139.0 (e), 134.5 (e), 132.2 (e), 129.6 (o), 129.1 (o), 127.8 (o), 127.5 (e), 127.2 (o), 124.2 (o), 119.9 (o), 112.6 (o), 94.7 (o), 70.3 (o), 56.4 (o), 46.7 (e), 46.4 (e), 36.7 (e), 35.0 (o), 29.5 (e), 21.4 (o); mass spectrum, m/z (relative intensity) [CI] 454 ($M^+ + 1$, 18), 436 (80), 298 (5), 251 (19), 212 (100), [EI] 298 (3), 241 (6), 155 (20), 91 (100); TLC (1:1 ethyl acetate–hexane) R_f 0.35; high-resolution mass spectroscopy (m/z) calcd for $C_{25}H_{27}NO_5S$ 453.1610, found 453.1590.

Minor product: **6b**, 32 mg (5%) as a colorless foam; $[\alpha]^{25}_D$ +13.2° (*c* 0.62, $CHCl_3$); IR ($CHCl_3$) 2.79, 3.31, 3.40, 5.95 (w), 6.02 (w), 6.25, 6.67, 6.85, 6.94, 7.46, 8.62, 9.09, 9.18 μm; ^1H NMR (470 MHz, $CDCl_3$) δ 1.78–1.96 (m, 2 H), 2.41 (s, 3 H) 2.64 (s, 3 H), 2.86–2.91 (m, 1 H), 3.08–3.13 (m, 1 H), 3.26 (dd, 1 H, J = 6.5, 19.6 Hz), 3.40 (d, 1 H, J = 19.6 Hz), 3.86 (s, 3 H), 4.51 (dd, 1 H, J = 4.6, 5.9 Hz), 4.80 (d, 1 H, J = 4.6 Hz), 5.95–5.99 (m, 2 H), 6.67 (s, 2 H), 6.70 (d, 1 H, J = 9.5 Hz), 7.28 (d, 1 H, J = 8.0 Hz), 7.57 (d, 1 H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 145.6 (e), 143.2 (e), 142.0 (e), 138.8 (e), 134.5 (e), 133.4 (e?), 132.7 (o), 129.5 (o), 127.1 (o), 126.8 (e), 125.6 (o), 124.8 (o), 119.7 (o), 112.7 (o), 88.4 (o), 63.9 (o), 56.4 (o), 46.5 (e), 45.6 (e), 37.4 (e), 34.8 (o), 29.5 (e), 21.3 (o); mass spectrum, m/z (relative intensity) [CI] 454 ($M^+ + 1$, 19) 436 (40), 251 (24), 212 (100), 157 (28), 89 (16), [EI] 453 (M^+, 11), 298 (21), 268 (19), 241 (78), 198 (35), 181 (25), 155 (38), 91 (100), 58 (52); TLC (1:1 ethyl acetate–hexane) R_f 0.12; high-resolution mass spectroscopy (m/z) calcd for $C_{25}H_{27}NO_5S$ 453.1610, found 453.1609.

3a(*R*),9b(*S*)-Dihydro-5-methoxy-9b-[2-(*N*-methylammonio)ethyl]phenanthro[4,4a,4b,5-*bcd*]furan-3(8*H*)-one Trifluoroacetate (7). The dienone **1c** (90 mg, 0.20 mmol) was dissolved in trifluoroacetic acid (2 mL) at room temperature. Evaporation of the reaction solution, after 1 min, gave spectrally homogeneous amine salt **7**: ^1H NMR (470 MHz, $CDCl_3$/Me_2SO-d_6) δ 2.12–2.22 (m, 1 H), 2.22–2.32 (m, 1 H), 2.64 (br s, 3+ H), 2.90 (br s, 1 H), 3.06 (br s, 1 H), 3.38 (dd, 1 H, J = 6.1, 20.0 Hz), 3.59 (d, 1 H, J = 20.0 hz), 3.82 (s, 3 H), 5.15 (s, 1 H), 5.92 (d, 1 H, J = 10.1 Hz), 6.12 (br s, 4 H), 6.41 (d, 1 H, J = 6.1 Hz), 6.68 (d, 1 H, J = 8.1 Hz), 6.74 (d, 1 H, J = 8.1 Hz), 9.19 (br s, 1 H), 9.38 (br s, 1 H); ^{13}C NMR ($CDCl_3$/Me_2SO-d_6) δ 193.2 (e), 144.1 (e), 143.3 (o), 141.8 (e), 137.6 (e), 133.5 (o), 130.2 (e), 125.9 (e), 123.9 (o), 119.6 (o), 112.7 (o), 85.7 (o), 55.5 (o), 46.6 (e), 44.7 (e), 34.2 (e), 32.3 (o), 29.5 (e). In practice, **7** was used directly after preparation.

