peak of highest amu was seen at $m/z$ 303 ($C_{20}H_{31}O_2$, $M^+ - CH_3$). Other significant peaks were at $m/z$ (relative intensity, composition) 272 (18.6, $C_{20}H_{32}$) 257 (12.4, $C_{19}H_{29}$), 191 (1.0, $C_{14}H_{23}$), 149 (21.6, $C_{11}H_{17}$), 137 (62.2, $C_{10}H_{17}$), 135 (47.3, $C_{10}H_{15}$), 109 (65.0, $C_8H_{13}$), and 95 (100, $C_7H_{11}$).

Reduction of 0.05 g of **22c,d** with $LiAlH_4$ gave **22a,b**.

**Reaction of 23a,b with Formic Acid.** A mixture of 0.17 g of **23a,b** and 2 mL of 97% formic acid was stirred at room temperature ($N_2$ atmosphere). The reaction was complete after 1 h. The mixture was neutralized with $NaHCO_3$ and extracted with ether. The usual workup followed by preparative TLC (hexane) gave 0.086 g of gummy **31** and 0.052 g of a mixture of olefins. The tricyclic hydrocarbon had the following: IR 2900 (br), 1445 (br), 1370, 968, 835 $cm^{-1}$; NMR $\delta$ 5.24 (q, $J$ = 8 Hz, H-14), 2.8 (septet, $J$ = 8 Hz, H-12), 1.56 (d, $J$ = 8, H-15), 1.54 (d, $J$ = 1 Hz, H-16), 0.97, 0.88, 0.88 (H-18, H-19, and H-20). Attempts to oxidize the 13,14-double bond selectively failed. An incorrect value was reported previously[8] for the molecular weight. The $^{13}C$ NMR spectrum is listed in Table II: mol wt calcd for $C_{20}H_{32}$ 272.2503, found (MS) 272.2519 (55.7%). Other significant ions in the high-resolution mass spectrum were at $m/z$ (relative intensity composition) 257 (100, $C_{19}H_{29}$), 215 (14.7, $C_{16}H_{23}$), 201 (15.1, $C_{15}H_{21}$), 175 (14.1, $C_{13}H_{19}$), 161 (14.8, $C_{12}H_{17}$), 147 (16.1, $C_{11}H_{15}$), 133 (29.6, $C_{10}H_{13}$), 121 (16.8, $C_9H_{13}$).

**8(17),13(16)-Labdadien-14-one (33).** Oxidation of 0.3 g of **17b,d** in 20 mL of pentane with 4 g of active $MnO_2$ in the manner described for oxidation of **18b,d** required 72 h for completion of the reaction. After the usual workup and preparative TLC (hexane–ether, 17:3) of the crude product there was obtained 0.26 g (89%) of **33** as a gum which slowly solidified and then melted at 58–59 °C: IR 3080, 1675, 1640, 1625, 1130, 980, 945, 890 $cm^{-1}$; NMR $\delta$ 5.97 (br) 5.75 (br) (H-16a,b), 4.84 (br) and 4.60 (br) (H-17a,b), 2.34 (Ac), 0.89, 0.81, and 0.68 (H-18, H-19, and H-20); mol wt calcd for $C_{20}H_{32}O$ 288.2453, found (MS) 288.2432 (10.2%). Other significant peaks in the high-resolution mass spectrum were at $m/z$ (composition, relative intensity) 273 ($C_{19}H_{29}O$, 14.6), 177 ($C_{13}H_{21}$, 14.2), 149 ($C_{10}H_{16}$, 23.4), and 137 ($C_{10}H_{17}$, 100).

**Reactions with $SnCl_4$.** (a) To a solution of 0.05 g of **24** in 8 mL of $CH_2Cl_2$ kept at −78 °C was added slowly with stirring 0.06 mL of $SnCl_4$. After 30 min the reaction was quenched with 10% $NaHCO_3$ solution and extracted with ether. After the usual workup the crude product was purified by preparative TLC (hexane–ether, 1:1) to give 0.02 g (40%) of a crystalline solid (**34**): 99–100 °C; IR (KBr) 3475, 1670, 1285, 1170, 1090, 950 $cm^{-1}$; NMR $\delta$ 6.80 (q, $J$ = 8 Hz, H-14), 2.81 (dd, $J$ = 18, 4 Hz, H-11a), 2.61 (dd, $J$ = 18, 4 Hz, H-11b), 1.85 (dd, $J$ = 8, 1 Hz, H-15), 1.70 (t, $J$ = 1 Hz, H-16), 1.12 (H-17), 0.87, 0.83, and 0.78 (H-18, H-19, and H-20); mol wt calcd for $C_{20}H_{34}O_2$ 306.2558, found (MS) 306.2517 (3.3%). Other significant peaks in the high-resolution mass spectrum were at $m/z$ (composition, relative intensity) 291 ($C_{19}H_{31}O_2$, 1.8), 288 ($C_{20}H_{32}O$, 19.9), 273 ($C_{19}H_{29}O$, 14.0), 221 ($C_{15}H_{25}O$, 18.4), 191 ($C_{14}H_{23}$, 26.8), 177 ($C_{13}H_{21}$, 25.3), and 175 ($C_{13}H_9$, 19.1).

(b) Ketone **33** (0.10 g) on treatment with 0.015 mL of $SnCl_4$ for 30 min at −78 °C in the manner described in the previous paragraph, a workup in the usual fashion, and preparative TLC (hexane–ether, 47:3) of the crude product afforded 0.015 g (15%) of gummy **35** which was a mixture of C-13 epimers as indicated by doubling of the methyl signals: IR 1690 (br), 1240, 1130, 1115 $cm^{-1}$; NMR $\delta$ 2.08 (Ac), 1.26 and 1.24 (H-17 of epimers), 0.88, 0.85, 0.84, 0.83, 0.80, and 0.79 (H-18, H-19, H-20, and epimers); mol wt calcd for $C_{20}H_{33}OCl$ 324.2219, found (MS) 324.2197 (12.1%). Other significant peaks in the high-resolution mass spectrum were at $m/z$ (composition, relative intensity) 309 ($C_{19}H_{30}OCl$, 10.4), 288 ($C_{20}H_{32}O$, 29.6), 273 ($C_{19}H_{29}O$, 29.5), and 266 ($C_{17}H_{27}Cl$, 54.1).

The more polar fraction yielded 0.022 g (23%) of **36** as a gum: IR 1665, 1640, 1290, 1255, 1180, 1145, 925, 875 $cm^{-1}$; NMR $\delta$ 6.34 (br, H-14), 2.27 (Ac), 1.11 (H-17), 0.96, 0.87, and 0.87 (H-18, H-19, and H-20); mol wt calcd for $C_{30}H_{32}O$ 288.2953, found (MS) 288.2464 (12.2%). Other significant peaks in the high-resolution mass spectrum were at $m/z$ (composition, relative intensity) 273 ($C_{19}H_{29}O$, 14), 191 ($C_{14}H_{22}$, 21), and 175 ($C_{13}H_{19}$, 9.7).

**Registry No.** **1a**, 3730-56-1; **5a**, 42401-43-4; **5b**, 42401-44-5; **8**, 42401-48-9; **9a**, 42401-49-0; **9b**, 83815-99-0; **9c**, 83816-00-6; **9d**, 83816-01-7; **9e**, 83816-02-8; **10a**, 83816-03-9; **10b**, 83816-04-0; **11a**, 83860-56-4; **11b**, 83816-05-1; **16a**, 61046-88-6; **16b**, 61091-77-8; **17a**, 83830-91-5; **17b**, 61091-79-0; **17c**, 83816-06-2; **17d**, 61091-80-3; **18a**, 83860-57-5; **18b**, 83860-58-6; **18c**, 83860-59-7; **18d**, 83860-60-0; **19**, 83860-61-1; **20a** (isomer 1), 83860-62-2; **20a** (isomer 2), 83860-68-8; **20b** (isomer 1), 83816-07-3; **20b** (isomer 2), 83860-69-9; **21a** (isomer 1), 83860-63-3; **21a** (isomer 2), 83860-70-2; **21b** (isomer 1), 83860-64-4; **21b** (isomer 2), 83860-71-3; **22a**, 61091-81-4; **22b**, 83860-65-5; **22c**, 83816-08-4; **22d**, 83860-66-6; **23a**, 61047-01-6; **23b**, 83860-67-7; **24a**, 83816-09-5; **24b**, 83816-10-8; **25**, 10395-42-3; **26**, 83816-11-9; **27**, 511-02-4; **28**, 83816-12-0; **31**, 83816-13-1; **33**, 20046-46-2; **34**, 83816-14-2; **35** (isomer 1), 83830-87-9; **35** (isomer 2), 83816-16-4; **36**, 83816-15-3; 2-fluoro-*N*-methylpyridinium tosylate, 58086-67-2; 2-fluoro-1,3-dimethylpyridinium tosylate, 59387-91-6.

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# Photochemistry of (*o*-Methylphenyl)alkadienes: Attempted Intramolecular Trapping of the Resulting *o*-Xylylenes[1a]

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The photochemistry of a series of *o*-methylphenyl dienes was investigated in order to determine if the resulting *o*-xylylenes could be trapped in an intramolecular Diels–Alder reaction in synthetically useful yields. Irradiation of **3** gave meta-isomer **4** as the major product along with lower yields of double bond migration product **5** and the desired cycloadduct **6**. The best yield of **6** (24%) was obtained by irradiation of **3** with a low-pressure mercury vapor lamp at low temperatures. The other compounds investigated gave none of the intramolecular Diels–Alder product of the *o*-xylylene. Irradiation of **17** gave only double bond migration product **18**. Irradiation of **22** gave an excellent yield of (2 + 2) cycloadduct **23**. Irradiation of **26** gave meta-isomer **28**, double bond migration product **27**, and **29**, a (2 + 2) cycloadduct of **28**.

