ORGANOMETALLICS

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Silicon in Synthesis. 18. Synthesis of Methyl Ketones and (*R*)-(+)-Frontalin Using (1-Chloro-1-(trimethylsilyl)ethyl)lithium for the Direct Conversion of Aldehydes and Ketones into α,β-Epoxy Trimethylsilanes

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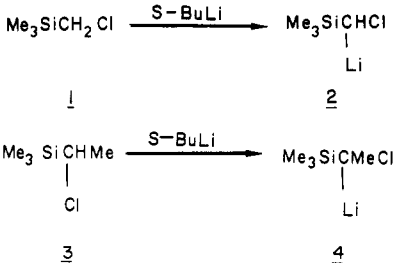
Treatment of (1-chloroethyl)trimethylsilane (3) with *sec*-butyllithium in THF at −78 °C gave (1-chloro-1-(trimethylsilyl)ethyl)lithium (4). The reagent 4 reacts with aldehydes and ketones to give epoxy trimethylsilanes, which on acid hydrolysis yield methyl ketones.

Introduction

While there are many methods available for the conversion of aldehydes and ketones into the homologous aldehyde, few of these procedures are applicable to providing the homologous methyl ketone.[1] As part of a general study of the uses of organosilicon reagents in synthesis, a convenient, and generally high yielding procedure for conducting this transformation is described that utilizes α,β-epoxy trimethylsilanes.

Since we had been able to selectively deprotonate (chloromethyl)trimethylsilane (1) to give the lithio species 2[2] its extension to (1-chloroethyl)trimethylsilane (3) appeared to be a plausible objective. It should be noted that the lithio species 4 is completely substituted and might be difficult to prepare because of steric hindrance. Furthermore 4, being completely substituted by $^-$Me, $^-$Cl, and $^-$SiMe$_3$, might be too sterically encumbered to undergo nucleophilic addition to aldehydes or ketones and merely act as a base toward enolizable systems.



Results

Initially (1-chloroethyl)trimethylsilane (3) was prepared from 2 by treatment with methyl iodide, albeit in very low yield (ca. 10%). Treatment of (1-chloroethyl)trichlorosilane with methylmagnesium bromide (3 equiv) also provided a route to 3, but while this work was in progress, the reagent 3 became commercially available.[3]

Since our experiences with the deprotonation of (chloromethyl)trimethylsilane (1) demonstrated with *sec*-butyllithium selectively gave 2, we treated (1-chloroethyl)-trimethylsilane with *sec*-butyllithium (1.5 mol in *n*-hexane or cyclohexane), at −78 °C, followed by warming to −55 °C to give solutions of (1-chloro-1-(trimethylsilyl)ethyl)lithium (4) (MCTC).[4]

Treatment of solutions of 4 in THF with a wide range of aldehydes and ketones gave in all cases α,β-epoxy trimethylsilanes (Table I). Suprisingly even very sterically hindered ketones, entries 11, 17 and 18 gave moderate

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(1) For a comprehensive review of nucleophilic acylation see: Lever, O. W., Jr. *Tetrahedron* **1976**, *32*, 1943. Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357. Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099 and references therein that described various Wittig and Horner-Wittig approaches. Martin, S. F. *Synthesis* **1979**, 633.

(2) Burford, C.; Cooke, F.; Roy, G.; Magnus, P. *Tetrahedron*, in press. Cooke, F.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 513. Burford, C.; Cooke, F.; Ehlinger, E.; Magnus, P. *J. Am. Chem. Soc.* **1977**, *99*, 4536.

(3) Sommer, L. H.; Whitmore, F. C. *J. Am. Chem. Soc.* **1946**, *68*, 485. $Me_3SiCHMeCl$ is commercially available from Petrarch Systems.

(4) The abbreviation MCTC is used for 1-chloro-1-(trimethylsilyl)ethyl carbanion.

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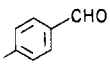
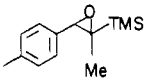
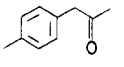
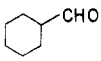
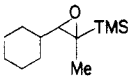
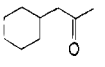
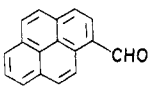
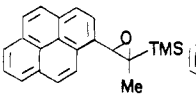
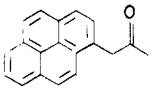
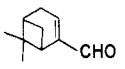
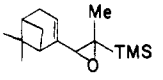
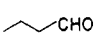
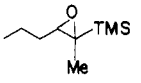
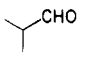
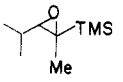
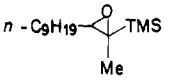
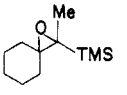
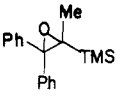
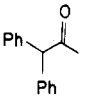
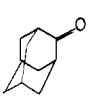
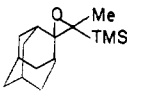
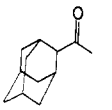
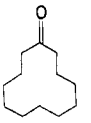
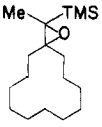
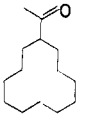
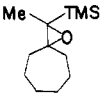
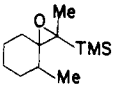
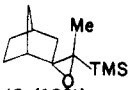
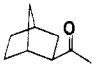
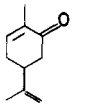
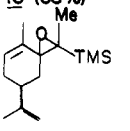
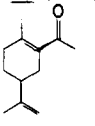
Table I

