π-Facial Selectivity in Diels–Alder Reactions of [4.3.2]Propella-2,4,8,10-tetraen-7-one and Its Derivatives. Synthesis of 2,5-Etheno[4.3.2]propella-3,8,10-trien-7-ones

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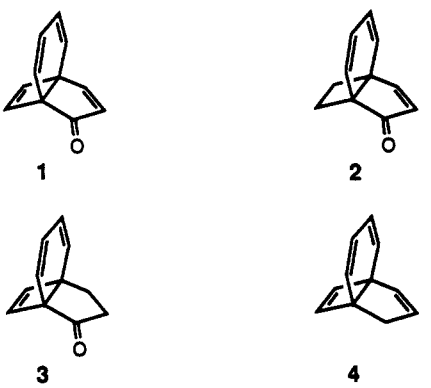
Received January 24, 1990

The Diels–Alder additions of dimethyl acetylenedicarboxylate, methyl propiolate, and maleic anhydride to [4.3.2]propella-2,4,8,10-tetraen-7-one (1), and its 8,9- and 10,11-dihydro derivatives, 2 and 3, and [4.3.2]propella-2,4,7,10-tetraene (4) occur stereoselectively at the face of cyclohexadiene ring syn to five-membered ring. The π-facial selectivity of the additions is rationalized in terms of difference in dihedral angles between the cyclohexadiene and two flanking rings. Treatment of the adduct of maleic anhydride to 1 with $Ni(PPh_3)_2(CO)_2$ gives 2,5-etheno[4.3.2]propella-3,8,10-trien-7-one (**5a**). The electronic absorption spectrum of **5a** exhibits characteristic longer wave absorptions compared with the corresponding partly saturated derivatives, suggesting the existence of longicyclic interaction among its four π-bonds. Irradiation of **5a** results in transannular [2 + 2] cycloaddition rather than cleavage into antiaromatic bicyclo[3.2.0]heptatrienone and benzene.

Recently we reported the synthesis of [4.3.2]propella-2,4,8,10-tetraen-7-one (1).[1] The Diels–Alder additions of acetylenic dienophiles or their equivalents to 1 can afford 2,5-etheno[4.3.2]propella-3,8,10-trien-7-ones (5), in which four isolated π-bond systems are arrayed in a longicyclic arrangement[2] in close proximity. Moreover, the compound 1 can undergo dienophilic attack on either of the two topologically distinctive faces of the cyclohexadiene ring, thereby providing an opportunity to study the effect of flanking four- and five-membered rings on the stereochemical course of Diels–Alder addition. π-Facial selectivity in Diels–Alder additions has attracted considerable attention in recent years.[3-12] In this paper we report the stereoselective additions of dienophiles to the cyclohexadiene moieties of 1, its dihydro derivatives, 2 and 3,



and [4.3.2]propella-2,4,7,10-tetraene (4)[13] at the face syn to the five-membered ring and discuss the probable cause of the observed π-facial selectivity. In addition, we report the spectroscopic properties of **5a** which suggest the presence of interaction among the four π-bond systems, possibly longicyclic in mode, and the result of a brief investigation on its photochemical behavior.

Results and Discussion

Additions of Dienophiles to 1 and Related Compounds. While the two π-faces of cyclohexadiene in 1 are distinguished sterically by virtue of the two different flanking rings, its diene unit is disposed unsymmetrically about the cyclopentenone ring. Therefore, in the addition of an asymmetric acetylenic dienophile to 1, the formation of four isomeric adducts is anticipated, resulting from the different face selections and regioselections, and in that of a symmetric dienophile the production of two isomers. Nuclear Overhauser effect (NOE) difference spectroscopy proved particularly useful for the elucidation of the stereochemistry of the adducts.

The reaction of 1 with dimethyl acetylenedicarboxylate (DMAD) proceeded smoothly at 80 °C to give a single adduct **5d** in 81% yield. Since the spectroscopic properties of the adduct, though consistent with the addition of

(1) Ohkita, M.; Tsuji, T.; Suzuki, M.; Murakami, M.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 1506.
(2) Goldstein, J.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 6193.
(3) (a) Martin, J. D.; Hill, R. K. *Chem. Rev.* **1961**, *61*, 537. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876. (c) Brown, F. K.; Houk, K. N.; Burnell, D. J.; Valenta, Z. *J. Org. Chem.* **1987**, *52*, 3050. (d) Kozikowski, A. P.; Nieduzak, T. R.; Springer, J. P. *Tetrahedron Lett.* **1986**, *27*, 819. Kozikowski, A. P.; Nieduzak, T. R.; Konoike, T.; Springer, J. P. *J. Am. Chem. Soc.* **1987**, *109*, 5167. (e) Paquette, L. A.; Vanucci, C.; Rogers, R. D. *Ibid.* **1989**, *111*, 5792.
(4) (a) Sugimoto, T.; Kobuke, Y.; Furukawa, J. *J. Org. Chem.* **1976**, *41*, 1457. See also: Kobuke, Y.; Sugimoto, T.; Furukawa, J.; Fueno, T. *J. Am. Chem. Soc.* **1972**, *94*, 3633. Hoffmann, R.; Levin, C. C.; Moss, R. A. *Ibid.* **1973**, *95*, 629.
(5) (a) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *Ibid.* **1989**, *111*, 8447 and references cited therein. (b) Chung, W.-S.; Turro, N. J.; Srivastava, S.; Li, H.; le Noble, W. J. *Ibid.* **1988**, *110*, 7882.
(6) (a) Anh, N. T. *Tetrahedron* **1973**, *29*, 3227. (b) Gleiter, R.; Ginsburg, D. *Pure Appl. Chem.* **1979**, *51*, 1301. (c) Böhm, M. C.; Gleiter, R. *Tetrahedron* **1980**, *36*, 3209. (d) Ginsburg, D. *Ibid.* **1983**, *39*, 2095.
(7) (a) Gleiter, R.; Paquette, L. A. *Acc. Chem. Res.* **1983**, *16*, 328. (b) Inagaki, S.; Fugimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054. (c) Mazzocchi, P. H.; Stahly, B.; Dodd, J.; Rondan, N. G.; Domelsmith, L. N.; Roseboom, M. D.; Caramella, P.; Houk, K. N. *Ibid.* **1980**, *102*, 6482.
(8) Brown, F. K.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 1971. Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108.
(9) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1989**, *109*, 663. See also: Fischer, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *Ibid.* **1988**, *110*, 4625. Tripathy, R.; Franck, R. W.; Onan, K. D. *Ibid.* **1988**, *110*, 3257.
(10) Williamson, K. L.; Li Hsu, Y.-F.; Lacko, R.; Youn, C. H. *J. Am. Chem. Soc.* **1969**, *91*, 6129. Williamson, K. L.; Li Hsu, Y.-F. *Ibid.* **1970**, *92*, 7385.
(11) Avenati, M.; Vogel, P. *Helv. Chim. Acta* **1982**, *65*, 204; **1983**, *66*, 1279.
(12) Hagenbuch, J.-P.; Vogel, P.; Pinkerton, A. A.; Schwarzenbach, D. *Helv. Chim. Acta* **1981**, *64*, 1818. See also: Mahaim, C.; Vogel, P. *Ibid.* **1982**, *65*, 866. Carrupt, P.-A.; Berchier, F.; Vogel, P. *Ibid.* **1985**, *68*, 1716 and references cited therein.

(13) Compound 4 was prepared by treating tosylhydrazone of 3 with butyllithium in ether.[14]
(14) Shapiro, R. H. *Org. React.* **1976**, *23*, 405.

