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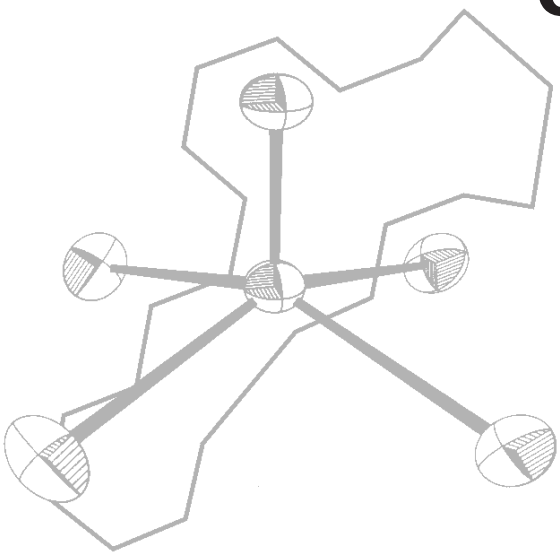

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Total Synthesis of the Pentacyclic Diterpenoid Tropone Hainanolidol

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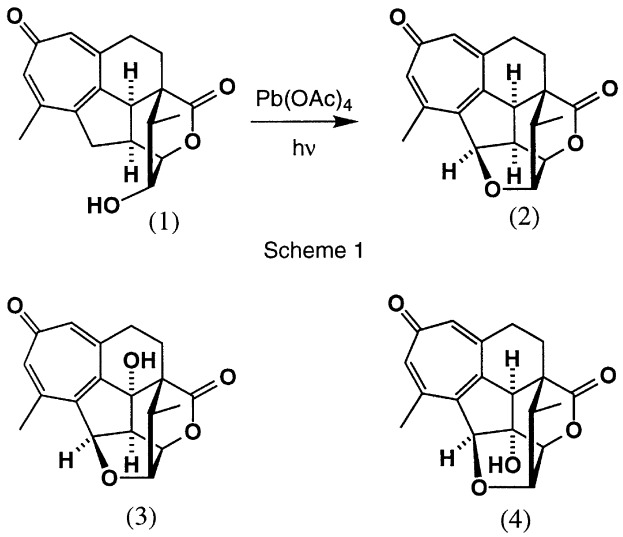
The total synthesis of the unusual diterpenoid tropone, hainanolidol (1), discovered in the bark of the yew species, *Cephalotaxus hainanensis*, has been completed in 26 steps from 3,5-dimethylanisole. The intramolecular cyclopropanation reaction of the aryl ring in (30) by means of the rhodium mandelate-catalysed reaction of the diazoacetyl function was used to assemble the 5/7 ring system of (31), at the same time elaborating a cycloheptatriene moiety that could be transformed subsequently to the tropone functionality in the target molecule. While removing the acetal protecting group from (31) an unexpected Mukaiyama–type aldol process was induced by $ZnBr_2$, affording (32), the structure of which was determined by X-ray analysis. With greater care, the aldehyde (33) could be obtained and the desired carbocyclic ring system completed by means of a base-catalysed aldol reaction with the newly formed hydroxyl being employed subsequently in the formation of the δ-lactone function in (35). Desilylation, reduction of the C-10 carbonyl function and brief exposure to acid finally afforded (1). This last step took advantage of the stability of the tropylium ion (40) to provide a 'thermodynamic sink' for the reaction outcome. The synthesis of (1) also constitutes a formal synthesis of the troponoid ether, harringtonolide (2), since this compound had been obtained previously from (1) by means of a transannular oxidation process. Methodology for the assembly of the tropone moiety in (1) and (2) was modelled on the simpler bi- and tricyclic systems, (13) and (22), respectively.

Keywords: Hainanolidol; diterpenoids; Yew bark; tropones; harringtonolide.

Introduction

The diterpenoid tropone, harringtonolide (2), was first isolated in North America from seeds of *Cephalotaxus harringtonia* (Taxaceae) and its structure established by X-ray crystallography.[1] At about the same time, (2) was independently discovered in the bark of the related Chinese species *Cephalotaxus hainanensis*, given the name hainanolide,[2] and found to have anti-neoplastic and anti-viral properties.[3] In *C. hainanensis*, (2) was accompanied by the closely related, but biologically inactive carbinol, hainanolidol (1), the structure of which was established by conversion into (2) by transannular oxidation with lead tetra-acetate (Scheme 1).[4] More recently, two further tropones of this type (3) and (4) have been discovered in *C. fortunei*.[5]



Scheme 1

In order to explore the chemistry and therapeutic potential of these unusual compounds, we have pursued a program of total synthesis that led initially to the preparation of carbinol (10) (R = H) as outlined in Scheme 2.[6] When attempts to convert (10) into (2) by means of an oxidative transannular process failed, we decided to modify our approach to incorporate an additional hydroxyl into the side chain with a view to forming the ether ring in harringtonolide (2) through nucleophilic displacement of a suitably activated substituent attached to C-12. We now report the details of this study which has culminated in the synthesis of *rac.*-hainanolidol (1) and the formal synthesis of harringtonolide by virtue of

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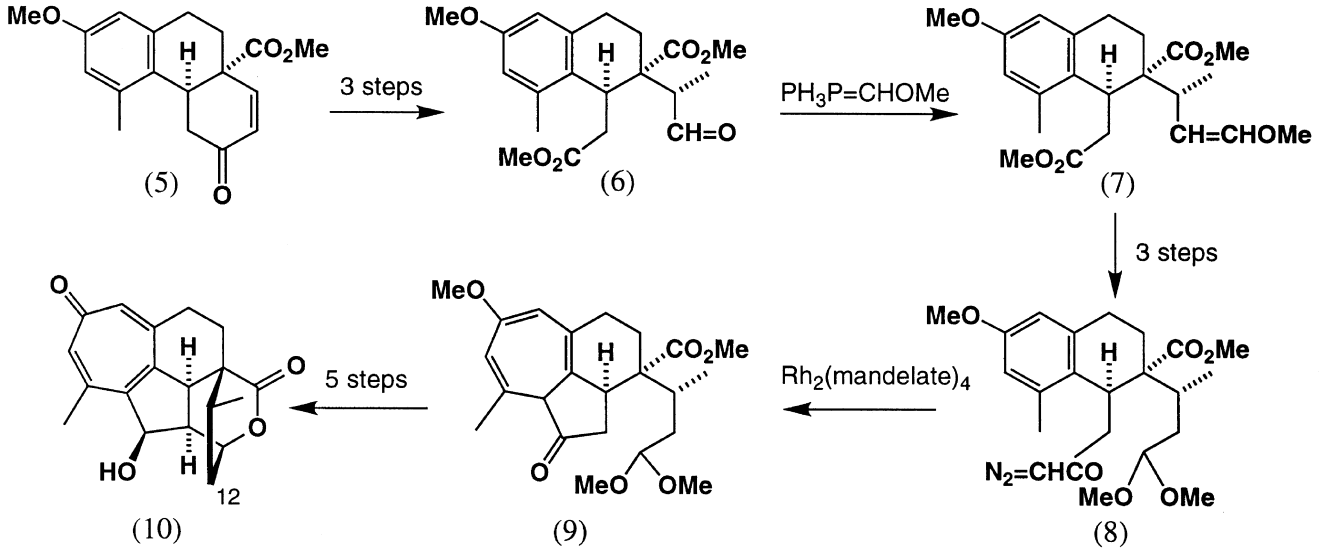


Scheme 2

the conversion (1) → (2). Model studies concerned with the elaboration of the tropone moiety found in this type of molecule are also described.

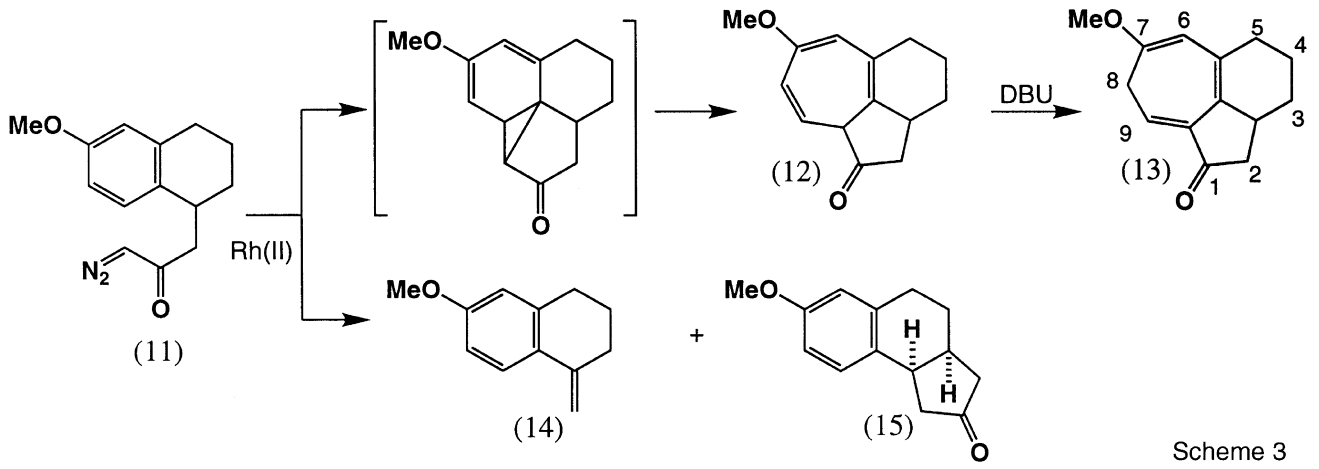
Results and Discussion

Model Studies on Tropone Formation

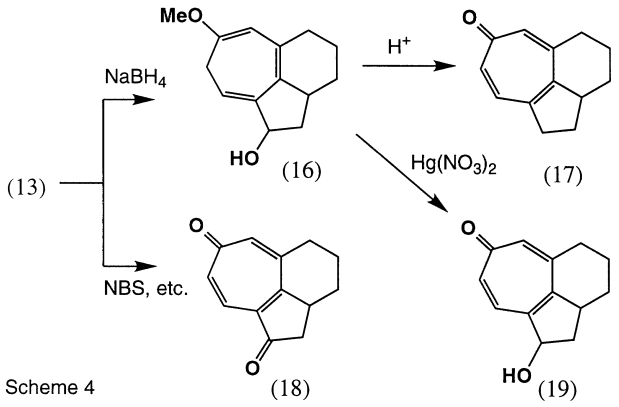
While developing the main synthetic approaches to (1) and (2), we also prepared a number of simpler analogues that were designed to assist in refining the methodology that would be required to prepare the tropone moiety in the target molecules. The first of these studies is summarized in Schemes 2 and 3. Diazoketone (11), a known compound,[7] was readily prepared, but its conversion into (12), by rhodium-catalysed intramolecular cyclopropanation,[8] occurred in disappointing yield. Two other major products, (14)[9] and (15)[10], were formed in similar amounts. Competing CH insertion to give (15) was not unexpected, while the formation of alkene (14) with concomitant loss of ketene also has precedent.[11] Ketone (12) was very prone to undergo oxidation, especially during chromatography, so isomerisation to (13) was usually carried out with this and subsequent examples before attempting resolution of the product mixture. For this particular series, we were able to obtain much better yields of (13) when copper(II) acetoacetate was employed as the cyclopropanation catalyst (ca 70%),[11] but with all other substrates, rhodium acetate or mandelate gave very acceptable results.

Our initial attempt at tropone formation was effected by bromination, then base-induced elimination of HBr following a procedure developed by Scott and Chamberlin.[12] Tropone (18) was obtained satisfactorily in this way, although we were alarmed to find that a clean sample displaying all the expected signals in an ^{1}H n.m.r. spectrum had completely decomposed 10 minutes later, affording a dark brown solution. Of even greater concern was the discovery that transformation of alcohol (16) to the corresponding tropone (19) by this procedure failed completely. We were relieved to find, however, that simple treatment of both (13) and (16) with mercury(II) nitrate furnished the tropones in acceptable yields. Curiously, (18) prepared in this way was reasonably stable.

Before proceeding further it was deemed advisable to examine these processes on a substrate that incorporated a methyl group at the cyclopropanation site, given the potential for a significant perturbation of the various conversions. Accordingly, diazoketone (20) was prepared from the parent dihydrocinnamic acid[13] and treated with



Scheme 3



Scheme 4

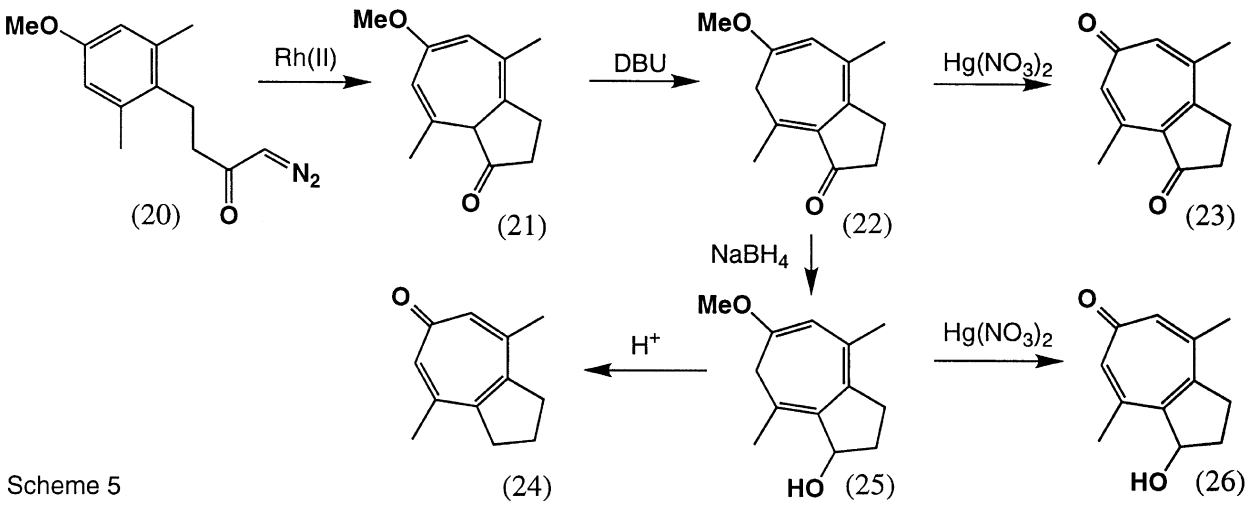
rhodium acetate. Transformation to (22) proceeded satisfactorily, as did subsequent treatment with mercury(II) nitrate to afford tropones (23) and (26) (Scheme 4). Thus encouraged, we returned to the main project.[14]

Synthesis of Hainanolidol (1)

