Bicyclo[3.3.0]octenones in Synthesis. An Approach to the Synthesis of the Antitumor Sesquiterpene Quadrone

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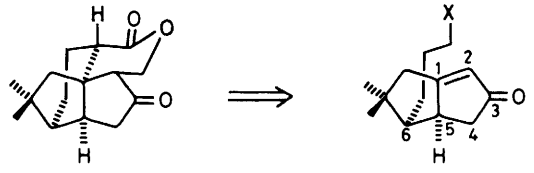
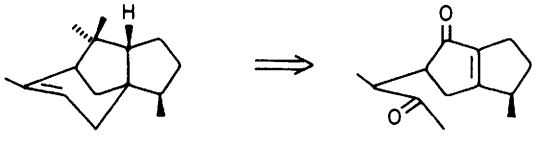
A synthetic approach to the antitumor sesquiterpene quadrone (**1**), based on intramolecular Michael reaction from a C-6 substituted bicyclo[3.3.0]oct-1(2)-en-3-one [*viz.* (**2**)] is outlined. The preparations of the bicyclo-octenones (**33b**), (**33a**), and (**41**), precursors of (**14**), (**15**), and (**16**) respectively, are described, but attempts to induce these substrates [and the nitrone (**42**)] to undergo intramolecular Michael reactions to the carbocyclic ring system in quadrone, met with total failure.

Treatment of the bromo ketone (**58**) with methanolic sodium methoxide resulted in smooth intramolecular alkylation producing the tricyclic dione (**59**) containing the carbocyclic ring system in quadrone (**1**).

The sesquiterpene quadrone is found in the broth of the fungus *Aspergillus terreus*. Its structure (**1**), which followed from direct *X*-ray measurements, was published in 1978.[1] Quadrone exhibits considerable inhibitory activity *in vitro* against human epidermoid carcinoma of the nasopharynx, and *in vivo* activity against p-388 lymphocytic leukemia in mice. Although the carbocyclic ring system in quadrone is unique, it does show ring features, *i.e.* bicyclo[3.3.0]octane, bicyclo[3.2.1]octane, and bicyclo[4.3.0]nonane, found in many other biologically important natural terpenes. Needless to say, the synthesis of quadrone has attracted the attentions of many research groups.[2] In this paper, we summarise the outcome of one of our approaches to quadrone based on the use of a C-6 substituted bicyclo[3.3.0]oct-1(2)-en-3-one [*viz.* (**2**)] as a key intermediate. In the accompanying paper, we describe how the related bicyclo[3.3.0]octenone (**4**) can be used to elaborate the tricyclic ring system found in the sesquiterpene cedrene (**3**).[3]

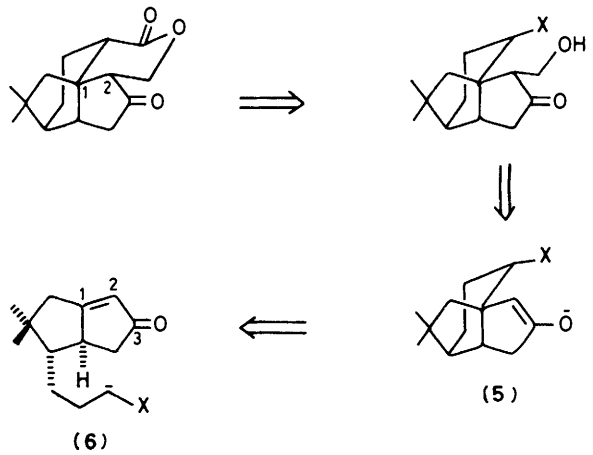


(**1**) (**2**)



(**3**) (**4**)

Our approach to the synthesis of quadrone (**1**) was based on the retrosynthetic analysis summarised in Scheme 1. In this approach, we envisaged introducing the cyclohexane ring and the hydroxymethyl residue at C-2 (later to become part of the lactone moiety) in quadrone, in a single step following intramolecular Michael reaction from (**6**) and trapping of the specific enolate (**5**) with formaldehyde (or its chemical equivalent). This general design had the attraction that a number of variations, including umpolung strategy, could be applied in order to generate the nucleophilic centre in the side chain of (**6**);† its only limitation was a stereochemical feature, since it was necessary to develop a synthesis of the key bicyclo-octenone intermediate (**2**) having the three-carbon side chain and the bridgehead hydrogen atom orientated *syn* to each other.



(**6**) (**5**)

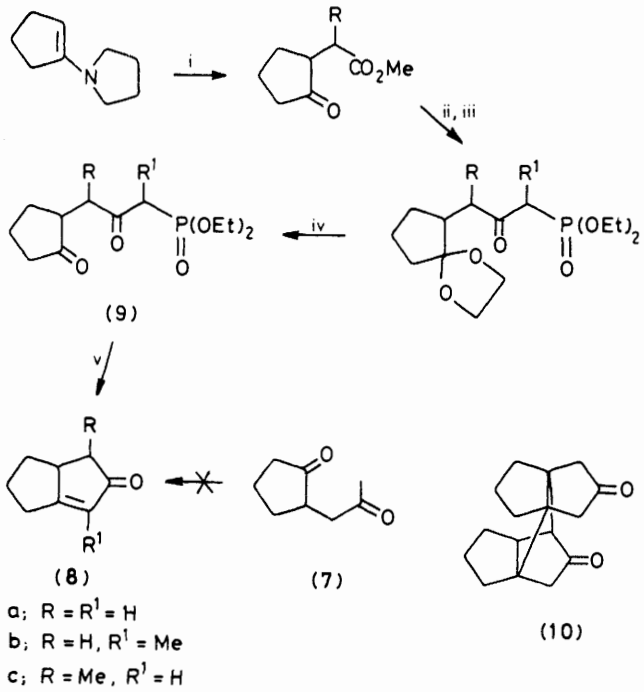
Scheme 1. X = Carbanion stabilizing group

We began our investigation of this approach to quadrone by first examining synthetic routes to bicyclo[3.3.0]oct-1(2)-en-3-ones. The most obvious approach to these enones was *via* aldolisation of appropriate 1,4-diones [*via* (**7**)].[5a] Since however the parent bicyclo-octenone (**8a**) cannot be produced by straightforward base-treatment of (**7**),[5b] we were attracted to a variant of this design using the intramolecular Wadsworth-Emmons reaction.[6] In a model study, the phosphonate ester intermediates (**9**) were first prepared by the procedure summarised in Scheme 2. Although the C-methyl substituted derivatives (**9b**) and (**9c**) were found to undergo smooth intramolecular olefination, leading to (**8b**) and (**8c**) respectively, much to our surprise, the unsubstituted phosphonate ester (**9a**) instead led largely to the novel dimer (**10**), derived *via* two successive Michael reactions from (**8a**) (for a full discussion of this work see ref. 7).

With the failure of the Wadsworth-Emmons reaction to provide a useful route to the parent bicyclo[3.3.0]octenone (**8a**)‡ we decided to modify our initial proposal for the synthesis of quadrone (Scheme 1), and incorporate a methyl group at C-2

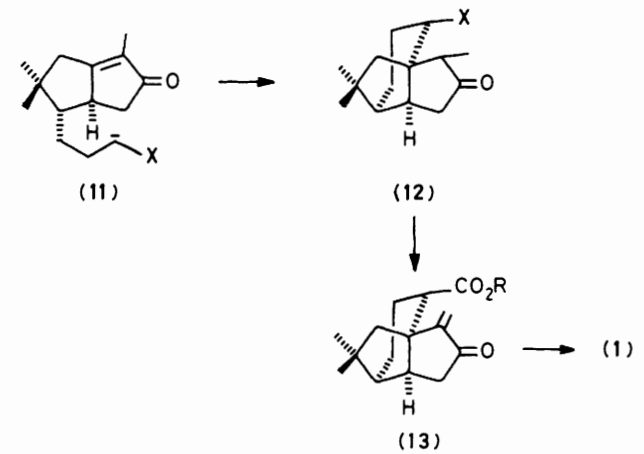
† For some recent demonstrations of the use of the intramolecular Michael reaction in synthesis see ref. 4.

‡ For an illustration of the use of the Wadsworth-Emmons reaction in the synthesis of carbaprostacyclin see ref. 8.



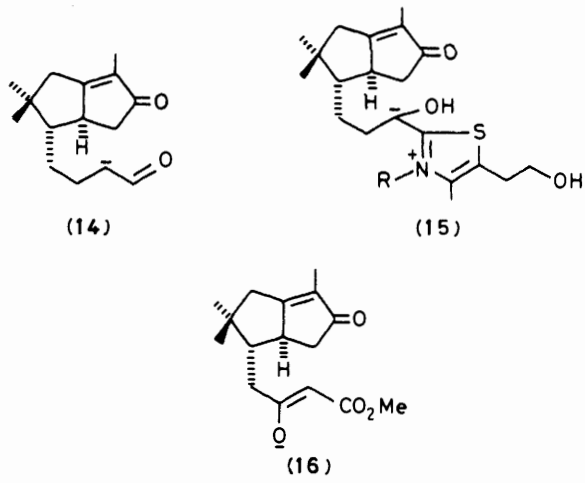
Scheme 2. *Reagents:* i, RCH(Br)CO_2Me; ii, $HO(CH_2)_2OH$, *p*-TSA; iii, $R^1CH_2P(O)(OEt)_2$, BuLi; iv, HCl; v, NaH, DME

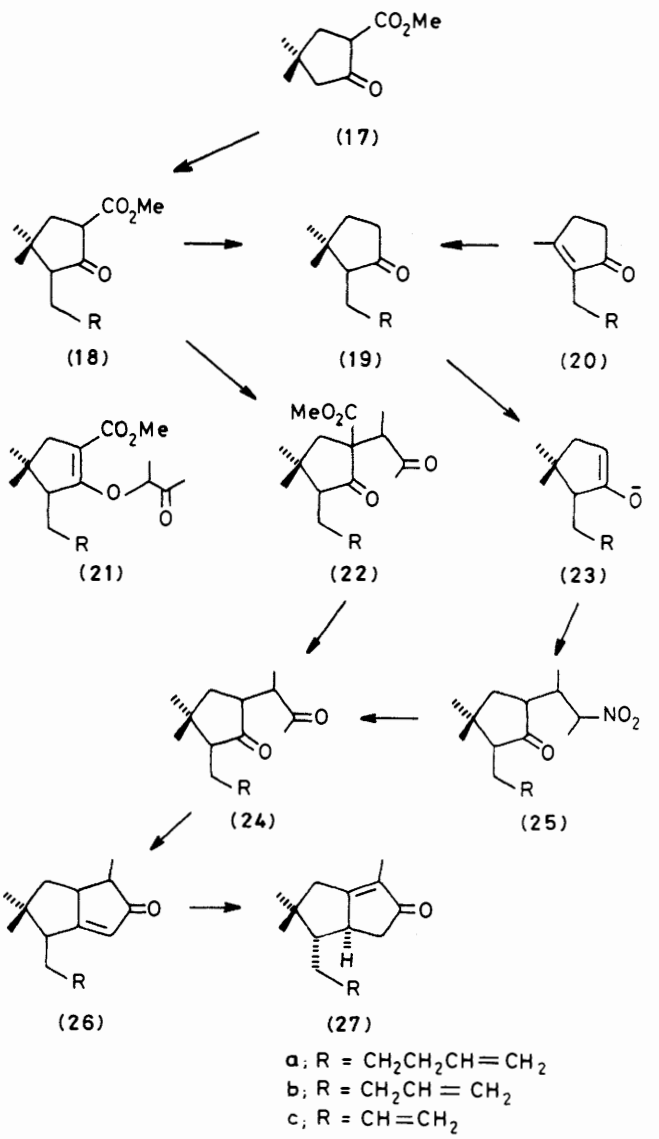
in the key bicyclo-octenone intermediate (**6**); these bicyclo-octenones could be obtained from appropriately substituted 1,4-diones by straightforward aldolisation.[5a] Our aim was to then replace the methyl group in (**12**) by the exocyclic methylene system (**13**) after the intramolecular Michael reaction (**11**) ⟶ (**12**) (Scheme 3).* To give us optimal flexibility in this new design, we also planned to synthesise a number of ω-alkenyl substituted bicyclo-octenones *viz.* (**27a**), (**27b**), and (**27c**) for elaboration to precursors of the carbanion intermediates (**14**), (**15**), and (**16**) respectively.