Intramolecular Diels–Alder reactions of *o*-xylylenes (*o*-quinodimethanes) have been extensively applied to the synthesis of polycyclic ring systems containing at least one aromatic ring (especially steroids) in recent years.[2] Al-

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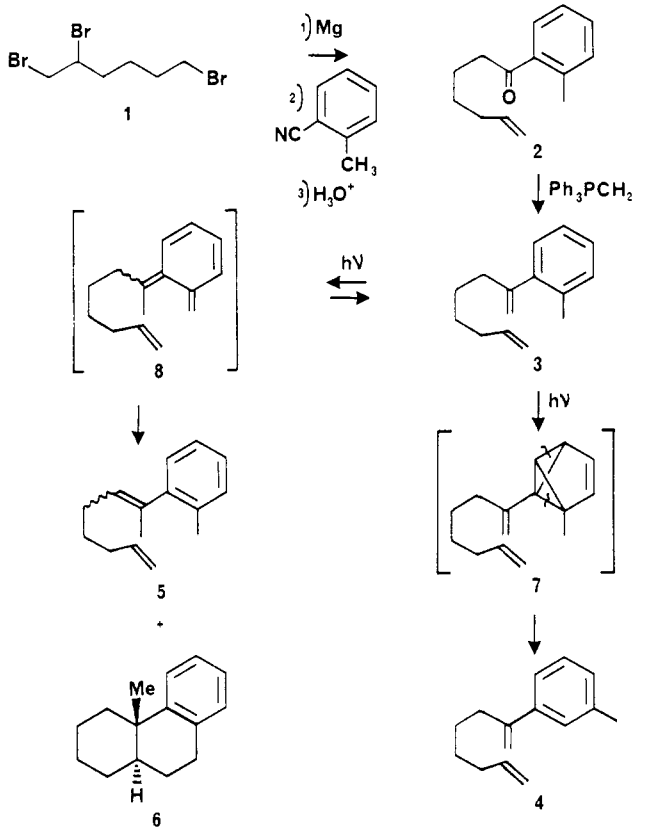
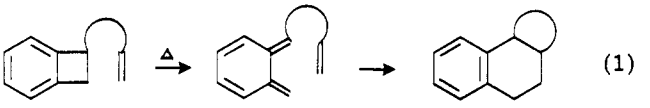
Scheme I




though a number of methods have been used to generate the o-xylylenes, the most commonly employed method has been the thermal ring opening of benzocyclobutenes as illustrated in eq 1. We have recently shown o-xylylenes,




(1)

generated photochemically from o-alkylstyrenes,[3] can be trapped in acceptable yields in intermolecular Diels–Alder reactions.[4,5] We report here our studies of the suitability of this method of generating o-xylylenes for intramolecular trapping. This method has the potential of introducing the angular methyl group, a ubiquitous feature of many natural products, as an integral feature of the reaction.

## Results and Discussion

Initial studies focused on the photochemistry of 2-(2-methylphenyl)-1,7-octadiene (3) since successful trapping of the o-xylylene would result in the formation of an octahydrophenanthrene, a common structural feature of numerous natural products. Compound 3 was prepared by the reaction of the Grignard reagent prepared from 1 with o-tolunitrile to give ketone 2 (Scheme I). Reaction of 2 with methylenetriphenylphosphorane gave 3.

Irradiation of 3 in benzene with a medium-pressure mercury vapor lamp gave 4 (37%), 5 (5%), and 6 (4%) after a 62% conversion of 3. The meta-isomer 4 was isolated by preparative GC and identified by comparison to an independently synthesized sample. The authentic sample of 4 was prepared from m-tolunitrile in the same manner as described for the preparation of 3. Minor products 5 and 6 were identified by comparison of their GC retention times on three different columns with those of authentic samples. The authentic sample of 5 was prepared by reaction of the Grignard reagent derived from 1 with o-methylacetophenone followed by dehydration of the resulting alcohol. This gave a 2.25:1 mixture of 3 and 5,[6] which were separated by preparative GC. Octahydrophenanthrene 6 was prepared as a mixture of cis and trans stereoisomers by the procedure of Barnes.[7] The isomers were separated by preparative GC, and their stereochemistries were assigned by NMR.[8] The product from the irradiation of 3 was found to have the trans stereochemistry. Irradiation of 3, with xanthone as a photosensitizer, gave a 34% yield of 5 at 71% conversion. In this case 5 was isolated by preparative GC and shown to have spectral properties that were identical with the independently synthesized sample.

The products formed upon irradiation of 3 are consistent with the mechanism previously proposed to account for the photochemistry of o-methylstyrene derivatives.[5] The formation of 4 presumably proceeds via benzvalene intermediate 7, a known[9] mechanism for the positional isomerization of benzene derivatives. Irradiation of 3 also produces a o-xylylene 8, initially as the E stereoisomer. The major reaction of (E)-8 is 1,5-hydrogen migration to regenerate 3. A smaller fraction of (E)-8 either cyclizes to 6 or undergoes geometrical isomerization to give (Z)-8, which is ultimately converted to 5. The formation of 7 is a singlet-state reaction since photosensitization of 3 results only in the formation of 5. In accord with previous results,[5] the sensitized conversion of 3 to 5 may involve either 8, which is too short-lived to be trapped under these conditions, or the triplet 1,4-biradical derived from 8.

Of the various strategies explored to increase the yield of 6, only the use of a low-pressure mercury vapor lamp was at all successful. McCullough and co-workers[10] have demonstrated that methyl-substituted o-xylylenes react by 1,5-hydrogen migrations to give styrene derivatives and that these reactions occur both thermally and photochemically.[11] Since o-xylylenes absorb at longer wavelengths than styrenes,[10] the use of the medium-pressure mercury vapor lamp, which has a considerable part of its light output above 300 nm, where 3 is transparent but where 8 is expected to absorb strongly, might cause a decrease in the lifetime of 8 and a resultant decrease in the yield of 6. This suggested that the use of a low-pressure

(1) (a) Presented in part at the 183rd National Meeting of the American Chemical Society, Las Vegas, NV, March 1982. (b) Boettcher Foundation Fellow, 1979–1980.

(2) For reviews and a few leading references see: (a) Oppolzer, W. *Synthesis* **1978**, 793–802. (b) Funk, R. L.; Vollhardt, K. P. C. *Chem. Soc. Rev.* **1980**, *9*, 41–61. (c) Kametani, T.; Nemoto, H. *Tetrahedron* **1981**, *37*, 3–16. (d) Djuric, S.; Sarkar, T.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 6885–6886. (e) Grieco, P. A.; Takigawa, T.; Schillinger, W. J. *J. Org. Chem.* **1980**, *45*, 2247–2251. (f) Nicolaou, K. C.; Barnette, W. E.; Ma, P. *Ibid.* **1980**, *45*, 1463–1470.

(3) Scully, F.; Morrison, H. *J. Chem. Soc., Chem. Commun.* **1973**, 529–530. Pratt, A. C. *Ibid.* **1974**, 183–184.

(4) Hornback, J. M.; Mawhorter, L. G.; Carlson, S. E.; Bedont, R. A. *J. Org. Chem.* **1979**, *44*, 3698–3703.

(5) Hornback, J. M.; Barrows, R. D., *J. Org. Chem.* **1982**, *47*, 4285–4291.

(6) Compound 5 was obtained as a mixture of geometrical isomers, which was not separated.

(7) Barnes, R. A. *J. Am. Chem. Soc.* **1953**, *75*, 3004–3008.

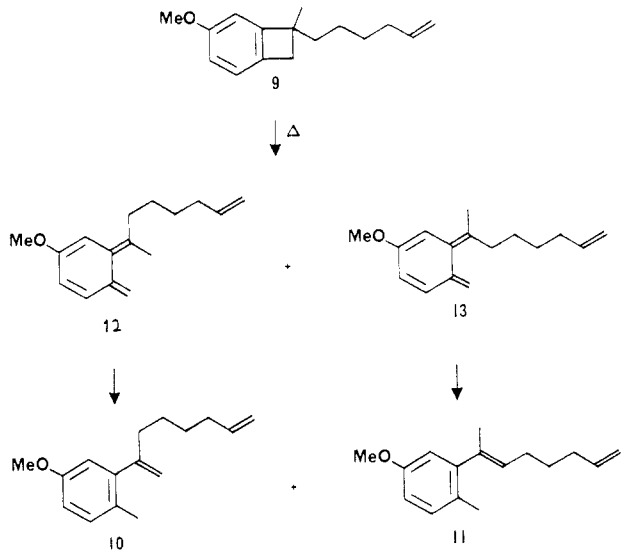
(8) Campbell, A. L.; Leader, H. N.; Sierra, M. G.; Spencer, C. L.; McCheshey, J. D. *J. Org. Chem.* **1979**, *44*, 2755–2757.

(9) Wilzbach, K. E.; Kaplan, L. *J. Am. Chem. Soc.* **1964**, *86*, 2307–2308. Kaplan, L.; Wilzbach, K. E.; Brown, W. G.; Yang, S. S. *J. Am. Chem. Soc.* **1965**, *87*, 675–676. Bryce-Smith, D.; Gilbert, A. *Tetrahedron* **1976**, *32*, 1309–1326.

(10) de Fonseka, K. K.; McCullough, J. J.; Yarwood, A. J. *J. Am. Chem. Soc.* **1979**, *101*, 3277–3282. McCullough, J. J. *Acc. Chem. Res.* **1980**, *13*, 270–276.

(11) The isomerization of (E)-8 to 3 is allowed thermally if suprafacial and allowed photochemically if antarafacial. The geometry of 8 is favorable for antarafacial hydrogen migration.[10]

Scheme II

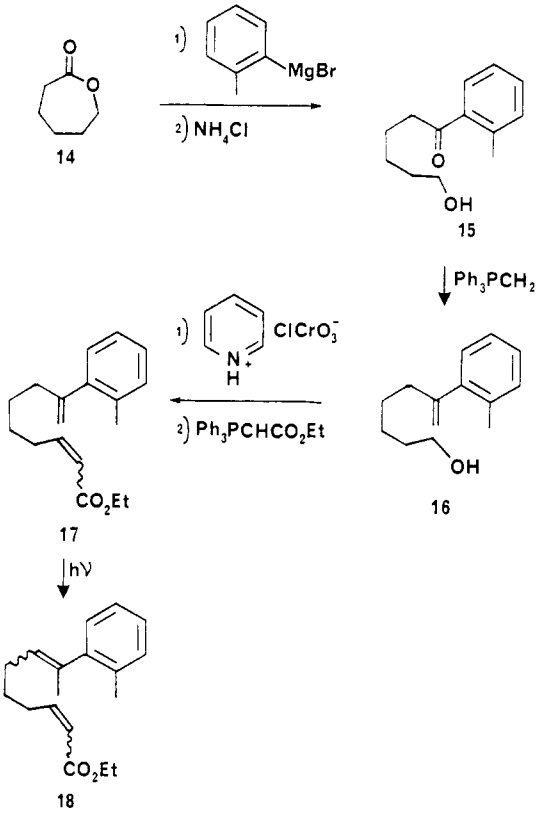



mercury vapor lamp, whose light output is primarily at 254 nm, might result in a higher yield of **6**. Irradiation of **3** in benzene at 7 °C with a low-pressure mercury vapor lamp resulted in the formation of **4** (51%) and **6** (24%) at 35% conversion of **3**. At higher temperatures the yields of both products decreased. Irradiation of **3** in benzene–acetonitrile at −10 °C with the same light source gave only a very slow reaction. Thus, the use of a low-pressure lamp did result in an increased yield of **6**, although the yield was still too low to be synthetically useful.

