Total Synthesis of Cyclopentanoid Natural Products

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The highly functionalised bicyclo[3.3.0]octanes (**5**) and (**6**) have been prepared by a sequence involving intramolecular Wittig reactions of the diketo ester (**9**) with vinyl phosphonium salts (**3**) and (**4**). Compounds (**5**) and (**6**) have then been used as starting materials for formal syntheses of (±)-chrysomelidial, (±)-loganin, and (±)-hirsutene. An intermediate used in the synthesis of (**5**) and (**6**) has been converted into a known precursor of (±)-sarkomycin.

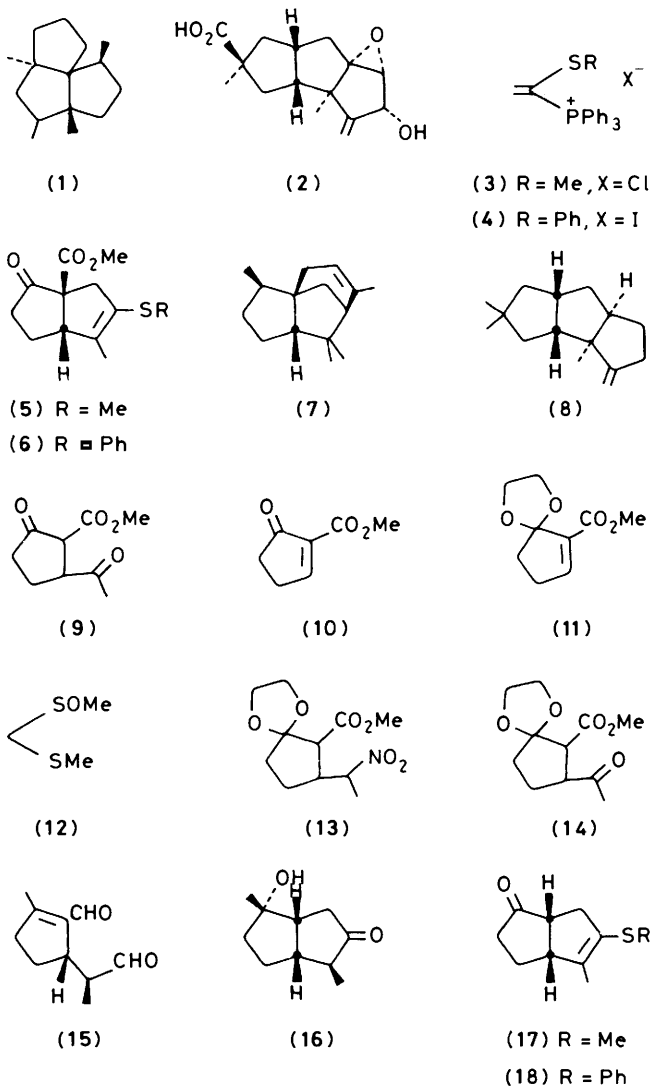
The discovery over recent years of a wide range of cyclopentane-containing natural products has created a demand for reactions which may be used to form five-membered carbocyclic rings. Although many classical ring forming reactions (*e.g.* Dieckmann, aldol) are applicable to five-membered rings, it has become necessary to develop more flexible annelation methods which allow greater control over the introduction of functionality.[1,2] Much of the current effort is directed towards the synthesis of fused pentacyclic systems such as the tricyclo-[6.3.0.0^{4,8}]undecane system found in isocomene, (**1**), and the tricyclo[6.3.0.0^{2,6}]undecane system of hirsutic acid, (**2**), and related compounds. This area of polyquinane synthesis has recently been comprehensively reviewed.[3]

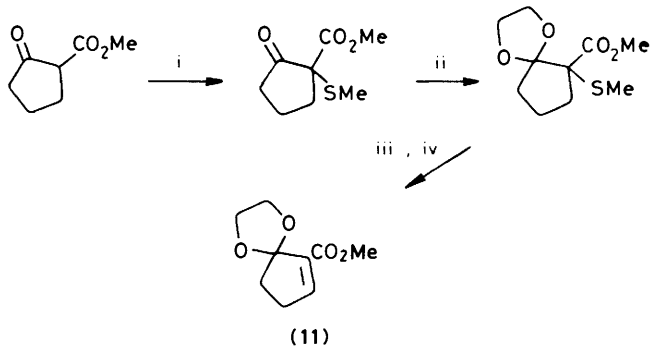
We have developed a synthesis of the vinyl phosphonium salts (**3**) and (**4**) and show their use in the synthesis of monocyclic cyclopentanoid natural products.[4,5] It was felt that the method should be capable of development to the preparation of polyquinane derivatives and in particular we were attracted by the possibility of producing the bicyclo-[3.3.0]octanes (**5**) and (**6**). The functionality present in these compounds makes them highly flexible for further development, and reactions can be envisaged which would allow modification of all eight positions around the bicyclo[3.3.0]octane skeleton. For example, it is apparent that tricyclic molecules such as cedrene, (**7**), and hirsutene, (**8**), should be derivable from (**5**) or (**6**).

We have published preliminary accounts of some of this work, including syntheses of sarkomycin,[6] chrysomelidial, and loganin.[7] We provide here full details of that work, together with further development in terms of a synthesis of hirsutene.

