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Synthetic studies toward the kempane diterpenes. Construction of a key tricyclic intermediate

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A synthetic sequence is described for construction of the tricyclic portion (**35**) of kempane diterpenes. The central stereochemistry was established by a Diels–Alder addition of 2,6-dimethyl-*para*-benzoquinone to a 5-membered, dithiane-protected diene, and the addition of acetylide, with very high chemoselectivity, provided a suitably functionalized handle that will be incorporated into the final seven-membered ring. The remaining stereogenic centres about the decalin moiety were established by a series of equilibration and reduction steps.

Introduction

The kempane diterpenes **1–5** (Fig. 1) are defined by a ring system that includes fused five-, two six- and seven-membered rings. The kempanes were isolated in very small amounts from the defensive secretions of termite soldiers of the species *Nasutitermes octopilis*, *Nasutitermes kempae* and *Bulbitermes singaporensis*.[1]

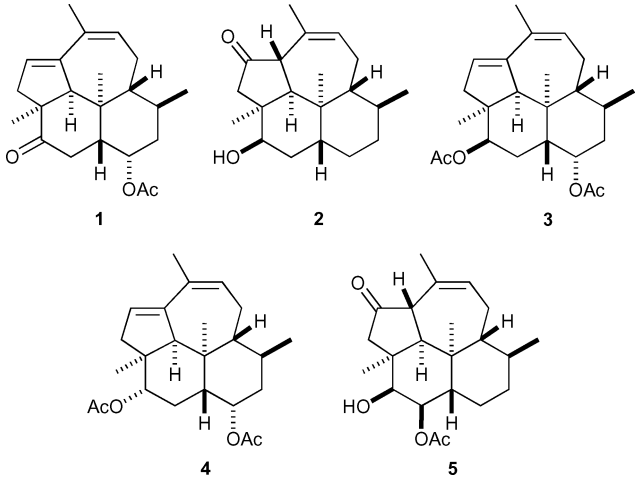

Fig. 1 Kempane diterpenes.

In spite of the significant synthetic challenge presented by the kempane diterpenes, efforts towards their synthesis have been surprisingly few. Dauben and co-workers[2] reported a route to **1** that included a number of inefficient steps, but, so far, this has been the only approach to have ended with a natural product. Paquette and co-workers[3] constructed a double-bond isomer of **2**, but they were unable to isomerize the double bond to produce the kempane. Work in our own laboratories resulted in the assembly of **6**,[4–6] which was designed to have functionality appropriately positioned to access kempanes **1–4** from a single, advanced intermediate. However, efforts to complete the synthesis of any kempane were thwarted by our inability to open the lactone ring in **6**. A closely related route, in which the lactone ring was opened early in the sequence, ended in failure when epimerization and conjugation of tricyclic compound **7** would not occur without the formation of a tetrahydrofuran moiety from the two methyl ethers, yielding the tetracyclic product **8** (Fig. 2).[6] Attempts to effect the

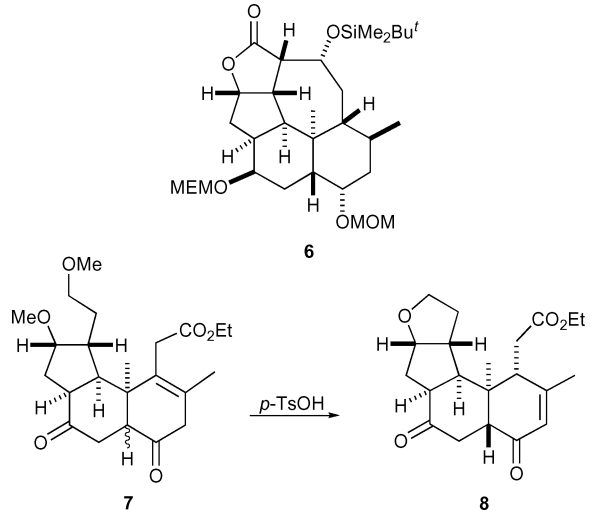

Fig. 2 End points in previous synthetic approaches.[6] ("MOM" = CH_2OCH_3, "MEM" = $CH_2OCH_2CH_2OCH_3$).

epimerisation and conjugation under conditions that did not produce the unwanted tetrahydrofuran were unsuccessful.

Our next approach was to construct a tricyclic molecule akin to **7**, bearing an oxygen function on the five-membered ring, but without the methoxyethyl chain. The significant questions to be answered were whether the relative stereochemistry about the decalin system could be achieved efficiently in a system in which formation of an extra five-membered ring would be impossible, and whether carbons to build the seven-membered ring could be added at the correct position and with the correct relative stereochemistry. The results of this investigation are presented here.

Results and discussion

The first target was the tricyclic compound **9** (Scheme 1). The bis(dimethyl acetal) of malonaldehyde was treated with 1,3-propanedithiol in the presence of boron trifluoride etherate to give the mono-dithiane **10**.[7] The anion of **10** reacted with iodo-acetal **11**, prepared by reaction of butanone with hydroiodic acid followed by protection as the ethylene acetal.[8] The product **12**, which had three protected carbonyls, was obtained in 84% yield. Treatment of **12** with aqueous HCl removed the oxygen-containing protecting groups, but the resulting keto–aldehyde was not isolated. Under the acidic conditions it underwent

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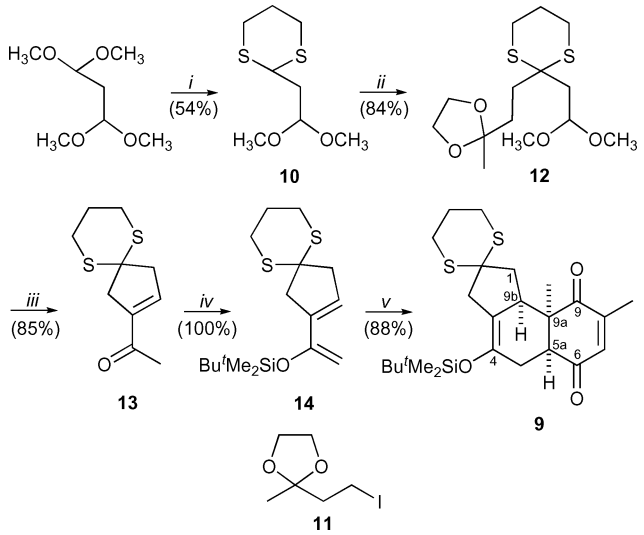
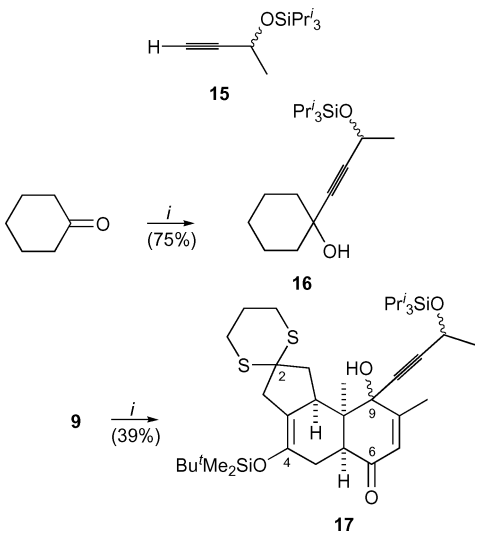


Scheme 1 Synthesis of tricyclic compound **9**. *Reagents and conditions*: *i*, $CH_2(CH_2SH)_2$, $BF_3{\cdot}Et_2O$; *ii*, BuLi, −25 °C, then **11**, 0 °C, 3 days; *iii*, 5% aqueous HCl, Δ, 3 h; *iv*, Bu^tMe_2SiOTf, Et_3N; *v*, 2,6-dimethyl-*p*-benzoquinone, toluene, Δ, 3 days.

aldol cyclization to produce the enone **13** in good yield. This was transformed quantitatively into the diene **14** with a silyl triflate in the presence of triethylamine. Heating **14** with 2,6-dimethyl-*para*-benzoquinone gave the Diels–Alder adduct **9** in excellent yield. (No regioisomeric Diels–Alder adduct was detected in the crude reaction mixture. Due to considerable overlap in the ^{1}H NMR spectrum of **9**, the regiochemistry and the stereochemistry of this reaction was ascertained by NMR analysis of subsequent compounds.) This reaction ensured the correct relative stereochemistry at two central positions, C-9a and C-9b.

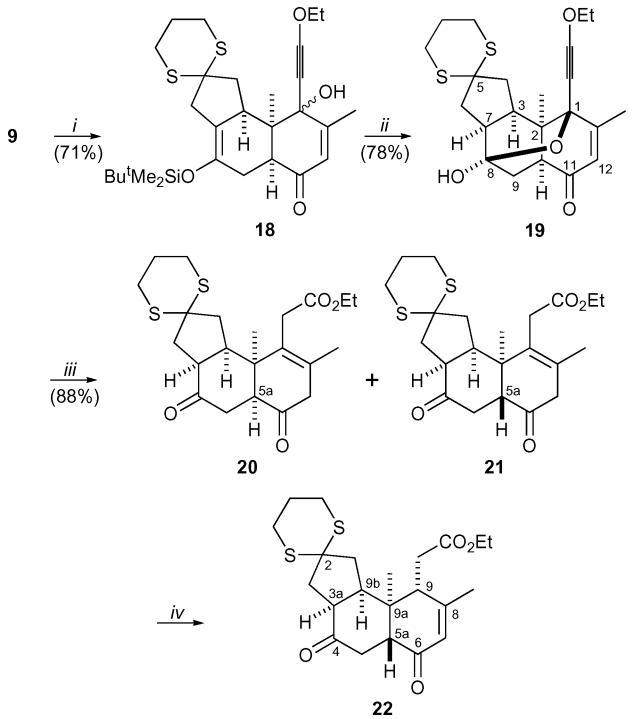
Additional carbons were needed to form the seven-membered ring. It had been shown that hydride reductions and additions of lithium acetylide to enediones similar to **9** took place with a very high preference for the "top" ketone (C-9) and from the face *syn* to the quaternary methyl (at C-9a).[5,6,9,10] Initially, **11** was treated with *t*-butyllithium and to the organolithium generated in this way was added **9**, but the result was a complex mixture. The lithium acetylide was prepared from triisopropylsilyl-protected 3-butyn-2-ol **15**. Whereas this reacted in 75% yield with cyclohexanone to produce **16** (Scheme 2), the acetylide's reaction with **9** occurred in only 39% yield. Nevertheless, the reaction had taken place with a high degree



Scheme 2 Reactions of the acetylide derived from **15**. *Reagents and conditions*: *i*, **15**, BuLi, −78 to 0 °C, then addition of the ketone.

of regioselectivity, although the product **17** was an epimeric mixture. In an attempt to deoxygenate the tertiary alcohol of **17**, the mixture was treated first with potassium fluoride in methanol, to remove the silyl enol ether, and then with zinc in acetic acid, following the same procedure used for **18** to **22**. The result of the latter step with **17** was a very complex mixture.

