Synthetic studies toward the kempane diterpenes. Diels–Alder additions to bicyclic dienes

Chunjian Liu, Guanglin Bao and D. Jean Burnell *

Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland, Canada A1B 3X7. E-mail: jburnell@mun.ca; Fax: 709-737-3702; Tel: 709-737-8535

Received (in Cambridge, UK) 5th June 2001, Accepted 2nd August 2001
First published as an Advance Article on the web 24th September 2001

Diels–Alder additions of 2,6-dimethyl-*p*-benzoquinone to the bicyclic dienes **24**, **30** and **32** took place with very high regio-, stereo- and facial selectivity. Reduction and then alkylation of a tetracyclic adduct with 1,3-dithienium tetrafluoroborate provided compound **56**, which has the correct stereochemistry at three key carbons for elaboration to the kempane diterpenes. Exploratory reactions with tricyclic model compounds and with tetracyclic adducts have been used to assess the development of the desired stereochemistry about the decalin moiety. X-Ray structures for **52**, **53** and **59** were determined.

Introduction

The kempanes (**1**–**3**, Fig. 1) are a small class of tetracyclic diterpenes that have been isolated in tiny amounts from the defensive secretions of soldiers of the termite species *Nasutitermes kempae* and *Nasutitermes octopilis*.[1] An apparently rearranged congener, rippertane (**4**), has also been isolated from other nasute termites.[2]

There has been only one successful total synthesis of **1**, by Dauben and co-workers.[3] Unfortunately, an attempt by Paquette's group[4] to synthesize **2** failed in the very last stage. In both Dauben's and Paquette's routes, the decalin system was used as the scaffold upon which first the five-, and then the seven-membered rings, were constructed. The only approach to **4** used α-santonin as the starting compound,[5] but the completion of this synthesis has not yet been published. In contrast with the earlier efforts towards **1** and **2**, we wanted to be able to produce all three kempanes from a common tetracyclic compound. This entailed a synthetic approach with intermediates carrying more functionality than either of the previous approaches. Herein are reported the results of exploratory reactions for the development of such a synthesis of the kempane diterpenes. This approach includes a number of options for the introduction of the methyl group at C-2a, and some model reactions to accomplish this are outlined. We previously communicated a route that produced the pentacyclic compound **5**, which bears oxygen functionality at all of the necessary positions, but **5** lacks the methyl group at C-2a.[6] The initial stages of that work are described in detail here, also.

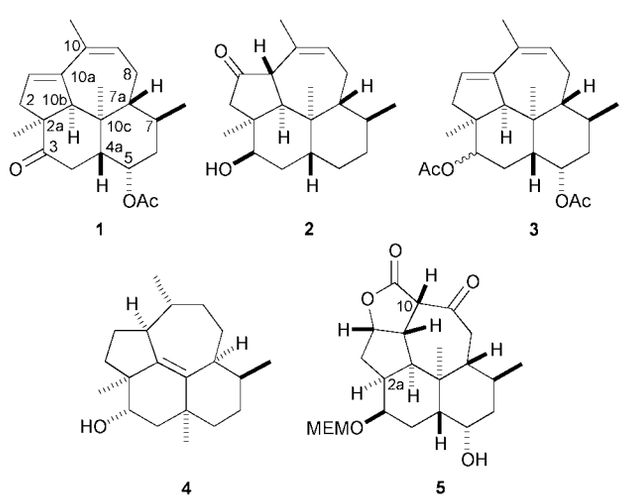
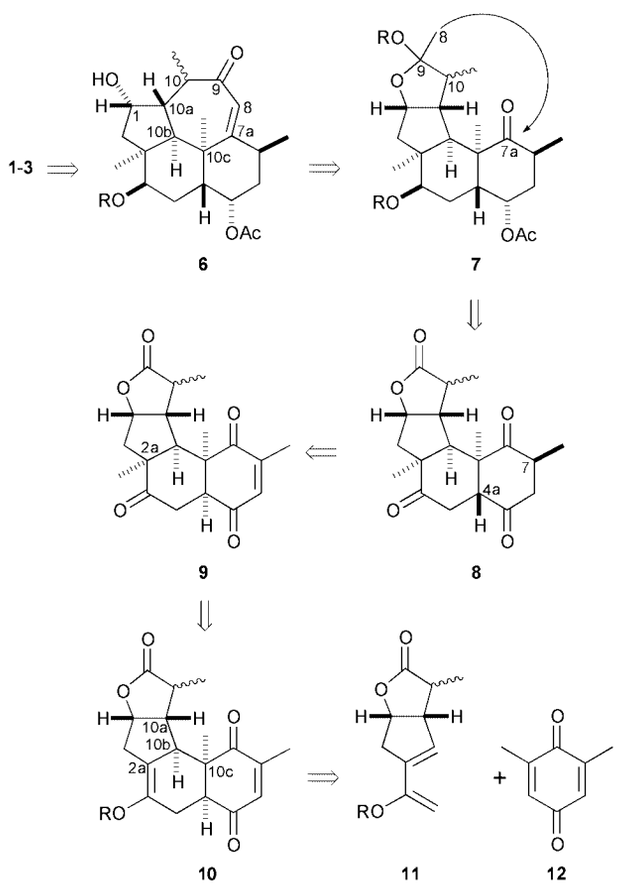


Fig. 1 Kempane diterpenes (**1**–**3**), rippertane (**4**) and the synthetic pentacyclic compound **5**.

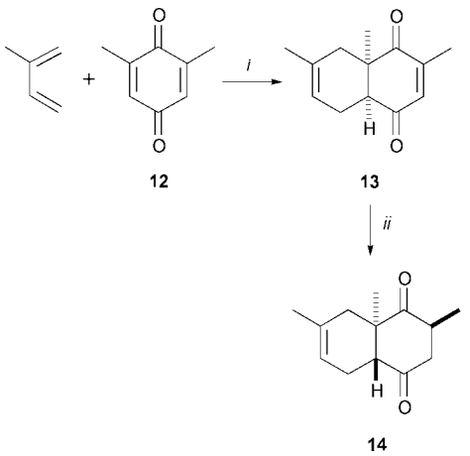
Results and discussion

Our initial retrosynthetic analysis is provided in Scheme 1. It is based on a conviction that establishing the correct relative stereochemistry at C-10a, C-10b and C-10c early in the synthetic sequence would allow for the development of the rest of the stereochemistry in a predictable manner. All three

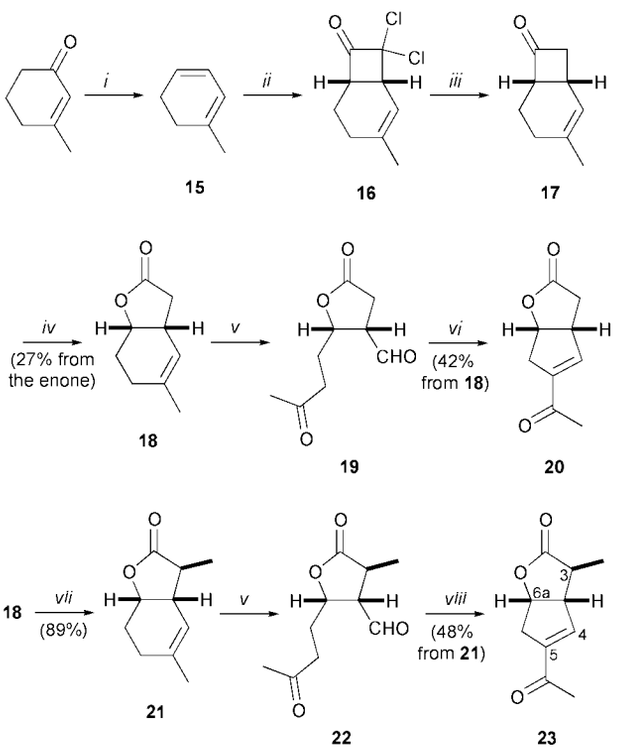


Scheme 1 Initial retrosynthetic analysis. (Compound numbering in this Scheme follows that of the kempanes.)

 DOI: 10.1039/b104924k

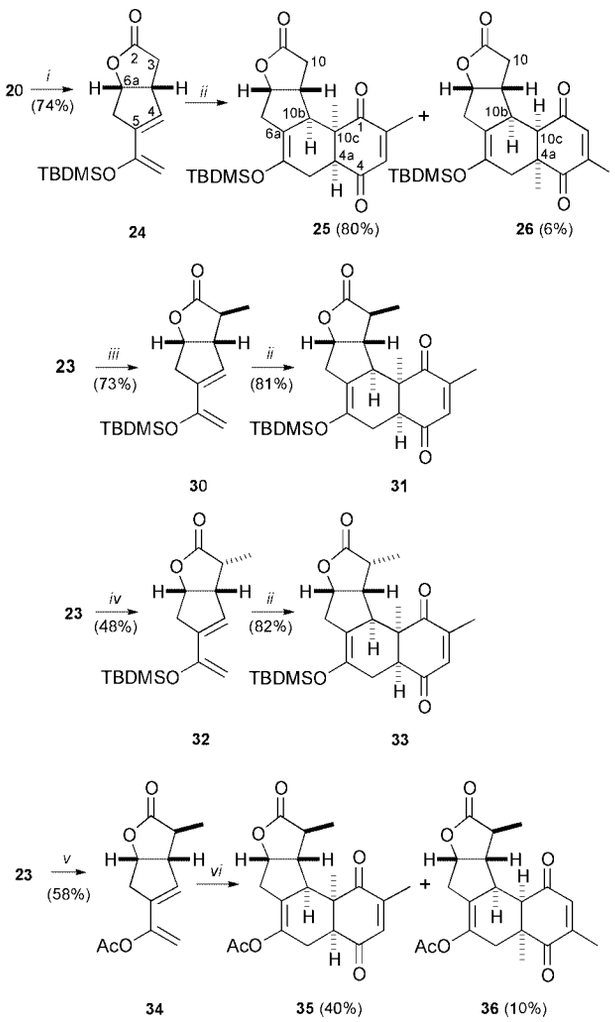


Scheme 2 Initial reactions in Dauben's synthesis[3] of **1**. *Reagents and conditions*: *i*, $BF_3{\cdot}Et_2O$; *ii*, Zn, AcOH, reflux.



Scheme 3 Synthesis of the diene precursors. *Reagents and conditions*: *i*, *1*. $TsNHNH_2$, HCl, THF, *2*. 2.2 equiv. MeLi, Et_2O, 0 °C; *ii*, $Cl_2CHCOCl$, Et_3N, RT; *iii*, Zn, NH_4Cl, MeOH; *iv*, H_2O_2, AcOH; *v*, *1*. O_3, CH_2Cl_2, −78 °C, *2*. Me_2S; *vi*, 1 : 1 5% aqueous HCl–THF, reflux, 12 h; *vii*, LDA, MeI, THF–HMPA, −78 °C; *viii*, (±)-CSA, C_6H_6, reflux, 25 h.

kempanes (**1**–**3**) might be derived from **6**, which would arise by opening the acetal of **7** and aldol cyclization to establish the C-7a–C-8 bond. The relative stereochemistry at C-4a and C-7 of **7** was expected to be established in **8** by equilibration following reduction of **9**. Methylation of the enol ether function on the convex side of compound **10** would take place *syn* to the methyl at C-10c. The rigid diene lactone **11** was adopted for the key Diels–Alder step to provide rapid access to an adduct with well-positioned functionality. In order to ascertain that these transformations, and their order, might be feasible, three processes needed to be examined. Firstly, and most importantly, it was imperative that the Diels–Alder addition of 2,6-dimethyl-*p*-benzoquinone (**12**) to a diene such as **11** be assessed. It was not clear if the stereochemistry at C-10 would influence the selectivity of the cycloaddition. Secondly, a process was needed for the addition of the methyl group at C-2a (**10** ⟶ **9**). The third objective was to examine the equilibration at C-4a and C-7 to



Scheme 4 Diels–Alder reactions of four bicyclic dienes. *Reagents and conditions*: *i*, TBDMSOTf, Et_3N; *ii*, **12**, toluene, reflux, 3 days; *iii*, LDA, TBDMSOTf, THF, −78 °C to RT; *iv*, LDA, TBDMSCl, THF–HMPA, −78 °C to RT; *v*, isopropenyl acetate, (±)-CSA, reflux, 4 days; *vi*, **12**, toluene, reflux, 12 days.

give a compound with the relative stereochemistry of **8**. This apparently trivial process was of some concern because of the low yield reported in the initial steps of Dauben's synthesis of **1**.[3] These are shown in Scheme 2. The Lewis acid-catalysed Diels–Alder reaction of **12** with isoprene, followed by reduction and equilibration of the adduct **13** gave the bicyclic diketone **14** in a yield of only 13%.

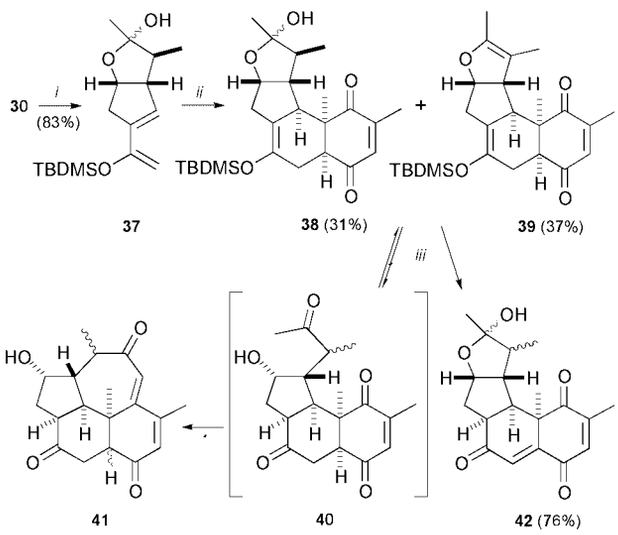
Our work began with the construction of possible precursors for a diene-lactone (Scheme 3). Enone-lactones **20** and **23** were prepared from 3-methylcyclohex-2-en-1-one by a process reminiscent of Corey's prostaglandin synthesis.[7] Addition of dichloroketene to diene **15** took place with complete chemo- and regiochemical control to provide **16**. Similar reactions have been reported by Harding *et al.*[8] Reductive removal of the chlorine atoms of **16** gave the ketone **17**, which in turn afforded only lactone **18** by a Baeyer–Villiger reaction with peroxyacetic acid. Ozonolysis of the double bond of **18** led to a rather unstable compound **19**, so aldol cyclization was carried out immediately with dilute HCl to give **20**. Our attempts to carry out the aldol cyclization under basic conditions led to very complex mixtures. The process outlined in Scheme 1 calls for a methyl-bearing diene (**11**), therefore **18** was methylated to give predominantly **21**. Ozonolysis produced unstable **22**, and aldol cyclization yielded **23**.

With enone-lactones **20** and **23** in hand, assessment could begin of the relative importance in the Diels–Alder reaction of two variables in the diene, *i.e.*, *i.* the presence and the relative stereochemistry of the methyl group at C-3, and *ii.* the identity

of the enol protecting group (Scheme 4). Firstly, the unmethylated diene **24** was obtained by treatment of **20** with TBDMS-triflate and triethylamine.[9] A toluene solution of **24** and the quinone **12** was heated under reflux for three days. Two adducts were detected in the crude product, and these were isolated by chromatography. The ^{1}H NMR data for the major adduct (80% yield) included nuclear Overhauser effect (NOE) enhancements that placed the methyl group on C-10c in the proximity of the hydrogens on C-10 and C-10b. These, and other NOE data, showed that the major adduct was the desired isomer **25**. The minor adduct, which was isolated in only 6% yield, was identified as **26**, the product of *endo* addition to the face of **24** *anti* to the lactone ring, but with regiochemistry opposite to the pathway that produced **25**. In the ^{1}H NMR spectrum of **26**, the resonances for the hydrogens on C-10b and C-10c were coupled (J = 5.3 Hz). Furthermore, NOE enhancements established that the methyl at C-4a was on the same side of the rings as the hydrogens on C-10b and C-10c and that the hydrogen on C-10c was close to a hydrogen on C-10. Whereas high *endo* selectivity should be expected for Diels–Alder reactions of quinones, it was gratifying that the regioselectivity was good† and the facial selectivity was excellent. Indeed, the facial selectivity with diene **24** was much superior to the facial selectivity reported by Overman and co-workers[11] for Diels–Alder reactions of 3-methyl-1-vinylcyclopentene, which might be considered a simple model for the facial alternatives in **24**.

The excellent stereoselectivity in the methylation of **18** to **21** and the lack of epimerization in the formation of **23** were compromised in the formation of diene **30** from **23**. A 6 : 1 mixture of the epimeric dienes **30** and **32**, respectively, was obtained when one equivalent of LDA was used to deprotonate **23**. Two equivalents of LDA provided a 1 : 6 mixture, with **32** being the major epimer. (This stereogenic centre would ultimately disappear in the kempanes.) It was not clear that the Diels–Alder additions of the epimeric dienes would have the same selectivity. The methyl group of diene **32** extends into the concave space of molecule, and it seemed likely that this would engender conformational changes that might alter the selectivity. Diene **30** reacted with **12** to give only one adduct, **31**, in 81% yield. The Diels–Alder reaction of **32** was like that of **30**, and an 82% yield of the desired adduct **33** was obtained. NMR analysis did not reveal any other Diels–Alder adducts. Thus, the methyl group has no significant influence in the Diels–Alder reaction that is the key for this approach to the kempanes. The acetoxy-substituted diene **34** was prepared from **23** in order to examine the effect of this difference on the reactivity of the diene. The Diels–Alder reaction of **34** was very sluggish, giving a yield of only 50% after heating it in toluene with an excess of **12** for 12 days. Furthermore, two inseparable Diels–Alder adducts, **35** and **36**, were obtained, in a ratio of only 4 : 1. Because of the poor reactivity of **34** and the modest regioselectivity, the use of an acetoxy-diene was not pursued further.

