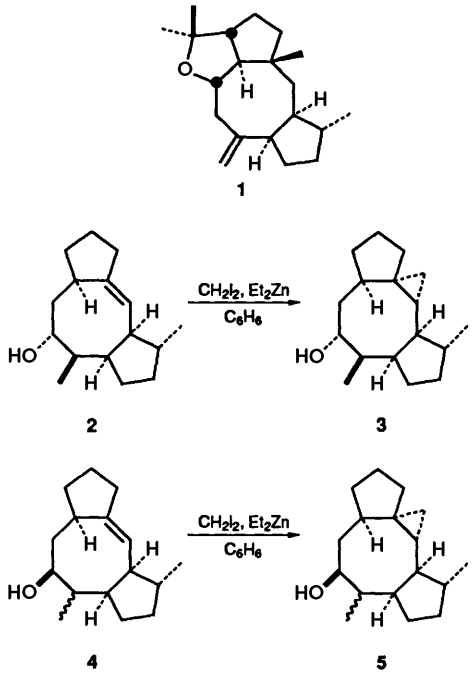
A Method for Intramolecular *Syn* Delivery of an Alkyl Group to the Proximal Olefinic Carbon in Cyclooct-5-enols†

Dirk Friedrich‡ and Leo A. Paquette*
Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210 USA

Various functionalized derivatives of *trans*-2,6-dimethylcyclooct-5-enol have been prepared and found to be recalcitrant to free radical or ionic six-ring cyclization with formation of a new carbon–carbon bond *syn* to the original hydroxy group at the pro-quaternary site. However, intramolecular *syn* delivery was achieved with complete regiocontrol by epoxidation/ring opening of the MOM ether, oxidation to the α,β-unsaturated ketone **35a**, Rh^{I}-catalysed hydrosilylation to give **36**, and exposure of this silyl enol ether to stannic chloride in the presence of 'proton sponge'. The pivotal ring closure leads in good yield to **32**, thereby solving the problem posed by untoward kinetic barriers to ring closure that are present under alternative conditions.

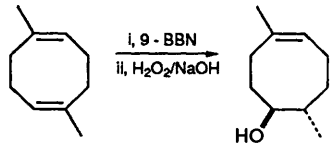
In the course of developing a synthetic approach to epoxydictymene **1**,[1] we have observed that the model cyclooctenols **2** and **4** uniformly undergo Simmons–Smith cyclopropanation from the less sterically hindered α face to give **3** and **5**, respectively.[2] The inability of the hydroxy group in **4** to coax the attacking carbenoid into *syn* addition[3] was construed to be an indication of substantive steric crowding within the interior of the tub conformation adopted by this medium-ring alcohol.

The cyclopropanation step was to be followed by the regiocontrolled hydrogenolysis of the strained ring so as to introduce the angular β-methyl group found in **1**. However, the



1 **2** **3** **4** **5**

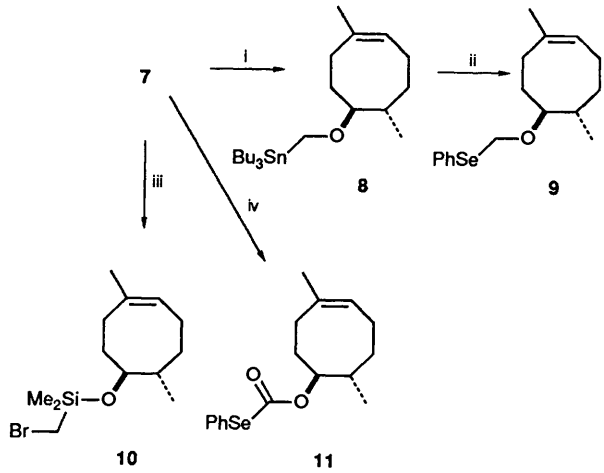
ineffectiveness of precomplexation as a means of achieving β attack prompted a search for an alternative means of transannular alkyl group delivery from hydroxy to the proximal olefinic centre. In view of the readily availability of the alcohol **7** from commercially available diene **6**, this substrate was selected as a test system for assessing possible ways in which a C–C bond could be introduced with regio- and stereo-specific generation of a quaternary centre.



6 **7**

Results and Discussion

Hydroboration of **6** with 9-BBN[4] allowed for controlled monohydroboration. However, because commercial **6** contains 25% of the 1,4-dimethyl isomer, preparative HPLC was required to acquire quantities of **7** sufficiently pure (>95%) for our purposes. Conversion of **7** into **8**–**14** was next performed in order to investigate several possible avenues of transannular alkylation (Schemes 1 and 2). The alkoxystannane **8**, obtained in 84% yield,[5] was utilized to produce the selenide **9** (93%).[6] Direct derivatization of the alcohol provided the bromomethylsilane **10** (99%),[7] the selenocarbonate **11** (86%),[6c,8] the



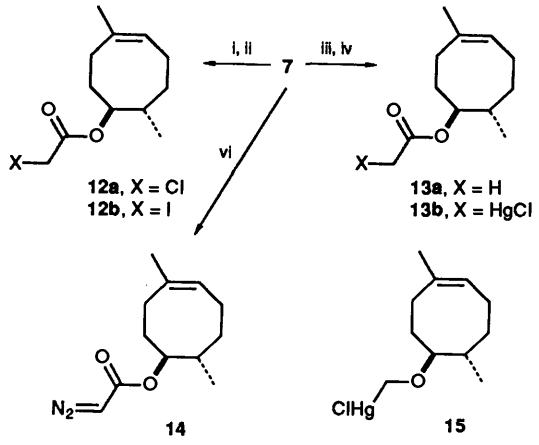
8 **9** **10** **11**

Scheme 1 *Reagents and conditions:* i, Bu_3SnCH_2I, KH, 18-crown-6; ii, BuLi, $(PhSe)_2$; iii, $ClMe_2SiCH_2Br$, Et_3N; iv, $COCl_2$, py; PhSeH, py

† This paper was submitted to mark the 150th anniversary of the Chemical Society/Royal Society of Chemistry.

‡ Postdoctoral Fellow of the Wigner-Stiftung der Technischen Universität Berlin (1989–1990) and the Deutsche Forschungsgemeinschaft (1990–1991).

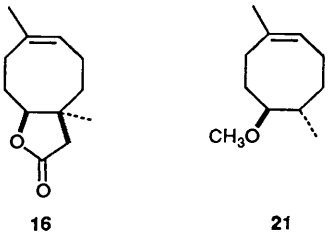
iodoacetate **12b** (94%),[9] the chloromercuriacetate **13b** (96%),[10] and the diazoacetate **14** (95%).[11] Attempts to obtain **15** by tin–lithium exchange of **8** and subsequent condensation with mercuric chloride failed. At −78 °C, a substantial amount of elemental mercury was formed alongside a quite complex mixture of unidentified products.



Scheme 2 *Reagents and conditions:* i, $ClCH_2COCl$, py; ii, NaI, acetone; iii, Ac_2O, py; iv, LDA, $HgCl_2$; v, $TsNHN{=}CHCOCl$, $PhNMe_2$; vi, Et_3N, CH_2Cl_2, 0 °C

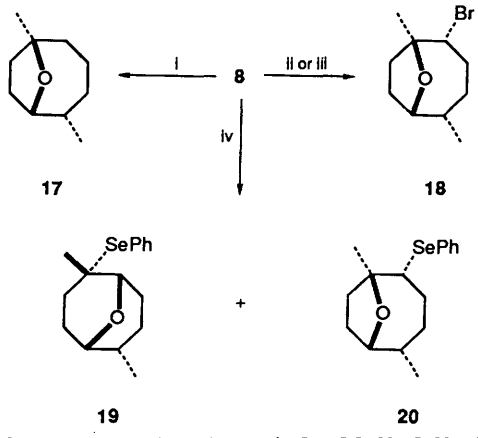
Attempted radical cyclization[6a,12] of the selenides **9** and **11** or the silane **10** under the usual conditions involving the slow addition of tributyltin hydride, triphenyltin hydride, or tris(trimethylsilyl)silane to refluxing benzene or toluene solutions containing AIBN[6–8] resulted only in net reduction. Alternative recourse to tributyltin hydride and triethylborane on solutions of **9** and **11** in benzene at 25 °C held open to the air[6c,13] did not alter the eventual outcome. Irradiation of **12b** at 254 or 300 nm in the presence of hexamethylditin[9] induced double bond migration, but not carbon–carbon bond formation. When heated in HMPA containing tetrakis(triphenylphosphine)palladium and 'proton sponge' at 80 °C for 18 h,[14] **12b** was observed to decompose slowly.

Our inability to accomplish the desired cyclization persisted when **13b** was exposed to palladium(II) salts and triethylamine in CD_3CN–$CDCl_3$ at room temperature or 330 K. Here again, several ill-defined substances were produced. Slow addition of **14** to a refluxing solution of a soluble Cu^{II} catalyst in toluene[11] gave rise in low yield to **16**. The main reaction pathway consisted of dimerization to the fumarate.



