2.3, 0.5 × 1 H), 4.16 (q, J = 7.1, 2 H), 4.0–4.26 (m, 0.5 × 1 H), 4.45 (dd, J = 9.2, 6.5, 0.5 × 1 H), 4.49 (dd, J = 9.4, 7.7, 0.5 × 1 H); ^{13}C NMR δ 14.0 (2 × CH_3), 36.8 (CH_2), 37.4 (CH_2), 37.8 (CH_2), 38.0 (CH_2), 41.2 (CH), 43.5 (CH), 44.2 (CH), 46.7 (2 × CH_2), 47.1 (CH), 61.3 (C), 61.7 (C), 62.3 (CH_2), 62.4 (CH_2), 71.2 (CH_2), 73.3 (CH_2), 169.2 (C=O), 169.5 (C=O), 175.8 (C=O), 176.1 (C=O). Anal. Calcd for $C_{11}H_{15}O_4Cl$: C, 53.55; H, 6.12; Cl, 14.37. Found: C, 53.51; H, 6.16; Cl, 12.1.

Oxidation of 13b with Mn(OAc)$_3$LiCl. Treating **13b** (1 g, 4.42 mmol) under the preceding conditions afforded 1.11 g of a crude product, the separation of which gave 98 mg (conv 90%) of unreacted **13b**; 269 mg of one diastereoisomer of **27b**; 137 mg of the other diastereomer of **27b**, and 226 mg of **28b** as a mixture of isomers.

Ethyl 4-(1-Chloromethyl)-3-(2-propenyl)-2-oxotetrahydrofuran-3-carboxylate (27b). First diastereoisomer: IR 1782 1739, 1643 cm^{-1}; ^{1}H NMR δ 1.24 (t, J = 7.1, 3 H), 1.54 (d, J = 6.5, 3 H), 2.56 (dd, J = 14.6, 5.0, 1 H), 2.63–2.97 (m, 2 H), 3.90 (dq, J = 10.4, 6.5, 1 H), 4.11 (dd, J = 10.6, 8.6, 1 H), 4.20 (q, J = 7.1, 2 H), 4.45 (t, J = 8.6, 1 H), 5.11–5.24 (m, 2 H), 5.55 (m, 1 H); ^{13}C NMR δ 14.1 (CH_3), 24.1 (CH_3), 36.5 (CH_2), 48.4 (CH), 56.6 (CH), 57.2 (C), 62.6 (CH_2), 69.9 (CH_2), 121.8 (=CH_2), 131.5 (=CH), 167.7 (C=O), 174.0 (C=O). Anal. Calcd for $C_{12}H_{17}O_4Cl$: C, 55.28; H, 6.57; Cl, 13.59. Found: C, 55.25; H, 6.44; Cl, 13.53. Second diastereoisomer: IR 1780, 1742, 1642 cm^{-1}; ^{1}H NMR δ 1.12 (t, J = 7.1, 3 H), 1.29 (d, J = 6.5, 3 H), 2.78–2.91 (m, 3 H), 3.87 (dd, J = 10.4, 8.6, 1 H), 3.91 (superimposed m, 1 H), 4.08 (q, J = 7.1, 2 H), 4.14 (t, J = 8.6, 1 H), 5.04–5.11 (m, 2 H), 5.41 (ddt, J = 16.2, 9.4, 6.6, 1 H); ^{13}C NMR δ 14.0 (CH_3), 23.6 (CH_3), 36.5 (CH_2), 48.4 (CH), 54.4 (CH), 57.6 (C), 62.4 (CH_2), 68.4 (CH_2), 121.8 (CH_2), 131.8 (CH), 167.8 (C=O), 173.9 (C=O). Anal. Calcd for $C_{12}H_{17}O_4Cl$: C, 55.28, H, 6.57; Cl, 13.59. Found: C, 55.28; H, 6.60; Cl, 13.50.

Ethyl 7-(chloromethyl)-6-methyl-3-oxa-2-oxobicyclo[3.3.0]octane-1-carboxylate (28b): IR 1774, 1738 cm^{-1}; ^{1}H NMR δ 0.95 (d, J = 7.1, 0.65 × 3 H), 1.01 (d, J = 7.3, 0.35 × 3 H), 1.21 (t, J = 7.1, 3 H), 1.6–2.8 (m, 5 H), 3.3–3.6 (m, 2 H), 4.04 (dd, J = 9.4, 2.8, 0.65 × 1 H), 4.16 (q, J = 7.1, 2 H), 4.24–4.45 (m, 0.35 × 2 H), 4.52 (dd, J = 9.4, 8.0, 0.65 × 1 H); ^{13}C NMR (major isomer) δ 13.6 (CH_3), 15.6 (CH_3), 35.5 (CH_2), 42.6 (CH), 52.3 (CH), 60.1 (C), 61.9 (CH_2), 71.79 (CH_2), 169.2 (C=O), 175.9 (C=O); (minor isomer) 12.8 (CH_3), 13.6 (CH_3), 35.8 (CH_2), 43.9 (CH), 44.4 (CH_2), 45.1 (CH), 54.4 (CH), 58.6 (C), 61.9 (CH_2), 69.7 (CH_2), 169.2 (C=O), the second C=O is not detected. Anal. Calcd for $C_{12}H_{17}O_4Cl$: C, 55.28; H, 6.57; Cl, 13.59. Found: C, 55.13; H, 6.60; Cl, 13.50.

Oxidation of 13c with Mn(OAc)$_3$LiCl. Treating **13c** (1 g, 4.16 mmol) led to 1.05 g of crude product. After column chromatography, 210 mg (conv 79%) of starting material, 82 mg of **28c** (as a 1:1 mixture of diastereoisomers), and 255 mg (37%) of **17c** were isolated successively.

Ethyl 7-(chloromethyl)-6,6-dimethyl-3-oxa-2-oxotetrahydrofuran-1-carboxylate (28c): IR 1776, 1738 cm^{-1}; ^{1}H NMR δ 0.81 (s, 0.5 × 3 H), 0.97 (s, 0.5 × 3 H), 1.14 (s, 0.5 × 3 H), 1.15 (s, 0.5 × 3 H), 1.32 (t, J = 7.1, 0.5 × 3 H), 1.33 (t, J = 7.1, 0.5 × 3 H), 1.95 (dd, J = 13.9, 12, 0.5 × 1 H), 2.05–2.38 (m, 2 H), 2.55 (AB part of a ABX, J_{AB} = 14, 0.5 × 2 H), 2.78 (d, J = 6.2, 0.5 × 1 H), 2.90 (dd, J = 8.3, 4, 0.5 × 1 H), 2.99 (dd, J = 13.9, 7.4, 0.5 × 2 H), 2.78 (d, J = 6.2, 0.5 × 1 H), 2.90 (dd, J = 8.3, 4, 0.5 × 1 H), 2.99 (dd, J = 13.9, 7.4, 0.5 × 1 H), 3.40 (dd, J = 10.8, 8.9, 0.5 × 1 H), 3.45 (t, J = 9, 0.5 × 1 H), 3.62 (dd, J = 9.5, 0.5 × 1 H), 3.64 (dd, J = 10.8, 4.9, 0.5 × 1 h), 4.27 (q, J = 7.1, 2 H), 4.27 (hidden m, 0.5 × 1 H), 4.33 (dd, J = 9.6, 4, 0.5 × 1 H), 4.50 (m, 1 H); ^{13}C NMR δ 14.0 (2 × CH_3), 15.7 (CH_3), 23.4 (CH_3), 23.7 (CH_3), 26.7 (CH_3), 35.7 (CH_2), 36.7 (CH_2), 43.8 (CH_2), 43.9 (2 × C), 44.1 (CH_2), 50.4 (CH), 53.2 (CH), 57.1 (CH), 58.0 (C), 58.3 (CH), 58.9 (C), 62.3 (CH_2), 62.4 (CH_2), 66.6 (CH_2), 68.0 (CH_2), 169.7 (C=O), 176.3 (C=O). Anal. Calcd for $C_{13}H_{19}O_4Cl$: C, 56.83; H, 6.97; Cl, 12.90. Found: C, 56.85; H, 6.88; Cl, 13.0.