Adducts **31** and **33** lack only two of the carbons required for the kempanes. Each adduct would need a methyl group at C-2a (kempane numbering) and a carbon that will become C-8 during the cyclization of the final, seven-membered ring (**7** ⟶ **6** in Scheme 1). It was decided to try to introduce the latter carbon much earlier in the reaction sequence than shown in Scheme 1. Treatment of diene **30** with methyllithium afforded the hemiacetal **37** as a 2.2 : 1 mixture of epimers (Scheme 5). Diels–Alder



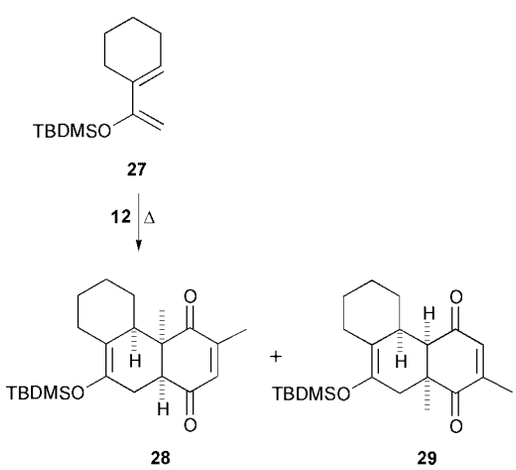
Scheme 5 Attempted opening and cyclization of hemiacetal. *Reagents and conditions*: *i*, MeLi, Et_2O; *ii*, **12**, toluene, reflux, 2 days; *iii*, 5% aqueous HCl–THF, RT, 24 h.

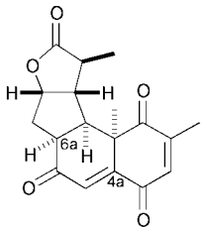
reaction of this mixture with the quinone **12** provided two products in almost equal amounts. These were **38**, still a mixture of epimers, and **39**, which was obviously derived from **38** by dehydration. The total yield of adduct was 68%. Cyclization of the seven-membered ring was attempted by adding the mixture of **38** and **39** to dilute acid. It was hoped that the methyl ketone **40**, unmasked by a reversible opening of the hemiacetal moiety of **38**, might undergo aldol closure with dehydration to give a tetracyclic product such as **41**. This approach was overly optimistic. None of the cyclized product was detected in the reaction mixture. Instead, the hydrolysed and oxidized epimeric mixture **42** was obtained. Therefore, the early introduction of C-8 and the immediate cyclization of the seven-membered ring was abandoned in favour of the original sequence (Scheme 1).

Next, the question of introduction of the methyl at the encumbered C-2a of the kempanes was addressed. Adding a carbon onto the silyl enol ether moiety in adduct **25**, **31** or **34** seemed like a way of ensuring that the carbon be added only at the desired position. Furthermore, the shape of these adducts, with *cis* ring junctions between the six-membered rings, was expected to allow the carbon to be added only onto the correct face. Attempts to methylate directly with, for instance, iodomethane failed, so attention turned to methods for indirect methylation. Most of these were failures as well. Some methods, *e.g.* $PhSCH_2Cl$ with $TiCl_4$,[12] returned the hydrolysed and oxidized compound, such as **43** from **31** (Fig. 2). This was the same result as just adding HCl to **31**.

Further experimentation with indirect approaches to methylation was carried out with a simpler tricyclic model compound **44** (Scheme 6). Although there are not many examples of cyclopropanation of TBDMS-enol ethers in the literature,[13] these

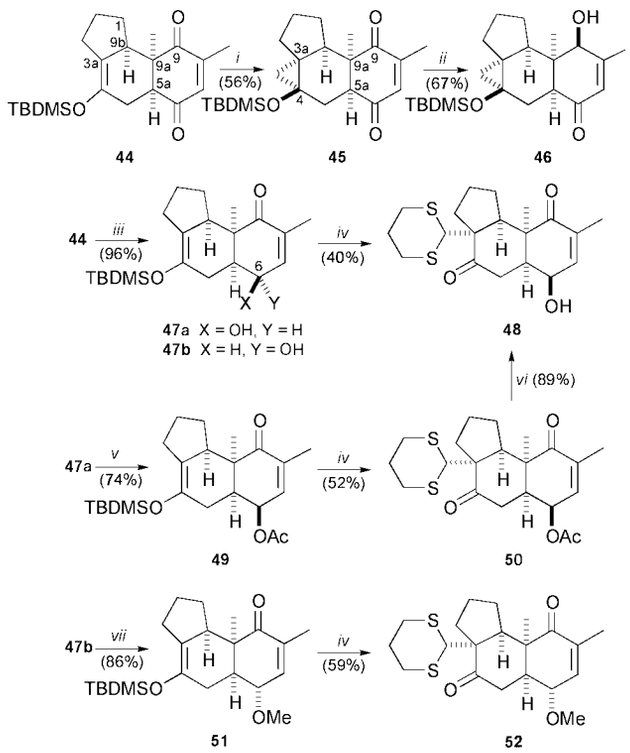
† 1-Substituents on butadiene generally greatly dominate over 2-substituents in determining the regioselectivity of Diels–Alder reactions with methyl-substituted *p*-benzoquinones, even when the 2-substituent is a stronger π-donor.[10] It was therefore very surprising that, in our hands, the reaction of quinone **12** with diene **27**, for which a 1-alkyl substituent and the oxygen substituent on the butadiene moiety should both direct the quinone to add in the same direction, gave **28** and **29** in ratio of only 2 : 1.





43

Fig. 2 Product from attempted methylation at C-6a.



Scheme 6 Model studies for the introduction of a methyl group at C-2a of the kempanes. *Reagents and conditions*: *i*, CH_2I_2, Et_2Zn; *ii*, $LiAl(OBu^t)_3H$, THF, 0 °C; *iii*, $NaBH_4$, $CeCl_3$; *iv*, with **47a**, 1,3-dithienium tetrafluoroborate, CH_2Cl_2–$MeNO_2$, −78 °C; *v*, Ac_2O, Et_3N, DMAP; *vi*, K_2CO_3, MeOH; *vii*, NaH, MeI.

silyloxycyclopropanes can be converted to α-methyl ketones with base[14] or acid.[13] Treatment of **44** and a large excess of CH_2I_2 with Et_2Zn gave the cyclopropanated compound **45** that had the desired stereochemistry at C-3a (from NOE experiments). Furthermore, monoreduction of **45** with a bulky hydride smoothly gave **46** with high chemo- and stereoselectivity.[15] This result suggested that the construction of the seven-membered ring *via* attack of a nucleophile onto the carbonyl at C-9a could be carried out selectively. It was then very disappointing when attempts to cyclopropanate the tetracyclic adduct **31** under similar conditions failed completely.

1,3-Dithienium tetrafluoroborate has been used to alkylate a trimethylsilyloxy alkene.[16] We found that the TBDMS enol ether derived from cyclohexanone was also alkylated with 1,3-dithienium tetrafluoroborate, in a yield of 88%. The reaction of this electrophile with **44** gave a complex mixture. In order to limit side-reactions, the carbonyl at C-6 of **44** was reduced. Monoreduction of enediones such as **44** with $NaBH_4$ in the presence of $CeCl_3$ is known to be regioselective, but not facially selective.[17] Thus, it was not surprising that the product was **47a**,**b**, a 1 : 1 mixture of epimers. Introduction of an excess of 1,3-dithienium tetrafluoroborate to **47a** gave **48** in modest yield, but it is important to note that the alkylation took place exclusively on the desired face of the silyl enol ether, *i.e.*, *syn* to the methyl at C-9a. Protection of the alcohol function of **47a** as the acetate **49** led to a significant improvement in the yield of

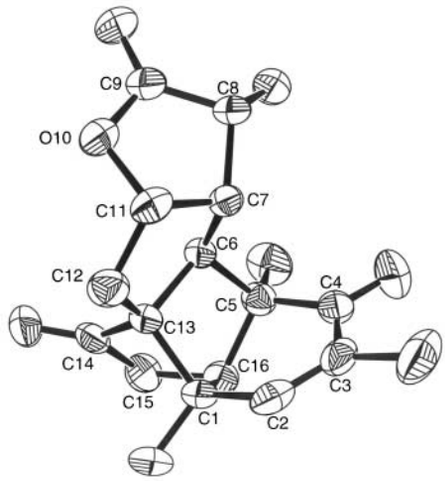
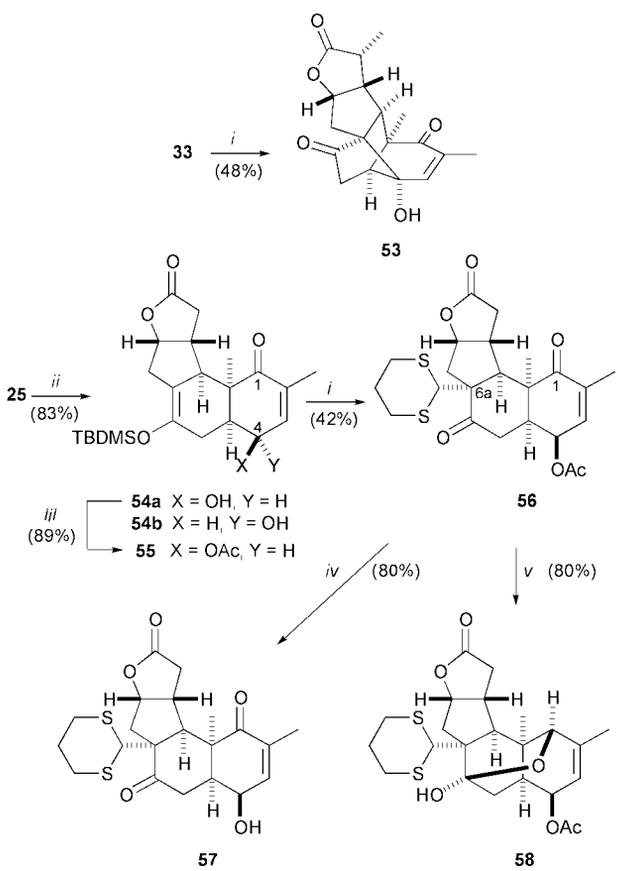


Fig. 3 X-Ray crystal structure of compound **53**.

alkylated product **50**. Methylation of **47b** followed by reaction with 1,3-dithienium tetrafluoroborate gave **52** as a single isomer in 59% yield. The structure of **52** was confirmed by X-ray crystallography.

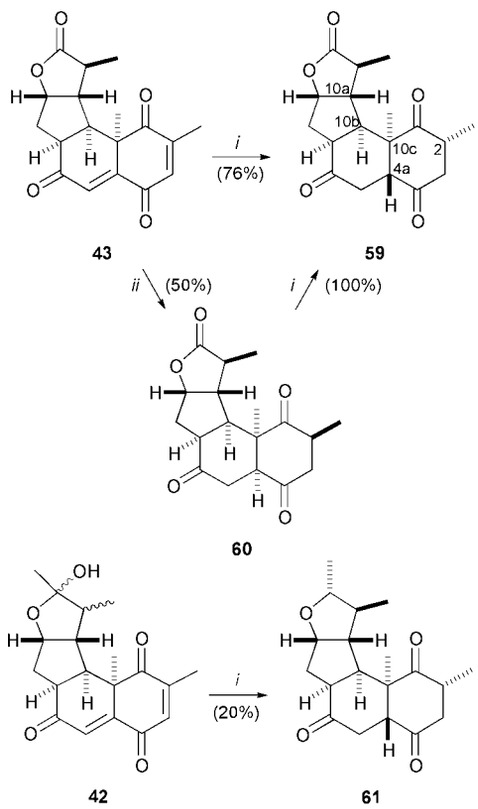
As shown in Scheme 7, addition of 1,3-dithienium tetrafluoroborate to the adduct **33** gave no dithiane-containing product. Instead, the product was the pentacyclic compound **53**, for which the structure was determined by X-ray analysis (Fig. 3). The same compound could be obtained by simply adding some HF to **33**. Reduction of adduct **25** with $NaBH_4$–$CeCl_3$[17] gave the 1 : 1 epimeric mixture **54a**,**b**, which was separated by chromatography. One isomer (**54a**) was acetylated (**55**) and treated with 1,3-dithienium tetrafluoroborate to give **56**. None



Scheme 7 Alkylation of tetracyclic Diels–Alder adducts with 1,3-dithienium tetrafluoroborate. *Reagents and conditions*: *i*, 1,3-dithienium tetrafluoroborate. CH_2Cl_2–$MeNO_2$, −78 °C; *ii*, $NaBH_4$, $CeCl_3$; *iii*, Ac_2O, Et_3N, DMAP; *iv*, K_2CO_3, MeOH; *v*, $NaBH_4$, MeOH–CH_2Cl_2.

of the compound with the opposite stereochemistry at C-6a was detected by NMR. Hydrolysis of the alkylated product could be carried out easily to give the alcohol **57**. Reduction of **56** with sodium borohydride took place from the convex face with a high degree of selectivity to yield the hemiacetal **58**.

Compound **43** had been produced in many unsuccessful methylation experiments. This compound was therefore convenient to use to study the reduction and equilibration process (**9** ⟶ **8** in Scheme 1) to establish the stereochemistry at C-2 and C-4a (Scheme 8). A similar process had proven to be very



Scheme 8 Reduction and equilibration study. *Reagents and conditions*: *i*, Zn, AcOH, Δ; *ii*, $TiCl_3$, H_2O, RT.

inefficient in Dauben's synthesis of **1** (Scheme 2).[3] Reduction of both double-bonds in **43** took place with zinc in hot acetic acid. The lactone ring was unaffected under these conditions, and two isomeric products were detected by NMR. The relative amounts of these changed during prolonged heating such that the initial minor product equilibrated to the major one, which was shown to be compound **59**. NOE data for this major product included a 9% enhancement of the signal for the hydrogen on C-10a and a 6% enhancement for the hydrogen on C-2 on saturation of the signal for the hydrogen on C-4a. This showed that the decalin ring-junction was *trans*, but the C-2 methyl was also *trans* to the C-4a hydrogen. The structure of **59** was corroborated by X-ray analysis, which showed that, at least in the solid state, the diketone ring was in a twisted conformation in which the C-2 methyl was pseudo-equatorial (Fig. 4). This was not the desired isomer for the synthesis of the kempanes. Attention was turned to the initially major isomer. Both double-bonds of **43** could be reduced quickly with $TiCl_3$ in water[18] at room temperature to give mainly the product that was identical with the initial major product from the reduction with zinc and acetic acid. The NOE data for this isomer included enhancements of the signals for both the C-2 and the C-4a hydrogens on saturation of the C-10c methyl signal. Thus, the compound was **60**. The configuration at C-2 was the desired one, but the decalin ring-junction was *cis*. Treatment of **60** with hot acetic acid gave **59**, but the desired isomer was never observed.

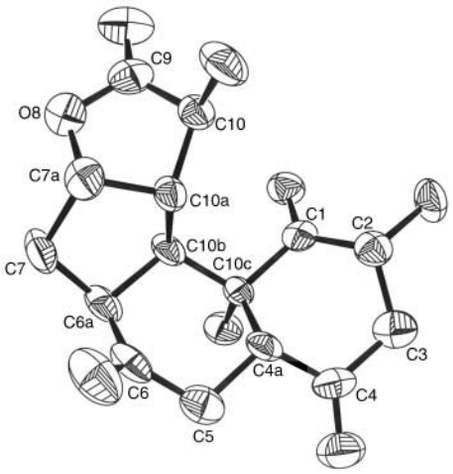


Fig. 4 X-Ray crystal structure for compound **59**.

In a similar manner, **42** was reduced by zinc in hot acetic acid to give a very complex mixture in which **61**, now a cyclic ether, was a major component.

Conclusions

While the route to the kempanes proposed in Scheme 1 contains elements that are feasible, some adjustments to the synthetic plan would be required. The key Diels–Alder reaction (**11** ⟶ **10**) was a selective and efficient reaction. Also, indirect introduction of the kempanes' C-2a methyl group (**10** ⟶ **9**) appeared to be possible through the reaction of the silyl enol ether with 1,3-dithienium tetrafluoroborate or *via* cyclopropanation, although the latter had failed with adduct **28**. The one attempt to cyclize the seven-membered ring (**7** ⟶ **6**) early in the synthetic sequence had not been encouraging, although reduction of a ketone function in the cyclopropanated model **42** and in the modified adduct **53** showed that this ketone was sufficiently unhindered that cyclization of the seven-membered ring onto this ketone might still be reasonably anticipated. Finally, it was clear that establishing the correct stereochemistry at C-4a and C-7 of the kempanes by equilibration would not take place as originally planned. These conclusions were instrumental in the design of a route, described in the following paper, that was ultimately successful in preparing the challenging ring system of the kempanes.