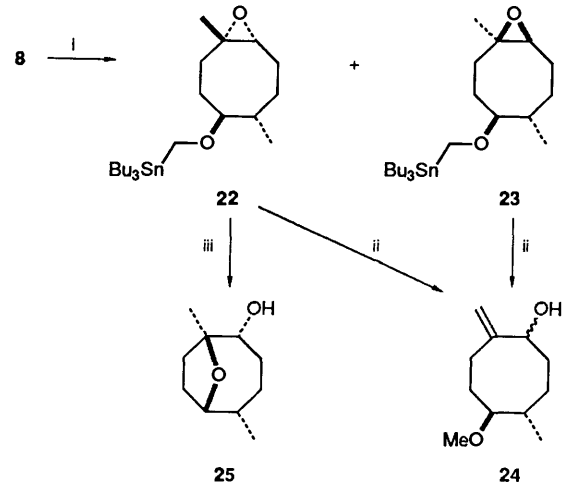
The situation changed dramatically when the stannane **8** was treated with a variety of electrophilic reagents.[15] However, although cyclization did materialize in most instances, the nucleophile was the ether oxygen and not the intended C–Sn σ bond. Examples illustrating the response to trifluoroacetic acid, cupric bromide (in MeCN), *N*-bromosuccinimide, and benzeneselenenyl chloride are shown in Scheme 3.

In contrast to precedent,[16] tin–lithium exchange in **8** did not result in ring closure at temperatures up to 25 °C. Following the addition of water, either pure **7** (in DME) or a mixture of **7** and **21** (in THF or THF–TMEDA) was isolated. *N*-(Phenylseleno)-



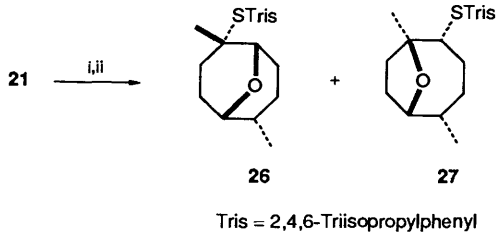
Scheme 3 *Reagents and conditions:* i, CF_3CO_2H, C_6H_6; ii, $CuBr_2$, CH_3CN; iii, NBS, $CHCl_3$; iv, PhSeCl, C_6H_6

phthalimide[15c,d] proved unreactive toward **8**, while *meta*-chloroperbenzoic acid promoted clean conversion into a mixture of the epoxystannanes **22** and **23** (Scheme 4). Transmetallation of these epoxides[17] resulted only in conversion into the epimeric allylic alcohols **24**. Although **22** (but not **23**) was sensitive to the presence of catalytic quantities of pyridinium tosylate or chloride,[18] only C–O bond formation leading to **25** occurred.



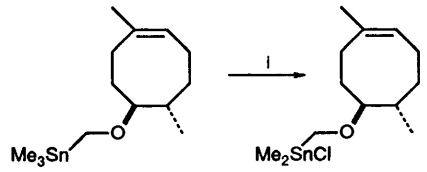
Scheme 4 *Reagents and conditions:* i, MCPBA; ii, BuLi; iii, Py·HOTs or 4-ClPy·HCl, MeCN–$CHCl_3$

The obvious kinetic bias for formation of a tetrahydrofuran ring was manifested again when the methyl ether **21** was subjected to Reetz conditions[19] in an attempt to introduce an angular methyl group directly (Scheme 5).



Scheme 5 *Reagents and conditions:* i, 2,4,6-$Pr^i_3C_6H_2SCl$; ii, Me_3Al

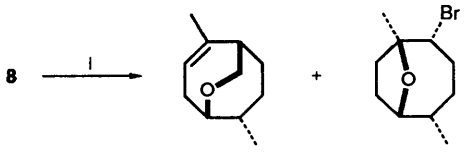
This pathway was not followed invariably. For example, the trimethylstannane **28** reacted cleanly with mercuric chloride in acetonitrile.[18] The lone product proved to be **29** resulting from selective methyl–tin cleavage (Scheme 6). No electrophilic attack on the double bond was in evidence.



28 29

Scheme 6 *Reagents and conditions:* i, $HgCl_2$, $CH_3CN/CHCl_3$

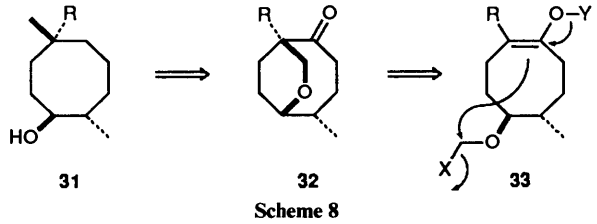
Transannular C–C bond formation was ultimately encountered when **8** was stirred with cupric bromide in dichloromethane[20] rather than in acetonitrile as before. However, the major product proved to be **30** where intramolecular reaction had clearly occurred at the less substituted olefinic carbon with double bond migration. The minor constituent was the previously characterized bromide **18** (Scheme 7). Small amounts of **30** were also formed on treatment of **8** with iodine in benzene solution.[21]



30 18

Scheme 7 *Reagents and conditions:* i, $CuBr_2$, CH_2Cl_2

Since conventional radical and ionic processes proved ineffective at accomplishing the desired objective, the polarity of the double bond was reversed in order to achieve the desired regiochemical outcome. The retrosynthetic analysis shown in Scheme 8 illustrates the manner in which an enol ether was expected to participate in directing proper introduction of a transannular C–C bond. When X = OR, the ring closure is seen to be a Mukaiyama-type reaction.[22]



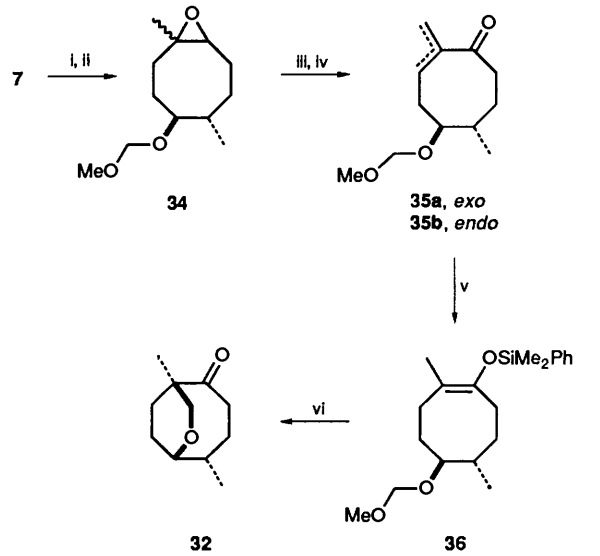
31 32 33

Scheme 8

Initial attempts to obtain the trimethylsilyl enol ether corresponding to **36** by reduction of **35** according to Saegusa[23] and direct addition of chlorotrimethylsilane proved inefficient. Considerable improvement was realized when a hydrosilylation alternative was employed[24] (Scheme 9), although the reluctance of the endocyclic enone **35b** to undergo 1,4-reduction in this manner persisted.

When **36** was treated with titanium tetrachloride in dichloromethane at −78 °C, the desired cyclization did indeed occur, but simple hydrolysis and cleavage of the MOM protecting group took place concurrently. Some improvement was noted when stannic chloride was substituted as Lewis acid; boron trifluoride–diethyl ether induced hydrolysis and unmasking of the hydroxy group exclusively. The most suitable conditions involved exposure of **36** to $SnCl_4$ catalysis in the presence of 'proton sponge' to guard against the build-up of hydrogen chloride in the reaction mixture. These optimal conditions afforded **32** in 69% isolated yield. The structural assignment to this bicyclic ketone was confirmed by extensive proton decoupling, $^1H/^1H$ COSY and $^1H/^{13}C$ COSY experiments.

This completely regioselective sequence constitutes a convenient means for installing a quaternary carbon at the appropriate distance from the site of hydroxy substitution. Furthermore, the new C–C bond is necessarily *syn* to the original OH functionality, thereby setting the state for ultimate conversion into an angular β-methyl group. Studies now in progress are aimed at adapting this methodology to a total synthesis of **1**.