Scheme 3.

The ω-alkenyl substituted bicyclo-octenones (**27**) were conveniently synthesised starting from the readily available β-keto ester (**17**) (Scheme 4). Thus, γ-alkylation of (**17**) using the appropriate alkenyl halide first gave (**18**), which on demethoxycarbonylation led to the substituted cyclopentanones (**19**). The same cyclopentanones could also be obtained by



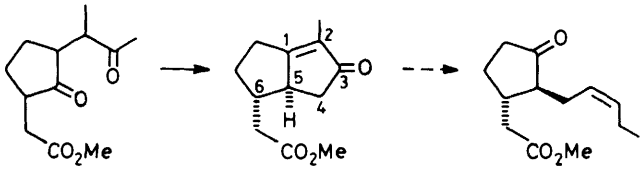


Scheme 4.

* We envisaged achieving this objective, for example, by phenylselenation of the thermodynamic enolate derived from (**12**), followed by oxidative elimination of the phenylselenyl group.

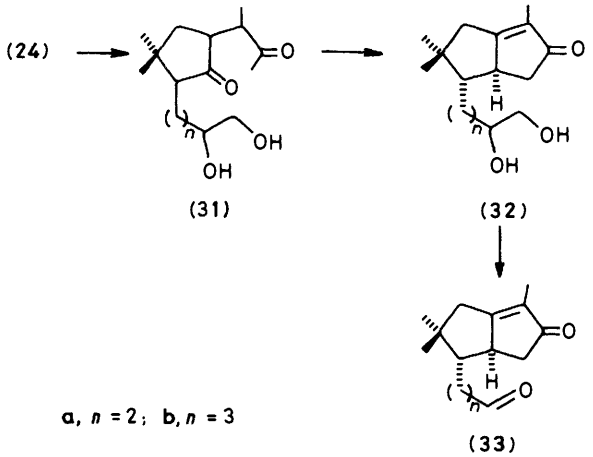
Michael addition of lithium dimethylcuprate to the corresponding cyclopentenones (**20**). Treatment of the cyclopentanones (**19**) in tetrahydrofuran at −78 °C with lithium hexamethyldisilazide produced the specific enolates (**23**) which reacted smoothly with 2-nitrobut-2-ene leading to the nitro ketones (**25**) in high yield.[9] Hydrolysis of (**25**), using sodium nitrite and n-propyl nitrite in dimethyl sulphoxide,[10] then provided the 1,4-diones (**24**). The use of lithium hexamethyldisilazide as base and 2-nitrobut-2-ene as alkylating agent in the sequence leading to (**24**) was significant since a number of alternative procedures based on the use of enamine, oxime, hydrazone, and trialkylsilyl derivatives of (**19**), and alkylating agents other than 2-nitrobut-2-ene, failed to yield any products resulting from *C*-alkylation under a range of conditions. In addition, although it was possible to alkylate the β-keto ester (**18**) with 3-bromobutan-2-one leading to (**22**), which could then be demethoxycarbonylated to (**24**), significant amounts (>50%) of the product (**21**), resulting from *O*-alkylation of (**18**), were produced concurrently.

Treatment of the 1,4-dione (**24**) with potassium t-butoxide in t-butyl alcohol resulted in smooth aldolisation, to (**26**), followed by isomerisation giving a single isomer of the bicyclo-[3.3.0]octenone (**27**). This aldolisation-isomerisation sequence is not without precedent,[5a] and furthermore has been shown to produce the *syn*-stereoisomer shown when the cyclopentanone precursor has an additional substituent at C-6. Thus, Sisido *et al.*[11] found that the substituted cyclopentanone (**28**) undergoes base-catalysed cyclisation producing only the *syn*-orientated enone (**29**) which they then used in a total synthesis of methyl jasmonate (**30**).



(**28**) (**29**) (**30**)

Having established a viable synthetic route to the ω-alkenyl substituted bicyclo-octenones (**27**), it came as an immense surprise when we found that it was not possible to oxidatively cleave the terminal double bonds in these substrates without cleaving the cyclopentenone double bonds simultaneously! Although there is ample precedent for effecting this type of selective oxidation,[12] in no instance, using a range of reagents, were we able to observe any selectivity. The problem was eventually overcome when we converted the ω-double bonds in the 1,4-dione intermediates (**24**) into the corresponding vicinal diols (**31**), and then effected aldolisation-rearrangement [to (**32**)] prior to oxidative cleavage with sodium periodate. Using this procedure we ultimately secured useful quantities of the aldehydes (**33a**) and (**33b**).



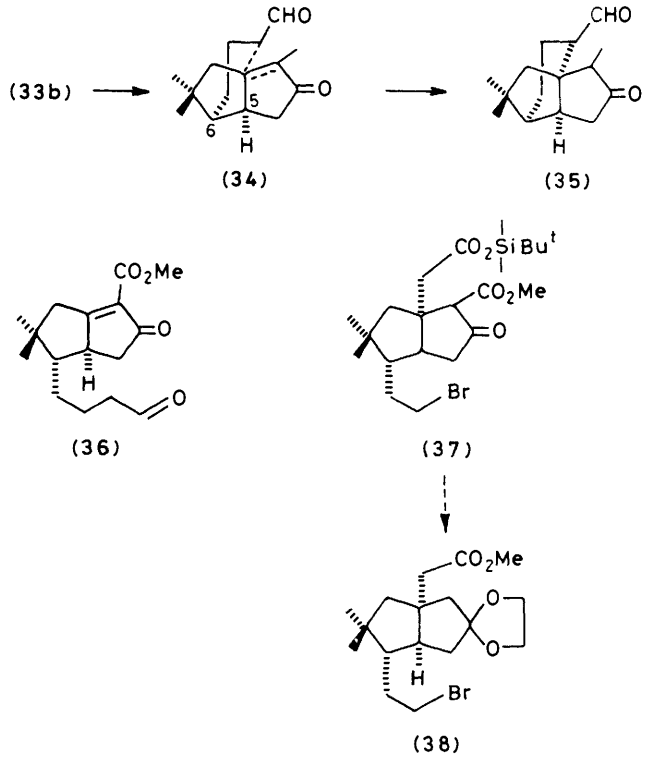
(**31**) (**32**)

a, *n* = 2; b, *n* = 3

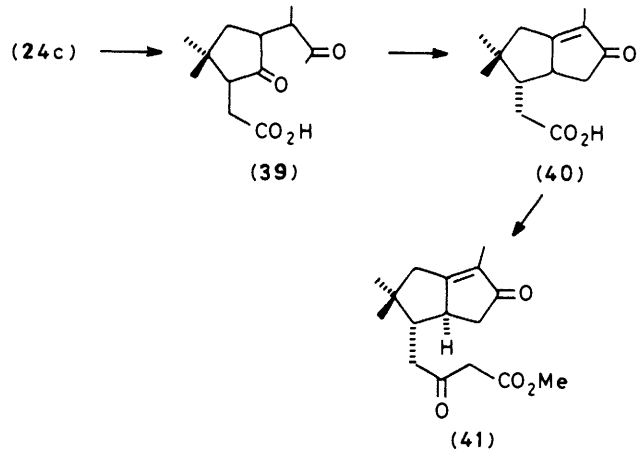
(**33**)

Attempts to induce the aldehyde (**33b**) to undergo intramolecular Michael reaction to the tricycle (**35**), using a range of reagents and reaction conditions, *met with total failure.* It was at this critical stage in our work that we became aware of Danishefsky's attempts to synthesise quadrone by a similar strategy, but employing the 'double-activated' Michael-acceptor precursor (**36**).[2a] He also met with failure, and ultimately modified the design using an intermolecular Michael reaction [leading to (**37**)] followed by intramolecular alkylation of (**38**) to create the cyclohexane ring in quadrone. A closely similar strategy to that of Danishefsky was subsequently published by Helquist *et al.*[2b]

The failure of (**33b**) [and (**36**)] to undergo intramolecular Michael reaction was most surprising, and is clearly of some mechanistic and theoretical interest. In a revealing paper which discusses torsional constraints in ring closure reactions, De Clercq[14] has suggested that one reason which might account for the failure of the Michael reaction in (**33b**), is the unfavourable torsional strain imposed at the C-5 to C-6 bond leading up to the transition state (**34**) between (**33b**) and (**35**). [For an analogous intramolecular Michael reaction leading to the ring system found in cedrene (**3**) see the accompanying paper.[3]]

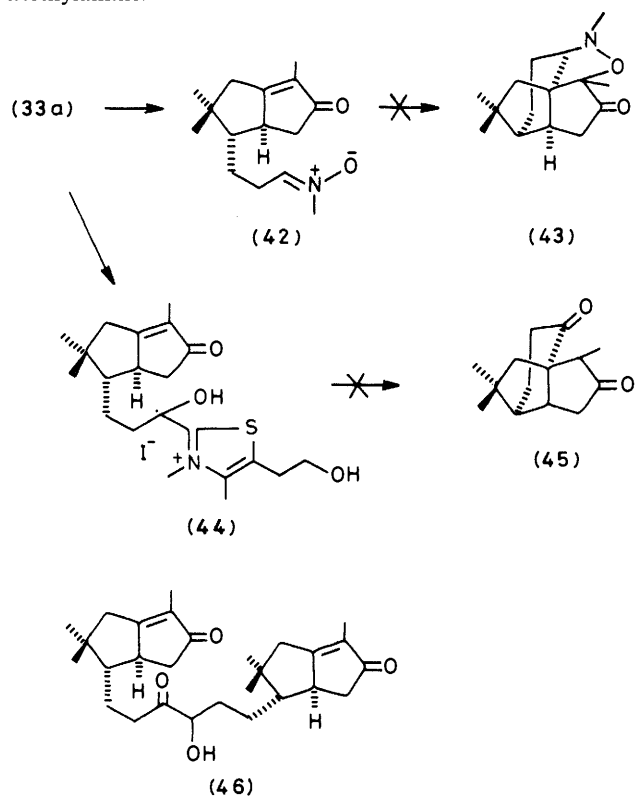


As a corollary to the general approach to quadrone summarised in Scheme 2, we also investigated by use of the β-keto ester (**41**), the nitrone (**42**) and of an umpolung design[14,15] involving the thiazolium salt (**44**) from (**33a**), to construct the cyclohexane ring in the sesquiterpene. The β-keto ester (**41**) was conveniently prepared starting from (**24c**) as shown in Scheme 5. All attempts to promote intramolecular reaction from (**41**) failed however, and starting material was recovered in most instances. In a similar vein, we were unable to detect the formation of the cyclisation product (**43**) during thermolysis of the nitrone (**42**) under a range of conditions,[16] and the

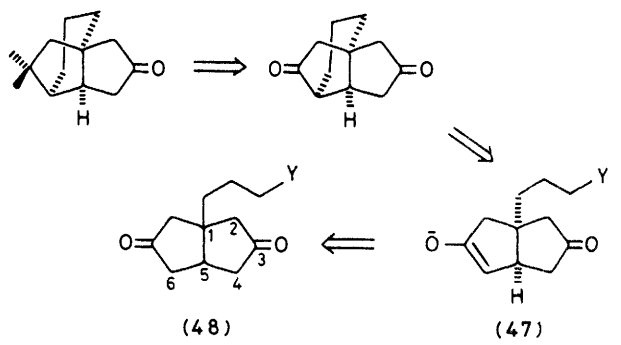


Scheme 5.

thiazolium salt (**44**) produced only the corresponding acyloin (**46**) instead of the tricylic dione (**45**), on treatment with triethylamine.