In contrast, addition of lithium ethoxyacetylide to **9** took place in better yield, but the product **18** was once again an epimeric mixture (Scheme 3). (The signals for the olefinic protons had the same chemical shift, which indicated that the two components of the product differed in stereochemistry, not in skeleton.) The epimers were not separated. The silyl group was removed from the mixture with potassium fluoride in methanol, but a single product was isolated. The yield (78%) indicated that both epimers of **18** must have reacted to form this product. Its ^{13}C NMR spectrum contained only one ketone signal, at δ 200.6, which was a conjugated ketone, and a signal at δ 99.1 ascribable to a hemi-acetal. The expected ketone at C-4 had formed a hemi-acetal with the tertiary alcohol, resulting in structure **19**. Compound **19** was heated in acetic acid in the presence of zinc metal. Deoxygenation took place smoothly to afford **20** and **21**, the *cis*- and the *trans*-decalin (C-5a epimers), in a 1 : 1 ratio. Each epimer had undergone concomitant conversion of the ethoxyalkyne moiety to the ethyl ester.[6]

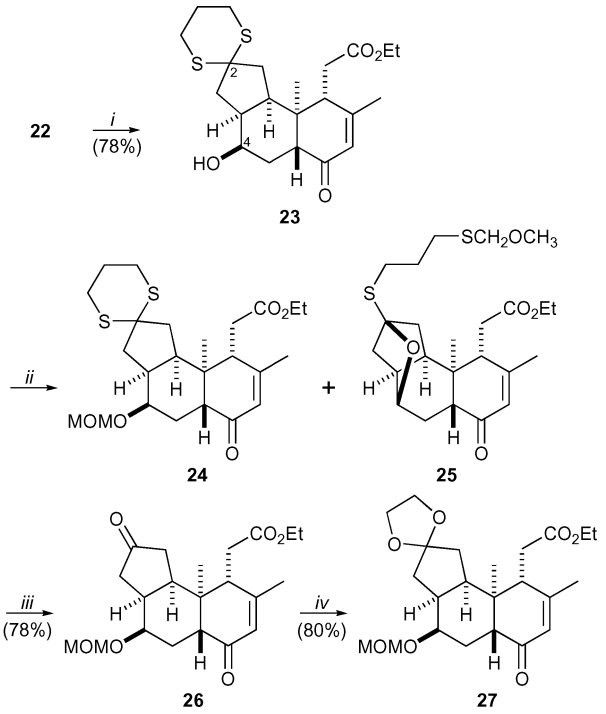


Scheme 3 Addition of ethoxyacetylide and deoxygenation. *Reagents and conditions*: *i*, ethoxyethyne, BuLi, −78 to 0 °C, then addition of **9**; *ii*, KF, CH_3OH; *iii*, Zn metal, CH_3CO_2H, Δ; *iv*, *p*-TsOH, C_6H_6, Δ, for yields see text.

Both **20** and **21** were converted to **22** by heating them as benzene solutions in the presence of *para*-toluenesulfonic acid. A significant difference in the rate and efficiency of the conversion to **22** was noted between **20** and **21**. The *cis*-decalin compound **20**, over a period of two days, gave only 45% of **22**, with some **20** being recovered. On the other hand, from the *trans*-decalin compound **21** an 81% yield of **22** was obtained after only six hours. This suggested that **20** epimerized slowly to **21** before reconjugation of the double bond. Nevertheless, **20** and **21** were converted to the same compound (**22**), which had the desired stereochemistry at C-5a and at C-9.

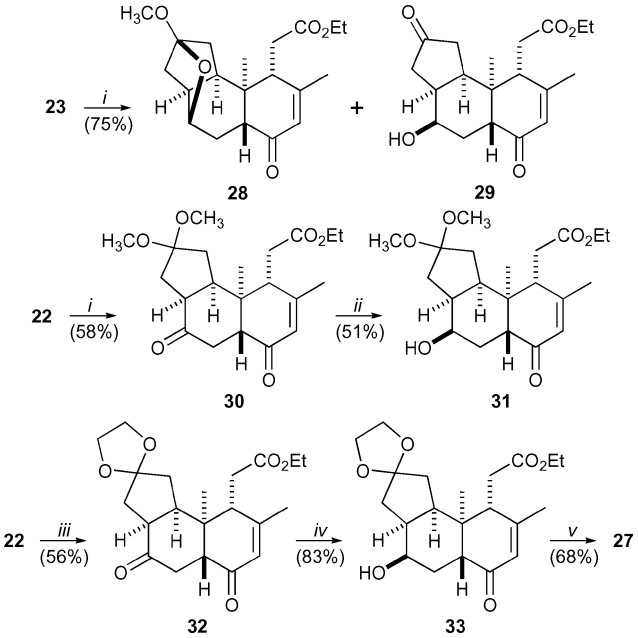
With a conjugated and an unconjugated ketone present in **22**, the opportunity was at hand to differentiate between the ketones. $LiAlH(O\text{–}Bu^t)_3$ reduced exclusively the unconjugated

ketone at C-4, but without any stereoselectivity. A 1 : 1 mixture of inseparable, epimeric alcohols was the result. However, L-Selectride reduced **22** with both chemo- and stereoselectivity affording **23** in good yield (Scheme 4). The axial arrangement of the hydroxyl was consistent with a narrow signal for the carbinolic methine in the ^{1}H NMR spectrum, but the relative stereochemistry was established unequivocally by measurement of NOEs. However, the axial alcohol of **23**, which matched the relative stereochemistry at C-4 of kempanes **2** and **3**, was in a congested environment, which made its protection troublesome. After much experimentation, the alcohol was converted to the methoxymethyl ether **24**, but the yield was modest and variable (30–55%). There was a significant amount (typically 15%) of a by-product in which the dithiane had opened to form a methoxymethyl thioether **25**. In spite of the low yield of **24**, the removal of its dithiane with mercury perchlorate in the presence of calcium carbonate,[11] giving **26**, and reprotection of the unconjugated carbonyl as the acetal **27** proceeded normally.



Scheme 4 Reduction and protection at C-4. *Reagents and conditions*: *i*, L-Selectride, THF, −78 °C; *ii*, CH_3OCH_2Cl, Pr^i_2NEt, CH_2Cl_2, Δ, for yields see text; *iii*, $Hg(ClO_4)_2$, $CaCO_3$, THF–H_2O; *iv*, 1,2-ethanediol, PPTS, C_6H_6, Δ. ("MOM" = CH_2OCH_3).

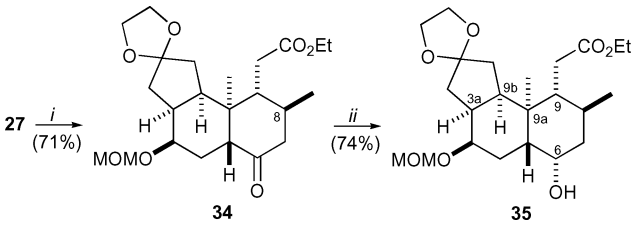
The disappointing yield of **24** led to an assessment of alternatives for the protection of the alcohol at C-4 and the switch of the dithiane to an acetal protecting group at C-2 (Scheme 5). The latter was necessary because a subsequent step was the dissolving-metal reduction of the double bond, conditions that would be incompatible with a dithiane. From the unprotected alcohol **23**, the direct conversion of dithiane to the dimethyl acetal using Stork's method,[12] with methanol and bis(trifluoroacetoxy)iodobenzene, gave a 1 : 1 mixture of the mixed acetal **28** and the ketone **29**, the product of simple deprotection, in a combined yield of 75%. The desired dimethyl acetal **30** was obtained from **23** under the same conditions, but the yield was a modest 58%. Reduction of **30** was less efficient, providing **31** in a yield of only 51%, and an attempt to protect **31** as the methoxymethyl ether, under the same conditions as for **23**, gave back only the unprotected alcohol. Starting again with **22**, the dithiane was converted directly to the dioxolane to give **32**, using 1,2-ethanediol and bis(trifluoroacetoxy)iodobenzene, but the yield was essentially the same as that for **30**. However,



Scheme 5 Alternative sequences for reduction at C-4 and switching the dithiane for an acetal at C-2. *Reagents and conditions*: *i*, CH_3OH, $PhI(OCOCF_3)_2$, RT; *ii*, K-Selectride, THF, −40 °C; *iii*, 1,2-ethanediol–CH_3CN (10 : 1), $PhI(OCOCF_3)_2$, RT; *iv*, L-Selectride, THF, −78 °C; *v*, CH_3OCH_2Cl, Pr^i_2NEt, CH_2Cl_2, RT. ("MOM" = CH_2OCH_3).

reduction of **32** occurred in 83% yield to provide **33**, and protection of **33** to give the methoxymethyl ether **27**, took place in higher yield than seen previously with **23**.

Treatment of **27** with lithium in liquid ammonia yielded compound **34**, in which the relative stereochemistry at C-8 was determined by measurement of NOEs to be the same as in the kempanes, *i.e.*, the methyl at C-8 was equatorial. Finally, reduction of the remaining ketone with L-Selectride was carried out with high stereoselectivity to give compound **35** with the hydroxyl in an axial position, which was the same relative stereochemistry at C-6 as in kempanes **1**, **3** and **4** (Scheme 6).



Scheme 6 Dissolving-metal reduction and reduction at C-6. *Reagents and conditions*: *i*, Li metal, NH_3, −55 °C, 5 min; *ii*, L-Selectride, THF, −78 °C. ("MOM" = CH_2OCH_3).

Conclusions

The approach to compound **35** described here used a Diels–Alder reaction to establish the central stereochemistry at C-9a and C-9b. Subsequent steps relied on equilibration and the stereoselectivity of hydride reductions to establish the rest of the stereogenic centres. Compound **35** represents the tricyclic portion of kempanes **1–4**, with all of the required stereochemistry and with the oxygen functions suitably differentiated. Experiments are underway aimed at the elongation of the two-carbon chain at C-9, cyclization of the seven-membered ring, addition of the methyl group at C-3a, and the modification of the oxygen functions in order to produce kempanes **1–4**.

Experimental

General

Melting points are uncorrected. NMR spectra are for $CDCl_3$ solutions, at 300 MHz for ^1H and 74.5 MHz for ^{13}C, unless specified otherwise. Shifts are relative to internal tetramethylsilane. Nuclear Overhauser effect (NOE) measurements were made using difference spectra. Assignments are based on 2-D experiments, DEPT or APT spectra (for ^{13}C) and the NOE measurements. ^{13}C NMR shifts are followed in parentheses by the number of attached hydrogens. "Chromatography" refers to flash chromatography on silica gel; elution was with hexanes containing an increasing proportion of ethyl acetate, unless otherwise noted. Compound **11** was prepared following a published procedure.[8]

2-(2,2-Dimethoxyethyl)-1,3-dithiane 10. A rapidly stirred mixture of $BF_3{\cdot}Et_2O$ (18 ml), glacial acetic acid (36 ml) and $CHCl_3$ (60 ml) was maintained at reflux. A solution of 1,3-propanedithiol (15 ml, 16 g, 0.15 mol) and malonaldehyde bis(dimethyl acetal) (100 ml, 0.60 mol) in $CHCl_3$ (350 ml) was added over 8 h. The mixture was allowed to cool to RT before it was washed with H_2O, 10% aqueous KOH solution and H_2O. The $CHCl_3$ solution was dried (K_2CO_3) and concentrated under vacuum. Vacuum distillation provided **10** (17 g, 54%) as an oil: bp 120–128 °C/2 mm Hg; δ_H 4.66 (1 H, t, *J* 5.8, C*H*$(OCH_3)_2$), 4.09 (1 H, t, *J* 7.2, C*H*$(SR)_2$), 3.34 (6 H, s, CH$(OCH_3)_2$), 2.95–2.78 (2 H, m), 2.16–2.08 (2 H, m), 2.03 (2 H, m) and 1.95–1.82 (2 H, m); δ_C 101.0 (*C*H$(OCH_3)_2$), 52.9 (CH$(OCH_3)_2$), 42.5 (C-2 of dithiane), 38.1 (2), 29.8 (2) and 25.6 (2); *m*/*z* 208.0588 (M^+, 1%, $C_8H_{16}O_2S_2$ requires 208.0592), 176 (34), 161 (10), 145 (12), 118 (40), 101 (21), 87 (12) and 75 (100).