Biphasic Cyclization of 7. The salt **7** prepared from dienone **1c** (400 mg, 0.91 mmol) was taken up in chloroform and added to a vigorously stirred biphasic mixture of chloroform/saturated sodium bicarbonate solution (10 mL each). After 20 min, the organic layer was separated and the aqueous phase extracted with dichloromethane (4×). The combined extract was dried over sodium sulfate and yielded 260 mg of amber glass. ^1H NMR (470 MHz, $CDCl_3$) analysis of this material showed the presence of three major products, neopinone–codeinone–unknown (10.0:1.7:1.9);[11] This material was purified by flash chromatography on acetone-deactivated silica gel (5%) using a chloroform–methanol gradient to give 170 mg (63%) of an amber semicrystalline material, which analyzed as neopinone–codeinone (1:1.5) by 470-MHz ^1H NMR: TLC (85:15 chloroform–methanol) R_f 0.35.

Such mixtures could be isomerized to codeinone by the method of Rapoport.[2] For example, 220 mg of a neopinone–codeinone mixture in dichloromethane (4 mL) under argon was treated with a solution of hydrogen chloride in ether (5.5 M, 0.55 mL). After 30 min at room temperature the mixture was partitioned between dichloromethane and 0.2 N sodium hydroxide solution (40 mL). The aqueous phase was extracted with several portions of dichloromethane and the combined extract washed with water (1×) and dried over sodium sulfate. The amber glass obtained by evaporation was reduced with sodium borohydride (100 mg) according to Gates[13] to yield 200 mg of codeine as a tan glass, homogeneous by 90-MHz ^1H NMR. Recrystallization from ether/chloroform/cyclohexane gave a tan powder, mp 151.5–153 °C (lit.[13] mp 157–158.5 °C).

Acknowledgment. We thank the NIH (GM 3269302) for the funds to support this research program and the Purdue University Biological Magnetic Resonance Laboratory (NIH RR01077) for access to the 470-MHz ^1H NMR spectrometer. We also thank T. Braish and M. Anderson for 470-MHz ^1H NMR spectra.

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Lanthanides in Organic Synthesis. 4. Reduction of α,β-Epoxy Ketones with Samarium Diiodide. A Route to Chiral, Nonracemic Aldols

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Received March 10, 1986

We recently described reduction of α-heterosubstituted ketones to the corresponding unsubstituted ketones utilizing samarium diiodide (SmI_2).[1] A variety of heterosubstituents can be reductively cleaved by this procedure under exceedingly mild conditions. Similar procedures applied to α,β-epoxy ketones result in formation of β-hydroxy ketones (aldols), of intense interest as key intermediates in construction of a variety of important natural products. Several methods have previously been developed for this particular process. Use of chromium(II) salts[2] and zinc/acetic acid,[3] as well as electrochemical methods,[4] often result in formation of enone or other byproducts, with corresponding decreases in yields of desired β-hydroxy ketones. Direct hydrogenation[5] has also been utilized, but the scope of this particular procedure has not been adequately delineated. At present, Al/Hg,[2h-j,6] NaTeH,[7] or NaI/NaOAc[8] appear to be reagents of choice for this particular transformation.