	substrate	epoxy silane (yield)	methyl ketone (yield)
1		 5 (96%)	 23 (90%)
2		 6 (70%)	 24 (95%)
3		 7 (78%)	 25 (82%)
4		 8 (89%)	
5		 9 (53%)	
6		 10 (82%)	
7		 11 (85%)	
8		 12 (96%)	 26 (86%)
9	PhCOPh	 13 (95%)	 27 (76%)
10		 14 (95%)	 28 (92%)
11		 15 (53%)	 29 (85%)
12		 16 (75%)	 30 (98%)
13		 17 (82%)	 31 (56%)
14		 18 (68%)	 32 (87%)
15		 19 (66%)	 33 (70%)
16		20 (40%)	34 (65%)
17		21 (40%)	35 (93%)
18		22 (35%)	36 (81%)

yields of epoxy trimethylsilanes. Also readily enolizable aldehydes and ketones gave reasonable (40–60%) yields of epoxy trimethylsilanes.

In the case of benzophenone, when it was added to MCTC at −78 °C, a deep blue solution was formed. This is indicative of a single electron transfer process,[5] although it may only constitute a small percentage of the reaction pathway. The nucleophilicity of MCTC is surprisingly, especially if we consider these reactions to be those of a carbanion. It is a bulky species that would be expected to function as a base rather than a nucleophile. Consequently it is attractive to speculate that MCTC adds, at least to hindered ketones, by an SET mechanism. (Scheme I).

Entry 18 converts the androstane derivative into progesterone (**36**). Although the epoxy trimethylsilane adduct **22** is only formed in moderate yield, its hydrolysis to the 20-ketone takes place in high yield. In general the hydrolysis of the adducts **5**–**7** and **8**–**18** proceeded in good yield to give the homologous methyl ketones **23**–**36**.

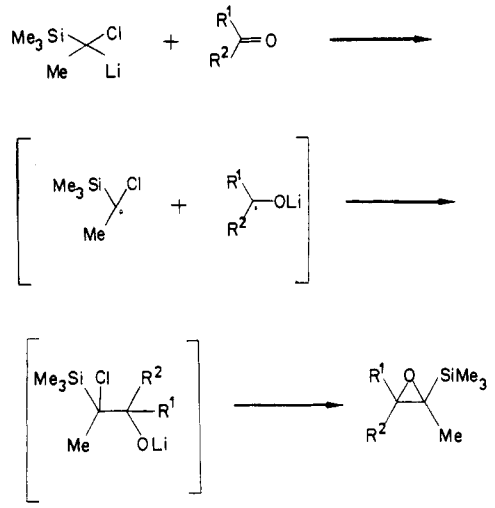
Synthesis of (*R*)-(+)-Frontalin. The reagent **4** appeared to be particularly suitable for a key step in the conversion of (3*R*)-(−)-linalool (**37**) into (*R*)-(+)-frontalin (**42**), the aggregation pheromone of the southern pine beetle *Dendroctonus frontalis*.[6]

Conversion of **37** into its trimethylsilyl ether **38** was achieved by conventional procedures (hexamethyldisilazane/pyridine/trimethylchlorosilane) (98%). Se-

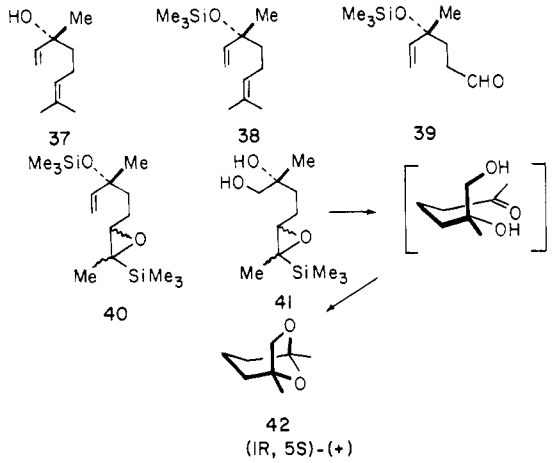
(5) Ashby, E. C.; Neumann, H. M.; Laemmie, J. T. *Acc. Chem. Res.* **1974**, *7*, 272.

(6) Kinzer, G. W.; Fentiman, A. F., Jr.; Page, T. F.; Foltz, R. L.; Vité, J. P. *Nature (London)* **1969**, *221*, 447.

Scheme I



lective ozonolysis of **38** (−78 °C, CH_2Cl_2, pyridine), followed by rapid isolation, gave after distillation the aldehyde **39** (65%). The aldehyde **39** was treated with **4**, at −78 °C,



and the reaction mixture warmed to 20 °C to give the epoxy trimethylsilane **40** (crude yield 95%; no attempt was made to purify this product). Crude **40** was ozonized in methanol and the intermediate ozonide reduced with sodium borohydride to give the diol **41** (65%, based on **39**). The diol was treated with boron trifluoride/diethyl ether in methanol at 0 °C and then warmed to 20 °C to give (*R*)-(+)-frontalin (**42**, 74%), bp 92–93 °C (100 mmHg).[7]

The overall yield from (3*R*)-(−)-linalool to (*R*)-(+)-frontalin is 23–29% as an average of several runs.

