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# Taxane Diterpene Synthesis Studies. Part 2: Towards Taxinine—Enantiospecific Construction of an AB-ring Substructure Incorporating both Quaternary Carbon Centres and Attempts to Annulate the C-ring*

*Martin G. Banwell*,[A,B] *Malcolm D. McLeod*,[A] *and Andrew G. Riches*[A]

[A] Research School of Chemistry, Institute of Advanced Studies, The Australian National University, Canberra ACT 0200, Australia.

[B] Author to whom correspondence should be addressed (e-mail: mgb@rsc.anu.edu.au).

In connection with efforts to develop an efficient total synthesis of the biologically active natural product taxinine **1**, the enzymatically-derived and monochiral *cis*-1,2-dihydrocatechol **7** was converted, over several steps including a Diels–Alder cycloaddition reaction, into the bicyclo[2.2.2]octan-2-one **18**. Reaction of the last compound with the organocerium reagent **22** afforded the 1,5-diene **23** which engaged in an anionic oxy-Cope rearrangement reaction to give, after *C*-methylation of the product enolate **25**, bicyclo[5.3.1]undecenone **27** embodying the AB-ring system of target **1**. Two methods for allylic oxidation of such products were developed and several unsuccessful attempts to effect a cyclization reaction so as to establish the taxane C-ring are described.

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## Introduction

The crystalline taxane diterpene taxinine **1** (Diagram 1) was first isolated by ethanol extraction of the needles of the Japanese yew around 1925.[1] This compound has since been identified in the needles, fruits, seeds, twigs, bark, and heartwood of many *Taxus* species. Its structure was established through a combination of NMR and chemical studies over 30 years ago[2] and subsequently confirmed by X-ray crystallographic methods.[3] As such taxinine was the first natural taxoid to be obtained in pure form and structurally characterized. Various studies have revealed that, unlike its structurally more complex and well known congener Taxol, compound **1** is a weakly cytotoxic agent.[4] Significantly, however, taxinine has been shown, among others, to increase the cellular accumulation of vincristine in multi-drug resistant tumour cells and must, therefore, be regarded as having therapeutic potential for resensitizing tumour cells to various anti-cancer agents.[4,5] As a consequence taxinine has attracted some attention as a synthetic target[6] although no total synthesis has been reported to date. That having been said, the preparation of closely related taxoids such as taxusin have been described by several groups.[7] Herein we detail an approach to the enantiomer of the natural product, namely *ent*-**1** (Diagram 1), that has culminated in the stereocontrolled synthesis of AB-ring substructures incorporating the synthetically demanding C8 quaternary carbon centre[8] as well as that at C15.

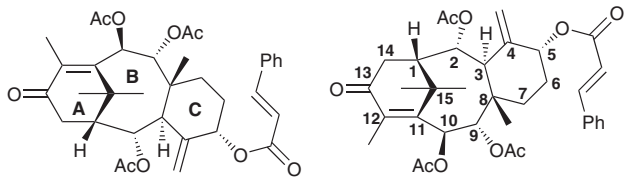


**Diagram 1.**

The retrosynthetic analysis of target *ent*-**1** employed in the present work is shown in Fig. 1 and exploits results detailed in Part 1 of this series.[9] It requires, in the closing stages, annulation of the taxane C-ring onto a bicyclo[5.3.1]undecenyl framework **2** incorporating the pivotal quaternary carbon centre C8 (taxane numbering). This centre was to be constructed by *C*-methylation of the enolate **3** which should, in turn, be accessible via anionic oxy-Cope rearrangement of the bicyclo[2.2.2]octane **4**, itself likely to be available through nucleophilic addition of an appropriately metallated alkene **5** to ketone **6**. Based on our earlier studies,[9,10] we anticipated that the bicyclo[2.2.2]octan-2-one **6** would be obtained by engaging *cis*-1,2-dihydrocatechol **7** in a Diels–Alder cycloaddition reaction with an appropriate dienophile.

*Certain aspects of this work have been reported in preliminary form: M. G. Banwell, P. Darmos, M. D. McLeod, D. C. R. Hockless, *Synlett* **1998**, 897. doi:10.1055/S-1998-1801

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The monochiral (>99.8% *e.e.*) diene **7** is readily generated by enzymatic dihydroxylation of toluene[11] and has already proven to be an important building block in the synthesis of terpenoids.[12] Since the enantiomeric form of diene **7** is also available[13] the successful implementation of the strategy defined here would provide, in a formal sense, access to substructures of the naturally occurring form, **1**, of taxinine. Additionally, we have described 'enantiomeric switching' regimes[9] which could well be employed here so as to provide access to precursors of taxinine **1** from diene **7**. The proposed use of the anionic oxy-Cope rearrangement **4** → **3** was inspired by the work of Martin et al.[14] who have highlighted the utility of this process in gaining access to the AB-ring system of taxanes, albeit in racemic form.

## Results and Discussion

In our initial attempts to implement the synthetic plan implied by Fig. 1 we elected, for the sake of simplicity, to target intermediates **5** and **6** wherein substituents X and Y are both hydrogen. Once proof-of-concept was obtained then appropriate variation of these substituents would be examined so as to enable introduction of the C9 and C10 acetate groups associated with target *ent*-**1**.

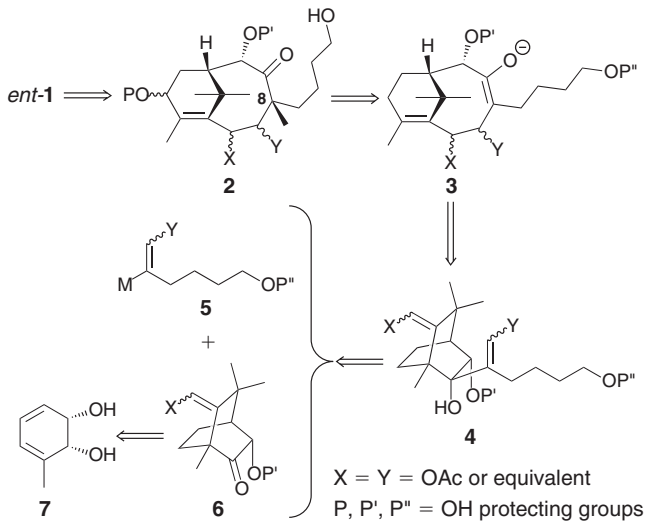
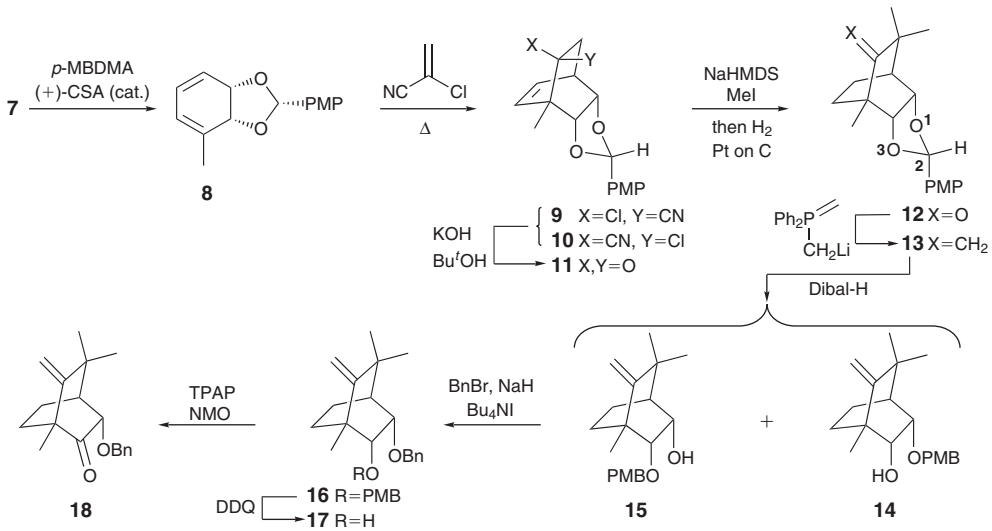
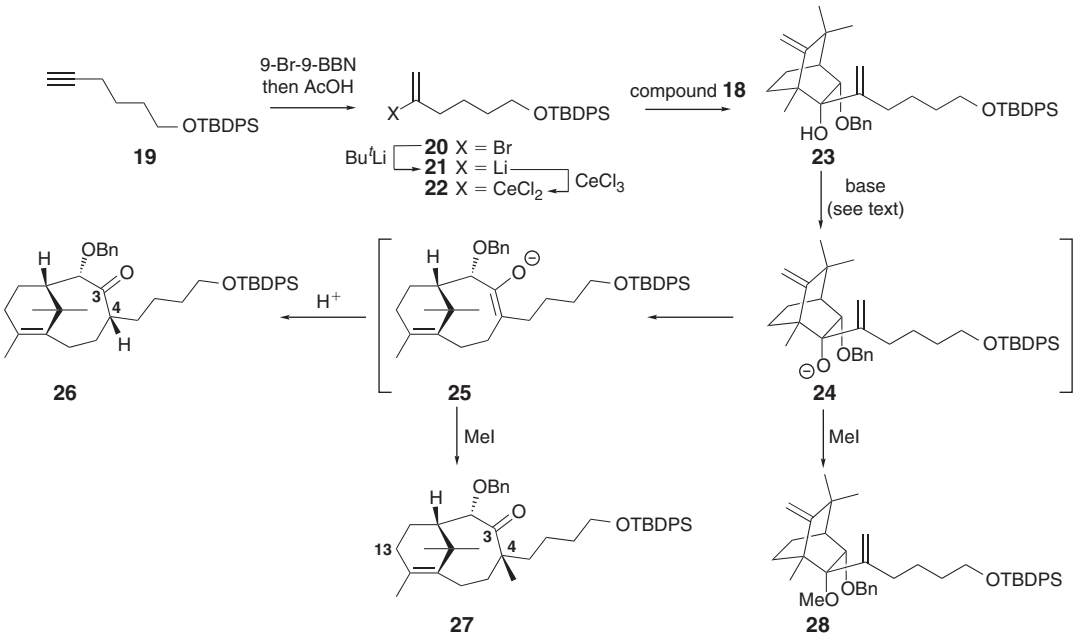



**Fig. 1.**

The synthesis of an 'operational' version of the generic structure **6**, namely bicyclo[2.2.2]octan-2-one **18**, is shown in Scheme 1 and this starts with the conversion of diol **7** into the corresponding *p*-methoxyphenyl (PMP) acetal **8** (53%) under conventional conditions. The product of this reaction was obtained as a single diastereomer and the stereoselective nature of this conversion most likely arises from the operation of a kinetically controlled process.[15] Reaction of diene **8** with α-chloroacrylonitrile, a well-known ketene equivalent used in Diels–Alder reactions,[16] provided a ca. 4 : 1 mixture of cycloadducts **9** and **10** which was immediately subjected to hydrolysis with potassium hydroxide in *t*-butanol, thus providing the ketone **11** as a white crystalline solid in 86% yield. *gem*-Dimethylation of compound **11** was achieved under standard conditions and the resulting product hydrogenated to give the saturated equivalent **12** (88% over two steps). Methylenation of this last ketone, as necessary for installation of one of the two double bonds required for the foreshadowed and pivotal anionic oxy-Cope rearrangement, proved somewhat problematic because of the hindered nature of the carbonyl group which is flanked by quaternary carbon centres. After considerable experimentation, two means for effecting this conversion were identified. The first involved using Cristau's diphenylphosphonium dimethyldiylide[17] which is much more reactive than the more commonly used 'parent' triphenylphosphonium methylide and under appropriate conditions the target methylenated product **13** was obtained in 99% yield. An alternate approach to this compound simply involved using the aforementioned parent ylide at 19 kbar. Under such conditions alkene **13** was obtained in 88% yield. The operational simplicity of the former process meant this was favoured in supporting the preparative work described from this point. Reductive ring-opening of the PMP-acetal unit within compound **13** could be achieved with diisobutylaluminium hydride (Dibal-H) to give a ca. 1 : 8




**Scheme 1.**




**Scheme 2.**

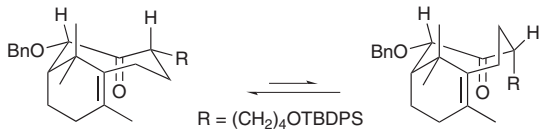



**Fig. 2.**

mixture of the chromatographically separable diol monoethers **14** (10%) and **15** (83%). The regioselectivity of this reaction is attributed to the preferential co-ordination of the reducing agent to that acetal oxygen remote from the bridgehead methyl group in substrate **13**. As a consequence the O1–C2 bond is cleaved preferentially. Conversion of the free hydroxy group within compound **15** into the corresponding benzyl ether **16** (92%) followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) mediated oxidative cleavage of the *p*-methoxybenzyl (PMB) moiety within the latter provided alcohol **17** (97%) which was oxidized to the ketone **18** in 98% yield using the Ley–Griffith reagent.[18]