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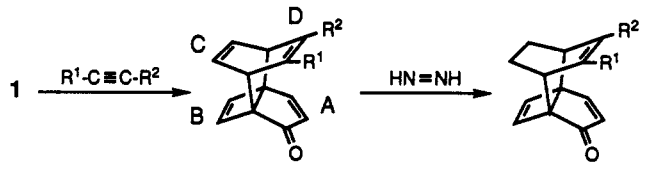
DMAD to the cyclohexadiene moiety, did not provide reliable information about the direction of addition, the adduct was reduced with diimide.[15] With this reagent, the unsubstituted double bond in the upper cyclohexadiene ring was reduced in preference to the other unsaturated moieties to give **6d**, which was subsequently examined by NOE experiments. In the ^{1}H NMR spectrum of **6d**,



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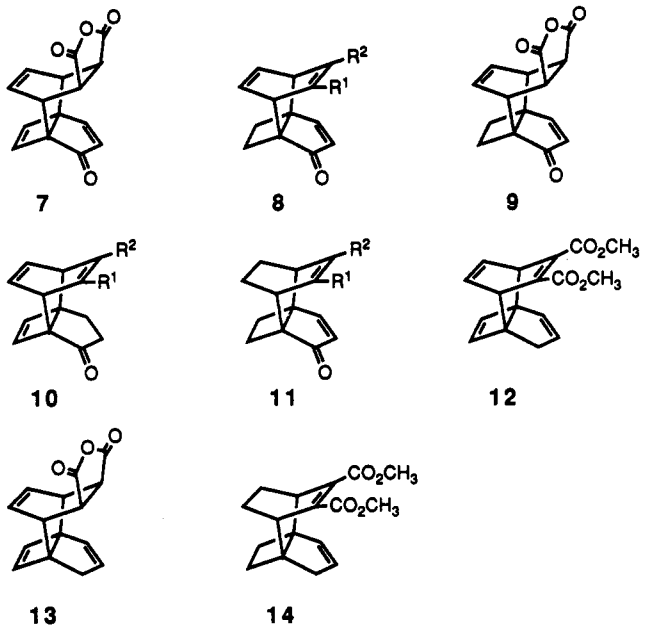
a, $R^1 = R^2 = H$; **b**, $R^1 = H$, $R^2 = CO_2CH_3$

c, $R^1 = CO_2CH_3$, $R^2 = H$; **d**, $R^1 = R^2 = CO_2CH_3$

methylene protons appear as a pair of multiplets at δ 1.2–1.6 and 1.8–2.2. Irradiation at δ 2.0, but not at δ 1.4, resulted in the significant enhancement of two doublet signals at δ 6.56 and 6.85 with a small vicinal coupling constant (J = 2.4 Hz) characteristic of cyclobutene protons.[16] Conversely, weak, yet distinct, positive NOEs were observed in the methylene and bridgehead proton signals at δ 1.8–2.2 and 3.4–3.5, respectively, upon irradiation of the cyclobutene protons. The mutual enhancements observed between the methylene and cyclobutene protons are clearly only consistent with the stereoselective addition of DMAD to the face of cyclohexadiene syn to the cyclopentenone ring.

The addition of methyl propiolate to **1** at 80 °C selectively afforded two of four possible [2 + 4] adducts in 63% and 22% yields. These adducts were readily isolated by column chromatography and identified as **5b** and **5c**, respectively, in the same way as described above.[17] Treatment of **5b** and **5c** with diimide led to preferential reduction of the upper unsubstituted double bond again to give **6b** and **6c**, respectively. Positive NOEs observed between the methylene and cyclobutene protons in both **6b** and **6c** are, as before, consistent only with the syn selective addition of methyl propiolate to **1** with respect to the cyclopentenone ring. Differentiation between **5b** and **5c** was made by examining the NOE between the β-proton of the enone moiety and the bridgehead proton adjacent to the methoxycarbonyl group which was readily distinguished from the other. Thus, the syn selectivity (with respect to the enone moiety) in the dienophile attack on **1** was confirmed for the second time. The addition of maleic anhydride to **1** also proceeded in the same syn-selective manner in the Alder mode and gave **7** as a sole product in a quantitative yield.

In order to examine the possibility that the π-face selective additions to **1** might somehow be induced as a consequence of longicyclic oribtal interaction among the π-bonds or might be dictated by an electronic factor such as secondary electronic interaction between the π-bonds



a, $R^1 = R^2 = H$; **b**, $R^1 = H$, $R^2 = CO_2CH_3$

c, $R^1 = CO_2CH_3$, $R^2 = H$; **d**, $R^1 = R^2 = CO_2CH_3$

of reactants[6] or the hyperconjugative interaction of incipient bonds,[5] the reactions of the dihydro derivatives, **2** and **3**,[1] and unoxygenated **4** were also studied. The cycloadditions of DMAD and maleic anhydride to **2** and **4**, and of DMAD to **3**, all proceeded with high stereoselectivity to give adducts resulting from the additions of the dienophiles to the face of cyclohexadiene syn to the five-membered ring; namely, the reactions of **2**, **3**, and **4** led to the selective formation of **8d** and **9**, **10d**, and **12** and **13**, respectively. The stereochemistry of the adducts was readily elucidated again by NOE experiments.[18] The structure of **10d** was further confirmed by its independent synthesis from **5d** by reduction of the enone moiety with triphenylstannane.[19] The additions of dienophiles to **1–4** in the same syn selective manner with respect to the five-membered ring strongly suggest that the observed π facial selectivity is characteristic of [4.3.2]propellane structure, hence is controlled by a steric effect rather than the electronic factors as mentioned above. The low regioselectivity observed in the reaction of electronically polarized methyl propiolate to **1** also suggests the relative unimportance of dipole–dipole or electrostatic interaction in steering the dienophiles toward the syn face.

π-Facial Selectivity in the Diels–Alder Reactions of 1 and Its Derivatives 2–4. The origin of π-facial selectivity in Diels–Alder cycloadditions has been considered variously as resulting from steric effects,[3] π-orbital distortion or tilting,[4,7] hyperconjugative interactions,[5] secondary orbital interactions,[6] torsional effects,[8] electrostatic interactions,[9] van der Waals–London interactions,[10] polarizability effects,[11] and product stability.[12] In his extensive study on addition reactions to unsaturated propellanes,[20,21] Ginsburg has shown that dienophiles stereo-

(15) (a) Hünig, S.; Müller, H. R.; Thier, W. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 271. (b) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; Benjamin: Menlo Park, CA, 1972.

(16) Accordingly, the multiplet at the lower field was assigned to the inner (endo) protons of methylenes and that at the higher field to the outer (exo) protons.

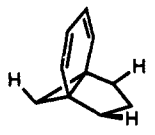
(17) In addition to **5b** and **5c**, the reaction afforded two very minor products in a ratio of ca. 2:1, amounts of which were insufficient for their structural analysis. Since their retention times in GLC analysis were much shorter compared with **5b** and **5c**, we suspect that they might result from unknown side reactions of **1** rather than the anti addition of methyl propiolate to **1**.

(18) The adduct **12** was reduced with diimide to **14** prior to NOE experiment. For details, see the Experimental Section.

(19) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

(20) (a) Ginsburg, D. *Propellanes*; Verlag Chemie: Weinheim, 1975. (b) Ginsburg, D. *Propellanes, Sequel I*; Department of Chemistry, Technion: Haifa, 1981. (c) Ginsburg, D. *Propellanes, Sequel II*; Department of Chemistry, Technion: Haifa, 1985.

selectively add to the face of a cyclohexadiene syn to the larger of two flanking rings unless an opposing stereoelectronic effect predominates. Ginsburg has rationalized these results on steric grounds. Thus, he has pointed out, for example, that a cyclopropane hydrogen syn to the cyclohexadiene ring in **15**, being in the middle of the molecule, effectively exerts more steric repulsion toward an incoming dienophile than the cyclopentane hydrogens which reside at the sides of the molecule.[6b,20h] His argument seems reasonable, but we believe that there may be an additional, possibly more important factor to be considered, i.e., the difference in dihedral angles between the cyclohexadiene and the two flanking rings. Thus, the smaller the size of the ring **16**, the wider is the dihedral angle α between the two planes *abc* and *def* and, in turn, the wider the angle α, the narrower the dihedral angle between the ring and plane *abed* becomes, even if the angle β between the geminal exocyclic bonds remains the same. In addition, the smaller a ring size is, the wider the angle β tends to be owing to the higher s character of the exocyclic hybrid orbital.[22] Therefore, in bicyclic 1,3-cyclo-



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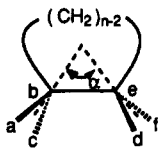