In summary, the reagent (1-chloro-1-(trimethylsilyl)-ethyl)lithium provides a convenient way of converting aldehydes and ketones into the homologous methyl ketones via epoxy trimethysilanes. The reagent **4** is suprisingly nucleophilic and even adds to 17-keto steroids, although in these cases in moderate yields.

Experimental Section

Gas chromatographic analyses were performed with a Perkin-Elmer 3920B instrument using 10% OV101 on chrom WHP (80–100) or 10% SE-30 on chrom DAW (100–120). Preparative layer chromatography was carried out by eluting with petroleum ether (bp 60–90 °C)/ethyl acetate (4:1) unless otherwise specified. Infrared spectra were recorded on a Perkin-Elmer 267 grating spectrometer and are for neat liquids unless otherwise specified. ^1H NMR spectra were recorded on a Varian A-60, a Varian EM-360, or a Varian EM-390 spectrometer for solutions in CCl_4, with tetramethylsilane (2%) as internal standard, unless stated otherwise. Mass spectral data were obtained using a double focussing consolidated electronic MS-9 mass spectrometer. All boiling points are uncorrected. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Solvents were dried and purified by standard techniques prior to use. Experiments involving alkyllithiums were conducted under argon or nitrogen. Transfer of liquids was carried out under a positive pressure of argon or nitrogen by using syringes oven dried to 160 °C.

sec-BuLi (1.1 or 1.3 M, in cyclohexane) was purchased from Foote Mineral Co. and found to be the most reliable source of this material. (1-Chloroethyl)trimethylsilane was purchased from Petrarch Systems Inc., distilled (bp 97 °C (760 mm) before use and stored over molecular sieves (4 Å).

General Procedure for the Preparation of (1-Chloro-1-(trimethylsilyl)ethyl)lithium. To a solution of *sec*-butyllithium (4.0 mL, 6.0 mmol, 1.5 M, in *n*-hexane or cyclohexane) in dry THF (8 mL) at −78 °C under dry argon was added (1-chloroethyl)-trimethylsilane (0.816 g, 6.0 mmol) in THF (2 mL). Tetramethylethylenediamine (1.0 equiv) can be added at this stage. It increases the rate of formation of (1-chloro-1-(trimethylsilyl)ethyl)lithium but has no other advantages. After the above mixture was stirred at ca. −55 to −60 °C for 0.5 h to ensure complete formation of **4** (MCTC), the solution was cooled to −78 °C and the carbonyl compound added. The mixture was kept for 0.5 h at −78 °C and then allowed to warm to 20 °C. In most cases, unless otherwise stated, the formation of epoxy trimethylsilane adduct was complete and the reaction was worked up by pouring the mixture into either saturated aqueous ammonium chloride solution or 1 N HCl and the mixture extracted with ether or dichloromethane. The extract was dried ($MgSO_4$) and evaporated and residue purified by either distillation under reduced pressure, plate layer chromatography, or recrystallization. In many cases the α,β-epoxy trimethylsilane adducts were isolated in ≥95% purity (GLC, NMR) and could be hydrolyzed directly to the corresponding methyl ketone.

[3-(4-Methylphenyl)-2-methyloxiranyl]trimethylsilane (5). To a solution of MCTC (6.0 mmol), prepared in the described manner, was added *p*-tolualdehyde (0.48 g, 4.0 mmol). The pale yellow solution immediately became a more intense yellow color. After being warmed to 20 °C, the mixture was worked up to give the epoxy trimethylsilane **5** (0.849 g, 96%), purified by distillation: bp 88–92 °C (0.75 mmHg); IR 3020, 2950, 1610, 1510, 1250, 860, 840 cm^{-1}; NMR δ 6.9 (4 H, b), 4.5 and 3.6 (1 H, 2 s, ratio 3:4 for the diastereomers), 2.2 (3 H, s), 1.2 and 0.80 (3 H, 2 s, ratio 3:4 for the diastereomers), 0.0 (9 H, 2 s separated by 2 Hz, used as an internal standard); MS, $C_{13}H_{20}OSi$, calcd 220.129, obsd 220.128. Anal. Calcd for $C_{13}H_{20}OSi$: C, 70.90; H, 9.1. Found: C, 70.69; H, 9.0.

1-*p*-Tolylpropan-2-one (23). To a solution of the epoxy trimethylsilane **5** (0.3 g, 1.36 mmol) in methanol (3 mL) was added 3 N $H_2H_2SO_4$ (1.0 mL), and the mixture was stirred at 20 °C for 1 h. The mixture was diluted with water (10 mL) and extracted with dichloromethane (3 × 5 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give after bulb-to-bulb distillation a colorless oil (0.181 g, 90%): IR 3020, 2960, 1710, 1610 cm^{-1}; NMR 6.8 (4 H, s), 3.3 (2 H, s), 2.1 (3 H, s), 1.8 (3 H, s); 2,4-dinitrophenylhydrazone, mp 135–136 °C (from benzene/petroleum ether) (lit.[8] 134–136 °C).