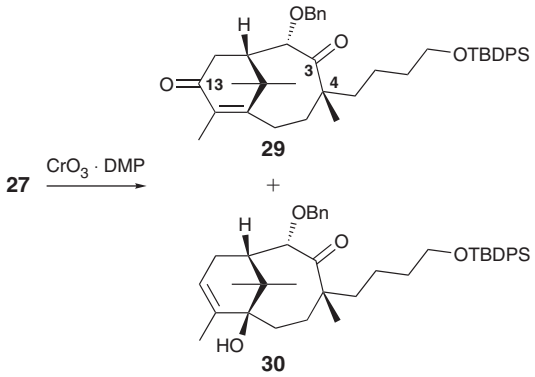
The specific form, **22** (Scheme 2), of the generic nucleophile **5** (Fig. 1) required for addition to the bicyclo[2.2.2]octan-2-one **18** was prepared by adding 9-bromo-9-borabicyclo[3.3.1]nonane (BBN)[19] to the known terminal alkyne **19**[20] and subjecting the resulting adduct to successive treatment with acetic acid then alkaline hydrogen peroxide. In this manner the bromoalkene **20** was obtained in 83% yield. Compound **20** could be lithiated using *t*-butyllithium and the resulting alkenyllithium transmetalled with anhydrous cerium trichloride to give compound **22** which was treated with ketone **18** at −78°C. After warming the reaction mixture to 18°C and quenching with ammonium chloride the anticipated 3°-alcohol **23** was obtained as a single diastereoisomer in 84% yield. The stereoselectivity of this conversion is attributed to the steric demands of the benzyloxy group which inhibits $\alpha$-face nucleophilic addition to the adjacent carbonyl moiety in substrate **18**. The assignment of stereochemistry follows from the successful participation of this compound in the anionic oxy-Cope rearrangement reaction (see below). Thus, on subjecting compound **23** to reaction with KH so as to form oxyanion **24** then warming the reaction mixture, so as to effect conversion of this species into the isomeric anion **25**, followed by quenching with ammonium chloride, afforded bicyclo[5.3.1]undecenone **26** (88%). This material was obtained as a single diastereoisomer and, based upon previous observations,[21] it is assumed that the side-chain has the α-configuration which arises through kinetically controlled *exo*-or β-face protonation of the precursor enolate **25**. Unfortunately, all attempts to alkylate ketone **26** by deprotonation to regenerate enolate **25** followed by trapping the latter with methyl iodide, so as to form the target dialkyl ketone **27**, failed. This outcome is attributed to an inability to regenerate the enolate **25** from **26**, a situation which is ascribed to the unfavourable orbital overlap between the $\alpha$-hydrogen and the carbonyl group in the preferred conformation (Fig. 2) of ketone **26**.[22] This explanation is supported by the observation that quenching anion **25** (derived by rearrangement of isomer **24**) with methyl iodide does indeed provide the desired dialkyl ketone **27** although only as a 1 : 10 mixture with the chromatographically inseparable protio-counterpart **26**. Rigorous exclusion of moisture failed to reduce the observed amount of the latter product, leading to speculation that deprotonation of alcohol **23** by the added hydride is rather slow with the result that this compound can protonate enolate **25** thus affording undesired non-methylated material **26**. To circumvent such difficulties an ‘internal quenching’ experiment was carried out wherein methyl iodide was present before the base was added to deprotonate alcohol **23**. Under such conditions (and

with KH as base) formation of compound **26** was completely suppressed but the target ketone **27** (45%) was accompanied by large quantities of the chromatographically separable *O*-methyl ether **28** (20%) arising from reaction of the methyl iodide with oxyanion **24**. Various adjustments to the base and solvent used in this conversion (Table 1) ultimately lead to the identification of conditions (Entry 4, Table 1)[23] wherein the desired compound **27** was the major product (84%).

Once again, the assignment of stereochemistry at C4 in compound **27** follows from previous observations[21] that reactions of enolate anions such as **25** with electrophiles occurs selectively at the *exo*- or β-face, thus affording an α-configured side-chain.

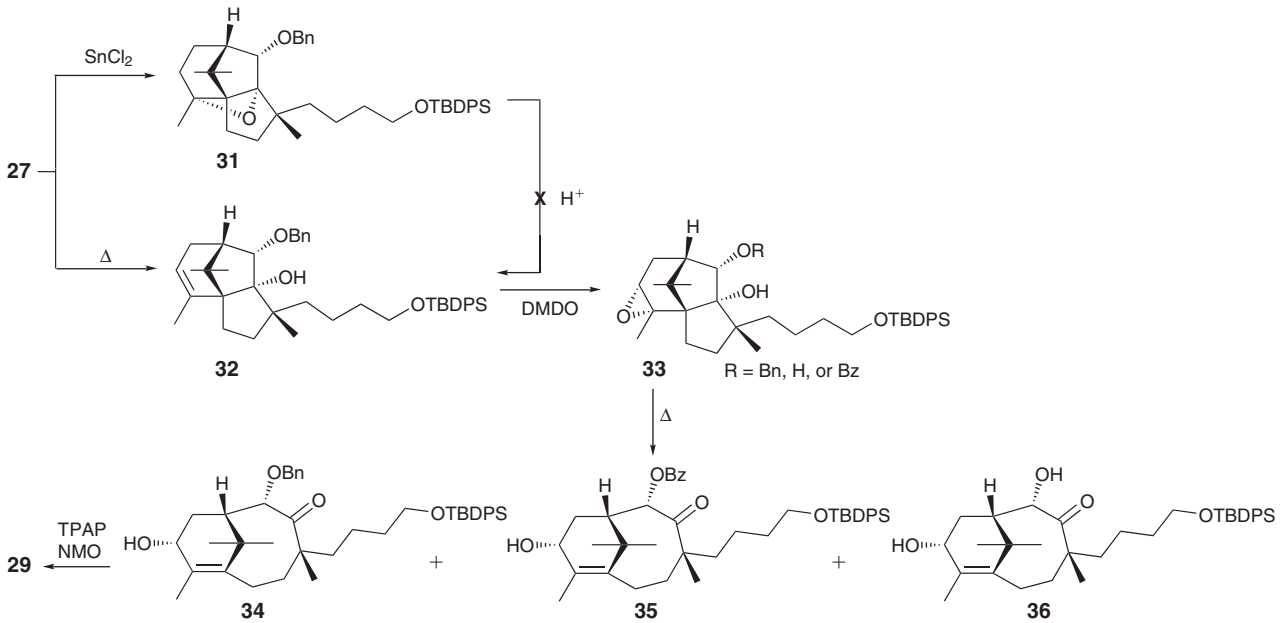
**Table 1. Product distributions arising from use of internal quench/alkylation regime during the anionic oxy-Cope rearrangement of compound 23**

| Entry | Scale [mmol] | Base/Solvent | **27** | **28** |
|---|---|---|---|---|
| 1 | 0.047 | KH/THF | 37% | 51% |
| 2 | 0.047 | KH/DME | 57% | 17% |
| 3 | 0.15 | KH/DME | 45% | 20% |
| 4 | 1.11 | KOBu$^t$/Et$_2$O | 84% | trace |




**Scheme 3.**

With significant quantities of compound **27** to hand efforts could be directed towards achieving allylic oxidation of this species so as to establish the C13 oxygen of taxinine. To these ends (Scheme 3) alkene **27** was treated with the $CrO_3$/3,5-dimethylpyrazole (DMP) complex,[24] a species known for its capacity to effect the desired conversion. Indeed, under appropriate conditions the target enone **29** was obtained albeit in low yield (17%) and accompanied by the rearranged allylic alcohol **30** (11%). As a consequence, a more circuitous but higher yielding method for forming compound **29** was developed (Scheme 4). In keeping with the behaviour of a related system,[21] compound **27** engaged in an $SnCl_2$-mediated transannular 'cycloaddition' of the C3 carbonyl group to the bridgehead alkene to give the oxetane **31** in 93% yield.[25] However, in contrast to earlier work involving a related system,[21] the latter could not be converted into the isomeric (and required) homoallylic alcohol **32** on exposure to various Brønsted or Lewis acids. Such difficulties could be circumvented by subjecting compound **27** to a thermally induced carbonyl-ene reaction[26] thus affording the tricyclic target **32** directly and in 96% yield. Subjection of the latter to epoxidation with dimethyl dioxirane (DMDO)[27] at 15°C afforded the unstable oxirane **33** which was not isolated but, rather, allowed to engage in a very facile and thermally promoted Eschenmoser–Grob fragmentation.[28] This afforded the target allylic alcohol **34** but it was accompanied by varying amounts of the benzoate **35** and diol **36** depending on the reaction stoichiometry, temperature and time (Table 2). Compound **35** presumably arises through DMDO-promoted benzylic oxidation of the benzyl ether moiety within **32**, **33**, and/or **34**. Co-product **36** may be generated through hydrolysis of benzoate **35** or




**Scheme 4.**

a hemi-acetal derived from ether **34**. Oxidation of allylic alcohol **34** with the Ley–Griffith reagent afforded the corresponding enone **29** in 97% yield and which proved identical, in all respects, with the material obtained by the more direct (but less efficient) route described immediately above.

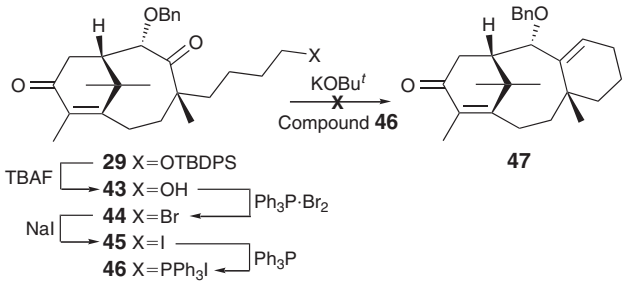
The efficiencies of the reaction sequences leading to compounds **27** and **29** were such that many hundreds of milligrams of these materials were available. As a consequence, the identification of methods for construction of the taxinine C-ring via cyclization between the C3 ketone and the terminus of the butyl side-chain attached at C4 of such substrates was pursued. Our initial approaches were very much influenced by Kajiwara's report[29] that $SmI_2$-mediated pinacolic coupling reactions can be used to effect formation of the C-ring of taxoids. To such ends, the TBDPS-ether within bicyclo[5.3.1]octenone **27** was cleaved using tetrabutylammonium fluoride (TBAF) and the ensuing alcohol **37** (99%) oxidized to the corresponding aldehyde **38** (84%) using the Dess–Martin periodinane (DMP) (Scheme 5).[30] With the requisite dicarbonyl compound in hand the foreshadowed reductive coupling reaction was pursued but exposure of compound **38** to samarium(II) iodide/lithium bromide[31] only provided the reduced and deoxygenated product **39** (12%) and the tricyclic diol **40** (63%). When samarium(II) iodide alone was employed then a 1 : 1 mixture of these same products was observed. The tricyclic product presumably arises via one electron reduction of the ketone carbonyl within precursor **38** followed by cyclization of the resulting ketyl radical anion onto the transannularly disposed double bond. Accompanying this process is the reduction of the aldehyde carbonyl so as to establish the 1°-alcohol unit observed in the final product **40**.

**Table 2. Product distributions observed in the DMDO-mediated epoxidation of tricyclic alkene 32**

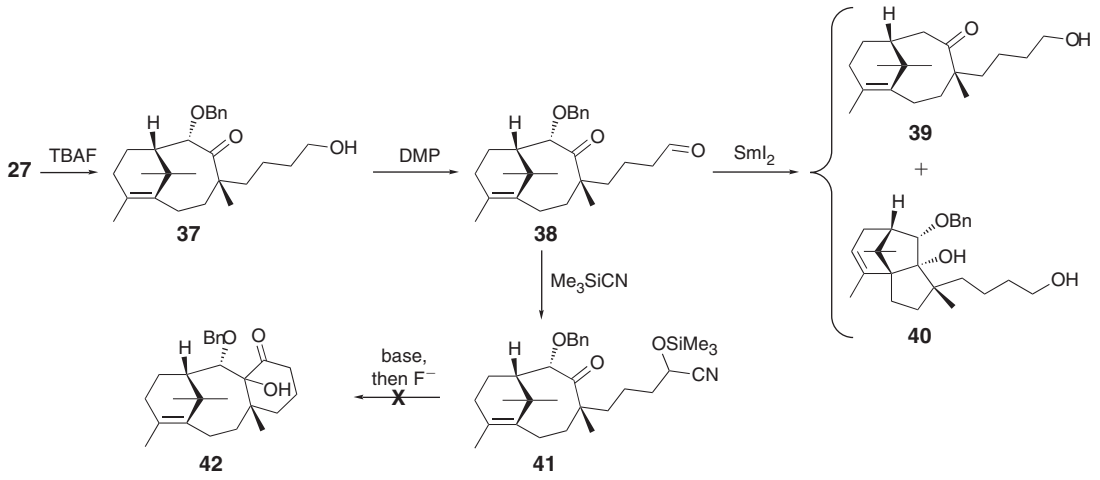
| Entry | eq. DMDO | Temp/Time | **34** | **35** | **36** |
|---|---|---|---|---|---|
| 1 | 3 | −20°C/8 h | 61% | – | 30% |
| 2 | 5 | 0°C/24 h | 10% | 15% | 65% |
| 3 | 10 | 0°C/20 h | 25% | – | 57% |

In the first step of efforts to form the C-ring through an intramolecular benzoin-type condensation reaction,[32] the keto-aldehyde was treated with trimethylsilylcyanide in the presence of triethylamine. However, the resulting material, tentatively identified as ca. 1 : 1 mixture of the diastereoisomeric cyanohydrin ethers **41** (69%), failed to engage in the desired cyclization reaction (which would have led to acyloin **42**) on exposure to a range of relevant conditions including those involving successive use of lithium diisopropylamide (LDA) then a fluoride ion source. Under such conditions only complex mixtures of products were obtained.

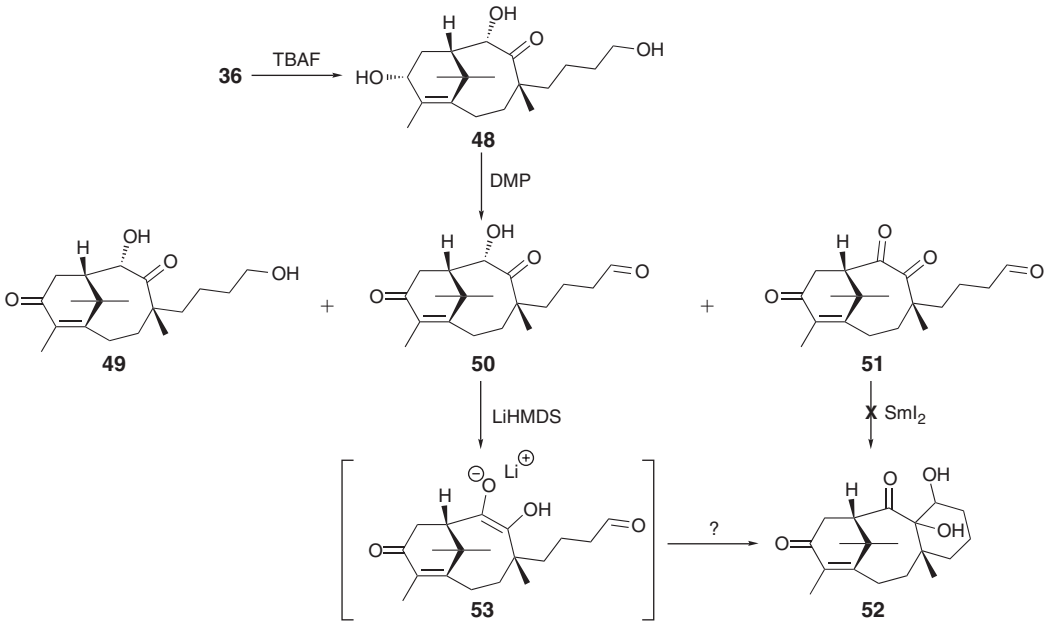
Intramolecular Wittig reactions involving treatment of a ketone with a suitably tethered ylide have proven useful in the formation of cyclohexenes.[33] In efforts to exploit such a process here, the TBDPS-ether **29** was deprotected using TBAF and the ensuing 1°-alcohol **43** (93%) (Scheme 6) then converted into the corresponding bromide **44** (96%) using $Ph_3P \cdot Br_2$.[34] Interestingly, when the equivalent conversion was attempted, directly,[35] on the TBDPS-ether **27** lacking an allylic oxygen at C13 (taxane numbering) only the previously observed oxetane **31** was obtained. Since reaction of bromide **44** with triphenylphosphine proved sluggish it was first converted, under Finkelstein conditions, into the corresponding iodide **45** (91%). Reaction of the latter halide with triphenylphosphine proceeded rapidly and the presumed phosphonium salt so formed was immediately treated with potassium *tert*-butoxide in an effort to generate the corresponding ylide which, of course, it was hoped would engage




**Scheme 6.**




**Scheme 5.**




**Scheme 7.**

in the desired intramolecular olefination reaction. Unfortunately, no evidence for the formation of the target cyclohexene **47** could be obtained.

