**(3*S*,7a*R*)-5-Oxo-3-phenyl-2,3,5,6,7,7a-hexahydropyrrolo[2,1-*b*]oxazole (10a).** Compound **10a** was obtained in 80% yield via method C using the (*S*)-phenylglycinol-derived succinimide **7a** (0.120 g, 0.55 mmol) and $NaBH_4$ (0.207 g, 5.5 mmol) in 10 mL of absolute ethanol. Workup afforded 107 mg of a colorless oil as a mixture of 5-ethoxy-2-pyrrolidinone diastereomers **8a** and approximately 10% of cyclized bicyclic lactam **10a**. This material was carried directly on to the next step. The bicyclic lactam was obtained in 96% yield from crude 5-ethoxy-2-pyrrolidinone **8a** (0.107 g, 0.43 mmol) and trifluoroacetic acid (0.49 g, 0.33 mL, 4.3 mmol) in 45 mL of $CH_2Cl_2$. This gave 84 mg (96%) of **10a** isolated as a slightly yellowish solid: mp 64–67 °C; $[\alpha]^{22}_D$ +154.1° (*c* 1.29, EtOH); FTIR ($CHCl_3$ film) 3018, 1706 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.16 (m, 1 H), 2.340–2.81 (m, 3 H), 3.810 (dd, 1 H, *J* = 8.7, 7.5 Hz), 4.56 (dd, 1 H, *J* = 8.7, 7.5 Hz), 510 (dd, 1 H, *J* = 7.5, 7.5 Hz), 5.28 (dd, 1 H, *J* = 6.2, 2.5 Hz, angular H), 7.21–7.37 (m, 5 H). Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.67; H, 6.34; N, 6.77.

**(3*S*,8a*R*)-3-Isopropyl-5-oxo-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (10d).** Compound **10d** was obtained in 77% yield via sodium borohydride reduction (0.96 g, 25.4 mmol) of (*S*)-valinol-derived glutarimide (0.51 g, 2.5 mmol) in 25 mL of absolute ethanol. Workup, as above, gave 450 mg of a colorless oil that proved to be mainly the cyclized material **10d**. However, it was still subjected to the cyclization step using trifluoroacetic acid (2.18 g, 1.47 mL, 19.1 mmol). Workup gave 281 mg of pure **10d**: $[\alpha]^{22}_D$ +19.4° (*c* 2.3, EtOH); FTIR (neat) 2960, 1654 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.86 (d, 3 H, *J* = 6.8 Hz), 0.88 (d, 3 H, *J* = 6.8 Hz), 1.39 (m, 1 H), 1.64 (m, 1 H), 1.87 (m, 1 H) 2.07–2.32 (m, 3 H), 2.49 (m, 1 H), 3.63 (dd, 1 H, *J* = 8.7, 6.9 Hz), 4.00 (dd, 1 H, 8.7, 7.2 Hz), 4.156 (m, 1 H), 4.70 (dd, 1 H, *J* = 8.7, 4.7 Hz). Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.22; H, 9.52; N, 7.77.

**(3*S*,5a*S*,9a*R*,9b*R*)-3-Isopropyl-5-oxo-2,3,6,7,8,9,9a,9b-octahydrooxazolo[2,3-*a*]isoindole (10e) and (3*S*,5a*R*,9a*S*,9b*R*)-3-Isopropyl-5-oxo-2,3,6,7,8,9,9a,9b-octahydrooxazolo[2,3-*a*]isoindole (10f).** Compounds **10e** and **10f** were obtained in 91% yield via method C using cyclohexane 1,2-dicarboximide **7e** (0.86 g, 3.6 mmol) and sodium borohydride (1.36 g, 36.0 mmol) in 30 mL of absolute ethanol. Workup gave 880 mg of a colorless oil composed of a mixture of ethoxy diastereomers **8e** and **8f** and 20% of cyclized material **10e** and **10f**. This mixture without any further handling, was subjected to the cyclization step. The material above (880 mg) and trifluoroacetic acid (3.7 g, 2.5 mL, 32.7 mmol) were dissolved in 50 mL of dichloromethane and gave 775 mg (99%) of cyclized products as a colorless oil.