Scheme 9 *Reagents and conditions:* i, $ClCH_2OMe$, Pr^2NEt; ii, MCPBA; iii, $LiNPr^i_2$, THF, 25 °C; iv, $(COCl)_2$, DMSO, CH_2Cl_2; EtN; v, $PhMe_2SiH$, $(Ph_3P)_3RhCl$, C_6H_6; vi, $SnCl_4$, proton sponge, CH_2Cl_2

Experimental

General experimental protocols have been described previously.[2,25] In addition *J* values are in Hz and ether refers to diethyl ether.

trans-2,6-*Dimethylcyclooct*-5-*enol* **7**.—Cycloocta-1,5-diene (16.7 g, 154.4 mmol) was added during 5 min to a solution of the borane–THF complex (1.0 mol dm^{-3}; 15 ml, 150 mmol) in dry tetrahydrofuran (500 ml). After initial cooling of the flask with tap water, the reaction mixture was stirred at room temperature for 24 h. Commercial dimethylcycloocta-1,5-diene (75:25 mixture of the 1,5- and 1,4-isomers, 20.0 g, 146.8 mmol) was introduced in one portion followed 18 h later by 20% aqueous NaOH (70 ml), water (40 ml) and 30% H_2O_2 (45 ml). The latter were added slowly at such a rate as to keep the exothermic oxidation under control. Once the mixture had cooled, the work-up consisted of partitioning between ether and brine, followed by drying and concentration of the organic phase. HPLC on silica gel (elution with light petroleum–ethyl acetate, 4:1) gave the isomeric alcohol mixture (15.6 g, 69%), from which **7** (8.45 g, 49%) was acquired as a colourless oil when rechromatographed in smaller batches; $\nu_{max}(CCl_4)/cm^{-1}$ 3625 and 3550–3250; δ_H(300 MHz; $CDCl_3$) 0.98 (3 H, d, *J* 7), 1.32 (1 H, dddd, *J* 14, 10, 6 and 4.5), 1.55–1.72 (2 H, m), 1.71 (3 H, br s), 1.84 (1 H, dddq, *J* 10, 7.5, 3.5 and 7), 1.92–2.06 (1 H, m), 2.07–2.31 (4 H, m), 3.54 (1 H, td, *J* 7.5 and 3.5) and 5.33 (1 H, br t, *J* 8); δ_C(75 MHz; $CDCl_3$) 18.3, 24.2, 25.0, 28.2, 35.2, 35.3, 37.2, 75.4, 123.4 and 137.4 (Found M^+, 154.1369. Calc. for $C_{10}H_{18}O$: *M*, 154.1358).

trans-2,6-*Dimethyl*-5-(*tributylstannylmethoxy*)*cyclooctene* **8**.—A solution of **7** (5.0 g, 32.4 mmol) in dry tetrahydrofuran (20 ml) was added during 5 min to a cold (0 °C), magnetically stirred suspension of oil-free potassium hydride (1.67 g, 41.6 mmol) in tetrahydrofuran (20 ml) and the mixture was stirred at

room temperature for 2 h. Following the introduction of 18-crown-6 (5.0 g, 18.9 mmol) in the same solvent (10 ml), (iodomethyl)tributylstannane (20.0 g, 46.4 mmol) in tetrahydrofuran (20 ml) was added dropwise at 0 °C during 10 min. The resulting thick slurry was stirred at room temperature for 1 h, quenched at 0 °C with water, and diluted with ether. Washing with water and brine, drying and evaporation gave a residue that was purified by flash chromatography on silica gel (elution with light petroleum) to give **8** as a colourless oil (13.18 g, 89%); $\nu_{max}(CCl_4)/cm^{-1}$ 1465, 1440, 1375 and 1060; δ_H(300 MHz, C_6D_6) 1.00 (9 H, t, *J* 7), 0.94–1.17 (6 H, m), 1.15 (3 H, d, *J* 7), 1.24–1.35 (1 H, m), 1.44 (6 H, tq, *J* 7.5 and 7), 1.73 (3 H, br s), 1.54–1.82 (8 H, m), 1.92 (1 H, dddq, *J* 10, 7.5, 3 and 7), 1.95–2.10 (2 H, m), 2.14–2.39 (3 H, m), 2.90 (1 H, td, *J* 7.5 and 3), 3.52 (1 H, d, *J* 9.5), 3.96 (1 H, d, *J* 9.5) and 5.36 (1 H, br t, *J* 8); δ_C(75 MHz, C_6D_6) 9.3 (3 C), 14.0 (3 C), 19.3, 24.9, 25.7, 27.8 (3 C), 28.9, 29.7 (3 C), 29.9, 36.0, 37.0, 60.3, 89.2, 123.2 and 137.2; $\delta_{Sn}(^{119}Sn$, 112 MHz, C_6D_6) −37.7 (Found: $M^+ - C_4H_9$, 401.1905. Calc. for $C_{19}H_{37}O^{120}Sn$: *M*, 401.1866).

trans-2,6-*Dimethyl*-5-(*phenylselenenylmethoxy*)*cyclooctene* **9**.—Butyllithium (1.5 mol dm^{-3} in hexane; 0.40 ml, 0.60 mmol) was added during 30 s to a cold (−78 °C), magnetically stirred solution of **8** (200 mg, 0.437 mmol) in dry tetrahydrofuran (6 ml). After 2.5 min, a solution of diphenyl diselenide (200 mg, 0.641 mmol) in tetrahydrofuran (2 ml) was added during 1 min at −78 °C. After an additional 10 min at this temperature, the cooling bath was removed and the reaction mixture was quenched with saturated aqueous ammonium chloride at 0 °C. The product was isolated by partitioning between light petroleum and brine, followed by flash chromatography on silica gel (elution with light petroleum, then light petroleum–ether, 50:1). Pure **9** was isolated as a colourless oil (132 mg, 93%); $\nu_{max}(CCl_4)/cm^{-1}$ 1575, 1475, 1435, 1375, 1080, 1065 and 690; δ_H(300 MHz, C_6D_6) 1.04 (3 H, d, *J* 7), 1.24 (1 H, dddd, *J* 14, 10.5, 6.5 and 5), 1.44–1.59 (2 H, m), 1.66 (3 H, br s), 1.77–2.07 (4 H, m), 2.08–2.26 (2 H, m), 3.44 (1 H, td, *J* 8 and 3.5), 5.08 (1 H, d, *J* 9.5 Hz), 5.20 (1 H, d, *J* 9.5), 5.31 (1 H, br t, *J* 8), 6.98–7.10 (3 H, m) and 7.63–7.69 (2 H, m); δ_C(75 MHz, C_6D_6) 19.3, 24.5, 25.7, 28.4, 30.9, 35.8, 36.8, 71.7, 82.6, 123.4, 126.8, 129.2 (2 C), 132.1, 132.6 (2 C) and 136.8 (Found: $M^+ - C_6H_5Se$, 167.1470. Calc. for $C_{11}H_{19}O$: *M*, 167.1436).

trans-5-(*Bromomethyldimethylsiloxy*)-2,6-*dimethylcyclooctene* **10**.—Bromomethylchlorodimethylsilane (0.50 ml, 3.67 mmol) was added during 5 min to a cold (0 °C), magnetically stirred solution of **7** (500 mg, 3.28 mmol), triethylamine (0.60 ml, 4.30 mmol) and 4-(dimethylamino)pyridine (40 mg) in dry dichloromethane (5 ml). The reaction mixture was stirred at room temperature for 1 h, diluted with light petroleum, and washed sequentially and rapidly with water, 5% HCl, water, and brine prior to drying. Filtration through silica gel (elution with light petroleum–ether, 9:1) and removal of solvent afforded pure **10** as a colourless oil (990 mg, 99%); $\nu_{max}(CCl_4)/cm^{-1}$ 2955, 2930, 1255, 1075, 1050 and 840; δ_H(300 MHz, C_6D_6) 0.21 (2 × 3 H, two resolved s, $\Delta\delta$ 0.05 ppm), 0.98 (3 H, d, *J* 7), 1.19 (1 H, dddd, *J* 14, 10.5, 6.5 and 4.5), 1.48–1.62 (2 H, m), 1.69 (3 H, br s), 1.82 (1 H, dddq, *J* 10.5, 8, 3.5 and 7), 1.90–2.07 (3 H, m), 2.28 (2 H, s), 2.10–2.38 (2 H, m), 3.56 (1 H, td, *J* 8 and 3.5) and 5.39 (1 H br, t, *J* 8); δ_C(75 MHz, C_6D_6) −2.7, −2.6, 16.5, 19.8, 24.5, 25.9, 28.4, 35.7, 36.1, 37.9, 77.0, 123.3 and 136.9 (Found: M^+, 306.0860. Calc. for $C_{13}H_{25}{}^{81}BrOSi$: *M*, 306.0838).

trans-2,6-*Dimethylcyclooct*-5-*enyl Phenylselenocarbonate* **11**.—A toluene solution of phosgene (0.93 mol dm^{-3}; 2.1 ml, 4.05 mmol) was added in one portion at room temperature to a solution of **7** (200 mg, 1.30 mmol) and pyridine (0.20 ml, 2.48 mmol) in dry tetrahydrofuran (10 ml). After 30 min, approximately 75% of the solvents were removed under reduced pressure without external heating in order to rid the system of excess of phosgene. After dilution with tetrahydrofuran (5 ml) and benzene (5 ml), pyridine (0.25 ml, 3.11 mmol) was again introduced, followed by a solution of benzeneselenol (270 mg, 1.72 mmol) in benzene (5 ml). The mixture was stirred at room temperature for 2 h, diluted with ether and washed sequentially with 5% HCl, water and brine. Purification was realized by flash chromatography on silica gel (elution with light petroleum–ether, 25:1) to give **11** as an almost colourless oil (376 mg, 86%); $\nu_{max}(CCl_4)/cm^{-1}$ 1725; δ_H(300 MHz, C_6D_6) 0.97 (3 H, t, *J* 7), 1.19 (1 H, dddd, *J* 14, 10.5, 6.5 and 4.5), 1.37 (1 H, dddd, *J* 14, 10, 4.5 and 3.5), 1.50–1.61 (1 H, m), 1.58 (3 H, br s), 1.72–2.12 (6 H, series of m), 5.02–5.10 (1 H, m), 5.22 (1 H, br t, *J* 8), 7.01–7.07 (3 H, m) and 7.61–7.69 (2 H, m); δ_C(75 MHz, C_6D_6) 18.9, 24.2, 25.5, 28.1, 32.4, 35.3, 36.4, 83.0, 123.5, 127.0, 128.9, 129.3 (2 C), 136.1 (2 C), 136.4 and 165.8 [Found: $M^+ - (C_6H_5Se + CO_2)$, 137.1369. Calc. for $C_{10}H_{17}$: *M*, 137.1330].

