Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c5ob02402a

Conversion of cycloalk-2-enones into 2-methylcycloalkane-1,3-diones—assessment of various Tamao-Fleming procedures and mechanistic insight into the use of the Me_3SiMe_2Si unit†

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Received 22nd November 2015,
Accepted 15th December 2015

DOI: 10.1039/c5ob02402a

www.rsc.org/obc

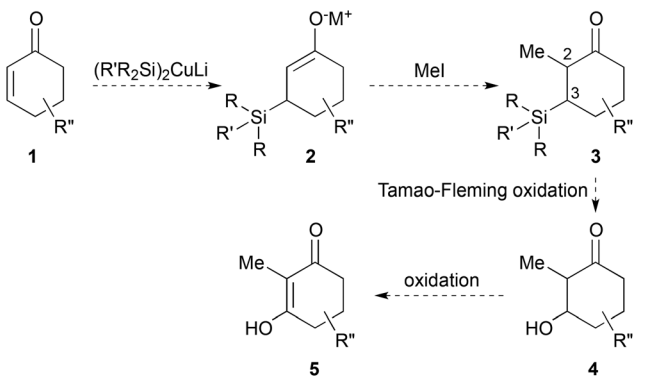
Conjugate addition of Me_3SiMe_2SiLi to cycloalk-2-en-1-ones, ketalization, Tamao–Fleming oxidation (Bu_4NF, then H_2O_2, $KHCO_3$), TPAP oxidation and acid hydrolysis generates 2-methyl cycloalkane-1,3-diones. Ketalization is needed in order to prevent addition of Me_3Si^- to the carbonyl. The pentamethyldisilanyl group has advantages over other silicon units that are used in Tamao–Fleming procedures.

Introduction

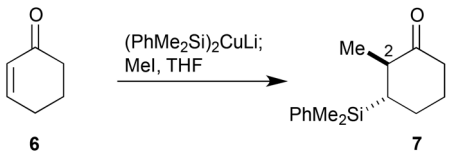
In connection with studies on a natural product synthesis we planned to convert a cyclohex-2-en-1-one substructure into the corresponding cyclohexane-1,3-dione carrying a methyl substituent at C(2). Our plan (Scheme 1) was to effect this transformation by conjugate addition of a silicon unit (**1** → **2**), followed by trapping of the intermediate enolate with MeI (**2** → **3**). The C(3)–Si bond would then be converted into a C–OH bond by Tamao–Fleming oxidation, and further oxidation of the resulting hydroxyl was expected to give the desired 1,3-dione (**3** → **4** → **5**). In this way a cyclohex-2-en-1-one (or its parent cyclohexanone) subunit would serve as a masked 2-methylcyclohexane-1,3-dione that could be liberated at a late stage of a synthesis when its reactivity would no longer interfere with other transformations. This approach to compounds of type **4** and **5** is more direct than one based on formation of a 2-methylcyclohex-2-en-1-one substructure from a cyclohexanone,[1] followed by epoxidation and reductive opening of the epoxide.[2] Conjugate additions of the type we contemplated, together with trapping of the resulting enolate by electrophiles, are known[3] and there are many examples in which a silicon–carbon bond is replaced by a carbon–oxygen bond.[4] Simple though this scheme appears, it proved to require considerable experimentation and could not be reduced to practice without incorporating protection–deprotection steps.

Results and discussion

We first added the $PhMe_2Si$ group to cyclohex-2-en-1-one and trapped the intermediate enolate with MeI (Scheme 2, **6** → **7**), as reported in the literature,[3c] and we then applied several of



Scheme 1 Synthetic plan.



Scheme 2 Conjugate addition and methylation of cyclohex-2-en-1-one.

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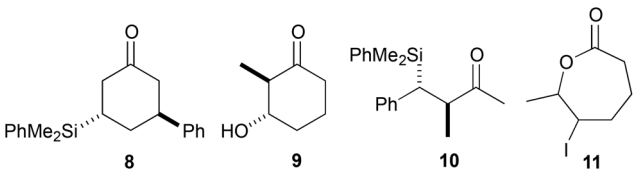
†Electronic supplementary information (ESI) available: NMR spectra of new compounds. See DOI: 10.1039/c5ob02402a

the standard methods for Tamao–Fleming oxidation that had been used successfully with compounds containing a ketone group.

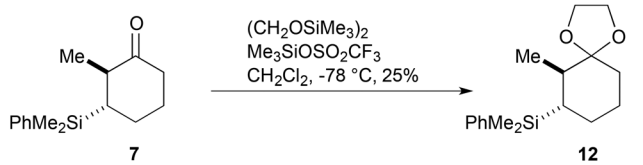
Treatment of **7** with $HBF_4{\cdot}OEt_2$ and then with *m*-CPBA, conditions that have been used with **8**,[5] failed to give **9**. Likewise, treatment with $Hg(OAc)_2$/AcOH/CF_3CO_2H, followed by AcOOH/AcOH, a reagent combination that worked for **10**,[5] were unsuccessful. A simple variation—use of $Hg(OCOCF_3)_2$ in AcOH–CF_3CO_2H, followed by addition of AcOOH, which gave an 85% yield in the case of a compound containing a cyclohexenone substructure[6]—again afforded PhOH as the only product we isolated. When we used ICl in Et_2O[7] on **7**, followed by *m*-CPBA, we obtained **11** in 12% yield, but not the desired hydroxy ketone **9**; in this last reaction, substitution of AcOOH for *m*-CPBA resulted in a complex mixture.



8 **9** **10** **11**

Ketone **7** appeared to be inert to $BF_3{\cdot}2AcOH$[5,8,9] at room temperature, apart from slow epimerization at C(2).

As attempts to carry out the Tamao–Fleming oxidation on *ketone* **7** were unsuccessful, we accepted that protection of the carbonyl was necessary. Formation of the ethylene ketal (**7** → **12**) was achieved, but only in 25% yield; use of CSA, ethylene glycol and $MeC(OMe)_3$ resulted in loss of the Ph group from the silicon unit. A brief attempt to improve the yield by use of catalytic *p*-TsNHOH[10,11] was unsuccessful, leading only to recovery of starting ketone **7**.



7 **12**

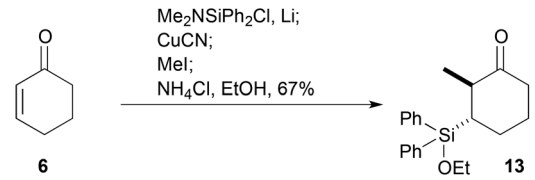
Scheme 3 Ketalization of compound **12**.

A sample of **12** was treated with Br_2 in AcOH and then with AcOOH/AcOH,[5] but no identifiable material was isolated.

Examination of different monosilicon units

At this point we decided to examine silicon groups other than $PhMe_2Si$ in the hope that at least one of the steps of the Tamao–Fleming oxidation would be facilitated.

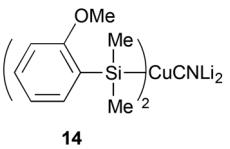
Cyclohex-2-en-1-one was therefore converted into **13** (67% yield) by conjugate addition and alkylation.[12] Treatment with *m*-CPBA and KHF_2 [13] again gave PhOH as the only isolated product (Scheme 4).



6 **13**

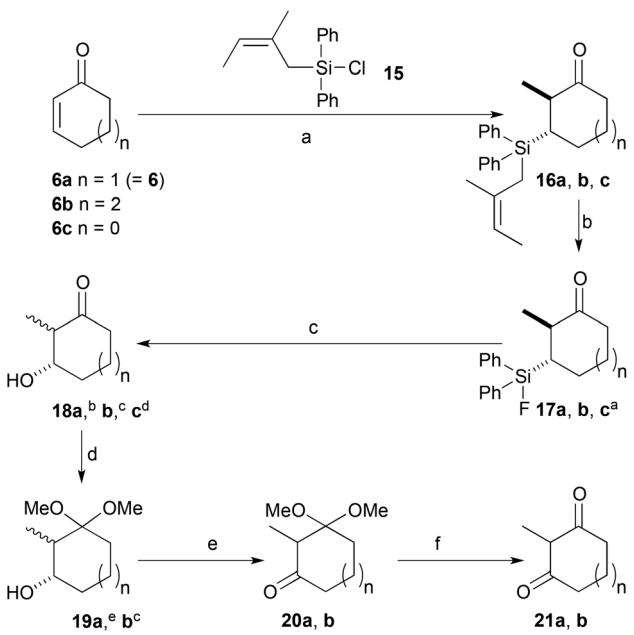
Scheme 4 Introduction of the $Ph_2(EtO)Si$ group.

The cuprate **14**[14] also seemed a promising candidate because of the ease with which the aryl group on silicon can be replaced to initiate the Tamao–Fleming sequence, but its generation is technically difficult and we were unsuccessful in the single attempt that we made.



14

We next prepared the allylic silane **16a** (Scheme 5), which was formed in 98% yield; the required cuprate is itself being easy[15] to make from chlorosilane **15**.