Experimental

General

Uncorrected melting points were determined on a Fisher–Johns apparatus. Infrared spectra were measured on a Mattson Polaris FT instrument. A General Electric GE 300-NB spectrometer provided the ^1H and ^{13}C NMR spectra (300 MHz for ^1H, 75 MHz for ^{13}C). Unless otherwise noted, $CDCl_3$ was the solvent. Shifts are relative to internal tetramethylsilane. Nuclear Overhauser effect (NOE) measurements were made using difference spectra. The NOE data have this form: saturated signal (enhanced signal, enhancement). ^{13}C NMR signals are followed in parentheses by the assignments (based on APT spectra and heterocorrelated spectra) or the number of attached hydrogens (*e.g.* 2 = CH_2). Mass spectra (EI) were usually obtained on a V. G. Micromass 7070HS instrument. The X-ray diffractometer was a Rigaku AFC6S instrument. Unless otherwise noted, solutions were "dried" by stirring with anhydrous $MgSO_4$ followed by filtration. "Chromatography" refers to flash column chromatography on silica gel; elution was generally with hexane containing an increasing proportion of ethyl acetate.

cis-8,8-Dichloro-3-methylbicyclo[4.2.0]oct-2-en-7-one 16

A mixture of 3-methylcyclohex-2-en-1-one (22.5 g, 200 mmol), *p*-tolylsulfonylhydrazine (38.4 g, 200 mmol) and 1.5 ml of concentrated HCl in THF (280 ml) was stirred at RT for 15 h. Three times, benzene (200 ml) was added to the red solution, and the mixture was concentrated under reduced pressure. The residue was solidified by trituration with diethyl ether and dried in a desiccator over $CaCl_2$ under vacuum for 24 h. The *p*-tolylsulfonylhydrazone (57.8 g) was a 2 : 1 mixture of stereoisomers by ^{1}H NMR: δ_H (for the major isomer) 7.85 (2 H, d, *J* 8.2), 7.31 (2 H, d, *J* 8.2), 5.94 (1 H, q, *J* 1.4), 2.42 (3 H, s), 2.24 (2 H, t, *J* 6.5), 2.05 (2 H, t, *J* 6.0), 1.81 (3 H, d, *J* 1.4) and 1.75 (2 H, m); δ_H (for the minor isomer) 7.86 (2 H, d, *J* 8.5), 7.31 (2 H, t, *J* 8.5), 6.13 (1 H, q, *J* 1.4), 2.42 (3 H, s), 2.32 (2 H, t, *J* 6.4), 2.15 (2 H, t, *J* 6.1), 1.87 (3 H, d, *J* 1.4) and 1.75 (2 H, m).

To a vigorously stirred suspension of the hydrazone mixture (28.9 g, 100 mmol) in anhydrous diethyl ether (150 ml) was added methyllithium (1.4 M in diethyl ether, 157 ml, 220 mmol) at 0 °C over 3 h. After stirring for an additional 15 h, water (200 ml) was cautiously added. The organic layer was extracted with pentane (3 × 60 ml), and the pentane extracts were combined with the diethyl ether solution. The combined solutions were washed with 5% aqueous HCl (2 × 60 ml), saturated aqueous $NaHCO_3$ (60 ml) and brine (60 ml). This solution of **15** was dried over anhydrous Na_2SO_4 then over solid KOH.

Dry triethylamine (26.8 ml, 193 mmol) and dichloroacetyl chloride (26.0 g, 175 mmol) in pentane were added at RT over 3 h. This was stirred for another 3.5 h. A precipitate was removed by filtration. The filtrate was washed with water (200 ml), saturated aqueous $NaHCO_3$ solution (3 × 130 ml) and brine (2 × 130 ml). The organic solution was dried and concentrated under reduced pressure. Distillation (75–91 °C/3 mmHg) of the residue provided crude **16** (11.4 g), which was used in the next step. An analytical sample was obtained by chromatography as a colourless oil: ν_{max}(film)/cm^{-1} 1804; δ_H 5.60 (1 H, m, 2-H), 4.05 (1 H, m, 6-H), 3.43 (1 H, m, 1-H), 2.15 (1 H, m, 5-H *anti* to 6-H), 1.99–1.92 (2 H, m, 4-H), 1.77 (3 H, s, 3-methyl), 1.65 (1 H, m, 5-H *syn* to 6-H); NOE data 4.05 (3.43, 1.3%; 2.15, 0.8%; 1.65, 1.2%), 2.15 (4.05, 1.3%; 1.65, 6%) and 1.65 (4.05, 2%; 2.15, 6%); δ_C 197.0 (C-7), 140.4 (C-3), 117.1 (C-2), 87.1 (C-8), 52.4 (C-6), 44.8 (C-1), 25.9 (C-4), 24.6 (3-methyl) and 19.4 (C-5); *m*/*z* 206 (M^+ + 2, 3%), 204.0103 (M^+, 5, $C_9H_{10}{}^{35}Cl_2O$ requires 204.0109), 105 (9), 94 (22), 91 (10), 79 (29), 77 (22) and 55 (100).

cis-3-Methylbicyclo[4.2.0]oct-2-en-7-one 17

To a vigorously stirred mixture of crude **16** (11.4 g, approximately 55.4 mmol) and NH_4Cl (23.5 g, 44.7 mmol) in methanol (300 ml) at 0 °C was added zinc dust (47.9 g, 730 mmol) in portions over 1 h. Stirring was continued at RT for 10 h. Diethyl ether (150 ml) was added and solid material was removed by filtration. The filtrate was concentrated under vacuum, and water (200 ml) was added to the residue. This was extracted with diethyl ether (4 × 50 ml). The combined organic extracts were washed with water (40 ml) and brine (40 ml), then dried and concentrated under vacuum. Distillation (70–80 °C/5 mmHg) provided **17** as a colourless oil. This was sufficiently pure to be used in the next step, but an analytical sample was obtained by chromatography: ν_{max} (film)/cm^{-1} 1778; δ_H 5.63 (1 H, q, *J* 1.3, 2-H), 3.49 (1 H, m, 6-H), 3.24 (1 H, ddd, *J* 16.8, 9.2 and 2.8, 8-H), 2.91 (1 H, m, 1-H), 2.54 (1 H, ddd, *J* 16.8, 3.7 and 2.6, 8-H), 2.05–1.94 (2 H, m, 4-H and 5-H), 1.80 (1 H, m, 4-H), 1.70 (3 H, s, 3-methyl) and 1.57 (1 H, m, 5-H); NOE data 3.49 (2.91, 2.2%), 3.24 (2.91, 1.7%; 2.54, 5%) and 2.54 (3.49, 4%); δ_C 212.2 (C-7), 135.8 (C-3), 122.6 (C-2), 56.3 (C-6), 52.3 (C-8), 26.2 (C-4), 24.4 (3-methyl), 23.4 (C-1) and 19.9 (C-5); *m*/*z* 136.0892 (M^+, 0.3%, $C_9H_{12}O$ requires 136.0888), 94 (84), 93 (16), 91 (14), 79 (100), 77 (22) and 55 (22).

cis-3a,6,7,7a-Tetrahydro-5-methylbenzofuran-2(3*H*)-one 18

To a solution of crude **17** (4.34 g, approximately 31.9 mmol) in glacial acetic acid (30 ml) at 0 °C was added 30% hydrogen peroxide (9.00 g, 79.4 mmol) over 10 min. The solution was stirred at 0 °C for 15 h before it was poured into water (100 ml), and dichloromethane (100 ml) was added. Solid Na_2CO_3 was introduced until gas evolution ceased. The aqueous layer was re-extracted with dichloromethane (3 × 40 ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (50 ml) and brine (50 ml). After drying over $MgSO_4$, the solution was concentrated under vacuum. Chromatography of the residue afforded **18** (4.05 g, overall 27% from 3-methylcyclohex-2-en-1-one) as a colourless oil: ν_{max}(film)/cm^{-1} 1779; δ_H 5.15 (1 H, broad s, 4-H), 4.72 (1 H, m, 7a-H), 2.97 (1 H, m, 3a-H), 2.75 (1 H, dd, *J* 17.1 and 8.5, 3-H *syn* to 3a-H), 2.27 (1 H, dd, *J* 17.1 and 2.9, 3-H *anti* to 3a-H), 2.18–2.07 (2 H, m, 6-H and 7-H), 1.90–1.71 (2 H, m, 6-H and 7-H) and 1.69 (3 H, s, 5-methyl); NOE data 5.15 (2.97, 1.4%; 2.27, 1.4%), 4.72 (2.97, 1.6%) and 2.75 (2.97, 1.2%; 2.27, 7%); δ_C 177.1 (C-2), 136.1 (C-5), 119.7 (C-4), 77.6 (C-7a), 36.3 (C-3), 34.8 (C-3a), 24.9 (2), 23.9 (2) and 23.7 (5-methyl); *m*/*z* 152.0845 (M^+, 24%, $C_9H_{12}O_2$ requires 152.0837), 141 (11), 110 (27), 95 (29), 93 (100), 86 (51), 81 (26), 79 (22), 77 (21), 68 (31), 67 (29) and 60 (34).

cis-5-Acetyl-3,3a,6,6a-tetrahydrocyclopenta[*b*]furan-2(2*H*)-one 20

Ozone was introduced into a solution of **18** (12.0 g, 79.0 mmol) in dichloromethane (750 ml) at −78 °C until a blue colour persisted. The excess ozone was removed by bubbling nitrogen through the solution until the blue colour disappeared. Dimethyl sulfide (45 ml) was added. The mixture was allowed to warm to RT as it was stirred overnight. The solvent and any remaining dimethyl sulfide were evaporated under vacuum. The residue (**19**) was immediately redissolved in THF (350 ml) and 5% aqueous HCl (350 ml) was added. The mixture was heated under reflux for 17 h. Most of the THF was evaporated under reduced pressure, and the remaining aqueous solution was extracted with ethyl acetate (4 × 50 ml). The combined organic extracts were washed with brine (2 × 50 ml), dried and concentrated under reduced pressure. Chromatography (silica gel, eluted with 3% methanol in chloroform) of the residue provided **20** (5.60 g, 42%) as a white solid: mp 109–111 °C; ν_{max}(CH_2Cl_2 solution)/cm^{-1} 1751, 1662 and 1617; δ_H 6.46 (1 H, d, *J* 1.3, 4-H), 5.18 (1 H, apparent t, *J* 5.5, 6a-H), 3.77 (1 H, m, 3a-H), 3.02–2.91 (2 H, m, 6-H), 2.88 (1 H, dd, *J* 18.0 and 10.2, 3-H *syn* to 3a-H), 2.56 (1 H, dd, *J* 18.0 and 2.0, 3-H *anti* to 3a-H) and 2.35 (3 H, s, $COCH_3$); δ_C 195.8 (*C*OCH_3), 175.5 (C-2), 143.9 (C-5), 141.0 (C-4), 82.3 (C-6a), 46.6 (C-3a), 37.8 (C-6), 32.4 (C-3) and 26.8 (CO*C*H_3); *m*/*z* 166.0628 (M^+, 8%, $C_9H_{10}O_3$ requires 166.0629), 151 (25), 122 (11), 95 (20), 67 (29), 65 (10), 51 (11) and 43 (100).

(3α,3aα,7aα)-3a,6,7,7a-Tetrahydro-3,5-dimethylbenzofuran-2(3*H*)-one 21

n-BuLi (7.72 ml of 2.5 M in hexane, 19.3 mmol) was added to a solution of diisopropylamine (2.81 ml, 21.2 mmol) in dry THF (26 ml) at 0 °C over 20 min. After stirring for 10 min, the solution was cooled to −78 °C. A solution of **18** (2.94 g, 19.3 mmol) in dry THF (26 ml) was introduced over 30 min. This was stirred for 30 min before iodomethane (3.04 g, 21.3 mmol) in hexamethylphosphoramide (4.16 g, 23.2 mmol) was added over 20 min, and this was stirred at −78 °C for 3 h. The solution was warmed to 0 °C, and dilute aqueous NH_4Cl solution (100 ml) was added at once followed by diethyl ether (300 ml). The organic layer was washed with water (3 × 80 ml) and brine (80 ml), dried (Na_2SO_4) and concentrated under vacuum. Chromatography provided **21** (2.87 g, 89%) as a colourless oil:

ν_{max}(film)/cm^{-1} 1773; δ_H 5.32 (1 H, m, 4-H), 4.67 (1 H, ddd, *J* 10.8, 6.8 and 4.1, 7a-H), 2.58 (1 H, m, 3a-H), 2.37 (1H, dq, *J* 7.5 and 7.5, 3-H), 2.08–1.70 (4 H, m, 6-H and 7-H), 1.71 (3 H, s, 5-methyl) and 1.31 (3 H, d, *J* 7.5, 3-methyl); NOE data 4.67 (2.58, 2%) and 1.31 (5.32, 1%; 2.58, 3%; 2.37, 4%); δ_C 179.7 (C-2), 136.0 (C-5), 119.4 (C-4), 75.9 (C-7a), 42.7 (C-3a), 41.7 (C-3), 26.1 (2), 25.6 (2), 23.5 (5-methyl) and 14.4 (3-methyl); *m*/*z* 166.0996 (M$^+$, 23%, $C_{10}H_{14}O_2$ requires 166.0994), 121 (9), 110 (17), 107 (28), 96 (14), 95 (17), 93 (81), 91 (20), 86 (17), 81 (17), 79 (29) and 74 (100).

(3α,3aα,7aα)-5-Acetyl-3,3a,6,6a-tetrahydro-3-methyl-2*H*-cyclopenta[*b*]furan-2-one 23

Ozone was introduced into a solution of **21** (3.05 g, 18.4 mmol) in dichloromethane (200 ml) at −78 °C until a blue colour persisted. Excess ozone was removed by bubbling nitrogen through the solution until the blue colour disappeared. Dimethyl sulfide (15 ml, 205 mmol) was added. The mixture attained RT while stirring overnight. Solvent and excess dimethyl sulfide were evaporated under reduced pressure to give a yellow oil (**22**), which was immediately redissolved in benzene (350 ml). (±)-Camphorsulfonic acid (0.43 g, 1.8 mmol) was added, and the mixture was heated under reflux in a Dean–Stark apparatus for 25 h. The cooled solution was washed with 5% aqueous $NaHCO_3$ solution (2 × 100 ml) and brine (2 × 100 ml), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography provided **23** (1.59 g, 48% from **21**) as a pale yellow oil: ν_{max}(film)/cm^{-1} 1769, 1670 and 1616m; δ_H 6.51 (1 H, d, *J* 1.7, 4-H), 5.20 (1 H, apparent dt, *J* 5.5 and 1.6, 6a-H), 3.41 (1 H, m, 3a-H), 2.98–2.82 (2 H, m, 6-H), 2.65 (1 H, qd, *J* 7.6 and 1.9, 3-H), 2.35 (3 H, s, $COCH_3$) and 1.42 (3H, d, *J* 7.6, 3-methyl); NOE data 5.20 (3.41, 2%; 2.98–2.82, 1.6%), 3.41 (6.51, 1.6%; 5.20, 2%; 1.42, 1.3%) and 1.42 (5.20, 1.6%; 3.41, 4%, 2.65, 5%); δ_C 195.9 (*C*OCH$_3$), 178.8 (C-2), 143.6 (C-5), 140.7 (C-4), 80.7 (C-6a), 54.7 (C-3a), 39.3 (C-3), 37.6 (C-6), 26.7 (CO*C*H$_3$) and 17.4 (3-methyl); *m*/*z* 180.0781 (M$^+$, 19%, $C_{10}H_{12}O_3$ requires 180.0786), 165 (22), 136 (16), 121 (17), 109 (15) and 43 (100).

cis-5-[1-(1,1-Dimethylethyl)dimethylsilyloxyethenyl]-3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one 24

To a solution of **20** (0.548 g, 3.30 mmol) and *tert*-butyldimethylsilyl triflate‡ (0.83 ml, 3.61 mmol) in dichloromethane (30 ml) at 0 °C was added triethylamine (0.60 ml, 4.30 mmol). After stirring the solution for 10 min, the solvent was evaporated under reduced pressure. Chromatography of the residue provided **24** (0.682 g, 74%) as a colourless oil: ν_{max}(film)/cm^{-1} 1778; δ_H 5.77 (1 H, broad s, 4-H), 5.16 (1 H, m, 6a-H), 4.36 (1 H, s, CH_2=), 4.33 (1 H, s, CH_2=), 3.61 (1 H, m, 3a-H), 2.83–2.80 (2 H, m, 6-H), 2.76 (1 H, dd, *J* 18.0 and 9.6, 3-H *syn* to 3a-H), 2.46 (1 H, dd, *J* 18.0 and 1.5, 3-H *anti* to 3a-H), 0.95 (9 H, s, SiC(CH$_3$)$_3$) and 0.17 (6H, s, Si(CH$_3$)$_2$); NOE data 5.16 (3.61, 3%) and 2.76 (3.61, 2%; 2.46, 7%); δ_C 176.4 (C-2), 152.4 (0), 140.2 (0), 127.3 (C-4), 94.8 (CH_2=), 83.4 (C-6a), 45.6 (C-3a), 39.0 (C-6), 33.5 (C-3), 25.7 (SiC(*C*H$_3$)$_3$), 18.2 (Si*C*(CH$_3$)$_3$) and −4.7 (Si(CH$_3$)$_2$); *m*/*z* 280.1496 (M$^+$, 0.6%, $C_{15}H_{24}O_3Si$ requires 280.1495), 223 (11), 181 (10), 117 (12), 75 (100) and 73 (14).