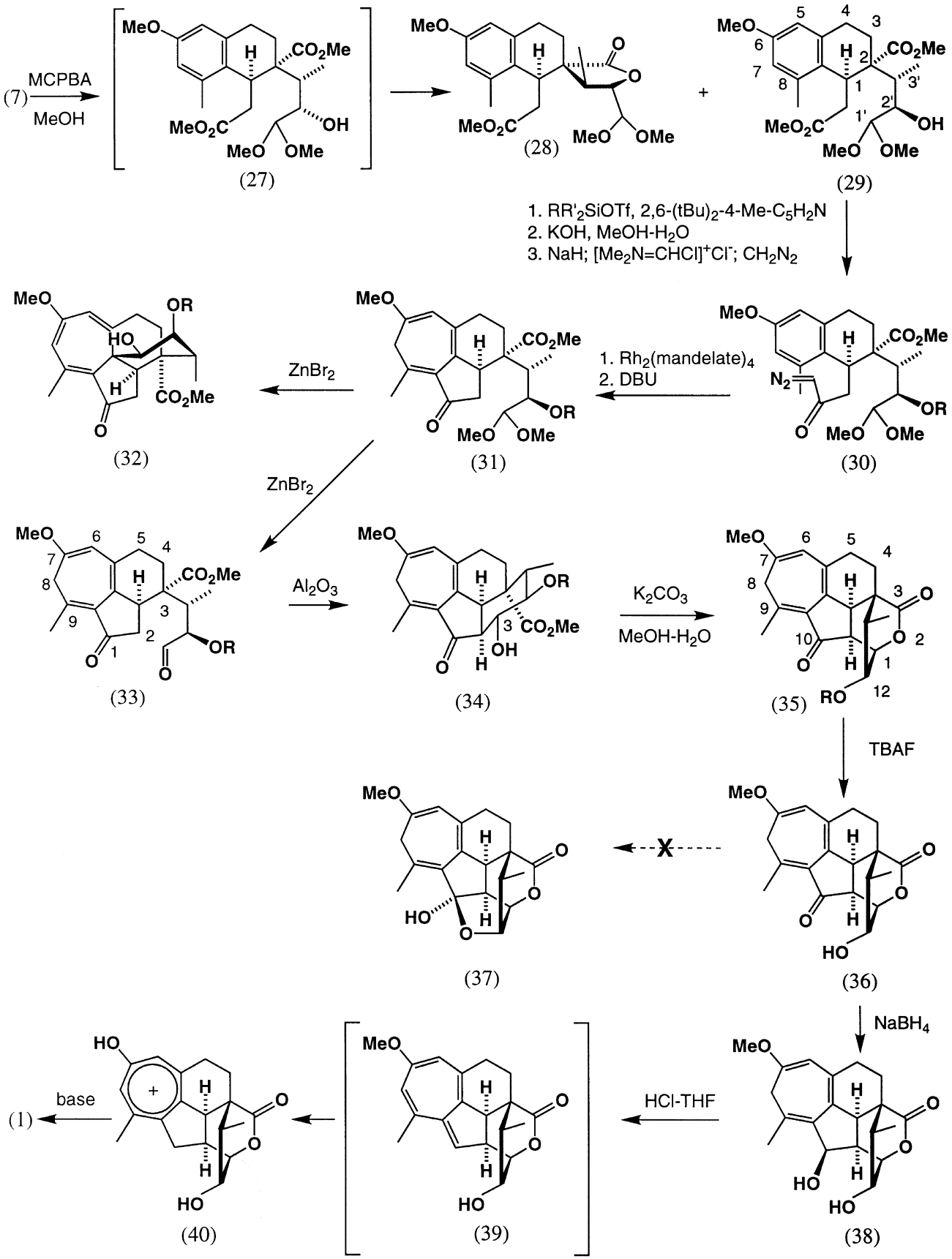
Intermediate (7)[6] was oxidised with *m*-chloroperoxybenzoic acid in MeOH with a view to forming an α-hydroxy acetal array from the enol ether function (Scheme 6). A 3 : 1 mixture of a hydroxy dimethyl acetal with a γ-lactone-containing product was obtained, the latter presumably arising from reaction between the newly introduced hydroxyl and the 3° ester group. A nOe experiment on this latter compound indicated that the methyl and acetal groups attached to the lactone ring were in a *trans* relationship, and therefore that the lactone possessed structure (28). The presumed hydroxy acetal precursor was accordingly assigned structure (27), and the major epimer structure (29). In the latter case, lactonization was presumably inhibited by the requirement for the methyl and acetal groups to adopt an eclipsed conformation. Following protection[15] of (29) as its *tert*-butyldimethylsilyl (TBDMS) ether,[16] the primary methyl ester was hydrolysed, and then diazoketone (30a) prepared by treating the sodium carboxylate with Vilsmeier reagent and adding the reaction mixture directly to an excess of diazomethane, affording (30a) in 80% overall yield from (29). This procedure, designed to avoid traces of adventitious HCl that are likely to accompany the isolation of acyl chlorides, has proven to be generally effective for acid-sensitive substrates.[17] Cyclopropanation[18] catalysed by rhodium mandelate[19] then furnished an unstable adduct that was immediately treated with DBU (1,8-Diazabicyclo[5.4.0]undec-7-ene (1,5-5)) to give the slightly less labile cycloheptatriene (31a) (84% overall yield).

In the expectation that chelation between the silyl ether and acetal functions would assist in the liberation of the aldehyde function from the dimethyl acetal group, (31a) was treated with $ZnBr_2$. Initial experiments with this reagent afforded (32a), presumably as a consequence of a Mukaiyama-like aldol process,[20] the structure being determined by single-crystal X-ray analysis (Fig. 1). With more carefully controlled conditions, however, aldehyde (33a) could be obtained as the major product (61% nett yield) and subsequent exposure to basic alumina gave the desired aldol product (34a) (76% yield). Only the equatorial 3α-epimer ($\delta_{3\beta H}$ 3.14 Hz, $J_{3,2}$ 8.7 Hz, $J_{3,3a}$ 10.2 Hz, $J_{3,OH}$ 2.1 Hz) was detected, suggesting that the aldol process was under thermodynamic control.[21] Treatment of (34a) with K_2CO_3 in aqueous MeOH furnished lactone (35a) in a very modest 33% yield, but this could be elevated to 65% by recycling recovered (34a).

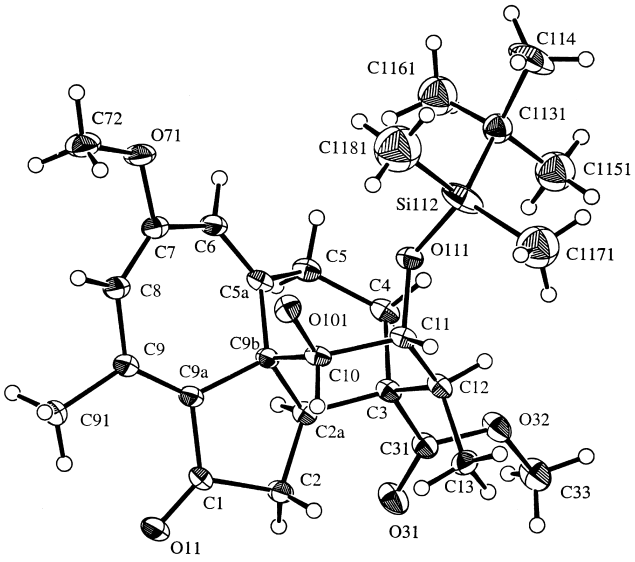
Unfortunately, as a consequence of the lactonization step, the TBDMS function was folded into a very hindered environment, and desilylation proved not to be possible. The alternative approach, involving removal of the TBDMS protecting group from (34a) prior to lactonization, was examined; however, while the parent diol was readily obtained, it could not be induced to lactonize, possibly because of additional hydrogen bonding with the adjacent hydroxyl. We therefore tried replacing the TBDMS group with the more labile isopropyldimethylsilyl function.[22] The sequence from acetal (29) to (31b) proceeded smoothly, but aldehyde (33b) was obtained in only 20% yield, and so we turned to the diethylisopropylsilyl (DEIPS)[23] protecting group. Yields previously obtained with the TBDMS group could be reproduced for the sequence (29) → (35c), and then desilylation was effected smoothly with tetrabutylammonium fluoride (TBAF). There was the



Scheme 5



Scheme 6 [Structures (30)-(35): a, R = $tBu(Me)_2Si$; b, R = $iPr(Me)_2Si$; c, R = $iPr(Et)_2Si$]



prospect that the resulting hydroxy ketone (36) might cyclize to the corresponding hemi-acetal (37), which could then be deoxygenated[24] to afford an immediate precursor to harringtonolide (2), but there was no indication of hemi-acetal formation.

Steric shielding of the upper face of the cyclopentanone ring was expected to steer the approach of reagents to the lower face, and so we were not surprised when reduction of (36) with sodium borohydride gave diol (38). Clearly, the *syn* relationship between the hydroxyls in this diastereomer does not readily allow ether formation by the usual S_N2 type of displacement; however, attempts to reverse the stereochemical outcome by means of a directed reduction using tetramethylammonium triacetoxyborohydride[25] to obtain the preferred 10α-epimer were unproductive. We had anticipated that this dilemma would probably arise when deciding to utilize (29) as an intermediate, knowing from earlier work that we were likely to obtain the 10β-epimer (38) from reduction of the cyclopentanone moiety. Alcohol (27) had been our preferred starting material, since it was expected to lead to 12-*epi*-(38), but apart from the question of yield, our attempts to open the lactone ring in (28) and prepare a silylated derivative of (27) proved to be impractical.

In order to bring the synthesis to a conclusion, we reluctantly decided to postpone the direct synthesis of harringtonolide (2) and, instead, delete the 10β-hydroxyl in (38) with a view to preparing hainanolidol (1). We were reasonably confident that this step could be combined with formation of the tropone moiety by ionisation of the protonated alcohol, leading ultimately to hainanolidol (1) *via* the tetraene (39) and tropylium ion (40). This expectation was reinforced by model experiments with (16) and (25) that furnished (17) and (24), respectively (Schemes 4, 5), the conversions depending on the intermediate tropylium moieties to provide a 'thermodynamic sink' for the reaction outcome. When briefly exposed to acid followed by base, (38) afforded in ca. 50% yield, a product with ^{1}H n.m.r. and mass spectral data matching those reported[2] for hainanolidol (1). Unfortunately, it has not been possible to obtain a sample of natural hainanolidol for direct comparison. In view of the conversion outlined in Scheme 1,[2] the preparation of (1) also constitutes a formal synthesis of harringtonolide (2).

Experimental

General

Microanalyses were conducted by the Australian National University Analytical Services Unit, Canberra. Low resolution EI mass spectra (70 eV) and high resolution accurate mass measurements were recorded on a VG Autospec double focussing mass spectrometer. Infrared spectra were recorded on Perkin-Elmer 683 or 1800 Fourier Transform Infrared spectrophotometers. ^{1}H n.m.r. and ^{13}C n.m.r. spectra were recorded on a Varian Gemini 300 spectrometer at 300 MHz and 75.5 MHz respectively. Analytical thin layer chromatography was carried out on Merck aluminium t.l.c. plates precoated with silica KG60 F_{254}. Flash chromatography was conducted on Merck Kieselgel 60 silica gel.

3-(6'-Methoxy-1',2',3',4'-tetrahydro-1'-naphthyl)-1-diazo-propan-2-one (11)

A solution of 6'-methoxy-1',2',3',4'-tetrahydro-1'-naphthylacetic acid (1.6 g, 7.2 mmol) in CH_2Cl_2 (10 ml) was carefully added to a mixture of oxalyl chloride (10 ml) and dimethyl formamide (1 drop). After stirring at room temperature for 10 min, the mixture was evaporated to dryness under high vacuum. Benzene (5 ml) was added, and the mixture again evaporated under high vacuum. The residue was dissolved in ether and added slowly to a freshly prepared solution of diazomethane in ether (excess). After 10 min, the yellow solution was passed down a column of silica to decompose the excess diazomethane. The pale yellow solution was evaporated to dryness to give 1.75 g of the crude *diazoketone* (11). Chromatography on silica gel (hexane/EtOAc, 8 : 1) gave pure diazoketone (1.6g, 90% yield), m.p. 84–86°C [Found: C, 69.0; H, 6.8; N, 11.2%; $M^{+\cdot}$, 216.1145. $C_{14}H_{16}N_2O_2$ requires C, 68.8; H, 6.6; N, 11.5%; $C_{14}H_{16}NO_2$ (M^+-N_2) requires $M^{+\cdot}$, 216.1150]. υ_{max} 2105, 1640, 1610, 1500 cm^{-1}. ^{1}H n.m.r. (300 MHz) δ 7.05, d, *J* 8.4 Hz, H8'; 6.71, dd, *J* 2.7, 8.4 Hz, H7'; 6.61, d, *J* 2.7 Hz, H5'; 5.75, s, CH=N_2; 3.76, s, OMe; 3.30-3.40, m, H1'; 2.50-2.80, 4H, m; 1.60-1.95, 4H, m. ^{13}C n.m.r. (75MHz) δ 194.1, C2; 157.5, C6'; 138.2, C4'a; 131.4, C8'a; 129.2, C8'; 113.54, 112.04, C5, C7; 55.1, OMe; 55.0, CH=N_2; 48.41, C1'; 33.80, C3; 29.74, 28.22, C2', C4'; 19.47, C3'.

7-Methoxy-1,2,2a,3,4,5,-hexahydro-(8H)-benz[cd]-azulen-1-one (13)

(a) A solution of diazoketone (11) (100 mg) in CH_2Cl_2 (25 ml) was added slowly over 3.5 hr (syringe pump) to a solution of $Rh_2(OAc)_4$ (3 mg) in CH_2Cl_2 (10 ml) at reflux. Analysis of the ^{1}H n.m.r. spectrum of the crude product indicated the formation of a 1 : 1.4 : 1.5 mixture of the desired triene (12) with alkene (14) and ketone (15), respectively. When the red solution was evaporated to dryness, and chromatographed on silica gel (hexane/EtOAc, 4 : 1), only (14) and (15) were recovered. In a repeat experiment, DBU (2 drops) was added to a solution of the crude product in CH_2Cl_2 (10 ml) and after 5 min, the solution washed with 1M HCl, brine and dried ($MgSO_4$). Chromatography on silica gel (hexane/EtOAc, 4 : 1) afforded:

Alkene (14)[10] (9.0 mg), ^{1}H n.m.r. (300 MHz) δ 7.59, d, *J* 8.7Hz, H8; 6.72, dd, *J* 2.7, 8.7 Hz H7; 6.61, d, *J* 2.7 Hz, H5; 5.33, 4.82, 2×d, *J* 1.3 Hz, =CH_2; 3.79, s, OMe; 2.81, m, 2H, H4; 2.50, m, 2H, H2; 1.85, m, 2H, H3.