Scheme 5 Use of Fleming's allylic silane. Reagents and conditions: for n = 1: (a) **15**, Li, THF, 0 °C, 12 h; CuCN, 0 °C, 2 h; cyclohexenone, –78 °C, 1.5 h; MeI, –78 °C to room temperature, 12 h, 98%. (b) $BF_3{\cdot}2AcOH$, CH_2Cl_2, 0 °C, 30 min, *ca.* 95%. (c) 30% H_2O_2, $NaHCO_3$, KF, THF–MeOH (1 : 1), 3 days, 68%. (d) HC$(OMe)_3$, PPTS, MeOH, 40 min, 97%. (e) TPAP, NMO, 4 Å sieves, CH_2Cl_2, 40 min, 91%. (f) 1 M HCl–THF (1 : 10), 99%. For n = 2: (a) **15**, Li, THF, 0 °C, 12 h; CuCN, 0 °C, 2 h; cycloheptenone, –78 °C, 1.5 h; MeI, –78 °C, 12 h, 90%. (b) $BF_3{\cdot}AcOH$, CH_2Cl_2, 0 °C, 10 min, 100%. (c) 30% H_2O_2, $NaHCO_3$, KF, THF–MeOH (1 : 1), 31 h, 64%. (d) HC$(OMe)_3$, PPTS, MeOH, 16 h, 81%. (e) TPAP, NMO, 4 Å sieves, CH_2Cl_2, 40 min, 98%. (f) 1 M HCl–THF (1 : 10), 30 min, 96%. For n = 0: (a) **15**, Li, THF, 0 °C, 12 h; CuCN, 0 °C, 3 h; cyclopentenone; –78 °C, 4 h; MeI, –78 °C, 12 h, 98%. (b) $BF_3{\cdot}2AcOH$, CH_2Cl_2, 0 °C, 30 min, 97%. (c) 30% H_2O_2, $NaHCO_3$, KF, THF–MeOH (1 : 1), 1.5 days, 36%. [a] *trans* : *cis* 11.5 : 1. [b] *trans* : *cis* 20 : 1. [c] Single *trans* isomer. [d] *trans* : *cis* 7 : 3. [e] *trans* : *cis* 5 : 1.

Treatment of **16a** with BF_3·2AcOH gave **17a** in *ca.* 95% yield. The compound partially decomposes on silica gel, but the crude material is satisfactory for the next step. Alternatively, treatment of **16a** with $HBF_4.OEt_2$ in CH_2Cl_2 gave the same product **17a** in 62% yield as a 3.4 : 1 *trans* : *cis* mixture of isomers. When the fluorosilane **17a** was exposed to the action of 30% H_2O_2 in the presence of $NaHCO_3$ and KF in THF–MeOH for 3 days at room temperature we obtained the desired hydroxy ketones **18a** in 68% yield as a 20 : 1 *trans* : *cis* mixture of stereoisomers; a four-day period gave 64% yield.

Oxidation of 3-hydroxy-2-methycyclohexan-1-one (18a) to 2-methylcyclohexane-1,3-dione (21a)

We now sought to oxidize the β-hydroxy ketones **18a** to the 1,3-diketone **21a**, and for these experiments it was convenient to make a supply of the β-hydroxy ketone (as a 3 : 1 mixture of *cis* and *trans* isomers) by a literature method.[16,17] We examined several oxidizing agents,[18] but usually obtained complex mixtures or only a small amount of the desired β-diketone **21a**. A common observation was the early appearance (tlc) of the desired product and its subsequent disappearance, while much starting hydroxy ketone remained.

In the light of the above findings, the β-hydroxy ketones **18a** were converted into the dimethoxy ketals **19a** using $HC(OMe)_3$ and PPTS. When TsOH was used as the catalyst the main pathway was dehydration, but with PPTS at room temperature only ketalization occurred and the yield was high (97%). TPAP oxidation to **20a** was also efficient and the desired 2-methylcyclohexane-1,3-dione **21a** was then liberated almost quantitatively by hydrolysis with hydrochloric acid[28] in THF.

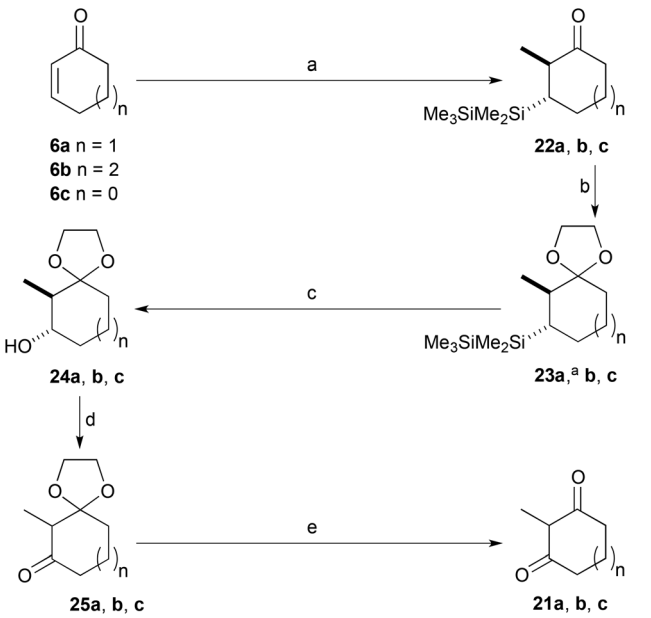
The sequence **6a** → **21a** of Scheme 5 defined a route to accomplish our aim of converting a cyclohex-2-en-1-one into a 2-methylcyclohexane-1,3-dione, and we next applied it to cyclohept-2-en-1-one (**6b**), a ketone that was best made by Saegusa oxidation[29] from cycloheptanone.[30]

Conjugate addition of the Fleming allylic silyl cuprate derived from **15** gave **16b** (90% yield); no *cis* isomer was isolated. Replacement of the allylic unit by fluorine was quantitative and the second stage of the Tamao–Fleming oxidation (**17b** → **18b**) afforded the keto alcohol in 64% yield as the *trans* isomer. Again, direct oxidation with TPAP generated some of the desired 1,3-diketone but this disappeared while much starting material remained. Accordingly, **18b** was ketalized (**18b** → **19b**) and then TPAP oxidation worked well (**19b** → **20b**, 98%). Finally, acid hydrolysis gave **21b**[31] (96%) which, according to its ^{1}H NMR spectrum, was in the diketo form and not enolized.

We also applied the method of Scheme 5 to cyclopent-2-en-1-one (**6c**). Formation of the conjugate addition product **16c** was very efficient (98%), as was replacement of the allylic unit by fluorine (**16c** → **17c**, 97%); however, the yield (36%) in the oxidation step of the Tamao–Fleming process **17c** → **18c** was too low to warrant studies on conversion to the 1,3-dione.

Use of the pentamethyldisilanyl group

During the course of our experimental work it became desirable to impose the additional requirement that the intermediate silane be of such a nature that a number of further reactions could be carried out before replacing the silicon unit by an oxygen. Both a phenyl and an allyl group on silicon rendered the compounds rather sensitive to acidic conditions; however, the $Me_3SiSiMe_2$– unit seemed ideal for conferring greater stability. This group has been used on only a few occasions[13,32,33] and so its merits have not yet been firmly established, but we applied it (Scheme 6) to the case of cyclohex-2-en-1-one for comparison with our earlier route, and then to cyclopent-2-en-1-one and cyclohept-2-en-1-one.

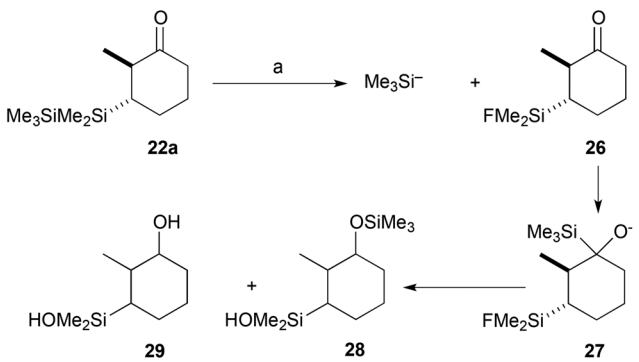


Scheme 6 Conversion of cycloalkenones to 2-methylcycloalkane-1,3-diones by use of the pentamethyldisilanyl group. Reagents and conditions: for n = 1: (a) $Me_3SiSiMe_3$, HMPA, MeLi, 0 °C, 30 min; dilute with THF at 0 °C over 30 min; cyclohexenone, −78 °C, 1 h; MeI, −78 °C to room temperature, 5 h, 88%. (b) Ethylene glycol, TsOH, PhH, reflux, Dean-Stark, 4.5 h, 91%. (c) Bu_4NF, THF, 15 min; 30% H_2O_2, $KHCO_3$, MeOH, 23 h, 71%. (d) TPAP, NMO, 4 Å sieves, CH_2Cl_2, 20 min, 95%. (e) 1 M HCl : THF (1 : 10), 10 h, 58% (78%, corrected for recovered **25a**). For n = 2: (a) $Me_3SiSiMe_3$, HMPA, MeLi, 0 °C, 40 min; dilute with THF at 0 °C over 40 min; cycloheptenone, −78 °C, 30 min; MeI, −78 °C, 20 min, 0 °C, 1 h, 85%. (b) Ethylene glycol, TsOH, PhH, reflux, Dean-Stark, 23 h, 83%. (c) Bu_4NF, THF, 30 min; 30% H_2O_2, $KHCO_3$, MeOH, 23 h, 69%. (d) TPAP, NMO, 4 Å sieves, CH_2Cl_2, 25 min, 94%. (e) 1 M HCl : THF (1 : 10), reflux, 17 h, 71% (82% corrected for recovered **25b**). For n = 0: (a) Me_3Si-$SiMe_3$, HMPA, MeLi, 0 °C, 30 min; dilute with THF at 0 °C over 40 min; cyclopentenone, −78 °C, 1 h; MeI, −78 °C to 0 °C, 3 h, 94%. (b) Ethylene glycol, TsOH, PhH, reflux, Dean-Stark, 6 h, 95%. (c) Bu_4NF, THF, 20 min; 30% H_2O_2, $KHCO_3$, MeOH, 20 h, 70%. (d) TPAP, NMO, 4 Å sieves, CH_2Cl_2, 30 min, 77%. (e) 1 M HCl : THF (1 : 10), 2.5 h, 71%. [a] Compound **23a** appeared (^{1}H NMR) to be a 5 : 1 mixture of *trans* and *cis* isomers.