However, it is important to note that this method of generating the *o*-xylylene did result in intramolecular cycloaddition, while a similar *o*-xylylene, generated by thermolysis of a benzocyclobutene, gave only the 1,5-hydrogen migration products. Thus, Kametani and coworkers[12] found that thermolysis of **9** (Scheme II) gave only styrene derivatives **10** and **11**, via *o*-xylylenes **12** and **13**. In this case, the 1,5-hydrogen migration of **12** to give **10** and **13** to give **11** is faster than the intramolecular Diels–Alder reaction of **12** or **13**. Once **10** or **11** is formed the reaction is over. In the photochemical example, the conversion of **8** to **3** is probably also much faster than the cycloaddition of **8** to give **6**. In this case, however, this is just an energy-wasting step since **3** is converted back to **8** upon continued irradiation. Thus, **8** has numerous chances to form **6** before the side reactions ultimately compete.

In addition to increasing the lifetime of the *o*-xylylene, the yield of the cycloadduct potentially could be increased by increasing the rate of the Diels–Alder reaction. Styrene derivative **17**, with an electron-withdrawing ester group on the dienophile, was synthesized to test this reasoning (Scheme III). Addition of the Grignard reagent derived from *o*-bromotoluene to a solution of ϵ-caprolactone (**14**) gave hydroxy ketone **15**. A Wittig reaction of **15** and methylenetriphenylphosphorane gave **16**. Oxidation of **16** to the aldehyde with pyridinium chlorochromate followed by a Wittig reaction with (carbethoxymethylene)triphenylphosphorane gave **17**. GC analysis showed **17** to be a mixture of two components in ca. 95:5 ratio. The major component was assigned as the *E* stereoisomer (**17a**) and the minor component as the *Z* stereoisomer (**17b**) on the basis of the known propensity of stabilized ylides to give the stereoisomer with the larger groups trans.[13]

Scheme III




Direct irradiation of **17** in benzene gave a 1.2:1 mixture of **17a** and **17b** along with a small amount of **18** (6%) after a 46% conversion of **17a** and **17b**. Isomer **18** was identified by comparison of its NMR spectrum with those of **17** and **5**. Irradiation of **17** in benzene with xanthone as a photosensitizer gave very similar results, a 1.6:1 mixture of **17a** and **17b** along with 5% of **18**. In neither irradiation was any of the possible octahydrophenanthrene product nor any of the meta isomer of **17** observed.

The photochemical behavior of **17** differs significantly from that of **3**. Direct irradiation of **3** gave the meta-isomer **4**, the double bond migration product **5**, and the cycloaddition product **6**, while sensitized irradiation gave only **5**. Similar results were observed in our previous studies[5] of the photochemistry of *o*-methylstyrene derivatives, that is, direct irradiation resulted in the formation of meta isomers and *o*-xylylenes, which could be trapped in Diels–Alder reactions, while sensitized irradiation gave only double bond migration products. The absence of both the meta isomer of **17** and the cycloaddition product in the direct irradiation and the similarity of the direct irradiation to the sensitized irradiation suggest that the direct irradiation of **17** also proceeds through the triplet excited state. If this is the case, then the interaction of the α,β-unsaturated ester chromophore and the styrene chromophore must result in an enhanced efficiency of intersystem crossing.[14] It is also interesting to note that cis–trans isomerization of the conjugated ester, a known reaction of the triplet state of similar esters,[15] was observed, while isomerization of the α,β-unsaturated ester to a β,γ-unsaturated ester, a known reaction of the singlet excited

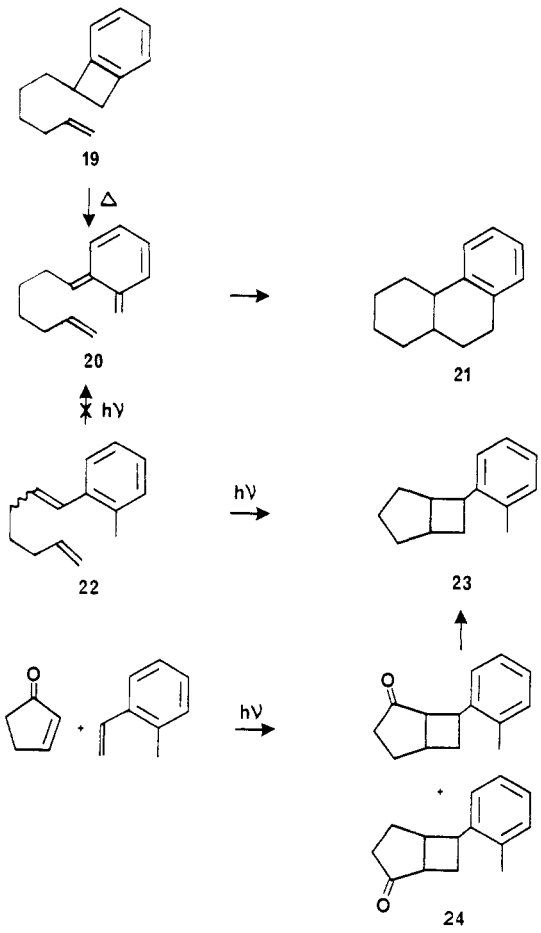
(12) Kametani, T.; Tsubuki, M.; Shiratori, Y.; Kato, Y.; Nemoto, H.; Ihara, M.; Fukumoto, K. *J. Org. Chem.* **1977**, *42*, 2672–2676.

(13) House, H. O. "Modern Synthetic Reactions", 2nd ed.; Benjamin: Menlo Park, CA, 1972; pp 701–702.

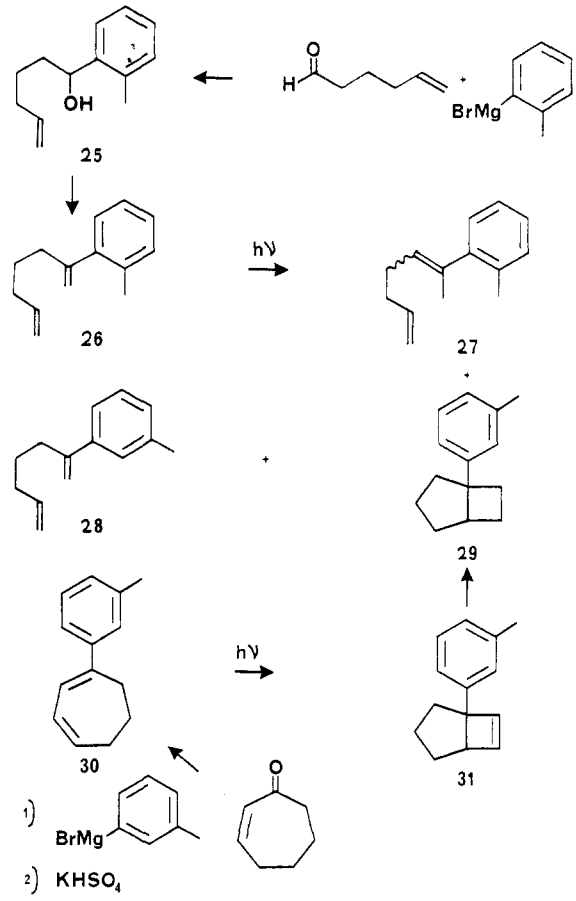
(14) The photochemistry of bichromophoric molecules can be quite different from that of the isolated chromophores. For a leading reference see: Morrison, H. A. *Acc. Chem. Res.* **1979**, *12*, 383–389.

(15) Barltrop, J. A.; Wills, J. *Tetrahedron Lett.* **1968**, 4987–4990. Jorgenson, M. J.; Gundel, L. *Ibid.* **1968**, 4991–4994.

Scheme IV




Scheme V




state of such esters, was not observed.

Another strategy to increase the lifetime of the o-xylylene and therefore increase the yield of the cycloaddition reaction is to limit the possible 1,5-hydrogen sigmatropic rearrangements that compete with the Diels–Alder reaction. Gowland and Durst[16] have shown that o-xylylene **20**, generated by thermolysis of benzocyclobutene **19**, gave **21** in 77% yield (Scheme IV). In the case of (*E*)-o-xylylene **20**, no 1,5-hydrogen migration can occur, and the cycloaddition proceeds in good yield. Therefore, the photochemical behavior of **22**, a potential source of **20**,[17] was investigated.

Styrene **22** was synthesized by reduction of **2** to the alcohol with lithium aluminum hydride followed by acid-catalyzed elimination of water. Irradiation of **22** in acetonitrile produced a single photoproduct in 86% yield. The $^1H$ and $^{13}C$ NMR spectra of this photoproduct revealed that it was not **21** but suggested that it was bicyclo[3.2.0]heptane derivative **23**. This structural assignment was confirmed by an independent synthesis. A photochemical (2 + 2) cycloaddition reaction of 2-cyclopentenone and o-methylstyrene gave **24**. GC analysis of **24** showed two peaks of approximately equal area, presumably the two possible regioisomers of the cycloadduct.[18] These isomers were not separated but were reduced to **23** by conversion to the tosylhydrazone followed by reaction with catecholborane. The sample of **23** thus obtained had spectral properties identical with those of the sample obtained from the irradiation of **22**.

