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# Stereocontrolled formation of spiro enones by radical cyclization of bromo acetals

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Dedicated to the memory of Professor R. U. Lemieux, FRS

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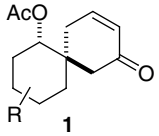
**Abstract**—Aldol condensation of ketones with 2-[[(1,1-(dimethylethyl)diphenylsilyl]oxy]propanal (**7**), dehydration, $NaBH_4$ reduction and treatment of the resulting alcohols with ethyl vinyl ether in the presence of NBS gives bromo acetals (e.g. **11**) that undergo 5-*exo*-trigonal radical cyclization, affording compounds that are easily converted into spiro enones (e.g. **16**). The stereochemistry at the spiro center is controlled by the stereochemistry at the hydroxyl-bearing carbon of the intermediate alcohol. 

## 1. Introduction and discussion

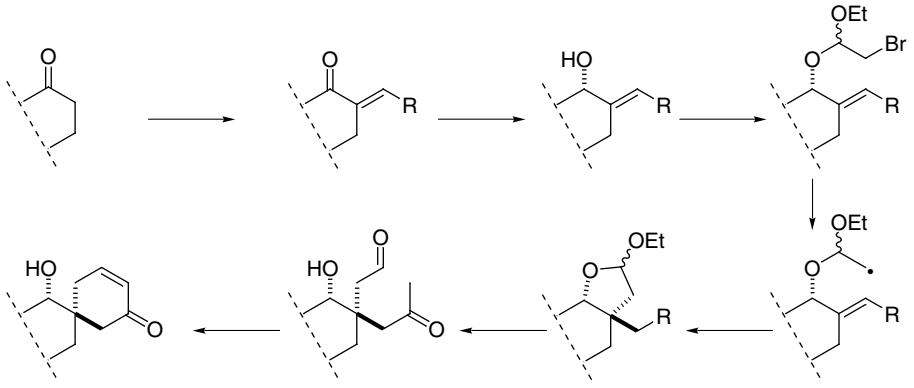
We describe a method for making spiro enones of type **1**, in such a way that the stereochemistry at the spiro center is controlled by the stereochemistry of an adjacent hydroxyl group.[1,2]




**1**

Our approach is based on the cyclization of Stork bromo acetals, as summarized in Scheme 1, where R is a group that is convertible into a methyl ketone unit [MeC(O)].

Radical cyclizations of halo acetals onto fully substituted $sp^2$ centers are known, as illustrated by the examples of Eqs. (1),[3] (2)[4] and (3),[5] but the process[6] does not appear to have been exploited specifically as a general and stereochemically controllable method for the preparation of spiro compounds. In developing the cyclization for this purpose, we felt that closure onto an exocyclic double bond, rather than one that is endocyclic, would be more convenient, because in the former case the requisite alkenes should be available easily by aldol condensation and dehydration.[7] On this basis, our initial approach (Scheme 2) called for conversion of cyclohexanone into the conjugated ketone **5**, which was prepared (though, without full characterization) by aldol condensation with aldehyde **3**,[8] followed by mesylation and treatment with DBU.




**Scheme 1.**

*Keywords*: spiro compounds; radical cyclization; enones.

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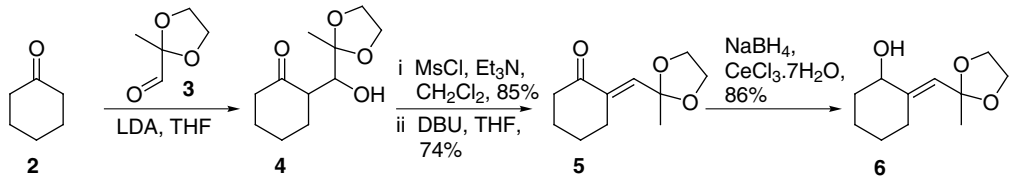
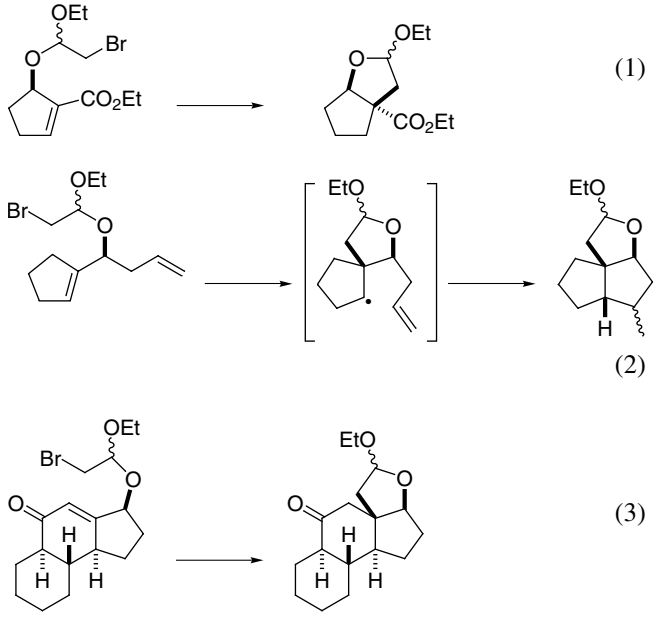
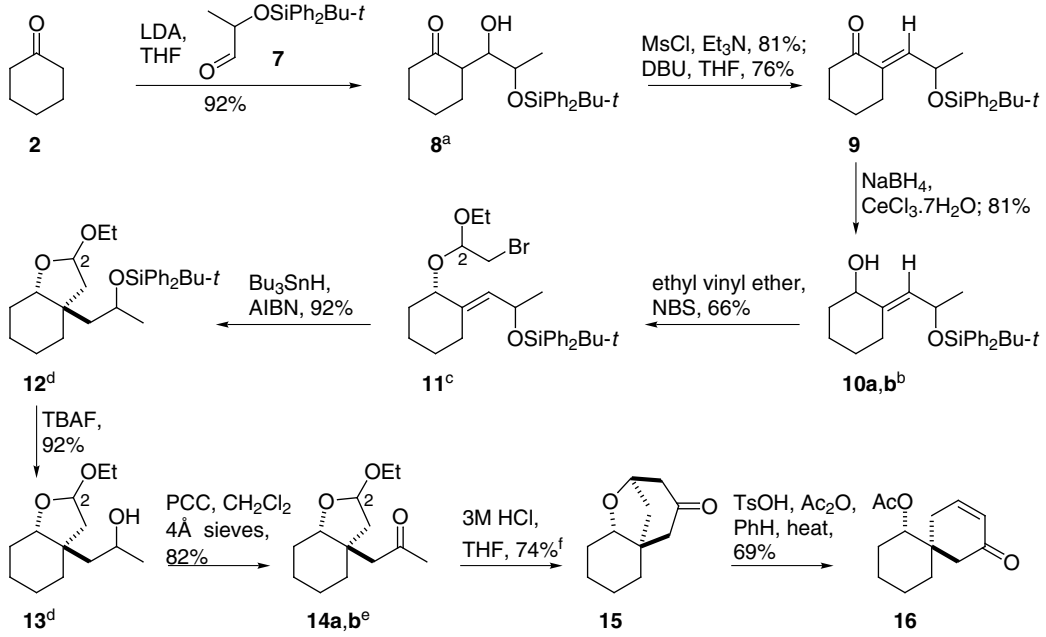



**Scheme 2.**

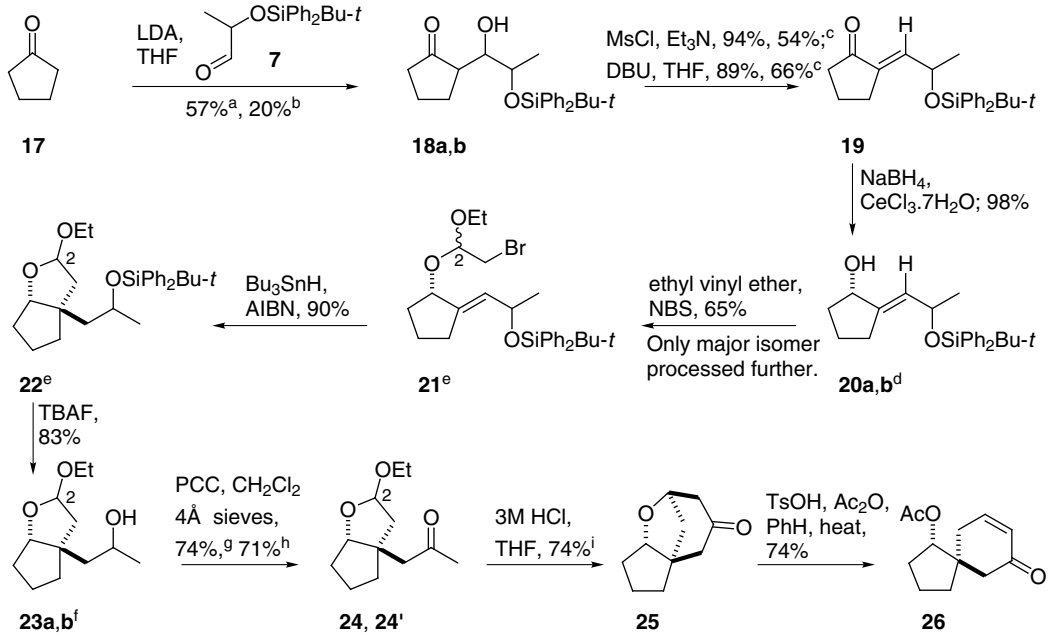



In the event, the derived alcohol **6** was very sensitive and it was not possible to attach the bromo acetal unit efficiently; the same was true in the corresponding diethyl ketal series. We therefore modified the process to that summarized in Scheme 3, and found that this revised approach could be implemented quite easily.

Aldol condensation of cyclohexanone with the readily available aldehyde **7**[9] gave the expected aldols **8**[10] and these were easily dehydrated by mesylation, followed by treatment with DBU. Enone **9** was obtained with the *E* geometry, as shown. Reduction with $NaBH_4$–$CeCl_3{\cdot}7H_2O$ afforded the expected alcohols **10**. The yield of the major alcohol was 65%, while that of the minor isomer was 16%; only the major alcohol was taken further. Treatment with ethyl vinyl ether in the presence of NBS served to generate the required bromo acetals **11** (66%) and these were best cyclized (**11**→**12**) by rapid heating (115°C) with a mixture of $Bu_3SnH$ (ca. 2 equiv.) and AIBN in PhMe, rather than by slow addition of the stannane. Under these optimized conditions,[11] the desired cyclization products **12** were isolated in high yield (92%), with the ring fusion stereochemistry being necessarily[12] as shown. The phenylseleno acetal corresponding to **11** (PhSe instead of Br), which was available in comparable yield to the bromo acetal (ethyl vinyl ether, PhSeBr, 70%) underwent radical cyclization in much poorer yield, and so only bromo acetals were used in subsequent work. Desilylation of **12** ($Bu_4NF$) and PCC oxidation converted the angular substituent into a methyl ketone,




**Scheme 3.** [a] One main isomer (ca. 80% of total). [b] Major isomer (**10a**) isolated in 65% yield, minor isomer (**10b**) isolated in 16% yield. Only major isomer was taken further. [c] Mixture (ca. 1:1) of two isomers differing in stereochemistry at C(2). Relative stereochemistry of ring and side chain stereogenic centers not assigned. [d] Two inseparable isomers (ca. 4:3) differing in stereochemistry at C(2). [e] Major isomer (**14a**) isolated in 41% yield, minor isomer (**14b**) in 31% yield. Compounds **14a** and **b** differ in stereochemistry at C(2). [f] Mixture of **14a** and **b** used.

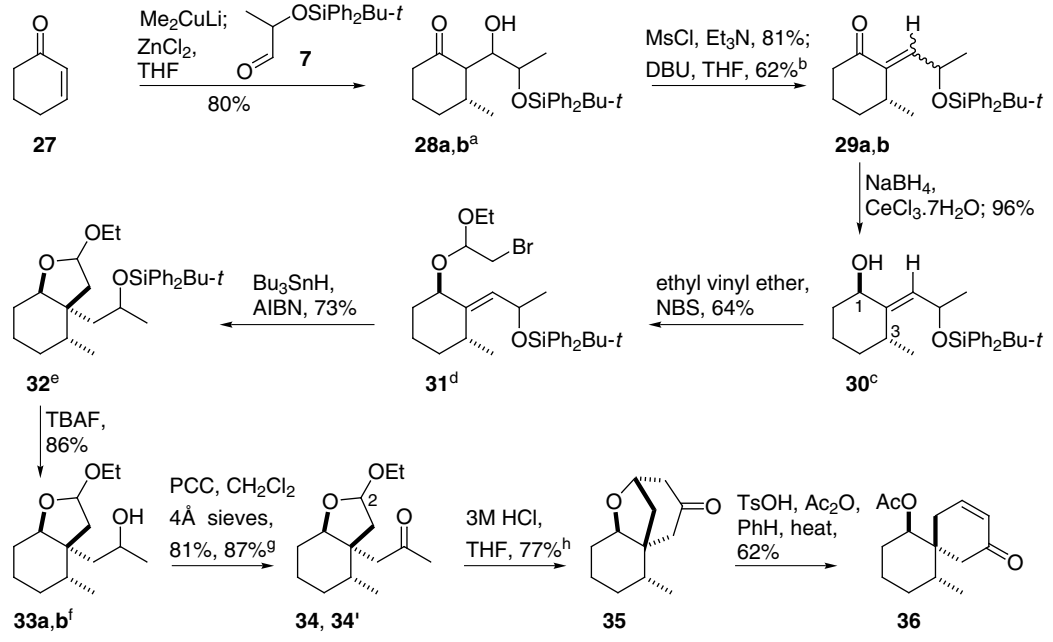



**Scheme 4.** [a] Yield of major aldol (**18a**), which contains trace impurities. [b] Yield of minor aldol (**18b**), which contains trace impurities. [c] First yield in each case corresponds to major aldol series. [d] Major isomer (**20a**) isolated in 55% yield, minor isomer (**20b**) isolated in 43% yield. Only major isomer was taken further. [e] Mixture (1:1) of two inseparable isomers differing in stereochemistry at C(2). [f] Major isomer (**23a**) isolated in 44% yield, minor isomer (**23b**) in 39% yield. The isomers differ in stereochemistry at C(2). [g] Yield of **24** from **23a** (major isomer of **23**). [h] Yield of **24′** from **23b** (minor isomer of **23**). Compounds **24** and **24′** differ in stereochemistry at C(2). [i] Mixture of **24** and **24′** used.