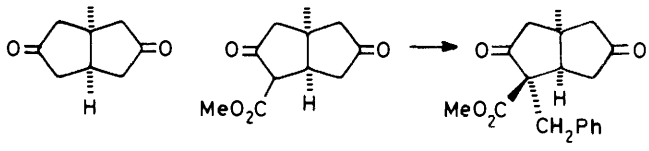


Contemporaneous with the above investigations, we briefly examined a second design to the carbocyclic ring system in quadrone which was based on the disconnection shown in Scheme 6. In this design we envisaged introducing the cyclohexane ring in the tricycle by way of intramolecular alkylation from the specific enolate (**47**). We were attracted to this approach since bicyclo-octanediones of the type (**48**) are easily available,[17] and also because we were confident that the specific enolate (**47**) could be obtained from (**48**) by way of introduction of an additional activating group at C-6 in the bicycle. Indeed, in a model study treatment of the bicyclo-octanedione (**49**) with methylmagnesium carbonate followed by anhydrous methanolic hydrogen chloride afforded a 60% yield of a single crystalline β-keto ester whose structure (**50**) followed

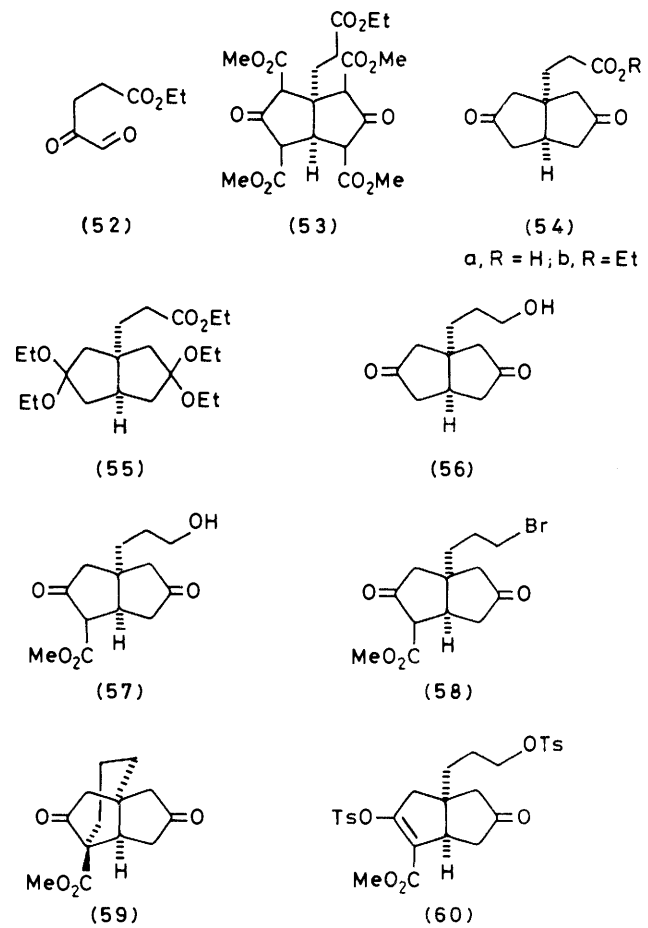


Scheme 6.

conclusively from *X*-ray measurements.* Subsequent treatment of the β-keto ester with sodium methoxide followed by benzyl bromide then led to the corresponding benzyl derivative (**51**).



We next investigated a synthesis of the substituted β-keto ester (**58**), required for intramolecular alkylation to the tricycle (**59**). Although Weiss *et al.* [18] have reported a synthesis of the diketo acid (**54a**) by direct condensation between dimethyl



* We thank Dr. M. J. Begley of this department for this information.

acetonedicarboxylate and 4,5-dioxopentanoic acid, we experienced considerable difficulty in reproducing their results. Ultimately, we obtained reproducible high yields (50—60%) of the acid (**54a**) by using the ethyl ester (**52**) of 4,5-dioxopentanoic acid, in place of the free carboxylic acid, following condensation with dimethyl acetonedicarboxylate and saponification-decarboxylation of the intermediate pentaester (**53**).

The diketo acid (**54a**) was next converted into the corresponding carbinol (**56**), following esterification to (**54b**), protection of the carbonyl groups as the bis-acetal (**55**), reduction using lithium aluminium hydride, and finally removal of the acetal-protecting groups with dilute hydrochloric acid. After protection of the carbinol (**56**) as the corresponding tetrahydropyranyl ether, treatment with methylmagnesium carbonate followed by methanolic hydrogen chloride gave rise to the β-keto ester (**57**). Finally, bromination of (**57**) using phosphorus tribromide then produced the corresponding bromide (**58**), which underwent smooth intramolecular cyclisation on dissolution in methanolic sodium methoxide giving the crystalline tricyclic dione ester (**59**). The same dione ester, whose structure was confirmed by *X*-ray measurements,* was also obtained when the bis-tosylate (**60**) produced from tosylation of the β-keto ester (**57**) was heated with sodium methoxide in methanol.

Experimental

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were run on a Unicam SP 200 or a Perkin-Elmer 710B instrument, and u.v. absorption data were recorded on a Unicam SP 800 instrument. ^{1}H N.m.r. spectra were determined on a Jeol JNM-MH100 n.m.r. spectrometer or a Perkin-Elmer R32 as dilute solutions in deuteriochloroform with tetramethylsilane as internal standard. Carbon-13 n.m.r. spectra were recorded on a Jeol NNM-PS-100 spectrometer at 25.15 MHz interfaced with a Nicolet 1085 20K computer. In both proton and carbon-13 n.m.r. spectra, signals are singlets except where one of the following designations is used: d = doublet, t = triplet, q = quartet, and m = multiplet. Splittings *J* are expressed in Hz. Molecular weights were determined from mass spectra, measured with an AEI MS 902 instrument.

All solvents for chromatography were redistilled, and ethereal solutions were dried over magnesium sulphate prior to evaporation.

4,4-Dimethyl-2-methoxycarbonylcyclopentan-1-one (**17**).—(*a*) A solution of 3,3-dimethylcyclopentan-1-one (11.12 g, 99.15 mmol)[19] in methylmagnesium carbonate solution (205 cm^3, 0.397 mol)[20] was heated at 100 °C for 2 h with stirring while a slow stream of N_2 was passed through the mixture. The cooled solution was added to briskly stirred saturated methanolic hydrogen chloride (550 cm^3) at −60 °C, and the mixture was then allowed to warm to room temperature with continued stirring for 22 h (care, CO_2 evolution!). The mixture was evaporated to half its original volume, and then extracted with ether (3 × 200 cm^3). The dimethylformamide layer was diluted with an equal volume of water and then extracted with a further three portions of ether (3 × 200 cm^3). The combined ethereal extracts were washed with saturated saline (2 × 150 cm^3) and then dried, evaporated, and distilled to give the β-keto ester as a colourless sweet smelling liquid (10.02 g, 60%), b.p. 108 °C at 18 mmHg, $\nu_{max.}$(film) 1 755 and 1 720 cm^{-1}; δ 1.08 (Me), 1.25 (Me), 1.9—2.32 (m, 2 H) 2.1 (CMe_2CH_2CO), 3.24 (t, *J* 10, $CHCO_2Me$), and 3.68 (OMe) (Found: C, 63.2; H, 8.1. $C_9H_{14}O_3$ requires C, 63.5; H, 8.3%).

(*b*) To a stirred suspension of sodium (13.73 g, 0.6 g-atom; cut into 2 mm cubes) in dry benzene (187 cm^3) under nitrogen was added dimethyl 3,3-dimethylhexane-1,6-dioate (62.24 g, 0.307 mol) and methanol (0.5 cm^3). The mixture was stirred and heated under reflux for 16 h and then allowed to cool. The excess of sodium was destroyed by the cautious addition of ice–water, and the mixture then acidified with 6M-hydrochloric acid. The organic phase was separated, and the aqueous layer was then extracted with ether (2 × 50 cm^3). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (40 cm^3) followed by saturated saline (2 × 40 cm^3) and then dried, evaporated, and distilled to give the β-keto ester (42.26 g, 81%) identical with that obtained under (*a*).

Dimethyl 3,3-Dimethylhexane-1,6-dioate.—A solution of 4,4-dimethylcyclohex-1-ene (26.46 g, 0.238 mol)[19] in benzene (85 cm^3) was added over 6.65 h to a vigorously stirred suspension of benzene (240 cm^3), water (710 cm^3), tetra-n-butylammonium hydrogen sulphate (2.37 g, 7 mmol), and potassium permanganate (115.2 g, 0.73 mol) whilst the temperature was maintained at 40 °C (ice-bath). When the temperature began to fall, the ice-bath was removed, and the mixture was allowed to come to room temperature with continued stirring (*ca.* 5 h). The black suspension was cooled to 5 °C, and then anhydrous sodium sulphite (144.5 g) was added, followed by concentrated hydrochloric acid (400 cm^3). The resulting white suspension was filtered, and the residue was then extracted with boiling chloroform (3 × 80 cm^3). The filtrate was separated, and the aqueous layer was then extracted with ethyl acetate (3 × 400 cm^3). The combined organic phases were dried and evaporated to leave the crude diacid as a white solid (38.75 g, 93%). The solid was dissolved in dry methanol (91.5 cm^3) and the solution was treated with concentrated sulphuric acid (5 cm^3), and then heated under reflux for 5 h. The solution was cooled and the methanol was then removed under reduced pressure at room temperature. The residue was poured into ice–water (300 cm^3) and then extracted with ether (4 × 150 cm^3). The combined ethereal extracts were washed with saturated aqueous sodium hydrogen carbonate (75 cm^3) and saturated saline solution (75 cm^3) and then dried, evaporated, and distilled to give the diester as a colourless liquid (37.35 g, 83%), b.p. 120—122 °C at 11 mmHg, $\nu_{max.}$ 1 740 cm^{-1}; δ 1.0 (CMe_2), 1.57—1.8 (m, 2 H), 2.18—2. 46 (m, 4 H), and 3.65 (CO_2Me).