Our final efforts to effect C-ring annulation involved attempts to exploit aldol condensation processes (Scheme 7). To such ends the TBDPS-ether **36** was desilylated using TBAF so as to generate triol **48** (95%). Reaction of the latter compound with one molar equivalent of DMP afforded a chromatographically separable mixture of diketone **49** (18%) and the tricarbonyl system **50** (46%). Use of two equivalents of DMP afforded compounds **49** and **50** in 21% and 68% yields, respectively. Increasing the mole ratio of oxidant to substrate to ca. 3.5 : 1 resulted in the tetracarbonyl system **51** (36%) being obtained as the only isolable reaction product. Attempts to effect a samarium iodide-mediated pinacolic coupling within polycarbonyl compound **51** and thereby form diol **52** were also unsuccessful.[36] A more tantalizing result was observed during efforts to effect an intramolecular aldol reaction of compound **50**. Thus, this tricarbonyl species was reacted with LiHMDS in the hope that the resulting acyloin-derived enolate **53** might engage in an aldol process to generate, after acidic work-up, the keto-diol **52**. Indeed, small amounts (11%) of a product isomeric (as judged by mass spectral analysis) with the starting material was obtained but the quantities of material obtained did not permit accumulation of sufficiently convincing NMR data to allow for unequivocal assignment of structure.

## Summary and Conclusions

The work detailed here demonstrates that the enantiomerically pure and readily accessible *cis*-1,2-dihydrocatechol **7** can be elaborated, via Diels–Alder and anionic oxy-Cope rearrangement reactions, into the AB-ring substructure, for example **27**, associated with *ent*-taxoids such as *ent*-taxinine. The propensity for such bicyclo[5.3.1]undecenones to engage in an intramolecular carbonyl ene reaction has been exploited in the installation of the C13 oxygen (taxane numbering) required in the target natural product. Further development of this approach requires the identification of an effective strategy for annulation of the taxoid C-ring onto the AB-ring systems such as **27** and **29**. Work directed towards such ends is now underway in these laboratories.

## Experimental

### *General*

General procedures and protocols have been described in Part 1[9] of this series.

### *Synthetic Studies*

*(2S,3aR,7aS)-3a,7a-Dihydro-2-(4-methoxyphenyl)-4-methyl-1,3-benzodioxole* ***8***

A magnetically stirred suspension of diol **4** (5.00 g, 39.6 mmol) in dichloromethane (150 mL) was treated with *p*-methoxybenzaldehyde dimethyl acetal (7.47 mL, 43.6 mmol) and the resulting mixture cooled to −20°C. (–)-Camphorsulfonic acid monohydrate (99 mg, 0.396 mmol) was then added in one portion which resulted in the rapid dissolution of suspended material. After 10 min the reaction mixture was quenched with $NaHCO_3$ (150 mL of a 5% w/v aqueous solution), the layers separated, and the aqueous phase extracted with dichloromethane (1 × 150 mL). The combined organic extracts were washed with brine (1 × 100 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give an oily solid. Recrystallization (petroleum spirit, 2 crops) of this material afforded *acetal* ***8*** (5.18 g, 53%) as pale-brown crystals, mp 101–102°C, $[\alpha]_D$+118 (*c* 2.0), $R_f$ 0.4 (15 : 85 v/v ethyl acetate/hexane), (Found: $M^{+\bullet}$ 244.1101, C 73.7, H 6.8. $C_{15}H_{16}O_3$ requires $M^{+\bullet}$ 244.1099, C 73.7, H 6.6%). $\nu_{max}/cm^{-1}$ 1664, 1613, 1585, 1519. $\delta_H$ (300 MHz) 7.39 (2 H, m), 6.88 (2 H, m), 6.02 (1 H, dd, *J* 9.8 and 5.6), 5.87 (1 H, dd, *J* 9.8 and 3.9), 5.78 (1 H, d, *J* 5.2), 5.68 (1 H, s), 4.70 (1 H, dd, *J* 9.3 and 3.9), 4.52 (1 H, dd, *J* 9.3), 3.80 (3 H, s), 1.95 (3 H, s). $\delta_C$ (75 MHz) 160.6, 133.8, 129.0, 128.4, 124.9, 121.5, 119.3, 113.7, 99.1, 75.0, 72.2, 55.2, 20.3. *m/z* (EI, 70 eV) 244 ($M^{+\bullet}$, 32%), 198 (68), 183 (13), 165 (13), 135 (100), 121 (21), 108 (51), 79 (48), 77 (49).

*(2S,3aS,4R,7S,7aR,8R)-8-Chloro-3a,4,7,7a-tetrahydro-2-(4-methoxyphenyl)-7-methyl-4,7-ethano-1,3-benzodioxole-8-carbonitrile* ***9*** *and (2S,3aS,4R,7S,7aR,8S)-8-Chloro-3a,4,7,7a-tetrahydro-2-(4-methoxyphenyl)-7-methyl-4,7-ethano-1,3-benzodioxole-8-carbonitrile* ***10***

A magnetically stirred solution of diene **8** (1.88 g, 7.69 mmol) in benzene (15 mL) was treated with 2-chloroacrylonitrile (1.84 mL, 23.1 mmol) and the resulting mixture heated at reflux for 48 h then cooled and concentrated under reduced pressure to afford a brown solid. This material was subject to flash chromatography (1 : 4 v/v ethyl acetate/hexane elution) to give, after concentration of the appropriate fractions ($R_f$ 0.3), a 4 : 1 mixture of the *title compounds* ***9*** and ***10*** (2.55 g, 100%) as a light-yellow oil (Found: C 65.5, H 5.4, N 4.5, Cl 10.4. $C_8H_8NO_3Cl$ requires C 65.2, H 5.5, N 4.2, Cl 10.7%). $\delta_H$ (300 MHz) (major) 7.38 (2 H, m), 6.89 (2 H, m), 6.38 (1 H, dd, *J* 8.1 and 6.6), 5.90 (1 H, d, *J* 8.1), 5.65 (1 H, s), 4.35 (2 H, s), 3.81 (3 H, s), 3.13 (1 H, m), 2.56 (1 H, dd, *J* 15.3 and 1.9), 2.25 (1 H, dd, *J* 15.3 and 4.0), 1.67 (3 H, s). $\delta_H$ (minor) 7.38 (2 H, m), 6.89 (2 H, m), 6.47 (1 H, app. t, *J* 7.4), 6.04 (1 H, d, *J* 8.2), 5.61 (1 H, s), 4.47 (1 H, dd, *J* 7.3 and 1.2), 4.40 (1 H, m), 3.81 (3 H, s), 3.13 (1 H, m), 2.68 (1 H, dd, *J* 14.9, 4.1), 2.19 (1 H, dd, *J* 14.9, 1.9), 1.68 (3 H, s). $\delta_C$ (75 MHz, $CDC1_3$) (major) 160.8, 132.2, 131.6, 128.8, 127.7, 118.7, 113.7, 103.9, 79.5, 78.0, 58.7, 55.3, 47.0, 42.3, 34.0, 17.5. $\delta_C$ (minor) 160.8, 134.5, 133.7, 128.8, 127.7, 119.2, 113.7, 103.2, 78.2, 77.9, 60.1, 55.2, 46.4, 42.4, 34.8, 17.2.

*(2S,3aS,4R,7S,7aR)-3a,4,7,7a-Tetrahydro-2-(4-methoxyphenyl)-7-methyl-4,7-ethano-1,3-benzodioxol-8-one* ***11***

A magnetically stirred suspension of a mixture of α-chloronitriles **9** and **10** (2.27 g, 6.84 mmol) in *tert*-butanol (68 mL) was treated with ground potassium hydroxide (1.92 g, 34.2 mmol), and the resulting mixture stirred at 70°C for 1.5 h. The cooled reaction was then quenched with water (70 mL) and extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with brine (1 × 50 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give an off-white solid. Subjection of this material to flash chromatography (1 : 3 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.3) afforded a white solid which was recrystallized (ether) to give the *title ketone* ***11*** (1.69 g, 86%) as white, crystalline masses, mp 136–137°C, $[\alpha]_D$ +257 (*c* 2.1), (Found: $M^{+\bullet}$ 286.1214, C 71.5, H 6.3. $C_{17}H_8O_4$ requires $M^{+\bullet}$ 286.1205, C 71.3, H 6.3%). $\nu_{max}/cm^{-1}$ 1726, 1613, 1585, 1519. $\delta_H$ (300 MHz) 7.43 (2 H, m), 6.89 (2 H, m), 6.49 (1 H, app. t, *J* 7.1), 5.88 (1 H, d, *J* 8.3), 5.72 (1 H, s) 4.52 (1 H, dd, *J* 7.3 and 3.8), 4.09 (1 H, d, *J* 6.9), 3.80 (3 H, s), 3.32 (1 H, m), 2.20 (1 H, dd, *J* 18.7 and 3.9), 1.95 (1 H, dd, *J* 18.7 and 2.1), 1.39 (3 H, s). $\delta_C$ (75 MHz) 209.8, 160.8, 134.0, 131.7, 128.7, 128.0, 113.7, 104.6, 79.9, 79.6, 55.2, 54.7, 35.2, 35.0, 14.3. *m/z* (EI, 70 eV) 286 ($M^{+\bullet}$, 18%), 198 (17), 149 (17), 136 (100), 121 (32), 108 (32), 91 (27), 77 (40).

*(2S,3aS,4S,7S,7aR)-3a,4,7,7a-Tetrahydro-2-(4-methoxyphenyl)-7,9,9-trimethyl-4,7-ethano-1,3-benzodioxol-8-one*

A magnetically stirred solution of ketone **11** (3.26 g, 11.4 mmol) in THF (45 mL) maintained at 0°C (ice bath) was treated with sodium hexamethyldisilazide (22.8 mL, 22.8 mmol) followed by methyl iodide (1.42 mL, 22.8 mmol). The reaction mixture was stirred for 6 h at 0°C with the addition of further sodium hexamethyldisilazide (22.8 mL, 22.8 mmol) and methyl iodide (1.42 mL, 22.8 mmol) after 2 and 4 h. The reaction mixture was then quenched with water (100 mL) and extracted with ether (3 × 100 mL). The combined organic extracts were washed with brine (1 × 100 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give an orange solid. Subjection of this material to flash chromatography (1 : 4 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.3) afforded a white solid which was recrystallized (ether) to give the *title ketone* (3.20 g, 89%) as white, crystalline masses, mp 117–118°C, $[\alpha]_D$ +230 (*c* 2.0), (Found: $M^{+\bullet}$ 314.1517, C 72.3, H 7.0. $C_{19}H_{22}O_4$ requires $M^{+\bullet}$ 314.1518, C 72.6, H 7.1%). $\nu_{max}/cm^{-1}$ 1722, 1614, 1586, 1519. $\delta_H$ (300 MHz) 7.43 (2 H, m), 6.89 (2 H, m), 6.46 (1 H, app. t, *J* 8.1), 5.80 (1 H, d, *J* 8.1), 5.68 (1 H, s), 4.79 (1 H, dd, *J* 7.6 and 3.4), 4.13 (1 H, d, *J* 6.8), 3.81 (3 H, s), 3.07, (1 H, m), 1.37 (3 H, s), 1.17 (3 H, s), 1.09 (3 H, s). $\delta_C$ (75 MHz) 214.0, 160.7, 135.4, 130.1, 128.8, 128.1, 113.7, 104.2, 79.5, 77.4, 55.3, 55.2, 46.4, 41.7, 28.4, 23.3, 14.6. *m/z* (EI, 70 eV) 314 ($M^{+\bullet}$, 13%), 198 (14), 178 (23), 163 (12), 149 (40), 136 (100), 121 (23), 109 (22).