The diastereomers **10e** and **10f** were separated by flash chromatography on 22 g of Amicon 50-$\mu$m silica gel using 15% ethyl acetate in hexane as eluent. The first eluting diasteromer **10e** was isolated (36%) as a white solid: mp 45–46 °C; $[\alpha]^{22}_D$ +54.8° (*c* 2.47, EtOH); FTIR (neat) ($CHCl_3$ film) 2932, 1708 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.89 (d, 3 H, *J* = 6.7 Hz), 0.92 (d, 3 H, *J* = 6.7 Hz), 0.97–1.77 (m, 8 H), 2.07 (m, 1 H), 2.56 (m, 1 H, C*H*$(CH_3)_2$), 2.84 (m, 1 H), 3.71–8.86 (m, 2 H)8 4.08 (dd, 1 H, *J* = 8.5, 7.0 Hz), 5.24 (d, 1 H, *J* = 5.1 Hz, angular H). Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 70.22; H, 9.57; N, 6.20. The second eluting diastereomer **10f** was isolated (64%) as a colorless oil: $[\alpha]^2_2D$ +32.5° (*c* 2.55, EtOH); FTIR (neat) 2933, 1714 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 0.88 (d, 3 H, *J* = 6.7 Hz), 0.96 (d, 3 H, *J* = 6.7 Hz), 1.27–1.73 (m, 8 H), 1.88 (m, 1 H), 2.29 (m, 1 H), 2.54 (m, 1 H), 3.67 (m, 2 H), 4.09 (m, 1 H), 4.86 (d, 1 H, *J* = 3.8 Hz, angular H).

**(3*S*,7a*R*)-3-Isopropyl-7a-methyl-5-oxo-2,3,5,6,7,7a-hexahydropyrolo[2,1-*b*]oxazole (11). Method D.** Valinol-derived succinimide **7b** (0.54 g, 2.9 mmol) was dissolved into 25 mL dry THF contained in a dry 50-mL flask equipped with magnetic stir bar, argon atmosphere, and rubber septum. To this stirring solution at room temperature was added methylmagnesium bromide (5.8 mL, 8.8 mmol, 3.0 equiv) over a 3-min period producing a cloudy yellowish mixture.[8] The mixture was stirred for 3 h at room temperature before being quenched by addition to 25 mL of saturated $NH_4Cl$ solution. This mixture was extracted with 3 × 25 mL portions of $Et_2O$, the combined organic extracts were dried ($K_2CO_3$), and the solvent was removed to afford 315 mg of a colorless oil. The aqueous extracts were evaporated and the resulting salts extracted with 2 × 50 mL of $Et_2O$, furnishing an additional 114 mg of product (73% overall yield). This material was carried on directly to the cyclization step without further purification. The crude adduct (430 mg, 2.1 mmol) was added to 50 mL of dichloromethane and trifluoroacetic acid (2.4 g, 1.6 mL, 21.3 mmol). After workup, 361 mg of **11** (93%) was obtained as a tan-colored oil: $[\alpha]^{22}_D$ +89.3° (*c* 2.60, EtOH); $[\alpha]^{22}_D$ lit.[9] +95.5° (*c* 2.8, EtOH); $^1H$ NMR ($CDCl_3$) $\delta$ 0.86 (d, 3 H, *J* = 6.6 Hz), 1.01 (d, 3 H, *J* = 6.6 Hz), 1.45 (s, 3 H, angular $CH_3$), 1.63 (m, 1 H, C*H*$(CH_3)_2$), 2.14 (m, 2 H), 2.45 (m, 1 H), 2.75 (m, 1 H), 3.56 (m, 1 H), 3.83 (dd, 1 H, *J* = 8.7, 6.2 Hz), 4.13 (dd, 1 H, *J* = 8.7, 7.5 Hz).

**Acknowledgment.** We are grateful to the National Institutes of Health and the Bristol-Myers Co. for financial support of portions of this work.

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## 4-[(*tert*-Butyldiphenylsilyl)oxy]-2-(tributylstannyl)-(*E*)-2-buten-1-ol: A Useful Precursor for Tetrahydrofuran Synthesis

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In the course of our studies toward the synthesis of the southern zone of avermectin $A_{2b}$,[1] we desired an efficient route to prepare cis-fused octahydrobenzofurans. In particular we required a methodology that permitted diastereoisomeric control in the construction of three contiguous asymmetric centers as well as the incorporation of an *E* exocyclic double bond. We wish to report that 4-[(*tert*-butyldiphenylsilyl)oxy]-2-(tributylstannyl)-(*E*)-2-buten-1-ol (**2**) has proven to be a valuable precursor to such functionalized octahydrobenzofurans, as well as a variety of other substituted tetrahydrofurans.

Critical to the approach was the formation of dianion **3**.[2] Diol **1**, which was prepared according to the procedure of Fleming et al.,[3] was regioselectively protected using *tert*-butyldiphenylsilyl chloride to provide the monosilyl derivative **2** (93%). Treatment of **2** with 2.1 equiv of *n*-butyllithium for 2 h at 35 °C in THF gave the dianion **3**. Maintenance of the temperature at −35 °C was crucial; higher temperatures led to severe decomposition of the dianion and lower temperatures led to its incomplete formation. A small amount of protonated dianion was recovered from each reaction. However, attempts to alter the basicity of the dianion by transmetalation with trimethylaluminum or cerium trichloride did not improve the yield. Reactions of dianion **3** with various carbonyl compounds are summarized in Scheme I.

