Calcd for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.93. Found: C, 68.09; H, 6.95.

Hydroxymethyl Ketal 25. To a solution of cyclopentanone **24b** (69.0 mg, 0.28 mmol) in 2 mL of THF at 0 °C was added $LiAl(O\text{-}t\text{-}Bu)_3H$ (143 g, 0.56 mmol). The reaction mixture was stirred for 5 h, diluted with brine, extracted with ether, and worked up to provide 59 mg (85%) of crude alcohols. NMR integration of methine proton signals showed a 12:1 ratio of hydroxy ketals **24c** and **24a**, respectively, which were inseparable on TLC: R_f 0.34 (40% EtOAc/hexanes); ^1H NMR (**24c**) δ 4.16 (m, 1 H), 3.85 (d, J = 6.9 Hz, 1 H), 3.59 (d, J = 6.9 Hz, 1 H), 2.47-2.18 (m, 3 H), 2.12-1.91 (m, 4 H), 1.90-1.70 (m, 4 H), 1.70-1.42 (m, 2 H), 1.09 (s, 3 H); IR 3583, 3446, 3015, 2947, 2903, 2868, 2232, 1449, 1081, 1062 cm^{-1}.

The mixture of ketals (55 mg, 0.22 mmol) was dissolved in 2 mL of CH_2Cl_2, cooled to 0 °C, and treated with 54 μL (0.44 mmol, 63 mg) of boron trifluoride etherate. After stirring for 2 h at 0 °C, the reaction mixture was diluted with brine, extracted with ether, and worked up to afford 49 mg of crude, isomerized ketal. Flash chromatography (20% EtOAc/hexanes) afforded the hydroxymethyl ketal **25** (36 mg, 66%): R_f 0.28 (20% EtOAc/hexanes); mp = 122-123 °C (ether/pentane); ^1H NMR δ 4.27 (d, J = 4.3 Hz, 1 H), 4.05 (dd, J = 12.4, 2.6 Hz, 1 H), 3.73 (dd, J = 12.4, 7.4 Hz, 1 H), 2.50 (ddd, J = 14.6, 8.4, 4.1 Hz, 1 H), 2.22-2.08 (m, 2 H), 2.05-1.67 (m, 7 H), 1.67-1.50 (m, 3 H), 1.12 (s, 3 H). Upon exchange with D_2O: δ 4.05 (dd, J = 12.4, 2.6 Hz, 1 H) → δ 4.05 (d, J = 12.4 Hz, 1 H); δ 3.73 (dd, J = 12.4, 7.4 Hz, 1 H) → δ 3.73 (d, J = 12.4 Hz, 1 H); δ 1.67-1.50 (m, 3 H) → δ 1.67-1.50 (m, 2 H); ^{13}C NMR δ 120.2, 105.5, 96.9, 81.5, 58.2, 57.1, 51.9, 35.6, 32.0, 27.3, 26.5, 22.6, 22.5, 16.5; IR: 3595, 3477, 2947, 2869, 2238, 1467, 1043. Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.68. Found: C, 67.52; H, 7.73.

Methods for the X-ray Solution of Structure 15. A crystal of dimensions 0.37 × 0.25 × 0.25 mm was mounted on a glass rod. Diffraction measurements were made on an Enraf-Nonius CAD-4 fully automated diffractometer by using graphite monochromatized Mo Kα radiation (λ = 0.710 73 Å). The unit cell was found by using 24 randomly selected reflections, and the indexing procedure produced the following monoclinic cell: a = 7.103 (2) Å, b = 10.998 (3) Å, and c = 16.142 (5) Å, with β = 95.44 (3). The volume is 1255 (1) Å^3, and the calculated density is 1.160 g/cm^3 for Z = 4. Systematic extinctions and an estimated density were the criterions used to uniquely establish the space group as $P2_1/c$ with 1 molecule of composition $C_{14}H_{21}ON$ comprising the asymmetric unit.

There were 2597 reflections collected with $2\theta \leq 52°$, with 749 (29%) observed ($I \geq 3\sigma I$). The structure was solved by direct methods, by using MULTAN80.[30] Eleven of the 16 non-hydrogen atoms were observed on the electron density map based on the phasing of 264 reflections ($E_{min} \geq 1.47$). The remaining five non-hydrogen atoms were located by using the weighted Fourier option in MULTAN80.

The carbon, oxygen, and nitrogen atoms were refined anisotropically. Hydrogen atoms were calculated by using SDP program HYDRO and added to the structure factor calculations. Full-matrix refinement of the non-hydrogen atoms and addition of the hydrogen atoms to the structure factor calculations, without refinement of their positions, has resulted in convergence to a standard crystallographic residual of 0.054 and a weighted residual of 0.049. All intramolecular bond distances and angles are within normal range.

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Registry No. 1, 90044-33-0; **2**, 101401-88-1; **8a**, 81328-62-3; **8b**, 99439-91-5; **9**, 4513-77-3; **9** (potassium enolate), 108060-96-4; **10**, 108060-88-4; **11**, 108060-89-5; **12**, 108060-90-8; **13**, 108060-91-9; **15**, 108060-92-0; **17**, 80963-36-6; **18**, 108060-93-1; **19**, 108060-94-2; **20**, 108060-95-3; **22**, 108060-97-5; **23a**, 108060-98-6; **23c**, 108060-99-7; **24a**, 108061-00-3; **24b**, 108061-01-4; **24c**, 108146-37-8; **25**, 108061-02-5; 2-methyl-1-cyclopentene-1-carboxaldehyde, 81328-61-2.

Supplementary Material Available: Tables I-V (ref 14) contain X-ray data (5 pages). Ordering information is given on any current masthead page.

(30) All data were generated on a VAX 11/750 (Digital Equipment Corporation) by using the Enraf-Nonius SDP-PLUS programs and MULTAN80, a system of computer programs for the automatic solution of crystal structures from X-ray diffraction data: Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Wolfson, M. M. The programs URANUS and SKKPUB, programs to generate plot and tables, respectively, were written by Simon Kay Kearsley, Yale University, 1985.

2,5-Cyclohexadien-1-one to Bicyclo[3.1.0]hexenone Photorearrangement. Development of the Reaction for Use in Organic Synthesis

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Contribution from the Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590. *Received January 13, 1987*

Abstract: 2,5-Cyclohexadien-1-ones (**8-14**) were prepared from derivatives of benzoic acid and benzonitrile by a Birch reductive alkylation-oxidation sequence. Photorearrangement of **9a** at 366 nm gave phenols **17** and **18** in a product ratio of 3:1, respectively; bicyclo[3.1.0]hexenone **15** was not detected even at short reaction times. Intermediate bicyclohexenone **15** presumably undergoes rapid photoisomerization to zwitterion **16**, which suffers competitive 1,2-migrations of the carbomethoxy group to give phenols **17** and **18**. In contrast, irradiation of **8a-e** produced a mixture of bicyclohexenones **19a-e** and **20a-e** in good to excellent yields. Continued irradiation (366 nm) of the mixtures of **19** and **20** gave predominately the diastereoisomeric series **19a-e** (~9:1 for the composition of **19** and **20**). None of the regioisomeric bicyclohexenones **22a-e** were detected. The photostabilizing effect of the enone β-methoxy group also was demonstrated in the context of 2,5-cyclohexadienone photochemistry; the 3,5-dimethoxy-substituted **12** was found to be photostable at 366 nm despite the fact that light is absorbed by **12**. 2,5-Dimethoxy-substituted **11** underwent slow photoconversion to phenol **35**, presumably via loss of formaldehyde in intermediate zwitterion **34**. Irradiation of the 2,6-dimethyl-substituted **10** gave phenol **38**. Replacement of the 4-carbomethoxy group with a cyano group provides a control element which allows isolation of bicyclohexenones from photorearrangement of 4,4-disubstituted 2,5-cyclohexadienones. Thus, **13a** photorearranged to **40a** and **41a** (**40a**:**41a**, 9:1) with no trace of phenolic byproducts; as expected, 3-methoxy-substituted **14** gave mainly **40b** (**40b**:**41b**, >95:5). Stereochemical studies with an enantiomerically pure 2,5-cyclohexadien-1-one **53a** demonstrated that photochemical interconversions of bicyclo[3.1.0]hexenones occur by external cyclopropane bond cleavage (bond "b" in structure **54**). These studies also demonstrated that there is a pathway for return of the excited state or primary photoproduct to racemized 2,5-cyclohexadienone, e.g., **53a** + **53b**. Bicyclohexenone **19b** was converted to lactone **63** (~quantitative yield) on treatment with $NaBH_4$ followed by acidification.

The most intensively studied photoreaction of 2,5-cyclohexadien-1-ones **1** is the rearrangement to bicyclo[3.1.0]hexenones **3** via intermediate zwitterions **2**. Although a great deal is known about the mechanism[1] of this photoconversion, there are relatively

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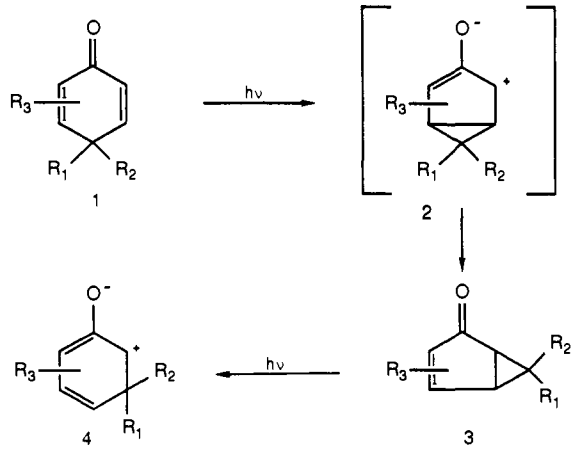
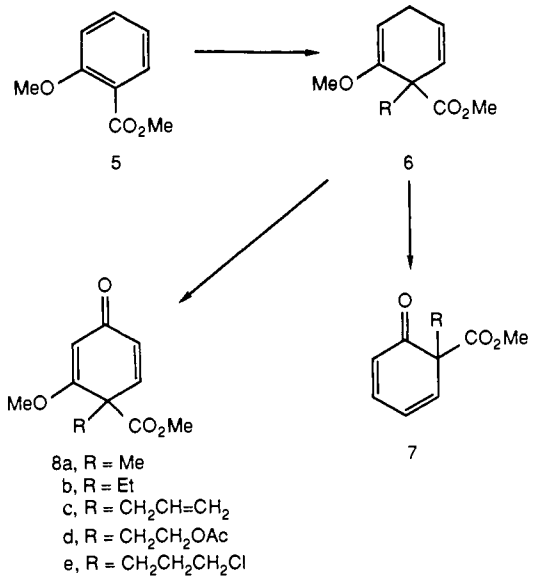


few examples of the use of 2,5-cyclohexadienone photochemistry as a strategic element in multistep organic synthesis.[2]

Functionalized bicyclo[3.1.0]hexenones appear to be particularly well-suited to the solution of problems centered in five- and six-membered ring construction. Part of our interest in this ring system is focused on the controlled conversion of bicyclo-[3.1.0]hexenones **3** to zwitterions of type **4** for use in intramolecular cycloaddition studies.[3] In this report, we present full details of syntheses and photorearrangements of a series of readily available 2,5-cyclohexadien-1-ones.[3c]

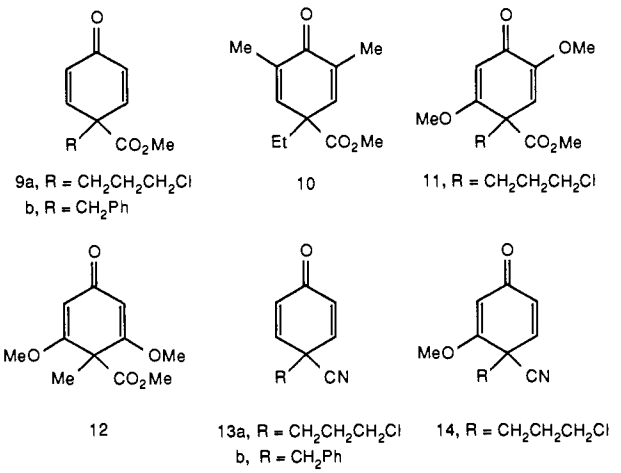
Results and Discussion

Preparation of 2,5-Cyclohexadien-1-ones. The Birch reduction–alkylation of *o*-methoxybenzoic acid esters and amides has provided a flexible route to 2,4-cyclohexadien-1-ones, e.g., **5** → **6** → **7**.[4] We now report that 1,4-cyclohexadienes **6** can be



converted to 2,5-cyclohexadien-1-ones **8a–e** by allylic oxidation with chromium-based reagents.[5] The efficiencies of four reagent systems for allylic oxidation have been examined: (1) Na_2CrO_4 in acetic acid–acetic anhydride,[6a] (2) CrO_3 in acetic acid–acetic anhydride,[6b] (3) pyridinium chlorochromate (PCC)[7a,b] in refluxing chloroform, and (4) pyridinium dichromate (PDC) in refluxing chloroform.[7c]

By using the reductive alkylation–oxidation sequence, benzoic acid, salicylic acid, 3,5-dimethylbenzoic acid, 2,5-dimethoxybenzoic acid, and 2,6-dimethoxybenzoic acid methyl esters can now be converted to 4-alkyl-4-(methoxycarbonyl)-2,5-cyclohexadien-1-ones **9a**, **9b**, **8a–e**, **10**, **11**, and **12**, respectively. Furthermore,



benzonitrile and 2-methoxybenzonitrile provide 2,5-cyclohexadienones **13a**, **13b**, and **14**, respectively, without significant reduction in overall yield as a result of elimination of HCN from

(1) For reviews of 2,5-cyclohexadienone photochemistry, see: (a) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183. (b) Chapman, O. L. *Adv. Photochem.* **1963**, *1*, 323. (c) Schaffner, K. *Adv. Photochem.* **1966**, *4*, 81. (d) Kropp, P. *Org. Photochem.* **1967**, *1*, 1. (e) Chapman, O. L.; Weiss, D. S. *Org. Photochem.* **1973**, *3*, 197. (f) Schuster, D. I. *Acc. Chem. Res.* **1978**, *11*, 65. (g) Schaffner, K.; Demuth, M. M. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3.