trans-2,6-*Dimethylcyclooct*-5-*enyl Chloroacetate* **12a**.—Chloroacetyl chloride (0.20 ml, 2.51 mmol) was added to a cold (0 °C), magnetically stirred solution of **7** (250 mg, 1.64 mmol), pyridine (0.50 ml, 6.2 mmol) and 4-(dimethylamino)pyridine (20 mg) in dry dichloromethane (5 ml). After being stirred for 2 h at room temperature, the reaction mixture was treated with water to destroy the excess of acid chloride, diluted with ether and washed sequentially with 5% HCl, water, dilute NaOH, water and brine. Drying and solvent evaporation gave **12a** as a faint yellow oil (362 mg, 96%); ν_{max}(neat)/cm^{-1} 1755 and 1730; δ_H(300 MHz, $CDCl_3$) 0.88 (3 H, d, *J* 7), 1.38 (1 H, dddd, *J* 13.5, 11, 6.5 and 4.5), 1.70 (3 H, br s), 1.54–1.71 (2 H, m), 1.96 (1 H, dddq, *J* 11, 7.5, 3.5 and 7), 2.13 (1 H, br ddd, *J* 14.5, 7 and 3.5), 2.28 (1 H, br ddd, *J* 14.5, 10.5 and 4), 1.97–2.30 (3 H, series of m), 4.01 (2 H, s), 4.85 (1 H, td, *J* 8.5 and 3.5) and 5.35 (1 H, br t, *J* 8); δ_C(75 MHz, $CDCl_3$) 18.2, 24.1, 25.3, 27.9, 32.1, 35.3, 35.9, 41.1, 80.0, 123.4, 136.4 and 166.7 (Found: M^+, 230.1040. Calc. for $C_{12}H_{19}{}^{35}ClO_2$: *M*, 230.1069).

trans-2,6-*Dimethylcyclooct*-5-*enyl Iodoacetate* **12b**.—A solution of **12a** (335 mg, 1.52 mmol) in acetone (6 ml) was stirred with sodium iodide (1.0 g, 6.67 mmol) and some anhydrous $MgSO_4$ with protection from light for 4 h at 25 °C. After dilution with ether, filtration and solvent evaporation, the residue was processed by partitioning between ether and water, and washing of the organic phase with dilute aqueous sodium thiosulphate and aqueous sodium hydrogencarbonate and then brine. Drying and solvent evaporation afforded **12b** as a light orange oil (459 mg, 98%); ν_{max}(neat)/cm^{-1} 1720; δ_H(300 MHz, $CDCl_3$) 0.91 (3 H, d, *J* 7) 1.38 (1 H, dddd, *J* 14, 11, 6 and 4.5), 1.54–1.70 (2 H, m), 1.71 (3 H, br s), 1.90–2.35 (6 H, series of m), 3.76 (2 H, s), 4.78 (1 H, td, *J* 8.5 and 3.5) and 5.34 (1 H, br t, *J* 8); δ_C(75 MHz, $CDCl_3$) −4.8, 18.3, 24.3, 25.2, 28.0, 31.8, 35.3, 35.9, 79.7, 123.3, 136.5 and 168.1 (Found: $M^+ - I$, 155.1400. Calc. for $C_{12}H_{19}O_2$: *M*, 155.1385).

trans-2,6-*Dimethylcyclooct*-5-*enol Chloromercuriacetate* **13b**.—Substitution of acetic anhydride (0.25 ml, 2.65 mmol) for chloroacetyl chloride as described for **12a** afforded acetate **13a** as a colourless oil (310 mg, 96%); ν_{max}(neat)/cm^{-1} 1735; δ_H(300 MHz, $CDCl_3$) 0.84 (3 H, d, *J* 7), 1.36 (1 H, dddd, *J* 13.5, 11, 6.5 and 4.5), 1.50–1.65 (2 H, m), 1.69 (3 H, br s), 1.88 (1 H, dddq, *J* 11, 7.5, 3.5 and 7), 2.00 (3 H, s), 2.13 (1 H, br ddd, *J* 14.5, 7 and 3.5), 2.25 (1 H, br ddd, *J* 14.5, 10.5 and 4), 1.91–2.28 (3 H, series of m), 4.76 (1 H, td, *J* 8.5 and 3.5) and 5.32 (1 H, br t, *J* 8); δ_C(75 MHz, $CDCl_3$) 18.2, 21.1, 24.2, 25.3, 28.1, 32.4, 35.3, 35.8, 77.5, 123.3, 136.5 and 170.4 (Found: M^+, 196.1452. Calc. for $C_{12}H_{20}O_2$: *M*, 196.1463).

A solution of the acetate (110 mg, 0.56 mmol) in dry tetra-

hydrofuran was added during 2 min to a cold (−78 °C), magnetically stirred solution of LDA [from diisopropylamine (0.12 ml, 0.856 mmol) and butyllithium (1.5 mol dm^{-3} in hexane; 0.05 ml, 0.75 mmol)] in tetrahydrofuran (4 ml). This mixture was stirred at −78 °C for 40 min, treated with a solution of mercuric chloride (500 mg, 1.84 mmol) in the same solvent and agitated for 30 min longer. Following the addition of saturated aqueous NH_4Cl and ether, the separated organic phase was washed with 5% HCl, water, and brine prior to drying and solvent evaporation to give **13b** as a colourless, viscous oil (243 mg, 99%); $\nu_{max}(CCl_4)/cm^{-1}$ 1710 and 1685; δ_H(300 MHz, C_6D_6) 0.93 (3 H, d, *J* 7), 1.28–1.62 (4 H, series of m), 1.68 (3 H, br s), 1.93 (2 H, s), 1.75–2.22 (5 H, series of m), 4.92 (1 H, ddd, *J* 9, 8 and 3.5) and 5.32 (1 H, br t, *J* 8); δ_C(75 MHz, C_6D_6) 18.9, 24.3, 25.7, 28.3, 30.8, 32.7, 35.7, 36.5, 77.8, 123.8, 136.5 and 171.4 (Found: $M^+ - C_2H_2O$, 390.0670. Calc. for $C_{10}H_{17}{}^{35}Cl^{202}HgO$: *M*, 390.0669).

trans-2,6-*Dimethylcyclooct*-5-*enyl Diazoacetate* **14**.—Freshly recrystallized glyoxylic acid chloride toluenesulphonylhydrazone (250 mg, 0.959 mmol) was added in one portion to a cold (0 °C) solution of **7** (100 mg, 0.648 mmol) in dry dichloromethane (6 ml). Upon addition of *N*,*N*-dimethylaniline (0.12 ml, 0.951 mmol), the initial pale yellow colour gradually darkened. After 15 min at 0 °C, TLC analysis indicated the esterification to be complete. Triethylamine (0.50 ml, 3.62 mmol) was introduced in one portion at 0 °C. After 30 min, the reaction mixture was diluted with ether and washed rapidly with 5% HCl, water and brine containing some $NaHCO_3$. Silica gel chromatography of the residue (elution with light petroleum–ether, 9:1) gave **14** as a pale yellow oil (138 mg, 95%); $\nu_{max}(CCl_4)/cm^{-1}$ 2120 and 1695; δ_H(300 MHz, C_6D_6) 0.92 (3 H, d, *J* 7), 1.24–1.58 (3 H, series of m), 1.63 (3 H, br s), 1.76–2.19 (6 H, series of m), 4.16–4.22 (1 H, br m), 5.01 (1 H, td, *J* 8.5 and 3.5) and 5.28 (1 H, br t, *J* 8); δ_C(75 MHz, C_6D_6) 18.4, 24.2, 25.6, 28.2, 32.8, 35.6, 36.5, 45.6, 77.9, 123.7, 136.5 and 165.7 (Found: M^+, 222.1334. Calc. for $C_{12}H_{18}N_2O_2$: *M*, 222.1368).