The dianion also smoothly added to a variety of epoxy aldehydes and epoxy ketones (Scheme II). Reaction of dianion **3** with 2,3-epoxycyclohexan-1-one resulted in the

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(2) Similar dianions have been formed from 2-bromoallyl alcohol, see: Corey, E. J.; Widiger, G. N. *J. Org. Chem.* **1975**, *40*, 2975. Schlosser, M.; Hammer, E. *Helv. Chim. Acta* **1974**, *57*, 2547.
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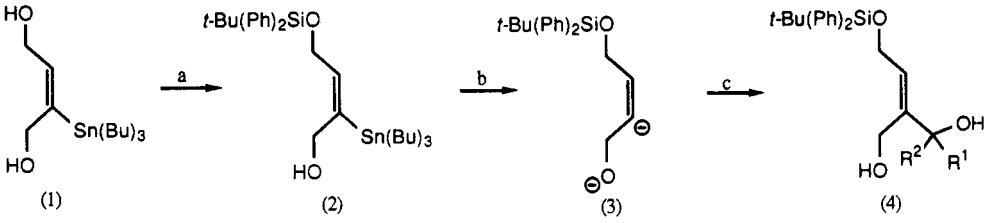
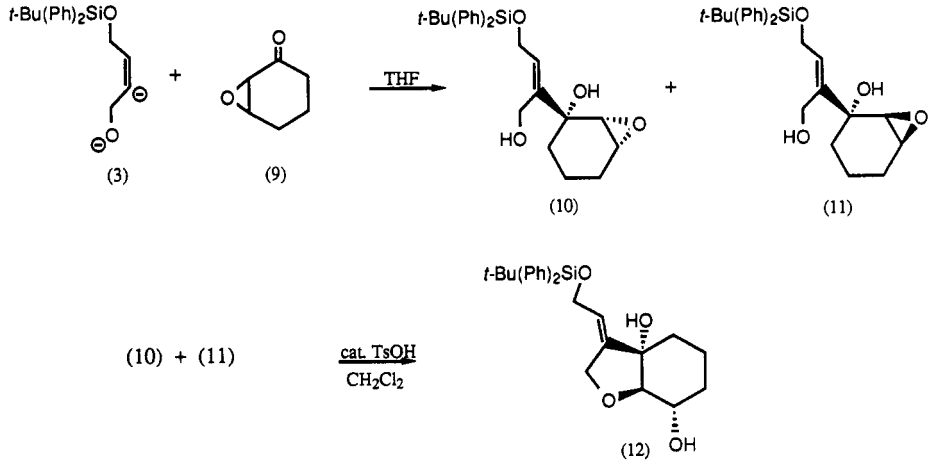
**Scheme I**

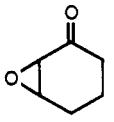
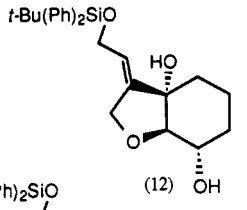
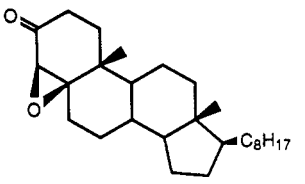
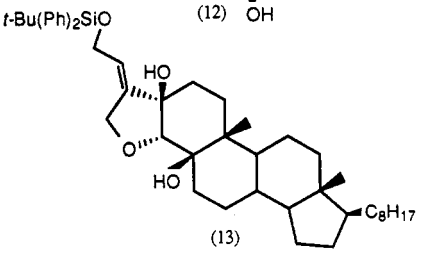
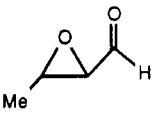
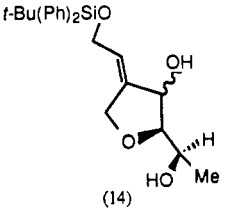



Reagents; a) *t*-Bu(Ph)$_2$SiCl, imidazole, DMF, 0°C. b) 2.1 eq. *n*-BuLi, THF, -35°C, 2 hr. c) $R^1R^2CO$, THF, -78°C.

| Entry | $R^1$ | $R^2$ | Yield | Entry | $R^1$ | $R^2$ | Yield |
|---|---|---|---|---|---|---|---|
| 1 | Ph | H | 72% (5) | 3 | *n*-$C_8H_{17}$ | $CH_3$ | 68% (7) |
| 2 | *n*-$C_4H_9$ | H | 70% (6) | 4 | $R^1 = R^2$ = cyclopentyl | | 64% (8) |

