Synthesis of Stable Analogues of TXA_2

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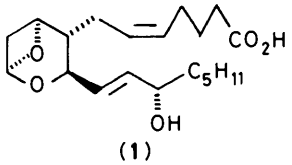
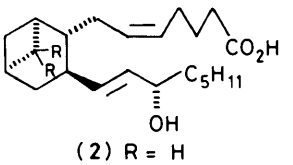
Intramolecular aldol condensations and intramolecular Lewis acid-catalysed alkylations are used in approaches to substituted bicyclo[3.3.1]nonanes and bicyclo[3.2.1]octanes, specifically the oxo esters (**7**), (**8**), and (**9**). A ring expansion to a cycloheptane derivative is observed on treatment of the cyclopentyl derivative (**18**) with acid, and the bicyclo[4.4.0]decane and bicyclo[4.3.0]nonane derivatives (**34**) and (**36**) are obtained from the prenyl derivatives (**30**) and (**35**) respectively. The oxo esters (**7**), (**8**), and (**9**) are converted into the stable TXA_2 analogues (**10**), (**11**), and (**12**) respectively, by a series of reactions which involve stereospecific functionalisation of their ketone and ester groups.

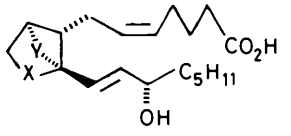
Thromboxane A_2 (TXA_2), (**1**), is an extremely potent compound which promotes the aggregation of blood platelets.[1] It is very unstable, and only recently has a total synthesis been reported.[2] There has been considerable effort directed towards the synthesis of stable analogues of TXA_2, with the aim of producing an antagonist of the natural material. In general, these analogues have involved replacement of one, or both, of the acetal oxygens of (**1**) by other atoms.[3] We were attracted by



(**1**)

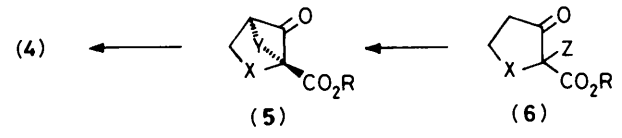


(**2**) R = H
(**3**) R = Me



(**4**)

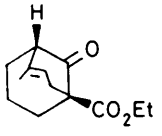
the reported analogues (**2**) and (**3**),[4,5] particularly the latter, which has an interesting biological profile. It was considered that analogues of the general type (**4**) would be of interest since a methyl group on the hydrocarbon bridge of the α-face might occupy a similar region of space as one of the methyl groups in (**3**), and this might have implications for interaction with the appropriate receptor. Furthermore, such analogues should be readily available *via* (**5**) from the cyclic β-oxo esters (**6**) (see Scheme 1). We describe the preparation of three compounds of



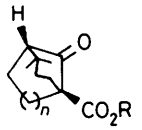
Scheme 1.

the type (**5**), where Y is a substituted three-carbon chain, specifically (**7**), (**8**), and (**9**), and their conversion into TXA_2 analogues (**10**), (**12**), and (**13**).

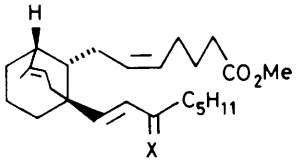
The obvious approach towards (**5**) is by intramolecular cyclisation of the enol or enolate from (**6**) (Z is the chain Y



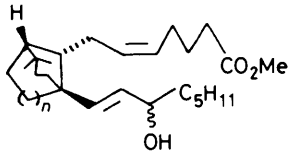
(**7**)



(**8**) *n* = 2, R = Et
(**9**) *n* = 1, R = Me



(**10**) X = OH, H
(**11**) X = O

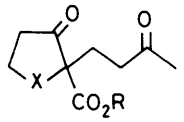


(**12**) *n* = 2
(**13**) *n* = 1

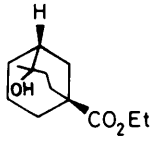
containing a suitable electrophilic functional group). Our efforts to achieve the conversion (**6**)→(**5**), have focussed on intramolecular aldol reactions and intramolecular Lewis acid-catalysed alkylations.

Aldol Condensations.—There are many examples in the literature of bicyclic ketones produced by aldol condensation.[6] Following established methods[7] the dioxo ester (**14**), prepared from ethyl 2-oxocyclohexanecarboxylate and methyl vinyl ketone, gave (**7**) (60%) on treatment with concentrated sulphuric acid. Variation of the concentration of sulphuric acid did not allow isolation of the hydroxy intermediate (**17**), while the use of other acid catalysts such as concentrated hydrochloric acid–acetic acid, stannic chloride and boron trifluoride, gave only the Robinson annulation product (**18**).

Cyclisation of the cyclopentane derivative (**15**) has been reported[7] to give the bicyclic hydroxy ester (**19**). Following the procedure described for the ethyl ester, we treated the methyl ester (**16**) with concentrated sulphuric acid. The product obtained did not show spectral or chemical properties consistent with the expected product (**20**). Rather the data suggested that the product was the lactone (**22**). Confirmation of the structure was obtained from an *X*-ray analysis (Figure 1). Repetition of the reaction described in the literature with the ethyl ester (**15**) gave a product (**23**) whose ^1H and ^{13}C n.m.r. spectra were superimposable on those of the lactone (**22**), except for the differences expected for the change from methyl to ethyl



(14) X = $(CH_2)_2$, R = Et
(15) X = CH_2, R = Et
(16) X = CH_2, R = Me



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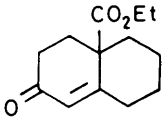

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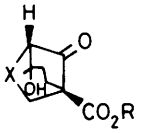
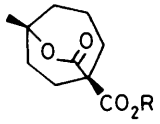
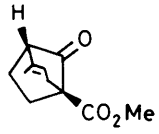


(19) X = CH_2, R = Et
(20) X = CH_2, R = Me
(21) X = S, R = Me

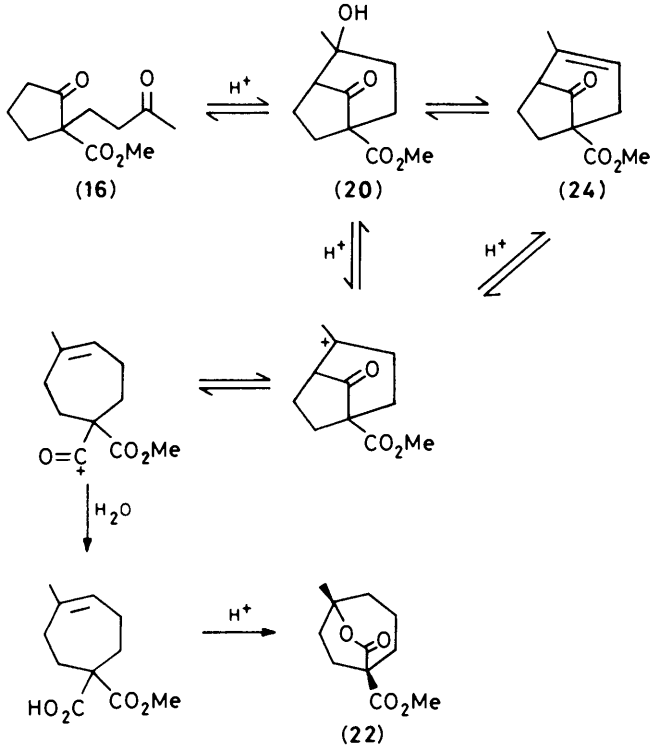


(22) R = Me
(23) R = Et



(24)

ester. There is no doubt, therefore, that the product previously reported to have structure (**19**) should be re-formulated as (**23**).[8] The proposed mechanism for the ring expansion is shown in Scheme 2. When short reaction times were used three products



Scheme 2.

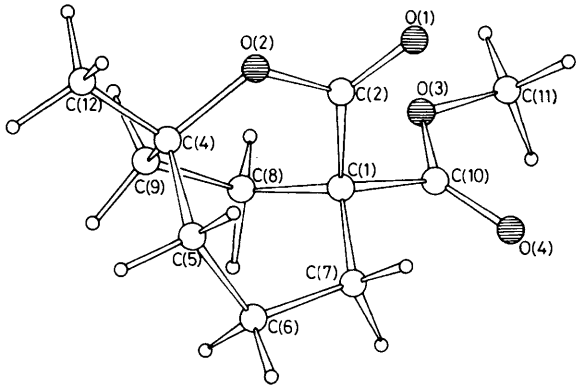
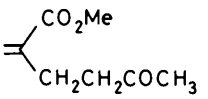


Figure 1. *X*-Ray structure of (**20**)

were observed, namely starting material (**16**), the lactone (**22**), and the bicycloalkene (**24**), which could be isolated in 31% yield by chromatography. Further treatment of (**24**) with concentrated sulphuric acid gave the lactone (**22**). Related rearrangements of cyclopentane to cycloheptane systems have been reported previously.[9]

Having investigated intramolecular aldol cyclisations of the carbocyclic systems (**14**) and (**16**) we then turned our attention to the heterocyclic compounds (**25**) and (**26**) readily available



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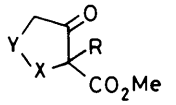


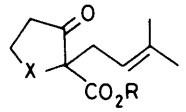
(25) X = CH_2, Y = S, R = $(CH_2)_2COCH_3$
(26) X = S, Y = CH_2, R = $(CH_2)_2COCH_3$
(27) X = CH_2, Y = S, R = H
(28) X = S, Y = CH_2 R = H
(29) X = CH_2, Y = S

from (**27**) and (**28**) respectively.[10,11] It is noteworthy that, during the Michael reaction between (**27**) and methyl vinyl ketone, a minor product isolated was the acrylic ester (**30**). A recent report[12] has shown that compounds of the type (**29**) on treatment with sodium hydroxide, afford acrylic esters. Indeed we found that reaction of (**25**) under the literature conditions gave cleanly the ester (**30**).

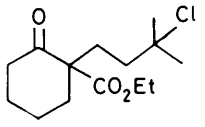
Treatment of the diketone (**25**) with concentrated sulphuric acid gave the bicyclic hydroxy ester (**21**).[12] In contrast, the diketone (**26**) gave largely decomposition products under similar conditions.

Lewis Acid-catalysed Alkylations.—The acid-catalysed α-alkylation of carbonyl compounds by coupling of S_N1 reactive substrates with enol derivatives has recently been reviewed.[13] Although most of the known examples are intermolecular, a few intramolecular reactions of this type are known, and we felt that useful compounds for our purposes could be generated by such reactions. Thus, alkylation of ethyl 2-oxocyclohexanecarboxylate with prenyl bromide gave the product (**31**) from alkylation at the primary position of the allyl halide. Addition of hydrogen chloride to (**31**) gave the tertiary chloride (**33**) which was converted into its enol silane (**34**) with ethyl trimethylsilylacetate–tetrabutylammonium fluoride.[14] However, treatment of (**34**) with titanium tetrachloride resulted only in desilylation, giving (**33**), while silver tetrafluoroborate gave (**31**).

It was hoped that treatment of (**31**) with trimethylsilyl trifluoromethanesulphonate (TMS triflate) would afford the



(31) X = $(CH_2)_2$, R = Et
(32) X = CH_2, R = Me



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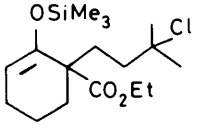

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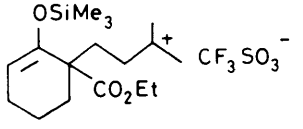
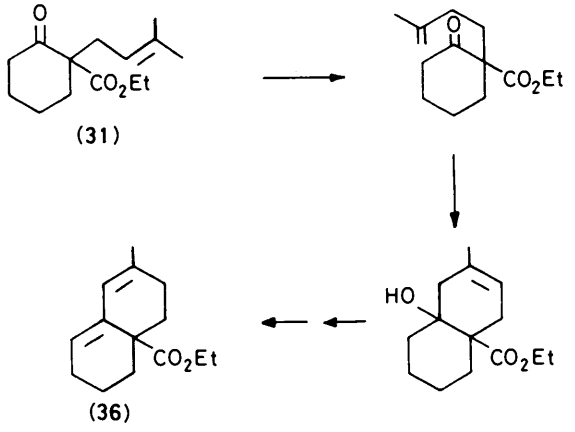


(35)

intermediate (**35**) which would then cyclise to give the desired compound (**8**). However, the product isolated from this reaction was not (**8**) but the transoid diene (**36**),[15] whose structure was confirmed by detailed examination of its ^1H and ^{13}C n.m.r. spectra. Furthermore, application of the Fieser-Woodward rules to the u.v. spectrum of (**36**) showed it to have a transoid diene component. It was found that the same product could be obtained by treating the oxo ester (**31**) with triflic acid or stannic chloride. T.l.c. monitoring of these reactions showed the presence of numerous intermediates which all eventually led to a single product. A possible mechanism involves an initial proton transfer, followed by an ene reaction. Subsequent dehydration and proton transfer would give the observed product (Scheme 3). A similar experiment with the cyclopentane derivative (**32**)

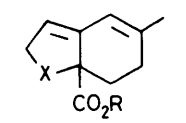


(31) (36)

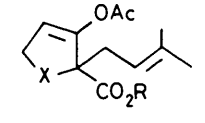
Scheme 3.

gave the bicyclo[4.3.0]nonane derivative (**37**). Similar cyclisations have been reported recently[16] using dimethylaluminium chloride although in these cases the product was a tertiary alcohol which is presumably an intermediate in our reactions.

