Reaction of Cyclic α-Hydroxy Epoxides with a Strong Base: A New 1,2-Rearrangement, Evidence for a Carbenoid Pathway

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Received January 30, 1995[⊗]

Abstract: Several substituted five- and six-membered cyclic α,β-unsaturated ketones are readily available by treatment of the corresponding α-hydroxy epoxides with an organolithium reagent. The reaction involves a new carbenoid 1,2-alkyl rearrangement. Evidence for the carbenoid intermediate has been obtained by an intramolecular trapping of the highly reactive species.

1. Introduction

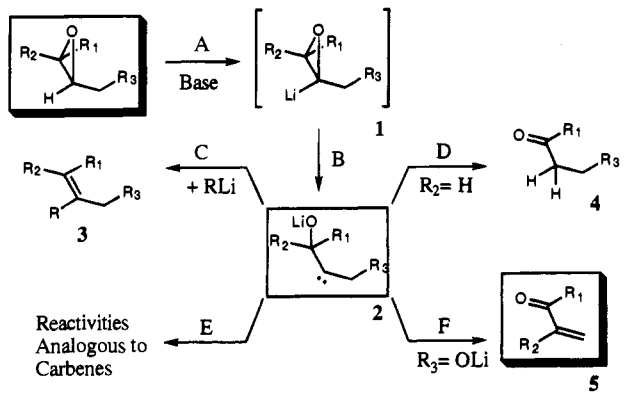
Epoxides in the presence of a strong base can exhibit many reactivities,[1] among which is the metalation of the oxirane ring (Scheme 1, path A). This highly reactive species **1** easily undergoes α-elimination (path B) leading to a carbenoid **2**.[2] An alkyllithium insertion followed by Li_2O elimination allows the stereospecific synthesis of olefins **3** (path C),[3] but the carbenoid **2** might also undergo carbene like reactivities (dimerizations,[4] C−H insertions,[5] cycloadditions[6]) (path E). While hydride migration furnishes isomerized ketone **4** (path D),[7] we report here the first example of an intramolecular alkyl 1,2-rearrangement, proceeding *via* a carbenoid stemmed from a metalated oxirane which leads to an α,β-unsaturated ketone **5** (R_3 = OLi) (path F).

2. Results and Discussion

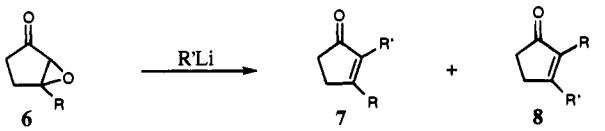
Hydride and carbon 1,2-shifts are classical intramolecular carbene reactions[8] which have recently stimulated much theoretical[9] and synthetic[10] interests, but only little is known about epoxide derived carbenoids.

We have observed, that, when treated with a 3-fold excess of an organolithium reagent, the cyclopentenone oxide[11] **6** leads, with good yields, to a mixture of two products **7** and **8** (Scheme 2).

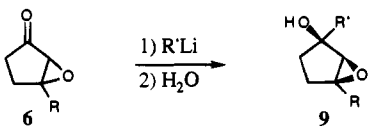
Scheme 1



Scheme 2



Scheme 3



We also noticed that, if the reaction is quenched after 10 min at −78 °C, the *syn* epoxy alcohol **9** is obtained regiospecifically with excellent diastereofacial selectivity[12] (>20: 1) (Scheme 3). Furthermore, when **9** was subjected to react with an excess of *n*-BuLi, the α,β-unsaturated ketones **7** and **8** were obtained within the same ratio.

The reaction mechanism is illustrated for the synthesis of the known dihydrojasmone[13] **14** and its regioisomer **16** (Scheme

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[⊗] Abstract published in *Advance ACS Abstracts,* December 1, 1995.

(1) Yandovskii, V. N.; Ershov, B. A. *Russ. Chem. Rev.* **1972,** *41,* 403−410.
(2) Crandall, J. K.; Apparu, M. *Org. React.* **1983,** 345−443.
(3) Doris, E.; Dechoux, L.; Mioskowski, C. *Tetrahedron Lett.* **1994,** *35,* 7943−7946.
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(6) Crandall, J. K.; Lin, L. H. C. *J. Am. Chem. Soc.* **1967,** *89,* 4526.
(7) Apparu, M.; Barrelle, M. *Tetrahedron* **1978,** *34,* 1541−1546.
(8) For a review on carbene chemistry, see: Jones, M., Jr.; Moss, R. A. *Carbenes*; Academic: New York; 1973; Vol. 1. Moss, R. A.; Jones, M. Jr. *Carbenes*; Academic: New York, 1975; Vol. 2. Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992,** *48,* 5385−5453. Also on carbenes with neighboring heteroatoms, see: Taylor K. G. *Tetrahedron* **1982,** *38,* 2751−2772.
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(10) Eaton, P. E.; White, A. J. *J. Org. Chem.* **1990,** *55,* 1321−1323. Bunz, U.; Herpich, W.; Podlech, J.; Polborn, K.; Pratzel, A.; Stephenson, D. S.; Szeimies, G. *J. Am. Chem. Soc.* **1994,** *116,* 7637−7641.
(11) Starting epoxy ketones were prepared according to Eschenmoser's procedure: Felix, D.; Wintner, C.; Eschenmoser, A. *Org. Synth.* **1976,** *55,* 52−56.
(12) No evidence of the attack of the organolithium reagent on the epoxide ring was found. The stereochemistry of the epoxy alcohol moiety was confirmed by *m*-CPBA epoxidation of the corresponding substituted allylic alcohol, see: Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979,** *101,* 159−169.
(13) Haruta, J.; Nishi, K.; Matsuda, S.; Akai, S.; Tamura, Y.; Kita, Y. *J. Org. Chem.* **1990,** *55,* 4853−4859.