**Scheme II**




| Epoxide | Product | Yield |
|---|---|---|
|  |  | 38% |
|  |  | 35% |
|  |  | 47% |

formation of a 2.2:1 mixture of diastereoisomers **10** and **11**, respectively (64%). Of this mixture, only **10** had the necessary stereochemistry for rapid cyclization. Thus treatment of **10** and **11** with a catalytic amount of *p*-toluenesulfonic acid afforded the single diastereoisomer, octahydrobenzofuran **12** (58%), along with recovery of the nonreactive epoxide **11**. The method was extended to 4$\beta$,5$\beta$-epoxycholestan-3-one and *trans*-2,3-epoxybutanal. The initial addition products were very acid sensitive and were normally not isolated. They were treated directly

with a catalytic amount of *p*-toluenesulfonic acid to yield the cyclization products. These results are summarized in Scheme II.

The cyclization examples illustrate the utility of 4-[(*tert*-butyldiphenylsilyl)oxy]-2-(tributylstannyl)-(*E*)-2-buten-1-ol as a precursor to a variety of functionalized tetrahydrofurans. Additionally the examples highlight the opportunity for stereoselectivity in bicyclic cases due to the exclusive cyclization of only one diastereoisomer. This resulted in diastereoisomeric control of three contiguous asymmetric centers. Further studies in this laboratory are focusing on the application of this methodology toward more complex avermectin targets.

## Experimental Section

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Infrared spectra were recorded as KBr disks or films on a Sargent Welch SP3-100, Perkin-Elmer 283, or Nicolet 7199 FT instrument. $^1$H NMR spectra were recorded on a JEOL FX270, Varian VXR-300, or Varian XL-400 spectrometer using tetramethylsilane as internal standard. Mass spectra were recorded on a VG7070F or VG70-250SE mass spectrometer. Microanalyses were determined at G. D. Searle and Company, Skokie, IL 60077. Samples for microanalyses that were oils were purified by flash chromatography, rotary evaporated, and subsequentially further evaporated at ca. 0.1 mmHg.

Hexane, diethyl ether, and ethyl acetate were purified by distillation. THF was dried by distillation under nitrogen from sodium benzophenone ketyl. DMF and $CH_2Cl_2$ were freshly distilled from $CaH_2$. All reactions were carried out under dry nitrogen. Silica gel for chromatography refers to the Merck product Kieselgel 60 (Art. 9385). Thin-layer chromatography was performed on Merck Kieselgel 60 F254 (Art. 5715).

**Preparation of 4-[(*tert*-Butyldiphenylsilyl)oxy]-2-(tributylstannyl)-(*E*)-2-buten-1-ol (2).**[4] To a solution of 2-(tributylstannyl)-(*E*)-2-butene-1,4-diol (2.50 g) in DMF (50 mL) at 0 °C was added imidazole (0.451 g) and *tert*-butyldiphenylsilyl chloride (1.83 g). The solution was stirred at 0 °C for 6 h, and crushed ice (2.5 g) was added. The solution was diluted with $Et_2O$ (200 mL), washed with saturated $NH_4Cl$ (3 × 50 mL), dried, and evaporated. Chromatography (80/20 hexanes/$Et_2O$) yielded **2** (3.62 g, 93%) as a colorless oil: IR (neat) 3490, 2950, 1470, 1430, 1110, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.80–0.91 (m, 15 H), 1.03 (s, 9 H), 1.25–1.36 (m, 6 H), 1.38–1.56 (m, 6 H), 4.08 (d, 2 H, $J$ = 6 Hz, $J_{^{119}Sn-H}$ = 20 Hz), 4.21 (d, 2 H, $J$ = 6 Hz), 5.72 (m, 1 H, $J_{^{119}Sn-H}$ = 31 Hz), 7.32–7.45 (m, 6 H), 7.65–7.70 (m, 4 H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 147.3, 138.1, 135.7, 133.8, 129.6, 127.6, 63.8, 61.3, 29.1, 27.3, 26.8, 19.1, 13.8, 10.0; mass spectrum (CI), *m/e* 559, 541, 489, 429, 303, 251, 199, 177, 119, 57, 41. Anal. Calcd for $C_{32}H_{52}O_2SiSn$: C, 62.44; H, 8.51. Found: C, 62.43; H, 8.23.