Triene (13) (11 mg) (Found: $M^{+\cdot}$, 216.1150. $C_{14}H_{16}O_2$ requires $M^{+\cdot}$, 216.1150). ^{1}H n.m.r. (300 MHz) δ 5.95, dd, *J* 6.1, 8.5 Hz, H9; 5.27, br s, H6; 3.59, s, OMe; 3.19, ddd, *J* 2.3, 8.5, 13.5 Hz, H8; 2.80-2.95, m, H2a; 2.73, dd, *J* 7.9, 17.8 Hz, H2; 2.45-2.55, 2H, m, H5, H'5; 2.20, dd, *J* 6.1, 13.5 Hz, H8'; 2.10, dd, *J* 8.7, 17.8 Hz, H'2; 1.95-2.05, 2H, m; 1.60-1.80, 1H, m; 1.15-1.30, 1H, m. ^{13}C n.m.r. (75MHz) δ 205.9, C1; 146.7, C7; 135.9, 134.4, 127.4, C5a, 9a, 9b;115.2, C9; 101.1, C6; 56.1, OMe; 45.9, C2a; 35.8, 32.6, C2, C8; 30.9, 29.6, C3, C5; 22.5, C4. Mass

spectrum *m/z* 216 (M, 100%), 201 (17), 188 (58), 174 (40), 160 (30), 145 (30), 128 (36), 115 (58), 91 (43).

Ketone (15) (19 mg), m.p. 64-66°C (lit.[9] 67-69°C) (Found: $M^{+\cdot}$, 216.1150. $C_{14}H_{16}O_2$ requires $M^{+\cdot}$, 216.1150). ^{1}H n.m.r. (300 MHz) δ 7.01, d, *J* 8.5 Hz, H8; 6.73, dd, *J* 2.7, 8.5 Hz, H7; 6.64, d, *J* 2.7 Hz, H5; 3.79, s, OMe; 3.48, m, 1H, H8b. ^{13}C n.m.r. (75MHz) δ 218.7, 157.8, 136.9, 130.3, 130.1, 113.5, 112.6, 55.2, 45.6, 45.1, 37.9, 34.9, 29.0, 24.4. Mass spectrum *m/z* 216 (M, 65%), 173 (100), 159 (40), 144 (13), 128 (18), 115 (34), 13 (103), 91 (22).

(b) A solution of diazoketone (11) (30 mg) in 1,2-dichloroethane (1 ml) was added slowly to a solution of $Cu(acac)_2$ (3 mg) in 1,2-dichloroethane (1 ml) at reflux. The red solution was evaporated to dryness, and chromatographed on silica gel (hexane/EtOAc, 4 : 1) to give 20 mg of the unstable *triene* (13) (75% yield).

7-Methoxy-1,2,2a,3,4,5,-hexahydro-(8H)-benz[cd]-azulen-1-ol (16)

A solution of the crude trienone (13) (600 mg) in MeOH (50 ml) was treated with $NaBH_4$ (100 mg) at 0 °C for 30 min. The solution was diluted with 0.1 M HCl in brine, and extracted thoroughly with EtOAc. The organic phase was dried over $MgSO_4$ and evaporated to give a pale yellow oil (635 mg, 88%). Chromatography on silica gel (hexane/EtOAc, 4 : 1) gave 410 mg (60% over two steps) of the unstable alcohol (16) (Found: $M^{+\cdot}$, 218.1310. $C_{14}H_{18}O_2$ requires $M^{+\cdot}$, 218.1307). ^{1}H n.m.r. (300 MHz) 5.30, m, H9; 5.02, s, H6; 4.58, dd, *J* 6.7, 8.5 Hz, H1; 3.51, s, OMe; 2.88, ddd, *J* 2.2, 8.4, 14.0 Hz, H8; 2.30-2.50, 6H, m; 1.97-2.08, 1H, m; 1.40-1.60, 1H, m; 1.00-1.25, 2H, m. ^{13}C n.m.r. (75MHz) 148.5, C7; 145.8, C9a, 134.7, 131.6, C5a, C9b; 110.3, C9; 99.4, C6; 72.6, C1; 55.4, OMe; 44.2, C2a; 38.2, 32.1, 31.3, 29.5, 22.5, C4.

1,2,2a,3,4,5-Hexahydro-(7H)-benz[cd]azulen-7-one (17)

A solution of the hydroxy triene (16) (55 mg, 200 μmol) in tetrahydrofuran (THF, 1 ml) was treated with 100 μl of concentrated HCl. After 10 min at room temperature, the mixture was quenched with saturated bicarbonate solution, and extracted thoroughly with EtOAc. The organic layer was dried over $MgSO_4$ and evaporated to dryness to give 45 mg (95%) of the crude material. Preparative t.l.c. on silica gel (EtOAc/chloroform, 1 : 1, plus 4% MeOH) gave the unstable *tropone* (17) in 50% yield (23 mg). ^{1}H n.m.r. (300 MHz) δ 7.10, 1H, d, *J* 11.9 Hz; 6.90, 1H, d, *J* 11.9 Hz; 6.89, 1H, s; 1.50–3.00, 10H, m; 1.20–1.35, 1H, m. ^{13}C n.m.r. (75MHz) δ 186.9, 149.7, 147.7, 146.6, 139.5, 139.1, 135.1, 46.4, 36.4, 33.1, 31.9, 28.2, 22.6.

1-Oxo-1,2,2a,3,4,5-hexahydro-(7H)-benz[cd]azulen-7-one (18)

(a) A solution of triene (13) (23 mg, 0.106 mmol) in THF (1.0 ml) at –78°C under an atmosphere of nitrogen was treated with a solution of *N*-bromosuccinimide (20.3 mg) in MeOH (5 ml) also cooled to –78°C and stirred for one h. Hunig's base (0.2 ml) was added and stirring continued at –78°C for 20 min. After evaporation of solvent the residue was extracted with carbon tetrachloride, again reduced to dryness and the residue dissolved in CH_2Cl_2 (3 ml). Dowex 50 (H^+) resin (ca 3.0 g) was added and the mixture stirred for 2 h, filtered and reduced to dryness, affording a yellow solid (20.3 mg). A ^{1}H n.m.r. spectrum indicated that this material was ca 90% *tropone* (18). Chromatography on silica gel (hexane/EtOAc, 1 : 2) led to extensive loss of material.

(b) A solution of methoxytriene (13) (150 mg, 0.69 mmol) in acetonitrile (7 ml) and water (1.5 ml) was treated with $Hg(NO_3)_2$ (225 mg, 0.69 mmol) and stirred under nitrogen at room temperature for 5 min. The solution was quenched in water (1 ml) and extracted with CH_2Cl_2 (2 × 2 ml). The organic phase was dried over $MgSO_4$ and evaporated to dryness to give 221 mg of a pale yellow solid. A portion of this crude material (28 mg) was purified by preparative t.l.c. on silica gel (EtOAc/chloroform, 1 : 1, plus 5% MeOH) to give 5.0 mg (18% yield) of *tropone* (18). (Found: $M^{+\cdot}$ 200.0834. $C_{13}H_{12}O_2$ requires M^+, 200.0837). ^{1}H n.m.r. (300 MHz) δ 7.38, 1H, d, *J* 11.6 Hz, H8; 7.01, 1H, m, H6; 6.98, ddd, *J* 1.1. 2.7, 11.6 Hz, H8; 3.08, 1H, m, H2a; 2.86, dd, *J* 7.0, 19.1 Hz, H2; 2.84, 1H, m, H5; 2.68, 1H, m, H'5; 2.30, 1H , m; 2.21, dd, *J* 4.0, 19.1 Hz, H'2; 1.90–1.80, 1H, m; 1.42–1.30, 1H, m; 1.15–1.35, 1H, m. ^{13}C n.m.r. (75MHz) δ 204.9, 187.3, 167.9, 146.2, 142.7, 140.0, 136.8, 128.9, 41.3, 37.4, 36.8, 27.1, 20.8.

1-Hydroxy-1,2,2a,3,4,5-hexahydro-(7H)-benz[cd]azulen-7-one (19)

A solution of hydroxytriene (16) (9.3 mg, 0.0887 mmol) in acetonitrile (5 ml) and water (1 ml) was treated with $Hg(NO_3)_2$ (20 mg) and stirred under nitrogen at room temperature for 5 min. The solution was quenched in water (1 ml) and extracted with CH_2Cl_2 (2 × 2 ml). The organic phase was dried over $MgSO_4$ and evaporated to dryness to give 11 mg of a pale yellow solid. This crude material was purified by preparative t.l.c. on silica gel (EtOAc/chloroform, 1 : 1, plus 5% MeOH) to give 3.3 mg (31% yield) of *tropone* (19). (Found: $M^{+\cdot}$, 202.0992. $C_{13}H_{14}O_2$ requires M^+, 202.0994). ^{1}H n.m.r. (300 MHz) δ 7.28, 1H, d, *J* 11.6 Hz; 6.90, 1H, d, *J* 11.6 Hz; 6.87, 1H, s; 4.92, 1H, m; 3.35–3.75, 1H, br s; 2.50–2.75, 4H, m; 2.05–2.15, 1H, m; 1.70–1.90, 2H, m; 1.40–1.60, 1H, m; 1.15–1.35, 1H, m. ^{13}C n.m.r. (75MHz) 186.9, 149.3, 147.7, 147.6, 139.9 (2×C), 133.7, 76.1, 42.6, 41.3, 32.7, 28.5, 21.9.

4-(2',6'-Dimethyl-4'-methoxyphenyl)-1-diazobutan-2-one (20)

Dimethylformamide (1 drop) was added to oxalyl chloride (6.25 ml, 0.072 mol) and stirred under nitrogen. The mixture was treated with a solution of 3-(2',6'-dimethyl-4-methoxyphenyl)-propanoic acid[13] (1.00 g) in CH_2Cl_2. The reaction mixture was allowed to evaporate under a flow of nitrogen with the aid of a warm water bath then placed under a high vacuum. Benzene (2 ml) and ether (100 ml) were added to the reaction mixture, the resulting solution then added slowly to a solution of diazomethane and stirred for 15 h. The mixture was then filtered through a silica gel column, eluting with ether, and evaporated to dryness. *Diazoketone* (20) was obtained as a yellow solid, m.p. 55–56°C (812 mg, 75% yield) (Found: C, 67.6; H, 7.2; N, 11.9%; $M^{+\cdot}$, 232.1212. $C_{13}H_{16}N_2O_2$ requires C, 67.2; H, 6.9; N, 12.1%; $M^{+\cdot}$, 232.1212). υ_{max} 2105, 1640, 1610, 1585 cm^{-1}. ^{1}H n.m.r. (300 MHz) δ 6.58, 2H, s, H3', H5'; 5.25, br s, H1; 3.75, s, OMe; 2.93–2.87, 2H, m, H4; 2.44–2.42, 2H, m, H3; 2.30, 6H, s, CH_3. ^{13}C n.m.r. (75 MHz) δ 194.2, 157.4, 137.3, 129.3, 113.5, 54.9, 54.2, 40.2, 24.2, 19.9.

6-Methoxy-4,8-dimethyl-2,3-dihydro-1(8aH)-azulenone (21)

A solution of diazoketone (20) (800 mg, 3.448 mmol) in dry CH_2Cl_2 (100 ml) was added slowly to a flask containing rhodium(II) acetate in dry CH_2Cl_2 (20 ml) under nitrogen. The reaction mixture was heated gently under reflux for 15 min, then the solvent was removed under reduced pressure to afford an unstable green oil which was used directly in the following experiments. υ_{max} 1740, 1630 cm^{-1}. ^{1}H n.m.r. (300 MHz) δ 5.81, s, H7; 5.67, s, H5; 3.61, s, OMe; 2.84–2.52, 5H, m; 1.86, s, Me; 1.83, s, Me. ^{13}C n.m.r. (75 MHz) δ 218.7, C1; 157.8, C6; 131.9, 126.4, 125.3, C3a, C4, C8; 120.3, C7; 107.6, C5; 54.6, OMe; 54.3, C8; 38.9, C2; 25.7, C2; 19.8, 18.2, 4-Me, 8-Me.

6-Methoxy-4,8-dimethyl-2,3-dihydro-1(7H)-azulenone (22)

A solution of crude ketone (21) in CH_2Cl_2 (50 ml) under nitrogen was treated with 200 μl of DBU. The reaction was quenched with pH 7 phosphate buffer (10 ml) and the organic layer washed with brine, then dried over $MgSO_4$ and evaporated to dryness to give 700 mg of an orange–brown oil. Chromatography on silica gel (pentane/EtOAc, 2 : 1), afforded *ketone* (22) (287 mg, 41% yield) as a yellow solid (Found: $M^{+\cdot}$, 204.1150. $C_{13}H_{16}O_2$ requires $M^{+\cdot}$, 204.1150). υ_{max} 1700, 1630, 1605 cm^{-1}. ^{1}H n.m.r. (300 MHz) δ 5.32, s, H5; 3.59, s, OMe; 2.75, 2H, dd, 6.7, 7.2 Hz, H2; 2.51, 2H, dd, 6.7, 7.2 Hz, H3; 2.46, 2H, s, H7; 2.42, s, 8-Me; 2.07, 4-Me. ^{13}C n.m.r. (75 MHz) 208.0, C1; 145.0, C6; 135.9, C8; 133.6, 132.3, 130.4, C3a, C4, C8a; 101.5, C5; 56.1, OMe; 41.8, C7; 37.8, C2; 24.6, C3; 20.7, 20.4, 4-Me, 8-Me. Mass spectrum *m/z* 204 (M, 98%), 189 (55), 161 (67), 147 (20), 131 (30), 119 (87), 105 (35), 91 (100).

2,3-Dihydro-4,8-dimethyl-6-oxo-1(6H)-azulenone (23)

A solution of the ketone (22) (20 mg, 0.098 mmol) in acetonitrile (5 ml) and water (1 ml) was treated with $Hg(NO_3)_2$ (31.8 mg) and stirred under nitrogen at room temperature for 5 min. The solution was quenched with water (1 ml) and extracted with CH_2Cl_2 (2 × 2 ml). The organic phase was dried over $MgSO_4$ and evaporated to dryness to give 32 mg of a gum. This crude material was purified by preparative t.l.c. on silica

gel (EtOAc/chloroform, 1 : 1) with 5% MeOH) to give 5.0 mg (27% yield) of *tropone* (23) (Found: $M^{+\cdot}$, 188.0837. $C_{12}H_{12}O_2$ requires $M^{+\cdot}$, 188.0837). υ_{max} 1710, 1620, 1600 cm^{-1}. ^1H n.m.r. (300 MHz) 7.06, 1H, d, *J* 2.3 Hz; 6.81, 1H, d, *J* 2.3 Hz; 2.97–2.94, 2H, m; 2.61–2.58, 2H, m; 2.55, 3H, s; 2.33, 3H, s. ^{13}C n.m.r. (75 MHz) 207.1, C1; 186.2, C6; 166.6, C3a; 143.7, 140.5 C5, C7; 144.0, 143.6, 140.5, C4, C8, C8a; 34.4, C2; 28.8, C3; 24.0, 23.3, 4-Me, 8-Me. Mass spectrum *m/z* 188 (M, 16%), 160 (80), 145 (12), 132 (29), 117 (100), 103 (13), 91 (40).