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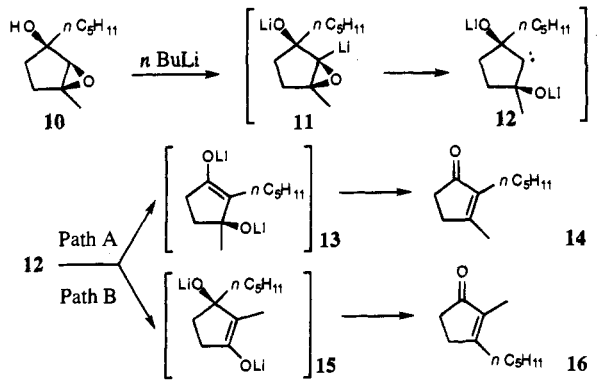
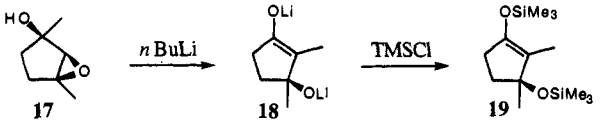
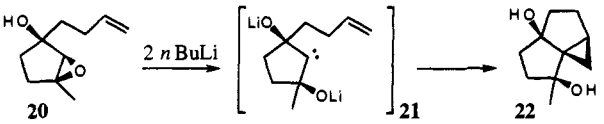
Scheme 4



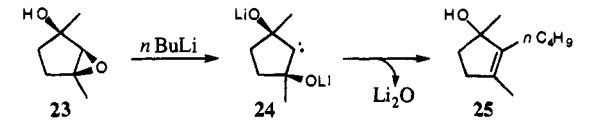
Scheme 5



Scheme 6



Scheme 7



4). The mechanistic pathway for this transformation invokes the carbenoid **12** as the key intermediate, which is generated by α-elimination of the metalated oxirane **11**. The highly reactive carbenoid can rearrange by processes A or B (e.g., intramolecular insertion) to yield intermediates **13** and **15**, which, after usual workup, furnish the α,β-unsaturated ketones **14** and **16**.

The presence of an intermediate alcoholate α,β-enolate as **18** has been demonstrated by trimethylsilyl chloride quenching of the reaction (Scheme 5). If treated under mild acidic aqueous conditions, **19** undergoes rearrangement into the corresponding α,β-unsaturated ketone.

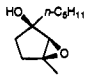
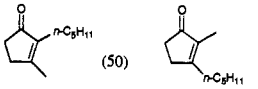
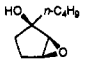
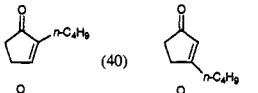
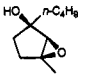
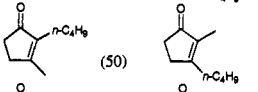
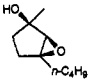
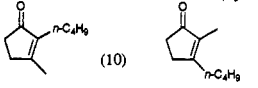
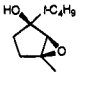
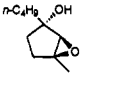
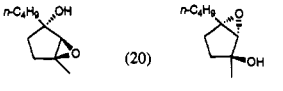
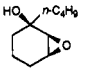
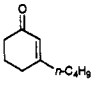
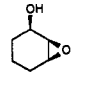
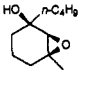
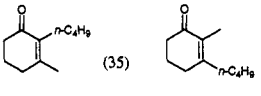
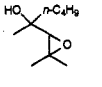
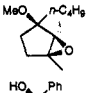
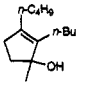
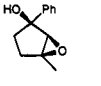
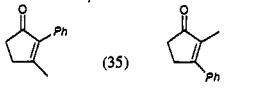
Evidence for a highly reactive carbenoid intermediate was obtained by an intramolecular trapping [2 + 1] cycloaddition reaction (Scheme 6). Thus, in the presence of an excess of *n*-BuLi, the epoxide **20** cyclopropanized into the tricyclic diol **22** in 20% yield.

Furthermore, we were also able to detect in some cases a by product resulting from *n*-BuLi insertion into **24** followed by Li_2O elimination leading to an allylic alcohol **25** (Scheme 7). The formation of this byproduct also argues for a carbenoid process.[14]

There is no evidence for the occurrence of an anionic mechanism during the key rearrangement step. If only 1 equiv of *n*-BuLi is used, the alcoholate initially formed is stable (no rearrangement was observed, even in the presence of excess lithium salts), suggesting that a second base equivalent is needed to metalate the oxirane ring. In order to find out the scope and limitations of this new reaction, many α-epoxy alcohols were synthesized and subjected to reaction with 3 equiv of *n*-BuLi.