**General Procedure for Carbonyl Addition to Dianion 3. Preparation of 2-(Hydroxymethyl)-4-[(*tert*-butyldiphenylsilyl)oxy]-1-phenyl-(*E*)-2-buten-1-ol (5).** To a solution of 4-[(*tert*-butyldiphenylsilyl)oxy]-2-(tributylstannyl)-(*E*)-2-buten-1-ol (0.303 g) in THF (7 mL) at −78 °C was added *n*-BuLi (0.67 mL of a 1.6 M solution in hexanes) dropwise. The reaction mixture was warmed to −35 °C for 2 h and then cooled to −78 °C. Benzaldehyde (0.058 g) in THF (1 mL) was added dropwise, and the solution was kept at −78 °C for 30 min and quenched with saturated $NH_4Cl$ (1 mL). The solution was diluted with $Et_2O$ (50 mL), washed with saturated $NH_4Cl$ (3 × 15 mL), dried, and evaporated. Chromatography (60/40 hexanes/$Et_2O$) yielded **5** (0.160 g, 72%) as a colorless oil: IR (neat) 3150–3650, 2880, 1440, 1120, 710 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.06 (s, 9 H), 1.97 (t, 1 H, $J$ = 6 Hz), 2.68 (d, 1 H, $J$ = 4 Hz), 3.91 (m, 2 H), 4.34 (m, 2 H), 5.30 (d, 1 H, $J$ = 4 Hz), 5.88 (t, 1 H, $J$ = 6 Hz), 7.33–7.43 (m, 11 H), 7.63–7.69 (m, 4 H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 141.8, 141.2, 135.60, 135.58, 133.3, 129.78, 129.75, 128.4, 127.7, 127.6, 126.1, 77.9, 60.3, 58.6, 26.8, 19.1; mass spectrum (CI), *m/e* 413, 397, 337, 279, 257, 239, 199, 179, 159, 143, 107, 91. Anal. Calcd for $C_{27}H_{32}O_3Si$: C, 74.96; H, 7.46. Found: C, 74.83; H, 7.59.

**Preparation of 3-(Hydroxymethyl)-1-[(*tert*-butyldiphenylsilyl)oxy]-(*E*)-2-octen-4-ol (6).** Valeraldehyde (0.051 g) was added to dianion **3** (0.4 mmol), prepared according to the general procedure, in THF (5 mL) at −78 °C to yield **6** (0.115 g, 70%) as a colorless oil: IR (neat) 3100–3700, 2860, 1470, 1435, 1120, 860, 705 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.91 (t, 3 H, $J$ = 6.0 Hz), 1.05 (s, 9 H), 1.20–1.38 (m, 4 H), 1.56–1.63 (m, 2 H), 1.92 (d, 1 H, $J$ = 4.0 Hz), 2.24 (t, 1 H, $J$ = 5.6 Hz), 4.07 (d, 2 H, $J$ = 5.6 Hz), 4.12 (m, 1 H), 4.31 (d, 2 H, $J$ = 6.0 Hz), 5.69 (t, 1 H, $J$ = 6.0 Hz), 7.36–7.46 (m, 6 H), 7.66–7.70 (m, 4 H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 142.0, 135.6, 133.3, 129.8, 128.6, 127.7, 76.6, 60.2, 58.3, 35.2, 28.0, 26.7, 22.6, 19.1, 14.0; mass spectrum (CI), *m/e* 377, 337, 275, 239, 199, 121, 95. Anal. Calcd for $C_{25}H_{36}O_3Si$: C, 72.77; H, 8.79. Found: C, 72.40; H, 8.69.

**Preparation of 1-[1-Hydroxy-4-[(*tert*-butyldiphenylsilyl)oxy]-(*E*)-2-buten-2-yl]cyclopentanol (8).** Cyclopentanone (0.043 g) was added to dianion **3** (0.5 mmol), prepared according to the general procedure, in THF (6 mL) at −78 °C to yield **8** (0.134 g, 64%) as a colorless oil: IR (neat) 3100–3700, 2980, 1480, 1140, 915, 740 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.05 (s, 9 H), 1.67–1.90 (m, 9 H), 2.33–2.38 (m, 1 H), 4.09 (d, 2 H, $J$ = 4 Hz), 4.32 (d, 2 H, $J$ = 6 Hz), 5.68 (t, 1 H, $J$ = 6 Hz), 7.36–7.46 (m, 6 H), 7.66–7.70 (m, 4 H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 144.2, 135.6, 133.4, 129.8, 127.7, 126.2, 84.7, 60.5, 59.3, 38.8, 26.8, 23.3, 19.1; mass spectrum (CI), *m/e* 433 ($M^+$ + Na), 375, 335, 315, 239, 227, 207; exact mass calcd for $C_{25}H_{34}O_3Si$ (M + $Na^+$) 433.2175, found (M + $Na^+$) 433.2201.