4,4-Dimethyl-2-methoxycarbonyl-5-pent-4-enylcyclopentan-1-one (**18a**).—4,4-Dimethyl-2-methoxycarbonylcyclopentan-1-one (5 g) was added over 0.25 h to an ice-cold stirred suspension of sodium hydride (0.78 g, 32.5 mmol) in dry tetrahydrofuran (80 cm^3) under nitrogen. The suspension was stirred at 0 °C for 1 h, and then cooled to −70 °C and treated with a solution of n-butyl-lithium (44 cm^3, 62.5 mmol), followed by hexamethylphosphoramide (5.3 cm^3, 29.4 mmol). The mixture was stirred at −70 °C for 0.5 h and then a solution of 1-iodopent-4-ene (6.1 g, 31.2 mmol) in dry tetrahydrofuran (7.3 cm^3) was added all at once. The resulting suspension was stirred at −70 °C for 0.5 h and then the cooling bath was removed and the mixture stirred for a further 1 h. The white suspension was poured into a mixture of water (27 cm^3), concentrated hydrochloric acid (9 cm^3), and ether (80 cm^3), and the organic phase was then separated. The aqueous layer was extracted with ether (40 cm^3), and the combined organic extracts were washed successively with 6M-hydrochloric acid (27 cm^3), saturated aqueous sodium hydrogen carbonate (27 cm^3) and saturated saline (27 cm^3). Evaporation of the dried ether extracts left a residue which was distilled under reduced pressure to give the β-keto ester as a colourless liquid (5 g, 71%), b.p. 98—100 °C at 0.1 mmHg; $\nu_{max.}$ (film) 1 755 and 1 720 cm^{-1}; δ 0.8—2.4 (m, 15 H), 3.2 (t, *J* 10, $CHCO_2Me$), 3.72 (OMe), 3.74 (OMe), 4.85—5.24 (m, $CH{:}CH_2$),

* We thank Dr. M. J. Begley of this department for this information.

and 5.54—6.06 (m, C*H*:CH_2); *m/z* 238.1558 ($C_{14}H_{22}O_3$ requires *M*, 238.1567).

3-(4,4-*Dimethyl*-2-*oxo*-3-*pent*-4-*enylcyclopentyl*)*butan*-2-*one* (**24a**).—A solution of 4,4-dimethyl-1-methoxycarbonyl-3-pent-4-enylcyclopentan-2-one (4.5 g, 17.7 mmol) in benzene (6.5 cm^3) was added to a stirred suspension of sodium hydride (20 mmol) in dry benzene (8 cm^3). The suspension was stirred for 0.25 h and then diluted with dimethylformamide (16 cm^3) and stirred until hydrogen evolution had ceased. 3-Bromobutan-2-one (18 mmol) was added, and the resulting suspension was stirred at 25 °C for 6 days and then poured into ether (60 cm^3). The separated organic layer was washed with ice-cold 5% aqueous sodium hydroxide (3 × 10 cm^3) and saturated saline (10 cm^3) and then dried and evaporated to leave a mixture (5.6 g) of the *C*- (**22a**) and *O*-alkylated (**21a**) esters as a mobile oil. The crude mixture was dissolved in dimethylformamide (175 cm^3) containing lithium iodide (34.67 g, 0.26 mol),[21] and the mixture was heated at reflux for 2 h under nitrogen. The solution was diluted with water (214 cm^3) and then acidified with 6M-hydrochloric acid and extracted with ether (5 × 200 cm^3). The combined ether extracts were washed with saturated saline (60 cm^3) and then dried and evaporated to leave an oily residue. This was chromatographed on silica gel G using chloroform–methanol 99:1 as eluant to give the ketone (**19a**) (1.09 g, 34%) and the 1,4-diketone (**24a**) (0.52 g, 12%) as a colourless sweet smelling oil, $\nu_{max.}$(film) 1 735, 1 710, and 1 640 cm^{-1}; δ 0.75—3.0 (m, 20 H), 2.0 (COMe), 2.1 (COMe), 4.68—5 (m, CH:CH_2), and 5.4—5.9 (m, C*H*:CH_2); *m/z* 250.1939 ($C_{16}H_{26}O_2$ requires *M*, 250.1933).

3-*Methyl*-2-*pent*-4-*enylcyclopent*-2-*en*-1-*one* (**20a**).—A solution of ethyl acetoacetate (15.84 g, 0.122 mol) in dry tetrahydrofuran (25 cm^3) was added over 0.5 h to a stirred suspension of sodium hydride (3.29 g, 0.134 mol) in dry tetrahydrofuran (300 cm^3) at 0 °C. The solution was stirred at 0 °C for a further 0.25 h and then n-butyl-lithium in hexane solution (0.128 mol) was added over 0.5 h to give an orange coloured suspension. After 0.3 h at 0 °C 1-iodopent-4-ene (26.3 g, 0.134 mol) in dry tetrahydrofuran (60 cm^3) was added over 0.15 h, and the cooling bath was then removed. The reaction mixture was stirred at room temperature for 0.5 h and then poured into a mixture of water (60 cm^3), concentrated hydrochloric acid (25 cm^3), and ether (180 cm^3). The organic phase was separated and the aqueous layer was extracted with ether (75 cm^3). The combined ethereal extracts were washed with saturated saline (50 cm^3), then dried and evaporated to give the β-ketoester (24.12 g, 99%), $\nu_{max.}$(film), 1 740, 1 710, and 1 640 cm^{-1}; δ 1.16 (t, *J* 8, OCH_2CH_3), 1.2—1.7 (m, 4 H), 1.8—2.18 (m, CH_2CH:CH_2), 2.52 (t, *J* 7, $COCH_2$), 3.29 (CH_2CO_2Et), 4.14 (q, *J* 8, OCH_2CH_3), 5.8—6.04 (m, CH:CH_2), 5.42—5.92 (m, C*H*:CH_2); *m/z* 198 ($C_{11}H_{18}O_3$ requires *M*, 198).

To a stirred suspension of sodium hydride (3.2 g, 0.13 mol) in dry dioxane (55 cm^3) under nitrogen at 25 °C was added the above β-keto ester (24.82, 0.125 mol) over 0.5 h. The mixture was stirred at room temperature for a further 0.5 h and then cooled to −20 °C. A solution of bromoacetone (23.6 g, 0.172 mol) in dioxane (22 cm^3) was added to the cooled suspension, and the mixture was then stirred at −5 °C for 0.75 h. The mixture was warmed to room temperature and then heated under reflux over 0.25 h. The fawn coloured suspension was diluted with aqueous sodium hydroxide (15.8 g of sodium hydroxide in 500 cm^3 water), and then slowly warmed to 70 °C over 1.5 h. The solution was heated at 70 °C for a further 1 h and then cooled and acidified with 2M-sulphuric acid. The aqueous solution was extracted with ether (4 × 200 cm^3), and the combined ethereal extracts were then dried, evaporated, and distilled to give the cyclopentenone as a sweet smelling colourless liquid (13.03 g, 64%), b.p. 120—122 °C at 12 mmHg, $\nu_{max.}$(film) 1 700 and 1 640 cm^{-1}; δ 1.35—1.6 (m, $CH_2CH_2CH_2$), 2.07 (:CCH_3) 1.95—255 (m, 8 H), 4.85—5.05 (m, CH:CH_2), 5.55—5.95 (m, C*H*:CH_2); *m/z* 164.1190 ($C_{11}H_{16}O$ requires *M*, 164.1201).

3,3-*Dimethyl*-2-*pent*-4-*enylcyclopentan*-1-*one* (**19a**).—Methyllithium solution (12 cm^3, 15.9 mmol) was added to a stirred suspension of copper(I) iodide (1.51 g, 8 mmol) in dry ether (15 cm^3) at −10 °C under nitrogen. The resulting lithium dimethylcuprate solution was then cooled to −20 °C and a solution of the cyclopentenone (**20a**) (0.8 g, 5 mmol) in dry ether (15 cm^3) was added over 0.3 h. The mixture was stirred at −20 °C for 0.75 h and then warmed to 0 °C and stirred for a further 1.25 h. A mixture of hexamethylphosphoramide (1 cm^3) triethylamine (1.75 cm^3) and trimethylsilyl chloride (1.5 cm^3) was added, and the mixture was then stirred at room temperature for 3 h. The dark suspension was poured into pentane (75 cm^3) containing ice-cold 5% hydrochloric acid (40 cm^3), and the mixture was then quickly filtered through a pad of Celite. The organic phase was separated, then washed with saturated saline (15 cm^3), dried, and evaporated to leave a mixture of the trimethylsilyl enol ether and starting material. The product mixtures from six experiments were combined and dissolved in methanol–water (4:1) (60 cm^3) and extracted with ether (2 × 60 cm^3). Evaporation of the dried ether extracts under reduced pressure left a mixture of the cyclopentanone and starting material. The mixture was separated by column chromatography on silica gel G using benzene–ether (2:1) as eluant to give the cyclopentanone as a sweet smelling liquid (3.36 g, 62%; 90% based on recovered starting material), b.p. 75 °C at 1 mmHg, $\nu_{max.}$(film) 1 735 and 1 640 cm^{-1}; δ 0.83 (Me), 1.38 (Me), 1.1—2.5 (m, 11 H), 4.97—5.25 (m, CH:CH_2), and 5.7—6.13 (m, C*H*:CH_2); *m/z* 180.1510 ($C_{12}H_{20}O$ requires *M*, 180.1514).

2-*But*-3-*enyl*-3,3-*dimethylcyclopentan*-1-*one* (**19b**).—Alkylation of the β-keto ester (**17**) with 1-bromobut-3-ene according to the procedure described for the preparation of the homologue (**18a**) first gave 5-but-3-enyl-4,4-dimethyl-2-methoxycarbonylcyclopentan-1-one (**18b**) (78%) as a sweet smelling liquid, b.p. 95—98 °C at 0.02 mmHg, $\nu_{max.}$(film) 1 760, 1 730, and 1 640 cm^{-1}; δ 0.85—2.5 (m, 13 H), 3.28 (t, *J* 10, C*H*CO_2Me), 3.77, 3.81 (OMe isomers), 4.95—5.23 (m, CH:CH_2), 5.62—6.10 (m, C*H*:CH_2).

A solution of the β-keto ester (**18b**) (10.32 g, 46 mmol) and lithium iodide (49 g, 0.575 mmol) in dimethylformamide (230 cm^3)[21] was heated under reflux for 2 h in an atmosphere of nitrogen. The cooled solution was diluted with water (300 cm^3) and then acidified with 6M-hydrochloric acid and extracted with ether (3 × 200 cm^3). The combined ether extracts were washed with saturated saline (2 × 75 cm^3) and then dried and evaporated. The residue was chromatographed on silica gel G using light petroleum (b.p. 40—60 °C)–ethyl acetate (95:5) as eluant to give the cyclopentanone as a colourless sweet smelling liquid (5.84 g, 76%), b.p. 42 °C at 0.05 mmHg; $\nu_{max.}$(film) 1 740 and 1 640 cm^{-1}; δ 0.82 (Me), 1.17 (Me), 1.3—2.4 (m, 9 H), 4.89—5.25 (m, CH:CH_2), and 5.58—6.04 (m, C*H*:CH_2); *m/z* 166 ($C_{11}H_{18}O$ requires *M*, 166). The 2,4-dinitrophenylhydrazone crystallised from ethanol and had m.p. 79—81 °C (Found: C, 59.1; H, 6.3; N, 16.4. $C_{17}H_{22}N_4O_4$ requires C, 58.9; H, 6.4; N, 16.2%).