(14) Crandall, J. K.; Lin, L. H. C. *J. Am. Chem. Soc.* **1967**, *89*, 4527.

Table 1. Examples of Rearrangement of α-Epoxy Alcohols

Entry	Substrate	Products (ratio[a] %)	Yield[b] (%)
1			74
2		 (50) (50)	70
3		 (40) (60)	67
4		 (50) (50)	78
5		 (10) (90)	71
6			77
7		 (20) (80)	90
8			55
9			63
10		 (35) (65)	59
11			85
12			95
13		 (35) (65)	64

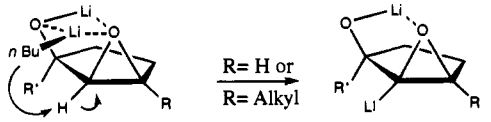
[a] Determined by 1H NMR analysis of the crude mixture. [b] Combined yields.

The migratory aptitudes of R and R', the prerogatives of the stereochemistry of the starting α-epoxy alcohols, and the extension of this unprecedented reaction to six-membered rings and acyclic systems were examined. Some examples starting from α-epoxy alcohols are given in Table 1.

The results stated in entries 4 and 5 suggest that a free divalent carbon intermediate is not involved and that the free carbene stage is probably bypassed.[15] This also indicates the partly concerted nature of the rearrangement and the favoring of the migration of the alkyl group originally bound to the OH bonded carbon. By analogy with entry 4, the α-methoxy epoxide (entry 12) also leads to a carbenoid such as **12**, but *n*-BuLi insertion followed by MeOLi elimination overwhelms the 1,2-rearrangement. This difference in reactivity between the α-alkoxy- and the α-alkyloxycarbenoid can be attributed to the migratory assistance of the oxygen anion[16] (primary stereoelectronic effect) which allows rearrangement. For a bis-alcoholate carbenoid

(15) Jones, M., Jr.; Moss. R. A. *Carbenes*; Academic: New York, 1973; Vol. 1, Chapter 2.

Scheme 8



26 27

intermediate such as **12**, strong electrostatic repulsions should forbid the organolithium insertion, thus favoring the 1,2-rearrangement, whereas for the α-methoxy epoxide, the electrostatic repulsions of the monoalcoholate carbenoid are minimized. In the latter process, the insertion reaction is faster than the rearrangement.

The methodology was extended to six-membered ring systems (entries 8, 9, and 10). The different ratios of rearranged products obtained in entries 3 and 8 suggest that strong stereoelectronic factors govern the carbenoid C-1,2 and H-1,2 rearrangements. Combined, the ratio recorded in entries 3, 4, 5, 6, and 13 indicates the following migratory aptitudes: hydride > methyl > *n*-butyl > aryl > *tert*-butyl.

As exemplified in entries 3, 8, and 9, the oxirane ring deprotonation takes place regiospecifically next to the hydroxyl group. The *cis* stereochemistry of the epoxy alcohol moiety allows the formation of stable lithium−epoxide complexes **26** between the alcoholate and the heterocyclic oxygen (Scheme 8), thus fixing the base in a position suitable for the ensuing deprotonation.[17]

Noncyclic hydroxyepoxide substrates (entry 11) failed to react *via* a carbenoid path but afforded the classical β-elimination product; the lack of geometric constraint should forbid the formation of a ternary complex identical to **26**. Consequently, in the absence of other overriding effects, the expected β-elimination on the bulky trisubstituted epoxide predominates.[18]

Because of the highly favorable configuration, *trans*-α-epoxy alcohol (entry 7)[19] was found to provide only a Payne-like rearrangement product,[20] indicating that severe stereochemical requirements are necessary to ensure α-metalation of the oxirane ring. The fast equilibration between both regioisomeric alcoholate epoxides could exclude the initial *n*-BuLi complexation which is a prerequisite prior to the metalation of the oxirane.[21]

The present study provides evidence for a new alkyl 1,2-carbenoid rearrangement achievable under basic conditions in cyclic α-epoxy alcohol systems. This reaction should have some further utility in effecting the straightforward conversion of cyclic α,β-epoxy ketones to alkylated α,β-unsaturated ketones,[22] which are of great importance in the synthesis of many natural products.