1,2-Dihydro-4,8-dimethyl-6-methoxy-1(7H)-azulen-1-ol (25)

A solution of the ketone (22) (513 mg, 2.51 mmol) in MeOH (20 ml) and THF (5 ml) under nitrogen was cooled to 0°C. $CeCl_3.H_2O$ and $NaBH_4$ (95 mg) were added to the mixture, whereupon H_2 gas evolved. The reaction was allowed to proceed for 10 min before being quenched in 0.1 M HCl (10 ml), extracted with ether (×3) and washed with brine. The extract was then dried over $MgSO_4$ and evaporated to dryness, giving the crude product (410 mg, 80%). Purification using a silica gel column (hexane/EtOAc, 4 : 1) gave the bright yellow *triene* (25) (30 mg, 25% yield) (Found: $M^{+\cdot}$, 206.1304. $C_{13}H_{18}O_2$ requires $M^{+\cdot}$, 206.1306). υ_{max} 3600, 1630, 1550 cm^{-1}. ^1H n.m.r. (300 MHz) δ 5.13, s, H5; 4.81, t, *J* 3 Hz, H1; 3.53, s, OMe; 2.77–2.72, 1H, m, H3; 2.61, d, *J* 12.9, 1.7 Hz, H7; 2.46, dt, *J* 15.9, 5.4 Hz, H'3; 2.14, d, *J* 12.9 Hz, H'7; 2.00, s, Me; 1.94, s, Me; 1.89–1.82, 2H, m, H2, H'2. ^{13}C n.m.r. (75 MHz) δ 147.4, C6; 139.3, 133.74, 129.25, 121.1, C3a, C4, C8, C8a; 100.6, C5; 73.7, C1; 55.5, OMe, 39.0, C7; 32.9, C2; 28.7 C3; 21.7, 21.2, 4-Me, 8-Me. Mass spectrum *m/z* 206 (M, 100%), 191 (70), 173 (53), 162 (95), 147 (35), 128 (30), 119 (55), 105 (40), 91 (83).

2,3-Dihydro-3-hydroxy-4,8-dimethyl-6(1H)-azulen-1-ol (26)

A solution of hydroxytriene (25) (18.3 mg, 0.0887 mmol) in acetonitrile (5 ml) and water (1 ml) was treated with $Hg(NO_3)_2$ (34 mg) and stirred under nitrogen at room temperature for 5 min. The solution was quenched in water (1 ml) and extracted with CH_2Cl_2 (2 × 2 ml). The organic phase was dried over $MgSO_4$ and evaporated to dryness to give 32 mg of a pale yellow solid. This crude material was purified by preparative t.l.c. on silica gel (EtOAc/chloroform, 1 : 1, plus 5% MeOH) to give 5.3 mg (31% yield) of *tropone* (26). (Found: $M^{+\cdot}$, 190.0993. $C_{12}H_{14}O_2$ requires $M^{+\cdot}$, 190.0994). υ_{max} 2950, 1620 cm^{-1}. ^1H n.m.r. (300 MHz) δ 6.87, 6.85, 2×s, H5, H7; 5.16, d, *J* 6.2 Hz, H1; 3.10, ddd, *J* 19.0, 8.2, 8.2 Hz, H3; 2.81, 1H, ddd, *J* 19.0, 9.0, 2.4 Hz, H'3; 2.40, s, Me; 2.19, s, Me; 2.16, m, H2; 1.94, m, H'2. ^{13}C n.m.r. (75 MHz) δ 186.2, C6;149.0, 146.5, 145.7, 145.4, C3a, C4, C8, C8a; 140.8, 140.3, C5, C7; 79.2, C3; 34.9, C2; 31.5, C-3; 21.7, 21.1, 4-Me, 8-Me. Mass spectrum *m/z* 190 (M,15%), 161 (29), 147 (100), 129 (27), 115 (15), 105 (23), 91 (28).

2,3-Dihydro-4,8-dimethyl-6(1H)-azulenone (24)

A solution of hydroxytriene (25) (20 mg, 0.097 mmol) in THF (1 ml) was treated with conc. HCl (100 µl) and stirred at room temperature for 10 min. The solution was quenched with saturated bicarbonate solution and extracted thoroughly with EtOAc. The organic phase was dried over $MgSO_4$ and evaporated to dryness to give 33 mg of an orange gum. This crude material was purified by preparative t.l.c. on silica gel (EtOAc/chloroform, 1 : 1 plus 5% MeOH) to give 8.6 mg (50% yield) of *tropone* (24) (Found: $M^{+\cdot}$, 174.1044. $C_{12}H_{14}O$ requires $M^{+\cdot}$, 174.1044). υ_{max} 1620 cm-^{1}. ^1H n.m.r. (300 MHz) δ 6.90, 2H, s, H5, H7; 2.90 4H, t, *J* 7.8 Hz, H1, H3; 2.20, 6H, s, 2×Me; 1.94–1.89, 2H, m, H2. ^{13}C n.m.r. (75 MHz) δ 186.0, C6; 147.4, 145.3, C3a, C4, C8, C8a; 139.5, C5, C7; 37.7, C1, C3; 25.7, C2; 21.1, 2×Me.

Methyl (4SR, 5SR, 1'SR, 2'SR)-3',4,4',5-Tetrahydro-6'-methoxy-5-(dimethoxymethyl)-4,8'-dimethyl-2-oxospiro[furan-3(2H),2'(1'H)-naphthalene]-1'-acetate (28) and Methyl (1SR, 2SR, 2'RS, 3'SR)-2-(1,1-dimethoxy-2'-hydroxy-but-3'-yl)-6-methoxy-8-methyl-1-methoxycarbonylmethyl-1,2,3,4-tetrahydro-2-naphthoate (29)

A solution of enol ether (7) (1.34 g, 3.44 mmol) in absolute MeOH (200 ml) was cooled to –5°C (ice–salt bath) and treated with *m*-chloroperoxybenzoic acid (mcpba) (50–55%, 1.90 g, *ca*. 5.77 mmol). The mixture was warmed to 10°C overnight and then treated with dimethyl sulfide (1 ml) and CH_2Cl_2. The solution was washed with sat. aq $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography on silica gel (hexane/EtOAc, 1 : 1) afforded the starting enol ether (7) (112 mg, 8% recovery) in addition to a more polar component. This was rechromatographed (hexane/EtOAc, 2 : 1) to give γ-lactone (28) (255 mg, 20% at 92% conversion) as an oil which crystallised on standing. Recrystallisation (EtOAc/pentane) gave white needles, m.p. 143°C (Found: C, 64.65; H, 7.69%. $C_{22}H_{30}O_7$ requires C, 65.01; H, 7.44%). R_f 0.19 (hexane/EtOAc, 2 : 1). υ_{max} (KBr) 2934s, 2914s, 2842s, 1768 (CO, s), 1728 (CO, s), 1613s, 1587s, 1280s, 1199s, 1174s, 1111s, 1084s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 6.59, 6.43, 2×1H, 2×d, $J_{5',7'}$ 2.5 Hz, H5', H7'; 4.40, 1H, d, $J_{6,5}$ 5.0 Hz, H6; 3.96, 1H, dd, $J_{5,4}$ 9.1 Hz, $J_{5,6}$ 5.0 Hz, H5; 3.73, 3.70, 2×3H, 2×s, 6'-OMe, 9'-CO_2Me; 3.69, 1H, obscured m, H1'; 3.48, 3.47, 2×3H, 2×s, 2×6-OMe; 2.87–2.82, 2H, m, H4'; 2.74, 1H, dd, J_{gem} 18.1 Hz, $J_{9',11}$ 9.2 Hz, H9'; 2.65, 1H, m, H4; 2.28, 1H, partially obscured dd, J_{gem} 18.1 Hz, $J_{9',1'}$ 1.9 Hz, H'9'; 2.25, 3H, s, 8'-Me; 2.00, 1H, m, H3'; 1.79, 1H, m, H'3'; 1.13, 3H, d, $J_{4\text{-Me},4}$ 6.8 Hz, 4-Me. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 177.2, C2; 172.7, **C**O_2Me; 157.0, C6'; 136.4, 135.5, C4a', C8'; 130.0, C8a'; 115.1, 110.2, C5', C7'; 105.4, C6; 80.9, C5; 56.2, 55.8, 54.8, 2×6-OMe, 6'-OMe; 51.7, CO_2**Me**; 47.0, C3; 39.7, C1'; 38.4, C9'; 37.1, C4; 26.4, 20.4, C4', C3'; 19.0, 8'-Me; 12.5, 4-Me. Mass spectrum *m/z* 406 (M^+, 6%), 343 (6), 311 (5), 287 (7), 269 (6), 257 (12), 225 (6), 201 (17), 186 (6), 172 (8), 128 (9), 91 (5), 75 (100), 62 (8).

Further elution afforded *hydroxy ester* (29) (846 mg, 61% at 92% conversion) as a yellow solid. recrystallisation (EtOAc/pentane) gave off-white mixed crystals, m.p. 140–142°C (Found: C, 62.84; H, 8.08%. $C_{22}H_{34}O_8$ requires C, 63.00; H, 7.81%). R_f 0.11 (hexane/EtOAc, 2 : 1). υ_{max} (KBr) 3517 (OH, s), 2999s, 2953s, 2934s, 2853s, 1742 (CO, s), 1729 (CO, s), 1606s, 1591s, 1470s, 1454s, 1430s, 1225s, 1147s, 988s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 6.44, 6.38, 2×1H, 2×d, $J_{5,7}$ 2.5 Hz, H5, H7; 4.33, 1H, br dd, $J_{1',2'}$ 6.8 Hz, $J_{2',3'}$ 2.5 Hz, H2'; 4.24, 1H, d, $J_{1',2'}$ 6.8 Hz, H1'; 4.10, 1H, m, H1; 3.68, 3H, s, 6-OMe; 3.53, 3H, s, 9-CO_2Me; 3.48, 3.41, 2×3H, 2×s, 1'-OMe, 2-CO_2Me; 3.31, 3H, s, 1'-OMe; 3.01, 1H, d, $J_{OH,2'}$ 2.7 Hz, OH; 2.86, 2H, m, H4; 2.78, 1H, dd, J_{gem} 14.3 Hz, $J_{9,1}$ 3.8 Hz, H9; 2.57, 1H, m, H3α; 2.24, 3H, s, 8-Me; 2.18, 1H, dd, J_{gem} 14.3 Hz, $J_{9,1}$ 9.5 Hz, H'9; 2.01, 1H, m, H3'; 1.56, 1H, dt, $J_{3\beta,3\alpha}$ 14.2 Hz, $J_{3\beta,4\alpha}$ 7.3 Hz, $J_{3\beta,4\beta}$ 7.3 Hz, H3β; 0.95, 3H, d, $J_{3',4'}$ 7.1 Hz, 3'-Me. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 176.5, 172.6, 9-**C**O_2Me, 2-**C**O_2Me; 157.5, C6; 137.1, 136.9, C4a, C8; 129.8, C8a; 113.5, 110.8, C5, C7; 105.5, C1'; 68.6, C2'; 55.6, 54.1, 2×1'-OMe; 54.7, 6-OMe; 53.1, C2; 51.6, 51.5, 9-CO_2**Me**, 2-CO_2**Me**; 39.2, C3'; 35.6, C1; 35.3, C9; 25.9, 25.4, C4, C3; 19.2, 8-Me; 8.6, 3'-Me. Mass spectrum *m/z* 438 (M^+, 16%), 406 (M^+ - MeOH, 26), 362 (15), 333 (21), 304 (27), 273 (13), 259 (7), 232 (14), 201 (36), 173 (18), 129 (7), 101 (14), 75 (100).

*Methyl (1*SR, *2*SR, *1'*SR, *2'*RS)*-6-methoxy-2-(1,1-dimethoxy-2'-t-butyldimethylsilyloxy-but-3'-yl)-1-methoxycarbonylmethyl-8-methyl-1,2,3,4-tetrahydro-2-naphthoate*

A solution of hydroxy acetal (29) (846 mg, 1.93 mmol) in CH_2Cl_2 (85 ml) was treated with TBDMS-triflate (1.00 ml, 4.35 mmol) and 2,6-di-*t*-butyl-4-methylpyridine (2.00 g, 9.74 mmol). The mixture was stirred at room temp. for 24 h and then diluted with sat. $NaHCO_3$ and extracted with Et_2O. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography on silica gel (hexane/EtOAc, 4 : 1) gave the *silyl ether* (874 mg, 82%) as an oil. (Found: C, 63.22; H, 9.04%. $C_{29}H_{48}O_8Si$ requires C, 63.01; H, 8.75%). R_f 0.57 (hexane/EtOAc, 2 : 1). υ_{max} (film) 2951s, 2930s, 2855s, 1737 (CO, br, s), 1613s, 1587s, 1463s, 1433s, 1255s, 1192s, 1162s, 1115s, 1090s, 1069s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 6.45, 6.39, 2×1H, 2×d, $J_{5,7}$ 2.5 Hz, H5, H7; 4.37, 1H, br d, $J_{1',2'}$ 3.6 Hz, H2'; 4.22, 1H, d, $J_{1',2'}$ 3.6 Hz, H1'; 3.96, 1H, br dd, $J_{1,9}$ 10.1 Hz, $J_{1,3\beta}$ 1.7 Hz, H1; 3.70, 3H, s, 6-OMe; 3.52, 3H, s, 9-CO_2Me; 3.46, 3.44, 2×3H, 2×s, 2-CO_2Me, 1'-OMe; 3.24, 3H, s, 1'-OMe; 2.97, 1H, br dd, J_{gem} 14.3 Hz, $J_{9,1}$ 3.5 Hz, H9; 2.89–2.84, 2H, m, H4; 2.44, 1H, m, H3α; 2.20, 3H, s, 8-Me; 2.26–2.12, 2H, m, H'9, H3'; 1.56, 1H, m, H3β; 0.99,

3H, d, $J_{3',4'}$ 7.1 Hz, 3'-Me; 0.88, 9H, s, $OSiMe_3$; 0.13, 6H, s, $OSiMe_2$. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 174.5, 173.4, 9-**C**O_2Me, 2-**C**O_2Me; 157.4, C6; 137.1, 137.0, C4a, C8; 131.0, C8a; 113.5, 111.0, C5, C7; 108.5, C1'; 70.4, C2'; 56.5, 55.7, 2×1'-OMe; 54.8, 6-OMe; 53.5, C2; 51.3, 51.2, 9-CO_2**Me**, 2-CO_2**Me**; 39.2, C3'; 36.3, C1; 35.0, C9; 26.1, OSiC**Me**$_3$; 25.9, 25.3, C4, C3; 19.3, 8-Me; 18.5, OSi**C**Me_3; 11.1, 3'-Me; –3.1, –4.8, OSi**Me**$_2$. Mass spectrum *m/z* 552 (M^+, 4%), 551 (M^+H, 13), 495 (4), 389 (6), 368 (16), 313 (13), 285 (8), 257 (9), 215 (23), 185 (9), 129 (31), 111 (22), 83 (47), 57 (100).