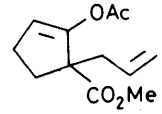
Cyclisation of (**31**) and (**32**) in the desired sense was eventually achieved by acid-catalysed cyclisation of the derived enol acetates.[13] Thus, treatment of (**31**) and (**32**) with isopropenyl acetate–toluene-*p*-sulphonic acid gave the enol acetates (**38**) and (**39**) respectively, which, with stannic chloride in dichloromethane, gave the bicyclic oxo esters (**8**) and (**9**) in high yield. The stannic chloride-catalysed cyclisations took a different course if the dichloromethane was excessively wet. Under these conditions the products isolated were ethyl 2-oxocyclohexanecarboxylate and methyl 2-oxocyclopentanecarboxylate respectively. This dealkylation is a reaction of the enol acetate and is not preceded by hydrolysis of the enol acetate, since (**31**) and (**32**) did not change under these conditions. Furthermore, dealkylation did not occur with the allyl substituted enol acetate (**40**), and this may indicate that the alkyl group lost must be able to form a carbocation more stable than the allyl cation.



(36) X = $(CH_2)_2$, R = Et
(37) X = CH_2, R = Me

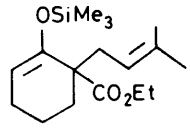


(38) X = $(CH_2)_2$, R = Et
(39) X = CH_2, R = Me



(40)

Other Approaches towards Bicyclo[3.3.1]*nonane Systems.*—It was hoped that Cope rearrangement of the enol silane (**41**) would afford (**42**) which could then be cyclised *via* an organoselenium intermediate, by analogy with previous work.[17] However, (**41**) did not change when heated to high temperatures in solution, while pyrolysis of the neat material gave (**31**), the product of desilylation, and (**43**), from subsequent decarboethoxylation, as the only isolated products. Furthermore, the anionic Cope rearrangement,[18] using the potassium enolate of (**31**), did not give the required product.



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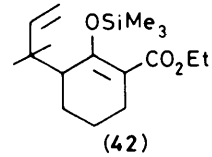

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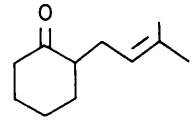

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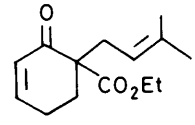


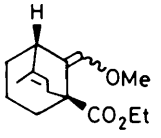
(44)

The formation of bicyclo[3.3.1]nonenes by means of palladium acetate-catalysed cyclisation of enol silanes containing a suitably positioned alkene functionality has recently been described by Kende.[19] Application of this methodology to the enol silane (**41**) gave only the α,β-unsaturated ketone (**44**), together with the hydrolysis product (**31**). The formation of enones under these conditions is now well established,[20] although Kende did not observe this pathway in his studies. It seems pertinent that the cases studied by Kende, which led to bicyclic systems, did not include a trisubstituted alkene. In our studies the alkene is trisubstituted and presumably the palladium acetate prefers to co-ordinate to the less crowded enol silane double bond, thus leading to the α,β-unsaturated ketone.

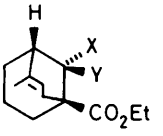
Conversion of (**7**), (**8**), *and* (**9**) into TXA_2 *Analogues.*—In all cases, the overall requirement is to convert the ketone carbonyl group into the α-side chain and the ester group to the ω-side chain of TXA_2. These conversions must be carried out with control of the stereochemistry, to give the *syn* isomer (*i.e.* the two side chains will be '*trans*' in the way the molecules are drawn). Molecular models suggest that for a derivative of (**7**) this arrangement represents the thermodynamically favoured situation, but for analogues derived from (**8**) and (**9**) it is

necessary to use methodology which will produce the thermodynamically unfavoured relative stereochemistry.

Synthesis of TXA_2 *Analogue* (**10**).—Several attempts to carry out Wittig reactions with (**7**) and various phosphoranes were unsuccessful, but a Wittig-Horner reaction with the anion of methoxymethyldiphenylphosphine oxide[21] gave a mixture of the isomeric enol ethers (**45**) in good yield. Acid-catalysed hydrolysis of this mixture gave a 2:1 epimeric mixture of the aldehydes (**46**) and (**47**), and treatment of this mixture with a catalytic amount of sodium ethoxide in ethanol caused complete conversion into a single isomer (**46**). Thus, our system was more efficient than that described by Corey in his synthesis of helminthosporal,[22] in which only 80% of the related aldehyde (**49**) was present at equilibrium. One carbon homologation of (**46**) was now necessary. This time, the phosphine oxide method was unsuccessful, owing to the very slow collapse of the hydroxy intermediate on treatment with sodium hydride. However, reaction between (**46**) and methoxymethyltriphenylphosphorane gave a mixture of enol ethers which was converted into the aldehyde (**48**) with mercuric acetate and potassium iodide.



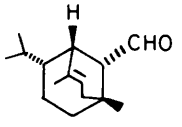
(**45**)



(**46**) X = CHO, Y = H

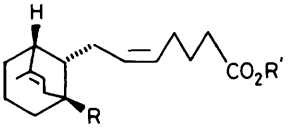
(**47**) X = H, Y = CHO

(**48**) X = CH_2CHO, Y = H



(**49**)

In order to confirm the relative stereochemistry present in (**48**), an *X*-ray analysis was performed on the dinitrophenylhydrazone derivative. This investigation (Figure 3) showed the required *syn* disposition of the CH_2CHO group in (**48**). With the required stereochemistry established, the α- and ω-side chains were now completed. Thus, the aldehyde (**48**) was treated with the potassium salt of 4-carboxybutyltriphenylphosphorane in tretrahydrofuran (THF), to give (**50**), with the required *Z* double bond.[23] The first attempts to modify the ester group in (**50**) involved reduction to the corresponding aldehyde (**51**)



(**50**) R = CO_2Et, R' = H

(**51**) R = CHO, R' = H

(**52**) R = CH_2OH, R' = H

(**53**) R = CH_2OH, R' = Me

(**54**) R = CHO, R' = Me

using di-isobutylaluminium hydride (Dibal), but under a range of conditions the reaction mixture always contained the desired aldehyde, the starting material, and the alcohol (**52**). It was thought that it would be more efficient and convenient to use sufficient Dibal to reduce the ester (**50**) to the alcohol (**52**) and then oxidise (**52**) to the aldehyde (**50**). Unfortunately, oxidation

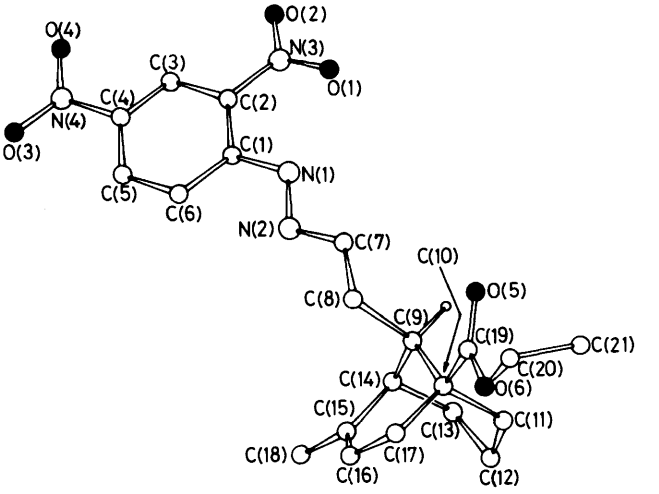
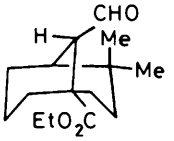


Figure 2. *X*-Ray structure of dinitrophenylhydrazone of (**48**). Hydrogen atoms (other than 9-H) have been omitted for clarity

of the hydroxy acid (**52**) with pyridinium chlorochromate (PCC) proceeded only in low yield. This problem was overcome by esterification of (**52**) with diazomethane, and PCC oxidation of the resulting hydroxy ester (**53**), thus giving the aldehyde (**54**) in high overall yield. The ω-side chain was now introduced by treatment of (**54**) with the sodium derivative of dimethyl 2-oxo-heptylphosphonate, to give the ketone (**11**) with the desired *E* configuration at the newly created double bond.[24] Finally, reduction of (**11**) with sodium borohydride gave, as expected, an epimeric mixture of the alcohols (**10**). No attempt was made to separate this mixture.

Synthesis of the TXA_2 *Analogue* (**11**).—Previous work in the area of the bicyclo[3.3.1]nonane system has shown that the molecule is in the twin-chair conformation.[25,26] Assuming that the same preferred conformation applies to derivatives of the oxo ester (**8**), then models show that the aldehyde (**55**) is the thermodynamically unfavourable isomer, due to the interaction between the aldehyde group and the axial methyl group [see (**55**)]. However, it was expected that, in the reduction of the α,β-unsaturated aldehyde (**61**) delivery of hydrogen would occur from the least hindered side giving (**56**) with the required stereochemistry. With this plan in mind, a method was sought for the conversion of (**8**) into the enal (**61**).

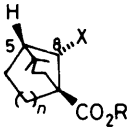


(**55**)

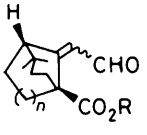
When the oxo ester (**8**) was treated with the anion from diethyl 2-(cyclohexylamino)vinyl phosphonate (**64**),[27] only a poor yield of (**61**) was obtained. However, on resorting to an organo-silicon based method, namely using the anion derived from the silylaldimine (**65**),[28] the desired α,β-unsaturated aldehyde (**61**) was obtained. Catalytic hydrogenation cleanly delivered the required aldehyde (**56**). This compound was rather unstable towards oxidation, so n.m.r. studies were more conveniently carried out on the derived acid (**57**). The ^{13}C n.m.r. spectrum of (**57**) showed only one set of peaks, thus suggesting the presence of only one isomer. Unfortunately, several attempts to prepare the '*cis*' isomer (**66**) *via* the thermodynamically favoured aldehyde (**67**) were plagued by the very low yield

(< 5%) in the reaction of (**8**) with the anion of methoxymethyldiphenylphosphine oxide. However, sufficient of the enol ethers (**71**) were obtained for a small scale acid hydrolysis, which showed the production of one aldehyde, presumably (**55**), which was epimerised to another aldehyde, presumed to be the thermodynamically favoured isomer (**67**), with base.

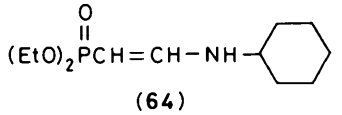
Conversion of the aldehyde (**56**) into the TXA_2 analogue (**12**) was then achieved using the method developed for converting (**48**) into (**10**), the yields being broadly similar.



(**55**) $n = 2$, X = CHO, R = Et
(**56**) $n = 2$, X = CH_2CHO, R = Et
(**57**) $n = 2$, X = CH_2CO_2H, R = Et
(**58**) $n = 1$, X = CHO, R = Me
(**59**) $n = 1$, X = CO_2H, R = Me
(**60**) $n = 1$, X = CH_2CHO, R = Me



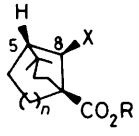
(**61**) $n = 2$, R = Et
(**62**) $n = 1$, R = Me
(**63**) $n = 1$, R = Et



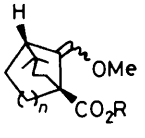
(**64**)

$Me_3SiCH_2CH{=}NBu^t$

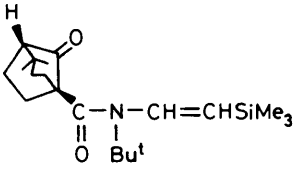
(**65**)



(**66**) $n = 2$, X = CH_2CO_2H, R = Et
(**67**) $n = 2$, X = CHO, R = Et
(**68**) $n = 1$, X = CHO, R = Me
(**69**) $n = 1$, X = CO_2H, R = Me
(**70**) $n = 1$, X = CH_2CHO, R = Me



(**71**) $n = 2$, R = Et
(**72**) $n = 1$, R = Me



(**73**)

Synthesis of TXA_2 *Analogue* (**13**).—It was expected that the methods used to prepare the analogue (**12**) from (**8**) could also be applied in this case, starting from the bicyclic oxo ester (**9**). However, these plans foundered at the first step, when the anion of the silylaldimine (**65**) gave only a small amount of the required α,β-unsaturated aldehyde (**62**) on reaction with (**9**). The major product appeared to be the amide (**73**). The anion from the vinyl phosphonate (**64**) did react with (**9**), but the yield of the required aldehyde was only 40%, and it had actually undergone transesterification to some extent to form a 1:2 mixture of (**62**) and (**63**).

In view of the fact that the bicyclo[3.3.1]nonane system (**8**) had reacted with the anion from methoxymethyldiphenylphosphine oxide only in very poor yield, it was a pleasant surprise to find that the same reaction carried out on the bicyclo[3.2.1]octane system (**9**) gave the enol ether (**72**), as a mixture of double bond isomers, in good yield, and this provided the basis for further development. Treatment of the enol ethers (**72**) with acid gave a single aldehyde which could be epimerised with sodium methoxide to a different aldehyde. It was thought that the initial aldehyde was (**58**) obtained by kinetic protonation of the enol ether from the least hindered side, and that this was converted into the thermodynamically more stable *anti* isomer (**68**) by base. The aldehydes (**58**) and (**68**) both underwent aerial oxidation in solution, to give the acids (**59**) and (**69**) respectively, and highfield n.m.r. studies on these latter compounds allowed confirmation of the stereochemistry. Of particular interest was the appearance of the signal for 8-H. In the spectrum of (**59**) it appeared as a double doublet with $J_{5,8} = 6$ Hz, whereas in the spectrum of (**69**) it was a singlet. Molecular models show that the dihedral angle between the protons on C-5 and C-8 in (**59**) and (**69**) are 45 and 90° respectively. Thus, the observed coupling constants are in good agreement with those predicted from the Karplus equation.

