$OCH_2CH{=}CH_2$), 5.04–5.36 [m, $CH_2CH{=}CH_2$ and $NCH(CO_2)_2$], 5.52 (dd, J = 3.7, 1.9 Hz, 4α-CH), 5.62–6.09 (m, $CH_2CH{=}CH_2$).

Acknowledgment. We thank Professor Y. Kishi for useful discussions. This research was supported by a grant from the United States–Israel Binational Science Foundation (BSF), Jerusalem, Israel.

Registry No. 11, 64804-09-7; **12a**, 85082-38-8; **12b**, 85082-39-9; **12c**, 85082-40-2; **12d**, 85082-41-3; **12e**, 85082-42-4; **13a** (isomer 1), 85082-43-5; **13a** (isomer 2), 85082-44-6; **13b** (isomer 1), 85082-45-7; **13b** (isomer 2), 85082-46-8; **13c** (isomer 1), 85082-47-9; **13c** (isomer 2), 85082-48-0; **13d** (isomer 1), 85082-49-1; **13d** (isomer 2), 85082-50-4; **13e** (isomer 1), 85082-51-5; **13e** (isomer 2), 85082-52-6; **14a** (isomer 1), 85082-53-7; **14a** (isomer 2), 85082-54-8; **14b** (isomer 1), 85082-55-9; **14b** (isomer 2), 85082-56-0; **14c** (isomer 1), 85082-57-1; **14c** (isomer 2), 85082-58-2; **14d** (isomer 1), 85082-59-3; **14d** (isomer 2), 85082-60-6; **14e** (isomer 1), 85082-61-7; **14e** (isomer 2), 85082-62-8; **15a** (isomer 1), 85082-63-9; **15a** (isomer 2), 85082-64-0; **15b** (isomer 1), 85082-65-1; **15b** (isomer 2), 85082-66-2; **15d** (isomer 1), 85082-67-3; **15d** (isomer 2), 85082-68-4; **16**, 85068-05-9; **17**, 85068-06-0; **18**, 85068-07-1; **19**, 85068-08-2; **20**, 85068-09-3; **21**, 85068-10-6; **22**, 85068-11-7; **23**, 85068-12-8; **25**, 85068-13-9; **26**, 85068-14-0; **27**, 85068-15-1; **28a**, 85068-16-2; **28b**, 85068-17-3; **28c**, 85068-18-4; **28d**, 85068-19-5; **28f**, 85068-20-8; **31**, 85068-21-9; **32**, 85068-22-0; **33**, 85068-23-1; **34**, 85068-24-2; **35**, 79196-76-2; **37**, 85068-25-3; **38a**, 85114-74-5; **38b**, 85114-75-6; **39a**, 85114-76-7; **39b**, 85114-77-8; (*E*)-**40**, 85114-78-9; (*Z*)-**40**, 85114-79-0; **41**, 85068-26-4; methyl (*E*)-4-hydroxybut-2-enoate, 29576-13-4; 3-phenylprop-2-ynyl alcohol, 1504-58-1; *tert*-butyl glyoxylate, 7633-32-1; thiophenol, 108-98-5; benzeneselenol, 645-96-5; diethyl mesoxalate, 609-09-6.

Supplementary Material Available: A drawing and tables containing atom coordinates, anisotropic temperature factors, hydrogen atom coordinates, bond lengths, and bond angles of *tert*-butyl (±)-1-oxahomocepham-5α-carboxylate (**26**) (5 pages). Ordering information is given on any current masthead page.

Electronic Control of Stereoselectivity. 18. Stereospecific Capture of Electrophiles by 9-Isopropylidenebicyclo[4.2.1]nona-2,4,7-triene[1]

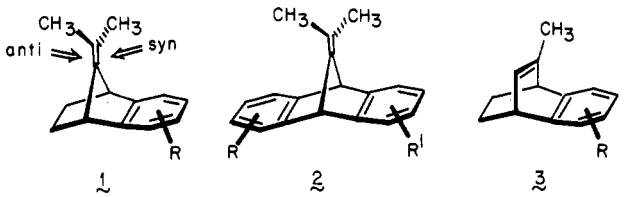
Kenneth E. Green and Leo A. Paquette*

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

Received September 2, 1982

The stereochemistry of addition of several weak electrophiles to the exocyclic double bond of the title compound (**4**) has been determined. Anti stereoselectivity was seen to operate exclusively in every example. The product structures were established by a combination of NMR spectroscopy, independent synthesis of the epimer, and (in one instance) X-ray crystallographic analysis. The causative factors that appear to underlie kinetically favored electrophilic attack in the indicated direction are discussed.