*Methyl (1*SR, 2SR, 1'SR, 2'RS)-6-methoxy-2-(1,1-dimethoxy-2'-dimethylisopropylsilyloxy-but-3'-yl)-1-methoxycarbonylmethyl-8-methyl-1,2,3,4-tetrahydro-2-naphthoate

This compound was prepared by the procedure described above for the TBDMS ether. ^1H n.m.r. δ (300 MHz, $CDC1_3$) 6.46, 6.38, 2×1H, 2×d, $J_{5,7}$, $J_{7,5}$ 2.5 Hz, H5, H7; 4.30, 1H, d, $J_{1',2'}$ 6.1 Hz, H2'; 4.13, 1H, d, $J_{1',2'}$ 6.1 Hz, H1'; 4.06, 1H, br dd, $J_{1,9}$ 9.5 Hz, $J_{1,9}$ 2.8 Hz, H1; 3.70, s, 3H, 6-OMe; 3.53, 3H, s, 9-CO_2 Me; 3.44, 3.42, 2×3H, 2×s, 2-CO_2Me; 3.44, 3.42, 2×3H, 2×s, 2-CO_2Me, 1'-OMe; 3.29, 3H, s, 1'-OMe; 2.87–2.80, 3H, m, H'9, H4; 2.57, 1H, m, H3α; 2.30, 3H, s, 8-Me; 2.18, 1H, dd J_{gem} 14.3 Hz, $J_{1,9}$ 9.7 Hz, H9; 2.11, 1H, br q, $J_{3',4'}$ 7.1 Hz, H3'; 1.58, 1H, m, H3β; 0.98, 3H, d, $J_{3',4'}$ 7.1 Hz, 3'-Me; 0.90, 7H, brs, *i*-propyl; 0.10, 0.09, 2×3H, 2×s, $SiMe_2$. ^{13}C n.m.r. δ (75.5 MHz, $CDC1_3$) 174.3, 173.2, 2×CO_2Me; 157.3, C6; 137.0, 136.6, C4a, C8; 131.0, C8a; 113.6, 110.9, C5, C7; 107.4, C1'; 70.4, C2'; 56.0, 6-OMe; 54.8, 2×1'-OMe; 52.7, C2; 51.4, 51.1, 2×CO_2**Me**; 39.5, C3'; 35.8, C1; 35.3, C9; 25.9, 25.3, C4, C3; 19.5, 8-Me; 17.0, SiCH**Me**$_2$; 15.0, Si**CH**Me_2; 9.9, 3'-Me; –3.8, –4.2, Si**Me**$_2$.

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)-*6-methoxy-2-(1,1-dimethoxy-2'-diethylisopropylsilyloxy-but-3'-yl)-1-methoxycarbonylmethyl-8-methyl-1,2,3,4-tetrahydro-2-naphthoate*

This compound was prepared by the procedure described above for the TBDMS ether. ^1H n.m.r. δ (300 MHz, $CDC1_3$) 6.45, 6.35, 2×1H, 2×d, $J_{5,7}$ 2.5 Hz, H5, H7; 4.38, 1H, d, $J_{1',2'}$ 5.1 Hz, H2'; 4.15, 1H, d, $J_{1',2'}$ 5.1 Hz, H1'; 4.00, 1H, br dd, $J_{1,9}$ 10.1 Hz, $J_{1,3\beta}$ 1.7 Hz, H1; 3.66, 3H, s, 6-OMe; 3.48, 3H, s, 9-CO_2Me; 3.42, 3.415, 2×3H, 2×s, 2-CO_2Me, 1'-OMe; 3.24, 3H, s, 1'-OMe; 2.86, 3H, m; 2.58, 1H, m; 2.20, 3H, s, 8-Me; 2.20–2.07, 2H, m; 1.56, 1H, m; 0.99–0.95, 16H, m, 3'-Me, DEIPS; 0.68–0.61, 4H, DEIPS. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 174.3, 173.1, 9-**C**O_2Me, 2-**C**O_2Me; 157.3, C6; 137.0, 136.7, C4a, C8; 130.8, C8a; 113.5, 110.8, C5, C7; 108.0, C1'; 70.2, C2'; 56.0, 55.4, 2×1'-OMe; 54.7, 6-OMe; 52.9, C2; 51.2, 51.0, 9-CO_2**Me**, 2-CO_2**Me**; 39.6, C3'; 35.8, C1; 35.0, C9; 25.8, 25.4,, C4, C3; 19.1, 8-Me; 17.6, 2×C, SiCH**Me**$_2$; 13.8, Si**C**HMe_2; 10.1, 3'-Me; 7.3, 7.2, $SiCH_2$**Me**; 4.4, 4.3, Si**CH**$_2$Me.

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)-*1-carboxymethyl-6-methoxy-2-(1,1-dimethoxy-2'-t-butyldimethylsilyloxy-but-3'-yl)-8-methyl-1,2,3,4-tetrahydro-2-naphthoate*

To a solution of the diester prepared above (874 mg, 1.58 mmol) in MeOH (65 ml) were added 5.2 N methanolic KOH (50 ml) and 5.2 N aq KOH (15 ml) and the mixture stirred overnight at room temp. The MeOH was then removed under reduced pressure and the residue diluted with Et_2O, cooled to 0°C and carefully acidified with 20% aq HCl. The mixture was extracted with Et_2O and the combined organic layers washed with sat. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated to afford the *title acid* (744 mg, 87%) as a colourless foam. Trituration of this material with Et_2O gave a crystalline solid, m.p. 80°C (Found: C, 62.29; H, 8.93%. $C_{28}H_{46}O_8Si$ requires C, 62.42; H, 8.61%). R_f 0.18 (hexane/EtOAc, 2:1). υ_{max} (KBr) 2998m, 2945s, 2853m, 1743 (CO, s), 1699 (CO, s), 1613m, 1586m, 1461m, 1273s, 1169s, 1103s, 1059s, 1048s, 832s, 774s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 6.46, 6.40, 2×1H, 2×d, $J_{5,7}$ 2.5 Hz, H5, H7; 4.37, 1H, br d, $J_{1',2'}$ 3.4 Hz, H2'; 4.22, 1H, d, $J_{1',2'}$ 3.4 Hz, H1'; 3.96, 1H, br d, $J_{1,9}$ 8.8 Hz, H1; 3.71, 3H, s, 6-OMe; 3.46, 3.42, 3.24, 3×3H, 3×s, 2×1'-OMe, 2-CO_2Me; 3.03, 1H, dd, J_{gem} 14.6 Hz, $J_{9,1}$ 2.7 Hz, H9; 2.89–2.85, 2H, m, H4; 2.61, 1H, m, H3α; 2.30, 3H, s, 8-Me; 2.22–2.12, 2H, m, H'9, H3'; 1.65, 1H, m, H3β; 1.00, 3H, d, $J_{3',4'}$ 7.0 Hz, 3'-Me; 0.87, 9H, s, $OSiCMe_3$; 0.14, 0.12, 2×3H, 2×s, $OSiMe_2$. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 179.3, CO_2H; 174.5, **C**O_2Me; 157.4, C6; 137.1, one peak overlapping, C4a, C8; 130.8, C8a; 113.6, 111.0, C5, C7; 108.6, C1'; 70.4, C2'; 56.8, 55.7, 2×1'-OMe; 54.8, 6-OMe; 53.5, C2; 51.3, CO_2**Me**; 39.2, C3'; 36.0, C1; 35.1, C9; 26.1, OSiC**Me**$_3$; 25.9, 25.3, C4, C3; 19.3, 8-Me; 18.5, OSi**C**Me_3; 11.2, 3'-Me; –3.1, –4.9, $OSiMe_2$. *m/z* 521 (M^+–OH, 6%), 495 (17), 477 (32), 431 (22), 389 (29), 357 (26), 311 (22), 273 (22), 255 (17), 232 (29), 215 (84), 143 (34), 115 (31), 75 (100).

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)-*1-carboxymethyl-6-methoxy-2-(1,1-dimethoxy-2'-dimethylisopropylsilyloxy-but-3'-yl)-8-methyl-1,2,3,4-tetrahydro-2-naphthoate*

This compound was prepared by the procedure described above for the TBDMS ether. ^1H n.m.r. δ (300 MHz, $CDCI_3$) 6.48, 6.39, 2×1H, 2×d, $J_{5,7}$ $J_{7,5}$ 2.5 Hz, H5, H7; 4.30, 1H, br d, $J_{1',2'}$ + 5.5 Hz, H2'; 4.13, 1H, d, $J_{1',2'}$ 5.5 Hz, H1'; 4.06, 1H, br dd, $J_{1,9}$ 9.4 Hz, $J_{1,9}$ 2.5 Hz, H1; 3.71, 3H, s, 6-OMe) 3.44, 3.39, 2×3H, 2×s, 2-CO_2Me, 1'-OMe; 3.30, 3H, s, 1'-OMe; 2.90–2.83, 3H, m, H9, H4; 2.60, 1H, m, H3α; 2.31, 3H, s, 8-Me; 2.18, 1H, dd, J_{gem} 14.7 Hz, $J_{9,1}$ 9.4 Hz, H'9; 2.10, 1H, br q, $J_{3',4'}$ 7.0 Hz, H3'; 1.56, 1H, m, H3β; 0.99, 3H, d, $J_{3',4'}$ 7.0, 3'-Me; 0.90, 7H, br s, *I*-propyl; 0.10, 0.09, 2×3H, 2×s, OSi**Me**$_2$. ^{13}C n.m.r. δ (75.5 MHz, $CDC1_3$) 178.9, **C**O_2H; 174.3, **C**O_2Me; 157.4, C6; 137.1, 136.7, C4a, C8; 131.0, C8a; 113, 8, 111.0, C5, C7; 107.6, C1'; 70.5, C2'; 56.4, 6-OMe; 54.9, 54.8, 2×1'-OMe; 52.9, C2; 51.2, CO_2**Me**; 39.6, C3'; 35.9, C1; 35.4, C9; 25.9, 25.4, C4, C3; 19.4, 8-Me; 17.0, SiCH**Me**$_2$; 15.0, Si**CH**Me_2; 10.1, 3'-Me; -3.7, -4.2, Si**Me**$_2$.

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)-*1-carboxymethyl-6-methoxy-2-(1,1-dimethoxy-2'-diethylisopropylsilyloxy-but-3'-yl)-8-methyl-1,2,3,4-tetrahydro-2-naphthoate*

This compound was prepared by the procedure described above for the TBDMS ether. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 10.5–11.2, 1H, br s, CO_2H; 6.45, 6.38, 2×1H, 2×d, $J_{5,7}$ 2.5 Hz, H5, H7; 4.37, 1H, br d, $J_{1',2'}$ 4.9 Hz, H2'; 4.15, 1H, d, $J_{1',2'}$ 4.9 Hz, H1'; 4.05, 1H, br d, $J_{1,9}$ 8.8 Hz, H1; 3.68, 3H, s, 6-OMe; 3.44, 3.42, 2×3H, 2×s, 2-CO_2Me, 1'-OMe; 3.26, 3H, s, 1'-OMe; 2.91, 1H, dd, J_{gem} 14.6 Hz, $J_{9,1}$ 2.7 Hz, H9; 2.83, 2H, m; 2.60, 1H, m; 2.31, 3H, s, 8-Me; 2.25–2.10, 2H, m; 1.53, 1H, m; 0.98–0.90, 16H, m, 3'-Me, DEIPS; 0.68–0.60, 4H, DEIPS. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 179.2, CO_2H; 174.3, **C**O_2Me; 157.4, C6; 137.1, 136.7, C4a, C8; 130.9, C8a; 113.7, 111.0, C5, C7; 108.2, C1'; 70.4, C2'; 56.4, 55.7, 2×1'-OMe; 54.8, 6-OMe; 53.0, C2; 51.1, CO_2**Me**; 39.7, C3'; 35.7, C1; 35.2, C9; 25.8, 25.5, C4, C3; 19.2, 8-Me; 17.6, 2×C, SiCH**Me**$_2$; 14.1, Si**C**HMe_2; 10.2, 3'-Me; 7.33, 7.28, $SiCH_2$**Me**; 4.5, 4.4, Si**CH**$_2$Me.

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)-*1-(3"-diazo-2"-oxopropyl)-6-methoxy-2-(1,1-dimethoxy-2'-t-butyldimethylsilyloxy-but-3'-yl)-8-methyl-1,2,3,4-tetrahydro-2-naphthoate (30a)*

A solution of the acid prepared above (99 mg, 0.184 mmol) in THF (5 ml) was treated with NaH (60% dispersion in oil, 8.9 mg, 0.223 mmol) and the mixture stirred at room temp. until gas evolution had ceased (*ca*. 20 min). Vilsmeier's reagent [prepared from oxalyl chloride (80 µl, 1.02 mmol) and dmf (79 µl, 1.02 mmol) in benzene (3 ml)] was then added and stirring continued for a further 30 min. The mixture, containing the intermediate acid chloride, was then poured into an ice-cold ethereal solution of diazomethane and allowed to stir for 5 min. Excess diazomethane was evaporated under a stream of nitrogen and then the mixture concentrated to dryness. Chromatography on silica gel (hexane/EtOAc, 2:1) afforded *diazoketone* (30a) (89 mg, 86%) as a yellow oil. (Found: C, 61.87; H, 8.01; N, 4.82%; M^+, 562.3077. $C_{29}H_{46}N_2O_7Si$ requires C, 61.89; H, 8.24; N, 4.98%; M^+, 562.3074). R_f 0.41 (hexane/EtOAc, 2:1). υ_{max} (film) 3094w, 2951s, 2856m, 2101 (CN_2, s), 1727 (CO, s), 1640 (CO, s), 1606s, 1321s, 1301s, 1250s, 1235s, 1200s, 1147s, 1117s, 1062s, 836s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 6.45, 6.40, 2×1H, 2×d, $J_{5,7}$ 2.3 Hz, H5, H7; 4.84, 1H, br s,

CH=N_2; 4.41, 1H, br d, $J_{1',2'}$ 3.5 Hz, H2'; 4.25, 1H, d, $J_{1',2'}$ 3.5 Hz, H1'; 3.97, 1H, br d, $J_{1,9}$ 9.9 Hz, H1; 3.71, 3H, s, 6-OMe; 3.48, 3.23, 6H, 3H, 2×s, 2×1'-OMe, CO_2Me; 2.93–2.85, 3H, m, H9, H4; 2.60, 1H, m, H3α; 2.26, 3H, s, 8-Me; 2.22–2.10, 2H, m, H'9, H3'; 1.54, 1H, m, H3β; 1.00, 3H, d, $J_{3',4'}$ 7.2 Hz, 3'-Me; 0.86, 9H, s, OSiCMe$_3$; 0.14, 0.13, 2×3H, 2×s, OSiMe$_2$. ^{13}C n.m.r. δ (75 MHz, CDCl$_3$) 194.5, **C**OCH=N_2; 174.4, **C**O_2Me; 157.4, C6; 137.5, 136.8, C4a, C8; 131.0, C8a; 113.3, 111.1, C5, C7; 108.6, C1'; 70.3, C2'; 56.8, CH=N_2; 55.9, 54.8, 54.8, 6-OMe, 2×1'-OMe; 53.5, C2; 51.3, CO_2**Me**; 39.2, C3'; 36.8, C1; 26.1, OSiC**Me**$_3$; 25.9, 25.5, C4, C3; 19.5, 8-Me; 18.5, OSi**C**Me$_3$; 11.2, 3'-Me; –3.0, –4.8, OSiMe$_2$; C9 not observed. Mass spectrum *m/z* 562 (M^+, 20%), 531 (39), 502 (61), 445 (36), 285 (58), 227 (37), 201 (51), 185 (27), 173 (39), 159 (22), 89 (71), 75 (100), 59 (24).

