Strain-assisted Reductive Ring Cleavage: Convenient Route to Bridged Eight-Membered Rings Present in Taxanes

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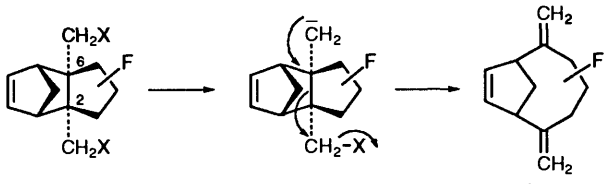
Reduction of 1,4-dimesyl entities embodied in several strained polycyclic systems with Zn–NaI–HMPA has been studied. While the dimesyl esters **9** and **15** gave exclusively C–C bond-cleaved products **10** and **24**, the dimesyl esters **18** and **20** gave both the ring-cleaved products **25** and **27** as well as the reduced products **26** and **28**. On the other hand, the dimesyl ester **23** afforded exclusively the reduced product **29**. The different reaction course observed has been ascribed to the release of strain associated with the trinorbornene systems. The ring-cleaved product **27** has been oxidised with RuO_4 to afford the dione **30**. Interestingly, oxidation of the diene **27** with OsO_4 was found to proceed with unprecedented chemoselectivity by oxidation of the non-conjugated methylene unit to afford the enone **31**.

Carbon–carbon bond cleavage, like carbon–carbon bond formation, is a useful transformation in organic synthesis. The cleavage is particularly advantageous over C–C bond formation in providing a variety of strategies[1–6] for the synthesis of medium and large rings and in stereoselective introduction of carbon appendages.[7] Ring expansion *via* oxidative fission[1] of carbon–carbon double bonds and by anion-[2] or radical-induced[3] cleavage of C–C σ bonds in bridged and small ring systems occurs smoothly. However, ring expansion through cleavage of σ bonds at the fusion of two rings larger than four membered requires either the process to be exothermic[4] or the ring-expanded product be highly stabilised through an intramolecular trap[5] or a molecular geometry[6] appropriate for continuous overlap of the participating orbitals. We herein describe a remarkable reductive process wherein the delicate balance between the two reaction courses, reduction and C–C bond fragmentation, is determined by the strain energies associated with the parent systems and the resultant ring-expanded products.



1 2 3

Scheme 1

As part of our interest to the synthesis of the anticancer diterpene taxol, a simple general process for the cleavage of a ring-fusion bond in the system **1** where a 5-membered ring is fused to a trinorbornene system was required. It was anticipated that generation of an anionic species **2** (Scheme 1) from a dihalogeno precursor **1** through metal–halogen exchange† might lead to Grob-type fragmentation to afford the bridged eight-membered-ring system **3** present in taxanes.[9] Successful realisation of this concept is presented[10] here.