2-(2,2-Dimethoxyethyl)-2-(3-[1,3-dioxolan-2-yl]butyl) -1,3-dithiane 12. *n*-Butyllithium (11.1 ml of a 2.5 M solution in hexane, 25.8 mmol) was added to a solution of **10** (5.38 g, 25.3 mmol) in dry THF (130 ml) at −40 °C. The solution was stirred for 2 h at −20 °C before the solution was cooled to −40 °C, and **11** (6.76 g, 27.9 mmol) was added. The mixture was maintained at 0 °C for 3 days. Much of the solvent was removed under vacuum before H_2O (50 ml) was added. The mixture was extracted with $CHCl_3$. The combined $CHCl_3$ extracts were washed with H_2O, 7% aqueous KOH solution and brine. The $CHCl_3$ solution was dried (K_2CO_3) and concentrated under vacuum. Chromatography provided **12** (6.84 g, 84%) as an oil: δ_H 4.66 (1 H, t, *J* 4.6, C*H*$(OCH_3)_2$), 3.95 (4 H, s, dioxolane), 3.35 (6 H, s, CH$(OCH_3)_2$), 2.83 (4 H, m, dithiane), 2.18 (2 H, d, *J* 4.6, CH_2CH$(OCH_3)_2$), 2.04 (2 H, m), 1.96 (2 H, apparent pentet, *J* 5.6, dithiane), 1.85 (2 H, m) and 1.34 (3 H, s, methyl on dioxolane); δ_C 109.8 (0), 102.4 (1), 64.5 (2 C, 2), 53.1 (2 C, 3), 50.8 (0), 41.5 (2), 33.2 (2), 33.1 (2), 26.0 (2 C, 2), 25.1 (2) and 23.9 (3); *m*/*z* 322.1277 (M^+, 2%, $C_{14}H_{26}O_4S_2$ requires 322.1272), 233 (3), 87 (21) and 75 (100).

2-Acetyl-6,10-dithiaspiro[4,5]dec-2-ene 13. A 5% aqueous HCl solution (80 ml) was added to a solution of **12** (2.31 g, 7.17 mmol) in THF (80 ml). This mixture was heated under reflux for 3 h. Most of the THF was evaporated under vacuum before the aqueous mixture was extracted with ethyl acetate. The combined extracts were washed with H_2O and brine. The solution was dried (Na_2SO_4), and the solvent was evaporated under vacuum. Chromatography yielded **13** (1.30 g, 85%) as a solid: mp 68–69 °C; ν_{max}(Nujol)/cm^{-1} 1704, 1655 and 1623; δ_H 6.67 (1 H, narrow m), 3.22 (2 H, narrow m), 3.11 (2 H, narrow m), 3.02 (2 H, ddd, *J* 14.3, 9.1 and 3.2, dithiane), 2.88 (2 H, ddd, *J* 14.3, 7.3 and 3.2, dithiane), 2.35 (3 H, s, COCH_3) and 2.16–1.94 (2 H, m, dithiane); δ_C 195.9 (0), 143.1 (0), 140.0 (1), 52.5 (0), 50.4 (2), 48.0 (2), 28.4 (2 C, 2), 26.4 (3) and 25.0 (2); *m*/*z* 214.0476 (M^+, 36%, $C_{10}H_{14}OS_2$ requires 214.0486), 181 (4), 171 (12), 140 (19), 108 (6), 106 (9), 97 (15), 45 (17) and 43 (100).

2-(1-((*tert*-Butyldimethylsilyl)oxy)vinyl)-6,10-dithiaspiro[4,5]-dec-2-ene 14. Dry triethylamine (1.10 ml, 7.90 mmol) was added to a solution of **13** (1.30 g, 6.07 mmol) and *tert*-butyldimethylsilyl triflate (1.57 ml, 6.68 mmol) in dry CH_2Cl_2 (50 ml) at 0 °C. After stirring for 10 min, the solvent was evaporated under vacuum. Chromatography afforded **14** (2.04 g, 100%) as an oil: ν_{max}(film)/cm^{-1} 1636 and 1590; δ_H 5.91 (1 H, broad s, 3-H), 4.27 (1 H, s, C=CH_2), 4.21 (1 H, s, C=CH_2), 3.02 (4 H, broad s, 1-H and 4-H), 2.93 (4 H, m, dithiane), 2.04 (2 H, broad m, dithiane), 0.94 (9 H, s, SiCMe$_2$*Bu*^{t}) and 0.16 (6 H, s, SiC*Me*$_2$Bu^t); δ_C 152.8 (0), 138.5 (0), 124.8 (1), 93.2 (2), 53.1 (0), 50.1 (2), 49.3 (2), 28.5 (2 C, 2), 25.7 (3 C, 3), 25.3 (2), 18.1 (0) and −4.7 (2 C, 3); *m*/*z* 328.1339 (M^+, 31%, $C_{16}H_{28}OS_2Si$ requires 328.1351), 271 (6), 221 (11), 197 (26), 165 (45) and 75 (100).

(5*aα*,9*aα*,9*bα*)-4-(*tert*-Butyldimethylsilyl)oxy-2,3,5,5*a*,9*a*,9*b*-hexahydro-8,9*a*-dimethyl-1*H*-benz[*e*]indene-2,6,9-trione, 2-(propylene thioacetal) derivative 9. A solution of diene **14** (2.84 g, 8.65 mmol) and 2,6-dimethyl-*para*-benzoquinone (2.38 g, 17.3 mmol) in dry toluene (100 ml) was heated at reflux for 3 days. The solvent was removed under vacuum, and chromatography (25% ether in hexane) gave **9** (3.53 g, 88%) as a solid: mp 162–164 °C; ν_{max}(Nujol)/cm^{-1} 1714, 1692 and 1622; δ_H 6.42 (1 H, narrow m, 7-H), 3.03–2.68 (9 H, m), 2.48 (1 H, dd, *J* 11.4 and 6.8), 2.40 (1 H, m), 2.19–2.01 (3 H, m), 1.96 (3 H, d, *J* 1.7, 8-CH_3), 1.38 (3 H, s, 9a-CH_3), 0.89 (9 H, s, SiC(CH_3)$_3$), 0.06 (3 H, s, SiCH_3) and 0.05 (3 H, s, SiCH_3); δ_C 202.2 (0), 200.1 (0), 148.6 (0, C-4), 138.8 (0, C-8), 133.4 (1, C-7), 117.1 (0, C-3a), 57.1 (1), 53.6 (0), 50.0 (0), 47.3 (1), 44.2 (2), 41.4 (2), 32.1 (2), 28.7 (2, S*C*H$_2$), 27.8 (2, SC*H*$_2$), 25.6 (3 C, 3, SiC(*C*H$_3$)$_3$), 25.6 (2, dithiane), 24.5 (3, 9a-*C*H$_3$), 18.0 (0, Si*C*(CH$_3$)$_3$), 16.6 (3, 8-*C*H$_3$), −3.9 (3, Si*C*H$_3$) and −4.0 (3, Si*C*H$_3$); *m*/*z* 464.1874 (M^+, 17%, $C_{24}H_{36}O_3S_2Si$ requires 464.1875), 389 (6), 366 (6), 358 (25), 357 (74), 75 (31) and 73 (100).

3-(Triisopropylsilyl)oxybut-1-yne 15. Chlorotriisopropylsilane (1.52 g, 7.9 mmol) was added to a solution of 3-butyn-2-ol (460 mg, 6.6 mmol) and imidazole (1.12 g, 16.5 mmol) in dry DMF (2.0 ml). The mixture was stirred at RT under argon for 15 h. H_2O (10 ml) was added. This was extracted with ethyl acetate. The ethyl acetate solution was washed with H_2O and brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography yielded **15** (1.49 g, 100%) as a liquid: δ_H 4.60 (1 H, dq, *J* 6.5 and 1.7, OC*H*), 2.38 (1 H, d, *J* 2.4, alkyne H), 1.46 (3 H, d, *J* 6.4, CH_3) and 1.06 (21 H, m, TIPS); δ_C 86.6, 71.0, 58.8, 25.6, 18.0, 17.9 and 12.2.

1-[3-(Triisopropylsilyl)oxybut-1-yn-1-yl]cyclohexanol 16. To a solution of **15** (129 mg, 0.57 mmol) in dry THF (5 ml) was introduced *n*-butyllithium (0.23 ml of a 2.5 M solution in hexane, 0.57 mmol) at −78 °C over 5 min. The solution was stirred for 30 min before it was transferred by double-headed needle to a solution of cyclohexanone (56 mg, 0.57 mmol) in dry THF (10 ml) at −78 °C. The mixture was stirred at −78 °C for 2 h and at 0 °C for 1 h. H_2O (10 ml) and then ether (100 ml) were added. The organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated under vacuum. Chromatography gave **16** as a liquid: δ_H 4.64 (1 H, q, *J* 6.5, OC*H*), 2.04 (1 H, s, O*H*), 1.86 (2 H, m), 1.60 (8 H, m) and 1.09 (21 H, m, TIPS).

(5*aα*,9*aα*,9*bα*)-4-(*tert*-Butyldimethylsilyl)oxy-2,3,5,5*a*,6,9,9*a*,9*b*-octahydro-9-hydroxy-8,9*a*-dimethyl-9-[3-(triisopropylsilyl)-oxybut-1-yn-1-yl]-1*H*-benz[*e*]indene-2,6-dione, 2-(propylene thioacetal) derivative 17 (mixture of epimers at C-9). To a solution of **15** (386 mg, 1.70 mmol) in dry THF (10 ml) was introduced *n*-butyllithium (0.68 ml of a 2.5 M solution in hexane, 1.7 mmol) at −78 °C over 5 min. The solution was stirred for 30 min before it was transferred by double-headed needle to a solution of **9** (628 mg, 1.35 mmol) in dry THF (10 ml) at −78 °C. The mixture was stirred at −78 °C for 2 h and at 0 °C for 1 h. H_2O (20 ml) and then ether (100 ml) were added. The aqueous layer was

re-extracted with ether. The combined ether layers were washed with H_2O and brine, dried (Na_2SO_4) and concentrated under vacuum. Chromatography gave **17** (52 mg, 39%) as a liquid: δ_H 5.81 (1 H, s, C*H*=CCH$_3$), 4.70 (1 H, q, *J* 6.4, CH$_3$C*H*O), 3.30 (1 H, dt, *J* 13.0 and 4.0), 2.88 (4 H, dq, *J* 28.0 and 4.8), 2.57 (1 H, m), 2.36 (4 H, m), 2.16 (3 H, s, CH_3), 2.02 (3 H, m), 1.69 (1 H, dd, *J* 14.4 and 4.3), 1.52 (6 H, m), 1.25 (1 H, s), 1.06 (18 H, d), 1.01 (3 H, s, CH_3), 0.84 (9 H, s, *t*-butyl), 0.12 (3 H, s, TIPS), 0.07 (3 H, s, CH_3 in TBS) and 0.03 (3 H, s, CH_3 in TBS); δ_C 196.8, 159.3, 140.8, 125.4, 116.1, 81.7, 76.2, 59.2, 53.3, 52.5, 46.2, 39.9, 34.7, 31.8, 29.1, 28.3, 26.0, 25.9, 25.5, 22.8, 19.1, 18.1, 16.8, 12.3, −3.4, −3.5 and −3.7.

