J = 9.6, 3.5 Hz), 2.53 (dd, 1 H, J = 9.6, 5.5 Hz), 6.94–7.56 (m, 14 H); UV (95% ethanol) 288, 237 nm (ϵ 11 200, 23 800); mass spectrum, m/e 308 (M$^+$), 293, 220, 214, 207, 206, 205, 179, 178, 129, 119, 105, 91, 77.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.31; H, 6.65.

The third fraction isolated from the chromatography column (21%) was identified as 1,3-diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (**13**) by comparison with an authentic sample.

The fourth fraction obtained from the column contained 84 mg of a white solid, mp 82–83 °C, whose structure was assigned as 1,2-diphenyl-3-methyl-4-vinylindene (**14**) on the basis of its spectral properties: IR (KBr) 2975, 1590, 1480, 1440, 1395, 1375, 1070, 1060, 990, 920, 805, 790, 760, 730, 695 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 2.51 (d, 3 H, J = 2.0 Hz), 4.85 (q, 1 H, J = 2.0 Hz), 5.33 (dd, 1 H, J = 10.9, 1.5 Hz), 5.63 (dd, 1 H, J = 17.3, 1.5 Hz), 6.93–7.68 (m, 14 H); UV (95% ethanol) 295, 253 nm (ϵ 20 150, 16 460); mass spectrum, m/e 308 (M$^+$, base), 293.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found; C, 93.40; H, 6.56.

The structure of this material was established by catalytic reduction to 1,2-diphenyl-3-methyl-4-ethylindene. A suspension containing 33 mg of **14** and 3 mg of 5% palladium on charcoal in 25 mL of ethanol was hydrogenated on a Paar shaker for 2 h at 15 psi. The solution was filtered and the solvent was removed under reduced pressure to give 1,2-diphenyl-3-methyl-4-ethylindene: UV (95% ethanol) 288 nm (ϵ 10 500); NMR ($CDCl_3$, 90 MHz) δ 1.37 (t, 3 H, J = 8.0 Hz), 2.67 (d, 3 H, J = 1.5 Hz), 3.04 (q, 2 H, J = 8.0 Hz), 4.82 (q, 1 H, J = 1.5 Hz), 6.8–7.4 (m, 14 H); mass spectrum, m/e 310 (M$^+$, base), 295, 281, 265, 203, 166, 105. The structure of this material was further established by comparison with an authentic sample.[27]

The extended photolysis (14 h) of cyclopropene 6 also produced two new compounds. Subsequent experiments showed that these materials were derived from a secondary photolysis of 1,2-dihydro-4-methyl-2,3-diphenylcyclopropa[a]naphthalene (**16**). The 1:1 mixture of isomers was separated by preparative thick-layer chromatography. The faster moving band contained a clear oil which resisted all attempts at crystallization. This material was assigned as 1-methyl-6,7-diphenyl-2,3-benzobicyclo-[3.2.0]hepta-2,6-diene (**20**) on the basis of its spectral properties: IR (neat) 3060, 3020, 2975, 2920, 2860, 1595, 1495, 1445, 1370, 1070, 1025, 910, 760, 775, 735, 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.66 (s, 3 H), 3.02 (d, 1 H, J = 3.5 Hz), 3.11 (d, 1 H, J = 8.6 Hz), 3.52 (dd, 1 H, J = 8.6, 3.5 Hz), 7.05–7.56 (m, 14 H); UV (95% ethanol) 291, 277 nm (ϵ 9200, 9100); mass spectrum, m/e 308 (M$^+$), 215, 178, 177, 131, 130 (base), 129, 115.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.08; H, 6.27.

The second band isolated was assigned as 3-methyl-4,5-diphenyl-1,2-benzocycloheptatriene (**19**) on the basis of its spectroscopic properties: mp 149–150 °C; IR (KBr) 3050, 3020, 2990, 2950, 2880, 1480, 1440, 1260, 1190, 1070, 980, 880, 840, 760, 745, 690 cm^{-1}; NMR ($CDCl_3$, 90

MHz) δ 2.33 (s, 3 H), 3.05 (dd, 1 H, J = 12.2, 6.7 Hz), 3.33 (dd, 1 H, J = 12.2, 7.9 Hz), 6.11 (br t, 1 H, J = 7.5 Hz), 6.92–7.70 (m, 14 H); ^{13}C NMR (ppm, $CDCl_3$) 22.3 (q, J = 128 Hz), 34.3 (t, J = 130 Hz), 125.5–130.8 (m), 137.6 (s), 138.4 (s), 140.3 (s), 140.6 (s), 141.3 (s), 141.4 (s); UV (95% ethanol) 242 nm (ε 28 100); mass spectrum, m/e 308 (M^+), 293, 231, 216, 215 (base), 178, 130, 91.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.39; H, 6.55.