(4aα,7aβ,10aβ,10bα,10cα)-6-[(1,1-Dimethylethyl)dimethylsilyloxy]-4a,5,7,7a,10,10a,10b,10c-octahydro-2,10c-dimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4,9-trione 25 and (4aα,7aβ,10aβ,10bα,10cα)-6-[(1,1-dimethylethyl)dimethylsilyloxy]-4a,5,7,7a,10,10a,10b,10c-octahydro-3,4a-dimethyl-1*H*-benz[6,7]indeno-[2,1-*b*]furan-1,4,9-trione 26

A solution of **24** (1.65 g, 5.89 mmol) and **12** (1.60 g, 11.8 mmol) in toluene (70 ml) was heated under reflux for 3 days. The solvent was evaporated under reduced pressure, and chromatography of the residue gave **25** (1.96 g, 80%) and **26** (0.141 g, 6%).

For **25**: pale yellow foam, ν_{max}(CCl$_4$)/cm^{-1} 1776 and 1681; δ_H 6.44 (1 H, t, *J* 1.5, 3-H), 5.06 (1 H, apparent dt, *J* 6.5 and 2.5, 7a-H), 3.61 (1 H, ddd, *J* 15.0, 8.2 and 2.5, 10a-H), 2.94 (1 H, broad t, *J* 8.4,10b-H), 2.93 (1 H, m, 7β-H), 2.79 (1 H, dd, *J* 17.7 and 8.4, 10β-H), 2.60 (1 H, broad d, *J* 18.1, 7α-H), 2.39 (1 H, m, 5α-H), 2.37 (1 H, dd, *J* 17.7 and 2.0, 10α-H), 2.28 (1 H, m, 4a-H), 2.13 (1 H, m, 5β-H), 1.97 (3 H, d, *J* 1.4, 2-methyl), 1.42 (3 H, s, 10c-methyl), 0.89 (9 H, s, SiC(CH$_3$)$_3$), 0.07 (3H, s, SiCH$_3$) and 0.05 (3H, s, SiCH$_3$); NOE data 3.61 (5.06, 8%; 2.79, 3%), 2.28 (3.61, 1%; 2.94, 8%; 2.79, 4%) and 1.42 (3.61, 5%; 2.94, 8%; 2.37, 8%; 2.28, 11%); δ_C 202.0 (0), 199.4 (0), 176.6 (C-9), 148.2 (C-2), 139.5 (C-6), 133.8 (C-3), 117.4 (C-6a), 85.2 (C-7a), 56.7 (C-10b), 53.3 (C-4a), 50.8 (C-10c), 41.2 (C-10a), 36.9 (C-10), 34.4 (C-7), 31.5 (C-5), 25.5 (SiC(*C*H$_3$)$_3$), 24.4 (10c-methyl), 18.0 (Si*C*(CH$_3$)$_3$), 16.5 (2-methyl), −3.9 (SiCH$_3$) and −4.0 (SiCH$_3$); *m*/*z* 416.1990 (M$^+$, 2%, $C_{23}H_{32}O_5Si$ requires 416.2019), 360 (11), 359 (35), 224 (21), 223 (37), 195 (12), 181 (21), 117 (20), 103 (16), 75 (100) and 73 (85).

For **26**: pale yellow foam, ν_{max}(CCl$_4$)/cm^{-1} 1775 and 1684; δ_H 6.49 (1 H, q, *J* 1.3, 2-H), 5.05 (1 H, td, *J* 6.5 and 1.9, 7a-H), 3.77 (1 H, m, 10a-H), 3.03 (1 H, d, *J* 5.3, 10c-H), 2.98 (1 H, m, 7β-H), 2.72 (1 H, dd, *J* 17.7 and 8.2, 10β-H), 2.59 (1 H, m, 7α-H), 2.52 (1 H, m, 10b-H), 2.36 (1 H, dd, *J* 17.7 and 2.1, 10α-H), 2.26 (1 H, dq, *J* 17.2 and 2.8, 5β-H), 1.99 (3 H, d, *J* 1.3, 3-methyl), 1.78 (1 H, dq, *J* 17.2 and 2.5, 5α-H), 1.37 (3 H, s, 4a-methyl), 0.90 (9 H, s, SiC(CH$_3$)$_3$), 0.08 (3H, s, SiCH$_3$) and 0.06 (3H, s, SiCH$_3$); NOE data 5.05 (3.77, 11%; 2.98, 6%; 2.72, 2%), 3.77 (5.05, 9%; 3.03, 1%; 2.72, 5%), 2.52 (3.77, 2%; 3.03, 11%; 1.37, 2%) and 1.37 (3.03, 14%; 2.52, 14%; 1.78, 7%); δ_C 202.9 (0), 198.5 (0), 176.9 (C-9), 146.7 (C-3), 139.3 (C-6), 136.9 (C-2), 116.1 (C-6a), 85.2 (C-7a), 51.8 (C-10c), 50.6 (C-4a), 43.7 (C-10b), 40.9 (C-10a), 37.7 (C-5), 35.5 (C-10), 33.6 (C-7), 25.5 (SiC(*C*H$_3$)$_3$), 21.3 (4a-methyl), 17.9 (Si*C*(CH$_3$)$_3$), 16.4 (3-methyl), −3.9 (SiCH$_3$) and −4.0 (SiCH$_3$); *m*/*z* 416.2036 (M$^+$, 6%, $C_{23}H_{32}O_5Si$ requires 416.2019), 360 (30), 359 (96), 251 (70), 223 (21), 195 (15), 194 (20), 181 (17), 75 (98) and 73 (100).

(3α,3aα,6aα)-5-[1-(1,1-Dimethylethyl)dimethylsilyloxyethenyl]-3,3a,6,6a-tetrahydro-3-methyl-2*H*-cyclopenta[*b*]furan-2-one 30 and (3α,3aβ,6aβ)-5-[1-(1,1-dimethylethyl)dimethylsilyloxyethenyl]-3,3a,6,6a-tetrahydro-3-methyl-2*H*-cyclopenta[*b*]furan-2-one 32

Method A. To a solution of diisopropylamine (0.14 ml, 1.00 mmol) in dry THF (4.0 ml) at 0 °C was added *n*-BuLi (2.5 M in hexane, 0.40 ml, 1.00 mmol) over 5 min. The solution was stirred for 20 min before it was transferred over 15 min by syringe to a solution of **23** (0.180 g, 1.00 mmol) and *tert*-butyldimethylsilyl triflate (0.28 ml, 1.2 mmol) in dry THF (5.0 ml) at −78 °C. This mixture was stirred at −78 °C for 1 h before it was allowed to warm to RT. Hexane (100 ml) was added. This solution was washed with water (3 × 30 ml) and brine (30 ml), dried (Na_2SO_4) and concentrated under reduced pressure. Preparative thin-layer chromatography (silica gel, 0.5 mm thickness, 25% ethyl acetate in hexane) provided **30** (214 mg, 73%) and a small amount of **32** (37 mg, 12%).

Method B. To a solution of diisopropylamine (0.23 ml, 1.75 mmol) in dry THF (5.0 ml) at 0 °C was added *n*-BuLi (2.5 M in hexane, 0.63 ml, 1.57 mmol) over 5 min. The solution was stirred for 10 min then cooled to −78 °C. A solution of **23** (0.128 g, 0.710 mmol) in dry THF (1.0 ml) was added over 10 min. This mixture was stirred at −78 °C for 30 min. Hexamethylphosphoramide (1.0 ml) was added followed by a solution of *tert*-butylchlorodimethylsilane (243 mg, 1.56 mmol) in dry THF (1.0 ml). The mixture was allowed to warm to RT, and

‡ The IUPAC name for triflate is trifluoromethanesulfonate.

it was stirred for 2 h before it was diluted with pentane (100 ml). This solution was washed with water (2 × 30 ml) and brine (30 ml), dried (Na_2SO_4) and concentrated under reduced pressure. Preparative TLC (silica gel, 0.5 mm thickness, 25% ethyl acetate in hexane) provided **32** (100 mg, 48%) and a small amount of **30** (16 mg, 8%).

For **30**: colourless crystals, mp 75–76.5 °C; ν_{max}(CH_2Cl_2 solution)/cm^{-1} 1772 and 1590; δ_H 5.80 (1 H, d, *J* 1.4, 4-H), 5.19 (1 H, apparent td, *J* 5.5 and 1.7, 6a-H), 4.36 (1 H, s, CH_2=), 4.33 (1 H, s, CH_2=), 3.25 (1 H, m, 3a-H), 2.88–2.73 (2 H, m, 6-H), 2.58 (1 H, qd, *J* 7.6 and 1.9, 3-H), 1.37 (3 H, d, *J* 7.6, 3-methyl), 0.96 (9 H, s, $SiC(CH_3)_3$) and 0.17 (6 H, s, $Si(CH_3)_2$); NOE data 5.19 (3.25, 7%; 2.88–2.73, 3%), 3.25 (5.80, 7%; 5.19, 8%; 2.58, 2%) and 1.37 (5.19, 1.3%; 3.25, 10%; 2.58, 10%); δ_C 179.9 (C-2), 152.4 (0), 140.0 (0), 127.1 (C-4), 94.8 (CH_2=), 81.7 (C-6a), 53.8 (C-3a), 40.2 (C-3), 38.9 (C-6), 25.7 ($SiC(CH_3)_3$), 18.2 ($SiC(CH_3)_3$), 17.4 (3-methyl), −4.7 ($Si(CH_3)_2$); *m*/*z* 294.1646 (M^+, 1%, $C_{16}H_{26}O_3Si$ requires 294.1649), 279 (1), 238 (8), 237 (7), 209 (18), 181 (14), 130 (18), 117 (18), 75 (100) and 73 (18).

For **32**: colourless oil, ν_{max}(film)/cm^{-1} 1772 and 1590; δ_H 5.86 (1 H, broad s, 4-H), 5.06 (1 H, m, 6a-H), 4.37 (1 H, s, CH_2=), 4.34 (1 H, s, CH_2=), 3.64 (1 H, apparent broad t, *J* 6.8, 3a-H), 2.89–2.75 (3 H, m, 3-H and 6-H), 1.27 (3 H, d, *J* 7.4, 3-methyl), 0.96 (9 H, s, $SiC(CH_3)_3$), 0.18 (3 H, s, $SiCH_3$) and 0.16 (3 H, s, $SiCH_3$); NOE data 5.06 (3.64, 4%), 3.64 (5.06, 4%) and 1.27 (5.86, 6%); δ_C 178.7 (C-2), 152.5 (0), 141.1 (0), 123.7 (C-4), 94.8 (CH_2=), 81.1 (C-6a), 50.6 (C-3a), 39.2 (C-6), 37.7 (C-3), 25.7 ($SiC(CH_3)_3$), 18.2 ($SiC(CH_3)_3$), 12.0 (3-methyl), −4.6 ($SiCH_3$) and −4.8 ($SiCH_3$); *m*/*z* 294.1651 (M^+, 0.4%, $C_{16}H_{26}O_3Si$ requires 294.1649), 238 (5), 237 (5), 209 (10), 181 (12), 130 (17), 117 (15), 75 (100) and 73 (15).

(4aα,7aβ,10β,10aβ,10bα,10cα)-6-[(1,1-Dimethylethyl)dimethylsilyloxy]-4a,5,7,7a,10,10a,10b,10c-octahydro-2,10,10c-trimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4,9-trione 31

A solution of diene **30** (295 mg, 1.00 mmol) and **12** (206 mg, 1.50 mmol) in dry toluene (10 ml) was heated under reflux for 3 days. The solvent was evaporated under reduced pressure. Signals attributable to only one adduct were detected in the ^1H NMR spectrum of the residue. Preparative TLC (silica gel, 0.5 mm thickness, 30% ethyl acetate in hexane) provided **31** (347 mg, 81%): colourless crystals, mp 134–135 °C; ν_{max}(CCl_4 solution)/cm^{-1} 1774 and 1682; δ_H 6.44 (1 H, q, *J* 1.4, 3-H), 5.14 (1 H, m, 7a-H), 3.14–3.00 (2 H, m, 7β-H and 10a-H), 2.94 (1 H, m, 4a-H), 2.45–2.34 (3 H, m, 5β-H, 7α-H and 10-H), 2.32 (1 H, m, 10b-H), 2.07 (1 H, m, 5α-H), 1.97 (3 H, d, *J* 1.4, 2-methyl), 1.41 (3 H, s, 10c-methyl), 1.31 (3H, d, *J* 7.3, 10-methyl), 0.89 (9H, s, $SiC(CH_3)_3$), 0.06 (3 H, s, $SiCH_3$) and 0.05 (3 H, s, $SiCH_3$); NOE data 5.14 (3.14–3.00, 9%), 2.94 (2.45–2.34, 8%; 2.32, 15%; 1.41, 1%), 2.32 (3.14–3.00, 5%; 2.94, 9%; 2.07, 5%), 1.41 (6.44, 2%; 3.14–3.00, 5%; 2.94, 9%; 2.45–2.34, 2%; 2.32, 16%) and 1.31 (3.14–3.00, 4%; 2.45–2.34, 5%); δ_C 201.8 (0), 199.6 (0), 179.5 (C-9), 148.1 (C-2), 139.6 (C-6), 133.8 (C-3), 116.8 (C-6a), 82.0 (C-7a), 56.5 (C-4a), 52.8 (C-10b), 51.0 (C-10c), 49.1 (C-10a), 43.1 (C-10), 34.6 (C-7), 31.6 (C-5), 25.5 ($SiC(CH_3)_3$), 24.8 (10c-methyl), 18.0 ($SiC(CH_3)_3$), 16.5 (2-methyl), 15.2 (10-methyl), −3.9 ($SiCH_3$) and −4.1 ($SiCH_3$); *m*/*z* 430.2157 (M^+, 10%, $C_{24}H_{34}O_5Si$ requires 430.2176), 415 (8), 373 (45), 238 (21), 237 (22), 209 (32), 181 (18), 131 (20), 130 (32), 117 (28), 75 (100) and 73 (81).

(4aα,7aβ,10α,10aβ,10bα,10cα)-6-[(1,1-Dimethylethyl)dimethylsilyloxy]-4a,5,7,7a,10,10a,10b,10c-octahydro-2,10,10c-trimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4,9-trione 33

A solution of diene **32** (123 mg, 0.418 mmol) and **12** (85 mg, 0.63 mmol) in dry toluene (5.0 ml) was heated under reflux for 3 days. The solvent was evaporated under reduced pressure. Signals attributable to only one adduct were detected in the ^1H NMR spectrum of the residue. Preparative TLC (silica gel, 0.5 mm thickness, 30% ethyl acetate in hexane) provided **33** (147 mg, 82%): colourless crystals, mp 131–133 °C; ν_{max}(CCl_4 solution)/cm^{-1} 1770 and 1682; δ_H 6.45 (1 H, q, *J* 1.4, 3-H), 5.08 (1 H, m, 7a-H), 3.70 (1 H, m, 10a-H), 2.98–2.83 (3 H, m, 4a-H, 7β-H and 10-H), 2.57–2.47 (2 H, m, 5-H and 7α-H), 2.41 (1 H, m, 10b-H), 2.03 (1 H, m, 5-H), 1.95 (3 H, d, *J* 1.4, 2-methyl), 1.37 (3 H, s, 10c-methyl), 1.25 (3H, d, *J* 7.6, 10-methyl), 0.88 (9 H, s, $SiC(CH_3)_3$), 0.05 (3 H, s, $SiCH_3$) and 0.04 (3 H, s, $SiCH_3$); NOE data 5.08 (3.70, 5%), 2.41 (2.98–2.83, 8%), 1.37 (3.70, 6%; 2.98–2.83, 8%) and 1.25 (2.98–2.83, 6%; 2.41, 7%); δ_C 202.2 (0), 199.7 (0), 179.4 (C-9), 147.9 (C-2), 140.0 (C-6), 133.9 (C-3), 119.4 (C-6a), 83.9 (C-7a), 57.1 (C-4a), 51.9 (C-10c), 46.7 (C-10b), 45.2 (C-10a), 38.6 (C-10), 35.5 (C-7), 31.7 (C-5), 25.5 ($SiC(CH_3)_3$), 25.5 (10c-methyl), 18.0 ($SiC(CH_3)_3$), 16.5 (2-methyl), 13.5 (10-methyl) and −4.0 ($Si(CH_3)_2$); *m*/*z* 430.2177 (M^+, 10%, $C_{24}H_{34}O_5Si$ requires 430.2176), 374 (17), 373 (48), 238 (25), 237 (22), 209 (29), 181 (17), 131 (26), 130 (28), 117 (34), 91 (21), 75 (96) and 73 (100).