Experimental Section

General Methods. ^1H and ^{13}C NMR spectra were recorded with a Bruker AC-200 spectrometer at 200 MHz (^1H) and 50 MHz (^{13}C) using $CHCl_3$ (7.27 ppm) and $CDCl_3$ (77 ppm) as internal standards, respectively. Chemical shifts are expressed in parts per million. Mass spectra were obtained on a Finnigan-4600 quadrupole spectrometer using either chemical (CI-NH_3) or electronic (EI-70 eV) ionisation mode. HRMS were recorded at the "Centre Régional des Mesures Physiques de l'Ouest". IR spectra were measured on a Perkin Elmer FT-IR 1600 spectrometer. Elemental analyses were carried out either at the Institute of Chemistry, University Louis Pasteur of Strasbourg or at the "Service de Microanalyses du CNRS" at Gif-sur-Yvette. THF was freshly distilled over Na-benzophenone prior to use. *n*BuLi was purchased from Aldrich Chemical Company. Analytical TLC were performed on Merck precoated TLC plates, silica gel 60 F_{254} (0.25 mm). Flash chromatography separations were performed on Merck silica gel 60 (230−400 mesh). Reaction vessels were flame-dried and allowed to cool under an inert atmosphere of argon.

α-Hydroxy Epoxides. A typical experimental procedure is provided for the synthesis of 2,5-dimethyl-6-oxa-bicyclo[3.1.0]hexan-2-ol (entry 1). Under Ar, at −78 °C, MeLi (1.4 mL of a 1.5 M solution in Et_2O, 1.2 equiv) was added dropwise to a stirred solution of 3-methyl-2-cyclopenten-1-one oxide (200 mg, 1.78 mmol, 1.0 equiv) in 15 mL of anhydrous THF. The mixture was stirred for 15 min at −78 °C, and the reaction was then quenched with water and extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated. The residual colorless liquid did not need further purification (225 mg, quantitative yield).

α,β-Unsaturated Ketones (1,2-Rearrangement). A typical experimental procedure is provided for the synthesis of 2,3-dimethyl-cyclopent-2-enone (entry 1). Under Ar, at −78 °C, *n*-BuLi (1.5 mL of a 1.6 M solution in hexane, 3.0 equiv) was added dropwise to a stirred solution of 2,5-dimethyl-6-oxa-bicyclo[3.1.0]hexan-2-ol (100 mg, 0.78 mmol, 1.0 equiv) in 8 mL of anhydrous THF. The mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was then quenched with water and extracted three times with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated. The residual liquid was chromatographed on silica gel (CH_2Cl_2 as eluent) to yield the desired α,β-unsaturated ketone (63 mg, 74%) as a colorless liquid.

2,3-Dimethyl-1,3-bis(trimethylsilanyloxy)cyclopentene (19). Under Ar, at −78 °C, *n*-BuLi (1.5 mL of a 1.6 M solution in hexane, 3.0 equiv) was added dropwise to a stirred solution of 2,5-dimethyl-6-oxa-bicyclo[3.1.0]hexan-2-ol (100 mg, 0.78 mmol, 1.0 equiv) in 8 mL of anhydrous THF. The mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was then quenched trimethylsilyl chloride at 0 °C (1 mL, 10 equiv) and concentrated under vacuum to dryness. The residue was diluted with Et_2O and filtered over Celite and the solvent was removed under vacuum. The crude product was pure enough to be spectroscopically analyzed: ^1H NMR ($CDCl_3$) δ 0.07 (s, 9H), 0.17 (s, 9H), 1.25 (s, 3H), 1.22−1.50 (m, 2H), 1.47 (t, J = 1.5 Hz, 3H), 1.90−1.95 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 0.6, 2.1, 26.2, 28.4, 31.1, 37.7, 83.9, 119.4, 147.3; MS (CI) *m/z* 183 (100). HRMS calcd for $C_{13}H_{28}O_2Si_2$ 272.1628, found 272.1620.

2-But-3-enyl-5-methyl-6-oxa-bicyclo[3.1.0]hexan-2-ol (20). ^1H NMR ($CDCl_3$) δ 1.40 (s, 3H), 1.47−1.62 (m, 5H), 1.90−2.01 (m, 1H), 2.12−2.20 (m, 2H), 2.52 (s, 1H), 3.08 (s, 1H), 4.92−5.07 (m, 2H), 5.74−5.96 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 17.9, 27.4, 30.5, 33.7, 35.4, 64.1, 68.1, 79.9, 114.5, 138.4; IR ($CHCl_3$) 3443 (OH) cm^{-1}; MS (EI) *m/z* 151 (100). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.38; H, 9.60. Found: C, 71.49; H, 9.97.

6-Methylhexahydrocyclopropa[c]pentalene-3a,6-diol (22). Under Ar, at −78 °C, *n*-BuLi (1.1 mL of a 1.6 M solution in hexane, 3.0 equiv) was added dropwise to a stirred solution of 2-but-3-enyl-5-methyl-6-oxa-bicyclo[3.1.0]hexan-2-ol (100 mg, 0.59 mmol, 1.0 equiv) in 6 mL of anhydrous THF. The mixture was allowed to warm to room temperature and stirred for an hour. The reaction was then quenched with water and extracted three times with AcOEt. The combined organic layers were dried over $MgSO_4$ and concentrated. The residual liquid was chromatographed on silica gel (CH_3OH:CH_2Cl_2, 5:95 as eluant) to yield the desired diol (19 mg, 20%) as a white solid: ^1H NMR ($CDCl_3$) δ AB part of an ABX (ν_A = 0.60, ν_B = 1.01, J_{AB} = 5.5 Hz, J_{AX} = 7.4 Hz, J_{BX} = 4.9 Hz, 2H), 1.02 (s, 3H), 1.15 (m, 1H), 1.43 (m, 1H), 1.67−2.19 (m, 7H), 2.72 (sbr, 2H); ^{13}C NMR ($CDCl_3$) δ 7.4, 23.1, 23.3, 25.1, 34.4, 36.5, 39.9, 47.1, 79.7, 89.7; IR ($CHCl_3$)

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3383 (OH) cm^{-1}; MS (EI) *m/z* 133 (100), 151 (58); HRMS calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1146.