(2) For a tabulation of photorearrangements of 2,5-cyclohexadienone to bicyclo[3.1.0]hexenones (with reaction yields), see: Krapcho, A. P. *Synthesis* **1976**, 425. A recent application of this photorearrangement to the synthesis of natural products can be found in the following: Caine, D.; Deutsch, H. *J. Am. Chem. Soc.* **1978**, *100*, 8030.

(3) (a) Schultz, A. G.; Myong, S. O.; Puig, S. *Tetrahedron Lett.* **1984**, *25* 1011. (b) Schultz, A. G.; Puig, S.; Wang, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 785. (c) For a preliminary partial account, see: Schultz, A. G.; Lavieri, F. P.; Macielag, M. *Tetrahedron Lett.* **1986**, *27*, 1481.

(4) (a) Schultz, A. G.; Dittami, J. P.; Lavieri, F. P.; Salowey, C.; Sundararaman, P.; Szymula, M. B. *J. Org. Chem.* **1984**, *49*, 4429. (b) Schultz, A. G.; Puig, S. *J. Org. Chem.* **1985**, *50*, 915. (c) Schultz, A. G.; Lavieri, F. P.; Snead, T. E. *J. Org. Chem.* **1985**, *50*, 3086.

(5) (a) To our knowledge, the first example of an oxidation of a 1,4-cyclohexadiene (e.g., methyl 1-(4-hydroxybutyl)-3-methylcyclohexa-2,5-diene-1-carboxylate) to a 4,4-disubstituted 2,5-cyclohexadien-1-one was reported by Marshall and Wuts. The 2,5-cyclohexadienone was obtained as an undesired byproduct from the oxidation of the primary alcohol: Marshall, J. A.; Wuts, P. G. M. *J. Org. Chem.* **1977**, *42*, 1794.

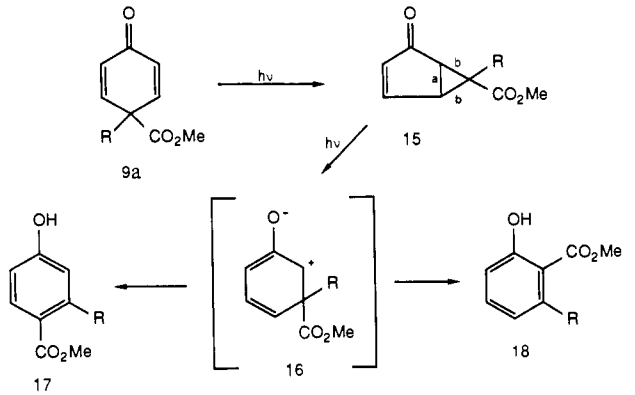
(6) (a) Marshall, C. W.; Ray, R. E.; Laos, I.; Riegel, B. *J. Am. Chem. Soc.* **1957**, *79*, 6308. (b) Nakayama, M.; Shinke, S.; Matsushita, Y.; Ohira, S.; Hayashi, S. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 184.

(7) (a) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647. (b) Bonadies, F.; DiFabio, R. *J. Org. Chem.* **1984**, *49*, 1647. (c) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

the product of Birch reduction–alkylation[8a] or from an intermediate in the oxidation step. We believe that these procedures for preparation of 2,5-cyclohexadien-1-ones provide a significant improvement in generality over methods previously described in the chemical literature.[8b,9]

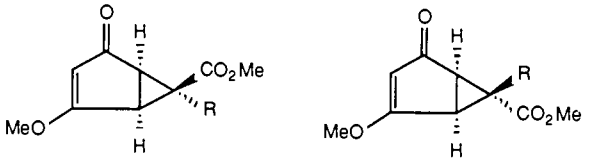
Photochemistry of 2,5-Cyclohexadien-1-ones. The photoreactions of 2,5-cyclohexadienones were performed in deaerated (N_2) benzene solutions with 366-nm light. The progress of reaction was monitored by either thin-layer chromatography (TLC) or gas chromatography.

Photorearrangement of 4-(chloropropyl)-4-(methoxycarbonyl)-2,5-cyclohexadien-1-one (**9a**) gave phenols **17** and **18** in a product ratio of 3:1, respectively. The exclusive formation of **17** and **18** is explained by initial photoconversion of **9a** to bicyclohexenone **15** (not detected even at short reaction times),



followed by rapid photoisomerization of **15** to zwitterion **16** via cyclopropane bond "a" cleavage. Subsequent 1,2-migrations of the carbomethoxy group in **16** would give phenols **17** and **18**. The exclusive migration of the carbomethoxy group rather than the chloropropyl group in zwitterion **16** is in accord with "migration tendencies" determined for carbethoxy relative to alkyl and aryl groups in the rearrangement of 4,4-disubstituted 2,5-cyclohexadien-1-ones to 4-alkyl- and 4-aryl-3-carbethoxyphenols in trifluoroacetic acid.[10a] A similar carbethoxy group migration has been observed in the photochemistry of 3-keto-9-carbethoxy-$\Delta^{1,4}$-hexahydronaphthalene.[10b]

In contrast to the photochemistry of **9a** (and **10**, vide infra), irradiation of **8a–e** produced a mixture of diastereoisomeric bicyclo[3.1.0]hexenones **19a–e** and **20a–e** in good to excellent yields.



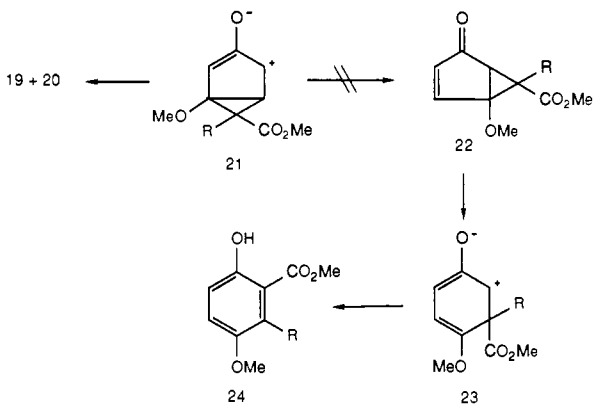
19a, R = Me
b, R = Et
c, R = $CH_2CH{=}CH_2$
d, R = CH_2CH_2OAc
e, R = $CH_2CH_2CH_2Cl$

20

Continued irradiation (366 nm) of the mixtures of **19** and **20** resulted in photoisomerization to give predominately the diastereoisomeric series **19a–e**, with selectivities on the order of 9:1 for the composition of **19** and **20**. Eventually, trace amounts of phenols began to accumulate in the photoreaction mixture. The dependence of product distribution on the wavelength of light used in the photolysis was examined for one 2,5-cyclohexadienone. Irradiation of **8e** through Pyrex glassware (≥300 nm) produced phenol **35** as the sole reaction product.

The assignment of bicyclohexenone stereochemistry rests on well-defined ^1H NMR spectral comparisons within the series **19a–e** and **20a–e**, and by X-ray analysis of **19e**.[11] Thus, the major diastereoisomer at photoequilibrium under direct irradiation conditions (366 nm) is that in which the CO_2Me group is endo related to the 3-methoxyenone chromophore.

Regioselectivity of Bicyclohexenone Formation. It is noteworthy that photogenerated zwitterion **21** rearranges to only **19** and **20** and not to **22**. The limit of detectability in these experiments



was ~2% of **22**. It might be argued, however (vide infra), that **22** would be photolabile under the 366-nm irradiation conditions and convert to zwitterion **23**, from which phenol **24** would be the expected product. Because only trace quantities of uncharacterized phenolic byproducts are observed in photoreactions of **8a–e**, we conclude that rearrangement of zwitterion **21** to bicyclohexenone **22** is not a significant competing reaction pathway.

In considering the reactivity of zwitterion **21** we can turn to the studies of Zimmerman and Pasteris.[12] They found that irradiation of 3-methoxy-4,4-diphenyl-2,5-cyclohexadienone (**25**)

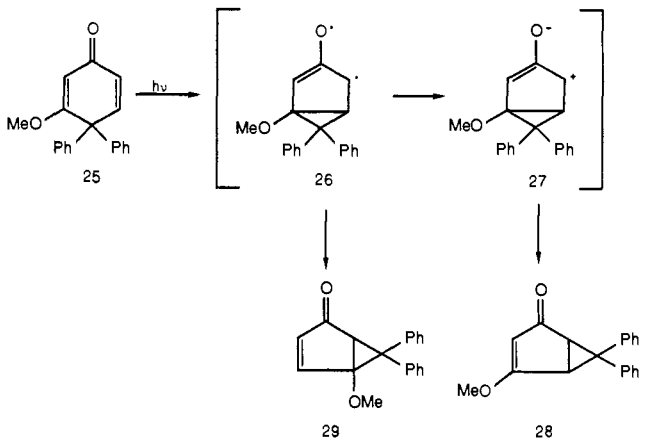
(8) (a) Schultz, A. G.; Macielag, M. *J. Org. Chem.* **1986**, *51*, 4983. (b) For another report of this same type of 2,5-cyclohexadienone construction, see: Beckwith, A. L. J.; Roberts, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 5893. Beckwith, A. L. J.; O'Shea, D. M.; Roberts, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 6408.

(9) (a) Waring, A. J. *Adv. Alicyclic Chem.* **1966**, *1*, 129. (b) Beard, C. C. In *Organic Reactions in Steroid Chemistry*; Fried, J.; Edwards, J. A., Ed.; Van Nostrand Reinhold Co.: New York, 1972; p 265. (c) Baird, R.; Winstein, S. *J. Am. Chem. Soc.* **1962**, *84*, 788. (d) Bubb, W. A.; Sternhell, S. *Tetrahedron Lett.* **1970**, 4499 and references cited therein. (e) Wynberg, H. *Chem. Rev.* **1960**, *60*, 169. (f) Hills, P. R.; McQuillin, F. J. *J. Chem. Soc. (London)* **1953**, 4060. (g) Jung, M. E. *Tetrahedron* **1976**, *32*, 3. (h) Zimmerman, H. E.; Schuster, D. I. *J. Am. Chem. Soc.* **1962**, *84*, 4527. (i) Zincke, T.; Suhl, R. *Chem. Ber.* **1906**, *39*, 4148. (j) Merchant, J. R.; Desai, V. B. *J. Chem. Soc. (London)* **1964**, 2258. (k) Muller, E.; Ley, K. *Chem. Ber.* **1955**, 601. (l) Bamberger, E. *Ann.* **1921**, *424*, 233, 297. (m) Wessely, F.; Hulzer, L.; Vilesek, H. *Monatsh. Chem.* **1953**, *84*, 655. (n) Fisher, A.; Henderson, G. N. *Tetrahedron Lett.* **1980**, *21*, 701. (o) Evans, D. A.; Hoffman, J. M.; Truesdale, L. K. *J. Am. Chem. Soc.* **1973**, *95*, 5822. (p) Evans, D. A.; Wong, R. Y. *J. Org. Chem.* **1977**, *42*, 350. (q) Liotta, D.; Saindance, M.; Barnum, C. *J. Org. Chem.* **1981**, *46*, 3370. (r) Criegee, R. In *Oxidation in Organic Chemistry*; Wiberg, K. D., Ed.; Academic Press: New York, 1965; Part A, p 289. (s) Wessely, F.; Sinwel, F. *Monatsh. Chem.* **1950**, *81*, 811, 1055. (t) Hecker, E.; Lattrell, R. *Angew. Chem.* **1962**, *74* 652. (u) Zbiral, E.; Saiko, O.; Wessely, F. *Monatsh. Chem.* **1964**, *95*, 512. (v) Hecker, E.; Lattrell, R. *Ann.* **1963**, *662*, 48. (w) Yamada, Y.; Hosaba, K.; Sanjah, H.; Suzuki, M. *J. Chem. Soc., Chem. Commun.* **1974**, 661. (x) Yamada, Y.; Kim, J.; Iguchi, K.; Suzuki, M. *Chem. Lett.* **1974**, 1399. (y) McKillop, A.; Perry, D. H.; Edwards, M.; Antus, S.; Farkas, L.; Nogradi, M.; Taylor, E. C. *J. Org. Chem.* **1976**, *41*, 282. (z) Nilsson, A.; Ronlaw, A.; Parker, V. D. *Tetrahedron Lett.* **1975**, *13*, 1107. (aa) Fisher, A.; Henderson, G. N. *Can. J. Chem.* **1979**, *57*, 552. (bb) Coppinger, G. M.; Campbell, T. W. *J. Am. Chem. Soc.* **1953**, *75*, 734. (cc) Capdevielle, P.; Maumy, M. *Tetrahedron Lett.* **1983**, *24*, 5611. (dd) Ronlan, A.; Parker, V. D. *J. Chem. Soc. C.* **1971**, 3214. (ee) Corey, E. J.; Barcza, S.; Klotmann, G. *J. Am. Chem. Soc.* **1969**, *91*, 4782. (ff) Iwata, C.; Morie, T.; Maezaki, N.; Shimamura, H.; Tanaka, T.; Imanishi, T. *J. Chem. Soc., Chem. Commun.* **1984**, 930. (gg) Iwata, C.; Fusaka, T.; Fujiwara, T.; Tomita, K.; Yamada, M. *J. Chem. Soc., Chem. Commun.* **1981**, 463. (hh) Mander, L. N. *Acc. Chem. Res.* **1983**, *16*, 48.