Acid-catalysed Cyclization of **8**.—Neat trifluoroacetic acid (0.20 ml, 2.60 mmol) was added at room temperature to a stirred solution of **8** (500 mg, 1.093 mmol) in benzene (6 ml). A second 0.20 ml portion of CF_3CO_2H was added 24 h later. After a total elapsed time of 60 h, most of the benzene was evaporated and the residual oil was partitioned between ether and brine containing some $NaHCO_3$. Flash chromatography on silica gel (elution with light petroleum–ether, 9:1) afforded pure **17** (115 mg, 68%) as a colourless volatile oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1470, 1450, 1375, 1120 and 1040; δ_H(300 MHz, $CDCl_3$) 0.76 (3 H, d, *J* 7), 1.29 (3 H, s), 1.10–2.00 (11 H, series of m), 4.20 (1 H, dtd, *J* 8, 4 and 1); δ_C(75 MHz, $CDCl_3$) 17.2, 23.7, 23.9, 29.6, 32.8, 38.6, 41.5, 42.8, 81.3 and 83.4 (Found: M^+, 154.1362. Calc. for $C_{10}H_{18}O$: *M*, 154.1358).

Brominative Cyclization of **8**.—*N*-Bromosuccinimide (60 mg, 0.336 mmol) was added in one portion at room temperature to a solution of **8** (100 mg, 0.219 mmol) in chloroform (5 ml, pretreated with K_2CO_3). After 5 min, the solvent was evaporated and the residue was purified by flash chromatography on silica gel (elution with light petroleum–ether, 6:1) to give **18** as a colourless oil (47.3 mg, 93%); δ_H(300 MHz, $CDCl_3$) 0.83 (3 H, d, *J* 7), 1.45 (3 H, s), 1.48–1.73 (3 H, m), 1.84–1.98 (2 H, m), 1.98–2.18 (2 H, m), 2.30–2.42 (1 H, m), 2.58–2.69 (1 H, m), 4.26 (1 H, t, *J* 5) and 4.36 (1 H, dt, *J* 5.5 and 5.5); δ_C(75 MHz, $CDCl_3$) 17.1, 25.7, 28.5, 28.8, 35.3, 35.6, 38.0, 63.0, 84.5 and 85.9 (Found: M^+, 234.0455. Calc. for $C_{10}H_{17}{}^{81}BrO$: *M*, 234.0443).

Phenylselenation of **8**.—Benzeneselenenyl chloride (50 mg, 0.261 mmol) in benzene (1 ml) was added during 2 min to a solution of **8** (100 mg, 0.219 mmol) in benzene (5 ml). After 5 min, the solvent was evaporated and the residue was purified by flash chromatography on silica gel (elution with light petroleum–ether, 6:1) to give an inseparable mixture of **19** and **20** as a colourless oil (59 mg, 87%); $\nu_{max}(CCl_4)/cm^{-1}$ 1575 and 700 (Found: M^+, 310.0834. Calc. for $C_{16}H_{22}{}^{80}SeO$: *M*, 310.0836).

For **19**: δ_H(300 MHz, $CDCl_3$) 0.87 (3 H, d, *J* 7), 1.58 (3 H, s), 1.49–2.56 (9 H, series of m), 3.63 (1 H, br s, *J* 6), 3.67 (1 H, br 5, *J* 5.5), 7.23–7.39 (3 H, m) and 7.51–7.64 (2 H, m); δ_C(75 MHz, $CDCl_3$) 18.4, 22.2, 27.4, 27.6, 27.9, 34.1, 34.4, 50.1, 71.4, 74.8, 128.5, 128.6 (2 C), 134.6 and 138.1 (2 C).

For **20**: δ_H(300 MHz, $CDCl_3$) 0.82 (3 H, d, *J* 7), 1.54 (3 H, s), 1.49–2.56 (9 H, series of m), 3.52 (1 H, dd, *J* 5.5 and 3.5), 4.30 (1 H, dt, *J* 6.5 and 4.5), 7.23–7.39 (3 H, m) and 7.51–7.64 (2 H, m); δ_C(75 MHz, $CDCl_3$) 17.2, 25.4, 28.6, 29.9, 32.7, 37.0, 39.1, 58.2, 84.5, 85.4, 126.8, 127.3, 129.0 (2 C) and 134.1 (2 C).

trans-5-*Methoxy*-2,6-*dimethylcyclooctene* **21**.—The methyl ether of **7** was prepared in conventional manner (KH, THF, 0 °C; excess of MeI, 0 °C to room temperature), purified by flash chromatography and isolated as a colourless volatile oil; δ_H(300 MHz, $CDCl_3$) 0.95 (3 H, d, *J* 7), 1.27 (1 H, dddd, *J* 14, 10.5, 5.5 and 5), 1.50–1.70 (2 H, m), 1.69 (3 H, br s), 1.81 (1 H, dddq, *J* 10.5, 7.5, 3.5 and 7), 1.94–2.37 (5 H, series of m), 2.92 (1 H, td, *J* 7.5 and 3), 3.30 (3 H, s) and 5.29 (1 H, br t, *J* 8); δ_C(75 MHz, $CDCl_3$) 18.7, 24.7, 25.2, 28.5, 29.9, 35.4, 36.5, 57.7, 85.6, 122.7 and 137.1 (Found: M^+, 168.1552. Calc. for $C_{11}H_{20}O$: *M*, 168.1514).

Epoxidation of **8**.—Purified *meta*-chloroperbenzoic acid (80 mg, 0.463 mmol) was added in one portion at room temperature to a vigorously stirred mixture of **8** (200 mg, 0.437 mmol) in dichloromethane (10 ml) and saturated aqueous $NaHCO_3$ (10 ml). After 30 min, the organic phase was separated, dried and evaporated. The residue was immediately subjected to flash chromatography on silica gel (elution with light petroleum–ether, 4:1). A 7:3 mixture of **22** and **23** was obtained as a colourless oil (172 mg, 83%) (Found: $M^+ - C_4H_9$, 417.1842. Calc. for $C_{19}H_{37}O_2{}^{120}Sn$: *M*, 417.1815).

For **22**: δ_H(300 MHz, C_6D_6) 1.01 (9 H, t, *J* 7), 1.06 (3 H, d, *J* 7), 1.27 (3 H, s), 0.95–2.05 (27 H, series of m), 2.55 (1 H, dd, *J* 10 and 4), 2.73 (1 H, td, *J* 7 and 2.5), 3.46 (1 H, d, *J* 9.5) and 3.84 (1 H, d, *J* 9.5); δ_C(75 MHz, C_6D_6) 9.3 (3 C), 13.9 (3 C), 17.9, 22.6, 25.9, 27.7 (3 C), 29.57, 29.63 (3 C), 31.0, 31.9, 36.8, 58.9, 60.7, 62.8 and 88.4; δ_{Sn}(^{119}Sn, 112 MHz, C_6D_6) −34.1.

For **23**: δ_H(300 MHz, C_6D_6) 1.01 (9 H, t, *J* 7), 1.07 (3 H, d, *J* 7), 1.28 (3 H, s), 0.96–1.81 (25 H, series of m), 1.94–2.11 (2 H, m), 2.51 (1 H, ddd, *J* 9, 5 and 1), 2.94 (1 H, ddd, *J* 10.5, 6 and 3.5), 3.56 (1 H, d, *J* 9.5) and 3.94 (1 H, d, *J* 9.5); δ_C(75 MHz, C_6D_6) 9.3 (3 C), 140.0 (3 C), 18.9, 21.7, 27.70, 27.73 (3 C), 29.56, 29.64 (3 C), 29.9, 33.8, 39.3, 58.6, 60.9, 62.0 and 87.4; δ_{Sn}(^{119}Sn, 112 MHz, C_6D_6) −34.2.

Acid-catalysed Isomerization of **22**.—A solution of the **22**/**23** mixture (7:3; 500 mg, 1.056 mmol) in chloroform (2 ml, pretreated with K_2CO_3) was added during 2 min to a solution of 4-chloropyridine hydrochloride (25 mg, 1.667 mmol) in acetonitrile–chloroform (1:1; 15 ml). After 1 h the reaction mixture was diluted with ether and washed with dilute HCl, water and brine containing $NaHCO_3$. Flash chromatography on silica gel (elution with light petroleum–ether, 4:1→1:2) afforded unchanged **23** as a colourless oil (151 mg, 30%; quantitative recovery) and **25** as a colourless oil (106 mg, 59%; 84% based upon amount of **22** originally present); $\nu_{max}(CCl_4)/cm^{-1}$ 3620 and 3550–3300; δ_H(300 MHz, $CHCl_3$) 0.74 (3 H, d, *J* 7), 1.28 (3 H, s), 1.36–1.51 (3 H, m), 1.52–1.63 (1 H, m), 1.73–

1.97 (4 H, m), 2.30 (1 H, br s), 2.28–2.40 (1 H, m), 3.72 (1 H, t, *J* 4.5) and 4.21 (1 H, ddd, *J* 7.5, 5 and 3.5); δ_C(75 MHz, $CDCl_3$) 17.3, 25.1, 26.8, 28.5, 32.0, 33.7, 38.4, 77.7, 84.0 and 85.2 (Found: M^+, 170.1328. Calc. for $C_{10}H_{18}O_2$: *M*, 170.1307).