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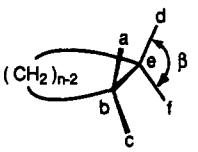

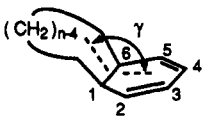

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hexadiene **17**, the smaller the size of flanking ring, the narrower the dihedral angle γ between the two rings will become. In order to evaluate the dihedral angle γ in the structure of **17**, molecular mechanics calculations were performed with MMP2.[23] The calculated angle γ in **17** varies from 124° to 116° and 107° when the ring annelated to cyclohexadiene is changed from cyclopentane to cyclobutane and cyclopropane, respectively.[24] Calculations also show that the cyclohexadiene ring in **1** will be essentially planar and the dihedral angle between the five- and six-membered rings will be 129°, wider by 12° than that between the four- and six-carbon rings. Similarly, difference in the magnitudes of corresponding dihedral angles in **4** is shown to come up to about 15°. Thus, in the Diels–Alder

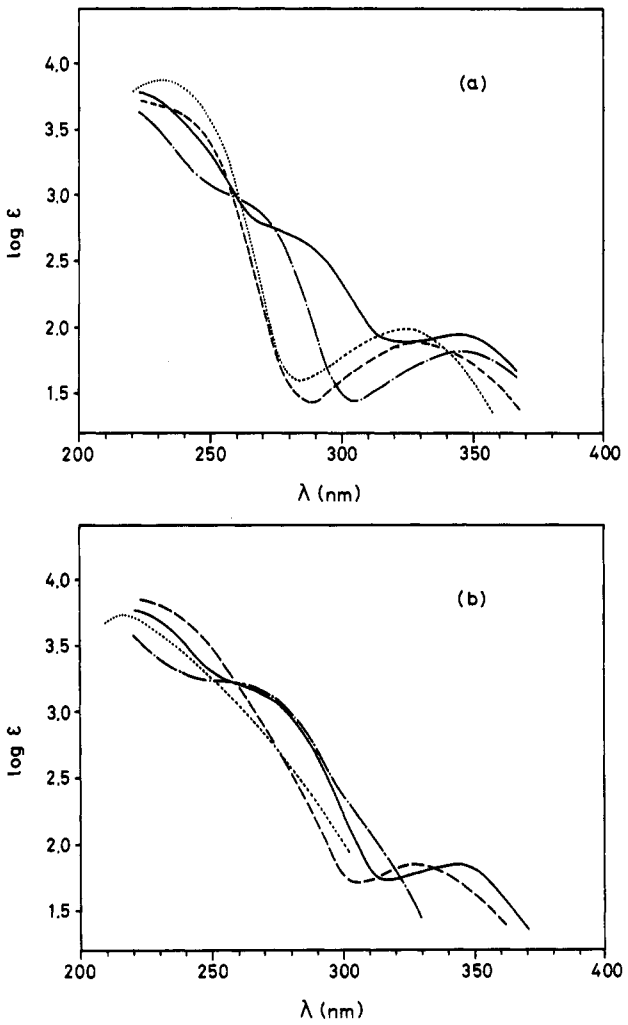


Figure 1. Electronic absorption spectra in ethanol: (a) **5a** (—), **7** (-·-), **9** (- - -), and **18** (···); (b) **5d** (—), **8d** (- - -), **10d** (-·-), and **19** (···).

reactions of **1** and the related compounds, **2–4**, the approach of dienophiles to the face of the cyclohexadiene syn to the five-membered ring should be sterically less encumbered than the anti approach, and we believe that this steric bias is largely responsible for the observed stereoselectivity.

Preparation of 5a. Treatment of **7** with $Ni(PPh_3)_2(CO)_2$ in refluxing diglyme[25] provided **5a** in 43% yield together with a small amount of the dihydro derivative **10a**.

Electronic Absorption Spectra of 5a and the Related Compounds. The electronic interaction among the isolated π-bond systems, A–D, of **5a** which are arrayed in a longicyclic topology is of considerable interest.[2,26] MMP2 calculations show that transannular distances between the upper, unsaturated cyclohexadiene carbons and proximate cyclobutene or cyclopentenone ring carbons are in the range of 2.9–3.0 Å. In this distance, considerable transannular π-orbital interactions are reasonably expected.[27,29]

(21) (a) Mayer, W. J. W.; Oren, I.; Ginsburg, D. *Tetrahedron* **1976**, *32*, 1005. (b) Rüttimann, A.; Ginsburg, D. *Ibid.* **1976**, *32*, 1009. *Ibid.* **1977**, *33*, 1163. (c) Kalo, J.; Photis, J. M.; Paquette, L. A.; Vogel, E.; Ginsburg, D. *Ibid.* **1976**, *32*, 1013. (d) Kalo, J.; Vogel, E.; Ginsburg, D. *Ibid.* **1977**, *33*, 1177. (e) Kalo, J.; Ginsburg, D. *Ibid.* **1978**, *34*, 2155. (f) Ashkenazi, P.; Kalo, J.; Rüttimann, A.; Ginsburg, D. *Ibid.* **1978**, *34*, 2161. (g) Ashkenazi, P.; Peled, M.; Vogel, E.; Ginsburg, D. *Ibid.* **1979**, *35*, 1321. (h) Ashkenazi, P.; Kaftory, M.; Grimme, W.; Heger, K.; Vogel, E.; Ginsburg, D. *Bull. Soc. Chim. Belg.* **1979**, *88*, 841. (i) Ashkenazi, P.; Gleiter, R.; von Philipsborn, W.; Bigler, P.; Ginsburg, D. *Tetrahedron* **1981**, *37*, 127. (j) Landheer, I.; Ginsburg, D. *Ibid.* **1981**, *37*, 143.

(22) (a) Greenberg, A.; Liebman, J. F. *Strained Organic Molecules*; Academic Press: New York, 1978. (b) Wiberg, K. B. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: Chichester, 1987.

(23) Sprague, J. T.; Tai, J. C.; Yuh, Y.; Allinger, N. L. *J. Comput. Chem.* **1987**, *8*, 581.

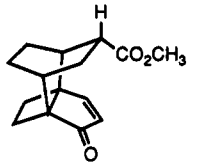
(24) According to molecular mechanics calculations (MMP2),[23] cyclohexadiene ring in **17** is not planar when $n = 4$ or 5. Dihedral angles between the planes C_1–C_6–C_5 and C_2–C_1–C_6 are 0°, 20°, and 1° when $n = 3$, 4, and 5, respectively.

(25) (a) Trost, B. M.; Chen, F. *Tetrahedron Lett.* **1971**, 2603. (b) Dauben, W. G.; Rivers, G. T.; Twieg, R. J.; Zimmermann, W. T. *J. Org. Chem.* **1976**, *41*, 887.

(26) Martin, H.-D.; Mayer, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 283.

(27) Resonance integral of −0.5 eV has been estimated for π-bonds separated by 3 Å in closely related 2,5-etheno[4.2.2]propella-3,7,9-triene.[28] See also: Heilbronner, E.; Bock, H. *Das HMO Modell und seine Anwendung*; Verlag Chemie: Weinheim, 1968. Dewar, M. J. S. *The Molecular Orbital Theory of Organic Chemistry*; McGraw Hill: New York, 1969.

The electronic absorption spectrum of **5a** was examined in comparison with those of related derivatives. Compound **5a** exhibits a prominent shoulder around 270 nm (ϵ 590), which is absent in the spectrum of a simple cyclopentenone derivative **18** (Figure 1a). Upon saturation of the double bond D, the shoulder was shifted to 250 nm (see the spectrum of **7**) and further reduction of double bond B caused disappearance of the shoulder to give a spectrum quite similar to that of **18** (see the spectrum of **9**). These observations suggest that the shoulders in the



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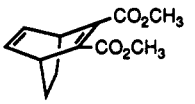

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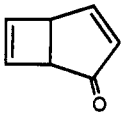
spectra of **5a** and **7** arise from longicyclic and laticyclic interactions[2] among their π-bonds, respectively. On the other hand, when the double bond D of **5a** was substituted with methoxycarbonyls as in **5d**, the shoulder was shifted to 255 nm, but did not appear to be appreciably shifted further upon reduction of double bond A to give **10d** (Figure 1b). Reduction of double bond B of **5d**, however, brought about further blue shift of the shoulder which eventually merged with a band at a shorter wavelength, and the spectrum of resultant **8d** was similar to that of **19** except for the region of n $\rightarrow$ π^* transition.