Supplementary Material Available: ^{1}H NMR spectra of compounds **1a–c**, **13a–c**, **10b + 11b**, **11b**, **21b**, **22b**, **23b**, and **23c** and ^{13}C NMR spectrum of **21b** (13 pages). Ordering information is given on any current masterhead page.

Vinyl Radical Cyclizations: Synthesis of Substituted Bicyclooctanols

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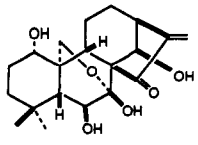
Received August 2, 1990

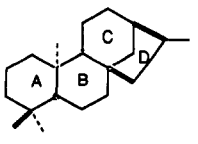
The preparation and free-radical bicyclic ring closure of 4-(2-bromo-2-propen-1-yl)cyclohexene **7** is described. The bicyclo[3.2.1] and -[2.2.2] alcohols **9** and **10** arising, respectively, from 5-*exo* and 6-*endo* (or 6-*exo*) modes of cyclization of a vinyl radical were isolated in a 1:1 ratio. Factors affecting the regiochemical outcome were investigated.

Introduction

Oridonin **1** is a member of a class of diterpenoids that have been isolated from various Rabdosia (Labiatae) species growing in China and Japan.[1] The *ent*-kaurane



1



2

structure **2** is a common feature of the majority of these diterpenoids. Its highly oxidized framework and its antitumor activity[1,2] make oridonin an attractive synthetic target. Our approach involves free-radical cyclization of a vinyl bromide for construction of the bicyclo[3.2.1]octanol derivative of the C/D subunit. This approach relies on precedent for intramolecular addition of vinyl radicals to carbon–carbion double bonds.[3-5]

(1) Fujita, E.; Node, M. *Diterpenoids of Rabdosia Species.* In Herz, W.; Grisebach, H.; Kirby, G. W.; Tamm, Ch. *Progress in the Chemistry of Natural Products*; Springer-Verlag: New York, 1984; Vol. 46, p 77.

(2) (a) Fuji, K.; Node, M.; Ito, N.; Fujita, E.; Takeda, S.; Unemi, N. *Chem. Pharm. Bull.* **1985**, *33*(3), 1038. (b) Node, M.; Sai, M.; Fuji, K.; Fujita, E. *Ibid.* **1983**, *31*(4), 1433.

(3) (a) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321 and references cited therein. See also: (b) Stork, G.; Mook, R., Jr. *Ibid.* **1983**, *105*, 3720. (c) Nozaki, K.; Oshima, K.; Utimoto, K.; **1987**, *109*, 2547. (d) Begley, M. J.; Ladlow, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1095. (e) Journet, M.; Samdja, W.; Malacria, M. *Syn. Lett.* **1990**, *320*.

(4) Marinovic, N. N.; Ramanathan, H. *Tetrahedron Lett.* **1983**, *24*, 1871.

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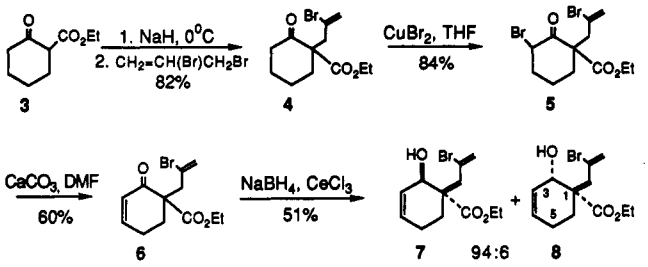
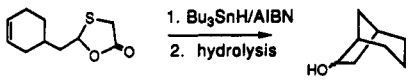
Scheme I

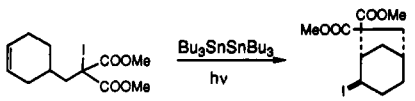


The regiochemical preference in the cyclization of vinyl radicals to form bicyclic structures parallels that of the alkyl analogues.[3] When both 5-*exo-trig* and 6-*endo-trig* modes of cyclization are possible, five-membered ring formation predominates. For instance, Yadav and Fallis[6] (eq 1) reported that radical cyclization of an oxathiolanone



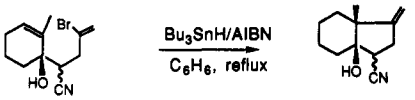
(1)

derivative of cyclohexene produced only the bicyclic [3.2.1] product. None of the [2.2.2] product was observed. Bicyclic ring closure by iodine atom transfer, performed by Curran,[7] also gave exclusively the 5-*exo* product (eq 2).



(2)

Similarly, Stork and Baine[3a] found that vinyl radical cyclization of an allylic alcohol also gave only the 5-*exo-trig* product (eq 3). On the basis of this, we anticipated that



(3)

allylic alcohol **7** would produce mainly the substituted bicyclo[3.2.1]octanol **9** via 5-*exo-trig* cyclization. We report the results of our studies, which indicate formation, however, of equal amounts of isomeric bicyclo[3.2.1]- and -[2.2.2]octanols **9** and **10**.

Results and Discussion

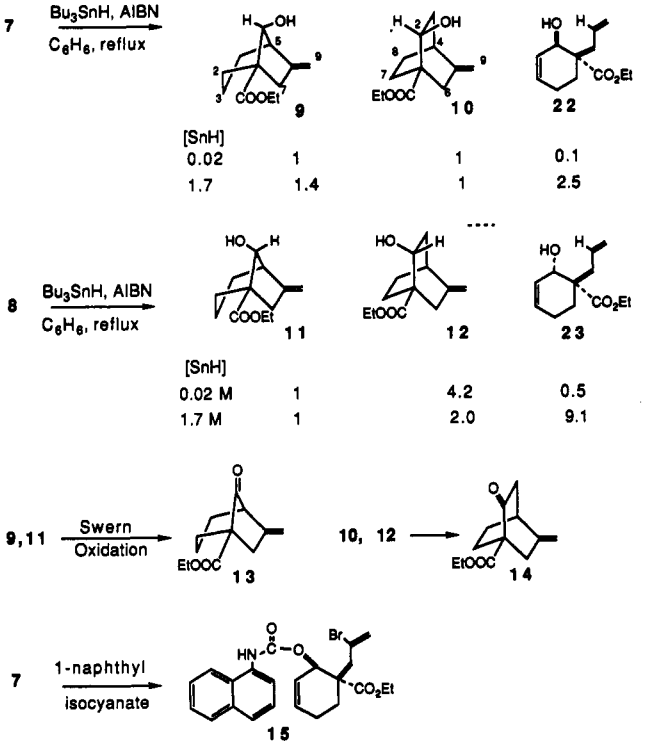
Our model studies involved investigation of the free-radical carbocyclization of allylic alcohol **7**. This was prepared as outlined in Scheme I.