*(2S,3aR,4S,7S,7aS)-Tetrahydro-2-(4-methoxyphenyl)-4,6,6-trimethyl-4,7-ethano-1,3-benzodioxol-5(4H)-one* ***12***

A solution of (2*S*,3a*S*,4*S*,7*S*,7a*R*)-3a,4,7,7a-tetrahydro-2-(4-methoxyphenyl)-7,9,9-trimethyl-4,7-ethano-1,3-benzodioxol-8-one (18.6 g, 59.1 mmol) in ethanol (180 mL) was purged with nitrogen and 10% platinum on carbon (5.87 g) was added. The atmosphere was exchanged for hydrogen (1 atmosphere) and the resulting mixture stirred at 18°C for 7 h then purged with nitrogen, filtered through a pad of Celite and the filtrate evaporated to give a white solid. This material was recrystallized (hexane) to afford *ketone* ***12*** (18.5 g, 99%) as colourless crystals, mp 127–128°C, $[\alpha]_D$ −21.8 (*c* 1.1), $R_f$ 0.4 (1 : 4 v/v ethyl acetate/hexane), (Found: $[M - H^{\bullet}]^+$ 315.1596, C 72.1, H 7.8. $C_{19}H_{24}O_4$ requires $[M - H^{\bullet}]^+$ 315.1596, C 72.1, H 7.7%). $\nu_{max}/cm^{-1}$ 1717, 1612, 1585, 1516. $\delta_H$ (300 MHz) 7.51 (2 H, m), 6.95 (2 H, m), 5.78 (1 H, s), 4.58 (1 H, m), 3.96 (1 H, m), 3.82 (3 H, s), 2.30–2.05 (3 H, complex m), 1.70 (1 H, m), 1.30 (1 H, m), 1.23 (3 H, s), 1.12 (3 H, s), 1.07 (3 H, s). $\delta_C$ (75 MHz) 218.7, 160.6, 128.2, 113.8, 103.8, 76.9, 74.0, 55.2, 48.0, 43.9, 41.5, 25.0, 23.4, 23.1, 17.0, 14.7 (one signal obscured or overlapping). *m/z* (EI, 70 eV) 316 ($M^{+\bullet}$, 45%), 315 (60), 285 (12), 135 (100), 121 (33), 108 (28), 94 (69).

*(2S,3aR,4R,7S,7aS)-Hexahydro-2-(4-methoxyphenyl)-4,6,6-trimethyl-5-methylene-4,7-ethano-1,3-benzodioxole* ***13***

*Method A*

A magnetically stirred suspension of dimethyl diphenylphosphonium iodide (2.05 g, 5.99 mmol) in THF (20 mL) maintained at −10°C (ice/salt bath) was treated with *n*-butyllithium (9.86 mL of a 1.58 M in THF, 15.6 mmol) resulting in the formation of a yellow solution. This was stirred at −10°C for 0.5 h and then at 18°C for 1.5 h whereupon it was re-cooled to 0°C and a solution of ketone **12** (1.26 g, 3.99 mmol) in THF (5 mL + 2 × 2.5 mL washings) was added via cannula. The reaction mixture was stirred for 0.5 h then *t*-butanol (1.91 mL, 20.0 mmol) was added dropwise producing a white precipitate. Stirring was continued for 0.5 h after which time the reaction mixture was quenched by the addition of water (40 mL) and extracted with diethyl ether (3 × 40 mL). The combined organic extracts were washed with brine (1 × 40 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a light-yellow oil. Subjection of this material to flash chromatography (7.5 : 92.5 v/v ethyl acetate/hexane elution) gave, after concentration of the appropriate fractions ($R_f$ 0.6 in 1 : 4 v/v ethyl acetate/hexane), a white solid. Recrystallization of this material (hexane) afforded *alkene* ***13*** (1.25 g, 99%) as crystalline masses, mp 62–64°C, $[\alpha]_D$ +29.3 (*c* 1.2), (Found: $[M - H^{\bullet}]^+$ 313.1807, C 76.7, H 8.0. $C_{20}H_{26}O_3$ requires $[M - H^{\bullet}]^+$ 313.1804, C 76.4, H 8.3%). $\nu_{max}/cm^{-1}$ 1641, 1615, 1588, 1518. $\delta_H$ (300 MHz) 7.52 (2 H, m) 6.95 (2 H, m), 5.72 (1 H, s), 4.94 (2 H, s), 4.46 (1 H, m), 3.83 (3 H, s), 3.75 (1 H, dd, *J* 8.7 and 1.5), 2.08 (1 H, m), 1.93 (1 H, m), 1.77 (1 H, m), 1.63 (1 H, m), 1.26 (3 H, s), 1.19–1.09 (1 H, partially obscured complex m), 1.17 (3 H, s), 1.10 (3 H, s). $\delta_C$ (75 MHz) 161.2, 160.5, 129.0, 128.4, 113.8, 106.2, 102.9, 79.4, 74.6, 55.3, 41.5, 39.7, 36.6, 30.8, 29.5, 24.8, 20.9, 15.1. *m/z* (EI, 70 eV) 314 ($M^{+\bullet}$, 47%), 313 (55), 163 (34), 162 (32), 149 (22), 147 (20), 145 (17), 135 (100), 121 (77), 119 (49), 107 (56), 105 (48), 93 (52), 91 (56), 77 (55).

*Method B*

A solution of ketone **12** (0.050 g, 0.158 mmol) and methyltriphenylphosphonium bromide (0.0847 g, 0.237 mmol) in THF (1.58 mL) contained in a polyethylene pipette bulb was treated with sodium hexamethyldisilazide (237 μL, 0.237 mmol) and the pipette bulb neck was secured firmly with a brass clamp. This vessel was subjected to 19 kbar for 2 h and then removed from the high pressure reactor. The contents

were concentrated under reduced pressure and the residue subjected to purification by flash chromatography and then recrystallization, as defined in Method A, thus providing the title ketone **13** (43 mg, 88%) identical, in all respects, with the material obtained as described immediately above.

*(1*R*,2*R*,3*S*,4*S*)-3-[(4-Methoxyphenyl)methoxy]-1,5,5-trimethyl-5-methylenebicyclo[2.2.2]octan-2-ol* ***14*** *and (1*S*,2*S*,3*R*,4*R*)-3-[(4-Methoxyphenyl)methoxy]-4,6,6-trimethyl-5-methylenebicyclo[2.2.2]octan-2-ol* ***15***

A magnetically stirred solution of acetal **13** (80 mg, 0.255 mmol) in a mixture of dichloromethane (0.63 mL) and pentane (0.63 mL) was cooled to −60°C then treated with diisobutylaluminium hydride (1.27 mL of a 1 M solution in hexane, 1.27 mmol). The resulting mixture was stirred at −60°C for 4 h then −40°C for 1.5 h after which it was carefully quenched with tartaric acid (10 mL of a 1 M aqueous solution) and the resulting biphasic mixture was stirred vigorously for 0.25 h then extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (1 × 30 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a light-yellow oil. Subjection of this material to flash chromatography (13 : 87 v/v ethyl acetate/hexane) afforded two fractions, A and B.

Concentration of fraction A [$R_f$ 0.5(3)] afforded *compound* ***14*** (7.9 mg, 10%) as a clear colourless oil, $[\alpha]_D$ +14.8 (*c* 1.5), (Found: $M^{+\bullet}$ 316.2036. $C_{20}H_{28}O_3$ requires $M^{+\bullet}$ 316.2038). $\nu_{max}/cm^{-1}$ 3508, 1638, 1613, 1586, 1514. $\delta_H$ (300 MHz) 7.28 (2 H, m), 6.89 (2 H, m), 4.88 (1 H, s), 4.84 (1 H, s), 4.56 (1 H, d, *J* 11.2), 4.48 (1 H, d, *J* 11.2), 3.89 (1 H, m), 3.81 (3 H, s), 3.41 (1 H, m), 1.90–1.65 (2 H, complex m), 1.65–1.50 (2 H, complex m), 1.18 (3 H, s), 1.11–1.05 (1 H, partially obscured complex m), 1.09 (3 H, s), 1.02 (3 H, s) (signal due to hydroxyl proton not observed). $\delta_C$ (75 MHz) 162.1, 159.3, 129.9. 129.4, 113.9, 105.6, 72.8, 71.8, 70.6, 55.3, 41.6, 40.9, 36.5, 30.5, 29.2, 24.5, 20.6, 15.5. *m*/*z* (EI, 70 eV) 316 ($M^{+\bullet}$, 6%), 195 (5), 135 (12), 121 (100).

Concentration of fraction B [$R_f$ 0.4(7)] afforded *compound* ***15*** (66.5 mg, 83%) as a clear colourless oil, $[\alpha]_D$ +18.4 (*c* 2.1), (Found: $M^{+\bullet}$ 316.2035. $C_{20}H_{28}O_3$ requires $M^{+\bullet}$ 316.2038). $\nu_{max}/cm^{-1}$ 3499, 1637, 1613, 1586, 1515. $\delta_H$ (300 MHz) 7.31 (2 H, m), 6.91 (2 H, m), 4.87 (1 H, s), 4.85 (1 H, s), 4.59 (1 H, d, *J* 11), 4.52 (1 H, d, *J* 11), 4.13 (1 H, m), 3.82 (3 H, s), 3.35 (1 H, d, *J* 6.5), 3.26 (1 H, br. d, *J* 7.2), 1.82–1.49 (4 H, complex m), 1.17 (3 H, s), 1.15 (3 H, s), 1.09 (1 H, partially obscured m), 1.04 (3 H, s). $\delta_C$ (75 MHz) 162.2, 159.4, 129.8, 129.7, 113.9, 105.6, 79.5, 75.1, 64.8, 55.2, 44.5, 40.7, 36.5, 30.7, 29.1, 25.2, 21.1, 14.7. *m*/*z* (EI, 70 eV) 316 ($M^{+\bullet}$, 6%), 195 (4), 135 (10), 121 (100).

*(1*R*,4*S*,5*S*,6*R*)-6-[(4-Methoxyphenyl)methoxy]-1,3,3-trimethyl-2-methylene-5-(phenylmethoxy)bicyclo[2.2.2]octane* ***16***

A magnetically stirred suspension of sodium hydride (462 mg, 19.3 mmol), tetrabutylammonium iodide (203 mg, 0.550 mmol), and benzyl bromide (1.31 mL, 11.0 mmol) in dimethylformamide (50 mL) was treated with a solution of alcohol **15** (1.74 g, 5.50 mmol) in dimethylformamide (3 mL + 2 × 1 mL washings), and the resulting mixture stirred at 18°C for 5 h then quenched (CAUTION!) by the addition of water (100 mL) and extracted with ether (3 × 50 mL). The combined organic extracts were washed with water (1 × 50 mL) and brine (1 × 50 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification of the resulting light-yellow oil by flash chromatography (1 : 9 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.4) gave *benzyl ether* ***16*** (2.05 g, 92%) as a clear colourless oil, $[\alpha]_D$ +98.5 (*c* 0.9), (Found: $M^{+\bullet}$ 406.2503. $C_{27}H_{34}O_3$ requires $M^{+\bullet}$ 406.2508). $\nu_{max}/cm^{-1}$ 1637, 1613, 1586, 1514. $\delta_H$ (300 MHz) 7.39–7.21 (7 H, complex m), 6.82 (2 H, m), 4.81 (1 H, s), 4.78 (1 H, s), 4.78 (1 H, d, *J* 11.5), 4.66 (1 H, d, *J* 12.1), 4.43 (1 H, d, *J* 12.1), 4.35 (1 H, d, *J* 11.5), 3.89 (1 H, dt, *J* 8.1 and 2.0), 3.79 (3 H, s), 3.19 (1 H, d, *J* 8.2), 2.05 (1 H, m), 1.87 (1 H, td, *J* 12.1 and 3.0), 1.67–1.54 (2 H, complex m), 1.14 (3 H, s), 1.12 (1 H, partially obscured m), 1.08 (3 H, s), 0.95 (3 H, s). $\delta_C$ (75 MHz) 162.5, 158.9, 138.9, 131.4, 129.5, 128.2, 127.9, 127.4, 113.4, 105.1, 78.6, 73.5, 70.8, 55.2, 40.8, 36.5, 30.7, 29.3, 25.6. 21.0, 15.7 (two signals obscured or overlapping). *m*/*z* (EI, 70 eV) 406 ($M^{+\bullet}$, 3%), 315 (7), 285 (13), 179 (12), 162 (20), 137 (15), 135 (25), 121 (100), 105 (13), 91 (68).

*(1*R*,2*R*,3*S*,4*S*)-1,5,5-Trimethyl-6-methylene-3-(phenylmethoxy)-bicyclo[2.2.2]octan-2-ol* ***17***

A rapidly stirred mixture of ether **16** (2.05 g, 5.04 mmol), dichloromethane (45 mL) and water (5 mL) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.72 g, 7.56 mmol). The ensuing deep-green suspension was stirred for 0.25 h then quenched with $NaHCO_3$ (50 mL of a saturated aqueous solution), the layers were separated, and the aqueous phase was extracted with dichloromethane (1 × 50 mL). The combined organic extracts were washed with brine (1 × 50 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow oil was subject to flash chromatography (1 : 9 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.4) gave *alcohol* ***17*** (1.40 g, 97%) as a clear, colourless oil, $[\alpha]_D$ +14.0 (*c* 2.2), (Found: $M^{+\bullet}$ 286.1934. $C_{19}H_{26}O_2$ requires $M^{+\bullet}$ 286.1933). $\nu_{max}/cm^{-1}$ 3516, 1638. $\delta_H$ (300 MHz) 7.38–7.32 (5 H, complex m), 4.89 (1 H, s), 4.85 (1 H, s), 4.64 (1 H, d, *J* 11.6), 4.58 (1 H, d, *J* 11.6), 3.92 (1 H, m), 3.46 (1 H, dd, *J* 8.5 and 1.7), 3.40 (1 H, broad s), 1.88–1.70 (2 H, complex m), 1.65–1.57 (2 H, complex m), 1.20 (3 H, s), 1.10 (1 H, partially obscured m), 1.10 (3 H, s), 1.04 (3 H, s). $\delta_C$ (75 MHz) 162.0, 137.8, 128.5, 127.9, 127.7, 105.6, 73.1, 72.0, 70.6, 41.5, 40.9, 36.5, 30.5, 29.2, 24.5, 20.6, 15.4. *m*/*z* (EI, 70 eV) 286 ($M^{+\bullet}$, 4%), 195 (21) 180 (12), 178 (27), 162 (23), 159 (18), 149 (18), 135 (64), 121 (32), 107 (27), 91 (100).