(10) (a) Marx, J. N.; Argyle, J. C.; Norman, L. R. *J. Am. Chem. Soc.* **1974**, *96*, 2121. (b) Kropp, P. J. *Tetrahedron Lett.* **1964**, 3647. (c) See: footnote 8 in Caine, D.; Deutsch, H.; Chao, S. T.; Van Derveer, D. G.; Bertrand, J. A. *J. Org. Chem.* **1978**, *43*, 1114 for additional information.

(11) We thank Dr. Yu Wang of the Department of Chemistry, Taiwan University, Roosevelt Rd., Section 4, Taipei, Taiwan, Republic of China, for the X-ray diffraction study of **19e**.

(12) An approximately 20% yield of the novel dienone photorearrangement product 3-methoxy-4,5-diphenylphenol also was obtained from irradiation of **25**. Zimmerman, H. E.; Pasteris, R. J. *J. Org. Chem.* **1980**, *45*, 4876.



in benzene produced bicyclohexenones **28** and **29** in a ratio of 1.4:1. In a separate experiment, zwitterion **27** (prepared by a nonphotochemical technique) was found to rearrange exclusively to **28**. To explain the concurrent photoproduction of **29**, Zimmerman suggested that rearrangement occurs from "an electronically excited (triplet) bridged species", **26**, the *photochemical precursor* of zwitterion **27**.

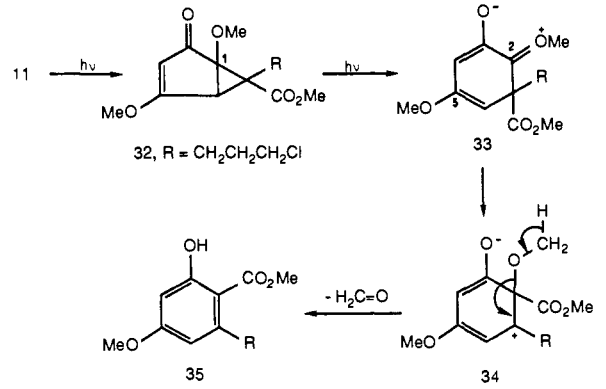
Our studies with 3-methoxy-4-(methoxycarbonyl)-2,5-cyclohexadien-1-ones **8a–e** and 3-methoxy-4-cyano-2,5-cyclohexadien-1-ones (vide infra) demonstrate that photorearrangements of these compounds occur exclusively to give the type **19** and **20** bicyclohexenones. This regiocontrol should be of use in synthetic applications of 2,5-cyclohexadienone photochemistry.

Photochemical Stability of Bicyclo[3.1.0]hexenones. Another potentially useful feature of the photorearrangements of **8a–e** is the excellent photochemical stability of the product bicyclo[3.1.0]hexenones **19a–e** and **20a–e**. These compounds undergo photointerconversion when irradiated with 366-nm light, but they do not easily photorearrange to phenols. This observation stands in marked contrast to the reactivity of the presumed intermediate **15** in the photorearrangement of **9** and to the photoreactivity recorded for most other bicyclo[3.1.0]hexenones.[1]

In the case of 3-methoxy-4,4-diphenyl-2,5-cyclohexadienone (**25**), for which unusual photoreactivity has been observed,[12] Zimmerman and Lynch[15] suggest that "the methoxy substituent lowers the energy of the $\pi \rightarrow \pi^*$ triplet sufficiently to permit reactivity competitive with the normal $n \rightarrow \pi^*$ type A rearrangement". In our case, the β-methoxy substituent acts as a photostabilization unit.

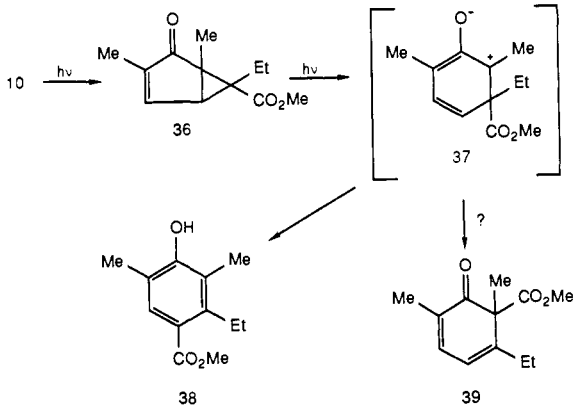
The enhanced photostability of β-methoxyenones also was demonstrated in the context of 2,5-cyclohexadienone photochemistry. The 3,5-dimethoxy-substituted 2,5-cyclohexadienone **12** was found to be photostable (366 nm), despite the fact that UV spectral data confirm that light is absorbed by **12** under the standard photolysis conditions.

We also have examined the photoreactivity of the 2,5-dimethoxy-substituted derivative **11** and have found that it is slowly converted to phenol **35**. This reaction is thought to occur by photorearrangement of **11** to the 1,4-dimethoxybicyclohexenone **32**, from which photozwitterionization (perhaps assisted by the



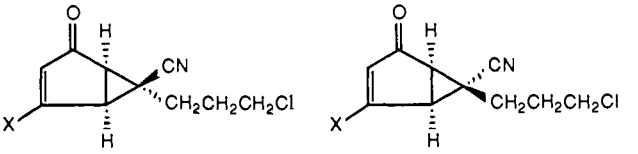
C(1) methoxy substituent) gives **33**. A 1,2-shift of the carbomethoxy group would give the new zwitterion **34**, and loss of formaldehyde would give phenol **35**. It is noteworthy that the methoxy substituents at C(2) and C(5) in **33** direct the methoxycarbonyl group migration to C(2), and, in contrast to the reactivity of zwitterion **16**, none of the phenol resulting from methoxycarbonyl group migration to C(4) was observed.

Irradiation of the 2,6-dimethyl-substituted derivative **10** provided phenol **38**. This example demonstrates that intermediate zwitterion **37**, without a methoxy group at C(5) as in **33**, undergoes methoxycarbonyl group rearrangement to C(4). Methoxycarbonyl group rearrangement to C(2) would have generated the photolabile 2,4-cyclohexadienone **39**.[1]



The control of the 2,5-cyclohexadienone photorearrangement by a β-methoxy substituent is expected to be generally useful for preparation of bicyclo[3.1.0]hexenones of type **19** and **20**. However, we also desired a control element that would provide bicyclo[3.1.0]hexenones from 4,4-disubstituted derivatives of type **9**. As already noted, **9** undergoes photorearrangement to phenols **17** and **18** via zwitterionization of bicyclo[3.1.0]hexenone **15** to give **16**.

We have uncovered an important control element in 2,5-cyclohexadienone photochemistry, as demonstrated by the rearrangement of the 4-cyano derivative **13a** to bicyclo[3.1.0]hexenones **40a** and **41a** with no trace of phenolic byproducts. With photo-

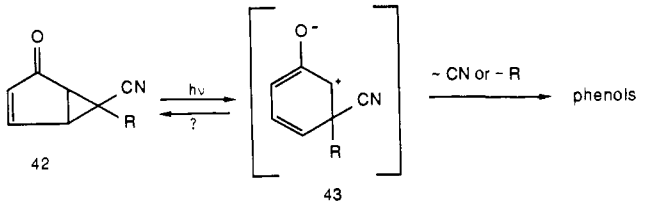


reactivity analogous to the series **8a–e**, irradiation of **13a** at 366 nm produces an initial mixture of bicyclo[3.1.0]hexenone diastereoisomers, but continued irradiation of the mixture for a total of 3 h results in the formation of predominately **40a** (**40a**:**41a**, 9:1). The 3-methoxy derivative **14** gives **40b** and **41b** as a 9:1 mixture after 3 h. After 8 h, the ratio of diastereoisomers is increased to >95:5, favoring the endo cyano isomer **40b**. No phenol formation was observed on extended irradiation of **40b** and **41b**.

The enhanced photostability of cyano-substituted bicyclo[3.1.0]hexenones **42** might, in principle, be a result of a retardation in the rate of photoisomerization to zwitterion **43**. This explanation appears attractive especially in light of the work of Gassman and Saito,[13] who showed that a β-cyano group is far more rate re-

(13) (a) Gassman, P. G.; Saito, K. *Tetrahedron Lett.* **1981**, *22*, 1311. (b) For more recent studies of the electronic effects of the cyano group, see: Gassman, P. G.; Talley, J. J. *Tetrahedron Lett.* **1981**, *22*, 5253. Gassman, P. G.; Guggenheim, T. L. *J. Org. Chem.* **1982**, *47*, 3023. Gassman, P. G.; Doherty, M. M. *J. Am. Chem. Soc.* **1982**, *104*, 3742. Dixon, D. A.; Eades, R. A.; Frey, R.; Gassman, P. G.; Hendewerk, M. L.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 3885.

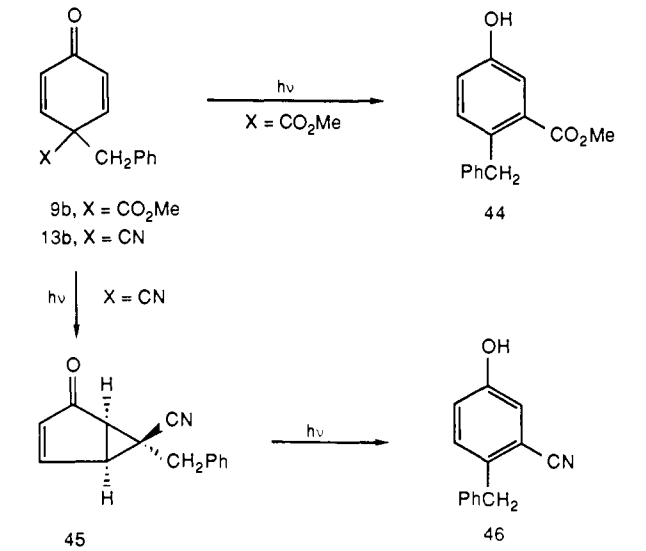
tarding than the α-cyano group in solvolyses of sulfonate esters. Remarkably, solvolyses of alkyl tosylates with a β-cyano substituent were found to occur at rates of $\sim 10^5$–10^8 slower than the homologous tosylates with a hydrogen atom in place of the cyano group. Thus, the zwitterionization of **42** may be inefficient because formation of a positive charge β to the cyano substituent in **43** would be disfavored.



42 43

Alternatively, it could be argued that zwitterions **43** are generated from **42** in reversible fashion, and the failure to observe cyano group migration is a result of a low "migration tendency" relative to the carbomethoxy group. Quantitative data concerning 1,2-rearrangements of the cyano group to an electron-deficient center do not appear to be available; however, Ingold and coworkers have reported the kinetics of 1,2-migration of the cyano group in 2-substituted 2,2-dimethylethyl radicals.[14] The cyano group was found to have an "unexpectedly low mobility" (k_r at 25 °C = 0.9 s^{-1}) relative to the pivaloyl group (1.7×10^5 s^{-1}). On the basis of the Ingold study and to the extent that zwitterion **43** had biradical character,[1] we might expect that the cyano group in **43** would have poorer mobility than a carbonyl-containing substituent such as the carbomethoxy group.

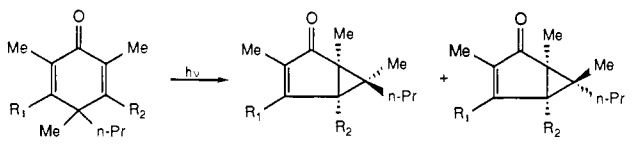
We sought a test of zwitterion formation through a derivative in which the group R would be expected to have unusually high mobility. In this way, photorearrangement of **42** to zwitterion **43** would be implicated by the isolation of a phenolic photoproduct. The derivative selected for study was 4-benzyl-4-cyano-2,5-cyclohexadien-1-one (**13b**).



As anticipated, a carefully monitored irradiation of **13b** (2 h) provided a 9:1 mixture of diastereoisomers, from which bicyclo[3.1.0]hexenone **45** was isolated in 74% yield. In contrast to **40a** and **40b**, however, continued irradiation of **45** over a total of 18 h photolysis time provided an 81% isolated yield of crystalline phenol **46**. Clearly, only the benzyl group has undergone 1,2-migration, presumably via the intermediacy of zwitterion **43** (R = CH_2Ph).

That a benzyl group has higher mobility than a carbomethoxy group in zwitterions **16** was demonstrated with **9b**. Photolysis of **9b** produced phenol **44** in 67% isolated yield. The formation of **44** might have been rationalized by a change in mechanism to that of a photochemical dienone–phenol type rearrangement, in which the carbomethoxy group undergoes exclusive migration. Such photorearrangements have been discovered by Zimmerman and Lynch in their study of 4,4-dinaphthyl-2,5-cyclohexadien-1-ones.[15] However, in view of the close structural similarity of **9b** and **13b**, we prefer to view the photorearrangement of **9b** to **44** as that involving bicyclo[3.1.0]hexenone **15** (R = CH_2Ph) and the type **16** zwitterion.