Sulphenylation of **21**.—2,4,6-Triisopropylbenzenesulphenyl chloride (100 mg, 0.360 mmol) in dry dichloromethane (1 ml) was added dropwise during 2 min to a cold (−15 °C), magnetically stirred solution of **21** (50 mg, 0.297 mmol) in dichloromethane (5 ml) until a faint yellow colour persisted. The reaction mixture was allowed to warm to room temperature and evaporated. The residue was purified by flash chromatography on silica gel (elution with light petroleum–ether, 15:1) to give an inseparable 5:6 mixture of **26** and **27** (72 mg, 62%) as a colourless oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1595, 1460, 1380, 1360, 1105, 1070, 1040 and 880; δ_H(300 MHz, $CDCl_3$) (for **26**) 0.90 (3 H, d, *J* 7), 1.12 (3 H, s), 3.64 (1 H, br t, *J* 5.5) and 3.69 (1 H, br d, *J* 6); (for **27**) 0.82 (3 H, d, *J* 7), 1.59 (3 H, s), 3.06 (1 H, dd, *J* 5 and 2.5) and 4.29 (1 H, br dt, *J* 6 and 4.5); (for **26** and **27**) 1.15–1.27 (18 H, m), 1.30–2.72 (9 H, series of m), 2.87 (1 H, sept, *J* 7), 3.84–4.04 (2 H, m) and 7.00 (2 H, s); δ_C(75 MHz, $CDCl_3$) (for **26**) 18.4, 22.6, 24.7, 25.8, 27.7, 34.1, 36.2, 52.4, 71.3, 75.7, 121.5 (2 C), 126.0, 149.8 and 154.7 (2 C); (for **27**) 17.3, 25.1, 27.7, 29.6, 29.8, 35.0, 39.4, 61.3, 84.9, 85.1, 121.8 (2 C), 127.7, 149.4 and 153.5 (2 C); (for **26** and **27**, partially unresolved isopropyl resonances) 23.83, 23.87, 23.91, 24.01, 24.04, 24.9, 313.3, 31.4, 32.0 and 34.2 (Found: M^+, 388.2810. Calc. for $C_{25}H_{40}OS$: *M*, 388.2800).

trans-2,6-*Dimethyl*-5-(*trimethylstannylmethoxy*)*cyclooctene* **28**.—This stannyl ether was obtained by Sn/Li exchange of **8** followed by treatment with Me_3SnCl in a fashion analogous to the preparation of the selenide **9**. Purification was achieved by flash chromatography on silica gel (elution with light petroleum, then light petroleum–ether, 25:1) to give **28** in 62% yield as a colourless oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1465, 1445, 1375, 1225, 1190, 1065 and 955; δ_H(300 MHz, C_6D_6) 0.21 (9 H, s), 1.14 (3 H, d, *J* 7), 1.28 (1 H, dddd, *J* 13.5, 10.5, 6 and 5), 1.52–1.68 (2 H, m), 1.71 (3 H, br s), 1.91 (1 H, dddq, *J* 10.5, 7.5, 3.5 and 7), 1.94–2.07 (2 H, br m), 2.16 (1 H, dddd, *J* 13.5, 10.5, 3.5 and 3), 2.30 (1 H, br ddd, *J* 14.5, 10.5 and 3.5), 2.20–2.34 (1 H, br m), 2.88 (1 H, td, *J* 7.5 and 3), 3.39 (1 H, d, *J* 9.5), 3.81 (1 H, d, *J* 9.5) and 5.36 (1 H, br t, *J* 8); δ_C(75 MHz; C_6D_6) −10.6 (3 C), 19.2, 24.8, 25.8, 28.8, 30.1, 36.1, 37.2, 61.2, 88.6, 123.3 and 137.1; δ_{Sn}(^{119}Sn, 112 MHz, C_6D_6) −24.1 (dd decet, *J* 20.5, 17.5 and 52.5) (Found: $M^+ - CH_3$, 317.0961. Calc. for $C_{13}H_{25}O^{120}Sn$: *M*, 317.0926).

Attempted Mercuriation of **28**.—A solution of **28** (60 mg, 0.181 mmol) in CD_3CN–$CDCl_3$ (1:1; 1.0 ml) was treated with powdered $HgCl_2$ (49 mg, 0.180 mmol) at room temperature. ^{1}H NMR analysis indicated clean conversion into **29** within 30 min with simultaneous appearance of an equivalent amount of CH_3HgCl (δ_H 1.00; δ_C 6.7). For **29**: δ_H(300 MHz, 1:1 CD_3CN–$CDCl_3$) 0.60 (6 H, s), 0.91 (3 H, d, *J* 7), 1.66 (3 H, br s), 1.18–2.30 (9 H, series of m), 2.97 (1 H, td, *J* 7.5 and 3), 3.82 (1 H, d, *J* 9.5), 4.10 (1 H, d, *J* 9.5) and 5.26 (1 H, br t, *J* 8); δ_C(75 MHz; 1:1 CD_3CN–$CDCl_3$) −0.4 (3 C), 19.0, 24.7, 25.6, 28.6, 30.3, 36.0, 37.2, 68.6, 88.2, 123.4 and 137.4; δ_{Sn}(^{119}Sn, 112 MHz, 1:1 CD_3CN–$CDCl_3$) 75.3.

Reaction of **8** *with Cupric Bromide*.—Dry, granular cupric bromide (500 mg, 2.24 mmol) was added in one portion to a solution of **8** (250 mg, 0.547 mmol) in dry dichloromethane (10 ml) at room temperature. The clear, colourless solution gradually became turbid. After 6 h, the reaction mixture was filtered, the solid residues were rinsed with ether, and the combined filtrates were diluted with ether and washed with 10% aqueous NH_4OH solution. Continued washing with 5% HCl, water and brine was followed by drying and solvent evaporation. Flash chromatography of the residue on silica gel (elution with light petroleum–ether, 6:1) gave **18** (19.2 mg, 15%) and **30** (48.5 mg, 53%) as a colourless, volatile oil; **30**: $\nu_{max}(CCl_4)/cm^{-1}$ 1450, 1425, 1380, 1265, 1190, 1165, 1135, 1095 and 850; δ_H(300 MHz, $CDCl_3$) 0.88 (3 H, d, *J* 7), 1.37 (1 H, tdd, *J* 13.5, 12 and 5.5), 1.56 (1 H, br ddt, *J* 13.5, 5.5 and 3.5), 1.64 (3 H, ddd, *J* 2.5, 1.5 and 1), 1.76 (1 H, tdd, *J* 13.5, 3.5 and 2), 1.83 (1 H, br, dddd, *J* 13.5, 5.5, 5 and 3.5), 1.99 (1 H br dddq, *J* 12, 5.5, 3.5 and 7), 2.26 (1 H, br dddq, *J* 18.5, 6.5, 3.5 and 1), 2.35 (1 H, br td, *J* 5 and 2), 2.56 (1 H, br dddq, *J* 18.5, 4, 2.5 and 2.5), 3.81 (1 H, dd, *J* 11 and 5), 3.83 (1 H, br dt, *J* 4 and 3.5), 4.14 (1 H, br d, *J* 11) and 5.46 (1 H, br ddq, *J* 6.5, 2.5 and 1.5); δ_C(75 MHz, $CDCl_3$) 19.4, 24.3, 27.2, 29.0, 30.2, 40.7, 44.7, 72.7, 80.9, 123.7 and 138.4 (Found: C, 79.35; H, 10.91%; M^+, 166.1370. $C_{11}H_{18}O$ requires C, 79.46; H, 10.91%; *M*, 166.1358).

1,2-*Epoxy*-5-(*methoxymethoxy*)-2,6-*dimethylcyclooctane* **34**.—Chloromethyl methyl ether (1.0 ml, 13.17 mmol) was added during 5 min to a cold (0 °C), magnetically stirred solution of **7** (812 mg, 5.26 mmol) and diisopropylethylamine (3.5 ml, 20.1 mmol) in dry dichloromethane (30 ml). The reaction mixture was stirred at room temperature for 10 h, treated with methanol (2 ml), and agitated overnight. Work-up afforded the MOM ether (1.182 g) as a colourless oil; δ_H(300 MHz, C_6D_6) 1.10 (3 H, d, *J* 7), 1.24 (1 H, dddd, *J* 14, 10.5, 6 and 5), 1.69 (3 H, br s), 1.63–1.70 (2 H, m), 1.84–2.05 (3 H, m), 2.10 (1 H, dddd, *J* 14, 10.5, 3.5 and 3), 2.13–2.28 (1 H, br m), 2.30 (1 H, br ddd, *J* 14.5, 10.5 and 3), 3.26 (3 H, s), 3.42 (1 H, td, *J* 8 and 3.5), 4.52 (1 H, d, *J* 7), 4.62 (1 H, d, *J* 7) and 5.33 (1 H, br t, *J* 8); δ_C(75 MHz, C_6D_6) 19.4, 24.6, 25.7, 28.7, 32.4, 36.0, 36.9, 55.3, 81.7, 96.3, 123.3 and 137.1 (Found: M^+, 198.1606. Calc. for $C_{12}H_{22}O_2$: *M*, 198.1620).