*(1*R*,3*S*,4*S*)-1,5,5-Trimethyl-6-methylene-3-(phenylmethoxy)bicyclo-[2.2.2]octan-2-one* ***18***

A magnetically stirred solution of alcohol **17** (1.39 g, 4.85 mmol) in dichloromethane (48 mL) was treated with 4-methylmorpholine *N*-oxide (1.71 g, 14.6 mmol) and powdered 4 Å molecular sieves (2.4 g) then tetrapropylammonium perruthenate (85 mg, 0.243 mmol). The resulting mixture was stirred at 18°C for 2.5 h then filtered through a pad of TLC-grade silica (dichloromethane washing), and the filtrate concentrated under reduced pressure to give a brown oil. Subjection of this material to flash chromatography (1 : 9 v/v diethyl ether/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.4) afforded *ketone* ***18*** (1.36 g, 98%) as a clear, colourless oil, $[\alpha]_D$ −70.2 (*c* 2.0), (Found $[M+H]^+$ 285.1858. $C_{19}H_{24}O_2$ requires $[M+H]^+$ 285.1855). $\nu_{max}/cm^{-1}$ 1729, 1637, 1607, 1586. $\delta_H$ (300 MHz) 7.40–7.28 (5 H, complex m), 4.94 (1 H, s), 4.93 (1 H, s), 4.91 (1 H, partially obscured d), 4.76 (1 H, d, *J* 12.0), 3.84 (1 H, m), 2.04 (1 H, m), 1.93–1.66 (4 H, complex m), 1.29 (3 H, s), 1.11 (6 H, s). $\delta_C$ (75 MHz) 212.5, 156.3, 138.0, 128.3, 127.8, 127.6, 108.0, 77.6, 72.4, 51.4, 44.3, 37.0, 32.1, 30.6, 28.8, 16.7, 16.4. *m*/*z* (EI, 70 eV) 285 ($[M+H]^+$, 8%), 179 (17), 178 (48), 165 (29), 163 (49), 147 (17), 137 (55), 135 (40), 123 (20), 121 (33), 119 (15), 109 (33), 107 (22), 105 (30), 95 (63), 91 (100).

*2-Bromo-6-(*tert*-butyldiphenylsilyloxy)hex-1-ene* ***20***

A magnetically stirred solution of 9-Br-9-BBN (1.23 g, 6.12 mmol) in dry dichloromethane (30 mL) and maintained under nitrogen was cooled to 0°C then 6-*tert*-butyldiphenylsilanyloxyhex-1-yne **19**[20] (1.72 g, 5.10 mmol) was added dropwise. Stirring was continued at 0°C for 3 h then glacial acetic acid (3.4 mL) was added and stirring continued at 0°C for a further 1 h before the addition of NaOH (140 mL of a 3 M aqueous solution) and hydrogen peroxide solution (6.8 mL of a 30% aqueous solution). Stirring was continued at 18°C for 0.5 h then the mixture was extracted with hexane (2 × 75 mL). The combined extracts were washed successively with water (1 × 150 mL), $NaHCO_3$ (1 × 150 mL of a saturated aqueous solution), and brine (1 × 150 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Subjection of the resulting light-yellow oil to flash chromatography (3 : 97 v/v ethyl acetate/hexane elution) gave the *alkenyl bromide* ***20*** (1.77 g, 83%)

as a clear, colourless oil. $\delta_H$ (300 MHz) 7.75–7.66 (4 H, complex m), 7.46–7.34 (6 H, complex m), 5.54 (1 H, m), 5.39 (1 H, d, *J* 1.6), 3.68 (2 H, t, *J* 6.1), 2.42 (2 H, t, *J* 6.7), 1.69–1.52 (4 H, complex m), 1.06 (9 H, s).

*(1*R*,2*S*,3*S*,4*S*)-2-{1-[4-(*tert*-Butyldiphenylsilyloxy)butyl]vinyl}-1,5,5-trimethyl-6-methylene-3-(phenylmethoxy)bicyclo[2.2.2]octan-2-ol* ***23***

Anhydrous cerium trichloride (1.413 g, 5.732 mmol; prepared by heating the heptahydrate at 150–160°C and 1 mmHg for 12 h) maintained under argon was treated with dry THF (14 mL). The resulting slurry was stirred at 18°C for 2 h then sufficient *tert*-butyllithium (ca. 5 drops of a 1.8 M solution in pentane) was added dropwise until an orange colour persisted. The resulting mixture was cooled to −78°C. In a separate flask, a solution of the alkenyl bromide **20** (2.393 g, 5.732 mmol) in dry THF (10 mL) was cooled to −78°C and *tert*-butyllithium (5.92 mL of a 1.8 M solution, 10.65 mmol) was added dropwise. After 0.33 h this solution was rapidly cannulated into the stirred slurry of $CeCl_3$. Stirring was continued at −78°C for 0.5 h before dropwise addition of a solution of the ketone **18** (1.164 g, 4.09 mmol) in THF (4 mL). The mixture was stirred at −78°C for 2 h then allowed to warm to 18°C over 1 h before being poured into $NH_4Cl$ (50 mL of a saturated aqueous solution) and extracted with ether (2 × 50 mL). The combined extracts were washed with brine (1 × 100 mL), then dried ($MgSO_4$) and evaporated to give a pale-yellow residue. Subjection of this material to flash chromatography (hexane to 5 : 95 v/v ethyl acetate/hexane gradient elution) gave, after concentration of the appropriate fractions ($R_f$ 0.25, 2.5 : 97.5 v/v ethyl acetate/hexane), the *title alcohol* ***23*** (1.82 g, 71%) as a colourless syrup, $[\alpha]_D$ −22.1° (*c* 0.8), (Found: $M^{+\bullet}$ 622.3849. $C_{41}H_{54}O_3Si$ requires $M^{+\bullet}$ 622.3842). $\nu_{max}/cm^{-1}$ 3522, 2960, 2931, 2869, 1471, 1461, 1427, 1110, 700. $\delta_H$ (300 MHz) 7.71–7.67 (4 H, complex m), 7.45–7.27 (11 H, complex m), 4.90 (1 H, broad s), 4.86 (1 H, broad s), 4.80 (1 H, s), 4.74 (1 H, s), 4.52 (2 H, s), 3.75 (1 H, t, *J* 1.8), 3.66 (2 H, m), 2.15 (1 H, m), 2.02–1.80 (2 H, complex m), 1.66–0.80 (9 H, complex m), 1.18 (3 H, s), 1.13 (3 H, s), 1.06 (9 H, s), 0.84 (3 H, s). $\delta_C$ (75 MHz) 160.5, 154.4, 137.8, 135.5, 134.1, 129.5, 128.3, 127.9, 127.8, 127.6, 110.5, 106.8, 78.5, 71.9, 64.0, 45.0, 44.5, 42.3, 37.1, 32.9, 32.7, 32.1, 29.4, 28.2, 26.9, 25.6, 19.2, 18.9, 16.4. *m/z* (EI, 70 eV) 622 ($M^{+\bullet}$, 0.6%), 605 (1), 604 (2), 565 (12), 457 (23), 241 (27), 199 (56), 135 (58), 91 (100).

*(1*S*,2*S*,4*S*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-8,11,11-trimethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-en-3-one* ***26***

A solution of the alcohol **23** (16 mg, 0.026 mmol) in dry THF (1 mL) was cannulated into a flask containing KH (2 mg, 0.051 mmol) maintained under nitrogen and the resulting mixture heated at reflux for 0.5 h after which time TLC analysis indicated complete consumption of starting material had occurred. As a consequence, the reaction mixture was cooled to 18°C then poured into $NH_4Cl$ (10 mL of a saturated aqueous solution) and extracted into ether (2 × 10 mL). The combined extracts were washed with brine (2 × 15 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a light-yellow oil. Subjection of this material to flash chromatography (5 : 95 v/v ethyl acetate/hexane) afforded, after concentration of the appropriate fractions ($R_f$ 0.2), the *title ketone* ***26*** (14 mg, 88%) as a clear colourless oil, $[\alpha]_D$ −1.8 (*c* 1.06), (Found: $M^{+\bullet}$ 622.3850. $C_{41}H_{54}O_3Si$ requires $M^{+\bullet}$ 622.3842). $\nu_{max}/cm^{-1}$ 3400, 2931, 2858, 1702, 1460, 1427, 1111, 701. $\delta_H$ (300 MHz) 7.75–7.63 (4 H, complex m), 7.45–7.20 (11 H, complex m), 4.43 (1 H, d, *J* 11.8), 4.22 (1 H, d, *J* 11.8), 4.20 (1 H, d, *J* 5.5), 3.61 (2 H, t, *J* 6.5), 2.55 (1 H, m), 2.40–2.24 (3 H, complex m), 2.18–0.80 (12 H, complex m), 1.43 (3 H, s), 1.41 (3 H, s), 1.08 (3 H, s), 1.04 (9 H, s). $\delta_C$ (75 MHz) 216.0, 138.1, 136.1, 135.5, 134.9, 134.0, 129.5, 128.2, 127.6(3), 127.5(9), 127.5(2), 84.7, 71.1, 63.7, 55.4, 51.1, 36.1, 34.0, 33.5, 32.8, 30.0, 28.4, 27.3, 26.9, 25.4, 23.9, 20.4, 19.2, 15.6. *m/z* (EI, 70 eV) 622 ($M^{+\bullet}$, 3%), 604 (13), 514 (31), 487 (30), 458 (49), 457 (100), 445 (38), 397 (40), 389 (41), 241 (30), 199 (50), 185 (20), 135 (26), 91 (100).

*(1*S*,2*S*,4*S*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-en-3-one* ***27***

A magnetically stirred solution of freshly sublimed potassium *t*-butoxide (540 mg, 4.816 mmol) in dry ether (10 mL) was treated with a mixture of methyl iodide (stored over $CaCl_2$) (300 μL, 4.816 mmol) and alcohol **23** (600 mg, 0.963 mmol). The resulting mixture was stirred at 18°C for 5 h during which time the formation of a white precipitate was observed. The mixture was then poured into $NH_4Cl$ (20 mL of a saturated aqueous solution). The separated aqueous phase was extracted with ether (2 × 10 mL) and the combined organic extracts were washed with brine (1 × 30 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Subjection of the ensuing light-yellow oil to flash chromatography (5 : 95 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.2) afforded the *bicyclic ketone* ***27*** (505 mg, 84%) as a clear, colourless syrup, $[\alpha]_D$ −39.5° (*c* 1.4), (Found: $M^{+\bullet}$ 636.3987. $C_{42}H_{56}O_3Si$ requires $M^{+\bullet}$ 636.3999). $\nu_{max}/cm^{-1}$ 2930, 1692, 1427, 1110, 700. $\delta_H$ (300 MHz) 7.68–7.65 (4 H, complex m), 7.45–7.26 (11 H, complex m), 4.43 (1 H, d, *J* 11.8), 4.35 (1 H, d, *J* 3.4), 4.32 (1 H, d, *J* 11.8), 3.69 (2 H, t, *J* 6.4), 2.43–2.27 (2 H, complex m), 2.15 (1 H, dd, *J* 7.6 and 3.2), 2.10–1.93 (3 H, complex m), 1.85–1.50 (7 H, complex m), 1.46 (3 H, s), 1.40 (3 H, s), 1.30–1.18 (2 H, complex m), 1.05 (12 H, m), 0.84 (3 H, s). $\delta_C$ (75 MHz) 212.3, 138.4, 136.7, 135.6, 134.3, 134.1, 129.5, 128.3, 127.7, 127.6, 127.5, 76.9, 70.4, 63.8, 54.1, 49.7, 36.4, 35.1, 33.4, 31.5, 29.7, 27.5, 26.9, 25.1, 24.6, 24.2, 21.9, 19.7, 19.2, 15.9. *m/z* (EI, 70 eV) 636 ($M^{+\bullet}$, 1%), 604 (1), 579 (3), 565 (3), 471 (35), 199 (51), 135 (28), 91 (100).

*(1*R*,2*S*,3*S*,4*S*)-4-[5-(2-methoxy-1,5,5-trimethyl-6-methylene-3-(phenylmethoxy)bicyclo[2.2.2]oct-2-yl)-hex-5-enyloxy]-*tert*-butyldiphenylsilane* ***28***

A solution of alcohol **23** (92 mg, 0.148 mmol), which had been dried azeotropically using toluene, in anhydrous DME (2 mL) was treated with methyl iodide (14 μL, 0.222 mmol) and the resulting mixture transferred, via cannula, into a sealable vial fitted with a septum and containing KH (7.1 mg, 0.177 mmol). The vial was sealed and the mixture heated at 50°C for 2 h. After cooling, the mixture was poured into $NH_4Cl$ (10 mL of a saturated aqueous solution) and extracted with ether (2 × 10 mL). The combined extracts were washed with brine (1 × 20 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow residue was subjected to flash chromatography (5 : 95 v/v to 1 : 9 ethyl acetate/hexane gradient elution) thus affording two fractions, A and B.

Concentration of fraction A ($R_f$ 0.2 in 5 : 95 v/v ethyl acetate/hexane elution) gave the C-*alkylated compound* ***27*** (42 mg, 45%) which was identical, in all respects, with the material obtained as described above.

Concentration of fraction B ($R_f$ 0.33 in 5 : 95 v/v ethyl acetate/hexane) gave the *title ether* ***28*** (19 mg, 20%) as a clear, colourless syrup, $[\alpha]_D$ −8.4° (*c* 1.0), (Found: $M^{+\bullet}$ 636.3988. $C_{42}H_{56}O_3Si$ requires $M^{+\bullet}$ 636.3999). $\nu_{max}/cm^{-1}$ 2958, 2931, 1471, 1462, 1427, 1110, 1100, 700. $\delta_H$ (300 MHz) 7.70–7.67 (4 H, complex m), 7.44–7.26 (11 H, complex m), 5.09 (1 H, broad s), 4.87 (1 H, broad s), 4.76 (1 H, s), 4.59 (1 H, s), 4.57 (1 H, d, *J* 12.0), 4.40 (1 H, d, *J* 12.0), 3.91 (1 H, broad s), 3.66 (2 H, t, *J* 6.2), 3.48 (3 H, s), 2.06 (1 H, m), 2.00–1.43 (10 H, complex m), 1.18 (3 H, s), 1.12 (3 H, s), 1.07 (9 H, s), 0.85 (3 H, s). $\delta_C$ (75 MHz) 160.9, 148.4, 139.1, 135.6, 134.1, 129.5, 128.1, 127.8, 127.6, 127.4, 114.1, 106.8, 84.8, 78.5, 71.3, 63.9, 57.3, 45.9, 41.6, 36.9, 33.1, 32.8, 31.7, 29.6, 28.4, 26.9, 25.4, 20.0, 19.2, 16.3. *m/z* (EI, 70 eV) 636 ($M^{+\bullet}$, 3%), 604 (3), 199 (58), 183 (23), 135 (41), 91 (100).

