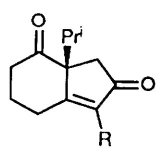
Polyfunctional Bicyclo[6.3.0]undecane Intermediates

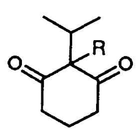
Alan P. Chorlton, Gareth A. Morris and James K. Sutherland *
Chemistry Department, Victoria University of Manchester, M13 9PL, UK

On thermolysis, 2-hydroxy-1-isopropyl-2-vinylbicyclo[4.3.0]non-6-en-8-one **18** undergoes oxy-Cope rearrangement followed by an 'ene' reaction to give 5-hydroxy-11-isopropyl-8-methyltricyclo-[6.3.0.0^{1,5}]undec-10-ene-9-one **21**, which is cleaved by $Pb(OAc)_4$–I_2 to 11-isopropyl-8-methylbicyclo-[6.3.0]undeca-1,10-diene-5,9-dione **23**. Aspects of the chemistry of the dione are explored.

In connection with a synthetic project we needed to prepare a number of polyfunctional bicyclo[6.3.0]undecane derivatives. In recent years a variety of routes to such compounds have been explored.[1] We chose to investigate the oxy-Cope rearrangement[2] (anionic or thermal) to generate the 8-membered ring, as some close analogues had been reported previously.[3,4] To this end, efficient routes to the diones **1** and **2** were required.

Isopropylation of 1,5-dimethoxycyclohexa-1,4-diene[5] followed by hydrolysis gave the dione **3**. Attempts to alkylate the intermediate dione with allyl bromide or ethyl bromoacetate were unsuccessful, but the dione **3** could be allylated using allyl acetate–$Pd(PPh_3)_4$–diazabicycloundecene[6] to form the alkene **4** (76%). Oxidation of the alkene **4** with OsO_4–$NaIO_4$ gave the aldehyde **5** (84%) which was converted into the acid **6** (91%) with CrO_3–AcOH–H_2O. Reaction of the acid **6** with Ac_2O–NaOAc formed the enol lactone **13** (87%). In the Dauben route[4] to the methylated series the ketonic carbonyl was protected as the ethylene acetal and then treated with $LiCH_2PO(OEt)_3$.





1; R = H
2; R = Me

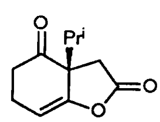
3; R = H
4; R = $CH_2CH{=}CH_2$
5; R = CH_2CHO
6; R = CH_2CO_2H
7; R = CH_2CO_2Et

8; R = CH_2COMe
9; R = CH_2COCH_2Br
10; R = $CH_2CH{=}CHMe$
11; R = $CH_2COCHBrMe$
12; R = CH_2COEt

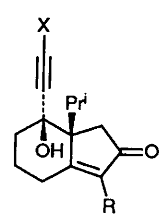
Presumably due to increased steric hindrance in the isopropyl series we were unable to prepare an acetal; in the hope that this hindrance would prevent reaction at the ketone, the lactone **13** was treated with $LiCH_2PO(OEt)_3$. The enone **1** was obtained but in only 24% yield and was accompanied by the ethyl ester **7** (23%); reaction with $LiCH(Me)PO(OEt)_3$ gave only the ester (45%).

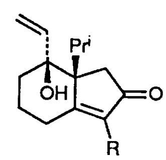
With this failure to exploit a common intermediate for the synthesis of the enones **1** and **2** we examined some individual approaches. Reaction of the dione **4** with $PdCl_2$–$CuCl_2$–O_2[7] gave the trione **8** (87%). As expected from related work, aldol cyclisation was difficult to achieve; indeed the conditions successful in the methylated series (KF, 18-crown-6, xylene) failed with the isopropyl compound. Trost overcame such a problem by use of the intramolecular Wittig reaction.[4] We were unable to prepare the required α-bromo ketone **9** by direct bromination, but reaction of the alkene **4** with *N*-bromosuccinimide (NBS)–Me_2SO–H_2O gave a bromohydrin which was oxidised with Jones' reagent to the ketone **9** (60%). Reaction of the bromide with Ph_3P–PhH effected only debromination. However it had been shown[8] that with $PhCOCH_2Br$, debromination can be dramatically reduced and the yield of phosphonium salt increased (from 3 to 92%) by the presence of a catalytic amount of Et_3N. When the bromide **9** was heated with Ph_3P–PhMe containing 5 mol% Et_3N the trione **8** (18%) and enone **1** (10%) were formed and 60% of bromide recovered; increasing the Et_3N to 1.5 mol gave the enone in 86% yield. In an attempt to prepare the homologue **2** by a similar route, the dione **3** was butenylated to give the alkene **10** (30% from but-2-enyl acetate, 48% from but-2-enyl ethyl carbonate). The alkene **10** reacted regiospecifically with NBS–Me_2SO–H_2O to give the bromohydrin which was oxidised to the ketone **11** [δ_H 1.7 (3 H, d, *J*/Hz 7]. The high regioselectivity of the addition may be accounted for by neighbouring group participation of a carbonyl oxygen in the favoured 5-*exo* mode. Reaction of the bromo ketone with Ph_3P–PhH–Et_3N brought about debromination to the ketone **12**.

The homologous ketone **2** was prepared using the annulation method developed by Yoshikoshi;[9] reaction of the dione **3** with 2-nitrobut-1-ene in boiling xylene containing KF gave the trione **12** (91%) which on extended reaction with NaH–PhH using vibro-mixing formed the dione **2** (61%). This five-step route allows the preparation of *ca.* 30 g batches in an overall yield of 31%. The dione **1** can also be prepared efficiently by this method. As expected, selective nucleophilic attack on the cyclohexanone carbonyl of the enedione **2** was possible with $NaBH_4$ to give the alcohol showing δ_H 3.52 (1 H, dd, *J*/Hz 7 and 2), in accord with bonding on the α face of the molecule; however neither of the enediones **1** or **2** reacted with vinylmagnesium bromide, presumably due to steric hindrance. The sterically less hindered lithium trimethylsilylethyne gave the adducts **14** and **15** from **1** and **2** respectively in excellent yields. The stereochemistry depicted is assumed on the basis of attack on the least hindered face of the molecule and has not been proven.