(5a*α*,9a*α*,9b*α*)-4-(*tert*-Butyldimethylsilyl)oxy-9-ethoxyethynyl-2,3,5,5*a*,6,9,9*a*,9*b*-octahydro-9-hydroxy-8,9*a*-dimethyl-1*H*-benz-[*e*]indene-2,6-dione, 2-(propylene thioacetal) derivative 18 (mixture of epimers at C-9). *n*-Butyllithium (0.43 ml of a 2.5 M solution in hexane, 1.1 mmol) was added over 5 min to a solution of ethoxyethyne (0.31 ml of a 50% by weight solution in hexane, 1.6 mmol) in dry THF (10 ml) at −78 °C. The solution was stirred for 30 min. It was transferred by double-tipped needle to a solution of **9** (248 mg, 0.534 mmol) in dry THF (10 ml) at −78 °C. The mixture was stirred at −78 °C for 2 h and then at 0 °C for 1 h. H_2O (10 ml) was added followed by ether (100 ml). The ether solution was washed with H_2O and brine. The solution was dried (Na_2SO_4), and the solvent was removed under vacuum. Chromatography yielded **18** (202 mg, 71%) as a foam: ν_{max}(Nujol)/cm^{-1} 3414, 2304 and 1692; δ_H 5.78 (1 H, s, 7-H of both isomers), 4.21–4.08 (2 H, m, OCH_2CH$_3$ of both isomers), 3.59 (1 H, s, O*H*), 3.15–1.90 (m), 2.14 (3 H, s, 8-CH_3 of major isomer), 2.12 (3 H, s, 8-CH_3 of minor isomer), 1.46–1.26 (m), 1.20 (3 H, s, 9a-CH_3 of major isomer), 0.95 (9 H, s, SiC(CH_3)$_3$ of minor isomer), 0.90 (9 H, s, SiC(CH_3)$_3$ of major isomer), 0.20 (3 H, s, SiCH_3 of minor isomer), 0.15 (3 H, s, SiCH_3 of minor isomer), 0.10 (3 H, s, SiCH_3 of major isomer) and 0.09 (3 H, s, SiCH_3 of major isomer); δ_C low field signals for major isomer 200.8 (0), 156.7 (0), 141.0 (0), 122.2 (1), 115.8 (0), 97.1 (0), 75.0 (0), 74.5 (0), 54.4 (1), 52.0 (0) and 48.2 (1); δ_C low field signals for minor isomer 196.7 (0), 162.0 (0), 140.2 (0), 125.9 (1), 116.3 (0), 95.3 (0), 74.2 (0), 73.8 (0), 53.4 (2), 51.8 (1) and 50.0 (1); δ_C high field signals for both/either isomer 46.3 (0), 45.6 (0), 44.9 (1), 43.3 (2), 42.4 (2), 41.5 (2), 40.4 (2), 33.1 (2), 28.9 (2), 28.4 (2), 28.1 (2), 27.6 (2), 26.0 (2), 25.6 (3), 25.4 (2), 20.3 (3), 18.5 (3), 18.0 (0), 14.7 (3), 14.5 (3), −3.5 (3), −3.6 (3), −3.7 (3) and −3.9 (3); *m*/*z* 534.2289 (M$^+$, 4%, $C_{28}H_{42}O_4S_2Si$ requires 534.2294), 505 (1), 488 (2), 427 (11), 357 (17), 261 (17), 75 (61) and 73 (100).

(1*R,2*R**,3*R**,7*S**,8*S**,10*S**)-1-(Ethoxyethynyl)-8-hydroxy-2,13-dimethyl-14-oxatetracyclo[6.5.1.0^{2,10}.0^{3,7}]tetradec-12-ene-5,11-dione, 5-(propylene thioacetal) derivative 19.** A solution of **18** (2.67 g, 5.00 mmol) and KF·2H_2O (2.35 g, 25.0 mmol) in methanol (260 ml) was stirred at RT for 14 h. Most of the methanol was removed under vacuum. H_2O was added, and this was extracted with ethyl acetate. The organic extract was washed with H_2O and brine, then dried ($MgSO_4$) and concentrated under vacuum. Chromatography gave **19** (1.64 g, 78%) as a solid: mp 181–183 °C; ν_{max}(Nujol)/cm^{-1} 3327, 2264 and 1666; δ_H 5.74 (1 H, br s, 12-H), 4.26 (2 H, q, *J* 7.1, OCH_2CH$_3$), 3.37 (1 H, dd, *J* 13.4 and 9.2, 4β-H), 3.08 (1 H, br s, O*H*), 3.03–2.76 (4 H, m, 2 × CH_2S), 2.65 (1 H, m, 7-H), 2.60 (1 H, m, 6-H), 2.45 (1 H, m, 3-H), 2.38 (1 H, m, 10-H), 2.33 (1 H, m, 6-H), 2.32 (1 H, m, 4α-H), 2.14 (1 H, t, *J* 12.3, 9α-H), 2.13 (3 H, d, *J* 1.3, 13-CH_3), 2.13–1.93 (2 H, m, dithiane), 1.70 (2 H, dd, *J* 13.5 and 4.4, 9β-H), 1.40 (3 H, t, *J* 7.1, OCH$_2$CH_3) and 1.05 (3 H, s, 2-CH_3), saturation of δ 3.37 (4β-H) led to NOEs at δ 2.45 (3-H) and 2.32 (4α-H), saturation of δ 1.70 (9β-H) led to a NOE at δ 2.14 (9α-H), saturation at δ 1.05 (2-CH_3) led to NOEs at δ 3.37 (4β-H), 2.45 (3-H) and 2.38 (10-H); δ_C 200.6 (0, C-11), 159.2 (0, C-13), 121.2 (1, C-12), 99.1 (0), 97.6 (0), 74.7 (2, O*C*H$_2$CH$_3$), 60.4 (0), 55.2 (0), 52.0 (1, C-10), 47.5 (1, C-3), 45.1 (1, C-7), 41.6 (2, C-4), 40.0 (2, C-6), 37.9 (0), 37.4 (0), 35.3 (2, C-9), 28.7 (2, *C*H$_2$S), 27.5 (2, *C*H$_2$S), 25.7 (2, dithiane), 20.5 (3, 13-*C*H$_3$), 19.1 (3, 2-*C*H$_3$) and 14.8 (3, OCH$_2$*C*H$_3$); *m*/*z* 420.1425 (M$^+$, 13%, $C_{22}H_{28}O_4S_2$ requires 420.1429), 392 (20), 374 (8), 350 (30), 348 (30), 179 (47), 175 (41), 172 (80), 151 (55), 137 (39), 107 (53), 106 (42), 98 (58), 91 (52) and 41 (100).

(3a*α*,5a*α*,9a*α*,9b*α*)-1,2,3,3*a*,4,5,6,7,9*a*,9*b*-Decahydro-8,9*a*-dimethyl-2,4,6-trioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(propylene thioacetal) derivative 20 and (3a*α*,5a*β*,9a*α*,9b*α*)-1,2,3,3*a*,4,5,6,7,9*a*,9*b*-decahydro-8,9*a*-dimethyl-2,4,6-trioxo-1*H*-benz-[*e*]inden-9-acetic acid ethyl ester, 2-(propylene thioacetal) derivative 21. A solution of **19** (1.62 g, 3.86 mmol) in glacial acetic acid (120 ml) was heated at reflux. Zinc dust (18 g, 0.28 mol) was added in portions until no more **19** remained by TLC. After cooling to RT, the mixture was filtered. The filtrate was poured into ethyl acetate (300 ml), H_2O (300 ml) was added, and this was stirred while solid Na_2CO_3 was added until evolution of CO_2 ceased. The aqueous layer was re-extracted with ethyl acetate. The combined organic solutions were washed with H_2O and brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography provided a 1 : 1 mixture of **20** and **21** (1.43 g, 88%). Repeated chromatography was used to separate the isomers.

*For **20**.* Viscous oil; ν_{max}(Nujol)/cm^{-1} 1712; δ_H 4.19 (2 H, m, OCH_2CH$_3$), 3.28 (1 H, d, *J* 17.0, CH_2CO$_2$), 3.25 (1 H, dd, *J* 16.8 and 1.4, 5β-H), 3.15 (1 H, d, *J* 21.1, 7-H), 3.13 (1 H, d, *J* 17.0, CH_2CO$_2$), 3.02 (1 H, br d, *J* 7.4, 5a-H), 2.89–2.70 (4 H, m, 2 × CH_2S), 2.87 (1 H, d, *J* 21.1, 7-H), 2.83 (1 H, m, 9b-H), 2.79 (1 H, m, 3a-H), 2.68 (1 H, dd, *J* 14.3 and 4.9, 1-H), 2.47 (1 H, ddd, *J* 16.8, 7.4 and 0.7, 5α-H), 2.29 (1 H, dd, *J* 14.3 and 8.5, 1-H), 2.06 (1 H, m, 3-H), 2.00–1.90 (2 H, m, dithiane), 1.77 (3 H, s, 8-CH_3), 1.51 (3 H, s, 9a-CH_3), 1.31 (1 H, m, 3-H) and 1.30 (3 H, t, *J* 7.6, OCH$_2$CH_3), saturation at δ 2.47 (5α-H) led to NOEs at δ 3.25 (5β-H) and 1.51 (9a-CH_3), saturation at δ 2.29 (1-H) led to NOEs at δ 2.83 (9b-H) and 2.68 (1-H), saturation at δ 1.51 (9a-CH_3) led to NOEs at δ 3.28 (CH_2CO$_2$), 3.13 (CH_2CO$_2$), 3.02 (5a-H), 2.83 (9b-H), 2.79 (3a-H) and 2.47 (5α-H); δ_C 208.5 (0), 208.0 (0), 171.3 (0), 130.0 (0), 128.9 (0), 61.0 (2, O*C*H$_2$CH$_3$), 53.5 (1, C-5a), 52.6 (0, C-2), 48.6 (1, C-2), 47.7 (1, C-9b), 45.6 (2, C-7), 44.1 (2 and 0, C-3 and C-9a), 42.3 (2, C-1), 34.2 (2, C-5), 33.7 (2, *C*H$_2$CO$_2$), 28.8 (2, *C*H$_2$S), 28.2 (2, *C*H$_2$S), 27.3 (3, 9a-*C*H$_3$), 25.2 (2, dithiane), 19.8 (3, 8-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m*/*z* 422.1565 (M$^+$, 56%, $C_{22}H_{30}O_4S_2$ requires 422.1585), 348 (9), 221 (15), 175 (46), 173 (20), 171 (16), 135 (32), 106 (65), 45 (37) and 41 (100).