The absorption at 270 nm in the spectrum of **5a** presumably arises from charge-transfer (CT) interaction between the enone moiety and the three formally isolated double bonds B, C, and D, and the introduction of the electronegative substituent on the double bond D would result in the diminution of the interaction. The similarity of the spectrum of **5d** to those of **7** and **10d** in the $\pi \rightarrow \pi^*$ region suggests that the absorption at 255 nm in the former principally arises from the laticyclic interactions among the π-bonds A, B, and C, and/or among the B, C, and D bonds. Expected through-bond orbital interaction between the upper cyclohexadiene and lower cyclopentenone π-bonds via the σ-bonds connecting the bridgehead carbons was not discernible in the absorption spectra of those compounds.[30,31] Thus the spectra of **8d** in the $\pi \rightarrow \pi^*$ region and of **9** were quite similar to those of **19** and **18**, respectively, and exhibited no particular absorption band ascribable to the through-bond CT interaction.

According to Goldstein and Hoffmann,[2] longicyclic interaction among π bonds in a (2,2,2,2) array leads to destabilization of the system. So far as the chemical property of **5a** is concerned, however, the effect was not appreciable.

Photolysis of 5. Thermal or photochemical expulsion of benzene from cyclohexadiene-annelated compound is a well-established method for the generation of electronically destabilized and/or sterically strained unsaturated species. In this respect compound **5** seemed to be a good precursor for unknown antiaromatic bicyclo[3.2.0]heptatrienone **20**,[32] since the latter species could be generated if the upper cyclohexadiene moiety in **5** were successfully cleaved by retro-Diels–Alder reaction or [4 + 4] cycloreversion. Irradiation of **5a** in methanol or acetone at ambient temperature, however, led only to quantitative intramolecular [2 + 2] cycloaddition to give **21**. On the other hand, photolysis of **5d** in methanol or ether produced only a trace of dimethyl phthalate, which could be regarded as an indicator of the desired reaction, and largely resulted in the formation of insoluble polymeric material. No particular electronic absorption ascribable to **20** was observed either, upon irradiation of **5d** in an EPA[33] matrix at 77 K.



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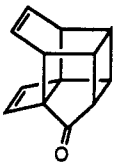

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Experimental Section

Melting points are uncorrected. Unless otherwise specified, all ^1H and ^{13}C NMR were recorded at 100 MHz in $CDCl_3$ in the High-Resolution NMR Laboratory, Hokkaido University. Mass spectra were recorded at an ionization voltage of 70 eV unless otherwise indicated. Elemental analyses were performed by the Center for Instrumental Analysis of Hokkaido University. GLC work was done with helium as a carrier gas with the following columns: A, 5% polyethylene glycol (PEG) 20M, 1 m; B, 10% PEG 20M, 1 m; C, 20% PEG 20M, 0.8 m; D, 5% silicone XE-60, 1 m; E, 10% silicone SE-30, 1 m. Preparative chromatography was performed on Merck Kieselgel 60 (70–230 mesh). HPLC analysis was conducted using a 3.9 mm × 30 cm column packed with μ-Porasil. The light source for photochemistry was a Halos (Eiko-sha, Japan) 450-W high-pressure Hg lamp. Dimethyl acetylenedicarboxylate (DMAD),[34] methyl propiolate,[35] dipotassium azodicarboxylate,[36] and dimethyl 2,3-bicyclo[2.2.2]-octa-2,5-dienedicarboxylate[37] were prepared following the known procedures. Other reagents and solvents were obtained from commercial sources and purified prior to use.

Preparation of 4. A mixture of 0.63 g of [4.3.2]propella-2,4,10-trien-7-one[1] (4.0 mmol) and 0.75 g of tosylhydrazine (4.0 mmol) in 20 mL of ethanol was heated at 75 °C for 2 h. After removal of the solvent in vacuo, the residue was dissolved in CH_2Cl_2 and passed through a short column of silica gel to remove colored matter. The evaporation of CH_2Cl_2 afforded 1.15 g of crystalline tosylhydrazone (88%): mp 148–150 °C dec; ^1H NMR δ 1.3–2.6 (m, 5 H), 2.43 (s, 3 H), 5.7–6.1 (m, 4 H), 5.83 (d, J = 2.5 Hz, 1 H), 5.97 (d, J = 2.5 Hz, 1 H), 7.30 (d, J = 8.3 Hz, 2 H), 7.84 (d, J = 8.3 Hz, 2 H); IR (KBr) 3220, 1392, 1346, 1166, 762, 716, 554 cm^{-1}; MS m/z 327 (M^+ + 1, 1.2), 326 (M^+, 0.5), 171 (100), 142 (35), 141 (40), 130 (52), 128 (35), 115 (52).

To a suspension of 0.82 g of the hydrazone (2.5 mmol) in 100 mL of ether was added 3.5 mL of 1.55 M butyllithium (5.4 mmol) in hexane at 0 °C. The resultant mixture was stirred at room temperature for 24 h and quenched with water. The aqueous solution was separated and extracted with pentane (100 mL × 2). The ethereal solution was combined with the extracts, dried with $MgSO_4$, and concentrated using a 22-cm Vigreux column. The residue was subjected to preparative GLC (20% Apiezone Grease L, 1.8 m, 140 °C and 20% PEG, 2 m, 140 °C) to give 154

(28) Gleiter, R.; Krennrich, G.; Bischof, P.; Tsuji, T.; Nishida, S. *Helv. Chim. Acta* **1986**, *69*, 962.

(29) For homoconjugative π,π-interaction in bicyclo[2.2.2]octadiene, see: Bischof, P.; Hashmall, J. A.; Heilbronner, E.; Hornung, V. *Helv. Chim. Acta* **1969**, *52*, 1745.

(30) (a) Hoffmann, R. *Acc. Chem. Res.* **1971**, *4*, 1. (b) Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 696. Paddon-Row, M. N. *Acc. Chem. Res.* **1982**, *15*, 245.

(31) (a) Dekkers, A. W. J. D.; Verhoeven, J. W.; Speckamp, W. N. *Tetrahedron* **1973**, *29*, 1691. (b) Pasman, P.; Rob, F.; Verhoeven, J. W. *J. Am. Chem. Soc.* **1982**, *104*, 5127.

(32) (a) Breslow, R.; Oda, M.; Sugimoto, T. *J. Am. Chem. Soc.* **1974**, *96*, 1639. (b) Balaban, A. T.; Banciu, M.; Ciorba, V. *Annulenes, Benzo-, Hetero-, Homo-Derivatives, and Their Valence Isomers, Vol. III*; CRC Press: Boca Raton, FL, 1987; p 115.

(33) A 5:5:2 mixture of ether, isopentane, and ethanol.

(34) Abbott, T. W. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 10.

(35) Henne, A. L.; Greenlee, K. W. *J. Am. Chem. Soc.* **1945**, *67*, 484.

(36) Berson, J. A.; Poonian, M. S.; Libbey, W. J. *J. Am. Chem. Soc.* **1969**, *91*, 5567.

(37) Rapoport, H.; Sheldrick, P. *J. Am. Chem. Soc.* **1963**, *85*, 1636.

mg f 4 (43%) as a colorless oil: ^{1}H NMR δ 2.25 (d, J = 17.6 Hz, 1 H), 2.53 (d, J = 17.6 Hz, 1 H), 5.66–5.95 (m, 6 H), 6.07 (d, J = 2.5 Hz, 1 H), 6.28 (d, J = 2.7 Hz, 1 H); ^{13}C NMR δ 40.95, 51.71, 61.92, 120.81, 121.71, 128.12 (two signals overlap), 130.40, 134.82, 139.64, 144.68; IR (neat) 3028, 786, 740, 730 cm^{-1}; UV λ_{max} (EtOH) 273 nm (ε 2300); MS m/z 142 (M$^+$, 47), 141 (71), 116 (63), 115 (100); HRMS calcd for $C_{11}H_{10}$ 142.0783, found 142.0758.