Retrosynthetic analysis suggested that (**5**) and (**6**) should be available from the diketo ester (**9**) and the vinyl phosphonium salts (**3**) and (**4**), respectively. Thus the first task was to establish a convenient synthesis of (**9**) and a route suggested itself involving addition of an acyl anion to the unsaturated keto ester (**10**). Although (**10**) can be prepared by selenoxide elimination,[8] and can be used in some cases for conjugate additions with nucleophiles,[9,10] it is nevertheless rather prone to polymerisation. We therefore decided to investigate the use of the corresponding acetal (**11**) which, it was expected, would be stable enough to be stored for long periods of time. The acetal (**11**) was readily prepared by standard methods, in 64% overall yield, from methyl 2-oxocyclopentanecarboxylate (Scheme 1).

A wide range of acyl anion equivalents has been described in recent years,[11] many of them being strongly basic reagents which must be used in aprotic solvents. Our first attempt to add an acyl anion to (**11**) used the commercially available sulphoxide (**12**).[12] Reaction between the lithio derivative of (**12**) and the ketal (**11**) gave only highly polar products which were not identified. It was postulated that the intermediate anion in the addition was being destroyed by acetal opening, followed by further reactions. If this were true, it might be possible to overcome the problem by choosing an acyl anion which could be used in a solvent capable of proton donation to the intermediate anion. In the event, treatment of a solution of (**11**) in nitroethane with tetramethylguanidine, resulted in conjugate addition of the nitronate anion to provide (**13**) as a 1.6:1 mixture of isomers (93%). Conversion of the mixture (**13**) into the ketone (**14**), also a mixture of isomers, was achieved either with buffered titanium trichloride[13] (77%) or with ozone followed by dimethyl sulphide.[14] The latter method, however,





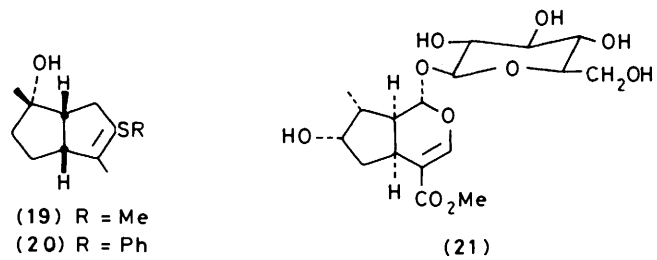
(11)

Scheme 1. *Reagents:* (i) NaH, *p*-TolylSO$_2$SMe; (ii) HOCH$_2$CH$_2$OH, H$^+$; (iii) NaIO$_4$; (iv) 110 °C, Ca CO$_3$.

always produced some unchanged starting material which had to be separated. The acetal group of (**14**) was hydrolysed with aqueous TFA (trifluoroacetic acid) to give the desired diketo ester (**9**) (79%) as a crystalline solid, which appeared to be a single isomer, presumably having a *trans* disposition of the acetyl and methoxycarbonyl groups. We could now turn our attention to the critical bicyclo[3.3.0]octane forming reaction. Formation of the anion of (**9**) with sodium hydride, followed by addition of the phosphonium salts (**3**) or (**4**) resulted in the desired bicyclic products (**5**) and (**6**) in yields of 97 and 83% respectively.

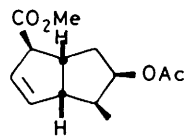
Synthesis of (±)-*Chrysomelidial.*—Chrysomelidial, (**15**), from the larval defence secretion of a chrysomelide beetle was reported in 1977.[15] Prior to our work, three total syntheses, two being non-stereospecific, and one formal synthesis of (**15**) had been described.[16] Both stereospecific routes proceeded through the bicyclo[3.3.0]octane (**16**), using the rigid nature of this system to establish the required relative stereochemistry. We felt that compounds (**5**) and (**6**) possessed ideal functionality for the preparation of (**16**).

Several methods for the demethoxycarbonylation of (**5**) and (**6**) were investigated. However, lithium or sodium chloride in DMSO (dimethyl sulphoxide),[17] sodium cyanide in DMSO[18] and propane-1,2-diol–sodium hydride[19] all gave mixtures and/or low yields of the desired product. The one reagent which did prove suitable for this conversion was sodium cyanide in HMPA (hexamethylphosphoric triamide),[20] which gave (**17**) (82%) or (**18**) (79%). Addition of methyl-lithium to (**18**) occurred stereospecifically to give the *endo* alcohol (**20**) (84%), but satisfactory hydrolysis of the vinyl sulphide in (**20**) did not prove possible. Use of titanium tetrachloride,[21] TFA,[22] or



(19) R = Me
(20) R = Ph

(21)



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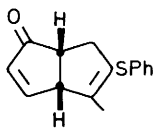

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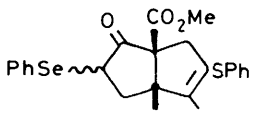

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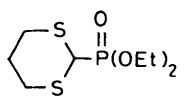

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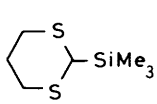

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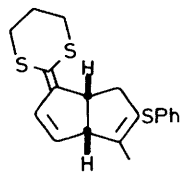

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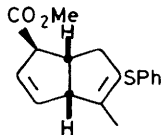

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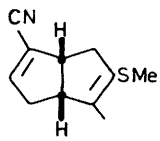

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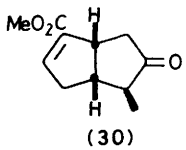

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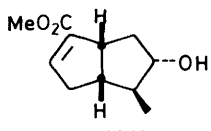

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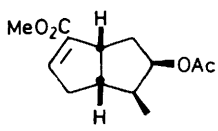
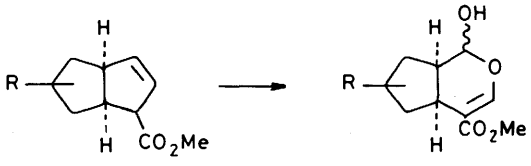