2-Butyl-1,3-dimethylcyclopenten-2-enol (25). ^1H NMR ($CDCl_3$) δ 0.92 (t, J = 6.8 Hz, 3H), 1.32 (s, 3H), 1.32−1.44 (m, 4H), 1.65 (s, 3H), 1.84−2.28 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.5, 23.2, 24.4, 26.1, 32.5, 34.0, 40.0, 85.4, 135.1, 140.2; IR (neat) 3352 (OH) cm^{-1}; MS (CI) *m/z* 151 (100), 186 (56); HRMS calcd for $C_{11}H_{20}O$ 168.1514, found 168.1514.

2,5-Dimethyl-6-oxa-bicyclo[3.1.0]hexan-2-ol (Entry 1). ^1H NMR ($CDCl_3$) δ 1.19 (s, 3H), 1.37 (s, 3H), 1.52 (m, 3H), 1.91 (m, 1H), 2.79 (s, 1H), 3.00 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 17.8, 22.8, 30.2, 35.2, 63.6, 68.5, 77.7; IR (neat) 3450 (OH) cm^{-1}; MS (CI) *m/z* 146 (100). Anal. Calcd for $C_7H_{12}O_2$: C, 65.58; H, 9.45. Found: C, 65.28; H, 9.72.

2,3-Dimethylcyclopent-2-enone (Entry 1). ^1H NMR ($CDCl_3$) δ 1.63 (m, 3H), 2.00 (s, 3H), 2.31 (m, 2H), 2.43 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 7.7, 17.0, 31.3, 34.0, 136.0, 169.9, 209.8; IR (neat) 1698 (CO), 1650 (C=C) cm^{-1}; MS (CI) *m/z* 111 (29), 128 (100), 145 (25). Anal. Calcd for $C_7H_{10}O$: C, 76.31; H, 9.17. Found: C, 76.55; H, 9.41.

5-Methyl-2-pentyl-6-oxabicyclo[3.1.0]hexan-2-ol (Entry 2). ^1H NMR ($CDCl_3$) δ 0.82 (t, J = 6.3 Hz, 3H), 1.18−1.64 (m, 11H), 1.35 (s, 3H), 1.89 (m, 1H), 2.72 (s, 1H), 3.01 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 17.7, 22.3, 22.6, 30.5, 32.2, 33.5, 36.4, 63.9, 68.3, 79.8; IR (neat) 3461 (OH) cm^{-1}; MS (CI) *m/z* 202 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.68; H, 10.96. Found: C, 71.30; H, 11.23.

3-Methyl-2-pentylcyclopent-2-enone (Entry 2). ^1H NMR ($CDCl_3$) δ 0.86 (t, J = 6.5 Hz, 3H), 1.16−1.45 (m, 6H), 2.04 (s, 3H), 2.15 (t, J = 6.7 Hz, 2H), 2.35 (m, 2H), 2.46 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.9, 17.1, 22.4, 22.9, 28.0, 31.4, 31.7, 34.2, 140.7, 170.0, 209.7; IR (neat) 1699 (CO), 1648 (C=C) cm^{-1}; MS (CI) *m/z* 167 (80), 184 (72), 333 (100).

2-Methyl-3-pentylcyclopent-2-enone (Entry 2). ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 6.7 Hz, 3H), 1.22−1.62 (m, 6H), 1.68 (s, 3H), 2.34−2.45 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 7.9, 13.9, 22.3, 26.8, 29.15, 31.14, 31.6, 34.0, 136.0, 174.0, 210.2; IR (neat) 1698 (CO), 1648 (C=C) cm^{-1}; MS (CI) *m/z* 167 (86), 184 (100). Anal. Calcd for $C_{11}H_{18}O$: C, 79.45; H, 10.93. Found: C, 79.60; H, 11.16.

2-Butyl-6-oxabicyclo[3.1.0]hexan-2-ol (Entry 3). ^1H NMR ($CDCl_3$) δ 0.91 (t, J = 6.9Hz, 3H), 1.31−1.75 (m, 9H), 2.03−2.14 (m, 2H), 3.25 (d, J = 2.7 Hz, 1H), 3.47 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 23.2, 25.2, 26.3, 32.1, 36.2, 56.6, 61.9, 79.9; IR (neat) 3423 cm^{-1}; MS (CI) *m/z* 174 (100). Anal. Calcd for $C_9H_{16}O_2$: C, 69.18; H, 10.34. Found: C, 69.45; H, 10.61.