In the case of **22**, formation of the (2 + 2) cycloadduct **23** was more efficient than the formation of o-xylylene **20**. Recent studies have demonstrated that many similar cycloadditions proceed via exciplexes.[19] Since chromophores separated by three methylene units give maximum efficiency in intramolecular eximer formation,[20] **22** might be expected to be more prone toward cycloaddition than **3**. Examination of the fluorescence spectrum of **22** showed an approximately 30–40% decrease in fluorescence intensity when compared to a model compound, 1-(2-methylphenyl)propene, probably due to eximer formation in the case of **22**, although no eximer emission was observed. This is in contrast with the behavior of **3**, which gave no (2 + 2) cycloadduct and which showed no decrease in fluorescence intensity when compared to 2-(2-methylphenyl)-1-butene.[5] It is interesting to note that Caldwell[21] has predicted that the cycloaddition of styrene with simple alkenes should readily occur.

The photochemistry of **26** was investigated to obtain further information on the effect of the length of the chain connecting the dienophile to the styrene chromophore (Scheme V). This compound has one less methylene unit than **3**, and the position of attachment of the chain differs

(16) Gowland, B. D.; Durst, T. *Can. J. Chem.* **1979**, *57*, 1462–1467.
(17) Styrene **22** would be expected[5] to initially produce the *Z* isomer of **20**. A subsequent geometrical isomerization would be necessary to produce (*E*)-**20**.
(18) Similar cycloadditions often result in the formation of regioisomeric adducts. Although the stereochemistry of **23** and **24** was not determined, they are presumed to be exo since this is the commonly observed stereochemistry of such cycloadducts. See: Turro, N. J. "Modern Molecular Photochemistry"; Benjamin/Cummings: Menlo Park, CA, 1978; pp 458–465. Chapman, O. L.; Lenz, G. "Organic Photochemistry"; Chapman, O. L. Ed.; Marcel Dekker: New York, 1967; Vol. 1, pp 294–307.
(19) For some leading references see: Caldwell, R. A.; Creed, D. *Acc. Chem. Res.* **1980**, *13*, 45–50. Lewis, F. D. *Ibid.* **1979**, *12*, 152–158. Gerhartz, W.; Poshusta, R. D.; Michl, J. *J. Am. Chem. Soc.* **1976**, *98*, 6427–6443.
(20) Hirayama, F. *J. Chem. Phys.* **1965**, *42*, 3163–3171.
(21) Caldwell, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 4004–4007.

from **22**. Compound **26** was synthesized by reaction of the Grignard reagent derived from *o*-bromotoluene with 5-hexenal[22] to give alcohol **25**, followed by oxidation and a Wittig reaction. Irradiation of **26** in benzene gave **27** (3%), **28** (26%), and **29** (15%) at 58% conversion of **26**. Sensitized irradiation of **26** gave 12% of **27** with *p*-dimethoxybenzene as the photosentizer and 32% of **27** along with a trace of **28** with xanthone as photosensitizer. The double bond migration isomer **27** was identified by comparison of its spectral properties with **5**. Photoproducts **28** and **29** were identified by comparison of their spectral properties with independently synthesized samples. Starting with *m*-bromotoluene, the synthesis of **28** was carried out similarly to that described for the preparation of **26**. Photoproduct **29** was synthesized as outlined in Scheme V. Reaction of 2-cycloheptenone with the Grignard reagent prepared from *m*-bromotoluene followed by dehydration of the resulting alcohol gave **30**. Irradiation of **30** gave **31**, which was hydrogenated to **29**.

The behavior of **26** upon irradiation was quite similar to that of **3**, with the exception that no Diels–Alder adduct of the *o*-xylylene was observed. Cycloadduct **29** was probably formed by a secondary photolysis of **28** since none of the ortho cycloadduct was observed. Indeed, irradiation of **28** (direct or sensitized) produced **29**. Furthermore, **26** showed no decrease in fluorescence intensity when compared to **3** or 2-(2-methylphenyl)-1-butene.

Since ketone **2** was available from the synthesis of **3**, the possibility that a trappable photoenol[23] might be generated upon irradiation of **2** was investigated. However, irradiation of **2** gave a 63% yield of acetophenone, the product of a Norrish Type II fragmentation.[24] In this case, therefore, the generation and trapping of the *o*-xylylene is unable to compete with the fragmentation. A related photoenol has been trapped intramolecularly;[25] however, no Norrish Type II reaction was possible in that example.

In summary, only irradiation of **3** produced the intramolecular Diels–Alder adduct of the *o*-xylylene and in only low yield. Competing reactions such as positional isomerization of the benzene ring, double bond migration, and (2 + 2) cycloadditions also occurred. However, the reaction of **3** did show some promising features since some of the cycloadduct **6** was formed, in contrast to the thermolysis of benzocyclobutene **9**. Furthermore, the cycloaddition gave the trans-ring junction found in many natural products. Increasing the rate of the Diels–Alder reaction (perhaps by restricting the conformations available to the *o*-xylylene) or increasing the lifetime of the *o*-xylylene might make this reaction synthetically useful.

## Experimental Section

**General Methods.** Boiling points are uncorrected; melting points are corrected. Nuclear magnetic resonance spectra were obtained on a Varian EM-360 or a Varian HA-100 spectrometer. Ultraviolet spectra were obtained on a Beckman Acta V spectrophotometer. Fluorescence spectra were obtained on a Perkin-Elmer MPF-36 spectrophotometer. Elemental analyses were obtained from Atlantic Microlab, Inc., Atlanta, GA.

Analytical GC employed a Hewlett-Packard 5750 chromatograph coupled to a Columbia Scientific Industries CSI 38 digital integrator. The following columns were used: column a, 1.8 m × 3.2 mm, 10% silicone gum rubber UCW-982 on 60/80 Chromosorb W; column b, 1.8 m × 3.2 mm, 10% SE-30 on 80/100 Chromosorb P; column c, 1.8 m × 3.2 mm, 3% OV-17 on 100/120 Chromosorb W; column d, 1.3 m × 3.2 mm, 15% FFAP on 60/80 Chromosorb W. Preparative GC employed an Aerograph A-700 chromatograph and a 3.65 m × 6.3 mm, 17% silicone gum rubber UCW-982 on 30/60 Chromosorb P (column f).

**Solvents.** All solvents used in photochemical experiments were purified and dried prior to use.

$Me_2SO$ was distilled from NaOH at reduced pressure (bp 50 °C (2–3 mmHg)) and stored over 4A molecular sieves.

THF was first dried over KOH and then distilled from $LiAlH_4$ under $N_2$.

Benzene was stirred over $H_2SO_4$ and decanted, and the process was repeated until darkening of the acid layer was slight. The benzene was distilled from $CaCl_2$ under $N_2$ after washing with $H_2O$ and $NaHCO_3$ solution.

Acetonitrile was stirred over CaH until gas evolution ceased, refluxed over CaH for 2 h, and finally distilled. The first 10% of the distillate was discarded.

Dichloromethane was washed with $H_2SO_4$, with $Na_2CO_3$ solution, and with $H_2O$, dried over $CaCl_2$, and distilled from $P_2O_5$.

Dioxane was purified as described for THF and stored at 0 °C over 4A molecular sieves in an amber glass bottle.

**1-(2-Methylphenyl)-6-hepten-1-one (2).** A three-necked flask, equipped with a reflux condenser and addition funnel, was charged with 22.3 g (0.92 mol) of Mg turnings and 250 mL of freshly dried THF. To this was added 19.6 g (0.063 mol) of 1,2,6-tribromohexane,[26] and the mixture was heated slightly to initiate the reaction. After the reaction had begun, an additional 93.0 g (0.30 mol) of 1,2,6-tribromohexane was added dropwise. This solution was heated to reflux for 1 h and cooled, and 29.3 g (0.25 mol) of *o*-tolunitrile was added dropwise. The resulting solution was heated to reflux for 3.5 h and then stirred overnight at room temperature. The solution was poured into 500 mL of ice-cold 20% HCl solution and stirred for 5 h at room temperature. The solution was extracted with three 200-mL portions of diethyl ether, and the extracts were combined, washed with three 100-mL portions of 10% HCl solution, with saturated $NaHCO_3$, and with $H_2O$, and dried over $MgSO_4$. Distillation yielded 33.8 g (67%) of **2**: bp 103–105 °C (0.7 mmHg); NMR ($CDCl_3$) $\delta$ 7.65–6.95 (m, 4 H, Ar), 6.00–4.75 (m, 3 H, C=CH), 2.77 (distorted t, 2 H, $CH_2$ $\alpha$ to C=O), 2.43 (s, 3 H, $ArCH_3$), 2.2–1.9 (m, 6 H, remaining $CH_2$'s); IR (neat) 1685, 732 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.08; H, 9.01.

**2-(2-Methylphenyl)-1,7-octadiene (3).** A solution of 21.4 g (0.060 mol) of methyltriphenylphosphonium bromide in 25 mL of dry $Me_2SO$ was added via syringe to a solution of methylsulfinyl carbanion (prepared[27] from 3.3 g (0.076 mol) of a 55% dispersion of NaH in mineral oil in 50 mL of dry $Me_2SO$ under an $N_2$ atmosphere). The resulting solution was allowed to stir for 10 min at room temperature, then 11.7 g (0.058 mol) of **2** was added via syringe, and the reaction mixture was stirred overnight at 55 °C. The solution was poured into 200 mL of $H_2O$ and extracted with pentane. The combined extracts were filtered, washed three times with $H_2O$, washed three times with 1:1 $Me_2SO$–$H_2O$, and dried over $MgSO_4$. The organic solution was filtered through 3 g of neutral alumina (activity I), and the alumina was eluted with an additional 500 mL of pentane. Distillation gave 8.3 g (71%) of **3**: bp 89 °C (1.1 mmHg); NMR ($CDCl_3$) $\delta$ 7.07 (m, 4 H, Ar), 6.00–4.7 (m, 5 H, C=CH), 2.50–1.82 (m, with a singlet superimposed at 2.67, 7 H, $ArCH_3$ and $CH_2$'s $\alpha$ to C=C), 1.78–1.13 (m, 4 H, remaining $CH_2$'s); IR (neat) 1630, 760, 738 $cm^{-1}$; $\lambda_{max}$ (heptane) <210 nm.