2-(3-*But*-3-*enyl*-4,4-*dimethyl*-2-*oxocyclopentyl*)-3-*nitrobutane* (**25b**).—Butyl-lithium solution (24.95 cm^3, 35.6 mmol) was added to a solution of hexamethyldisilazane (5.8 g, 35.8 mmol) in dry tetrahydrofuran (100 cm^3) at −20 °C under nitrogen. The solution was stirred at −20 °C for 0.5 h and then cooled to −78 °C and treated with a solution of the cyclopentanone (**19b**)

(5.27 g, 31.3 mmol) in dry tetrahydrofuran (4 cm^3) over 1 h. The resulting lemon coloured solution was stirred at −78 °C for 1 h and then 2-nitrobut-2-ene (4.8 g, 48 mmol) was added all at once. The deep yellow mixture was stirred at −78 °C for 2 h and then quenched with 3M-acetic acid (30 cm^3). The cooling bath was removed, and when the mixture had warmed to room temperature the organic phase was separated. The aqueous layer was extracted with ether (50 cm^3), and the combined organic phases were then washed with saturated aqueous sodium hydrogen carbonate (16 cm^3) followed by saturated saline (25 cm^3). The dried organic phase was evaporated to leave the nitro ketone (8.05 g, 95%) as a pungent, yellow oil, $\nu_{max.}$(film) 1 740, 1 640, and 1 550 cm^{-1}; δ 0.8—2.6 (complex m, 21 H), 4.4—5 (m, $CHNO_2$), 4.9—5.2 (m, $CH{:}CH_2$), 5.6—6.06 (m, $CH{:}CH_2$); *m/z* 267.1816 ($C_{15}H_{25}NO_3$ requires *M*, 267.1834).

3-[3-*But*-3-*enyl*-4,4-*dimethyl*-2-*oxocyclopentyl*]*butan*-2-*one* (**24b**).—The nitro ketone (**25b**) (8.05 g, 30.1 mmol) followed by n-propyl nitrite (5.6 g, 62.7 mmol) were added to a solution of dry sodium nitrite (10.84 g, 0.156 mol) in dry dimethyl sulphoxide (63 cm^3) under nitrogen, and the resulting mixture was stirred at room temperature in subdued light for 46 h. The solution was poured into a mixture of dichloromethane (160 cm^3) and water (40 cm^3), and the organic phase was then separated. The aqueous layer was extracted with dichloromethane (200 cm^3), and the combined organic extracts were washed with water (80 cm^3) followed by saturated saline (80 cm^3). Evaporation of the dried extracts left an oil which was chromatographed on silica gel C using light petroleum (b.p. 40—60 °C)–ethyl acetate as eluant to furnish the pure 1,4-diketone as a colourless oil (4.53 g, 80%), $\nu_{max.}$(film) 1 730, 1 710, and 1 640 cm^{-1}; δ 0.8—30 (m, 18 H), 2.15, 2.23 (COMe isomers), 4.95—5.21 ($CH{:}CH_2$), and 5.6—6.1 (m, $CH{:}CH_2$); *m/z* 236.1766 ($C_{15}H_{24}O_2$ requires *M*, 236.1776).

6-*But*-3-*enyl*-2,7,7-*trimethylbicyclo*[3.3.0]*oct*-1(2)-*en*-3-*one* (**27b**).—A solution of the 1,4-diketone (**24b**) (0.52 g) in dry t-butyl alcohol (6.5 cm^3) was added to a stirred solution of potassium t-butoxide (0.32 g, 2.85 mmol in dry t-butyl alcohol (13 cm^3) under nitrogen, and the red solution was then heated under reflux for 3 h. The cooled solution was poured into saturated saline–water (1:1) (52 cm^3), and then acidified with 6M-hydrochloric acid and extracted with ether (4 × 100 cm^3). The combined ethereal extracts were washed with 2M-hydrochloric acid (30 cm^3), followed by saturated saline. The extracts were then dried and evaporated to leave an oil, which was purified by column chromatography on silica gel (50—100 mesh) using chloroform–methanol (99:1) as eluant to give the bicyclo[3.3.0]octenone as a pale yellow oil (250 mg, 52%); $\lambda_{max.}$(EtOH) 238 nm; $\nu_{max.}$(film) 1 700 and 1 660 cm^{-1}; δ 1.0 (Me), 1.07 (Me), 1.2—2.87 (m, 10 H), 1.63 (:CMe), 4.85—5.12 (m, $CH{:}CH_2$) and 5.52—6.03 (m, $CH{:}CH_2$); δ_C 8.29 (q), 24.99 (q), 28.9 (t), 29.4 (q), 32.73 (t), 42.49 (t), 42.7, 48.63 (d), 53.87 (d), 114.82 (t), 131.76, 138.55 (d), 181.35, and 209.92 p.p.m.; *m/z* 218.1662 ($C_{15}H_{20}O$ requires *M*, 218.1671).

3-[3-(4,5-*Dihydroxypentyl*)-4,4-*dimethyl*-2-*oxocyclopentyl*]-*butan*-2-*one* (**31b**).—A solution of the 1,4-diketone (**24a**) (95 mg, 0.38 mmmol) in dry pyridine (0.5 cm^3) was added to a stirred solution of osmium tetraoxide (100 mg, 0.39 mmol) in dry pyridine (1 cm^3) under nitrogen. The solution turned black rapidly, and was stirred at room temperature for 6 h. A solution of sodium bisulphite (0.18 g) in water (3 cm^3) and pyridine (2 cm^3) was then added, and the mixture was stirred at room temperature for a further 0.25 h. The orange-red solution was extracted with chloroform (6 × 5 cm^3), and the combined organic extracts were then washed with saturated saline (5 cm^3). The dried and evaporated extracts were chromatographed on silica gel (50—100 mesh) using 9:1 ethyl acetate–methanol as eluant to give the dihydroxy dione as a yellow unstable oil (70 mg, 65%), $\nu_{max.}$(film) 3 400, 1 735, and 1 710 cm^{-1}; δ 0.83—1.97 (m, 20 H), 2.15, 2.23 (COMe, isomers), and 3.2—3.9 (m, 5 H), which was not purified further.

6-(4,4-*Dihydroxypentyl*)-2,7,7-*trimethylbicyclo*[3.3.0]*oct*-1(2)-*en*-3-*one* (**32b**).—A solution of the dihydroxy dione (**31b**) (70 mg) in t-butyl alcohol (1 cm^3) was added to a stirred solution of potassium t-butoxide (36 mg, 0.319 mmol) in dry t-butyl alcohol (1.5 cm^3) under nitrogen, and the resulting mixture was then heated under reflux for 3 h. The cooled mixture was poured into saturated saline (3 cm^3) and then acidified with 6M-hydrochloric acid and extracted with ether (4 × 5 cm^3). The combined ethereal extracts were dried, evaporated, and chromatographed on silica gel (50—100 mesh) using ethyl acetate–methanol (9:1) as eluant to give the bicyclo-[3.3.0]octenone as a pale yellow oil (34 mg, 52%), $\lambda_{max.}$(EtOH) 240 nm; $\nu_{max.}$(film) 3 400, 1 700, and 1 640 cm^{-1}; δ 1.06 (Me), 1.14 (Me), 1.3—2.9 (m, 12 H), 1.7 (:C*Me*), and 3.2—4.2 (m, 5 H).

2,7,7-*Trimethyl*-6-(4-*oxobutyl*)*bicyclo*[3.3.0]*oct*-1(2)-*en*-3-*one* (**33b**).—Sodium periodate (24 mg) was added to a stirred solution of the diol (**32b**) (27 mg, 0.1 mmol) in methanol–water (1:1) (0.5 cm^3) at 0 °C under nitrogen, and the mixture was then stirred at 0 °C for 0.75 h. The suspension was diluted with saturated saline (0.5 cm^3) and then extracted with chloroform (4 × 3 cm^3). The combined chloroform extracts were dried and then evaporated to leave the aldehyde as a colourless oil (23 mg, 100%); $\lambda_{max.}$(EtOH) 240 nm; $\nu_{max.}$(film) 2 725, 1 720, 1 700, and 1 660 cm^{-1}; δ 1.07 (Me) 1.14 (Me), 1.3—2.85 (m, 12 H), 1.7 (:CMe), and 9.81 (t, *J* 2, CHO); *m/z* 234.1628 ($C_{15}H_{22}O_2$ requires *M*, 234.1620).

3-[3-(3,4-*Dihydroxybutyl*)-4,4-*dimethyl*-2-*oxocyclopentyl*]-*butan*-2-*one* (**31a**).—A solution of the 1,4-diketone (**24b**) (1.83 g) in pyridine (20 cm^3) was added to a stirred solution of osmium tetraoxide (2 g, 7.77 mmol) in dry pyridine (20 cm^3) under nitrogen and the resulting black solution was stirred at room temperature for 6 h. A solution of sodium bisulphite (3.6 g) in water (39 cm^3) and pyridine (29 cm^3) was added, and the mixture was then stirred for 0.5 h. The red solution was extracted with chloroform (5 × 80 cm^3), and the combined organic extracts were washed with saturated saline (2 × 100 cm^3). The dried and evaporated extracts were chromatographed on silica gel (50—100 mesh) using ethyl acetate–methanol (9:1) as eluant to furnish the dihydroxy dione as an unstable pale brown oil (1.74 g, 83%), $\nu_{max.}$(film) 3 420, 1 730, and 1 710 cm^{-1}; δ 0.85—2.0 (m, 18 H), 2.18, 2.24 (COMe, isomers), 2.74 (br, 2 × OH), and 3.45—4.85 (m, 3 H).

6-(3,4-*Dihydroxybutyl*)-2,7,7-*trimethylbicyclo*[3.3.0]*oct*-1(2)-*en*-3-*one* (**32a**).—A solution of the dihydroxy dione (**31a**) (0.3 g) in t-butyl alcohol (4.5 cm^3) was added to a stirred solution of potassium t-butoxide (from 56.5 mg of potassium, 1.44 mg-atom) in dry t-butyl alcohol (6.75 cm^3) under nitrogen. The solution was heated at 100 °C for 3 h, and then cooled, diluted with saturated saline (13.5 cm^3), acidified with 6M-hydrochloric acid, and extracted with ether (3 × 20 cm^3). The combined ether extracts were washed with saturated saline (10 cm^3), and then dried and evaporated to leave a green oil. The oil was chromatographed on silica gel G using 9:1 ethyl acetate–methanol as eluant to afford the bicyclo[3.3.0]octenone as a colourless glass (115 mg, 41%), $\lambda_{max.}$ 239 nm; $\nu_{max.}$(film) 3 400, 1 700, and 1 660 cm^{-1}; δ 1.06 (Me), 1.14 (Me), 1.2—2.8 (m, 10 H), 1.67 (:CMe), 3.42—3.78 (m, 3 H), and 3.73 (br, 2 × O*H*); *m/z* 252.1728 ($C_{15}H_{24}O_3$ requires *M*, 252.1725).