The two aldehydes (**58**) and (**68**) were now homologated to give the aldehydes (**60**) and (**70**). The latter two compounds were shown by ^1H n.m.r. to be different; thus (**58**) was not being epimerised to (**68**) under the conditions of the Wittig reaction.

Having satisfied the stereochemical requirements of the synthesis, the route from (**60**) to the TXA_2 analogue (**13**) proceeded without event.

The TXA_2 analogues (**10**), (**12**), and (**13**) have all been tested as TXA_2 antagonists, but none of them has shown any useful activity.

Experimental

Dry tetrahydrofuran (THF) was obtained by distillation from potassium. Dry diethyl ether was obtained by distillation from lithium aluminium hydride. Dry di-isopropylamine, and dichloromethane were obtained by distillation from calcium hydride. Short column chromatography was carried out using either Merck '7736' or '7734' silica gel. Light petroleum refers to the fraction boiling in the range 40—60 °C. N.m.r. data were obtained from Jeol–C60, Bruker WP80, Bruker WM250 and Varian EM390 instruments. Values are quoted in Hz. Spectra were recorded in $CDCl_3$ solution with $SiMe_4$ as an internal standard. I.r. spectra were obtained on a Pye Unicam SP200 spectrophotometer as liquid films unless otherwise stated. Mass spectral data were obtained from AEI MS9, AEI MS30 and Kratos MS25 instruments. They were run with electron impact (e.i.) and chemical ionization (c.i.). High resolution spectra (e.i.) usually had M^+ too weak for accurate measurement, so the ($M^+ - H_2O$) peak was measured. Low resolution (c.i.) spectra all showed a large ($M^+ + 1$) peak. All the compounds described are racemic.

Ethyl 2-Oxo-1-(3-oxobutyl)cyclohexanecarboxylate (**14**).—To a mixture of ethyl 2-oxocyclohexanecarboxylate (6.3 g, 37 mmol) and methyl vinyl ketone (10 cm^3, 120 mmol) was added triethylamine (5.6 cm^3, 39 mmol) with swirling and cooling. The reaction mixture was cooled in an ice-bath for 1 h and then allowed to stand at room temperature for 1 week. The unchanged methyl vinyl ketone and triethylamine were distilled off under reduced pressure, and the residue was dissolved in ether (40 cm^3). The ethereal extract was washed successively with 2M hydrochloric acid (20 cm^3), 2M aqueous sodium hydroxide (20 cm^3) and water (20 cm^3), and then dried ($MgSO_4$) and evaporated to give the product (**14**) (8.6 g, 97%), b.p. 70 °C at 0.4 mmHg; $\nu_{max.}$ 1 720, 1 710, 1 445, 1 365, 1 130, and 1 095 cm^{-1}; δ_H (90 MHz) 4.25 (2 H, q, J 7 Hz, CO_2CH_2), 2.7—1.4 (15 H, complex), and 1.2 (3 H, t, J 7 Hz, $CO_2CH_2CH_3$).

Ethyl 4-*Methyl*-9-*oxobicyclo*[3.3.1]*non*-3-*ene*-1-*carboxylate* (**7**).—Concentrated sulphuric acid (10 cm^3) was added dropwise, with stirring, to ethyl 2-oxo-1-(3-oxobutyl)cyclohexanecarboxylate (**14**) (10 g, 42 mmol) cooled in an ice-bath. The resulting solution was left at 0 °C for 1 h and then at room temperature for 45 min. The mixture was then poured into a slurry of ice and water and extracted with ether (3 × 25 cm^3). The combined ether extracts were washed successively with saturated aqueous sodium hydrogen carbonate (2 × 15 cm^3) and water (1 × 20 cm^3), dried ($MgSO_4$), and evaporated. The crude residue was purified by column chromatography using ether–hexane (1:9) to give the product (**7**) (5.5 g, 59.5%); $\nu_{max.}$ 1 730, 1 710, 1 450, 1 280, 1 255, and 1 230 cm^{-1} (lit.,[7] 1 730 and 1 720 cm [1]); δ_H (250 MHz) 5.65 (1 H, t, =CH), 4.23 (2 H, q, *J* 7 Hz, CO_2CH_2), 3.34 [br d, *endo*-2-H], 2.73 (br t, *endo*-8-H), 2.05—1.85 (4 H, complex), 1.69 (3 H, s, 2-Me), 1.65 (1 H, m, *exo*-7-H), and 1.3 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

Methyl 2-*Oxo*-1-(3-*oxobutyl*)*cyclopentanecarboxylate* (**16**).—A solution of methyl 2-oxocyclopentanecarboxylate (5 g, 35 mmol), methyl vinyl ketone (3 cm^3, 35.4 mmol), triethylamine (1.2 cm^3, 8.6 mmol), and dry benzene was allowed to stand at room temperature for 7 days. The volatile components were removed under reduced pressure and the residue was distilled under vacuum to give the product (**16**) (4.8 g, 65%), b.p. 124—126 °C at 0.5 mmHg (Found: C, 62.45; H, 7.8. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.60%); $\nu_{max.}$ 1 750, and 1 720 cm^{-1}; δ_H (60 MHz) 3.8 (3 H, s, CO_2CH_3), and 2.9—1.5 (13 H, complex).

Methyl 5-*Methyl*-7-*oxo*-6-*oxabicyclo*[3.2.2]*nonane*-1-*carboxylate* (**22**).—Concentrated sulphuric acid (1 cm^3) was added with swirling to methyl 2-oxo-1-(3-oxobutyl)cyclopentanecarboxylate (**16**) (0.5 g, 2.4 mmol) cooled in an ice-bath. The mixture was allowed to stand at room temperature overnight and was then poured onto ice and water (10 cm^3). The aqueous solution was neutralised with saturated aqueous sodium hydrogen carbonate, and the solid product was filtered off and washed with water. The solid was recrystallised from methanol–water to give the product (**22**) (0.3 g, 60%), m.p. 100—102 °C (Found: C, 62.45; H, 7.75. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.60%); $\nu_{max.}$(KBr) 1 740, and 1 720 cm^{-1}; δ_H (250 MHz) 3.8 (3 H, s, CO_2CH_3), 2.6 (1 H, m, 2-H), 2.2—1.7 (9 H, complex), and 1.42 (3 H, s, OCH_3); δ_C (62.85 MHz), 172.9 (ester carbonyl), 171.9 (C-7), 82.9 (C-5), 52.6 (CH_3 of ester), 51.9 (C-1), 38.0, 30.9, 30.0, 29.6 (5-Me), 24.7 and 20.6; *m/z* 212 (M^+).

Methyl 4-*Methyl*-8-*oxobicyclo*[3.3.1]*oct*-3-*ene*-1-*carboxylate* (**24**).—Concentrated sulphuric acid (4 cm^3) was added with swirling to methyl 2-oxo-1-(3-oxobutyl)cyclopentanecarboxylate (**16**), (4.6 g, 20 mmol) cooled in an ice-bath. The mixture was allowed to stand in the ice-bath for 30 min, and was then poured onto iced water (25 cm^3). The aqueous solution was extracted with ether (3 × 25 cm^3) and the combined ether extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 20 cm^3), dried ($MgSO_4$), and evaporated. Column chromatography with ethyl acetate–light petroleum (1:9) gave the product (**24**) (1.32 g, 31.5%) (Found: C, 67.85; H, 7.20. $C_{11}H_{14}O_3$ requires C, 68.00; H, 7.25%); $\nu_{max.}$ 1 755, 1 725, 1 440, 1 280, 1 235, 1 215, 1 080, and 1 020 cm^{-1}; δ_H (250 MHz) 5.3 (1 H, br s, =CH), 3.77 (3 H, s, CO_2CH_3), 3.2 (1 H, dq, *endo*-2-H), 2.8—2.6 (m, 2 H *exo*-2-H and *endo*-6-H), 2.45 (m, 1 H 5-H), 2.2—2.0 (complex, 3 H), and 1.73 (s, 3 H 4-Me).

Ethyl 2-*Oxo*-1-(3-*oxobutyl*)*cyclopentanecarboxylate* (**15**).—This was prepared as for (**16**) above. Distillation gave the product (**15**) (76%), b.p. 118—120 °C at 0.5 mmHg (lit.,[7] b.p. 140—142 °C at 2.4 mmHg); $\nu_{max.}$ 1 750, 1 720, 1 370, 1 260, 1 165, and 1 030 cm^{-1}; δ_H (90 MHz) 4.25 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.9—1.6 (13 H, complex), and 1.2 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

Ethyl 5-*Methyl*-7-*oxo*-6-*oxabicyclo*[3.2.2]*nonane*-1-*carboxylate* (**23**).—This was prepared from (**15**) as for (**22**) above (yield 73%), m.p. 57—58 °C (lit.,[7] m.p. 61—62 °C); $\nu_{max.}$(Nujol) 1 740, 1 715, 1 450, 1 200, and 1 050 cm^{-1}; δ_H (250 MHz) 4.25 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.6 (1 H, m, 2-H), 2.2—1.7 (9 H, complex), 1.4 (3 H, s, CH_3), and 1.3 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$); δ_C (62.85 MHz) 172.8 (ester carbonyl), 171.3 (lactone carbonyl), (C-5), 61.5 (CO_2CH_2), 51.8 (C-1) 38.05, 30.9, 30.0, 29.6 (5-Me), 24.6, 20.6, and 13.8 ($CO_2CH_2CH_3$).

Methyl 4-*Oxo*-3-(3-*oxobutyl*)*tetrahydrothiophene*-3-*carboxylate* (**25**).—This was prepared from (**27**) as for (**16**) above. The crude product was chromatographed with ethyl acetate–light petroleum (5:95) increasing to (20:80), to give methyl 2-ethylidene-5-oxohexanoate (12%); $\nu_{max.}$ 1 720, 1 635, 1 450, 1 200, 1 040, and 820 cm^{-1}; δ_H (80 MHz) 6.2 (1 H, s, HC^c=CCO$_2$Me) 5.6 (1 H, s, HC^t=CCO$_2$Me), 3.25 (3 H, s, CO_2CH_3) 2.6 (4 H, m, CH_2CH_2), 2.1 (3 H, s, $COCH_3$), and the product (**24**) (47%) (Found: C, 52.3; H, 6.15. $C_{10}H_{14}O_4S$ requires C, 52.15; H, 6,15%); $\nu_{max.}$ 1 730, 1 450, 1 390, and 1 050 cm^{-1}; δ_H (80 MHz) 3.75 (3 H, s, CO_2CH_3), 3.4 (2 H, d, *J* 5 Hz, SCH_2CO), and 3.0—2.0 (9 H, complex); *m/z* 230 (M^+).

Methyl 4-*Hydroxy*-4-*methyl*-8-*oxo*-6-*thiabicyclo*[3.2.1]-*octane*-1-*carboxylate* (**21**).—This was prepared from (**25**) as for (**7**) above. The crude product was chromatographed with ethyl acetate–light petroleum (1:4) to give the product (**21**) (40%), m.p. 85.5—88 °C (lit.,[12] m.p. 88—89 °C) (Found: C, 51.95; H, 6.1. $C_{10}H_{14}O_4$ requires C, 52.15; H, 6.15%); $\nu_{max.}$(KBr) 3 400, 1 760, 1 735, 1 305, 1 240, 1 135, and 905 cm^{-1}; δ_H (80 MHz) 3.9 (1 H, s, 5-H), 3.8 (3 H, s, CO_2CH_3), 3.6 (1 H, d, *J* 11 Hz, *endo*-7-H), 3.1 (1 H, s, OH), 2.7 (1 H, d, *J* 11 Hz, *exo*-7-H), 2.55—1.5 (3 H, complex), 1.4 (3 H, s, 4-CH_3), 1.25 (1 H, s, *exo*-3-H); *m/z* 230 (M^+), 213 (M^+ − OH), 199 (M^+ − OCH_3), and 171 (M^+ − CO_2CH_3).

Methyl 3-*Oxo*-2-(3-*oxobutyl*)*tetrahydrothiophene*-2-*carboxylate* (**26**).—This was prepared from (**28**) as for (**16**) above. The volatile components were removed on the rotary evaporator and a white solid crystallised to give the product (**26**) (79%), m.p. 52.5—54.5 °C (Found: C, 52.65; H, 6.35. $C_{10}H_{14}O_4$ requires C, 52.15; H, 6.15%); $\nu_{max.}$(KBr) 1 740, 1 730, 1 710, 1 245, 1 070, and 900 cm^{-1}; δ_H (80 MHz) 3.75 (3 H, s, CO_2CH_3), 3.4—2.2 (8 H, complex), 2.1 (3 H, s, $OCCH_3$); *m/z* 230 (M^+).