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.70; H, 10.13.

**7-(2-Methylphenyl)-1,6-octadiene (5).** A three-necked flask, equipped with a reflux condenser and addition funnel, was charged with 1.1 g (0.045 mol) of Mg turnings and 150 mL of freshly dried THF. To this mixture, under a $N_2$ atmosphere, was added a small portion of 5.0 g (0.016 mol) of 1,2,6-tribromohexane[26] in 10 mL of THF. After the reaction had started, the remaining tribromide was added dropwise. The solution was heated to reflux for 1 h. To this Grignard reagent was added 1.6 g (0.01 mol) of *o*-

(22) Viola, A. *J. Am. Chem. Soc.* **1965**, *87*, 1150–1151.
(23) Sammes, P. G. *Tetrahedron* **1976**, *32*, 405–422.
(24) Turro, N. J. "Modern Molecular Photochemistry"; Benjamin/Cummings: Menlo Park, CA, 1978; pp 386–392.
(25) Quinkert, G. *Chimia* **1977**, *31*, 225.
(26) Lamb, R. C.; Ayers, P. W. *J. Org. Chem.* **1962**, *27*, 1441–1442.
(27) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128–1129.

methylacetophenone, and the solution was heated to reflux for 3.5 h and then allowed to stir overnight at room temperature. The solution was poured into 250 mL of ice-cold 20% HCl solution and stirred for 2 h at room temperature. The solution was extracted with pentane. The combined extracts were washed with 10% HCl solution, with saturated $NaHCO_3$ solution, and with water and dried over $MgSO_4$. The solvent was removed in vacuo.

The remaining amber oil was added to 40 mL of HMPA and heated to reflux for 1.5 h. After the reaction mixture had cooled, it was poured into 200 mL of water and extracted with pentane. The combined extracts were washed with water, with $NaHSO_3$ solution, and again with water and then dried over $MgSO_4$. The solvent was removed in vacuo to leave a mixture of **3** and **5**.

Preparative GC (column f, 130 °C) afforded 0.83 g of **5** in the second fraction; NMR ($CDCl_3$) $\delta$ 7.10 (br s, 4 H, Ar) 5.97–4.73 (m, 4 H, C=CH), 2.43–1.10 (m, 12 H, with singlets superimposed at 1.92 and 2.14, $\alpha$-$CH_3$, o-$CH_3$, $CH_2$'s); IR (neat) 1635, 895, 739, 710 $cm^{-1}$; $\lambda_{max}$ (heptane) 240 nm ($\epsilon$ 9500).

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.97; H, 9.98.

**1-(3-Methylphenyl)-6-hepten-1-one (32).** Ketone **32** was prepared from 9.1 g (0.37 mol) of Mg turnings, 41.2 g (0.14 mol) of 1,2,6-tribromohexane,[26] and 11.1 g (0.095 mol) of *m*-tolunitrile by the same method as described for the preparation of **2**. Distillation yielded 8.0 g (42%) of **32**: bp 110 °C (0.75 mmHg); NMR ($CDCl_3$) $\delta$ 7.77–7.45 (m, 2 H, Ar), 7.40–7.10 (m, 2 H, Ar), 6.0–4.7 (m, 3 H, C=CH), 2.97 (distorted t, 2 H, $CH_2$ $\alpha$ to C=O), 2.28 (s, 3 H, $ArCH_3$), 2.14–1.10 (m, 6 H, remaining $CH_2$'s); IR (neat) 1785, 780, 721 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.93; H, 8.77.

**2-(3-Methylphenyl)-1,7-octadiene (4).** Compound **4** was prepared from 5.0 g (0.025 mol) of **32**, 10.3 g (0.030 mol) of methyltriphenylphosphonium bromide, and 1.6 g (0.037 mol) of a 55% dispersion of NaH in mineral oil in a procedure similar to that described for the preparation of **3**. After dry-column chromatography on silica gel with hexane as eluent, distillation afforded 2.0 g (40%) of **4**: bp 96–97 °C (0.77 mmHg); NMR ($CDCl_3$) $\delta$ 7.3–6.9 (m, 4 H, Ar), 6.07–4.67 (m, 5 H, C=CH), 2.9–1.2 (m, with a singlet superimposed at 2.35, 11 H, $ArCH_3$ and $CH_2$'s); IR (neat) 1585, 785, 718 $cm^{-1}$.

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.91; H, 10.18.

**1-(2-Methylphenyl)-6-hydroxyhexan-1-one (15).** A three-necked flask, equipped with a reflux condenser and addition funnel, was charged with 4.1 g (0.17 mol) of Mg turnings and 100 mL of 60:40 anhydrous ether and dry benzene and was heated to 55 °C under a $N_2$ atmosphere. To this warm solution was added 44.5 g (0.17 mol) of *o*-bromotoluene over a 30-min period. Once the addition was complete, the resulting solution was heated to reflux for 1 h. The resulting Grignard solution was poured into an addition funnel connected to a 250-mL three-necked flask. The flask contained 18.2 g (0.16 mol) of $\epsilon$-caprolactone in 100 mL of anhydrous ether at −10 °C under a $N_2$ atmosphere. After the addition funnel containing the Grignard had been purged with $N_2$, the reagent was added slowly. Once this addition was complete, the mixture was stirred for 90 min, at which time 20 mL of saturated $NH_4Cl$ solution was slowly added. After the completion of the hydrolysis, the mixture was filtered and the precipitate washed with 100 mL of benzene. The filtrate was washed three times with $H_2O$ and dried over $MgSO_4$. Removal of the solvent left 34.5 g of a clear amber oil which proved to be pure enough to use in the synthesis of **16**. However, distillation gave 20.5 g (62%) of **15**: bp 138–140 °C (0.35 mmHg); NMR ($CDCl_3$) $\delta$ 7.32 (m, 4 H, Ar), 3.40 (m, 2 H, $CH_2O$), 3.05 (br s, 1 H, OH), 2.79 (distorted t, 2 H, protons on C-2), 2.38 (s, 3 H, $ArCH_3$), 2.11–1.23 (m, 6 H, remaining $CH_2$'s); IR (neat) 3430, 1680, 745, 720 $cm^{-1}$.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.81. Found: C, 75.71; H, 8.83.

**6-(2-Methylphenyl)-6-hepten-1-ol (16).** Compound **16** was prepared from 97.0 g (0.27 mol) of methyltriphenylphosphonium bromide, 35 g (0.17 mol) of undistilled **15**, and 11.7 g (0.49 mol) of a 55% mineral oil dispersion of NaH in the same manner as described for the preparation of **3**. Distillation gave 22.5 g (64%) of **16**: bp 124–125 °C (0.65 mmHg); NMR ($CDCl_3$) $\delta$ 7.01 (m, 4 H, Ar), 5.09 (narrow m, 1 H, C=CH) 4.79 (narrow m, 1 H, C=CH), 3.40 (m, 2 H, $CH_2O$), 3.07 (br s, 1 H, OH), 2.23 (s, 3 H, $ArCH_3$), 1.75–1.05 (m, 8 H, $CH_2$'s); IR (neat) 3430, 747, 710 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{20}$: C, 82.30; H, 9.87. Found: C, 82.03; H, 9.57.

**Ethyl 8-(2-Methylphenyl)-2,8-nonadienoate (17).** To a cold slurry of 10.8 g (0.05 mol) of pyridinium chlorochromate and 0.88 g (0.011 mol) of anhydrous sodium acetate in 60 mL of dry $CH_2Cl_2$ was added 7.3 g (0.035 mol) of **16** in 50 mL of dry $CH_2Cl_2$. The solution was stirred at 0 °C for 1.5 h and then allowed to warm to room temperature. After stirring for 2.5 h, the mixture was diluted with 5 volumes of anhydrous ether, and the solution was decanted from the solids. The remaining black tar was stirred in 200 mL of ether with a glass stirring rod until the residue became granular, and then the etheral solution was filtered. The organic layers were combined and filtered through Florisil. Removal of the solvent left 7.2 g of 6-(2-methylphenyl)-6-heptenal (**33**): IR (neat) 2760, 1730, 710 $cm^{-1}$.

To a solution of 12.5 g (0.036 mol) of (carbethoxymethylene)triphenylphosphorane in 100 mL of dry $CH_2Cl_2$ was added slowly, with stirring, 7.2 g (0.036 mol) of **33** under $N_2$. After the resulting mixture had been heated to reflux for 3.5 h, the solution was evaporated to 30% of its original volume and diluted with 200 mL of petroleum ether (bp 30–60 °C). The solution was filtered, and the precipitate was washed with an additional 150 mL of petroleum ether. The extracts and the filtrate were combined. Removal of the solvent left 12.1 g of a clear oil. Distillation gave 6.0 g (65%) of **17**, bp 136–138 °C (0.5 mmHg); NMR ($CDCl_3$) $\delta$ 7.05 (narrow m, 4 H, Ar), 5.82 (narrow m, 1 H, vinyl proton $\alpha$ to C=O), 5.57 (narrow m, 1 H, vinyl proton $\beta$ to C=O), 5.09 (narrow m, 1 H, vinyl proton on C-9), 4.78 (narrow m, 1 H, vinyl proton on C-9), 4.04 (q, $J$ = 6.4 Hz, 2 H, $OCH_2$), 2.90–1.02 (m, with a singlet superimposed at 2.21, 14 H, $CH_2$'s, $ArCH_3$, $CH_3$ of ethyl); IR (neat) 1730, 1188, 890, 747, 710 $cm^{-1}$; $\lambda_{max}$ (heptane) <210 nm; GC analysis showed **17** to be 95% trans and 5% cis.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.39; H, 8.89.

**1-(2-Methylphenyl)-6-hepten-1-ol (34).** A solution of 1.5 g (0.074 mol) of **2** in 50 mL of anhydrous ether was added dropwise, over a 1-h period, to a slurry of 3.5 g (0.093 mol) of $LiAlH_4$ in 200 mL of anhydrous ether at 0 °C. The resulting solution was stirred for 2.5 h while being warmed to room temperature, followed by a slow addition of 8 mL of $H_2O$ to the recooled solution (0 °C). This solution was stirred for another 2.5 h and filtered, and the filtrate was dried over $MgSO_4$. Distillation afforded 13.5 g (90%) of **34**: bp 115–116 °C (0.8 mmHg); NMR ($CDCl_3$) $\delta$ 7.21 (m, 4 H, Ar), 6.00–5.57 (m, 3 H, C=CH), 2.42 (s, 1 H, OH), 2.32–1.12 (m, with a singlet superimposed at 2.21, 12 H, $ArCH_3$, $CH_2$'s and CH); IR (neat) 3400, 900, 735 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.71. Found: C, 82.28; H, 9.90.