Reaction of 1 with DMAD. A mixture of 13 mg of 1 (82 μmol) and 150 μL of DMAD was heated at 80 °C under nitrogen. After 6 h, GLC analysis (column A, 100–220 °C) showed the complete consumption of 1 and the formation of a single product. The excess DMAD was removed in vacuo, and the residue was subjected to preparative GLC to give 20 mg of **5d** (81%) as a colorless solid: mp 102–103 °C; ^{1}H NMR δ 3.74 (s, 6 H), 3.95–4.17 (m, 2 H), 6.01 (d, J = 5.6 Hz, 1 H), 6.22–6.49 (m, 2 H), 6.23 (d, J = 2.2 Hz, 1 H), 6.55 (d, J = 2.2 Hz, 1 H), 7.41 (d, J = 5.6 Hz, 1 H); IR (KBr) 2960, 1740–1700, 1640, 1605, 1340, 1270, 1240, 1220, 1060, 820, 790, 690 cm^{-1}; UV λ_{max} (EtOH) 255 (ε 1600, sh), 345 nm (70); MS m/z 298 (M$^+$, 1), 239 (77), 163 (32), 104 (100), 76 (67). Anal. Calcd for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73. Found: C, 68.67; H, 4.89.

Reaction of 1 with Methyl Propiolate. A mixture of 18 mg of 1 (0.11 mmol) and 220 μL of methyl propiolate was heated at 80 °C under nitrogen. After 20 h, GLC analysis (column A, 100–220 °C) showed the almost complete consumption of 1 and the formation of two products in a ratio of ca. 3:1. The excess methyl propiolate was evaporated in vacuo, and the residue was chromatographed on silica gel. Elution with ether/hexane (1:4) afforded the major product **5b**, which was further purified by preparative GLC (17 mg, 62%). Elution with ether/hexane (1:1) produced the minor adduct **5c**, which was further purified by preparative GLC (6 mg, 22%). **5b**: mp 111–112 °C; ^{1}H NMR δ 3.70 (s, 3 H), 3.87–3.98 (dd, J = 5.1, 5.9 Hz, 1 H), 4.21 (d, J = 6.1 Hz, 1 H), 5.91 (d, J = 5.6 Hz, 1 H), 6.11–6.48 (m, 2 H), 6.21 (d, J = 2.4 Hz, 1 H), 6.58 (d, J = 2.4 Hz, 1 H), 7.27 (d, J = 5.9 Hz, 1 H), 7.36 (d, J = 5.6 Hz, 1 H); IR (KBr) 1710, 1700, 1345, 1260, 1080, 790 cm^{-1}; UV λ_{max} (EtOH) 230 (ε 5100, sh), 250 (1800, sh), 345 nm (70); MS m/z 240 (M$^+$, 6), 181 (79), 180 (44), 153 (50), 152 (45), 104 (86), 76 (100). Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.06; H, 4.91. A positive NOE was induced in the signal due to the β-proton of the enone moiety in **5b** upon irradiation of the bridgehead proton adjacent to the methoxycarbonyl group. **5c**: mp 155–156 °C; ^{1}H NMR δ 3.72 (s, 3 H), 3.79–3.89 (m, 1 H), 4.33–4.38 (m, 1 H), 5.94 (d, J = 5.6 Hz, 1 H), 6.25–6.34 (m, 3 H), 6.54 (d, J = 2.4 Hz, 1 H), 7.28 (d, J = 6.1 Hz, 1 H), 7.31 (d, J = 5.6 Hz, 1 H); IR (KBr) 1710, 1695, 1260, 1240, 790 cm^{-1}; UV λ_{max} (EtOH) 250 (ε 1400, sh), 340 nm (70); MS m/z 240 (M$^+$, 8), 181 (12), 180 (12), 152 (18), 104 (100), 76 (70). Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.15; H, 5.07.

Reaction of 1 with Maleic Anhydride. A solution of 24 mg of 1 (0.15 mmol) and 30 mg of maleic anhydride (0.31 mmol) in 0.15 mL of benzene was heated at 70 °C for 5 h under nitrogen. The preparative GLC (column D, 190 °C) of the reaction mixture afforded 38 mg of **7** (97%): mp 214–216.5 °C; ^{1}H NMR δ 3.05–3.25 (m, 2 H), 3.51–3.73 (m, 2 H), 6.07 (d, J = 5.6 Hz, 1 H), 6.13 (d, J = 2.6 Hz, 1 H), 6.06–6.33 (m, 2 H), 6.42 (d, J = 2.6 Hz, 1 H), 7.64 (d, J = 5.6 Hz, 1 H); IR (KBr) 1860, 1780, 1770, 1695, 1690, 1220, 1090, 920, 790 cm^{-1}; UV λ_{max} (EtOH) 220 (ε 4300, sh), 250 (1200, sh), 347 nm (70); MS m/z 254 (M$^+$, 6), 181 (9), 156 (100), 128 (96), 76 (35). Anal. Calcd for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96. Found: C, 70.67; H, 3.95. Irradiation of the acid anhydride ring protons at δ 3.05–3.25 induced positive NOEs in the signals due to the bridgehead and cyclopentenone ring protons.

Reaction of 2 with DMAD. A mixture of 30 mg of **2** (0.19 mmol) and 0.15 mL of DMAD was heated at 80 °C for 12 h under nitrogen. GLC analysis (column D, 80–220 °C) showed the complete consumption of **2** and the formation of a single adduct. The reaction mixture was chromatographed on silica gel to isolate the adduct, which was crystallized from hexane to give 48 mg of **8d**. From the mother liquid, additional 9 mg of **8d** was obtained by preparative GLC (a combined yield, 100%): mp 118–118.5 °C; ^{1}H NMR δ 1.75 (br s, 4 H), 3.72 (s, 6 H), 4.07–4.23 (m, 2 H), 6.24 (d, J = 5.5 Hz, 1 H), 6.55–6.73 (m, 2 H), 7.50 (d, J = 5.5 Hz, 1 H); IR (KBr) 3074, 2940, 1712, 1706, 1634, 1440, 1346, 1286, 1070, 770 cm^{-1}; UV λ_{max} (EtOH) 335 nm (ε 110); MS m/z 300 (M$^+$, 2), 269 (12), 241 (82), 163 (100), 106 (57), 78 (38); HRMS calcd for $C_{17}H_{16}O_5$ 300.0997, found 300.0975. Upon irradiation of the cyclobutane protons at δ 1.75, positive NOEs were induced in the signals due to the olefinic protons of the upper cyclohexadiene ring at δ 6.55–6.73, bridgehead protons at δ 4.07–4.23, and β-proton of the enone moiety at δ 7.50. The same effects were observed in the methylene and bridgehead protons upon irradiation of the olefinic protons of the cyclohexadiene moiety.

Reaction of 2 with Maleic Anhydride. A solution of 40 mg of **2** (0.25 mmol) and 50 mg of maleic anhydride (0.5 mmol) in benzene was refluxed for 36 h under nitrogen. GLC analysis (column D, 80–220 °C) showed the almost complete consumption of **2** and the formation of a single adduct. The reaction mixture was chromatographed on silica gel to give 63 mg of crude crystalline product (97%), which was crystallized from hexane/benzene (1:1) to give 46 mg of pure **9** (71%): mp 184–185 °C; ^{1}H NMR δ 1.6–2.1 (m, 4 H), 2.8–3.0 (m, 2 H), 3.30–3.65 (m, 2 H), 6.39 (d, J = 5.5 Hz, 1 H), 6.45–6.65 (m, 2 H), 7.70 (d, J = 5.5 Hz, 1 H); IR (KBr) 2944, 1856, 1776, 1694, 1240, 938 cm^{-1}; UV λ_{max} (EtOH) 220 (ε 5300), 330 nm (80); MS m/z 256 (M$^+$, 46), 228 (9), 183 (23), 158 (19), 130 (100), 115 (21); HRMS calcd for $C_{15}H_{12}O_4$ 256.0736, found 256.0725. Irradiation of (i) the β-proton of the enone moiety at δ 7.70, (ii) the acid anhydride ring protons at δ 2.8–3.0, and (iii) the cyclobutane ring protons at δ 1.6–2.1 induced positive NOEs in the signals due to (i) the acid anhydride ring protons and one of the bridgehead protons, (ii) the β-proton of the enone moiety, and (iii) the olefinic protons in the upper cyclohexene ring and β-proton of the enone moiety, respectively.