Ethyl 1-(3-*Methylbut*-2-*enyl*)-2-*oxocyclohexanecarboxylate* (**31**).—Sodium hydride (50% dispersion in oil; 0.28 g, 5.9 mmol) was placed in a three-necked flask under nitrogen and washed with hexane (× 3). Dimethylformamide (10 cm^3) was added, and to this suspension ethyl 2-oxocyclohexanecarboxylate (1 g, 5.9 mmol) was then added slowly by cannula over 15 min. The resulting pale yellow solution was stirred for a further 20 min before 1-bromo-3-methylbut-2-ene (1 cm^3, 8.9 mmol) was added. A white solid appeared after 1 h and the reaction was complete in 2 h. The mixture was partitioned between dilute hydrochloric acid (50 cm^3) and ether (20 cm^3). The aqueous layer was extracted with ether (2 × 25 cm^3) and the combined ether extracts were washed with water (2 × 25 cm^3), dried ($MgSO_4$), and evaporated to give a yellow oil, which when subjected to bulb-to-bulb distillation gave the pure product (**31**) (1.3 g, 93%), b.p. 104—106 °C at 0.5 mmHg (Found: C, 70.15; H, 9.85. $C_{14}H_{22}O_3$ requires C, 70.55; H, 9.30%); $\nu_{max.}$ 1 735, and 1 712 cm [1]; δ_H (250 MHz) 5.08 (1 H, t, *J* 4.5 Hz, CH=), 4.17 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.63—2.24 (5 H, complex), 2.1—1.36 (11 H, complex), and 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

Methyl 1-(3-*Methylbut-2-enyl*)-2-*oxocyclopentanecarboxylate* (**32**).—This was prepared from methyl 2-oxocyclopentanecarboxylate as for (**31**) above; yield 95% (Found: C, 68.7; H, 8.6. $C_{12}H_{18}O_3$ requires C, 68.54; H, 8.63%); $\nu_{max.}$ 1 755, 1 730, 1 460, 1 445, and 1 415 cm^{-1}; δ_H (80 MHz) 5.05 (1 H, t, *J* 5 Hz, C*H*=CMe$_2$), 3.7 (3 H, s, CO_2CH_3), 2.75—1.75 (8 H, complex), 1.7 (3 H, s, =CCH_3), and 1.6 (3 H, s, =CCH_3).

Ethyl 1-(3-*Chloro*-3-*methylbutyl*)-2-*oxocyclohexanecarboxylate* (**33**).—A stream of hydrogen chloride was bubbled through a stirred solution of ethyl 1(3-methylbut-2-enyl)-2-oxocyclohexanecarboxylate (**31**) (2 g, 8.4 mmol) in anhydrous ether (10 cm^3) for 2 min at −78 °C. The mixture was then slowly warmed to room temperature, whilst being gently aspirated with nitrogen. Residual hydrochloric acid was removed by stirring an ethereal solution of the product with sodium hydrogen carbonate until the ether layer was neutral. The sodium hydrogen carbonate was filtered off, and the ether evaporated to give the product (**33**) (2.2 g, 95%) which was not further purified; $\nu_{max.}$ 1 735sh, 1 710, 1 450, 1 370, and 1 020 cm^{-1}; δ_H (250 MHz) 3.23 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.6—2.4 (2 H, m, CH_2CO) 2.1—1.4 (10 H, complex), 1.58 [3 H, s, $(CH_3)_2C$], and 1.28 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

Ethyl 1-(3-*Chloro*-3-*methylbutyl*)-2-*trimethylsilyloxycyclohex*-2-*enecarboxylate* (**34**).—Ethyl 1-(3-chloro-3-methylbutyl)-2-oxocyclohexanecarboxylate (**33**) (1 g, 3.64 mmol) and ethyl trimethylsilylacetate (0.7 cm^3, 3.8 mmol) were added to a solution of tetrabutylammonium fluoride (1M in THF; 0.2 cm^3, 20 mmol) under nitrogen at 0 °C. A reaction took place immediately, accompanied by slight evolution of heat, and the colour changed to brown. The resulting mixture was stirred for a further 2 h and then diluted with hexane, filtered, and concentrated. The crude product was subjected to bulb-to-bulb distillation to yield pure product (**34**) (950 mg, 76%), b.p. 220 °C (bath temp.) at 0.5 mmHg; $\nu_{max.}$ 1 725, 1 660, 1 250, 930, and 845 cm^{-1}; δ_H (250 MHz) 4.85 (1 H, t, *J* 4 Hz, CH=), 4.15 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.1—1.6 (10 H, complex), 1.55 [6 H, s $(CH_3)_2C$], 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), and 0.2 [9 H, s, $Si(CH_3)_3$].

Ethyl 4-*Methylbicyclo*[4.4.0]*deca*-4,6-*dienecarboxylate* (**36**). —(*a*) *Using trimethylsilyl trifluoromethanesulphonate.* To a stirred solution of ethyl 1-(3-methylbut-2-enyl)-2-oxocyclohexanecarboxylate (**31**) (100 mg, 0.42 mmol) in dichloromethane (10 cm^3) under nitrogen, at 0 °C, was added trimethylsilyltrifluoromethanesulphonate (2 drops). The mixture was slowly allowed to reach room temperature. After 3 h water (10 cm^3) was added and the layers separated. The aqueous layer was extracted with ether (2 × 10 cm^3) and the combined organic extracts were dried ($MgSO_4$) and evaporated. The crude product was chromatographed with ethyl acetate–hexane (5:95) to give the product (**36**) (60 mg, 64%) (Found: M^+, *m/z* 220.1458. $C_{14}H_{20}O_2$ requires *M*, 220.1464); $\lambda_{max.}$(EtOH) 231 (18 000 dm^3 mol^{-1} cm^{-1}), 239 (18 000), and 247sh nm (12 400); $\nu_{max.}$ 1 720, 1 445, 1 230, 1 195, 1 150, 1 090, and 1 025 cm^{-1}; δ_H (250 MHz) 5.85 (1 H, s, CH=, 5-H), 5.55 (1 H, br s, 7-H), 4.15 (2 H, t, *J* 7 Hz, CO_2CH_2), 2.3—1.85 (6 H, complex), 1.7 (3 H, s, MeC=), 1.65—1.25 (4 H, complex), and 1.2 (3 H, t, $CO_2CH_2CH_3$); δ_C (62.86 MHz) 175.6 (s, CO_2Me), 135.3 (s, C-6), 134.2 (s, C-4), 124.8 (d, C-7), 123.6 (d, C-5), 60.45 (t, CO_2CH_2), 46.02 (s, C-1), 34.5 (t, C-10), 34.0 (t, C-2), 28.5 (t, C-3), 25.4 (t, C-8), 23.4 (q, 4-CH_3), 19.5 (t, C-9), and 14.3 (q, $CO_2CH_2CH_3$).

(*b*) *Using stannic chloride.* Ethyl 1-(3-methylbut-2-enyl)-2-oxocyclohexanecarboxylate (**31**) (0.1 g, 0.42 mmol) was added to a solution of stannic chloride (0.02 cm^3, 0.17 mmol) in dichloromethane (25 cm^3) cooled in an ice-bath. The reaction mixture was allowed to reach room temperature, when water (2 drops) was added and the whole stirred for 16 h. Further water (25 cm^3) was added and the aqueous layer was extracted with ether (2 × 15 cm^3) and the combined extracts were dried ($MgSO_4$) and evaporated. The crude product was chromatographed with ethyl acetate–hexane (5:95) to give the product (**36**) (63 mg, 68%).

(*c*) *Using trifluoromethanesulphonic acid.* To a stirred solution of ethyl 1-(3-methylbut-2-enyl)-2-oxocyclohexanecarboxylate (**31**) (0.1 g, 0.42 mmol) in dichloromethane (10 cm^3) under nitrogen, at 0 °C, was added trifluoromethanesulphonic acid (0.035 cm^3, 0.4 mmol). The mixture was slowly allowed to reach room temperature and then stirred for 3 h. T.l.c. indicated that (**36**) was the major product.

Ethyl 4-*Methylbicyclo*[4.4.0]*deca*-4,6-*dienecarboxylate* (**36**) *from Ethyl* 1-(3-*Methylbut*-2-*enyl*)-2-*trimethylsilyloxycyclohex*-2-*enecarboxylate* (**41**).—To a stirred solution of (**41**) (0.1 g, 0.32 mmol) in dichloromethane (10 cm^3) under nitrogen, at 0 °C, was added trifluoromethanesulphonic acid (0.035 cm^3, 0.4 mmol). The mixture was slowly allowed to reach room temperature and then stirred for 3 h. The crude product was chromatographed with ethyl acetate–hexane (10:90) to give the product (**36**) (45 mg, 64%).

Methyl 4-*Methylbicyclo*[4.3.0]*nona*-4,6-*dienecarboxylate* (**37**).—This was prepared from methyl 1-(3-methylbut-2-enyl)-2-oxocyclopentanecarboxylate (**32**) and trimethylsilyl trifluoromethanesulphonate, as for (**36**) above; yield 65% (Found: M^+, *m/z* 192.1156. $C_{12}H_{16}O_2$ requires M^+, 192.1150); $\nu_{max.}$ 1 725, 1 450, 1 440, 1 260, and 1 190 cm^{-1}; δ_H (80 MHz) 6.05 (1 H, s, 5-H), 5.5 (1 H, br s, 7-H), 3.7 (3 H, s, CO_2CH_3), 2.7—1.3 (8 H, complex), and 1.7 (3 H, s, 4-CH_3).

Ethyl 2-*Acetoxy*-1-(3-*methylbut*-2-*enyl*)*cyclohex*-2-*enecarboxylate* (**38**).—Ethyl 1-(3-methylbut-2-enyl)-2-oxocyclohexanecarboxylate (**31**) (1 g, 4.2 mmol) was heated with isopropenyl acetate (15 cm^3) and toluene-*p*-sulphonic acid monohydrate (100 mg) for 24 h with slow removal of the generated acetone. The mixture was cooled and diluted with hexane (30 cm^3), and the organic layer was washed with aqueous sodium hydrogen carbonate (15 cm^3), dried ($MgSO_4$), and evaporated. The crude product was chromatographed with ethyl acetate–hexane (5:95) to give the product (**38**) (0.8 g, 75.4%, based on recovered starting material of 0.1 g) (Found: C, 68.6; H, 8.7. $C_{16}H_{24}O_4$ requires C, 68.55; H, 8.65%); $\nu_{max.}$ 1 763, 1 728, and 1 670 cm^{-1}; δ_H (90 MHz), 5.57 (1 H, t, *J* 3.5 Hz, AcOC=C*H*), 5.1 (1 H, t, *J* 5 Hz, C*H*=CMe$_2$), 4.1 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.45 (2 H, d, *J* 7 Hz, CH_2CH=CMe$_2$), 2.15 (3 H, s, $OCOCH_3$), 1.65 (6 H, 2 s, CH_3), 2.15—1.65 (6 H, complex), and 1.2 (3 H, t, *J* 7 Hz).

Methyl 2-*Acetoxy*-1-(3-*methylbut*-2-*enyl*)*cyclopent*-2-*enecarboxylate* (**39**).—Methyl 1-(3-methylbut-2-enyl)-2-oxocyclopentanecarboxylate (**32**) (8.4 g, 40 mmol) was heated with isopropenyl acetate (70 cm^3) and toluene-*p*-sulphonic acid (3 g) for 7 d, with slow removal of the generated acetone by distillation. In order to ensure complete reaction, it was necessary to distil away some of the isopropenyl acetate (35 cm^3) with the acetone. The mixture was cooled and diluted with ether (40 cm^3) and water (25 cm^3). The aqueous layer was extracted with ether (3 × 20 cm^3) and the combined ether extracts were washed with aqueous sodium hydrogen carbonate (2 × 20 cm^3) dried ($MgSO_4$), and evaporated. The crude product was chromatographed with ethyl acetate–light petroleum (1:9) to give the rather unstable product (**39**) (9 g, 89%); $\nu_{max.}$ 1 775, 1 745, 1 670, 1 450, and 1 390 cm^{-1}; δ_H (80 MHz) 5.75 (1 H, t, *J* 3.5 Hz, AcOC=C*H*), 5.05 (1 H, t, *J* 5 Hz, C*H*=CMe$_2$), 3.75 (3 H, s, CO_2CH_3), 2.8—1.8 (6 H, complex), 1.7 (3 H, s, =CCH_3), and 1.6 (3 H, s, =CCH_3).

Ethyl 4,4-*Dimethyl*-9-*oxobicyclo*[3.3.1]*nonanecarboxylate* (**8**).—Ethyl 2-acetoxy-1-(3-methylbut-2-enyl)cyclohex-2-enecarboxylate (**38**) (227 mg, 0.81 mmol) was added to a solution of stannic chloride (0.15 cm^3, 1.3 mmol) in dichloromethane (50 cm^3) cooled in an ice-bath. The reaction mixture was allowed to reach room temperature and was stirred for 3 h after the addition of water (2 drops). Further water (25 cm^3) was added to the reaction mixture and the aqueous layer was extracted with ether (2 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated and the crude product was chromatographed with ethyl acetate–hexane (5:95) to give the product (**8**) (188 mg, 98%) (Found: M^+, *m/z* 238.1596. $C_{14}H_{22}O_3$ requires *M*, 238.1569); $\nu_{max.}$ 1 730, 1 710, 1 460, 1 370, 1 160, and 1 060 cm^{-1}; δ_H (80 MHz) 4.2 (2 H, q, *J* 7 Hz, CO_2CH_2), 3.0—1.45 (11 H, complex), 1.3 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.05 (3 H, s, CH_3), and 0.95 (3 H, s, CH_3).