Triplet-Sensitized Irradiation of 1,2-Diphenyl-3-methyl-3-(*o*-vinylphenyl)cyclopropene (6) in Benzene. A solution containing 607 mg of 6 and 67 mg of thioxanthen-9-one in 500 mL of anhydrous benzene was irradiated for 2.5 h under an argon atmosphere with a 450-W Hanovia mercury arc lamp equipped with a Uranium filter sleeve. The solvent was removed under reduced pressure and the resulting yellow oil was chromatographed on a 2.5 × 1.5 cm silica gel column, using hexane as the eluent. The solvent was removed under reduced pressure and the resulting colorless oil was subjected to chromatography on a 100 × 1.5 cm silica gel column, using a 9% benzene–hexane mixture as the eluent. The first component isolated from the column contained 382 mg (63%) of 1,6-methanocycloprop[*a*]indene **7**. The second component isolated was a crystalline solid (211 mg, 35%) whose structure was assigned as 4b,4c,9b,9c-tetrahydro-9c-methyl-4c-phenyl-5*H*-benzo[*b*]cyclopropa[*lm*]fluorene (**22**) on the basis of its spectral properties: mp 133–134 °C; IR (KBr) 3010, 2890, 1485, 1445, 1380, 1115, 1075, 1035, 1020, 980, 820, 790, 760, 750, 725, 705 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.43 (s, 3 H), 2.61 (s, 1 H), 2.73 (dd, 1 H, J = 15.3, 3.3 Hz), 3.31 (dd, 1 H, J = 15.3, 3.3 Hz), 3.87 (t, 1 H, J = 3.3 Hz), 6.88–7.40 (m, 13 H); ^{13}C NMR (ppm, $CDCl_3$) 16.3 (q, J = 126 Hz), 32.5 (t, J = 129 Hz), 33.5 (d, J = 156 Hz), 44.4 (s), 49.9 (d, J = 135 Hz), 122.4–129.3 (m), 133.3 (s), 141.5 (s), 145.9 (s), 146.2 (s); UV (95% ethanol) shoulder 233 nm (ε 16 900); mass spectrum, m/e 308 (M^+, base), 294, 293, 231, 216, 215, 115, 91.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.72; H, 6.68.

Triplet-Sensitized Irradiation of 1,3-Diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (13) in Benzene. A solution containing 166 mg of **13** and 23 mg of thioxanthen-9-one in 200 mL of anhydrous benzene was irradiated for 2 h under an argon atmosphere with a 450-W Hanovia mercury arc lamp equipped with a Uranium filter sleeve. The solvent was removed under reduced pressure and the resulting yellow solid was chromatographed on a 15 × 1.5 cm silica gel column, using hexane as the eluent. The first component isolated contained 77 mg (46%) of 1,6-methanocycloprop[*a*]indene (**28**). The second component isolated from the column contained 88 mg (53%) of a white crystalline solid whose structure was identified as 4b,4c,9b,9c-tetrahydro-4c-methyl-9c-phenyl-5*H*-benzo[*b*]cyclopropa[*lm*]fluorene (**43**) on the basis of its spectral properties: mp 123–124 °C; IR (KBr) 3030, 2990, 2890, 1605, 1495, 1475, 1450, 1440, 775, 760, 745, 730, 720, 710, 700, 685 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.28 (s, 3 H), 2.67 (s, 1 H), 2.79 (dd, 1 H, J = 15.2, 2.8 Hz), 3.34 (dd, 1 H, J = 15.2, 2.8 Hz), 3.61 (t, 1 H, J = 2.8 Hz), 6.57–7.41 (m, 13 H); mass spectrum, m/e 308 (M^+), 294, 293, 216, 215 (base).

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.33; H, 6.59.