While 9-isopropylidenebenzonorbornenes (**1**) preferably



1 **2** **3**

enter into bonding from the anti direction with weakly electrophilic reagents,[2,3] strong electrophiles are captured with remarkably exclusive syn π-facial stereoselectivity.[3,4] Dissimilar functional groups in otherwise more symmetrical 11-isopropylidenedibenzonorbornadienes (**2**) are likewise capable of modulating stereoselection when lesser reactive agents are involved.[5] This may well be a consequence of the importance of long-range homoaromatic involvement by the aryl rings in the corresponding transition states.[3,6] Since comparable through-space coupling is nonoperational in benzobicyclo[2.2.2]octadienes (**3**), stereoelectronic control is seen neither in these systems[7] nor their dibenzo counterparts.[8] The experimental data relating to the more powerful electrophiles correlate most reasonably with initial π-complexation to the aromatic rings, thus constituting a special case of guided electrophilic capture.[5]

The presumed existence of a direct link between π-facial stereoselectivity and the development of extended positive-charge stabilization in **1** and **2**, at least when such reagents as *m*-chloroperbenzoic acid, *N*-bromosuccinimide, *N*-methyltriazolinedione, singlet oxygen, and dichlorocarbene are involved, has prompted the present investigation. The question at issue was whether electrophile stereoselection could be utilized as an experimental tool

(1) Part 17: Hayes, P. C.; Paquette, L. A. *J. Org. Chem.*, in press.
(2) Paquette, L. A.; Hertel, L. W.; Gleiter, R.; Böhm, M. C. *J. Am. Chem. Soc.* **1978**, *100*, 6510.
(3) Paquette, L. A.; Hertel, L. W.; Gleiter, R.; Böhm, M. C.; Beno, M. A.; Christoph, G. G. *J. Am. Chem. Soc.* **1981**, *103*, 7106.
(4) Hertel, L. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1979**, *101*, 7620.
(5) Paquette, L. A.; Klinger, F.; Hertel, L. W. *J. Org. Chem.* **1981**, *46*, 4403.
(6) Secondary orbital interactions have been implicated as significant contributors to the stereoselectivity of singlet oxygen capture in these systems [Okada, K.; Mukai, T. *J. Am. Chem. Soc.* **1978**, *100*, 6509]. The photoelectron spectrum of 9-isopropylidenebenzonorbornadiene has been independently measured, and the extent of orbital splitting arising from the exo- and endocyclic double bonds estimated [Haselbach, E.; Rossi, M. *Helv. Chim. Acta* **1976**, *59*, 278; Pfaendler, H. R.; Tanida, H.; Haselbach, E. *Ibid.* **1974**, *57*, 383]. Additionally, ^{13}C NMR spectroscopy has revealed that the exocyclic double bond in 7-methylenenorbornene is polarized due to homoconjugation [Hoffmann, R.; Kurz, H. *Chem. Ber.* **1975**, *108*, 119; see also, Paquette, L. A.; Oku, M.; Farnham, W. B.; Olah, G. A.; Liang, G. *J. Org. Chem.* **1975**, *40*, 700].
(7) Paquette, L. A.; Bellamy, F.; Wells, G. J.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1981**, *103*, 7122.
(8) Cristol, S. J.; Kochansky, M. C. *J. Org. Chem.* **1975**, *40*, 2171.

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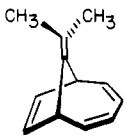
with which to assess the importance of homoaromaticity and its particular topological distribution within a given molecule as it enters into chemical reaction. Triene **4**

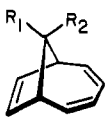


4

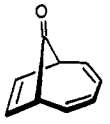
5

became the focus of our attention because of its obvious relationship to the bicyclo[4.2.1]nona-2,4,7-trienyl cation (**5**), an intermediate originally expected to exhibit homoaromatic (2π3C) and bicycloaromatic (6π7C) character.[9]

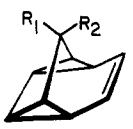
Although the experimental tests that have been brought to bear on the electronic nature of **5** have been many,[10-14] the true character of this species remains unclear. Not only do the syn and anti tosylates **6a** and **6b** exhibit an identical



6a, R_1 = H, R_2 = OTs
b, R_1 = OTs, R_2 = H
c, R_1 = H, R_2 = OCH_3



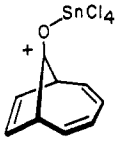
7



8

solvolysis rate at 50.0 °C in aqueous methanol (their k's do differ in other solvents[12c]) but also similar product mixtures are obtained from both epimers.[13] Furthermore, all of the products are structurally rearranged (*cis*-dihydroindenyl derivatives predominate), indicating that **5** does not persist when the transition state is attained late on the reaction coordinate. This inability to produce a cation of undistorted geometry can be partially overcome by making recourse to deamination. Photolysis of the tosylhydrazone of **7** in methanolic sodium methoxide afforded **6c** as a major product (46.4%).[13] Nonetheless, a clear distinction has not yet been made between the extent to which π participation may be involved and the possible onset of an intramolecular Diels–Alder reaction that delivers **8** prior to ionization.