Cyclization results are outlined in Scheme II. A benzene solution of tributyltin hydride (0.044 M) and a catalytic amount of azobisisobutyronitrile (AIBN) was added slowly to a refluxing solution of allylic alcohol **7** (0.025 M) in benzene. Cyclization produced a mixture of products **9** and **10** in a 1:1 ratio (determined by HPLC and GCMS with use of a carbowax column).

A combination of methods was used to assign the structures of **9** and **10**. Gross structures were determined on the basis of ^{1}H NMR data including 2D-COSY NMR splitting assignments. The IR spectra indicated hydroxyl (3554 and 3544 cm^{-1}) and *exo*-methylene functionalities (1654 and 1662 cm^{-1}) for **9** and **10**, respectively.

To obtain further structural evidence, the alcohols were oxidized to the corresponding ketones **13** and **14**. The infrared spectrum of **13** was characteristic of an ester and

Scheme II



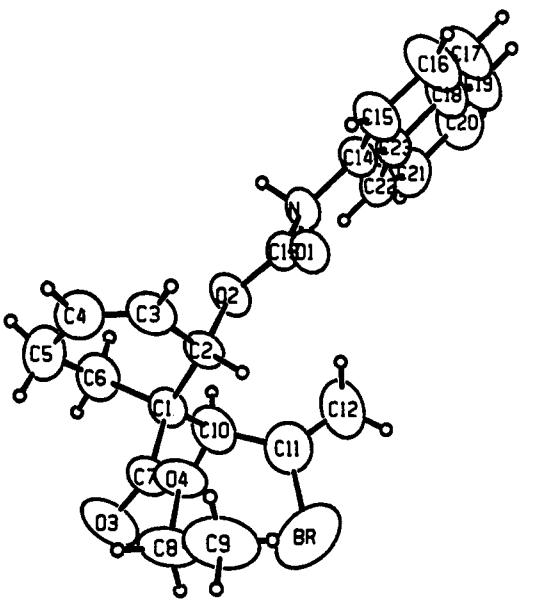
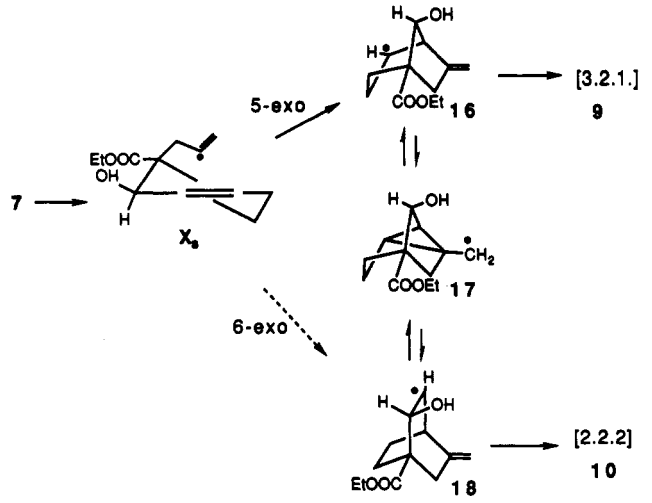


Figure 1. X-ray structure of compound **15**.

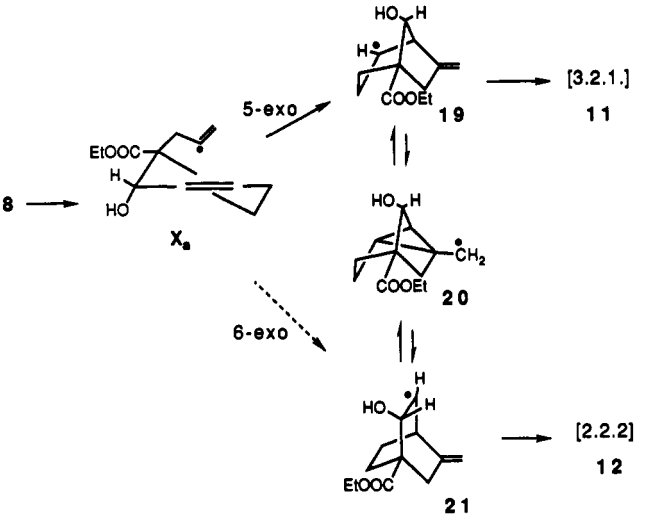
a five-membered ring ketone (1760, 1730 cm^{-1}), whereas **14** showed a single carbonyl stretch at 1740 cm^{-1}. ^{13}C NMR DEPT (distortionless enhancement by polarization transfer) spectra were determined to assign carbon multiplicities. A major structural difference between ketones **13** and **14** is the presence of a CHC=O subunit in **13** and a CH_2C=O subunit in **14**. Methine carbons appear in the DEPT spectra of **13** at δ 54 and of **14** at δ 38. Conversely, the methylene carbons of **13** are at δ 39, 38, 37, and 18, whereas those of **14** are at δ 44, 34, 26, and 25. The methine of **13** at δ 54 and the methylene of **14** at δ 44 are considered to be adjacent to carbonyl carbons, which cause a downfield shift of 10–14 ppm.[8] On the basis of these

(5) For reviews see: Curran, D. P. *Synthesis* **1988**, *417* and 489.
(6) Yadav, V.; Fallis, A.-G. *Tetrahedron Lett.* **1989**, *30*, 3283.
(7) Curran, D. P.; Chang, C. T. *J. Org. Chem.* **1989**, *54*, 3140.
(8) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; John Wiley & Sons: New York, 1981; p 267–269.

Scheme III



Scheme IV

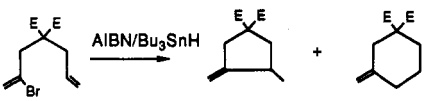


and the X-ray data discussed in the following text, we assigned the bicyclo[3.2.1]- and -[2.2.2]octanol structures to **9** and **10**, respectively.

We were interested in determining if the stereochemistry of the OH groups in the allylic alcohols affected the ratio of cyclization products. Consequently, the absolute configuration of alcohol **7** was determined by a single-crystal X-ray structure of its urethane derivative **15** (Figure 1). This revealed the OH group of the major alcohol epimer (**7**) to be cis to the allyl group. Free-radical cyclization of (minor) alcohol **8** produced bicyclo[3.2.1]octanol **11** and bicyclo[2.2.2]octanol **12** in the ratio of 1:4.2 (determined by HPLC and GCMS). Oxidation of [3.2.1] alcohol epimers **9** and **11** provided the same ketone **13** as evidenced by IR and GCMS data. Similarly, both [2.2.2] alcohols **10** and **12** afforded ketone **14**.