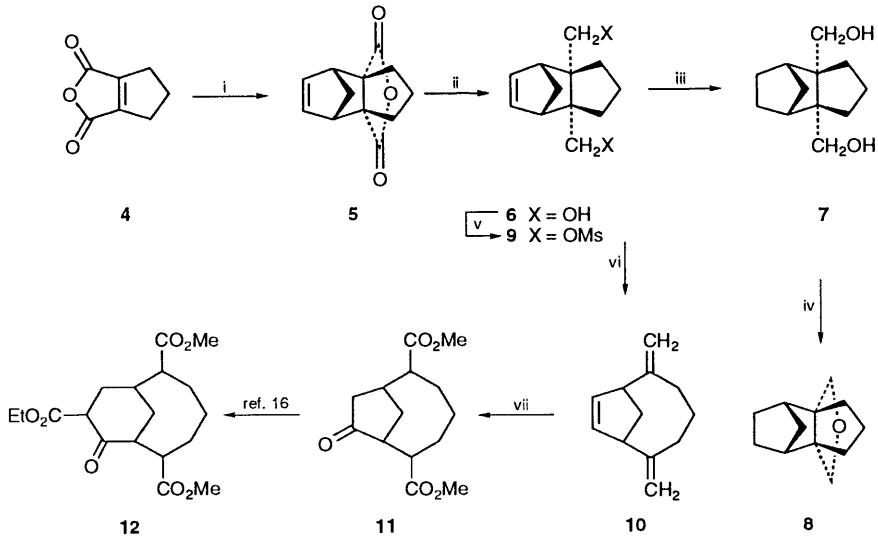
Results and Discussion

Tricyclo[5.2.1.$0^{2,6}$]decenes required for this investigation were obtained through Diels–Alder reaction of cyclopentadiene with appropriate dienophiles. For example, reaction[11] of cyclopentene-1,2-dicarboxylic anhydride **4** with cyclopentadiene afforded the anhydride **5** (Scheme 2). Reduction of the anhydride **5** with $LiAlH_4$ (LAH) in refluxing tetrahydrofuran (THF) gave the diol **6** in nearly quantitative yield. An attempt to prepare the corresponding diiodide directly from the diol **6** by using Lange's procedure[12] (I_2–PPh_3–imidazole) gave a complex reaction mixture. Considering that addition of I_2 to the double bond of diol **6** with intramolecular participation of OH would make the reaction complicated, the saturated diol **7**, obtained by hydrogenation of diol **6**, was chosen for this study. However, reaction of the diol **7** with I_2–PPh_3–imidazole did not produce the desired diiodo derivative. The only product isolated, in 79% yield, was assigned the structure **8**, m.p. 188 °C, on the basis of NMR spectral data. The diol **6** was then converted into the dimesyl derivative **9** in quantitative yield. Attempted displacement of the mesyloxy groups in compound **9** by iodide with NaI in refluxing acetone led to complete recovery of starting material **9**. When heated‡ with NaI in hexamethylphosphoric triamide (HMPA), the dimesyl compound **9** gave a mixture of at least four components (TLC). Generation of the anionic species **3** directly from the dimesyl compound was next considered.

Fuzimoto[14] has shown that mesyl esters can be reduced directly and very efficiently when heated with powdered Zn and NaI in 1,2-dimethoxyethane (DME) or HMPA. Subsequently it was shown[15] that reduction of mesyl esters under these conditions involves radical or anionic intermediates. Intrigued by this observation, we heated the dimesyl species **9** with a suspension of powdered Zn and NaI in HMPA for 5 h at 90–110 °C (oil-bath temp.). As expected, only the ring-cleaved product **10** was obtained, in 82% yield as a liquid after column chromatography. The structure could be assigned easily from its ^1H NMR spectrum by the appearance of four olefinic protons at δ 4.61 in addition to a two-olefinic-proton singlet at δ5.78. Additional support in favour of structure **10** was obtained by the appearance of two olefinic carbons at δ_C 154.1 (s) and 110.8 (t) attributable to *exo* methylene units at C-2 and C-6, in addition to the C-8, C-9 olefinic carbons at δ 135.5 (d) in the ^{13}C NMR spectrum of the product. Further evidence

† Bailey *et al.* have reported that 1,2-bis(iodomethyl)cyclobutane on treatment with Bu^{t}Li in pentane at −23 °C results in Grob-type cleavage of cyclobutane (ref. 8).

‡ Paquette *et al.* have demonstrated that a 1,4-dimesyl system embodied in a highly strained cage system undergoes C–C bond cleavage on simple heating with NaI in hexamethylphosphoric triamide (ref. 13).

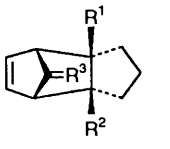


Scheme 2 *Reagents and conditions:* i, cyclopentadiene, THF, $AlCl_3$, 0°C; ii, $LiAlH_4$, THF, reflux; iii, H_2, 10% Pd–C, EtOH; iv, I_2–PPh_3–imidazole, CH_2Cl_2; v, $MeSO_2Cl$–NEt_3–DMAP, CH_2Cl_2, 0°C; vi, Zn–NaI, HMPA, 90–110 °C; vii, (*a*) BH_3, THF, 0 °C, 3 mol dm^{-3} NaOH, 30% H_2O_2; (*b*) Jones' reagent, acetone, 0 °C.

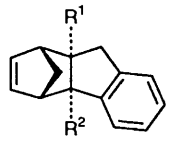
in support of structure **10** was obtained by transformation of the triene **10** into the known keto diester **11**[16] through hydroboration, Jones oxidation and treatment of diazomethane. The keto diester **10** has already been transformed[16] into the bicyclo[5.3.1]undecane **12**, the AB ring system of taxanes. Thus, the transformation of anhydride **4** into triester **12** represents an excellent route for entry into the taxane family.

To test the generality of this ring-cleavage process and to get insight about the structural requirement for the observed C–C bond cleavage suppressing normal reduction, a number of dimesyl esters having a *syn* arrangement of the mesyloxymethyl groups around the bond to be cleaved were chosen. The dimesyl derivatives **15**, **18** and **23** were obtained from the known adducts **13**,[17] **16**[16] and **21**,[18] respectively, through LAH reduction and mesylation of the corresponding diols **14**, **17** and **22**. The dimesyl compound **20** was obtained from the diol **17** through hydrogenation to compound **19** and its subsequent mesylation. The mesyl compounds were heated with powdered Zn and NaI in HMPA in an oil-bath preset to 90–110 °C under magnetic stirring. Sonication of the reaction mixture for 2 h before heating gave significant improvements in yield. The results are summarised in Table 1.