General interest in use of epoxides as intermediates in organic synthesis has intensified as a direct result of the development of the Sharpless asymmetric epoxidation reaction.[9] This procedure allows generation of chiral, nonracemic α,β-epoxy alcohols possessing several different

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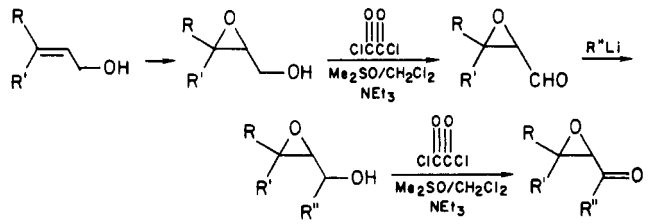
substitution patterns. Since these intermediates can be converted by straightforward techniques to α,β-epoxy ketones, this process, coupled with reductive ring opening of the epoxide, results in a general synthesis of chiral, nonracemic aldol products. In this paper, we report our results on reduction of α,β-epoxy ketones using SmI_2, providing a facile route to β-hydroxy ketones.

Results and Discussion

Substrates required for the present study were prepared in one of two ways. In the first route, readily available enones were converted directly into α,β-epoxy ketones by olefin epoxidation utilizing basic hydrogen peroxide.[10] Because we desired an approach that would take advantage of the Sharpless epoxidation reaction, a straightforward route from allylic alcohols[11] was also developed. Epoxidation of requisite allylic alcohols was followed by Swern oxidation,[12] generating α,β-epoxy aldehydes. Addition of organolithium reagent and subsequent Swern oxidation led to the desired α,β-epoxy ketone.



Substrates prepared by these routes were treated with 2 equiv of SmI_2 in THF–MeOH solvent at −90 °C. (Reaction of 2,3-epoxycyclohexanone at −78 °C resulted in yields 10–15% lower than those performed at −90 °C.) As far as we can determine, reduction of all substrates was complete within minutes under these conditions. Reactions were quenched at this temperature with saturated aqueous K_2CO_3 or, preferably, pH 8 phosphate buffer. Simple workup followed by flash chromatography[13] or Kugelrohr distillation led to excellent isolated yields of desired products (Table I).

Results outlined in Table I attest to the generality of the procedure. Primary, secondary, and tertiary alcohol aldol products can all be generated in high yields (entries 1–3). Acyclic as well as cyclic substrates encompassing a variety of substitution patterns can be utilized. While stereochemistry is retained β to the carbonyl (entry 8), stereochemical integrity at the α-position is lost during reduction (entry 6). We have encountered only one epoxy ketone resistant to reduction. Thus, the epoxide derived from carvone gave no detectable amount of the desired product, but only 34% of the starting material could be recovered from the reaction mixture. We had previously found that similar α-heterosubstituted ketones were also resistant to reduction.[1]

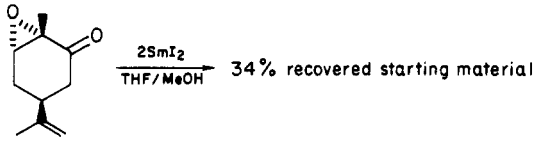
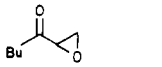
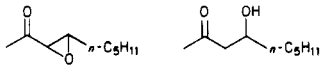
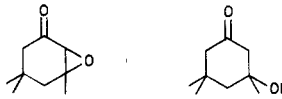
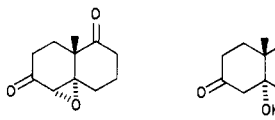
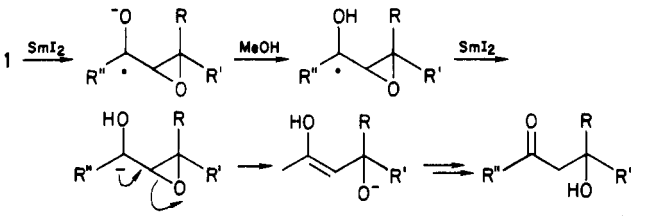


Table I. Reduction of α,β-Epoxy Ketones with Samarium Diiodide. Synthesis of β-Hydroxy Ketones

entry	α,β-epoxy ketone	product	% isolated yield (GC)
1			97
2			81
3			(79)
4			74
5			82
6			79[a]
7			79[b]
8			76

[a] Ratio of diastereomers, 2.3:1. [b] A single diastereomer was isolated.