(3-Cyclohexyl-2-methyloxiranyl)trimethylsilane (6). To a stirred solution of MCTC (1.3 equiv) at −78 °C was added cyclohexanecarboxaldehyde (0.19 mL, 1.59 mmol, 1.0 equiv). The mixture was warmed to 20 °C and worked up in the usual way to give **6** (0.25 g, 70%): bp 65 °C (0.275 mmHg); IR 2920, 2850, 1450, 1410, 1250, 870, 850 cm^{-1}; NMR δ 0.0 (9 H, 2 s in the ratio 2:1, separated by 2.5 Hz, for the diastereomers), 0.8–1.7 (11 H, b), 1.0 (3 H, d, diastereomers), 2.15 (1 H, d, J = 7 Hz); MS, $C_{12}H_{24}OSi$, calcd 212.160, obsd 212.160.

1-Cyclohexylpropan-2-one (24). The epoxy trimethylsilane **6** (0.25 g) was treated with 20% aqueous methanolic H_2SO_4 for 1 h and the mixture heated at reflux to give the ketone **24** (0.141

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g, 95%): IR 1710 cm^{-1}; NMR δ 0.80–1.75 (11 H, b), 2.05 (3 H, s), 2.15 (2 H, d, J = 6 Hz); 2,4-dinitrophenylhydrazone, mp 96–97 °C (lit.[9] 97–98 °C).

[3-(1-Pyrenyl)-2-methyloxiranyl]trimethylsilane (7). To a solution of MCTC at −78 °C, prepared from (1-chloroethyl)-trimethylsilane (2.7 mL, 0.017 mol, 5 equiv) *sec*-BuLi (1.4 M), and TMEDA (2.6 mL) in THF (8 mL), was added pyrenecarboxaldehyde (1.0 g, 1 equiv) in THF (2 mL). After the mixture was warmed to 20 °C, the orange solution was poured into saturated aqueous NH_4Cl solution (50 mL) and extracted with ethyl acetate (2 × 30 mL). The extract was washed with water (2 × 30 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give 1.3 g of crude **7**. Purification by PLC on silica gel, eluting with 4:1 petroleum ether/EtOAc, gave pure **7** (1.1 g, 78%): mp 100–102 °C; IR (Nujol mull) 2920, 2850, 1250, 850, 840, 830, 710 cm^{-1}; NMR δ 0.1 (9 H, s), 0.7 (3 H, s), 4.3 (1 H, s), 7.6–7.9 (9 H, m). Anal. Calcd for $C_{22}H_{22}OSi$: C, 80.03; H, 6.71. Found: 79.88; H, 6.79.

1-(1-Pyrenyl)propan-2-one (25). The epoxy trimethylsilane **7** (0.30 g) was dissolved in 90% formic acid (3 mL) and stirred at 20 °C for 1 h. Evaporation under reduced pressure and purification of the residue by PLC gave **25** (0.20 g, 82%): mp 83–84 °C (lit.[10] mp 85–86 °C); IR (Nujol mull) 1705 cm^{-1}; NMR δ 2.1 (3 H, s), 4.3 (2 H, s), 7.6–8.0 (9 H, m).

[3-(2-(6,6-Dimethylbicyclo[3.1.1]hept-2-enyl))-2-methyloxiranyl]trimethylsilane (8). To a solution of MCTC at −78 °C, prepared from (1-chloroethyl)trimethylsilane (1.55 mL, 9.98 mmol, 1.5 equiv), *sec*-BuLi (1.1 M, 9 mL), and TMEDA (1.5 mL) in THF (20 mL), was added freshly distilled myrtenal (1.0 g, 6.65 mmol) in THF (2 mL). After the mixture was warmed to 20 °C over 1.5 h, workup gave a liquid that was distilled to give **8** (1.5 g, 89%): bp 95 °C (10.5 mmHg); IR (2920, 2900, 1245, 840 cm^{-1}; NMR δ 0.35 (9 H, s), 1.0 (3 H, s), 1.3 (1 H, s), 1.4 (1 H, s), 1.5 (3 H, s), 1.6 (2 H, s), 2.1–2.6 (5 H, b s), 3.1 (1 H, b s), 5.4 (1 H, b s); MS, $C_{15}H_{26}SiO$, calcd 250.175, obsd 250.175.

(3-Propyl-2-methyloxiranyl)trimethylsilane (9). To a solution of MCTC at −78 °C, prepared from (1-chloroethyl)trimethylsilane (0.50 g, 2.76 mmol) and *sec*-BuLi (1.5 M, 1.84 mL (2.76 mmol) in THF (3 mL), was added *n*-butyraldehyde (0.176 mL, 2.0 mmol). After being warmed to 10 °C over 1 h, the mixture was worked up in the usual way to give the **epoxy trimethylsilane 9** (0.183 mg, 53%): IR 2960, 1460, 1250, 840 cm^{-1}; NMR δ 0.1 (9 H, s), 1.1 (3 H, s), 0.7–2.1 (8 H, m); MS, $C_9H_{20}SiO$, calcd 172.129, obsd 172.128.

(3-Isopropyl-2-methyloxiranyl)trimethylsilane (10). To a solution of MCTC (1.3 equiv) at −78 °C was added isobutyraldehyde (0.144 mL, 1.59 mmol, 1.0 equiv). After being warmed to 10 °C over 1 h, the mixture was worked up in the usual way to give **10** (0.20 g, 82%, ≥95% pure by VPC): bp 60 °C (0.25 mmHg); NMR δ 0.0 (9 H, 2 s, ratio 4:1 for diastereoisomers), 0.85–1.15 (6 H, m), 1.15 (3 H, s), 2.15 (1 H, m), 3.6 (1 H, m); MS, $C_9H_{20}SiO$, calcd 172.129, obsd 172.128.