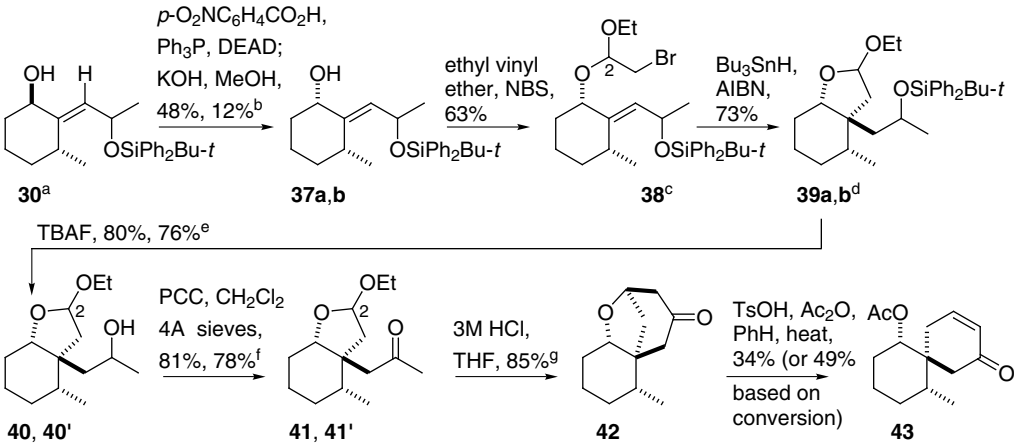
and then exposure to mineral acid caused hydrolysis of the lactol ethyl ethers to the corresponding lactols, and induced, formally, aldol condensation, dehydration and intramolecular Michael addition, leading to **15**. Finally, the enone system was liberated[13] (**15→16**) by heating in PhH with $Ac_2O$ and a catalytic amount of $TsOH{\cdot}H_2O$.

Although use of **7**, as opposed to **3**, means that more complex stereoisomer mixtures have to be handled, the silyl ether series based on **7** has the important advantage that it does not involve any especially sensitive intermediates.

We then repeated the sequence, starting from cyclopentanone; the results were entirely comparable, and are summarized in Scheme 4.




**Scheme 5.** [a] Major isomer (**28a**) isolated in 72% yield, minor isomer (**28b**) isolated in 8% yield. [b] Mixture of isomers of **28** used. Yield of major fraction (**29a**, two isomers (ca. 8:1), both with *E* geometry) 53%, yield of minor fraction (**29b**, two isomers (ca. 5:1), both with *Z* geometry) 9%. Only major fraction (**29a**) taken forward. [c] Two inseparable isomers (ca. 8:1). [d] Four isomers (ca. 8:8:1:1). [e] Four isomers. [f] Yield of major fraction (**33a**) 44%, yield of minor fraction (**33b**) 42%, each fraction consisting of two isomers (both ca. 6:1). [g] Yield from **33a** (major fraction of **33**) was 81%; yield from **33b** (minor fraction of **33**) was 87%. Both **34** and **34′** were single isomers differing in stereochemistry at C(2). [h] A 1:1 mixture of **34** and **34′** was used.




**Scheme 6.** [a] An 8:1 mixture of isomers. [b] Yield of major isomer (**37a**) 48% overall. Yield of minor isomer (**37b**) 12%. Only major isomer was taken further. [c] Two isomers (ca. 1:1) differing in stereochemistry at C(2). [d] Yield of major isomer (**39a**) 49%, yield of minor isomer (**39b**) 24%. [e] Yield of **40** from **39a** (major isomer of **39**) 80%, yield of **40′** from **39b** (minor isomer of **39**) 76%. Isomers **40** and **40′** differ in stereochemistry at C(2). [f] Yield of **41** from **40** (major isomer series) 81%, yield of **41′** from **40′** (minor isomer series) 78%. [g] Ketones **41** and **41′** were mixed (ca. 2:1) before treatment with HCl.

The experiments leading to **16** and **26** suggest that the method is general, and so we next established that the stereochemistry of the spiro center could indeed be reversed by appropriate manipulation of the stereochemistry of the adjacent oxygen function. To this end, the route of Scheme 3 was modified so as to incorporate a methyl group as a stereochemical marker in the 6-membered ring (see Scheme 5). A conjugate addition-aldol condensation served to convert 2-cyclohexenone into **28a**,**b** (Scheme 5), and from that point, our standard sequence of reactions was applied, as shown. The presence of the methyl group increased the number of isomers in the intermediate stages, but this complication disappears, of course, near the end of the sequence. Both isomers of aldol **28** and the major fraction of enone **29** (53% yield, consisting of two isomers, each with *E* geometry) were used for the subsequent steps. The *E* geometry for **29a** was established by the characteristic chemical shift of the vinylic hydrogen ($\delta$ 6.4). Both isomers of the minor fraction of **29** had *Z* geometry ($\delta$ 5.6). Compound **30** was obtained as an 8:1 mixture of *E* isomers, and the relative stereochemistry at C(1) and C(3) of each component was inferred by observation of an NOE (ca. 5%) between C(1)*H* and the C(3)C*H*$_3$ hydrogens. For comparison, alcohol **37a** (see later) was also examined, and in this case, no NOE enhancement between the corresponding hydrogens was observed. The *trans* relationship of the hydroxyl and methyl groups in **30** is that expected for the usual axial hydride delivery in $NaBH_4$ reduction of ketones **29a**. The bromo acetals **31** were obtained as a mixture of four isomers (ca. 8:8:1:1). The corresponding product of radical cyclization (**32**) was also obtained as a mixture of four isomers. In this case, however, the isomer ratio could not be determined from the $^1$H NMR spectrum, but the presence of two major and two minor isomers was clear from the $^{13}$C NMR spectrum. Desilylation ($Bu_4NF$) afforded alcohols **33** as a separable mixture of two fractions in yields of 44 and 42%, each consisting of two isomers, and in both cases, the isomer ratio was ca. 6:1. After oxidation, each fraction gave a single isomer of general structure **34**/**34′** in good yield (>80%), and both the ketones **34** and **34′**, which differ only in the stereochemistry at C(2), then afforded the same tricyclic product **35**. This was converted under the standard conditions into spiro enone **36**.

We have also shown that **30** can serve as a common intermediate for generating both stereochemistries at the spiro carbon. To do this, alcohols **30** (as an 8:1 isomer mixture) were subjected to Mitsunobu inversion (Scheme 6, **30**→**37a**,**b**), and the major alcohol (**37a**) was converted into bromo acetals **38**. These were subjected to radical cyclization and the individual products (**39a**, 49% and **39b**, 24%) were separately desilylated. Oxidation of the resulting alcohols (**40**→**41** and **40′**→**41′**) gave the expected ketones. Samples of these were mixed and converted into the polycyclic ketone **42** by the action of hydrochloric acid. Finally, treatment with $Ac_2O$ in the presence of $TsOH{\cdot}H_2O$ yielded spiro enone **43**, isomeric with that (**36**) obtained from alcohols **30**.

## 2. Conclusion

The above experiments show that the present methodology can be used to make spiro enones in a manner that allows control of the stereochemistry of the spiro center so that either stereochemistry can be generated.

## 3. Experimental

### 3.1. General

The same general procedures as used previously[14] were followed. The symbols s, d, t and q used for $^{13}$C NMR signals indicate zero, one, two and three attached hydrogens, respectively. In cases where the number of signals is less than expected, we assume this is due to coincident chemical shifts.

**3.1.1. 2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1-hydroxypropyl]cyclohexanone (8).** A solution of cyclohexanone (0.90 mL, 8.67 mmol) in THF (15 mL) was added dropwise to a stirred and cooled (−78°C) solution

of LDA [generated by dropwise addition of BuLi (2.5 M, in hexane, 3.9 mL, 9.7 mmol) to *i*-$Pr_2NH$ (1.4 mL, 10.0 mmol) in THF (60 mL) at 0°C, followed, after 15 min, by cooling to −78°C]. After 1 h, aldehyde **7**[9] (1.384 g, 4.428 mmol) in THF (20 mL) was added quickly. Stirring was continued for 50 min at −78°C, and the reaction was quenched with saturated aqueous $NH_4Cl$ (9 mL). The cooling bath was removed and stirring was continued until the mixture had reached room temperature. The mixture was diluted with $Et_2O$ (150 mL), washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2×20 cm), using 1:6 EtOAc–hexane, gave alcohols **8** as a mixture of four isomers (one isomer being the major component, ca. 80% of the total) ($^{13}C$ NMR) (1.669 g, 92%): FTIR ($CH_2Cl_2$, cast) 3520, 2932, 2857, 1696 $cm^{-1}$; exact mass (HR electrospray) *m/z* calcd for $C_{25}H_{34}NaO_3Si$ 433.217493, found 433.216764.

**3.1.2. (*E*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]cyclohexanone (9).** *(a) Methanesulfonic acid 2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-(2-oxocyclohexyl)propyl ester*. $MeSO_2Cl$ (0.96 mL, 12.4 mmol) was added dropwise to a stirred and cooled (0°C) solution of alcohols **8** (1.6334 g, 3.9778 mmol) and $Et_3N$ (2.8 mL, 20 mmol) in $CH_2Cl_2$ (64 mL). The cooling bath was left in place, but was not recharged. Stirring was continued for 6 h, the solution was quenched with saturated aqueous $NaHCO_3$ (15 mL), diluted with $Et_2O$ (200 mL), washed with water and brine, dried ($MgSO_4$), and filtered through a pad (4×3 cm) of silica gel, using $Et_2O$ (100 mL) as a rinse. Evaporation of the filtrate gave the crude mesylates (1.5785 g, 81%), which were used immediately for next step.

*(b) (E)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propylidene]cyclohexanone (9)*. DBU (1.0 mL, 6.7 mmol) was added dropwise to a stirred solution of the above mesylates (1.5785 g, 3.2298 mmol) in THF (26 mL). After 1 h, the mixture was diluted with $Et_2O$ (200 mL) and washed with water, 5% hydrochloric acid, and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.5×25 cm), using 1:10 EtOAc–hexane, gave enone **9** (0.9631 g, 76%): FTIR ($CH_2Cl_2$, cast) 2931, 2889, 2857, 1691, 1624 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.07 (s, 9H), 1.22 (d, $J$=6.3 Hz, 3H), 1.26–1.40 (m, 1H), 1.50–1.62 (m, 1H), 1.62–1.82 (m, 2H), 2.00 (ddd, $J$=7.0, 6.0, 2.0 Hz, 2H), 2.26 (ddd, $J$=17.6, 9.0, 5.6 Hz, 1H), 2.40 (dt, $J$=17, 5 Hz, 1H), 4.52 (dq, $J$=8, 6.3 Hz, 1H), 6.54 (dt, $J$=8, 1.2 Hz, 1H), 7.3–7.5 (m, 6H), 7.62–7.74 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) $\delta$ 19.2 (s), 23.0 (q), 23.3 (t), 23.4 (t), 26.7 (t), 26.9 (q), 66.0 (d), 127.5 (d), 127.6 (d), 129.6 (d), 129.7 (d), 133.8 (s), 133.9 (s), 134.1 (s), 135.8 (d), 135.9 (d), 141.5 (d), 201.3 (s); exact mass (HR electrospray) *m/z* calcd for $C_{25}H_{32}NaO_2Si$ 415.206929, found 415.207259. The *E* geometry was assigned by comparison of the chemical shift of the vinyl hydrogen with values reported for the model compounds (*E*)-2-ethylidenecyclohexanone[15] and (*Z*)-2-ethylidenecyclohexanone.[15]

**3.1.3. (*E*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]cyclohexanol (10a,b).** $NaBH_4$ (6.9 mg, 0.18 mmol) was added in small portions to a stirred and cooled (0°C) solution of enone **9** (44.6 mg, 0.114 mmol) and $CeCl_3·7H_2O$ (65 mg, 0.17 mmol) in MeOH (1.5 mL) and THF (0.4 mL). After 1 h, the mixture was quenched with saturated aqueous $NH_4Cl$ (0.3 mL), diluted with $Et_2O$ (20 mL), and filtered through a pad (2×2 cm) of silica gel, using $Et_2O$ (20 mL) as a rinse. The organic filtrate was washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1×20 cm), using 1:10 EtOAc–hexane, gave alcohols **10** as two separable isomers, **10a** (less polar) (29.2 mg, 65%) and **10b** (more polar) (7.3 mg, 16%).

Isomer **10a**: FTIR ($CH_2Cl_2$, cast) 3387, 2931, 2892, 2857, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 0.96 (d, $J$=4.3 Hz, 1H), 1.05 (s, 9H), 1.10–1.50 (m, 7H, including a doublet at $\delta$ 1.20, $J$=6.2 Hz), 1.55–1.78 (m, 3H), 1.80–2.05 (m, 1H), 3.81–3.91 (m, 1H), 4.65 (dq, $J$=8.3, 6.2 Hz, 1H), 5.37 (dd, $J$=8.3, 1.0 Hz, 1H), 7.30–7.50 (m, 6H), 7.65–7.75 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 75.5 MHz) $\delta$ 19.2 (s), 22.6 (t), 25.0 (q), 26.0 (t), 26.7 (t), 27.0 (q), 35.6 (t), 66.1 (d), 73.1 (d), 126.5 (d), 127.4 (d), 127.6 (d), 129.46 (d), 129.54 (d), 134.6 (s), 134.9 (s), 135.9 (d), 136.1 (d), 139.5 (s); exact mass (HR electrospray) *m/z* calcd for $C_{25}H_{34}NaO_2Si$ 417.222579, found 417.222943.

Isomer **10b**: FTIR ($CH_2Cl_2$, cast) 3358, 2931, 2892, 2857, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 200 MHz) $\delta$ 1.07 (s, 9H), 1.11–1.61 (m, including a doublet at $\delta$ 1.21, $J$=6.2 Hz, 9H in all), 1.61–1.88 (m, 2H), 1.95–2.15 (m, 1H), 3.84–3.95 (m, 1H), 4.65 (dq, $J$=8.3, 6.2 Hz, 1H), 5.44 (d, $J$=8.3 Hz, 1H), 7.27–7.50 (m, 6H), 7.60–7.78 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 50.3 MHz) $\delta$ 19.2 (s), 22.8 (t), 25.0 (q), 26.3 (t), 26.9 (t), 27.0 (q), 35.7 (t), 65.9 (d), 73.2 (d), 126.1 (d), 127.3 (d), 127.5 (d), 129.4 (d), 129.5 (d), 134.6 (s), 134.7 (s), 135.8 (d), 135.9 (d), 139.9 (s); exact mass (HR electrospray) *m/z* calcd for $C_{25}H_{34}NaO_2Si$ 417.222579, found 417.222279.