Methyl 4,4-*Dimethyl*-8-*oxobicyclo*[3.2.1]*octanecarboxylate* (**9**).—This was prepared from methyl 2-acetoxy-1-(3-methylbut-2-enyl)cyclopentanecarboxylate (**39**) as for (**8**) above; yield 88%, m.p. 63.5—65.0 °C (Found: C, 68.2; H, 8.7. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.60%); $\nu_{max.}$(KBr) 1 750, 1 720, 1 470, 1 445, 1 280, 1 135, and 1 075 cm^{-1}; δ_H (80 MHz) 3.75 (3 H, s, CO_2CH_3), 2.6—1.1 (9 H, complex), 1.0 [6 H, s, $=C(CH_3)_2$]; δ_H (80 MHz, C_6D_6) 3.5 (3 H, s, CO_2CH_3), 2.7—1.9 (2 H, m), 1.8—0.9 (7 H, complex), 0.85 (3 H, s, $=CCH_3$), and 0.55 (3 H, s, $=CCH_3$).

Ethyl 1-(3-*Methylbut*-2-*enyl*)-2-*trimethylsilyloxycyclohexanecarboxylate* (**41**).—Chlorotrimethylsilane (0.8 cm^3, 6.3 mmol) was added to a stirred mixture of ethyl 1-(3-methylbut-2-enyl)-2-oxocyclohexanecarboxylate (**23**) (1 g, 4.2 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.95 cm^3, 6.4 mmol) in dichloromethane (5 cm^3) at 40 °C. The mixture was heated at reflux, under nitrogen, for 5 h. The resulting mixture was diluted with hexane (15 cm^3), washed with water (10 cm^3), and saturated aqueous sodium hydrogen carbonate (5 cm^3), dried ($MgSO_4$), and evaporated. The crude product was subjected to bulb-to-bulb distillation to afford pure product (**41**) (1.15 g, 88%); $\nu_{max.}$ 1 730, 1 665, 1 620, 1 445, 1 250, 845, and 755 cm^{-1}; δ_H (60 MHz) 4.85 (1 H, t, *J* 7 Hz, CH=CO), 4.55 (1 H, t, *J* 4 Hz, $CH{=}CMe_2$), 3.88 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.15 (2 H, d, *J* 7 Hz, $CH_2CH{=}$), 1.75 (2 H, m, $CH_2CH{=}CMe_2$), 1.5 [6 H, 2 s, $=C(CH_3)_2$], 1.6—1.2 (4 H, complex), 1.3 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), and 0.2 [9 H, s, $Si(CH_3)_3$].

Investigation of the Reaction of Palladium(II) *Acetate with Ethyl* 1-(3-*Methylbut*-2-*enyl*)-2-*trimethylsilyloxyhex*-2-*enecarboxylate* (**41**).—A solution of ethyl 1-(3-methylbut-2-enyl)-2-trimethylsilyloxyhex-3-enecarboxylate (**41**) (0.092 g, 0.3 mmol) in anhydrous dichloromethane (3 cm^3) and acetonitrile (3 cm^3) was added dropwise by cannula to a solution of palladium(II) acetate (0.067 g, 0.3 mmol) in anhydrous acetonitrile (3 cm^3). The resulting solution was stirred overnight at room temperature. Two products were isolated by column chromatography. They were identified as the desilylated starting material (**31**) and the α,β-unsaturated ketone, ethyl 1-(3-methylbut-2-enyl)-2-oxocyclohex-3-enecarboxylate (**44**); $\nu_{max.}$ 1 730, 1 690, 1 630, 1 450, and 1 395 cm^{-1}; δ_H (80 MHz) 6.9 (1 H, m, $CH{=}CHCO$), 6.05 (1 H, d, *J* 8 Hz, $=CHCO$), 5.1 (1 H, t, *J* 4 Hz), 4.15 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.8—1.8 (6 H, complex), 1.75 (3 H, s, $=CCH_3$), 1.7 (3 H, s, $=CCH_3$), and 1.2 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

Ethyl 9-*Formyl*-4-*methylbicyclo*[3.3.1]*non*-3-*enecarboxylate* (**46**) *and* (**47**).—Methoxymethyldiphenylphosphine oxide (0.296 g, 1.05 mmol) in dry THF (6 cm^3) was added by cannula to a solution of lithium di-isopropylamide [from di-isopropylamine (0.14 cm^3, 1 mmol) and butyl-lithium (1.44M in hexane; 0.7 cm^3, 1. mmol)] in THF (6 cm^3) and the mixture was stirred at 0 °C for 10 min. The deep red mixture was cooled to −78 °C and ethyl 4-methyl-9-oxobicyclo[3.3.1]non-3-enecarboxylate (**7**) (0.219 g, 0.88 mmol) in dry THF (0.5 cm^3) was added dropwise by cannula. The solution was allowed to warm to room temperature and then stirred for 30 min. Saturated aqueous ammonium chloride solution (10 cm^3) and ether (10 cm^3) were then added. The aqueous layer was extracted with ether (3 × 10 cm^3), and the combined organic layers were dried ($MgSO_4$) and evaporated to give a yellow oil which was dissolved in dry THF (12 cm^3) and stirred with sodium hydride (60% dispersion in oil; 0.06 g, 2.5 mmol) for 2 h. The mixture was filtered through Hyflo to remove the gelatinous precipitate of sodium diphenylphosphinite. The residue was washed with ether (30 cm^3) and the combined organic fractions were evaporated. The crude product was chromatographed with ethyl acetate–light petroleum (1:4) to give a geometric mixture of two enol ether (**45**); $\nu_{max.}$ 1 725, 1 670, 1 660, 1 460, 1 450, 1 160, and 1 120 cm^{-1}.

The enol ethers (**45**) were dissolved in ethanol (5 cm^3) with dilute hydrochloric acid (3 drops) and stirred for 7 h. The ethanol was then evaporated under reduced pressure, and ether (10 cm^3) and water (5 cm^3) were added. The layers were separated and the aqueous layer extracted with ether (2 × 10 cm^3). The combined ether extracts were dried ($MgSO_4$) and evaporated to give a mixture of aldehydes (**46**) and (**47**) (0.213 g, 91%). The ^1H n.m.r. spectra indicated the presence of two epimeric aldehydes (**46**) and (**47**) in the ratio of 2:1.

Ethyl syn-9-*Formyl*-4-*methylbicyclo*[3.3.1]*non*-3-*enecarboxylate* (**46**).—The mixture of the two epimeric aldehydes (**46**) and (**47**) (83 mg, 0.35 mol) was dissolved in ethanol (5 cm^3) and a very small amount of sodium was added. The resulting solution was left at room temperature for 14 h. Dilute hydrochloric acid was then added until the solution was neutral. Ethanol was removed on the rotary evaporator and ether (10 cm^3) and water (10 cm^3) were added; the layers were separated and the aqueous layer extracted with ether (2 × 10 cm^3). The combined ether extracts were dried ($MgSO_4$) and evaporated, to afford the product (**46**) (79 mg, 96%) (Found: C, 71.05; H, 8.65. $C_{14}H_{20}O_3$ requires C, 71.15; H, 8.5%); $\nu_{max.}$ 1 700, 1 450, 1 300, 1 270, 1 145, 1 125, 1 040, and 940 cm^{-1}; δ_H (200 MHz) 9.7 (1 H, s, CHO), 5.57 (1 H, brs, =CH), 4.25 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.64—1.4 (9 H, complex), and 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

Ethyl syn-9-*Formylmethyl*-4-*methylbicyclo*[3.3.1]*non*-3-*enecarboxylate* (**48**).—To a stirred solution of di-isopropylamine (0.38 cm^3, 2.7 mmol) in THF (8 cm^3), maintained at 0 °C, was added butyl-lithium (1.44M in hexane; 1.88 cm^3, 1.7 mmol). The solution was stirred for 20 min at this temperature after which toluene (6 cm^3) was added followed by methoxymethyltriphenylphosphonium chloride (0.93 g, 2.7 mmol). The bright red solution was stirred at 0 °C for 15 min before the aldehyde (**46**) (0.303 g, 1.28 mmol) in toluene (1 cm^3) was added dropwise at the same temperature. After 45 min, t.l.c. indicated that the reaction was complete, and the mixture was quenched with ice–water (25 cm^3) and ether (70 cm^3). The organic layer was separated and the aqueous phase re-extracted with ether (2 × 25 cm^3). The combined organic layers were dried ($MgSO_4$) and evaporated to afford an oily residue which was chromatographed with ethyl acetate–light petroleum (1:3) to give the mixture of enol ethers; $\nu_{max.}$ 1 725, 1 675, 1 660, 1 460, 1 450, 1 060, and 1 020 cm^{-1}; δ_H (60 MHz) 5.5 (3 H, m, $CH{=}$), 4.0 (2 H, q, *J* 7 Hz, CO_2CH_2), 3.5 (2.5 H, s, OCH_3), 3.3 (0.5 H, s, OCH_3), 2.5—1.0 (9 H, m), 1.7 (3 H, s, $=CCH_3$), and 1.2 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

The enol ethers were dissolved in THF (13.6 cm^3) and water (1.5 cm^3), stirred under argon, and treated with mercuric acetate (0.721 g, 2.3 mmol). After 1 h at room temperature, the yellow

mixture was poured into 7% aqueous potassium iodide solution (100 cm^3) and extracted with benzene (2 × 75 cm^3). The combined organic layers were washed with 7% aqueous potassium iodide (2 × 50 cm^3), dried ($MgSO_4$), and evaporated, and the crude product chromatographed with ethyl acetate–light petroleum (40:60) to give the product (**48**) [0.24 g, 75% from (**45**)] (Found: C, 71.75; H, 8.8. $C_{15}H_{22}O_3$ requires C, 71.95; H, 8.85%); $\nu_{max.}$ 2 705, 1 725, 1 495, 1 450, 1 260, 1 130, 1 115, 1 090, and 1 005 cm^{-1}; δ_H (200 MHz) 9.42 (1 H, s, CHO), 5.55 (1 H, s, =CH), 4.25 (2 H, q, *J* 7 Hz, $CO_2CH_2CH_3$), 2.9—2.55 (2 H, m, CH_2CHO), 2.2—1.4 (9 H, complex), 1.7 (3 H, s, $=CCH_3$), and 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$).

The dinitrophenylhydrazone of the aldehyde (**48**) was prepared, m.p. 156—158 °C and submitted to *X*-ray analysis.

(Z)-7-[5-(*Ethoxycarbonyl*)-2-*methylbicyclo*[3.3.1]*non*-2-*en*-syn-9-*yl*]*hept*-5-*enoic Acid* (**50**).—Potassium t-butoxide (2.46 g, 22 mmol) and (4-carboxybutyl)triphenylphosphonium bromide (4.86 g, 11 mmol) were quickly ground together and then placed in a dry two-necked flask under nitrogen. THF (125 cm^3) was distilled onto the solids to give a bright orange solution which was stirred for 30 min. A solution of the aldehyde (**48**) (1 g, 4 mmol) in dry THF (15 cm^3) was added in a single portion with stirring and the resulting solution was stirred for 1 h. Saturated aqueous ammonium chloride (50 cm^3) was added, followed by dilute hydrochloric acid until the mixture was acidic, and then ether (25 cm^3) was added. The layers separated and the aqueous layer was extracted with ether (3 × 25 cm^3). The combined ether extracts were dried ($MgSO_4$) and evaporated to yield a viscous oil, which was chromatographed with ethyl acetate–light petroleum (40:60) to give the product (**50**) (1.6 g, 87%) (Found: C, 69.25; H, 8.7. $C_{20}H_{30}O_4$ requires C, 69.75; H, 8.75%); $\nu_{max.}$ 2 700—2 500br, 1 740—1 710, 1 445, 1 255, 1 070, 1 040, and 870 cm^{-1}; δ_H (200 MHz), 5.55 (br, s, C*H*=CMe), 5.35 (2 H, m, CH=CH), 4.15 (2 H, q, *J* 7 Hz, CO_2CH_2), 2.6 (1 H, m), 2.34 (2 H, t, *J* 7 Hz, CH_2CO_2H), 1.35—2.2 (18 H, complex), and 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$); *m/z* 334 (M^+), 319 ($M^+ - CH_3$).