(3α,3aα,6aα)-5-[(1-Acetoxy)ethenyl]-3,3a,6,6a-tetrahydro-3-methyl-2*H*-cyclopenta[*b*]furan-2-one 34

A solution of **23** (180 mg, 1.00 mmol) and (±)-camphorsulfonic acid (20 mg, 0.09 mmol) in isopropenyl acetate (5.0 ml, 45 mmol) was heated under reflux for 4 days. The excess isopropenyl acetate was evaporated under reduced pressure. Preparative TLC (silica gel, 0.5 mm thickness, 60% ethyl acetate in hexane) provided **34** (130 mg, 58%) as a pale yellow oil: ν_{max}(film)/cm^{-1} 1765, 1648 and 1602; δ_H 5.64 (1 H, d, *J* 1.1, 4-H), 5.20 (1 H, td, *J* 5.9 and 1.2, 6a-H), 5.00 (1 H, d, *J* 2.0, CH_2=), 4.98 (1 H, d, *J* 2.0, CH_2=), 3.27 (1 H, m, 3a-H), 2.93 (1 H, ddt, *J* 17.3, 5.9 and 1.7, 6-H), 2.83 (1 H, dd, *J* 17.3 and 1.2, 6-H), 2.57 (1 H, qd, *J* 7.6 and 2.1, 3-H), 2.22 (3 H, s, $COCH_3$) and 1.37 (3 H, d, *J* 7.6, 3-methyl); δ_C 179.4 (C-2), 168.7 ($COCH_3$), 149.0 (0), 136.3 (0), 127.7 (C-4), 105.5 (CH_2=), 81.1 (C-6a), 54.0 (C-3a), 39.9 (C-3), 38.8 (C-6), 20.8 ($COCH_3$) and 17.3 (3-methyl).

(4aα,7aβ,10β,10aβ,10bα,10cα)-6-Acetoxy-4a,5,7,7a,10,10a,10b,10c-octahydro-2,10,10c-trimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4,9-trione 35 and (4aα,7aβ,10β,10aβ,10bα,10cα)-6-acetoxy-4a,5,7,7a,10,10a,10b,10c-octahydro-3,4a,10-trimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4,9-trione 36

A solution of **34** (107 mg, 0.481 mmol) and **12** (73 mg, 0.53 mmol) in dry toluene (5.0 ml) was heated under reflux. After 4 days another 110 mg (0.808 mmol) of 2,6-dimethyl-1,4-benzoquinone was added and the solution was heated under reflux for 8 days. The solvent was evaporated under reduced pressure. Preparative TLC (silica gel, 0.5 mm thickness, 60% ethyl acetate in hexane) gave a pale yellow foam (83 mg, 50%) consisting of an inseparable 4 : 1 mixture of **35** and **36**, respectively. The following NMR data were obtained from the adduct mixture.

For **35**: δ_H 6.45 (1 H, apparent t, *J* 1.4, 3-H), 5.19 (1 H, m, 7a-H), 3.18 (1 H, dd, *J* 13.2 and 5.8, 10a-H), 3.02 (1 H, m, 4a-H), 2.90 (1 H, m, 7β-H), 2.62 (1 H, m), 2.51–2.39 (3 H, m), 2.19 (1 H, m), 2.10 (3 H, s, $COCH_3$), 1.99 (3 H, d, *J* 1.4, 2-methyl), 1.44 (3 H, s, 10c-methyl) and 1.32 (3 H, d, *J* 7.4, 10-methyl); NOE data 6.45 (1.99, 1%), 5.19 (3.18, 5%; 2.90, 3%), 3.18 (5.19, 6%), 1.44 (3.02, 8%) and 1.32 (3.18, 7%); δ_C 201.4, 198.8, 179.1, 168.4, 148.1, 137.4, 133.8, 127.1, 81.8, 55.9, 52.8, 51.1, 48.9, 43.2, 34.4, 28.7, 24.4, 20.6, 16.5 and 15.3.

Discernable signals for **36**: δ_H 6.63 (1 H, q, *J* 1.4, 2-H), 4.94 (1 H, m, 7a-H), 2.17 (3 H, s, $COCH_3$), 2.02 (3 H, d, *J* 1.4, 3-methyl), 1.40 (3 H, d, *J* 7.7, 10-methyl) and 1.25 (3 H, s, 10c-methyl); δ_C 137.3, 81.2, 57.1, 53.8, 42.2, 42.0, 35.1, 33.6, 21.7, 20.7, 17.7 and 16.4.

(2α,3α,3aα,6aα)- and (2α,3β,3aβ,6aβ)-5-[1-(1,1-Dimethylethyl)-dimethylsilyloxyethenyl]-3,3a,6,6a-tetrahydro-2-hydroxy-2,3-dimethyl-2*H*-cyclopenta[*b*]furan 37

To a solution of **30** (458 mg, 1.56 mmol) in anhydrous diethyl ether (20 ml) at −30 °C was added methyllithium (1.28 ml of a 1.4 M solution in diethyl ether, 1.79 mmol) over 6 min. The mixture was allowed to warm to 0 °C over 2.5 h. Water (50 ml) was added, and the aqueous layer was extracted with diethyl ether (3 × 25 ml). The combined organic solutions were washed with brine (2 × 30 ml), dried and concentrated under reduced pressure. Chromatography afforded a white solid, **37** (403 mg, 83%), as a 2.2 : 1 mixture of epimers: $\nu_{max}(CCl_4)/cm^{-1}$ 3404 (broad) and 1588; for the *major epimer*: δ_H 5.94 (1 H, d, *J* 2.0, 4-H), 4.87 (1 H, m, 6a-H), 4.29 (1 H, s, CH_2=), 4.28 (1 H, s, CH_2=), 3.06 (1 H, m, 3a-H), 2.76–2.67 (2 H, m), 2.51 (1 H, m), 1.44 (3 H, s, 2-methyl), 1.13 (3 H, d, *J* 7.0, 3-methyl), 0.97 (9 H, s, $SiC(CH_3)_3$), 0.18 (3 H, s, $SiCH_3$) and 0.17 (3 H, s, $SiCH_3$); clearly discernable signals for the *minor epimer*: δ_H 6.04 (1 H, d, *J* 1.3, 4-H), 1.36 (3 H, s, 2-methyl) and 1.04 (3 H, d, *J* 7.2, 3-methyl).

(4aα,7aβ,10β,10aβ,10bα,10cα)-6-[(1,1-Dimethylethyl)dimethylsilyloxy]-5,7,7a,9,10,10a,10b,10c-octahydro-9-hydroxy-2,9,10,10c-tetramethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4(4a*H*)-dione 38and(4aα,7aβ,10aβ,10bα,10cα)-6-[(1,1-dimethylethyl)dimethylsilyloxy]-5,7,7a,10a,10b,10c-hexahydro-2,9,10,10c-tetramethyl-1*H*-benz[6,7]-indeno[2,1-*b*]furan-1,4(4a*H*)-dione 39

A solution of **37** (2.2 : 1 epimeric mixture; 111 mg, 0.357 mmol) and **12** (97.2 mg, 0.714 mmol) in toluene (5.0 ml) was heated under reflux for 48 h. The solvent was evaporated under reduced pressure. Preparative TLC (silica gel, 0.5 mm thickness, 30% ethyl acetate in hexane) gave **38** (50 mg, 31%), as an 8 : 1 mixture of epimers at C-9, and **39** (57 mg, 37%).

NMR data for **38**: *major epimer*: δ_H 6.38 (1 H, narrow m, 3-H), 4.89 (1 H, apparent q, *J* 7.7, 7a-H), 3.05–2.83 (3 H, m), 2.33 (1 H, m), 2.18–2.01 (2 H, m), 1.94 (3 H, broad s, 2-methyl), 1.67 (1 H, m), 1.47 (3 H, s), 1.39 (3 H, s), 1.22 (1 H, m), 1.03 (3 H, d, *J* 6.8, 10-methyl), 0.87 (9 H, s), 0.04 (3 H, s) and 0.02 (3 H, s); δ_C 201.5, 200.4, 148.4, 138.0, 133.3, 119.7, 108.0, 81.3, 56.9, 51.4, 49.8, 36.3, 31.7, 26.0, 25.6, 25.2, 18.0, 16.5, 12.4, −3.9 and −4.2; clearly discernable signals for the *minor epimer*: δ_H 6.49 (1 H, s, 3-H), 5.07 (1 H, m, 7a-H), 0.97 (3 H, d, *J* 7.5, 10-H), 0.93 (9 H, s), 0.19 (3 H, s) and 0.14 (3 H, s).

For **39**: pale yellow solid, mp 128–129.5 °C; $\nu_{max}(CCl_4)/cm^{-1}$ 1681; δ_H 6.38 (1 H, s, 3-H), 5.06 (1 H, apparent q, *J* 7.5, 7a-H), 3.68 (1 H, d, *J* 8.3, 10a-H), 3.12 (1 H, dd, *J* 15.3 and 7.6, 7β-H), 2.94 (1 H, apparent t, *J* 8.9, 4a-H), 2.41–2.32 (2 H, m, 5-H and 10b-H), 2.19–2.00 (2 H, m, 7α-H and 5-H), 1.95 (3 H, d, *J* 1.3, 2-methyl), 1.72 (3 H, s, 9-methyl), 1.56 (3 H, s, 10-methyl), 1.43 (3 H, s, 10c-methyl), 0.88 (9H, s, $SiC(CH_3)_3$), 0.05 (3 H, s, $SiCH_3$) and 0.03 (3 H, s, $SiCH_3$); NOE data 5.06 (3.68, 7%; 3.12, 3%) and 1.43 (3.68, 8%; 2.94, 6%; 2.41–2.32, 4%); δ_C 201.9 (0), 200.5 (0), 148.4 (0), 145.7 (0), 137.8 (0), 133.3 (1), 118.1 (0), 104.6 (0), 82.5 (1), 57.2 (1), 53.5 (1), 51.5 (0), 50.5 (1), 36.9 (2), 31.9 (2), 25.6 (3), 24.9 (3), 18.0 (0), 16.6 (3), 11.8 (3), 10.6 (3), −3.9 (3) and −4.2 (3); *m*/*z* 428.2374 (M^+, 3%, $C_{25}H_{36}O_4Si$ requires 428.2383), 332 (5), 291 (10), 275 (6), 247 (5), 179 (7), 109 (14), 75 (32) and 73 (100).

(6aα,7aβ,10aβ,10bα,10cα)-6a,7,7a,9,10,10a,10b,10c-Octahydro-9-hydroxy-2,9,10,10c-tetramethyl-1*H*-benz[6,7]indeno[2,1-*b*]-furan-1,4,6-trione 42

A solution of **37** (2.2 : 1 epimeric mixture; 845 mg, 2.72 mmol) and **12** (680 mg, 5.00 mmol) in toluene (40 ml) was heated under reflux for 70 h. The solvent was evaporated under reduced pressure, and the residue (**38** and **39**) was redissolved in THF (40 ml). To this was added 5% aqueous HCl (20 ml), and the mixture was stirred at RT for 24 h. Ethyl acetate (160 ml) was added and the organic solution was washed with water (3 × 50 ml) and brine (50 ml). The solution was dried, concentrated under reduced pressure and subjected to chromatography, which provided **42** (472 mg, 52% from **37**) as a mixture composed mainly of two isomers (approximately 2 : 1). Selected NMR data for **42**: *major isomer*: δ_H 6.99 (1 H, broad s), 6.58 (1 H, s), 2.15 (3 H, broad s), 1.57 (3 H, s), 1.44 (3 H, s) and 0.78 (3 H, d, *J* 6.7); δ_C 200.3, 197.6, 185.5, 151.1, 149.7, 139.3, 138.6, 127.7, 109.5, 83.0, 81.8, 52.6, 52.5, 51.2, 48.8, 35.9, 30.6, 25.7, 17.1 and 13.8; *minor isomer*: δ_H 6.98 (1 H, broad s), 6.55 (1 H, s), 2.15 (3 H, broad s), 1.60 (3 H, s), 1.36 (3 H, s) and 0.72 (3 H, d, *J* 7.2); δ_C 201.4, 197.3 and 186.0.

(6aα,7aβ,10β,10aβ,10bα,10cα)-6a,7,7a,10a,10b,10c-Hexahydro-2,10,10c-trimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,4,6,9(6a*H*)-tetraone 43

To a solution of **41** (335 mg, 0.778 mmol) in THF (16 ml) was added 8 ml of 10% aqueous HCl. After stirring at RT for 24 h, ethyl acetate (80 ml) was added. The organic layer was washed with water (3 × 25 ml) and brine (25 ml), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue afforded **43** (150 mg, 61%) as yellow crystals: mp 180–182 °C; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1767, 1667 and 1624; δ_H ($CDCl_3$) 7.00 (1 H, q, *J* 1.4), 6.61 (1 H, s), 4.72 (1 H, apparent q, *J* 9.2), 3.19–2.99 (3 H, m), 2.82 (1 H, m), 2.16 (3 H, d, *J* 1.4), 2.05 (1 H, m), 1.86 (1 H, m), 1.64 (3 H, s) and 1.12 (3 H, d, *J* 7.5); δ_H (CD_3COCD_3) 7.10 (1 H, q, *J* 1.4, 3-H), 6.40 (1 H, s, 5-H), 4.72 (1 H, apparent q, *J* 8.2, 7a-H), 3.34 (1 H, apparent t, *J* 6.7, 6a-H), 3.23 (1 H, dd, *J* 8.8 and 6.1, 10b-H), 2.84 (1 H, m, 7β-H), 2.75 (1 H, dq, *J* 7.5 and 4.8, 10-H), 2.33 (1 H, apparent td, *J* 9.1 and 4.7, 10a-H), 2.15 (3 H, d, *J* 1.4, 2-methyl), 1.91 (1 H, m, 7α-H), 1.70 (3 H, s, 10c-methyl) and 1.07 (3 H, d, *J* 7.5, 10-methyl); NOE data (CD_3COCD_3): 4.72 (2.84, 1.6%; 2.33, 7%), 3.23 (2.75, 12%; 1.91, 2%; 1.70, 1%), 1.91 (4.72, 2%; 3.34, 4%; 3.23, 2%; 2.84, 6%), 1.70 (7.10, 1.2%; 6.40, 2%; 3.34, 10%; 3.23, 9%) and 1.07 (2.33, 6%); δ_C ($CDCl_3$) 198.4, 197.3, 185.1, 179.7, 150.7, 149.7, 139.0, 127.4, 80.9, 52.8, 50.6, 48.6, 47.9, 41.6, 36.5, 30.4, 18.0 and 17.1; δ_C (CD_3COCD_3) 199.6 (0), 198.9 (0), 186.3 (0), 180.3 (C-9), 152.1 (0), 150.5 (0), 139.9 (C-3), 127.6 (C-5), 81.8 (C-7a), 53.6 (C-10b), 51.5 (C-10c), 48.8 (C-6a), 48.8 (C-10a), 42.5 (C-10), 36.9 (C-7), 30.5 (10c-methyl), 17.9 (10-methyl) and 17.1 (2-methyl); *m*/*z* 314.1162 (M^+, 45%, $C_{18}H_{18}O_5$ requires 314.1154), 296 (16), 286 (22), 268 (22), 253 (15), 241 (28), 217 (21), 213 (24), 188 (22), 176 (100), 148 (42), 120 (23), 96 (18), 94 (45), 91 (53), 79 (42) and 77 (34).

(5aα,9aα,9bα)-4-[(1,1-Dimethylethyl)dimethylsilyloxy]-2,3,5,5a,9a,9b-hexahydro-8,9a-dimethyl-1*H*-benz[*e*]indene-6,9-dione 44

A solution of 1-{[(1,1-dimethylethyl)dimethylsilyloxy]ethenyl}-cyclopentene§ (3.64 g, 16.2 mmol) and **12** (4.46 g, 32.4 mmol) in toluene (200 ml) was heated under reflux for 3 days. The solvent was evaporated under reduced pressure. Chromatography of the residue gave **44** (4.86 g, 83%) as a viscous oil: ν_{max}(film)/cm^{-1} 1683 and 1624; δ_H 6.41 (1 H, s, 7-H), 2.87 (1 H, t, *J* 8.0, 5a-H), 2.42–2.10 (5 H, m), 1.95 (3 H, d, *J* 0.8, 8-methyl), 1.39 (3 H, s, 9a-methyl), 0.89 (9 H, s, $SiC(CH_3)_3$), 0.05 (3 H, s, $SiCH_3$) and 0.04 (3 H, s, $SiCH_3$); NOE data: 1.39 (2.87, 4%); δ_C 202.4 (0), 200.5 (0), 148.7 (0), 137.3 (0), 133.5 (C-7), 120.8 (0), 57.1 (C-5a), 50.4 (C-9a), 49.4 (C-9b), 31.8 (2), 28.0 (2), 27.8 (2), 25.6 ($SiC(CH_3)_3$), 24.8 (9a-methyl), 24.5 (2), 17.9 ($SiC(CH_3)_3$), 16.5 (8-methyl) and −4.1 ($Si(CH_3)_2$); *m*/*z* 360.2134 (M^+, 2%, $C_{21}H_{32}O_3Si$ requires 360.2119), 345 (1), 303 (3), 244 (2), 211 (3), 168 (8), 167 (7) and 75 (100).