2,7,7-*Trimethyl*-6-(3-*oxopropyl*)*bicyclo*[3.3.0]*oct*-1(2)-*en*-3-*one* (**33a**).—Sodium periodate (106 mg) was added to a stirred solution of the diol (**32a**) (113 mg, 0.45 mmol) in methanol–water (2:1) (2.4 cm^3) at 5 °C under nitrogen. The mixture was stirred at 5 °C for 0.75h, and then diluted with saturated saline (7 cm^3). The solution was extracted with chloroform (4 × 20 cm^3) and the combined chloroform extracts were then dried and evaporated to leave the bicyclo[3.3.0]octenone as a colourless mobile oil (94.6 mg, 97%); $\lambda_{max.}$(EtOH) 239 nm; $\nu_{max.}$(film) 2 730, 1 725, 1 700, and 1 660 cm^{-1}; δ 1.08 (Me), 1.26 (Me), 1.7 (:CMe), 1.2—2.85 (m, 10 H), and 9.82 (t, *J* 2, CHO).

3,3-*Dimethyl*-2-*prop*-2-*enylcyclopentan*-1-*one* (**19c**).—Methyllithium solution (60 cm^3, 79.5 mmol) was added to a stirred suspension of copper(I) iodide (7.55 g, 40 mmol) in dry ether (75 cm^3) at −10 °C under nitrogen. The resulting lithium dimethylcuprate solution was cooled to −20 °C and a solution of allethrone (3.4 g, 25 mmol)[22] in dry ether (75 cm^3) was then added over 0.3 h. The mixture was stirred at −20 °C for 0.75 h, and then warmed to 0 °C and stirred for a further 1.25 h. To the resulting turbid, yellow suspension was added a mixture of hexamethylphosphoramide (5 cm^3), triethylamine (8.75 cm^3), and trimethylsilyl chloride (7.5 cm^3), and the mixture was then stirred at room temperature for 2.5 h. The dark suspension was poured into pentane (375 cm^3) containing ice-cold hydrochloric acid (190 cm^3), and then quickly filtered through a pad of Celite. The organic phase was separated, washed with saturated saline (62.5 cm^3), and then dried and evaporated to give a mixture (5.6 g) of the trimethylsilyl enol ether of (**19c**) and starting material as a yellow oil.

The trimethylsilyl enol ether–allethrone mixture was dissolved in a mixture of tetrahydrofuran (27 cm^3) and 2M-hydrochloric acid (27 cm^3), and then shaken for 1 h at room temperature. The mixture was extracted with ether (2 × 25 cm^3), and the combined ether extracts were then washed with saturated saline (25 cm^3). The organic phase was dried and evaporated under reduced pressure to leave a mixture of the cyclopentanone and starting allethrone. The mixture was separated by column chromatography on silica gel G using chloroform as eluant to give the cyclopentanone (2.4 g, 63%; 79% based on recovered starting material) as a colourless liquid, $\nu_{max.}$(film) 1 735 and 1 640 cm^{-1}; δ 0.86 (Me), 1.19 (Me), 1.56—2.54 (m, 7 H), 4.85—5.13 (m, CH:CH_2), 5.7—6.01 (m, C*H*:CH_2); *m/z* 152.1199 ($C_{10}H_{16}O$ requires *M*, 152.1202).

3-(4,4-*Dimethyl*-2-*oxo*-3-*prop*-2-*enylcyclopentyl*)*butan*-2-*one* (**24c**).—The cyclopentanone (**19c**) was alkylated with 2-nitrobut-2-ene according to the general procedure described for the preparation of the analogue (**25b**), and gave 2-[4,4-dimethyl-2-oxo-3-prop-2-enylcyclopentyl]-3-nitrobutane (**25c**) as a yellow oil (95%), $\nu_{max.}$(film) 1 740, 1 640, and 1 550 cm^{-1}; δ 0.85—2.8 (m, 19 H), 4.5—5.1 (m, $CHNO_2$), 4.98—5.37 (m, CH:CH_2), 5.76—6.2 (m, C*H*:CH_2); *m/z* 253.1667 ($C_{14}H_{23}NO_3$ requires *M*, 253.1678).

The nitro ketone was then hydrolysed to the corresponding 1,4-diketone, $\nu_{max.}$(film) 1 730, 1 710, and 1 640 cm^{-1}; δ 0.8—3.0 (m, 16 H), 2.06, 2.13 (COMe, isomers), 4.88—5.19 (m, CH:CH_2), and 5.5—6.0 (m, C*H*:CH_2); *m/z* 222.1603 ($C_{14}H_{22}O_2$ requires *M*, 222.1619) by the procedure described earlier for the preparation of the analogue (**24b**).

3-(3-*Carboxymethyl*-4,4-*dimethyl*-2-*oxocyclopentyl*)*butan*-2-*one* (**39**).—A solution of potassium permanganate (0.102 g, 0.57 mmol) and sodium periodate (5.31 g, 11.36 mmol) in water (255 cm^3) was added to a stirred solution of the 1,4-diketone (**24c**) (0.71 g, 3.19 mmol) and potassium carbonate (0.852 g, 6.18 mmol) in a 4:1 mixture of water and t-butyl alcohol (1 000 cm^3). The resulting purple solution was stirred at room temperature for 6 h. The excess of oxidant was reduced by addition of sodium bisulphite, and the solution was then evaporated to 250 cm^3 under reduced pressure. The residue was acidified with concentrated hydrochloric acid and then extracted with ether using a continuous extractor (24 h). The combined ethereal extracts were then dried and evaporated to leave the diketo acid as a pale yellow oil (0.72 g, 95%), $\nu_{max.}$(film) 1 720 cm^{-1}; δ 0.9—1.4 (m, 3 × Me), 1.4—3.2 (complex m, 7 H), and 2.2, 2.27 (COMe, isomers).

6-*Carboxymethyl*-2,7,7-*trimethylbicyclo*[3.3.0]*oct*-1(2)-*en*-3-*one* (**40**).—A solution of the 1,4-diketo acid (**39**) (0.6 g, 2.5 mmol) in aqueous potassium hydroxide (0.7 g potassium hydroxide in 25 cm^3 water) was heated under reflux with stirring for 22 h. The cooled solution was acidified with concentrated hydrochloric acid, and then extracted with chloroform (4 × 40 cm^3). The combined organic extracts were washed with saturated saline (20 cm^3), and then dried and evaporated to leave an oily solid. The enone was obtained by trituration of the oil with ether, and the resulting white solid was recrystallised from ethyl acetate–hexane to give the pure acid as colourless crystals (0.3 g, 55%), m.p. 161—162 °C; $\lambda_{max.}$(EtOH) 238 nm; $\nu_{max.}$(KBr disc) 1 710 and 1 640 cm^{-1}; δ 1.06 (Me), 1.27 (Me), 1.7 (:CMe), 2.0—2.9 (m, 8 H), and 5.3—6.5 (br, CO_2H); δ_c 8.32 (q), 25.11 (q), 28.87 (q), 34.14 (t), 41.08 (t), 42.14 (t), 42.87, 48.69 (d), 50.66 (d), 132.5, 176.54, 181.92, and 211.71 p.p.m. (Found: C, 70.0; H, 8.20; *M*, *m/z* 222.1240. $C_{13}H_{18}O_3$ requires C, 70.2; H, 8.2%; *M*, 222.1256).

6-(3-*Methoxycarbonyl*-2,7,7-*trimethyl*-2-*oxopropyl*)*bicyclo*-[3.3.0]*oct*-1(2)-*en*-3-*one* (**41**).—Oxalyl chloride (0.2 cm^3) was added to a stirred suspension of the acid (**40**) (100 mg, 0.45 mmol) in dry benzene under nitrogen at 10 °C. The mixture was allowed to warm to room temperature and stirred for 2 h. The benzene and excess of oxalyl chloride were removed in a stream of dry nitrogen and the last traces were then removed under reduced pressure to leave the crude acid chloride as a yellow oil.

A solution of the acid chloride in dry dichloromethane (0.4 cm^3) was added to an ice-cold solution of Meldrum's acid (71.2 mg, 0.492 mmol) and dry pyridine (78 mg, 0.988 mmol) in dry dichloromethane (0.4 cm^3). The mixture was stirred at 0 °C for 1 h, and then at room temperature for 1 h. The solution was washed with 2M-hydrochloric acid (0.3 cm^3) followed by water (0.3 cm^3), and then dried and evaporated to leave the crude acylated Meldrum's acid (150 mg).

The acylated Meldrum's acid in dry methanol (2 cm^3) was heated under reflux for 2 h. The cooled solution was evaporated, and the crude oil was then chromatographed on silica gel G using chloroform–ether (95 : 5) as eluant to give the β-*keto ester* as a colourless oil (27.5 mg, 22%), $\lambda_{max.}$(EtOH) 273 nm; $\nu_{max.}$($CHCl_3$) 1 740, 1 710, 1 695, and 1 660 cm^{-1}; δ 1.04 (Me), 1.11 (Me), 1.68 (:CMe), 1.6—2.7 (complex m, 8 H), 3.49 (CH_2CO_2Me), and 3.77 (CO_2Me); *m/z* 278.1524 ($C_{16}H_{22}O_4$ requires *M*, 278.1518).

Preparation of the Nitrone (**42**).—1M-Sodium ethoxide was added to a stirred solution of *N*-methylhydroxylamine hydrochloride (32 mg) in dry ethanol (3.6 cm^3) at 0—5 °C under nitrogen until the suspension was alkali to phenolphthalein. The suspension was warmed to 10 °C, and then a solution of the enone aldehyde (**33a**) (78 mg) in dry ethanol (0.7 cm^3) was introduced. The mixture was stirred at 25 °C for 21 h and then filtered. Evaporation of the filtrate left the nitrone as a white solid (78 mg, 89%) which crystallised from methylene dichloride–hexane to give white crystals, m.p. 90—92 °C (decomp.), $\lambda_{max.}$(EtOH) 236 nm; $\nu_{max.}$($CHCl_3$) 1 700 and 1 660 cm^{-1}; δ 1.07 (Me), 1.16 (Me), 1.0—2.8 (m, 10 H), 1.68 (:CMe),

3.75 (NMe), and 6.81 (t, *J* 6, :C*H*); *m/z* 249.1750 ($C_{15}H_{23}NO_2$ requires *M*, 249.1729).

Preparation of the Acyloin (**46**).—5-Hydroxyethyl-3,4-dimethylthiazolium iodide (0.28 g)[14] and dry triethylamine (0.3 cm^3) were added to a stirred solution of the enone aldehyde (**33a**) (94 mg) in dry isopropyl alcohol (10 cm^3) under nitrogen. The mixture was heated under reflux for 14 h, and then cooled and diluted with water (25 cm^3). The mixture was extracted with ethyl acetate (5 × 15 cm^3), and the combined extracts were then washed with water (10 cm^3) followed by saturated saline (10 cm^3). Evaporation of the dried extracts left a residue which was chromatographed on silica using ethyl acetate–methanol (95:5) as eluant to give the acyloin (35 mg, 37%) as a colourless glass, $\lambda_{max.}$(EtOH) 239 nm; $\nu_{max.}$(film) 3 540, 1 710, and 1 660 cm^{-1}; δ 1.05—1.16 (m, CMe_2), 1.6—1.7 (m, :CMe), 1.4—2.8 (m, 22 H), and 4.02—4.3 (m, C*H*OH); *m/z* 440.2916 ($C_{28}H_4O_4$ requires *M*, 440.2926).