Silver(I)-Induced Rearrangement of 1,3-Diphenyl-2-methyl-3-(*o*-vinylphenyl)cyclopropene (13) in Benzene. A solution containing 64 mg of **13** and 300 mg of silver perchlorate in 25 mL of anhydrous benzene was heated at 56 °C for 14 h. The resulting solution was washed several times with a sodium sulfide solution followed by a saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent under reduced pressure left 62 mg of a colorless oil which contained a 64:36 mixture of 2-methyl-4-vinyl-1,3-diphenylindene (**44**) [NMR ($CDCl_3$, 90 MHz) δ 1.68 (s, 3 H), 4.38 (br s, 1 H), 4.82 (dd, 1 H, J = 11.0, 1.5 Hz), 5.52 (dd, 1 H, J = 17.2, 1.5 Hz), 6.40 (dd, 1 H, J = 17.2, 11.0 Hz), 6.98–7.53 (m, 13 H)] and 2-methyl-1-phenyl-3-(*o*-vinylphenyl)indene (**45**) as judged by NMR analysis. The structure of **45** was confirmed by comparison with an independently synthesized sample.

To a stirred suspension of activated magnesium (38 mmol) prepared according to the method of Rieke[74] in 100 mL of tetrahydrofuran at 60 °C was added 3.50 g of *o*-bromovinylbenzene. The mixture was allowed to reflux for 40 min and was then cooled to room temperature. To the above Grignard solution was added 582 mg of 2-methyl-3-phenyl-1-indanone[75] in 15 mL of anhydrous ether. The reaction mixture was stirred for 3 h and was carefully quenched by the addition of a saturated ammonium chloride solution. The reaction mixture was stirred until both phases became clear and then the organic phase was taken up in ether. The resulting ethereal layer was washed twice with water and a saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent under reduced pressure left a light yellow oil. The resulting indanol obtained was used without further purification. To the above indanol was added 20 mL of glacial acetic acid, 2 mL of concentrated sulfuric acid, and 2 mL of water. The reaction mixture was stirred at room temperature for 10 min and then 30 mL of water was added. The excess acid was carefully neutralized with crystalline sodium carbonate and the mixture was extracted three times with benzene. The combined benzene extracts were washed with a saturated sodium bicarbonate solution, water, and a saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvent under reduced pressure left a yellow oil which was chromatographed on a 15 × 5 cm silica gel column, using hexane as the eluent. The structure of the resulting colorless oil (628 mg, 65%) was assigned as 2-methyl-1-phenyl-3-(*o*-vinylphenyl)indene (**45**) and was identical with the minor product obtained from the silver ion catalyzed reaction of **13**: IR (neat) 3070, 3040, 2990, 2940, 2920, 1600, 1500, 1475, 1470, 1465, 1460, 1450, 1115, 1050, 940, 805, 790, 780, 770, 735, 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.70 (s, 3 H), 4.43–4.53 (m, 1 H), 5.03–5.22 (m, 1 H), 5.70 (dd, 1 H, J = 17.5, 1.3 Hz), 6.50–7.84 (m, 14 H); UV (95% ethanol) 250 nm (ε 15 700); mass spectrum, m/e 308 (M^+), 293, 215, 185 (base), 183, 105, 104, 103, 91, 77.

Anal. Calcd for $C_{24}H_{20}$: C, 93.46; H, 6.54. Found: C, 93.36; H, 6.59.

Preparation of 1,2-Diphenyl-3-methyl- (23) and 1,3-Diphenyl-2-methyl-3-(*o*-propenylphenyl)cyclopropene (25). To a stirred suspension of activated magnesium prepared according to the method of Rieke[74] in 150 mL of refluxing tetrahydrofuran was added 3.30 g of *o*-bromoisopropenylbenzene. The mixture was heated at reflux for 45 min and was then added to a stirred slurry containing 2.50 g of diphenylmethylcyclopropenylium perchlorate in 100 mL of anhydrous tetrahydrofuran at −78 °C under a nitrogen atmosphere. The mixture was worked up in the normal fashion and chromatographed on silica gel to give 0.38 g (14%) of **23**, mp 70–71 °C: IR (KBr) 3095, 3080, 3015, 2960, 2925, 2860, 1820, 1640, 1600, 1485, 1450, 1435, 1375, 1305, 1265, 1160, 900, 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.95 (s, 3 H), 1.97 (b s, 3 H), 4.88–5.00 (m, 1 H), 5.01–5.13 (m, 1 H), 6.98–7.83 (m, 14 H); UV (95% ethanol) 317 and 227 nm (ε 22 500 and 31 000); mass spectrum, m/e 322 (M^+, base), 307, 231, 230, 215, 205, 178, 91.

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.04; H, 6.89.