We considered the pathways by which the bicyclo[3.2.1] and -[2.2.2] alcohols could arise (Schemes III and IV). There are four possibilities: (1) 5-*exo-trig* ring closure of radical X_a from **7** can generate radical **16**, which could be trapped by a hydrogen atom donor to give [3.2.1] product **9** or rearrange via the cyclopropylcarbinyl radical **17** to [2.2.2] radical **18** and lead to a mixture of [3.2.1] and [2.2.2] products. (2) Similarly, cyclization by a 6-*exo-trig* pathway can also produce a mixture of products via radical **18**. Alternatively, there may be competition between 5-*exo-trig* and 6-*exo-trig* modes of cyclization (3) with or (4) without cyclopropylcarbinyl rearrangement. The ratio of products could be a reflection of the extent of each mode of cyclization, the ratio of the two intermediate radicals **16** and **18**, their rate of equilibration, and their relative rates of hydrogen atom capture.

In order to determine if rearrangement were taking place, the reaction was examined with use of varying concentrations of tributyltin hydride and the product ratios were determined by GCMS with use of a carbowax column. An increase in the concentration of stannane is expected to result in the capture of the initially formed bicyclic radical, thereby minimizing any rearrangement to **17**. (This procedure was suggested to us by Prof. D. Curran.) At concentrations of tin hydride between 0.017 and 0.028 M, the ratio of products **9** [3.2.1] and **10** [2.2.2] from allylic alcohol **7** remained at 1:1. Use of 1.7 M tin hydride only increased the ratio of **9** to **10** to 1.4, and **22** (reduced **7**) was also formed in moderate yield (**22**:**9**:**10** 2.5:1.4:1). This contrasts with the results of Stork[9] (eq 4) in which the ratio of 5-*exo* to 6-*endo* product for formation of monocyclic products was found to increase substantially with stannane concentration.



				[Bu_3SnH]
	3	:	1	0.02 M
	97	:	1	1.7 M

(4)

At 1.7 M stannane concentration, allylic alcohol **8** gave the reduced starting material **23** and cyclized products **11** and **12** in the ratio of 9:1:2.

These data are consistent with the first alternative mechanism, if interpreted as follows. Studies summarizing the regiochemistry of radical reactions[5] conclude that ring closures that proceed by the 5-*exo-trig* mode occur more often than those employing the 6-*endo* (or 6-*exo*) mode. Vinyl radical additions to alkenes result in the formation of homoallylic radicals that may rearrange unimolecularly at very rapid rates (10^5–10^8)[9,10] via cyclopropylcarbinyl radicals.[9,10] Hydrogen atom transfer to alkyl radicals by tin hydrides is a second-order reaction and occurs at 0.74 × 10^6 for cyclohexyl radicals.[11] Consequently, 1.7 M Bu_3SnH is sufficient to capture the initially formed bicyclic radicals (**16** and **19**) at a rate that may be competitive with rearrangement, but 0.025 M Bu_3SnH is not. One may then assume the following: (1) All bicyclic radicals, once formed, rearrange rapidly via a cyclopropylcarbinyl intermediate (e.g., **17**). (2) At equilibrium (low Bu_3SnH concentration), the concentrations of **16** and **18** (from **7**) are equal, as are those of **19** and **21** (from **8** via X_a, Scheme III). The calculated[12] enthalpies of formation of **9**–**12** vary by no more than 1 kcal. (3) Tin hydride capture of radicals **16** and **18** proceeds at similar rates, but the reaction of **19** is slower than that of **21** due to steric congestion caused by the *syn*-hydroxyl group of **19**. Thus, the ratio of **9** to **10** would be close to 1, while that of **12** to **11** should be greater than 1.4. The rate of equilibration of **19** and **21** (via **20**) is slower than the rate of equilibration of **16** and **18** (via **17**). If this were true, then a change to a high Bu_3SnH

(9) Stork, G.; Mook R., Jr. *Tetrahedron Lett.* **1986**, *27*, 4529.

(10) (a) Beckwith, A. L. J.; O'Shea, D. M. *Tetrahedron Lett.* **1986**, *27*, 4525. (b) Beckwith, A. L. J.; Bowry, V. W. *J. Org. Chem.* **1989**, *54*, 2681. (c) Newcomb, M.; Glenn, A. G.; Williams, W. G. *Ibid.* **1989**, *54*, 2675.

(11) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739.

(12) **9** (-135 kcal/mol); **10** (-134 kcal/mol); **11** (-134 kcal/mol); **12** (-134 kcal/mol). Enthalpies of formation were calculated by use of PCMODEL, an MM2 program based on W. C. Still's, as modified by P. Gajewski et al. (Serena Software, Bloomington, IN).

concentration could increase the ratio of **11** to **12** (e.g., from 1:4.2 to 1:2), due to competitive capture of the radical (**19**), initially formed by 5-*exo-trig* ring closure but have little effect on the ratio of **9** to **10** (which changed from 1.0 to 1.4). We can offer, however, no rationale for why the rearrangements would proceed at different rates. Note: these data are also consistent with formation of *only* **16** (and **19**) from the initial vinyl radical X_a (X_a), *both* **16** and **18** (**19** and **21**), but *not* **18** (**21**) alone. If the ratio of products were determined only by the relative rates of formation (and capture) of **16** and **18** (or **19** and **21**), with no intervening rearrangement, then the product ratios should not vary with tin hydride concentration.

Finally, the rate constant for cyclization of a vinyl radical is the same order of magnitude as that or hydrogen abstraction from stannane by a vinyl radical (3×10^8).[5] At high tin hydride concentrations (1.7 M), cyclization is therefore accompanied by reduction of X_a to **22** and X_s to **23**. The larger effect on X_s (**23**:**11** + **12** = 9:3; **22**:**9** + **10** = 2.5:2.4) could mean that X_s closes faster to **16** than X_a closes to **19**.

Experimental Section

General Methods. Melting points were determined in open capillaries and are uncorrected. GCMS analyses were performed with a cross-linked methyl silicone column. For separation of polar compounds, a carbowax column was used. Analytical HPLC was conducted with two 4 mm × 30 cm μ-Porasil silica columns in series and a differential refractometer. Preparative HPLC separations were performed with use of a 8 mm × 10 cm column with a μ-Porasil radial PAK 8-mm cartridge.

Flash chromatography was performed according to the method described by W. C. Still[13] with silica gel 60 (230–400 mesh). Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. CH_2Cl_2, benzene, and DMF were distilled over CaH_2 and stored over molecular sieves. Other solvents were used as purchased.