(3-Nonyl-2-methyloxiranyl)trimethylsilane (11). To a solution of MCTC (1.3 equiv) at −78 °C was added *n*-decanal (0.3 mL, 159 mol, 1.0 equiv). After being warmed to 10 °C over 1 h, the mixture was worked up in the usual way to give **11** (0.35 g, 85%): bp 90 °C (0.100 mmHg); IR 2950, 2920, 1250, 850 cm^{-1}; NMR δ 0.10 (9 H, s), 0.7–1.0 (3 H, m), 1.15 (3 H, s), 1.20–1.25 (15 H, b), 3.6 (1 H, m). No satisfactory MS or microanalytical data could be obtained. Hydrolysis of **11** gave *n*-decyl methyl ketone in low yield (ca. 20%); 2,4-dinitrophenylhydrazone, mp 81 °C (lit.[11] 81 °C).

Trimethyl(2-methyl-1-oxaspiro[2.5]oct-2-yl)silane (12). To a solution of MCTC (2.4 mmol) at −78 °C was added cyclohexanone (0.21 mL, 2.0 mmol). After being warmed to 10 °C over 1.5 h, the mixture was worked up in the usual way to give the epoxy trimethylsilane **12** (0.38 g, 96%) after purification by PLC: IR 2920, 2850, 1450, 1250, 860, 840, 755 cm^{-1}; NMR δ 2.4–1.2 (10 H, m), 1.1 (3 H, s), 0.1 (9 H, s); MS, $C_{11}H_{22}OSi$, calcd 198.144, obsd 198.144.

Cyclohexyl Methyl Ketone (26). The epoxy trimethylsilane **12** (0.134 g) in methanol (3 mL) was treated with 6 N H_2SO_4 (0.5 mL) at 20 °C for 20 min. Workup gave **26** (0.083 g, 86%): IR 1710 cm^{-1}; NMR δ 2.5–0.7 (11 H, m), 2.0 (3 H, s).

(3,3-Diphenyl-2-methyloxiranyl)trimethylsilane (13). To a solution of MCTC (2.4 mmol) at −78 °C was added benzophenone (0.237 g, 1.30 mmol). After being warmed to 0 °C over 1 h, the mixture was worked up in the usual way to give **13** (0.36 mg, 95%) after purification by PLC: IR 2960, 1495, 1450, 1250, 860, 840, 760 cm^{-1}; NMR δ 7.5–7.0 (10 H, m), 1.0 (3 H, s), 0.0 (9 H, s); MS, $C_{18}H_{22}OSi$, calcd 282.144, obsd 282.145.

Dibenzyl Ketone (27). The epoxy trimethylsilane **13** (0.185 g) in methanol (3 mL) was treated with 6 N H_2SO_4 at 50 °C for 2 h. Workup gave **27** (0.105 g, 76%)[12] after purification by PLC.

(3′-Methylspiro[adamantane-2,2′-oxiran]-2′-yl)trimethylsilane (14). To a solution of MCTC (1.95 mmol) at −78 °C was added 2-adamantanone (0.225 g, 1.50 mmol). After 35 min at −78 °C the above mixture was worked up to give **14** (0.355 g, 95%) after purification by PLC: IR 2910, 2850, 1450, 1250, 860, 840, 755 cm^{-1}; NMR δ 2.2–0.8 (14 H, m), 1.2 (3 H, s), 0.1 (9 H, s). Anal. Calcd for $C_{15}H_{26}OSi$: C, 72.00; H, 10.40. Found: C, 71.74; H, 10.29.

Methyl Adamantyl Ketone (28). The epoxy trimethylsilane **14** (0.32 g, 1.28 mmol) in methanol (8 mL) was treated with 6 N H_2SO_4 (1 mL) at 20 °C for 1.5 h. Workup gave **28** (0.210 g, 92%) after purification by PLC; 2,4-dinitrophenylhydrazone, mp 150–153 °C (from benzene/petroleum ether; lit.[13] mp 153.4–153.9 °C).

Trimethyl(2-methyl-1-oxaspiro[2.11]undec-2-yl)silane (15). To a solution of MCTC (4.5 mmol) at −78 °C was added cyclododecanone (0.547 g, 3.0 mmol). After 10 min the above mixture was warmed to 0 °C over 1 h and worked up in the usual way to give **15** (0.450 g, 53%) purified by bulb-to-bulb distillation to remove the starting ketone: IR 2920, 2850, 1470, 1250, 840, 755 cm^{-1}; NMR δ 1.4 (22 H, b), 1.2 (3 H, s), 0.1 (9 H, s); MS, $C_{17}H_{34}OSi$, calcd 282.238, obsd 282.238.