**1-(2-Methylphenyl)-1,6-heptadiene (22).** A small distillation apparatus was charged with 13.3 g (0.063 mol) of **34** and 0.7 g of $KHSO_4$. The mixture was heated for 2 h at 120–125 °C (20–23 mmHg), after which the pressure was lowered and 10.4 g (86%) of **22** was collected: bp 90–91 °C (1.0 mmHg); NMR ($CDCl_3$) $\delta$ 7.10 (m, 4 H, Ar), 6.45–4.75 (m, 5 H, C=CH) 2.4–1.2 (m, with a singlet superimposed at 2.21, 9 H, $ArCH_3$, $CH_2$'s); IR (neat) 960, 900, 735 $cm^{-1}$; $\lambda_{max}$ (heptane) <250 nm.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C 89.95; H, 10.00.

**6-(2-Methylphenyl)bicyclo[3.2.0]heptane (23).** A solution of 1.0 g (0.12 mol) of 2-cyclopentenone and 7.2 g (0.061 mol) of *o*-methylstyrene in 200 mL of benzene was irradiated through quartz in the preparative photochemical apparatus for 3.2 h. After the solvent had been removed in vacuo, the residue was distilled, affording 1.4 g (67%) of **24**: bp 116–117 °C (0.2 mmHg); NMR ($CDCl_3$) $\delta$ 7.39–6.80 (m, 4 H, Ar), 2.83–1.52 (m, 12 H, with a singlet superimposed at 2.09); IR (neat) 1728, 751, 720 $cm^{-1}$; GC analysis (column d, 130 °C) showed two peaks of approximately equal area.

The tosylhydrazone derivative of **24** was prepared from 1.4 g (7.0 mmol) of **24** and 1.5 g (8.4 mmol) of *p*-toluenesulfonylhydrazine according to the procedure of Hutchins et al.[28] Removal

(28) Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1973**, *95*, 3662–3668.

of the ethanol afforded 2.4 g (90%) of the tosylhydrazone derivative, mp 178–181 °C.

The tosylhydrazone derivative was cleanly reduced by adding 6.91 mmol of catecholborane to a cooled solution of 2.4 g (6.24 mmol) of the tosylhydrazone derivative of **24** in $CHCl_3$ according to the procedure outlined by Kabalka and Baker.[29] This procedure afforded 0.80 g (68%) of **23**, whose spectral data were the same as those of the sample obtained from the photolysis of **22**.

**1-(2-Methylphenyl)-5-hexen-1-ol (25).** A three-necked flask, equipped with a reflux condenser and addition funnel, was charged with 1.6 g (0.066 mol) of Mg turnings and 100 mL of a 50:50 mixture of anhydrous ether and dry benzene. The solution was heated to 55 °C under $N_2$. To this warm solution was added 15.7 g (0.06 mol) of *o*-bromotoluene over a 30-min period. Once the addition was complete, the resulting solution was heated to reflux for 1 h and cooled to 0 °C. To the resulting Grignard reagent was added 4.5 g (0.04 mol) of 5-hexenal[22] over a 5-min period. The resulting mixture was heated to reflux for 6 h and then stirred overnight at room temperature. Hydrolysis was carried out by a slow addition of 7 mL of saturated $NH_4Cl$ solution. The reaction mixture was filtered, and the precipitate was washed with 150 mL of ether. The organic layers were combined, washed three times with $H_2O$, and dried over $MgSO_4$. Distillation afforded 6.7 g (88%) of **25**, bp 106–108 °C (0.8 mmHg); NMR ($CDCl_3$) $\delta$ 7.10 (m, 4 H, Ar), 6.01–4.55 (m, 3 H, C=CH), 2.41 (s, 1 H, OH), 2.32–1.23 (m, with a singlet superimposed at 2.22, 10 H, $ArCH_3$, $CH_2$'s and CH); IR (neat) 3300, 740 $cm^{-1}$.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.01; H, 9.55.

**2-(2-Methylphenyl)-1,6-heptadiene (26).** To a solution of 5.0 g (0.024 mol) of pyridinium chlorochromate in 30 mL of dry $CH_2Cl_2$ at 0 °C was added 3.0 g (0.016 mol) of **25** in 30 mL of dry $CH_2Cl_2$. The resulting mixture was allowed to stir overnight at room temperature. Ether (300 mL) was added, and the solvent was decanted. To the remaining black tar was added 200 mL of ether, and this was stirred with a glass rod until the residue became granular. The organic layers were combined and filtered through Florisil. Distillation yielded 2.7 g (90%; 97% pure by GC analysis) of 1-(2-methylphenyl)-5-hexen-1-one (**35**): bp 98–99 °C (1.1 mmHg); NMR ($CDCl_3$) $\delta$ 7.68 (m, 1 H, Ar), 7.08 (narrow m, 3 H, Ar), 6.19–4.70 (m, 3 H, C=CH), 2.85 (t, $J$ = 3.5 Hz, 2 H, $CH_2$ $\alpha$ to C=O), 2.45 (s, 3 H, $ArCH_3$), 2.20–1.60 (m, 4 H, remaining $CH_2$'s; IR (neat) 1680, 740 $cm^{-1}$.

Compound **26** was prepared from 2.0 g (0.011 mol) of **35**, 7.6 g (0.022 mol) of methyltriphenylphosphonium bromide and 1.0 g (0.023 mol) of a 55% mineral oil dispersion of NaH in the same manner as described fro the preparation of **3**. Distillation yielded 1.3 g (66%) of **26**: bp 67–68 °C (0.85 mmHg); NMR ($CDCl_3$) $\delta$ 7.05 (narrow m, 4 H, Ar), 6.05–4.20 (m, 5 H, C=CH), 2.61–1.12 (m, with a singlet superimposed at 2.21, 9 H, $ArCH_3$, $CH_2$'s); IR (neat) 780, 740 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.36; H, 9.61.

**1-(3-Methylphenyl)-5-hexen-1-ol (36).** Compound **36** was prepared from 15.7 g (0.06 mol) of *m*-bromotoluene, 1.6 g (0.066 mol) of Mg turnings, and 4.1 g (0.042 mol) of 5-hexenal[22] according to the procedure outlined for the preparation of **25**. Distillation gave 5.1 g (92%) of **36**: bp 106–108 °C (0.9 mmHg); NMR ($CDCl_3$) $\delta$ 7.07 (m, 4 H, Ar), 6.01–4.31 (m, 3 H, C=CH), 2.82 (s, 1 H, OH), 2.31–1.09 (m, with a singlet superimposed at 2.28, 10 H, $ArCH_3$, $CH_2$'s, CH); IR (neat) 3340, 785, 700 $cm^{-1}$.

Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.04; H, 9.54.

**2-(3-Methylphenyl)-1,6-heptadiene (28).** Oxidation of 4.5 g (0.024 mol) of **36** with 7.8 g (0.036 mol) of pyridinium chlorochromate, in the same manner as described for the preparation of **35**, gave 3.2 g (47%) of 1-(3-methylphenyl)-5-hexen-1-one (**37**): bp 114–115 °C (1.4 mmHg); NMR ($CDCl_3$) $\delta$ 7.63 (m, 1 H, Ar), 7.21 (narrow m, 3 H, Ar), 6.00–4.78 (m, 3 H, C=CH), 2.87 (br t, $J$ = 3.7 Hz, 2 H, $CH_2$ $\alpha$ to C=O), 2.42–1.59 (m, with a singlet superimposed at 2.34, 7 H, $ArCH_3$ and remaining $CH_2$'s); IR (neat) 1680, 779, 696 $cm^{-1}$.

Compound **28** was prepared from 3.0 g (0.016 mol) of **37**, 11.5 g (0.032 mol) of methyltriphenylphosphonium bromide, and 1.39 g (0.032 mol) of a 55% mineral oil dispersion of NaH according to the procedure outlined for the preparation of **26**. The crude oil contained a small amount of **37**, which was removed by chromatography on silica gel with hexane as eluent. Distillation yielded 1.5 g (50%) of **28**: bp 86–87 °C (1.0 mmHg); NMR ($CDCl_3$) $\delta$ 7.10 (m, 4 H, Ar), 6.05–4.47 (m, 5 H, C=CH), 2.71–0.90 (m, with a singlet superimposed at 2.31, 9 H, $ArCH_3$, $CH_2$'s); IR (neat) 790, 708 $cm^{-1}$.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.24; H, 9.75.

**1-(3-Methylphenyl)bicyclo[3.2.0]hept-6-ene (31).** A three-necked flask, equipped with a condenser and addition funnel, was charged with 2.6 g (0.11 mol) of Mg turnings and 100 mL of anhydrous ether, under a $N_2$ atmosphere. To this solution was added 28.3 g (0.108 mol) of *m*-bromotoluene over a 10-min period, and the entire mixture was refluxed overnight. After the mixture was cooled to 0 °C, 4.0 g (0.036 mol) of cyclohept-2-enone was added over a 5-min period. The resulting mixture was stirred at 0 °C for 30 min. The solution was cooled to −10 °C, and 13.5 mL of saturated $NH_4Cl$ solution was slowly added. After filtration, the combined organic layers were washed three times with $H_2O$ and dried over $MgSO_4$. Removal of the solvent left 7.8 g of 1-(3-methylphenyl)cyclohept-2-en-1-ol (**38**) as an amber oil. Dehydration of **38** was accomplished by heating the alcohol over 50 mg of $KHSO_4$ at 100 °C (22–25 mmHg) for 60 min as previously described for the preparation of **22**. Lowering the pressure afforded 3.2 g (48%) of 1-(3-methylphenyl)-1,3-cycloheptadiene (**30**): bp 112–113 °C (1.3 mmHg); NMR ($CDCl_3$) $\delta$ 7.02 (m, 4 H, Ar), 6.00–5.75 (m, 3 H, C=CH), 2.28 (s, 3 H, $ArCH_3$), 2.73–1.80 (m, 4 H, $CH_2$'s); IR (neat) 777, 698 $cm^{-1}$. Compound **30** showed noticeable changes in the NMR spectrum after standing for 7 days in a refrigerator.