(32)

mercuric chloride[23] all released the carbonyl group but also caused unwanted side reactions, including dehydration of the tertiary alcohol. Use of mercuric chloride with calcium carbonate or mercuric oxide[24] gave no reaction. The solution to the problem turned out to lie with the corresponding methylthio series. Thus methyl-lithium addition to (**17**) gave the *endo* alcohol (**19**) (75%). After considerable experimentation it was found that selective hydrolysis of the vinyl sulphide in (**19**) could be achieved with mercuric chloride in aqueous acetonitrile if the reaction was carefully monitored by t.l.c. A similar study with the phenylthio compound (**20**) showed that its hydrolysis was slower and concurrent dehydration was unavoidable. The desired ketone (**16**) (69%) has the methyl group in the more stable *exo* configuration. The spectral data for synthetic (**16**) were consistent with the assigned structure and its melting point matched that quoted in the literature.[16] Since (**16**) has been converted into chrysomelidial, our method constitutes a formal total synthesis of the natural compound.

Synthesis of (±)-*Loganin*.—The iridoid glucoside loganin, (**21**), is a widely distributed biosynthetic intermediate in the plant world which has attracted considerable attention as a synthetic target.[25] One of the major approaches has been to establish the relative stereochemistry in a bicyclo[3.3.0]octane which is then oxidatively cleaved to give the loganin ring system (Scheme 2). Particularly attractive to us was the bicyclo-



Scheme 2.

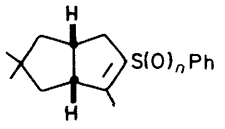
[3.3.0]octene (**22**), used as an intermediate in Fleming's synthesis. We felt that our bicyclo[3.3.0]octanes (**17**) and (**18**) should provide access to (**22**). The initial problem was the conversion of (**18**) into the corresponding α,β-unsaturated ketone (**23**). Attempts to perform this transformation using sulphoxide[26] or selenoxide[8] methodology were unrewarding, in that it proved impossible to isolate satisfactory yields of the desired monosulphenylated or monoselenated ketone under any of the wide range of conditions investigated. It was possible to isolate the monoselenated product (**24**) (mixture of isomers) by using (**6**) as the substrate, but attempts to demethoxycarbonylate (**24**) appeared to result in loss of selenium too, giving (**18**). The desired enone (**23**) was, however, readily prepared by Pd^{II} catalysed oxidation of the corresponding silyl enol ether.[27] Thus reaction of (**18**) with trimethylsilyl chloride–DBU (diazabicycloundecene), followed by treatment with palladium(II) acetate–benzoquinone gave the enone (**23**) (69%). We chose to homologate the carbonyl group of (**23**) to the desired ester *via* the ketone thioacetal. Treatment of enone (**23**) with the anion from the phosphonate (**25**)[28] gave 1,4-addition only, while the anion from (**26**)[29] in THF (tetrahydrofuran) at 78 °C gave a mixture of 1,2- and 1,4-addition. However, this latter reaction in the mixed solvent hexane–THF (1.8:1)[30] gave the desired 1,2-addition adduct (**27**) (58%). It was hoped that Hg^{2+} catalysed hydrolysis of (**27**) would produce the useful intermediate (**28**). Unfortunately, (**27**) was unstable to storage, and treatment with mercuric chloride–methanol–water gave a complex mixture of products.

We therefore turned to more traditional chemistry to accomplish the desired synthesis. Treatment of ketone (**17**) with sodium cyanide gave the cyanohydrin, which was dehydrated to give the nitrile (**29**) [69% from (**17**)]. Reaction of (**29**) with concentrated H_2SO_4–methanol, and aqueous work-up, gave the keto-ester (**30**) as a single isomer, assumed to have the thermodynamically more stable *exo* methyl group. Completion of the synthesis involved stereospecific reduction of (**30**) to the *endo* alcohol (**31**), followed by mesylation, and S_N2 displacement with acetate, to give the *exo* acetate (**32**). Finally, deconjugation of the α,β-unsaturated ester was achieved by brief treatment of (**32**) with LDA (lithium di-isopropylamide), followed by quenching with methanol, which afforded (**22**) (39%), whose ^1H n.m.r. and i.r. spectra closely matched those of an authentic sample.

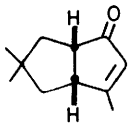
Synthesis of (±)-*Hirsutene*.—Hirsutene (**8**) is the simplest member of the hirsutane family of natural products, which, since its isolation in 1976,[31] has become a common synthetic target. It appeared to us that bicyclo[3.3.0]octanes (**5**) and (**6**) possessed suitable functionality for modification to hirsutene. The major requirement would be the development of a method for adding a third five-membered ring. Our original plan was to oxidise the vinyl sulphone, and then add a suitable nucleophile to its now electrophilic double bond. Application of this approach began with alkylation of (**6**) to the *gem*-dimethyl compound followed by demethoxycarbonylation and Wolff–Kishner reduction to give the vinyl sulphide (**33**) [67% from (**6**)]. Oxidation of (**33**) with *m*-chloroperbenzoic acid gave, in quantitative yield, the desired sulphone (**34**). Unfortunately, all attemps to add nucleophiles to the double bond of (**34**) proved fruitless and, consistently, starting material was recovered. Particularly disappointing for our plans was the fact that that organocuprates showed no tendency to react. It seems likely that the lack of reactivity of (**34**) results from combined effects of steric hindrance and the lower activation of the β-carbon by a sulphone group relative to a carbonyl group. It has been reported that the closely related enone (**35**) is susceptible to cuprate additions.[32]