Methyl Cyclododecyl Ketone (29). The epoxy trimethylsilane **15** (0.325 g, 1.25 mmol) in methanol (3 mL) was treated with 3 N H_2SO_4 (1.0 mL) at 20 °C for 15 min. Workup gave **29** (0.223 g, 85%) purified by bulb-to-bulb distillation: IR 2920, 2850, 1705 cm^{-1}; NMR δ 2.6–2.1 (1 H, m), 2.0 (3 H, s), 1.3 (22 H, b s); 2,4-dinitrophenylhydrazone, mp 145–146 °C (from benzene/petroleum ether; lit.[14] 144.5 °C).

Trimethyl(2-methyl-1-oxaspiro[2.6]non-2-yl)silane (16). To a solution of MCTC (1.5 equiv) at −78 °C was added cycloheptanone (1.05 g). After being warmed to 20 °C over 1.5 h, the mixture was worked up to give **16** (1.4 g, 75%): bp 93 °C (1.5 mmHg): IR 2920, 1250, 860, 840 cm^{-1}; NMR δ 0.15 (9 H, s), 1.3 (3 H, s), 1.5–1.9 (12 H, b); MS, $C_{12}H_{24}OSi$, calcd 212.160, obsd 212.160.

Methyl Cycloheptyl Ketone (30). The epoxy trimethylsilane **16** (0.60 g, 2.8 mmol) in 90% formic acid (8 mL) was stirred at 20 °C for 0.5 h. Evaporation and distillation (bp 40 °C (0.15 mmHg) gave **30** (0.385 g, 98%).[15]

Trimethyl(2,2′-dimethyl-1-oxaspiro[2.5]oct-2-yl)silane (17). To a solution of MCTC (1.5 equiv) at −78 °C was added 2-methylcyclohexanone (2.0 g, 1 equiv). After the mixture was warmed to 20 °C of 1.5 h, workup gave the epoxy trimethylsilane **17** (3.13 g, 82%): bp 48–51 °C (10.1 mmHg); IR 2960, 1250, 860, 840 cm^{-1}; NMR δ 0.1 (9 H, s), 1.0 (3 H, s), 1.15 (3 H, s), 1.2 (3 H, s), 1.4–2.0 (9 H, b); MS, $C_{12}H_{24}OSi$, calcd 212.160, obsd 212.160. Anal. Calcd for $C_{12}H_{24}OSi$: C, 67.92; H, 11.32. Found: C, 67.72; H, 11.20.

***trans*-1-Acetyl-2-methylcyclohexane (31).** The epoxy trimethylsilane **17** (0.90 g, 4.24 mmol) in 90% formic acid (3 mL) was stirred at 20 °C for 0.5 h. Evaporation and distillation gave **31** (0.33 g, 52%): bp 38 °C (0.4 mmHg); NMR δ 0.8 (3 H, d, J = 6 Hz), 1.3–1.8 (9 H, b m), 2.1 (3 H, s), 2.3–2.6 (1 H, b).[16]

(3′-Methylspiro[bicyclo[2.2.1]heptane-1,2′-oxiran]-2′-yl)trimethylsilane (18). To a solution of MCTC (2.0 equiv) at −78 °C was added norcamphor (1.0 g, 1.0 equiv). After being warmed

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to 20 °C over 1.5 h, workup gave the **epoxy trimethylsilane 18** (1.3 g, 68%): bp 75–78 °C (1.5 mmHg); IR 2950, 1250, 860, 840 cm^{-1}; NMR δ 0.1 and 0.15 (9 H, 2 s, 1:1), 0.5 (1 H, d, J = 3 Hz), 0.8 (1 H, b s), 1.1 and 1.2 (3 H, 2 s, 1:1), 1.4–2.0 (6 H, b m), 2.3 (2 H, b s); MS, $C_{12}H_{22}OSi$, calcd 210.144, obsd 210.145.

2-Acetylbicyclo[2.2.1]heptane (32). The epoxy trimethylsilane **18** (0.15 g) in 20% aqueous THF (3 mL) was treated with 3 N HCl (0.5 mL) at 20 °C for 1 h. Workup gave **32** (0.085 g, 87%): bp 80 °C (bulb-to-bulb at 1.5 mmHg; IR 1710 cm^{-1}.[17]

(5-Isopropyl-2-methyl-3-methylspiro[cyclohex-2-ene-1,2′-oxiran]-2′-yl)trimethylsilane (19). To a solution of MCTC (1.3 equiv) at −78 °C was added carvone (2.1 mL, 1.0 equiv). After the mixture was warmed to 20 °C over 1.5 h, workup gave **19** (2.88 g, 86%). Distillation at 0.03 mmHg gave two fractions: bp 61–63 °C (1.65 g, 50%) and bp 68–73 °C (0.18 g, 16%; (epimers); IR 2960, 1645, 1450, 1375, 1250, 900, 850 cm^{-1}; NMR (on mixture of epimers) δ 0.1 (9 H, 2 s), 1.1–1.2 (3 H, d), 1.6 (6 H, d), 2.2–2.2 (5 H, b m), 4.6 (2 H, s), 5.6–6.0 (1 H, m); MS, $C_{15}H_{26}OSi$, calcd 250.175, obsd 250.176.