Photoisomerization of Bicyclo[3.1.0]hexenones. In 1969, Rodgers and Hart[16] reported that the stereoselectivity of the photorearrangement of 2,5-cyclohexadienones to bicyclo[3.1.0]-hexenones was sensitive to steric factors. With the series **47a–c**,

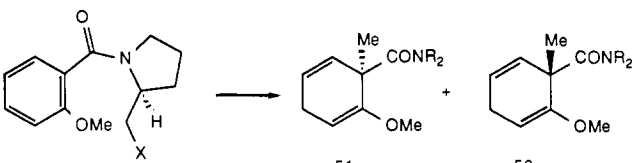


47a, $R_1 = R_2 = H$
b, R_1 = Me; $R_2 = H$
c, $R_1 = R_2$ = Me

48 49

they showed that formation of the type **48** diastereoisomer increased at the expense of **49** as the R_1 and R_2 substituents increased in size. Photointerconversion of **48** and **49** was not reported in the Rodgers and Hart paper. Both the Zimmerman and Schuster research groups have demonstrated that bicyclohexenone epimers do not interconvert under a variety of photochemical conditions.[17] Thus, photoisomerizations of **19** to **20** and **40** to **41** appear to be without precedent, although, the photosensitized epimerization of the structurally related bicyclo[3.1.0]hex-2-ene-6-*endo*-carboxylic acid and its methyl ester has been demonstrated to occur by cleavage of an external cyclopropyl bond.[18]

We have studied the mechanism of bicyclo[3.1.0]hexenone photoisomerization by irradiation of enantiomerically pure 3-methoxy-4-methyl-4-(methoxycarbonyl)-2,5-cyclohexadienone (**53**).[19] This material was prepared from *o*-methoxybenzamide **50b** by utilization of our recently reported method for performing



50a, X = OH
b, X = OCH_2OMe

51 52

an enantioselective Birch reductive alkylation.[20] The ratio of diastereoisomers **51** and **52** produced by reductive alkylation of **50b** was determined to be 260:1 by quantitative gas chromatographic and GC/MS analyses. The enantiomeric purities of **53a** ($[\alpha]_D^{24}$ −71.4°, *c* 1.71 in MeOH) and derived bicyclohexenones **54** and **55** were determined by ^1H NMR studies with the chiral

(14) Lindsay, D. A.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 7087.

(15) Zimmerman, H. E.; Lynch, D. C. *J. Am. Chem. Soc.* **1985**, *107*, 7745. For a related photorearrangement, see: ref 12.

(16) Rodgers, T. R.; Hart, H. *Tetrahedron Lett.* **1969**, 4845 and references cited therein for similar observations.

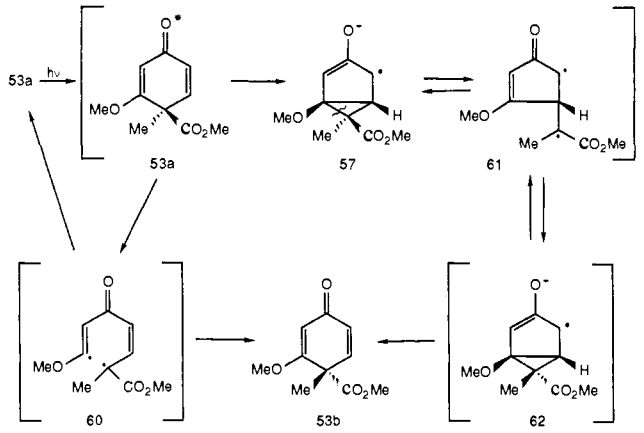
(17) (a) Zimmerman, H. E.; Grunewald, J. O. *J. Am. Chem. Soc.* **1967**, *89*, 5163. (b) Curran, W. V.; Schuster, D. I. *J. Chem. Soc., Chem. Commun.* **1968**, 699. (c) Schuster, D. I.; Curran, W. V. *J. Org. Chem.* **1970**, *35*, 4192. (d) Schuster, D. I.; Prabhu, K. V.; Adcock, S.; van derVeen, J. J.; Fujiwara, H. *J. Am. Chem. Soc.* **1971**, *93*, 1557.

(18) (a) Garin, D. L.; Cooke, D. J. *J. Chem. Soc., Chem. Commun.* **1972**, 33. (b) For the photochemical interconversion of cis and trans isomers of 5,6-dibiphenylylbicyclo[3.1.0]hexan-2-one, see: Zimmerman, H. E.; Jian-hua, X.; King, R. K.; Caufield, C. E. *J. Am. Chem. Soc.* **1985**, *107*, 7724; related earlier work is noted in ref 3 of this paper.

(19) An analogous mechanistic probe was used in the study of bicyclo-[3.1.0]hex-2-ene photochemistry, see: ref 15.

(20) (a) Schultz, A. G.; Sundararaman, P. *Tetrahedron Lett.* **1984**, *25*, 4591. (b) Schultz, A. G.; Sundararaman, P.; Macielag, M.; Lavieri, F. P.; Welch, M. *Tetrahedron Lett.* **1985**, 4575. (c) McCloskey, P. J.; Schultz, A. G. *Heterocycles* **1987**, *25*, 437.

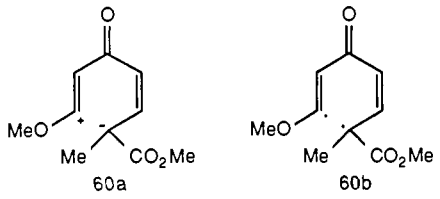
Scheme II



shift reagent tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III), i.e., Eu(hfc)$_3$.[3c]

After 20% photoconversion of enantiomerically pure **53a**, recovered 2,5-cyclohexadienone was found to be a 5:1 mixture of enantiomers **53a** and **53b**, respectively (Scheme I). Photoproducts **54** and **55** were each obtained as a 5:1 mixture of enantiomers, as evidenced by the chiral ^{1}H NMR shift reagent study. Furthermore, **55** exhibited a rotation of $[\alpha]_D^{25}$ + 205°. That recovered 2,5-cyclohexadienone and bicyclohexenones were all obtained as 5:1 mixtures of enantiomers is considered to be a fortuituous occurrence resulting from the arbitrarily selected period of photolysis. Complete photorearrangement of **53a** produced **54** ($[\alpha]_D^{23}$ −130°; 3:1 mixture of enantiomers) and nearly racemic **55** ($[\alpha]_D^{31}$ +14.0°). Finally, irradiation of **54** (the 3:1 mixture of enantiomers, isolated by chromatography on silica gel) provided a 1:3 mixture of enantiomers **55** and **56** ($[\alpha]_D^{23}$ −106°), respectively, after 50% photoconversion of **54**. Significantly, recovered **54** had not lost optical activity.

These data reveal several important details about the mechanism of photorearrangement of 2,5-cyclohexadienones to bicyclohexenones. First, it is clear that there is a pathway for return of the excited state of **53a** to **53a** and the enantiomer **53b**. This pathway may involve cleavage of one or both of the ring bonds to C(4) in **53a** to give, for example, **60** (Scheme II). Intermediate **60** could be zwitterionic **60a** or biradicaloid **60b**. It is noteworthy



that zwitterion **60a** should be stabilized by both the methoxy and carbomethoxy groups. Reformation of the 2,5-cyclohexadienone ring from **60** would be expected to give **53a** and the enantiomer **53b**.

Alternatively, it is possible that racemization of **53a** occurs via cleavage of an external cyclopropane bond in an intermediate **57** or **58**. As shown for **57** in Scheme II, the indicated bond cleavage would generate **61** as either a zwitterion or a biradical-type of intermediate. Reformation of the cyclopropane ring could give either **57** or the diastereoisomer **62**, and regeneration of a 2,5-cyclohexadienone from **62** would provide **53b**.

Schuster and Liu[21] have shown by an analysis of kinetic data that a photochemically generated zwitterion can return to the starting 2,5-cyclohexadien-1-one. The availability of a variety of enantiomerically pure 2,5-cyclohexadien-1-ones by modification of the enantioselective Birch reductive alkylation[20] provides a unique opportunity to study substituent effects on the photoracemization of 2,5-cyclohexadien-1-ones. Preliminary data indicate that substitution of the strongly electron-withdrawing carbomethoxy group for mildly electron-withdrawing or electron-donating groups will eliminate photoracemization, but these results will be described elsewhere.

The second observation concerning the chemistry outlined in Scheme I is that both diastereomeric zwitterions **57** and **58** are produced by photorearrangement of **53a**. We presume that **57** and **58** rearrange to **54** and **55**, respectively, by the "slither" mechanism.[1] In subsequent studies, we hope to devise tactics that will provide some measure of control of stereoselectivity of zwitterion formation, possibly by steric effects already uncovered by Rodgers and Hart.[16]

The third observation is that the photochemical interconversion of bicyclo[3.1.0]hexenones, specifically **54** and **56**, must occur by external cyclopropane bond "b" cleavage, rather than internal cyclopropane bond "a" cleavage. In separate experiments with racemic materials, it was demonstrated that irradiation of a mixture of **19a** and **20a** resulted in photoisomerization to give predominately the *endo*-methoxycarbonyl diastereoisomer **19a** (95%), unreacted **20a**, and a trace of phenolic products. On the other hand, irradiation of pure **19a** did not result in detectable photoisomerization to **20a**.

The fourth observation is that the pathway for conversion of **54** into **56** does not include a detectable shunt to starting 2,5-cyclohexadienone.[22] This may mean that **54** and **55** never revert to zwitterion **57** and **58**, despite the fact that bicyclohexenone interconversion must occur by cleavage of a "b" bond. However, the uncertainties associated with the presence of two type-"b" bonds in **54** and two possible pathways for racemization of **53a** (Scheme II) preclude a more definitive statement at this time.

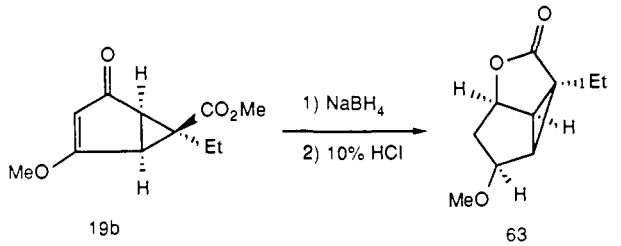
Finally, as indicated earlier, photoexcited **53a** does not rearrange to bicyclohexenone **59** (Scheme I). The absence of **59** and the stability of **54**–**56** toward photoconversion to phenols greatly simplified the product study outlined in Scheme I. These technical considerations suggest that further work with benzoic acid derived 2,5-cyclohexadienones could reveal additional mechanistic subtleties that may be difficult to unravel with more conventional substrates.

Conclusion

This study which is focused on the development of the 2,5-cyclohexadien-1-one photorearrangement for use in organic synthesis has uncovered several important mechanistic details. The synthetic and mechanistic developments include the following: (1) A wide range of 4-alkyl-4-(methoxycarbonyl)-2,5-cyclohexadien-1-ones and 4-alkyl-4-cyano-2,5-cyclohexadien-1-ones are now available from benzoic acid and benzonitrile derivatives by the Birch reductive alkylation strategy. (2) These 2,5-cyclohexadienones may be prepared in enantiomerically pure form by use of the chiral auxiliary technique. (3) Photolysis of 4-alkyl-4-(methoxycarbonyl)-2,5-cyclohexadienones (except for the 4-benzyl derivative **9b**) results in formation of phenolic products via exclusive 1,2-migration of the methoxycarbonyl group in an intermediate zwitterion. Photolysis of 4-alkyl-4-cyano-2,5-cyclohexadienones provides bicyclo[3.1.0]hexenones in excellent yield. (4) Photorearrangements of 4-alkyl-4-(methoxycarbonyl)-3-methoxy-2,5-cyclohexadien-1-ones and the corresponding nitriles are regiospecific to give diastereoisomeric mixtures of bicyclo[3.1.0]hexenones. Continued irradiation produces a ≥9:1 mixture of bicyclohexenone diastereoisomers favoring the endo methoxycarbonyl and endo cyano configurations. The photochemical interconversion of bicyclo[3.1.0]hexenones has been found to occur by external cyclopropane bond cleavage (bond "b" in structure **54**). (5) Stereochemical studies with an enantiomerically pure 2,5-cyclohexadien-1-one have conclusively demonstrated that there is a pathway for return of the excited state and/or primary photoproduct to the starting 2,5-cyclohexadienone. (6) The excellent chemical yields obtained for photogeneration of bicyclohexenones of type **19** suggest that these compounds will

(21) Schuster, D. I.; Liu, K.-C. *Tetrahedron* **1981**, *37*, 3329.

(22) The consequences of various cyclopropane bond cleavages in bicyclo[3.1.0]hexenone photochemistry are discussed in ref 1a, p 192.



19b 63

be useful synthetic intermediates. In this regard, it is noteworthy that **19b** is converted to lactone **63** in ~quantitative yield on treatment with $NaBH_4$ in ethanol, followed by acidification of the reaction mixture. Derivatives of **63** should be useful in prostanoid[23] and other cyclopentanoid natural product syntheses.