On the other hand, the importance of through-space interaction in these systems is not subject to question. Using photoelectron spectroscopy, Schweig and his coworkers determined that although **7** is not bicycloconjugated, the n-molecular orbital of the carbonyl group interacts directly with the butadiene moiety with which it is homoconjugated.[15] When the carbonyl group is increasingly polarized by complexation to stannic chloride as in **9**, homoconjugation between these two segments of the molecule is observably enhanced.[16] Similar effects



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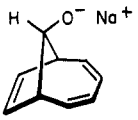
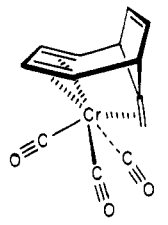


10

operate in **10**. Thus, there would appear to be little or no direct involvement of the nonconjugated double bond with C_9 under neutral, cationic, or anionic conditions. CNDO/2 calculations performed on **5** have indicated that this cation (when fully dissociated and unsolvated) can significantly stabilize itself (7 kcal/mol) by tipping its electron-deficient center away from the etheno bridge to the extent of 10°. Accompanying this distortion is a displacement of the butadiene unit toward the two-carbon bridge by 30° (11 kcal/mol).[16] The implication here is, of course, that structural bending within **5** as indicated produces an exothermic change that delivers a cation conceivably stabilized by as much as 18 kcal/mol.

However, a caveat remains. Dreiding models of **4** reveal the tetraene to be nontrivially strained, with the exocyclic double bond at C_9 being nearly coplanar with the bridgehead (C_1, C_6) carbons and C_7–C_8 double bond.[17] An almost planar five-membered ring results. To the extent that this conformation is relatively inflexible, those reagents that attack C_9 must be relegated to anti approach because of substantial steric shielding on the syn surface by the diene bridge. This view is fully consistent with the stereochemical outcome of nucleophilic additions to ketone **7**.[10a,12b,18a,19] Remarkably, the five-membered ring in chromium tricarbonyl complex **11** is also approximately planar (to



11

within 0.2 Å).[20] For unknown reasons, the liquid tetraene avoids conventional complex formation to C_7,C_8 and the diene unit (from below plane)[21] and bonds exclusively to $Cr(CO)_3$ to give **11**, where the exocyclic C=C vector lies approximately perpendicular to the butadiene plane. This unusual arrangement has not been encountered elsewhere. If the conformational features discussed above are common to **4** and its congeners, one would be guided to expect that syn addition of electrophiles to the exocyclic double bond of such systems would be inhibited on steric grounds.

Results

Access to **4** was gained by Wittig condensation of **7**[10a,18] with isopropylidenetriphenylphosphorane.[22] The first

(9) (a) Goldstein, M. J. *J. Am. Chem. Soc.* **1967**, *89*, 6357. (b) Goldstein, M. J.; Hoffmann, R. *Ibid.* **1971**, *93*, 6193.
(10) (a) Antkowiak, T. A.; Sanders, D. C.; Trimitsis, G. B.; Press, J. B.; Shechter, H. *J. Am. Chem. Soc.* **1972**, *94*, 5366. (b) Sanders, D. C.; Shechter, H. *Ibid.* **1973**, *95*, 6858.
(11) Kende, A. S.; Bogard, T. L. *Tetrahedron Lett.* **1967**, 3383.
(12) (a) Diaz, A. F.; Fulcher, J.; Sakai, M.; Winstein, S. *J. Am. Chem. Soc.* **1974**, *96*, 1264. (b) Diaz, A.; Fulcher, J. *Ibid.* **1974**, *96*, 7954. (c) Diaz, A.; Fulcher, J. *Ibid.* **1976**, *98*, 798.
(13) Kirmse, W.; Voigt, G. *J. Am. Chem. Soc.* **1974**, *96*, 7598.
(14) (a) Schipper, P.; Buck, H. M. *J. Am. Chem. Soc.* **1978**, *100*, 5507. (b) Paquette, L. A.; Broadhurst, M. J. *J. Org. Chem.* **1973**, *38*, 1893.
(15) Shafer, W.; Schmidt, H.; Schweig, A.; Hoffmann, R. W.; Kurz, H. *Tetrahedron Lett.* **1974**, 1953.
(16) Diaz, A.; Fulcher, J.; Cetina, R.; Rubio, M.; Reynoso, R. *J. Org. Chem.* **1975**, *40*, 2459.
(17) Similar considerations have been earlier applied to ketone **7**: (a) ref 10a. (b) Schuster, D. I.; Kim. C. W. *J. Org. Chem.* **1975**, *40*, 505.
(18) (a) Sakai, M.; Childs, R. F.; Winstein, S. *J. Org. Chem.* **1972**, *37*, 2517. (b) Paquette, L. A.; Meisinger, R. H.; Wingard, R. E., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 2155. (c) Kurabayashi, K.; Mukai, T. *Tetrahedron Lett.* **1972**, 1049.
(19) Miyashi, T.; Hazato, A.; Mukai, T. *J. Am. Chem. Soc.* **1982**, *104*, 891.
(20) Jameson, G. B.; Salzer, A. *Organometallics* **1982**, *1*, 689.
(21) Salzer, A. *J. Organomet. Chem.* **1976**, *107*, 79; **1976**, *117*, 245.
(22) Wittig, G.; Wittenburg, D. *Justus Liebigs Ann. Chem.* **1957**, *606*, 1.