Methyl(Z)-7-[5-(*Hydroxymethyl*)-2-*methylbicyclo*[3.3.1]*non*-2-*en*-syn-9-*yl*]*hept*-5-*enoate* (**53**).—The acid ester (**50**) (0.191 g, 0.57 mmol) and toluene (5 cm^3) were placed in a flame-dried, three-necked flask fitted with a nitrogen inlet, and cooled to −78 °C. Di-isobutylaluminium hydride (25% w/w in toluene; 1.1 cm^3, 1.7 mmol), was slowly added over 5 min. When t.l.c. indicated that the reaction was complete, water (5 cm^3) was added and the reaction mixture allowed to reach room temperature. Dilute hydrochloric acid (15 cm^3) and ether (10 cm^3) were added and the layers separated; the aqueous layer was then extracted with ether (3 × 10 cm^3). An ethereal solution of diazomethane was added to the combined organic extracts, which were then dried ($MgSO_4$) and evaporated. The crude product was chromatographed with ethyl acetate–light petroleum (3:7) to give the product (**53**) (0.15 g, 87%) (Found: C, 74.65; H, 9.95; O, 15.7. $C_{19}H_{30}O_3$ requires C, 74.45; H, 9.85; O, 15.66%); $\nu_{max.}$ 3 450br, 1 740, 1 445, 1 380, 1 025, and 1 050 cm^{-1}; δ_H (80 MHz) 5.5 (3 H, complex, C*H*=), 3.7 (3 H, s, CO_2CH_3), 3.5 (1 H, d, *J* 11 Hz, CH_2OH), 3.2 (1 H, d, *J* 11 Hz, CH_2OH), 2.5—1.2 (21 H, complex), and 2.1 (1 H, s, OH); *m/z* 306 (M^+) and 275 (M^+ − OMe).

Methyl (Z)-7-(5-*Formyl*-2-*methylbicyclo*[3.3.1]*non*-2-*en*-syn-9-*yl*)*hept*-5-*enoate* (**54**).—Pyridinium chlorochromate (0.2 g, 0.93 mmol) was suspended in anhydrous dichloromethane (2 cm^3) and the alcohol (**52**) (0.2182 g, 0.71 mmol) in dichloromethane (1 cm^3) was then added in one portion to the magnetically stirred suspension. After 4 h, dry diethyl ether (10 cm^3) was added and the supernatant liquid was decanted from the black gum. The insoluble residue was washed with dry diethyl ether (3 × 5 cm^3) and the combined ether solutions were passed through a short silica gel column. The solvent was removed to give the product (**54**) (0.199 g, 92%); $\nu_{max.}$ 2 875, 1 740, 1 720, 1 445, and 1 240 cm^{-1}; δ_H (80 MHz), 9.4 (1 H, s, CHO), 5.55 (1 H, br s, C*H*=CMe), 5.35 (2 H, m, CH=CH), 3.65 (3 H, s, CO_2CH_3), and 2.6—1.2 (21 H, complex).

Methyl (Z)-7-[(E)-5-(3-*oxo*-*oct*-1-*enyl*)-2-*methylbicyclo*-[3.3.1]*non*-2-*en*-syn-9-*yl*]*hept*-5-*enoate* (**11**).—To a suspension of sodium hydride (80% dispersion in oil; 0.0285 g, 0.72 mmol) in THF (2 cm^3), under nitrogen, was added dimethyl 2-oxoheptylphosphonate (0.152 g, 0.686 mmol) in THF (1 cm^3) by cannula. A yellow solution was formed initially. After 5 min a white precipitate was deposited and after 10 min the reaction mixture had completely solidified. After 30 min the aldehyde (**54**) (0.1986 g, 0.65 mmol) in THF (3 cm^3) was added by cannula. The resulting solution was stirred at room temperature for 48 h. Saturated aqueous ammonium chloride (10 cm^3) and ether (10 cm^3) were added, and the layers were separated. The aqueous layer was extracted with ether (2 × 10 cm^3) and the combined ether extracts were dried ($MgSO_4$) and evaporated.

The crude product was chromatographed with ethyl acetate–light petroleum (1:4) to give the product (**11**) (0.225 g, 87%) (Found: C, 77.95; H, 10.05. $C_{26}H_{40}O_3$ requires C, 77.95; H, 10.05%); $\nu_{max.}$ 1 740, 1 675, 1 625, and 1 380 cm^{-1}; δ_H (200 MHz) 6.75 (1 H, d, *J* 15.5 Hz, OCCH=), 6.1 (1 H, d, *J* 15.5 Hz, CH=CHCO), 5.57 (1 H, br s, C*H*=CMe), 5.35 (2 H, m, CH=CH), 3.67 (3 H, s, CO_2CH_3), 2.55 (2 H, t, *J* 7 Hz, CH_2CO), 2.4—1.15 (27 H, complex), and 0.9 (3 H, m, CH_3); *m/z* 400 (M^+).

Methyl (Z)-7-[5-(3-*Hydroxyoct*-1-*enyl*)-2-*methylbicyclo*-[3.3.1]*non*-2-*en*-syn-9-*yl*]*hept*-5-*enoate* (**10**).—The enone (**11**) (0.0537 g, 0.134 mmol) was dissolved in methanol (2 cm^3) and the solution cooled to 0 °C. Sodium borohydride (20 mg, 0.53 mmol) was then added and the reaction was carefully monitored by t.l.c. When the reaction was complete, water (2 cm^3) was added and the methanol was removed under reduced pressure. Ether (3 cm^3) was added to the residue and the layers were separated. The aqueous layer was extracted with ether (2 × 5 cm^3), and the combined ethereal extracts were dried ($MgSO_4$) and evaporated. The crude product was chromatographed with ethyl acetate–light petroleum to give the product (**10**) (0.0515 g, 96%) (Found: M^+, *m/z* 402.3130. $C_{26}H_{42}O_3$ requires *M*, 402.3134); $\nu_{max.}$ 3 450br, 1 745, 1 450, 1 160, and 980 cm^{-1}; δ_H (80 MHz) 5.5 (3 H, complex, CH=C), 4.1 (1 H, m, C*H*–OH), 3.65 (3 H, s, CO_2CH_3), 2.4—1.0 (32 H, complex), and 0.9 (3 H, t, CH_2CH_3).

Ethyl 4,4-*Dimethyl*-(Z)-9-(2-*oxoethylidene*)*bicyclo*[3.3.1]-*nonanecarboxylate* (**61**).—To a stirred solution of di-isopropylamine (3.8 cm^3, 27 mmol) in THF (50 cm^3) at 0 °C was added butyl-lithium (1.53M in hexane; 17.75 cm^3, 27 mmol) and the solution was stirred for 30 min before *N*-butyl-2-(trimethylsilyl)acetaldehyde imine (**28**) (4.46 g, 26 mmol) was added. The deep red reaction mixture was stirred for 15 min, cooled to −78 °C, and treated with ethyl 4,4-dimethyl-9-oxobicyclo-[3.3.1]nonanecarboxylate (**8**) (2.5 g, 10.5 mmol). The resulting mixture was warmed to *ca.* −20 °C over 3 h and then quenched with water (20 cm^3). Solid oxalic acid was added to bring the pH to 4.5 and the mixture was stirred for 30 min. The reaction mixture was poured onto brine (40 cm^3) and extracted with ether (3 × 40 cm^3). The combined organic extracts were washed with saturated aqueous sodium hydrogencarbonate, dried ($MgSO_4$), and evaporated. The crude product was chromatographed with ethyl acetate–light petroleum (15:85) to give the product (**61**) (1.9 g, 69%); $\nu_{max.}$ 1 730, 1 685, 1 625, 1 400, 1 375, 1 240, 1 160, and 850 cm^{-1}; δ_H (80 MHz) 9.5 (1 H, d, *J* 9

Hz, CHO), 5.8 (1 H, d, *J* 9 Hz, CH=), 4.1 (2 H, q, *J* 7 Hz, $CO_2CH_2CH_3$), 2.6—1.4 (11 H, complex), 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.0 (3 H, s, CCH_3), and 0.9 (3 H, s, CCH_3).

Ethyl syn-9-(*Formylmethyl*)-4,4-*dimethylbicyclo*[3.3.1]-*nonanecarboxylate* (**56**).—The α,β-unsaturated aldehyde (**61**) (141.8 mg, 0.56 mmol) was dissolved in ethyl acetate (5 cm^3) and light petroleum (5 cm^3), and 10% palladium on carbon catalyst (100 mg) was then added. The reaction mixture was then subjected to standard hydrogenation conditions. Hydrogen (12.5 cm^3) was taken up within 1 h and t.l.c. indicated that the reaction had gone to completion. The mixture was filtered through Hyflo and the filtrate then evaporated, to give the product (**56**) (139 mg, 98%); $\nu_{max.}$ 2 720, 1 725, 1 400, 1 375, 1 260, 1 160, 1 060, and 1 050 cm^{-1}; δ_H (80 MHz) 9.65 (1 H, t, *J* 2.5 Hz, CHO), 4.1 (3 H, m, $CO_2CH_2CH_3$), 2.6 (2 H, m, CH_2CHO), 2.2—1.3 (11 H, complex), 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.05 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3).

The aldehyde (**56**) rapidly oxidised in deuteriochloroform solution to 2-(5-carboxymethyl-2,2-dimethylbicyclo[3.3.1]-nonan-*syn*-9-ylethanoic acid (**57**), m.p. 116—118 °C (Found: C, 68.15; H, 9.35. $C_{16}H_{26}O_4$ requires C, 68.05; H, 9.3%); $\nu_{max.}$(KBr) 3 450br, 1 720, 1 705, 1 395, 1 370, 1 340, 1 220, and 1 160 cm^{-1}; δ_H (400 MHz) 4.1 (3 H, m, $CO_2CH_2CH_3$), 2.5 (3 H, m, CH_2CO_2H and 1-H), 2.1—1.3 (11 H, complex), 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.05 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3).

(Z)-7-[-5-*Ethoxycarbonyl*-2,7-*dimethylbicyclo*[3.3.1]*nonan*-syn-9-*yl*]*hept*-5-*enoic Acid*.—This was prepared from (**56**) as for (**50**) above; yield 74% (Found: C, 70.8; H, 9.9. $C_{21}H_{24}O_4$ requires C, 70.97; H, 10.12%); $\nu_{max.}$ 3 300br, 1 720, 1 440, 1 380, 1 240, 1 160, and 1 045 cm^{-1}; δ_H (400 MHz) 9.3—8.5 (br s, OH), 5.4 (2 H, m, CH=CH), 4.1 (2 H, m, $CO_2CH_2CH_3$), 2.4 (3 H, t, *J* 7 Hz, CH_2CO_2H), 2.3—1.34 (20 H, complex), 1.25 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.05 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3); δ_C (20 MHz, $CDCl_3$), 179.4 (C=O), 177.9 (C=O), 130.2 (CH=), 129.1 (CH=), 60.1 (*C*-CO_2Et), 46.6, 45.9, 40.4, 40.05, 35.8, 35.4, 33.46, 32.4, 31.6, 29.7, 29.1, 26.8, 25.5, 24.5, 21.1, and 14.2.

Methyl (Z)-7-(-5-*Hydroxymethyl*-1,2-*dimethylbicyclo*[3.3.1]-*nonan*-syn-9-*yl*)*hept*-5-*enoate*.—This was prepared as for (**53**) above; yield 74% [Found: *m/z* 304.2387. $C_{20}H_{32}O_2$ requires $M^+ - H_2O$, 304.2392); $\nu_{max.}$ 3 500 br, 1 720, 1 440, 1 200, and 1 020 cm^{-1}; δ_H (80 MHz) 5.5 (2 H, m, CH=), 3.75 (3 H, s, CO_2CH_3), 3.4 (1 H, d, *J* 11 Hz, CH_2OH), 3.0 (1 H, d, *J* 11 Hz, CH_2OH), 2.5—1.2 (18 H, complex), 1.5 (1 H, s, OH), 1.1 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3).

Methyl (Z)-7-[-5-*Formyl*-2,2-*dimethylbicyclo*[3.3.1]*nonan*-9-*yl*]*hept*-5-*enoate*.—This was prepared as for (**54**) above; yield 100%; $\nu_{max.}$ 2 730, 1 740, 1 475, 1 380, and 1 175 cm^{-1}; δ_H (80 MHz) 9.4 (1 H s, CHO), 5.4 (2 H, m, CH=CH), 3.7 (3 H, s, CO_2CH_3), 1.5—1.2 (18 H, complex), 1.02 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3).

Methyl (Z)-7-[5-(3-*Oxo*-(E)-*oct*-1-*enyl*-2,2-*dimethylbicyclo*[3.3.1]*nonan*-syn-9-*yl*]*hept*-5-*enoate*.—This was prepared as for (**11**) above. The crude product was chromatographed with ethyl acetate–light petroleum (1:3) to give the product (79%) [Found: *m/z* 416.3300 (M^+). $C_{27}H_{44}O_3$ requires 416.3290]; $\nu_{max.}$ 1 720, 1 660, 1 600, 1 440, 1 345, and 1 145 cm^{-1}; δ_H (80 MHz) 6.7 (1 H, d, *J* 16 Hz, =CHCO), 5.95 (1 H, d, *J* 16 Hz, CH=CHCO), 5.35 (2 H, m, CH_2CH=CH), 3.7 (3 H, s, CO_2CH_3), 2.7—1.1 (31 H, complex), 0.95 (3 H, s, CCH_3), and 1.05 (3 H, s, CCH_3); *m/z* 416 (M^+), 345, 317, 151, and 99.

Methyl (Z)-7-[5-(3-*Hydroxy*-(E)-*oct*-1-*enyl*)-2,2-*dimethylbicyclo*[3.3.1]*nonan*-syn-9-*yl*]*hept*-5-*enoate* (**12**).—This was prepared as for (**10**) above; yield 96% [Found: *m/z*, 400.3340 ($M^+ - H_2O$). $C_{27}H_{44}O_2$ requires 400.3341]; $\nu_{max.}$ 3 400 br, 1 720, 1 440, 1 345, 1 010, and 960 cm^{-1}; δ_H (80 MHz) 5.4 (4 H, m, CH=CH), 4.0 (2 H, m, CH_2OH), 3.7 (3 H, s, CO_2CH_3), 2.4—1.1 (30 H, complex), 1.05 (3 H, s, CCH_3), 0.95 (3 H, s, CCH_3), 1.5 (1 H, s, OH).