An additional advantage of the Me_3SiMe_2Si group is that formation of a cuprate is unnecessary, as the second silicon modifies the properties of the anion $Me_3SiMe_2Si^-$ in a way that causes it to add 1,4 to cycloalk-2-en-1-ones.

We generated Me_3SiMe_2SiLi in the manner reported in the literature,[33] although we found it was better to prolong to 30 min the initial period after addition of MeLi, and that the subsequent dilution with THF should be done slowly[32d] (over *ca.* 30 min). With this procedure, addition to cyclohexenone (Scheme 6, **6a** → **22a**) was efficient (88% yield). Unlike the situation with $PhMe_2Si$ (*cf.* Scheme 3, **7** → **12**) ketalization (**22a** → **23a**) was easily achieved in the presence of TsOH, reflecting the stability of the pentamethyldisanyl group to acid. The Tamao–Fleming steps provided the hydroxy ketal **24a** (71%), and oxidation (95%) took the route as far as **25a**. The final acid hydrolysis (78%) was best stopped before completion, at least when using HCl–THF, which was the only reagent we examined.

The above sequence was not the first we tried with the pentamethyldisilane reagent. Initially, we did not protect the ketone and we found that in the Tamao–Fleming step three byproducts were formed that revealed details of the mechanism and established the need for ketone protection (Scheme 7). While we did not deduce the structure of one of these byproducts the other two were clearly **28** and **29** (of undetermined stereochemistry), and we interpret their formation as resulting from attack of the Me_3Si^- anion[34] on the ketone carbonyl (**26** → **27**), followed by Brook rearrangement to **28**. On the basis of this proposal we obviously had to protect the ketone carbonyl before the Tamao–Fleming sequence. We did examine the possibility of using acetone as a sacrificial trap for Me_3Si^-, but this modification did not alter the outcome.



Scheme 7 Byproducts from reaction of fluoride with **23a**. Reagent: (a) Bu_4NF, THF.

We next applied the procedure to the case of cyclohept-2-en-1-one (Scheme 6, **6b**) and found that each of the steps (**6b** → **21b**) proceeded without incident.

Finally, in view of the difficulties we had met with cyclopent-2-en-1-one (see Scheme 5, **6c** → **18c**), we applied the pentamethyldisilane approach to this ketone; again all the steps worked smoothly (Scheme 6, **6c** → **21c**).

Conclusions

Conversion of cycloalk-2-en-1-ones into 2-methylcycloalkane-1,3-diones, using conjugate addition of a silicon group, enolate trapping with MeI and Tamao–Fleming oxidation is most reliably achieved if the intermediate β-silyl ketone is converted into a ketal before applying the Tamao–Fleming conditions. The presence of a silicon unit carrying a phenyl (as in **7**, Scheme 3) or allyl substituent (as in **16a,b,c**, Scheme 5) renders the compounds sensitive to acids and this restricts the types of transformations that can be carried out. The efficiency of the Tamao–Fleming oxidation steps with the allylsilane are comparable to the corresponding steps in the pentamethyldisilanyl series but the far greater stability of the Me_3SiMe_2Si unit is a significant advantage, and this silicon unit deserves to be more widely used, especially where other structural features of the substrate are immune to attack by Me_3Si^-.

Experimental

Solvents used for chromatography were distilled before use. Commercial thin layer chromatography plates (silica gel, Merck 60F-254) were used. Silica gel for flash chromatography was Merck type 60 (230–400 mesh). Dry solvents were prepared under an inert atmosphere and transferred by syringe or cannula. The symbols s, d, t and q used for ^{13}C NMR spectra indicate zero, one, two, or three attached hydrogens, respectively, the assignments being made from APT spectra. Solutions were evaporated under water pump vacuum and the residue was then kept under oil pump vacuum. High resolution electrospray mass spectrometric analyses were done with an orthogonal time of flight analyzer and electron ionization mass spectra were measured with a double-focusing sector mass spectrometer.

6-Iodo-7-methyloxepan-2-one (11)

ICl (0.43 mL, 0.43 mmol) was added to a stirred solution of **7** (50 mg, 0.21 mmol) in Et_2O (1.0 mL) (Ar atmosphere). After 3 h, the reaction mixture was cooled to 0 °C and *m*-CPBA (149 mg, 0.82 mmol, purified from wet commercial material) was added, followed by a solution of Et_3N (34 μL, 0.25 mmol) in Et_2O (1 mL). The ice bath was left in place, but not recharged, and stirring was continued overnight. The mixture was quenched with saturated aqueous $Na_2S_2O_3$ (*ca.* 5 mL) and saturated aqueous $NaHCO_3$ (*ca.* 5 mL) and then extracted with Et_2O (2 × 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.8 × 15 cm), using a 5–10% EtOAc–hexanes gradient, gave **11** (6 mg, 12%) as an oil:

FTIR ($CDCl_3$, cast) 2958, 1736, 1443, 1239, 1043 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.62–1.72 (m, 1 H), 1.82–1.93 (m, 1 H), 1.96 (d, J = 7.0 Hz, 3 H), 1.93–2.01 (m, 1 H), 2.22–2.29 (m, 1 H), 2.42–2.51 (m, 1 H), 2.57–2.66 (m, 1 H), 3.93–4.01 (m, 1 H), 4.22–4.30 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2 (t), 23.9 (q), 27.1 (t), 29.2 (d), 29.4 (t), 84.3 (d), 170.4 (s); exact mass (ESI) m/z calcd for $C_7H_{11}INaO_2$ $(M + Na)^+$ 276.9696, found 276.9692. Additional small signals in the ^{13}C NMR spectrum suggested the presence of a second stereoisomer.

Dimethyl[*trans*-6-methyl-1,4-dioxaspiro[4,5]decan-7-yl]-phenylsilane (12)

$(Me_3SiOCH_2)_2$ (340 mg, 1.65 mmol) in CH_2Cl_2 (2 mL) and $CF_3SO_2OSiMe_3$ (8.0 μL, 0.045 mmol) were added sequentially to a stirred and cooled (−78 °C) solution of **7** in CH_2Cl_2 (3 mL) (Ar atmosphere). Stirring was continued for 4 h and the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (*ca.* 15 mL) and extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.8 × 15 cm), using 3% EtOAc–hexanes, gave **12** (33 mg, 25%) as an oil: FTIR ($CDCl_3$, cast) 3068, 2975, 2879, 1878 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.28 (s, 3 H), 0.31 (s, 3 H), 0.81 (d, J = 6.5 Hz, 3 H), 1.05–1.18 (m, 2 H), 1.31 (td, J = 13.5, 4.0 Hz, 1 H), 1.43–1.53 (m, 1 H), 1.56–1.63 (m, 1 H), 1.63–1.72 (m, 2 H), 1.75–1.82 (m, 1 H), 3.84–4.00 (m, 4 H), 7.30–7.36 (m, 3 H), 7.46–7.52 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −3.0 (q), −2.9 (q), 14.3 (q), 25.5 (t), 27.7 (t), 29.6 (d), 35.3 (t), 41.7 (d), 65.0 (t), 65.1 (t), 110.8 (s), 127.6 (d), 128.6 (d), 133.8 (d), 139.7 (s); exact mass (EI) calcd for $C_{17}H_{26}O_2Si$ $(M)^+$ 290.1702, found 290.1705.

trans-3-(Ethoxydiphenylsilyl)-2-methylcyclohexan-1-one (13)

A solution of the dimethylaminodiphenylsilyl cuprate reagent was prepared as follows: lithium wire (113 mg, 16.4 mmol) was cut into strips (*ca.* 1 cm long), washed with dry hexane, blotted and weighed. The strips were quickly cut into small pieces (1–2 mm) and transferred to a round-bottomed flask containing Me_2NPh_2SiCl (2.16 mL, 8 mmol) in THF (16 mL) (Ar atmosphere). The mixture was stirred vigorously for 5 min and then at 0 °C for 4 h to generate a dark green solution.

Dry CuCN (kept for 12 h under oilpump vacuum, 358 mg, 4.0 mmol) was added to another flask containing THF (4 mL) and HMPA (6 mL) and the mixture was stirred and cooled (0 °C) (Ar atmosphere). The silyllithium solution was taken up into a syringe and added dropwise over *ca.* 5 min to the stirred CuCN mixture. After the addition, stirring was continued at 0 °C for 0.5 h and then at −78 °C for 4.5 h to generate the cuprate reagent.