We believe the reaction mechanism closely resembles that of dissolving metal reductions of ketones in the initial steps.[14] Reaction of SmI_2 with the ketone generates a ketyl, which is rapidly protonated by methanol. Further reduction by the second equivalent of SmI_2 produces a carbanion, inducing ring-opening of the epoxide. Tautomerization of the resulting enol provides the observed ketone, with loss of stereochemistry at the position adjacent to the carbonyl.



We have utilized the Sharpless asymmetric epoxidation reaction[9,15] to demonstrate use of this procedure for synthesis of chiral, nonracemic aldol products. Epoxidation of (*E*)-2-octen-1-ol with $Ti(OiPr)_4$/*t*-BuOOH/L-(+)-diethyl tartrate led to a 78% isolated yield of (2*S*,3*S*)-2,3-epoxy-1-octanol (95% ee by capillary GLC analysis of the MTPA ester[16]). Swern oxidation[12] generated the desired aldehyde, which was treated with methyllithium to provide the

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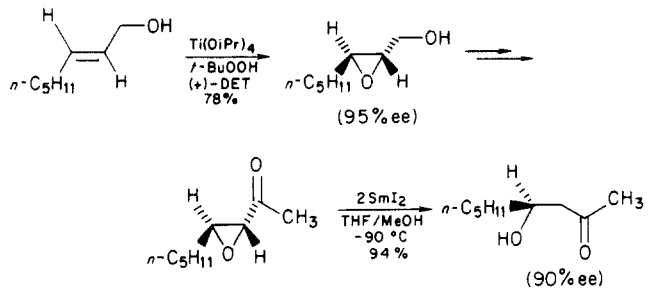

corresponding secondary alcohol. A second Swern oxidation led to the requisite α,β-epoxy ketone. Treatment of this substrate with SmI_2 under the standard conditions allowed isolation of (*S*)-4-hydroxy-2-nonanone in 94% isolated yield (90% ee by ^1H NMR analysis using $Eu(hfc)_3$ shift reagent[17]). It is clear that under these conditions, little if any retroaldol–aldol equilibration occurs that would serve to racemize the β-hydroxy ketone product. As a consequence, the sequence described above should allow access into a variety of chiral, nonracemic aldol products that might be difficult to acquire by more traditional procedures.[18]

Experimental Section

All boiling points and melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 727B spectrophotometer. ^1H NMR spectra were recorded by using $CDCl_3$ as solvent with $CHCl_3$ (δ 7.2) or Me_4Si (δ 0.00) as the internal standard. ^{13}C NMR spectra were recorded by using $CDCl_3$ as both solvent and internal standard (δ 77.00). Packed column gas–liquid chromatographic analyses were conducted with GLC columns (10 ft × $^1/_8$ in.) packed with Carbowax 20M (3% on AW-DMCS Chromosorb W) or SE-30 (5% on AW-DMCS Chromosorb W). Capillary gas–liquid chromatographic analyses were performed with 25-m SE-54 or OV-17 fused silica capillary columns. Flash chromatography[13] was carried out under standard procedures. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon immediately prior to use. Methanol was dried over 3-Å molecular sieves. All reactions were conducted under a positive pressure of argon, utilizing standard bench-top techniques for the handling of air-sensitive materials.[19]

Reduction of α,β-Epoxy Ketones with SmI_2. General Procedure. To a slurry of the Sm powder[20] (0.32 g, 2.1 mmol) in THF (2 mL) at room temperature was added a solution of 1,2-diiodoethane[21] (0.56 g, 2.0 mmol) in THF (2 mL). The resultant olive-green slurry was stirred at ambient temperature for 1 h, after which time the resulting dark blue slurry of SmI_2 formed was cooled to −90 °C (liquid N_2/methanol) and treated with a solution of the α,β-epoxy ketone (1.0 mmol) in MeOH (1 mL) and THF (2 mL). The resultant brown mixture was stirred for 5 min at −90 °C, quenched at this temperature by addition of saturated aqueous K_2CO_3 or pH 8 phosphate buffer, and then warmed to room temperature. The aqueous phase was extracted with Et_2O (5 × 10 mL), and the combined extracts were dried ($MgSO_4$).