**3.1.4. (*E*)-[[1-[2-(2-Bromo-1-ethoxyethoxy)cyclohexylidene]-2-propyl]oxy](1,1-dimethylethyl)diphenylsilane (11).** NBS (0.7472 g, 4.198 mmol), dry $CH_2Cl_2$ (18.5 mL) and ethyl vinyl ether (1.35 mL, 14.1 mmol) were mixed under Ar in a 50-mL round-bottomed flask until a homogeneous solution was obtained. This solution was added dropwise by syringe to a stirred and cooled (0°C) solution of alcohol **10a** (i.e. major isomer) (0.5523 g, 1.3995 mmol) in $CH_2Cl_2$ (7.5 mL), the reaction mixture being protected from light by aluminum foil. The cold bath was left in place, and stirring was continued for 25 h. The mixture was then diluted with $CH_2Cl_2$ (100 mL), washed with 10% aqueous $Na_2S_2O_3$, water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2×20 cm), using 1:25 EtOAc–hexane, gave bromo acetals **11** (0.4925 g, 66%) as a mixture [1:1 ($^1H$ NMR)] of two isomers: FTIR ($CH_2Cl_2$, cast) 2965, 2931, 2857 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 300 MHz) $\delta$ 0.8–1.10 (m, 4H), 1.10–1.56 (m, 15H), 1.56–2.10 (m, 4H), 3.10–3.60 (m, 4H), 3.70–3.78 (m, 0.5H), 3.98–4.07 (m, 0.5H), 4.52–4.62 (m, 1H), 4.62–4.78 (m, 1H), 5.63 (d, $J$=8.2 Hz, 0.5H), 5.67 (d, $J$=8.3 Hz, 0.5H), 7.16–7.35 (m, 6H), 7.72–7.88 (m, 4H); $^{13}C$ NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.5 (q), 15.6 (q), 19.4 (s), 21.5 (t), 22.2 (t), 25.3 (q), 26.2 (t), 27.2 (q), 27.4 (t), 27.7 (t), 32.7 (t), 32.9 (t), 34.0 (t), 34.3 (t), 61.8 (t), 62.0 (t), 66.3 (d), 66.4 (d), 77.4 (d), 78.1 (d), 98.9 (d), 100.6 (d), 127.9 (d),

128.0 (d), 129.0 (d), 129.9 (d), 130.0 (d), 131.5 (d), 134.56 (s), 134.61 (s), 134.96 (s), 134.99 (s), 136.2 (d), 136.3 (d), 136.8 (s), 137.9 (s); exact mass (HR electrospray) *m/z* calcd for $C_{29}H_{41}{}^{79}BrNaO_3Si$ 567.190605, found 567.191218.

**3.1.5. (3a*R**,7a*S**)-3a-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propyl]-2-ethoxyoctahydrobenzofuran (12).** $Bu_3SnH$ (0.37 mL, 1.37 mmol) and AIBN (21 mg, 0.13 mmol) were added to a stirred solution of bromo acetals **11** (0.3952 g, 0.7243 mmol) in PhMe (50 mL). The flask was then lowered into a preheated oil bath set at 115°C (continued stirring). After 1.5 h, the mixture was cooled to room temperature and the solvent was evaporated. Flash chromatography of the residue over silica gel (1.5×20 cm), using 1:30 EtOAc–hexane, gave acetals **12** (0.3100 g, 92%) as a mixture [ca. 4:3 ($^1$H NMR)] of two isomers, differing in stereochemistry at C(2): FTIR ($CH_2Cl_2$, cast) 2931, 2857 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 0.80–1.80 (m, 24H), 1.85–2.15 (m, 3H), 3.30–3.45 (m, 1H), 3.45–3.96 (m, 2H), 3.96–4.12 (m, 1H), 5.05–5.18 (two t, *J*=5.1, 4.5 Hz, 1H), 7.15–7.28 (m, 6H), 7.63–7.9 (m, 4H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.4 (q), 15.5 (q), 16.8 (s), 19.2 (s), 20.2 (t), 21.3 (t), 21.6 (t), 21.7 (t), 25.2 (t), 25.5 (q), 25.8 (q), 27.0 (q), 27.5 (t), 30.5 (t), 31.8 (t), 41.1 (s), 42.1 (s), 43.4 (t), 44.8 (t), 46.2 (t), 47.7 (t), 63.2 (t), 63.5 (t), 68.1 (d), 79.4 (d), 82.8 (d), 103.0 (d), 103.8 (d), 127.8 (d), 128.0 (d), 129.5 (d), 129.7 (d), 134.2 (s), 135.2 (s), 136.0 (d), 136.1 (d); exact mass (HR electrospray) *m/z* calcd for $C_{29}H_{42}NaO_3Si$ 489.280094, found 489.280630.

**3.1.6. 1-[(3a*R**,7a*S**)-2-Ethoxyoctahydrobenzofuran-3a-yl]-2-propanol (13).** $Bu_4NF$ (1.0 M in THF, 3.5 mL, 3.5 mmol) was added dropwise to a stirred solution of acetals **12** (0.4090 g, 0.8763 mmol) in THF (30 mL). The stirred mixture was warmed to 45°C for 150 min, cooled to room temperature, diluted with $Et_2O$ (120 mL), and washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1×20 cm), using 1:4 EtOAc–hexane, gave alcohols **13** (185 mg, 92%) as a chromatographically inseparable mixture [ca. 4:3 ($^1$H NMR)] of two isomers, differing in stereochemistry at C(2): FTIR ($CH_2Cl_2$, cast) 3443, 2969, 2931, 2861 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 0.92–1.50 (m, 13H), 1.50–1.75 (m, 1.5H), 1.77–2.12 (m, 4H), 2.63 (brs, 0.5H), 3.25–3.45 (m, 1H), 3.55–3.95 (m, 3H), 5.05–5.20 (m, 1H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.3 (q), 15.4 (q), 20.3 (t), 21.5 (t), 21.7 (t), 21.9 (t), 25.2 (t), 25.4 (q), 25.6 (q), 28.1 (t), 31.27 (t), 31.33 (t), 42.0 (s), 42.3 (s), 42.6 (t), 43.8 (t), 47.4 (t), 63.3 (t), 63.6 (t), 64.2 (d), 64.3 (d), 79.7 (d), 82.8 (d), 103.2 (d), 104.4 (d); exact mass *m/z* calcd for $C_{13}H_{24}O_3$ 228.17255, found 228.17290.

**3.1.7. 1-[(3a*R**,7a*R**)-2-Ethoxyoctahydrobenzofuran-3a-yl]-2-propanone (14a,b).** A solution of alcohols **13** (26.8 mg, 0.117 mmol) in $CH_2Cl_2$ (1 mL) was added dropwise to a stirred mixture of PCC (38.0 mg, 0.176 mmol), powdered 4 Å molecular sieves (150 mg) and $CH_2Cl_2$ (1 mL). After 3 h, the mixture was diluted with $Et_2O$ (10 mL), and filtered through a pad (2×1.5 cm) of silica gel, using $Et_2O$ (20 mL) as a rinse. Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.6×15 cm), using 1:9 EtOAc–hexane, gave ketones **14** as two separable isomers, **14a** (less polar) (11.0 mg, 41%) and **14b** (more polar) (8.2 mg, 31%), differing in stereochemistry at C(2).

Isomer **14a**: FTIR ($CH_2Cl_2$, cast) 2974, 2933, 2862, 1712 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 0.96–1.24 (m, 1H), 1.17–1.24 (t, *J*=7.0 Hz, 3H), 1.24–1.45 (m, 4H), 1.55–1.72 (m, 1H), 1.65 (s, 3H), 1.72–1.85 (m, 2H), 1.92 (dd, *J*=13.6, 4 Hz, 1H), 1.95–2.07 (m, 1H), 2.35 (d, *J*=16.0 Hz, 1H), 2.42 (dd, *J*=13.6, 6 Hz, 1H), 3.41 (dq, *J*=9.6, 7.0 Hz, 1H), 3.72 (t, *J*=3 Hz, 1H), 3.93 (dq, *J*=9.6, 7.0 Hz, 1H), 5.15 (dd, *J*=6, 4 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.3 (q), 20.1 (t), 21.6 (t), 25.5 (t), 30.3 (t), 30.7 (q), 41.5 (s), 46.3 (t), 46.8 (t), 63.4 (t), 79.5 (d), 103.0 (d), 205.0 (s); exact mass *m/z* calcd for $C_{13}H_{22}O_3$ 226.15689, found 226.15672.

Isomer **14b**: FTIR ($CH_2Cl_2$, cast) 2973, 2931, 2862, 1716 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 1.09–1.31 (m, 2H), 1.21 (t, *J*=7 Hz, 3H), 1.31–1.45 (m, 1H), 1.45–1.60 (m, 2H), 1.60–1.72 (m, 1H), 1.70 (s, 3H), 1.84 (d, *J*=16 Hz, 1H), 1.90–2.17 (m, 3H), 2.19–2.29 (m, 2H), 3.41 (dq, *J*=10, 7 Hz, 1H), 3.58 (t, *J*=5 Hz, 1H), 3.94 (dq, *J*=10, 7.0 Hz, 1H), 5.11 (dd, *J*=6.5, 3.0 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.4 (q), 21.5 (t), 21.7 (t), 28.0 (t), 30.4 (t), 31.1 (q), 41.7 (s), 43.5 (t), 49.1 (t), 63.6 (t), 81.8 (d), 103.9 (d), 205.4 (s); exact mass *m/z* calcd for $C_{13}H_{22}O_3$ 226.15689, found 226.15692.

**3.1.8. (1*R**,6*R**,8*S**)-7-Oxatricyclo[6.3.1.0$^{1,6}$]dodecan-10-one (15).** A solution of ketones **14a** and **b** (ca. 4:3) (0.1359 g, 0.6004 mmol) in a mixture of 3 M HCl (30 mL) and THF (6 mL) was refluxed (85°C) for 24 h, cooled to room temperature, and extracted with EtOAc (100 mL). The aqueous layer was washed with EtOAc (2×50 mL), and the combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1×20 cm), using 1:1 EtOAc–hexane, gave tricyclic ketone **15** (80.1 mg, 74%) as a solid: FTIR ($CH_2Cl_2$, cast) 2934, 2861, 1716 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 360 MHz) $\delta$ 0.64–0.90 (m, 3H), 0.91–1.10 (m, 2H), 1.17–1.27 (m, 1H), 1.29–1.45 (m, 2H), 1.73–1.84 (m, 1H), 1.84 (t, *J*=16.8 Hz, 2H), 1.99–2.07 (m, 1H), 2.16 (dt, *J*=16.8, 2.6 Hz, 1H), 2.60–2.71 (m, 1H), 3.49 (dd, *J*=10.4, 4.4 Hz, 1H), 4.15–4.21 (m, 1H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 21.4 (t), 23.2 (t), 32.0 (t), 32.5 (t), 36.1 (t), 42.1 (s), 49.3 (t), 56.4 (t), 73.4 (d), 82.1 (d), 207.1 (s); exact mass *m/z* calcd for $C_{11}H_{16}O_2$ 180.11504, found 180.11500.

**3.1.9. Acetic acid (1*R**,6*R**)-10-oxospiro[5.5]undec-8-en-1-yl ester (16).** A solution of ketone **15** (50.2 mg, 0.279 mmol), $TsOH{\cdot}H_2O$ (47 mg, 0.27 mmol), and $Ac_2O$ (0.40 mL, 4.2 mmol) in PhH (55 mL) was heated at 85°C for 40 h, cooled, and evaporated. The residue was diluted with $Et_2O$ (100 mL), washed with water, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1×15 cm), using 1:4 EtOAc–hexane, gave spiro enone **16** (42.5 mg, 69%): FTIR ($CH_2Cl_2$, cast) 3035, 2938, 2864, 1734, 1680, 1621 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 400 MHz) $\delta$ 0.85–1.14 (m, 4H), 1.24–1.42 (m, 2H), 1.45–1.55 (m, 1H), 1.55–1.65 (m, 1H), 1.68 (s, 3H), 1.82 (dt, *J*=19.0, 1.5 Hz, 1H), 2.11 (dt, *J*=19.0, 3.0 Hz, 1H), 2.15 (d, *J*=15.4 Hz, 1H), 2.37 (d,

$J$=15.4 Hz, 1H), 4.63 (dd, $J$=9.0, 4.0 Hz, 1H), 5.96–6.02 (m, 1H), 6.16 (ddd, $J$=9.6, 5.2, 2.8 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 75.5 MHz) $\delta$ 20.6 (t), 21.1 (q), 23.0 (t), 26.3 (t), 30.1 (t), 32.2 (t), 40.3 (s), 47.6 (t), 77.0 (d), 128.9 (d), 147.5 (d), 170.2 (s), 198.8 (s); exact mass $m/z$ calcd for $C_{13}H_{18}O_3$ 222.12560, found 222.12578.

**3.1.10. 2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1-hydroxypropyl]cyclopentanone (18a,b).** The procedure described for **8** was followed, using cyclopentanone (1.72 mL, 19.5 mmol) in THF (34 mL), LDA (21.4 mmol) in THF (140 mL), aldehyde **7**[9] (3.0450 g, 9.7446 mmol) in THF (48 mL), and a final reaction time of 1 h. Flash chromatography of the crude product over silica gel (2.5×25 cm), using 1:10 EtOAc–hexane, gave aldols **18** as two fractions, **18a** (more polar) (2.2118 g, 57%) and **18b** (less polar) (0.7671 g, 20%), each of which contained trace impurities ($^1$H NMR).

Fraction **18a**: FTIR ($CH_2Cl_2$, cast) 3491, 2961, 2931, 2886, 2857, 1723 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 0.97–2.30 (m, 7H), 1.10 (s, 9H), 1.12 (d, $J$=7.0 Hz, 3H), 3.62 (dt, $J$=8.5, 2.8 Hz, 1H), 3.77 (dd, $J$=2.5, 0.6 Hz, 1H), 3.89 (dq, $J$=6.3, 2.8 Hz, 1H), 7.35–7.47 (m, 6H), 7.69–7.79 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) $\delta$ 17.0 (q), 19.1 (s), 20.4 (t), 26.5 (t), 26.9 (q), 38.0 (t), 50.2 (d), 71.0 (d), 75.8 (d), 127.4 (d), 127.44 (d), 129.47 (d), 129.5 (d), 133.8 (s), 134.1 (s), 135.7 (d), 222.3 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{24}H_{32}NaO_3Si$ 419.201843, found 419.202002.

Fraction **18b**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 0.96–2.42 (m, 10H), 1.08 (s, 9H), 3.66 (ddd, $J$=8.0, 4.0, 2.0 Hz, 1H), 4.01 (dq, $J$=7.5, 3.6 Hz, 1H), 4.07 (d, $J$=2.0 Hz, 1H), 7.35–7.50 (m, 6H), 7.65–7.78 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) $\delta$ 18.7 (q), 19.3 (s), 21.0 (t), 27.1 (q), 27.2 (t), 78.7 (t), 50.1 (d), 70.9 (d), 76.1 (d), 127.5 (d), 127.8 (d), 129.7 (d), 129.8 (d), 133.6 (s), 134.3 (s), 135.75 (d), 135.8 (d), 136.0 (d), 223.7 (s).