*(1*S*,2*S*,4*S*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-ene-3,9-dione* ***29*** *and (1*S*,2*S*,4*S*,7*S*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-7-hydroxy-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-8-en-3-one* ***30***

A magnetically stirred suspension of chromium trioxide (53 mg, 0.534 mmol) in dry dichloromethane (4 mL) was cooled to −20°C and 3,5-dimethylpyrazole (58 mg, 0.534 mmol) was added. After stirring the reaction mixture for 0.33 h at −20°C it had become homogeneous

and brick-red in colour. A solution of the bicyclic ketone **26** (17 mg, 0.0267 mmol) in dry dichloromethane (1 mL) was then added dropwise and the temperature maintained between −15 and −10°C for 5 h, after which time most of the starting material had been consumed as judged by TLC analysis. Consequently, the reaction mixture was quenched, at −15 to −20°C, by addition of NaOH (2 mL of a 5 M aqueous solution) with vigorous stirring of the resultant mixture in an ice-bath for 0.5 h. The separated aqueous phase was extracted with ether (3 × 5 mL) and the combined organic phases was washed with HCl (1 × 15 mL of a 1 M aqueous solution) and brine (1 × 15 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography (3 : 97 to 1 : 4 v/v ethyl acetate/hexane gradient elution) affording two fractions, A and B.

Concentration of the fraction A ($R_f$ 0.5) gave the *endione* ***29*** (3 mg, 17%) as a clear, colourless syrup, $[\alpha]_D$ −76.3° (*c* 0.9), (Found: $M^{+\bullet}$ 650.3797. $C_{42}H_{54}O_4Si$ requires $M^{+\bullet}$ 650.3791). $\nu_{max}/cm^{-1}$ 2929, 1695, 1668, 1111, 701. $\delta_H$ (300 MHz) 7.68–7.64 (4 H, complex m), 7.45–7.25 (11 H, complex m), 4.50 (1 H, d, *J* 3.4), 4.41 (1 H, d, *J* 11.5), 4.27 (1 H, d, *J* 11.5), 3.69 (2 H, t, *J* 6.3), 3.11 (1 H, d, *J* 19.5), 2.63 (1 H, dd, *J* 19.5, 6.6), 2.60–2.45 (2 H, complex m), 2.28 (1 H, d, *J* 13.6), 2.13 (1 H, m), 1.81 (1 H, m), 1.75–0.80 (6 H, complex m), 1.67 (3 H, s), 1.50 (3 H, s), 1.30 (1 H, m), 1.14 (3 H, s), 1.05 (9 H, s), 0.92 (3 H, s). $\delta_C$ (75 MHz) 212.8, 198.6, 157.3, 137.8, 135.8, 135.5(5), 135.5(2), 134.0, 129.6, 128.4, 127.8, 127.7, 127.6, 75.7, 70.5, 63.5, 50.0, 49.9, 37.3, 35.1, 33.8, 33.2, 31.9, 31.5, 26.9, 26.1, 24.9, 24.5, 19.5, 19.2, 14.6. *m*/*z* (EI, 70 eV) 650 ($M^{+\bullet}$, 2%), 607 (3), 593 (32), 270 (24), 199 (44), 179 (32), 135 (32), 91 (100).

Concentration of fraction B ($R_f$ 0.4) afforded *compound* ***30*** (2 mg, 11%) as a clear colourless oil (Found: $[M - H_2O]^{+\bullet}$ 634.3849. $C_{42}H_{56}O_4Si$ requires $[M - H_2O]^{+\bullet}$ 634.3842). $\nu_{max}/cm^{-1}$ 3540, 2929, 1703, 1111, 701. $\delta_H$ (300 MHz) 7.67–7.64 (4 H, complex m), 7.42–7.26 (11 H, complex m), 5.32 (1 H, broad m), 4.70 (1 H, d, *J* 1.8), 4.44 (1 H, d, *J* 11.8), 4.21 (1 H, d, *J* 11.8), 3.69 (2 H, t, *J* 6.3), 2.50 (1 H, m), 2.20–0.80 (3 H, complex m), 1.72 (3 H, broadened s), 1.28 (3 H, s), 1.08 (3 H, s), 1.04 (9 H, s), 0.87 (3 H, s). *m*/*z* (EI, 70 eV) 634 ($[M - H_2O]^{+\bullet}$, 0.3%), 595 (0.5), 409 (10), 199 (40), 135 (22), 133 (21), 91 (100).

*(1*R*,3a*S*,4*R*,7*S*,8*S*,8a*R*)-1-[(4-*tert*-Butyldiphenylsilyloxy)butyl]-hexahydro-1,4,9,9-tetramethyl-8-(phenylmethoxy)-1*H*-3a,7-methanoazulen-4,8a-oxide* ***31***

A magnetically stirred solution of the silyl ether **27** (15 mg, 0.0235 mmol) in $CDCl_3$ (0.5 mL) was treated with $SnCl_2 \cdot 2H_2O$ (0.3 mg, 0.0012 mmol) and the resulting mixture stirred at 18°C for 1 h after which time $^1$H NMR analysis showed efficient formation of the oxetane **31**. No further change was observed on standing at 18°C for 48 h. At this time the reaction mixture was poured into $NaHCO_3$ (10 mL of a saturated aqueous solution) and extracted with diethyl ether (2 × 10 mL). The combined extracts were washed with brine (2 × 10 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give essentially pure *oxetane* ***31*** (14 mg, 93%) as a clear, colourless syrup, $[\alpha]_D$ 0.0° (*c* 1.0), $R_f$ 0.25 (1 : 9 v/v ethyl acetate/hexane). $\delta_H$ (300 MHz) 7.74–7.71 (4 H, complex m), 7.46–7.26 (11 H, complex m), 4.66 (1 H, d, *J* 12.0), 4.37 (1 H, d, *J* 12.0), 3.99 (1 H, d, *J* 5.6), 3.69 (2 H, m), 2.40–2.26 (3 H, complex m), 1.93–1.87 (2 H, complex m), 1.73 (2 H, m), 1.66–1.05 (8 H, complex m), 1.24 (3 H, s), 1.10 (9 H, s), 1.01 (3 H, s), 0.94 (3 H, s), 0.77 (3 H, s). $\delta_C$ (75 MHz) 138.4, 135.6, 134.3(1), 134.2(6), 129.4, 128.5, 128.1, 127.5, 96.9, 84.3, 75.8, 71.5, 64.1, 63.1, 50.7, 45.3, 44.2, 37.4, 35.0, 34.1, 33.6, 27.3, 26.9, 23.4, 21.4, 21.3, 20.9, 20.5, 19.2, 17.2. *m*/*z* (EI, 70 eV) 579 ($[M - C_4H_9^{\bullet}]^+$, 1%), 561(2), 528 (2), 501 (2), 471 (38), 411 (24), 255 (18), 199 (50), 91 (100).

*(1*R*,3a*R*,7*S*,8*S*,8a*R*)-1-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-2,3,7,8-tetrahydro-1,4,9,9-tetramethyl-8-(phenylmethoxy)-1*H*-3a,7-methanoazulen-8a(6*H*)-ol* ***32***

A solution of the bicyclic silyl ether **27** (240 mg, 0.377 mmol) in sodium-dried xylene (3 mL) was heated at reflux for 3 h then cooled to 18°C and concentrated under reduced pressure. Subjection of the resulting yellow oil to flash chromatography (5 : 95 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.4) gave the *tricyclic alcohol* ***32*** (231 mg, 96%) as a colourless syrup, $[\alpha]_D$ −7.8° (*c* 1.2), (Found: $M^{+\bullet}$ 636.3991. $C_{42}H_{56}O_3Si$ requires $M^{+\bullet}$ 636.3999). $\nu_{max}/cm^{-1}$ 3540 (br), 2930, 1471, 1453, 1428, 1101, 700. $\delta_H$ (300 MHz) 7.69–7.66 (4 H, complex m), 7.41–7.26 (11 H, complex m), 5.34 (1 H, broad m), 4.55 (1 H, d, *J* 11.5), 4.44 (1 H, d, *J* 11.5), 4.13 (1 H, d, *J* 5.6), 3.67 (2 H, t, *J* 6.3), 3.10 (1 H, broad s), 2.36 (1 H, broad d, *J* 17.1), 2.05–1.89 (2 H, complex m), 1.88–1.67 (2 H, complex m), 1.63–1.20 (11 H, complex m), 1.04 (12 H, s), 1.02 (3 H, s), 0.99 (3 H, s). $\delta_C$ (75 MHz) 141.5, 138.4, 135.6, 134.2, 129.4, 128.3, 127.7, 127.5, 120.4, 92.3, 81.1, 71.9, 66.2, 64.1, 47.7, 46.8, 39.8, 39.5, 38.5, 33.9, 27.6, 26.9, 25.3, 24.4, 23.0, 22.9, 22.7, 22.4, 19.2 (one resonance obscured or overlapping). *m*/*z* (EI, 70 eV) 636 ($M^{+\bullet}$, 2.5%), 618 (1), 579 (5), 528 (50), 471 (52), 459 (34), 411 (31), 403 (24), 199 (63), 135 (64), 91 (100).

*(1*S*,2*S*,4*S*,9*R*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-9-hydroxy-4,8,11,11-tetramethylbicyclo[5.3.1]undec-7-en-3-one* ***34****, (1*S*,2*S*,4*S*,9*R*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-9-hydroxy-4,8,-11,11-tetramethyl-2-oxobicyclo[5.3.1]undec-7-en-2-yl Benzoate* ***35****, and (1*S*,2*S*,4*S*,9*R*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-2,9-dihydroxy-4,8,11,11-tetramethylbicyclo[5.3.1]undec-7-en-3-one* ***36***

*Method A*

A mixture of tricyclic alcohol **32** (106 mg, 0.166 mmol) and anhydrous potassium carbonate (50 mg) was cooled in an ice-salt bath and an ice-cold solution of dimethyldioxirane (ca. 0.01 M in acetone, 5.0 mL, 0.499 mmol) was added slowly. The resulting mixture was stirred at ca. −20°C for 8 h then warmed to 18°C, filtered, and the filtrate concentrated under reduced pressure. The residue was taken up in dry toluene (5 mL) and the resulting solution heated at reflux for 2 h. The cooled reaction mixture was then subjected to flash chromatography (1 : 4 to 1 : 1 v/v ethyl acetate/hexane gradient elution) affording two fractions, A and B.

Concentration of fraction A ($R_f$ 0.3 in 1 : 4 v/v ethyl acetate/ hexane) gave *compound* ***34*** (66 mg, 61%) as a clear, colourless syrup, $[\alpha]_D$ −6.6° (*c* 0.8), (Found: $M^{+\bullet}$ 652.3930. $C_{42}H_{56}O_4Si$ requires $M^{+\bullet}$ 652.3948). $\nu_{max}/cm^{-1}$ 3535, 2930, 1682, 1454, 1110, 701. $\delta_H$ (300 MHz) 7.67–7.62 (4 H, complex m), 7.45–7.24 (11 H, complex m), 4.41 (1 H, d, *J* 11.8), 4.41 (1 H, d, *J* 3.3), 4.35 (1 H, d, *J* 11.8), 4.03 (1 H, broad d, *J* 10.2), 3.70 (2 H, t, *J* 6.2), 2.60 (1 H, m), 2.43–0.80 (3 H, complex m), 1.70 (3 H, s), 1.39 (3 H, s), 1.05 (9 H, s), 0.93 (3 H, s), 0.84 (3 H, s). $\delta_C$ (75 MHz) 217.9, 137.9, 137.4, 135.5, 134.0, 129.5, 128.4, 127.7(8), 127.7(5), 127.6, 70.5, 67.3, 63.6, 50.6, 50.3, 36.4, 33.3, 33.2, 31.5, 30.4, 30.3, 29.3, 26.9, 24.9, 24.7, 24.4, 19.6, 19.2, 17.5 (one resonance obscured or overlapping). *m*/*z* (EI, 70 eV) 652 ($M^{+\bullet}$, 0.7%), 634 (2.4), 593 (3), 577 (6), 543 (7), 487 (26), 459 (40), 295 (21), 233 (27), 199 (66), 164 (40), 135 (81), 91 (100).

Concentration of fraction B ($R_f$ 0.1 in 1 : 4 v/v ethyl acetate/hexane) gave *compound* ***36*** (28 mg, 30%) as a clear, colourless syrup, $[\alpha]_D$ +9.1° (*c* 1.2), (Found: $[M - C_4H_9^{\bullet}]^+$ 505.2772. $C_{35}H_{50}O_4Si$ requires $[M - C_4H_9^{\bullet}]^+$ 505.2774). $\nu_{max}/cm^{-1}$ 3536, 3434, 2931, 1673, 1111, 701. $\delta_H$ (300 MHz) 7.69–7.65 (4 H, complex m), 7.45–7.26 (6 H, complex m), 4.62 (1 H, d, *J* 3.7), 4.03 (1 H, broad d, *J* 10.6), 3.71 (2 H, t, *J* 6.3), 2.60 (1 H, m), 2.38 (1 H, m), 2.20–1.05 (13 H, complex m), 1.71 (3 H, s), 1.47 (3 H, s), 1.06 (9 H, s), 0.96 (3 H, s), 0.94 (3 H, s). $\delta_C$ (75 MHz) 222.7, 138.4, 135.5, 135.0, 134.0, 129.5, 127.6, 70.2, 67.1, 63.6, 53.0, 50.5, 36.6, 33.3, 32.8, 31.0, 30.2, 28.7, 26.8, 24.8, 24.6, 19.5, 19.2, 17.5 (one resonance obscured or overlapping). *m*/*z* (EI, 70 eV) 505 ($[M - C_4H_9^{\bullet}]^+$, 12%), 487 (66), 409 (28), 295 (32), 271 (37), 233 (35), 199 (100), 135 (81).

*Method B*

A mixture of the tricyclic alcohol **32** (216 mg, 0.339 mmol) and anhydrous potassium carbonate (200 mg) was cooled in an ice-salt bath then an ice-cold solution of dimethyldioxirane (ca. 0.01 M in acetone, 17.0 mL, 1.69 mmol) was added slowly. The resulting mixture was stirred at 0°C for 24 h then filtered, and the filtrate concentrated under reduced pressure. The ensuing residue was taken up in toluene (10 mL) and the resulting solution heated at reflux for 2 h then cooled to 18°C and concentrated under reduced pressure. The resulting yellow residue was

subject to flash chromatography (1 : 4 to 2 : 3 v/v ethyl acetate/hexane gradient elution) thus giving three fractions A–C.