*For **21**.* Solid; mp 161–163 °C; ν_{max}(Nujol)/cm^{-1} 1715; δ_H 4.16 (2 H, q, *J* 7.2, OCH_2CH$_3$), 3.30 (1 H, d, *J* 17.4, CH_2CO$_2$), 3.24 (1 H, dd, *J* 12.0 and 5.1, 5a-H), 3.10 (1 H, d, *J* 20.7, 7-H), 3.09 (1 H, d, *J* 17.4, CH_2CO$_2$), 3.04 (1 H, dd, *J* 14.1 and 2.2), 2.98–2.71 (4 H, m, 2 × CH_2S), 2.90 (1 H, m, methine), 2.82 (1 H, d, *J* 20.7, 7-H), 2.78 (1 H, m, methine), 2.67 (1 H, dd, *J* 18.1 and 12.0, 5α-H), 2.55 (1 H, dd, *J* 18.1 and 5.1, 5β-H), 2.25 (1 H, dd, *J* 14.4 and 7.9), 2.19 (1 H, dd, *J* 14.1 and 7.8), 2.15–1.90 (2 H, m, dithiane), 1.77 (1 H, dd, *J* 14.4 and 10.1), 1.71 (3 H, s, 8-CH_3), 1.27 (3 H, t, *J* 7.2, OCH$_2$CH_3) and 1.07 (3 H, s, 9a-CH_3); δ_C 209.8 (0), 207.4 (0), 171.2 (0), 131.1 (0), 130.4 (0), 61.0 (2, O*C*H$_2$CH$_3$), 53.3 (0, C-2), 49.1 (1, C-5a), 48.5 (1 and 1, C-3a and C-9b), 46.1 (2, C-7), 44.7 (0, C-9a), 43.5 (2 and 2, C-1 and C-3), 35.3 (2, C-5), 33.5 (2, *C*H$_2$CO$_2$), 28.8 (2, *C*H$_2$S), 28.4 (2, *C*H$_2$S), 24.9 (2, dithiane), 21.3 (3, 9a-*C*H$_3$), 19.8 (3, 8-*C*H$_3$) and 14.2 (3, OCH$_2$*C*H$_3$); *m*/*z* 422.1570 (M$^+$, 71%, $C_{22}H_{30}O_4S_2$ requires 422.1585), 377 (8), 315 (9), 249 (23), 221 (35), 214 (41), 201 (20), 175 (84), 173 (100), 172 (56), 135 (58), 107 (37), 99 (34), 98 (36), 91 (41), 43 (45) and 41 (70).

(3a*α*,5a*β*,9a*α*,9b*α*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-8,9*a*-dimethyl-2,4,6-trioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(propylene thioacetal) derivative 22.

*From **20**.* A solution of **21** (680 mg, 1.61 mmol) and *p*-TsOH monohydrate (306 mg, 1.61 mmol) in benzene (80 ml) was heated at reflux for 2 days. After cooling to RT, ethyl acetate (150 ml)

was added, and the solution was washed with saturated aqueous $NaHCO_3$ solution (until gas evolution ceased) and brine. The solution was dried ($MgSO_4$) and concentrated under vacuum. Chromatography provided **22** (304 mg, 45%).

*From **21***. As for **20** except the reaction time was 6 h, and the yield of **22** after chromatography was 81%.

*For **22***. Solid; mp 144–146 °C; ν_{max}(Nujol)/cm^{-1} 1712 and 1672; δ_H 5.95 (1 H, narrow m, 7-H), 4.24 (2 H, m, OCH_2CH$_3$), 3.26 (1 H, br d, *J* 10.0, 9-H), 3.03–2.69 (4 H, m, 2 × CH_2S), 2.97 (1 H, m, 3-H), 2.90 (1 H, dd, *J* 13.4 and 4.3, 5a-H), 2.85–2.71 (4 H, m), 2.58 (1 H, dd, *J* 17.0 and 1.8, CH_2CO$_2$), 2.47 (1 H, dd, *J* 17.0 and 9.6, CH_2CO$_2$), 2.45 (1 H, dd, *J* 15.6 and 13.4, 5α-H), 2.11–1.98 (2 H, m, dithiane), 1.96 (1 H, dd, *J* 14.8 and 7.7, 3-H), 1.91 (3 H, t, *J* 1.2, 8-CH_3), 1.77 (1 H, t, *J* 14.4, 1-H), 1.32 (3 H, t, *J* 7.1, OCH$_2$CH_3) and 1.08 (3 H, s, 9a-CH$_3$), saturation at δ 3.26 (9-H) led to NOEs at δ 2.90 (5a-H), 2.79 (m, likely 1-H), 2.47 (CH_2CO$_2$) and 1.77 (1-H), saturation at δ 1.08 (9a-CH_3) led to NOEs at 2.85–2.71, 2.58 (CH_2CO$_2$), 2.47 (CH_2CO$_2$) and 2.45 (5α-H); δ_C 208.8 (0, C-4), 197.5 (0, C-6), 173.1 (0, *C*O$_2$), 159.3 (0, C-8), 126.4 (1, C-7), 61.3 (2, O*C*H$_2$CH$_3$), 51.7 (0, C-2), 50.6 (1), 49.7 (1, C-5a), 48.7 (1), 45.5 (1, C-9), 42.2 (2, C-1), 41.3 (0, C-9a), 40.5 (2, C-3), 35.9 (2, C-5), 31.5 (2, *C*H$_2$CO$_2$), 29.0 (2, *C*H$_2$S), 28.8 (2, *C*H$_2$S), 25.0 (2, dithiane), 21.8 (3, 8-*C*H$_3$), 15.6 (3, 9a-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m*/*z* 422.1566 (M$^+$, 41%, $C_{22}H_{30}O_4S_2$ requires 422.1585), 249 (19), 221 (19), 214 (13), 175 (100), 173 (31), 172 (19), 135 (25), 107 (19), 43 (33) and 41 (33).

(3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-4-hydroxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(propylene thioacetal) derivative 23. L-Selectride (Aldrich Chemical Co., 0.30 ml of a 1.0 M solution in THF, 0.30 mmol) was added to a solution of **22** (85 mg, 0.20 mmol) in dry THF (20 ml) at −78 °C, and the solution was stirred at −78 °C for 3 h. The reaction was quenched by addition of 5% aqueous NaOH (2 ml). The solution was warmed to RT. Ethyl acetate (100 ml) was added, and this solution was washed with H_2O and brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography provided **23** (66 mg, 78%) as a solid: mp 75–77 °C; ν_{max}(Nujol)/cm^{-1} 3427, 1714 and 1670; δ_H 5.90 (1 H, br s, 7-H), 4.23 (2 H, m, OCH_2CH$_3$), 3.97 (1 H, br s, 4-H), 3.24 (1 H, br d, *J* 10.2, 9-H), 3.08–2.75 (4 H, m, 2 × CH_2S), 2.93 (1 H, dd, *J* 11.6 and 2.9, 5a-H), 2.53–2.17 (8 H, m), 2.13 (1 H, m, 3a-H), 2.12–1.93 (2 H, m, dithiane), 1.87 (3 H, br s, 8-CH_3), 1.56 (1 H, ddd, *J* 15.5, 11.6 and 2.1, 5α-H), 1.31 (3 H, t, *J* 7.4, OCH$_2$CH_3) and 0.87 (3 H, s, 8-CH_3), saturation at δ 3.97 (4-H) led to NOEs at δ 2.38, 2.13 (3a-H) and 1.56 (5α-H), saturation at δ 3.24 (9-H) led to NOEs at δ 2.93 (5a-H) and 2.53–2.32, saturation at δ 1.87 (8-CH_3) led to NOEs at δ 2.51, 2.38 and 1.56 (5α-H); δ_C 200.6 (0, C-6), 173.3 (0, *C*O$_2$), 158.9 (0, C-8), 126.7 (1, C-7), 68.0 (1, C-4), 61.0 (2, *C*H$_2$CO$_2$), 52.8 (0, C-2), 46.7 (1, C-9b), 45.4 (2), 45.3 (1, C-9), 43.6 (1, C-5a), 42.9 (2), 41.2 (0, C-9a), 40.3 (1, C-3a), 31.4 (2, *C*H$_2$CO$_2$), 29.2 (2, *C*H$_2$S), 29.0 (2, *C*H$_2$S), 27.4 (2, C-5), 25.0 (2, dithiane), 21.7 (3, 8-*C*H$_3$), 15.6 (3, 9a-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m*/*z* 424.1735 (M$^+$, 31%, $C_{22}H_{32}O_4S_2$ requires 424.1742), 406 (7), 391 (8), 361 (5), 349 (5), 317 (15), 251 (26), 222 (28), 221 (32), 196 (21), 185 (29), 177 (86), 175 (30), 173 (25), 149 (29), 135 (54), 107 (39), 106 (33), 91 (44), 67 (44), 55 (31), 43 (59) and 41 (100).

(3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-4-(methoxy)methoxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(propylene thioacetal) derivative 24 and (1*R,3*S**,4*R**,5*S**,9*S**,11*R**,12*S**)-1-(3-(methoxy)thiomethyl)thiopropyl-4,6-dimethyl-14-oxa-8-oxotetracyclo[9.2.1.0^{3,12}.0^{4,9}]tetradec-6-en-5-acetic acid ethyl ester 25.** A solution of **23** (100 mg, 0.236 mmol), Pr$^i_2$NEt (0.54 ml, 3.1 mmol) and chloro(methoxy)methane (0.18 ml, 2.4 mmol) in CH_2Cl_2 (10 ml) was heated at reflux for 2 days. The solution was cooled to RT. The solution was washed with 1% aqueous HCl and brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography gave **24** (60 mg, 55%) and **25** (16 mg, 15%).

*For **24***. Oil; ν_{max}(film)/cm^{-1} 1713; δ_H 5.90 (1 H, narrow m, 7-H), 4.71 (1 H, d *J* 6.9, OCH_2O), 4.55 (1 H, *J* 6.9, OCH_2O), 4.23 (2 H, m, OCH_2CH$_3$), 3.73 (1 H, br s, 4-H), 3.42 (3 H, s, OCH_3), 3.25 (1 H, br d, *J* 10.3, 9-H), 3.06 (1 H, m, CH_2S), 2.94 (1 H, m, CH_2S), 2.80–2.65 (2 H, m, CH_2S), 2.79 (1 H, dd, *J* 12.4 and 3.0, 5a-H), 2.61–2.30 (6 H, m), 2.26 (1 H, m, 3a-H), 2.12 (2 H, m, 3-H$_2$), 2.07 (1 H, m, dithiane), 1.92 (1 H, m, dithiane), 1.88 (3 H, narrow m, 8-CH_3), 1.41 (1 H, ddd, *J* 15.5, 12.2 and 2.1, 5α-H), 1.32 (3 H, t, J 7.8, OCH$_2$CH_3) and 0.83 (3 H, s, 9a-CH_3), saturation at δ 3.73 (4-H) led to NOEs at δ 4.71 (OCH_2O), 4.55 (OCH_2O), 2.26 (3a-H), 2.12 (3-H) and 1.41 (5α-H), saturation at δ 3.25 (9-H) led to NOEs at δ 2.79 (5a-H) and 2.61–2.30, saturation at δ 0.83 led to NOEs at δ 2.61–2.30 and 1.41 (5α-H); δ_C 200.6 (0, C-6), 173.4 (0, *C*O$_2$), 159.2 (0, C-8), 126.7 (1, C-7), 95.6 (2, O*C*H$_2$O), 73.5 (1, C-4), 61.0 (2, O*C*H$_2$CH$_3$), 56.3 (3, O*C*H$_3$), 53.5 (0, C-2), 46.9 (1, C-9b), 45.5 (1, C-9), 44.3 (1, C-5a), 43.8 (2, C-3), 41.8 (2, C-1), 41.1 (0, C-9a), 39.0 (1, C-3a), 31.5 (2, *C*H$_2$CO$_2$), 29.1 (2, *C*H$_2$S), 29.0 (2, *C*H$_2$S), 25.4 (2, dithiane), 24.3 (2, C-5), 21.8 (3, 8-*C*H$_3$), 15.7 (3, 9a-*C*H$_3$) and 14.2 (3, OCH$_2$*C*H$_3$); *m*/*z* 468.1995 (M$^+$, 31%, $C_{24}H_{36}O_5S_2$ requires 468.2002), 424 (10), 423 (16), 233 (29), 221 (20), 177 (33), 135 (17) and 45 (100).