§ The diene was produced by treatment of 1-acetylcyclopentene with TBDMS-OTF and Et_3N.

[(3aα,4β,5aα,9aα,9bα)-4-[(1,1-Dimethylethyl)dimethylsilyloxy]-2,3,3a,4,5,5a,9a,9b-octahydro-3a,4-methano-8,9a-dimethyl-1*H*-benz[*e*]indene-6,9-dione 45

To a solution of **44** (117 mg, 0.325 mmol) in dry toluene (5 ml) was added diethylzinc (1.95 ml of a 1.0 M solution in hexane, 1.95 mmol), and diiodomethane (0.32 ml, 3.9 mmol) at RT. The mixture was stirred at RT for 2 h. The mixture was poured into an aqueous saturated NH_4Cl solution (20 ml). This was extracted with diethyl ether (4 × 30 ml). The combined extracts were washed with water (20 ml), brine (20 ml), dried and concentrated under reduced pressure. Chromatography of the residue provided **45** (68 mg, 56%) as an oil: ν_{max}(film)/cm^{-1} 1726, 1697 and 1622; δ_H 6.30 (1 H, m, 7-H), 2.38–2.13 (4 H, m), 1.97 (3 H, d, *J* 1.6, 8-methyl), 1.94 (1 H, m), 1.83 (1 H, dd, *J* 12.6 and 1.7), 1.77 (1 H, dd, *J* 3.8 and 1.2), 1.64 (1 H, m), 1.41 (2 H, m), 1.24 (3 H, s, 9a-methyl), 0.79 (9 H, s, $SiC(CH_3)_3$), 0.71 (1 H, d, *J* 5.3, cyclopropyl), 0.36 (1 H, d, *J* 5.3, cyclopropyl), 0.010 (3 H, s, $SiCH_3$) and 0.009 (3 H, s, $SiCH_3$); NOE data: 1.24 (0.36, 5%); δ_C 202.7 (0), 201.1 (0), 150.6 (C-8), 132.4 (C-7), 58.2 (C-4), 57.4 (1), 53.0 (1), 50.2 (0), 34.8 (2), 33.3 (2), 31.0 (0), 28.3 (2), 27.7 (C-1), 26.0 (2), 25.6 ($SiC(CH_3)_3$), 24.7 (9a-methyl), 17.7 ($SiC(CH_3)_3$), 16.6 (8-methyl), −3.2 ($SiCH_3$) and −4.0 ($SiCH_3$); *m*/*z* 374.2273 (M^+, 2%, $C_{22}H_{34}O_3Si$ requires 374.2275), 317 (7), 181 (33), 149 (18), 75 (71) and 73 (100).

(3aα,4β,5aα,9β,9aα,9bα)-4-[(1,1-Dimethylethyl)dimethylsilyloxy]-1,2,3,3a,4,5,5a,9,9a,9b-decahydro-9-hydroxy-3a,4-methano-8,9a-dimethyl-6*H*-benz[*e*]inden-6-one 46

$LiAl(OBu^t)_3H$ (0.22 ml of a 1.0 M solution in THF, 0.22 mmol) was added to a solution of **45** (68 mg, 0.18 mmol) in dry THF (5 ml) at 0 °C, and this solution was stirred at 0 °C for another 2 h. Water (2 ml) was added slowly followed by ethyl acetate (100 ml) and brine (20 ml). The organic layer was dried and concentrated under reduced pressure. Chromatography of the residue gave **46** (45.5 mg, 67%) as a white solid: mp 144–146 °C; ν_{max}(Nujol)/cm^{-1} 1712 and 1658; δ_H 5.77 (1 H, s, 7-H), 3.82 (1 H, d, *J* 8.8, 9-H), 2.33 (1 H, dd, *J* 13.3 and 5.6), 2.09 (3 H, d, *J* 1.2, 8-methyl), 2.06–1.58 (m), 1.41 (1 H, dd, *J* 12.4 and 5.9), 1.11 (2 H, m), 0.87 (3 H, s, 9a-methyl), 0.82 (9 H, s, $SiC(CH_3)_3$), 0.82 (1 H, d, *J* 5.5, cyclopropyl), 0.46 (1 H, d, *J* 5.5, cyclopropyl), 0.06 (3 H, s, $SiCH_3$) and 0.04 (3 H, s, $SiCH_3$); δ_C 202.4 (C-6), 157.4 (C-8), 123.3 (C-7), 73.8 (C-9), 58.3 (C-4), 52.6 (1), 52.2 (1), 37.8 (C-9a), 35.4 (2), 34.0 (2), 30.8 (C-9b), 27.9 (cyclopropyl), 27.5 (2), 26.3 (9a-methyl), 26.0 (2), 25.6 ($SiC(CH_3)_3$), 22.1 (8-methyl), 17.7 ($SiC(CH_3)_3$), −3.2 ($SiCH_3$) and −4.0 ($SiCH_3$); *m*/*z* 376.2431 (M^+, 1%, $C_{22}H_{36}O_3Si$ requires 376.2434), 319 (4), 301 (4), 277 (3), 181 (15), 75 (67), 73 (100) and 41 (22).

(5aα,6β,9aα,9bα)-4-[(1,1-Dimethylethyl)dimethylsilyloxy]-1,2,3,5,5a,6,9a,9b-octahydro-6-hydroxy-8,9a-dimethyl-9*H*-benz[*e*]inden-9-one 47a and (5aα,6α,9aα,9bα)-4-[(1,1-dimethylethyl)dimethylsilyloxy]-1,2,3,5,5a,6,9a,9b-octahydro-6-hydroxy-8,9a-dimethyl-9*H*-benz[*e*]inden-9-one 47b

To a solution of **44** (360 mg, 1.00 mmol) and $CeCl_3 \cdot 7H_2O$ (373 mg, 1.00 mmol) in methanol (10 ml) at 0 °C was added $NaBH_4$ (26.6 mg, 0.70 mmol) over 5 min. The mixture was stirred for 2 min before 40 ml of a dilute aqueous NH_4Cl solution was added. This was extracted with ethyl acetate (4 × 25 ml). The combined extracts were washed with water (2 × 25 ml) and brine (25 ml), dried and concentrated under reduced pressure. Chromatography of the residue gave **47a** and **47b** (347 mg, 96%) as a 1 : 1 mixture. These epimers were ultimately separated by repeated chromatography.

For **47a**: colourless viscous oil; ν_{max}(Nujol)/cm^{-1} 3421 (broad) and 1713; δ_H 6.34 (1 H, d, *J* 1.2, 7-H), 4.93 (1 H, m, 6-H), 2.53–2.43 (m), 2.33–2.19 (m), 1.91–1.78 (m), 1.74 (3 H, s, 8-methyl), 1.43 (1 H, m), 1.28 (3 H, s, 9a-methyl), 0.90 (9 H, s, $SiC(CH_3)_3$), 0.04 (3 H, s, $SiCH_3$) and 0.02 (3 H, s, $SiCH_3$); NOE data: 4.93 (6.34, 4%; 1.28, 7%); δ_C 202.7 (C-9), 144.1 (C-7), 138.1 (0), 134.2 (0), 121.4 (0), 67.9 (C-6), 50.9 (1), 50.2 (1), 47.9 (C-9a), 28.9 (2), 28.0 (2), 25.7 ($SiC(CH_3)_3$), 25.0 (2), 22.0 (9b-methyl), 18.0 ($SiC(CH_3)_3$), 15.9 (2-methyl), −4.0 ($SiCH_3$) and −4.1 ($SiCH_3$); *m*/*z* 317 (M^+ − 45, 2%), 262 (4), 244 (8), 229 (6), 175 (11), 149 (100), 147 (26), 121 (30), 98 (68), 91 (23), 75 (27), 55 (28) and 43 (34).

For **47b**: pale yellow viscous oil; ν_{max}(Nujol)/cm^{-1} 3393 (broad) and 1712; δ_H 6.51 (1 H, d, *J* 2.1, 7-H), 4.32 (1 H, m, 6-H), 2.46–2.23 (m), 2.16–1.98 (m), 1.79 (3 H, d, *J* 0.9, 8-methyl), 1.66 (1 H, dd, *J* 9.2 and 3.5), 1.55–1.41 (m), 1.34 (3 H, s, 9a-methyl), 1.24 (1 H, m), 0.93 (9 H, s, $SiC(CH_3)_3$), 0.12 (3 H, s, $SiCH_3$) and 0.11 (3 H, s, $SiCH_3$); δ_C 202.7 (C-9), 144.7 (C-7), 137.7 (0), 135.2 (0), 121.1 (0), 66.7 (C-6), 49.5 (1), 49.0 (1), 45.3 (C-9a), 30.2 (2), 29.9 (2), 25.7 ($SiC(CH_3)_3$), 25.2 (9a-methyl), 25.1 (2), 22.5 (2), 18.1 ($SiC(CH_3)_3$), 16.1 (8-methyl), −4.0 ($SiCH_3$) and −4.2 ($SiCH_3$); *m*/*z* 362 (M^+, 1%), 317 (2), 264 (16), 149 (10), 138 (14), 98 (13), 75 (100) and 73 (23).

(3aα,5aα,6β,9aα,9ba)-3a-(1,3-Dithian-2-yl)-1,2,3,3a,4,5,5a,6,9a,9b-decahydro-6-hydroxy-8,9a-dimethyl-9*H*-benz[*e*]indene-4,9-dione 48

To a solution of **47a** (101 mg, 0.279 mmol) in dry dichloromethane (3.0 ml) at −78 °C under argon was added over 5 min a solution of 1,3-dithienium tetrafluoroborate (172 mg, 0.836 mmol) in dry nitromethane (1.0 ml). After the solution was stirred for another 20 min at −78 °C, it was allowed to warm to RT. The mixture was poured into saturated aqueous $NaHCO_3$ solution (10 ml), and this was extracted with ethyl acetate (3 × 20 ml). The combined organic extracts were washed with brine (20 ml) and dried. The solution was concentrated under reduced pressure, and chromatography of the residue provided **48** (34 mg, 40%) as a white solid: mp 171–172 °C; ν_{max}(Nujol)/cm^{-1} 3407 (broad) and 1712; δ_H 6.34 (1 H, d, *J* 1.5, 7-H), 4.86 (1 H, apparent t, *J* 2.2, 6-H), 4.34 (1 H, s, 2-H of dithiane), 2.91–2.77 (m), 2.66 (1 H, dd, *J* 9.0 and 5.7), 2.29 (1 H, dd, *J* 17.8 and 9.2), 2.14–2.05 (m), 1.97–1.79 (m), 1.75 (3 H, s, 8-methyl), 1.68 (m) and 1.40 (3 H, s, 9a-methyl); δ_C 211.6 (C-4), 201.8 (C-9), 140.6 (C-7), 136.1 (C-8), 67.1 (C-6), 63.5 (C-3a), 58.1 (C-2 of dithiane), 53.0 (1), 48.5 (C-9a), 47.6 (1), 36.9 (2), 33.5 (2), 31.8 (2), 31.6 (2), 28.7 (2), 25.7 (2), 24.2 (2), 23.4 (9a-methyl) and 15.9 (8-methyl); *m*/*z* 366.1330 (M^+, 6%, $C_{19}H_{26}O_3S_2$ requires 366.1322), 349 (7), 348 (21), 228 (17) and 119 (100).

(5aα,6β,9aα,9bα)-6-Acetoxy-4-[(1,1-dimethylethyl)dimethylsilyloxy]-1,2,3,5,5a,6,9a,9b-octahydro-8,9a-dimethyl-9*H*-benz[*e*]inden-9-one 49

To a solution of **47a** (544 mg, 1.50 mmol) in dry dichloromethane at RT was added acetyl chloride (0.71 ml, 7.5 mmol), triethylamine (1.05 ml, 7.50 mmol) and 4-(dimethylamino)-pyridine (DMAP) (36.7 mg, 0.30 mmol). This solution was stirred at RT for 24 h. The mixture was diluted with dichloromethane (100 ml) before it was washed with brine (2 × 20 ml), dried and concentrated under reduced pressure. Chromatography of the residue provided **49** (478 mg, 74%) as a yellow oil; ν_{max}(film)/cm^{-1} 1736 and 1674; δ_H 6.44 (1 H, s, 7-H), 5.92 (1 H, apparent t, *J* 2.5, 6-H), 2.98 (1 H, m), 2.90 (1 H, m), 2.73 (1 H, m), 2.57–2.53 (2 H, m), 2.40 (1 H, dd, *J* 17.3 and 12.9), 2.12 (3 H, s, CH_3CO_2), 2.08 (m), 1.94 (1 H, m), 1.84 (3 H, 8-methyl), 1.67 (1 H, m), 1.50 (3 H, 9a-methyl), 0.92 (9 H, s, $SiC(CH_3)_3$) and 0.1 (6 H, s, $Si(CH_3)_2$); δ_C 198.5 (C-9), 170.1 (CH_3CO_2), 139.6 (C-7), 138.0 (0), 137.4 (0), 136.8 (0), 68.2 (C-8), 49.1 (C-9a), 46.5 (1), 36.0 (2), 35.7 (2), 29.3 (2), 25.7 ($SiC(CH_3)_3$), 21.7 (2), 21.4 (9a-methyl), 21.0 (CH_3CO_2), 18.1 ($SiC(CH_3)_3$), 15.9 (8-methyl) and −3.6 ($Si(CH_3)_2$); *m*/*z* 404.2372 (M^+, 2%, $C_{23}H_{36}O_4Si$ requires 404.2381), 303 (6), 285 (5), 191 (9), 149 (100), 147 (21), 121 (21), 98 (79), 75 (32) and 43 (85).

(3aα,5aα,6β,9aα,9ba)-6-Acetoxy-3a-(1,3-dithian-2-yl)-1,2,3,3a,4,5,5a,6,9a,9b-decahydro-8,9a-dimethyl-9*H*-benz[*e*]indene-4,9-dione 50

To a solution of **49** (415 mg, 1.10 mmol) in dry dichloromethane (10 ml) at −78 °C under argon was added over 5 min a solution of 1,3-dithienium tetrafluoroborate (600 mg, 2.91 mmol) in dry nitromethane (2.0 ml). After the solution was stirred for another 20 min at −78 °C, it was allowed to warm to RT. The mixture was poured into saturated aqueous $NaHCO_3$ solution (20 ml), and this was extracted with ethyl acetate (3 × 40 ml). The combined organic extracts were washed with brine (20 ml) and dried. The solution was concentrated under reduced pressure, and chromatography of the residue provided **50** (233 mg, 52%) as a yellow oil: δ_H 6.26 (1 H, s, 7-H), 5.83 (1 H, apparent t, *J* 2.4, 6-H), 4.30 (1 H, s, 2-H of dithiane), 2.99 (1 H, m), 2.92–2.82 (2 H, m), 2.71 (1 H, dd, *J* 14.6 and 8.0), 2.66 (1 H, dd, *J* 5.9 and 3.6), 2.32 (1 H, dd, *J* 18.8 and 10.1), 2.26 (1 H, m), 2.17–2.08 (4 H, m), 2.05 (3H, s, CH_3CO_2), 1.95–1.79 (3 H, m), 1.76 (3 H, s, 8-methyl), 1.66 (1 H, s) and 1.46 (3 H, s, 9a-methyl); NOE data: 4.30 (2.99, 3%; 2.71 and 2.66, 12%), 1.46 (5.83, 12%; 4.30, 2%; 2.99, 3%; 2.71 and 2.66, 17%); δ_C 210.5 (C-4), 201.2 (C-9), 170.2 (CH_3CO_2), 137.4 (C-8), 136.5 (C-7), 69.4 (C-6), 63.3 (C-3a), 57.8 (C-2 of dithiane), 52.6 (1), 48.5 (C-9a), 44.8 (1), 37.2 (2), 33.4 (2), 31.7 (2), 31.5 (2), 28.6 (2), 25.6 (2), 24.1 (2), 23.4 (9a-methyl), 20.9 (CH_3CO_2) and 15.9 (8-methyl).

Hydrolysis of 50 to 48

To a solution of **50** (197 mg, 0.480 mmol) in methanol (10 ml) at RT was added a solution of K_2CO_3 (335 mg, 2.40 mmol) in water (2 ml). The mixture was stirred at RT for 2 h. A 1% aqueous HCl solution (5 ml) was added to the mixture, and this was extracted ethyl acetate (3 × 20 ml). The combined extracts were washed with brine (20 ml) and dried. The solution was concentrated under reduced pressure, and chromatography of the residue afforded **48** (89%).