1-*Methylbicyclo*[3.3.0]*octane*-3,7-*dione* (**49**).—The dione was prepared from pyruvaldehyde and dimethyl acetonedicarboxylate. It had m.p. 121—123 °C (n-hexane) (lit.,[17] m.p. 120 °C), $\nu_{max.}$ 1 730 cm^{-1}; δ 1.34 (Me), 2.0—2.9 (m, 5 H), and 2.34 (CH_2); δ_c 26.2 (q), 42.8 (d), 43.7 (t), 43.7, 50.4 (t), and 217 p.p.m. (Found: C, 71.2; H, 8.1. Calc. for $C_9H_{12}O_2$: C, 71.0; H, 7.95%). The dione produced a corresponding bisdioxolane, a colourless oil, $\nu_{max.}$(film) 2 950 and 2 900 cm^{-1}; δ 1.2 (Me), 1.5—2.18 (m, 9 H), 3.84 (OCH_2 CH_2O); δ_c 29.7 (q), 41.9 (t), 44.8, 45.6 (d), 49.4 (t), 63.9 (t), 64.2 (t), and 118.1 p.p.m. (Found: C, 64.9; H, 8.8. $C_{13}H_{20}O_4$ requires C, 65.0; H, 8.4%).

4-*Methoxycarbonyl*-1-*methylbicyclo*[3.3.0]*octane*-3,7-*dione* (**50**).—A solution of 1-methylbicyclo[3.3.0]octane-3,7-dione (3.8 g, 25 mmol) in methylmagnesium carbonate solution[20] (51.5 cm^3, 0.1 mol) was heated at 65 °C for 2 h with a slow stream of nitrogen passing through the solution. The mixture was cooled, and then added cautiously to a stirred solution of anhydrous methanolic hydrogen chloride at −65 °C. The solution was allowed to warm to room temperature over 22 h. The resulting pale yellow solution was evaporated to half its original volume, and then extracted with ether (2 × 300 cm^3). The dimethylformamide salt layer was diluted with an equal volume of water and then extracted with a further three portions of ether (3 × 200 cm^3). The combined ethereal extracts were dried and then evaporated to leave an oil which crystallised with time. Trituration with ether afforded the β-keto ester as a white solid (3.27 g, 62%). An analytical sample was obtained by recrystallisation from isopropyl alcohol and had m.p. 71—72 °C, $\nu_{max.}$(KBr disc) 1 720 cm^{-1}; δ 1.4 (Me) 2.2—3.0 (m, 7 H), 3.0—3.2 (m, C*H*CO_2Me), and 3.8 (CO_2CH_3) (Found: C, 63.0; H, 7.2%; *m/z* 210. $C_{11}H_{14}O_4$ requires C, 62.8; H, 6.7% *M*, 210).

4-*Benzyl*-4-*methoxycarbonyl*-1-*methylbicyclo*[3.3.0]*octane*-3,7-*dione* (**51**).—Benzyl bromide (283 mg) was added to a stirred solution of the β-keto ester (**50**) (315 mg, 1.5 mmol) in 2M-sodium methoxide (0.75 cm^3, 1.5 mmol) and the mixture was then stirred at room temperature for 24 h. The mixture was diluted with water (2 cm^3), acidified with 6M-hydrochloric acid, and then extracted with benzene (2 × 10 cm^3). The combined organic extracts were dried and evaporated to leave an oil, which on crystallisation from n-hexane–ether gave the β-keto ester as a colourless crystalline solid (140 mg, 37%), m.p. 69—70 °C, $\nu_{max.}$(KBr disc) 1 740 and 1 610 cm^{-1}; δ 1.03 (Me) 1.71—3.43 (complex m, 9 H), 3.64 (CO_2CH_3), 6.89—7.22 (m, Ph); δ_c 28.77 (q), 40.3, 40.6, 41.3, 49.8, 50.5, 52.1, 53.0, 66.3, 127.3, 128.5, 130.8, 135.7, 170.7, 214.3, and 216.7 p.p.m. (Found: C, 72.0; H, 7.1%; *m/z* 300. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%; *M*, 300).

Ethyl 4,5-*Dioxopentanoate* (**52**).—A stream of dry ozone–oxygen mixture was passed through a vigorously stirred suspension of ethyl benzyl-laevulinate (34.84 g, 0.23 mol)[23] in dry methanol (300 cm^3) at −10 °C. On completion of reaction (t.l.c. analysis) the resulting light green solution was purged with dry nitrogen for 0.5 h. The solution was hydrogenated at room temperature and atmospheric pressure over 5% palladium on calcium carbonate (1.75 g). The mixture absorbed one equivalent of hydrogen, and was then evaporated to dryness. The residue was dissolved in water (75 cm^3) and then washed with hexane (4 × 60 cm^3) to remove the benzaldehyde. The aqueous extract was evaporated under reduced pressure to leave the keto aldehyde ester as an unstable green oil (21.95 g, 92.5%), $\nu_{max.}$(film) 3 450 and 1 720 cm^{-1}; δ 1.22 (t, *J* 7, OCH_2CH_3), 2.0—3.0 (m, 4 H), 4.1 (q, *J* 7, OCH_2CH_3), and 4.8—5.4 (m, 1 H), which was used immediately without further purification.

1-(2-*Carboxyethyl*)*bicyclo*[3.3.0]*octane*-3,7-*dione* (**54a**).—Dimethyl acetonedicarboxylate (48.3 g) was added, all at once, to a stirred solution of ethyl 4,5-dioxopentanoate (21.95 g, 0.138 mol) in aqueous sodium bicarbonate buffer (0.167M; 950 cm^3), and the light green solution was then stirred at room temperature for 4 days. The resulting dark green solution was acidified with 6M-hydrochloric acid and then extracted with chloroform (2 × 650 cm^3). The combined chloroform extracts were dried and evaporated to give the pentaester (**53**) (63.8 g) as an orange oil. The oil was dissolved in 25% hydrochloric acid (1.27 dm^3), and the solution was heated under reflux for 6 h. The cooled solution was evaporated under reduced pressure to one-fifth of its original volume, and then extracted with ethyl acetate (5 × 400 cm^3). Evaporation of the dried extracts followed by chromatography in silica gel (50—100 mesh) using chloroform–methanol (95:5) as eluant gave a mixture of the ethyl ester (**54b**) (3.96 g, 12%) and the diketo acid (**54a**) (17.38 g, 60%). The diketo acid crystallised from ethyl acetate–hexane, and had m.p. 108—110 °C (lit.,[18] m.p. 101—102 °C); $\nu_{max.}$(KBr) 1 700 cm^{-1}; δ 1.78—2.8 (m, 9 H), 2.48 (CH_2), and 10.7 (CO_2H); δ_c 30.2 (t), 33.4 (t), 41.8, 43.7 (t), 47.0 (d), 47.8 (t), 178.1, and 216.3 p.p.m. (Found: C, 62.7; H, 6.8. Calc. for $C_{11}H_{14}O_4$: C, 62.9; H, 6.7%).

1-(3-*Ethoxycarbonylethyl*)*bicyclo*[3.3.0]*octane*-3,7-*dione* (**54b**).—The diketo acid (**54a**) (13.78 g, 65 mmol) was esterified with diethyl sulphate by the usual method, to afford the ethyl ester as a colourless solid (12.4 g, 79.5%), m.p. 60 °C; b.p. 158 °C at 0.1 mmHg; $\nu_{max.}$(KBr) 1 730 cm^{-1}; δ 1.26 (t, *J* 7, OCH_2CH_3), 1.8—2.9 (m, 9 H), 1.31 (CH_2), and 4.13 (q, *J* 7, OCH_2CH_3); δ_c 14.2 (q), 30.5 (t), 33.7 (t), 41.8 (t), 43.7 (t), 47.1 (d), 47.8 (t), 60.8 (t), 172.6, and 216.1 p.p.m.

1-(3-*Ethoxycarbonylethyl*)-3,3,7,7-*tetraethoxybicyclo*[3.3.0]-*octane* (**55**).—Concentrated sulphuric acid (10 drops) was added to a stirred solution of the diketo ester (**54b**) (12.4 g, 52 mmol) in dry ethanol (2.65 cm^3, 57.6 mmol) and triethyl orthoformate (17.34 g, 0.117 mol). The solution was set aside at room temperature for 1.5 h, and then neutralised by addition of triethylamine (2.65 cm^3). The mixture was evaporated to dryness, and then partitioned between ether (250 cm^3) and water (50 cm^3). The organic phase was separated, and the aqueous layer was then extracted with ether (250 cm^3). The combined ethereal extracts were dried (Na_2SO_4) and evaporated to leave the acetal as a colourless oil (20.1 g, 99%), $\nu_{max.}$(film) 1 730 cm^{-1}; δ 1.19 (t, *J* 8, OCH_2CH_3), 1.24 (t, *J* 7, $CO_2CH_2CH_3$), 1.7—2.4 (m, 13 H), 3.42 (q, *J* 8, OCH_2CH_3), 4.08 (q, *J* 7, $CO_2CH_2CH_3$), which was used without further purification.

1-(3-*Hydroxypropyl*)*bicyclo*[3.3.0]*octane*-3,7-*dione* (**56**).—A solution of the acetal ester (**55**) (20.1 g) in dry ether (100 cm^3)

was added to a stirred suspension of lithium aluminium hydride (2 g, 52.5 mmol) in dry ether (250 cm^3) under nitrogen at such a rate as to maintain a gentle reflux. The mixture was cooled, and the excess of lithium aluminium hydride was destroyed by careful additon of water. The resulting white suspension was filtered, and the residue was then washed several times with ether. The combined ether filtrates were dried (Na_2SO_4) and evaporated to leave the alcohol (17.4 g, 97%) as a colourless oil, $\nu_{max.}$(film) 3 400 and 2 900 cm^{-1}; δ 1.16 (t, *J* 8, OCH_2CH_3), 1.4—2.2 (m, 13 H), 3.45 (q, *J* 8, OCH_2CH_3), 3.4—3.8 (m, CH_2OH). The alcohol (17.37 g, 50.5 mmol) was dissolved in ethanol (87 cm^3), then treated with 2M-hydrochloric acid (87 cm^3), and the resulting mixture was stirred at room temperature for 2 h. The solution was neutralised by the addition of solid potassium carbonate, and then extracted with ether (3 × 250 cm^3). Evaporation of the dried extracts left an oil which was chromatographed on silica gel (50—100 mesh) using chloroform–methanol (9:1) as eluant to give the *diketo alcohol* (8.2 g, 82%) as a colourless oil, b.p. 165 °C (decomp.) at 0.1 mmHg, $\nu_{max.}$(film) 3 450 and 1 730 cm^{-1}; δ 1.5—2.8 (m, 13 H), 1.9 (OH), and 3.6—3.8 (m, CH_2O); δ_c 28.5 (t), 35.4 (t), 41.9 (d), 43.9 (t), 47.4, 48.2 (t), 62.45 (t), and 217.4 p.p.m. The *p*-nitrobenzoate derivative recrystallised from ethanol and had m.p. 122—123 °C; $\nu_{max.}$(film) 1 730, 1 600, and 1 530 cm^{-1}; δ 1.73—2.88 (m, 9 H), 2.2 (CH_2), 4.48 (t, *J* 7, CH_2O), 8.26—8.48 (m, $PhNO_2$) (Found: C, 62.8; H, 5.45; N, 4.0. $C_{18}H_{19}NO_6$ requires C, 62.6; H, 5.55; N, 4.1%).