The second component isolated from the column contained 0.052 g (7%) of **25** as a crystalline solid: mp 92–93 °C; IR (KBr) 3125, 3025, 1820, 1620, 1510, 1400, 1380, 1080, 1040, 900, 795, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.80 (b s, 3 H), 2.39 (s, 3 H), 4.80–4.91 (m, 1 H), 4.92–5.02 (m, 1 H), 6.90–7.80 (m, 14 H); UV (95% ethanol) 262 nm (ε 24 000); m/e 322 (M^+, base), 307, 292, 229, 215, 91.

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.02; H, 6.88.

Thermolysis of 1,2-Diphenyl-3-methyl-3-(*o*-2-propenylphenyl)cyclopropene (23). A solution containing 46 mg of **23** in 0.5 mL of a pyridine–benzene (1:4) mixture was heated in a sealed tube at 160 °C for 25 min. The solvent was removed under reduced pressure and the resulting residue was chromatographed on a thick-layer plate to give 44 mg (96%) of a white solid, mp 115–116 °C, whose structure was assigned as 1,1a,6,6a-tetrahydro-1a,6-dimethyl-1,6a-diphenyl-1,6-methanocycloprop[*a*]indene (**24**) on the basis of its spectral properties: IR (KBr) 3105, 2950, 1605, 1500, 1460, 1380, 1260, 1080, 1030, 900, 750, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.33 (s, 3 H), 1.35 (s, 3 H), 1.63 (d, 1 H, J = 9.0 Hz), 2.61 (d, 1 H, J = 9.0 Hz), 6.96–7.50 (m, 14 H); UV (95% ethanol) shoulder 218 nm (ε 25 600).

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.06; H, 6.90.

This same material was also obtained when a sample of **23** was irradiated in the presence of thioxanthone through a Uranium glass filter sleeve.

Thermolysis of 1,3-Diphenyl-2-methyl-3-(*o*-2-propenylphenyl)cyclopropene (25). A solution containing 21 mg of **25** in 0.3 mL of a pyridine–benzene (1:4) mixture was heated in a sealed tube at 160 °C for 15 min. The solvent was removed under reduced pressure and the resulting residue was purified by thick-layer chromatography to give 20 mg (95%) of a white solid, mp 109–110 °C, whose structure is assigned as 1,1a,6,6a-tetrahydro-1,6-dimethyl-1a,6a-diphenyl-1,6-methanocycloprop[*a*]indene (**26**) on the basis of its spectral properties: IR (KBr) 3150, 3000, 1605, 1540, 1460, 1380, 1280, 1200, 1080, 1040, 780, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.42 (s, 3 H), 1.43 (d, 1 H, J = 9.0 Hz), 1.56 (s, 3 H), 2.30 (d, 1 H, J = 9.0 Hz), 6.60–7.30 (m, 14 H); UV (95% ethanol) 247 nm (ε 14 900).

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Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.07; H, 6.89.

This same material was also obtained when a sample of **25** was irradiated in the presence of thioxanthone through a Uranium glass filter sleeve.

Preparation of 1,2-Diphenyl-3-methyl-3-(*o*-vinylbenzyl)cyclopropene (46) and 1,3-Diphenyl-2-methyl-3-(*o*-vinylbenzyl)cyclopropene (48). To a stirred suspension containing 7.00 g of lithium aluminum hydride in 500 mL of anhydrous ether under a nitrogen atmosphere was added, via continuous extraction by means of a Soxhlet extractor, 10.00 g of α-carboxy-*o*-toluic acid. The reaction mixture was allowed to reflux for 24 h. The excess lithium aluminum hydride was quenched by the addition of 3 mL of ethyl acetate followed by heating for 10 min at reflux. To the cooled reaction mixture was added 7 mL of water and 7 mL of a 15% sodium hydroxide solution followed by 21 mL of water. The aluminum salts were filtered and the resulting ethereal solution was washed with a saturated sodium bicarbonate solution followed by a saturated sodium chloride solution. The ethereal layer was dried over magnesium sulfate and the solvent was removed under reduced pressure. The resulting colorless oil (6.43 g, 76%) was identified as *o*-(2-hydroxyethyl)benzyl alcohol by its characteristic NMR spectrum: NMR ($CDCl_3$, 100 MHz) δ 2.65 (t, 2 H, J = 6.0 Hz), 3.52 (br t, 2 H, J = 6.0 Hz), 4.33 (br s, 2 H), 4.88 (br s, 2 H), 6.82–7.20 (m, 4 H). The above diol was used without further purification.