Reaction of the vinyl sulphone (**34**) with butyl-lithium gave an orange solution of the corresponding anion which could be quenched with a range of electrophiles to give the products of α-alkylation in high yield. It was felt that, by use of a suitable electrophile, this result could be adapted to enable us to build on the third ring of hirsutene. Our first approach involved trapping the anion of (**34**) with 1,3-dibromopropane thus producing (**36**) as a 7:1 isomer mixture (83%). The major isomer was presumed to be that with the *exo* 3-bromopropyl group, formed by approach of the alkylating agent from the convex face of the molecule. This mixture was converted into the corresponding iodide, and then the nitro alkenes (**37**) with silver nitrite.[33] It was now planned to use an intramolecular nitrile oxide cycloaddition to form the third cyclopentane ring,[34] the desired product being the isoxazoline (**38**). Cleavage of the heterocyclic ring would provide a route to (**39**), which has previously been converted into hirsutene.[10] Thus, the major isomer from the mixture (**37**) was subjected to the usual conditions for nitrile oxide formation (phenyl isocyanate–triethylamine–benzene).[35] Consumption of the starting nitro compound occurred, but it did not prove possible to isolate any of the desired product. An inspection of molecular models shows a severe interaction between the two protons shown in (**38**) and this may prevent the reaction from taking the desired course.

The solution to our problem lay in the observation that desulphonylation of (**40**) (10:1 mixture of isomers), prepared by alkylation of the anion from (**34**) with the iodo acetal[36] (**41**) (77%), gave the alkene (**42**) (90%), in which the double bond had moved into the thermodynamically more stable position, and the stereochemical complication had been eliminated. Hydrolysis of the acetal gave the corresponding aldehyde (**43**) (75%). This latter compound has previously been converted into



(33) n = O
(34) n = 2



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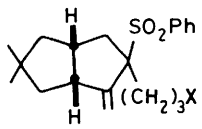
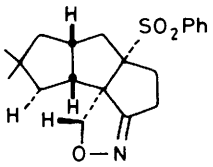


(36) X = Br
(37) X = NO_2



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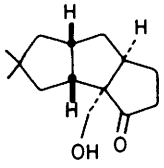

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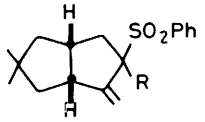
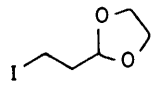


(40) R = $(CH_2)_2CH$ (O, O)

(44) R = $(CH_2)_2C{\equiv}CMe$



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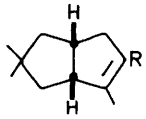
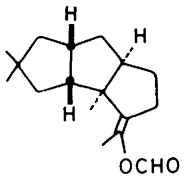


(42) R = $(CH_2)_2CH$ (O, O)

(43) R = $(CH_2)_2CHO$

(45) R = $(CH_2)_2C{\equiv}CMe$



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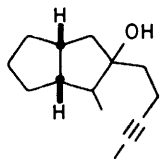

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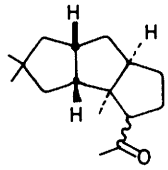

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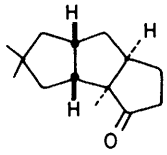
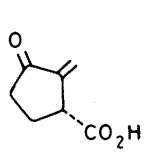


(49)

hirsutene[31] and the spectral data for our compound were consistent with the assigned structure and with the limited literature data available.

A better approach to hirsutene resulted from the alkylation of the anion from (**34**) with 5-iodopent-2-yne, prepared from commerically available pent-3-yne-1-ol. The product (**44**) (72%, 6:1 mixture of isomers) was desulphonylated to give (**45**) (87%) which was cyclised with formic acid to the tricyclic enol formate (**46**) (56%). It has been shown that the related cyclisation of (**47**) gives only the desired, *cis*, *anti*, *cis* ring fusion.[37] The cyclisation of (**45**) had to be carefully monitored to avoid conversion of the product (**46**) into the ketone (**48**), which could also be obtained by treatment of (**46**) with potassium hydroxide in methanol. Finally, cleavage of the double bond in (**46**) was accomplished with an excess of ruthenium dioxide to give the ketone (**49**) (42%), a well known precursor of hirsutene.[10] The 250 MHz ^{1}H n.m.r. spectrum of our synthetic material was superimposable on that of an authentic sample.

Synthesis of (±)-*Sarkomycin*.—Sarkomycin (**50**) is the simplest member of the cyclopentanoid family of antibiotic–



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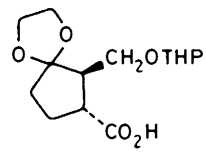
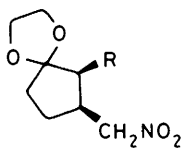


(51)



(52) R = CO_2Me
(53) R = CH_2OH
(54) R = CH_2OTHP

antitumour agents. Early syntheses of sarkomycin were largely non-regioselective and the first regiocontrolled approach was only recently described.[9] Sarkomycin itself is rather unstable and thus synthetic efforts have been largely directed towards a stable precursor which can be readily converted into the natural product. Such an intermediate is (**51**), which, on treatment with acid, yields sarkomycin.[9] The ready addition of a nitronate anion to the keto ester (**11**), which we had used in the synthesis of the diketo ester (**9**), suggested itself as a route towards (**51**).

Treatment of (**10**) in nitromethane with tetramethylguanidine gave a 12:1 mixture of two products (77%). The major product appears to be the *cis* isomer (**52**), an assignment which is based on the observed coupling constant of 8 Hz between the proton α to the ester and the adjacent methine proton. Selective reduction of the ester was achieved with aluminium hydride, prepared from aluminium chloride and lithium aluminium hydride,[38] and the product alcohol (**53**) (85%) was then protected as its THP ether (79%). The primary nitro group was directly oxidised to the carboxylic acid with basic potassium permanganate[39] to give the desired sarkomycin percursor (**51**) (50%). Comparison with the published data suggested that our compound was identical with that previously described,[9] and that epimerisation had occurred during the final reaction to give the *trans* isomer.