4-Methoxycarbonyl-1-(3-hydroxypropyl)bicyclo[3.3.0]*octane-3,7-dione* (**57**).—Toluene-p-sulphonic acid (0.1 g), followed by dihydropyran (2.9 cm^3) were added to a stirred solution of the diketoalcohol (**56**) (1.96 g, 10 mmol) in dry dioxane (20 cm^3). The solution was stirred at room temperature for 0.25 h, and then neutralised by the addition of methanol (0.5 cm^3) and concentrated ammonia (0.5 cm^3). The mixture was evaporated to dryness and the residue was then partitioned between chloroform (100 cm^3) and saturated aqueous sodium hydrogen carbonate (30 cm^3). The organic layer was separated, then dried, and evaporated. The residue was chromatographed on silica gel G using chloroform–ether (4:1) as eluant to give the tetrahydropyranyl ether (2.4 g, 84%) as a pale yellow oil, $\nu_{max.}$ (film) 1 740 cm^{-1}; δ 1.36—2.73 (complex m, 19 H), 3.2—3.88 (m, 2 × CH_2O), and 4.46 (br, OC*H*O).

A stirred solution of the tetrahydropyranyl ether (1.96 g) in methylmagnesium carbonate solution (21.6 cm^3, 40 mmol) was heated at 105—110 °C for 2.5 h with a slow stream of nitrogen passing through the mixture. After 0.5 h the mixture set solid and dimethylformamide (10 cm^3) was added to dissolve the solid. The mixture was cooled to room temperature, and then added to anhydrous methanolic hydrogen chloride (60 cm^3) at −60 °C with vigorous stirring. The solution was allowed to warm to room temperature with continued stirring for 20 h and then evaporated to half its original volume. The mixture was diluted with an equal volume of water and extracted with chloroform (2 × 50 cm^3). The combined chloroform extracts were dried and then evaporated to leave the β-keto ester as an oil (1.78 g, 70%), $\nu_{max.}$(film) 3 450, 1 740, and 1 710 cm^{-1}; δ 1.5—2.9 (m, 11 H), 3.02—3.23 (m, $CHCO_2Me$), 3.5—3.8 (m, CH_2O), and 3.75 (CO_2CH_3).

1-(3-Bromopropyl)-4-methoxycarbonylbicyclo[3.3.0]*octane-3,7-dione* (**58**).—A mixture of the alcohol (**57**) (0.63 g) and pyridine (20 μl) in ether (2.5 cm^3) was added to a stirred solution of pyridine (70 μl, 0.847 mmol) and phosphorus tribromide (0.25 g, 0.92 mmol) in dry ether (25 cm^3) at −5 °C under nitrogen. The mixture was stirred at −5 °C for 1 h, and then warmed to room temperature and stirred for a further 16 h. The mixture was dissolved in chloroform (15 cm^3) and then washed with water (2 × 5 cm^3). Evaporation of the dried chloroform extracts left an oil which was chromatographed on silica gel G using chloroform–ether (6:4) as eluant to give the bromide as a colourless oil (50 mg, 7%); $\nu_{max.}$(film) 1 740, 1 660, and 1 620 cm^{-1}; δ 1.6—2.6 (m, 11 H), 3.04—3.21 (m, $CHCO_2Me$), 3.38 (t, *J* 6, CH_2Br), and 3.71 (CO_2CH_3); *m/z* 316.0322 ($C_{13}H_{17}BrO_4$ requires *M*, 316.0311).

Enol Tosylate (**60**) *of 1-(3-Tosyloxypropyl)-4-methoxycarbonylbicyclo*[3.3.0]*octane-3,7-dione*.—Toluene-*p*-sulphonyl chloride (0.5 g) was added to an ice-cold stirred solution of the alcohol (**57**) (0.32 g) in dry pyridine (5 cm^3), and the mixture was then kept at 0 °C for 16 h before being poured into ice–water (50 g). The mixture was extracted with benzene (2 × 50 cm^3), and the combined benzene extracts were washed with cold 2M-hydrochloric acid (2 × 20 cm^3) followed by water (25 cm^3). Evaporation of the dried (K_2CO_3) extracts left a residue which was chromatographed on silica gel G using benzene–ether (1:1) as eluant to give the enol tosylate (130 mg, 18%) as a viscous oil, $\nu_{max.}$(film) 1 730 and 1 640 cm^{-1}, δ 1.5—2.9 (m, 11 H), 2.5 (ArMe), 3.65 (OMe), 4.0—4.2 (m, OCH_2), and 7.4—8.0 (m, ArCH); *m/z* 562 ($C_{27}H_{30}S_2O_3$ requires *M*, 562).

A small amount of the tosylate of the carbinol (**56**) was also recovered by chromatography. The tosylate exhibited the following spectral characteristics, $\nu_{max.}$ 1 730 and 1 600 cm^{-1}; δ 1.5—2.7 (m, 9 H), 2.17 (CH_2), 2.39 (ArMe), 3.94—4.1 (m, CH_2O), 7.36 (d, *J* 9, 2 × :C*H*), and 7.81 (d, *J* 9, 2 × :C*H*), which were identical with those obtained for an authentic sample produced from direct tosylation of the carbinol (**56**).

Preparation of the Tricyclic Dione (**59**).—A solution of the bromide (**58**) (50 mg) in dry oxygen-free methanol (10 cm^3) was added over 0.5 h to a stirred solution of sodium methoxide (from 4 mg Na) in methanol (4 cm^3). The mixture was allowed to warm to 25 °C when it was stirred for a further 21 h. The mixture was diluted with water (2 cm^3), and then acidified with 6M-hydrochloric acid and extracted with benzene (2 × 5 cm^3). Evaporation of the dry benzene extracts left a residue which crystallised from hexane–ether to give the tricyclic dione (26 mg, 70%) as white crystals, m.p. 108 °C, $\nu_{max.}$(KBr) 1 740 and 1 720 cm^{-1}; δ 1.55—2.06 (m, 6 H), 2.16—2.67 (m, 7 H), and 3.71 (OMe); δ_c 19.4, 33.5, 35.4, 40.8, 44.3, 45.7, 48.9, 52.2, 53.3, 63.6, 170.35, 211.9, and 215.3 p.p.m. (Found: C, 65.95; H, 6.75; *m/z* 236.1052. $C_{13}H_{16}O_4$ requires C, 66.1; H, 6.8% *M*, 236.1049).

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References

1 R. L. Ranieri and G. J. Carlton, *Tetrahedron Lett.*, 1978, 499; G. J. Calton, R. L. Ranieri, and M. A. Espenshade, *J. Antibiot.*, 1978, **31**, 38.
2 (*a*) S. Danishefsky, K. Vaughan, R. Gadwood, and K. Tsuzuki, *J. Am. Chem. Soc.*, 1980, **102**, 4262; *ibid.*, 1981, **103**, 4136; (*b*) W. K. Bornack, S. S. Bhagwat, J. Ponton, and P. Helquist, *ibid.*, 1981, **103**, 4647; (*c*) S. D. Burke, C. W. Murtiashaw and M. S. Dike, *J. Org. Chem.*, 1982, **47**, 1349; (*d*) A. B. Smith, B. A. Wexler and J. Slade, *Tetrahedron Lett.*, 1982, **23**, 1631; (*e*) A. S. Kende, B. Roth, P. J. Sanfilippo, and T. J. Blacklock, *J. Am. Chem. Soc.*, 1982, **104**, 5808; (*f*) K. Takeda, Y. Shimono, and E. Yoshii, *ibid.*, 1983, **105**, 563.
3 M. Horton and G. Pattenden, *J. Chem. Soc., Perkin Trans 1*, 1984, following paper.
4 G. Stork, J. D. Winkler, and N. A. Saccomano, *Tetrahedron Lett.*, 1983, **24**, 465 and refs. cited therein; S. D. Burke, C. W. Mutrisashaw, and M. S. Dike, *J. Org. Chem.*, 1982, **47**, 1349; I. A. Blair, L. N. Mander, P. H. C. Mundill, and S. G. Pyne, *Aust. J. Chem.*, 1981, **34**, 1887 and refs. cited therein; B. M. Trost, C. D. Shuey, F. DiNinno, and S. S. McElvain *J. Am. Chem. Soc.*, 1979, **101**, 1284; see also ref. 3.

5 (*a*) See L. A. Paquette, 'Topics in Current Chemistry,' 1979, **79**, 41; (*b*) A. Marfat and P. Helquist, *Tetrahedron Lett.*, 1978, 4217.
6 (*a*) P. A. Grieco and C. S. Pogonowski, *Synthesis*, 1973, 425; (*b*) R. D. Clark, L. G. Kozar, and C. H. Heathcock, *Synth. Commun.*, 1975, 1; (*c*) E. Piers, B. Abeysekera, and J. R. Scheffer, *Tetrahedron Lett.*, 1979, 3279.
7 M. J. Begley, K. Cooper, and G. Pattenden, *Tetrahedron Lett.*, 1981, **22**, 257; *Tetrahedron*, 1981, **37**, 4503; P. A. Aristoff, *Synth. Commun.*, 1983, **13**, 145.
8 P. A. Aristoff, *J. Org. Chem.*, 1981, **46**, 1954.
9 J. E. McMurry and J. Melton, *J. Org. Chem.*, 1973, **38**, 4367.
10 N. Kornblum and P. A. Wade, *J. Org. Chem.*, 1973, **38**, 1418.
11 K. Sisido, S. Kurozumi, and K. Utimoto, *J. Org. Chem.*, 1969, **34**, 2661.
12 See: (*a*) G. Slomp, Jr., and J. L. Johnson, *J. Am. Chem. Soc.*, 1958, **80**, 915; (*b*) W. H. Parsons, R. H. Schlessinger, and M. L. Queseda, *J. Am. Chem. Soc.*, 1980, **102**, 889; (*c*) T. Veysoglu, L. A. Mitscher, and J. K. Swayze, *Synthesis*, 1980, 807; (*d*) G. Pattenden and D. Whybrow, *J. Chem. Soc., Perkin Trans 1*, 1981, 1046.
13 P. J. De Clercq, *Tetrahedron*, 1981, **37**, 4277.
14 H. Stetter, *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 639.
15 For a recent illustration of this design see: B. M. Trost, C. D. Shuey, F. DiNinno, and S. S. McElvain, *J. Am. Chem. Soc.*, 1979, **101**, 1284.
16 See: J. J. Tufariello, *Acc. Chem. Res.*, 1979, **12**, 396; W. Oppolzer and J. I. Grayson, *Helv. Chim. Acta*, 1980, **63**, 1706.
17 U. Weiss and J. M. Edwards, *Tetrahedron Lett.*, 1968, 4885.
18 J. Oehldrich, J. M. Cook, and U. Weiss, *Tetrahedron Lett.*, 1976, 4549.
19 H. Pines, P. J. Pavlik, and V. N. Ipatieff, *J. Am. Chem. Soc.*, 1951, **73**, 5738.
20 H. L. Finkbeiner and M. Stiles, *J. Am. Chem. Soc.*, 1963, **85**, 616.
21 P. D. G. Dean, *J. Chem. Soc.*, 1965, 6655; *cf.* A. P. Krapcho and A. J. Lovey, *Tetrahedron Lett.*, 1973, 957.
22 G. Pattenden and R. Storer, *J. Chem. Soc., Perkin Trans 1*, 1974, 1603.
23 S. H. Zaheer, I. K. Kacker, and N. Shanmukha Rao, *Chem. Ber.*, 1956, **89**, 351.

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