To a stirred solution containing 21.78 g of *o*-(2-hydroxyethyl)benzyl alcohol in 250 mL of carbon tetrachloride was added 76.0 g of triphenylphosphine. The resulting mixture was allowed to stir for 60 h at room temperature and was taken up in pentane, cooled to 0 °C, and filtered to remove most of the triphenylphosphine oxide. The filtrate was concentrated under reduced pressure and was then chromatographed on a 30 × 5 cm silica gel column, using hexane as the eluent. The resulting colorless liquid (17.77 g, 66%) was identified as *o*-(2-chloroethyl)benzyl chloride on the basis of its characteristic NMR spectrum: ($CDCl_3$, 100 MHz) δ 3.05 (t, 2 H, J = 7.5 Hz), 3.61 (t, 2 H, J = 7.5 Hz), 4.48 (s, 2 H), 7.01–7.39 (m, 4 H); IR (neat) 3005, 2940, 2860, 1495, 1455, 1440, 1330, 1310, 1295, 1265, 1255, 1225, 1095, 1060, 835, 770, 755, 740, 720, 715 cm^{-1}.

To a stirred solution containing 8.74 g of the above dichloride in 100 mL of anhydrous ether at 0 °C was added with stirring 12.95 g of potassium *tert*-butoxide. The resulting mixture was allowed to stir for 2 h at 0 °C under a nitrogen atmosphere. The excess potassium *tert*-butoxide was removed by adding 40 mL of water, and the resulting ethereal solution was washed 3 times with water followed by a saturated sodium chloride solution. The ethereal layer was dried over magnesium sulfate, and the solvent was removed under reduced pressure to give 6.63 g (94%) of *o*-vinylbenzyl chloride as a colorless liquid: NMR ($CDCl_3$, 100 MHz) δ 4.61 (s, 2 H), 5.38 (dd, 1 H, J = 10.5, 2.0 Hz), 5.72 (dd, 1 H, J = 17.5, 2.0 Hz), 7.09 (dd, 1 H, J = 17.5, 10.5 Hz), 7.15–7.63 (m, 4 H).

To a stirred suspension of magnesium turnings in 5 mL of anhydrous ether under a nitrogen atmosphere was added over a 10-min period 2.74 g of *o*-vinylbenzyl chloride in 20 mL of anhydrous ether. The reaction mixture was heated at reflux for 45 min and was then cooled to room temperature. The resulting solution of *o*-vinylbenzyl magnesium chloride was added to a stirred suspension containing 1.25 g of 1-methyl-2,3-diphenylcyclopropenylium perchlorate in 75 mL of anhydrous ether at −78 °C under a nitrogen atmosphere. The mixture was allowed to warm to 5 °C over a 12-h interval. After the mixture was quenched with a saturated ammonium chloride solution, the organic layer was washed with water and dried over magnesium sulfate. Removal of the solvent under reduced pressure left a light yellow oil which was chromatographed on a 100 × 1.5 cm silica gel column, using hexane as the eluent. The first component isolated from the column contained a white crystalline solid (0.689 g, 53%) which was identified as 1,2-diphenyl-3-methyl-3-(*o*-vinylbenzyl)cyclopropene (**46**) on the basis of its spectral properties: mp 51–52 °C; IR (KBr) 3050, 3005, 2905, 1810, 1495, 1445, 1385, 1370, 1075, 1030, 990, 915, 755, 735, 690 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.50 (s, 3 H), 3.19 (s, 2 H), 5.01 (dd, 1 H, J = 10.9, 1.4 Hz), 5.40 (dd, 1 H, J = 17.3, 1.4 Hz), 6.94 (dd, 1 H, J = 17.3, 10.9 Hz), 7.11–7.55 (m, 14 H); UV (95% ethanol) 339, 322 (ϵ 19 100, 32 500); mass spectrum, m/e 322 (M^+), 308, 307, 293, 291, 215, 205 (base).

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.09; H, 6.90.