Exclusive C–C bond cleavage was observed for the dimesyl derivatives **9** and **15** (entries 1 and 2), while significant amounts of reduction products **26** and **28** were formed with the ring-cleaved products **25** and **27** from reaction of the mesyl compounds **18** and **20** (entries 3 and 4). The dimesyl compound **23** (entry 5) on the other hand produced only the reduced product **29**. As all the dimesyl compounds used have the same molecular geometry suitable for a Grob-type fragmentation *via* the intermediate carbanion **2**, it was expected that all the mesyl esters would give only the ring-cleaved products if molecular geometry were the only factor required for cleavage. While the dimesyl compound **9** suffers from angle strain as well as non-bonded interaction involving the hydrogens at C-3, C-4 and C-5 with the C-10 hydrogen, the resultant eight-membered-ring system **10** experiences transannular interactions comparable to the non-bonded interaction in the dimesyl compound. Thus, the driving force for the fragmentation is possibly the release of angle strain associated with the trinorbornene unit. This is further supported when both the *exo* dimesyl compound **15** and its corresponding *endo* dimesyl isomer, where the angle strain has been increased at the expense of reduced non-bonded interaction, also gave only the ring-cleaved product **24**. Incorporation of an aromatic ring in the eight-membered ring as in compounds **26** and **28** minimises the transannular interaction with concomitant increase in angle strain due to bond-angle deformation. Hence, during reaction of the dimesyl compounds **18** and **20** the release of strain energy is less compared with that in the reaction of compounds **9** and **15** and reduction of the intermediate carbanion competes with fragmentation giving rise to some reduced products. The importance of the angle strain for the fragmentation is further demonstrated when the dimesyl compound **23** incorporated in a bicyclo[2.2.2]octane system failed to undergo fragmentation, producing only the reduced product **29**.



13 R^1R^2 = CO(O)CO, R^3 = CMe_2
14 R^1 = R^2 = CH_2OH, R^3 = CMe_2
15 R^1 = R^2 = CH_2OMs, R^3 = CMe_2



16 R^1R^2 = CO(O)CO
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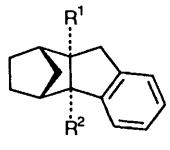
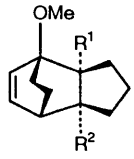
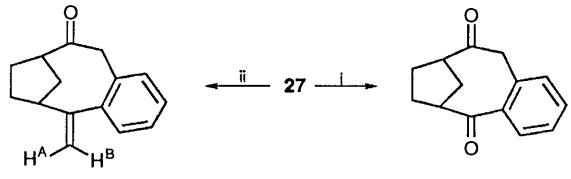


19 R^1 = R^2 = CH_2OH
20 R^1 = R^2 = CH_2OMs



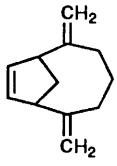
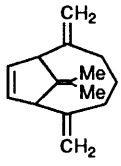
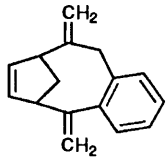
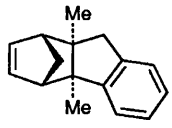
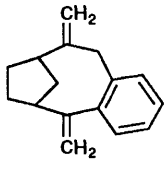
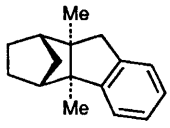
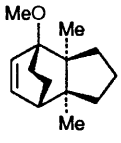
21 R^1R^2 = CO(O)CO
22 R^1 = R^2 = CH_2OH
23 R^1 = R^2 = CH_2OMs



31 **30**

Scheme 3 *Reagents and conditions:* i, $RuCl_3 \cdot xH_2O$–$NaIO_4$, CCl_4–MeCN–water, room temp.; ii, OsO_4–$NaIO_4$, Et_2O–water.

Table 1 Reaction of dimesyl compounds with Zn–NaI in HMPA

Entry	Dimesylate	Product(s)	Yield (%)
1	**9**	 **10**	82[a]
2	**15**	 **24**	74[a]
3	**18**	 **25** +  **26**	80:20[b]
4	**20**	 **27** +  **28**	70:30[b]
5	**23**	 **29**	76[a]

[a] Yields refer to chromatographically isolated products. [b] Percentage of products in the crude reaction mixture as determined from ^{1}H NMR spectroscopy.

To extend the scope of this ring-cleavage process toward further functionalisation necessary for the synthesis of taxane diterpenes, the ring-cleaved product **27** was subjected to oxidation (Scheme 3). Oxidation of compound **27** with catalytic amount of $RuCl_3$ and $NaIO_4$ under Sharpless conditions gave the diketone **30**. The structure of the oxidation product of the diene **27** as the diketone was quite evident from the disappearance of the olefinic protons in the ^{1}H NMR spectrum and olefinic carbons in the ^{13}C NMR spectrum and from the presence of aromatic conjugated and non-conjugated carbonyl groups at δ 208.9 and 212.9, respectively. Interestingly, it was noted that by using a catalytic amount of OsO_4–$NaIO_4$ in aqueous diethyl ether, oxidation of the styrenic bond in compound **27** was found to be slower compared with oxidation of the non-conjugated methylene unit and the enone **31** could be isolated in 74% yield after a period of 16 h. That, during oxidation with OsO_4, the non-conjugated olefinic unit was oxidised was clearly evident by the disappearance of only the upfield olefinic protons at δ 4.57 and 4.74 of the diene **27** and the presence of olefinic protons H^A at δ 4.93 (d, J 3) and H^B at δ 5.26 (dd, J 3 and 1.5) in the ^{1}H NMR spectrum of the product. Similarly, the ^{13}C NMR spectrum of the product showed the presence of aromatic conjugated methylene carbons at δ_C 155.2(s) and 115.0(t) and only the non-conjugated carbonyl group at δ_C 211.9(s). The enone **31** could be further oxidised to the diketone **30** by reaction with the $RuCl_3$–$NaIO_4$ system. The diketone **30** and the enone **31** represent the tricyclic taxane nucleus suitably functionalised for further elaboration.