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)*-1-(3"-diazo-2"-oxopropyl)-6-methoxy-2-(1,1-dimethoxy-2'-dimethylisopropylsilyloxy-but-3'-yl)-8-methyl-1,2,3,4-tetrahydro-2-naphthoate (30b)*

This compound was prepared by the procedure described above for the TBDMS ether. ^{1}H n.m.r. δ (300 MHz, CDC1$_3$) 6,46, 6.39, 2×1H, 2×d, $J_{5,7}$ 2.5 Hz, H5, H7; 4.91, 1H, br s, CH=N_2; 4.33, 1H, d, $J_{1',2'}$ 5.6 Hz, H2'; 4.15, 1H, d, $J_{1',2'}$ 5.6 Hz, H1'; 4.02, 1H, br d, $J_{1,9}$ 9.7 Hz, H1; 3.70, 3H, s, 6-OMe; 3.48, 3.45, 2×3H, 2×s, 2-CO_2Me, 1'-OMe; 3.29, 3H, s, 1'-OMe; 2.88–2.83, 2H, m, H4; 2.76, 1H, dd, J_{gem} 12.9 Hz, $J_{9,1}$ 3.1 Hz, H9; 2.58, 1H, m, H3α; 2.26, 3H, s, 8-Me; 2.15–2.08, 2H, m, H3', H9; 1.55, 1H, m, H3β; 0.98, 3H, d, $J_{3',4'}$ 7.1 Hz, 3'-Me; 0.89, 7H, br s, *i*-propyl 1; 0.10, 0.09, 2×3H, 2×s, Si**Me**$_2$. ^{13}C n.m.r. δ (75.5 MHz, CDC1$_3$) 194.4, **C**OCH=N_2; 174.3, CO_2Me; 157.4, C6; 137.4, 136.4, C4a, C8; 131.0, C8a; 113.5, 111.1, C5, C7; 107.6, C14; 70.3, C2'; 55.0, 54.9, 6-OMe, 2×1'-OMe; 52.8, C2; 51.2, CO_2**Me**; 42.0, CH=N_2; 39.5, C3'; 36.6, C1; 25.9, 25.5, C4, C3; 19.5, 8-Me; 17.0, SiCH**Me**$_2$; 15.0, SiCH**Me**$_2$; 10.0, 3'-Me; –3.7, –4.1, Si**Me**$_2$.

*Methyl (1*SR, *2*SR, *1*'SR, *2*'RS)*-1-(3"-diazo-2"-oxopropyl)-6-methoxy-2-(1,1-dimethoxy-2'-diethylisopropylsilyloxy-but-3'-yl)-8-methyl-1,2,3,4-tetrahydro-2-naphthoate (30c)*

This compound was prepared by the procedure described above for the TBDMS ether. ^{1}H n.m.r. δ (300 MHz, CDCl$_3$) 6.45, 6.38, 2×1H, 2×d, $J_{5,7}$ 2.4 Hz, H5, H7; 4.86, 1H, br s, CH=N_2; 4.40, 1H, br d, $J_{1',2'}$ 5.3 Hz, H2'; 4.19, 1H, d, $J_{1',2'}$ 5.3 Hz, H1'; 4.10, 1H, br d, $J_{1,9}$ 8.1 Hz, H1; 3.70, 3H, s, 6-OMe; 3.48, 3.47, 3.27, 3×3H, 3×s, 2×1'-OMe, CO_2Me; 2.90–2.75, 3H, m; 2.60, 1H, m; 2.24, 3H, s, 8-Me; 2.20–2.10, 2H, m; 1.52, 1H, m; 1.05–0.95, 16H, m, 3'-Me, DEIPS; 0.70–0.60, 4H, DEIPS. ^{13}C n.m.r. δ (75 MHz, CDCl$_3$) 194.3, **C**OCH=N_2; 174.0, **C**O_2Me; 157.1, C6; 137.2, 136.3, C4a, C8; 130.6, C8a; 113.2, 110.8, C5, C7; 107.8, C1'; 70.4, C2'; 56.2, CH=N_2; 55.4, 54.5, 54.5, 6-OMe, 2×1'-OMe; 52.7, C2; 50.8, CO_2**Me**; 39.4, C3'; 36.3, C1; 36.1, C9; 25.6, 25.3, C4, C3; 19.1, 8-Me; 17.4, 2×C, SiCH**Me**$_2$; 13.7, Si**C**HMe$_2$; 9.9, 3'-Me; 7.2, 7.1, SiCH$_2$**Me**; 4.3, 4.2, Si**C**H$_2$Me.

*Methyl (2a*SR, *3*SR, *2*'RS, *3*'SR)*-2,2a,3,4,5,8-Hexahydro-7-methoxy-3-(1,1-dimethoxy-2'-t-butyldimethylsilyloxy-but-3'-yl)-9-methyl-1-oxo-1H-benz[cd]azulene-3-carboxylate (31a)*

A solution of diazoketone (13a) (180 mg, 0.32 mmol) in CH_2Cl_2 (5 ml) was treated with Rh_2(mandelate)$_4$ (10 mg, 0.012 mmol) and the mixture heated at reflux for 10 min under an atmosphere of nitrogen. DBU (2 drops) was added and the solution stirred for *ca*. 2 min, then diluted with CH_2Cl_2 and washed with 0.5 N HCl and 2 N NaOH. The organic phase was dried, filtered and concentrated under reduced pressure. Chromatography on silica gel (hexane/EtOAc, 2 : 1) gave *cycloheptatriene* (31a) (112 mg, 65%) as an oil. (Found: C, 64.71; H, 8.63%; M^+, 534.3020. $C_{29}H_{46}O_7Si$ requires C, 65.14; H, 8.67%; M^+, 534.3013). R_f 0.49 (hexane/EtOAc, 2 : 1). υ_{max} (film) 2953s, 2931s, 2856s, 1726 (CO, s), 1709 (CO, s), 1258s, 1220s, 1196s, 1151s, 1104s, 1060s, 835s cm^{-1}. ^{1}H n.m.r. δ (300 MHz, CDCl$_3$) 5.15, 1H, br s, H6; 4.08, 1H, d, $J_{1',2'}$ 4.9 Hz, H1'; 3.72, 1H, br d, $J_{1',2'}$ 4.9 Hz, H2'; 3.66, 3H, s, 7-OMe; 3.58, 3H, s, CO_2Me; 3.33, 3.32, 2×3H, 2×s, 2×1'-OMe; 3.18, 1H, m, H2a; 2.88, 1H, dd, J_{gem} 12.4 Hz, $J_{8,6}$ 1.8 Hz, H8; 2.76–2.53, 4H, m, H2, H5; 2.42, 3H, s, 9-Me; 2.39–2.31, 2H, m, H4α, H3'; 2.14, 1H, br d, J_{gem} 12.4 Hz, H'8; 2.04, 1H, m, H4β; 0.94, 3H, partially obscured d, 3'-Me; 0.92, 9H, s, OSiCMe$_3$; 0.14, 0.11, 2×3H, 2×s, OSiMe$_2$. ^{13}C n.m.r. δ (75 MHz, CDCl$_3$) 206.4, C1; 177.7, **C**O_2Me; 146.3, C7; 135.8, 135.1, 131.1, 131.1, C9, C9a, C9b, C5a; 107.1, C1'; 99.5, C6; 73.4, C2'; 56.0, 7-OMe; 55.3, 54.9, 2×1'-OMe; 51.6, CO_2**Me**; 48.6, C3; 42.0, 41.6, C2, C8; 41.4, 36.8, C2a, C3'; 29.9, 27.0, C5, C4; 26.3, OSiC**Me**$_3$; 20.5, 9-Me; 18.7, OSi**C**Me$_3$; 9.9, 10-Me; –3.2, –4.1, OSiMe$_2$. Mass spectrum *m/z* 534 (M^+, 7%), 502 (16), 445 (22), 339 (21), 327 (13), 286 (51), 271 (16), 255 (30), 243 (25), 227 (20), 202 (20), 159 (26), 89 (60), 75 (100), 59 (45).

*Methyl (2a*SR, *3*SR, *2*'RS, *3*'SR)*-2,2a,3,4,5,8-Hexahydro-7-methoxy-3-(1,1-dimethoxy-2'-dimethylisopropylsilyloxy-but-3'-yl)-9-methyl-1-oxo-1H-benz[cd]azulene-3-carboxylate (31b)*

This compound was prepared by the procedure described above for the TBDMS ether. ^{1}H n.m.r. δ (300 MHz, CDC1$_3$) 5.14, 1H, br s, H6; 4.08, 1H, d, $J_{1',2'}$ 6.7 Hz, H1'; 3.69, 1H, br d, $J_{1',2'}$ 6.7 Hz H2'; 3.66, 3H, s, 7-OMe; 3.57, 3H, s, 3-CO_2Me; 3.32, 3.29, 2×3H, 2×s, 2×1'-OMe; 3.24, 1H, m, H2α; 2.89, 1H, dd, J_{gem} 12.4 Hz, $J_{8,6}$ 1.9 Hz, H8; 2.77, 2.56, 3H, m, H2, H5, H'5; 2.46, 1H, m, H2'; 2.40, 3H, s, 9-Me; 2.34–2.24, 2H, m, H42, H10; 2.11, 1H, br d, J_{gem} 12.4 Hz, H'8; 2.65, 1H, m, H4β; 0.95–0.92, 10H, m, 3'-Me, *i*-propyl; 0.08, 6H, br s, Si**Me**$_2$. ^{13}C n.m.r. δ (75.5 MHz, CDC1$_3$) 206.3, C1; 177.4, 3-**C**O_2Me; 146.5, C7; 135.9, 135.1, 132.0, 132.0, C9, C9a, C9b, C5a; 105.7, C1'; 99.7, C6; 73.6, C2'; 56.1, 7-OMe; 54.9, 53.6, 2×1'-OMe; 51.6, CO_2**Me**; 48.7, C2; 42.1, 41.8, C2, C8; 41.7, 37.2, C2, C10; 29.8, 27.6, C5, C4; 20.5, 9-Me; 17.2, 17.1, SiCH**Me**$_2$; 15.0, Si**C**HMe$_2$; 9.3, 3'-Me; –3.8, –3.9, Si**Me**$_2$.

*Methyl (2a*SR, *3*SR, *2*'RS, *3*'SR)*-2,2a,3,4,5,8-Hexahydro-7-methoxy-3-(1,1-dimethoxy-2'-diethylisopropylsilyloxy-but-3'-yl)-9-methyl-1-oxo-1H-benz[cd]azulene-3-carboxylate (31c)*

This compound was prepared by the procedure described above for the TBDMS ether. ^{1}H n.m.r. δ (300 MHz, CDCl$_3$) 5.15, 1H, br s, H6; 4.11, 1H, d, $J_{1',2'}$ 6.5 Hz, H1'; 3.75, 1H, br d, $J_{1',2'}$ 6.5 Hz, H2'; 3.66, 3H, s, 7-OMe; 3.59, 3H, s, CO_2Me; 3.34, 3.31, 2×3H, 2×s, 2×1'-OMe; 3.2, 1H, m; 2.90, 1H, dd, J_{gem} 12.3 Hz, $J_{8,6}$ 1.8 Hz, H8; 2.75–2.60, 4H, m; 2.42, 3H, s, 9-Me; 2.52, 1H, m; 2.35, 1H, m; 2.13, 1H, d, J_{gem} 12.3 Hz, H'8; 2.04, 1H, m) 1.04–0.94, 16H, m, 3'-Me, DEIPS; 0.71–0.63, 4H, DEIPS. ^{13}C n.m.r. δ (75 MHz, CDCl$_3$) 206.0, C1; 177.3, **C**O_2Me; 146.3, C7; 135.7, 134.8, 131.9, 131.7, C9, C9a, C9b, C5a; 105.7, C1'; 99.5, C6; 73.6, C2'; 55.9, 7-OMe; 54.7, 53.6, 2×1'-OMe; 51.4, CO_2**Me**; 48.6, C3; 41.8, 41.6, C2, C8; 41.5, 37.2, C2a, C3'; 29.7, 27.4, C5, C4; 20.3, 8-Me; 17.65, 17.6, SiCH**Me**$_2$; 13.7, Si**C**HMe$_2$; 9.2, 3'-Me; 7.3, 7.2, SiCH$_2$**Me**; 4.4, 4.3, Si**C**H$_2$Me.

*Methyl (2a*SR, *3*SR, *9b*SR, *10*SR, *11*RS, *12*SR)*-3-(2'-t-Butyldimethylsilyloxy-1'-oxo-but-3'-yl)-2,2a,3,4,5,8-hexahydro-7-methoxy-9-methyl-1-oxo-1H-benz[cd]azulene-3-carboxylate (33a) and Methyl (2a*SR, *3*SR, *2*'RS, *3*'SR*)-11-t-Butyldimethyl silyloxy-1,2,2a,3,4,5-hexahydro-10-hydroxy-7-methoxy-9,12-dimethyl-1-oxo-3,9a-propano-9a*H*-benz[*cd*]azulene-3-carboxylate (32a)*

A mixture of acetal (31a) (100 mg, 0.19 mmol) and $ZnBr_2$ (47 mg, 0.21 mmol) in CH_2Cl_2 (7.5 ml) was stirred at room temp., under an atmosphere of nitrogen, for 18 h. The solution was then diluted with CH_2Cl_2, washed with 2 N NaOH and water, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography on silica gel (hexane/EtOAc, 2 : 1) gave the starting acetal (31a) (9 mg, 9% recovery) and aldehyde (33a) (51 mg, 56% at 91% conversion) as a pale yellow solid. Recrystallisation (EtOAc/pentane) gave a white solid, m.p. 110–112°C (Found: C, 65.92; H, 8.65%; M^+, 488.2591. $C_{27}H_{40}O_6Si$ requires C, 66.36; H, 8.25%; M^+, 488.2594). R_f 0.52 (hexane/EtOAc, 2 : 1). υ_{max} (KBr) 3012m, 2968m, 2951m, 2926m, 2853m, 1726 (CO, s), 1706 (CO, s), 1614s, 1259s, 1232s, 1221s, 1201s, 1176s, 1154s, 1121s, 1103s, 1020s, 841s cm^{-1}. ^{1}H n.m.r. δ (300 MHz, CDCl$_3$) 9.59, 1H, d, $J_{1',2'}$ 1.4 Hz, H1'; 5.15, 1H, br s, H6; 4.07, 1H, m, H2'; 3.72, 3H,

s, 7-OMe; 3.59, 3H, s, CO_2Me; 3.37, 1H, m, H2a; 2.91, 1H, dd, J_{gem} 12.3 Hz, $J_{8,6}$ 1.8 Hz, H8; 2.68–2.52, 2H, m, H5; 2.67, 1H, dd, J_{gem} 18.1 Hz, $J_{2,2a}$ 9.5 Hz, H2; 2.41, 3H, s, 9-Me; 2.45–2.35, 2.26–2.09, 1H, 3H, 2×m, H4α, H4β, H8, H3'; 0.96, 9H, s, $OSiCMe_3$; 0.95, 3H, d, $J_{3',4'}$ 7.5 Hz, 3'-Me; 0.12, 0.05, 2×3H, 2×s, $OSiMe_2$. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 205.1, C1; 204.2, C1'; 176.7, **C**O_2Me; 146.7, C7; 135.6, 135.3, 131.8, 131.6, C9, C9a, C9b, C5a; 99.7, C6; 79.0, C2'; 56.1, 7-OMe; 52.1, CO_2**Me**; 48.4, C3; 42.1, 41.6, C2, C8; 41.6, 39.4, C2a, C3'; 29.4, 27.3, C4, C3; 25.9, OSiC**Me**$_3$; 20.5, 9-Me; 18.3, OSi**C**Me_3; 10.1, 3'-Me; -4.0, -4.6, $OSiMe_2$. Mass spectrum *m/z* 488 (M^+, 95%), 431 (87), 339 (48), 271 (30), 255 (79), 227 (40), 202 (60), 169 (42), 143 (52), 73 (100), 59 (43).