A solution of 2.0 g (0.01 mol) of **30** in 275 mL of dry pentane was irradiated through quartz in the preparative photochemical apparatus for 1.1 h. Distillation yielded 1.4 g (70%) of **31**: bp 88–89 °C (1.0 mmHg); NMR ($CDCl_3$) $\delta$ 7.05 (narrow m, 4 H, Ar), 6.12 (d, $J$ = 2.4 Hz, 1 H, C=CH), 5.91 (d, $J$ = 2.4 Hz, 1 H, C=CH), 3.08 (m, 1 H, C-5 bridge proton), 2.28 (s, 3 H, $ArCH_3$), 2.30–1.15 (m, 6 H, $CH_2$'s); IR (neat) 778, 740, 698 $cm^{-1}$.

Anal. Calcd for $C_{14}C_{16}$: C, 91.25; H, 8.75. Found: C, 91.27; H, 8.73.

**1-(3-Methylphenyl)bicyclo[3.2.0]heptane (29).** Compound **31** (1.1 g, 0.006 mol) was hydrogenated (Parr apparatus) over 0.026 g of 10% Pd/C catalyst in 50 mL of ethanol at 32 psi. The reaction mixture was filtered through Celite, and the ethanol was removed. Chromatography on silica gel, with hexane as eluent, and distillation yielded 0.85 g (77%) of **29**: bp 85–86 °C (1.0 mmHg); NMR ($CDCl_3$) $\delta$ 7.02 (m, 4 H, Ar), 2.89 (m, 1 H, C-5 bridge proton), 2.30 (s, 3 H, $ArCH_3$), 2.54–1.15 (m, 10 H, $CH_2$'s); IR (neat) 778, 698 $cm^{-1}$; $^{13}C$ NMR ($CDCl_3$) $\delta$ 150.86, 137.43, 127.97, 125.93, 125.75, 122.19, 52.36, 44.54, 43.43, 34.32, 31.34, 26.20, 21.65, 21.42.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.92; H, 10.05.

**1-(2-Methylphenyl)-1-propene (39).** Compound **39** was prepared from 4.0 g (0.03 mol) of *o*-methylbenzaldehyde, 16.0 g (0.043 mol) of ethyltriphenylphosphonium bromide, and 2.1 g (0.047 mol) of a 55% mineral oil dispersion of NaH in the same manner described earlier for **3**. Distillation afforded 3.1 g (79%) of **39**: bp 46–48 °C (1.5 mmHg) (lit.[30] bp 79.5 °C (15 mmHg)).

**Photochemical Apparatus.** Preparative irradiations were conducted with a water-cooled, quartz immersion well and a Hanovia 450-W medium-pressure mercury vapor lamp. A Pyrex filter, which fit inside the immersion well, was used for sensitized runs. The outer vessels were either 250 or 500 mL in size and were water cooled. The photolysis solutions were continuously purged with a stream of oxygen-free nitrogen.[31]

Analytical irradiations employed the same light source and immersion well, mated with a "merry-go-round" apparatus with eight positions for quartz or Pyrex tubes. The tubes were 10–15

(29) Kabalka, G. W.; Baker, J. D., Jr. *J. Org. Chem.* **1975**, *40*, 1834–1835.

(30) Levina, R. Y.; Grinberg, I. K. *J. Gen. Chem. USSR* **1937**, *7*, 2306–2308.

(31) Meites, L.; Meites, T. *Anal. Chem.* **1948**, *20*, 984–985.

mL in capacity, and the contents were degassed with a stream of oxygen-free nitrogen[31] for 5 min prior to irradiation. Analysis was done by GC, using internal standards.

Low-pressure irradiations employed a Pen-Ray Model SCT-4 photochemical immersion lamp, which emits primarily at 254 nm. The solutions were purged continuously with oxygen-free nitrogen.[31]

**Direct Irradiation of 2-(2-Methylphenyl)-1,7-octadiene (3).** A solution of 5.0 g (0.025 mol) of **3** in 500 mL of benzene was irradiated through quartz in the preparative photochemical apparatus for 66 h. After the solvent had been removed in vacuo, the residue was distilled, and **4** was isolated from the fraction boiling at 87–90 °C (1.1 mmHg) by preparative GC (column f, 130 °C). The sample of **4** obtained had the same spectral data as those of an authentic sample.

An analytical photolysis of 10 mL of 0.053 M **3** in benzene, after 28 h of irradiation through quartz, showed, by GC analysis (column a, temperature programmed from 160 to 200 °C) using naphthalene as an internal standard, a 62% conversion of **3**, a 37% yield of **4**, a 5% yield of **5**, and a 2–4% yield of **6**. Compounds **5** and **6** were identified by comparison of their GC retention times with those of authentic samples, independently synthesized by alternative routes, on three different columns (column a, temperature programmed from 160 to 200 °C; column b, temperature programmed from 105 to 200 °C; column c, temperature programmed from 150 to 200 °C).

An analytical photolysis, using a low-pressure lamp immersed in 365 mL of 0.0026 M **3** in benzene at reflux, after 100 h of irradiation, showed, by GC analysis (column a, temperature programmed from 160 to 200 °C) using naphthalene as an internal standard, a 47% conversion of **3** to **4** (19%) and **6** (7%).

Another analytical photolysis, using a low-pressure lamp immersed in 365 mL of 0.003 M **3** in benzene at 7 °C, after 200 h of irradiation, showed, by GC analysis (column a, temperature programmed from 160 to 200 °C) using naphthalene as an internal standard, a 35% conversion of **3** to **4** (51%) and **6** (24%).

**Sensitized Irradiation of 2-(2-Methylphenyl)-1,7-octadiene (3).** A solution of 2.0 g (0.01 mol) of **3** and 5.0 g (0.03 mol) of xanthone in 500 mL of benzene was irradiated through Pyrex in the preparative photochemical apparatus for 43 h. After the solvent had been removed in vacuo, the residue was distilled and **5** was isolated from the fraction boiling at 84–87 °C (1.1 mmHg) by preparative GC (column f, 130 °C). The sample of **5** obtained had the same spectral data as an authentic sample.

An analytical photolysis of 10 mL of 0.052 M **3** and 0.15 M xanthone in benzene, after 33 h of irradiation through Pyrex, showed, by GC analysis (column a, temperature programmed from 160 to 200 °C) using naphthalene as an internal standard, a 71% conversion of **3** to give a 34% yield of **5**.

**Direct Irradiation of Ethyl 8-(2-Methylphenyl)-2,8-nonadienoate (17).** A solution of 1.0 g (0.004 mol) of **17**, 95% trans and 5% cis, in 250 mL of benzene was irradiated through quartz in the preparative photochemical apparatus for 4.5 h. Removal of the solvent in vacuo left a mixture of **17** and **18**.

This mixture was separated into individual fractions by preparative GC (column f, 180–186 °C). Collection of the first eluted sample afforded 0.18 g of **17b**.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.40; H, 8.90.

The collection of the second eluted fraction afforded 0.16 g of **17a**.

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.68; H, 9.18.

Collection of the third fraction yielded 0.015 g of **18**: NMR ($CDCl_3$) $\delta$ 7.02 (m, 4 H, Ar), 6.10–5.50 (m, 2 H, CH=CHCO$_2$), 5.46–4.72 (m, 1 H, vinyl proton on C-7), 4.18 (q, 2 H, $J$ = 7.0 Hz, OCH$_2$), 2.81–1.02 (m, with a singlet superimposed at 2.20 ($o$-CH$_3$) and another singlet superimposed at 1.89, ($\alpha$-CH$_3$) 14 H, $o$-CH$_3$, $\alpha$-CH$_3$, CH$_2$'s, CH$_3$ of ethyl); IR (neat) 1720, 1670, 1260, 1180, 780 cm$^{-1}$; $\lambda_{max}$ (heptane) <240 nm ($\epsilon$ 9500).

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.35; H, 8.90.

An analytical photolysis of 10 mL of 0.016 M **17** (5% **17b**, 95% **17a**) in benzene, after 8.2 h of irradiation through quartz, showed, by GC analysis (column b, 175 °C) using xanthone as an internal standard, a 46% conversion of **17** and a 6% yield of **18** (based on the amount of **17** that reacted). A constant ratio of 1:1.2 **17b** and **17a**, respectively, was reached.

**Sensitized Irradiation of Ethyl 8-(2-Methylphenyl)-2,8-nonadienoate (17).** A 10-mL solution of 0.016 M **17** and 0.01 M xanthone in benzene was irradiated through Pyrex for 8.2 h. GC analysis (column b, 175 °C) showed a 36% conversion of **17** and a 5% yield of **18** (based on the amount of **17** that reacted). A constant ratio of 1:1.6 of **17b**:**17a** was reached.

**Direct Irradiation of 1-(2-Methylphenyl)-1,6-heptadiene (22).** A solution of 1.0 g (5.4 mmol) of **22** in 275 mL of dry acetonitrile was irradiated through quartz in the preparative photochemical apparatus for 4.8 h. The solvent was removed in vacuo, and the residue was distilled to remove the high-boiling fractions. The distillate, boiling at 82–86 °C (0.65 mmHg), was chromatographed on activated alumina with hexane as eluent. Distillation of the first band gave 90% of **23**: bp 82–83 °C (0.65 mmHg); NMR ($CDCl_3$) $\delta$ 7.03 (m, 4 H, Ar), 3.19–1.27 (m, with a singlet superimposed at 2.14, 14 H, ArCH$_3$, CH$_2$'s, CH's); $^{13}$C NMR ($CDCl_3$) $\delta$ 144.55, 135.39, 129.90, 125.81, 125.29, 124.93, 45.06, 39.28, 34.09, 33.62, 33.21, 31.28, 25.45, 20.13; IR (neat) 748, 719 cm$^{-1}$.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.89; H, 10.04.