The second component isolated from the column contained a white crystalline solid (0.592 g, 45%) whose structure was identified as 1,3-diphenyl-2-methyl-3-(*o*-vinylbenzyl)cyclopropene (**48**) on the basis of its spectral properties: mp 75–76 °C; IR (KBr) 2995, 1840, 1595, 1485, 1440, 1380, 1035, 1000, 920, 905, 775, 765, 760, 745, 700, 690 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 2.11 (s, 3 H), 3.43 (d, 1 H, J = 14.5 Hz), 3.83 (d, 1 H, J = 14.5 Hz), 5.15 (dd, 1 H, J = 11.0, 1.4 Hz), 5.54 (dd, 1 H, 17.3, 1.4 Hz), 6.82–7.44 (m, 15 H); UV (95% ethanol) 253 nm (ϵ 24 400); mass spectrum, m/e 322 (M^+), 320, 307, 305, 229, 215, 206, 205 (base), 203, 202, 117, 115.

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 92.92; H, 7.01.

Thermolysis of 1,2-Diphenyl-3-methyl-3-(*o*-vinylbenzyl)cyclopropene (46). A solution containing 93 mg of **46** in 0.5 mL of a 20% pyridine–benzene mixture was heated in a sealed tube at 175 °C for 190 h. The solvent was removed under reduced pressure and the resulting yellow solid was chromatographed on a 2.5 × 1.5 cm silica gel column, using hexane as the eluent. The white solid obtained (86.5 mg, 93%) was identified as ($1\alpha,1a\beta,7\alpha,7a\beta$)-1,1a,7,7a-tetrahydro-1a-methyl-1,7a-diphenyl-1,7-methano-2*H*-cyclopropa[*b*]naphthalene (**47**) on the basis of its spectral properties: mp 153–154 °C; IR (KBr) 2935, 2840, 1580, 1470, 1420, 1365, 770, 760, 735, 695 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.09 (s, 3 H), 2.11 (dd, 1 H, J = 11.0, 2.5 Hz), 2.84 (dd, 1 H, J = 11.0, 9.6 Hz), 3.08 (d, 1 H, J = 17.7 Hz), 3.54 (d, 1 H, J = 17.7 Hz), 3.61 (dd, 1 H, J = 9.6, 2.5 Hz), 6.97–7.30 (m, 14 H); UV (95% ethanol) 223 nm (ϵ 20 700); mass spectrum, m/e 322 (M^+), 219, 218 (base), 217, 215, 202, 84.

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.08; H, 6.89.

Thermolysis of 1,3-Diphenyl-2-methyl-3-(*o*-vinylbenzyl)cyclopropene (48). A solution containing 97 mg of **48** in 0.5 mL of a 20% pyridine–benzene mixture was heated in a sealed tube at 176 °C for 54 h. The solvent was removed under reduced pressure and the yellow solid that was obtained was chromatographed on a 2.5 × 5 cm silica gel column, using hexane as the eluent. The major component isolated was a white solid (88.4 mg, 91%) whose structure was assigned as ($1\alpha,1a\beta,7\alpha,7a\beta$)-1,1a,7,7a-tetrahydro-1-methyl-1a,7a-diphenyl-1,7-methano-2*H*-cyclopropa[*b*]naphthalene (**49**) on the basis of its spectral properties: mp 129–130 °C; IR (KBr) 3005, 2925, 2840, 1580, 1500, 1490, 1445, 1385, 1370, 1035, 1030, 781, 765, 760, 735, 710, 695 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 1.55 (s, 3 H), 2.31 (dd, 1 H, J = 11.0, 2.4 Hz), 2.85 (dd, 1 H, J = 11.0, 9.8 Hz), 3.09 (d, 1 H, J = 18.0 Hz), 3.30 (dd, 1 H, J = 9.8, 2.4 Hz), 3.65 (d, 1 H, J = 18.0 Hz), 6.70–7.23 (m, 14 H); mass spectrum, m/e 322 (M^+), 205 (base), 181, 180, 149, 131, 115, 105, 103, 93, 91, 77.

Anal. Calcd for $C_{25}H_{22}$: C, 93.12; H, 6.88. Found: C, 93.03; H, 6.94.