Cyclohex-2-en-1-one (0.43 mL, 4 mmol) in THF (5.0 mL) was added dropwise to the cooled (−78 °C) cuprate solution and stirring was continued for 1.5 h. MeI (2.5 mL, 40 mmol) was added and stirring at −78 °C was continued overnight (large silvered Dewar filled with dry ice/acetone). The mixture was then quenched with a slurry of saturated aqueous NH_4Cl (2.14 g, 40 mmol) in absolute ethanol (10 mL) and stirred at room temperature for 24 h. The mixture was then diluted with Et_2O (150 mL), washed with water (100 mL), and the organic extract was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using a 5–20% EtOAc–hexanes gradient, gave the *trans* isomer **13** (906 mg, 67%) as a thick oil: FTIR ($CDCl_3$, cast) 3069, 2972, 1709, 1445 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (d, J = 6.5 Hz, 3 H), 1.13 (t, J = 7.0 Hz, 3 H), 1.52–1.68 (m, 2 H), 1.68–1.80 (m, 1 H), 1.99 (br d, J = 16.0 Hz, 1 H), 2.06–2.15 (m, 1 H), 2.15–2.30 (m, 2 H), 2.38 (br d, J = 13.5 Hz, 1 H), 3.60–3.70 (m, 2 H), 7.38–7.50 (m, 6 H), 7.60–7.69 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.2 (q), 18.2 (q), 26.6 (t), 30.0 (t), 33.3 (d), 42.0 (t), 45.7 (d), 59.4 (t), 127.9 (d), 128.0 (d), 130.0 (d), 130.1 (d), 133.3 (s), 133.5 (s), 135.1 (d), 135.2 (d), 214.3 (s); exact mass (ESI) m/z calcd for $C_{21}H_{26}NaO_2Si$ $(M + Na)^+$ 338.1702, found 338.1707.

trans-2-Methyl-3-{[(2*Z*)-2-methylbut-2-en-1-yl]diphenylsilyl}-cyclohexan-1-one (16a)

A solution of the allyl silyl cuprate reagent was prepared as follows: lithium wire (65.5 mg, 9.5 mmol) was cut into strips (*ca.* 1 cm), washed with dry hexane, blotted and weighed. The strips were quickly cut into pieces (1–2 mm) and transferred into a cooled (0 °C) round-bottomed flask containing chloro[(2*Z*)-2-methylbut-2-en-1-yl]diphenylsilane (**15**)[15] (717.5 mg, 2.5 mmol) in THF (5 mL) (Ar atmosphere). The reaction mixture was stirred overnight to produce a deep dark green solution.

Dry CuCN (kept for 12 h under oilpump vacuum, 112 mg, 1.25 mmol) was added to another flask containing THF (1 mL) and the mixture was stirred and cooled (0 °C) (Ar atmosphere). The silyllithium solution was taken up into a syringe and added dropwise over *ca.* 5 min to the stirred CuCN mixture. After the addition, stirring was continued at 0 °C for 2 h to generate the cuprate reagent.

The solution of the cuprate reagent was cooled to −78 °C, and cyclohex-2-en-1-one (0.10 mL, 1.0 mmol) was added dropwise (Ar atmosphere). Stirring was continued for 1.5 h at −78 °C. MeI (0.62 mL, 10 mmol) was then added, the cold bath was left in place, but not recharged, and stirring was continued overnight, by which time the mixture had reached room temperature. The mixture was then quenched with saturated aqueous NH_4Cl (*ca.* 15 mL) and stirring was continued for 15 min. The mixture was then extracted with Et_2O (3 × 30 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.3 × 18 cm), using 10% EtOAc–hexanes, gave the *trans* isomer **16a** (355 mg, 98%) as an oil: FTIR ($CDCl_3$, cast) 3069, 2933, 1709, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.96 (d, J = 7.0 Hz, 3 H), 1.08 (d, J = 6.5 Hz, 3 H), 1.47 (s, 3 H), 1.70–1.60 (m, 2 H), 1.82–1.70 (m, 1 H), 2.12 (d, J = 4.0 Hz, 2 H), 2.25–2.00 (m, 4 H), 2.39 (br d, J = 13.0 Hz, 1 H), 4.94 (q, J = 6.5 Hz, 1 H), 7.45–7.32 (m, 6 H), 7.62–7.54 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5 (q), 15.7 (q), 19.4 (t), 26.5 (q), 27.5 (t), 30.1 (t), 33.0 (d), 41.9 (t), 46.7 (d), 118.6 (d), 127.6 (d), 127.8 (d), 129.4 (d), 129.5 (d), 132.0 (s), 133.9 (s),

134.3 (s), 135.50 (d), 135.52 (d), 214.1 (s); exact mass (ESI) calcd for $C_{24}H_{30}NaOSi$ $(M + Na)^+$ 385.1958, found 385.1961.

trans-3-(Fluorodiphenylsilyl)-2-methylcyclohexan-1-one (17a)

$BF_3{\cdot}2AcOH$ (0.51 mL, 1.98 mmol) was added to a stirred and cooled (0 °C) solution of **16a** (240 mg, 0.66 mmol) in CH_2Cl_2 (12 mL) (Ar atmosphere). Stirring was continued for 30 min, and the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (*ca.* 20 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to give the *trans* isomer **17a** (196 mg, 95%) as an oil: FTIR ($CDCl_3$, cast) 3071, 2935, 1709, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (d, J = 6.5 Hz, 3 H), 1.62–1.82 (m, 3 H), 1.88–1.89 (m, 1 H), 2.10–2.20 (m, 1 H), 2.24–2.34 (m, 1 H), 2.37–2.48 (m, 2 H), 7.34–7.54 (m, 6 H), 7.60–7.74 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.99 (q), 15.01 (q), 26.41 (t), 26.43 (t), 29.9 (t), 33.8 (d), 33.9 (d), 41.9 (t), 45.2 (d), 128.3 (d), 130.85 (d), 130.88 (d), 131.9 (s), 132.0 (s), 132.2 (s), 132.3 (s), 134.3 (d), 134.36 (d), 134.39 (d), 134.4 (d), 213.0 (s); exact mass (EI) calcd for $C_{19}H_{21}OFSi$ $(M)^+$ 312.1346, found 312.1344.

3-Hydroxy-2-methylcyclohexan-1-one (18a)[35] from (17a)

KF (53 mg, 0.90 mmol), $NaHCO_3$ (214 mg, 2.55 mmol) and H_2O_2 (30 wt% in water, 0.25 mL, 2.40 mmol) were added sequentially to a stirred solution of **17a** (94 mg, 0.30 mmol) in THF (2 mL) and MeOH (2 mL) (Ar atmosphere). Stirring was continued for 72 h. Without aqueous workup, silica gel (*ca.* 1 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top a column of flash chromatography silica gel (1.3 × 15 cm) made up with hexanes. Flash chromatography, using a 10–30% acetone-hexanes gradient, gave **18a** (26 mg, 68%) as an oil which was a 20 : 1 mixture of *trans* and *cis* isomers. The material had: FTIR ($CDCl_3$, cast) 3428, 2937, 2873, 1708, 1035 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (signals of major isomer only) δ 1.17 (d, J = 6.5 Hz, 3 H), 1.48–1.60 (m, 1 H), 1.69–1.80 (m, 2 H), 1.96–2.06 (m, 1 H), 2.21–2.12 (m, 1 H), 2.23–2.33 (m, 1 H), 2.34–2.46 (m, 2 H), 3.44–3.54 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) (signals of major isomer only) δ 10.8 (q), 20.8 (t), 33.8 (t), 40.4 (t), 53.9 (d), 75.9 (d), 210.4 (s); exact mass (EI) calcd for $C_7H_{12}O_2$ $(M)^+$ 128.0837, found 128.0837.

3,3-Dimethoxy-2-methylcyclohexan-1-ol (19a)

Pyridinium *p*-toluenesulfonate (287 mg, 1.14 mmol) and $CH(OMe)_3$ (0.84 mL, 7.6 mmol) were added sequentially to a stirred solution of **18a** (97 mg, 0.76 mmol) in MeOH (4.5 mL) (Ar atmosphere). After 40 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (*ca.* 10 mL) and stirring was continued for 5 min. The mixture was extracted with Et_2O (3 × 20 mL) and the combined organic extracts were dried ($MgSO_4$) and evaporated to afford **19a** (128 mg, 97%) as an oil which was a 5 : 1 mixture of *trans* and *cis* isomers. A small sample of the *trans* isomer was separated; it had: FTIR ($CDCl_3$, cast) 3421, 2951, 2829, 1067 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (d, J = 7.0 Hz, 3 H), 1.28–1.39 (m, 1 H), 1.39–1.52 (m, 2 H), 1.52–1.65 (m, 3 H), 1.65–1.72 (m, 1 H), 2.22 (dq, J = 10.5, 6.0 Hz, 1 H), 3.16 (s, 3 H), 3.18 (s, 3 H), 3.94 (ddd, J = 10.5, 9.5, 4.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.8 (q), 18.9 (t), 26.3 (t), 28.8 (t), 40.4 (d), 47.2 (q), 47.7 (q), 70.3 (d), 103.3 (s); exact mass (EI) calcd for $C_9H_{18}O_3$ $(M)^+$ 174.1256, found 174.1257.

3,3-Dimethoxy-2-methylcyclohexan-1-one (20a)

N-Methylmorpholine *N*-oxide (129 mg, 1.11 mmol), powdered 4 Å molecular sieves (369 mg) and Pr_4NRuO_4 (26 mg, 0.074 mmol) were added sequentially to a stirred solution of **19a** (128 mg, 0.74 mmol) in CH_2Cl_2 (1.5 mL) (Ar atmosphere). After 40 min, the reaction mixture was filtered through a short pad of silica gel and the filtrate was evaporated to give **20a** (115 mg, 91%) as an oil: FTIR ($CDCl_3$, cast) 2957, 2832, 1716, 1175 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.14 (d, J = 7.5 Hz, 3 H), 1.56–1.67 (m, 1 H), 1.76–1.86 (m, 2 H), 1.93–2.01 (m, 1 H), 2.18–2.26 (m, 1 H), 2.46 (ddd, J = 15.0, 13.0, 7.0 Hz, 1 H), 2.75 (qt, J = 7.5, 1.5 Hz, 1 H), 3.16 (s, 3 H), 3.17 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.4 (q), 19.2 (t), 26.0 (t), 36.1 (t), 47.5 (q), 47.8 (q), 51.8 (d), 103.6 (s), 211.9 (s); exact mass (EI) calcd for $C_9H_{16}O_3$ $(M)^+$ 172.1099, found 172.1096.