Concentration of fraction A [$R_f$ 0.3(2) in 1 : 4 v/v ethyl acetate/hexane] afforded the allylic alcohol **34** (22 mg, 10%) identical, in all respects, with the material obtained as described above.

Concentration of fraction B ($R_f$ 0.3 in 1 : 4 v/v ethyl acetate/hexane) afforded the *benzoate* ***35*** (34 mg, 15%) as a clear colourless oil, $[\alpha]_D$ +8.3° (*c* 0.94), (Found: $[M - H_2O]^{+\bullet}$ 648.3637. $C_{42}H_{54}O_5Si$ requires $[M - H_2O]^{+\bullet}$ 648.3635). $\nu_{max}/cm^{-1}$ 3541, 2931, 1720, 1688, 1272, 1111, 707. $\delta_H$ (300 MHz) 8.08 (2 H, m), 7.69–7.65 (4 H, complex m), 7.58 (1 H, m), 7.47–7.34 (8 H, complex m), 6.03 (1 H, d, *J* 3.4), 4.10 (1 H, broad m), 3.69 (2 H, t, *J* 6.4), 2.69 (1 H, m), 2.50–2.12 (5 H, complex m), 1.85–0.82 (8 H, complex m), 1.75 (3 H, s), 1.58 (3 H, s), 1.04 (9 H, s), 1.03 (3 H, s), 0.97 (3 H, s). $\delta_C$ (75 MHz) 215.0, 165.1, 137.5, 135.9, 135.6, 134.0, 134.1, 133.3, 129.8, 129.5, 128.4, 127.6, 71.6, 67.1, 63.6, 50.9, 50.8, 36.7, 33.4, 33.3, 31.8, 30.2, 29.7, 26.9, 24.9, 24.7, 24.6, 19.6, 19.2, 17.6. *m/z* (EI, 70 eV) 648 ($[M - H_2O]^{+\bullet}$, 0.4%), 609 (2), 591 (3), 588 (3), 531 (5), 487 (24), 469 (15), 303 (26), 199 (39), 135 (25), 105 (100).

Concentration of fraction C ($R_f$ 0.1 in 1 : 4 v/v ethyl acetate/hexane) afforded the diol **36** (124 mg, 65%) identical, in all respects, with the material obtained as described above.

*Method C*

Treatment of the tricyclic alcohol **32** (76 mg, 0.119 mmol) with dimethyldioxirane (ca. 0.01 M in acetone, 11.6 mL, 1.162 mmol) in the presence of dry potassium carbonate (200 mg) at 0°C for 20 h followed by thermolysis in boiling toluene, as above, gave a light-yellow oil on work-up. Subjection of this material to flash chromatography (1 : 4 to 1 : 1 v/v ethyl acetate/hexane gradient elution) afforded two fractions A and B.

Concentration of fraction A ($R_f$ 0.3 in 1 : 4 v/v ethyl acetate/hexane) gave *compound* ***34*** (19 mg, 25%) which was identical, in all respects, with the material obtained as described above.

Concentration of fraction B ($R_f$ 0.1 in 1 : 4 v/v ethyl acetate/hexane) gave *compound* ***36*** (37 mg, 57%) which was identical, in all respects, with the material obtained as described above.

*(1*S*,2*S*,4*S*)-4-[4-(*tert*-Butyldiphenylsilyloxy)butyl]-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]-undec-7-ene-3,9-dione* ***29*** *(from* ***34****)*

A magnetically stirred solution of the alcohol **34** (66 mg, 0.101 mmol) in dry dichloromethane (10 mL) was treated with *N*-methylmorpholine-*N*-oxide (18 mg, 0.152 mmol) and 4 Å molecular sieves (50 mg). The resulting mixture was stirred at 18°C for 0.25 h then treated with tetrapropylammonium perruthenate (3.6 mg, 0.0101 mmol). The ensuing mixture was stirred at 18°C for 3 h then filtered through a pad of TLC-grade silica gel and the solids thus retained washed with ethyl acetate (10 mL). The combined filtrates were concentrated under reduced pressure and the residue subject to flash chromatography (1 : 4 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions ($R_f$ 0.3) gave the enone **29** (64 mg, 97%) as a clear, colourless syrup which was identical, in all respects, with the material obtained previously.

*(1*S*,2*S*,4*S*)-4-(4-Hydroxybutyl)-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-en-3-one* ***37***

A magnetically stirred solution of the silyl ether **27** (474 mg, 0.761 mmol) in dry THF (35 mL) was treated with TBAF (1.52 mL of a 1.0 M in THF, 1.52 mmol) and the resulting mixture stirred at 18°C for 3 h. The reaction mixture was poured into $NH_4Cl$ (50 mL of a saturated aqueous solution) and extracted with ether (2 × 100 mL). The combined organic extracts were washed with brine (2 × 50 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The light-yellow residue thus obtained was subjected to flash chromatography (2 : 3 v/v ethyl acetate/hexane elution) giving, after concentration of the appropriate fractions ($R_f$ 0.5), the *title alcohol* ***37*** (301 mg, 99%) as a clear, colourless oil (Found: $M^{+\bullet}$ 398.2824. $C_{26}H_{38}O_3$ requires $M^{+\bullet}$ 398.2821). $\delta_H$ (300 MHz) 7.33–7.26 (5 H, complex m), 4.42 (1 H, d, *J* 11.8), 4.35 (1 H, d, *J* 3.9), 4.32 (1 H, d, *J* 11.8), 3.68 (2 H, t, *J* 6.5), 2.38 (2 H, m), 2.16 (1 H, m), 2.08–1.94 (2 H, complex m), 1.83–1.15 (11 H, complex m), 1.51 (3 H, s), 1.40 (3 H, s), 1.06 (3 H, s), 0.88 (3 H, s). $\delta_C$ (75 MHz) 212.4, 138.3, 136.7, 134.4, 128.3, 127.7, 127.6, 76.9, 70.4, 62.8, 54.0, 49.6, 36.3, 35.7, 33.4, 31.8, 29.7, 27.5, 25.0, 24.5, 24.2, 21.8, 19.9, 15.9. *m/z* (EI, 70 eV) 398 ($M^{+\bullet}$, 3%), 307 (7), 290 (18), 165 (53), 137 (67), 135 (53), 121 (38), 109 (38), 105 (38), 95 (71), 91 (100).

*(1*S*,2*S*,4*S*)-4-{4,10,11,11-Tetramethyl-5-oxo-6-(phenylmethoxy)bicyclo[5.3.1]undec-7-en-4-yl}butyraldehyde* ***38***

A magnetically stirred solution of alcohol **37** (269 mg, 0.675 mmol) in dry dichloromethane (60 mL) was treated with Dess–Martin periodinane (429 mg, 1.012 mmol) and the resulting mixture stirred at 18°C for 2 h then treated with $NaHCO_3$ (50 mL of a saturated aqueous solution) and $Na_2S_2O_3$ (50 mL of a saturated aqueous solution). The resulting mixture was stirred vigorously until all suspended solids were dissolved. The organic layer was then separated and the aqueous phase extracted with dichloromethane (2 × 50 mL). The combined organic phases were washed with brine (2 × 100 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1 : 3 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.4) gave the *aldehyde* ***38*** (224 mg, 84%) as a colourless, crystalline solid, mp 78–80°C, $[\alpha]_D$ −87.4° (*c* 0.9), (Found: $M^{+\bullet}$ 396.2662. $C_{26}H_{36}O_3$ requires $M^{+\bullet}$ 396.2664). $\nu_{max}/cm^{-1}$ 2931, 1724, 1693, 1455, 1101, 734. $\delta_H$ (300 MHz) 9.80 (1 H, t, *J* 1.4), 7.33–7.25 (5 H, complex m), 4.42 (1 H, d, *J* 11.9), 4.35 (1 H, d, *J* 2.9), 4.33 (1 H, d, *J* 11.9), 2.57–2.30 (4 H, complex m), 2.18–1.92 (4 H, complex m), 1.73–1.20 (7 H, complex m), 1.47 (3 H, s), 1.40 (3 H, s), 1.05 (3 H, s), 0.88 (3 H, s). $\delta_C$ (75 MHz) 212.0, 202.6, 138.3, 136.7, 134.5, 128.3, 127.7, 127.6, 76.8, 70.5, 54.0, 49.6, 44.6, 36.3, 35.5, 31.7, 29.7, 27.4, 25.0, 24.4, 24.1, 21.9, 16.4, 15.9. *m/z* (EI, 7 eV) 396 ($M^{+\bullet}$, 4%), 305 (7), 288 (20), 256 (28), 165 (64), 137 (65), 135 (51), 121 (40), 109 (32), 95 (80), 91 (100).

*(1*S*,4*R*)-4-(4-Hydroxybutyl)-4,8,11,11-tetramethylbicyclo[5.3.1]-undec-7-en-3-one* ***39*** *and (1*R*,3a*R*,7*S*,8*S*,8a*R*)-4-(4-Hydroxybutyl)-1,4,9,9-tetramethyl-2,3,7,8-tetrahydro-8-(phenylmethoxy)-1*H*-3a,7-methanoazulen-8a(6*H*)-ol* ***40***

Lithium bromide (42 mg), which had been dried at 18°C and 1 mm Hg for 5 h, was dissolved in dry THF (200 mL) and the resulting solution was deoxygenated by the freeze-pump-thaw method (3 cycles and using nitrogen as replacement gas). Freshly prepared $SmI_2$ (611 μL of a 0.1 M solution in THF, 0.061 mmol) was added, followed by a deoxygenated solution of the keto-aldehyde **38** (11 mg, 0.0278 mmol). Since the blue colour of $SmI_2$ was discharged before addition of the substrate was complete additional quantities of this reagent (2 mL of a 0.1 M solution in THF, 0.2 mmol) were added until a blue colour persisted. The resulting mixture was allowed stir for 16 h at 18°C then quenched by addition of $Na_2S_2O_3$ (3 mL of a 2 M aqueous solution) and extracted with ether (2 × 10 mL). The combined organic phases was washed with brine (2 × 20 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (1 : 4 to 2 : 3 v/v ethyl acetate/hexane gradient elution) thus giving two fractions, A and B.

Concentration of fraction A ($R_f$ 0.5 in 1 : 4 v/v ethyl acetate/hexane) gave a clear colourless oil tentatively identified as *compound* ***39*** (1 mg, 12%) (Found: $M^{+\bullet}$ 292.2395. $C_{19}H_{32}O_2$ requires $M^{+\bullet}$ 292.2402). $\nu_{max}/cm^{-1}$ 3400, 2980, 1676, 1459, 1373, 1039. $\delta_H$ (300 MHz) 3.67 (2 H, m), 2.92 (1 H, dd, *J* 11.9 and 2.6), 2.38 (1 H, m), 2.24–0.80 (16 H, complex m), 1.48 (3 H, s), 1.39 (3 H, s), 1.04 (3 H, s), 0.92 (3 H, s). *m/z* (EI, 70 eV) 292 ($M^{+\bullet}$, 47%), 274 (11), 220 (37), 219 (38), 201 (33), 178 (100), 163 (50), 135 (66), 121 (76), 107 (60), 91 (49).

Concentration of fraction B ($R_f$ 0.3 in 1 : 4 v/v ethyl acetate/hexane) gave *compound* ***40*** (7 mg, 63%) as a clear, colourless syrup, $[\alpha]_D$ + 36.7° (*c* 0.55), (Found: $[M - CH_3^{\bullet}]^+$ 385.2730. $C_{26}H_{38}O_3$ requires $[M - CH_3^{\bullet}]^+$ 385.2743). $\nu_{max}/cm^{-1}$ 3400, 2942, 1464, 1067. $\delta_H$ (300 MHz) 7.38–7.26 (5 H, complex m), 4.58 (1 H, d, *J* 11.4), 4.52

(1 H, d, *J* 11.4), 4.07 (1 H, d, *J* 5.0), 3.66 (3 H, m), 3.40 (1 H, broad s), 2.40 (1 H, m), 2.03 (1 H, m), 1.90–0.80 (12 H, complex m), 1.13 (3 H, s), 1.01 (3 H, s), 0.99 (3 H, s), 0.89 (3 H, s). $\delta_C$ (75 MHz) 138.2, 128.6, 128.1, 90.9, 80.5, 71.7, 62.8, 61.6, 47.2, 47.1, 41.6, 38.7, 38.0, 34.9, 33.4, 29.2, 28.5, 26.2, 25.7, 22.9, 22.1, 20.6, 18.7 (one resonance obscured or overlapping). *m*/*z* (EI, 70 eV) 385 ([M − $CH_3^•$]$^+$, 2%), 309 (31), 294 (26), 292 (29), 279 (29), 149 (23), 109 (30), 107 (31), 95 (35), 91 (100).

*(1*S*,2*S*,4*S*)-4-(4-Hydroxybutyl)-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-ene-3,9-dione* ***43***

A magnetically stirred solution of the silyl ether **29** (15 mg, 0.0235 mmol) in dry THF (2 mL) was treated with TBAF (35 mL of a 1.0 M solution in THF, 0.035 mmol) and the resulting mixture stirred at 18°C for 1 h then poured into $NH_4Cl$ (5 mL of a saturated aqueous solution) and extracted twice with ether (3 × 10 mL). The combined organic extracts were washed with brine (2 × 30 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting light-yellow oil was subjected to flash chromatography (4 : 1 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.4) gave the *alcohol* ***43*** (9 mg, 93%) as a clear, colourless oil, $[\alpha]_D$ −16.0° (*c* 1.06), (Found: $M^{+•}$ 412.2610. $C_{26}H_{36}O_4$ requires $M^{+•}$ 412.2614). $\nu_{max}/cm^{-1}$ 3402, 2924, 1693, 1662, 1454, 1072. $\delta_H$ (300 MHz) 7.36–7.26 (5 H, complex m), 4.50 (1 H, d, *J* 3.2), 4.41 (1 H, d, *J* 11.6), 4.28 (1 H, d, *J* 11.6), 3.68 (2 H, t, *J* 6.3), 3.12 (1 H, d, *J* 19.5), 2.67–2.47 (3 H, complex m), 2.30 (1 H, broad d, *J* 14.3), 2.16 (1 H, m), 1.83 (1 H, m), 1.75–0.80 (7 H, complex m), 1.71 (3 H, s), 1.50 (3 H, s), 1.14 (3 H, s), 0.95 (3 H, s). $\delta_C$ (75 MHz) 212.9, 198.6, 157.4, 137.7, 135.8, 128.4, 127.8, 127.7, 75.7, 70.6, 62.5, 50.0, 49.8, 37.3, 35.0, 33.7, 33.2, 32.2, 31.8, 26.1, 24.7, 24.5, 19.7, 14.6. *m*/*z* (EI, 70 eV) 412 ($M^{+•}$, 0.8%), 369 (0.8), 321 (7), 293 (13), 270 (30), 179 (51), 91 (100).