1-Acetyl-2-methyl-5-isopropenylcyclohexene (33). The epoxy trimethylsilane **19** (0.20 g) in 90% formic acid (1.0 mL) was stirred at 20 °C for 2 h. Evaporation and distillation at 0.05 mm gave the enone **33** (70%): IR 2920, 1680, 1645 cm^{-1}; NMR δ 1.5–1.8 (10 H, m), 1.9 (3 H, s), 2.2 (3 H, s), 4.7 (2 H, s); MS, $C_{12}H_{18}O$, calcd 178.136, obsd 178.136. Anal. Calcd for $C_{12}H_{18}O$: C, 80.90; H, 10.11. Found: C, 80.96; H, 10.4.

(1,2,3,4,5,6,7,8-Octahydro-3′-methylspiro[anthracene-1,2′-oxiran]-2′-yl)trimethylsilane (20). To a solution of MCTC (1.3 equiv) at −78 °C was added 1,2,3,4,5,6,7,8-octahydro-1-oxaanthracene (2.0 g, 1.0 equiv). After the mixture was warmed to 20 °C over 1.5 h, workup gave **20** (1.2 g, 40%) purified by PLC: IR 2920, 1250, 860 cm^{-1}; NMR δ 0.1 (9 H, s), 1.3 (3 H, 2 s, epimers), 1.7–2.0 (6 H, b m), 5.6–5.8 (1 H, b s), 6.8–7.0 (1 H, b s); MS, $C_{19}H_{28}OSi$, calcd 300.191, obsd 300.191.

1-Acetyl-1,2,3,4,5,6,7,8-octahydroanthracene (34). The epoxy trimethylsilane **20** (0.135 g, 0.45 mmol) in 90% formic acid (1 mL) was stirred at 20 °C for 2 h. Evaporation and purification (PLC) gave **34** (0.070 g, 65%): IR 1700, 1430, 1350, 790 cm^{-1}; NMR δ 0.8–1.0 (2 H, b), 1.2 (2 H, b), 1.6–1.9 (6 H, b), 2.0 (3 H, s), 2.7 (4 H, b), 5.6 (1 H, m), 6.6 (1 H, s), 6.8 (1 H, s); MS, $C_{16}H_{20}O$, calcd 228.151, obsd 228.152.

(3-Methoxy-3′-methylspiro[1,3,5-estratriene-17,2′-oxiran]-2′-yl)trimethylsilane (21). To a solution of MCTC (3.2 equiv) at −78 °C was added estrone methyl ether (0.5 g, 1.0 equiv). After the mixture was warmed to 20 °C over 2 h, workup gave the crude mixture (0.58 g) which was purified by PLC to give **21** (0.3 g, 40%): mp 128 °C (from benzene/hexane); IR (Nujol mull) 2920, 1250 cm^{-1}; NMR (CCl_4) δ 0.1 (9 H, s), 0.2 (9 H, s) for epimers at C-20, 3:1, 0.8 (3 H, s), 0.9 (3 H, s), 1.0 (3 H, s), 1.2 (3 H, s), 1.3 (3 H, s), 1.5–2.3 (14 H, m), 2.7–2.9 (3 H, m), 3.6 (3 H, s), 6.3–7.1 (3 H, m). Anal. Calcd for $C_{24}H_{36}O_2Si$: C, 75.00; H, 9.37. Found: 74.90; H, 9.44.

3-Methoxy-17-acetyl-1,3,5-estratriene (35). The epoxy trimethylsilane **21** (0.05 g) in 90% formic acid (3 mL) was stirred at 20 °C for 1 h. Evaporation and purification (PLC) of the residue gave **35** (0.038 g, 93%); mp 132–134 °C (from EtOAc/petroleum ether; lit.[18] mp 134–136 °C). Anal. Calcd by $C_{21}H_{28}O_2$: C, 80.79; H, 9.04. Found: C, 80.83; H, 9.05.

(3-Methoxy-3′-methylspiro[androst-3,5-diene-17,2′-oxiran]-2′-yl)trimethylsilane (22). To a solution of MCTC (3.0 equiv) at −78 °C was added 3-methoxyandrost-3,5-dien-17-one (1.0 g, 1 equiv). After the mixture was warmed to 20 °C, workup gave **22** (0.5 g, 38% after purification by PLC). Hydrolysis of **22** (0.5 g) in ether (5 mL)/6 N HCl (3 mL) gave progesterone (**36**) (0.32 g, 81%), mp 122–123 °C (from ethanol; lit.[19] mp 121 °C).

Trimethylsilyl Ether of (−)-Linalool (38). (3*R*)-(−)-Linalool (**37** (10.0 g, 0.078 mol) in pyridine (10 mL) was treated with hexamethyldisilazane (12.6 g, 0.078 mol), followed by chlorotrimethylsilane (3.68 g, 0.034 mol). After 24 h at 20 °C, the mixture was filtered through celite, and the filtrate was washed with aqueous $NaHCO_3$, extracted with ether (150 mL), dried ($MgSO_4$), evaporated. The residue was distilled under vacuum to give **38** (14.4 g, 98%): bp 45 °C (0.17 mm Hg); IR 2950, 1450, 1370, 1250, 1175, 920 cm^{-1}; NMR δ 0.0 (9 H, s), 1.2 (3 H, s), 1.5 (6 H, d, J = 4 Hz), 1.3–2.0 (4 H, m), 4.65–4.85 (1 H, m), 4.85–5.15 (2 H, m), 5.55–6.0 (1 H, m); $[\alpha]^{24}_D$ −3.47[1]° (neat liquid). Anal. Calcd $C_{13}H_{26}OSi$: C, 68.95; H, 11.57. Found: 69.08; H, 11.69.