**3.1.11. (*E*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]cyclopentanone (19) from 18a (major isomer of 18).** *(a) Methanesulfonic acid 2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-(2-oxocyclopentyl)propyl ester.* The procedure described for mesylation of **8** was followed, using $MeSO_2Cl$ (0.44 mL, 5.7 mmol), alcohol **18a** (i.e. major isomer of **18**) (0.7360 g, 1.8557 mmol), $Et_3N$ (1.3 mL, 9.3 mmol) and $CH_2Cl_2$ (35 mL), and a reaction time of 4 h. The crude mesylate (0.8280 g, 94%) was used immediately for next step.

*(b) (E)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propylidene]cyclopentanone (**19**).* The procedure described for **9** was followed, using DBU (0.54 mL, 3.6 mmol) and the above mesylates (0.8280 g, 1.744 mmol) in THF (17 mL). Flash chromatography of the crude product over silica gel (1.5×20 cm), using 1:10 EtOAc–hexane, gave enone **19** (0.5850 g, 89%): FTIR ($CH_2Cl_2$, cast) 2963, 2930, 2891, 2857, 1722, 1657 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 1.06 (s, 9H), 1.25 (d, $J$=6.4 Hz, 3H), 1.50–1.70 (m, 1H), 1.70–1.80 (m, 1H), 1.92–2.06 (m, 1H), 2.12–2.30 (m, 3H), 4.44 (dq, $J$=7.6, 6.4 Hz, 1H), 6.50 (dt, $J$=8.2, 2.7 Hz, 1H), 7.30–7.50 (m, 6H), 7.62–7.75 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75.5 MHz) $\delta$ 19.1 (s), 19.8 (t), 23.1 (q), 26.4 (t), 26.9 (q), 38.1 (t), 67.8 (d), 127.5 (d), 127.6 (d), 129.66 (d), 129.70 (d), 133.8 (s), 134.0 (s), 134.6 (s), 135.8 (d), 135.9 (d), 138.0 (d), 207.5 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{24}H_{30}NaO_2Si$ 401.191279, found 401.191571. The $E$ geometry was assigned on the basis of the chemical shift arguments used for **9**.

**3.1.12. (*E*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]cyclopentanone (19) from 18b (minor isomer of 18).** *(a) Methanesulfonic acid 2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-(2-oxocyclopentyl)propyl ester.* The procedure described for mesylation of **8** was followed, using $MeSO_2Cl$ (0.45 mL, 5.8 mmol), alcohol **18b** (i.e. minor isomer of **18**) (0.7485 g, 1.887 mmol), $Et_3N$ (1.3 mL, 9.3 mmol) and $CH_2Cl_2$ (36 mL), and a reaction time of 6 h. The crude mesylate (0.4875 g, 54%) was used immediately for next step.

*(b) (E)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propylidene]cyclopentanone (**19**).* The procedure described for **9** was followed, using DBU (0.32 mL, 2.1 mmol), the above mesylates (0.4875 g, 1.027 mmol) in THF (10 mL), and a reaction time of 45 min. Flash chromatography of the crude product over silica gel (1.5×20 cm), using 1:15 EtOAc–hexane, gave enone **19** (0.2560 g, 66%), spectroscopically identical with material obtained from the major isomer series.

**3.1.13. (*E*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]cyclopentanol (20a,b).** The procedure described for **10a**,**b** was followed, using $NaBH_4$ (0.3680 g, 9.725 mmol), enone **19** (2.4240 g, 6.4027 mmol), $CeCl_3{\cdot}7H_2O$ (3.4210 g, 9.1817 mmol),and MeOH (74 mL). Flash chromatography of the crude product over silica gel (2.5×25 cm), using 1:8 EtOAc–hexane, gave alcohols **20** as two separable isomers, **20a** (less polar) (1.3555 g, 55%) and **20b** (more polar) (1.0530 g, 43%).

Isomer **20a**: FTIR ($CH_2Cl_2$, cast) 3432, 2962, 2930, 2891, 2857 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 0.64 (d, $J$=6.0 Hz, 1H), 1.07 (s, 9H), 1.18–1.58 (m, 3H), 1.27 (d, $J$=6.0 Hz, 3H), 1.63–1.84 (m, 3H), 4.15 (q, $J$=6.0 Hz, 1H), 4.43 (dq, $J$=8.0, 6.0 Hz, 1H), 5.47 (dq, $J$=8.0, 2.0 Hz, 1H), 7.33–7.48 (m, 6H), 7.66–7.75 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) $\delta$ 19.1 (s), 21.5 (t), 23.9 (q), 26.5 (t), 27.0 (q), 35.1 (t), 68.1 (d), 75.2 (d), 127.4 (d), 127.6 (d), 128.3 (d), 129.6 (d), 134.3 (s), 135.0 (s), 135.8 (d), 136.0 (d), 144.3 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{24}H_{32}NaO_2Si$ 403.206929, found 403.207043.

Isomer **20b**: FTIR ($CH_2Cl_2$, cast) 3340, 2962, 2930, 2892, 2857 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.08 (s, 9H), 1.26 (d, $J$=6.0 Hz, 3H), 1.30–1.43 (m, 1H), 1.46–1.60 (m, 3H), 1.62–1.75 (m, 2H), 1.91–2.03 (m, 1H), 4.25 (s, 1H), 4.39 (dq, $J$=8.0, 6.0 Hz, 1H), 5.61 (dd, $J$=8.0, 1.0 Hz, 1H), 7.32–7.48 (m, 6H), 7.66–7.75 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) $\delta$ 19.2 (s), 22.1 (t), 24.1 (q), 26.3 (t), 27.0 (q), 35.0 (t), 68.0 (d), 75.6 (d), 127.3 (d), 127.5 (d), 128.7 (d), 129.4 (d), 129.5 (d), 134.46 (s), 134.50 (s), 135.86 (d), 135.93 (d), 144.4 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{24}H_{32}NaO_2Si$ 403.206929, found 403.207247.

**3.1.14. (*E*)-[[1-[2-(2-Bromo-1-ethoxyethoxy)cyclopentylidene]-2-propyl]oxy](1,1-dimethylethyl)diphenylsilane (21).** The procedure described for **11** was followed, using NBS (1.8235 g, 10.245 mmol), dry $CH_2Cl_2$ (46 mL), ethyl vinyl ether (3.3 mL, 34 mmol), alcohol **20a** (i.e. major isomer) (1.3000 g, 3.4155 mmol) in 18 mL $CH_2Cl_2$ (18 mL), and a reaction time of 18 h. Flash chromatography of the crude product over silica gel (2×20 cm), using 1:40 EtOAc–hexane, gave bromo acetals **21** (1.1870 g, 65%) as a chromatographically inseparable mixture [ca. 1:1 ($^1$H NMR) of two isomers: FTIR ($CH_2Cl_2$, cast) 2965, 2930, 2891, 2857 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 360 MHz) $\delta$ 1.12 (t, $J$=7.0 Hz, 1.5H), 1.13 (t, $J$=7.0 Hz, 1.5H), 1.23 (s, 4.5H), 1.24 (s, 4.5H), 1.30 (d, $J$=6.2 Hz, 2H), 1.32 (d, $J$=6.2 Hz, 2H), 1.38–1.58 (m, 2H), 1.58–1.80 (m, 3H), 3.15–3.31 (m, 2H), 3.31–3.42 (m, 1H), 3.42–3.53 (m, 1H), 4.12–4.20 (m, 1H), 4.44–4.58 (m, 1H), 4.70 (t, $J$=5.5 Hz, 0.5H), 4.77 (t, $J$=5.5 Hz, 0.5H), 5.85 (d, $J$=8.5 Hz, 0.5H), 5.90 (dq, $J$=8.5, 2.0 Hz, 0.5H), 7.15–7.30 (m, 6H), 7.75–7.85 (m, 4H); $^{13}$C NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.2 (q), 19.2 (s), 21.6 (t), 22.0 (t), 23.9 (q), 24.0 (q), 25.8 (t), 26.3 (t), 26.8 (q), 27.0 (q), 32.1 (t), 32.2 (t), 32.3 (t), 33.4 (t), 60.7 (t), 60.8 (t), 68.2 (d), 79.0 (d), 79.8 (d), 99.6 (d), 100.1 (d), 127.56 (d), 127.6 (d), 129.3 (d), 129.5 (d), 129.59 (d), 129.63 (d), 130.3 (d), 134.3 (s), 134.4 (s), 134.6 (s), 134.7 (s), 136.0 (d), 136.1 (d), 136.2 (d), 140.4 (s), 141.0 (s); exact mass (HR electrospray) *m/z* calcd for $C_{28}H_{39}{}^{79}BrNaO_3Si$ 553.174955, found 553.175107.

**3.1.15. (3a*R**,7a*S**)-3a-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propyl]-2-ethoxyhexahydrocyclopenta[*b*]furan (22).** The procedure described for **12** was followed, using $Bu_3SnH$ (0.57 mL, 2.11 mmol), AIBN (33 mg, 0.20 mmol), bromo acetals **21** (0.6860 g, 1.290 mmol), PhMe (90 mL), and a reaction time of 1 h. Flash chromatography of the crude product over silica gel (1.5×20 cm), using 1:40 EtOAc–hexane, gave acetals **22** (0.5290 g, 90%) as a chromatographically inseparable mixture [ca. 1:1 ($^1$H NMR)] of two isomers, differing in stereochemistry at C(2): FTIR ($CH_2Cl_2$, cast) 2961, 2931, 2898, 2857 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 400 MHz) $\delta$ 1.10 (d, $J$=6.0 Hz, 1.5H), 1.11 (d, $J$=6.0 Hz, 1.5H), 1.16 (t, $J$=7.0 Hz, 1.5H), 1.17 (t, $J$=7.0, 1.5H), 1.19–2.24 (m, 9H), 1.22 (s, 4.5H), 1.25 (s, 4.5H), 2.43 (d, $J$=13 Hz, 0.5H), 2.51 (dd, $J$=14, 6.0 Hz, 0.5H), 3.30–3.41 (m, 1H), 3.74–3.90 (m, 1H), 4.04 (sextet, $J$=6.0 Hz, 0.5H), 4.14 (sextet, $J$=6.0 Hz, 0.5H), 4.19 (d, $J$=5.0 Hz, 1H), 5.06 (dd, $J$=5.6, 2.0 Hz, 0.5H), 5.13 (d, $J$=5.0 Hz, 0.5H), 7.15–7.30 (m, 6H), 7.75–7.90 (m, 4H); $^{13}$C NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.2 (q), 15.3 (q), 19.15 (s), 19.20 (s), 24.3 (t), 24.5 (t), 25.2 (q), 25.4 (q), 27.0 (q), 27.1 (q), 32.8 (t), 34.0 (t), 38.8 (t), 39.5 (t), 46.0 (t), 46.1 (t), 49.9 (s or t), 50.9 (s or t), 51.29 (s or t), 51.35 (s or t), 62.0 (t), 62.7 (t), 68.9 (d), 69.1 (d), 90.7 (d), 92.8 (d), 104.7 (d), 105.2 (d), 127.6 (d), 127.7 (d), 129.5 (d), 129.6 (d), 129.65 (d), 129.7 (d), 134.3 (s), 134.4 (s), 135.0 (s), 135.3 (s), 136.0 (d), 136.07 (d), 136.12 (d); exact mass (HR electrospray) *m/z* calcd for $C_{28}H_{40}NaO_3Si$ 475.26444, found 475.264908.

**3.1.16. 1-[(3a*R**,7a*S**)-2-Ethoxyhexahydrocyclopenta[*b*]-furan-3a-yl]-2-propanol (23a,b).** The procedure described for **13** was followed, using $Bu_4NF$ (1.0 M in THF, 2.5 mL, 2.5 mmol), acetals **22** (0.4750 g, 1.049 mmol) in THF (44 mL), and a reaction time of 4 h. Flash chromatography of the crude product over silica gel (1×20 cm), using 1:6 EtOAc–hexane, gave alcohols **23** as two isomers, **23a** (more polar) (99.8 mg, 44%) and **23b** (less polar) (88.0 mg, 39%), differing in stereochemistry at C(2).

Isomer **23a**: FTIR ($CH_2Cl_2$, cast) 3432, 2967, 2908 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 400 MHz) $\delta$ 1.01 (d, $J$=6.2 Hz, 3H), 1.15–1.44 (m, 4H), 1.19 (t, $J$=7.1 Hz, 3H), 1.51–1.65 (m, 2H), 1.87–1.96 (m, 1H), 1.96–2.06 (m, 1H), 2.08 (dd, $J$=13.7, 1.8 Hz, 1H), 2.17–2.30 (m, 2H), 3.36 (dq, $J$=9.4, 7.1 Hz, 1H), 3.61–3.72 (m, 1H), 3.89 (dq, $J$=9.4, 7.1 Hz, 1H), 4.30 (d, $J$=4.7 Hz, 1H), 5.16 (dd, $J$=5.9, 1.85 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.4 (q), 24.2 (t), 25.5 (q), 34.2 (t), 38.6 (t), 46.3 (t), 49.6 (t), 52.1 (s), 63.0 (t), 65.8 (d), 92.2 (d), 105.8 (d); exact mass (HR electrospray) *m/z* calcd for $C_{12}H_{22}NaO_3$ 237.146665, found 237.146728.

Isomer **23b**: FTIR ($CH_2Cl_2$, cast) 3455, 2960 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 1.10–1.25 (m, 1H), 1.12 (t, $J$=7.1 Hz, 3H), 1.21 (d, $J$=6.2 Hz, 3H), 1.29–1.52 (m, 4H), 1.52–1.74 (m, 3H), 1.92–2.03 (m, 1H), 2.34 (d, $J$=13.8 Hz, 1H), 3.28 (dq, $J$=9.6, 7.1 Hz, 1H), 3.31 (s, 1H), 3.75 (dq, $J$=9.6, 7.1 Hz, 1H), 3.92–4.08 (m, 1H), 4.68 (d, $J$=5.0 Hz, 1H), 5.03 (d, $J$=5.4 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.2 (q), 24.2 (t), 24.7 (q), 33.6 (t), 43.1 (t), 44.9 (t), 48.6 (t), 51.1 (s), 62.6 (t), 65.0 (d), 89.3 (d), 105.0 (d); exact mass (HR electrospray) *m/z* calcd for $C_{12}H_{22}NaO_3$ 237.146665, found 237.146457.