**Preparation of 3-(Hydroxymethyl)-1-[(*tert*-butyldiphenylsilyl)oxy]-4-methyl-(*E*)-2-dodecen-4-ol (7).** 2-Decanone (0.139 g) was added to dianion **3** (0.7 mmol), prepared according to the general procedure, in THF (8 mL) at −78 °C to yield **7** (0.231 g, 68%) as a colorless oil: IR (neat) 3140–3700, 2940, 1470, 1440, 1390, 1120, 1080, 860, 720 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.89 (t, 3 H, $J$ = 6 Hz), 1.05 (s,9 H), 1.20–1.31 (br s, 12 H), 1.32 (s, 3 H), 1.59 (m, 2 H), 1.98 (br s, 1 H), 2.41 (br s, 1 H), 4.08 (br s, 2 H), 4.32 (d, 2 H, $J$ = 6 Hz), 5.71 (t, 1 H, $J$ = 6 Hz), 7.37–7.48 (m, 6 H), 7.67–7.72 (m, 4 H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 146.0, 135.6, 133.4, 129.8, 127.7, 126.8, 76.0, 60.5, 58.4, 41.6, 31.9, 30.0, 29.6, 29.3, 28.1, 26.8, 24.1, 22.6, 19.1, 14.1; mass spectrum (CI), *m/e* 407, 329, 267, 199, 139, 121, 107, 93, 69, 43. Anal. Calcd for $C_{30}H_{46}O_3Si$: C, 74.63; H, 9.61. Found: C, 74.53; H, 9.84.

**Preparation of 3(*R*,*S*)-Hydroxy-2(*R*,*S*)-[1(*R*,*S*)-hydroxyethyl]-4-[3-[(*tert*-butyldiphenylsilyl)oxy]-(*E*)-propylidene]-2,3,4,5-tetrahydrofuran (14).** *trans*-2,3-Epoxybutan-1-al[5] (0.128 g) was added to dianion **3** (1.5 mmol), prepared according to the general procedure, in THF (18 mL) at −78 °C. The solution was stirred for 10 min followed by the addition of 5% $NH_4Cl$ (5 mL). The reaction mixture was diluted with $Et_2O$ (100 mL), washed with 5% $NH_4Cl$ (3 × 20 mL), dried, and evaporated. The crude reaction mixture was diluted with dichloromethane (30 mL), *p*-toluenesulfonic acid (0.010 g) was added, and the solution was stirred for 45 min. $Et_2O$ (100 mL) was added, and the solution was washed with saturated $NH_4Cl$ (3 × 25 mL) and saturated $NaHCO_3$ (3 × 25 mL), dried, and evaporated. Chromatography (60/40 $Et_2O$/hexanes) yielded **14** (0.288 g, 47%) as a colorless oil: IR (neat) 3120–3680, 2880, 1440, 1120, 720 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.05 (s, 9 H), 1.29 (d, 3 H, $J$ = 6 Hz), 1.75 (d, 1 H, $J$ = 6 Hz), 1.94 (d, 1 H, $J$ = 4 Hz), 3.32 (dd, 1 H, $J$ = 8, 6 Hz), 3.94 (m, 1 H), 4.17 (d, 2 H, $J$ = 4 Hz), 4.33 (s, 2 H), 4.49 (m, 1 H), 5.65 (m, 1 H), 7.37–7.48 (m, 6 H), 7.60–7.65 (m, 4 H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 141.9, 135.6, 133.8, 129.8, 127.7, 121.8, 87.0, 77.2, 73.3, 68.2, 68.1, 61.9, 29.7, 26.8, 18.9; mass spectrum (CI), *m/e* 355 ($M^+$ − *t*-Bu), 337, 243, 199, 129, 95; exact mass calcd for $C_{20}H_{23}O_4Si$ ($M^+$ − *t*-Bu) 355.1366, found ($M^+$ − *t*-Bu) 355.1349.

**Preparation of [1*S*(*R*),2*S*(*R*),6*S*(*R*)]-2-Hydroxy-2-[1-(hydroxymethyl)-3-[(*tert*-butyldiphenylsilyl)oxy]-(*E*)-1-propen-1-yl]-7-oxabicyclo[4.1.0]heptane, 10 (Major), and [1*S*(*R*),2*R*(*S*),6*S*(*R*)]-2-Hydroxy-2-[1-(hydroxymethyl)-3-[(*tert*-butyldiphenylsilyl)oxy]-(*E*)-1-propen-1-yl]-7-oxabicyclo[4.1.0]heptane, 11 (Minor).** 2,3-Epoxycyclohexan-1-one

(4) The same regioselective protection was observed when *tert*-butyldimethylsilyl chloride was used in place of *tert*-butyldiphenylsilyl chloride.