The MOM ether (1.13 g) was treated with *meta*-chloroperbenzoic acid in the predescribed manner to afford a 2:1 mixture of the epoxides **34** (1.088 g, 100%); δ_H(300 MHz, C_6D_6) 1.01 (2 × 3 H, pair of unresolved d, *J* 7) 1.23 (3 H, s), 1.25 (3 H, s), 1.00–1.60 (2 × 5 H, series of m), 1.65–2.07 (2 × 4 H, series of m), 2.45 (1 H, ddd, *J* 9, 5 and 1), 2.50 (1 H, dd, *J* 10 and 4), 3.21 (3 H, s), 3.22 (3 H, s), 3.24–3.31 (1 H, m), 3.44 (1 H, ddd, *J* 10.5, 6.5 and 3.5), 4.43 (1 H, d, *J* 6.5), 4.49 (1 H, d, *J* 7), 4.52 (1 H, d, *J* 6.5) and 4.54 (1 H, d, *J* 7); δ_C(75 MHz, C_6D_6) 18.1, 19.0, 21.5, 22.5, 25.7, 27.8, 29.9, 30.9, 31.6, 31.8, 32.2, 34.0, 36.8, 39.3, 55.2, 55.3, 58.5, 58.7, 61.7, 62.7, 79.7, 80.1, 95.9 and 96.5 [Found: $M + H^+$ 215.12 (FAB). Calc. for $C_{12}H_{23}O_3$ 215.16].

Ring Opening and Oxidation of **34**.—Unpurified **34** (1.040 g) in dry tetrahydrofuran (10 ml) was added to a cold (−78 °C) solution of LDA [from diisopropylamine (4.0 ml, 28.54 mmol) and butyllithium (1.5 mol dm^{-3} in hexane: 12.0 ml, 18.0 mmol)] in tetrahydrofuran (60 ml). After being stirred overnight at room temperature, the reaction mixture was diluted with ether and worked up as before to give a mixture of allylic alcohols (1.083 g).

The major portion of this material (1.027 g) was subjected to Swern oxidation as follows. A solution of oxalyl chloride (0.90 ml, 10.32 mmol) in dry dichloromethane (60 ml) was treated at −78 °C with dimethyl sulphoxide (3.50 ml, 49.3 mmol) in the same solvent (5 ml). After 20 min, the allylic alcohols in dichloromethane (5 ml) were slowly introduced, followed after a further 20 min by neat triethylamine (10.0 ml, 71.7 mmol). After a further 10 min at −78 °C, the cooling bath was removed. Once room temperature had been reached, the mixture was diluted with ether and washed with 5% HCl, water and brine. Immediate purification by flash chromatography on silica gel (elution with light petroleum–ether, 2:1) afforded a mixture of the enones **35a** and **35b** in a reproducible 7:3 ratio (723 mg of colourless oil, 75% overall from **7**); ν_{max}(neat)/cm^{-1} 1690, 1655

and 1605 (Found: M^+, 212.1427. Calc. for $C_{12}H_{20}O_3$: *M*, 212.1412).

For **35a**: δ_H(300 MHz, C_6D_6) 0.92 (3 H, d, *J* 7), 0.95–2.62 (9 H, series of m), 3.18 (3 H, s), 3.28 (1 H, td, *J* 8 and 2.5), 4.40 (1 H, d, *J* 6.5), 4.48 (1 H, d, *J* 6.5), 4.91 (1 H, dt, *J* 2 and 1) and 5.52 (1 H, d, *J* 2); δ_C(75 MHz, C_6D_6) 18.9, 30.3, 31.1, 33.0, 37.6, 39.7, 55.4, 80.6, 95.9, 117.9, 150.2 and 205.5.

For **35b**: δ_H(300 MHz, C_6D_6) 0.88 (3 H, d, *J* 6.5), 0.95–2.62 (7 H, series of m), 1.92 (3 H, br s), 3.07 (1 H, ddd, *J* 9.5, 4.5 and 3), 3.20 (3 H, s), 4.42 (1 H, d, *J* 7), 4.56 (1 H, d, *J* 7) and 5.99 (1 H, ddq, *J* 8.5, 8 and 1.5); δ_C(75 MHz, C_6D_6) 19.6, 20.5, 28.3, 32.8, 35.8, 41.6, 55.5, 80.9, 95.7, 134.1, 140.6 and 202.3.

trans-1-(*Dimethylphenylsiloxy*)-5-(*methoxymethoxy*)-2,6-*dimethylcyclooctene* **36**.—A solution of the enones **35a**/**35b** (70:30; 710 mg, 3.34 mmol) and dimethylphenylsilane (580 mg, 4.26 mmol) in dry benzene (15 ml) was stirred at room temperature under nitrogen in the presence of tris(triphenylphosphine)-rhodium chloride (50 mg) for 12 h and then heated at 70 °C for 7 h. Evaporation of the solvent followed by flash chromatography on silica gel (elution with light petroleum–ether, 9:1) gave **36** (503 mg, 62% based on the availability of **35a**; **35b** proved unreactive) as a colourless oil; δ_H(300 MHz, C_6D_6) 0.45 (6 H, two narrowly resolved s), 1.06 (3 H, d, *J* 7), 1.76 (3 H, br s), 1.22–2.27 (9 H, series of m), 3.24 (3 H, s), 3.40–3.48 (1 H, m), 4.50 (1 H, d, *J* 6.5), 4.59 (1 H, d, *J* 6.5), 7.21–7.33 (3 H, m) and 7.63–7.72 (2 H, m); δ_C(75 MHz, C_6D_6) −0.4 (2 C), 16.7, 18.9, 29.1, 31.2, 34.3, 34.6, 37.8, 55.2, 81.3, 96.4, 113.4, 128.1 (2 C), 129.8, 133.6 (2 C), 138.7 and 145.0 (Found: M^+, 348.2128. Calc. for $C_{20}H_{32}O_3Si$: *M*, 348.2121).

Transannular Cyclization of **36**.—Neat stannic chloride (0.30 ml, 2.56 mmol) was added dropwise at room temperature to a solution of 1,8-bis(dimethylamino)naphthalene (80 mg, 0.373 mmol) in dry dichloromethane (90 ml). After 5 min, the cloudy pink solution was cooled to −78 °C and **36** (250 mg, 0.717 mmol) in dichloromethane (10 ml) was introduced during 10 min. After slow warming to 20 °C and overnight stirring, the mixture was diluted with ether and quenched with saturated aqueous $NaHCO_3$. The organic phase was washed with 5% HCl, water and brine and then dried and evaporated. Flash chromatography of the residue on silica gel (elution with light petroleum–ether, 2:1) afforded **32** (90.8 mg, 69%) as a colourless oil; $\nu_{max}(CCl_4)/cm^{-1}$ 1690; δ_H(300 MHz, $CDCl_3$) 0.88 (3 H, d, *J* 7), 0.96 (3 H, s), 1.51 (1 H, br ddd, *J* 15, 9.5 and 2), 1.61 (1 H, dtd, *J* 15, 12 and 1.5), 1.75 (1 H, dddd, *J* 14.5, 8, 2 and 1), 1.85 (1 H, br dddd, *J* 15, 8.5, 7 and 2), 1.96 (1 H, dddd, *J* 15, 11, 8 and 1.5), 2.10 (1 H, ddddq, *J* 12, 7, 3.5, 1 and 7), 2.20 (1 H, ddddd, *J* 14.5, 11, 9.5, 7 and 1), 2.63 (1 H, ddd, *J* 14, 8.5 and 1.5), 3.10 (1 H, ddd, *J* 14, 12 and 2), 3.61 (1 H, dd, *J* 11.5 and 1.5), 3.81 (1 H, d, *J* 11.5) and 4.05 (1 H, br ddd, *J* 7, 3.5 and 1); δ_C(75 MHz, $CDCl_3$) 17.9, 18.7, 23.2, 28.0, 30.0, 39.6, 42.7, 45.9, 66.7, 75.0 and 215.6 (Found: C, 72.82; H, 9.85%; M^+, 182.1309. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.85%; *M*, 182.1307).

Acknowledgements

We thank the National Institutes of Health (Grant GM-30827) for generous financial support.