3-Hydroxy-2-methylcyclohex-2-en-1-one (21a)[17] from (20a)

A solution of **20a** (115 mg, 0.67 mmol) in a 1 : 10 mixture (3.5 mL) of hydrochloric acid (1 M) and THF was stirred for 3.5 h. Evaporation of the solvent gave **21a** (84 mg, 99%) as a solid: ^1H NMR (500 MHz, DMSO-d_6) δ 1.53 (s, 3 H), 1.80 (quintet, J = 6.5 Hz, 2 H), 2.28 (br s, 4 H), 10.3 (br s, 1 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 7.2, 20.5, 30.2 (br s), 109.5.

trans-2-Methyl-3-{[(2*Z*)-2-methylbut-2-en-1-yl]diphenylsilyl}-cycloheptan-1-one (16b)

A solution of the allyl silyl cuprate reagent was prepared as follows: lithium wire (196.6 mg, 28.5 mmol) was cut into strips (*ca.* 1 cm), washed with dry hexane, blotted and weighed. The strips were quickly cut into pieces (1–2 mm) and transferred to a cooled (0 °C) round-bottomed flask containing allyl silane **15** (2.15 g, 7.5 mmol) in THF (5 mL) (Ar atmosphere). The mixture was stirred overnight to produce a dark green solution.

Dry CuCN (kept for 12 h under oilpump vacuum, 336 mg, 3.75 mmol) was added to another flask containing THF (1 mL) and the mixture was stirred and cooled (0 °C) (Ar atmosphere). The silyl lithium solution was taken up into a syringe and added dropwise over *ca.* 5 min to the stirred CuCN mixture. After the addition, stirring was continued at 0 °C for 2 h to generate the cuprate reagent.

The solution of the cuprate reagent was cooled to −78 °C, and cyclohept-2-en-1-one (347.4 mg, 3.0 mmol) was added dropwise (Ar atmosphere). Stirring was continued for 1.5 h at −78 °C, MeI (1.89 mL, 30 mmol) was then added and stirring at −78 °C was continued overnight (large silvered Dewar filled with dry ice/acetone). The mixture was then quenched with

saturated aqueous NH_4Cl (*ca.* 25 mL) and stirring was continued for 15 min. The mixture was extracted with Et_2O (3 × 75 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using a 5–10% EtOAc–hexanes gradient, gave **16b** (1.02 g, 90%) as an oil which was the *trans*-isomer: FTIR ($CDCl_3$, cast) 3069, 2929, 2857, 1701, 1445 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, J = 7.0 Hz, 3 H), 1.00–1.12 (m, 1 H), 1.19 (d, J = 6.5 Hz, 3 H), 1.26–1.34 (m, 1 H), 1.36–1.46 (m, 2 H), 1.52 (s, 3 H), 1.84–2.00 (m, 2 H), 2.06–2.20 (m, 3 H), 2.22–2.30 (m, 1 H), 2.60 (dq, J = 10.5, 7.0 Hz, 1 H), 2.75 (td, J = 10.5, 3.0 Hz, 1 H), 5.01 (q, J = 6.5 Hz, 1 H), 7.30–7.42 (m, 6 H), 7.50–7.60 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7 (q), 18.7 (t), 19.2 (q), 26.2 (t), 26.6 (q), 28.5 (d), 30.0 (t), 32.1 (t), 39.2 (t), 49.9 (d), 118.6 (d), 127.7 (d), 127.8 (d), 129.4 (d), 129.5 (d), 132.3 (s), 134.7 (s), 134.8 (s), 135.4 (d), 135.5 (d), 216.7 (s); exact mass (ESI) calcd for $C_{25}H_{32}NaOSi$ $(M + Na)^+$ 399.2115, found 399.2119.

trans-3-(Fluorodiphenylsilyl)-2-methylcycloheptan-1-one (17b)

$BF_3{\cdot}2AcOH$ (0.13 mL, 0.91 mmol) was added to a stirred and cooled (0 °C) solution of **16b** (114 mg, 0.30 mmol) in CH_2Cl_2 (5 mL) (Ar atmosphere). After 10 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (*ca.* 10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford **17b** (99 mg, 100%) as an oil which was the *trans*-isomer: FTIR ($CDCl_3$, cast) 3072, 2927, 1702, 1122 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.13 (dd, J = 7.0, 1.0 Hz, 3 H), 1.04–1.20 (m, 1 H), 1.30–1.52 (m, 3 H), 1.84–1.98 (m, 2 H), 2.03 (dd, J = 15.0, 5.5 Hz, 1 H), 2.28–2.38 (m, 1 H), 2.67 (dq, J = 11.0, 7.0 Hz, 1 H), 2.75 (td, J = 12.0, 2.5 Hz, 1 H), 7.38–7.46 (m, 4 H), 7.46–7.52 (m, 2 H), 7.60–7.66 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.57 (q), 18.59 (q), 26.0 (t), 28.11 (t), 28.13 (t), 29.0 (d), 29.1 (d), 31.6 (t), 39.4 (t), 48.6 (d), 128.25 (d), 128.27 (d), 130.87 (d), 130.90 (d), 131.4 (s), 131.5 (s), 132.4 (s), 132.5 (s), 134.43 (d), 134.44 (d), 134.5 (d), 216.2 (s); exact mass (ESI) calcd for $C_{20}H_{23}FNaOSi$ $(M)^+$ 349.1394, found 349.1401.

trans-3-Hydroxy-2-methylcycloheptan-1-one (18b)[36]

KF (51 mg, 0.87 mmol), $NaHCO_3$ (208 mg, 2.48 mmol) and H_2O_2 (30 wt% in water, 0.24 mL, 2.32 mmol) were added sequentially to a stirred solution of **17b** (95 mg, 0.29 mmol) in a mixture of THF (2 mL) and MeOH (2 mL) (Ar atmosphere). Stirring was continued for 31 h. The reaction was quenched with solid $Na_2S_2O_3$ (2.30 g, 14.6 mmol) and stirring was continued for a further 15 min. Without aqueous workup, silica gel (*ca.* 2 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top of a column of flash chromatography silica gel (1.8 × 18 cm) made up with hexanes. Flash chromatography, using a 10–15% acetone–hexanes gradient, gave **18b** (26.5 mg, 64%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 3431, 2934, 2863, 1695, 1036 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.20 (d, J = 7.0 Hz, 3 H), 1.42–1.54 (m, 1 H), 1.56 (d, J = 5.0 Hz, 1 H), 1.68–1.97 (m, 5 H), 2.42–2.55 (m, 2 H), 2.66–2.74 (m, 1 H), 3.57–3.64 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6 (q), 24.2 (t), 24.7 (t), 37.2 (t), 42.6 (t), 54.3 (d), 73.7 (d), 214.2 (s); exact mass (EI) calcd for $C_8H_{14}O_2$ $(M)^+$ 142.0994, found 142.0995.

trans-3,3-Dimethoxy-2-methylcycloheptan-1-ol (19b)

Pyridinium *p*-toluenesulfonate (155 mg, 0.62 mmol) and $CH(OMe)_3$ (1.8 mL, 16.4 mmol) were added sequentially to a stirred solution of **18b** (58 mg, 0.41 mmol) in MeOH (6 mL) (Ar atmosphere). After 16 h, the reaction mixture was quenched with Et_3N (0.17 mL, 1.23 mmol) and stirring was continued for 15 min. The solution was applied directly to the top of a column (1.3 × 18 cm) of flash chromatography silica gel made up with 3% Et_3N in hexanes. Flash chromatography, using 10% acetone–hexanes, gave **19b** (63 mg, 81%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 3526, 2942, 2832, 1461, 1043 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (d, J = 7.5 Hz, 3 H), 1.40–1.66 (m, 3 H), 1.70–1.90 (m, 5 H), 2.38–2.46 (m, 1 H), 3.16 (s, 3 H), 3.26 (s, 3 H), 3.69–3.74 (m, 1 H), 3.76 (d, J = 9.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3 (q), 19.5 (t), 21.1 (t), 28.7 (t), 30.7 (t), 42.2 (d), 47.7 (q), 48.3 (q), 72.6 (d), 106.7 (s); exact mass (ESI) calcd for $C_{10}H_{20}NaO_3$ $(M + Na)^+$ 211.1305, found 211.1305.

3,3-Dimethoxy-2-methylcycloheptan-1-one (20b)

N-Methylmorpholine *N*-oxide (66 mg, 0.57 mmol), powdered 4 Å molecular sieves (113 mg) and Pr_4NRuO_4 (8.0 mg, 0.023 mmol) were added sequentially to a stirred solution of **19b** (43 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) (Ar atmosphere). After 40 min, the solution was applied directly onto a column of flash chromatography silica gel (1.3 × 8 cm) made up with hexanes. Flash chromatography, using 10% acetone-hexanes, gave **20b** (41 mg, 98%) as an oil: FTIR ($CDCl_3$, cast) 2947, 2831, 1694, 1109 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.22 (d, J = 8.0 Hz, 3 H), 1.48–1.56 (m, 1 H), 1.67–1.89 (m, 4 H), 1.98–2.06 (m, 1 H), 2.54–2.64 (m, 2 H), 2.92–3.01 (m, 1 H), 3.14 (s, 3 H), 3.20 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.1 (q), 23.0 (t), 24.0 (t), 32.0 (t), 43.4 (t), 47.7 (q), 48.1 (q), 53.8 (d), 101.9 (s), 212.7 (s); exact mass (ESI) calcd for $C_{10}H_{18}NaO_3$ $(M + Na)^+$ 209.1148, found 209.1146.