13



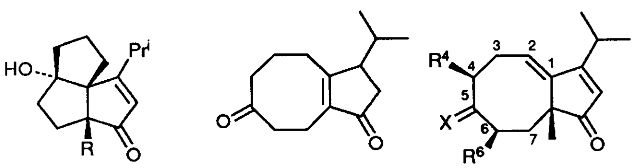


14; R = H, X = $SiMe_3$
15; R = Me, X = $SiMe_3$
16; R = X = H
17; R = Me, X = H

18; R = H
19; R = Me

It would be advantageous if the oxy-Cope rearrangement could be effected on the silylalkyne **15** or on the alkyne **17**, since additional functionality would be introduced. To this end the reaction mixture from the acetylene addition to the dione **2** was allowed to stand at 25 °C for 30 min instead of being quenched at 15 °C; however a mixture of at least six products was formed.

Reaction of **15** with KF and 18-crown-6 brought about desilylation, which could have been achieved more simply using Bu_4NF–THF (tetrahydrofuran). Attempts to bring about rearrangement of **17** thermally or with KH led to mixtures of products. Lindlar reduction of the alkynes **16** and **17** gave the alkenes **18** and **19**, which were recovered after exposure to KH–THF at 25 °C; on boiling, mixtures of products were formed similar to these obtained on reaction with KH and 18-crown-6 in THF at 0 °C. Reaction of the alkene **18** with KOH–MeOH at 65 °C gave the tricycle **20** [40%; ν_{max}/cm^{-1} 3350, 1710 and 1620; δ_H 6.08 (1 H, s), 2.8 (1 H, sep, *J*/Hz 7), 1.20 (3 H, d, *J*/Hz 7) and 1.18 (3 H, d, *J*/Hz 7]. The λ_{max}/nm of 245 did not agree with the calculated value (226) and may be due to interaction of the hydroxy group with the enone unit. When the alkene **18** was heated in $O(CH_2CH_2OH)_2$ the tricycle **20** was formed (50%), along with the enedione **22** (30%; ν_{max}/cm^{-1} 1705 and 1615; λ_{max}/nm 240). Reduction of the enedione **22** with H_2–Pd gave the dihydro product (ν_{max}/cm^{-1} 1750 and 1705), and reaction of **22** with KOH–MeOH effected a quantitative conversion into the tricycle **20**. From these results it is apparent that rearrangement can only be achieved under conditions where the initial product is thermally unstable, forming the tricycle **20** by aldol (or 'ene') reaction and the conjugated ketone **22** by prototropic migration. Reaction of the homologue **19** with KH–THF gave 5% of the tricycle **21** [λ_{max}/nm 246; ν_{max}/cm^{-1} 3500, 1700 and 1640; δ_H 6.1 (1 H, s), 2.8 (1 H, sep, *J*/Hz 7), 1.2 (3 H, d, *J*/Hz 7), 1.1 (3 H, d, *J*/Hz 7) and 1.0 (3 H, s)]. Attempts to trap the intermediate with Me_3SiCl were unsuccessful. On heating the alcohol **19** in $O(CH_2CH_2OH)_2$ an 86% yield of the tricycle **21** was obtained.



20; R = H
21; R = Me

22

23; R^4 = R^6 = H, X = O
24; R^4 = R^6 = H, X = OH
25; R^4 = ^{2}H, R^6 = H, X = O
26; R^4 = Me, R^6 = H, X = O
27; R^4 = H, R^6 = Me, X = O
28; R^4 = Br, R^6 = H, X = O

Since the tricycle **21** was readily available, we examined its conversion into a bicyclo[6.3.0]undecane derivative. To effect this by a conventional retro-aldol reaction was implausible but generation of an alkoxy radical which could fragment to an 8-membered ring seemed possible. To this purpose the alcohol **21** was treated with $Pb(OAc)_4$–I_2–PhH,[10] which resulted in formation of the diene **23** (86%) (ν_{max}/cm^{-1} 1703 and 1692; λ_{max}/nm 278).

To confirm the structure and obtain information on conformation relevant to the chemistry of the molecule an extensive NMR analysis was carried out. The protons of the 8-membered ring divide into two groups of 4- and 5-spins respectively; the analysis of the comparatively weakly coupled 4 spin group is straightforward. The 5-spin group poses two problems: the very strong coupling between the protons 3-H and 4-H, and the near-exact degeneracy between 4-H and the isopropyl methine. The programme DAVSYM2,[11] which fits to the complete spectral bandshape and hence does not require the assignment of individual lines, was used to refine the parameters for the 4-spin group and to analyse the 5-spin ABCDX system.

A well-digitised proton spectrum of **23** was edited to remove sections of baseline, a calculated isopropyl CH multiplet was

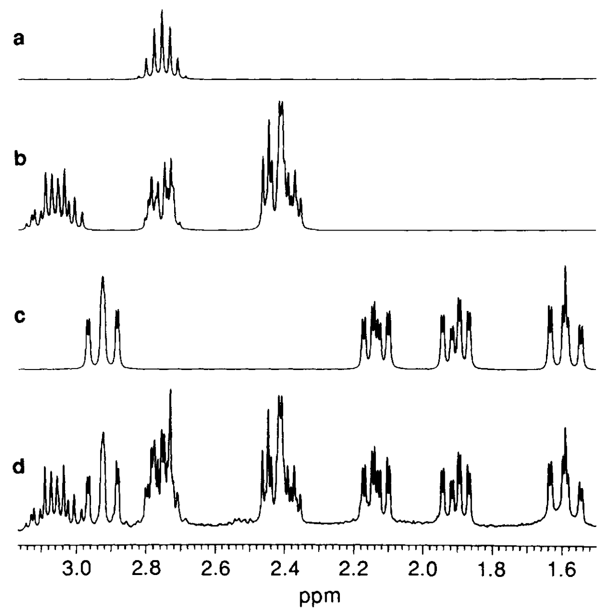


Fig. 1 **a** Simulated isopropyl CH multiplet at 2.75 ppm; **b** and **c** simulated spectra of the 4-spin (5-ring) and 5-spin (8-ring) systems respectively, after refinement with DAVSYM2; and **d** high field region of the experimental 300 MHz ^{1}H NMR spectrum of **19**, to which subspectra **b** and **c** were fitted