2-Butylcyclopent-2-enone (Entry 3). ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 7.0 Hz, 3H), 1.25−1.55 (m, 4H), 2.16 (m, 2H), 2.38 (m, 2H), 2.53 (m, 2H), 7.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.4, 24.4, 26.4, 29.8, 34.6, 146.5, 157.3, 210.1; IR (neat) 1699 (C=O), 1670 (C=C) cm^{-1}; MS (CI) *m/z* 139 (52), 156 (100). Anal. Calcd for $C_9H_{14}O$: C, 78.20; H, 10.23. Found: C, 78.45; H, 10.12.

3-Butyl-cyclopent-2-enone (Entry 3). ^1H NMR ($CDCl_3$) δ 0.91 (t, J = 7.1 Hz, 3H), 1.29−1.60 (m, 4H), 2.39 (m, 4H), 2.55 (m, 2H), 5.92 (t, J = 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.4, 29.1, 31.5, 33.2, 35.2, 129.3, 183.3, 210.2; IR (neat) 1709 (C=O), 1676 (C=C) cm^{-1}; MS (CI) *m/z* 139 (87), 156 (100). Anal. Calcd for $C_9H_{14}O$: C, 78.20; H, 10.23. Found: C, 78.59; H, 9.95.

2-Butyl-5-methyl-6-oxabicyclo[3.1.0]hexan-2-ol (Entry 4). ^1H NMR ($CDCl_3$) δ 0.92 (t, J = 6.8 Hz, 3H), 1.38−1.72 (m, 9H), 1.43 (s, 3H), 1.96 (m, 1H), 2.02 (s, 1H), 3.07 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7, 17.7, 23.0, 25.0, 30.4, 33.4, 36.1, 63.9, 68.2, 79.7; IR (neat) 3459 (OH) cm^{-1}; MS (CI) *m/z* 153 (22), 188 (100). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.78; H, 10.80.

5-Butyl-2-methyl-6-oxabicyclo[3.1.0]hexan-2-ol (Entry 5). ^1H NMR ($CDCl_3$) δ 0.91 (t, J = 6.7 Hz, 3H), 1.22 (s, 3H), 1.30−1.68 (m, 9H), 1.95 (m, 1H), 2.24 (sbr, 1H), 3.03 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.6, 22.7, 27.3, 28.2, 31.5, 35.2, 66.8, 67.6, 77.6; IR (neat) 3456 (OH) cm^{-1}; MS (CI) *m/z* 153 (21), 188 (100). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.70; H, 10.89.

2-Butyl-3-methylcyclopent-2-enone (Entries 4 and 5). ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.9 Hz, 3H), 1.18−1.42 (m, 4H), 2.05 (s, 3H), 2.16 (t, J = 7.2 Hz, 2H), 2.35 (m, 2H), 2.47 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.8, 17.2, 22.6, 22.7, 30.5, 31.4, 34.3, 140.7, 170.0, 209.8; IR (neat) 1698 (C=O), 1645 (C=C) cm^{-1}; MS (CI) *m/z* 153 (60), 170 (100). Anal. Calcd for $C_{10}H_{16}O$: C, 78.88; H, 10.61. Found: C, 79.02; H, 10.49.

3-Butyl-2-methylcyclopent-2-enone (Entries 4 and 5). ^1H NMR ($CDCl_3$) δ 0.94 (t, J = 7.1 Hz, 3H), 1.29−1.56 (m, 4H), 1.69 (t, J = 1.8 Hz, 3H), 2.34−2.54 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 7.9, 13.8, 22.6, 29.2, 29.3, 30.9, 34.1, 136.0, 174.0, 210.3; IR (neat) 1701 (C=O), 1647 (C=C) cm^{-1}; MS (CI) *m/z* 153 (59), 170 (100). Anal. Calcd for $C_{10}H_{16}O$: C, 78.88; H, 10.61. Found: C, 78.87; H, 10.74.

2-*tert*-Butyl-4-methyl-6-oxabicyclo[3.1.0]hexan-2-ol (Entry 6). ^1H NMR ($CDCl_3$) δ 0.93 (s, 9H), 1.23−1.54 (m, 2H), 1.37 (s, 3H), 1.94 (m, 2H), 2.23 (s, 1H), 3.20 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 17.8, 25.0, 32.2, 32.8, 35.6, 66.1, 67.6, 84.4; IR (neat) 3488 (OH) cm^{-1}; MS (CI) *m/z* 153 (62), 170 (22), 188 (100). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.22; H, 10.76.

3-*tert*-Butyl-2-methylcyclopent-2-enone (Entry 6). ^1H NMR ($CDCl_3$) δ 1.23 (s, 9H), 1.83 (t, J = 2.1 Hz, 3H), 2.30 (m, 2H), 2.52 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.0, 27.7, 28.7, 33.4, 35.6, 134.9, 180.0, 210.8; IR (neat) 1700 (C=O), 1685 (C=C) cm^{-1}; MS (CI) *m/z* 153 (90), 170 (100). Anal. Calcd for $C_{10}H_{16}O$: C, 78.88; H, 10.61. Found: C, 78.96; H, 10.73.