In summary, the cyclopentenone acetal (**11**) has been shown to be a useful precursor to 3-substituted cyclopentanones, and the bicyclo[3.3.0]octanes (**5**) and (**6**) have been demonstrated to be versatile precursors to complex cyclopentane-containing natural products. Further investigations are currently being undertaken.

Experimental

Materials and Techniques.—Dry tetrahydrofuran (THF) was obtained by distillation from potassium. Dry ether was obtained by distillation from lithium aluminium hydride. Dry di-isopropylamine, benzene, dichloromethane and HMPA (hexamethylphosphoramide) were obtained by distillation from calcium hydride. Short column chromatography was carried out using either Merck '7736' or '7734' silica gel. ^{1}H N.m.r. data were obtained from JEOL-C60, Bruker WP80, Perkin-Elmer R34, and Bruker AM250 instruments. ^{13}C N.m.r. data were obtained from a Bruker WP80 spectrometer. Spectra were recorded in $CDCl_3$ solution with $SiMe_4$ as an internal standard. I.r. spectra were obtained on Pye Unicam WP200 and SP3-100 spectrophotometers as liquid films unless otherwise stated. Mass spectral data were obtained from AEI MS9 and Kratos MS25 instruments. Light petroleum refers to the fraction boiling in the range 40—60 °C. Ether refers to diethyl ether.

Methyl 1-Methylthio-2-oxocyclopentanecarboxylate.—A solution of methyl 2-oxocyclopentanecarboxylate (50 g, 0.35 mol) in THF (500 ml) was added dropwise to a mechanically stirred suspension of sodium hydride (60% dispersion in oil; 14.8 g, 0.37 mol, previously washed with hexane) in THF (100 ml) at 0 °C under nitrogen. After completion of the addition the

solution was stirred at room temperature for 20 min and methyl thiotosylate (73 g, 0.36 mol) in THF (200 ml) was added over 5 min. The reaction mixture was stirred at room temperature for 4 h during which time a white solid was precipitated. The mixture was filtered under suction and the filter cake was thoroughly washed with ether. The solvent was removed from the filtrate, and the residue was partitioned between ether and water. The aqueous layer was extracted with ether and the combined organic extracts were washed with brine, dried ($MgSO_4$), and then evaporated to give the crude product as a yellow oil (100%). A small portion of the sample was chromatographed with ethyl acetate–light petroleum (10:90) to obtain an analytical sample as an oil (Found: C, 51.25; H, 6.55. $C_8H_{12}O_3S$ requires C, 51.03; H, 6.43%); $\nu_{max.}$ 1 755 and 1 740 cm^{-1}; δ_H 2.08 (3 H, s, SMe), 1.70—2.50 (6 H, series of m), and 3.70 (3 H, s, OMe).

Methyl 6-Methylthio-1,4-dioxaspiro[4.4]*nonane-6-carboxylate*.—A mixture of the crude product from above (65 g, 0.35 mol), ethylene glycol (100 ml), and toluene-*p*-sulphonic acid (1.5 g) were refluxed in benzene (600 ml) under a Dean-Stark trap. After 48 h, g.l.c. analysis indicated almost complete disappearance of starting material. The cooled reaction mixture was washed once with saturated aqueous sodium hydrogen carbonate and several times with water. Drying of the organic layer ($MgSO_4$), removal of the solvent, and distillation gave the product as a yellow oil (68 g, 83% from methyl 2-oxocyclopentanecarboxylate), b.p. 115—120 °C at 5 mmHg [Found: *m/z* 232.0777 (M^+). $C_{10}H_{16}O_4S$ requires 232.0769]; $\nu_{max.}$ 1 730 cm^{-1}; δ_H 1.60—2.50 (6 H, series of m), 2.02 (3 H, s, SMe), 3.63 (3 H, s, OMe), and 3.77—4.15 (4 H, m, OCH_2CH_2O).

Methyl 1,4-Dioxaspiro[4.4]*non-6-ene-6-carboxylate* (**11**).—A suspension of sodium periodate (32.1 g, 0.15 mol) in water (200 ml) was added dropwise to a mechanically stirred solution of methyl 6-methylthio-1,4-dioxaspiro[4.4]nonene-6-carboxylate (34 g, 0.15 mol) in methanol (400 ml) at 0 °C. After completion of the addition the reaction mixture was stirred at room temperature for 24 h during which time a white solid was precipitated. The reaction mixture was filtered and the filter cake was thoroughly washed with methanol. The solvent was removed from the filtrate at <40 °C and the residue was partitioned between water and dichloromethane. The aqueous layer was extracted with dichloromethane and the combined organic layers were dried ($MgSO_4$) and evaporated to give the crude sulphoxide mixture. Column chromatography with ethyl acetate–light petroleum (40:60) followed by methanol–ethyl acetate (10:90) gave a diastereoisomeric pair of sulphoxides as an oil (32.1 g, 88%); $\nu_{max.}$ 1 738 and 1 060 cm^{-1}; δ_H 1.65—2.75 (6 H, series of m), 2.17 (3 H, s, SOMe), 3.55—4.21 (4 H, m, OCH_2CH_2O), and 3.36 (3 H, s, OMe).