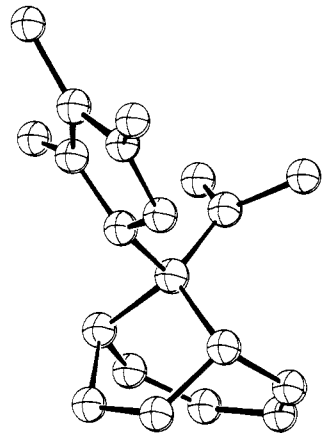
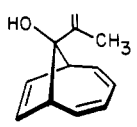
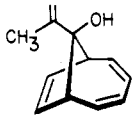


Figure 1. Computer-generated perspective drawing of the final X-ray model of urazole **15** (courtesy of J. Clardy and L. S. Bass).

reaction studied was singlet oxygenation. Irradiation of cold (0 °C), oxygen-saturated acetone solutions of **4** and methylene blue for 2 h, followed by direct reduction of the resulting hydroperoxide with sodium borohydride, afforded an isomerically pure, crystalline allylic alcohol in greater than 90% yield. The product was established as anti isomer **12** on the basis of an unequivocal synthesis of its



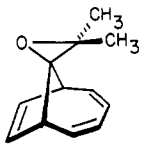
12



13

syn epimer (**13**), which takes advantage of the known propensity of **7** to add organometallic[10a,18a,19] and hydride reagents[10a,12b,18a] from that direction syn to the etheno bridge. Indeed, exposure of the ketone to the Grignard reagent derived from 2-bromopropene gave rise efficiently and exclusively to **13**. With both isomers in hand, it became quite apparent that (a) the multiplet due to H_2–H_5 in **12** appears at higher field than that in **13**, a circumstance likely attributable to shielding by the superpositioned isopropenyl double bond, (b) the H_7–H_8 multiplet is not comparably affected in **13**, and (c) the methyl group in **12** is upfield shifted relative to that in the syn epimer, presumably as a consequence of the conjugated diene anisotropy effect.

When **4** was treated with *m*-chloroperbenzoic acid, equally high-yield conversion to a single epoxide occurred. The stereochemical purity of this crystalline substance was deduced by means of ^1H and ^{13}C NMR spectroscopy in tandem with VPC analysis. Clear definition of its anti stereostructure (**14**) was accomplished by ring opening with lithium diethylamide to give **12**.



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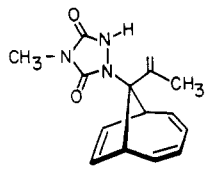
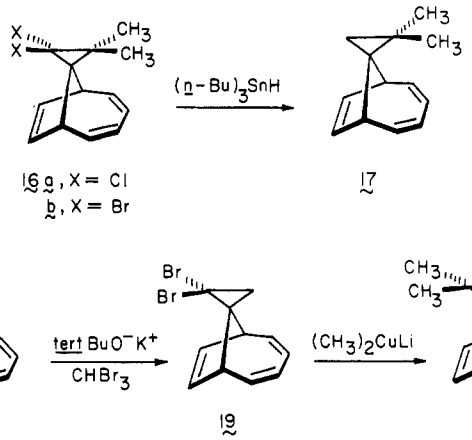


15

The stereoselection observed in the ene reaction of **4** with *N*-methyltriazolinedione was also completely anti. Although the appearance of the H_2–H_5 multiplet in **15** centered at δ 5.90 and the methyl singlet at δ 1.70 agreed well with the parameters exhibited by **12**, these features were not considered to be adequately confirmatory of structure. An X-ray crystal structure analysis was therefore undertaken, the results of which are depicted in Figure 1. As a consequence, the parallelism between **12** and **15** is seen to hold completely.