Ethyl 1-(2-Bromo-2-propenyl)-2-oxocyclohexanecarboxylate (4). To a suspension of NaH (4.8 g of 97% solid, 0.20 mol) in 150 mL of dry *N,N*-dimethylformamide (DMF)[14] at 0 °C was added a solution of ethyl 2-oxocyclohexanecarboxylate (34.0 g, 0.200 mol) in 50 mL of dry DMF under a N_2 atmosphere. After the mixture was stirred for 1 h, 40 g (0.20 mol) of 2,3-dibromopropene in 50 mL of DMF was added and stirring was continued at room temperature overnight. The mixture was poured into ice–water (50 mL) and extracted with ether (3 × 25 mL). The combined ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Distillation of the residue afforded 47.3 g (82%) of **4** as a colorless liquid: bp 115 °C (0.5 Torr); FTIR (CCl_4) 2981, 2942, 2867, 1718, 1656, 1624 cm^{-1}; ^1H NMR (200 MHz) δ 1.29 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.63 (m, 4 H), 2.15 (m, 2 H), 2.43 (dd, J = 4.7 Hz, 5.4, 2 H, $CH_2CH_2C{=}O$), 2.79, 3.21 (AB q, J = 15.0 Hz, $CH_2C(Br){=}CH_2$), 4.22 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.55 (s, 1 H, $C(Br){=}CH_2$), 5.62 (s, 1 H, $C(Br){=}CH_2$); GCMS, m/z (relative intensity) 245 (1.5), 243 ($M^+ - OCH_2CH_3$, 1.7), 209 (85), 163 (69), 137 (100). Anal. Calcd for $C_{12}H_{1}37BrO_3$: C, 49.87; H, 5.88; Br, 27.64. Found: C, 49.52; H, 5.94; Br 27.56.

Ethyl 3-Bromo-1-(2-bromo-2-propenyl)-2-oxocyclohexanecarboxylate (5). A mixture of 6.0 g (0.02 mol) of ketone **4** and 9.0 g (0.04 mol) of $CuBr_2$[15] dissolved in 100 mL of dry THF was stirred at room temperature for 2 days, during which time a white solid precipitated. The mixture was filtered, and the filtrate was diluted with water (50 mL) and extracted with chloroform (3 × 25 mL). The combined organic layers were washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Distillation afforded 6.41 g (84%) of **5** (as a mixture of isomers) as an oil: bp 130–135 °C (1.0 Torr); FTIR (CCl_4) 2980, 2940, 2871, 1731, 1624 cm^{-1}; ^1H NMR (200 MHz) δ 1.30 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.57 (m, 1 H), 1.92 (m, 3 H), 2.66 (m, 2 H), 2.87, 3.26 (AB q, J = 15.0 Hz, $CH_2C(Br){=}CH_2$), 4.25 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 4.76 (dd, J = 5.9 Hz, 6.3, 1 H, $CHBrC{=}O$), 5.58 (s, 1 H, $CH_2{=}$), 5.67 (s, 1 H, $CH_2{=}$); GCMS m/z (no M^+), 289 ($M^+ - Br$, 25), 217 (30.1), 215 ($M^+ - Br - COOEt$, 32.9), 135 ($M^+ - 2Br - COOEt$, 100). Anal. Calcd for $C_{12}H_{16}Br_2O_3$: C, 39.17; H, 4.35. Found: C, 39.55; H, 4.55.

Ethyl 1-(2-Bromo-2-propenyl)-2-oxo-3-cyclohexenecarboxylate (6). A mixture of bromo ketone **5** (3.0 g, 8.2 mmol) and $CaCO_3$[16] (2.0 g, 20 mmol) in 30 mL of dry DMF was heated at 120 °C overnight (18 h). The mixture was cooled and filtered. The filtrate was diluted with 30 mL of water and extracted with ether (3 × 25 mL). The ether was washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification of the crude product by flash chromatography (5:1 hexane–ethyl acetate) provided 1.42 g of **6** as an oil (60%): FTIR (CCl_4) 3036, 2981, 2930, 2869, 1734, 1686, 1624 cm^{-1}; ^1H NMR (200 MHz) δ 1.25 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 2.05 (m, 1 H), 2.45 (m, 1 H), 2.65 (m, 2 H), 3.01, 3.28 (AB q, J = 14.9 Hz, $CH_2C(Br){=}CH_2$), 4.18 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.58 (s, 1 H, $C(Br){=}CH_2$), 5.69 (s, 1 H, $C(Br){=}CH_2$), 6.05 (dd, J = 10.2, 0.9 Hz, 1 H, $CH{=}CHC{=}O$), 6.96 (m, 1 H, $CH{=}CHC{=}O$); GCMS m/z (no M^+), 243 (3), 241 ($M^+ - OEt$, 3), 207 ($M^+ - Br$, 72), 133 ($M^+ - Br - COOEt$, 53), 68 (100). Anal. Calcd for $C_{12}H_{15}BrO_3$: C, 50.22; H, 5.23. Found: C, 50.25; H, 5.43.

Ethyl 1-(2-Bromo-2-propenyl)-2-hydroxy-3-cyclohexenecarboxylate (7, 8). To a solution of enone **6** (12.0 g, 42.0 mmol) and $CeCl_3 \cdot 7H_2O$[17] (15.7 g, 42.0 mmol) in 150 mL of methanol was added $NaBH_4$ (1.59 g, 42.0 mmol) in 60 mL of methanol at 0 °C. The mixture was stirred for 2 h at room temperature, then diluted with ice–water (50 mL), acidified with 1.0 N HCl, and extracted with ether (3 × 30 mL). The organic layer was washed with water and brine, dried ($MgSO_4$), and evaporated under reduced pressure to afford 10.55 g of an oil. Flash chromatography (5:1 hexane–ethyl acetate) provided 5.38 g of **7** (45%) and 0.73 g of **8** (6%) (51% overall yield). GCMS analysis of the crude product on a carbowax column showed that the alcohols were in the ratio of 94:6. **7**: FTIR (CCl_4) 3529, 3033, 2981, 2935, 2870, 1731, 1624 cm^{-1}; ^1H NMR (200 MHz) δ 1.29 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.99 (m, 4 H, CH_2CH_2), 2.63 (br s, 1 H, OH), 2.74, 3.09 (AB q, J = 14.9 Hz, 2 H, $CH_2CBr{=}CH_2$), 4.18 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 4.46 (d, J = 1.8 Hz, 1 H, CHOH), 5.54 (d, J = 14.4 Hz, 1 H, $CH{=}CH$), 5.65 (dd, J = 14.2, 3.2 Hz, 1 H, $CH{=}CH$); 5.74 (s, 1 H, $CBr{=}CH_2$); 5.79 (s, 1 H, $CBr{=}CH_2$); GCMS m/z (no M^+), 270 ($M^+ - H_2O$, 0.1), 221 (14.14), 219 (14.50), 209 ($M^+ - Br$, 100), 163 ($M^+ - Br - EtOH$, 47), 135 (35), 111 (68), 91 (34), 79 (45). Anal. Calcd for $C_{12}H_{17}BrO_3$: C, 49.87; H, 5.88; Found: C, 49.07; H, 6.05. **8**: FTIR (CCl_4) 3603, 3516, 3032, 2980, 2927, 2848, 1739, 1624 cm^{-1}; ^1H NMR (200 MHz) δ 1.28 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.9 (m, 1 H, H-6_{ax}), 2.15 (m, 3 H, H-$5_{a,b}$, H-6_{eq}), 2.73, 2.95 (AB q, J = 14.7 Hz, 2 H, $CH_2Br{=}CH_2$), 2.99 (br s, 1 H, OH), 4.11 (br s, 1 H, CHOH), 4.21 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.56 (dd, J = 15.6, 1.54 Hz, 1 H, $CH{=}CH$), 5.65 (d, J = 15.6 Hz, 1 H, $CH{=}CH$), 5.79 (s, 1 H, $CBr{=}CH_2$), 5.80 (s, 1 H, $CBr{=}CH_2$); GCMS m/z (no M^+), 221 (22), 219 (21), 209 (51), 163 (44), 135 (31), 111 (100), 91 (50), 79 (57). Anal. Calcd for $C_{12}H_{17}BrO_3$: C, 49.87; H, 5.88; Br, 27.64. Found: C, 49.37; H, 5.64; Br, 27.46.