2-Butyl-6-oxa-5-methylbicyclo[3.1.0]hexan-2-ol (Entry 7). Prepared according to ref 19: ^1H NMR ($CDCl_3$) δ 0.93 (t, J = 6.9 Hz, 3H), 1.37−1.90 (m, 11H), 1.50 (s, 3H), 3.05 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.0, 17.6, 23.1, 26.0, 29.9, 34.5, 37.1, 64.4, 66.8, 80.9; IR (neat) 3424 (OH) cm^{-1}; MS (CI) *m/z* 153 (22), 188 (100). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.39; H, 10.44.

5-Butyl-6-oxa-2-methylbicyclo[3.1.0]hexan-2-ol (Entry 7). ^1H NMR ($CDCl_3$) δ 0.91 (t, J = 7.0 Hz, 3H), 1.26−1.91 (m, 11H), 1.40 (s, 3H), 3.02 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.7, 24.0, 27.7, 28.2, 31.3, 35.7, 66.8, 68.3, 78.2; IR (neat) 3384 (OH) cm^{-1}; Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.31; H, 10.77.

2-Butyl-7-oxabicyclo[4.1.0]heptan-2-ol (Entry 8). ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3H), 1.21−1.70 (m, 11H), 1.96 (td, J = 4.6 Hz and J = 15.0 Hz, 1H), 2.61 (sbr, 1H), 2.98 (d, J = 3.9 Hz, 1H), 3.31 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 15.1, 23.1, 23.7, 24.7, 33.5, 39.2, 55.5, 58.5, 68.7; IR (neat) 3422 (OH) cm^{-1}; MS (CI) *m/z* 153 (23), 170 (37), 188 (100). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.53; H, 10.68. Found: C, 70.36; H, 10.85.

3-Butylcyclohex-2-enone (Entry 8). ^1H NMR ($CDCl_3$) δ 0.93 (t, J = 7.0 Hz, 3H), 1.26−1.53 (m, 5H), 1.95−2.05 (m, 2H), 2.18−2.39 (m, 5H), 5.88 (t, J = 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.3, 22.7, 29.0, 29.7, 37.3, 37.8, 125.6, 166.8, 200.0; IR (neat) 1680 (C=O), 1672 (C=C) cm^{-1}; MS (CI) *m/z* 153 (33), 170 (100). Anal. Calcd for $C_{10}H_{16}O$: C, 78.88; H, 10.61. Found: C, 78.69; H, 10.64.

7-Oxabicyclo[4.1.0]heptan-2-ol (Entry 9). ^1H NMR ($CDCl_3$) δ 1.19−1.54 (m, 4H), 1.72−1.78 (m, 2H), 3.11 (sbr, 1H), 3.26 (m, 2H), 3.90−3.98 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 18.5, 22.7, 28.3, 55.2, 55.4, 67.1; IR (neat) 3415 (OH) cm^{-1}; MS (CI) *m/z* 132 (100). Anal. Calcd for $C_6H_{10}O_2$: C, 63.12; H, 8.85. Found: C, 63.03; H, 9.10.

Cyclohex-2-enone (Entry 9). ^1H NMR ($CDCl_3$) δ 1.95−2.05 (m, 2H), 2.28−2.43 (m, 4H), 6.00 (dt, J = 1.9 Hz and J = 10.1 Hz, 1H), 6.97 (dt, J = 4.0 Hz and J = 10.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.3, 25.2, 37.6, 129.3, 150.4, 199.1; IR (neat) 1685 (CO), 1682 (C=C) cm^{-1}.

2-Butyl-6-methyl-7-oxabicyclo[4.1.0]heptan-2-ol (Entry 10). ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 6.8 Hz, 3H), 1.10−1.58 (m, 11H), 1.31 (s, 3H), 1.91 (m, 1H), 2.51 (s, 1H), 2.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 15.8, 23.2, 25.0, 29.6, 34.1, 40.0, 61.5, 65.7, 68.9; IR (neat) 3430 (OH) cm^{-1}; MS (CI) *m/z* 167 (82), 184 (20), 202 (100).

2-Butyl-3-methylcyclohex-2-enone (Entry 10). ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 3H), 1.22−1.32 (m, 6H), 1.89 (m, 1H), 1.91 (s, 3H), 2.24−2.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.8, 20.9, 22.1, 22.6, 24.7, 31.1, 32.7, 37.7, 135.8, 154.5, 198.5; IR (neat) 1660 (CO), 1639 (C=C) cm^{-1}; MS (CI) *m/z* 167 (100), 184 (55). Anal. Calcd for $C_{11}H_{18}O$: C, 79.45; H, 10.93. Found: C, 79.63; H, 11.09.

3-Butyl-2-methylcyclohex-2-enone (Entry 10). ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 6.7 Hz, 3H), 1.20−1.47 (m, 6H), 1.74 (s, 3H), 1.89 (m, 2H), 2.21 (m, 2H), 2.28-2.37 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 10.3, 13.7, 22.3, 22.6, 29.5, 30.6, 34.8, 37.5, 130.5, 159.0, 199.3; IR (neat) 1666 (CO), 1647 (C=C) cm^{-1}; MS (CI) *m/z* 167 (60), 184 (100). Anal. Calcd for $C_{11}H_{18}O$: C, 79.45; H, 10.93. Found: C, 79.70; H, 11.15.