**3.1.17. 1-[(3a*R**,7a*R**)-2-Ethoxyhexahydrocyclopenta[*b*]-furan-3a-yl]-2-propanone (24) from 23a (major isomer of 23).** The procedure described for **14a**,**b** was followed, using alcohol **23a** (i.e. major isomer) (87.0 mg, 0.406 mmol) in $CH_2Cl_2$ (3.6 mL), PCC (0.1326 g, 0.6149 mmol), powdered 4 Å molecular sieves (704 mg), $CH_2Cl_2$ (3.6 mL), and a reaction time of 3 h. Flash chromatography of the crude product over silica gel (1×15 cm), using 1:4 EtOAc–hexane, gave ketone **24** (64.0 mg, 74%), whose stereochemistry at C(2) with respect to the quaternary center was not established. Compound **24** had: FTIR ($CH_2Cl_2$, cast) 2971, 2901, 1718 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 1.17 (t, $J$=7.1 Hz, 3H), 1.32–1.74 (m, 3H), 1.64 (s, 3H), 1.92–2.06 (m, 1H), 1.94 (dd, $J$=13.5, 5.8 Hz, 1H), 2.04 (s, 2H), 2.06–2.26 (m, 2H), 2.29 (dd, $J$=13.5, 1.8 Hz, 1H), 3.37 (dq, $J$=9.4, 7.1 Hz, 1H), 3.86 (dq, $J$=9.4, 7.1 Hz, 1H), 4.18 (dd, $J$=5.7, 1.3 Hz, 1H), 5.11 (dd, $J$=5.8, 1.8 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.4 (q), 24.5 (t), 30.4 (q), 34.5 (t), 39.2 (t), 46.7 (t), 50.6 (s), 53.5 (t), 63.0 (t), 91.4 (d), 105.4 (d), 205.1 (s); exact mass *m/z* calcd for $C_{12}H_{20}O_3$ 212.14125, found 212.14062.

**3.1.18. 1-[(3a*R**,7a*R**)-2-Ethoxyhexahydrocyclopenta[*b*]-furan-3a-yl]-2-propanone (24′) from 23b (minor isomer of 23).** The procedure described for **14a**,**b** was followed, using alcohol **23b** (i.e. minor isomer) (74.0 mg, 0.345 mmol) in $CH_2Cl_2$ (3 mL), PCC (0.1117 g, 0.5180 mmol), powdered 4 Å molecular sieves (500 mg), $CH_2Cl_2$ (3 mL), and a reaction time of 3.5 h. Flash chromatography of the crude product over silica gel (1×15 cm), using 1:4 EtOAc–hexane, gave ketone **24′** (0.0521 g, 71%), whose stereochemistry at C(2) with respect to the quaternary center was not established. Compounds **24** and **24′** have different stereochemistry at C(2). Compound **24′** had: FTIR ($CH_2Cl_2$,

cast) 2941, 2902, 2868, 1718 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 400 MHz) $\delta$ 1.14 (t, $J$=7.1 Hz, 3H), 1.34 (ddd, $J$=6.1 Hz, 1H), 1.51–1.75 (m, 3H), 1.64 (s, 3H), 1.78 (dd, $J$=13.4, 4.9 Hz, 1H), 1.81–1.88 (m, 1H), 1.93–2.00 (m, 1H), 2.16 (d, $J$=13.4 Hz, 1H), 2.41 (d, $J$=17.8 Hz, 1H), 2.79 (d, $J$=17.8 Hz, 1H), 3.31 (dq, $J$=9.6, 7.1 Hz, 1H), 3.74 (dq, $J$=9.6, 7.1 Hz, 1H), 4.28 (d, $J$=4.8 Hz, 1H), 5.06 (d, $J$=4.9 Hz, 1H); $^{13}C$ NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.5 (q), 24.5 (t), 30.3 (q), 33.2 (t), 39.7 (t), 46.7 (t), 50.2 (s), 53.2 (t), 62.2 (t), 89.4 (d), 104.5 (d), 205.8 (s); exact mass $m/z$ calcd for $C_{12}H_{20}O_3$ 212.14125, found 212.14120.

**3.1.19. (1*R**,5*R**,7*S**)-6-Oxatricyclo[5.3.1.0$^{1,5}$]undecan-9-one (25).** The procedure described for **15** was followed, using ketones **24** and **24′** (ca. 1:1) (74.0 mg, 0.349 mmol), 3 M HCl (17 mL), THF (3.6 mL), and a reflux time of 36 h. Flash chromatography of the crude product over silica gel (1×15 cm), using 1:3 EtOAc–hexane gave ketone **25** (43 mg, 74%): FTIR ($CH_2Cl_2$, cast) 2954, 2877, 1715 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.84–0.95 (m, 1H), 1.15 (d, $J$=11.2 Hz, 1H), 1.23–1.45 (m, 2H), 1.48–1.62 (m, 3H), 1.64 (ddt, $J$=11.2, 5.6, 2.8 Hz, 1H), 1.80 (dd, $J$=17.8, 2.8 Hz, 1H), 2.16 (d, $J$=17 Hz, 1H), 2.26 (dt, $J$=17, 2.0 Hz, 1H), 2.58 (dq, $J$=17.8, 2.0 Hz, 1H), 3.91 (t, $J$=5.6 Hz, 1H), 4.17 (dt, $J$=5.4, 2.7 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) $\delta$ 23.6 (t), 33.2 (t), 34.0 (t), 40.6 (t), 48.3 (t), 50.9 (s), 53.5 (t), 76.4 (d), 88.5 (d), 209.8 (s); exact mass $m/z$ calcd for $C_{10}H_{14}O_2$ 166.09938, found 166.09960.

**3.1.20. Acetic acid (1*R**,5*R**)-9-oxospiro[5.4]dec-7-en-1-yl ester (26).** The procedure described for **16** was followed, using ketone **25** (15.2 mg, 0.091 mmol), $TsOH{\cdot}H_2O$ (15.5 mg, 0.089 mmol), $Ac_2O$ (0.13 mL, 1.4 mmol), PhH (18 mL), and a reaction time of 20 h. Flash chromatography of the crude product over silica gel (0.6×10 cm), using 1:3 EtOAc–hexane, gave enone **26** (14.1 mg, 74%): FTIR ($CH_2Cl_2$, cast) 2958, 2879, 1736, 1680 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.56–1.86 (m, 5H), 2.06 (s, 3H), 2.08–2.19 (m, 1H), 2.27 (dd, $J$=16.0, 1.0 Hz, 1H), 2.29 (ddt, $J$=19.0, 5.0, 1.4 Hz, 1H), 2.46 (d, $J$=16.0 Hz, 1H), 2.57 (dt, $J$=19.0, 2.8 Hz, 1H), 4.85 (dd, $J$=6.4, 4.0 Hz, 1H), 6.04 (dq, $J$=10.0, 2.0 Hz, 1H), 6.93 (ddd, $J$=10.0, 5.0, 3.3 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) $\delta$ 20.1 (t), 21.1 (q), 29.9 (t), 31.8 (t), 34.4 (t), 47.3 (t), 47.6 (s), 80.6 (d), 129.5 (d), 148.7 (d), 170.4 (s), 198.4 (s); exact mass $m/z$ calcd for $C_{12}H_{16}O_3$ 208.10994, found 208.11036.

**3.1.21. 2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1-hydroxypropyl]-3-methylcyclohexanone (28a,b).** MeLi (1.4 M in $Et_2O$, 4.28 mL, 6.0 mmol) was added dropwise to a stirred and cooled (0°C) suspension of CuI (0.571 g, 3.00 mmol) in $Et_2O$ (30 mL). After 5 min, 2-cyclohexenone (0.145 mL, 1.5 mmol) was added, and stirring was continued at 0°C for 30 min. $ZnCl_2$ solution (1.0 M in $Et_2O$, 3.0 mL, 3.0 mmol) was then added, the mixture was cooled to −78°C, and aldehyde **7**[9] (0.94 g, 3.0 mmol) in $Et_2O$ (10 mL) was added dropwise. Stirring at −78°C was continued for 1 h, and saturated aqueous $NH_4Cl$ (20 mL), followed by water (30 mL) were added. The cooling bath was removed, and stirring was continued until the mixture attained room temperature. The mixture was extracted with $Et_2O$ (3×50 mL), and the combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2×15 cm), using 1:10 EtOAc–hexane, gave aldols **28** as two fractions, **28a** (less polar) (0.4619 g, 72%) and **28b** (more polar) (54.7 mg, 8%), each consisting ($^1H$ and $^{13}C$ NMR) of a single isomer.

Isomer **28a**: FTIR ($CH_2Cl_2$, cast) 3515, 2957, 2932, 2858, 1695, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.06 (s, 9H), 1.12 (d, $J$=6.5 Hz, 3H), 1.21 (d, $J$=6.1 Hz, 3H), 1.29–1.42 (m, 1H), 1.55–2.19 (m, 6H), 2.58 (dd, $J$=10.5, 1.8 Hz, 1H), 3.13 (brs, 1H), 3.49 (dd, $J$=8.0, 1.8 Hz, 1H), 4.07 (dq, $J$=8.0, 6.1 Hz, 1H), 7.30–7.50 (m, 6H), 7.60–7.72 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) $\delta$ 19.3 (s), 20.2 (q), 20.6 (q), 26.4 (t), 27.0 (q), 33.8 (t), 36.6 (d), 42.6 (t), 56.6 (d), 71.2 (d), 74.8 (d), 127.5 (d), 127.6 (d), 129.6 (d), 129.7 (d), 133.8 (s), 134.2 (s), 135.8 (d), 135.9 (d), 216.3 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{26}H_{36}NaO_3Si$ 447.233143, found 447.233532.

Isomer **28b**: FTIR ($CH_2Cl_2$, cast) 3462, 2957, 2931, 2858, 1702, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.98 (d, $J$=6.7 Hz, 3H), 1.01 (d, $J$=6.2 Hz, 3H), 1.08 (s, 9H), 1.34–1.46 (m, 1H), 1.68–2.08 (m, 4H), 2.22–2.48 (m, 3H), 2.74 (brs, 1H), 3.67 (t, $J$=5.0 Hz, 1H), 4.09 (dq, $J$=6.2, 5.0 Hz, 1H), 7.30–7.50 (m, 6H), 7.60–7.80 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) $\delta$ 19.4 (s), 20.0 (q), 20.3 (q), 24.4 (t), 27.1 (q), 31.1 (t), 35.4 (d), 41.8 (t), 58.2 (d), 71.1 (d), 75.3 (d), 127.5 (d), 127.7 (d), 129.6 (d), 129.8 (d), 133.5 (s), 134.4 (s), 135.9 (d), 214.1 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{26}H_{36}NaO_3Si$ 447.233143, found 447.233639.

**3.1.22. (*E*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]-3-methylcyclohexanone (29).** *(a) Methanesulfonic acid 2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1-(6-methyl-2-oxocyclohexyl)propyl ester.* The procedure described for mesylation of **8** was followed, using $MeSO_2Cl$ (1.2 mL, 15 mmol), alcohols **28a** and **b** (2.0430 g, 4.8108 mmol), $Et_3N$ (3.4 mL, 24 mmol), and $CH_2Cl_2$ (80 mL), and a reaction time of 4 h. The crude mesylates were obtained (1.9542 g, ca. 81%) were used immediately for next step.

*(b) (E)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propylidene]-3-methylcyclohexanone (29a,b).* The procedure described for **9** was followed, using DBU (1.8 mL, 12 mmol), the above mesylates (1.9542 g, 3.8870 mmol) in THF (40 mL), and a reaction time of 24 h. Flash chromatography of the crude product over silica gel (3×20 cm), using 1:10 EtOAc–hexane, gave enone **29** as two fractions, **29a** (more polar) (0.8343 g, 53%) and **29b** (less polar) (0.1450 g, 9%), each fraction consisting of two isomers ($^1H$ NMR).

Fraction **29a** [two isomers, ca. 8:1 ($^1H$ NMR)]: FTIR ($CH_2Cl_2$, cast) 3071, 3049, 2960, 2931, 2891, 2857, 1691, 1629, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 360 MHz) $\delta$ 0.61 (d, $J$=7.2 Hz, 0.3H), 0.81 (d, $J$=7.3 Hz, 2.7H), 1.02 (s, 8.0H), 1.04 (s, 1.0H), 1.20 (d, $J$=6.4 Hz, 0.3H), 1.25 (d, $J$=6.3 Hz, 2.7H), 1.20–2.80 (m, 7H), 4.48–4.60 (m, 1H), 6.32 (dd, $J$=9.0, 1.0 Hz, 0.9H), 6.45 (dd, $J$=8.0, 0.7 Hz, 0.1H), 7.30–7.50 (m, 6H), 7.60–7.72 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz) $\delta$ 18.5 (t), 18.8 (t), 19.1 (s), 19.2 (q), 21.0 (q),

24.1 (q), 24.15 (q), 26.88 (q), 26.9 (q), 30.27 (d), 30.3 (t), 30.4 (t), 30.9 (d), 40.6 (t), 40.7 (t), 65.5 (d), 66.0 (d), 127.5 (d), 127.6 (d), 129.6 (d), 129.67 (d), 129.7 (d), 133.5 (s), 134.0 (s), 134.1 (s), 134.2 (s), 135.8 (d), 135.82 (d), 135.9 (d), 136.0 (d), 139.3 (s), 139.7 (d), 140.1 (d), 201.9 (s), 203.0 (s); exact mass (HR electrospray) *m/z* calcd for $C_{26}H_{34}NaO_2Si$ 429.222579, found 429.222573. The *E* geometry for both components of this (major) fraction was inferred from the characteristic chemical shift ($\delta$ 6.45) of the vinyl hydrogen.

Fraction **29b** [two isomers, ca. 5:1 ($^1$H NMR)]: FTIR ($CH_2Cl_2$, cast) 3515, 2957, 2932, 2858, 1695, 1589 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 0.90–1.90 (m, 20H), 2.05–2.60 (m, 2H), 4.65–4.85 (m, 1H), 5.54–5.65 (m, 1H), 7.25–7.42 (m, 6H), 7.60–7.68 (m, 4H); $^{13}$C NMR ($CDCl_3$, 100.6 MHz) $\delta$ 18.3 (q), 19.2 (t), 20.2 (t), 20.9 (q), 23.5 (s), 24.1 (q), 24.4 (q), 26.9 (q), 27.0 (q), 31.3 (t), 33.6 (t), 27.5 (d), 38.3 (d), 42.0 (t), 42.2 (t), 67.2 (d), 67.8 (d), 127.4 (d), 127.43 (d), 127.5 (d), 127.54 (d), 129.4 (d), 129.5 (d), 133.3 (s), 134.6 (s), 135.8 (d), 135.86 (d), 135.9 (d), 138.0 (d), 139.9 (s), 140.4 (s), 141.3 (d), 203.7 (s), 204.1 (s); exact mass (HR electrospray) *m/z* calcd for $C_{26}H_{34}NaO_2Si$ 429.222579, found 429.223320. The *Z* geometry for both components of this (minor) fraction was inferred from the characteristic chemical shift ($\delta$ 5.54–5.65) of the vinyl hydrogen.