An analytical photolysis of 10 mL of 0.03 M **22** in $CH_3CN$, after 5.3 h of irradiation through quartz, showed, by GC analysis (column b, temperature programmed from 100 to 130 °C) using naphthalene as an internal standard, a 99% conversion of **22**, with an 86% yield of **23**.

**Direct Irradiation of 2-(2-Methylphenyl)-1,6-heptadiene (26).** A solution of 0.7 g (3.8 mmol) of **26** in 275 mL of benzene was irradiated through quartz in the preparative photochemical apparatus for 6.2 h. Removal of the solvent in vacuo left a mixture of **26–29**.

Compound **27** was identified by comparison of its GC retention times with those of an authentic sample on three separate columns (column a, 120 °C; column b, 130 °C; column c, 110 °C).

Compounds **28** and **29** were separated by preparative GC (column f, 165 °C). Collection of the second peak afforded 0.23 g (32%) of **28**. The sample of **28** obtained had the same spectral data as those of an authentic sample. Collection of the third peak afforded 0.098 g (14%) of **29**. The sample of **29** obtained had the same spectral data as those of an authentic sample.

An analytical photolysis of 10 mL of 0.021 M solution of **26** in benzene, after 11.5 h of irradiation through quartz, showed, by GC analysis (column b, 120 °C) using naphthalene as an internal standard, a 58% conversion of **26**, yielding **27** (3%), **28** (26%), and **29** (15%), based on reacted starting material.

**Irradiation of 2-(2-Methylphenyl)-1,6-heptadiene (26) in the Presence of *p*-Dimethoxybenzene.** A solution of 0.5 g (2.7 mmol) of **26** and 1.0 g (7.2 mmol) of $p$-dimethoxybenzene in 275 mL of benzene was irradiated through quartz in the preparative photochemical apparatus for 7 h. Removal of the solvent in vacuo left an approximately 50:50 mixture of **26**:**27**, which was separated by preparative GC (column f, 150 °C).

Collection of the first peak, followed by column chromatography on silica gel with hexane as eluent, to remove the last traces of $p$-dimethoxybenzene, yielded 0.06 g (12%) of **27**: NMR ($CDCl_3$) $\delta$ 7.12 (m, 4 H, Ar), 5.85–4.69 (m, 4 H, C=CH), 2.42–1.49 (m, 10 H, with two singlets superimposed at 2.21 and 1.92, representing the $o$-CH$_3$ and $\alpha$-CH$_3$ groups, respectively, and CH$_2$'s); IR (neat) 755, 720 cm$^{-1}$.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; 9.74. 9.89. Found: C, 90.07; H, 9.89.

**Sensitized Irradiation of 2-(2-Methylphenyl)-1,6-heptadiene (26).** An analytical photolysis of 10 mL of 0.021 M **26** and 0.021 g of xanthone (0.011 M), in benzene after 11.5 h of irradiation through Pyrex, showed, by GC analysis (column b, 120 °C) using 2-methylnaphthalene as an internal standard, a 59% conversion of **26**, yielding **27** (32%) and **28** (2%).

**Direct Irradiation of 2-(3-Methylphenyl)-1,6-heptadiene (28).** A solution of 0.6 g (32 mmol) of **28** in 275 mL of benzene was irradiated through quartz in the preparative photochemical

apparatus for 1.9 h. Removal of the solvent in vacuo left a mixture of **28** and **29**.

Compounds **28** and **29** were separated by preparative GC (column f, 155 °C). Collection of the second peak afforded 0.11 g (19%) of **29**, whose spectral data were identical with those of an authentic sample.

An analytical photolysis of 10 mL of 0.015 M **28** in benzene, after 7.7 h of irradiation through quartz, showed, by GC analysis (column b, 120 °C) using naphthalene as an internal standard, a 65% conversion of **28**, yielding **29** (34%).

**Sensitized Irradiation of 2-(3-Methylphenyl)-1,6-heptadiene (28).** An analytical photolysis of 10 mL of 0.016 M **28** and 0.024 g of xanthone in benzene, after 7.7 h of irradiation through Pyrex, showed, by GC analysis (column b, 120 °C) using 2-methylnaphthalene as an internal standard, a 60% conversion of **28** to give **29** in 50% yield.

**Direct Irradiation of 1-(2-Methylphenyl)-6-hepten-1-one (2).** A solution of 5.0 g (0.025 mol) of **2** in 500 mL of benzene was irradiated through quartz in the preparative photochemical apparatus for 9.1 h. After the solvent had been removed in vacuo, the residue was distilled and 2.1 g (63%) of *o*-methylacetophenone was isolated from the fraction boiling at 56–57 °C (1.7 mmHg). Spectral comparison with an authentic sample confirmed the structural assignment.

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**Registry No.** **1**, 81536-61-0; **2**, 83845-35-6; **3**, 83845-36-7; **4**, 83845-37-8; **5**, 83845-38-9; **6**, 70561-39-6; **14**, 502-44-3; **15**, 83845-39-0; **16**, 83861-69-2; *cis*-**17**, 83845-40-3; *trans*-**17**, 83845-59-4; **18**, 83845-41-4; **22**, 73357-80-9; **23**, 83845-42-5; **24** (isomer 1), 83845-43-6; **24** (isomer 1) tosyl hydrazone, 83845-44-7; **24** (isomer 2), 83845-60-7; **24** (isomer 2) tosyl hydrazone, 83845-61-8; **25**, 83845-45-8; **26**, 83845-46-9; **27**, 83845-47-0; **28**, 83845-48-1; **29**, 83845-49-2; **30**, 83845-50-5; **31**, 83845-51-6; **32**, 83845-52-7; **33**, 83845-53-8; **34**, 83845-54-9; **35**, 83845-55-0; **36**, 83845-56-1; **37**, 83845-57-2; **38**, 83845-58-3; **39**, 14918-24-2; $Ph_3PCHCO_2Et$, 1099-45-2; *o*-tolunitrile, 529-19-1; *o*-bromotoluene, 95-46-5; 2-cyclopentenone, 930-30-3; *o*-methylstyrene, 611-15-4; 5-hexenal, 764-59-0; methyltriphenylphosphonium bromide, 1779-49-3.

# Asymmetric Synthesis of Enantiomeric Cyclophosphamides

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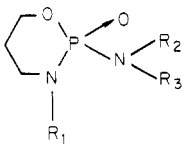
An efficient asymmetric synthesis of the enantiomers of cyclophosphamide was developed on the basis of three important steps: (1) a highly stereospecific synthesis of the 2-chloro-2-oxo-1,3,2-oxazaphosphorinane ring from an optically active amino alcohol and phosphoryl chloride (diastereomer ratio obtained is 10:1 to 12:1); (2) the use of the diethanolamine derivative as an intermediate for introduction of the mustard group; (3) a novel, simple, and effective method for cleaving an *N*-benzyl group by sulfuric acid in toluene, instead of hydrogenolysis.

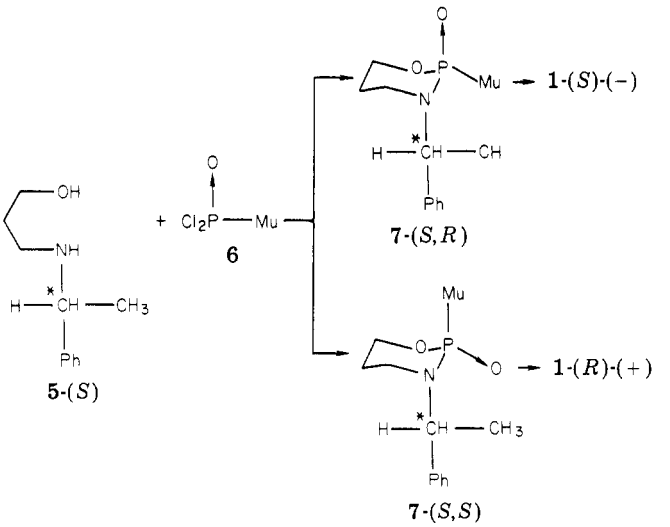
It is still an open question whether (−)-(*S*)-cyclophosphamide [2-[bis(2-chloroethyl)amino]-2-oxo-1,3,2-oxazaphosphorinane, (*S*)-**1**] is a therapeutically more effective antineoplastic agent[2] than the racemic mixture. Since the first resolution[3,4] of cyclophosphamide **1**, a number of



**1**, $R_1$ = H; $R_2$ = $CH_2CH_2Cl$; $R_3$ = $CH_2CH_2Cl$
**2**, $R_1$ = $CH_2CH_2Cl$; $R_2$ = H; $R_3$ = $CH_2CH_2Cl$
**3**, $R_1$ = $CH_2CH_2Cl$; $R_2$ = $CH_2CH_2Cl$; $R_3$ = $CH_2CH_2Cl$
**4**, $R_1$ = $CH_2CH_2Cl$; $R_2$ = H; $R_3$ = $CH_2CH_2OSO_2CH_3$

synthetic methods have been developed leading to the optically active forms of **1** and the related compounds, iphosphamide (**2**), trophosphamide (**3**), and sulphosphamide (**4**). A stereospecific synthesis of the enantiomers of **2**[5] and of **3**[5] was reported recently. Resolution of **3** by a platinum complex was also reported.[6] Absolute configurations of the levorotatory form of **1** as *S*[7a] and of the

Scheme I[a]



[a] Mu = $N(CH_2CH_2Cl)_2$.

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(2) Cox, P. J.; Farmer, P. B.; Jarman, M.; Jones, M.; Stec, W. J. *Biochem. Pharmacol.* **1976**, *25*, 993.

(3) Kinas, R.; Pankiewicz, K.; Stec, W. J. *Bull. Acad. Pol. Sci., Ser. Sci. Chem.* **1975**, *23*, 981.

(4) (a) Zon, G. *Tetrahedron Lett.* **1975**, 3139. (b) Zon, G.; Brandt, J. A.; Egan, W. *J. Natl. Cancer Inst.* **1977**, *58*, 1117.

(5) Ludeman, S. M.; Bartlett, D. L.; Zon, G. *J. Org. Chem.* **1979**, *44*, 1163.

(6) Wroblewsky, A. E.; Verkade, J. G. *J. Am. Chem. Soc.* **1979**, *101*, 7719.

0022-3263/83/1948-0098$01.50/0 