(5) Prepared according to: Wellman, G. R.; Lam, B.; Anderson, E. L.; White, E. *Synthesis* **1976**, 547.

(0.095 g) was added to dianion **3** (0.85 mmol), prepared according to the general procedure, in THF (10 mL) at −78 °C. The solution was stirred for 45 min followed by the addition of 5% $NH_4Cl$ (5 mL). $Et_2O$ (100 mL) was added, and the solution was washed with saturated NaCl (3 × 25 mL), dried and evaporated. A crude $^1H$ NMR analysis (400 MHz, $CDCl_3$) at this point showed a 2.2:1 ratio of diastereoisomers **10** and **11**. Chromatography (60/40 $Et_2O$/hexanes) yielded **10** and **11** (0.239 g, 64%) in a 1.8:1 ratio of diastereoisomers as a colorless oil: IR (neat) 3140–3700, 2950, 1480, 1120, 710 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9 H), 1.15–2.01 (m, 6 H), 2.10 (t, 1 H, $J$ = 6.8 Hz, minor diastereoisomer), 2.67 (s, 1 H, major diastereoisomer), 2.75 (t, 1 H, $J$ = 6.8 Hz, major diastereoisomer), 2.80 (s, 1 H, minor diastereoisomer), 3.03 (d, 1 H, $J$ = 3.6 Hz, minor diastereoisomer), 3.13 (d, 1 H, $J$ = 4.0 Hz, major diastereoisomer), 3.27 (t, 1 H, $J$ = 4.0 Hz, minor diastereoisomer), 3.41 (m, 1 H, major diastereoisomer), 4.08 (m, 2 H, major diastereoisomer), 4.18 (m, 2 H, minor diastereoisomer), 4.36 (d, 2 H, $J$ = 6.0 Hz, minor diastereoisomer), 4.40 (d, 2 H, $J$ = 6.0 Hz, major diastereoisomer), 5.71 (t, 1 H, $J$ = 6.0 Hz, major diastereoisomer), 6.00 (t, 1 H, $J$ = 6.0 Hz, minor diastereoisomer), 7.37–7.48 (m, 6 H), 7.60–7.81 (m, 4 H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 143.0, 135.7, 133.3, 129.8, 128.8, 127.8, 73.0, 60.4, 58.2, 56.9, 53.4, 31.6, 26.8, 22.6, 19.0, 15.9; mass spectrum (CI), $m/e$ 439 ($M^+$ + H), 421, 403, 199, 185, 165. Anal. Calcd for $C_{26}H_{34}O_4Si$: C, 71.19; H, 7.81. Found: C, 71.17; H, 8.19.

**Preparation of [4a*S*(*R*),7*S*(*R*),7a*R*(*S*)]-3-[3-[(*tert*-Butyldiphenylsilyl)oxy]-(*E*)-propylidene]octahydrobenzofuran-4a,7-diol (12).** *p*-Toluenesulfonic acid (0.010 g) was added to a 2.2:1 solution of **10** and **11** (0.120 g) in dichloromethane (20 mL) and stirred for 45 min. $Et_2O$ (75 mL) was added, and the solution was washed with saturated $NH_4Cl$ (3 × 15 mL) and saturated $NaHCO_3$ (3 × 15 mL), dried, and evaporated. Chromatography (60/40 $Et_2O$/hexanes) yielded **12** (0.069 g, 58%) as a colorless oil: IR (neat) 3120–3700, 2940, 1460, 1125, 710 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9 H), 1.10–1.28 (m, 1 H), 1.34–1.47 (m, 1 H), 1.62–1.71 (m, 2 H), 1.76–1.85 (m, 1 H), 1.92–1.99 (m, 1 H), 2.26 (s, 1 H), 2.44 (d, 1 H, $J$ = 2.8 Hz), 3.38 (m, 1 H), 3.59 (d, 1 H, $J$ = 6.8 Hz), 4.18 (m, 2 H), 4.24, 4.41 (AB q, 2 H, $J$ = 14 Hz), 5.57 (m, 1 H), 7.35–7.47 (m, 6 H), 7.62–7.69 (m, 4 H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 141.4, 135.5, 133.3, 129.8, 127.7, 120.1, 88.4, 77.8, 68.9, 66.9, 61.8, 31.9, 30.0, 26.7, 19.0, 18.6; mass spectrum (CI), $m/e$ 439 ($M^+$ + H), 421, 403, 199, 165, 147, 121. Anal. Calcd for $C_{26}H_{34}O_4Si$: C, 71.19; H, 7.81. Found: C, 71.08; H, 8.14.