Radical Cyclization[4] of Allylic Alcohol 7. To a refluxing solution of allylic alcohol **7** (0.28 g, 1 mmol) in 40 mL of dry benzene was added during 1 h tributyltin hydride (0.25 mL, 1.1 mmol) and AIBN (10 mg) dissolved in 25 mL of benzene. Heating was continued for an additional 1 h. After removal of the solvent under reduced pressure, the residue was dissolved in ether (25 mL) and stirred with saturated aqueous KF (20 mL) for 2 h, and the white precipitate of tributyltin fluoride was filtered. The filtrate was extracted with ether (3 × 25 mL), washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by flash chromatography (5:1 hexane–ethyl acetate) to afford 0.16 g of a mixture of **9** and **10** (80%) as an oil. A portion of the purified product mixture was separated by HPLC to afford **9** (17.3 mg) and **10** (18.7 mg). The approximate 1:1 ratio of products was confirmed by GCMS analysis of the crude product with use of a carbowax

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column. The ratio found was **9:10** = 0.996:1.000. ***syn*-Ethyl 8-hydroxy-6-methylenebicyclo[3.2.1]octane-1-carboxylate (9)**: FTIR (CCl_4) 3544, 3073, 2982, 2941, 2860, 1735, 1662 cm^{-1}; ^1H NMR (300 MHz) δ 1.29 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.67 (m, 5 H) 1.92 (m, H-2_{ax}), 2.46, 2.88 (AB q, J = 17.0 Hz, $CH_2C{=}CH_2$), 2.73 (s, H-5), 2.88 (d, J = 17.0 Hz, 1 H, H-7_a), 2.99 (s, 1 H, OH), 3.95 (s, 1 H, CHOH), 4.22 (q, J = 7.0 Hz, 2 H, CH_2CH_3), 5.03 (s, 2 H, C=CH_2); GCMS m/z 210 (M^+, 8), 119 ($M^+ - CO_2Et - H_2O$, 100), 91 (59), 79 (35); HRMS calcd for $C_{12}H_{17}O_3$ (M - H) 209.1178, found 209.1140. ***syn*-Ethyl 2-hydroxy-5-methylenebicyclo-[2.2.0]octane-1-carboxylate (10)**: FTIR (CCl_4) 3554, 3072, 2982, 2939, 2869, 1734, 1654 cm^{-1}; ^1H NMR (300 MHz) δ 1.31 (t, J = 7.0 Hz, 3 H, CH_2CH_3), 1.60 (m, 4 H, CH_2CH_2), 1.90 (m, H-7_b), 2.22 (ddd, J = 13.4, 9.8, 2.9 Hz, H-7_a), 2.35 (t, J = 2.7, H-4), 2.47 (dd, J = 16.8, 1.6, H-6_b), 2.89 (dd, J = 16.6, 2.2, H-6_a), 2.91 (d, J = 2.6, 1 H, OH), 4.20 (q, J = 7.0, 2 H, CH_2CH_3), 4.28 (d, J = 1.3, 1 H, CHOH), 4.72 (d, J = 1.4, 1 H, C=CH_2), 4.84 (d, J = 1.4, 1 H, C=CH_2); GCMS m/z 210 (M^+, 4.9), 119 ($M^+ - CO_2Et - H_2O$, 70.1), 91 (100), 79 (22); HRMS calcd for $C_{12}H_{17}O_3$ (M - H) 209.1178, found 209.1172.

Cyclizationn of Alcohol 7 under Varying Concentrations of Tributyltin Hydride. The previous procedure for radical cyclization of alcohol **7** was repeated with use of the following: (1) alcohol **7** (0.5 g, 1.7 mmol) dissolved in 85 mL of benzene, with tributyltin hydride (0.67 mL, 2.55 mmol) and 15 mg of AIBN dissolved in 25 mL of benzene, and (2) alcohol **7** (0.2 g, 0.69 mmol) dissolved in 30 mL of benzene, tributyltin hydride (0.36 mL, 1.38 mmol) and 15 mg of AIBN dissolved in 20 mL of benzene. GCMS analysis of the reaction mixture indicated that the products **9** and **10** were in the ratio of 1:1.

Radical Cyclization of Alcohol 7 under High Tributyltin Hydride Concentration. To a refluxing solution **7** (0.10 g, 0.347 mmol) in 8 mL of benzene was added a solution of tributylin hydride (4.5 mL, 0.017 mol) and AIBN (10 mg) dissolved in 2 mL of benzene. Heating was continued for an additional 1 h. Excess tributyltin hydride was distilled off under reduced pressure, leaving 0.15 g of crude product. GCMS analysis of the residue showed a mixture of products **22**, **9**, and **10** (retention times: 28.6, 31.1, and 30.4 min, respectively) in a ratio of 2.5:1.4:1. Compound **22** was identified as the reduced starting material by comparison of the GCMS data with that of **23** (vide infra): GCMS m/z 210 (M^+, 0.3), 169 (M^+ - allyl, 37), 151 ($M^+ - H_2O$ - allyl, 26), 141 (67), 119 ($M^+ - H_2O$ - COOEt, 36), 113 (74), 95 (100), 79 (52).

Urethane Derivative of Allylic Alcohol 7. The allylic alcohol **7** (0.2g, 0.69 mmol) and freshly distilled 1-naphthyl isocyanate (0.12 mL, 0.87 mmol) were mixed and heated under N_2 at 60–70 °C for 2.5 h. After the mixture was cooled to room temperature, 4 mL of petroleum ether (30–60) was added and the mixture was boiled for 1 min and then filtered. The filtrate was cooled in ice to allow crystallization to take place and afforded 0.12 g of **15** (37%) as white crystals. Recrystallization from CCl_4–hexane (1:3) gave crystalline needles (mp 106–107 °C) that were suitable for X-ray analysis: FTIR (CCl_4) 3444, 3045, 2984, 2932, 1738, 1625, 1531 cm^{-1}; ^1H NMR (200 MHz) 1.25 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.62 (m, 1 H), 2.15 (m, 3 H), 2.75, 2.99 (AB q, J = 15.1 Hz), 4.16 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.55 (s, 1 H, CHO–), 5.58 (dd, J = 13.9, 1.8 Hz, 1 H, CH=CH), 5.65 (d, J = 13.7 Hz, 1 H, CH=CH), 5.97 (s, 1 H, CBr=CH_2), 5.98 (s, 1 H, CBr=CH_2), 6.95 (br s, 1 H, NH), 7.73 (m, 7H); GCMS m/z 378 (M^+ - Br, 2), 334 (10), 143 (100), 91 (5), 79 (45); HRMS calcd for $C_{23}H_{23}BrNO_4$ (M - H) 456.0889, found 456.0810.