2-Methylcycloheptan-1,3-dione (21b)[31] from (20b)

A 1 : 10 mixture (0.2 mL) of hydrochloric acid (1 M) and THF was added to a stirred solution of **20b** (41.5 mg, 0.22 mmol) in THF (2 mL). After 30 min, the solvent was evaporated to afford **21b** (30 mg, 96%) as an oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (d, J = 7.0 Hz, 3 H), 1.84–1.94 (m, 2 H), 2.00–2.10 (m, 2 H), 2.46–2.55 (m, 2 H), 2.55–2.64 (m, 2 H), 3.73 (q, J = 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.2 (q), 25.8 (t), 43.4 (t), 60.9 (d), 208.0 (s).

trans-2-Methyl-3-{[(2*Z*)-2-methylbut-2-en-1-yl]diphenylsilyl}-cyclopentan-1-one (16c)

A solution of the allyl silyl cuprate reagent was prepared as follows: lithium wire (196.6 mg, 28.5 mmol) was cut into strips

(*ca.* 1 cm), washed with dry hexane, blotted and weighed. The strips were quickly cut into small pieces (1–2 mm) and transferred into a cooled (0 °C) round-bottomed flask containing the allyl silane **15** (2.15 g, 7.5 mmol) in THF (15 mL) (Ar atmosphere). The mixture was stirred overnight to produce a dark green solution.

Dry CuCN (kept for 12 h under oilpump vacuum, 336 mg, 3.75 mmol) was added to another flask containing THF (5 mL) and the mixture was stirred and cooled (0 °C) (Ar atmosphere). The silyl lithium solution was taken up into a syringe and added dropwise over *ca.* 5 min to the stirred CuCN mixture. After the addition, stirring was continued at 0 °C for 3 h to generate the cuprate reagent.

The solution of the cuprate reagent was cooled to −78 °C, and cyclopent-2-en-1-one (383.5 mg, 3.38 mmol) was added dropwise (Ar atmosphere). Stirring was continued for 4 h at −78 °C, MeI (1.89 mL, 30 mmol) was then added and stirring at −78 °C was continued overnight (large silvered Dewar filled with dry ice/acetone). The mixture was then quenched with saturated aqueous NH_4Cl (*ca.* 20 mL) and stirring was continued for 15 min. The mixture was filtered through a short pad of Celite, and then extracted with Et_2O (3 × 75 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using a 3–10% EtOAc–hexanes gradient, gave **16c** (1.15 g, 98%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 3069, 2965, 1737, 1427 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.03 (d, J = 7.0 Hz, 3 H), 1.15 (d, J = 6.5 Hz, 3 H), 1.53 (s, 3 H), 1.59–1.74 (m, 2 H), 1.78–1.86 (m, 1 H), 2.04–2.28 (m, 5 H), 4.99 (q, J = 6.5 Hz, 1 H), 7.32–7.47 (m, 6 H), 7.54–7.62 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6 (q), 15.3 (q), 18.2 (t), 23.0 (t), 26.5 (q), 29.8 (d), 37.6 (t), 46.2 (d), 118.4 (d), 127.7 (d), 127.9 (d), 129.65 (d), 129.71 (d), 131.8 (s), 133.3 (s), 133.7 (s), 135.6 (d), 222.0 (s); exact mass (ESI) calcd for $C_{23}H_{28}NaOSi$ $(M + Na)^+$ 371.1802, found 371.1801.

3-(Fluorodiphenylsilyl)-2-methylcyclopentan-1-one (17c)

BF_3·2AcOH (0.96 mL, 6.78 mmol) was added to a stirred and cooled (0 °C) solution of **16c** (0.79 g, 2.26 mmol) in CH_2Cl_2 (15 mL) (Ar atmosphere). After 30 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (*ca.* 30 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford **17c** (657 mg, 97%) as an oil which was an 11.5 : 1 mixture of *trans* and *cis* isomers. The material had: FTIR ($CDCl_3$, cast) 3071, 2966, 1739, 1122 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (signals of major isomer only) δ 1.07 (d, J = 7.0 Hz, 3 H), 1.66–1.90 (m, 2 H), 2.02–2.22 (m, 3 H), 2.32 (dd, J = 16.5, 9.0 Hz, 1 H), 7.36–7.55 (m, 6 H), 7.63–7.74 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) (signals of major isomer only) δ 14.80 (q), 14.81 (q), 22.0 (t), 22.1 (t), 30.6 (d), 30.7 (d), 37.61 (t), 37.62 (t), 45.0 (d), 128.28 (d), 128.32 (d), 131.01 (d), 131.02 (d), 131.03 (d), 131.04 (d), 131.4 (s), 131.5 (s), 131.7 (s), 131.9 (s), 134.30 (s), 134.32 (d), 134.4 (d), 134.5 (d), 220.94 (s), 220.95 (s); exact mass (ESI) calcd for $C_{18}H_{19}FNaOSi$ $(M + Na)^+$ 321.1081, found 321.1079.

3-Hydroxy-2-methylcyclopentan-1-one (18c)[16]

KF (191 mg, 3.30 mmol), $NaHCO_3$ (785 g, 9.35 mmol) and H_2O_2 (30 wt% in water, 0.90 mL, 8.80 mmol) were added sequentially to a stirred solution of **17c** (328 mg, 1.10 mmol) in THF (5 mL) and MeOH (5 mL) (Ar atmosphere), and stirring was continued for 39 h. Without aqueous workup, silica gel (*ca.* 2 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top of a column of flash chromatography silica gel (1.8 × 18 cm) made up with hexanes. Flash chromatography, using a 10–15% acetone–hexanes gradient, gave **18c** (44.8 mg, 36%) as an oil which was a 7 : 3 mixture of *trans* and *cis* isomers. The material had: FTIR ($CDCl_3$, cast) 3440, 2969, 2877, 1741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.11 (d, J = 7.0 Hz, 0.9 H), 1.14 (d, J = 7.0 Hz, 2.1 H), 1.46 (d, J = 7.5 Hz, 0.3 H), 1.80 (d, J = 7.5 Hz, 0.7 H), 1.81–1.90 (m, 0.7 H), 2.00–2.45 (m, 3.6 H), 2.51 (qdd, J = 9.5, 3.5, 1.5 Hz, 0.7 H), 3.96–4.04 (m, 0.7 H), 4.50 (br s, 0.3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.8 (q), 11.8 (q), 29.8 (t), 30.0 (t), 33.9 (t), 36.1 (t), 50.0 (d), 52.5 (d), 72.7 (d), 76.6 (d), 217.5 (s), 218.7 (s); exact mass (EI) calcd for $C_6H_{10}O_2$ $(M)^+$ 114.0681, found 114.0680.

trans-2-Methyl-3-(pentamethyldisilan-1-yl)cyclohexan-1-one (22a)

MeLi (1.6 M in Et_2O, 1.88 mL, 3.0 mmol) was added slowly to a stirred and cooled (0 °C) solution of $Me_3SiSiMe_3$ (1.25 mL, 6.0 mmol) in HMPA (4.0 mL) (Ar atmosphere). After 30 min, the reaction mixture was diluted in a dropwise manner with THF (12.0 mL) over 30 min and the solution was then cooled to −78 °C. Cyclohex-2-en-1-one (0.16 mL, 1.5 mmol) was added dropwise over 30 min, and stirring was continued for 1 h. MeI (1.02 mL, 15.0 mmol) in THF (3 mL) was then added slowly to the reaction mixture, the cold bath was left in place, but not recharged, and stirring was continued for 5 h during which time the mixture reached room temperature. The mixture was quenched with saturated aqueous NH_4Cl (*ca.* 3 mL) and stirring was continued for 5 min. The mixture was then washed with water (20 mL) and extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using a 5–10% EtOAc–hexanes gradient, gave **22a** (321 mg, 88%) as an oil which was the *trans*-isomer: FTIR ($CDCl_3$, cast) 2948, 2894, 1711 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06–0.18 (m, 15 H), 1.06 (d, J = 6.5 Hz, 3 H), 1.00–1.08 (m, 1 H), 1.57 (qd, J = 12.5, 4.0 Hz, 1 H), 1.73 (qt, J = 12.5, 4.0 Hz, 1 H), 1.82–1.90 (m, 1 H), 2.12–2.20 (m, 1 H), 2.27–2.39 (m, 2 H), 2.39–2.46 (dm, J = 13.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −3.8 (q), −3.6 (q), −1.3 (q), 15.2 (q), 28.3 (t), 30.5 (t), 35.1 (d), 41.9 (t), 47.3 (d), 214.3 (s); exact mass (EI) calcd for $C_{11}H_{23}OSi_2$ $(M - CH_3)^+$ 227.1288, found 127.1285.