Experimental Section

^1H NMR spectra were recorded on Varian T-60 (60-MHz), varian XL-200 (200-MHz); and Hitachi-Perkin-Elmer R-600 (60-MHz) NMR spectrometers (tetramethylsilane internal standard). ^{13}C NMR spectra were obtained on the Varian XL-200 and IBM WP-100SY spectrometers. Infrared spectra were obtained on either a Perkin-Elmer 137b or 298 spectrometer, and ultraviolet spectra were recorded on a Perkin-Elmer 552 spectrometer. Mass spectra were obtained on Hewlett-Packard 5987A GC–MS system (methane, chemical ionization gas). Optical rotations were obtained on Perkin-Elmer 241 polarimeter. Elemental analyses were determined by Spang Microanalytical Laboratories, Eagle Harbor, MI. The light source for all photochemistry was a Hanovia 450-W medium pressure mercury arc lamp. The lamp was placed in a water-cooled Pyrex immersion well. Reaction vessels containing solutions to be irradiated were attached to the immersion well and were saturated with nitrogen prior to irradiation. The Hanovia lamp in the Pyrex immersion well fitted with Corning color filters 0-25 and 7-54 was employed as the 366-nm light source. Purifications by flash chromatography used either Baker silica gel with a 40-μm average particle diameter or Baker neutral alumina with a 50–200 μm average particle diameter.

Birch Reduction–Alkylation of Benzoic Acid and Cyanobenzene Derivatives. 6-(2-Acetoxyethyl)-6-carbomethoxy-1-methoxy-1,4-cyclohexadiene (6d) was prepared in 85% yield by the method reported for **6a**, **6b**, **6c** and **6e**.[4a,c] Flash chromatography (silica gel, hexane–ethyl acetate, 3:1) gave **6d** as a colorless oil: ^1H NMR ($CDCl_3$) δ 2.06 (m, 4 H), 2.40 (m, 1 H), 2.84 (m, 2 H), 3.55 (s, 3 H), 3.68 (s, 3 H), 3.96 (m, 2 H), 4.88 (t, 1 H, J = 2 Hz), 5.44 (d, 1 H, J = 10 Hz), 5.92 (m, 1 H); IR (film) 2940, 1730, 1680 cm^{-1}; CIMS, m/z 255 (M^+ + 1). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.13. Found: C, 61.23; H, 7.08%.

3-Carbomethoxy-3-(3-chloropropyl)-1,4-cyclohexadiene was prepared in 64% yield from the lithium enolate as described for **6d**. Flash chromatography (silica gel, hexane–ethyl acetate, 13:1) provided an oil: ^1H NMR ($CDCl_3$) δ 1.6–1.86 (m, 4 H), 2.64 (m, 2 H), 3.51 (t, 2 H, J = 6 Hz), 3.69 (s, 3 H), 5.71 (m, 2 H), 5.93 (m, 2 H); IR (film) 1728, 1430, 1232 cm^{-1}; CIMS, m/z (rel intensity) 215 (M^+ + 1, 100), 179 (68), 155 (46), 137 (30), 119 (35). Anal. Calcd for $C_{11}H_{15}O_2Cl$: C, 61.54; H, 7.04. Found: C, 61.43; H, 7.09.

3-Benzyl-3-carbomethoxy-1,4-cyclohexadiene was prepared in 78% yield as described for **6d**. Flash chromatography (silica gel, hexane–ethylacetate, 8:1) provided a colorless oil: ^1H NMR ($CDCl_3$) δ 2.39 (d, 1 H, J = 22 Hz), 2.55 (d, 1 H, J = 22 Hz), 3.01 (s, 2 H), 3.68 (s, 3 H), 6.84 (s, 4 H), 7.13 (m, 2 H), 7.21–7.40 (m, 3 H); IR (film) 3080, 3060, 3025, 2950, 2920, 2860, 2815, 1722, 1490, 1450, 1430 cm^{-1}; CIMS, m/z (rel intensity) 229 (M^+ + 1, 20), 197 (44), 169 (100), 91 (75).

3-Carbomethoxy-1,4-dimethyl-3-ethyl-1,4-cyclohexadiene was prepared in quantitative yield as described for **6d** (oil): ^1H NMR ($CDCl_3$) δ 0.71 (t, 3 H, J = 7.4 Hz), 1.60 (q, 2 H, J = 7.4 Hz), 1.72 (s, 6 H), 2.40 (s, 2 H), 3.63 (s, 3 H), 5.39 (s, 2 H); IR (film) 2970, 1725, 1430, 1225, 1185 cm^{-1}; CIMS, m/z (rel intensity) 195 (M^+ + 1, 100.00), 135 (35.17).

3-Carbomethoxy-3-(3-chloropropyl)-1,4-dimethoxy-1,4-cyclohexadiene was prepared in 77% yield from the lithium enolate as described for **6d**. Flash chromatography (silica gel, hexane–ethyl acetate, 5:1) provided an oil: ^1H NMR ($CDCl_3$) δ 1.6–1.9 (m, 3 H), 2.1 (m, 1 H), 2.88 (m, 2 H), 3.52 (t, two overlapping s at 3.54 and 3.56, 8 H, J = 6 Hz), 3.68 (s, 3 H), 4.34 (s, 1 H), 4.80 (t, 1 H, J = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 27.9, 28.4, 32.8, 45.3, 52.1, 52.3, 54.5, 54.7, 92.9, 94.9, 152.6, 156.1, 174.6; IR (film) 1720, 1650, 1430, 1385 cm^{-1}; CIMS, m/z (rel intensity) 275 (M^+ + 1, 100), 243 (67), 239 (67), 215 (22), 197 (23), 179 (14).

(23) For the use of compounds closely related to **63** in prostaglandin-directed synthetic studies: (a) Corey, E. J. *Ann. N.Y. Acad. Sci.* **1970**, *180*, 24. (b) Corey, E. J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1972**, *94*, 4014.

Allylic Oxidations of 1,4-Cyclohexadiene Derivatives. Method A. Oxidation with Sodium Chromate. 4-(2-Acetoxyethyl)-4-carbomethoxy-3-methoxy-2,5-cyclohexadien-1-one (8d).[19] To a solution of **6d** (0.172 g, 0.676 mmol) in acetic acid (4.0 mL) and acetic anhydride (0.5 mL) at room temperature was added sodium chromate (0.219 g, 1.35 mmol). The reaction mixture was stirred at room temperature for 48 h and then neutralized with a saturated solution of sodium bicarbonate. The mixture was dissolved in ethyl acetate (50 mL) and water (50 mL). The organic phase was washed with brine (1 × 50 mL), dried over sodium sulfate, and concentrated to give crude **8d** as a pale yellow oil. Flash chromatography (silica gel, hexane–ethyl acetate, 2:1) gave **8d** (0.060 g, 33%) as a colorless oil: ^1H NMR ($CDCl_3$) δ 1.98 (s, 3 H), 2.42 (m, 1 H), 2.60 (m, 1 H), 3.73 (s, 3 H), 3.80 (s, 3 H), 3.90 (m, 2 H), 5.76 (s, 1 H), 6.36 (d, 1 H, J = 8 Hz), 6.56 (d, 1 H, J = 8 Hz); IR (film) 2950, 1740, 1650, 1600, 1230 (br) cm^{-1}; CIMS, m/z 269 (M^+ + 1).

Method B. Oxidation with Chromium Trioxide. 4-Carbomethoxy-3-methoxy-4-(2-propenyl)-2,5-cyclohexadien-1-one (8c). A solution of chromium trioxide (1.48 g, 14.8 mmol), acetic anhydride (2.6 mL), and acetic acid (5.5 mL) was cooled to 7 °C and diluted with benzene (5.5 mL). To the stirred solution was added **6c** (0.617 g, 2.96 mmol) in benzene (1 mL). After 1 h at 7 °C, the reaction mixture was diluted with ethyl acetate (250 mL) and carefully quenched with a saturated solution of sodium bicarbonate (250 mL). The organic phase was washed with water (1 × 250 mL) and brine (1 × 250 mL), dried over sodium sulfate, and concentrated. Flash chromatography (silica gel, hexane–ethyl acetate, 3:1) gave **8c** (0.29 g, 45%) as a colorless solid (mp 45.0–46.0 °C): ^1H NMR ($CDCl_3$) δ 2.78 (dd, 1 H, J = 8 Hz, J = 13 Hz), 2.95 (dd, 1 H, J = 8 Hz, J = 13 Hz), 3.71 (s, 3 H), 3.75 (s, 3 H), 5.10 (m, 2 H), 5.42 (m, 1 H), 5.70 (s, 1 H), 6.33 (d, 1 H, J = 8 Hz), 6.53 (d, 1 H, J = 8 Hz); IR (film) 2940, 1730, 1650, 1590, 1360 cm^{-1}; CIMS, m/z 223 (M^+ + 1). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.92; H, 6.28.

Method C. Oxidation with Pyridinium Dichromate. 4-Carbomethoxy-4-ethyl-3-methoxy-2,5-cyclohexadien-1-one (8b). A solution of **6b** (2.07 g, 10.6 mmol) and pyridinium dichromate (31.8 mmol, 11.95 g) in ethanol free chloroform (100 mL) was refluxed for 24 h with continuous removal of water by a Dean-Stark apparatus. The reaction mixture was filtered through a pad of Florisil (hexane–ethyl acetate, 1:1) and concentrated to a volume of 100 mL. The concentrated solution was washed with 10% HCl (1 × 100 mL), water (1 × 100 mL), and brine (1 × 100 mL), then dried over magnesium sulfate, and concentrated to give **8b** (2.13 g) as a pale yellow oil. Flash chromatography on silica gel (hexane–ethyl acetate, 1:1) provided **8b** (1.21 g, 54%) as a pale yellow solid (mp 84–85 °C); ^1H NMR ($CDCl_3$) δ 0.65 (t, 3 H, J = 7.6 Hz), 1.99 (6 line m, 1 H), 2.27 (6 line m, 1 H), 3.67 (s, 3 H), 3.73 (s, 3 H), 5.70 (s, 1 H), 6.30 (dd, 1 H, J = 9.9 Hz, J = 1.1 Hz), 6.42 (d, 1 H, J = 9.9 Hz); IR (film) 2970, 1735, 1655, 1625, 1595, 1220 cm^{-1}; EIMS, m/z (rel intensity) 210 (M^+, 35.96), 151 (84.60), 121 (21.33), 59 (100.00). Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 63.13; H, 6.98.

4-Carbomethoxy-3-methoxy-4-methyl-2,5-cyclohexadien-1-one (8a) was prepared by method C from **6a** in 40% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 1:1) provided **8a** as a colorless solid, mp 90.5–92.5 °C: ^1H NMR ($CDCl_3$) δ 1.59 (s, 3 H), 3.72 (s, 3 H), 3.79 (s, 3 H), 5.68 (s, 1 H), 6.30 (d, 1 H, J = 9 Hz), 6.59 (d, 1 H, J = 9 Hz); IR (KBr) 2940, 1740, 1650, 1600, 1220 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 274 nm (8840), 228 nm (21 000); CIMS, m/z 197 (M^+ + 1).

4-Carbomethoxy-4-(3-chloropropyl)-3-methoxy-2,5-cyclohexadien-1-one (8e) was prepared by method B from **6e** in 60% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 3:2) provided **8e** as a pale yellow solid, mp 64–66 °C: ^1H NMR ($CDCl_3$) δ 1.4–1.64 (m, 2 H), 2.18 (m, 1 H), 2.41 (m, 1 H), 3.52 (t, 2 H, J = 7 Hz), 3.73 (s, 3 H), 3.79 (s, 3 H), 5.76 (s, 1 H), 6.37 (d, 1 H, J = 9 Hz), 6.52 (d, 1 H, J = 9 Hz); IR (KBr) 1730, 1650, 1590 cm^{-1}; CIMS, m/z (rel intensity) 259 (M^+ + 1, 100), 223 (30), 199 (7); UV (MeOH) λ_{max} (ϵ) 275.3 nm (10 120), 236.4 nm (13 720). Anal. Calcd for $C_{12}H_{15}O_4Cl$: C, 55.71; H, 5.84. Found: C, 55.89; H, 6.00.

4-Carbomethoxy-4-(3-chloropropyl)-2,5-cyclohexadien-1-one (9a) was prepared by method B from 3-carbomethoxy-3-(3-chloropropyl)-1,4-cyclohexadiene in 75% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 2.4:1) provided **9a** as a pale yellow solid; mp 61–63 °C: ^1H NMR ($CDCl_3$) δ 1.70 (m, 2 H), 2.17 (m, 2 H), 3.54 (t, 2 H, J = 6 Hz), 3.78 (s, 3 H), 6.44 (d, 2 H, J = 10 Hz), 7.06 (d, 2 H, J = 10 Hz); IR (KBr) 1730, 1665, 1628, 1445, 1400 cm^{-1}; CIMS, m/z (rel intensity) 229 (M^+ + 1, 100), 197 (10), 193 (22); UV (MeOH) λ_{max} (ϵ) 239.3 nm (12 728). Anal. Calcd for $C_{11}H_{13}O_3Cl$: C, 57.78; H, 5.73. Found: C, 57.83; H, 5.68.