Methyl 4,4-*Dimethyl*-8-(2-*oxoethylidene*)*bicyclo*[3.2.1]-*octanecarboxylate* (**62**) *and Ethyl* 4,4-*Dimethyl*-8-(2-*oxoethylidene*)*bicyclo*[3.2.1]*octanecarboxylate* (**63**).—Into a three-necked round-bottomed flask (25 cm^3) fitted with a nitrogen inlet, septum and magnetic stirrer were placed sodium hydride (42.3 mg, 0.1 mmol, 60% dispersion in oil) and anhydrous THF (1 cm^3). A solution of diethyl 2-(cyclohexylamino)vinyl phosphonate (**64**) (233.1 mg, 0.9 mmol) in THF (1 cm^3) was added dropwise by cannula over a period of 10 min, during which time the temperature was maintained at 0—5 °C with an ice-bath. The mixture was stirred for 15 min at 0—5 °C before a solution of methyl 4,4-dimethyl-8-oxobicyclo[3.2.1]octane-carboxylate (**9**) (158.9 mg, 0.76 mmol) in THF (2 cm^3) was added dropwise by cannula over 10 min at 0 °C. The resulting mixture was stirred and heated at 40 °C overnight. The mixture was then poured into cold water (10 cm^3) and extracted with ether (3 × 10 cm^3). The combined ether extracts were washed with saturated aqueous brine (5 cm^3) and evaporated under reduced pressure. The residue was dissolved in benzene (6 cm^3), and then water (18 cm^3) and oxalic acid dihydrate (0.8 g) were added. The resulting solution was stirred under reflux for 2 h. The layers were separated and the aqueous layer was extracted with ether (2 × 10 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was chromatographed with ethyl acetate–light petroleum (5:95), to give two products, methyl 4,4-dimethyl-8-(2-oxoethylidene)bicyclo[3.2.1]octanecarboxylate (**62**) (27.2 mg, 15%); $\nu_{max.}$ 1 735, 1 680, 1 635, 1 400, 1 380, 1 200, 1 165, 1 130, and 1 095 cm^{-1}; δ_H (80 MHz) 9.5 (1 H, d, *J* 11 Hz, CHO), 5.75 (1 H, d, *J* 11 Hz, CH=), 3.7 (3 H, s, CO_2CH_3), 2.5—1.2 (9 H, complex), 1.0 (3 H, s, CCH_3), 0.9 [3 H, s, $C(CH_3)$], and ethyl 4,4-dimethyl-8-(2-oxoethylidene)bicyclo[3.3.1]octanecarboxylate (**63**) (57.6 mg, 30%); $\nu_{max.}$ 2 730, 1 725, 1 675, 1 625, 1 375, and 1 160 cm^{-1}; δ_H (80 MHz) 9.9 (1 H, d, *J* 11 Hz, CHO), 5.9 (1 H, d, *J* 11 Hz, =CH), 4.7 (2 H, q, *J* 7 Hz, $CO_2CH_2CH_3$), 3.1 (1 H, d, *J* 5 Hz, 5-H), 2.5—1.4 (8 H, complex), 1.2 (3 H, t, *J* 7 Hz, $CO_2CH_2CH_3$), 1.0 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3).

Methyl syn-8-*Formyl*-4,4-*dimethylbicyclo*[3.2.1]*octanecarboxylate* (**58**).—This was prepared from (**9**) as for (**46**) and (**47**) above. The crude product was chromatographed with ethyl acetate–light petroleum (1:4) to give the enol ethers (**72**); $\nu_{max.}$ 1 735, 1 705, 1 275, 1 165, 1 130, and 1 080 cm^{-1}; δ_H (80 MHz) 5.85 (0.2 H, s, HC=), 5.65 (0.8 H, s, HC=), 3.75 (0.6 H, s, CO_2CH_3), 3.7 (2.4 H, s, CO_2CH_3), 3.55 (0.6 H, s, OCH_3), 3.45 (2.4 H, s, OCH_3), 2.7—1.1 (9 H, complex), and 0.75 [6 H, s, $C(CH_3)_2$]. The enol ethers (**72**) were dissolved in ethanol (30 cm^3) with a few drops of dilute hydrochloric acid and stirred for 5 h. The ethanol was evaporated under reduced pressure and then ether (40 cm^3) and water (25 cm^3) were added. The layers were separated, and the aqueous phase was extracted with ether (2 × 25 cm^3). The combined ether extracts were dried ($MgSO_4$) and evaporated to give the product (**58**) [1.07 g, 69% from (**9**)]; $\nu_{max.}$ 1 730, 1 400, 1 380, 1 280, 1 235, 1 200, 1 170, and 1 080 cm^{-1}; δ_H (80 MHz) 10.0 (1 H, s, CHO), 3.7 (3 H, s, CO_2CH_3), 2.9 (1 H, d, *J* 5 Hz, 5-H), 2.4 (1 H, br, s, 8-H), 2.2—1.0 (8 H, complex), and 0.9 (3 H, s, CCH_3). In $CDCl_3$ solution, the aldehyde (**58**) was oxidised with time to give the acid (**59**) (Found: C, 64.65; H, 8.3. $C_{13}H_{20}O_4$ requires C, 64.98; H, 8.39%); $\nu_{max.}$ 3 300br, 1 735, 1 700, 1 280, 1 230, 1 195, 1 175, and 1 075 cm^{-1}; δ_H (400 MHz) 3.69 (3 H, s, CO_2CH_3), 3.09 (1 H dd, *J* 2

6 Hz, 8-H), 2.3 (3 H, m), 2.4 (1 H, dt, H_3 *endo*), 1.2—1.3 (5 H, m), 0.95 (3 H, s, CCH_3), and 0.87 (3 H, s, CCH_3).

Methyl anti-8-*Formyl*-4,4-*dimethylbicyclo*[3.3.1]*octanecarboxylate* (**68**).—The aldehyde (**58**) (303 mg, 1.3 mmol) was dissolved in methanol (5 cm^3) and a very small amount of sodium was added. The resulting solution was left at room temperature for 14 h after which dilute hydrochloric acid was added until the solution was neutral. Methanol was removed on the rotary evaporator and ether (10 cm^3) and water (5 cm^3) were added. The layers were separated, and the aqueous phase was extracted with ether (2 × 5 cm^3). The combined ether extracts were dried ($MgSO_4$) and evaporated to give the product (**68**) (298 mg, 98%); $\nu_{max.}$ 2 730, 1 730, 1 280, 1 235, 1 200, and 1 170 cm^{-1}; δ_H (80 MHz) 9.5 (1 H, s, CHO), 3.7 (3 H, s, CO_2CH_3), 3.0 (1 H, s, 8-H), 2.2—1.1 (9 H, complex), 1.05 (3 H, s, CCH_3), and 0.95 (3 H, s, CCH_3). In $CDCl_3$ solution the aldehyde (**68**) was oxidised to give the acid (**69**), m.p. 127—130 °C (Found: C, 65.15; H, 8.3. $C_{13}H_{20}O_4$ requires C, 65.0; H, 8.4%); $\nu_{max.}$(KBr) 3 430br, 1 730, 1 705, 1 285, 1 245, 1 170, and 1 080 cm^{-1}; δ_H (250 MHz) 3.7 (3 H, s, CO_2CH_3), 3.1 (1 H, s, 8-H), 2.25 (1 H, m, 7-H *exo*), 2.05 (1 H, t, *J* 3.5 Hz, 5-H), 1.81 (1 H, tdd, 2-H), 1.6 (1 H, m, 7-H *endo*), 1.55 (1 H, ddd, 2-H *endo*), 1.4 (1 H, tdd, 3-H *endo*), 1.25 (1 H, m, 3-H *exo*), 1.05 (3 H, s, CH_3), and 0.95 (3 H, s, CH_3).

Methyl syn-8-(*Formylmethyl*)-4,4-*dimethylbicyclo*[3.2.1]*octanecarboxylate* (**60**).—This was prepared from (**58**) as for (**48**) above. The crude product was chromatographed with ethyl acetate–light petroleum (15:85) to give the product (**60**) (0.898 g, 77%); $\nu_{max.}$ 2 700, 1 720, 1 440, 1 270, 1 160, and 1 070 cm^{-1}; δ_H (80 MHz) 9.7 (1 H, br s, CHO), 3.65 (3 H, s, CO_2CH_3), 2.75 (2 H, m, CH_2CHO), 2.1—1.1 (9 H, complex), 1.0 (3 H, s, CCH_3), and 0.9 (3 H, s, CCH_3).

Methyl anti-8-*Formylmethyl*-4,4-*dimethylbicyclo*[3.2.1]*octanecarboxylate* (**70**).—This was prepared from (**68**) as for (**48**) above, yield 84%; $\nu_{max.}$ 2 700, 1 725, 1 465, 1 280, 1 165, and 1 070 cm^{-1}; δ_H (80 MHz) 9.7 (1 H, br s, CHO), 3.65 (3 H, s, CO_2CH_3), 2.85—1.15 (11 H, complex), 1.05 (3 H, s, CCH_3), and 0.87 (3 H, s, CCH_3).

(Z)-7-[5-*Methoxycarbonyl*-2,2-*dimethylbicyclo*[3.2.1]*octan*-syn-8-*yl*]*hept*-5-*enoic Acid*.—This was prepared from (**60**) as for (**53**) above. The crude product was chromatographed with ethyl acetate–light petroleum (35:65) to give the product (85%) [Found: *m/z* 304.2039 ($M^+ - H_2O$). $C_{19}H_{28}O_3$ requires 304.2038]; $\nu_{max.}$ 3 300br, 1 735, 1 720, 1 470, 1 450, 1 250, 1 170, 1 080, and 1 050 cm^{-1}; δ_H (80 MHz) 10.45 (br s, CO_2H), 5.4 (2 H, m, CH=CH), 3.65 (3 H, s, CO_2CH_3), 2.5—1.15 (16 H, complex), 1.0 (3 H, s, CCH_3), and 0.85 (3 H, s, CCH_3).

Methyl (Z)-7-[5-*Hydroxymethyl*-2,2-*dimethylbicyclo*[3.2.1]*octan*-syn-8-*yl*]*hept*-5-*enoate*.—This was prepared as for (**55**) above. The crude product was chromatographed with ethyl acetate–light petroleum (1:4) to give the product (90%) [Found: *m/z* 290.2242 ($M^+ - H_2O$). $C_{19}H_{30}O_2$ requires 290.2245]; $\nu_{max.}$ 3 400br, 2 900, 2 830, 1 720, 1 420, 1 345, 1 080, and 1 020 cm^{-1}; δ_H (80 MHz) 5.5 (2 H, m, CH=CH), 3.7 (3 H, s, CO_2CH_3), 3.4 (2 H, s, CH_2OH), 2.5—1.2 (9 H, complex), 1.0 (3 H, s, CCH_3), and 0.85 (3 H, s, CCH_3).

Methyl (Z)-7-[5-*Formyl*-2,2-*dimethylbicyclo*[3.2.1]*octan*-syn-8-*yl*]*hept*-5-*enoate*.—This was prepared as for (**61**) above; yield 100%; $\nu_{max.}$ 2 750, 1 740, 1 470, 1 380, and 1 170 cm^{-1}; δ_H (80 MHz) 9.4 (1 H, s, CHO), 5.35 (2 H, m, CH=CH), 3.7 (3 H, s, CO_2CH_3), 2.5—1.1 (18 H, complex), 1.02 (3 H, s, CCH_3), and 0.9 (3 H, s, CCH_3).

Table 1. Final fractional co-ordinates for non-hydrogen atoms (× 10^4) with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
O(1)	2 243(2)	5 778(3)	8 408(2)
O(2)	5 067(2)	6 778(3)	9 162(2)
O(3)	2 789(2)	641(3)	6 856(2)
O(4)	2 419(3)	1 929(5)	5 562(3)
C(1)	4 762(3)	3 661(4)	7 129(2)
C(2)	3 908(3)	5 462(4)	8 275(2)
C(4)	7 109(3)	6 547(4)	8 960(2)
C(5)	7 565(3)	7 556(5)	8 163(3)
C(6)	7 338(4)	5 957(6)	6 839(3)
C(7)	5 429(3)	4 826(5)	6 425(3)
C(8)	6 366(3)	2 390(4)	7 412(2)
C(9)	7 631(3)	4 035(4)	8 462(2)
C(10)	3 185(3)	2 003(5)	6 413(3)
C(11)	1 215(3)	− 864(5)	6 338(3)
C(12)	7 956(4)	7 993(5)	10 190(3)

Methyl (Z)-7-{-5-[(E)-(3-*Oxo*-*oct*-1-*enyl*)]-2,2-*dimethylbicyclo*[3.3.1]*octan*-syn-8-*yl*}*hept*-5-*enoate*.—This was prepared as for (**56**) above. The crude product was chromatographed with ethyl acetate–light petroleum (15:85) to give the product (82%) (Found: C, 77.35; H, 10.4. $C_{26}H_{42}O_3$ requires C, 77.55; H, 10.50%); $\nu_{max.}$ 1 730, 1 670, 1 630, 1 450, 1 365, 1 280, and 1 025 cm^{-1}; δ_H (80 MHz) 6.75 (1 H, d, *J* 17 Hz, =CHCO), 6.0 (1 H, d, *J* 17 Hz, C*H*=CHCO), 5.35 (2 H, m, CH=CH), 3.65 (3 H, s, CO_2CH_3), and 2.7—0.8 (35 H, complex).