Reaction of 3 with DMAD. A mixture of 20 mg of **3** (0.13 mmol) and 0.2 mL of DMAD was heated at 80 °C for 2 h under nitrogen. GLC analysis (column A, 100–220 °C) showed the production of a single major adduct. The yield of isomeric adducts was less than 1%, if any. After removal of the excess DMAD in vacuo, the residue was subjected to preparative GLC to give 27 mg of **10d** (71%) as colorless crystals: mp 69–70 °C; ^{1}H NMR δ 1.86–2.03 (m, 2 H), 2.44 (ddd, J = 4, 8, 17 Hz, 1 H), 3.08 (ddd, J = 8.5, 9.5, 18 Hz, 1 H), 3.76 (s, 3 H), 3.79 (s, 3 H), 3.87–3.95 (m, 1 H), 4.04–4.12 (m, 1 H), 6.11 (d, J = 2.4 Hz, 1 H), 6.29–6.43 (m, 3 H); IR (KBr) 2960, 1730, 1710, 1635, 1600, 1440, 1280, 1240, 1120, 1064, 780 cm^{-1}; UV λ_{max} (EtOH) 255 nm (ε 1700, sh); MS m/z 300 (M$^+$, 1), 241 (32), 163 (100), 78 (36). Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.89; H, 5.35. Upon irradiation of the β-methylene protons of the cyclopentanone ring at δ 1.86–2.03, positive NOEs were observed in the signals due to one of the bridgehead protons at δ 3.87–3.95 and one of the cyclobutene protons at δ 6.4, but not in those due to the olefinic protons of the upper cyclohexadiene moiety.

Reaction of 4 with DMAD. A mixture of 54 mg of **4** (0.38 mmol) and 0.4 mL of DMAD (3.3 mmol) was heated at 70 °C under argon. After 3 h, GLC analysis (column B, 80–220 °C) showed the complete consumption of **4** and the formation of a single product. The column chromatography of the mixture on silica gel followed by preparative GLC (column D, 150 °C) afforded 108 mg of **12** (100%): mp 72.5–73 °C; ^{1}H NMR δ 2.32 (d, J = 18 Hz, 1 H), 2.41 (d, J = 18 Hz, 1 H), 3.74 (s, 3 H), 3.77 (s, 3 H), 3.75–3.96 (m, 2 H), 5.63 (br s, 2 H), 5.99 (d, J = 2.7 Hz, 1 H), 6.17–6.36 (m, 3 H); IR (KBr) 1712, 1634, 1600, 1438, 1282, 1070, 808 cm^{-1}; UV λ_{max} (EtOH) 245 nm (ε 1500, sh); MS m/z 284 (M$^+$, 0.2), 253 (2.3), 195 (23), 163 (47), 90 (100), 89 (35); HRMS calcd for $C_{17}H_{16}O_4$ 284.1049, found 284.1063.

Reaction of 4 with Maleic Anhydride. A solution of 16 mg of **4** (0.11 mmol) and 22 mg of maleic anhydride (0.22 mmol) in 0.8 mL of benzene was heated at 70 °C. After 9 h, GLC analysis (column D, 80–220 °C) showed the complete consumption of **4** and the formation of a single product. The preparative GLC of the reaction mixture afforded 25 mg of the product to which the structure **13** was assigned on the basis of its spectroscopic property (93%): mp 167.5–168.5 °C. The stereoselective addition of maleic anhydride to **4** at the face of cyclohexadiene ring syn to the C_5-ring in the Alder mode was unambiguously proved by NOE experiments. Thus, irradiation at δ 1.79 led to positive NOEs in signals at δ 2.28 and 2.56–2.62 but not in those at δ 2.42 and 2.74–2.80, while irradiation at δ 2.60 induced a positive NOE in a signal at δ 1.79 but not in an absorption at δ 1.96. On the other hand, irradiation at δ 5.10 led to weak but distinct NOEs in signals at δ 2.42 and 2.78–2.80, whereas that at δ 5.26 did not induce an appreciable NOE in the other signals: ^{1}H NMR (270 MHz, C_6D_6) δ 1.79 (ddd, J = 18, 2, 2 Hz, 1 H, allylic endo), 1.96 (ddd, J = 18,

2, 2 Hz, 1 H, allylic exo), 2.28 (dd, J = 8, 3 Hz, 1 H, acid anhydride ring H proximal to C_5-ring CH_2), 2.42 (dd, J = 8, 3 Hz, 1 H, acid anhydride ring H distal to C_5-ring CH_2), 2.56–2.62 (m, 1 H, bridgehead H proximal to C_5-ring CH_2), 2.74–2.80 (m, 1 H, bridgehead H distal to C_5-ring CH_2), 5.07–5.12 (m, 1 H, C_5-ring olefinic H distal to CH_2), 5.26 (ddd, J = 6, 2, 2 Hz, 1 H, C_5-ring olefinic H adjacent to CH_2), 5.44 (d, J = 2.6 Hz, 1 H, C_4-ring H), 5.60 (d, J = 2.6 Hz, 1 H, C_4-ring H), 5.60–5.71 (m, 2 H, C_6-ring olefinic H); IR (KBr) 1858, 1774, 1222, 1090, 918, 904, 814, 804, 732 cm^{-1}; MS m/z 240 (M^+, 6), 168 (33), 167 (87), 142 (100), 141 (41), 116 (32), 115 (34), 105 (31); HRMS calcd for $C_{15}H_{12}O_3$ 240.0786, found 240.0783.

Reduction of 5d with Diimide. To a magnetically stirred solution of 10 mg of **5d** (34 mmol) in 2 mL of acetonitrile containing 50 μL of acetic acid was portionwise added dipotassium azodicarboxylate, and the reaction was monitored by GLC (column E, 100–220 °C). When 10 equiv of the salt was added, the magnitude of a major product peak became maximum. The mixture was neutralized with $NaHCO_3$ and extracted with ether. The ethereal extract was washed with water, dried with $MgSO_4$, and concentrated. The product was purified by successively subjecting the residue to preparative HPLC (ether/hexane, 1:1) and GLC (colume E, 180 °C) to give 3 mg of **6d** as a colorless oil (30%), which crystallized in a few days: mp 72–74 °C; ^1H NMR δ 1.2–1.6 (m, 2 H), 1.8–2.2 (m, 2 H), 3.43–3.51 (m, 2 H), 3.74 (s, 3 H), 3.75 (s, 3 H), 6.09 (d, J = 5.6 Hz, 1 H), 6.56 (d, J = 2.4 Hz, 1 H), 6.85 (d, J = 2.4 Hz, 1 H), 7.39 (d, J = 5.6 Hz, 1 H); IR (KBr) 2948, 1740, 1720, 1698, 1632, 1436, 1278 cm^{-1}; UV λ_{max} (EtOH) 225 (ε 7000, sh), 340 nm (60); MS m/z 300 (M^+, 22), 272 (28), 269 (21), 244 (44), 213 (100), 153 (25); HRMS calcd for $C_{17}H_{16}O_5$ 300.0998, found 300.0972. Upon irradiation of the methylene protons at δ 1.8–2.2, positive NOEs were observed in the signals due to the cyclobutene protons at δ 6.56 and 6.85, but not in those due to the cyclopenenone ring protons at δ 6.09 and 7.39. Conversely, irradiation at δ 6.5 led to NOEs in the signals due to the methylene and bridgehead protons at δ 1.8–2.2 and 3.4–3.5, respectively. Irradiation of the methylene protons at δ 1.2–1.6 did not induce appreciable NOE in the olefinic proton signals.