4-Benzyl-4-carbomethoxy-2,5-cyclohexadien-1-one (9b) was prepared by method B from 3-benzyl-3-carbomethoxy-1,4-cyclohexadiene in 59% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 3:1)

provided **9b** as an oil: ^{1}H NMR ($CDCl_3$) δ 3.22 (s, 2 H), 3.71 (s, 3 H), 6.30 (d, 2 H, J = 10 Hz), 7.09 (d, J = 10 Hz, overlapping at 7.09–7.28, 7 H); IR (film) 3080, 3060, 3025, 1728, 1662, 1627, 1602, 1492, 1430, 1400 cm^{-1}; CIMS, m/z (rel intensity) 243 (M^+ + 1, 2), 91 (100). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.27; H, 5.98.

4-Carbomethoxy-4-ethyl-2,6-dimethyl-2,5-cyclohexadien-1-one (10) was prepared by method C from 3-carbomethoxy-1,4-dimethyl-3-ethyl-1,4-cyclohexadiene in 80% yield (oil): ^{1}H NMR ($CDCl_3$) δ 0.78 (t, 3 H, J = 7.4 Hz), 1.91 (q with overlapping s at 1.90, 8 H, J = 7.4 Hz), 3.70 (s, 3 H), 6.74 (s, 2 H); IR (film) 2970, 1730, 1670, 1640, 1430, 1220 cm^{-1}; CIMS, m/z (rel intensity) 209 (M^+ + 1, 100.00), 181 (10.67), 177 (11.31). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.23; H, 7.78.

4-Carbomethoxy-4-(3-chloropropyl)-2,5-dimethoxy-2,5-cyclohexadien-1-one (11) was prepared by method B from 3-carbomethoxy-3-(3-chloropropyl)-1,4-dimethoxy-1,4-cyclohexadiene in 49% yield. Flash chromatography (silica gel, hexane–ethyl acetate 1:1) provided **11** (mp 83–85 °C): ^{1}H NMR ($CDCl_3$) δ 1.47 (m, 2 H), 2.17 (m, 1 H), 2.38 (m, 1 H), 3.52 (t, 2 H, J = 6 Hz), 3.71 (s, 3 H), 3.72 (s, 3 H), 3.79 (s, 3 H), 5.33 (s, 1 H), 5.80 (s, 1 H); IR (film) 1725, 1635, 1600, 1430 cm^{-1}; CIMS, m/z (rel intensity) 289 (M^+ + 1, 100), 257 (12), 253 (24), 229 (4); UV (MeOH) λ_{max} (ϵ) 284.0 nm (3678), 253.3 nm (13 729). Anal. Calcd for $C_{13}H_{17}O_5Cl$: C, 54.08; H, 5.94. Found: C, 53.88; H, 5.78.

4-Carbomethoxy-3,5-dimethoxy-4-methyl-2,5-cyclohexadien-1-one (12) was prepared by method B from 6-carbomethoxy-1,5-dimethoxy-6-methyl-1,4-cyclohexadiene[4a] in 20% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 2:1) provided **12**, mp 118–119 °C: ^{1}H NMR ($CDCl_3$) δ 1.66 (s, 3 H), 3.73 (s, 3 H), 3.77 (s, 6 H), 5.53 (s, 2 H); IR (KBr) 3000, 2940, 1750, 1650, 1630, 1600, 1440, 1360, 1210, 1130 cm^{-1}; CIMS, m/z (rel intensity) 227 (M^+ + 1); UV (MeOH) λ_{max} (ϵ) 280 nm (7400), 241 nm (19 940), 206 nm (6700). Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.29; H, 6.19%.

4-(3-Chloropropyl)-4-cyano-2,5-cyclohexadien-1-one (13a) was prepared by method C from 3-(3-chloropropyl)-3-cyano-1,4-cyclohexadiene[8a] in 67% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 3:1) provided **13a** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.93 (m, 2 H), 2.22 (m, 2 H), 3.61 (t, 2 H, J = 6 Hz), 6.53 (d, 2 H, J = 10 Hz), 6.88 d, 2 H, J = 10 Hz); IR (film) 2238, 1670, 1630, 1445 cm^{-1}; CIMS, m/z (rel intensity) 196 (M^+ + 1, 100), 169 (48), 160 (42), 120 (20); UV (MeOH) λ_{max} (ϵ) 226.4 nm (10 837). Anal. Calcd for $C_{10}H_{10}NOCl$: C, 61.39; H, 5.15. Found: C, 61.06; H, 5.30.

4-Benzyl-4-cyano-2,5-cyclohexadien-1-one (13b) was prepared by method B from 3-benzyl-3-cyano-1,4-cyclohexadiene[8a] in 63% yield. Flash chromatography (silica gel, hexane–ethyl acetate, 3:1) provided **13b** as a colorless solid. An analytical sample was prepared by recrystallization from dichloromethane–hexane, mp 111–113 °C: ^{1}H NMR ($CDCl_3$) δ 3.16 (s, 2 H), 6.40 (d, 2 H, J = 10 Hz), 6.84 (d, 2 H, J = 10 Hz), 7.22–7.38 (m, 5 H); IR (film) 2228, 1662, 1627, 1603, 1490, 1445, 1390 cm^{-1}; CIMS, m/z (rel intensity) 210 (M^+ + 1, 100), 183 (8), 120 (90). Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30. Found: C, 80.47; H, 5.44.

4-(3-Chloropropyl)-4-cyano-3-methoxy-2,5-cyclohexadien-1-one (14) was prepared by method B from 6-(3-chloropropyl)-6-cyano-1-methoxy-1,4-cyclohexadiene[8a] in 40% yield. Flash chromatography (silica gel, methylene chloride–ethyl acetate, 9:1) provided **14** as a pale yellow solid, mp 63–65 °C; ^{1}H NMR ($CDCl_3$) δ 1.74 (m, 2 H), 2.34 (m, 2 H), 3.55 (t, 2 H, J = 6 Hz), 3.89 (s, 3 H), 5.75 (d, 1 H, J = 1 Hz), 6.43 (dd, 1 H, J = 10 Hz, J = 1 Hz), 6.64 (d, 1 H, J = 10 Hz); IR (KBr) 2250, 1670, 1640, 1610, 1455 cm^{-1}; CIMS, m/z (rel intensity) 226 (M^+ + 1, 100), 199 (30), 190 (16), 150 (31); UV (MeOH) λ_{max} (ϵ) 271.1 nm (7387), 228.2 nm (9632). Anal. Calcd for $C_{11}H_{12}NO_2Cl$: C, 58.54; H, 5.36. Found: C, 58.43; H, 5.31.

Photolysis of 2,5-Cyclohexadienones. 6-Carbomethoxy-4-methoxy-6-methylbicyclo[3.1.0^{1,5}]hex-3-en-2-ones (19a and 20a). A solution of **8a** (0.120 g, 0.612 mmol) in benzene (12 mL) was purged with N_2 for 10 min before irradiation at 366 nm for 8 h. After concentration of the reaction mixture, flash chromatography (alumina, hexane–ethyl acetate, 1:1) gave diastereomers **20a** (44 mg, 37%) and **19a** (50 mg, 42%). **20a** was distilled in a Kugelrohr apparatus (85 °C, 0.8 mmHg) to give **20a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 3 H), 2.60 (d, 1 H, J = 6 Hz), 2.84 (d, 1 H, J = 6 Hz), 3.73 (s, 3 H), 3.85 (s, 3 H), 5.02 (s, 1 H); IR (film) 2940, 1730, 1690, 1590 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 272 nm (8310), 215 nm (8870); CIMS, m/z 197 (M^+ + 1).

19a was distilled in a Kugelrohr apparatus (85 °C, 0.8 mmHg) to give **19a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 3 H), 2.26 (d, 1 H, J = 6 Hz), 2.44 (d, 1 H, J = 6 Hz), 3.68 (s, 3 H), 3.80 (s, 3 H), 4.80 (s, 1 H); IR (film) 2940, 1730, 1690, 1590 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 261 nm (6420); CIMS, m/z 197 (M^+ + 1).

6-Carbomethoxy-6-ethyl-4-methoxybicyclo[3.1.0^{1,5}]hex-3-en-2-ones (19b and 20b) were prepared by irradiation of **8b** in benzene solution at 366 nm for 3 h. Flash chromatography (silica gel, hexane–ethyl acetate, 1:1) provided **20b** (48%) as an oil: ^{1}H NMR ($CDCl_3$) δ 0.93 (t, 3 H, J = 7.2 Hz), 1.80 (8 line m, 2 H), 2.55 (dd, 1 H, J = 5.7 Hz, J = 1.2 Hz), 2.82 (dd, 1 H, J = 5.7 Hz, J = 0.9 Hz), 3.68 (s, 3 H), 3.80 (s, 3 H), 4.97 (s, 1 H); IR (film) 2945, 1725, 1687, 1660, 1580, 1225 cm^{-1}; EIMS, m/z (rel intensity) 210 (M^+, 12.14), 182 (38.08), 151 (53.47), 150 (54.51), 59 (100.00).

Another chromatographic fraction provided **19b** (24%), mp 72–74 °C: ^{1}H NMR ($CDCl_3$) δ 0.97 (t, 3 H, J = 7.9 Hz), 1.58 (8 line m, 2 H), 2.21 (d, 1 H, J = 5.0 Hz), 2.39 (d, 1 H, J = 5.0 Hz), 3.65 (s, 3 H), 3.76 (s, 3 H), 4.73 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.92, 28.70, 31.55, 35.17, 52.22, 56.62, 58.94, 98.64, 169.64, 186.34, 198.64; IR (film) 2980, 1725, 1685, 1580, 1360, 1237 cm^{-1}; EIMS, m/z (rel intensity) 210 (M^+, 17.38), 182 (76.06), 151 (64.76), 150 (88.12), 59 (100.00). Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 63.01; H, 6.69.

6-Carbomethoxy-4-methoxy-6-(2-propenyl)bicyclo[3.1.0^{1,5}]hex-3-en-2-ones (19c and 20c) were prepared by irradiation of **8c** in benzene solution at 366 nm for 4 h. Flash chromatography (silica gel, hexane–ethyl acetate, 2:1) provided **20c** (40%) as an oil: ^{1}H NMR ($CDCl_3$) δ 2.4–2.8 (m, 3 H), 2.89 (d, 1 H, J = 6 Hz), 3.70 (s, 3 H), 3.83 (s, 3 H), 5.06 (m, 3 H), 5.70 (m, 1 H); IR (film) 2950, 1720, 1680, 1580 cm^{-1}; CIMS, m/z 223 (M^+ + 1).

Also isolated was **19c** (41%) as an oil: ^{1}H NMR ($CDCl_3$) δ 2.3–2.5 (m, 4 H), 3.68 (s, 3 H), 3.81 (s, 3 H), 4.82 (s, 1 H), 5.14 (m, 2 H), 5.77 (m, 1 H); IR (film) 2950, 1730, 1680, 1580 cm^{-1}; CIMS, m/z 223 (M^+ + 1).

6-(2-Acetoxyethyl)-6-carbomethoxy-4-methoxybicyclo[3.1.0^{1,5}]hex-3-en-2-ones (19d and 20d) were prepared by irradiation of **8d** in benzene solution at 366 nm for 6 h. Flash chromatography (alumina, hexane–ethyl acetate, 2:1) provided **20d** (40%) as an oil: ^{1}H NMR ($CDCl_3$) δ 2.04 (s, 3 H), 2.1–2.3 (m, 2 H), 2.58 (d, 1 H, J = 6 Hz), 2.88 (d, 1 H, J = 6 Hz), 3.74 (s, 3 H), 3.86 (s, 3 H), 4.15 (m, 2 H), 5.04 (s, 1 H); IR (film) 2950, 1740, 1680, 1650, 1590 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 273 nm (5580), 212 nm (7430); CIMS, m/z 269 (M^+ + 1).

Also isolated was **19d** (27%) as an oil: ^{1}H NMR ($CDCl_3$) δ 1.9–2.1 (m with overlapping s at 2.04, 5 H), 2.32 (d, 1 H, J = 6 Hz), 2.51 (d, 1 H, J = 6 Hz), 3.68 (s, 3 H), 3.80 (s, 3 H), 4.16 (br t, 2 H, J = 6 Hz), 4.82 (s, 1 H); IR (film) 2950, 1730, 1690, 1650 cm^{-1}; CIMS, m/z 269 (M^+ + 1). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.29; H, 6.12.

6-Carbomethoxy-6-(3-chloropropyl)-4-methoxybicyclo[3.1.0^{1,5}]hex-3-en-2-ones (19e and 20e) were prepared by irradiation of **8e** in benzene solution at 366 nm for 3 h. Flash chromatography (silica gel, hexane–ethyl acetate, 1:1) provided **20e** (31%) as an oil: ^{1}H NMR ($CDCl_3$) δ 1.76 (m, 2 H), 1.99 (m, 2 H), 2.58 (d, 1 H, J = 6 Hz), 2.89 (d, 1 H, J = 6 Hz), 3.53 (m, 2 H), 3.71 (s, 3 H), 3.84 (s, 3 H), 5.03 (s, 1 H); IR (film) 1725, 1690, 1590, 1435 cm^{-1}; CIMS, m/z (rel intensity) 259 (M^+ + 1, 100), 227 (6), 223 (24); UV (MeOH) λ_{max} (ϵ) 273.8 nm (7259). Anal. Calcd for $C_{12}H_{15}O_4Cl$: C, 55.71; H, 5.84. Found: C, 55.35; H, 6.05.