Further elution afforded *alcohol* (32a) (15 mg, 16% at 91% conversion) as a yellow solid. Recrystallisation (EtOAc/pentane) gave small colourless prisms, m.p. 242–244°C (Found: C, 66.11; H, 8.53. $C_{27}H_{40}O_6Si$ requires C, 66.36; H, 8.28%). R_f 0.35 (hexane/EtOAc, 2 : 1). υ_{max} (KBr) 3567 (OH, s), 2952m, 2931m, 2856m, 1732 (CO, s), 1686 (CO, s), 1644m, 1603w, 1535s, 1253m, 1230m, 1193s, 1163s, 1126s, 1096s, 1072s, 1042s, 837s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 5.89, 1H, m, H6; 5.22, 1H, d, $J_{6,8}$ 2.4 Hz, H8; 3.82–3.77, 2H, m, H10, H11; 3.72, 3H, s, 7-OMe; 3.65, 3H, s, CO_2Me; 2.81–2.67, 2.60–2.44, 1.94, 3H, 4H, 1H, 3×m, H2, H2a, H12, H4, H5; 2.43, 3H, s, 9-Me; 2.33, 1H, dd, $J_{OH,10}$ 12.2 Hz, $J_{OH,11}$ 1.4 Hz, OH; 1.01, 3H, d, *J* 7.7 Hz, 12-Me; 0.91, 9H, s, $OSiCMe_3$; 0.12, 0.08, 2×3H, 2×s, $OSiMe_2$. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 203.3, C1; 176.8, **C**O_2Me; 161.7, C7; 146.2, 144.5, C5a, C9; 124.7, C9b; 121.5, C6; 106.3, C8; 76.9, 75.0, C10, C11; 54.8, 7-OMe; 51.9, CO_2**Me**; 51.0, C2b; 44.2, C9b; 44.1, 42.0, C2a, C12; 40.6, C2; 33.8, 29.9, C4, C5; 25.7, OSiC**Me**$_3$; 23.1, 6-Me; 18.4, OSi**C**Me_3; 18.1, 12-Me; –4.7, –5.3, $OSiMe_2$. Mass spectrum *m/z* 488 (M^+, 74%), 470 (7), 431 (26), 399 (20), 371 (7), 339 (9), 285 (100), 255 (26), 227 (51), 202 (14), 167 (10), 149 (34), 115 (9), 99 (12), 73 (22).

*Methyl (2a*SR, *3*SR, *2'*RS, *3'*SR)*-3-(2'-Diethylisopropylsilyloxy-1'-oxo-but-3'-yl)-2,2a,3,4,5,8-hexahydro-7-methoxy-9-methyl-1-oxo-1H-benz[cd]azulene-3-carboxylate (33c)*

This compound was prepared by the procedure described above for the TBDMS ether. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 9.6, 1H, s, H1'; 5.15, 1H, br s, H6; 4.15, 1H, m, H2'; 3.71, 3H, s, 7-OMe; 3.59, 3H, s, CO_2Me; 3.40–3.30, 1H, m; 2.90, 1H, dd, J_{gem} 12.4 Hz, $J_{8,6}$ 2.0 Hz, H8; 2.75–2.50, 4H, m; 2.41, 3H, s, 9-Me; 2.26–2.12, 3H, m; 0.96, 9H, s, $OSiCMe_3$; 1.04–0.89, 16H, m, 3'-Me, DEIPS; 0.78–0.60, 4H, DEIPS. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 205.1, C1; 203.7, C1'; 176.7, **C**O_2Me; 146.7, C7; 135.6, 135.2, 131.8, 131.7, C9, C9a, C9b, C5a; 99.7, C6; 79.8, C2'; 56.1, 7-OMe; 52.0, CO_2**Me**; 48.3, C3; 42.2, 41.6, C2, C8; 41.5, 39.4, C2a, C3'; 29.4, 27.2, C4, C3; 17.5, 2×C, SiCH**Me**$_2$; 13.2, Si**C**HMe_2; 12.0, 3'-Me; 7.3, 7.2, $SiCH_2$**Me**; 4.3, 4.2, Si**C**H_2Me.

*Methyl (1*SR, *2*SR, *3*RS,*3a*SR,*10a*RS,*10b*SR)*-2-t-Butyldimethylsilyloxy-1,2,3,3a,6,9,10,10b-octahydro-3-hydroxy-7-methoxy-1,5-dimethyl-4-oxocyclohept[bc]acenaphthylene-10a(4H)-carboxylate (34a)*

A solution of aldehyde (33a) (45 mg, 0.092 mmol) in CH_2Cl_2 (5 ml) was treated with basic, activated alumina (1 g) and the resultant suspension stirred at room temp. for 16 h. The mixture was then filtered and the retained solids washed with CH_2Cl_2. Concentration of the filtrate and chromatography of the residue on silica gel (hexane/EtOAc, 4 : 1) afforded carbinol (34a) (28 mg, 62%) as a colourless solid. Recrystallisation (EtOAc/pentane) gave white prisms, m.p. 135–138°C (Found: C, 66.22; H, 8.45%; M^+, 488.2594. $C_{27}H_{40}O_6Si$ requires C, 66.36; H, 8.25%; M^+, 488.2594). R_f 0.57 (hexane/EtOAc, 2 : 1). υ_{max} (KBr) 3515 (OH, m), 2952m, 2928m, 2855m, 1717 (CO, s), 1692 (CO, s), 1631m, 1600m, 1264m, 1219m, 1194s, 1103s, 1062s, 836s cm^{-1}. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 5.16, 1H, br s, H8; 3.74, 1H, dd, $J_{2,1}$ 10.3 Hz, $J_{2,3}$ 8.7 Hz, H2; 3.73, 3H, s, 7-OMe; 3.59, 3H, s, CO_2Me; 3.18, 1H, br d, $J_{10b,3a}$ 7.2 Hz, H10b; 3.14, 1H, ddd, $J_{3,3a}$ 10.2 Hz, $J_{3,2}$ 8.7 Hz, $J_{3,OH}$ 2.1 Hz, H3; 2.94, 1H, dd, J_{gem} 12.6 Hz, $J_{6,8}$ 2.0 Hz, H6; 2.92, 1H, dd, $J_{3a,3}$ 10.2 Hz, $J_{3a,10b}$ 7.2 Hz, H3a; 2.54, 1H, d, $J_{OH,3}$ 2.1 Hz, OH; 2.42, 3H, s, 5-Me; 2.44–2.33, 2H, 1H, 2×m, H9α, H10; 2.21, 1H, br d, J_{gem} 12.6 Hz, H6; 1.83–1.71, 2H, m, H1, H9β; 1.02, 3H, d, *J* 7.0 Hz, 1-Me; 0.89, 9H, s, $OSiCMe_3$; 0.12, 0.10, 2×3H, 2×s, $OSiMe_2$. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 206.7, C4; 175.8, **C**O_2Me; 146.7, C7; 138.9, C5; 132.7, 130.5, 129.9, C4a, C8a, C10c; 99.2, C8; 75.7, 73.3, C2, C3; 56.8, C3a; 56.1, 7-OMe; 51.6, CO_2**Me**; 47.2, C10a; 42.1, C6; 42.0, C10b; 35.8, C1; 27.3, 26.6, C9, C10; 26.1, OSiC**Me**$_3$; 20.9, 5-Me; 18.6, OSi**C**Me_3; 12.4, 1-Me; –3.7, –4.4, $OSiMe_2$. Mass spectrum *m/z* 488 (M^+, 44%), 431 (100), 401 (44), 371 (38), 356 (55), 339 (28), 75 (70).

*Methyl (1*SR, *2*SR, *3*RS,*3a*SR,*10a*RS,*10b*SR)*-2-diethylisopropylsilyloxy-1,2,3,3a,6,9,10,10b-octahydro-3-hydroxy-7-methoxy-1,5-dimethyl-4-oxocyclohept[bc]acenaphthylene-10a(4H)-carboxylate (34c)*

This compound was prepared by the procedure described above for the TBDMS ether. ^1H n.m.r. δ (300 MHz, $CDCl_3$) 5.14, 1H, br s, H8; 3.82, 1H, dd, $J_{2,1}$ 10.4 Hz, $J_{2,3}$ 8.8 Hz, H2; 3.72, 3H, s, 7-OMe; 3.58, 3H, s, CO_2Me; 3.18, 1H, br d, $J_{10b,3a}$ 7.2 Hz, H10b; 3.11, 1H, ddd, $J_{3,3a}$ 10.2 Hz, $J_{3,2}$ 8.7 Hz, $J_{3,OH}$ 2.1 Hz, H3; 2.92, 1H, dd, J_{gem} 12.6 Hz, $J_{6,8}$ 2.0 Hz, H6; 2.88, 1H, dd, $J_{3a,3}$ 10.2 Hz, $J_{3a,10b}$ 7.2 Hz, H3a; 2.62, 1H, d, $J_{OH,3}$ 2.1 Hz, OH; 2.48–2.33, 2H, 1H, 2×m, H9α, H10; 2.40, 3H, s, 5-Me; 2.17, 1H, d, J_{gem} 12.6 Hz, H'6; 1.78–1.65, 2H, m, H1, H9β; 1.01–0.93, 16H, m, 3'-Me, DEIPS; 0.78–0.60, 4H, DEIPS. ^{13}C n.m.r. δ (75 MHz, $CDCl_3$) 206.9, C4; 175.8, **C**O_2Me; 146.8, C7; 139.0, C5; 132.7, 130.6, 129.8, C4a, C8a, C10c; 99.2, C8; 75.4, 73.4, C2, C3; 57.0, C3a; 56.1, 7-OMe; 51.6, CO_2**Me**; 47.2, C10a; 42.1, C6; 42.0, C10b; 35.7, C1; 27.2, 26.5, C9, C10; 20.9, 5-Me; 17.5, 2×C, SiCH**Me**$_2$; 13.2, Si**C**HMe_2; 12.0, 3'-Me; 7.3, 7.2, $SiCH_2$**Me**; 4.3, 4.2, Si**C**H_2Me.

*Methyl (1*SR, *2*SR, *3*RS,*3a*SR,*10a*RS,*10b*SR)*-1,2,3,3a,6,9,10,10b-octahydro-2,3-Dihydroxy-7-methoxy-1,5-dimethyl-4-oxocyclohept[bc]acenaphthylene-10a(4H)-carboxylate*

Silyl ether (34a) (5.5 mg, 11.3 μmol) was dissolved in THF (1 ml) and treated with TBAF (23 μl of a 1 M solution in THF, 23 μmol). The solution was stirred at room temp. under an atmosphere of nitrogen for 1 h, after which time t.l.c. indicated that reaction was incomplete. A further aliquot of TBAF was added (10 μl, 10 μmol) and stirring continued for another 30 min. The mixture was then diluted with water and extracted with Et_2O. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Chromatography on silica gel (hexane/EtOAc, 1 : 2) afforded the *title diol* (2.1 mg, 50%). ^1H n.m.r. δ (300 MHz, $CDCl_3$) 5.15, 1H, br s, H8; 3.74, 1H, dd, $J_{2,1}$ 10.7 Hz, $J_{2,3}$ 9.0 Hz, H2; 3.73, 3H, s, 7-OMe; 3.58, 3H, s, CO_2Me; 3.22, 1H, br d, $J_{10b,3a}$ 7.1 Hz, H10b; 3.15, 1H, dd, $J_{3,3a}$ 10.1 Hz, $J_{3,2}$ 9.0 Hz, H3; 2.96, 1H, dd, J_{gem} =12.5 Hz, $J_{6,8}$ 2.1 Hz, H6; 2.93, 1H, dd, $J_{3a,3}$ 10.1 Hz, $J_{3a,10b}$ 7.1 Hz, H3a; 2.49–2.41, 2.36, 2H, 1H, 2×m, H9, H10α; 2.21, 1H, br d, J_{gem} 12.5 Hz, H'6; 1.86–1.73, 2H, m, H1, H10β; 1.58, 2H, br s, 2×OH; 1.07, 3H, d, $J_{1\text{-}Me,1}$ 6.8 Hz, 1-Me.

*(1*RS, *3a*RS, *10a*SR, *10b*SR *11*SR, *12*SR)*-12-t-Butyldimethylsilyloxy-3a,5,8,10,10a,10b-hexahydro-7-methoxy-9,11-dimethyl-10-oxo-1,3a-ethano-1H-cyclohept[3,4]indeno[1,7-cd]pyran-3(4H)-one (35a)*

A solution of (34a) (4.0 mg) was dissolved in MeOH (1 ml), and treated with a saturated solution of K_2CO_3 in MeOH/H_2O (1 : 1). The solution was stirred vigorously for 1 h, then diluted with brine (10 ml) and thoroughly extracted with CH_2Cl_2. The organic phase was washed with brine, and dried over $MgSO_4$ before being evaporated to dryness. The residue was carefully chromatographed on silica gel (hexane/EtOAc, 6 : 1) to provide *lactone* (35a) in 33% yield as a mixture with starting material (34a) (47%) and the Δ^6-isomer of (34a) (18%). ^1H n.m.r. δ (300 MHz, $CDC1_3$) 5.27, 1H, s, H6; 4.83, 1H, t, *J* 4.4 Hz, H1; 3.68, 1H, dd, *J* 2.9, 4.4 Hz, H12; 3.59, 3H, s, OMe; 3.10–3.20, 2H, m, **AB**X, H10a, H10b; 3.06, 1H, dd, *J* 2.0, 12.8 Hz, H8; 2.78, 1H, br dd, *J* 7.7, 18.1 Hz, H5; 2.42, 1H, m, H'5; 2.39, 3H, s, 9-Me; 2.20, 1H, dd, *J* 7.7,

14.2 Hz, H4; 2.00, 1H, m, obscured, H11; 2.00, 1H, d, *J* 12.4 Hz, H'8; 1.92, 1H, ddd, *J* 7.7, 12.6, 14.2 Hz, H'4; 1.06, 3H, d, *J* 7.4 Hz, 11-Me; 0.89, 9H, s, $OSiCMe_3$; 0.12, 0.09, 2×3H, 2×s, $OSiMe_2$.