*For **25***. Oil; ν_{max}(film)/cm^{-1} 1713; δ_H 5.90 (1 H, narrow m, 7-H), 4.62 (2 H, s, SCH_2O), 4.30 (1 H, m, 11-H), 4.19 (2 H, m, OCH_2CH$_3$), 3.34 (3 H, s, OCH_3), 3.23 (1 H, br d, *J* 9.7, 5-H), 2.83 (1 H, m, 9-H), 2.82 (2 H, m, CH_2S), 2.70 (2 H, t, *J* 6.8, CH_2S), 2.45 (1 H, dd, *J* 16.4 and 3.3, CH_2CO$_2$), 2.33 (1 H, dd, *J* 16.4 and 9.7, CH_2CO$_2$), 2.32 (1 H, m, 12-H), 2.31–2.03 (4 H, m), 1.96 (2 H, pentet, *J* 6.8, SCH$_2$CH_2CH$_2$S), 1.89 (1 H, m, 2-H), 1.88 (3 H, br s, 6-CH_3), 1.78 (1 H, br d, *J* 9.7, 13-H), 1.59 (1 H, ddd, *J* 15.9, 11.5 and 2.2, 10α-H), 1.29 (3 H, t, *J* 7.1, OCH$_2$CH_3) and 0.81 (3 H, s, 4-CH_3), saturation at δ 4.30 (11-H) led to NOEs at δ 2.32 (12-H) and 1.59 (10α-H), saturation at δ 3.23 (5-H) led to NOEs at δ 2.83 (9-H), 2.33 (CH_2CO$_2$) and 1.89 (2-H), saturation at δ 0.81 (4-CH_3) led to NOEs at δ 2.45 (CH_2CO$_2$), 2.33 (CH_2CO$_2$), 2.32 (12-H) and 1.59 (10α-H); δ_C 200.2 (0, C-8), 173.1 (0, *C*O$_2$), 158.7 (0, C-6), 126.8 (1, C-7), 91.3 (2, C-1), 77.5 (1, C-11), 75.4 (2, S*C*H$_2$O), 61.1 (2, O*C*H$_2$CH$_3$), 55.7 (3, O*C*H$_3$), 44.8 (1, C-5), 44.7 (2, C-13), 43.4 (1, C-3), 42.5 (1, C-9), 41.7 (0, C-4), 39.6 (2, C-2), 38.8 (1, C-12), 31.4 (2, *C*H$_2$CO$_2$), 30.4 (2, SCH$_2$*C*H$_2$CH$_2$S), 30.0 (2, *C*H$_2$S), 28.0 (2, *C*H$_2$S), 24.3 (2, C-10), 22.1 (3, 6-*C*H$_3$), 14.3 (3, 4-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m*/*z* 423.1648 (M$^+$, 17%, $C_{22}H_{31}O_4S_2$, M$^+$ − CH_2OCH_3, requires 423.1662), 221 (3), 177 (5), 151 (14), 84 (14), 49 (24) and 45 (100).

(3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-4-(methoxy)methoxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester 26. To a solution of **24** (25 mg, 0.053 mmol) in THF–H_2O (5 : 1, 6 ml) was added $CaCO_3$ (7 mg, 0.07 mmol) and a solution of $Hg(ClO_4)_2$ (26 mg, 0.065 mmol) in H_2O (0.5 ml). The resulting mixture was stirred at RT for 14 h. Ethyl acetate (100 ml) was added, and the solution was washed with saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated under vacuum. Chromatography gave **26** (15.5 mg, 78%) as a solid: mp 133–134 °C; ν_{max}(Nujol)/cm^{-1} 1714 and 1666; δ_H 5.92 (1 H, br s, 7-H), 4.60 (1 H, d, *J* 7.4, OCH_2O), 4.43 (1 H, d, *J* 7.4, OCH_2O), 4.20 (2 H, br q, *J* 7.2, OCH_2CH$_3$), 3.93 (1 H, m, 4-H), 3.32 (3 H, s, OCH_3), 3.19 (1 H, br d, *J* 9.4, 9-H), 2.79 (1 H, dd, *J* 11.9 and 3.0, 5a-H), 2.59 (1 H, dd, *J* 17.0 and 13.2, 1-H), 2.49–2.21 (7 H, m), 2.15 (1 H, dd, *J* 17.0 and 8.1, 1-H), 1.88 (3 H, br s, 8-CH_3), 1.48 (1 H, ddd, *J* 15.4, 11.9 and 1.9, 5α-H), 1.30 (3 H, t, *J* 7.2, OCH$_2$CH_3) and 0.90 (3 H, s, 9a-CH_3), saturation of δ 3.93 (4-H) led to NOEs at δ 4.60 (OCH_2O), 4.43 (OCH_2O), 2.43 (3a-H) and 1.48 (5α-H), saturation of δ 3.19 (9-H) led to NOEs at δ 2.79 (5a-H), 2.59 (1-H), 2.39 (CH_2CO$_2$) and 2.15 (1-H), saturation of δ 0.90 (9a-CH_3) led to NOEs at δ 2.43 (3a-H), 2.39 (CH_2CO$_2$) and 1.48 (5α-H); δ_C 216.8 (0, C-2), 200.0 (0, C-6), 172.7 (0, *C*O$_2$),

159.3 (0, C-8), 126.7 (1, C-7), 95.2 (2, O*C*H_2O), 74.1 (1, C-4), 61.2 (2, O*C*H_2CH$_3$), 56.2 (3, O*C*H_3), 45.4 (1, C-9b), 45.1 (1, C-9), 43.7 (2, C-3), 43.0 (1, C-5a), 41.7 (0, C-9a), 38.8 (2, C-1), 36.7 (1, C-3a), 31.5 (2, *C*H_2CO$_2$), 24.3 (2, C-5), 21.8 (3, 8-*C*H_3), 15.0 (3, 9a-*C*H_3) and 14.1 (3, OCH$_2$*C*H_3); *m/z* 378.2042 (M$^+$, 3%, $C_{21}H_{30}O_6$ requires 378.2042), 333 (3), 317 (3), 316 (5), 259 (5), 233 (6), 221 (6), 159 (5), 95 (10) and 45 (100).

From 26 to (3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-decahydro-4-(methoxy)methoxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(ethylene acetal) derivative 27. A solution of **26** (73.5 mg, 0.194 mmol), 1,2-ethanediol (0.11 ml, 1.9 mmol) and pyridinium *para*-toluenesulfonate (10 mg, 0.039 mmol) in benzene (20 ml) was heated at reflux for 16 h. After the solution cooled to RT, it was diluted with ethyl acetate (100 ml), and this solution was washed with saturated aqueous $NaHCO_3$ solution and brine. The solution was dried ($MgSO_4$) and concentrated under vacuum. Chromatography provided **27** (65 mg, 80%) as a solid: mp 91.5–93 °C; δ_H 5.89 (1 H, narrow m, 7-H), 4.68 (1 H, d, *J* 6.9, OC*H*$_2$O), 4.55 (1 H, d, *J* 6.9, OC*H*$_2$O), 4.21 (2 H, m, OC*H*$_2$CH$_3$), 3.97–3.75 (4 H, m, OC*H*$_2$C*H*$_2$O), 3.79 (1 H, narrow m, 4-H), 3.42 (3 H, s, OC*H*$_3$), 3.19 (1 H, br d, *J* 10.3, 9-H), 2.78 (1 H, dd, *J* 12.1 and 3.1, 5a-H), 2.52 (1 H, br d, *J* 17.0, C*H*$_2$CO$_2$), 2.34 (1 H, dd, *J* 17.0 and 10.3, C*H*$_2$CO$_2$), 2.31 (1 H, m, 5β-H), 2.24–1.97 (5 H, m), 1.85 (3 H, narrow m, 8-C*H*$_3$), 1.73 (1 H, dd, *J* 16.9 and 5.3, 1-H), 1.40 (1 H, ddd, *J* 14.8, 12.1 and 2.2, 5α-H), 1.30 (3 H, t, *J* 7.2, OCH$_2$C*H*$_3$) and 0.82 (3 H, s, 9a-H); δ_C 200.8 (0, C-6), 173.2 (0, *C*O$_2$), 159.4 (0, C-8), 126.7 (1, C-7), 117.1 (0, C-2), 95.7 (2, O*C*H$_2$O), 74.5 (1, C-4), 64.5 (2, C*H*$_2$O), 63.5 (2, C*H*$_2$O), 60.9 (2, O*C*H$_2$CH$_3$), 55.9 (3, O*C*H$_3$), 46.7 (1), 45.4 (1, C-9), 43.8 (1, C-5a), 41.4 (0, C-9a), 39.6 (2), 37.6 (1), 37.5 (2, C-1), 31.5 (2, *C*H$_2$CO$_2$), 24.6 (2, C-5), 21.9 (3, 8-*C*H$_3$), 15.3 (3, 9a-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m/z* 422.2309 (M$^+$, 16%, $C_{23}H_{34}O_7$ requires 422.2304), 377 (14), 361 (15), 99 (20), 89 (19), 87 (31), 86 (46), 84 (40) and 45 (100).

(1*R,3*S**,4*R**,5*S**,9*S**,11*R**,12*S**)-1-Methoxy-4,6-dimethyl-14-oxa-8-oxotetracyclo[9.2.1.0^{3,12}.0^{4,9}]tetradec-6-en-5-acetic acid ethyl ester 28 and (3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-decahydro-4-hydroxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]-inden-9-acetic acid ethyl ester 29.** A mixture of **23** (81 mg, 0.19 mmol) and [bis(trifluoroacetoxy)iodo]benzene (127 mg, 0.286 mmol) in CH_3OH (3.0 ml) was stirred at RT for 4 h. Ethyl acetate (100 ml) was added, and this solution was washed with saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated under vacuum. Chromatography gave a mixture of **28** and **29** (1 : 1 ratio, 75% combined) as a solid. Repeated chromatography gave an enriched sample of **28** and a homogeneous sample of **29**.

*For **28**.* ν_{max}(Nujol)/cm^{-1} 1713; δ_H 5.90 (1 H, m, 7-H), 4.30 (1 H, br s, 11-H), 4.19 (2 H, m, OC*H*$_2$CH$_3$), 3.77 (3 H, s, OC*H*$_3$), 3.23 (1 H, m, 5-H), 2.96–2.76 (3 H, m), 2.49–2.01 (6 H, m), 1.89 (1 H, m), 1.88 (3 H, br s, 6-C*H*$_3$), 1.59 (1 H, ddd, *J* 15.6, 12.2 and 2.2, 10α-H), 1.29 (3 H, t, *J* 7.2, OCH$_2$C*H*$_3$) and 0.81 (3 H, s, 4-C*H*$_3$); δ_C 200.2, 173.1, 158.7, 126.8, 91.3, 77.5, 61.1, 55.4, 44.8, 43.3, 42.4, 41.7, 39.6, 38.8, 31.4, 28.2, 24.3, 22.1, 14.3 and 14.1; *m/z* 348 (M$^+$, 5%), 316 (60), 221 (31), 149 (23), 135 (55), 122 (62), 95 (58), 86 (70), 84 (100) and 41 (91).