The mixture of sulphoxides (32 g, 0.13 mol) was dissolved in toluene (500 ml) containing powdered calcium carbonate (15 g, 0.15 mol) and refluxed for 16 h. The cooled reaction mixture was filtered and the solvent was removed. Column chromatography with ethyl acetate–light petroleum–triethylamine (20:80:1) gave the product (**11**) as a yellow oil (20.7 g, 87%) [Found: *m/z* 184.0732 (M^+). $C_9H_{12}O_4$ requires 184.0736]; $\nu_{max.}$ 1 725 and 1 638 cm^{-1}; δ_H 1.90—2.52 (4 H, series of m), 3.63 (3 H, s, OMe), 3.81—4.26 (4 H, m, OCH_2CH_2O), and 6.95 (1 H, t, vinyl H).

Methyl 7-(1-Nitroethyl)-1,4-dioxaspiro[4.4]*nonane-6-carboxylate* (**13**).—A mixture of ester (**11**) (6 g, 32.6 mmol), nitroethane (10.8 ml, 150 mmol), and tetramethylguanidine (0.75 g, 0.82 ml, 6.5 mmol) was stirred under nitrogen at room temperature for 3 days. The orange–red solution was acidified to pH 6 with 2M-HCl and extracted with ether. The organic extracts were dried ($MgSO_4$) and evaporated and column chromatography of the residue with ethyl acetate–light petroleum (20:80) gave the product (**13**) (7.73 g, 92%) as a mixture of two isomers (1.6:1, stereochemistry undefined). The product could also be purified by distillation to give (**13**) in 90% yield, b.p. 160—168 °C at 3—4 mmHg.

Major isomer (higher R_F) m.p. 68—70 °C (ether) (Found: C, 51.0; H, 6.65; N, 5.35. $C_{11}H_{17}NO_6$ requires C, 50.96; H, 6.61; N, 5.40%); $\nu_{max.}$(KBr) 1 722, 1 550, 1 370, and 1 078 cm^{-1}; δ_H 1.54 (3 H, d, *J* 7 Hz, *Me*$CHNO_2$), 1.70—2.95 (6 H, series of m), 3.71 (3 H, s, OMe), 3.95 (4 H, br s, OCH_2CH_2O), and 4.50—4.95 (1 H, m, $CHNO_2$).

Minor isomer (lower R_F) m.p. 66—68 °C (Found: C, 51.5; H, 6.7; N, 5.34%); $\nu_{max.}$ 1 730, 1 555, and 1 370 cm^{-1}; δ_H 1.49 (3 H, d, *J* 6 Hz, *Me*$CHNO_2$), 1.60—3.00 (6 H, series of m), 3.74 (3 H, s, *OMe*), 3.95 (4 H, br s, OCH_2CH_2O), and 4.42—4.90 (1 H, m, $CHNO_2$).

Methyl 7-Acetyl-1,4-dioxaspiro[4.4]*nonane-6-carboxylate* (**14**).—(i) *Using* $TiCl_3$. To a stirred solution of sodium methoxide [prepared from sodium (2.65 g, 0.115 mol) in methanol (50 ml)] was added a solution of a nitroester (**13**) (29.5 g, 0.11 mol) in methanol (200 ml). The mixture was stirred under nitrogen for 20 min. A solution of ammonium acetate (211 g, 2.74 mol) in water (690 ml) was added to $TiCl_3$ solution (15% w/v; 465 ml, 0.46 mol) under a nitrogen atmosphere in a pressure equalised dropping funnel, and the mixture was rapidly added to the anion solution. After being stirred for 1.5 h at room temperature the reaction mixture was extracted several times with ether. The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (×2) and brine, dried ($MgSO_4$), and evaporated to give the product (**14**) as an inseparable mixture of two isomers (19.6 g, 77%); $\nu_{max.}$ 1 738, 1 710, and 1 170 cm^{-1}; δ_H 1.52—2.50 (7 H, series of m, *Me*CO at 2.15, 2.20), 2.90—3.53 (2 H, series of m, $CHCO_2Me$ and *CH*COMe), 3.69, 3.72, (3 H, 2s, OMe), and 3.97 (4 H, br s, OCH_2CH_2O).

(ii) *Using ozone*. To a stirred solution of sodium methoxide, prepared by dissolving sodium (1.96 g, 0.085 mol) in methanol (50 ml), was added a solution of the nitro ester (**13**) (20 g, 0.077 mol) in methanol (250 ml). The mixture was cooled to −78 °C and O_3–O_2 was bubbled through until a pale blue colour persisted (*ca.* 3 h). The mixture was left at −78 °C for 30 min and then purged with nitrogen to remove excess of O_3. Dimethyl sulphide (5 ml) was added, and the mixture was allowed to reach room temperature overnight. The volatile materials were removed on a rotary evaporator and the residue was dissolved in ether. The ether solution was washed with water and brine, dried ($MgSO_4$), and evaporated and column chromatography of the residue with ethyl acetate–light petroleum (20:80 ⟶ 40:60) gave starting material (**13**) (4.10 g) and the product (**14**) (10.97 g, 63%); yield based on recovered starting material (80%).