**3.1.23. (1*R**,*E*,3*R**)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propylidene]-3-methylcyclohexanol (30).** The procedure described for **10a**,**b** was followed, using $NaBH_4$ (53.5 mg, 1.41 mmol), enones **29a** (two isomers, major fraction of **29**) (0.3790 g, 0.9320 mmol), $CeCl_3{\cdot}7H_2O$ (0.498 g, 1.34 mmol), and MeOH (10 mL). Flash chromatography of the crude product over silica gel (2×20 cm), using 1:8 EtOAc–hexane, gave alcohols **30** as a chromatographically inseparable mixture [ca. 8:1 ($^1$H NMR)] of two isomers (0.3665 g, 96%): FTIR ($CH_2Cl_2$, cast) 3380, 3070, 3048, 2964, 2930, 2857 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 0.72 (d, *J*=7.3 Hz, 0.3H), 0.89 (d, *J*=7.4 Hz, 2.7H), 0.92–1.70 (m, 6H), 1.06 (s, 9H), 1.22 (d, *J*=6.2 Hz, 3H), 1.97–2.08 (m, 1H), 2.50–2.68 (m, 1H), 4.08 (t, *J*=5.4 Hz, 1H), 4.73 (dq, *J*=8.3, 6.2 Hz, 1H), 5.44 (dd, *J*=7.9, 1.8 Hz, 0.1H), 5.49 (dd, *J*=8.3, 1.9 Hz, 0.9H), 7.30–7.50 (m, 6H), 7.62–7.78 (m, 4H); $^{13}$C NMR ($CDCl_3$, 50.3 MHz) $\delta$ 19.0 (q), 19.2 (s), 19.6 (t), 25.3 (q), 27.0 (q), 31.2 (d), 31.8 (t), 37.6 (t), 66.1 (d), 68.7 (d), 123.8 (d), 127.4 (d), 127.5 (d), 129.4 (d), 129.5 (d), 134.7 (s), 134.8 (s), 135.8 (d), 136.0 (d), 143.6 (s); the spectrum showed some peaks from minor isomer: $\delta$ 17.5 (q), 19.5 (t), 25.4 (q), 31.0 (d), 32.8 (t), 66.5 (d), 68.4 (d), 123.3 (d), 127.4 (d), 143.3 (s); exact mass (HR electrospray) *m/z* calcd for $C_{26}H_{36}NaO_2Si$ 431.238229, found 431.238955.

As described in Section 1, NOE measurements established that the OH and ring $CH_3$ groups are *trans* for both the major and minor isomers of **30**.

**3.1.24. [[1-[(2*R**,*E*,6*R**)-2-(2-Bromo-1-ethoxyethoxy)-6-methylcyclohexylidene]-2-propyl]oxy](1,1-dimethylethyl)diphenylsilane (31).** The procedure described for **11** was followed, using NBS (0.4663 g, 2.620 mmol), dry $CH_2Cl_2$ (12 mL), ethyl vinyl ether (0.84 mL, 8.8 mmol), alcohols **30** (0.3570 g, 0.8735 mmol) in $CH_2Cl_2$ (5 mL), and a reaction time of 24 h. Flash chromatography of the crude product over silica gel (2×20 cm), using 1:20 EtOAc–hexane, gave bromo acetals **31** (0.315 g, 64%) as a mixture [ca. 8:8:1:1 ($^1$H NMR)] of four isomers: FTIR ($CH_2Cl_2$, cast) 3070, 3048, 2965, 2930, 2889, 2858 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 300 MHz) $\delta$ 0.50–0.78 (m, 3H), 0.90–1.45 (m, 20H), 1.78–1.98 (m, 1H), 2.35–2.55 (m, 1H), 3.05–3.56 (m, 4H), 3.88–4.10 (m, 1H), 4.55–4.88 (m, 2H), 5.86–6.10 (m, 1H), 7.18–7.32 (m, 6H), 7.74–7.90 (m, 4H); $^{13}$C NMR ($C_6D_6$, 75.5 MHz) $\delta$ 15.4 (q), 15.42 (q), 18.67 (q), 18.7 (q), 19.5 (s), 20.0 (t), 20.1 (t), 20.2 (t), 25.6 (q), 25.7 (q), 27.2 (q), 31.6 (d), 31.7 (d), 31.8 (d), 32.0 (t), 32.3 (t), 32.4 (t), 32.6 (t), 33.2 (t), 35.0 (t), 35.6 (t), 36.0 (t), 36.5 (t), 61.0 (t), 61.3 (t), 66.6 (d), 66.63 (d), 67.1 (d), 73.1 (d), 73.7 (d), 73.8 (d), 73.9 (d), 100.6 (d), 100.9 (d), 101.1 (d), 101.3 (d), 125.5 (d), 125.7 (d), 126.0 (d), 127.8 (d), 127.9 (d), 129.7 (d), 129.9 (d), 130.2 (d), 134.8 (s), 135.1 (s), 136.2 (d), 136.3 (d), 136.35 (d), 136.45 (d), 136.47 (d), 140.7 (s), 141.0 (s); exact mass (HR electrospray) *m/z* calcd for $C_{30}H_{43}{}^{79}BrNaO_3Si$ 581.206255, found 581.206942.

**3.1.25. (3a*R**,4*S**,7a*S**)-3a-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propyl]-2-ethoxyoctahydro-4-methylbenzofuran (32).** The procedure described for **12** was followed, using $Bu_3SnH$ (0.20 mL, 0.74 mmol), AIBN (12.5 mg, 0.08 mmol), bromo acetals **31** (0.2702 g, 0.4828 mmol), PhMe (35 mL), and a reaction time of 1.5 h. Flash chromatography of the crude product over silica gel (1.5×20 cm), using 1:25 EtOAc–hexane, gave acetals **32** (0.170 g, 73%) as a mixture of four isomers ($^1$H NMR): FTIR ($CH_2Cl_2$, cast) 3070, 3049, 2959, 2931, 2858 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 400 MHz) $\delta$ 0.55–2.40 (m, 29H), 3.25–3.55 (m, 1H), 3.75–4.20 (m, 3H), 4.95–5.06 (m, 1H), 7.15–7.30 (m, 6H), 7.70–7.90 (m, 4H); $^{13}$C NMR ($C_6D_6$, 50.3 MHz) $\delta$ 13.7 (q), 15.6 (q), 15.8 (q), 16.0 (q), 16.4 (q), 17.0 (s), 19.39 (s), 19.41 (s), 20.4 (q), 20.9 (t), 21.0 (t), 25.4 (t), 25.5 (t), 25.6 (q), 25.9 (q), 26.4 (q), 26.5 (t), 27.0 (t), 27.2 (q), 27.3 (q), 28.6 (t), 29.8 (t), 29.9 (t), 34.5 (d), 34.7 (d), 36.0 (d), 36.7 (d), 37.1 (t), 37.7 (t), 37.8 (t), 37.9 (t), 41.8 (s), 42.3 (s), 43.0 (t), 43.26 (t), 43.34 (t), 45.2 (t), 45.6 (t), 63.2 (t), 63.4 (t), 64.0 (t), 67.9 (d), 68.2 (d), 68.3 (d), 76.4 (d), 77.5 (d), 79.9 (d), 80.3 (d), 102.4 (d), 102.8 (d), 103.3 (d), 127.8 (d), 128.3 (d), 129.8 (d), 129.85 (d), 129.9 (d), 130.0 (d), 130.1 (d), 134.3 (s), 134.5 (s), 134.56 (s), 134.6 (s), 135.16 (s), 135.2 (s), 136.2 (d), 136.3 (d); exact mass (HR electrospray) *m/z* calcd for $C_{30}H_{44}NaO_3Si$ 503.295744, found 503.295796.

**3.1.26. 1-[(3a*R**,4*S**,7a*S**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanol (33a,b).** The procedure described for **13** was followed, using $Bu_4NF$ (1.0 M in THF, 1.0 mL, 1.0 mmol), acetals **32** (four isomers) (0.1615 g, 0.3359 mmol) in THF (15 mL), and a reaction time of 4 h. Flash chromatography of the crude product over silica gel (1×20 cm), using 1:4 EtOAc–hexane, gave alcohol **33** as two fractions, **33a** (less polar) (36.0 mg, 44%) and **33b** (more polar) (34.5 mg, 42%), each fraction consisting two isomers.

Fraction **33a** [(two isomers, ca. 6:1 ($^1$H NMR)]: FTIR ($CH_2Cl_2$, cast) 3438, 2960, 2931 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 400 MHz) $\delta$ 0.73 (d, *J*=7.0 Hz, 3H), 0.78 (s, 1H), 0.95 (d,

$J$=6.2 Hz, 3H), 1.06–1.23 (m, 2H), 1.25 (t, $J$=7.1 Hz, 3H), 1.29–1.62 (m, 4H), 1.74–2.50 (m, 5H), 3.48 (dq, $J$=9.5, 7.1 Hz, 1H), 3.74–3.87 (m, 1H), 4.01 (dq, $J$=9.5, 7.1 Hz, 1H), 4.49 (t, $J$=2.8 Hz, 1H), 5.15 (dd, $J$=5.8, 4.0 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 100.6 MHz) (signals for major isomer only) $\delta$ 15.6 (q), 16.2 (q), 21.1 (t), 25.5 (t), 26.3 (q), 30.0 (t), 36.2 (d), 36.6 (t), 43.0 (t), 45.9 (s), 63.4 (t), 64.5 (d), 77.7 (d), 102.5 (d); exact mass $m/z$ calcd for $C_{14}H_{26}O_3$ 242.18820, found 242.18760.

Fraction **33b** [(two isomers, ca. 6:1 ($^1$H NMR)]: FTIR ($CH_2Cl_2$, cast) 3438, 2961, 2931, 2875 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 360 MHz) $\delta$ 0.69 (brs, 1H), 0.81 (d, $J$=7.0 Hz, 3H), 0.94 (d, $J$=6.2 Hz, 3H), 0.94–1.50 (m, 9H), 1.60–2.17 (m, 4H), 2.26–2.56 (m, 1H), 3.49 (dq, $J$=9.6, 7.0 Hz, 1H), 3.50–3.62 (m, 1H), 4.01 (dq, $J$=9.6, 7.0 Hz, 1H), 4.14 (t, $J$=3.5 Hz, 1H), 5.18 (dd, $J$=6.8, 2.2 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 50.3 MHz) (signals for major isomer only) $\delta$ 15.8 (q), 16.5 (q), 21.0 (t), 26.3 (q), 26.7 (t), 30.0 (t), 34.4 (d), 38.1 (t), 41.9 (t), 44.0 (s), 63.9 (t), 64.7 (d), 80.9 (d), 103.4 (d); exact mass $m/z$ calcd for $C_{14}H_{26}O_3$ 242.18820, found 242.18790.

**3.1.27. 1-[(3a*R**,4*R**,7a*R**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanone (34) from 33a (major fraction of 33).** The procedure described for **14a**,**b** was followed, using alcohols **33a** (two isomers, major fraction of **33**) (30.0 mg, 0.124 mmol) in $CH_2Cl_2$ (3 mL), PCC (41 mg, 0.19 mmol), powdered 4 Å molecular sieves (180 mg), $CH_2Cl_2$ (1.2 mL), and a reaction time of 2 h. Flash chromatography of the crude product over silica gel (1×15 cm), using 1:2 EtOAc–hexane, gave ketone **34** as a single isomer (24 mg, 81%): FTIR ($CH_2Cl_2$, cast) 2932, 1719 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 360 MHz) $\delta$ 0.69 (d, $J$=7.0 Hz, 3H), 0.89 (dq, $J$=13.2, 3.2 Hz, 1H), 1.19–1.51 (m, 4H), 1.21 (t, $J$=7.1 Hz, 3H), 1.68–1.80 (m, 1H), 1.73 (s, 3H), 1.83 (d, $J$=15.5 Hz, 1H), 1.98–2.07 (m, 1H), 2.17 (d, $J$=15.5 Hz, 1H), 2.23 (dd, $J$=13.9, 4.4 Hz, 1H), 2.38 (dd, $J$=13.9, 6.0 Hz, 1H), 3.43 (dq, $J$=9.4, 7.1 Hz, 1H), 3.94 (dq, $J$=9.4, 7.1 Hz, 1H), 4.02 (t, $J$=2.8 Hz, 1H), 5.10 (dd, $J$=5.9, 4.5 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.5 (q), 17.1 (q), 20.7 (t), 25.5 (t), 30.0 (t), 31.6 (q), 35.7 (d), 41.8 (t), 43.1 (t), 46.0 (s), 63.6 (t), 79.0 (d), 102.9 (d), 205.7 (s); exact mass $m/z$ calcd for $C_{14}H_{24}O_3$ 240.17255, found 240.17280.

**3.1.28. 1-[(3a*R**,4*R**,7a*R**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanone (34′) from 33b (minor fraction of 33).** The procedure described for **14a**,**b** was followed, using alcohols **33b** (i.e. minor fraction) (10.0 mg, 0.0413 mmol) in $CH_2Cl_2$ (1 mL), PCC (14 mg, 0.065 mmol), powdered 4 Å molecular sieves (60 mg), $CH_2Cl_2$ (0.5 mL), and a reaction time of 5 h. Flash chromatography of the crude product over silica gel (0.6×15 cm), using 1:5 EtOAc–hexane, gave ketone **34′** as a single isomer (8.6 mg, 87%). Compounds **34** and **34′** have different stereochemistry at C(2).

Compound **34′**: FTIR ($CH_2Cl_2$, cast) 2932, 2874, 1716 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 400 MHz) $\delta$ 0.73 (d, $J$=7.0 Hz, 3H), 0.87–1.01 (m, 1H), 1.20 (t, $J$=7.1 Hz, 3H), 1.32–1.44 (m, 3H), 1.70 (s, 3H), 1.76–1.92 (m, 1H), 1.91 (d, $J$=16.0 Hz, 1H), 2.01–2.11 (m, 1H), 2.15 (d, $J$=16.0 Hz, 1H), 2.21 (d, $J$=1.9 Hz, 1H), 2.35–2.46 (m, 1H), 2.49 (dd, $J$=13.6, 7.1 Hz, 1H), 3.42 (dq, $J$=9.6, 7.1 Hz, 1H), 3.91 (t, $J$=3.4 Hz, 1H), 3.94 (dq, $J$=9.6, 7.1 Hz, 1H), 5.13 (dd, $J$=7.1, 1.9 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.7 (q), 17.0 (q), 20.7 (t), 26.8 (t), 30.0 (t), 31.8 (q), 34.2 (d), 41.5 (t), 41.9 (t), 44.3 (s), 64.1 (t), 80.5 (d), 103.6 (d), 206.3 (s); exact mass $m/z$ calcd for $C_{14}H_{24}O_3$ 240.17255, found 240.17227.