4-Methyl-4-((trimethylsilyl)oxy)hex-5-en-1-al (39). Linalool trimethylsilyl ether **38** (3.0 g) in CH_2Cl_2 (100 mL) and pyridine (1.05 g) at −78 °C was treated with ozone until the disappearance of starting material (ca. 15 min). The mixture was filtered through celite into water (100 mL) containing dimethyl sulfide (2 mL). The organic layer was separated, washed with water (100 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give an oil. The oil was dissolved in ether, filtered through celite, dried ($MgSO_4$), and distilled to give **39** (1.6 g, 65%): bp 34–35 °C (10.37 mmHg); IR 2950, 2820, 2720, 1725, 1250, 1050, 845 cm^{-1}; NMR δ 0.0 (9 H, s), 1.2 (3 H, s), 1.6–2.3 (4 H, m), 4.6–5.2 (2 H, m), 5.3–6.0 (1 H, m), 9.6 (1 H, t, J = 2 Hz); $[\alpha]^{24}_D$ +1.54[1]° (neat).

Reaction of MCTC with 39. To a solution of MCTC (1.3 equiv) at −78 °C was added freshly distilled **39** (1.0 g, 1 equiv). After the mixture was warmed to 20 °C and worked up, **40** (1.35 g, 95%) was obtained. This material was used directly in the next step. Crude **40** (1.0 g) was ozonized in methanol (10 mL) at −78 °C until a faint blue color persisted. To this mixture $NaBH_4$ (0.30 g) was added at 0 °C, and the mixture was worked up to give the diol **41** (0.5 g, 65%): IR 3400, 2960, 1250, 845, 790 cm^{-1}; NMR δ 0.1 (9 H, s), 1.0 (4 H, b), 1.2 (3 H, b s), 1.5 (3 H, b s), 3.1 (2 H, b s). This product (0.5 g) was dissolved in methanol (2 mL) at 0 °C and BF_3·Et_2O (1 mL) added. After 2 h at 20 °C the mixture was quenched with saturated aqueous $NaHCO_3$, extracted with light petroleum ether, dried ($NaSO_4$), and carefully evaporated to give frontalin **42** (0.21 g, 74%): $[\alpha]^{24}_D$ +52.6° (neat liquid); bp 92–93 °C (100 mmHg); IR 2920, 1120, 1020, 840 cm^{-1}; NMR δ 1.48 (3 H, s), 1.57 (3 H, s), 1.8 (6 H, b s), 3.58, 4.04, (2 H, AB quartet), J_{AB} = 7 Hz).[20]

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Registry No. 3, 7787-87-3; **4**, 81897-57-6; **5** isomer 1, 81874-73-9; **5** isomer 2, 81874-74-0; **6** isomer 1, 81874-75-1; **6** isomer 2, 81897-62-3; **7**, 81874-76-2; **8**, 81874-77-3; **9**, 65164-99-0; **10** isomer 1, 81874-78-4; **10** isomer 2, 81874-79-5; **11**, 81874-80-8; **12**, 65206-59-9; **13**, 65164-95-6; **14**, 65164-96-7; **15**, 65164-97-8; **16**, 81874-81-9; **17**, 81874-82-0; **18**, 81874-83-1; **19**, 81874-84-2; **20** epimer 1, 81874-87-5; **20** epimer 2, 81897-58-7; **21** epimer 1, 81897-59-8; **21** epimer 2, 81897-60-1; **22**, 81897-61-2; **23**, 2096-86-8; **23** DNP, 81874-85-3; **24**, 103-78-6; **24** dnp, 81874-89-7; **25**, 70644-22-3; **26**, 823-76-7; **27**, 102-04-5; **28**, 22635-58-1; **28** DNP, 22635-57-0; **29**, 28925-00-0; **29** DNP, 28924-98-3; **30**, 6713-48-0; **31**, 5222-61-7; **32**, 58654-66-3; **33**, 81874-86-4; **34**, 81874-88-6; **35**, 1624-73-3; **36**, 57-83-0; **37**, 126-91-0; **38**, 67604-71-1; **39**, 67604-72-2; **40**, 67604-73-3; **41**, 67604-74-4; **42**, 57919-96-1; *p*-tolualdehyde, 104-87-0; cyclohexanecarboxaldehyde, 2043-61-0; pyrenecarboxaldehyde, 3029-19-4; myrtenal, 564-94-3; *n*-butyraldehyde, 123-72-8; isobutyraldehyde, 78-84-2; *n*-decanal, 112-31-2; *n*-decyl methyl ketone, 6175-49-1; *n*-decyl methyl ketone DNP, 81874-90-0; cyclohexanone, 108-94-1; benzophenone, 119-61-9; 2-adamantanone, 700-58-3; cyclododecanone, 830-13-7; cycloheptanone, 502-42-1; 2-methylcyclohexanone, 583-60-8; norcamphor, 497-38-1; carvone, 2244-16-8; 1-oxa-1,2,3,4,5,6,7,8-octahydroanthracene, 5440-71-1; estrone methyl ether, 1624-62-0; 3-methoxyandrost-3,5-dien-17-one, 57144-06-6.

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