Methyl 2-Acetyl-5-oxocyclopentane-1-carboxylate (**9**).—The acetal (**14**) (11.2 g, 0.05 mol) was stirred in TFA–H_2O (2:1; 45 ml) for 6 h at room temperature. The bulk of the TFA was removed under reduced pressure and the residue was partitioned between ether and saturated aqueous sodium chloride. The aqueous layer was extracted several times with ether and the combined organic extracts were dried ($MgSO_4$) and evaporated. Column chromatography with ethyl acetate–light petroleum (40:60) gave (**9**) as an off-white solid which was washed with a small amount of ether to give pure product (**9**) as a white solid (7.15 g, 79%), m.p. 81—82 °C (Found: C, 58.75; H, 6.6. $C_9H_{12}O_4$ requires C, 58.68; H, 6.57%); $\nu_{max.}$(KBr) 1 760, 1 735, and 1 705 cm^{-1}; δ_H 1.60—2.70 (4 H, series of m), 2.29 (3 H, s, MeCO), 3.55—3.90 (2 H, m, *CH*COMe and $CHCO_2Me$), and 3.79 (3 H, s, OMe); δ_C 23.9, 28.6, 37.9, 52.2, 52.6, 56.3, 168.5, 206.6, and 208.6.

Methyl 4-*Methyl*-8-*oxo*-3-*phenylthiobicyclo*[3.3.0]*oct*-3-*ene*-1-*carboxylate* (**6**).—To a suspension of sodium hydride (60% dispersion in mineral oil; 598 mg, 15 mmol, previously washed with hexane) in THF (5 ml) at 0 °C under nitrogen, was added a solution of diketo ester (**9**) (2.5 g, 13.6 mmol) in THF (60 ml). The mixture was stirred at room temperature for 15 min after which the vinylphosphonium salt (**4**) (7.3 g, 13.9 mmol) was added. After the mixture had been stirred at room temperature for 20 min it was refluxed for 1 h. The THF was removed on the rotary evaporator and the residue was partitioned between ether and 2M-HCl. The aqueous layer was extracted with ether–ethyl acetate and the combined organic extracts were washed with water and brine. Drying ($MgSO_4$) and solvent removal gave an oil which was chromatographed with ethyl acetate–light petroleum (20:80) to give the product (**6**) as a white solid (3.40 g, 83%), m.p. 79—81 °C (Found: C, 67.5; H, 6.05; S, 10.35. $C_{17}H_{18}O_3S$ requires C, 67.52; H, 6.00; S, 10.61%); $\nu_{max.}$(KBr) 1 750, 1 715, 1 635w, and 1 580w cm^{-1}; δ_H 1.88 (3 H, s, MeC=C), 2.12—2.58 (4 H, series of m), 2.75 (1 H, d, *J* 20 Hz, AB system), 3.08 (1 H, d, *J* 20 Hz, AB system), 3.68 (4 H, s, OMe and allylic CH), and 7.15—7.33 (5 H, m, SPh); δ_C 13.1(q), 23.2(t), 36.0(t), 42.9(t), 52.5(q), 57.1(d), 63.2(s), 126.8(d), 127.4(s), 129.0(d), 130.4(d), 133.7(s), 141.0(s), 170.4(s), and 215.0(s).

Methyl 4-*Methyl*-3-*methylthio*-8-*oxobicyclo*[3.3.0]*oct*-3-*ene*-1-*carboxylate* (**5**).—Treatment of diketo ester (**9**) (3 g, 16.3 mmol) with sodium hydride (60% dispersion in mineral oil; 716 mg, 17.9 mmol) and the vinylphosphonium salt (**3**) (7.25 g, 19.56 mmol) in a similar manner to that described above, followed by work-up and column chromatography with ethyl acetate–light petroleum (30:70) gave the product (**5**) as an oil (3.78 g, 97%) (Found: C, 60.15; H, 6.8. $C_{12}H_{16}O_3S$ requires C, 59.99; H, 6.75%); $\nu_{max.}$ 1 745, 1 722, and 1 620w cm^{-1}; δ_H 1.60—1.78 (3 H, m, MeC=C), 2.00—2.58 (4 H, series of m), 2.23 (3 H, s, SMe), 2.72—3.38 (2 H, series of m, allylic CH_2), 3.50—3.70 (1 H, broad unresolved signal, allylic CH), and 3.72 (3 H, s, OMe); δ_C 12.6(q), 14.4(q), 23.1(t), 35.8(t), 42.0(t), 52.6(q), 57.2(d), 63.2(s), 129.2(s), 133.8(s), 170.5(s), and 215.9(s); *m/z* 240 (M^+), 181 ($M - CO_2Me$).

6-*Methyl*-7-*phenylthiobicyclo*[3.3.0]*oct*-6-*en*-2-*one* (**18**).—Finely powdered sodium cyanide (0.665 g, 13.6 mmol) was dissolved in HMPA (60 ml) at 75 °C under nitrogen. The β-keto ester (**6**) (2 g, 6.6 mmol) in HMPA (15 ml) was added dropwise to the stirred solution. After completion of the addition, stirring was continued at 75 °C for 1 h. The mixture was cooled and poured into 2M-HCl (300 ml) and extracted with carbon tetrachloride. The combined extracts were thorougly washed with 2M-NaOH (×2), to reverse any cyanohydrin formation, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (10:90) gave the product (**18**) as a colourless oil (1.27 g, 79%) (Found: C, 73.4; H, 6.7. $C_{15}H_{16}OS$ requires C, 73.73; H, 6.60%); $\nu_{max.}$ 3 060, 1 740, 1 627w, and 1 585 cm^{-1}; δ_H 1.89 (3 H, s, MeC=C), 2.02—2.38 (4 H, series of m), 2.50—2.73 (3 H, m, allylic CH_2 and angular CH), 3.47 (1 H, br s, allylic C*H*), and 7.10—7.30 (5 H, m, SPh).