2-(3,3-Dimethyloxiranyl)hexan-2-ol (Entry 11). ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 6.3 Hz, 3H), 1.24 (s, 3H), 1.32 (s, 3H), 1.51 (s, 3H), 1.36−1.55 (m, 6H), 2.08 (s, 1H), 2.67 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 18.3, 23.0, 25.3, 25.9, 43.8, 58.8, 68.8, 69.1; IR (neat) 3493 (OH) cm^{-1}; MS (CI) *m/z* 155 (52), 190 (100). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.70; H, 11.72. Found: C, 69.77; H, 11.30.

2,4-Dimethyloct-1-ene-3,4-diol (Entry 11). ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 6.6 Hz, 3H), 1.04 (s, 3H), 1.21−1.50 (m, 6H), 1.81 (s, 3H), 2.12 (s,1H), 2.42 (d, J = 4 Hz, 1H), 3.92 (d, J = 4 Hz, 1H), 4.96 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.5, 22.1, 23.2, 25.8, 39.4, 74.5, 80.2, 114.6, 145.1; IR ($CHCl_3$) 3415 (OH) cm^{-1}; MS (CI) *m/z* 190 (100). Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.70; H, 11.72. Found: C, 69.85; H, 11.35.

4-Butyl-4-methoxy-1-methyl-6-oxabicyclo[3.1.0]hexane (Entry 12). Under Ar, at 0°C, NaH (60 mg of a 60% suspension in oil, 1.2 equiv) was added portionwise to a stirred solution of 2-butyl-5-methyl-6-oxabicyclo[3.1.0]hexan-2-ol (200 mg, 1.17 mmol, 1.0 equiv) in 4 mL of anhydrous THF. Methyl iodide (0.11 mL, 1.5 equiv) was at this stage added dropwise. The mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was then cautiously quenched with water and extracted three times with Et_2O. The combined organic layers are dried over $MgSO_4$ and concentrated. The residual liquid is chromatographed on silica gel (ether: hexane, 1:9 as eluant) to yield the desired methoxy epoxide (185 mg, 86%) as a colorless liquid. ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J = 6.7 Hz, 3H), 1.32−1.68 (m, 9H), 1.42 (s, 3H), 1.93 (m, 1H), 3.11 (s, 1H), 3.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 14.0, 18.0, 23.2, 24.9, 28.4, 30.1, 33.6, 51.5, 61.9, 65.3, 84.3; IR (neat) 1090 (OMe) cm^{-1}; MS (CI) *m/z* 153 (48), 185 (34), 202 (100). Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.68; H, 10.96. Found: C, 71.87; H, 10.70.

2,3-Dibutyl-1-methylcyclopent-2-enol (Entry 12). ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 5.6 Hz, 3H), 0.92 (t, J = 5.6 Hz, 3H), 1.20−2.40 (m, 16H), 1.31 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 22.7, 23.3, 24.4, 26.0, 28.7, 30.1, 31.2, 32.9, 40.0, 85.4, 139.2, 140.2; IR (neat) 3423 (OH) cm^{-1}; MS (CI) *m/z* 193 (100).

3-Methyl-2-phenyl-6-oxabicyclo[3.1.0]hexan-2-ol (Entry 13). ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 3H), 1.66−1.88 (m, 2H), 1.97−2.12 (m, 2H), 2.41 (s, 1H), 3.29 (s, 1H), 7.25−7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.8, 31.0, 37.9, 65.5, 66.8, 81.2, 124.5, 127.4, 128.5, 129.8, 132.8; IR (neat) 3440 (OH) cm^{-1}; MS (CI) *m/z* 173 (10), 190 (32), 208 (100).

3-Methyl-2-phenylcyclopent-2-enone (Entry 13). ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 3H), 2.54 (d, J = 5.5 Hz, 2H), 2.65 (d, J = 5.5 Hz, 2H), 7.40−7.55 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.8, 30.7, 34.7, 124.9, 127.4, 128.1, 129.0, 131.7, 140.2, 208.7; IR (neat) 1698 (CO), 1623 (C=C) cm^{-1}; MS (CI) *m/z* 173 (10), 190 (100), 207 (14).

2-Methyl-3-phenylcyclopent-2-enone (Entry 13). ^{1}H NMR ($CDCl_3$) δ 1.96 (t, J = 1.9 Hz, 3H), 2.54 (m, 2H), 2.90 (m, 2H), 7.25−7.53 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 9.8, 29.2, 33.9, 115.2, 127.0, 128.5, 129.5, 136.3, 136.4, 209.8; IR (neat) 1695 (CO), 1635 (C=C) cm^{-1}; MS (CI) *m/z* 190 (100).

Acknowledgment. The authors thank Alain Valleix for MS measurements and Dorothée Deuring for helpful discussions. The "Institut de Recherche Servier" is gratefully acknowledged for financial support to Eric Doris.

JA950292H