The foregoing developments led us to examine next the behavior of **4** toward electron-deficient carbenes such as $:CCl_2$ and $:CBr_2$. Upon being heated with sodium trichloroacetate in a tetrachloroethylene–glyme (1:1) solvent system, a homogeneous dichlorocyclopropane was obtained. Its ^1H NMR spectrum proved to be almost completely superimposable upon that of the dibromocyclopropane produced from the action on **4** of potassium *tert*-butoxide and bromoform in pentane solution. Accordingly, the two adducts were considered to possess identical topology.

If stereochemical crossover had not materialized in either of these dihalocarbene insertion reactions, the two products should be **16a** and **16b**, respectively. Suitable stereochemical correlation was realized as follows. In a process designed to deliver hydrocarbon **17**, **16b** was subjected to tri-*n*-butyltin hydride reduction. Particularly noteworthy are the chemical shifts of its cyclopropyl (δ 0.4) and methyl proton signals (δ 1.0). To arrive at **20**, the known methylene derivative **18**[10b,14b,23] was dibromocyclopropanated as before. *gem*-Dimethylation of **19** with lithium dimethylcuprate[24] ensued. In the case of **20**, the key proton absorptions were seen at δ 0.15 and 1.08, respectively. The enhanced long-range shielding reflected in the cyclopropyl protons of **20** relative to **17** conform to the diene magnetic anisotropy effects noted earlier for **12** and **13**. However, a reverse correlation exists for the methyl resonances, those in **17** appearing at lower field. This phenomenon is observed because of the obvious enhancement in distance and dihedral angle relative to the diene π network to which the methyl protons are subjected. These geometric differences are adequate cause for substantial change in long-range shielding[25] and may also be accompanied by differences in electron-density gradients.



16a, X = Cl
b, X = Br

17

18 **19** **20**

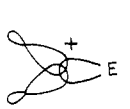
In an effort to broaden the range of electrophiles, **4** was also treated with *N*-bromosuccinimide (1.5 equiv) in 5–10% aqueous glyme at 0–20 °C. Although the polyolefin was rapidly consumed, no allylic bromide could be isolated. Similar behavior was noted with *tert*-butyl hypochlorite (1 equiv) in methyl formate in the absence of light at 0–20

(23) (a) Reetz, M. T.; Hoffmann, R. W.; Schaefer, W.; Schweig, A. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 81. (b) Hoffmann, R. W.; Kurz, H. *Chem. Ber.* **1975**, *108*, 119.
(24) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 3911.
(25) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: London, 1969; pp 83–88.

°C.[3,26] Attempts to acylate 7 with acetic anhydride and zinc chloride[3,27] at −70 and −20 °C were equally ill-fated.

Discussion

We have demonstrated that addition reactions of weakly electrophilic reagents to 4 proceed at the exocyclic double bond with complete anti stereoselectivity within the experimental limits of detection. Consequently, there is no question that this bridged polyolefin can clearly distinguish between the two stereochemical pathways open for bonding to its isopropenyl group. However, one must question whether the observed stereoselectivity is electronic or steric in origin. The success realized earlier with 1 and 2 derives in large part from the fact that these substrates have the ability to distinguish stereochemically between bridged (21) and open ion (22) pathways. When weak electrophiles are



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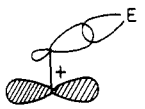
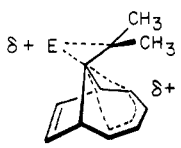


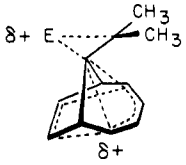
22

involved, homoaromatic charge delocalization is called into play for the purpose of polarizing the attacking reagent and causing it to engage in bonding. More powerful electrophiles are dependent neither on polarization nor on long-range stabilization in the olefin and seemingly engage in transient arene complex formation.

Should 4 behave analogously, positive charge delocalization would materialize between C_9 and the C_2–C_5 diene unit as illustrated in 23. However, an interaction of this



23



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type is dihomocyclopentadienyl in nature and undoubtedly disfavored electronically.[28] On the other hand, the geometric boundaries arrived at by CNDO/2 calculations[16] may more closely approximate the true nature of the cationic species in question. Added involvement of the etheno bridge as in 24 lifts the energetic disadvantages present in 23 and provides for the intervention of a stabilized intermediate or transition state.

Although charge dispersal as in 24 *may* lead to kinetically favored anti attack, topological factors are believed to contribute most heavily to this stereoselection. In the ground-state geometry of 4, 18, and related molecules, the C_9 bridge would appear to be so acutely tilted toward the butadiene segment that the anti surface of the exocyclic double bond is solely accessible for bonding. Any energetic advantage that may be gained by syn attack and development of homoaromatic interaction with the pπ orbitals at C_7 and C_8 is not capable of realization because of this sizable steric constraint. Consequently, 9-alkylidenebicyclo[4.2.1]nonatrienes are not useful probes for assessing possible homoaromatic and bicycloaromatic interactions that may develop during their capture by electrophilic reagents.