*For **29**.* Mp 143–145 °C; ν_{max}(Nujol)/cm^{-1} 1714 and 1661; δ_H 5.92 (1 H, narrow m, 7-H), 4.20 (2 H, m, OC*H*$_2$CH$_3$), 4.15 (1 H, narrow m, 4-H), 3.21 (1 H, m, 9-H), 2.91 (1 H, dd, *J* 12.2 and 3.2, 5a-H), 2.66 (1 H, dd, *J* 16.8 and 12.6, 1-H), 2.49–2.10 (8 H, m), 1.88 (3 H, t, *J* 1.3, 8-C*H*$_3$), 1.67 (1 H, ddd, *J* 16.0, 12.2 and 2.4, 5a-H), 1.65 (1 H, br s, O*H*), 1.29 (3 H, t, *J* 7.2, OCH$_2$C*H*$_3$) and 0.90 (3 H, s, 9a-H); δ_C 217.6 (0, C-2), 200.3 (0, C-6), 172.7 (0, *C*O$_2$), 159.4 (0, C-8), 126.6 (1, C-7), 68.4 (1, C-4), 61.2 (2, O*C*H$_2$CH$_3$), 45.4 (1), 45.1 (1, C-9), 43.7 (2), 42.4 (1, C-5a), 41.8 (0, C-9a), 39.1 (2, C-1), 36.8 (1), 31.5 (2, *C*H$_2$CO$_2$), 28.4 (2, C-5), 21.9 (3, 8-*C*H$_3$), 14.9 (3, 9a-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m/z* 334.1784 (M$^+$, 31%, $C_{19}H_{26}O_5$ requires 334.1779), 317 (21), 316 (100), 301 (24), 298 (21), 243 (26), 229 (33), 227 (46), 222 (32), 221 (48), 185 (26), 149 (35), 148 (34), 135 (88), 123 (33), 122 (51), 95 (91), 91 (44), 67 (38) and 41 (48).

(3*aα*,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-2,2-dimethoxy-8,9*a*-dimethyl-4,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester 30. A mixture of **22** (153 mg, 0.362 mmol) and [bis(trifluoroacetoxy)iodo]benzene (321 mg, 0.724 mmol) in CH_3OH (5.0 ml) was stirred at RT for 10 min. The mixture was poured into saturated aqueous $NaHCO_3$ solution (20 ml), and this was extracted with ethyl acetate. The organic solution was washed with brine, dried ($MgSO_4$), and concentrated under vacuum. Chromatography provided **30** (79 mg, 58%) as a solid: mp 156–158 °C; ν_{max}(Nujol)/cm^{-1} 1713 and 1666; δ_H 5.94 (1 H, m, 7-H), 4.22 (2 H, m, OC*H*$_2$CH$_3$), 3.23 (1 H, m, 9-H), 3.16 (3 H, s, OC*H*$_3$), 3.15 (3 H, s, OC*H*$_3$), 2.88 (1 H, dd, *J* 12.9 and 4.7, 5α-H), 2.77 (1 H, dd, *J* 13.0 and 1.7), 2.77–2.66 (2 H, m), 2.61–2.37 (6 H, m), 2.13 (1 H, dd, *J* 13.0 and 6.8), 1.90 (3 H, s, 8-C*H*$_3$), 1.74 (1 H, dd, *J* 14.0 and 8.4), 1.49 (1 H, t, *J* 13.0), 1.31 (3 H, t, *J* 6.5, OCH$_2$C*H*$_3$) and 1.04 (3 H, s, 9a-H); δ_C 209.3 (0), 197.8 (0), 172.8 (0), 159.4 (0), 126.4 (1), 109.1 (0), 61.2 (2), 49.4 (3), 48.9 (3), 48.7 (3 and 3), 47.5 (1), 45.0 (1), 41.5 (0), 35.8 (2), 35.2 (2), 34.2 (2), 31.7 (2), 21.9 (3), 15.1 (3) and 14.1 (3); *m/z* 378 (M$^+$, 2), 346 (2), 204 (86), 149 (20), 86 (30), 84 (51), 77 (100) and 57 (30).

(3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-4-hydroxy-2,2-dimethoxy-8,9*a*-dimethyl-6-oxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester 31. A solution of **30** (105 mg, 0.278 mmol) and K-Selectride (Aldrich Chemical Co., 0.34 ml of a 1.0 M solution in THF, 0.34 mmol) in dry THF (20 ml) was stirred at −78 °C for 3 h and then at 0 °C for 4 h. After addition of 5% aqueous NaOH solution (5 ml) and then H_2O, the mixture was extracted with ethyl acetate. The ethyl acetate extract was washed with brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography yielded **31** (54 mg, 51%) as a solid: mp 93–95 °C; ν_{max}(Nujol)/cm^{-1} 3438 and 1714; δ_H 5.89 (1 H, narrow m, 7-H), 4.21 (2 H, m, OC*H*$_2$CH$_3$), 4.03 (1 H, narrow m, 4-H), 3.34 (1 H, br s O*H*), 3.23 (3 H, s, OC*H*$_3$), 3.20 (3 H, s, OC*H*$_3$), 3.20 (1 H, m, 9-H), 2.95 (1 H, dd, *J* 12.3 and 3.5, 5a-H), 2.49 (1 H, dd, *J* 16.9 and 1.2, C*H*$_2$CO$_2$), 2.34 (1 H, dd, *J* 16.9 and 10.3, C*H*$_2$CO$_2$), 2.29 (1 H, m, 1-H), 2.24 (1 H, dt, *J* 14.7 and 3.1, 5β-H), 2.17–1.94 (4 H, m), 1.88 (1 H, m, 1-H), 1.85 (3 H, br s, 8-C*H*$_3$), 1.50 (1 H, ddd, *J* 14.7, 12.3 and 2.3, 5α-H), 1.30 (3 H, t, *J* 7.1, OCH$_2$C*H*$_3$) and 0.82 (3 H, s, 9a-C*H*$_3$), saturation of δ 2.95 (5a-H) led to an NOE at δ 3.20 (9-H), saturation of δ 0.82 (9a-C*H*$_3$) led to NOEs at δ 2.49 (C*H*$_2$CO$_2$), 2.34 (C*H*$_2$CO$_2$), 2.17–1.94 and 1.50 (5α-H); δ_C 200.8 (0, C-6), 173.1 (0, *C*O$_2$), 158.8 (0, C-8), 126.8 (1, C-7), 111.5 (0, C-2), 68.5 (1, C-4), 61.0 (2, O*C*H$_2$CH$_3$), 49.4 (3, O*C*H$_3$), 48.9 (3, O*C*H$_3$), 46.3 (1, C-9b), 44.8 (1, C-9), 43.1 (1, C-5a), 41.6 (0, C-9a), 40.0 (2, C-3), 39.9 (1, C-3a), 37.5 (2, C-1), 31.6 (2, *C*H$_2$CO$_2$), 27.1 (2, C-5), 21.8 (3, 8-*C*H$_3$), 15.4 (3, 9a-*C*H$_3$) and 14.1 (3, OCH$_2$*C*H$_3$); *m/z* 380 (M$^+$, 18%), 349 (25), 348 (58), 316 (18), 303 (30), 275 (27), 261 (29), 260 (28), 221 (91), 201 (32), 187 (38), 177 (57), 147 (52), 135 (100), 111 (41), 105 (42), 97 (71), 95 (58), 79 (42), 67 (56), 55 (43), 43 (42) and 41 (83).

(3*aα*,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-8,9*a*-dimethyl-2,4,6-trioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(ethylene acetal) derivative 32. A solution of **22** (115 mg, 0.272 mmol) in CH_3CN (1.0 ml) followed by [bis(trifluoro-xsacetoxy)iodo]benzene (181 mg, 0.408 mmol) were added to 1,2-ethanediol (5 ml). The mixture was stirred for 10 min at RT before it was poured into saturated aqueous $NaHCO_3$ solution. This was extracted with ethyl acetate. The ethyl acetate solution was washed with brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography afforded **32** (57 mg, 56%) as a foam: ν_{max}(Nujol)/cm^{-1} 1713 and 1667; δ_H (500 MHz) 5.94 (1 H, br s, 7-H), 4.22 (2 H, m, OC*H*$_2$CH$_3$), 3.94 (1 H, m, OC*H*$_2$CH$_2$O), 3.89 (2 H, apparent t, *J* 6.6, OC*H*$_2$CH$_2$O), 3.81 (1 H, m,

OCH_2CH_2O), 3.18 (1 H, br d, *J* 9.8, 9-H), 2.87 (1 H, dd, *J* 13.0 and 4.0, 5a-H), 2.84 (1 H, br d, *J* 14.2, 3-H), 2.77 (1 H, br t, *J* 8.8, 3a-H), 2.75 (1 H, dd, *J* 15.7 and 4.0, 5β-H), 2.57 (1 H, br d, *J* 17.2, CH_2CO_2), 2.56 (1 H, m, 9b-H), 2.45 (dd, *J* 17.2 and 9.8, CH_2CO_2), 2.44 (1 H, dd, *J* 15.7 and 13.0, 5α-H), 1.98 (1 H, dd, *J* 13.1 and 6.5, 1α-H), 1.89 (3 H, br s, 8-CH_3), 1.85 (1 H, dd, *J* 14.2 and 8.8, 3-H), 1.57 (1 H, t, *J* 13.1, 1β-H), 1.31 (3 H, t, *J* 6.7, OCH_2CH_3) and 1.08 (3 H, s, 9a-CH_3), saturation of δ 3.18 led to NOEs at δ 2.87 (5a-H), 2.57 (CH_2CO_2), 2.45 (CH_2CO_2), 1.98 (1α-H) and 1.57 (1β-H), saturation of δ 1.08 led to NOEs at δ 2.77 (3a-H), 2.57 (CH_2CO_2), 2.45 (CH_2CO_2) and 2.44 (5α-H); δ_C (125 MHz) 209.2 (0, C-4), 197.6 (0, C-6), 172.8 (0, *C*O_2), 159.4 (0, C-8), 126.4 (1, C-7), 115.1 (0, C-2), 64.6 (2, O*C*H_2CH_2O), 64.0 (2, O*C*H_2CH_2O), 61.2 (2, O*C*H_2CH_3), 50.1 (1, C-9b), 49.3 (1, C-5a), 47.7 (1, C-3a), 45.3 (1, C-9), 41.5 (0, C-9a), 37.1 (2, C-1), 36.0 (2, C-3), 36.0 (2, C-5), 31.6 (2, *C*H_2CO_2), 21.8 (3, 8-*C*H_3), 15.1 (3, 9a-*C*H_3) and 14.1 (3, OCH_2*C*H_3); *m/z* 376.1883 (M^+, 52%, $C_{21}H_{28}O_6$ requires 376.1884), 361 (6), 303 (29), 287 (14), 221 (14), 175 (15), 168 (19), 135 (20), 127 (31), 126 (62), 99 (76), 87 (27), 86 (100) and 55 (37).