This investigsation demonstrates that reduction of a 1,4-dimesyl system embodied in tricyclo[5.2.1.$0^{2,6}$]decenes with Zn–NaI in HMPA leads to cleavage of the central C–C bond leading to ring expansion to give bridged eight-membered rings. The driving force for the ring cleavage has been attributed to the release of angle strain associated with the trinorbornene unit.

Experimental

The compounds described are all racemates. M.p.s were measured in open capillary tubes and are uncorrected. IR spectra of solids (KBr) and liquids (neat) were recorded on a Perkin-Elmer model PE-298 instrument. ^{1}H NMR spectra were

recorded at 200 MHz and 60 MHz on Varian Associates XL-200 and EM-360L spectrometers with $SiMe_4$ as internal standard. *J* Values are given in Hz. ^{13}C NMR spectra were recorded at 25 MHz on a JEOL FX-100 spectrometer. Sonication was carried out in a common ultrasonic cleaner (Julabo USR3, 100 W, operating at 35 kHz) partially filled with water at 15–20 °C. The organic extracts were dried over anhydrous Na_2SO_4. Column chromatography was performed on silica gel (60–120 mesh). Elemental analyses were performed by Mr. P. P. Bhattacharya and Mr. S. Sarkar of this laboratory.

General Procedure for Preparation of the Diols.—endo-2,6-*Bis(hydroxymethyl)tricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*ene* **6**. The general procedure for synthesis of the diols is illustrated by the synthesis of the diol **6**. To a magnetically stirred suspension of LAH (500 mg, 12 mmol) in THF (7 cm^3) was added dropwise a solution of the anhydride **5** (500 mg, 2.5 mmol) in THF (3 cm^3) under N_2. The mixture was then refluxed for 3 h. The reaction mixture was cooled in ice and quenched by sequential addition of water (0.5 cm^3), aq. NaOH (0.5 cm^3; 15%) and water (1.5 cm^3). The mixture was stirred for 15 min. The granular precipitate was filtered off, and washed with hot THF (4 × 15 cm^3). The combined filtrate and washings were dried. The solvent was removed under reduced pressure to afford *diol* **6** (470 mg, 98%), m.p. 178 °C (Found: C, 74.05; H, 9.3. $C_{12}H_{18}O_2$ requires C, 74.18; H, 9.33%); ν_{max}/cm^{-1} 3320; δ_H(200 MHz; $CDCl_3$) 1.38–2.16 (8 H, m), 2.44 (2 H, t, *J* 2), 3.38 (2 H, br), 3.50 (4 H, ABq, *J* 20) and 6.18 (2 H, t, *J* 2).

exo-2,6-*Bis(hydroxymethyl)*-10-*isopropylidenetricyclo*-[5.2.1.$0^{2,6}$]*dec*-8-*ene* **14**. A solution of the *exo*-adduct **13** (400 mg, 1.64 mmol) in THF (12 cm^3) was reduced with LAH (310 mg, 8.2 mmol) to afford the *diol* **14** (370 mg, 97%), m.p. 182 °C (Found: C, 76.6; H, 9.4. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%); ν_{max}/cm^{-1} 3500; δ_H (60 MHz; $CDCl_3$) 1.23–1.96 (12 H, m with a singlet at δ 1.56), 2.90 (2 H, t, *J* 1), 3.16 (2 H, br s), 3.63 (4 H, ABq, *J* 14) and 6.36 (2 H, t, *J* 1).

endo-2,10-*Bis(hydroxymethyl)tetracyclo*[9.2.1.$0^{2,10}$.$0^{3,8}$]-*tetradeca*-3,5,7,12-*tetraene* **17**. A solution of the anhydride **16** (500 mg, 1.98 mmol) in THF (14 cm^3) was reduced with LAH (220 mg, 5.79 mmol) to afford the *diol* **17** (450 mg, 95%), m.p. 142 °C (Found: C, 79.25; H, 7.5. $C_{16}H_{18}O_2$ requires C, 79.31; H, 7.49%); ν_{max}/cm^{-1} 3400–3100; δ_H(200 MHz; $CDCl_3$) 1.16–1.46 (2 H, m), 2.61 (1 H, br s), 2.66 (1 H, br s), 2.76 (1 H, d, *J* 17), 3.46–3.74 (5 H, m), 3.70 (1 H, d, *J* 17), 4.17 (1 H, d, *J* 12), 6.26 (2 H, br s) and 7.12–7.36 (4 H, m).