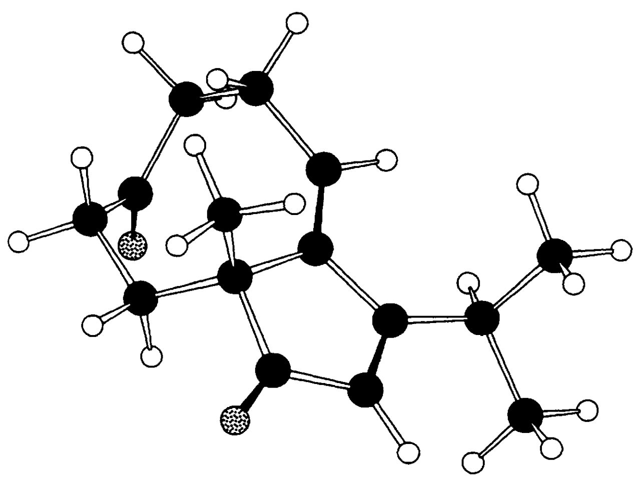


Fig. 2 Computed model of **23** using CHARMe programme

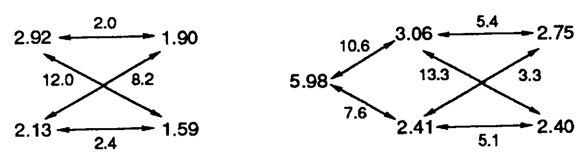


Fig. 3 δ and *J* values for 4- and 5-spin systems

substracted at 2.75 ppm, and the resultant 8 sections of spectrum were transferred to a Cyber 176 mainframe. Convergence of DAVSYM2 for the 5-spin system was critically dependent on starting parameters; some 50 runs, typically of 1 min duration, were needed before a satisfactory fit was obtained. Final agreement factors 'R' were 2.2 and 3.9% respectively for the 4- and 5-spin systems; the latter figure is particularly gratifying given the uncertainties involved in subtracting the overlapping isopropyl multiplet. The simulated component parts of the high field region of the proton spectrum of **29** may be compared with the experimental spectrum in Fig. 1. In Fig. 3 the $J^{1,3}$ values revealed by the simulation are compared with the dihedral angles derived from an energy minimised model (Fig. 2) of the diene **23** produced by the CHARMe programme on a

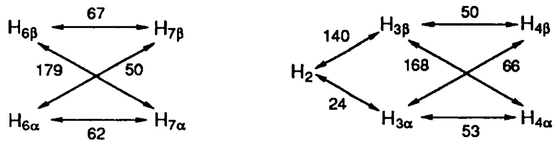
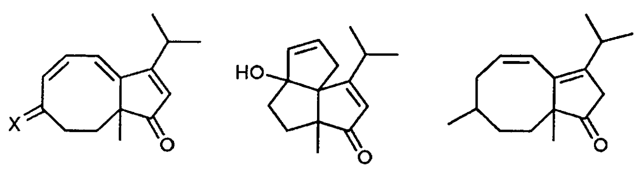


Fig. 4 Torsion angles from CHARMe calculation. α,β Refers to orientation relative to angular methyl.

Silicon Graphics IRIS-4D workstation. The dihedral angles of the model (Fig. 3) are consistent with the J^3 values and in particular show that one hydrogen is antiperiplanar to two vicinal hydrogens.

The model suggested that proton removal to form enolate and its reaction with electrophiles should both occur from the β face of the molecule. Modelling of the alkene isomers corresponding to the regioisomeric enolates showed the 6-ene to be marginally more stable (1 kcal)* than the 4-ene, but the difference is probably too small to be significant. In the event, reaction of the dione **23** with $LiNPr^i_2$–THF followed by quenching with D_2O gave > 75% of a monodeuterio compound **25**; from the NMR spectrum it was apparent that the signal at δ 2.92 was no longer present and that the signal at δ 1.59 was now a broadened doublet indicating 6-H abstraction and deuteriation from the β face. This enolate did not react with MeI; however when an enolate was generated using $LiNPr^i_2$–THF–$PO(NMe_2)_3$ and treated with MeI, an 8:2 mixture [capillary GC(CGC)] of monomethyl derivatives was formed. To our surprise the major product was apparently the 4-methyl isomer **26**, since the 4-spin system was intact and the signal at δ 2.75 had disappeared. We were unable to determine whether the minor isomer was a stereo- or a regio-isomer; the latter is strongly indicated by reaction of the enolate with Bu^tMe_2SiCl forming an 8:2 mixture (CGC) of enol ethers. Generation of an enolate using $LiN(SiMe_3)_2$–THF–$PO(NMe_2)_3$ followed by methylation reversed the isomer ratios giving the 6-methyl compound **27** as the predominant isomer. It is difficult to rationalise these results, but they do afford opportunities for some selective reactions at both C-4 and C-6. Bromination of the $LiNPr^i_2$-derived enolate gave the 4-bromo compound **28** which was converted into the triene **29** on reaction with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) in Me_2NCHO. Attempts to prepare the deconjugated diene by reduction of the triene **29** led to the tricycle **31**.



29; X = O
30; X = H, OH
31
32

However, reduction of the triene **29** with $NaBH_4$ formed the alcohol **30**, which on reduction with Li–NH_3 gave the diene **32**. On treatment with base the diene **32** was converted into the conjugated isomer identical with the product obtained from $NaBH_4$ reduction of the dione **23**. A variety of attempts to prepare a triene from the 4-methyl ketone **24** were unsuccessful.

Experimental

Light petroleum refers to the fraction b.p. 60–80 °C. Extracts were dried using Na_2SO_4. NMR spectra were measured in $CDCl_3$ at 300 MHz, J values are given in Hz. IR spectra were measured in $CHCl_3$ and UV spectra in EtOH.