(5aα,6α,9aα,9bα)-4-[(1,1-Dimethylethyl)dimethylsilyloxy]-1,2,3,5,5a,6,9a,9b-octahydro-6-methoxy-8,9a-dimethyl-9*H*-benz[*e*]inden-9-one 51

To a solution of **47b** (690 mg, 1.90 mmol) in THF (30 ml) at RT was added sodium hydride (235 mg, 9.50 mmol) and iodomethane (1.2 ml, 19 mmol). This was stirred at RT for 12 h. Ice-cold water (30 ml) was added, and this solution was extracted with ethyl acetate (4 × 50 ml). The combined extracts were washed with brine (2 × 40 ml), dried and concentrated under reduced pressure. Chromatography provided **51** (614 mg, 86%) as a pale yellow oil: ν_{max}(film)/cm^{-1} 1712, 1674 and 1625; δ_H 6.58 (1 H, s, 7-H), 3.76 (1 H, m, 6-H), 3.43 (3 H, s, OCH_3), 2.46–2.22 (m), 2.15–2.07 (m), 1.79 (3 H, s, 8-methyl), 1.73 (1 H, m), 1.56–1.41 (3 H, m), 1.34 (3 H, s, 9a-methyl), 0.93 (9 H, s, $SiC(CH_3)_3$) and 0.10 (6 H, s, $Si(CH_3)_2$); δ_C 203.0 (C-9), 139.8 (C-7), 137.8 (0), 135.4 (0), 120.8 (0), 76.1 (C-6), 57.0 (OCH_3), 49.4 (1), 46.0 (1), 45.6 (C-9a), 30.8 (2), 29.9 (2), 25.7 ($SiC(CH_3)_3$), 25.2 (9a-methyl), 23.1 (2), 18.1 ($SiC(CH_3)_3$), 16.2 (8-methyl), −4.0 ($SiCH_3$) and −4.1 ($SiCH_3$); *m*/*z* 376.2444 (M^+, <1%, $C_{22}H_{36}O_3Si$ requires 376.2432), 361 (1), 280 (3), 225 (13), 205 (11), 152 (100), 112 (26), 75 (46) and 73 (35).

(3aα,5aα,6α,9aα,9ba)-3a-(1,3-Dithian-2-yl)-1,2,3,3a,4,5,5a,6,9a,9b-decahydro-6-methoxy-8,9a-dimethyl-9*H*-benz[*e*]indene-4,9-dione 52

A solution of 1,3-dithienium tetrafluoroborate (153 mg, 0.744 mmol) in dry nitromethane (1.0 ml) was added over 5 min to a solution of **51** (140 mg, 0.372 mmol) in dry dichloromethane (3.0 ml) at −78 °C under argon. The solution was stirred at −78 °C for 20 min before it was allowed to warm to RT. The mixture was added to a saturated aqueous $NaHCO_3$ solution (20 ml). This was extracted with ethyl acetate (3 × 40 ml). The combined extracts were washed with brine (20 ml), dried and concentrated under reduced pressure. Chromatography of the residue gave **52** (83.5 mg, 59%) as a white solid: mp 226–228 °C; ν_{max}(Nujol)/cm^{-1} 1745, 1710 and 1661; δ_H 6.69 (1 H, s, 7-H), 4.84 (1 H, s, 2-H of dithiane), 3.65 (1 H, dt, *J* 10.1 and 2.0, 6-H), 3.49 (3 H, s, OCH_3), 3.09 (1 H, dd, *J* 13.8 and 6.0), 2.95 (1 H, dd, *J* 7.8 and 3.1), 2.89 (1 H, dt, *J* 6.6 and 1.5), 2.84 (1 H, m), 2.70 (1 H, dd, *J* 13.6 and 2.5), 2.59 (1 H, dt, *J* 14.1 and 8.7), 2.43 (1 H, m), 2.13 (2 H, dq, *J* 14.0 and 3.3), 1.88 (1 H, ddd, *J* 13.7, 10.3 and 3.1), 1.81 (3 H, t, *J* 1.6, 8-methyl), 1.70 (3 H, s, 9a-methyl), 1.56 (1 H, m), 1.43 (1 H, dd, *J* 12.6 and 6.5), 1.29 (1 H, m) and 0.96 (1 H, m); NOE data: 4.84 (3.09, 7%; 1.70, 9%), 1.70 (4.84, 11%; 3.09, 4%; 2.43, 5%); δ_C 210.0 (C-4), 201.0 (C-9), 142.3 (C-7), 135.7 (C-8), 75.3 (C-6), 63.3 (C-3a), 57.8 (OCH_3), 56.5 (C-2 of dithiane), 53.4 (1), 50.1 (1), 45.6 (C-9a), 36.4 (2), 31.8 (2), 31.1 (2, 2C), 27.9 (2), 26.2 (9a-methyl), 25.8 (2), 22.8 (2) and 16.3 (8-methyl); *m*/*z* 380.1484 (M^+, 1%, $C_{20}H_{28}O_3S_2$ requires 380.1478), 262 (4), 221 (8), 152 (18), 149 (13), 135 (15), 119 (100), 112 (29) and 69 (15).

X-Ray crystal structure determination for 52

A colourless irregular crystal of dimensions 0.35 × 0.10 × 0.40 mm was mounted on a glass fibre: $C_{20}H_{28}O_3S_2$, *M* = 380.56, orthorhombic, *a* = 21.765(7), *b* = 14.725(6), *c* = 11.857(6) Å, *V* = 3800(2) Å^3, *T* = 299 K, space group *Pbca* (no. 61), *Z* = 8, μ(Cu-Kα) 26.67 cm^{-1}, 3219 reflections collected, 2257 observed ($I > 2.00\sigma(I)$); *R* = 0.094, R_w = 0.092, goodness of fit = 6.93.

(1*R,4*S**,5*R**,9*R**,10*S**,11*S**,12*R**, 15*S**)-5-Hydroxy-7,9,12-trimethyl-14-oxapentacyclo[8.6.0.0^{1,5}.0^{4,9}.0^{11,15}]hexadec-6-ene-2,8,13-trione 53**

A solution of 1,3-dithienium tetrafluoroborate (24.0 mg, 0.116 mmol) in nitromethane (1.0 ml) was added to a solution of **33** (50.0 mg, 0.116 mmol) in dry dichloromethane (3.0 ml) at −78 °C. The mixture was stirred at this temperature for 20 min before it was allowed to warm to RT. Ethyl acetate (25 ml) was added, and this solution was washed with a saturated aqueous $NaHCO_3$ solution (2 × 20 ml) and brine (2 × 20 ml). The solution was dried (Na_2SO_4) and concentrated under reduced pressure. Preparative TLC provided **53** (18 mg, 48%) as colourless crystals: mp >220 °C (dec.); ν_{max}(Nujol)/cm^{-1} 3405, 1748 and 1669; δ_H (CD_3COCD_3) 7.00 (1 H, s, 6-H), 5.20 (1 H, s, OH, removed with D_2O), 4.90 (1 H, t, *J* 5.7), 2.80 (1 H, m), 2.66–2.44 (3 H, m), 2.35 (1 H, d, *J* 16.2), 2.08–2.01 (3 H, m), 1.83 (3 H, d, *J* 1.4, 7-methyl), 1.35 (3 H, s, 9-methyl) and 0.98 (3 H, d, *J* 7.2, 12-methyl); δ_C (CD_3COCD_3) 209.0, 200.8, 178.0, 149.4, 138.3, 88.6, 83.5, 76.1, 59.6, 55.9, 54.7, 48.1, 39.3, 37.2, 26.6, 18.1, 15.1 and 12.1; *m*/*z* 316.1306 (M^+, 62%, $C_{18}H_{20}O_5$ requires 316.1310), 288 (10), 205 (18), 178 (17), 165 (36), 151 (100), 137 (14), 123 (12), 91 (13) and 79 (15).

X-Ray crystal structure determination for 53

A colourless irregular crystal of dimensions 0.40 × 0.30 × 0.15 mm was mounted on a glass fibre: $C_{18}H_{20}O_5$, *M* = 316.35, tetragonal, *a* = 9.055(3), *c* = 18.635(6) Å, *V* = 1527.8(7) Å^3, *T* = 299 K, space group $P4_3$ (no. 78), *Z* = 4, μ(Mo-Kα) 1.0 cm^{-1}, 1588 reflections collected, 1409 unique (R_{int} = 0.022); 1045 observed ($I > 1.50\sigma(I)$); *R* = 0.033, R_w = 0.033, goodness of fit = 1.36.

(4α,4aβ,7aα,10aα,10bβ,10cβ)-6-[(1,1-Dimethylethyl)dimethylsilyloxy]-4,4a,5,7,7a,10,10b,10c-octahydro-4-hydroxy-2,10c-dimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,9(10a*H*)-dione 54a and (4α,4aα,7aβ,10aβ,10bα,10cα)-6-[(1,1-dimethylethyl)dimethylsilyloxy]-4,4a,5,7,7a,10,10b,10c-octahydro-4-hydroxy-2,10c-dimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,9(10a*H*)-dione 54b

To a solution of **25** (858 mg, 2.06 mmol) and $CeCl_3 \cdot 7H_2O$

(775 mg, 2.06 mmol) in methanol (20 ml) at 0 °C was added sodium borohydride (55.7 mg, 1.44 mmol) in small portions over 5 min. After stirring for another 2 min, dilute aqueous NH_4Cl solution (40 ml) was added. This was extracted with ethyl acetate (4 × 40 ml). The combined extracts were washed with water (2 × 40 ml) and brine (40 ml), dried and concentrated under reduced pressure. Chromatography of the residue provided a 1 : 1 epimeric mixture of alcohols **54a** and **54b** (712 mg, 83%). Further careful chromatography did separate these isomers.

For **54a**: pale yellow solid, mp 100–102 °C; ν_{max}(Nujol)/cm^{-1} 3422 and 1712; δ_H 6.38 (1 H, s, 3-H), 5.05 (1 H, dt, *J* 6.2 and 2.6, 7a-H), 4.96 (1 H, m, 4-H), 3.89 (1 H, m), 2.90 (1 H, dd, *J* 6.3 and 2.7), 2.82 (1 H, dd, *J* 17.7 and 9.0), 2.64 (1 H, broad s), 2.57–2.45 (m), 2.41 (1 H, d, *J* 2.7), 2.35 (1 H, d, *J* 2.4), 2.31–2.21 (m), 2.05–1.97 (1 H, m), 1.75 (3 H, s, 2-methyl), 1.29 (3 H, s, 10c-methyl), 0.90 (9 H, s, $SiC(CH_3)_3$), 0.06 (3 H, s, $SiCH_3$) and 0.04 (3 H, s, $SiCH_3$); NOE data 3.89 (5.05, 7%; 2.82, 4%) and 1.29 (4.96, 12%; 3.89, 5%); δ_C 202.3 (C-1), 177.4 (C-9), 142.1 (C-3), 140.6 (0), 133.9 (0), 117.3 (0), 86.0 (C-7a), 67.5 (C-4), 54.9 (10), 49.7 (1), 48.3 (C-10c), 41.2 (1), 37.6 (2), 34.4 (2), 28.6 (2), 25.6 ($SiC(CH_3)_3$), 21.4 (10c-methyl), 17.9 ($SiC(CH_3)_3$), 15.8 (2-methyl), −3.8 ($SiCH_3$) and −4.0 ($SiCH_3$); *m*/*z* 418.2191 (M^+, 5%, $C_{23}H_{34}O_5Si$ requires 418.2174), 281 (8), 224 (15), 223 (25), 138 (100), 121 (20), 117 (18), 75 (95) and 73 (97).

For **54b**: white solid, mp 128–130 °C; ν_{max}(Nujol)/cm^{-1} 3416, 1746, 1708 and 1665; δ_H 6.54 (1 H, t, *J* 1.7, 3-H), 4.91 (1 H, dt, *J* 7.1 and 2.6, 7a-H), 4.25 (1 H, m, 4-H), 3.03 (1 H, dd, *J* 15.7 and 7.1, 10a-H), 2.86 (1 H, apparent q, *J* 8.6), 2.58 (1 H, dd, *J* 18.2 and 8.3), 2.38–2.29 (m), 2.26–2.17 (m), 2.14–2.02 (m), 1.80 (3 H, s, 2-methyl), 1.41 (3 H, s, 10c-methyl), 0.93 (9 H, s, $SiC(CH_3)_3$), 0.11 (3 H, s, $SiCH_3$) and 0.10 (3 H, s, $SiCH_3$); NOE data: 4.91 (3.03, 4%; 2.86, 5%), 4.25 (2.86, 5%), 2.86 (4.91, 7%; 4.25, 5%) and 1.41 (2.14–2.02, 10%); δ_C 210.8 (C-1), 176.9 (C-9), 142.9 (C-3), 140.0 (0), 135.3 (0), 117.1 (0), 83.9 (C-7a), 67.0 (C-4), 51.9 (1), 48.8 (1), 45.6 (C-10c), 42.0 (1), 35.2 (2), 33.1 (2), 30.4 (2), 25.6 ($SiC(CH_3)_3$), 25.2 (10c-methyl), 18.0 ($SiC(CH_3)_3$), 16.1 (2-methyl), −4.0 ($SiCH_3$) and −4.1 ($SiCH_3$); *m*/*z* 418.2198 (M^+, 5%, $C_{23}H_{34}O_5Si$ requires 418.2174), 359 (9), 281 (13), 224 (7), 223 (15), 138 (100), 117 (10), 75 (61) and 73 (50).

(4α,4aβ,6aβ,7aα,10aα,10bβ,10cβ)-4-Acetoxy-6a-(1,3-dithian-2-yl)-4,4a,5,6a,7,7a,10,10a,10b,10c-decahydro-2,10c-dimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,6,9-trione 56

The formation of **55** followed the same procedure as for **49**. 1,3-Dithienium tetrafluoroborate (498 mg, 2.42 mmol) in dry nitromethane (2.0 ml) was added over 5 min to a solution of **55** (371 mg, 0.805 mmol) in dry dichloromethane (10 ml) at −78 °C. The solution was stirred at −78 °C for 20 min before it was allowed to warm to RT. The mixture was poured into a saturated aqueous $NaHCO_3$ solution (20 ml). This was extracted with ethyl acetate (3 × 40 ml). The combined organic extracts were washed with brine (20 ml), dried and concentrated under reduced pressure. Compound **56** (157 mg, 42%) was difficult to separate by chromatography from the hydrolysis by-product. For **56**: mp 192–195 °C; ν_{max}(Nujol)/cm^{-1} 1708 and 1669; δ_H 6.29 (1 H, s, 3-H), 5.87 (1 H, m, 4-H), 5.14 (1 H, t, *J* 6.4, 7a-H), 4.16 (1 H, s, 2-H of dithiane), 3.62 (1 H, m), 3.15 (1 H, m), 2.98–2.82 (6 H, m), 2.50 (1 H, m), 2.38 (1 H, ddd, *J* 20.7, 18.7 and 1.4), 2.11 (3 H, s, CH_3CO_2), 2.07 (1 H, m), 1.78 (1 H, m), 1.74 (3 H, d, *J* 2.6, 2-methyl) and 1.46 (3 H, s, 10c-methyl); NOE data: 5.87 (3.15, 8%; 1.46, 10%) and 1.46 (5.87, 12%; 3.62, 8%; 2.77, 8%); δ_C 208.0 (C-6), 201.3 (C-1), 176.6 (C-9), 170.1 (CH_3CO_2), 137.9 (C-3), 136.9 (C-2), 86.0 (C-7a), 69.7 (C-4), 63.0 (C-6a), 59.9 (1), 56.2 (C-2 of dithiane), 49.3 (C-10c), 44.6 (1), 42.2 (1), 38.7 (2), 38.3 (2), 37.8 (2), 32.2 (2), 31.5 (2), 25.3 (2), 22.1 (10c-methyl), 20.9 (CH_3CO_2) and 15.7 (2-methyl); *m*/*z* 464.1307 (M^+, <1%, $C_{23}H_{28}O_6S_2$ requires 464.1326), 241 (2), 119 (100) and 43 (22).

(4α,4aβ,6aβ,7aα,10aα,10bβ,10cβ)-6a-(1,3-Dithian-2-yl)-4,4a,5,6a,7,7a,10,10a,10b,10c-decahydro-4-hydroxy-2,10c-dimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-1,6,9-trione 57

To a solution of **56** (35 mg, 0.075 mmol) in methanol (2.0 ml) was added a solution of K_2CO_3 (105 mg, 0.753 mmol) in water (1.0 ml). The mixture was stirred at RT for 2 h. Ethyl acetate (100 ml) was added and the solution was washed with 1% aqueous HCl (10 ml) and brine (10 ml). The solution was dried and concentrated under reduced pressure. Chromatography of the product provided **57** (22.5 mg, 80%) as a white solid: mp 264–267 °C; ν_{max}(Nujol)/cm^{-1} 1713 and 1674; δ_H (CD_3SOCD_3) 6.41 (1 H, s, 3-H), 4.99 (1 H, m, 7a-H), 4.66 (1 H, broad s, 4-H), 4.43 (1 H, s, 2-H of dithiane), 3.44 (1 H, m), 2.94–2.70 (m), 2.62 (1 H, d, *J* 5.1), 2.53 (1 H, dd, *J* 15.6 and 4.2), 2.48 (1 H, m), 2.38 (1 H, dd, *J* 18.0 and 1.8), 2.25 (1 H, d, *J* 15.0), 2.10 (1 H, dd, *J* 17.1 and 7.8), 2.01 (1 H, m), 1.60 (3 H, s, 2-methyl) and 1.31 (3 H, s, 10c-methyl); NOE data 4.99 (3.44, 7%; 2.48, 2%), 4.43 (2.94–2.70, 6%; 2.62, 4%) and 1.31 (4.66, 7%; 3.44, 6%; 2.62, 6%); δ_C (CD_3SOCD_3) 208.5 (C-6), 202.5 (C-1), 177.0 (C-9), 144.7 (C-3), 133.7 (C-2), 85.0 (C-7a), 65.6 (C-4), 63.2 (C-6a), 60.5 (1), 56.0 (C-2 of dithiane), 48.7 (C-10c), 46.6 (1), 41.6 (1), 37.1 (2), 37.0 (2), 31.0 (2), 30.8 (2), 25.5 (2), 22.3 (10c-methyl) and 15.6 (2-methyl); *m*/*z* 422.1229 (M^+, <1%, $C_{21}H_{26}O_5S_2$ requires 422.1229), 286 (1), 241 (4), 119 (100) and 57 (12).