endo-2,6-*Bis(hydroxymethyl)*-1-*methoxytricyclo*[5.2.2.$0^{2,6}$]*undec*-8-*ene* **22**. A solution of the anydride **21** (250 mg, 1 mmol) in dry THF (10 cm^3) was refluxed with LAH (150 mg, 4 mmol) in dry THF (7 cm^3) for 3.5 h to afford the *diol* **22** (240 mg, 100%), m.p. 164 °C (Found: C, 70.2; H, 9.5. $C_{14}H_{22}O_3$ requires C, 70.55; H, 9.31%); ν_{max}/cm^{-1} 3360; δ_H(60 MHz; $CDCl_3$) 1.43–1.90 (10 H, m), 2.23 (1 H, br s), 3.23–3.50 (4 H, m), 3.33 (3 H, s), 3.90–4.36 (2 H, br s) and 6.20–6.33 (2 H, m).

endo-2,6-*Bis(hydroxymethyl)tricyclo*[5.2.1.$0^{2,6}$]*decane* **7**. A solution of the unsaturated diol **6** (500 mg, 2.57 mmol) in ethanol (20 cm^3) was stirred magnetically in the presence of Pd–C (50 mg, 10%) under H_2 for 2 h. The catalyst was filtered off and the solvent was removed from the filtrate to afford the *saturated diol* **7** (500 mg, 100%), m.p. 228 °C (Found: C, 73.6; H, 10.6. $C_{12}H_{20}O_2$ requires C, 73.43; H, 10.27%); δ_H(200 MHz; $CDCl_3$) 1.04–2.02 (14 H, m), 2.80 (2 H, br s), 3.58 (2 H, d, *J* 12) and 3.86 (2 H, d, *J* 12).

Reaction of the Saturated Diol **7** *with* I_2–PPh_3–*Imidazole. Synthesis of the Tetrahydrofuran Derivative* **8**.—To a magnetically stirred solution of Ph_3P (1.58 g, 6.02 mmol) and imidazole (400 mg, 6 mmol) in CH_2Cl_2 (8 cm^3) was added slowly iodine (3 g, 11.8 mmol). The mixture was stirred until it became homogeneous. A solution of the diol **7** (420 mg, 2.14 mmol) in CH_2Cl_2 (2 cm^3) was slowly added to the reaction mixture. After the mixture had been stirred for 2 h, the solvent was removed. The residual black sticky mass was dissolved in water and was extracted with hexane (3 × 20 cm^3). The combined extract was washed successively with aq. sodium thiosulfate (5%) and brine, and dried. The crude material obtained after removal of hexane was chromatographed to afford *tetracycle* **8** (300 mg, 79%), m.p. 188 °C (Found: C, 80.6; H, 10.2. $C_{12}H_{18}O$ requires C, 80.85; H, 10.18%); δ_H(60 MHz; CCl_4) 0.86–1.83 (12 H, m), 1.96 (2 H, br s), 2.90 (2 H, d, *J* 10) and 3.90 (2 H, d, *J* 10).

General Procedure for Preparation of the Dimesyl Esters.—The general procedure is illustrated by the synthesis of the dimesyl compound **9**.

endo-2,6-*Bis(mesyloxymethyl)tricyclo*[5.2.1.$0^{2,6}$]*dec*-8-*ene* **9**. To a magnetically stirred and cooled (ice–salt-bath) solution of the diol **6** (350 mg, 1.8 mmol) in CH_2Cl_2 (7 cm^3) were added dropwise and sequentially triethylamine (0.750 cm^3, 5.3 mmol), 4-(dimethylamino)pyridine (DMAP) (5 mg) and methanesulfonyl chloride (0.330 cm^3, 4.2 mmol). The mixture was stirred at this temp. for 30 min and at room temp. for 30 min. The reaction mixture was then poured into cold water (5 cm^3) and extracted with CH_2Cl_2. The extract was washed successively with water, 10% aq. HCl, and saturated aq. $NaHCO_3$, and was dried. Removal of solvent under reduced pressure afforded the dimesyl compound **9** (600 mg, 96%), m.p. 122 °C; δ_H(200 MHz; $CDCl_3$) 1.42–2.08 (8 H, m), 2.74 (2 H, br s), 3.06 (6 H, s), 3.95 (4 H, s) and 6.35 (2 H, br s). Attempted purification to give an analytically pure sample led to rapid decomposition.

exo-10-*Isopropylidene*-2,6-*bis(mesyloxymethyl)tricyclo*[5.2.1.-0.^{2,6}]*dec*-8-*ene* **15**. A solution of the diol **14** (200 mg, 0.85 mmol) in CH_2Cl_2 (4 cm^3) was treated with methanesulfonyl chloride (0.168 cm^3, 2.16 mmol), triethylamine (0.4 cm^3, 2.8 mmol) and DMAP (5 mg) to afford the dimesyl compound **15** (310 mg, 100%), m.p. 176 °C; δ_H(60 MHz; $CDCl_3$) 1.40–2.06 (12 H, m with a singlet at δ 1.63), 3.06 (6 H, s), 3.30 (2 H, t, *J* 1), 4.13 (4 H, ABq, *J* 10) and 6.36 (2 H, t, *J* 1).