X-ray Analysis of 15. The crystals were triclinic, space group $P21/C$ with a = 21.596 (20) Å, b = 11.169 (0) Å, c = 9.405 (0) Å for $C_{23}H_{24}BrNO_4$. A crystal measuring 0.20 × 0.20 × 6.0 mm was used for data collection. The structure was solved by direct methods using 3767 reflections. The *N*-naphthylcarbamoyloxy group proved to be cis to the 2-bromo-2-propenyl group.

Swern Oxidation[18] of the Mixture of 9 and 10. To a solution of oxalyl chloride (0.18 mL, 2.34 mmol) in 5 mL of dry CH_2Cl_2 maintained at –78 °C was added a solution of dimethyl sulfoxide (DMSO, 0.3 mL, 3.9 mmol) in 10 mL of CH_2Cl_2, and the mixture was stirred for 2 min. The mixture of alcohols **9** and **10** (0.4 g, 1.90 mmol) in 10 mL of CH_2Cl_2 was added during 5 min. Stirring was continued for 45 min, and then triethylamine (1.2 mL, 9.4 mmol) was added. After 5 min, the mixture was allowed to warm to room temperature, water (25 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The organic layer was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography of the crude product (5:1 hexane–ethyl acetate) gave **13** (0.1568 g, 40%) and **14** (0.1400 g, 35%) as pale yellow oils. **Ethyl 6-methylene-8-oxo-bicyclo[3.2.1]octane-1-carboxylate (13)**: FTIR (CCl_4) 3070, 2950, 1758, 1729, 1661, 1447, 1367, 1290 cm^{-1}; ^1H NMR (300 MHz) δ 1.28 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.68 (m, H-3_{eq}), 1.85 (m, H-4_{eq}), 2.10 (m, 3 H, H-2_{eq}, -3_{ax}, -4_{ax}), 2.36 (m, H-2_{ax}), 2.73 (dd, J = 17.4, 2.1 Hz, H-7_b), 2.97 (m, H-5), 3.29 (dd, J = 17.4, 2.5 Hz, H-7_a), 4.21 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.05 (s, 2 H, C=CH_2); ^{13}C NMR (300 MHz) DEPT δ 14 (CH_3), 18 (CH_2), 37 (CH_2), 39 (CH_2), 40 (CH_2), 54 (CH), 59 (quaternary C), 61 (OCH_2), 108 (=CH_2), 143 (C=CH_2), 171 (C=OO), 213 (C=O); GCMS m/z 208 (M^+, 6), 163 (M^+ - OEt, 26), 162 (M^+ - HOEt, 100), 135 (M^+ - COOEt, 5), 107 (44), 91 (43), 79 (36); HRMS calcd for $C_{12}H_{17}O_3$ (M + H) 209.1178, found 209.1169. **Ethyl 5-methylene-2-oxobicyclo-[2.2.0]octane-1-carboxylate (14)**: FTIR (CCl_4) 3073, 2940, 1741, 1660, 1467 cm^{-1}; ^1H NMR (300 MHz) δ 1.28 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.89 (m, 3 H, H-2_b, H-$3_{a,b}$), 2.34 (m, H-2_a), 2.41 (d, J = 2.8 Hz, 2 H, H-7), 2.64 (dd, J = 17.8, 2.1 Hz, H-6_b), 2.73 (t, J = 2.8 Hz, H-4), 2.99 (dd, J = 17.8, 2.5 Hz, H-6_a), 4.23 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 4.81 (s, 1 H, C=CH_2), 4.96 (s, 1 H, C=CH_2); ^{13}C NMR (300 MHz) DEPT δ 15 (CH_3), 25 (CH_2), 26 (CH_2), 34 (CH_2), 38 (CH), 44 (CH_2), 56 (quaternary C), 61 (OCH_2), 108 (=CH_2), 145 (C=CH_2), 170 (C=OO), 210 (C=O); GCMS m/z 208 (M^+, 27), 163 (M^+ - OEt, 45), 162 (M^+ - HOEt, 56), 135 (M^+ - COOEt, 58), 107 (76), 93 (100), 91 (99), 79 (48). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.30; H, 7.77.

Oxidation of Alcohols 9 and 10. Alcohol **9** (3.5 mg, 0.016 mmol) and alcohol **10** (6.7 mg, 0.032 mmol) were oxidized separately according to the procedure described previously with use of oxalyl chloride (59 μL, 0.63 mmol), DMSO (100 μL, 1.3 mmol), and triethylamine (0.42 mL, 2.9 mmol). The GCMS and IR data of the corresponding ketones isolated are identical with those obtained for **13** and **14**, respectively.

Cyclization of Allylic Alcohol 8. A solution of alcohol **8** (0.1214 g, 0.4215 mmol) in 20 mL of dry benzene and a solution of tributyltin hydride (0.12 mL, 0.4637 mmol) and 10 mg of AIBN in 10 mL of benzene were combined as previously for alcohol **7**. After removal of the solvent, GCMS analysis of the crude reaction product mixture showed two components with M^+ of 210 in the ratio of 4.2:1. The crude product was purified by flash chromatography to remove excess tributyltin hydride. A portion of the crude product was further separated by HPLC to afford **11** (2.9 mg, 3.3%) and **12** (11.7 mg, 13.3%). ***anti*-Ethyl 8-hydroxy-6-methylenebicyclo[3.2.1]octane-1-carboxylate (11)**: FTIR (CCl_4) 3568, 3072, 2981, 2940, 2869, 1714, 1661, 1464, cm^{-1}; ^1H NMR (200 MHz) δ 1.26 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.61 (m, 4 H, CH_2CH_2), 1.73 (s, 2 H, CH_2), 2.10 (m, H-5), 2.56 (d, J = 1.9 Hz, 2 H, H-$7_{a,b}$), 2.69 (br s, 1 H, OH), 4.12 (q, J = 7.2 Hz, 3 H, CH_2CH_3, 4.12 (s, CHOH), 4.88 (br s, 1 H, C=CH_2), 4.94 (br s, 1 H, C=CH_2); GCMS m/z 210 (M^+, 8), 119 ($M^+ - CO_2Et - H_2O$, 100), 91 (52), 79 (35). ***anti*-Ethyl 2-hydroxy-5-methylene-bicyclo[2.2.2]octane-1-carboxylate (12)**: FTIR (CCl_4) 3468, 3069, 2938, 2869, 1715, 1653, 1447 cm^{-1}; ^1H NMR (200 MHz) δ 1.51 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.90 (m, 4 H, CH_2CH_2), 2.30 (m, 2 H, CH_2CHOH), 2.46 (dt, J = 18.1, 2.7 Hz H-6_a), 2.56 (m, H-4), 2.87, (dt, J = 18.1, 2.7 Hz, H-6_b), 3.49 (br s, OH), 4.36 (s, 1 H, CHOH), 4.40 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 4.90 (d, J = 1.7 Hz, 1 H, C=CH_2), 5.04 (d, J = 1.7 Hz, 1 H, C=CH_2); GCMS m/z 210 (M^+, 6), 119 ($M^+ - CO_2Et - H_2O$, 71), 93 (100), 91 (89), 79 (35).