1,1,1,2,2-Pentamethyl-2-[*trans*-6-methyl-1,4-dioxaspiro[4,5]-decan-7-yl]disilane (23a)

Ethylene glycol (0.46 mL, 8.16 mmol) and TsOH (7.0 mg, 0.04 mmol) were added sequentially to a solution of **22a**

(99 mg, 0.41 mmol) in C_6H_6 (4 mL). The solution was refluxed for 4.5 h, using a Dean-Stark apparatus. The solution was cooled, quenched with saturated aqueous $NaHCO_3$ (*ca.* 20 mL) and extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford **23a** (107 mg, 91%) as an oil which was a 5 : 1 mixture of *trans* and *cis* isomers. The material had: FTIR ($CDCl_3$, cast) 2943, 2882, 1245 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (signals of major isomer only) δ 0.01–0.18 (m, 15 H), 0.87–0.94 (m, 3 H), 0.94–1.01 (m, 1 H), 1.07–1.20 (m, 1 H), 1.33 (td, J = 13.5, 4.0 Hz, 1 H), 1.44–1.55 (m, 1 H), 1.64–1.76 (m, 3 H), 1.81 (br d, J = 13.0 Hz, 1 H), 3.87–4.03 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) (signals of major isomer only) δ −3.6 (q), −3.4 (q), −1.2 (q), 14.4 (q), 25.7 (t), 28.6 (t), 30.1 (d), 35.4 (t), 42.5 (d), 64.9 (t), 65.1 (t), 110.8 (s); exact mass (EI) calcd for $C_{13}H_{27}O_2Si_2$ $(M - CH_3)^+$ 271.1550, found 271.1550.

6-Methyl-1,4-dioxaspiro[4,5]decan-7-ol (24a)[37]

Bu_4NF (1.0 M in THF, 1.80 mL, 1.80 mmol) was added slowly to a stirred solution of **23a** (85.8 mg, 0.30 mmol) in THF (5.0 mL) (Ar atmosphere) and stirring was continued for 15 min. MeOH (5.0 mL), H_2O_2 (30 wt% in water, 0.73 mL, 7.18 mmol) and $KHCO_3$ (119.7 mg, 1.20 mmol) were added sequentially and stirring was continued for 23 h. Without aqueous workup, silica gel (*ca.* 2 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top a column of flash chromatography silica gel (1.8 × 18 cm) made up with hexanes. Flash chromatography, using a 3–10% acetone–hexanes gradient, gave **24a** (37 mg, 71%) as an oil which was the *trans* isomer containing a trace of the *cis* isomer: FTIR ($CDCl_3$, cast) 3415, 2940, 2883, 1040 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.01 (d, J = 7.0 Hz, 3 H), 1.34–1.45 (m, 2 H), 1.45–1.56 (m, 1 H), 1.67–1.81 (m, 3 H), 1.81–1.88 (m, 1 H), 2.33 (br s, 1 H), 3.53–3.61 (m, 1 H), 3.88–4.00 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.1 (q), 19.2 (t), 31.9 (t), 32.8 (t), 45.8 (d), 64.6 (t), 64.8 (t), 73.6 (d), 111.0 (s); exact mass (EI) calcd for $C_9H_{16}O_3$ $(M)^+$ 172.1099, found 172.1100.

6-Methyl-1,4-dioxaspiro[4,5]decan-7-one (25a)[38]

N-Methylmorpholine *N*-oxide (96.7 mg, 0.83 mmol), powdered 4 Å molecular sieves (275 mg) and Pr_4NRuO_4 (19.3 mg, 0.055 mmol) were added sequentially to a stirred solution of **24a** (94.8 mg, 0.55 mmol) in CH_2Cl_2 (8 mL) (Ar atmosphere). After 20 min, the solution was applied directly to a column of flash chromatography silica gel (1.3 × 8 cm) made up with hexanes. Flash chromatography, using 10% acetone–hexanes, gave **25a** (89.3 mg, 95%) as an oil: FTIR ($CDCl_3$, cast) 2948, 2884, 1716 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (d, J = 6.5 Hz, 3 H), 1.68–1.91 (m, 3 H), 1.99–2.02 (m, 1 H), 2.22–2.32 (m, 1 H), 2.40–2.48 (m, 1 H), 2.73 (q, J = 7.0 Hz, 1 H), 3.88–4.03 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.5 (q), 20.0 (t), 34.0 (t), 39.9 (t), 54.4 (d), 65.3 (t), 65.6 (t), 111.9 (s), 209.3 (s); exact mass (EI) calcd for $C_9H_{14}O_3$ $(M)^+$ 170.0943, found 170.0941.

3-Hydroxy-2-methylcyclohex-2-en-1-one (21a)[17] from (25a)

A 1 : 10 mixture (0.3 mL) of hydrochloric acid (1 M) and THF was added to a stirred solution of **25a** (51 mg, 0.30 mmol) in THF (3 mL) and stirring was continued for 10 h. Without aqueous workup, silica gel (*ca.* 1 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top of a column of flash chromatography silica gel (1.5 × 15 cm) made up with hexanes. Flash chromatography, using a 10–20% acetone–hexanes gradient, gave **21a** [22.2 mg, 58%, 78% corrected for recovered **25a** (12.9 mg)]: ^1H NMR (500 MHz, DMSO-d_6) δ 1.53 (s, 3 H), 1.80 (quintet, J = 6.5 Hz, 2 H), 2.28 (br s, 4 H), 10.3 (br s, 1 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 7.2, 20.5, 30.2 (br s), 109.5.

trans-2-Methyl-3-(pentamethyldisilan-1-yl)cycloheptan-1-one (22b)

MeLi (1.6 M in Et_2O, 4.45 mL, 7.12 mmol) was added slowly to a stirred and cooled (0 °C) solution of $Me_3SiSiMe_3$ (2.97 mL, 14.2 mmol) in dry HMPA (9.5 mL) (Ar atmosphere). After 40 min, the reaction mixture was diluted over 40 min in a dropwise manner with THF (12.0 mL) and the solution was cooled to −78 °C. Cyclohept-2-en-1-one (392 mg, 3.56 mmol) was added slowly and stirring was continued for 30 min. MeI (2.24 mL, 35.6 mmol) in THF (7 mL) was added slowly and, after 20 min, the cooling bath was replaced with an ice bath and stirring was continued for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (*ca.* 5 mL) and stirring was continued for 5 min. The mixture was diluted with water (40 mL) and extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using a 1–5% EtOAc–hexanes gradient, gave **22b** (779 mg, 85%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 2948, 2852, 1703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.02–0.16 (m, 15 H), 0.69 (t, J = 10.0 Hz, 1 H), 0.96–1.07 (m, 1 H), 1.11 (d, J = 7.0 Hz, 3 H), 1.23–1.35 (m, 1 H), 1.44 (qt, J = 13.0, 3.0 Hz, 1 H), 1.76–1.98 (m, 3 H), 2.22–2.32 (m, 1 H), 2.46 (dq, J = 10.5, 7.0 Hz, 1 H), 2.69 (td, J = 12.0, 3.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.5 (q), −3.2 (q), −1.4 (q), 19.1 (q), 26.1 (t), 29.6 (d), 30.1 (t), 32.1 (t), 39.2 (t), 50.2 (d), 216.9 (s); exact mass (EI) calcd for $C_{12}H_{25}OSi_2$ $(M - CH_3)^+$ 241.1444, found 241.1444.

1,1,1,2,2-Pentamethyl-2-[*trans*-6-methyl-1,4-dioxaspiro[4,6]-undecan-7-yl]disilane (23b)

Ethylene glycol (0.70 mL, 12.3 mmol) and TsOH (10.6 mg, 0.062 mmol) were added sequentially to a solution of **22b** (158 mg, 0.616 mmol) in C_6H_6 (6 mL) and the mixture was refluxed for 23 h, using a Dean-Stark apparatus. The solution was cooled, quenched with saturated aqueous $NaHCO_3$ (*ca.* 10 mL) and water (20 mL), and extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1.8 × 15 cm), using a 1–5% EtOAc–hexanes gradient,

gave **23b** (154 mg, 83%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 2945, 2683, 1244 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ −0.10–0.20 (m, 15 H), 0.52–0.64 (m, 1 H), 1.01 (d, J = 7.0 Hz, 3 H), 1.08–1.20 (m, 1 H), 1.42–1.58 (m, 2 H), 1.58–1.68 (m, 3 H), 1.80–1.92 (m, 3 H), 3.80–3.95 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.5 (q), −3.9 (q), −1.3 (q), 20.6 (q), 23.6 (t), 28.9 (t), 31.8 (d), 32.6 (t), 33.3 (t), 42.4 (d), 63.5 (t), 64.4 (t), 114.4 (s); exact mass (EI) calcd for $C_{14}H_{29}O_2Si_2$ $(M - CH_3)^+$ 285.1706, found 285.1699.

trans-6-Methyl-1,4-dioxaspiro[4,6]undecan-7-ol (24b)

Bu_4NF (1.0 M in THF, 2.56 mL, 2.56 mmol) was slowly added to a stirred solution of **23b** (133 mg, 0.44 mmol) in THF (4.0 mL) (Ar atmosphere) and stirring was continued for 30 min. MeOH (4.0 mL), H_2O_2 (30 wt% in water, 1.08 mL, 10.6 mmol) and $KHCO_3$ (176 mg, 1.76 mmol) were added sequentially and stirring was continued for 23 h. The reaction mixture was evaporated. Et_2O (*ca.* 10 mL) and silica gel (*ca.* 2 g) were added and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top a column of flash chromatography silica gel (1.5 × 15 cm) made up with hexanes. Flash chromatography, using a 10–15% acetone–hexanes gradient, gave **24b** (56.8 mg, 69%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 3434, 2933, 2692, 1458 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (d, J = 7.0 Hz, 3 H), 1.44–1.57 (m, 2 H), 1.61–1.74 (m, 2 H), 1.74–1.94 (m, 4 H), 2.04–2.14 (m, 1 H), 3.03 (d, J = 7.0 Hz, 1 H), 3.64 (d, J = 6.0 Hz, 1 H), 3.84–4.04 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1 (q), 20.8 (t), 22.0 (t), 33.3 (t), 33.4 (t), 47.6 (d), 64.1 (t), 64.6 (t), 76.8 (d), 113.8 (s); exact mass (EI) calcd for $C_{10}H_{18}O_3$ $(M)^+$ 186.1256, found 186.1257.