endo-2,10-*Bis(mesyloxymethyl)tetracyclo*[9.2.1.$0^{2,10}$.$0^{3,8}$]-*tetradeca*-3,5,7,12-*tetraene* **18**. A solution of the diol **17** (480 mg, 2 mmol) in CH_2Cl_2 (10 cm^3) was treated with methanesulfonyl chloride (0.4 cm^3, 5 mmol), triethylamine (0.98 cm^3, 7 mmol) and DMAP (10 mg) to afford the dimesyl compound **18** (710 mg, 90%), m.p. 98 °C; δ_H 1.43 (2 H, m), 2.70–3.33 (10 H, m with two singlets at δ 2.83 and 3.06 for SO_2Me), 3.96–4.73 (4 H, m), 6.38 (2 H, t, *J* 1–2) and 7.03–7.36 (4 H, m).

endo-2,10-*Bis(mesyloxymethyl)tetracyclo*[9.2.1.$0^{2,10}0^{3,8}$]-*tetradecane* **20**. A solution of the unsaturated diol **17** (500 mg, 2.06 mmol) in ethanol (20 cm^3) was stirred magnetically in the presence of Pd–C (80 mg, 10%) under H_2 for 2 h. The catalyst was filtered off and the solvent was removed from the filtrate to afford the diol **19** (500 mg, 100%), m.p. 137 °C; δ_H(200 MHz; $CDCl_3$) 1.0–1.96 (6 H, m), 2.11 (1 H, br s), 2.20 (1 H, br s), 2.68 (1 H, d, *J* 17), 3.50–3.62 (2 H, m), 3.70 (1 H, d, *J* 17), 4.0–4.32 (4 H, m) and 7.04–7.44 (4 H, m).

A solution of the saturated diol **19** (200 mg, 0.82 mmol) in CH_2Cl_2 (4 cm^3) was treated with methanesulfonyl chloride (0.170 cm^3, 2.19 mmol), triethylamine (0.400 cm^3, 2.8 mmol) and DMAP (5 mg) to afford the dimesyl compound **20** (325 mg, 100%), m.p. 118 °C; δ_H(60 MHz; $CDCl_3$) 1.2–1.3 (6 H, m), 1.63 (2 H, br s), 2.36 (2 H, br s), 2.8 (3 H, s), 3.03 (3 H, s), 4.26–4.76 (4 H, m) and 7.2 (4 H, s).

endo-1-*Methoxy*-2,6-*bis(mesyloxymethyl)tricyclo*[5.2.2.$0^{2,6}$]-*undec*-8-*ene* **23**. A solution of the diol **22** (200 mg, 0.84 mmol) in CH_2Cl_2 (4.5 cm^3) was treated with methanesulfonyl chloride (0.16 cm^3, 2 mmol), triethylamine (0.37 cm^3, 2.7 mmol) and DMAP (5 mg) to afford the dimesyl compound **23** (300 mg, 92%) as a yellow liquid; δ_H(60 MHz; $CDCl_3$) 1.26–2.16 (10 H,

m), 2.52 (1 H, br s), 2.93 (6 H, s), 3.33 (3 H, s), 3.80–4.33 (4 H, m), 6.30 (1 H, br s) and 6.35 (1 H, br s).

Reaction of the Dimesyl Esters with Zn–NaI *in HMPA.—General procedure.* A suspension of freshly activated Zn powder (20 mmol), powdered anhydrous NaI (6 mmol) and a dimesyl compound (1 mmol) in HMPA (dried over molecular sieves 4 Å) (8 cm^3) was sonicated for 2 h. The mixture was then heated in an oil-bath (preset at 90–110 °C) for 3–5 h under N_2. The reaction mixture was cooled, and diluted with pentane (25 cm^3). The undissolved material was filtered off. The filtrate was washed successively with aq. sodium thiosulfate (5%) and water (4 × 10 cm^3), dried, and concentrated, and the residual liquid was purified by column chromatography to afford the pure product.

2,6-*Dimethylenebicyclo*[5.2.1]*dec*-8-*ene* **10** was obtained from the dimesyl ester **9** as a *clear liquid* (82%) (Found: C, 89.9; H, 10.3. $C_{12}H_{16}$ requires C, 89.93; H, 10.06%); ν_{max}/cm^{-1} 2960, 2930, 1635, 1460, 1440 and 900; δ_H(60 MHz; CCl_4) 1.30–2.73 (8 H, m), 3.44 (2 H, br d, *J* 9), 4.61 (4 H, m) and 5.78 (2 H, s); δ_C 154.1(s), 135.5(d), 110.8(t), 52.1(d), 38.8(t), 37.1(t) and 29.4(t).