Methyl (Z)-7-{5-[(E)-3-*Hydroxyoct*-1-*enyl*]-2,2-*dimethylbicyclo*[3.3.1]*octan*-syn-8-*yl*}*hept*-5-*enoate* (**13**).—This was prepared as for (**10**) above; yield 98% [Found: *m/z* 386.3187 ($M^+ - H_2O$). $C_{26}H_{42}O_2$ requires 386.185]; $\nu_{max.}$ 3 400, 1 720, 1 440, 1 345, 1 010, and 955 cm^{-1}; δ_H (80 MHz) 5.7—5.0 (4 H, complex, CH=CH), 4.05 (2 H, m, CH_2OH), 3.65 (3 H, s, CO_2CH_3), 2.5—1.1 (28 H, complex), 0.95 (3 H, s, CCH_3), 0.85 (3 H, s, CCH_3), and 1.7 (1 H, OH).

X-*Ray Study of Compound* (**22**).—*Crystal data*. $C_{11}H_{16}O_4$, M_r = 212.3. Space group $P\bar{1}$, *a* = 7.177(s), *b* = 6.699(2), *c* = 12.898(4) Å, α = 119.0(1), β = 91.8(1), γ = 88.5(1)°, *U* = 539.8 $Å^3$, D_m = 1.32, *Z* = 2, D_c = 1.31 $mg\,m^{-3}$; λ = 0.710 69 Å, μ(Mo-K_α) = 0.06 mm^{-1}, *F*(000) = 228.

X-*Ray intensity measurements*. A crystal of approximate dimensions 0.25 × 0.30 × 0.40 mm was mounted with the *c* axis coincident with the ω axis of a Stoe Stadi 2 two-circle diffractometer. Data were collected using the background ω scan-background technique. Corrections for Lorentz and polarisation effects were applied, but not for absorption. Of 1 794 unique reflections collected, 1 317 had $I/\sigma(I) > 3.0$ and were used for the final stages of structure analysis.

Structure Determination and Refinement.—The presence of two molecules in the unit cell led us initially to attempt a solution in the centrosymmetric space group $P\bar{1}$ (confirmed by subsequent analysis to be the correct space group). The structure was solved by multisolution direct methods.[29] Full-matrix refinement with anisotropic thermal parameters for all non-hydrogen atoms gave the final *R* = 0.047 and *R'* = 0.052. Hydrogen atoms were included in positions calculated from the geometry of the molecule (C–H 1.08 Å) and common isotropic thermal parameters applied to the methyl and to the methylene hydrogens refined to final values of *U* = 0.109(6), 0.070(3) $Å^2$ respectively. Scattering factors were calculated[30] using an analytical approximation and the final weighting scheme adopted was $w = 1.6410/[^2(F_o) + 0.0011(F_o)^2]$. Final atomic parameters are given in Table 1, bond distances and angles in

Table 2. Bond distances (Å) and angles (°) with estimated standard deviations in parentheses†

Bond distances (Å)

C(1)–C(2)	1.517(3)	C(4)–C(9)	1.516(3)
C(1)–C(7)	1.546(4)	C(4)–C(12)	1.518(4)
C(1)–C(8)	1.548(3)	C(5)–C(6)	1.519(4)
C(1)–C(10)	1.538(3)	C(6)–C(7)	1.532(3)
C(2)–O(1)	1.211(2)	C(8)–C(9)	1.549(3)
C(2)–O(2)	1.333(3)	C(10)–O(3)	1.326(3)
O(2)–C(4)	1.488(2)	C(10)–O(4)	1.192(3)
C(4)–C(5)	1.523(4)	O(3)–C(11)	1.446(3)

Bond angles (°)

C(2)–C(1)–C(7)	109.1	C(5)–C(4)–C(9)	114.6
C(2)–C(1)–C(8)	109.6	C(5)–C(4)–C(12)	110.2
C(2)–C(1)–C(10)	106.3	C(9)–C(4)–C(12)	111.5
C(7)–C(1)–C(8)	112.3	C(4)–C(5)–C(6)	115.9
C(7)–C(1)–C(10)	108.5	C(5)–C(6)–C(7)	115.6
C(8)–C(1)–C(10)	110.8	C(6)–C(7)–C(1)	113.8
C(1)–C(2)–O(1)	123.3	C(1)–C(8)–C(9)	112.7
C(1)–C(2)–O(2)	117.6	C(8)–C(9)–C(4)	114.0
O(1)–C(2)–O(2)	119.1	C(1)–C(10)–O(3)	111.4
C(2)–O(2)–C(4)	119.1	C(1)–C(10)–O(4)	124.7
O(2)–C(4)–C(5)	108.7	O(3)–C(10)–O(4)	123.9
O(2)–C(4)–C(9)	107.6	C(10)–O(3)–C(11)	117.5
O(2)–C(4)–C(12)	103.7		

† Estimated standard deviation for all bond angles is 0.2°.

Table 3. Final fractional co-ordinates for non-hydrogen atoms ($\times 10^4$) with estimated standard deviations in parentheses.

Atom	*x*	*y*	*z*
O(1)	−1 044(3)	7 334(4)	3 759(8)
O(2)	−1 900(2)	9 431(4)	4 614(6)
O(3)	−233(3)	14 212(4)	2 140(8)
O(4)	−1 426(3)	14 054(4)	3 316(7)
O(5)	3 334(2)	904(4)	121(6)
O(6)	3 682(2)	−168(4)	−692(6)
N(1)	448(2)	7 238(4)	2 349(7)
N(2)	1 266(3)	6 594(4)	1 618(7)
N(3)	−1 228(3)	8 705(5)	3 846(8)
N(4)	−712(4)	13 493(5)	2 688(8)
C(1)	176(3)	8 736(5)	2 431(8)
C(2)	−650(3)	9 500(5)	3 160(8)
C(3)	−923(3)	11 043(6)	3 205(8)
C(4)	−404(3)	11 867(5)	2 637(8)
C(5)	416(3)	11 197(6)	1 968(8)
C(6)	692(3)	9 656(5)	1 901(8)
C(7)	1 471(3)	5 171(6)	1 607(9)
C(8)	2 301(3)	4 232(5)	842(9)
C(9)	2 737(3)	3 250(5)	2 355(8)
C(10)	3 432(3)	1 894(5)	1 597(8)
C(11)	3 762(3)	921(6)	3 222(8)
C(12)	4 070(4)	1 787(6)	4 844(8)
C(13)	3 416(4)	3 243(6)	5 461(9)
C(14)	3 134(3)	4 153(6)	3 803(9)
C(15)	3 860(3)	4 637(6)	2 934(10)
C(16)	4 314(3)	3 799(6)	1 504(9)
C(17)	4 140(3)	2 400(5)	608(8)
C(18)	4 063(4)	6 059(6)	3 776(10)
C(19)	3 069(3)	865(5)	293(9)
C(20)	3 434(4)	−1 255(6)	−1 954(9)
C(21)	3 200(4)	−2 492(6)	−984(10)

Table 2. All calculations were carried out on an IBM 4341 computer using the SHELX computing package.[29]

X-Ray Study of the Dinitrophenylhydrazone Derivative of Compound (**48**).—*Crystal data.* $C_{21}H_{26}N_4O_6$, M_r = 430.4.

Table 4. Bond distances (Å) and angles (°) with estimated standard deviations in parentheses

Bond distances (Å)

C(1)–N(1)	1.378(6)	C(9)–C(10)	1.601(6)
C(1)–C(2)	1.491(7)	C(9)–C(14)	1.506(8)
C(1)–C(6)	1.378(8)	C(10)–C(11)	1.580(8)
C(2)–N(3)	1.412(8)	C(10)–C(17)	1.526(8)
C(2)–C(3)	1.420(7)	C(10)–C(19)	1.486(8)
N(3)–O(1)	1.250(6)	C(11)–C(12)	1.505(8)
N(3)–O(2)	1.287(6)	C(12)–C(13)	1.602(7)
C(3)–C(4)	1.326(8)	C(13)–C(14)	1.547(9)
C(4)–N(4)	1.501(7)	C(14)–C(15)	1.500(9)
C(4)–C(5)	1.445(7)	C(15)–C(16)	1.373(8)
N(4)–O(3)	1.203(7)	C(15)–C(18)	1.497(8)
N(4)–O(4)	1.265(7)	C(16)–C(17)	1.474(7)
C(5)–C(6)	1.418(7)	C(19)–O(5)	1.210(7)
N(1)–N(2)	1.451(6)	C(19)–O(6)	1.409(6)
N(2)–C(7)	1.302(7)	O(6)–C(20)	1.417(7)
C(7)–C(8)	1.557(7)	C(20)–C(21)	1.496(9)
C(8)–C(9)	1.575(8)		

Bond angles (°)

N(1)–C(1)–C(2)	124.7(5)	C(10)–C(9)–C(14)	107.0(4)
N(1)–C(1)–C(6)	120.4(4)	C(9)–C(10)–C(11)	110.8(4)
C(2)–C(1)–C(6)	114.8(4)	C(9)–C(10)–C(17)	111.9(4)
C(1)–C(2)–N(3)	121.1(4)	C(9)–C(10)–C(19)	110.3(4)
C(1)–C(2)–C(3)	123.8(5)	C(11)–C(10)–C(17)	110.9(4)
N(3)–C(2)–C(3)	115.1(4)	C(11)–C(10)–C(19)	103.5(4)
C(2)–N(3)–O(1)	118.4(4)	C(17)–C(10)–C(19)	109.0(5)
C(2)–N(3)–O(2)	118.4(4)	C(10)–C(11)–C(12)	113.2(4)
O(1)–N(3)–O(2)	123.2(5)	C(11)–C(12)–C(13)	111.0(4)
C(2)–C(3)–C(4)	118.4(5)	C(12)–C(13)–C(14)	112.4(5)
C(3)–C(4)–N(4)	117.1(5)	C(13)–C(14)–C(15)	110.1(5)
C(3)–C(4)–C(5)	120.4(5)	C(13)–C(14)–C(9)	110.5(5)
N(4)–C(4)–C(5)	122.5(5)	C(9)–C(14)–C(15)	108.9(5)
C(4)–N(4)–O(3)	115.8(5)	C(14)–C(15)–C(16)	121.7(5)
C(4)–N(4)–O(4)	121.2(5)	C(14)–C(15)–C(18)	115.2(5)
O(3)–N(4)–O(4)	123.0(4)	C(16)–C(15)–C(18)	123.1(6)
C(4)–C(5)–C(6)	121.7(5)	C(15)–C(16)–C(17)	125.6(5)
C(5)–C(6)–C(1)	120.8(4)	C(16)–C(17)–C(10)	111.4(4)
C(1)–N(1)–N(2)	120.8(4)	C(10)–C(19)–O(5)	123.8(5)
N(1)–N(2)–C(7)	116.4(4)	C(10)–C(19)–O(6)	111.8(4)
N(2)–C(7)–C(8)	125.7(5)	O(5)–C(19)–O(6)	124.4(5)
C(7)–C(8)–C(9)	111.1(5)	C(19)–O(6)–C(20)	118.6(4)
C(8)–C(9)–C(10)	115.9(4)	O(6)–C(20)–C(21)	112.1(5)
C(8)–C(9)–C(14)	111.2(4)		

Space group $P\bar{1}$, a = 16.456(6), b = 9.266(4), c = 7.220(3) Å, α = 94.8(1), β = 89.8(1), γ = 79.9(1)°, U = 1 080.0 Å^3, D_m = 1.33, Z = 2, D_c = 1.32 mg m^{-3}, λ = 0.710 69 Å, μ(Mo-K_α) = 0.07 mm^{-1}, $F(000)$ = 456.0.

X-Ray intensity measurements. A crystal of approximate dimensions 0.15 × 0.20 × 0.30 mm was mounted with the c axis coincident with the ω axis of a Stoe Stadi 2 two-circle diffractometer. Data were collected using the background ω scan-background technique. Corrections for Lorentz and polarisation effects were applied, but not for absorption. Of 2 379 unique reflections collected 1 496 had $I/\sigma(I) > 3$ and were used for the final stages of structure analysis.

Structure determination and refinement. The structure was solved by multisolution direct methods[29] in the centrosymmetric space group $P\bar{1}$ (shown by subsequent analysis to be correct). All hydrogen atoms were located but their positions were not refined (hydrogens associated with carbon atoms were located in ideal positions calculated from the geometry of the molecule, C–H 1.08 Å). Full-matrix refinement with anisotropic thermal parameters for all non-hydrogen atoms gave the final R = 0.059, R' = 0.054. Scattering factors were calculated[30]

using an analytical approximation and the final weighting scheme adopted was $w = 4.5552/[^2(F_o) + 0.0002(F_o)^2]$. Final atomic parameters are given in Table 3, bond distances and angles in Table 4. All calculations were carried out on an IBM 4341 computer using the SHELX computing package.[29]

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