2-Allyl-2-isopropylcyclohexane-1,3-dione **4**.—2-Isopropylcyclohexane-1,3-dione (3 g) and $Pd(PPh_3)_4$ (0.6 g) were dissolved in THF (75 cm^3) and DBU (3.05 cm^3) and allyl acetate (2.33 g) were added. The reaction mixture was stirred for 24 h in the dark. Most of the THF was removed under reduced pressure and the concentrated solution was purified by flash chromatography (light petroleum–Et_2O) (6:1) to give the *dione* **4** as a colourless oil (2.88 g); ν_{max}/cm^{-1} 1725 and 1680 (Found: M^+, 194.1307. $C_{12}H_{18}O_2$ requires M, 194.1307).

2-Formylmethyl-2-isopropylcyclohexane-1,3-dione **5**.—Finely powdered $NaIO_4$ (2.87 g) was added to the dione **4** (1.3 g), Et_2O (18 cm^3), water (18 cm^3) and OsO_4 (85 mg) over 45 min with continuous stirring. After 12 h the mixture was extracted with EtOAc. The combined extracts were washed with brine, dried and concentrated. Flash chromatography of the residue (light petroleum–Et_2O) (8:1) gave the *dione* **5** (1.1 g), m.p. 63–64 °C (Found: C, 67.2; H, 8.3. $C_{11}H_{16}O_2$ requires C, 67.4; H, 8.2%) which was oxidised with CrO_3–AcOH to the *acid* **6**, m.p. 209–210 °C (Found: C, 62.5; H, 7.7. $C_{11}H_{16}O_4$ requires C, 62.3; H, 7.6%). Reaction of **6** with Ac_2O–NaOAc gave the *enol lactone* **13**, m.p. 48–49 °C (Found: C, 68.0; H, 7.4. $C_{11}H_{14}O_3$ requires C, 68.0; H, 7.2%).

2-(3-Bromo-2-oxopropyl)-2-isopropylcyclohexane-1,3-dione **9**.—The alkene **4** (2.88 g) and dry DMSO (dimethyl sulphoxide) (50 cm^3) were cooled to 10 °C with stirring under N_2. Water (0.534 cm^3) was added followed by NBS (5.28 g) and stirring was continued for 1 h. Brine was added followed by extractions with Et_2O. The combined extracts were washed with brine, dried and evaporated under reduced pressure to give a brown oil (5 g); ν_{max}/cm^{-1} 3600 and 1705; δ_H 4.5–3.8 (1 H, m), 3.4 (4 H, m), 1.5 (3 H, d, J 7), 1.0 (3 H, d, J 7) and 0.85 (3 H, d, J 7) (Found: M^+, 290.0511 and 292.0497. $C_{12}H_{19}BrO_3$ requires M, 290.0518 and 292.0498). The bromohydrin (5 g) was dissolved in Me_2CO (100 cm^3). Jones' reagent (8 mol dm^{-3}; 10 cm^3) was added with stirring. After 12 h brine was added followed by extractions with EtOAc. The extracts were combined, washed with brine, dried and evaporated to give a brown oil (3.5 g). Purification of this by flash chromatography (light petroleum–Et_2O, 1:1) gave the *bromo ketone* **9** as a light brown solid (2.56 g), m.p. 84–85 °C (Found: C, 50.0; H, 3.7%; M^+, 288.0366 and 290.0343. $C_{12}H_{17}BrO_3$ requires C, 49.8; H, 5.9%; M, 288.0362 and 290.0342).

2-Isopropyl-2-(2-oxopropyl)cyclohexane-1,3-dione **8**.—$CuCl_2$ (2.3 g), $PdCl_2$ (0.822 g), Me_2NCHO (28 cm^3) and water (2.8 cm^3) were stirred under an O_2 atmosphere for 10 min. The alkene **4** (4.5 g) in Me_2NCHO (5 cm^3) was added to the reaction mixture and stirring continued for 12 h. HCl (2 mol dm^{-3}) was added followed by extractions with Et_2O; the combined extracts were washed with brine, dried and concentrated to give the *trione* **8** (4.14 g), m.p. 70–71 °C (light petroleum–Et_2O) (Found: C, 68.4; H, 8.7. $C_{12}H_{18}O_3$ requires C, 68.6; H, 8.6%); δ_H 3.15 (2 H, s) and 2.15 (3 H, s); ν_{max}/cm^{-1} 1710 and 1690.

2-(But-2-enyl)-2-isopropylcyclohexane-1,3-dione **10**.—2-Isopropylcyclohexane-1,3-dione (3 g) and Pd $(PPh_3)_4$ (0.6 g) were dissolved in THF (75 cm^3) and DBU (3.05 cm^3) and but-2-enyl acetate (2.33 g) were added. The reaction mixture was stirred for 24 h in the dark. Most of the THF was removed under reduced pressure and the concentrated solution was purified by flash chromatography (light petroleum–Et_2O) (6:1) to give the *dione* **10** as a colourless oil (1.94 g); ν_{max}/cm^{-1} 1725 and 1690 (Found: M^+, 208.1461. $C_{13}H_{20}O_2$ requires M, 208.1463).

* 1 cal = 4.186 J.

2-(3-*Bromo*-2-*oxobutyl*)-2-*isopropylcyclohexane*-1,3-*dione* **11**.—The alkene **10** (50 mg) and dry DMSO (2 cm^3) were cooled to 10 °C with stirring under N_2. Water (0.086 cm^3) was added followed by NBS (110 mg) and stirring was continued for 1 h. Brine was added followed by extractions with Et_2O. The combined organic extracts were washed with brine and dried. The solvents were removed under reduced pressure to give a brown oil (70 mg); ν_{max}/cm^{-1} 3600 and 1705; δ_H 4.5–3.8 (2 H, m), 1.5 (3 H, d, *J* 7) and 1.0 and 0.85 (3 H, d, *J* 7) (Found: M^+, 306.0659 and 304.0677. $C_{13}H_{21}BrO_3$ requires *M*, 306.0654 and 304.0674).