Also isolated was **19e** (48%), mp 95–97 °C: ^{1}H NMR ($CDCl_3$) δ 1.68–1.98 (m, 4 H), 2.28 (d, 1 H, J = 6 Hz), 2.49 (d, 1 H, J = 6 Hz), 3.60 (t, 2 H, J = 6 Hz), 3.67 (s, 3 H), 3.79 (s, 3 H), 4.78 (s, 1 H); IR ($CHCl_3$) 1720, 1680, 1580, 1435 cm^{-1}; CIMS, m/z (rel intensity) 259 (M^+ + 1, 100), 227 (9), 223 (27); UV (MeOH) λ_{max} (ϵ) 264.1 nm (8420). Anal. Calcd for $C_{12}H_{15}O_4Cl$: C, 55.71; H, 5.84. Found: C, 55.77; H, 5.79.

Methyl 2-(3-Chloropropyl)-4-hydroxybenzoate (17) and Methyl 2-(3-Chloropropyl)-6-hydroxybenzoate (18). A solution of **9a** (24 mg, 0.10 mmol) in benzene (2.4 mL) was purged with nitrogen for 15 min before irradiation at 366 nm for 3 h. Concentration of the reaction mixture followed by flash chromatography (silica gel, hexane–ethyl acetate, 3:1) gave **17** (11 mg, 46% yield) and **18** (3 mg, 13%). **17** was recrystallized from ether–hexane, mp 96–98 °C; ^{1}H NMR ($CDCl_3$) δ 2.10 (m, 2 H), 3.13 (t, 2 H, J = 6 Hz), 3.61 (t, 2 H, J = 6 Hz), 3.89 (s, 3 H), 5.50 (br s, 1 H, D_2O exchangeable), 6.76 (dd, overlapping br s at 6.79, 2 H, J = 9 Hz, J = 3 Hz), 7.96 (d, 1 H, J = 9 Hz); IR (KBr) 3260, 1665, 1610, 1565, 1433 cm^{-1}; CIMS, m/z (rel intensity) 229 (M^+ + 1, 84), 197 (8), 193 (100). Anal. Calcd for $C_{11}H_{13}O_3Cl$: C, 57.78; H, 5.73. Found: C, 57.79; H, 5.64.

18 was isolated as an oil: ^{1}H NMR ($CDCl_3$) δ 2.05 (m, 2 H), 3.11 (t, 2 H, J = 6 Hz), 3.61 (t, 2 H, J = 6 Hz), 4.01 (s, 3 H), 6.80 (d, 1 H, J = 8 Hz), 6.92 (d, 1 H, J = 8 Hz), 7.37 (t, 1 H, J = 8 Hz), 11.22 (s, 1 H, D_2O exchangeable); IR (film) 3500–2500 (br), 1665, 1610, 1575, 1450 cm^{-1}; CIMS, m/z (rel intensity) 229 (M^+ + 1, 100), 197 (17), 193 (42). Anal. Calcd for $C_{11}H_{13}O_3Cl$: C, 57.78; H, 5.73. Found: C, 57.73; H, 5.84.

Methyl 2-(3-Chloropropyl)-6-hydroxy-4-methoxybenzoate (35). A solution of **11** (40 mg, 0.16 mmol) in benzene (4 mL) was purged with nitrogen for 15 min before irradiation through Pyrex glassware for 12

h. Concentration of the reaction mixture followed by flash chromatography (silica gel, hexane–ethyl acetate, 3.5:1) afforded **35** (32 mg, 80%), mp 56–58 °C: ^{1}H NMR ($CDCl_3$) δ 2.01 (m, 2 H), 3.03 (t, 2 H, J = 6 Hz), 3.57 (t, 2 H, J = 6 Hz), 3.80 (s, 3 H), 3.93 ns, 3 H), 6.33 (d, 1 H, J = 3 Hz), 6.37 (d, 1 H, J = 3 Hz), 11.77 (s, 1 H, D_2O exchangeable); IR (KBr) 3500–2500 (br), 1650, 1610, 1575, 1435 cm^{-1}; CIMS, m/z (rel intensity) 259 (M^+ + 1, 100), 227 (14), 223 (44). Anal. Calcd for $C_{12}H_{15}O_4Cl$: C, 55.71; H, 5.84. Found: C, 55.81; H, 5.79.

Phenol **35** also was obtained in 69% yield by irradiation of **11** at 366 nm for 54 h.

Methyl 2-Ethyl-4-hydroxy-3,5-dimethylbenzoate (38) was prepared by irradiation of **10** in acetone for 6 h as described for **19a** and **20a**. Flash chromatography (silica gel, hexane–ethyl acetate, 4:1) provided **38** (34%), mp 98–99 °C: ^{1}H NMR ($CDCl_3$) δ 1.15 (t, 3 H, J = 7.4 Hz), 2.21 (s, 6 H), 2.92 (q, 2 H, J = 7.4 Hz), 3.82 (s, 3 H), 4.97 (s, 1 H, D_2O exchangeable), 7.53 (s, 1 H); IR ($CDCl_3$) 3600, 1720, 1435, 1210 cm^{-1}; CIMS, m/z (rel intensity) 209 (M^+ + 1, 100.00). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.02; H, 7.74.

6-(3-Chloropropyl)-6-cyanobicyclo[3.1.0^{1,5}]hex-3-en-2-ones (40a and 41a) were prepared by irradiation of **13a** in benzene solution at 366 nm for 3 h. Flash chromatography (silica gel, hexane–ethyl acetate, 2.5:1) provided **40a** (60%), mp 51–52 °C: ^{1}H NMR ($CDCl_3$) δ 1.92 (m, 2 H), 2.08 (m, 2 H), 2.36 (d, 1 H, J = 5 Hz), 2.82 (dd, 1 H, J = 5 Hz, J = 3 Hz), 3.62 (t, 2 H, J = 6 Hz), 6.08 (d, 1 H, J = 6 Hz), 7.64 (dd, 1 H, J = 6 Hz, J = 3 Hz); IR ($CHCl_3$) 2220, 1700, 1570, 1438 cm^{-1}; CIMS, m/z (rel intensity) 196 (M^+ + 1, 100), 168 (29), 160 (19); UV (MeOH) λ_{max} (ϵ) 249.9 nm (4144). Anal. Calcd for $C_{10}H_{10}NOCl$: C, 61.39; H, 5.15. Found: C, 61.26; H, 5.22.

Also isolated was **41a** (7% yield) as an oil: ^{1}H NMR ($CDCl_3$) δ 1.79–2.14 (m, **4** H), 2.66 (d, 1 H, J = 5 Hz), 3.20 (dd, 1 H, J = 5 Hz, J = 3 Hz), 3.57 (m, 2 H), 6.13 (d, 1 H, J = 6 Hz), 7.51 (dd, 1 H, J = 6 Hz, J = 3 Hz).

6-(3-Chloropropyl)-6-cyano-4-methoxybicyclo[3.1.0^{1,5}]hex-3-en-2-ones (40b and 41b) were prepared by irradiation of **14** in benzene solution at 366 nm for 3 h. Flash chromatography (silica gel, hexane–ethyl acetate, 1:1) provided **40b** (64%), mp 95–97 °C: ^{1}H NMR ($CDCl_3$) δ 1.80 (m, 2 H), 2.12 (m, 2 H), 2.38 (d, 1 H, J = 6 Hz), 2.63 (d, 1 H, J = 6 Hz), 3.77 (t, 2 H, J = 6 Hz), 3.91 (s, 3 H), 5.08 (s, 1 H); IR ($CHCl_3$) 2220, 1690, 1590, 1438 cm^{-1}; CIMS, m/z (rel intensity) 226 (M^+ + 1, 100), 198 (7), 190 (11); UV (MeOH) λ_{max} (ϵ) 264.0 nm (12481). Anal. Calcd for $C_{11}H_{12}NO_2Cl$: C, 58.54; H, 5.36. Found: C, 58.30; H, 5.36.

Also isolated was **41b** (9%) as an oil: ^{1}H NMR ($CDCl_3$) δ 1.82–2.18 (m, 4 H), 2.68 (d, 1 H, J = 6 Hz), 2.94 (d, 1 H, J = 6 Hz), 3.58 (m, 2 H), 3.88 (s, 3 H), 5.09 (s, 1 H); IR (film) 2220, 1690, 1590, 1442 cm^{-1}; CIMS, m/z (rel intensity) 226 (M^+ + 1, 100), 198 (2), 190 (11); UV (MeOH) λ_{max} (ϵ) 267.2 nm (6769).

Methyl 2-Benzyl-5-hydroxybenzoate (44). A solution of **9b** (48 mg, 0.2 mmol) in benzene (5 mL) was purged with nitrogen for 15 min before irradiation at 366 nm for 2 h. Concentration of the reaction mixture followed by flash chromatography (silica gel, hexane–ethyl acetate, 3:1) gave **44** (32 mg, 67%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 3.79 (s, 3 H), 4.30 (s, 2 H), 5.20 (s, 1 H, exchangeable with D_2O), 6.94 (dd, 1 H, J = 8 Hz, J = 2 Hz), 7.09–7.32 (m, 6 H), 7.40 (d, 1 H, J = 2 Hz).

6-Benzyl-6-cyanobicyclo[3.1.0^{1,5}]hex-3-en-2-one (45). A solution of **13b** (42 mg, 0.2 mmol) in benzene (4 mL) was purged with nitrogen for 15 min before irradiation at 366 nm for 2 h. Concentration of the reaction mixture followed by flash chromatography (silica gel, hexane–ethyl acetate, 3:1) gave **45** (31 mg, 74%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 2.43 (d, 1 H, J = 5 Hz), 2.86 (m, 1 H), 2.93 (d, 1 H, J = 16 Hz), 3.07 (d, 1 H, J = 16 Hz), 6.08 (d, 1 H, J = 5 Hz), 7.24–7.42 (m, 5 H), 7.61 (m, 1 H); IR (film) 3060, 2238, 1700, 1333 cm^{-1}; CIMS, m/z (rel intensity) 210 (M^+ + 1, 100), 182 (38). Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30. Found: C, 80.29; H, 5.21.

2-Benzyl-5-hydroxybenzonitrile (46). A solution of **13b** (42 mg, 0.2 mmol) in benzene (4 mL) was purged with nitrogen for 15 min before irradiation at 366 nm for 18 h. Concentration of the reaction mixture followed by flash chromatography (silica gel, hexane–ethyl acetate, 4;1) gave **46** (34 mg, 81%) as a colorless solid. An analytical sample was prepared by recrystallization from chloroform–hexane, mp 100–102 °C: ^{1}H NMR ($CDCl_3$) δ 4.10 (s, 2 H), 5.44 (s, 1 H, exchangeable with D_2O), 7.00 (dd, 1 H, J = 8 Hz, J = 2 Hz), 7.11 (d, 1 H, J = 2 Hz), 7.14 (d, 1 H, J = 8 Hz), 7.18–7.36 (m, 5 H); IR ($CHCl_3$) 3600–3100 (br), 2230, 1605, 1580, 1490, 1440 cm^{-1}; CIMS, m/z (rel intensity) 210 (M^+ + 1, 100), 132 (52). Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30. Found: C, 80.25; H, 5.18.

2-Methoxy-1-[[2(*S*)-(hydroxymethyl)pyrrolidinyl]carbonyl]benzene (50a). To a stirred solution of L(+)-prolinol (1.03 g, 10.3 mmol) and triethylamine (1.36 g, 13.4 mmol) in dry dichloromethane (32 mL) at 0 °C was added a solution of *o*-anisoyl chloride (1.60 g, 9.38 mmol) in dry dichloromethane (14 mL). The resulting solution was stirred at 0 °C for 1 h and then at room temperature for 24 h. The reaction mixture was washed with 5% hydrochloric acid (1 × 20 mL), saturated sodium bicarbonate (1 × 20 mL), and brine (1 × 20 mL). After drying over anhydrous magnesium sulfate, the solvent was removed under reduced pressure; flash chromatography (silica gel, ethyl acetate–methanol, 20:1) gave **50a** (1.81 g, 82%) as a colorless solid. An analytical sample was prepared by recrystallization from ethyl acetate–ether, mp 100–103 °C: ^{1}H NMR ($CDCl_3$) δ 1.54–1.87 (m, 3 H), 2.16 (m, 1 H), 3.31 (m, 2 H), 3.72 (m, 1 H), 3.86 (m, overlapping s at 3.82, 4 H), 4.38 (m, 1 H), 4.98 (br s, 1 H, exchangeable with D_2O), 6.94–7.06 (m, 2 H), 7.30–7.44 (m, 2 H); IR ($CHCl_3$) 3400, 1600, 1490, 1460, 1430 cm^{-1}; $[\alpha]_D^{20}$ -97.3° (c 1.16, $CHCl_3$); CIMS, m/z (rel intensity) 236 (M^+ + 1, 100). Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.17; H, 7.13.