Experimental Section

Proton magnetic resonance spectra were obtained with a Varian EM-390 spectrometer; apparent splittings are given in all cases. ^{13}C NMR spectra were recorded on a Bruker WP-80 spectrometer. Infrared spectra were determined on a Perkin-Elmer Model 467 instrument. Mass spectra were recorded on an AEI-MS9 spectrometer at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Lab., Herlev, Denmark.

9-Isopropylidenebicyclo[4.2.1]nona-2,4,7-triene (4). To a stirred suspension of isopropyltriphenylphosphonium bromide (1.06 g, 2.75 mmol) in anhydrous tetrahydrofuran (60 mL) was added *n*-butyllithium in hexane (2.1 mL of 1.36 M, 2.85 mmol) under a nitrogen atmosphere. The red solution was stirred at room temperature for 1 h prior to dropwise addition of ketone 7 (310 mg, 2.35 mmol).[10a,17] The reaction mixture was heated at reflux for 10 h, cooled, and filtered through a pad of Celite. The filtrate was washed with water and brine, dried, and evaporated to leave a brown oil. Distillation of this material in a Kugelrohr apparatus (120 °C, 1.5 torr) afforded 186 mg (50%) of 4 as a viscous oil: ^1H NMR ($CDCl_3$) δ 6.3–5.6 (m, 4 H), 5.4 (d, J = 6 Hz, 2 H), 3.7 (d, J = 6 Hz, 2 H), 1.7 (s, 6 H); mass spectrum, m/e calcd (M^+) 158.1095, obsd 158.1100.

Anal. Calcd for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 90.98; H, 8.89.

Singlet Oxygenation of 4. A solution of 4 (150 mg, 0.95 mmol) in acetone (10 mL) was admixed with 10 mL of a saturated solution of methylene blue in the same solvent, cooled to 0 °C, and irradiated with a 500-W tungsten filament bulb while being oxygenated. After 2 h, the solvent was removed in vacuo and methanol (25 mL) was added followed by sodium borohydride (359 mg, 9.5 mmol). This mixture was stirred at room temperature for 4 h, concentrated under reduced pressure, and partitioned between ether and water. The organic phase was separated, and the aqueous layer was reextracted with ether. The combined ethereal layers were washed with 5% sodium hydroxide solution and water prior to drying and solvent removal. There was obtained 150 mg (90.5%) of 12 as a homogeneous white solid: mp 59–60 °C (from hexanes); IR (cm^{-1}, $CHCl_3$) 3600–3380, 2925, 900, 675, 640; ^1H NMR ($CDCl_3$) δ 5.85 (m, 4 H), 5.3 (m, 2 H), 4.9 (m, 2 H), 3.19 (m, 2 H), 1.85 (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 143.22, 132.54, 124.67, 121.13, 114.87, 81.37, 53.45, 17.67; mass spectrum, m/e calcd (M^+) 174.1044, obsd 174.1050.

***syn*-9-Isopropenylbicyclo[4.2.1]nona-2,4,7-trien-9-ol (13).** The Grignard reagent of 2-bromopropene (278 mg, 2.3 mmol) was prepared in 10.2 mL of anhydrous tetrahydrofuran with 56 mg (2.3 mmol) of magnesium turnings by heating at reflux for 20 min after dropwise addition of the bromide. Upon cooling to room temperature, a solution of 7 (200 mg, 15.2 mmol) in tetrahydrofuran (1 mL) was introduced slowly, and the reaction mixture was stirred at room temperature for 12 h. With ice cooling, saturated ammonium chloride solution was added, the reaction mixture was filtered, and the filtrate was evaporated. The residue was dissolved in ether, dried, and concentrated in vacuo to leave a yellowish oil that was distilled in a Kugelrohr apparatus (50 °C, 0.2 torr). There was obtained 192 mg (73%) of 13 as a colorless oil, which crystallized upon cooling: mp 31–32 °C; IR (cm^{-1}, neat) 3560, 3020, 1640, 1100–1020, 890, 870, 822, 742, 680; ^1H NMR ($CDCl_3$) δ 6.2 (m, 4 H), 5.3 (m, 2 H), 4.92 (m, 2 H), 3.18 (m, 2 H), 1.92 (m, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 146.52, 134.82, 125.89, 123.80, 111.76, 74.96, 51.61, 19.42; mass spectrum, m/e calcd (M^+) 174.1044, obsd 174.1049.

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.38; H, 8.26.

Epoxidation of 4. A nitrogen-blanketed, magnetically stirred solution of 4 (40 mg, 0.253 mmol) in dichloromethane (10 mL) was cooled to −78 °C, treated with *m*-chloroperbenzoic acid (51.4 mg, 0.255 mmol), and stirred for 5 h before warming to room temperature. After an additional 6 h, water was added, the organic

(26) (a) Cooper, R. G. D. *Tetrahedron Lett.* **1980**, *21*, 781. (b) Offermann, W.; Vogtle, F. *Synthesis* **1977**, 272.