The bromohydrin (70 mg) was dissolved in Me_2CO (10 cm^3). Jones' reagent (8 mol dm^{-3}; 1 cm^3) was added with stirring. After 5 h, brine was added followed by extractions with EtOAc. The extracts were combined, washed with brine and dried. Removal of solvent gave a brown oil (61 mg). Purification by flash chromatography (light petroleum–Et_2O) (1:1) gave the *bromo ketone* **11** as a light brown oil (33 mg); δ_H 3.2 (2 H, s), 1.7 (3 H, d, *J* 7) and 0.9 (6 H, d, *J* 7) (Found: M^+, 304.0496 and 302.0514. $C_{13}H_{19}O_3Br$ requires *M*, 304.0499 and 302.05181).

3a-*Isopropyl*-3,3a,5,6-*tetrahydro*-7H-*indene*-2,4-*dione* **1**.—(*a*) The trione **8** (105 mg) in dry PhH (1 cm^3) was added to the vibrated suspension of NaH (48 mg, 50%) in dry benzene (1.5 cm^3) under N_2. The reaction mixture was boiled for 4 h and then AcOH (0.09 cm^3) and water (2 cm^3) were added, followed by extractions with Et_2O. The extracts were combined, washed with saturated aqueous $NaHCO_3$ and dried; removal of solvent gave the *dione* **1** (62 mg), m.p. 79–80 °C (light petroleum–Et_2O) (Found: C, 74.8; H, 8.5%; M^+, 192.1145. $C_{12}H_{16}O_2$ requires C, 75.0; H, 8.33%; *M*, 192.1150); λ_{max}/nm 238; ν_{max}/cm^{-1} 1705, 1690 and 1625: δ_H 5.8 (1 H, s).

(*b*) The bromo ketone **9** (4 g), PPh_3 (3.62 g), Et_3N (2.88 cm^3) in PhMe (150 cm^3) were heated under reflux for 24 h in a N_2 atmosphere. After cooling the mixture was filtered, the filtrate concentrated, and the residue purified by flash chromatography (PhMe–EtOAc, 9:1) to give the dione **1** (2.3 g).

Preparation of 4-*Hydroxy*-3a-*isopropyl*-4-*trimethylsilylethynyl*-3,3a,4,5,6,7-*hexahydroinden*-2-*one* **14** *and* 4-*Hydroxy*-3a-*isopropyl*-1-*methyl*-4-*trimethylsilylethynyl*-3,3a,4,5,6,7-*hexahydroinden*-2-*one* **15**.—(*a*) Me_3SiCCH (5.68 cm^3) and THF (92 cm^3) were cooled to −78 °C under N_2. BuLi (1.6 mol dm^{-3}; 25.12 cm^3) was added dropwise over 5 min with stirring. After 30 min the dione **2** (6.9 g) in THF (35 cm^3) was added to the reaction mixture over 10 min. After 15 min the mixture was warmed to −5 °C and saturated aqueous NH_4Cl was added followed by extractions with Et_2O. The combined extracts were washed with brine, dried, and evaporated to give the *alkyne* **15** (11.12 g), m.p. 105–106 °C (light petroleum–Et_2O) (Found: C, 70.8; H, 9.0%; M^+, 220.1463. $C_{18}H_{28}O_2Si$ requires C, 71.0 H, 9.2%; *M*, 304.1858); λ_{max}/nm 242; ν_{max}/cm^{-1} 3600, 2108, 1710 and 1618; δ_H 2.64 and 2.30 (1 H, *J* 20), 2.60 (1 H, br d, *J* 8), 2.4 (1 H, septet, *J* 7), 1.66 (3 H, s), 1.18 and 0.6 (3 H, d, *J* 7) and 0.08 (9 H, s).

(*b*) In a similar manner the dione **1** (50 mg) was converted into the *alkyne* **14** (73 mg), m.p. 101–103 °C (light petroleum–Et_2O) (Found: C, 70.2; H, 9.2%; M^+, 290.1702. $C_{17}H_{26}O_2Si$ requires C, 70.3; H, 9.0%; *M*, 290.1702); λ_{max}/nm 242; ν_{max}/cm^{-1} 3600, 2180 and 1710; δ_H 5.84 (1 H, s), 2.66 and 2.26 (1 H, d, *J* 19), 1.07 and 0.62 (3 H, d, *J* 7) and 0.08 (9 H, s).

2-*Isopropyl*-2-(2-*oxobutyl*)*cyclohexane*-1,3-*dione* **12**.—2-Isopropylcyclohexane-1,3-dione (50 g) and dry KF (18.8 g) in xylene (800 cm^3) were stirred under N_2 for 30 min. 2-Nitrobut-1-ene (49.18 g) was added to the reaction mixture, which was stirred and boiled for 16 h. Most of the xylene was removed under reduced pressure and the concentrated solution was chromatographed on silica gel (light petroleum–Et_2O) to give the *trione* **12** (67.5 g), crystallised from Et_2O, m.p. 65.5–67 °C (Found: C, 69.4; H, 8.9%; M^+, 224.1414. $C_{13}H_{20}O_3$ requires C, 69.64; H, 8.9%; *M*, 224.1412); ν_{max}/cm^{-1} 1710 and 1690; δ_H 3.15 (2 H, s), 3.0 (2 H, q, *J* 7), 2.1 (3 H, t, *J* 7) and 0.9 (6 H, d, *J* 7).

3a-*Isopropyl*-1-*methyl*-3,3a,5,6-*tetrahydro*-7H-*indene*-2,4-*dione* **1**.—The trione **12** (13.44 g) in dry PhH (60 cm^3) was added to a vibrated suspension of NaH (50%, 5.76 g) in dry PhH (90 cm^3) under N_2. The reaction mixture was boiled for 52 h. After cooling, AcOH (12 cm^3) and water (80 cm^3) were added, followed by extraction with Et_2O. The combined extracts were washed with saturated aqueous $NaHCO_3$ and evaporated to give the *dione* **2** as a light brown solid (7.85 g), crystallised from light petroleum–Et_2O, m.p. 82 °C (Found: C, 75.8; H, 8.7%; M^+, 206.1311. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.7%; *M*, 206.1307); λ_{max}/nm 244; ν_{max}/cm^{-1} 1705 and 1655; δ_H 2.9 and 2.1 (1 H, d, *J* 19), 1.7 (3 H, s) and 0.8 and 0.7 (3 H, d, *J* 7).