Direct Irradiation of 1,2-Diphenyl-3-methyl-3-(*o*-vinylbenzyl)cyclopropene (46) in Benzene. A solution of 367 mg of **46** in 400 mL of anhydrous benzene was irradiated for 3 h under an argon atmosphere with a 550-W Hanovia mercury arc lamp equipped with a Pyrex filter sleeve. The solvent was removed under reduced pressure and the resulting yellow oil was chromatographed on a 100 × 1.5 cm silica gel column, using hexane as the eluent. The first two fractions isolated from the column (180 mg, 49%) contained a complex mixture of trienes and were not characterized. The third component isolated from the column (78 mg, 21%) was identified as 2-methyl-8-vinyl-3,4a-diphenyl-1,4a-dihydroazulene (**50**) on the basis of its characteristic NMR spectrum: NMR ($CDCl_3$, 90 MHz) δ 1.65 (s, 3 H), 3.44 (br d, 1 H, J = 22.5 Hz), 3.78 (br d, 1 H, J = 22.5 Hz), 5.13 (br d, 1 H, J = 11.0 Hz), 5.28 (br d, 1 H, J = 18.0 Hz), 5.50–5.68 (m, 1 H), 6.10–6.58 (m, 5 H), 6.65 (dd, 1 H, J = 18.0, 11.0 Hz), 6.83–7.37 (m, 8 H). The fourth component isolated from the column (62 mg, 17%) was identified as 1,3-diphenyl-2-methyl-3-(*o*-vinylbenzyl)cyclopropene (**48**) on the basis of its spectral properties and by comparison with an independently synthesized sample.

Rate Studies. Stock solutions which were 10^{-3} M in the appropriate cyclopropene, 10^{-4} M in hexachlorobenzene (internal standard), containing 5.0 mL of anhydrous pyridine and 20 mL of anhydrous benzene, were prepared. From each stock solution, 0.5-mL aliquots were withdrawn, degassed, and sealed under vacuum in 5-mm thick-walled glass ampules. The ampules were immersed in a thermostated (±0.1 °C) oil bath at the designated temperatures and samples were periodically withdrawn for analysis. The product concentrations were determined by HPLC, using a Waters Associates ALC 201 liquid chromatograph equipped with an Altex 4.6 mm × 250 mm Ultrasphere-ODS 5 μm column interfaced to a Hewlett Packard 3380A integrator.

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Registry No. 6, 70913-08-5; **7**, 70913-09-6; **8**, 62937-87-5; **9**, 70913-10-9; **13**, 70913-11-0; **14**, 85282-87-7; **15**, 85282-88-8; **16**, 85282-89-9; **17**, 75032-46-1; **19**, 85282-90-2; **20**, 85282-91-3; **22**, 80949-69-5; **23**, 85282-92-4; **24**, 85282-93-5; **25**, 85282-94-6; **26**, 85282-95-7; **28**,

80949-68-4; **30**, 70913-12-1; **31**, 50397-92-7; **32**, 62937-86-4; **33**, 65086-21-7; **34**, 85282-96-8; **36**, 85282-97-9; **43**, 80949-70-8; **44**, 85282-98-0; **45**, 85282-99-1; **46**, 70913-17-6; **47**, 70913-19-8; **48**, 70913-18-7; **49**, 70913-20-1; **50**, 85283-00-7; *o*-bromovinylbenzene, 2039-88-5; diphenylmethylcyclopropenylium perchlorate, 72612-89-6; benzyne, 462-80-6; **18**, 51310-25-9; **12**, 67177-31-5; 2-methyl-3-phenylindanone, 52957-74-1; *o*-bromoisopropenylbenzene, 7073-70-3; α-carboxy-*o*-toluic acid, 89-51-0; *o*-(2-hydroxyethyl)benzyl alcohol, 6346-00-5; *o*-(2-chloroethyl)benzyl chloride, 78317-75-6; *o*-vinylbenzyl chloride, 22570-84-9.

Conformational Analysis by NMR Spectrometry of the Highly Substituted Cyclic Tetrapeptides, Chlamydocin and Ala⁴-Chlamydocin. Evidence for a Unique Amide Bond Sequence in Dimethyl-d_6 Sulfoxide

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Abstract: The solution conformations of chlamydocin, *cyclo*(Aib-Phe-D-Pro-L-Aoe), and Ala⁴-chlamydocin, *cyclo*[Aib-Phe-D-Pro-L-Ala), have been investigated by ^1H and ^{13}C nuclear magnetic resonance spectroscopy in dimethyl-d_6 sulfoxide. Two conformations of these molecules are present in ratios of approximately 6:4. The conformers interconvert slowly on the NMR time scale, and this slow interconversion is due to a cis–trans isomerization of one amide bond. The 12-membered ring system of conformer I in dimethyl-d_6 sulfoxide is characterized by four transoid amide bonds, with two bis γ-turn intramolecular hydrogen bonds. Conformer II, which is found only in mixed solvents that contain high concentrations of Me_2SO, has a cis,trans,trans,trans amide bond sequence. Low-temperature NOE was utilized to determine amide bond geometry in conformer II. Circular dichroism data in different solvents are recorded. Approximate torsional angles of the minor conformer (conformer II) derived from the NMR data and Dreiding models are Aib ϕ +70°, ψ +75°, ω −160°; Phe ϕ +150°, ψ −105°, ω +20°; D-Pro ϕ +85°, ψ −140°, ω +165°; Ala (Aoe) ϕ −105°, ψ +80°, ω −160°, respectively. The cis,trans,trans,trans ring conformation of a cyclic tetrapeptide has not been described previously.