(27) (a) Beak, P.; Berger, K. R. *J. Am. Chem. Soc.* **1980**, *102*, 3848. (b) Deno, N. C.; Chafetz, H. *Ibid.* **1952**, *74*, 3940. (c) Groves, J. K.; Jones, N. *J. Chem. Soc. C* **1968**, 2215, 2354, 2898; **1968**, 608. (d) Meerwein, H. *Justus Liebigs Ann. Chem.* **1927**, *455*, 227. (e) Dilthey, W. *Chem. Ber.* **1938**, *71*, 1350. (f) Dubois, M.; Cazaux, M. *Bull. Soc. Chim. Fr.* **1975**, *1-2*, 265, 269. (g) Hoffmann, H. M. R.; Tsushima, T. *J. Am. Chem. Soc.* **1977**, *99*, 6008.

(28) Breslow, R.; Hoffman, J. M., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 2110 and references cited therein.

layer was separated, and the aqueous phase was twice extracted with dichloromethane. The combined organic solutions were washed with saturated sodium bicarbonate solution and brine prior to drying and solvent evaporation. There was isolated 40.8 mg (92.7%) of **14** as a colorless crystalline solid, mp 62–63 °C (from hexanes); ^{1}H NMR ($CDCl_3$) δ 6.16–5.66 (m, 4 H), 5.40 (m, 2 H), 2.80 (m, 2 H), 1.24 (s, 6 H); ^{13}C NMR (ppm, $CDCl_3$) 131.96, 124.43, 123.12, 75.06, 61.66, 48.69, 21.46; mass spectrum, *m/e* calcd (M^+) 174.1045, obsd 174.1096.

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.42; H, 8.03.

Ring Opening of 14. To a cold (0 °C) solution of diethylamine (70.9 mg, 0.971 mmol) in anhydrous ether (3 mL) was added 0.7 mL of 1.38 M *n*-butyllithium in hexane. After 30 min of stirring, **14** (50 mg, 0.287 mmol) in anhydrous ether (3 mL) was added and the reaction mixture was stirred at room temperature for 12 h. Water and ether were added, the aqueous layer was extracted with ether (2×), and the combined organic phases were washed with 10% ammonium chloride solution, water, and saturated sodium bicarbonate solution prior to drying. Following solvent evaporation, the residue was purified by preparative TLC on silica gel (elution with ethyl acetate–petroleum ether, 1:1.5). There was isolated 11.6 mg (23.7%) of **12** with spectral properties identical with these described above.

***N*-Methyltriazolinedione Addition to 4.** A solution of *N*-methyltriazolinedione (71.5 mg, 0.63 mmol) in ethyl acetate was added dropwise during 1 h to a nitrogen-blanketed solution of **4** (100 mg, 0.63 mmol) in the same solvent (3 mL). The reaction mixture was stirred at room temperature for 12 h, water and ether were added, and the separated organic phase was dried and evaporated. The residue was recrystallized from ethyl acetate to furnish 62.5 mg (36.4%) of **15**; mp 199 °C dec; ^{1}H NMR ($CDCl_3$) δ 5.90 (m, 4 H), 5.3 (br s, 2 H), 4.9 (m, 2 H), 4.1 (m, 2 H), 3.0 (s 3 H), 1.70 (s, 3 H); ^{13}C NMR (ppm, $CDCl_3$) 154.68, 151.86, 137.54, 132.20, 125.98, 120.50, 118.36, 75.30, 48.40, 25.05, 18.25; mass spectrum, *m/e* calcd (M+) 271.1321, obsd 271.1330.

Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32. Found: C, 66.04; H, 6.47.

Dichlorocarbene Addition to 4. A solution of **4** (50 mg, 0.317 mmol) and sodium trichloroacetate (1.165 g, 6.3 mmol) in 30 mL of 1:1 tetrachloroethylene–glyme was heated at reflux for 18 h, cooled, diluted with water, and extracted with ether (3 × 10 mL). The combined organic layers were washed with saturated sodium bicarbonate, 10% ammonium chloride, and saturated brine solutions prior to drying and solvent evaporation. The residue was recrystallized from hexanes to give 61.1 mg (84.3%) of **16a**: mp 132 °C; ^{1}H NMR ($CDCl_3$) δ 5.95 (m, 4 H), 5.3 (m, 2 H), 3.20 (m, 2 H), 1.1 (s, 6 H); ^{13}C NMR (ppm, $CDCl_3$) 134.25, 124.39, 122.40, 46.18, 42.01, 29.34, 20.40, 19.87; mass spectrum, *m/e* calcd (M^+) 240.0473, obsd 240.0479.