10-*Isopropylidene*-2,6-*dimethylenebicyclo*[5.2.1]*dec*-8-*ene* **24** was obtained from the dimesyl derivative **15** as a clear liquid (74%), b.p. 80–85 °C (0.4 mmHg) (bath temp.) (Found: C, 90.15; H, 10.0. $C_{15}H_{20}$ requires C, 89.93; H, 10.06%); ν_{max}/cm^{-1} 2930, 1630, 1440, 895 and 770; δ_H(60 MHz; CCl_4) 1.56 (2 H, m), 1.70 (6 H, s), 2.26 (4 H, m), 3.96 (2 H, br s), 4.70 (4 H, br s) and 5.76 (2 H, d, *J* 1.5); δ_C 151.3 (s), 134.9 (d), 111.3 (t), 56.1 (d), 38.3 (t), 26.8 (t) and 20.6 (q); *m*/*z* (%) 200 (M^+, 45), 185 (100), 171 (20), 157 (45), 143 (34), 128 (26), 115 (16), 106 (10), 91 (8) and 77 (4).

2,10-*Dimethylenetricyclo*[9.2.1.$0^{3,8}$]*tetradeca*-3,5,7,12-*tetraene* **25** and endo-2,10-*dimethyltetracyclo*[9.2.1.$0^{2,10}$.$0^{3,8}$]*tetradeca*-3,5,7,12-*tetraene* **26** were obtained from the dimesyl substrate **18** as ~80:20 mixture in 73% yield. Chromatography through a long column of silica gel afforded pure compound **25** (10%), b.p. 95–100 °C (10 mmHg) (bath temp.) (Found: C, 92.0; H, 8.0. $C_{16}H_{16}$ requires C, 92.26; H, 7.74%); ν_{max}/cm^{-1} 2980, 2930, 1640, 1610, 1480 and 1445; δ_H(60 MHz; CCl_4) 0.83–1.46 (2 H, m), 2.43–3.03 (2 H, m), 3.33 (1 H, br d, *J* 8), 3.76 (1 H, br d, *J* 8), 4.70 (1 H, d, *J* 2.5), 4.80 (1 H, t, *J* < 1), 5.05 (1 H, t, *J* 1–2), 5.16 (1 H, t, *J* 1–2), 5.6 (1 H, m), 6.03 (1 H, m) and 6.76–7.30 (4 H, m) and a fraction ~90% enriched with compound **26** (Found: C, 91.6; H, 8.5. $C_{16}H_{18}$ requires C, 91.37; H, 8.63%); δ_H(60 MHz; CCl_4) (from mixture) 1.0 (3 H, s), 1.10 (3 H, s), 1.26 (2 H, t, *J* < 1), 2.50 (1 H, br s), 2.60 (1 H, br s), 2.90 (2 H, s), 6.20 (2 H, br s) and 7.06 (4 H, s).

2,10-Dimethylenetricyclo[9.2.1.$0^{3,8}$]tetradeca-3,5,7-triene **27** and 2,10-dimethyltetracyclo[9.2.1.$0^{2,10}$.$0^{3,8}$]tetradeca-3,5,7-triene **28** were obtained from the dimesyl compound **20** as ~70:30 mixture in 86% yield, which on careful column chromatography afforded compound **27** (64% yield containing ~10% of compound **28**); ν_{max}/cm^{-1} 2950, 1635, 1605, 1485, 1440 and 895; δ_H 1.36–2.33 (6 H, m), 2.66–3.50 (4 H, m), 4.57 (1 H, d, *J* 3), 4.74 (1 H, d, *J* 3), 4.90 (1 H, d, *J* 3), 5.23 (1 H, m) and 6.90–7.30 (4 H, m). The diene was characterised by its conversion into the dione **30**.

endo-1-*Methoxy*-2,6-*dimethyltricyclo*[5.2.2.$0^{2,6}$]*undec*-8-*ene* **29** was obtained from the dimesyl substrate **23** as the only product (76%) as a clear liquid (Found: C, 81.3; H, 10.7. $C_{14}H_{22}O$ requires C, 81.50; H, 10.75%); δ_H 1.06 (3 H, s), 1.26 (3 H, s), 1.13–2.33 (10 H, m), 3.43 (3 H, s), 3.96 (1 H, br d, *J* 3), 5.46 (1 H, dd, *J* 6 and 3) and 6.08 (1 H, d, *J* 6).

Dimethyl 8-*oxobicyclo*[5.2.1]*decane*-2,6-*dicarboxylate* **11**. A solution of the triene **10** (120 mg, 0.75 mmol) in THF (20 cm^3) was treated with a solution of diborane (34%; 0.8 cm^3, 3.47 mmol) in THF at 0 °C for 3 h and then left overnight in a refrigerator. The excess of diborane was decomposed by careful addition of a few drops of water. To the mixture was added aq. sodium hydroxide (3 mol dm^{-3}; 27 cm^3) followed by dropwise addition of aq. hydrogen peroxide (30%; 27 cm^3). The reaction mixture was stirred at room temp. for 1 h and was then extracted with ethyl acetate (4 × 15 cm^3). The extract was washed with brine, dried, and concentrated under reduced pressure to afford the trihydroxy compound (110 mg) as a viscous mass; ν_{max}/cm^{-1} 3400br.