Chlamydocin, *cyclo*[Aib¹-L-Phe²-D-Pro³-L-(2-amino-8-oxo-9,10-epoxydecanoic acid)] (**1**),[1-3] is a cytostatic agent that appears to have an unusual mechanism of action. At concentrations near 2 nM, chlamydocin inhibits tritiated thymidine incorporation into calf thymus lymphocytes stimulated with phytohemaglutinin,[4] an assay that is sensitive to any agent interfering with rapid normal uptake of DNA precursors by the rapidly growing cells.[5] This strong inhibition parallels chlamydocins's behavior in an in vivo mouse mastocytoma assay (EC_{50} = 0.3 ng/mL).[2] The site of action is not known, but the low effective concentrations in these assay systems necessitate a very specific interaction between this site and chlamydocin, an interaction that requires both the cyclic tetrapeptide ring system and the intact epoxy ketone group.[2,3]

Conformations for the chlamydocin ring system have been determined in the solid state[6] and in nonpolar solvents.[7] The all-transoid[1c] bis γ-turn conformation (Figure 1F) was first identified in dihydrochlamydocin (**2**), the reduced carbonyl analogue of **1**, by Flippen and Karle[6] and subsequently was found for (Gly¹,Ala⁴)-chlamydocin (**3**), *cyclo*(D-Phe-Pro)$_2$ (**4**),[8] Ala⁴-chlamydocin (**5**), and chlamydocin in chloroform solution.[7] However, the all-transoid conformation is readily disrupted by hydrogen-bonding solvents. In view of the importance of the cyclic tetrapeptide ring system to the biological activity of chlamydocin, we have studied its conformation in dimethyl sulfoxide.

We report here the results of NMR studies to determine the conformations of **1** and **5** in dimethyl sulfoxide. Low-temperature nuclear Overhauser effect (NOE) difference spectra[9,10] were used to assign amide bond geometries in one conformation that rapidly interconverts at room temperature. Conformations are proposed for **1**, **5**, and (Gly¹,Ala⁴)-chlamydocin (**3**) in Me_2SO. Evidence is presented for a previously unobserved cyclic tetrapeptide conformation with three trans and one cis amide bond in the 12-membered ring system.

Experimental Section

Detailed descriptions of experimental methods used for solvent titrations, for concentration and temperature dependency measurements of amide proton chemical shifts, and for Tempo titration measurements were reported in earlier papers.[7,8] Dimethyl-d_6 sulfoxide and 2,2,6,6-tetramethyl-1-piperdinyloxy free radical (Tempo) were obtained from Aldrich Co., Inc. For NOE experiments in Me_2SO-d_6 the spectra were obtained at 50 °C in order to reduce the correlation times and to increase NOE enhancements. In some cases, spectra were obtained in mixed solvent pairs of Me_2SO-d_6/chloroform-*d* at lower temperatures to suppress conformational interconversions and saturation transfer. Samples of **1** and **5**, stored in Me_2SO for months, were recovered by evaporation of solvent in vacuo at room temperature and reanalyzed by TLC and NMR.

cyclo[Aib-L-Phe-D-Pro-L-[3,3,3-$^2H_3$]Ala] (**6**) was synthesized from 3,3,3-trideuterioalanine by using the methods reported for the synthesis of the protio compound.[11]

(1) (a) Abstracted in part from: Jasensky, R. D., Ph.D. Thesis, University of Wisconsin, Madison, WI, 1979. (b) Abbreviations used follow IUPAC–IUB tentative rules as described in: *J. Biol. Chem.* **1972**, *247*, 977. Additional abbreviations used: Aib, α-aminoisobutyric acid; Aoe, 2-amino-8-oxo-9,10-epoxydecanoic acid. Superscripts to amino acids in a peptide chain designate the point of substitution relative to the parent compound. (c) Transoid amide bonds are defined as amide bonds with the torsion angle ω deviating from 0° or 180°.

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