With 14 equiv of dipotassium azodicarboxylate, **5d** was further reduced to give **11d** as the major product. The reaction was worked up as described above and the product was isolated by preparative GLC (column D, 200 °C): mp 106–107 °C; ^1H NMR δ 1.26–1.96 (m, 4 H), 2.06–2.56 (m, 4 H), 3.18 (m, 1 H), 3.29 (m, 1 H), 3.72 (s, 6 H), 6.34 (d, J = 5.6 Hz, 1 H), 7.50 (d, J = 5.6 Hz, 1 H); IR (KBr) 1720, 1705, 1440, 1285, 1260, 1080 cm^{-1}; MS m/z 302 (M^+, 5), 271 (21), 246 (95), 242 (33), 215 (100); HRMS calcd for $C_{17}H_{18}O_5$ 302.1153, found 302.1142.

Reduction of 5b with Diimide. Treatment of 23 mg of **5b** (0.096 mmol) in 10 mL of acetonitrile containing 2 mL of acetic acid with 195 mg of dipotassium azodicarboxylate (1.2 mmol) at room temperature and subsequent separation of products by preparative GLC (column D, 180 °C) afforded 10 mg of **6b** (43%), 2 mg of **11b** (8%), and 4 mg of 18 (17%). **6b**: mp 117–119 °C; ^1H NMR δ 1.21–1.49 (m, 2 H), 1.78–2.05 (m, 2 H), 3.22–3.29 (m, 1 H), 3.63–3.67 (m, 1 H), 3.71 (s, 3 H), 6.00 (d, J = 5.8 Hz, 1 H), 6.54 (d, J = 2.5 Hz, 1 H), 6.87 (d, J = 2.5 Hz, 1 H), 7.13 (d, J = 6.4 Hz, 1 H), 7.36 (d, J = 5.8 Hz, 1 H); IR (KBr) 3028, 2952, 1700, 1688, 1616, 1438, 1368, 1264, 1228, 1078 cm^{-1}; UV λ_{max} (EtOH) 225 (ε 7100), 340 nm (60); MS m/z 242 (M^+, 39), 214 (46), 186 (41), 155 (100), 127 (39); HRMS calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0960; positive NOEs were observed in the signals due to the cyclobutane protons at δ 6.54 and 6.87 upon irradiation of the methylene protons at δ 1.78–2.05. 18: ^1H NMR δ 1.52–1.81 (m, 6 H), 2.09–2.19 (m, 3 H), 2.32–2.62 (m, 4 H), 3.59 (s, 3 H), 6.26 (d, J = 5.6 Hz, 1 H), 7.63 (d, J = 5.6 Hz, 1 H); IR (neat) 2948, 1708, 1616, 1572, 1440, 1262, 1086, 824, 756 cm^{-1}; UV λ_{max} (EtOH) 231 (ε 7600), 325 nm (100); MS m/z 246 (M^+, 38), 218 (98), 186 (43), 158 (100), 132 (88), 131 (53); HRMS calcd for $C_{15}H_{18}O_3$ 246.1257, found 246.1266.

Reduction of 5c with Diimide. Treatment of 4 mg of **5c** in acetonitrile/acetic acid with 20 equiv of dipotassium azodicarboxylate and subsequent purification of product by preparative GLC (column D, 180 °C) provided 2 mg of **6c**: mp 101–102 °C; ^1H NMR δ 1.14–1.28 (m, 2 H), 1.96–2.02 (m, 2 H), 3.15–3.21 (m, 2 H), 3.72 (s, 3 H), 6.00 (d, J = 5.6 Hz, 1 H), 6.56 (d, J = 2.4 Hz, 1 H), 6.83 (d, J = 2.4 Hz, 1 H), 7.11 (d, J = 6.8 Hz, 1 H), 7.31 (d, J = 5.6 Hz, 1 H); IR (KBr) 1710, 1690, 1620, 1440, 1260, 1230, 1090 cm^{-1}; MS (23 eV) m/z 242 (M^+, 57), 214 (100), 155 (92); HRMS calcd for $C_{15}H_{14}O_3$ 242.0942, found 242.0939. Upon irradiation of the endo protons of the upper cyclohexene moiety at δ 1.96–2.02, positive NOEs were induced in the signals due to the cyclobutene protons at δ 6.56 and 6.83, but not in those to the enone protons.

Reduction of 12 with Diimide. To a mixture of 71 mg of **12** (0.25 mmol) and 0.3 g of dipotassium azodicarboxylate in 9 mL of acetonitrile was added 1 mL of acetic acid at room temperature, and the reaction was monitored by GLC (column D, 150 °C). When additional acetic acid (1.5 mL) and the salt (0.5 g) were added, a secondary reduction product appeared, and, therefore, the reaction was discontinued. The mixture was poured into a mixture of 70 mL of ether and 50 mL of Na_2CO_3, and the aqueous solution separated from the ethereal layer was extracted with 30 mL of ether. The ethereal solutions were combined, dried with $MgSO_4$, and concentrated to give 72 mg of residue, which was subjected to preparative GLC repeatedly (column D, 180 °C and column B, 190 °C) to give 25 mg of a reduction product as a colorless oil to which the structure **14** was assigned on the basis of its spectroscopic property. Each signal in the 500-MHz ^1H NMR spectrum of **14** could be assigned unambiguously on the basis of chemical shift, examination of coupling pattern aided by double resonance technique, and NOE experiments. Thus, irradiation of protons at δ 1.81–1.89 and 1.95–2.02 led to mutual positive NOEs in their absorptions, whereas that of protons at δ 1.13–1.23 and 1.57–1.66 did not induce appreciable NOE in the absorptions due to the four- and six-membered ring methylene protons, respectively: ^1H NMR (500 MHz, C_6D_6) δ 1.13–1.23 (m, 2 H, C_6-ring exo), 1.47–1.55 (m, 1 H, C_4-ring exo), 1.57–1.66 (m, 1 H, C_4-ring exo), 1.81–1.89 (m, 2 H, C_6-ring endo), 1.95–2.02 (m, 2 H, C_4-ring endo), 2.17 (dt, J = 17, 2 Hz, 1 H, C_5-ring allylic), 2.61 (br d, J = 17 Hz, 1 H, C_5-ring allylic), 2.92 (br s, 1 H, bridgehead), 3.02 (br s, 1 H, bridgehead), 3.40 (s, 3 H, methoxyl), 3.45 (s, 3 H, methoxyl), 5.48–5.51 (m, 1 H, olefinic), 5.63 (dt, J = 5, 2 Hz, 1 H, olefinic); IR (neat) 1722, 1628, 1436, 1348, 1272, 1074, 736 cm^{-1}; UV λ_{max} (EtOH) 221 nm (ε 5200); MS m/z 288 (M^+, 10), 260 (31), 232 (100), 201 (62), 115 (20), 91 (20); HRMS calcd for $C_{17}H_{20}O_4$ 288.1362, found 288.1336.

Treatment of 5d with Triphenylstannane. A mixture of 30 mg of **5d** (0.10 mmol) and 300 mg of triphenylstannane (0.85 mmol) in 5 mL of benzene was refluxed for 3 days. The resultant mixture was treated with aqueous methanol and filtered through a short pad of Celite 535. The filtrate was washed with brine and dried with $MgSO_4$. After removal of the solvent, the residue was chromatographed on silica gel eluted with ether/hexane (1:1). The eluent was concentrated, and the residue was subjected to preparative GLC (column D, 170 °C) to give 4 mg of **10d** (13%). The spectroscopic properties of the product were identical with those of the adduct obtained from **3** and DMAD.