Preparation of 4-*Ethynyl*-4-*hydroxy*-3a-*isopropyl*-3,3a,-4,5,6,7-*hexahydroinden*-2-*one* **16** *and* 4-*Ethynyl*-4-*hydroxy*-3a-*isopropyl*-1-*methyl*-3,3a,4,5,6,7-*hexahydroinden*-2-*one* **17**.—(*a*) The alkyne **15** (10.18 g), THF (100 cm^3) and Bu_4NF (1 mol dm^{-3}; 36.85 cm^3) were stirred at ambient temperature for 30 min. HCl (2 mol dm^{-3}) was added, the organic layer was separated and the aqueous layer was extracted with ether. The extracts were combined, washed with water, then brine, and dried. Concentration followed by flash chromatography (light petroleum–Et_2O, 1:1) afforded the *alkyne* **17** (6.95 g), m.p. 142–145 °C (Found: C, 77.5; H, 8.8%; M^+, 232.1458. $C_{15}H_{20}O_2$ requires C, 77.6; H, 8.6%; *M*, 232.1458); λ_{max}/nm 244; ν_{max}/cm^{-1} 3600, 2185, 1710 and 1620; δ_H 2.7 and 2.35 (1 H, d, *J* 20), 2.6 (1 H, bd, *J* 8), 2.4 (1 H, septet, *J* 7), 2.25 (1 H, s), 1.7 (3 H, s), and 1.2 and 0.62 (3 H, d, *J* 7).

(*b*) The silylalkyne **14** (0.68 g), was converted into a similar way into the *alkyne* **16** (0.46 g), m.p. 134–135 °C (light petroleum–Et_2O) (Found: C, 76.9; H, 8.4%; M^+, 218.1310. $C_{14}H_{18}O_2$ requires C, 77.1; C, 8.3%; *M*, 218.1307); λ_{max}/nm 236; ν_{max}/cm^{-1} 3600, 3300, 1705 and 1680; δ_H 5.9 (1 H, s), 2.65 and 2.35 (1 H, d, *J* 19), 2.6 (1 H, d, *J* 8), 2.28 (1 H, s), 1.68 (3 H, s) and 1.2 and 0.62 (3 H, d, *J* 7).

Preparation of 4-*Hydroxy*-3a-*isopropyl*-4-*vinyl*-3,3a,4,5,6,7-*hexahydroinden*-2-*one* **18** *and* 4-*Hydroxy*-3a-*isopropyl*-1-*methyl*-4-*vinyl*-3,3a,4,5,6,7-*hexahydroinden*-2-*one* **19**.—The alkyne **17** (6.5 g) was dissolved in EtOAc (50 cm^3). Lindlar catalyst (65 mg) was added and the reaction mixture was stirred under an atmosphere of H_2 for 5 h at ambient temperature. The catalyst was removed by filtration through Celite and the EtOAc was removed. Purification of the residue by flash chromatography (light petroleum–Et_2O, 3:1) afforded the *alkene* **19**, m.p. 111–112 °C (5.5 g) (light petroleum–Et_2O) (Found: C, 76.7; H, 9.3%; M^+, 234.1617. $C_{15}H_{22}O_2$ requires C, 76.7; H, 9.4%; *M*, 234.1620); λ_{max}/nm 248; ν_{max}/cm^{-1} 3500, 1705 and 1615; δ_H 6.0 (1 H, dd, *J* 4 and 14), 5.4 (1 H, d, *J* 18), 5.15 (1 H, d, *J* 14), 2.75 (1 H, dd, *J* 3), 1.95 (1 H, bs), 1.7 (3 H, s) and 1.2 and 0.6 (3 H, d, *J* 7).

The alkyne **16** (35 mg) was reduced in a similar fashion to the *alkene* **18**, m.p. 108–109 °C (light petroleum–Et_2O) (Found: C, 73.5; H, 9.2%; M^+, 220.1461. $C_{14}H_{20}O_2$ requires C, 73.1; H, 9.1%; *M*, 220.1463); λ_{max}/nm 241; ν_{max}/cm^{-1} 3550, 3400, 1710 and 1618; δ_H 6.0 (1 H, dd, *J* 4 and 14), 5.9 (1 H, s), 5.3 (1 H, d, *J* 18), 5.1 (1 H, d, *J* 14), 2.75 (1 H, dd, *J* 8 and 3), 2.55 (1 H, m), 1.9 (1 H, br s), 1.72 (3 H, s) and 1.2 and 0.62 (3 H, d, *J* 7).

Pyrolysis of the Alkene **18**.—The alkene **18** (40 mg) was boiled in diethylene glycol (5 cm^3) for 2 h under an atmosphere of N_2. After dilution with water the mixture was extracted with Et_2O. The extracts were combined, washed with brine, dried and evaporated. Separation by flash chromatography (light petroleum–Et_2O) (7:3) gave the *8-hydroxy-2-isopropyltricyclo-*[6.3.0.0^{1,5}]*undec-2-en-4-one* **20** (20 mg), m.p. 79 °C (light petroleum) (Found: C, 76.3; H, 9.2%; M^+, 220.1463. $C_{14}H_{20}O_2$ requires C, 76.4; H, 9.2%; *M*, 220.1463); λ_{max}/nm 245; ν_{max}/cm^{-1} 3500, 3300, 1700 and 1640; δ_H 6.08 (1 H, s); and the *bicyclo*[6.3.0]*undecenedione* **23** as an oil (12 mg); λ_{max}/nm 240; ν_{max}/cm^{-1} 1705 and 1620; δ_H 2.84 (1 H, br s), 2.76 (1 H, m) and 1.0 and 0.66 (3 H, d, *J* 7) (Found: M^+, 220.1463. $C_{14}H_{20}O_3$ requires *M*, 220.1463).