*(1*S*,2*S*,4*S*)-4-(4-Bromobutyl)-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-ene-3,9-dione* ***44***

A magnetically stirred solution of the alcohol **43** (9 mg, 0.0218 mmol) in dry dichloromethane (2 mL) was treated with $Ph_3P \cdot Br_2$ (327 μL of a 0.1 M solution in dichloromethane, 0.0327 mmol) and the resulting mixture was stirred at 18°C for 1 h and then poured into water and extracted with dichloromethane (2 × 10 mL). The combined organic extracts were washed with brine (2 × 40 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The ensuing light-yellow oil was subjected to flash chromatography (1 : 3 v/v ethyl acetate/hexane elution) and concentration of the appropriate fractions ($R_f$ 0.5) afforded the *alkyl bromide* ***44*** (10 mg, 96%) as a clear, colourless oil (Found: $M^{+•}$ 474.1767. $C_{26}H_{35}{}^{79}BrO_3$ requires $M^{+•}$ 474.1770). $\nu_{max}/cm^{-1}$ 2924, 1694, 1666, 1454, 1098, 1068. $\delta_H$ (300 MHz) 7.37–7.27 (5 H, complex m), 4.50 (1 H, d, *J* 3.3), 4.41 (1 H, d, *J* 11.5), 4.29 (1 H, d, *J* 11.5), 3.46 (2 H, t, *J* 6.4), 3.12 (1 H, d, *J* 19.5), 2.68–2.48 (3 H, complex m), 2.33 (1 H, broad d, *J* 14.3), 2.17 (1 H, m), 1.95–1.79 (3 H, complex m), 1.72 (3 H, s), 1.72–0.80 (4 H, m), 1.51 (3 H, s), 1.15 (3 H, s), 0.95 (3 H, s). $\delta_C$ (75 MHz) 212.7, 198.5, 157.3, 137.7, 135.8, 128.4, 127.9, 127.7, 75.6, 70.6, 49.9, 49.8, 37.3, 35.1, 33.9, 33.7, 32.9, 32.1, 30.9, 26.1, 24.8, 24.5, 21.7, 14.6. *m*/*z* (EI, 70 eV) 476 and 474 ($M^{+•}$, both 3%), 433 (3) and 431 (3), 385 (32) and 383 (32), 357 (97) and 355 (100), 270 (40), 179 (61), 91 (100).

*(1*S*,2*S*,4*S*)-4-(4-Iodobutyl)-4,8,11,11-tetramethyl-2-(phenylmethoxy)bicyclo[5.3.1]undec-7-ene-3,9-dione* ***45***

A magnetically stirred solution of the alkyl bromide **44** (9 mg, 0.0189 mmol) in acetone (2 mL) was treated with anhydrous sodium iodide (11 mg, 0.0757 mmol) and the resulting mixture heated at reflux for 4 h. The cooled reaction mixture was concentrated under reduced pressure and the residue partitioned between ether (5 mL) and $Na_2S_2O_3$ (5 mL of a ca. 0.1 M aqueous solution). The separated organic phase was washed with brine (1 × 5 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give *alkyl iodide* ***45*** (9 mg, 91%) as a clear, colourless, but unstable oil. $\delta_H$ (300 MHz) 7.37–7.25 (5 H, complex m), 4.51 (1 H, d, *J* 3.3), 4.41 (1 H, d, *J* 11.5), 4.29 (1 H, d, *J* 11.5), 3.24 (2 H, t, *J* 6.6), 3.11 (1 H, d, *J* 19.5), 2.68–2.49 (3 H, complex m), 2.33 (1 H, broad d, *J* 14.2), 2.17 (1 H, m), 1.90–1.20 (7 H, complex m), 1.72 (3 H, s), 1.51 (3 H, s), 1.15 (3 H, s), 0.95 (3 H, s).

*(1*S*,2*S*,4*S*,9*R*)-2,9-Dihydroxy-4-(4-hydroxybutyl)-4,8,11,11-tetramethylbicyclo[5.3.1]undec-7-en-3-one* ***48***

A magnetically stirred solution of the diol **36** (60 mg, 0.107 mmol) in dry THF (5 mL) was treated with TBAF (1.0 M solution in THF, 320 μL, 0.320 mmol), the resulting mixture stirred at 18°C for 5 h then poured into ammonium chloride (10 mL of a saturated aqueous solution) and extracted with ethyl acetate (4 × 20 mL). The combined extracts were washed with brine (1 × 15 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was subjected to flash chromatography (ethyl acetate elution) to give, after concentration of the appropriate fractions ($R_f$ 0.4), the *triol* ***48*** (33 mg, 95%) as a clear, colourless oil, $[\alpha]_D$ +17.8° (*c* 1.4), (Found: $M^{+•}$ 324.2302. $C_{19}H_{32}O_4$ requires $M^{+•}$ 324.2301). $\nu_{max}/cm^{-1}$ 3400, 2940, 1675, 1461, 1408, 1011, 731. $\delta_H$ (300 MHz) 4.60 (1 H, d, *J* 3.7), 4.01 (1 H, broad d, *J* 10.6), 3.67 (2 H, t, *J* 6.5), 2.59 (1 H, m), 2.43–1.20 (5 H, complex m), 1.72 (3 H, s), 1.45 (3 H, s), 0.97 (3 H, s), 0.92 (3 H, s). $\delta_C$ (75 MHz) 222.5, 138.4, 135.0, 70.2, 67.1, 62.6, 53.0, 50.4, 36.6, 33.3, 33.0, 31.2, 30.1, 28.6, 24.7, 24.6, 19.7, 17.5, 17.4. *m*/*z* (EI, 70 eV) 324 ($M^{+•}$, 3%), 306 (6), 291 (10), 233 (17), 211 (23), 149 (26), 137 (35), 136 (32), 135 (100), 133 (46), 121 (45).

*Oxidations of Triol* ***54****. Formation of (1*S*,2*S*,4*S*)-2-Hydroxy-4-(4-hydroxybutyl)-4,8,11,11-tetramethylbicyclo[5.3.1]undec-7-ene-3,9-dione* ***49*** *and (1*S*,2*S*,4*R*)-4-{2-Hydroxy-4,8,11,11-tetramethyl-5,9-dioxobicyclo[5.3.1]undec-7-en-4-yl}butyraldehyde* ***50***

*Method A*

A magnetically stirred solution of the triol **48** (11 mg, 0.0339 mmol) in dry dichloromethane (2 mL) maintained at 0°C was treated with the Dess–Martin periodinane (14.4 mg, 0.0339 mmol) and the resulting mixture stirred at 0°C for 1 h. The reaction mixture was then quenched by the successive addition of $Na_2S_2O_3$ (2 mL of a saturated aqueous solution) then $NaHCO_3$ (2 mL of a saturated aqueous solution) and the resulting slurry stirred vigorously for 0.5 h. The separated aqueous phase was extracted with dichloromethane (2 × 5 mL) and the combined organic phases washed with brine (2 × 10 mL), then dried ($MgSO_4$) filtered, and concentrated under reduced pressure. Subjection of the resulting light-yellow oil to flash chromatography (2 : 3 v/v ethyl acetate/hexane to ethyl acetate gradient elution) gave two fractions, A and B.

Concentration of fraction A ($R_f$ 0.3, 4 : 1 v/v ethyl acetate/hexane) yielded *compound* ***49*** (2 mg, 18%) as a clear colourless oil, $[\alpha]_D$ −73.4° (*c* 1.0), (Found: $M^{+•}$ 322.2141. $C_{19}H_{30}O_4$ requires $M^{+•}$ 322.2144). $\nu_{max}/cm^{-1}$ 3400, 2926, 1685 (sh), 1654, 1460, 1058. $\delta_H$ (300 MHz) 4.69 (1 H, dd, *J* 8.3 and 3.7), 3.69 (2 H, t, *J* 6.3), 3.16 (1 H, broad d, *J* 8.3), 2.64–2.53 (3 H, complex m), 2.43–2.17 (3 H, complex m), 2.00–1.20 (8 H, complex m), 1.72 (3 H, s), 1.57 (3 H, s), 1.17 (3 H, s), 1.03 (3 H, s). $\delta_C$ (75 MHz) 217.8, 197.7, 159.0, 135.6, 69.3, 62.6, 51.8, 50.2, 37.6, 35.1, 33.2, 32.8, 31.8, 31.1, 26.1, 25.5, 24.3, 19.5, 14.6. *m*/*z* (EI, 70 eV) 323 ([M + H]$^+$, 35%), 322 ($M^{+•}$, 7), 279 (20), 238 (35), 203 (20), 180 (100), 165 (34), 151 (43), 137 (37), 121 (62).

Concentration of fraction B ($R_f$ 0.6, 4 : 1 v/v ethyl acetate/hexane) yielded *compound* ***50*** (5 mg, 46%) as a clear, colourless syrup, $[\alpha]_D$ −103.0° (*c* 1.0), (Found: $M^{+•}$ 320.1988. $C_{19}H_{28}O_4$ requires $M^{+•}$ 320.1988). $\nu_{max}/cm^{-1}$ 3411, 2924, 1720, 1687, 1662, 1461, 1058. $\delta_H$ (300 MHz) 9.81 (1 H, t, *J* 1.1), 4.69 (1 H, m), 3.14 (1 H, d, *J* 8.7), 2.70–2.20 (5 H, complex m), 1.94 (1 H, m), 1.70–0.80 (7 H, complex m), 1.68 (3 H, s), 1.57 (3 H, s), 1.16 (3 H, s), 1.04 (3 H, s). $\delta_C$ (75 MHz) 217.4, 201.9, 197.6, 158.8, 135.6, 69.3, 51.8, 50.1, 44.2, 37.6, 35.0, 32.8, 31.7, 30.9, 26.0, 25.2, 24.2, 15.7, 14.6. *m*/*z* (EI, 70 eV) 320 ($M^{+•}$, 6%), 305 (8), 248 (55), 236 (37), 231 (26), 180 (67), 165 (21), 151 (28), 149 (34), 142 (100), 121 (38), 100 (27), 84 (42).

*Method B*

Treatment of triol **48** (34 mg, 0.105 mmol) with Dess–Martin periodinane (89 mg, 0.210 mmol) at 0°C for 4 h as described above gave diol **49** (7 mg, 21%) and the aldehyde **50** (23 mg, 68%).

*(1*S*,4*S*)-4-{4,8,11,11-Tetramethyl-5,6,9-trioxobicyclo[5.3.1]undec-7-en-4-yl}butyraldehyde **51***

A magnetically stirred solution of triol **48** (14 mg, 0.0431) in dichloromethane (2 mL) was treated with the Dess–Martin periodinane (60 mg, 0.141 mmol) and the resulting mixture stirred at 18°C for 4 h. The reaction mixture was then worked up as described above and the resulting light-yellow oil subject to flash chromatography (3 : 7 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions ($R_f$ 0.5) then gave the *title compound **51*** (5 mg, 36%) as a clear, colourless syrup, $[\alpha]_D$ −97.7° (*c* 0.4), (Found: $M^{+\bullet}$ 318.1834. $C_{19}H_{26}O_4$ requires $M^{+\bullet}$ 318.1831). $\nu_{max}/cm^{-1}$ 2938, 1722, 1696, 1677, 1462, 1376, 875. $\delta_H$ (300 MHz) 9.81 (1 H, t, *J* 1.1), 3.06–2.34 (7 H, complex m), 2.13 (1 H, m), 1.94 (1 H, m), 1.77 (3 H, s), 1.74–1.10 (4 H, complex m), 1.42 (3 H, s), 1.28 (3 H, s), 1.23 (3 H, s). $\delta_C$ (75 MHz) 210.6, 207.6, 201.9, 196.2, 157.3, 137.6, 59.4, 48.4, 44.1, 35.8, 33.5, 32.2, 31.3, 26.0, 24.8, 24.5, 15.3, 15.0 (one resonance obscured or overlapping). *m*/*z* (EI, 70 eV) 318 ($M^{+\bullet}$, 12%), 290 (17), 222 (64), 221 (59), 203 (55), 178 (100), 150 (46), 135 (71), 122 (41), 107 (80), 91 (32).

*Attempted Cyclization of Compound **50***

A magnetically stirred solution of the compound **50** (9 mg, 0.0281) in THF (2 mL) was cooled to −78°C and LiHMDS (56 μL of a 1.0 M solution in THF) was added dropwise. Stirring was continued at −78°C for 0.25 h then the reaction mixture was allowed to warm to 18°C over 0.5 h, before quenching with $NH_4Cl$ (5 mL of a saturated aqueous solution). The resulting mixture was extracted with ethyl acetate (2 × 10 mL) and the combined extracts were washed with brine (2 × 10 mL), then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Subjection of the resulting light-yellow oil to flash chromatography (ethyl acetate) gave, after concentration of the appropriate fractions ($R_f$ 0.2), ca. 1 mg of a colourless syrup that is isomeric with the starting material (Found: $M^{+\bullet}$ 320.1986. $C_{19}H_{28}O_4$ requires $M^{+\bullet}$ 320.1988). $\nu_{max}/cm^{-1}$ 3424, 2924, 1662, 1603, 1461, 1302, 1058, 731. *m*/*z* 321 ($[M+H]^+$, 7%), 320 ($M^{+\bullet}$, 8), 305 (18), 291 (10), 236 (70), 180 (100), 165 (37), 151 (47), 137 (26), 135 (24), 121 (61), 91 (24), 67 (28).

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