**Preparation of 3,4-[4-[3-[(*tert*-Butyldiphenylsilyl)oxy]-(*E*)-propylidene]tetrahydrofurano]-5β-cholestane-3β,5-diol (13).** 4β,5β-Epoxycholestan-3-one[6] (0.512 g) was added to dianion **3** (1.28 mmol), prepared according to the general procedure, in THF (15 mL) at −78 °C. The solution was stirred for 45 min followed by the addition of 5% $NH_4Cl$ (5 mL). The reaction mixture was diluted with $Et_2O$ (100 mL), washed with 5% $NH_4Cl$ (3 × 20 mL), dried, and evaporated. The crude reaction mixture was diluted with dichloromethane (30 mL), *p*-toluenesulfonic acid (0.010 g) was added, and the solution was stirred for 45 min. $Et_2O$ (100 mL) was added, and the solution was washed with saturated $NH_4Cl$ (3 × 25 mL) and saturated $NaHCO_3$ (3 × 25 mL), dried, and evaporated. Chromatography (60/40 $Et_2O$/hexanes) yielded **13** (0.325 g, 35%) as a white solid: mp 51–52 °C; IR (KBr disk) 3200–3640, 2980, 1380, 1140, 710 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.69 (s, 3 H), 0.82–2.10 (m, 37 H), 0.98 (s, 3 H), 1.05 (s, 9 H), 2.25 (br s, 1 H), 2.93 (s, 1 H), 2.96 (br s, 1 H), 4.18 (m, 2 H), 4.37 (m, 2 H), 5.86 (t, 1 H, $J$ = 6.4 Hz), 7.37–7.48 (m, 6 H), 7.66–7.71 (m, 4 H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 141.2, 135.7, 135.6, 133.3, 129.8, 128.8, 127.7, 72.9, 67.4, 67.3, 60.5, 58.8, 56.2, 55.9, 48.1, 42.5, 39.7, 39.5, 36.10, 36.07, 35.8, 35.2, 31.3, 30.2, 28.4, 28.3, 28.2, 28.0, 26.8, 24.3, 23.8, 22.8, 22.6, 21.4, 19.1, 18.6, 18.4, 11.9; mass spectrum (CI), $m/e$ 733 ($M^+$ + Li), 691, 453, 327. Anal. Calcd for $C_{47}H_{70}O_4Si$: C, 77.63; H, 9.70. Found: C, 77.36; H, 9.98.

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## Characterization of 2-Siloxyoxiranes Formed by Epoxidation of Silyl Enol Ethers with Dimethyldioxirane

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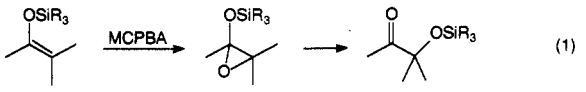
The oxidation of silyl enol ethers by peroxy acids involves the intermediacy of 2-siloxyoxiranes (eq 1).[1] Under the normally acidic reaction conditions, however, these intermediates quickly rearrange to the corresponding α-siloxy carbonyl compounds, and few 2-siloxyoxiranes have been isolated or characterized.[2,3] We have examined dimethyldioxirane as a reagent for the preparation of 2-siloxyoxiranes. Dioxirane reagents[4,5] are efficient yet mild oxidants, react well at low temperatures, and should not promote acid-catalyzed rearrangement of the siloxyoxirane products. Two recent reports of the epoxidation of alkyl enol ethers by dioxirane reagents prompts us to report our results.[6]



(1)

Initial attempts to isolate the epoxides formed by the reaction of dimethyldioxirane with simple *tert*-butyldimethylsilyl enol ethers met with limited success. α-Siloxy and α-hydroxy carbonyl compounds arising from the rearrangement of the siloxyoxirane intermediates[1] were often predominant. To minimize the rearrangement upon workup, we performed the reactions directly in acetone-$d_6$ using dimethyldioxirane-$d_6$. Dimethyldioxirane-$d_6$ was prepared from acetone-$d_6$ and aqueous potassium caroate and was distilled as a solution in wet acetone-$d_6$ (see the Experimental Section).[7] The reagent thus prepared could be dried over $MgSO_4$, but was generally used wet since $MgSO_4$ catalyzed some decomposition of the dioxirane.

Silyl enol ethers **1a–g** reacted with 1 equiv of dimethyldioxirane-$d_6$ in acetone-$d_6$ at −78 °C (Scheme I). After 2–5 min, each reaction mixture was warmed to room temperature and immediately examined by $^1H$ NMR and mass spectrometry (EI, low resolution). An aliquot of each product solution was evaporated at 0 °C under reduced pressure and examined by infrared spectroscopy. Thus, the analysis of each product solution was complete within 15–30 min after product formation.

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