*(1*RS, *3a*RS, *10a*SR, *10b*SR *11*SR, *12*SR)-*12-Diethylisopropylsilyloxy-3a,5,8,10,10a,10b-hexahydro-7-methoxy-9,11-Dimethyl-10-oxo-1,3a-ethano-1*H-*cyclohept[3,4]indeno[1,7-cd]pyran-3(4*H*)-one (35c)*

A solution of (34c) (190 mg, 0.48 mmol) was dissolved in MeOH (1 ml), and treated with a saturated solution of K_2CO_3 in MeOH/H_2O (1 : 1). The solution was stirred vigorously for 30 min, then diluted with brine (10 ml) and thoroughly extracted with CH_2Cl_2. The organic phase was washed with brine, and dried over $MgSO_4$ before being evaporated to dryness. The residue was carefully chromatographed on silica gel (hexane/EtOAc, 6 : 1) to provide the title compound in 30% yield, with a recovery of 30% of the starting material. (Found: C, 68.68; H, 8.40%; M^+, 470.2483. $C_{27}H_{38}O_5Si$ requires C, 68.90; H, 8.14%; M^+, 470.2488). ^{1}H n.m.r. δ (300 MHz, $CDC1_3$) 5.26, 1H, s, H6; 4.88, 1H, t, *J* 4.4 Hz, H1; 3.70, 1H, dd, *J* 2.9, 4.4 Hz, H12; 3.58, 3H, s, OMe; 3.10–3.20, 2H, m, **AB**X, H10a, H10b; 3.06, 1H, dd, *J* 2.0, 12.8 Hz, H8; 2.78, 1H, br dd, *J* 7.7, 18.1 Hz, H5; 2.42, 1H, m, H'5; 2.39, 3H, s, 9-Me; 2.18, 1H, dd, *J* 7.7, 14.2 Hz, H4; 2.02, 1H, m, obscured, H11; 2.00, 1H, d, *J* 12.4 Hz, H'8; 1.92, 1H, ddd, *J* 7.7, 12.6, 14.2 Hz, H'4; 1.04, 3H, d, *J* 7.4 Hz, 11-Me; 0.75–0.9, 13H, m, DEIPS; 0.4–0.6, 4H, m, DEIPS. ^{13}C n.m.r. δ (75 MHz, $CDC1_3$) 200.6, C10; 176.2, C3; 145.3, C7; 134.0, 133.5, 131.7, 131.3, C5a, C5b, C9a, C9b; 100.1, C6; 78.8, C1; 73.7, C12; 56.2, OMe; 47.7, C3b; 42.6, C3a; 42.3, C10a; 41.0, C8; 35.2, C11; 27.8, C5; 23.5, C4; 20.1, 9-Me; 16.9, 11-Me; 47.7, 3b; 42.6, C3a; 42.3, C8; 41.0, C10a; 35.2, C11; 27.8, C5; 23.5, C4; 19.8, 9-Me; 16.9, 16.8, SiCH**Me**$_2$; 16.75, 11-Me; 12.4, Si**C**HMe$_2$; 6.7, 2×C, $SiCH_2$**Me**; 3.4, 3.2, Si**CH**$_2$Me. Mass spectrum *m/z* 470 (M^+, 37%), 442 (14), 441 (39), 428 (40), 427 (100).

*(1*RS, *3a*RS, *10a*SR, *10b*SR *11*SR, *12*SR)-*3a,5,8,10,10a,10b-Hexahydro-12-hydroxy-7-methoxy-9,11-dimethyl-10-oxo-1,3a-ethano-1*H-*cyclohept[3,4]indeno[1,7-*cd*]pyran-3(4*H*)-one (36)*

Silyl ether (35c) (52 mg, 0.11 mmol) was dissolved in THF (3 ml) and the solution was cooled to 0°C. The solution was treated with TBAF (0.1 ml of a 1M solution in THF), and allowed to stir for 5 min. The orange mixture was quenched with ice water (10 ml) and extracted with EtOAc. The organic phase was washed with brine, dried over magnesium sulphate, and evaporated to dryness. Chromatography on silica gel (hexane/EtOAc, 1 : 2) provided the deprotected *alcohol* (36) in 85% yield. (Found: 342.1458. $C_{20}H_{22}O_5$ requires 342.1467). ^{1}H n.m.r. δ (300 MHz, $CDC1_3$) 5.29, 1H, br s, H6; 4.94, 1H, t, *J* 4.9 Hz, H1; 3.76, 1H, q, *J* 4.15 Hz, H12; 3.64, 3H, s, OMe; 3.24, 1H, dd, *J* 4.9, 12.5 Hz, H10a; 3.16, 1H, br d, *J* 12.5 Hz, H10b; 3.07, 1H, dd, *J* 2.0, 12.8 Hz, H8; 2.80, 1H, dd, *J* 7.7, 18.1 Hz, H5; 2.45, 1H, m, H'5; 2.39, 3H, s, 9-Me; 2.18, 1H, dd, *J* 7.7, 14.2 Hz, H4; 2.03, 1H, d, *J* 12.4 Hz, H'8; 1.90–2.08, 2H, m, H'4, H11; 1.09, 3H, d, *J* 7.3 Hz, 11-Me. ^{13}C n.m.r. δ (75 MHz, $CDC1_3$) 203.7, C10; 176.2, C3; 145.9, C7; 134.6, 134.1, 132.5, 130.4, C5a, C5b, C9a, C9b; 100.6, C6; 78.3, C1; 74.1, C2; 56.1, OMe; 47.4, C3b; 42.6, C3a; 42.5, C8; 41.1, C10a; 33.5, C11; 27.8, C5; 23.2, C4; 20.1, 9-Me; 16.9, 11-Me. Mass spectrum *m/z* 342 (M^+, 100%), 327 (66), 296 (5), 281 (7), 267 (16), 265 (16), 251 (10).

*(1*RS, *3a*RS, *10a*SR, *10b*SR *11*SR, *12*SR)-*3a,5,8,10,10a,10b-Hexahydro-10,12-dihydroxy-7-methoxy-9,11-dimethyl-1,3a-ethano-1*H-*cyclohept[3,4]indeno[1,7-*cd*]pyran-3(4*H*)-one (38)*

To ketone (36) (31 mg, 0.091 mmol) dissolved in MeOH (2 ml), was added $NaBH_4$ (10 mg, excess). The reaction mixture was stirred at room temp until complete by t.l.c. (40 minutes). The mixture was diluted with brine (5 ml) and acidified to pH 3 with 0.5M HCl. The aqueous phase was extracted with EtOAc, and the organic extracts were washed with brine, dried over Mg_2SO_4 and evaporated to dryness. The crude material (30 mg) appeared to be ~80% pure by n.m.r. analysis. The sample was purified by preparative t.l.c. (silica, hexane/EtOAc, 1 : 3) to give pure *diol* (38) (10 mg). This sample degraded significantly during the overnight ^{13}C n.m.r. δ acquisition. (Found: 344.1623. $C_{20}H_{22}O_5$ requires 344.1623). ^{1}H n.m.r. δ (300 MHz, $CDC1_3$) 5.58, 1H, d, *J* 5.2 Hz, H6; 5.12, 1H, br s, H10; 4.77, 1H, dd, *J* 3.3, 4.8 Hz, H1; 3.70, 1H, m, H12; 3.60, 3H, s, OMe; 3.10, 1H, d, *J* 12.8 Hz, H10b; 2.85, 1H, m, obscured, H10a; 2.82, 1H, dd, *J* 1.9, 12.8 Hz, H8; 2.65, 1H, dd, *J* 7.7, 18.1 Hz, H5; 2.33, 1H, m, H'5; 2.08, 1H, d, *J* 12.8 Hz, H'8; 2.05, 1H, m, obscured, H4; 2.02, 3H, s, 9-Me; 1.87, 1H, q, *J* 6.8Hz, H11; 1.80, 1H, ddd, *J* 7.7, 12.6, 14.2 Hz, H'4; 1.06, 3H, d, *J* 7.0 Hz, 11-Me. ^{13}C n.m.r. δ (75 MHz, $CDC1_3$) 177.0, C3; 148.6, C7; 139.6, 131.2, 127.4, 119.0, C5a, C5b, C9a, C9b; 99.8, C6; 77.5, 76.4, 72.6, C1, C9, C12; 55.8, OMe; 48.8, C3b; 43.7, C3a; 42.4, C8; 40.6, C10a; 33.2, C11; 28.1, C5; 23.1, C4; 20.1, 9-Me; 16.7, 11-Me. Mass spectrum *m/z* 344 (M^+, 91%), 329 (28), 327 (32), 326 (100), 325 (46), 311 (34), 267 (12), 239 (14), 217 (22), 214 (22).

(±)-Hainanolidol (1)

A sample of (38) (4 mg) was dissolved in THF (2 ml) and treated with 0.1 ml of conc. HCl. After standing for 10 min at room temp, the mixture was quenched with sat. aqu. $NaHCO_3$ solution (5 ml) and extracted with EtOAc. The organic phase was dried over $MgSO_4$, and evaporated to dryness. The crude material was purified by preparative t.l.c. (silica, EtOAc/chloroform, 1 : 1, with 5% MeOH) to give ~2 mg of the title compound. (Found: 312.1354. $C_{19}H_{20}O_4$ requires 312.1361). λ_{max} (EtOH) 240 (log ε 4.50), 321 (4.05). υ_{max} (neat) 3100 (s, br), 1760s, 1620s, 1590m, 1530m cm^{-1}. ^{1}H n.m.r. δ (500 MHz, $CDC1_3$) 6.92, 1H, br s, H8; 6.84, 1H, br s, H6; 4.57, 1H, t, *J* 4.2 Hz, H1; 3.80, 1H, dd, *J* 1.6, 4.5, 5.7 Hz, H12; 3.70, 1H, d, *J* 18.5 Hz, H10β; 3.49, 1H, d, *J* 10.9, H10b; 3.24, 1H, dd, *J* 18.5, 11.1, H10α; 3.16, 1H, m, H10a; 2.89, 1H, m, H5; 2.80, 1H, m, H'5; 2.42, 1H, m, H4; 2.33, 3H, s, 9-Me; 1.85, 1H, dt, *J* 14.6, 7.6 Hz, H'4; 1.45, 1H, m, H11; 0.99, 3H, d, *J* 7.1Hz, 11-Me. ^{13}C n.m.r. δ (75 MHz, $CDC1_3$) 184.2, C7; 177.0, C3; 141.5, C8; 138.0, 6; 145.4, 144.7, 142.1, 139.0, C5a, C5b, C9a, C9b; 77.6, C1; 75.6 C12; 51.5, C3b; 44.3, C3a; 37.2, C10a; 37.4, C11; 30.4, C5; 25.0, C4; 21.6, 9-Me; 16.9, 11-Me. Mass spectrum *m/z* 312 ($M^{+\cdot}$, 47%), 285 (6), 284 (44), 238 (21), 221 (34), 207 (81), 197 (33). 196 (80), 181 (34), 169 (33), 167 (55), 165 (47), 155 (42), 153 (48), 143 (100, 128 (40), 115 (25).

Hainanolidol (lit.)[2]. λ_{max} 240 (log ε 4.50), 321 (4.05). υ_{max} 3100 (s, br), 1760s, 1620s, 1590m, 1530m cm^{-1}. ^{1}H n.m.r. δ (60 MHz, $CDC1_3$) 6.90, 2H, m, H6, H8; 4.62, 1H, t, H1; 3.78, 1H, t, H12; 3.65–3.0, 5H, m; 2.9–2.3, 3H, m; 2.24, 3H, s, 9-Me; 1.94, 1H, m; 1.54, 1H, m; 1.02, 3H, d, 11-Me. Mass spectrum *m/z* 312 ($M^{+\cdot}$, 78%), 285 (11), 284 (51), 238 (13), 221 (23), 207 (63), 197 (26). 196 (73), 181 (23), 169 (23), 167 (39), 165 (32), 155 (34), 153 (33), 143 (100, 128 (28), 115 (13).

X-ray Structure Determination of Alcohol (16a)

Crystal Data. $C_{27}H_{40}O_6Si$, M_r 488.69, monoclinic, *C*2/*c*, *a* 25.170(4), *b* 10.904(2), *c* 21.132(2) Å, β 114.208(9)°, *V* 5290(1) Å^3, *Z* 8, D_x 1.227 g cm^{-3}, λ (Cu Kα) 1.5418 Å, μ 10.74 cm^{-1}, *F*(000) 2112, *T* 213 K, *R* 0.085 for 2787 observed reflections.

Data Collection And Processing: A yellow prismatic crystal of size 0.3 × 0.2 × 0.1 mm was mounted on a quartz fibre. All measurements were made on a Rigaku AFC6R four-circle diffractometer with graphite monochromated Cu Kα radiation and a rotating anode generator. Lattice parameters were obtained from least-squares analysis of the setting angles of 25 reflections with 43.5 < θ < 47.3°. Intensity data were collected at a temperature of 213 K using the ω-2θ scan technique to a maximum 2θ value of 120°. The total number of reflections measured was 4310. Equivalent reflections were merged to yield 3938 unique data (R_{int} 0.062), of which 2787 with I > 3σ(I) were used in structure solution and refinement. Structure solution was by direct methods.[26] Refinement[27] with anisotropic displacement factors for all non-hydrogen atoms gave rise to unacceptably large ratios between maximum and minimum displacements of atoms C(115), C(116), C(117) and C(118), all within the $OSi(CH_3)_2(C_4H_{12})$ group, suggesting that these atoms were disordered. Consequently these atoms were each split over two sites and the relative populations were refined. Restraints were imposed on bond distances involving the disordered atoms. Hydrogen atoms attached to carbon atoms were included at calculated positions (those cor-

responding to the minor orientation of the disordered $OSi(CH_3)_2(C_4H_9)$ group were omitted); the alcohol hydrogen atom on O(101) was not located. Full matrix least-squares refinement on F using 299 parameters gave final R 0.085. The weighting scheme used was $w = [\sigma^2(F) + 0.0001F^2]^{-1}$ and the maximum shift/error ratio in the final cycle was 0.04. The maximum and minimum heights in the final difference map were 0.64 and –0.53 e $Å^{-3}$ with the major features being located in the disordered region of the structure. Neutral-atom scattering factors with anomalous dispersion corrections were used throughout.[28]

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