(1*R**,2*R**,3*R**,4*R**,8*S**,10*S**,11*S**,13*S**,14*R**)-14-Acetoxy-10-(1,3-dithian-2-yl)-11-hydroxy-2,16-dimethyl-7,17-dioxapentacyclo[9.5.1.0^{2,13}.0^{3,10}.0^{4,8}]heptadec-15-en-6-one 58

To a solution of **56** (34.5 mg, 0.074 mmol), in 1 : 1 methanol–dichloromethane (4 ml) at 0 °C was added sodium borohydride (4.3 mg, 0.11 mmol). The mixture was stirred at 0 °C for 10 min, then at RT for 2 h. The mixture was poured into a dilute aqueous NH_4Cl solution (10 ml), which was extracted with ethyl acetate (4 × 20 ml). The combined extracts were washed with brine (20 ml), dried and concentrated under reduced pressure. Chromatography gave **58** (27.5 mg, 80%) as a white solid: mp 242–243.5 °C; ν_{max}(Nujol)/cm^{-1} 1765 and 1714; δ_H 5.42 (1 H, m, 14-H), 5.40 (1 H, s, 15-H), 5.06 (1 H, m, 8-H), 4.14 (1 H, s, 2-H of dithiane), 3.62 (1 H, d, *J* 1.3, 1-H), 3.03–2.85 (3 H, m), 2.83–2.72 (3 H, m), 2.53–2.45 (2 H, m), 2.38 (1 H, m), 2.21–1.94 (4 H, m), 2.09 (3 H, s, CH_3CO_2), 1.86 (3 H, 16-methyl) and 0.93 (3 H, 2-methyl); NOE data: 2.38 (5.42, 8%; 4.14, 7%) and 0.93 (5.42, 12%; 3.62, 5%; 3.03–2.85, 5%; 2.53–2.45, 6%); δ_C 176.6 (0), 170.8 (0), 138.4 (C-16), 121.7 (C-15), 98.2 (C-11), 86.3 (C-8), 74.5 (C-1), 71.6 (C-14), 58.8 (C-10), 58.7 (1), 57.9 (C-2 of dithiane), 41.1 (1), 37.3 (1), 36.2 (2), 35.3 (2), 31.8 (2), 31.3 (2), 25.5 (2), 21.5 (16-methyl), 21.2 (CH_3CO_2) and 18.2 (2-methyl); *m*/*z* 466.1493 (M^+, 2%, $C_{23}H_{30}O_6S_2$ requires 466.1484), 243 (11), 119 (100) and 43 (21).

(2α,4aβ,6aα,7aβ,10β,10aβ,10bα,10cα)-2,4a,5,6a,7,7a,10,10a,10b,10c-Decahydro-2,10,10c-trimethyl-3*H*-benz[6,7]indeno-[2,1-*b*]furan-1,4,6,9-tetraone 59

To a solution of **43** (80 mg, 0.25 mmol) in glacial acetic acid (10 ml) heated under reflux was added zinc dust (0.98 g, 15 mmol) in portions until the solution was colourless and TLC indicated that **43** was completely consumed. The mixture was heated under reflux for an additional 7 h. The mixture was filtered, and the filtrate was poured into ethyl acetate (100 ml) and water (40 ml). Solid Na_2CO_3 was added until CO_2-evolution ceased. The aqueous layer was re-extracted with ethyl acetate (2 × 15 ml). The combined organic layers were washed with water (2 × 30 ml) and brine (30 ml), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue gave a 6 : 1 ratio of **59** and **60** (combined 62 mg, 76%). Crystallization from dichloromethane and ethyl acetate gave a small sample of homogeneous **59** as a solid: mp >220 °C (dec.); ν_{max}(Nujol)/cm^{-1} 1754 and 1705; δ_H (CD_2Cl_2) 4.80 (1 H,

apparent broad q, *J* 7.5, 7a-H), 3.42 (1 H, dd, *J* 9.9 and 7.1, 4a-H), 3.02–2.89 [3 H, m, 2-H (m), 6a-H (t) and 7β-H (dd)], 2.84 (1 H, dd, *J* 19.0 and 7.5, 3β-H), 2.82 (1 H, dd, *J* 9.5 and 7.0, 10b-H), 2.61–2.58 (2 H, m, 5-H_2), 2.49 (1 H, qd, *J* 7.5 and 3.6, 10-H), 2.26 (1 H, dd, *J* 19.0 and 12.6, 3α-H), 1.98 (1 H, apparent dt, *J* 9.5 and 3.6, 10a-H), 1.51 (1 H, m, 7α-H), 1.30 (3 H, s, 10c-methyl), 1.17 (3 H, d, *J* 6.2, 2-methyl) and 1.11 (3 H, d, *J* 7.5, 10-methyl); NOE data: 4.80 (3.02–2.89 [7β-H], 3%; 1.98, 4%), 3.43 (3.02–2.89 [2-H], 6%; 2.61–2.58, 1%; 1.98, 9%), 1.98 (4.80, 5%; 3.43, 9%; 1.11, 1%), 1.30 (3.02–2.89 [6a-H], 5%; 2.82, 16%; 2.61–2.58, 5%; 2.26, 2%), 1.17 (3.02–2.89 [2-H], 6%; 2.26, 3%) and 1.11 (2.49, 4%; 1.98, 4%); δ_C (CD_2Cl_2) 212.8 (0), 208.7 (0), 206.7 (0), 179.9 (C-9), 81.7 (C-7a), 56.3 (C-10b), 50.5 (C-6a), 49.5 (C-4a), 48.0 (C-10c), 47.2 (C-10a), 42.5 (C-3), 42.3 (C-2), 42.2 (C-10), 36.7 (C-5), 32.5 (C-7), 21.8 (10c-methyl), 18.2 (10-methyl) and 13.8 (2-methyl); *m/z* 318.1446 (M^+, 22%, $C_{18}H_{22}O_5$ requires 318.1466), 221 (7), 207 (100), 179 (12), 161 (27), 152 (19), 121 (14), 112 (15), 109 (17), 93 (16), 55 (41), 42 (32) and 41 (45).

X-Ray crystal structure determination for 59¶

A colourless irregular crystal of dimensions 0.40 × 0.20 × 0.20 mm was mounted on a glass fibre: $C_{18}H_{22}O_5$, M = 318.37, monoclinic, a = 6.942(7), b = 27.82(1), c = 7.998(4) Å, β 94.95(7)°, V = 1539(2) Å^3, T = 299 K, space group $P2_1/n$ (no. 14), Z = 4, μ(Mo-Kα) 0.99 cm^{-1}, 3045 reflections collected, 2809 unique (R_{int} = 0.121); 1331 observed ($I > 2.00\sigma(I)$); R = 0.093, R_w = 0.094, goodness of fit = 3.21.

(2α,4aβ,6aβ,7aα,10α,10aα,10bβ,10cβ)-2,4a,5,6a,7,7a,10,10a,10b,10c-Decahydro-2,10,10c-trimethyl-3*H*-benz[6,7]indeno-[2,1-*b*]furan-1,4,6,9-tetraone 60

To a solution of **43** (28 mg, 0.089 mmol) in acetone (2.0 ml) was added in small portions a 20% aqueous solution of $TiCl_3$ (0.24 ml, 0.38 mmol) at RT. The solution was stirred for 20 min before it was poured into 25 ml of brine. This was extracted with ethyl acetate (3 × 15 ml). The combined organic solutions were washed with water (20 ml) and brine (20 ml), dried and concentrated under reduced pressure. Chromatography of the residue provided **60** (14 mg, 50%) as a white solid: 178–180 °C; ν_{max}(Nujol)/cm^{-1} 1770 and 1710; δ_H 4.78 (1 H, apparent q, *J* 7.2, 7a-H), 3.49 (1 H, m, 4a-H), 3.27 (1 H, m, 2-H), 3.05–2.92 (4 H, m), 2.74 (1 H, dd, *J* 9.6 and 7.7, 10b-H), 2.53 (1 H, m, 5β-H), 2.49 (1 H, dq, *J* 9.5 and 5.0, 10-H), 2.26 (1 H, dd, *J* 19.6 and 13.4, 3α-H), 1.68 (3 H, s, 10c-methyl), 1.67 (1 H, m, 10a-H), 1.58 (1 H, m, 7β-H), 1.20 (3 H, d, *J* 6.4, 2-methyl) and 1.13 (3 H, d, *J* 7.5, 10-methyl); NOE data: 3.49 (3.27, 6%; 2.53, 1%; 1.68, 1%) and 1.20 (3.27, 8%; 2.26, 2%); δ_C 211.9 (0), 207.0 (0), 206.2 (0), 179.3 (C-9), 81.6 (C-7a), 55.4 (C-10b), 54.1 (C-4a), 49.6 (C-6a), 47.92 (C-10c), 47.87 (C-10a), 42.3 (C-3), 41.9 (C-10), 39.0 (C-2), 34.6 (C-5), 31.9 (C-7), 28.0 (10c-methyl), 17.6 (10-methyl) and 13.6 (2-methyl); *m/z* 318.1447 (M^+, 44%, $C_{18}H_{22}O_5$ requires 318.1466), 290 (11), 276 (17), 248 (12), 245 (11), 231 (22), 221 (18), 207 (100), 161 (22), 152 (46), 109 (36), 99 (32), 93 (37), 91 (32), 79 (42), 77 (32), 69 (51), 55 (91), 42 (77) and 41 (84).

(2α,4aβ,6aα,7aβ,9α,10β,10aβ,10bα,10cα)-4a,5,6a,7,7a,9,10,10a,10b,10c-Decahydro-2,9,10,10c-tetramethyl-3*H*-benz[6,7]indeno-[2,1-*b*]furan-1(2*H*),4,6-trione 61

A solution of **42** (0.258 g, 0.781 mmol) in glacial acetic acid (40 ml) heated under reflux as zinc dust (1.45 g, 21.7 mmol) was added in portions until the solution became colourless and TLC indicated that **42** was completely consumed. The mixture was heated for another 10 h. After cooling, the mixture was filtered, and the filtrate was added to ethyl acetate (80 ml) and water (80 ml). Solid Na_2CO_3 was added until CO_2-evolution ceased. The aqueous layer was re-extracted with ethyl acetate (2 × 30 ml). The combined organic layers were washed with water (30 ml) and brine (30 ml), dried and concentrated under reduced pressure. Chromatography of the residue provided **61** (50 mg, 20%) as a colourless solid: mp 179–181 °C; ν_{max}(Nujol)/cm^{-1} 1709; δ_H 4.36 (1 H, m, 7a-H), 3.52 (1 H, dd, *J* 10.4 and 6.5, 4a-H), 3.42 (1 H, dq, *J* 8.8 and 6.1, 9-H), 3.06 (1 H, m, 2-H), 3.05 (1 H, t, *J* 7.7, 6a-H), 2.86 (1 H, dd, *J* 9.6 and 7.0, 3β-H), 2.81 (1 H, dd, *J* 12.6 and 6.9, 10b-H), 2.74 (1 H, dd, *J* 13.6 and 7.7, 7β-H), 2.59 (2 H, m, 5-H_2), 2.26 (1 H, dd, *J* 19.6 and 13.4, 3α -H), 1.70 (1 H, m, 10a-H), 1.57–1.49 (2 H, m, 7α -H and 10-H), 1.30 (3 H, s, 10c-methyl), 1.23 (3 H, d, *J* 6.1, 9-methyl), 1.20 (3 H, d, *J* 6.4, 2-methyl) and 0.80 (3 H, d, *J* 6.7, 10-methyl); NOE data 4.36 (3.42, 4%; 2.74, 4%; 1.70, 3%), 3.52 (3.06, 7%; 1.70, 6%), 1.70 (4.36, 5%; 3.52, 10%; 0.80, 1%), 1.30 (3.05, 8%; 2.81, 6%, 2.59, 6%) and 0.80 (3.42, 4%; 3.06, 2%; 1.70, 3%; 1.57–1.49, 2%); δ_C 212.0 (0), 209.1 (0), 207.0 (0), 85.8 (C-9), 83.1 (C-7a), 55.7 (C-10b), 53.2 (C-10a), 53.1 (C-6a), 48.9 (C-4a), 47.5 (C-10c), 47.4 (C-10), 42.0 (C-3), 41.5 (C-2), 36.2 (C-5), 30.3 (C-7), 21.8 (10c-methyl), 18.7 (9-methyl), 17.0 (10-methyl) and 13.4 (2-methyl); *m/z* 318.1839 (M^+, 12%, $C_{19}H_{26}O_4$ requires 318.1831), 207 (9), 178 (10), 161 (23), 152 (11), 136 (10), 121 (14), 112 (100), 97 (68), 55 (37), 43 (52) and 41 (35).

Acknowledgements

We are very grateful to Mr David O. Miller of this Department for the X-ray crystal structures. This research was supported by a grant from the Natural Sciences and Engineering Research Council of Canada.

References

1 R. Baker and S. Walmsley, *Tetrahedron*, 1982, **38**, 1899; G. D. Prestwich, *Tetrahedron*, 1982, **38**, 1911; K. Nakanishi, T. Goto, S. Itô, S. Natori and S. Nozoe, *Natural Products Chemistry*, vol. 3, Oxford University Press, Oxford, 1983, pp. 136–138.
2 G. D. Prestwich, S. G. Spanton, J. W. Lauher and J. Vrkoč, *J. Am. Chem. Soc.*, 1980, **102**, 6825.
3 W. G. Dauben, I. Farkas, D. P. Bridon, C.-P. Chuang and K. E. Henegar, *J. Am. Chem. Soc.*, 1991, **113**, 5883.
4 L. A. Paquette, D. R. Sauer, D. G. Cleary, M. A. Kinsella, C. M. Blackwell and L. G. Anderson, *J. Am. Chem. Soc.*, 1992, **114**, 7375; D. F. Taber, *Tetrahedron Lett.*, 1993, **34**, 1883.
5 P. Metz, S. Bertels and R. Fröhlich, *J. Am. Chem. Soc.*, 1993, **115**, 12595.
6 C. Liu and D. J. Burnell, *J. Am. Chem. Soc.*, 1997, **119**, 9584.
7 E. J. Corey and T. Ravindranathan, *Tetrahedron Lett.*, 1971, 4753.
8 K. E. Harding, J. B. Strickland and J. Pommerville, *J. Org. Chem.*, 1988, **53**, 4877.
9 M. Ihara, Y. Ishada, K. Fukumoto and T. Kametani,, *Chem. Pharm. Bull.*, 1985, **33**, 4102; L. N. Mander and S. P. Sethi, *Tetrahedron Lett.*, 1984, **25**, 5953.
10 C. Schmidt, S. D. Sabnis, E. Schmidt and D. K. Taylor, *Can. J. Chem.*, 1971, **49**, 371; R. A. Dickinson, R. Kubela, G. A. MacAlpine, Ž. Stojanac and Z. Valenta, *Can. J. Chem.*, 1972, **50**, 2377; F. Bohlmann, W. Mathar and H. Schwartz, *Chem. Ber.*, 1977, **110**, 2028; J. Das, R. Kubela, G. A. MacAlpine, Ž. Stojanac and Z. Valenta, *Can. J. Chem.*, 1979, **57**, 3308.
11 M. J. Fisher, W. J. Hehre, S. D. Kahn and L. E. Overman, *J. Am. Chem. Soc.*, 1988, **110**, 4625.
12 I. Paterson and I. Fleming, *Tetrahedron Lett.*, 1979, 995.
13 A. J. Ragauskas and J. B. Stothers, *Can. J. Chem.*, 1985, **63**, 2969; A. Abad, C. Agulló, M. Arnó, A. C. Cuñat, B. Meseguer and R. J. Zaragozá, *J. Org. Chem.*, 1998, **63**, 5100.
14 W. P. Weber, *Silicon Reagents for Organic Synthesis*, Springer, New York, 1983, pp. 235–238.
15 C. Liu and D. J. Burnell, *J. Org. Chem.*, 1997, **62**, 3683.
16 I. Paterson and L. G. Price, *Tetrahedron Lett.*, 1981, **22**, 2829.
17 C. Liu and D. J. Burnell, *Tetrahedron Lett.*, 1997, **37**, 6573.
18 L. C. Blaszczak and J. E. McMurry, *J. Org. Chem.*, 1974, **39**, 258.

¶ CCDC reference number(s) 164940–164942. See http://www.rsc.org/suppdata/p1/b1/b104924k/ for crystallographic files in .cif or other electronic format.