6-Methyl-1,4-dioxaspiro[4,6]undecan-7-one (25b)

N-Methylmorpholine *N*-oxide (44.4 mg, 0.38 mmol), powdered 4 Å molecular sieves (127 mg) and Pr_4NRuO_4 (8.9 mg, 0.025 mmol) were added sequentially to a stirred solution of **24b** (47.2 mg, 0.253 mmol) in CH_2Cl_2 (5 mL) (Ar atmosphere). After 25 min, the solution was applied directly to the top of a column of flash chromatography silica gel (1.3 × 8 cm) made up with hexanes. Flash chromatography, using 10% acetone–hexanes, gave **25b** (44 mg, 94%) as an oil: FTIR ($CDCl_3$, cast) 2980, 2886, 1703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.14 (d, J = 7.0 Hz, 3 H), 1.60–1.86 (m, 5 H), 1.92–2.02 (m, 1 H), 2.48–2.64 (m, 2 H), 2.96 (q, J = 7.0 Hz, 1 H), 3.86–4.02 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.6 (q), 23.9 (t), 24.0 (t), 37.6 (t), 43.1 (t), 55.6 (d), 64.7 (t), 65.1 (t), 109.4 (s), 212.4 (s); exact mass (EI) calcd for $C_{10}H_{16}O_3$ $(M)^+$ 184.1099, found 184.1099.

2-Methylcycloheptane-1,3-dione (21b)[31] from (25b)

A 1 : 10 mixture (1.0 mL) of hydrochloric acid (1 M) and THF was added to a stirred solution of **25b** (40.7 mg, 0.22 mmol) in THF (3 mL). The mixture was refluxed for 17 h and then cooled to room temperature. Silica gel (*ca.* 1 g) was added to the mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top of a column of flash chromatography silica gel (1.5 × 10 cm) made up with hexanes. Flash chromatography, using a 5–10% acetone–hexanes gradient, gave **21b** [22 mg, 71% or 82% corrected for recovered **25b** (5.4 mg)] as an oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (d, J = 7.0 Hz, 3 H), 1.84–1.94 (m, 2 H), 2.00–2.10 (m, 2 H), 2.46–2.55 (m, 2 H), 2.55–2.64 (m, 2 H), 3.73 (q, J = 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.2 (q), 25.8 (t), 43.4 (t), 60.9 (d), 208.0 (s).

trans-2-Methyl-3-(pentamethyldisilan-1-yl)cyclopentan-1-one (22c)

MeLi (1.6 M in Et_2O, 1.88 mL, 3.0 mmol) was added slowly to a stirred and cooled (0 °C) solution of $Me_3SiSiMe_3$ (1.25 mL, 6.0 mmol) in dry HMPA (4.0 mL) (Ar atmosphere). After 30 min, the reaction mixture was diluted over 40 min in a dropwise manner with THF (12.0 mL) and the orange solution was then cooled to −78 °C. Cyclopent-2-en-1-one (0.15 mL, 1.5 mmol) was added dropwise over *ca.* 5 min and stirring was continued for 1 h. MeI (1.02 mL, 15.0 mmol) in THF (3 mL) was added slowly, the cold bath was left in place, but not recharged, and stirring was continued for 3 h during which time the mixture reached room temperature. The mixture was quenched with saturated aqueous NH_4Cl (*ca.* 3 mL) and stirring was continued for 5 min. The mixture was then diluted with water (30 mL) and extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.8 × 18 cm), using 10% EtOAc–hexanes, gave **22c** (322 mg, 94%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 2952, 2894, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06–0.14 (m, 15 H), 1.00–1.10 (m, 1 H), 1.11 (d, J = 7.0 Hz, 3 H), 1.54–1.66 (m, 1 H), 1.91 (sextet, J = 6.5 Hz, 1 H), 1.99–2.08 (m, 1 H), 2.08–2.18 (m, 1 H), 2.33 (dd, J = 19.0, 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.5 (q), −4.9 (q), −1.5 (q), 15.1 (q), 23.9 (t), 31.6 (d), 38.2 (t), 46.7 (d), 222.6 (s); exact mass (EI) calcd for $C_{11}H_{24}OSi_2$ $(M)^+$ 228.1366, found 228.1365.

1,1,1,2,2-Pentamethyl-2-[*trans*-6-methyl-1,4-dioxaspiro[4,4]-nonan-7-yl]disilane (23c)

Ethylene glycol (1.24 mL, 22.1 mmol) and TsOH (19 mg, 0.11 mmol) were added sequentially to a solution of **22c** (253 mg, 1.11 mmol) in C_6H_6 (10 mL). The solution was refluxed for 6 h, using a Dean-Stark apparatus. The solution was cooled, quenched with saturated aqueous $NaHCO_3$ (*ca.* 20 mL) and water (*ca.* 10 mL) and extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford **23c** (285 mg, 95%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 2951, 2879, 1245 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.02–0.12 (m, 15 H), 0.86–1.00 (m, 1 H), 0.93 (d, J = 7.0 Hz, 3 H), 1.40–1.51 (m, 1 H), 1.68–1.81 (m, 3 H), 1.84–1.92 (m, 1 H), 3.82–3.98 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −5.7 (q), −4.8 (q), −1.5 (q), 14.5 (q), 24.4 (t), 30.4 (d), 36.2 (t), 43.5 (d), 64.6 (t), 64.8 (t), 119.2 (s); exact mass (EI) calcd for $C_{12}H_{25}O_2Si_2$ $(M - CH_3)^+$ 257.1393, found 257.1393.

***trans*-6-Methyl-1,4-dioxaspiro[4.4]nonan-7-ol (24c)**[37]

Bu_4NF (1.0 M in THF, 1.10 mL, 1.10 mmol) was slowly added to a stirred solution of **23c** (50.1 mg, 0.184 mmol) in THF (4.0 mL) (Ar atmosphere). After 20 min MeOH (4.0 mL), H_2O_2 (30 wt% in water, 0.45 mL, 4.42 mmol) and $KHCO_3$ (74 mg, 0.74 mmol) were added sequentially and stirring was continued for 20 h. Without aqueous workup, silica gel (*ca.* 1 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top a column of flash chromatography silica gel (1.3 × 15 cm) made up with hexanes. Flash chromatography, using a 10–20% acetone–hexanes gradient, gave **24c** (20.6 mg, 70%) as an oil which was the *trans* isomer: FTIR ($CDCl_3$, cast) 3425, 2968, 1457 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.97 (d, J = 7.0 Hz, 3 H), 1.56–1.66 (m, 1 H), 1.81 (ddd, J = 13.5, 10.0, 7.0 Hz, 1 H), 1.88–2.00 (m, 2 H), 2.02–2.15 (m, 2 H), 3.81 (br s, 1 H), 3.85–3.96 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.5 (q), 30.9 (t), 31.1 (t), 49.0 (d), 64.4 (t), 64.8 (t), 77.5 (d), 116.8 (s); exact mass (EI) calcd for $C_8H_{14}O_3$ $(M)^+$ 158.0943, found 158.0943.

6-Methyl-1,4-dioxaspiro[4.4]nonan-7-one (25c)[39]

N-Methylmorpholine *N*-oxide (67.6 mg, 0.58 mmol), powdered 4 Å molecular sieves (193 mg) and Pr_4NRuO_4 (TPAP, 13.5 mg, 0.0385 mmol) were added sequentially to a stirred solution of **24c** (60.9 mg, 0.385 mmol) in CH_2Cl_2 (6 mL) (Ar atmosphere). After 30 min, the solution was applied directly to the top of a column of flash chromatography silica gel (1.5 × 6 cm) made up with hexanes. Flash chromatography, using 15% acetone–hexanes, gave **25c** (46.5 mg, 77%) as an oil: FTIR ($CDCl_3$, cast) 2979, 2886, 1748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (d, J = 7.0 Hz, 3 H), 2.04 (dt, J = 13.5, 10.5 Hz, 1 H), 2.12–2.20 (m, 1 H), 2.30–2.40 (m, 1 H), 2.42–2.51 (m, 2 H), 3.97–4.07 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.2 (q), 32.1 (t), 36.6 (t), 51.6 (d), 65.2 (t), 65.4 (t), 114.4 (s), 215.5 (s); exact mass (EI) calcd for $C_8H_{12}O_3$ $(M)^+$ 156.0786, found 156.0787.

3-Hydroxy-2-methylcyclopent-2-en-1-one (21c)[40]

A 1 : 10 mixture (1.0 mL) of hydrochloric acid (1 M) and THF was added to a stirred solution of **25c** (40.5 mg, 0.26 mmol) in THF (5 mL) and stirring was continued for 2.5 h. Without aqueous workup, silica gel (*ca.* 1 g) was added to the reaction mixture and the solvent was evaporated *in vacuo* at room temperature (rotary evaporator, water pump). The residue was added to the top of a column of flash chromatography silica gel (1.3 × 10 cm) made up with hexanes. Flash chromatography, using a 30–50% acetone–hexanes gradient, gave **21c** (20.6 mg, 71%) as a solid: mp 208–210 °C (lit.[40] 214–216 °C); ^1H NMR (500 MHz, DMSO-d_6) δ 1.46 (s, 3 H), 2.33 (s, 4 H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 5.8, 30.0, 111.5.

Acknowledgements

We thank NSERC for financial support and Professor M. Lopp (Department of Chemistry, Tallinn Technical University) for experimental details on the preparation of 3-hydroxy-2-methylcyclohexanone.

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