Anal. Calcd for $C_{13}H_{14}Cl_2$: C, 64.75; H, 5.85. Found: C, 64.42; H, 5.79.

Dibromocarbene Addition to 4. A cold (0 °C) stirred mixture of **4** (40 mg, 0.17 mmol) and potassium *tert*-butoxide (48 mg, 0.43 mmol) in pentane (10 mL) was treated with bromoform (30 μL, 0.34 mmol). After 10 h, pentane and water were added, and the aqueous phase was extracted with pentane. The combined organic layers were washed with brine, dried, and evaporated to leave a solid, which was taken up in petroleum ether and eluted through a short silica column. Evaporation of the eluate gave 25.2 mg (45%) of **16b**, which was reduced without further purification: ^{1}H NMR ($CDCl_3$) δ 6.02 (m, 4 H), 5.4 (m, 2 H), 3.32 (m, 2 H), 1.1 (s, 6 H).

Butyltin Hydride Reduction of 16b. A solution of **16b** (75 mg, 0.23 mmol) and tri-*n*-butyltin hydride (66.93 mg, 0.23 mmol) in benzene (2 mL) was heated at 70 °C for 4 h and stirred at room temperature for 8 h. The solvent was evaporated, and the residual brown oil was purified by preparative VPC (0.25 in. × 6 ft 5% SE-30 on Chromosorb G, 150 °C) to give 25.7 mg (65%) of **17** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.2–5.8 (m, 4 H), 5.35 (m, 2 H), 2.6 (d, J = 6 Hz, 2 H), 1.0 (s, 6 H), 0.4 (s, 2 H); ^{13}C NMR (ppm, $CDCl_3$) 137.29, 123.84, 123.08, 50.42, 27.40, 23.08, 20.40, 19.53; mass spectrum, *m/e* calcd (M^+) 172.1252, obsd 172.1258.

Dibromocyclopropanation of 18. A cold (−20 °C), magnetically stirred slurry of potassium *tert*-butoxide (524.6 mg, 4.68 mmol) in pentane (20 mL) containing **18** (203 mg, 1.56 mmol) was treated dropwise with bromoform (1.18 g, 4.68 mmol) during 2 h. After 3 h at −20 °C and 8 h at room temperature, the reaction mixture was processed as described above to give a solid residue, which was purified by preparative TLC (silica gel, petroleum ether). There was obtained 344 mg (73%) of **19** as an unstable colorless solid: ^{1}H NMR ($CDCl_3$) δ 6.2–5.8 (m, 4 H), 5.4 (m, 2 H), 3.3 (m, 2 H), 1.4 (s, 2 H); ^{13}C NMR (ppm, $CDCl_3$) 133.89, 125.58, 123.44, 50.29, 48.93, 44.22, 29.74.

Methyl–Halogen Exchange in 19. Cuprous iodide (3.73 g, 19.7 mmol) in cold (0 °C) anhydrous ether (30 mL) was treated dropwise with ethereal methyllithium (39.4 mmol). The resulting clear solution was stirred at room temperature for 2 h and recooled to −20 °C prior to slow addition of **19** (595 mg, 1.97 mmol). Following 96 h of stirring at −20 °C, the reaction mixture was poured into cold saturated ammonium chloride solution and filtered. The separated organic phase was washed with saturated ammonium chloride solution, water, and brine before drying and solvent removal. Kugelrohr distillation of the residual brown oil (70 °C, 1.5 mm) afforded 99.4 mg (29.3%) of **20** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.2–5.8 (m, 4 H), 5.4 (m, 2 H), 2.9 (m, 2 H), 1.08 (s, 6 H), 0.15 (s, 2 H); ^{13}C NMR (ppm, $CDCl_3$) 136.89, 127.70, 123.55, 46.03, 22.74, 21.54, 20.77, 15.30.

Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.80; H, 9.30.

Acknowledgment. This investigation was supported by the National Cancer Institute (Grant CA-12115) to whom we are deeply appreciative.

Registry No. **4**, 85454-50-8; **7**, 34733-74-9; **12**, 85454-51-9; **13**, 85454-52-0; **14**, 85454-53-1; **15**, 85454-54-2; **16a**, 85454-55-3; **16b**, 85454-56-4; **17**, 85454-57-5; **18**, 38898-39-4; **19**, 85454-58-6; **20**, 85548-92-1; isopropyltriphenylphosphonium bromide, 1530-33-2; *n*-butyllithium, 109-72-8; *N*-methyltriazolinedione, 13274-43-6; dichlorocarbene, 1605-72-7; dibromocarbene, 4371-77-1; tri-*n*-butyltin hydride, 688-73-3.