Preparation of 8-Hydroxy-2-isopropyl-5-methyltricyclo-[6.3.0.0^{1,5}]*undec-2-en-4-one* **21**.—The alkene **19** (6.7 g) was boiled in diethylene glycol (60 cm^3) for 10 min under an atmosphere of N_2. After cooling, water and Et_2O were added. The organic layer was separated and the aqueous layer extracted with Et_2O. The combined extracts were washed with brine, dried and concentrated to give the *tricycle* **21** (5.95 g), m.p. 82 °C (light petroleum) (Found: 76.9; H, 9.4%; M^+, 334.1615. $C_{15}H_{22}O_2$ requires C, 76.9; H, 9.4%; *M*, 234.1620); λ_{max}/nm 245; ν_{max}/ cm^{-1} 3500, 1700 and 1640; δ_H 6.1 (1 H, s), 2.8 (1 H, septet, *J* 7), 1.4 (1 H, dt, *J* 12) and 1.2 and 1.1 (3 H, d, *J* 7) and 1.0 (3 H, s).

Preparation of 11-Isopropyl-8-methylbicyclo[6.3.0]*undec-1,10-diene-5,9-dione* **23**.—The tricycle **21** (2.26 g), $Pb(OAc)_4$ (14.97 g) and I_2 (4.29 g) were boiled in dry PhH (50 cm^3) for 10 min under N_2. The solution was cooled and saturated aqueous $Na_2S_2O_5$ and Et_2O were added to give a yellow precipitate which was filtered off. The organic layer was separated, washed with brine, dried and concentrated to a brown oil. Flash chromatography (light petroleum–Et_2O, 2:3) of the latter gave the *dione* **23** (1.93 g), m.p. 83–84 °C (light petroleum–Et_2O) (Found: C, 77.4; H, 8.7%; M^+, 232.1463. $C_{15}H_{20}O_2$ requires C, 77.6; H, 8.6%; *M*, 232.1458); λ_{max}/nm 278; ν_{max}/cm^{-1} 1703, 1692 and 1605.

Methylation of the Dione **23**.—(*a*) Pr^i_2NH (0.66 cm^3) and THF (15 cm^3) were cooled to −78 °C under N_2. BuLi (1.6 mol dm^{-3}; 2.96 cm^3) was added. After 5 min the diene **23** (1 g) in THF (5 cm^3) was added dropwise, followed by HMPA (hexamethylphosphoramide) (0.824 cm^3). After 5 min MeI was added to the reaction mixture. The mixture was stirred for 3 h and then allowed to warm to ambient temperature when saturated aqueous NH_4Cl was added to it. The mixture was extracted with Et_2O and the combined extracts were concentrated to give a brown oil which, on flash chromatography (light petroleum–Et_2O, 2:3), gave starting material (16 mg) and the methylated isomers as a waxy solid (700 mg). GLC and NMR spectroscopy of the latter indicated that the *6-methyl compound* **27**; λ_{max}/nm 276; ν_{max}/cm^{-1} 1705 and 1605; δ_H 6.04 (1 H, dd, *J* 11 and 8), 5.98 (1 H, s), 3.1 (2 H, m), 2.1 (1 H, m), 1.96 (1 H, m), 1.54 (1 H, bt, *J* 7) and 1.15 and 1.05 (3 H, d, *J* 7) (Found: M^+, 246.1623. $C_{16}H_{22}O_2$ requires *M*, 246.1620), was contaminated with the *4-methyl isomer* **26**.

(*b*) The tricycle (0.54 g), HMPA (0.48 cm^3) and the THF (10 cm^3) were cooled to 0 °C under N_2 with stirring. $LiN(SiMe_3)_2$ (1 mol dm^{-3}; 2.8 cm^3) was added. After 10 min MeI (0.217 cm^3) was added to the reaction mixture followed by saturated aqueous $NaHCO_3$. The mixture was extracted with Et_2O and the extract concentrated to give a yellow oil (0.48 g). GLC and NMR spectroscopy of the latter indicated that *1-isopropyl-4,8-dimethylbicyclo*[6.3.0]*undeca-1,10-diene-5,9-dione* **26** was the major (80%) product; λ_{max}/nm 278; ν_{max}/cm^{-1} 1705 and 1605; δ_H 6.04 (1 H, dd, *J* 10.8 and 7.8), 5.98 (1 H, s), 3.1 (1 H, td, *J* 13.2 and 2.4), 2.8 (2 H, m), 2.45 (2 H, m), 2.1 (1 H, dd, *J* 8.2 and 2.2), 1.92 (1 H, m), 1.55 (1 H, dt, *J* 12 and 2.2), 1.34 (3 H, s), 1.25 and 1.13 (3 H, d, *J* 6.8) and 1.2 and 0.83 (3 H, d, *J* 7) (Found: M^+, 246.1620. $C_{16}H_{22}O_2$ requires *M*, 246.1620).

Bromination of the Dione **23**.—The enolate (*ex* LDA–HMPA) of the dione **23** (1 g) was prepared as above. After 5 min Br_2 (0.26 cm^3) in CH_2Cl_2 (2 cm^3) was added to the reaction mixture. Saturated aqueous $NaHCO_3$ was added after 1 min and the mixture extracted with Et_2O. Concentration of the extract gave a dark brown oil which, on flash chromatography (light petroleum–Et_2O, 4:1), gave the *bromide* **28** (0.8 g); λ_{max}/nm 278; ν_{max}/cm^{-1} 1710 and 1615; δ_H 6.0 (1 H, dd, *J* 10.8 and 7.8), 5.95 (1 H, s), 3.8 (1 H, m), 2.95 (2 H, m), 2.85 (1 H, td, *J* 13.2 and 2.4), 2.7 (1 H, m), 1.85 (1 H, m), 1.48 (1 H, dt, *J* 12 and 2), 1.32 (3 H, s) and 1.22 and 1.10 (3 H, d, *J* 7) (Found: M^+, 310.0569 and 312.0549. $C_{15}H_{19}BrO_2$ requires *M*, 310.0574 and 312.0556).