Treatment of 7 with $Ni(CO)_2(PPh_3)_2$. A magnetically stirred suspension of 60 mg of **7** (0.23 mmol) and 226 mg of $Ni(CO)_2(PPh_3)_2$ (0.35 mmol) in 5 mL of anhydrous diglyme was refluxed under argon for 40 min while the color of suspension changed from yellow-green to dark brown. The reaction mixture was cooled to room temperature and filtered through a short pad of Florisil, which was washed with 60 mL of ether. The filtrate was combined with the washing, washed with water (2 × 50 mL), dried with $MgSO_4$, concentrated, and chromatographed on silica gel. After PPh_3 (88 mg) was eluted out with hexane, the column was eluted with ether/hexane (1:1) to give a mixture of **5a** and **10a**, which was subjected to preparative GLC (column C, 180 °C) to give 18 mg of **5a** (43%) and 5 mg of **10a** (12%). **5a**: mp 189–190 °C (in a sealed capillary); ^1H NMR δ 3.55–3.72 (m, 1 H), 2.73–3.90 (m, 1 H), 5.92 (d, J = 5.6 Hz, 1 H), 6.11–6.42 (m, 5 H), 6.55 (d, J = 2.4 Hz, 1 H), 7.34 (d, J = 5.6 Hz, 1 H); ^{13}C NMR δ 42.3, 42.4, 64.4 (two signals overlap), 132.7, 132.9, 133.7, 134.4, 136.9 (two signals overlap), 144.0, 161.7, 207.5; IR (KBr) 3060, 2960, 1695, 1572, 1548, 1346, 1260, 1220, 820, 784 cm^{-1}; UV λ_{max} (EtOH) 220 (ε 6200, sh), 273 (590, sh), 345 nm (90); MS m/z 182 (M^+, 49), 181 (84), 154 (64), 153 (91), 152 (51), 104 (43), 102 (29), 76 (100). Anal. Calcd for $C_{13}H_{10}O$: C, 85.69; H, 5.53. Found: C, 85.65; H, 5.51. **10a**: mp 172–173 °C; ^1H NMR δ 1.78 (dd, J = 5.6, 10.0 Hz, 2 H), 2.34 (dt, J = 18.0, 5.6 Hz, 1 H), 3.05 (dt, J = 18.0, 10.0 Hz, 1 H), 3.50–3.73 (m, 2 H), 6.08 (d, J = 2.4 Hz, 1 H), 6.20 (dd, J = 5.1,

5.6 Hz, 1 H), 6.29 (dd, J = 5.1, 5.6 Hz, 1 H), 6.37 (d, J = 2.4 Hz, 1 H), 6.45–6.53 (m, 2 H); IR (KBr) 3050, 2950, 1724, 1348, 1210, 770 cm^{-1}; UV λ_{max} (EtOH) 230 (ϵ 1800, sh), 298 nm (180); MS (23 eV) m/z 184 (M^+, 30), 183 (100), 155 (20), 142 (20), 141 (95), 106 (30), 78 (63); HRMS calcd for $C_{13}H_{12}O$ 184.0887, found 184.0874.

Photochemical Transformation of 5a into 21. A solution of 9 mg of **5a** in 2 mL of methanol was deaerated by bubbling argon and irradiated with a high-pressure Hg lamp through Pyrex at 12 °C. After 20 min, GLC analysis (column A, 160 °C) showed the quantitative conversion of **5a** into a single product, which was obtained as a colorless solid after removal of the solvent and identified as **21**: mp 72–73 °C; ^1H NMR δ 2.38 (m, 1 H), 2.91–3.29 (m, 4 H), 3.44 (ddd, J = 1.0, 5.6, 5.9 Hz, 1 H), 6.09–6.23 (m, 3 H), 6.42 (ddd, J = 1.0, 5.9, 8.3 Hz, 1 H); ^{13}C NMR δ 33.6, 37.6, 39.5, 42.7, 44.0, 50.1, 58.8 (two signals overlap), 127.3, 128.3, 132.4, 139.9, 217.9; IR (film) 3050, 2970, 1755, 1378, 1298, 1260, 1212, 1026, 790, 760, 738, 716, 684 cm^{-1}; MS (23 eV) m/z 182 (M^+, 4), 181 (12), 154 (21), 153 (100), 152 (15), 128 (12), 104 (7); HRMS calcd for $C_{13}H_{10}O$ 182.0714, found 182.0712.

Acknowledgment. Financial support of this research by the Ministry of Education, Science, and Culture, Japanese Government (Grant-in-Aid for Scientific Research, No. 62470018) is gratefully acknowledged.

Carbanion-Accelerated Claisen Rearrangements. 7. Phosphine Oxide and Phosphonate Anion Stabilizing Groups[1a]

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Received July 2, 1990

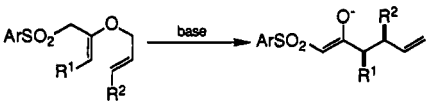
The utility of phosphine oxide and phosphonate groups has been examined in the context of the carbanion-accelerated Claisen rearrangement (CACR). Both of the groups permit the construction of substituted allyl vinyl ethers by allyl oxide addition to phosphorus-substituted allenes. Extensive optimization was required to suppress isomerization of both the allenes and the vinyl ethers. Using potassium dimsylate and lithium chloride as the base, both the phosphine oxides and phosphonates rearranged readily at room temperature with complete regioselectivity in good yield (62–93%). The phosphonates also showed a high level of diastereoselectivity (92% de). The characteristic features of the CACR were compared with the original arylsulfone version.

Introduction

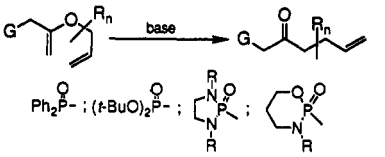
Recent reports from our laboratories[2] have documented the viability and synthetic potential of the carbanion-accelerated Claisen rearrangement (CACR) of allyl vinyl ethers (Scheme I). To date, these studies have focused on the use of the arylsulfonyl stabilizing group, and the results can be summarized as follows: (1) >300-fold rate acceleration over the thermal version, (2) complete regioselectivity, (3) high tolerance for substitution on the allyl vinyl ether (up to tetrasubstituted), (4) exclusive formation of trans olefins, and (5) high internal diastereoselectivity (90% de) for the syn or anti isomers.

To determine the effects of other anion stabilizing groups on rate and selectivity, we considered sulfoxides, sulfoximines, and sulfilimines, but found these sulfur-based groups problematic in preparation and rearrangement of the functionalized allyl vinyl ethers.[2] In contemplating alternative anion-stabilizing moieties, it became quickly apparent that the phosphorus-based groups offered a number of attractive advantages: (1) the ease of access to allenylphosphorus precursors,[3] (2) a well-established chemistry of phosphorus-stabilized allyl anions,[4] (3) potentially tunable reactivity in the choice of phosphorus derivative based on differences in pK_a (phosphine oxide, phosphonate, phosphonamidate, phosphonamide, et al.),[5] (4) the opportunity for manipulation of the keto phosphonate product,[6] and finally (5) the potential for chiral modification of the phosphorus to investigate auxiliary-based asymmetric induction.[7]

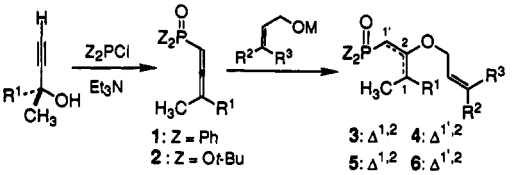
Scheme I



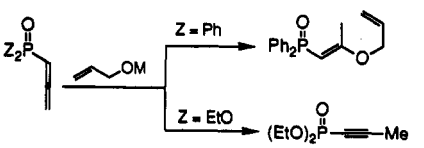
Scheme II



Scheme III



Scheme IV



(1) (a) Taken in part from Marlin, J. E. Ph.D. Thesis, University of Illinois, Urbana, IL, 1987. (b) Present Address: FJSRL/NC, USAF Academy, CO 80840.

(2) (a) Denmark, S. E.; Harmata, M. A.; White, K. S. *J. Am. Chem. Soc.* **1989**, *111*, 8878. (b) Harmata, M. A. Ph.D. Thesis, University of Illinois, Urbana, IL, 1985.

(3) Mark, V. In *Mechanism of Molecular Migrations*; Thyagajaran, B. S., Ed.; Wiley: New York, 1969; Vol. 3, pp 320–431.

(4) Biellmann, J.-F.; Ducep, J.-B. *Org. React.* **1982**, *27*, 1.

(5) (a) The pK_a of diphenylbenzylphosphine oxide is 24 (DMSO). Streitwieser, A., Jr.; Juaristi, E.; Nebenzahl, L. L. In *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: New York, 1980; Vol. 5A, p 359. (b) The pK_a of diethylbenzylphosphonate is 28 (DMSO). Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

(6) Walker, B. J. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: New York, 1979; Chapter 3.

0022-3263/91/1956-1003$02.50/0