References

1 N. Enoki, A. Furusaki, K. Suehiro, R. Ishida and T. Matsumoto, *Tetrahedron Lett.*, 1983, **24**, 4341.
2 L. A. Paquette, D. Friedrich and R. D. Rogers, *J. Org. Chem.*, 1991, **56**, in the press.
3 B. D. Challand, G. Kornis, G. L. Lange and P. de Mayo, *J. Chem. Soc., Chem. Commun.*, 1967, 704; B. D. Challand, H. Hikino, G. Kornis, G. Lange and P. de Mayo, *J. Org. Chem.*, 1969, **34**, 794; C. D. Poulter, E. C. Friedrich and S. Winstein, *J. Am. Chem. Soc.*, 1969, **91**, 6892; J. A. Staroscik and B. Rickborn, *J. Org. Chem.*, 1972, **37**, 738; N. Kawabata, T. Nakagawa, T. Nakao and S. Yamashita, *J. Org. Chem.*, 1977, **42**, 3031.
4 R. S. Matthews and J. K. Whitesell, *J. Org. Chem.*, 1975, **40**, 3312; G. Mehta and K. S. Rao, *J. Am. Chem. Soc.*, 1986, **108**, 8015.
5 M. Pereyre, J.-P. Quintard and A. Rahm, *Tin in Organic Synthesis*, Butterworths, 1987; D. Seyferth and S. B. Andrews, *J. Organomet. Chem.*, 1971, **30**, 151; D. Seyferth, S. B. Andrews and R. L. Lambert, Jr., *J. Organomet. Chem.*, 1972, **37**, 69; W. C. Still, *J. Am. Chem. Soc.*, 1978, **100**, 1481; W. C. Still and A. Mitra, *J. Am. Chem. Soc.*, 1978, **100**, 1927; W. C. Still, J. H. McDonald, III, D. B. Collum and A. Mitra, *Tetrahedron Lett.*, 1979, **20**, 593; K. Mori and S. Kuwahara, *Tetrahedron*, 1982, **38**, 521.
6 (*a*) A. L. J. Beckwith and P. E. Pigon, *Austr. J. Chem.*, 1986, **39**, 77. Compare: (*b*) J. E. Baldwin, R. M. Adlington and J. Robertson, *Tetrahedron*, 1989, **45**, 909; (*c*) D. L. J. Clive, H. W. Manning and T. L. B. Boivin, *J. Chem. Soc., Chem. Commun.*, 1990, 972.
7 H. Nishiyama, T. Kitajima, M. Matsumoto and K. Itoh, *J. Org. Chem.*, 1984, **49**, 2298; G. Stork and M. Kahn, *J. Am. Chem. Soc.*, 1985, **107**, 500; E. Magnol and M. Malacria, *Tetrahedron Lett.*, 1986, **27**, 2255; M. Koreeda and I. A. George, *Chem. Lett.*, 1990, 83.
8 J. Pfenninger, C. Henberger and W. Graf, *Helv. Chim. Acta*, 1980, **63**, 2328; M. D. Bachi and E. Bosch, *Tetrahedron Lett.*, 1986, **27**, 641.
9 D. P. Curran and C.-T. Chang, *Tetrahedron Lett.*, 1987, **28**, 2477. Compare: G. A. Kraus and K. Landgrebe, *Tetrahedron Lett.*, 1984, **25**, 3939; *Tetrahedron*, 1985, **41**, 4039; M. Degueil-Castaing, B. De Jeso, G. A. Kraus, K. Landgrebe and B. Maillard, *Tetrahedron Lett.*, 1986, **27**, 5927.
10 R. C. Larock and D. E. Stinn, *Tetrahedron Lett.*, 1989, **30**, 2767; R. C. Larock, D. E. Stinn and M.-Y. Kuo, *Tetrahedron Lett.*, 1990, **31**, 17.
11 E. J. Corey and A. G. Myers, *Tetrahedron Lett.*, 1984, **25**, 3559; S. F. Martin, R. E. Austin and C. J. Oalman, *Tetrahedron Lett.*, 1990, **31**, 4731.
12 A. L. J. Beckwith and C. H. Schiesser, *Tetrahedron*, 1985, **41**, 3925; J. D. Winkler and V. Sridar, *J. Am. Chem. Soc.*, 1986, **108**, 1708; *Tetrahedron Lett.*, 1988, **29**, 6219; J. D. Winkler, V. Sridar and M. G. Siegel, *Tetrahedron Lett.*, 1989, **30**, 4943.
13 K. Nozaki, K. Oshima and K. Utimoto, *Tetrahedron Lett.*, 1988, **29**, 6125, 6127.
14 M. Mori, I. Oda and Y. Ban, *Tetrahedron Lett.*, 1982, **23**, 5315; M. Mori, Y. Kubo and Y. Ban, *Tetrahedron Lett.*, 1982, **23**, 1519; M. Mori, N. Kanda, I. Oda and Y. Ban, *Tetrahedron*, 1985, **41**, 5465.
15 (*a*) D. J. Peterson and M. D. Robbins, *Tetrahedron Lett.*, 1972, **13**, 2135; (*b*) D. J. Peterson, M. D. Robbins and J. R. Hansen, *J. Organomet. Chem.*, 1974, **73**, 237; (*c*) K. C. Nicolaou, D. A. Claremon, W. E. Barnette and S. P. Seitz, *J. Am. Chem. Soc.*, 1979, **101**, 3706; (*d*) K. C. Nicolaou, *Tetrahedron*, 1981, **37**, 4097; (*e*) Y. Ueno, M. Ohta and M. Okawara, *Tetrahedron Lett.*, 1982, **23**, 2577; (*f*) Z. N. Parnes, G. I. Bolestova, J. S. Akhrem, M. E. Vol'pin and D. N. Kursanov, *J. Chem. Soc., Chem. Commun.*, 1980, 748; (*g*) T. L. Macdonald and S. Mahaligam, *J. Am. Chem. Soc.*, 1980, **102**, 2113; (*h*) T. L. Macdonald, S. Mahaligham and D. E. O'Dell, *J. Am. Chem. Soc.*, 1981, **103**, 6767.
16 C. A. Broka, W. J. Lee and T. Shen, *J. Org. Chem.*, 1988, **53**, 1336.
17 D. R. Williams and J. Grote, *J. Org. Chem.*, 1983, **48**, 134; R. J. Linderman, D. M. Graves, W. R. Kwochka, A. F. Ghannam and T. V. Anklekar, *J. Am. Chem. Soc.*, 1990, **112**, 7438.
18 D. D. Davis, R. L. Chambers and H. T. Johnson, *J. Organomet. Chem.*, 1970, **25**, C13; S. Teratake, *Chem. Lett.*, 1974, 1123; S. Teratake and S. Morikawa, *Chem. Lett.*, 1975, 1333; I. Fleming and C. J. Urch, *Tetrahedron Lett.*, 1983, **24**, 4591; E. Murayama, T. Kikuchi, K. Sasaki, N. Sootome and T. Sato, *Chem. Lett.*, 1984, 1897; J. F. Kadow and C. R. Johnson, *Tetrahedron Lett.*, 1984, **25**, 5255; I. Fleming and M. Rowley, *Tetrahedron Lett.*, 1985, **26**, 3857; C. R. Johnson and J. F. Kadow, *J. Org. Chem.*, 1987, **52**, 1493.
19 M. T. Reetz and T. Seitz, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 1028; M. R. Reetz, J. Westermann and R. Steinbach, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 900, 901; M. T. Reetz, B. Wenderoth, R. Peter, R. Steinbach and J. Westermann, *J. Chem. Soc., Chem. Commun.*, 1980, 1202; M. T. Reetz, J. Westermann and R. Steinbach, *J. Chem. Soc., Chem. Commun.*, 1981, 237; M. T. Reetz and J. Westermann, *J. Org. Chem.*, 1983, **48**, 254.
20 A. N. Kashin, N. A. Bumagin, I. P. Beletskaya and O. A. Reutov, *Zh. Org. Khim.*, 1973, **9**, 1769.
21 D. E. Seitz, G. L. Tonnesen, S. Hellman, R. N. Hanson and S. J. Adelstein, *J. Organomet. Chem.*, 1980, **186**, C33.
22 T. Mukaiyama, *Org. React.*, 1982, **28**, 238; A. Alexakis, M. J.

Chapdelaine, G. H. Posner and A. W. Rumquist, *Tetrahedron Lett.*, 1978, **19**, 4205; G. S. Cockerill, P. Kocienski and R. Treadgold, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2093, 2101; J. H. Hutchinson, G. Pattenden and P. L. Myers, *Tetrahedron Lett.*, 1987, **28**, 1313; M. Mortimore, G. S. Cockerill, P. Kocienski and R. Treadgold, *Tetrahedron Lett.*, 1987, **28**, 3747; P. Kocienski, S. D. A. Street, C. Yeates and S. F. Campbell, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2171; R. J. Linderman and A. Godfrey, *J. Am. Chem. Soc.*, 1988, **110**, 6249.

23 (*a*) T. Tsuda, T. Hayashi, H. Satomi, T. Kawamoto and T. Saegusa, *J. Org. Chem.*, 1986, **51**, 537; (*b*) T. Tsuda, H. Satomi, T. Hayashi and T. Saegusa, *J. Org. Chem.*, 1987, **52**, 439.

24 I. Ojima, M. Nihonyanagi, Y. Kogure, M. Kumagari, S. Horiuchi and K. Nakatsugawa, *J. Organomet. Chem.*, 1975, **94**, 449.

25 D. Friedrich and L. A. Paquette, *J. Org. Chem.*, 1991, **56**, in the press.

Paper 1/00849H
Received 21*st February* 1991
Accepted 7*th March* 1991