**3.1.29. (1*R**,2*R**,6*R**,8*S**)-2-Methyl 7-oxatricyclo-[6.3.1.0$^{1,6}$]dodecan-10-one (35).** The procedure described for **15** was followed, using ketones **34** and **34′** (ca. 2:1) (16.0 mg, 0.067 mmol), 3 M HCl (3.3 mL), THF (0.68 mL), and a reflux time of 36 h. Flash chromatography of the crude product over silica gel (0.6×20 cm), using EtOAc–hexane, gave tricyclic ketone **35** (10 mg, 77%): FTIR ($CH_2Cl_2$, cast) 2939, 2867, 1716 cm$^{-1}$; $^1$H NMR ($CD_2Cl_2$, 400 MHz) $\delta$ 0.96 (d, $J$=7.2 Hz, 3H), 1.20–1.82 (m, 7H), 1.92–2.04 (m, 1H), 2.22 (d, $J$=17.5 Hz, 1H), 2.28 (d, $J$=17.5 Hz, 1H), 2.40–2.58 (m, 3H), 3.75 (dd, $J$=11.0, 6.0 Hz, 1H), 4.47 (ddd, $J$=6.4, 3.7, 1.6 Hz, 1H); $^{13}$C NMR ($CD_2Cl_2$, 100.6 MHz) $\delta$ 16.7 (q), 18.4 (t), 28.1 (t), 30.4 (t), 34.1 (d), 39.0 (t), 45.9 (s), 49.6 (t), 52.1 (t), 73.6 (d), 87.7 (d), 210.4 (s); exact mass $m/z$ calcd for $C_{12}H_{18}O_2$ 194.13068, found 194.13115.

**3.1.30. Acetic acid (1*R**,5*R**,6*R**)-5-methyl-10-oxospiro-[5.5]undec-8-en-1-yl ester (36).** The procedure described for **16** was followed, using ketone **35** (4.8 mg, 0.025 mmol), TsOH·$H_2O$ (4.0 mg, 0.02 mmol), $Ac_2O$ (0.04 mL, 0.4 mmol, PhH (4.5 mL), and a reaction time of 28 h. Flash chromatography of the crude product over silica gel (0.6×25 cm), using 2:5 EtOAc–hexane, gave spiro enone **36** (3.6 mg, 62%): FTIR ($CH_2Cl_2$, cast) 2938, 2868, 1734, 1680 cm$^{-1}$; $^1$H NMR ($C_6D_6$, 360 MHz) $\delta$ 0.66 (d, $J$=7.2 Hz, 3H), 0.87–1.02 (m, 1H), 1.12–1.58 (m, 5H), 1.62–1.74 (m, 1H), 1.69 (s, 3H), 1.88–2.05 (m, 2H), 2.27 (d, $J$=16.0 Hz, 1H), 2.29 (d, $J$=16.0 Hz, 1H), 5.06 (dd, $J$=6.5, 3.5 Hz, 1H), 6.02 (dt, $J$=10.1, 2.1 Hz, 1H), 6.19 (dt, $J$=10.1, 4.2 Hz, 1H); $^{13}$C NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.7 (q), 19.5 (t), 20.3 (q), 25.8 (t), 28.5 (t), 31.1 (t), 33.8 (d), 42.1 (s or t), 42.8 (s or t), 72.9 (d), 129.2 (d), 146.3 (d), 168.8 (s), 196.6 (s); exact mass $m/z$ calcd for $C_{14}H_{20}O_3$ 236.14125, found 236.14145.

**3.1.31. (1*R**,*E*,3*S**)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propylidene]-3-methylcyclo-hexanol (37a,b).** *(a) 4-Nitrobenzoic acid (1R*,E,3S*)-2-[2-[[(1,1-dimethylethyl)diphenylsilyl]oxy]propylidene]-3-methylcyclohexyl ester.* $Ph_3P$ (0.802 g, 3.06 mmol) and 4-nitrobenzoic acid (0.5117 g, 3.06 mmol) were added successively to a stirred and cooled (0°C) solution of allylic alcohols **30** (8:1 mixture of isomers) (0.6253 g, 1.530 mmol) in dry THF (15 mL). DEAD (0.48 mL, 3.05 mmol) was added dropwise, and stirring was continued for 90 min at 0°C. The mixture was then diluted with $Et_2O$ (150 mL), washed successively with saturated aqueous $NaHCO_3$, water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.5×30 cm), using 1:15 EtOAc–hexane, gave the crude nitrobenzoates (0.785 g), which were used directly in next step.

*(b) (1R*,E,3S*)-2-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-propylidene]-3-methylcyclohexanol (**37a,b**).* KOH (0.79 g, 14 mmol) was added to a stirred solution of the above crude

nitrobenzoates (ca. 0.785 g, ca. 1.407 mmol) in MeOH (50 mL), and stirring was continued for 4 h. The solvent was evaporated and the residue was diluted with water (50 mL) and extracted with $Et_2O$ (2×50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1.5×40 cm), using 1:8 EtOAc–hexane, gave alcohols **37** as two separable isomers, **37a** (more polar) (0.299 g, 48%) and **37b** (less polar) (0.0765 g, 12%).

Isomer **37a**: FTIR ($CH_2Cl_2$, cast) 3387, 3070, 3048, 2931, 2857, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.00–1.48 (m, 8H), 1.06 (s, 9H), 1.23 (d, $J$=6.2, 3H), 1.78–1.98 (m, 2H), 2.26–2.38 (m, 1H), 4.12 (t, $J$=2.5 Hz, 1H), 4.64 (dq, $J$=8.3, 6.2 Hz, 1H), 5.45 (d, $J$=8.3 Hz, 1H), 7.28–7.48 (m, 6H), 7.60–7.75 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 50.3 MHz) $\delta$ 15.0 (t), 19.1 (s), 21.4 (q), 25.0 (q), 26.9 (q), 29.9 (d), 31.9 (t), 33.5 (t), 65.3 (d), 74.9 (d), 127.4 (d), 127.5 (d), 129.4 (d), 129.5 (d), 133.0 (d), 134.4 (s), 134.5 (s), 135.8 (d), 135.9 (d), 141.9 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{26}H_{36}NaO_2Si$ 431.238229, found 431.237534.

Isomer **37b**: FTIR ($CH_2Cl_2$, cast) 3578, 3463, 3070, 3049, 2931, 2857, 1589 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 0.72 (s, 1H), 0.78 (d, $J$=7.3, 3H), 1.07 (s, 9H), 1.18–1.52 (m, 4H), 1.22 (d, $J$=7.2 Hz, 3H), 1.74–1.95 (m, 2H), 2.32–2.45 (m, 1H), 3.98 (t, $J$=2 Hz, 1H), 4.65 (dq, $J$=7.8, 6.3 Hz, 1H), 5.32 (d, $J$=7.8 Hz, 1H), 7.30–7.52 (m, 6H), 7.60–7.80 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 75.5 MHz) $\delta$ 15.0 (t), 19.2 (s), 19.9 (q), 24.9 (q), 27.0 (q), 29.4 (d), 32.7 (t), 33.3 (t), 66.1 (d), 74.4 (d), 127.4 (d), 127.6 (d), 129.6 (d), 132.9 (d), 134.3 (s), 134.8 (s), 135.9 (d), 136.1 (d), 136.3 (d), 141.0 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{26}H_{36}NaO_2Si$ 431.238229, found 431.237429.

**3.1.32. [[1-[(2*R**,*E*,6*S**)-2-(2-Bromo-1-ethoxyethoxy)-6-methylcyclohexylidene]-2-propyl]oxy]-(1,1-dimethylethyl)diphenylsilane (38).** The procedure described for **11** was followed, using NBS (0.353 g, 1.98 mmol), dry $CH_2Cl_2$ (9 mL), ethyl vinyl ether (0.64 mL, 6.6 mmol), alcohol **37a** (i.e. major isomer) (0.2702 g, 0.6612 mmol) in $CH_2Cl_2$ (4 mL), and a reaction time of 26 h. Flash chromatography of the crude product over silica gel (1.5×40 cm), using 1:20 EtOAc–hexane, gave bromo acetals **38** as a chromatographically inseparable mixture [ca. 1:1 ($^1H$ NMR)] of isomers (0.2319 g, 63%): FTIR ($CH_2Cl_2$, cast) 3070, 3048, 2964, 2931, 2857 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 400 MHz) $\delta$ 0.66–1.46 (m, 22H), 1.83–2.06 (m, 2H), 2.28–2.42 (m, 1H), 3.05–3.4 (m, 4H), 3.84 (t, $J$=1.5 Hz, 0.5H), 4.05 (t, $J$=2 Hz, 0.5H), 4.58 (t, $J$=5.4 Hz, 0.5H), 4.72 (dd, $J$=6.0, 4.7 Hz, 0.5H), 4.74–4.88 (m, 1H), 5.54 (d, $J$=8.3 Hz, 0.5H), 5.60 (d, $J$=8.3 Hz, 0.5H), 7.16–7.28 (m, 6H), 7.72–7.88 (m, 4H); $^{13}C$ NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.2 (q), 15.4 (q), 15.8 (t), 15.9 (t), 19.4 (s), 20.6 (q), 20.7 (q), 25.2 (q), 25.5 (q), 27.16 (q), 27.2 (q), 30.3 (d), 30.6 (d), 32.2 (t), 32.3 (t), 32.5 (t), 32.9 (t), 33.4 (t), 60.6 (t), 61.3 (t), 65.9 (d), 78.3 (d), 80.0 (d), 98.8 (d), 100.9 (d), 127.8 (d), 127.9 (d), 129.8 (d), 130.0 (d), 133.4 (d), 134.7 (s), 134.76 (s), 134.8 (s), 135.4 (d), 136.1 (d), 136.2 (d), 137.8 (s), 139.9 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{30}H_{43}{}^{79}BrNaO_3Si$ 581.206255, found 581.205692.

**3.1.33. (3a*R**,4*R**,7a*S**)-3a-[2-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]propyl]-2-ethoxyoctahydro-4-methylbenzofuran (39a,b).** The procedure described for **12** was followed, using $Bu_3SnH$ (0.15 mL, 0.56 mmol), AIBN (9.0 mg, 0.055 mmol), bromo acetals **38** (0.194 g, 0.3466 mmol), PhMe (25 mL), and a reaction time of 1 h. Flash chromatography of the crude product over silica gel (1.5×30 cm), using 1:40 EtOAc–hexane gave acetals **39** as two separable isomers, **39a** (more polar) (82 mg, 49%) and **39b** (less polar) (40 mg, 24%), differing in stereochemistry at C(2).

Isomer **39a**: FTIR ($CH_2Cl_2$, cast) 3070, 3048, 2931, 2857 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 400 MHz) $\delta$ 0.82 (d, $J$=7.0 Hz, 3H), 0.87–1.73 (m, 24H), 2.07 (dd, $J$=13.5, 6.2 Hz, 1H), 2.34 (dd, $J$=14.5, 5.0 Hz, 1H), 3.42 (dq, $J$=9.4, 7.1 Hz, 1H), 3.96 (dq, $J$=9.4, 7.1 Hz, 1H), 4.02–4.13 (m, 2H), 5.09 (dd, $J$=6.1, 2.6 Hz, 1H), 7.16–7.28 (m, 6H), 7.75–7.90 (m, 4H); $^{13}C$ NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.3 (q), 16.9 (q), 17.2 (t), 19.1 (s), 25.5 (q), 26.7 (t), 27.0 (q), 28.1 (t), 31.3 (d), 42.0 (t), 45.6 (t), 46.7 (s), 63.0 (t), 68.3 (d), 80.6 (d), 103.2 (d), 127.5 (d), 128.0 (d), 129.5 (d), 129.6 (d), 134.5 (s), 135.2 (s), 136.1 (s); exact mass (HR electrospray) $m/z$ calcd for $C_{30}H_{44}NaO_3Si$ 503.295744, found 503.295658.

Isomer **39b**: FTIR ($CH_2Cl_2$, cast) 3070, 3048, 2965, 2931, 2857 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.68 (d, $J$=6.7 Hz, 3H), 0.85–1.75 (m, 22H), 1.84–2.07 (m, 2H), 2.05 (dd, $J$=13.4, 5.4 Hz, 1H), 2.23 (dd, $J$=14.6, 5.4 Hz, 1H), 3.44 (dq, $J$=9.5, 7.0 Hz, 1H), 3.97 (dq, $J$=9.5, 7.0 Hz, 1H), 4.12–4.23 (m, 2H), 5.18 (t, $J$=5.7 Hz, 1H), 7.16–7.30 (m, 6H), 7.75–7.92 (m, 4H); $^{13}C$ NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.7 (q), 17.4 (q), 19.4 (s), 23.3 (t), 26.4 (q), 27.31 (q), 30.6 (t), 31.5 (t), 34.5 (d), 39.3 (t), 47.7 (s or t), 49.2 (s or t), 63.7 (t), 68.3 (d), 80.2 (d), 104.6 (d), 127.8 (d), 128.3 (d), 129.8 (d), 129.9 (d), 134.7 (s), 135.6 (s), 136.4 (d); exact mass (HR electrospray) $m/z$ calcd for $C_{30}H_{44}NaO_3Si$ 503.29519, found 503.29536.

**3.1.34. 1-[(3a*R**,4*R**,7a*S**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanol (40) from 39a (major isomer of 39).** The procedure described for **13** was followed, using $Bu_4NF$ (1.0 M in THF, 0.5 mL, 0.5 mmol), acetals **39a** (i.e. major isomer) (80 mg, 0.17 mmol) in THF (7 mL), and a reaction time of 6 h. Flash chromatography of the crude product over silica gel (1×30 cm), using 1:4 EtOAc–hexane, gave alcohol **40** (32 mg, 80%): FTIR ($CH_2Cl_2$, cast) 3439, 2960, 2930 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.77 (d, $J$=6.8 Hz, 3H), 1.05–1.75 (m, 8H), 1.15 (t, $J$=7.1 Hz, 3H), 1.18 (d, $J$=6.1 Hz, 3H), 1.89 (dd, $J$=13.8, 1.6 Hz, 1H), 1.98 (dd, $J$=13.8, 6.0 Hz, 1H), 2.08 (dd, $J$=14.7, 9.7 Hz, 1H), 2.81 (brs, 1H), 3.34 (dq, $J$=9.5, 7.1 Hz, 1H), 3.84 (dq, $J$=9.5, 7.1 Hz, 1H), 4.01–4.13 (m, 1H), 4.29 (dd, $J$=5.4, 4.1 Hz, 1H), 5.04 (dd, $J$=6.0, 1.6 Hz, 1H); $^{13}C$ NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.3 (q), 16.9 (q), 18.3 (t), 25.7 (q), 26.1 (t), 27.4 (t), 34.6 (d), 38.7 (t), 45.5 (s or t), 47.8 (s or t), 63.0 (t), 64.5 (d), 80.7 (d), 103.3 (d); exact mass $m/z$ calcd for $C_{14}H_{26}O_3$ 242.18820, found 242.18826.