Without further characterization the trihydroxy compound was oxidized in ice-cold acetone (4 cm^3) with Jones' reagent (0.7 mol dm^{-3}; 3 cm^3) for 1 h. The solvent was then removed and the residue was diluted with water (5 cm^3) and extracted with ethyl acetate (3 × 10 cm^3). The extract was washed with brine and dried. Removal of solvent furnished a semisolid material which, on treatment with an ethereal solution of diazomethane followed by column chromatography, afforded the keto diester **11** (120 mg, 64%) as a liquid. This material was found to be identical by IR and ^1H NMR spectroscopy with the sample[16] prepared by a different route.

2,10-*Dioxotricyclo*[9.2.1.$0^{3,8}$]*tetradeca*-3,5,7-*triene* **30**. A mixture of the diene **27** (100 mg, 0.5 mmol) as obtained above, $NaIO_4$ (950 mg, 4.28 mmol), $RuCl_3 \cdot xH_2O$ (~5 mg) in a mixture of CCl_4 (6 cm^3), MeCN (6 cm^3), and water (12 cm^3) was stirred vigorously at room temp. for 16 h. The reaction mixture after dilution with water was extracted with CH_2Cl_2 (3 × 10 cm^3). The extract was washed successively with aq. $NaHCO_3$ (5%) and brine, and was dried. Removal of solvent, followed by column chromatography, afforded the *reduced product* **28** (20 mg, 20%) [light petroleum (60–80 °C) as eluent] (Found: C, 90.15; H, 9.8. $C_{16}H_{20}$ requires C, 90.50; H, 9.49%); ν_{max}/cm^{-1} 2945, 2940, 1590, 1480 and 1375; δ_H 1.10 (3 H, s), 1.16 (3 H, s), 1.2–2.2 (8 H, m), 2.86 (2 H, s) and 6.96 (4 H, s); *m*/*z* (%) 212 (M^+, 11), 182 (42), 154 (100), 144 (43), 129 (28) and 115 (19); and the *diketone* **30** (66 mg, 65%) as a liquid [light petroleum (60–80 °C)–diethyl ether (4:1) as eluent] (Found: C, 78.3; H, 6.4. $C_{14}H_{14}O_2$ requires C, 78.48; H, 6.59%); ν_{max}/cm^{-1} 1685 and 1600; δ_H(100 MHz; $CDCl_3$) 1.44–2.56 (6 H, m), 2.72–3.40 (2 H, m), 3.58 (2 H, ABq, *J* 16) and 7.0–7.68 (4 H, m); δ_C 28.8 (t), 29.3 (t), 34.1 (t), 45.3 (t), 52.9 (d), 53.5 (d), 126.1 (d). 127.7 (d), 129.5 (d), 129.6 (s), 130.3 (d), 140.9 (s), 208.9 (s, C-2) and 212.9 (s, C-10); *m*/*z* (%) 214 (M^+, 36), 186 (7), 173 (61), 145 (100), 117 (52) and 90 (87).

2-*Methylene*-10-*oxotricyclo*[9.2.1.$0^{3,8}$]*tetradeca*-3,5,7-*triene* **31**. A mixture of the diene **27** (110 mg, 0.54 mmol), $NaIO_4$ (260 mg, 3.7 mmol) and OsO_4 (cat.) in diethyl ether (5 cm^3)–water (1.5 cm^3) was stirred vigorously for 16 h. After dilution with water the reaction mixture was extracted with diethyl ether (3 × 5 cm^3). The extract was washed with brine and dried. Removal of solvent, followed by column chromatography, afforded the starting diene (30 mg recovery) and the enone **31** (60 mg, 74% based on consumed diene) [hexane–diethyl ether (4:1) as eluent]; ν_{max}/cm^{-1} 1690, 1620 and 1595; δ_H(60 MHz; CCl_4) 1.16–4.16 (10 H, m), 4.93 (1 H, d, *J* 3, H^A), 5.26 (1 H, dd, *J* 3.1, H^B) and 6.86–7.73 (4 H, m); δ_C 30.0 (t), 31.2 (t), 37.9 (t), 46.2 (t), 51.5 (d), 115.02 (t), 126.9 (d), 127.7 (d), 128.7 (d), 129.8 (d), 132.5 (s), 142.4 (s), 155.2 (s) and 211.9 (s, C-10); *m*/*z* (%) 212 (M^+, 69), 183 (18), 171 (76), 145 (100), 128 (73), 115 (75) and 91 (37).

Oxidation of this enone with RuO_4 as above afforded a dione identical with the dione **30** by ^1H NMR spectroscopy.

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