1-Hydroxy-3-heptanone. With the general procedure above, 1,2-epoxy-3-heptanone (0.13 g, 1.0 mmol) was reduced to provide 0.12 g (97%) of 1-hydroxy-3-heptanone[22] after flash chromatography (30% EtOAc in hexanes): IR (neat) 3420, 1710 cm^{-1}; ^1H NMR δ 3.8 (t, J = 5 Hz, 2 H), 2.6 (t, J = 5 Hz, 2 H), 2.4 (t, J = 6 Hz, 2 H), 1.7–1.0 (m, 4 H), 0.8 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 211.95, 57.83, 44.25, 43.03, 25.67, 22.22, 13.77; exact mass calcd for $C_7H_{14}O_2$ 130.0994, found 130.0982.

4-Hydroxy-2-nonanone. With the general procedure above, 3,4-epoxy-2-nonanone (0.16 g, 1.0 mmol) was reduced to provide 0.13 g (81%) of 4-hydroxy-2-nonanone[23] after Kugelrohr distillation: bp 60 °C (0.1 mmHg); IR ($CHCl_3$) 3520, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1–3.7 (m, 1 H), 3.0 (s, 1 H), 2.6 (s, 1 H), 2.5 (d, J = 3 Hz, 1 H), 2.0 (s, 3 H), 1.5–1.0 (m, 8 H), 0.8 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 209.74, 67.40, 49.94, 36.33, 31.56, 30.57, 24.95, 22.42, 13.83.

4-Hydroxy-4-methyl-2-pentanone. With the general procedure described above, 3,4-epoxy-4-methyl-2-pentanone (0.11 g, 1.0 mmol) was reduced to afford 79% of 4-hydroxy-4-methyl-2-pentanone[24] by GLC analysis (10 ft. × $^1/_8$ in. 3% Carbowax 20M on AW/DMCS Chromosorb W, 100–180 °C at 60 deg/min).

3-Hydroxycyclohexanone. With the general procedure above, cyclohexenone oxide (0.11 g, 1.0 mmol) was reduced to provide 0.084 g (74%) of 3-hydroxycyclohexanone:[25] bp 80 °C (0.1 mmHg); IR (neat) 3600, 3450, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1 (m, 1 H), 3.0 (s, 1 H), 2.8–1.1 (m, 8 H); ^{13}C NMR δ 210.42, 69.48 50.27, 40.82, 32.57, 20.56.

3-Hydroxy-3,5,5-trimethylcyclohexanone. With the general procedure above, isophorone oxide (0.15 g, 1.0 mmol) was reduced to provide 0.13 g (82%) of 3-hydroxy-3,5,5-trimethylcyclohexanone[7] after Kugelrohr distillation: bp 85 °C (0.1 mmHg); IR ($CHCl_3$) 3580, 3410, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4 (s, 2 H), 2.3 (s, 1 H), 2.2 (s, 2 H), 1.7 (s, 2 H), 1.3 (s, 3 H), 1.1 (s, 3 H), 1.0 (s, 3 H); ^{13}C NMR δ 211.34, 74.69, 53.90, 53.71, 49.76, 35.51, 33.01, 32.25, 28.30; exact mass calcd for $C_9H_{16}O_2$ 156.1150 found 156.1158.

2-Acetylcyclohexanol. With the general procedure above (K_2CO_3 workup), 1-acetyl-1,2-epoxycyclohexane (0.14 g, 1.0 mmol) was reduced to provide 0.11 g (79%) of a mixture of *cis*- and *trans*-2-acetylcyclohexanol[7] after Kugelrohr distillation: bp 85 °C (1.0 mmHg); IR (neat) 3440, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1 (s, 0.5 H), 3.6 (dt, J = 6, 9 Hz, 0.5 H), 3.1 (s, 0.5 H), 2.9–2.8 (m, 0.5 H), 2.5–2.2 (m, 1 H), 2.1 (s, 3 H), 2.0–1.0 (m, 8 H); ^{13}C NMR δ 213.80, 212.79, 70.52, 66.02, 58.70, 53.74, 33.68, 31.78, 28.91, 28.59, 27.63, 25.11 (2 C), 24.10, 22.96, 19.58; exact mass calcd for $C_8H_{14}O_2$ 142.0994, found 142.0982.