2-Methoxy-1-[[2(*S*)-[(methoxymethoxy)methyl]pyrrolidinyl]carbonyl]benzene (50b). To a stirred solution of **50a** (1.18 g, 5.0 mmol) in dry dichloromethane (25 mL) at 0 °C was added chloromethyl methyl ether (1.21 g, 15.0 mmol) followed by triethylamine (1.5 g, 15.0 mmol). The resulting suspension was maintained at 0 °C for 1 h and then stirred at 25 °C for 12 h. The reaction mixture was washed with 1% hydrochloric acid (1 × 10 mL), saturated sodium bicarbonate (1 × 10 mL), water (1 × 10 mL), and brine (1 × 10 mL). After drying over magnesium sulfate, the solvent was removed under reduced pressure; flash chromatography (silica gel, ethyl acetate) gave **50b** (1.15 g, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$) suggested the presence of a mixture of rotational isomers δ 1.64–2.14 (m, 4 H), 3.17–3.39 (s, 3 H), 3.14–3.34 (m, 2 H), 3.72–3.90 (m, overlapping with singlets at 3.82, 3.83, 5 H), 4.37, 4.70 (m, 2 H), 4.46 (m, 1 H), 6.90–7.04 (m, 2 H), 7.24–7.40 (m, 2 H); IR (film) 2940, 2875, 2825, 1600, 1405 cm^{-1}; $[\alpha]_D^{22}$ -120.1° (c 0.61, CH_3OH); CIMS, m/z (rel intensity) 280 (M^+ + 1, 100), 248 (60), 135 (50). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58. Found: C, 64.69; H, 7.66.

(6*R*)-6-[[2-(*S*)-[(Methoxymethoxy)methyl]pyrrolidinyl]carbonyl]-6-methyl-1-methoxy-1,4-cyclohexadiene (51). A solution of **50b** (0.25 g, 0.89 mmol) in dry tetrahydrofuran (4.5 mL) and *tert*-butyl alcohol (66 mg, 0.89 mmol) was cooled to −78 °C. Liquid ammonia (60 mL, predried over sodium amide) was distilled into the reaction mixture. Potassium metal (77 mg, 2.2 equiv) was added to the stirred ammonia solution. Methyl iodide (0.25 g, 1.79 mmol) was added, and the resulting yellow solution was stirred for 1 h at −78 °C. Solid ammonium chloride was added, and the mixture was allowed to warm to room temperature. Brine (20 mL) was then added, and the mixture was extracted with chloroform (3 × 20 mL). The combined organic extracts were washed with 10% sodium thiosulfate (1 × 20 mL), water (1 × 20 mL), and brine (1 × 20 mL). After drying over magnesium sulfate the solvent was removed under reduced pressure to give **51** and **52** as a 99.7:0.3 mixture of diastereomers by analytical GC. Flash chromatography (silica gel, dichloromethane–ethyl acetate, 4:1) gave **51** (0.24 g, 89%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3 H), 1.68–1.98 (m, 4 H), 2.74–2.92 (m, 2 H), 3.28 (m, 1 H), 3.38 (s, 3 H), 3.48–3.71 (m, overlapping s at 3.54, 5 H), 3.78 (dd, 1 H, J = 10 Hz, J = 3 Hz), 4.34 (m, 1 H), 4.57–4.79 (m, 3 H), 5.53 (dt, 1 H, J = 10 Hz, J = 2 Hz), 5.78 (m, 1 H); IR (film) 3000, 2950, 2940, 2885, 2825, 1615, 1405 cm^{-1}; $[\alpha]_D^{20}$ -29.4° (c 0.26, $CHCl_3$); CIMS, m/z (rel intensity) 296 (M^+ + 1, 100), 264 (82), 172 (40), 142 (28). Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53. Found: C, 64.92; H, 8.46.

(2*R*)-2-[[(*N*-Carbomethoxy-(*S*)-2-pyrrolidinyl)methoxy]carbonyl]-2-methylcyclohex-3-en-1-one. A solution of methanol (100 mL), concentrated HCl (15 mL), and **51** (2.10 g, 7.11 mmol) was refluxed for 3 h. The reaction was carefully quenched with solid sodium bicarbonate, diluted with CH_2Cl_2 (500 mL), filtered, and concentrated to give the rearranged amine, which was immediately protected as a carbamate by reaction with methyl chloroformate (20 mL) and sodium bicarbonate (1 g) in 50 mL of CH_2Cl_2 (overnight at room temperature). Flash chromatography (silica gel, hexane–ethyl acetate, 2:1) gave (2*R*)-2-[[(*N*-carbomethoxy-(*S*)-2-pyrrolidinyl)methoxy]carbonyl]-2-methylcyclohex-3-en-1-one as a colorless oil (1.03 g, 49%): ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 3 H), 1.6–2.0 (m, 4 H), 2.4–2.8 (m, 4 H), 3.32 (m, 2 H), 3.64 (s, 3 H), 4.10 (m, 3 H), 5.68 (d, 1 H, J = 8 Hz), 5.97 (m, 1 H); IR (film) 2960, 2880, 1720 (br), 1440 cm^{-1}; CIMS, m/z 296 (M^+ + 1).

(2*R*)-6-[[(*N*-Carbomethoxy-(*S*)-2-pyrrolidinyl)methoxy]carbonyl]-1-methoxy-6-methyl-1,4-cyclohexadiene. A solution of (2*R*)-2-[[(*N*-carbomethoxy-(*S*)-2-pyrrolidinyl)methoxy]carbonyl]-2-methylcyclohex-3-en-1-one (0.684 g, 2.32 mmol), dry methanol (45 mL), trimethyl orthoformate (30 mL), and concentrated H_2SO_4 (15 drops) was refluxed for 22 h. Neutralization of the reaction mixture with solid sodium bicarbonate followed by filtration, concentration of the filtrate, and flash chromatography (silica gel, hexane–ethyl acetate, 2:1) gave (2*R*)-6-[[(*N*-carbomethoxy-(*S*)-2-pyrrolidinyl)methoxy]carbonyl]-1-methoxy-6-methyl-1,4-cyclohexadiene (0.717 g, 99%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 3 H), 1.6–2.0 (m, 4 H), 2.81 (m, 2 H), 3.30 (m, 2

H), 3.52 (s, 3 H), 3.66 (s, 3 H), 4.09 (m, 3 H), 4.75 (s, 1 H), 5.47 (d, 1 H, J = 8 Hz), 5.76 (m, 1 H); IR (film) 2960, 1710 (br), 1450, 1380 cm^{-1}; CIMS, m/z 310 ($M^+ + 1$).

(6*R*)-6-Carbomethoxy-1-methoxy-6-methyl-1,4-cyclohexadiene. A solution of (2*R*)-6-[[(*N*-carbomethoxy-(*S*)-2-pyrrolidinyl)methoxy]-carbonyl]-1-methoxy-6-methyl-1,4-cyclohexadiene (0.582 g, 1.88 mmol) in dry methanol (25 mL) and sodium methoxide (0.610 g, 11.3 mmol) was refluxed for 12 h. The reaction mixture was dissolved in ether (100 mL), and water (100 mL) was added. The organic phase was washed with brine (1 × 100 mL), dried over sodium sulfate, and chromatographed on neutral alumina (hexane–ethyl acetate, 2:1) to give (6*R*)-6-carbomethoxy-1-methoxy-6-methyl-1,4-cyclohexadiene (0.275 g, 80%) as a colorless oil, identical with ^1H NMR and IR to the corresponding racemic material **6a**.

(4*R*)-4-Carbomethoxy-3-methoxy-4-methyl-2,5-cyclohexadien-1-one (53a) was prepared from (6*R*)-6-carbomethoxy-1-methoxy-6-methyl-1,4-cyclohexadiene as described for the preparation of **8a**. The ^1H NMR, infrared, and mass spectra of **53a** were identical with those of **8a**. The optical rotation of **53a** was $[\alpha]_D^{24}$ −71.4° (c 1.71, methanol).

Irradiation of 53a for 1 h. A solution of **53a** (70 mg, 0.36 mmol) in benzene (7 mL) was purged with nitrogen for 15 min before irradiation at 366 nm for 1 h. The reaction mixture was concentrated, and flash chromatography (silica gel, hexane–ethyl acetate, 1:1) provided bicyclohexenones **54** and **55** and recovered 2,5-cyclohexadienone **53** as 5:1 mixture of enantiomers.

The ratio of enantiomers in each case was determined by ^1H NMR spectroscopy by using the chiral shift reagent tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III); i.e., $Eu(hfc)_3$. A 0.28 M stock solution of $Eu(hfc)_3$ in deuteriated chloroform was prepared, and 5-μL aliquots of the stock solution were added to the NMR sample tubes containing **53**, **54**, or **55**. When base line separation of a diagnostic proton signal was obtained (usually after the addition of several 5-μL aliquots of stock solution), the peaks were integrated. A comparison of the size of the integrals obtained in this manner provided the ratio of enantiomers. In the case of 2,5-cyclohexadienone **53**, the diagnostic proton that had base line separation was the vinyl proton attached to C(5). For bicyclohexenones **54** and **55**, the diagnostic proton that had base line separation in each case was the vinyl proton attached to C(3).

Irradiation of 53a for 9 h. A solution of **53a** (0.125 g, 0.64 mmol) in benzene (12 mL) was purged with nitrogen for 15 min before irradiation at 366 nm for 9 h. Flash chromatography provided bicyclohexenones **54** (52 mg) and **55** (43 mg). ^1H NMR spectroscopic examination of **54** showed that it was a 3:1 mixture of enantiomers. This mixture gave an optical rotation of $[\alpha]_D^{23}$ −130° (c 0.48, methanol). ^1H NMR spectroscopic examination of **55** showed that it was nearly racemic. This mixture gave an optical rotation of $[\alpha]_D^{31}$ +14.0° (c 0.84, methanol).

Irradiation of the 3:1 Mixture of Enantiomers of 54. A solution of **54** (23 mg) containing a 3:1 mixture of enantiomers in benzene (2.5 mL) was purged with nitrogen for 10 min before irradiation at 366 nm for 4 h. The reaction mixture was concentrated, and flash chromatography (silica gel, hexane–ethyl acetate, 1:1) provided a 1:3 mixture of **55** and **56** (11.3 mg) $[\alpha]_D^{23}$ −106° (c 0.23, methanol). Also recovered was **54** (6.3 mg) as a 3:1 mixture of enantiomers.

4-Ethyl-7-methoxytricyclo[3.3.0^{1,5}.0^{4,6}]oxaoctan-3-one (63). The bicyclohexenone **19b** (150 mg, 0.71 mmol) was dissolved in anhydrous ethanol (25 mL). To this solution was added sodium borohydride (108 mg, ~4 equiv). After stirring 16 h, the reaction mixture was carefully quenched with 10% HCl. Water was added to dissolve the salts, and the solution was stirred 2 h at room temperature. After extracting with chloroform, the organic layer was washed with water and saturated sodium bicarbonate and then dried over magnesium sulfate to give **63** (103 mg, 100%) as a colorless oil of high purity: ^1H NMR ($CDCl_3$) δ 0.98 (t, 3 H, J = 8 Hz), 1.48 (six line multiplet, 1 H, J = 8 Hz), 1.88–2.04 (m, 2 H), 2.12 (d, 1 H, J = 10 Hz), 2.18 (t, 1 H, J = 5 Hz), 2.94 (t, 1 H, J = 5 Hz), 3.45 (s, 3 H), 4.36 (t, 1 H, J = 7 Hz), 4.86 (brs, 1 H); ^{13}C NMR ($CDCl_3$) 10.75, 23.33, 37.72, 37.97, 46.35, 56.39, 80.55, 81.31, 176.91 (one carbon missing); IR (film) 2925, 1760, 1090, 985 cm^{-1}; CIMS, m/z (rel intensity) 183 ($M^+ + 1$, 10.63), 151 (93.55), 107 (100.00). Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74. Found: C, 65.83; H, 7.77.

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Vinyl Alcohol: Generation and Decay Kinetics in Aqueous Solution and Determination of the Tautomerization Equilibrium Constant and Acid Dissociation Constants of the Aldehyde and Enol Forms

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Abstract: Vinyl alcohol was generated in aqueous solution by Norrish type II photoelimination of 5-hydroxy-2-pentanone and by the acid-catalyzed hydrolysis of a ketene acetal (1-(vinyloxy)-1-methoxyethene) and an ortho ester (2-(vinyloxy)-2-phenyl-1,3-dioxolane), and rates of isomerization of this enol to acetaldehyde catalyzed by hydronium and hydroxide ions and formic and acetic acid buffers were measured. Rates of enolization of acetaldehyde, determined by iodine scavenging and catalyzed by hydronium and hydroxide ions, were also measured. These data lead to two concordant, independent determinations of the tautomerization equilibrium constant for acetaldehyde in aqueous solution whose average is $K_E = (5.89 \pm 0.81) \times 10^{-7}$, $pK_E = 6.23 \pm 0.06$. They also give $K_a^E = (3.13 \pm 0.17) \times 10^{-11}$, $pK_a^E = 10.50 \pm 0.02$, for the dissociation constant of vinyl alcohol ionizing as an oxygen acid, and $K_a^K = (1.85 \pm 0.27) \times 10^{-17}$, $pK_a^K = 16.73 \pm 0.06$, for the dissociation constant of acetaldehyde ionizing as a carbon acid; all equilibrium constants are concentration quotients and refer to aqueous solution at ionic strength 0.10 M. Kinetic solvent isotope effects on both enolization and ketonization suggest that reaction occurs by a stepwise rather than a concerted mechanism.

There has been a resurgence of interest lately in the chemistry of simple enols.[1] This was sparked by the demonstration that vinyl alcohol, the prototype enol, is not especially unstable in aqueous solution,[2] and it has included invention of new methods for estimating enol contents of simple aldehydes and ketones[3] as well as the re-examination of stable, sterically crowded "Fuson" enols.[4] We have contributed to this activity by devising methods for preparing enols in aqueous solution under conditions where

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