**3.1.35. 1-[(3a*R**,4*R**,7a*S**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanol (40′) from 39b (minor isomer of 39).** The procedure described for **13** was

followed, using $Bu_4NF$ (1.0 M in THF, 0.25 mL, 0.25 mmol), acetals **39b** (i.e. minor isomer) (38 mg, 0.08 mmol) in THF (4 mL), and a reaction time of 6 h. Flash chromatography of the crude product over silica gel (1×30 cm), using 1:4 EtOAc–hexane, gave alcohol **40′** (14.5 mg, 76%). Compounds **40** and **40′** have different stereochemistry at C(2).

Compound **40′**: FTIR ($CH_2Cl_2$, cast) 3417, 2960, 2930, 2874 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.73 (d, $J$=6.8 Hz, 3H), 0.96–1.18 (m, 3H), 1.02 (d, $J$=6.2 Hz, 3H), 1.21–1.36 (m, 2H), 1.25 (t, $J$=7.1 Hz, 3H), 1.48–1.61 (m, 2H), 1.65 (dd, $J$=13.3, 6.1 Hz, 1H), 1.70 (dd, $J$=14.9, 9.2 Hz, 1H), 1.86–2.10 (m, 2H), 2.11 (dd, $J$=13.2, 5.4 Hz, 1H), 3.47 (dq, $J$=9.5, 7.1 Hz, 1H), 3.80–3.90 (m, 1H), 4.00 (dq, $J$=9.5, 7.1 Hz, 1H), 4.35 (dd, $J$=10.8, 6.6 Hz, 1H), 5.29 (t, $J$=5.7 Hz, 1H); $^{13}C$ NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.7 (q), 17.5 (q), 23.4 (t), 26.2 (q), 30.7 (t), 31.5 (t), 34.6 (d), 39.3 (t), 46.7 (s or t), 49.0 (s or t), 63.8 (t), 64.9 (d), 80.9 (d), 104.9 (d); exact mass $m/z$ calcd for $C_{14}H_{26}O_3$ 242.18820, found 242.18795.

**3.1.36. 1-[(3a*R**,4*R**,7a*S**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanone (41) from 40 (major isomer series).** The procedure described for **14a**,**b** was followed, using alcohol **40** (major isomer series) (26 mg, 0.11 mmol) in $CH_2Cl_2$ (2.6 mL), PCC (36 mg, 0.17 mmol), powdered 4 Å molecular sieves (156 mg), $CH_2Cl_2$ (1 mL), and a reaction time of 3 h. Flash chromatography of the crude product over silica gel (0.6×25 cm), using 1:2 EtOAc–hexane, gave ketone **41** (20.8 mg, 81%): FTIR ($CH_2Cl_2$, cast) 2931, 2872, 1715 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.77 (d, $J$=6.9 Hz, 3H), 0.98–1.08 (m, 1H), 1.19 (t, $J$=7.1 Hz, 3H), 1.26–1.39 (m, 2H), 1.44–1.65 (m, 2H), 1.46 (dd, $J$=13.5, 1.4 Hz, 1H), 1.69 (s, 3H), 1.88–1.99 (m, 1H), 2.10–2.20 (m, 1H), 2.12 (dd, $J$=13.5, 6.2 Hz, 1H), 2.37 (d, $J$=17.5 Hz, 1H), 3.05 (d, $J$=17.5 Hz, 1H), 3.38 (dq, $J$=9.5, 7.1 Hz, 1H), 3.89 (dq, $J$=9.5, 7.1 Hz, 1H), 4.52 (dd, $J$=6.9, 5.0 Hz, 1H), 5.07 (dd, $J$=6.2, 1.4 Hz, 1H); $^{13}C$ NMR ($C_6D_6$, 50.3 MHz) $\delta$ 15.6 (q), 17.3 (q), 19.1 (t), 28.6 (t), 29.0 (t), 31.3 (d or q), 31.6 (d or q), 39.6 (t), 45.9 (s or t), 49.5 (s or t), 63.3 (t), 81.4 (d), 103.0 (d), 206.6 (s); exact mass $m/z$ calcd for $C_{14}H_{24}O_3$ 240.17255, found 240.17226.

**3.1.37. 1-[(3a*R**,4*R**,7a*S**)-2-Ethoxyoctahydro-4-methylbenzofuran-3a-yl]-2-propanone (41′) from 40′ (minor isomer series).** The procedure described for **14a**,**b** was followed, using alcohol **40′** (minor isomer series) (13 mg, 0.05 mmol) in $CH_2Cl_2$ (1.5 mL), PCC (18 mg, 0.08 mmol), powdered 4 Å molecular sieves (80 mg), $CH_2Cl_2$ (0.5 mL), and reaction time of 3 h. Flash chromatography of the crude product over silica gel (0.6×30 cm), using 1:2 EtOAc–hexane, gave ketone **41′** (10 mg, 78%). Compounds **41** and **41′** have different stereochemistry at C(2).

Compound **41′**: FTIR ($CH_2Cl_2$, cast) 2931, 1716 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.70 (d, $J$=6.8 Hz, 3H), 0.90–1.33 (m, 3H), 1.21 (t, $J$=7.1 Hz, 3H), 1.50 (d of pentets, $J$=13.1, 3.4 Hz, 1H), 1.69–2.05 (m, 3H), 1.75 (dd, $J$=13.5, 6.1 Hz, 1H), 1.81 (s, 3H), 2.03 (dd, $J$=13.5, 5.2 Hz, 1H), 2.06 (d, $J$=15.1 Hz, 1H), 2.30 (d, $J$=15.1 Hz, 1H), 3.42 (dq, $J$=9.5, 7.1 Hz, 1H), 3.93 (dq, $J$=9.5, 7.1 Hz, 1H), 4.26 (dd, $J$=10.7, 6.7 Hz, 1H), 5.14 (dd, $J$=6.1, 5.2, 1H); $^{13}C$ NMR ($C_6D_6$, 100.6 MHz) $\delta$ 15.6 (q), 17.7 (q), 23.1 (t), 30.6 (t), 31.3 (t), 32.0 (q), 35.0 (d), 37.8 (t), 49.5 (t), 50.7 (s), 63.8 (t), 81.1 (d), 104.6 (d), 206.8 (s); exact mass $m/z$ calcd for $C_{14}H_{24}O_3$ 240.17255, found 240.17271.

**3.1.38. (1*R**,2*S**,6*R**,8*S**)-2-Methyl-7-oxatricyclo[6.3.1.0$^{1,6}$]-dodecan-10-one (42).** The procedure described for **15** was followed, using ketones **41** and **41′** (ca. 2:1 mixture of isomers) (17.5 mg, 0.073 mmol), 3 M HCl (3.6 mL), THF (0.75 mL), and a reflux time of 6 h. Flash chromatography of the crude product over silica gel (0.6×30 cm), using 1:3 EtOAc–hexane, gave tricyclic ketone **42** (12 mg, 85%): FTIR ($CH_2Cl_2$, cast) 2933, 2859, 1718 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.65 (d, $J$=6.7 Hz, 3H), 0.70–1.40 (m, 7H), 1.74–1.84 (m, 3H), 2.02 (dt, $J$=16.9, 2.6 Hz, 1H), 2.27 (d, $J$=16.9 Hz, 1H), 2.66 (ddt, $J$=16.4, 4.0, 2.0 Hz, 1H), 3.54 (d, $J$=10.5, 6.4 Hz, 1H), 4.20 (ddd, $J$=6.7, 4.3, 1.1 Hz, 1H); $^{13}C$ NMR ($C_6D_6$, 100.6 MHz) $\delta$ 17.6 (q), 22.7 (t), 30.8 (t), 32.5 (t), 32.7 (t), 36.7 (d), 47.0 (s), 49.5 (t), 54.2 (t), 73.5 (d), 83.5 (d), 207.7 (s); exact mass $m/z$ calcd for $C_{12}H_{18}O_2$ 194.13068, found 194.13072.

**3.1.39. Acetic acid (1*R**,5*S**,6*S**)-5-methyl-10-oxospiro-[5.5]undec-8-en-1-yl ester (43).** The procedure described for **16** was followed, using ketone **42** (11 mg, 0.06 mmol), $TsOH·H_2O$ (10 mg, 0.057 mmol), $Ac_2O$ (0.08 mL, 0.9 mmol), PhH (12 mL), and a reaction time of 23 h. Flash chromatography of the crude product over silica gel (0.6×30 cm), using 1:6 EtOAc–hexane, gave spiro enone **43** (4.5 mg, 34% or 49% after correction for recovered starting material): FTIR ($CH_2Cl_2$, cast) 3034, 2938, 2863, 1739, 1678 $cm^{-1}$; $^1H$ NMR ($C_6D_6$, 360 MHz) $\delta$ 0.50 (d, $J$=6.7 Hz, 3H), 0.65–1.22 (m, 5H), 1.27 (dt, $J$=13.7, 3.8 Hz, 1H), 1.56–1.73 (m, 2H), 1.58 (s, 3H), 2.00 (ddd, $J$=20, 3.6, 2.6 Hz, 1H), 2.16 (d, $J$=16.3 Hz, 1H), 2.29 (d, $J$=16.3 Hz, 1H), 4.46 (dd, $J$=10.7, 4.1 Hz, 1H), 5.94 (dt, $J$=10.2, 2.3 Hz, 1H), 6.13 (dt, $J$=10.2, 4.1 Hz, 1H); $^{13}C$ NMR ($C_6D_6$, 75.5 MHz) $\delta$ 17.5 (q), 20.5 (q), 22.8 (t), 25.1 (t), 26.7 (t), 29.1 (t), 40.7 (d), 43.2 (s), 46.6 (t), 79.3 (d), 129.5 (d), 146.7 (d), 169.3 (s), 197.4 (s); exact mass $m/z$ calcd for $C_{14}H_{20}O_3$ 236.14125, found 236.14138.

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## References

1. Review on stereocontrolled synthesis of spiro compounds: (a) Sannigrahi, M. *Tetrahedron* **1999**, *55*, 9007–9071. Reviews on generation of quaternary carbon centers: (b) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 389–401. (c) Martin, S. F. *Tetrahedron* **1980**, *36*, 419–460. (d) Fuji, K. *Chem. Rev.* **1993**, *93*, 2037–2066.
2. For a different approach to spiro compounds, in which the stereochemistry is also controlled by the stereochemistry of

an alcohol, see: Batey, R. A.; Harling, J. D.; Motherwell, W. B. *Tetrahedron* **1992**, *48*, 8031–8052.
3. Yamane, T.; Ishizaki, M.; Suzuki, M.; Takahashi, M.; Hiroya, K.; Takano, S.; Ogasawara, K. *Heterocycles* **1996**, *42*, 65–69.
4. Yadav, J. S.; Praveen, K. T. K.; Gadgil, V. R. *Tetrahedron Lett.* **1992**, *33*, 3687–3690.
5. Stork, G.; Mah, R. *Tetrahedron Lett.* **1989**, *30*, 3609–3612.
6. For other examples of radical cyclization onto the fully substituted terminus of a double bond, see, for example: Refs. 3, 4, and (a) Stork, G.; Mook, Jr., R.; Biller, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741–3742. (b) Begley, M. J.; Bhandal, H.; Hutchinson, J. H.; Pattenden, G. *Tetrahedron Lett.* **1987**, *28*, 1317–1320. (c) Hutchinson, J. H.; Pattenden, G.; Myers, P. L. *Tetrahedron Lett.* **1987**, *28*, 1313–1316. (d) Begley, M. J.; Cheshire, D. R.; Harrison, T.; Hutchinson, J. H.; Myers, P. L.; Pattenden, G. *Tetrahedron* **1989**, *45*, 5215–5246. (e) Middleton, D. S.; Simpkins, N. S.; Terrett, N. K. *Tetrahedron* **1990**, *46*, 545–564. (f) Srikrishna, A.; Sharma, G. V. R.; Nagaraju, S. *Synth. Commun.* **1992**, *22*, 1221–1230. (g) Srikrishna, A.; Viswajanani, R.; Sattigeri, J. A. *J. Chem. Soc., Chem. Commun.* **1995**, 469–470. (h) Srikrishna, A.; Viswajanani, R.; Yelamaggad, C. V. *Tetrahedron Lett.* **1995**, *36*, 1127–1128. (i) Hoffmann, H. M. R.; Herden, U.; Breithor, M.; Rhode, O. *Tetrahedron* **1997**, *53*, 8383–8400. (j) Kim, S.; Oh, D. H. *Synlett* **1998**, 525–527. (k) Srikrishna, A.; Kumar, P. P.; Reddy, T. J. *Tetrahedron Lett.* **1998**, *39*, 5815–5818. (l) Tsukuda, T.; Watanabe, M.; Ontsuka, H.; Hattori, K.; Shirai, M.; Shimma, N. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1825–1828.
7. Formation of spiro compounds (without stereochemical control) by radical cyclization of bromo acetals onto an endocyclic double bond: see, for example, Harrison, T.; Pattenden, G.; Myers, P. L. *Tetrahedron Lett.* **1988**, *29*, 3869–3872.
8. Fujisawa, T.; Kooriyama, Y.; Shimizu, M. *Tetrahedron Lett.* **1996**, *37*, 3881–3884.
9. Asao, N.; Shimada, T.; Sudo, T.; Tsukada, N.; Yazawa, K.; Gyoung, Y. S.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 6274–6282.
10. The material was one main isomer with trace amounts of what we assume to be three other isomers. The isomer ratio could not be determined from the $^{1}$H NMR spectrum, but the presence of sets of small signals in the $^{13}$C NMR spectrum revealed the minor components.
11. Cf. Stork, G.; Ouerfelli, O. *New J. Chem.* **1992**, *16*, 95–98.
12. The ring fusion is necessarily *cis*: Clive, D. L. J.; Cheshire, D. R.; Set, L. *J. Chem. Soc., Chem. Commun.* **1987**, 353–355.
13. Cf. Stork, G.; Atwal, K. S. *Tetrahedron Lett.* **1983**, *24*, 3819–3822.
14. Clive, D. L. J.; Wickens, P. L.; Sgarbi, P. W. M. *J. Org. Chem.* **1996**, *61*, 7426–7437.
15. Piers, E.; Morton, H. E.; Chong, M. J. *Can. J. Chem.* **1987**, *65*, 78–87.