2-(1-Hydroxy-1-methylethyl)-5-methylcyclohexanone. With the general procedure above, pulegone oxide[26] (0.17 g, 1.0 mmol) was reduced to provide 0.14 g (79%) of 2-(1-hydroxy-1-methylethyl)-5-methylcyclohexanone[27] after Kugelrohr distillation: bp 70 °C (0.01 mmHg); IR (neat) 3500, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.8 (s, 1 H), 0.98 (s, 6 H), 0.79 (d, J = 5.4 Hz, 3 H), 2.4–0.7 (m, 8 H); ^{13}C NMR δ 215.03, 71.22, 58.70, 51.43, 35.44, 33.86, 28.80, 28.43, 25.59, 22.17.

***trans*-Hexahydro-4a-hydroxy-8a-methyl-1,6(2*H*,5*H*)-naphthalenedione.** With the general procedure above, (1aα,4aα,8a*R**)-tetrahydro-4a-methyl-1a*H*-naphth[1,8a-*b*]oxirene-2,5(3*H*,6*H*)-dione[28] (0.19 g, 1.0 mmol), was reduced to provide 0.14 g (76%) of *trans*-hexahydro-4a-hydroxy-8a-methyl-1,6-(2*H*,5*H*)-naphthalenedione after recrystallization from ether: mp 186–187 °C; IR ($CHCl_3$/Me_2SO) 3330, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.9–1.5 (m, 13 H), 1.3 (s, 3 H); ^{13}C NMR ($CDCl_3$/Me_2SO-d_2) δ 213.59, 209.74, 79.04, 50.56, 49.87, 36.95, 35.93, 32.18, 27.35, 19.92, 19.79; exact mass calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1105.

(*S*)-4-Hydroxy-2-nonanone. With the general procedure above, (3*R*,4*S*)-3,4-epoxy-2-nonanone (0.16 g, 1.0 mmol, 95% ee) was reduced to provide 0.15 g (94%) of (*S*)-4-hydroxy-2-nonanone[21] after Kugelrohr distillation: bp 85 °C (1.0 mmHg); IR ($CHCl_3$) 3520, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1–3.7 (m, 1 H),

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2.8 (s, 1 H), 2.6 (s, 1 H), 2.5 (d, J = 3 Hz, 1 H), 2.0 (s, 3 H), 1.5–1.0 (m, 8 H), 0.8 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 209.79, 67.56, 49.94, 36.36, 31.76, 30.77, 25.11, 22.61, 14.03. ^{1}H NMR analysis ($CDCl_3$, 0.02 M, $C(O)CH_3$, $\Delta\Delta\delta$ 0.15 ppm) using Eu(hfc)$_3$, tris-[3-heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III) (1.1 equiv), as the chiral shift reagent[17] indicated a 95:5 mixture of isomers (90% ee).

Acknowledgment. We thank Dr. Bruce LaBelle for performing the critical chemical shift reagent study and the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (GM 35249) for their generous support of our program. An instrumentation grant from the National Institutes of Health (RR 01709) is also gratefully acknowledged.

An Asymmetric Synthesis of Enantiomerically Pure (*S*)-(+)-Linalool (3,7-Dimethyl-1,6-octadien-3-ol) and a Formal Synthesis of (*R*)-(−)-Linalool

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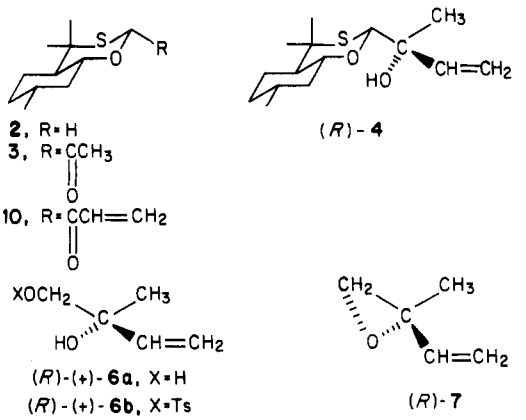
Received December 30, 1985