Preparation of 11-Isopropyl-8-methylbicyclo[6.3.0]*undeca-1,3,10-triene-5,9-dione* **29**.—The bromo ketone **28** (500 mg) was dissolved in DMF (10 cm^3) and DBU (0.26 cm^3) added. After 2 h water was added and the mixture extracted with Et_2O. The extracts were combined, washed with water and brine, dried and concentrated. The resulting brown oil was purified by flash chromatography (light petroleum–Et_2O, 3:2) to give the *triene* **29** (230 mg); λ_{max}/nm 326 and 243; ν_{max}/cm^{-1} 1710 and 1640; δ_H 6.7 (1 H, d, *J* 7), 6.06 (1 H, s), 6.0 (1 H, d, *J* 12.5), 2.96 (2 H, m), 2.32 (1 H, bd, *J* 12), 2.1 (1 H, t, *J* 14), 1.9 (1 H, m), 1.24 (6 H, dd, *J* 7) and 1.2 (3 H, s) (Found: M^+, 230.1302. $C_{15}H_{18}O_2$ requires *M*, 230.1307).

Preparation of 5-Hydroxy-11-isopropyl-8-methylbicyclo-[6.3.0]*undec-1,3,10-trien-9-one* **30**.—$CeCl_3$ (595 mg) was dissolved in hot Pr^iOH (10 cm^3) and the solution cooled to 0 °C. The trienedione **29** (330 mg) was added to it, followed by $NaBH_4$ (60 mg). The reaction mixture was then stirred at 10 °C for 3 h. After this it was diluted with water and CH_2Cl_2; the aqueous layer was then extracted with CH_2Cl_2. The extracts were combined, washed with brine, dried and concentrated to give the alcohol **30** (270 mg); λ_{max}/nm 294; ν_{max}/cm^{-1} 3520, 3400, 1710 and 1620; δ_H 6.3 (1 H, d, *J* 3), 6.15 (1 H, dd, *J* 7 and 3), 6.07 (1 H, s), 5.8 (1 H, dd, *J* 6), 4.0 (1 H, br s), 2.9 (1 H, septet, *J* 7) and 1.24 and 1.20 (3 H, d, *J* 7), 0.96 (3 H, s) (Found: M^+, 232.1463. $C_{15}H_{20}O_2$ requires *M*, 232.1462).

Reduction of the Trieneol **30**.—Li (18 mg) was added to liquid NH_3 (10 cm^3) under N_2 with stirring. The resulting dark blue solution was stirred for 15 min and then the trienol (15 mg) in THF (2 cm^3) was added over 1 min. On discharge of the blue colouration (*ca.* 1 min) NH_4Cl was added and NH_3 evaporated. Water and Et_2O were added, the organic layer was separated, and the aqueous layer was extracted with Et_2O. The extracts were combined, washed with brine, dried and concentrated to give the *diene* **32** (12 mg); ν_{max}/cm^{-1} 3400, 1750 and 1640; δ_H 6.1 (1 H, d, *J* 10.5), 5.8 (1 H, m), 3.08 (1 H, m), 2.9 and 2.84 (1 H, dd, *J* 20 and 2), 0.98 (3 H, s) and 0.96 (6 H, d, *J* 7) (Found: M^+, 234.163 21; $C_{15}H_{20}O_2$ requires *M*, 234.1619).

Silylation of the Dienedione **23** *Enolates*.—The dione **23** (500 mg) was converted into the enolates with $LiNPr^i_2$–HMPA as above. Bu^tMe_2SiCl (480 mg) in THF (1 cm^3) was added to the reaction mixture which was then stirred at −78 °C for 10 min before being allowed to warm to 0 °C. Saturated aqueous $NaHCO_3$ was added to the mixture which was then extracted with diethyl ether. The combined extracts were washed with brine, dried and concentrated to give the *ethers* (520 mg). GC showed the presence of two *ethers* (8:2). The major product showed λ_{max}/nm 276; ν_{max}/cm^{-1} 1705 and 1610; δ_H 6.1 (1 H, t, *J* 10.5), 6.0 (1 H, s), 5.0 (1 H, t, *J* 10.5), 3.1 (1 H, m), 1.25 (3 H, s), 1.12 and 1.08 (3 H, d, *J* 7), 0.86 (9 H, s) and 0.05 (6 H, s) (Found: M^+, 346.2327. $C_{21}H_{34}O_2Si$ requires *M*, 346.2308). The minor product showed δ_H 6.0 (1 H, t, *J* 10.5), 5.9 (1 H, s), 4.85

(1 H, t, J 10.5), 2.18 (3 H, s), 1.08 and 1.04 (3 H, d, J 7), 0.80 (9 H, s) and 0.03 (6 H, s).

The enolate prepared using $LiN(SiMe_3)_2$ gave the same two products with the ratio reversed.

Acknowledgements

We thank the SERC for financial support and Professor G. Haegele, University of Düsseldorf for providing the programme DAVSYM2.

References

1 G. Pattenden and A. M. Birch, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1913; L. A. Paquette, D. R. Andrews and P. J. Springer, *J. Org. Chem.*, 1983, **48**, 1148; S. L. Schreiber, T. Sammakia and W. E. Crowe, *J. Am. Chem. Soc.*, 1986, **108**, 3128.

2 D. A. Evans and A. M. Golob, *J. Am. Chem. Soc.*, 1975, **97**, 4765.

3 S. Swaminathan, J. P. John and S. R. Ramachandran, *Tetrahedron Lett.*, 1962, 729; S. Swaminathan, R. Uma and K. Rajagopalan, *Tetrahedron Lett.*, 1984, 5825.

4 W. G. Dauben and D. J. Hart, *J. Org. Chem.*, 1977, **42**, 3787.

5 E. Piers and J. R. Grierson, *J. Org. Chem.*, 1977, **42**, 3755.

6 B. M. Trost and D. P. Curran, *J. Am. Chem. Soc.*, 1980, **102**, 5699.

7 J. Tsuji, I. Shimizu and K. Yamamoto, *Tetrahedron Lett.*, 1976, 2975.

8 M. Ohta, K. K. Fukui, R. Sudo and M. Masuke, *J. Org. Chem.*, 1968, **33**, 3504.

9 A. Yoshikoshi, T. Yanami, M. Miyashita, M. Kato, Y. Itagaki and K. Matsuara, *J. Org. Chem.*, 1977, **42**, 2779.

10 C. Mystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner and A. Wettstein, *Helv. Chim. Acta*, 1962, **45**, 1317.

11 W. Boenigk, Doctorial Thesis, University of Düsseldorf, 1984.

Paper 0/05553K
Received 10*th December* 1990
Accepted 25*th January* 1991