(3*aα*,4β,5*a*β,9α,9*aα*,9*bα*)-1,2,3,3*a*,4,5,6,9,9*a*,9*b*-Decahydro-4-hydroxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(ethylene acetal) derivative 33. L-Selectride (Aldrich Chemical Co., 1.5 ml of a 1.0 M solution in THF, 1.5 mmol) was added to a solution of **32** (466 mg, 1.24 mmol) in dry THF (50 ml) at −78 °C. The solution was stirred at −78 °C for 3 h. The reaction was quenched by addition of 5% aqueous NaOH solution (5 ml). The mixture was warmed to RT before ethyl acetate (200 ml) was added. This was washed with H_2O and brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography gave **33** (387 mg, 83%) as a solid: mp 95–97 °C; ν_{max}(Nujol)/cm^{-1} 3467, 1722 and 1673; δ_H (500 MHz) 5.88 (1 H, s, 7-H), 4.21 (2 H, m, OCH_2CH_3), 4.04 (1 H, narrow m, 4-H), 3.95–3.85 (4 H, m, OCH_2CH_2O), 3.19 (1 H, br d, *J* 10.0, 9-H), 2.94 (1 H, dd, *J* 11.7 and 2.8, 5a-H), 2.49 (1 H, br d, *J* 17.5, CH_2CO_2), 2.34 (1 H, dd, *J* 17.5 and 10.0, CH_2CO_2), 2.31 (1 H, t, *J* 14.0), 2.23 (1 H, dt, *J* 15.0 and 2.8, 5β-H), 2.17–2.01 (4 H, m), 1.88 (1 H, m, 1-H), 1.85 (3 H, s, 8-CH_3), 1.53 (1 H, ddd, *J* 14.8, 12.0 and 3.0, 5α-H), 1.30 (3 H, t, *J* 7.0, OCH_2CH_3) and 0.82 (3 H, s, 9a-CH_3), saturation of δ 3.19 (9-H) led to NOEs at δ 2.94 (5a-H), 2.49 (CH_2CO_2), 2.34 (CH_2CO_2) and 1.88 (1-H), saturation of δ 1.53 (5α-H) led to NOEs at δ 4.04 (4-H) and 2.23 (5β-H), saturation of δ 0.82 (9a-H) led to NOEs at δ 2.49 (CH_2CO_2), 2.34 (CH_2CO_2), 2.17–2.01 and 1.53 (5α-H); δ_C (125 MHz) 200.8 (0), 173.2 (0), 159.0 (0), 126.8 (1), 117.1 (0), 68.6 (1), 64.3 (2), 64.2 (2), 61.0 (2), 46.8 (1), 45.1 (1), 43.1 (1), 41.6 (2), 41.1 (0), 39.2 (1), 38.7 (2), 31.6 (2), 27.6 (2), 21.8 (3), 15.4 (3) and 14.1 (3); *m/z* 378.2036 (M^+, 46%, $C_{21}H_{30}O_6$ requires 378.2041), 333 (21), 229 (51), 221 (31), 182 (42), 177 (42), 168 (49), 152 (38), 147 (36), 135 (73), 127 (85), 126 (63), 99 (94), 95 (65), 87 (67), 86 (100), 67 (40), 55 (46), 45 (36) and 43 (61).

From 33 to 27. A mixture of **33** (255 mg, 0.674 mmol), Pr^i_2NEt (0.88 ml, 5.0 mmol) and chloro(methoxy)methane (0.28 ml, 3.4 mmol) in CH_2Cl_2 (20 ml) was stirred at RT for 24 h. CH_2Cl_2 (100 ml) was added, and the solution was washed with H_2O and brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography provided **27** (193 mg, 68%).

(3*aα*,4β,5*a*β,8β,9α,9*aα*,9*bα*)-Perhydro-4-(methoxy)methoxy-8,9*a*-dimethyl-2,6-dioxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(ethylene acetal) derivative 34. To dry ammonia (60 ml, distilled from sodium) at −78 °C was added lithium metal (14.5 mg, 2.07 mmol). This was warmed to −50 °C, and a solution of **27** (125 mg, 0.296 mmol) in 1,4-dioxane–ether (1 : 1, 14 ml) was introduced over 1 min. The mixture was stirred for 5 min. Sufficient anhydrous NH_4Cl was added to discharge the blue colour. The mixture was allowed to warm in order to evaporate the ammonia. To the remainder was added H_2O (100 ml), and this was extracted with ethyl acetate. The ethyl acetate solution was washed with brine, dried ($MgSO_4$) and concentrated under vacuum. Chromatography gave **34** (89 mg, 71%) as a solid: mp 151–152 °C; ν_{max}(Nujol)/cm^{-1} 1714; δ_H (500 MHz) 4.64 (1 H, d, *J* 7.0, OCH_2O), 4.54 (1 H, d, *J* 7.0, OCH_2O), 4.16 (2 H, m, OCH_2CH_3), 3.95–3.83 (3 H, m, OCH_2CH_2O), 3.78 (1 H, m, OCH_2CH_2O), 3.75 (1 H, narrow m, 4-H), 3.41 (3 H, s, OCH_3), 2.80 (1 H, d, *J* 11.8, 5a-H), 2.54 (1 H, d, *J* 16.5, CH_2CO_2), 2.32 (1 H, dd, *J* 14.0 and 4.5, 7α-H), 2.20–1.93 (8 H, m), 1.87 (1 H, br m, 8-H), 1.86 (1 H, dd, *J* 12.0 and 5.5), 1.52 (1 H, ddd, *J* 14.8, 11.8 and 1.7, 5α-H), 1.27 (3 H, t, *J* 7.0, OCH_2CH_3), 0.95 (3 H, d, *J* 6.5, 8-CH_3) and 0.72 (3 H, s, 9a-CH_3), saturation of δ 3.75 (4-H) led to NOEs at δ 4.64 (OCH_2O), 4.54 (OCH_2O), *ca.* 2.17 (3a-H) and 1.52 (5α-H), saturation of δ 0.95 (8-CH_3) led to NOEs at δ 2.32 (7α-H), *ca.* 2.09 (7β-H) and 1.87 (8-H), saturation of δ 0.72 (9a-CH_3), led to NOEs at δ 2.54 (CH_2CO_2), *ca.* 2.17 (3a-H), *ca.* 2.02 (CH_2CO_2), 1.87 (8-H) and 1.52 (5α-H); δ_C (125 MHz) 212.5 (0, C-6), 173.6 (0, *C*O_2), 117.4 (0, C-2), 95.8 (2, OCH_2O), 74.6 (1, C-4), 64.5 (2, OCH_2), 63.5 (2, OCH_2), 60.6 (2, OCH_2CH_3), 55.9 (3, OCH_3), 49.8 (2, C-7), 47.2 (1), 46.6 (1, C-3a), 46.1 (1), 42.1 (0, C-9a), 39.2 (2), 37.8 (1), 36.5 (2), 36.4 (1, C-8), 33.5 (2, *C*H_2CO_2), 24.9 (2, C-5), 20.0 (3, 8-*C*H_3), 15.8 (3, 9a-*C*H_3) and 14.1 (3, OCH_2*C*H_3); *m/z* 424.2432 (M^+, 6%, $C_{23}H_{36}O_7$ requires 424.2459), 379 (24), 364 (8), 363 (8), 199 (36), 126 (19), 125 (22), 99 (30), 87 (36), 86 (62) and 45 (100).

(3*aα*,4β,5*a*β,6α,8β,9α,9*aα*,9*bα*)-Perhydro-6-hydroxy-4-(methoxy)methoxy-8,9*a*-dimethyl-2-oxo-1*H*-benz[*e*]inden-9-acetic acid ethyl ester, 2-(ethylene acetal) derivative 35. L-Selectride (Aldrich Chemical Co., 0.24 ml of a 1.0 M solution in THF, 0.24 mmol) was added to a solution of **34** (68 mg, 0.16 mmol) in dry THF (10 ml) at −78 °C. The solution was stirred at −78 °C for 2 h. The reaction was quenched by addition of 5% aqueous NaOH solution (1 ml). The mixture was warmed to RT before ethyl acetate (100 ml) was added. This was washed with H_2O and brine, dried (Na_2SO_4) and concentrated under vacuum. Chromatography afforded **35** (53 mg, 79%) as a solid: mp 105–106 °C; ν_{max}(Nujol)/cm^{-1} 3535 and 1722; δ_H (500 MHz) 4.69 (1 H, d, *J* 7.2, OCH_2O), 4.60 (1 H, d, *J* 7.2, OCH_2O), 4.12 (2 H, m, OCH_2CH_3), 3.93–3.83 (3 H, m, OCH_2CH_2O), 3.87 (1 H, narrow m, 6-H), 3.77 (1 H, m, OCH_2CH_2O), 3.76 (1 H, narrow m, 4-H), 3.42 (3 H, s, OCH_3), 2.44 (1 H, d, *J* 16.5, CH_2CO_2), 2.22 (1 H, m, 3a-H), 2.13 (1 H, d, *J* 14.0, 3β-H), 2.05–1.97 (2 H, m, 3α-H and CH_2CO_2), 1.93 (1 H, m, 1-H), 1.89–1.78 (5 H, m), 1.76 (1 H, m, 7-H), 1.61 (1 H, br d, *J* 11.0, 9-H), 1.61 (1 H, m, 5β-H), 1.40 (1 H, ddd, *J* 14.8, 11.5 and 3.2, 7-H), 1.25 (3 H, t, *J* 7.3, OCH_2CH_3), 1.00 (3 H, s, 9a-CH_3) and 0.83 (3 H, d, *J* 7.0, 8-CH_3), saturation of δ 3.87 (6-H) led to NOEs at δ 1.84 (5a-H), 1.76 (7-H), 1.61 (5β-H) and 1.40 (7-H), saturation of δ 3.76 (4-H) led to NOEs at δ 4.69 (OCH_2O), 4.60 (OCH_2O), 2.22 (3a-H), 2.13 (3β-H), 1.85 (likely 5α-H), 1.61 (5β-H) and 1.00 (9a-CH_3), saturation of δ 1.00 (9a-CH_3) led to NOEs at δ 2.44 (CH_2CO_2), 2.22 (3a-H), 2.05–1.97 (CH_2CO_2) and 1.89–1.80 (5α-H and 8-H), saturation of δ 0.83 (8-CH_3) led to NOEs at δ 1.89–1.82 (8-H), 1.76 (7-H), 1.61 (9-H) and 1.40 (7-H); δ_C (125 MHz) 174.5 (0, *C*O_2), 117.7 (0, C-2), 96.3 (2, OCH_2O), 76.5 (1, C-4), 72.5 (1, C-6), 64.4 (2, OCH_2), 63.4 (2, OCH_2), 60.2 (2, OCH_2CH_3), 55.7 (3, OCH_3), 48.8 (1, C-5a), 47.4 (1, C-9), 43.3 (2, C-7), 39.3 (2, C-3), 38.3 (1, C-3a), 37.5 (0, C-9a), 36.4 (2, C-1), 35.5 (1), 33.4 (2, *C*H_2CO_2), 30.4 (2, C-5), 29.1 (1), 19.6 (3, 8-*C*H_3), 17.5 (3, 9a-*C*H_3) and 14.1 (3, OCH_2*C*H_3); *m/z* 426.2647 (M^+, 1%, $C_{23}H_{38}O_7$ requires 426.2615), 381 (3), 366 (2), 365 (2), 349 (2), 199 (28), 125 (12), 99 (23), 87 (14), 86 (29) and 45 (100).

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