Radical Cyclization of Alcohol 8 under High Tributyltin Hydride Concentration. Alcohol **8** (100 mg, 0.347 mmol) in 8 mL of benzene was reacted with a solution of tributyltin hydride (4.5 mL, 0.017 mol) and AIBN (10 mg) in 2 mL of benzene according to the procedure described for **7**. After removal of the solvent, GCMS analysis of the residue showed that the mixture contained the reduced starting material **23** (ethyl 1-allyl-2-hydroxy-3-cyclohexenecarboxylate) with **12** and **11** in the ratio of 9.1:2:1. (Retention times 28.58, 29.81, and 30.99 min, respectively.) Separation by HPLC afforded **Ethyl 1-allyl-2-**

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hydroxy-3-cyclohexenecarboxylate (23) as an oil: IR (CCl_4) 3500, 3080, 3040, 2980, 1740, 1640 cm^{-1}; ^1H NMR (200 MHz) δ 1.26 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.99 (m, 1 H), 2.06 (m, 3 H), 2.32 (dd, J = 13.8, 7.9 Hz, 1 H, $CH_2CH{=}CH_2$), 2.44 (dd, J = 13.8, 7.3 Hz, 1 H, $CH_2CH{=}CH_2$), 3.05 (d, J = 8.6 Hz, 1 H, OH), 4.10 (d, J = 7.6 Hz, 1 H, CHOH), 4.19 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.06 (d, J = 11.9 Hz, 1 H, CH=CH), 5.08 (dd, J = 11.9, 3.6 Hz, 1 H, CH=CH), 5.78 (m, 3 H, $CH{=}CH_2$); GCMS m/z 210 (M^+) 169 (M^+ - allyl, 13), 151 ($M^+ - H_2O$ - allyl, 22), 141 (75), 119 ($M^+ - H_2O$ - COOEt, 38), 113 (98), 95 (100), 79 (51).

Oxidation of the Alcohols 11 and 12. The mixture of alcohols 11 and 20 (30 mg, 0.1428 mmol) was oxidized by the Swern procedure with oxalyl chloride (59 μL, 0.65 mmol), DMSO (100 μL, 1.30 mmol), and triethylamine (0.42 mL, 3.0 mmol). A portion of the product mixture was separated by HPLC to give 13 (1.5 mg, 5%) and 14 (3.2 mg, 11%). These products were identical with those obtained by the oxidation of alcohols 9 and 10 as shown by the identity of IR and GCMS spectra.

Oxidation of Alcohol 12. Alcohol 12 (11.7 mg, 0.057 mmol) was oxidized with oxalyl chloride (11.2 μL, 0.12 mmol), DMSO (19 μL, 0.25 mmol), and triethylamine (80 μL, 0.56 mmol). The GCMS and IR data of the isolated ketone are identical with those of ketone 14.

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Supplementary Material Available: X-ray crystallography material for urethane 15 (10 pages). Ordering information is given on any current masthead page.

Total Synthesis of Dehydroambliol-A and Its Unnatural *Z* Isomer†

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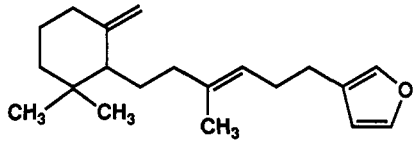
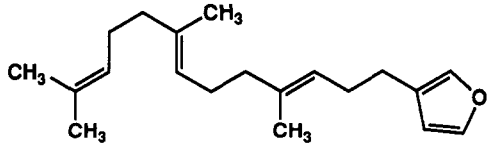
Convergent total syntheses of dehydroambliol-A (1a), its unnatural *Z* isomer 1b, and ambliofuran (2) are described. The syntheses utilized 2-(3′-furyl)-1,3-dithiane (6) as a common intermediate. Analysis of their proton and carbon magnetic resonance spectra confirm that in the natural product dehydroambliol-A and in synthetic dehydroambliol-A the Δ^7-bond possesses the *E* geometry, while in the unnatural isomer of dehydroambliol-A, the Δ^7-bond is of the *Z* configuration.

The isolation and structure elucidation of several metabolites from the class of marine sponge known as *Dysidea amblia* has been reported.[1] By use of a combination of spectroscopic and degradative chemical studies, a diterpenoid-based structure was suggested for dehydroambliol-A (1) and ambliofuran (2).



Dehydroambliol-A (1)

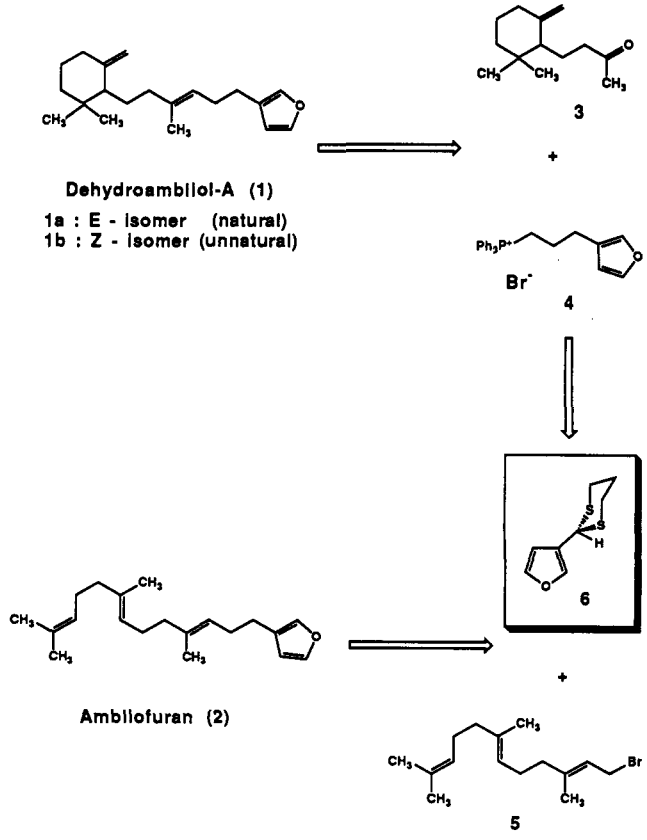
1a : E - isomer (natural)
1b : Z - isomer (unnatural)



Ambliofuran (2)

Although a synthesis of ambliofuran (2) has been reported recently,[2] the total synthesis of dehydroambliol-A (1) has not been described. We wish to report the synthesis of the natural product dehydroambliol-A (1a) and its unnatural Z isomer 1b. In addition, an alternative synthesis of ambliofuran (2) is described.

Scheme I. Retrosyntheses of Dehydroambliol-A (1) and Ambliofuran (2)



† This work was abstracted from the thesis research of C.V.M. presented to the Graduate School of Rutgers University in partial fulfillment of the requirements of the Ph.D. degree.

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