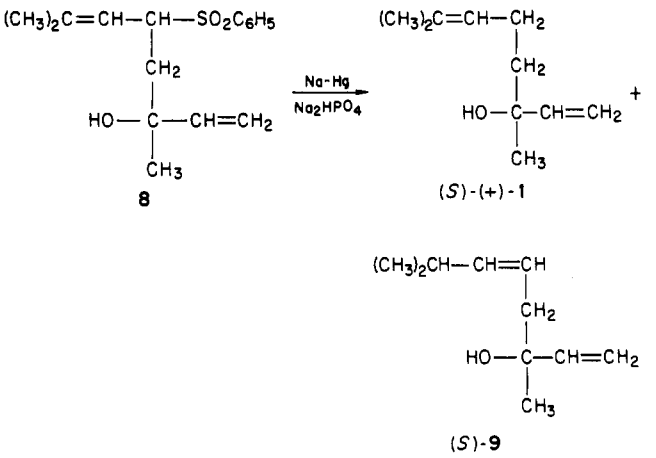
The terpene alcohol linalool (1) occurs in nature in both dextrorotatory (coriandrol) and levorotatory (licareol) forms as a constituent of essential oils,[1] and the correct configuration of the (−)-isomer as *R* was established in the 1960s by two groups of investigators.[2] Although the *dl* isomer has been synthesized by several routes, it has, so far, been only partially resolved.[3] However, a synthesis of enantiomerically pure (−)-**1** in nine steps from a resolved precursor [(*S*)-$C_6H_5CH_2OC(CH_3)(CO_2C_2H_5)CO_2H$[4]] has been reported.[5] We describe here a synthesis of enantiomerically pure (+)-**1** using our previously published[6] asymmetric synthesis employing the readily accessible oxathiane **2**[7] as the chiral template (Scheme I).

Treatment of **3**, obtained from **2** as described,[8] with vinylmagnesium bromide and magnesium chloride at −78 °C gave carbinol (*R*)-**4** in 84% de (92:8 ratio of diastereomers). The major diastereomer was obtained in pure form (as checked by NMR) by recrystallization (52% yield) and was cleaved by *N*-chlorosuccinimide–silver nitrate[9] to (*R*)-2-hydroxy-2-methyl-3-butenal [(*R*)-CH_2=CH(CH_3)C(OH)CHO, (*R*)-**5**], reduced in situ by sodium borohydride to (*R*)-(+)-**6a**, in 62% yield. The latter was converted to the primary mono-*p*-toluenesulfonate (*R*)-(+)-**6b** (83% yield) which, on treatment with ground potassium hydroxide in tetrahydrofuran yielded (*R*)-1,2-epoxy-2-methyl-3-butene (isoprene 1,2-monoepoxide, **7**).

Scheme I



Scheme II



Compounds **5**, **6a**, and **7** are chiral isoprenoid synthons. Since direct conversion of **7** to the monoterpene linalool **1** with prenyl organometallic reagents $(CH_3)_2C$=$CHCH_2M$ appears unfeasible,[10,11] **7** was allowed to react with the anion of prenyl phenyl sulfone, $(CH_3)_2C$=$CHCH_2SO_2C_6H_5$ as previously reported by Julia.[5,10] Reduction of sulfone **8** with sodium amalgam in anhydrous methanol led to linalool, as previously described,[5,10] along with the expected position isomer **9** (Scheme II). Use of the modified reducing conditions described by Trost,[12] i.e., use of disodium hydrogen phosphate (Na_2HPO_4) in the amalgam reduction, improved the ratio of **1**:**9** from the reported[10] 2:1 to 3:1, and **1** could be separated from the position isomer **9** by chromatography on silica gel (gradient elution) to give chemically and enantiomerically pure (+)-**1**. Chemical purity was checked by comparison of proton and ^{13}C NMR spectra with those of authentic samples of (+)-linalool; enantiomeric purity (≥99% ee) was determined by using a chiral shift reagent, Eu(hfc)$_3$.[13]

(*S*)-(−)-**6a** in 94% ee was similarly asymmetrically synthesized from the acryloyl derivative of **2**, **10**, obtained by treating the lithium derivative of **2** with acrolein followed by Swern oxidation.[14] Reaction of **10** with methylmagnesium bromide followed by oxathiane cleavage and sodium borohydride reduction (vide supra) gave (*S*)-(−)-**6a**. Unfortunately the diastereomer of (*S*)-**4** obtained in the

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