6-*Methyl*-7-*methylthiobicyclo*[3.3.0]*oct*-6-*en*-2-*one* (**17**).—Treatment of the keto ester (**5**) (3.78 g, 15.7 mmol) with sodium cyanide (1.54 g, 31.5 mmol) in a manner similar to that above, followed by work-up and column chromatography with ethyl acetate–light petroleum (25:75) gave the product (**17**) as a colourless oil (2.37 g, 82%) (Found: C, 66.1; H, 7.85. $C_{10}H_{14}OS$ requires C, 65.89; H, 7.74%; $\nu_{max.}$ 1 730, 1 615w cm^{-1}; δ_H 1.82 (3 H, s, MeC=C), 1.94—2.16 (4 H, m), 2.19 (3 H, s, SMe), 2.60—2.82 (3 H, m, allylic CH_2 and angular CH), and 3.25—3.55 (1 H, broad unresolved signal, allylic C*H*).

exo-2,6-*Dimethyl*-7-*phenylthiobicyclo*[3.3.0]*oct*-6-*en*-endo-2-*ol* (**20**).—The ketone (**18**) (400 mg, 1.64 mmol) was dissolved in dry ether (8 ml) and cooled to −78 °C under nitrogen. Methyllithium (1.6M solution in diethyl ether; 2.1 ml, 3.28 mmol) was added. The mixture was stirred for 10 min at −78 °C after which i.r. analysis indicated that the reaction had gone to completion (disappearance of C=O stretch). The reaction mixture was poured into 2M-HCl and extracted with ether. The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate dried ($MgSO_4$), and evaporated to give pure product (**20**) as a slightly yellow oil (356 mg, 84%); $\nu_{max.}$ 3 500, 1 640w, and 1 595 cm^{-1}; δ_H 1.28 (3 H, s, MeCOH), 1.40—2.10 (8 H, series of m), 2.40—2.55 (3 H, m), 3.20 (1 H, broad unresolved signal, allylic CH), and 7.10—7.35 (5 H, m, SPh).

exo-2,6-*Dimethyl*-7-*methylthiobicyclo*[3.3.0]*oct*-6-*en*-endo-2-*ol* (**19**).—Treatment of the ketone (**17**) (154 mg, 0.82 mmol) with methyl-lithium (1.6M solution in diethyl ether; 1.54 ml, 2.46 mmol) in a similar manner to that above, followed by work-up and column chromatography with ethyl acetate–light petroleum (10:90) gave the product (**19**) as a colourless oil (122 mg, 75%) (Found: C, 66.3; H, 9.4. $C_{11}H_{18}OS$ requires C, 66.63; H, 9.15%); $\nu_{max.}$ 3 440 and 1 625w cm^{-1}; δ_H 1.29 (3 H, s, MeCOH), 1.40—2.0 (8 H, series of m), 2.10—2.70 (3 H, series of m), 2.28 (3 H, s, SMe), and 3.10 (1 H, broad unresolved signal, allylic C*H*).

endo-6-*Hydroxy*-exo-2,exo-6-*dimethylbicyclo*[3.3.0]*octan*-3-*one* (**16**).—Mercuric chloride (413 mg, 1.52 mmol) in acetonitrile–water (3:1, 3 ml) was added to a solution of the alcohol (**19**) (100 mg, 0.51 mmol) in the same solvent (3 ml). The mixture was refluxed for 1 h, cooled, and filtered through HiFlo Supercel. The filter aid was washed thoroughly with ether and the combined filtrate and washings were poured into a separating funnel containing aqueous sodium sulphide. The aqueous layer was extracted with ether and the combined extracts were washed with water and dried ($MgSO_4$). Solvent removal and column chromatography with ethyl acetate–light petroleum (20:80) gave the product (**16**) as white crystals (59 mg, 69%), m.p. 57.5—58.5 °C (lit.,[16] 58—59 °C); $\nu_{max.}$(KBr) 3 500 and 1 735 cm^{-1}; δ_H 1.05 (3 H, d, *J* 8 Hz, MeCC=O), 1.32 (3 H, s, *Me*COH), 1.55 (1 H, br s, OH), and 1.70—2.50 (9 H, series of m).

6-*Methyl*-7-*phenylthiobicyclo*[3.3.0]*octa*-3,6-*dien*-2-*one* (**23**).—To a solution of the ketone (**18**) (500 mg, 2.05 mmol) in dry dichloromethane (8 ml) was added freshly distilled trimethylsilyl chloride (0.39 ml, 3.08 mmol) and 1,8-diazabicyclo-[5.4.0]undec-7-ene (0.52 ml, 3.49 mmol). The mixture was refluxed for 1.5 h under nitrogen, cooled, and diluted with pentane (10 ml). The organic solution was washed with 1% aqueous HCl and saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated to give the crude silyl enol ether (630 mg). To a solution of the crude ether (630 mg, 2 mmol) in dry acetonitrile under nitrogen was added palladium acetate (225 mg, 1 mmol) and *p*-benzoquinone (109 mg, 1 mmol). The reaction mixture was left overnight at room temperature, filtered, and evaporated. Column chromatography with diethyl ether–light petroleum (4:96) gave the product (**23**) as a pale yellow oil (496 mg, 69%) (Found: C, 74.25; H, 6.0. $C_{15}H_{14}OS$ requires C, 74.34; H, 5.82%); $\nu_{max.}$ 3 110w, 1 720, 1 645w, and 1 595 cm^{-1}; δ_H 1.97 (3 H, s, MeC=C), 2.45—3.15 (3 H, m, allylic CH_2 and angular CH), 3.92 (1 H, br s, allylic C*H*), 6.15 (1 H, dd, *J* 6 Hz, 2 Hz), 7.22 (5 H, s, SPh), and 7.85 (1 H, dd, *J* 6 Hz, 3 Hz).

6-(1,3-*Dithian*-2-*ylidene*-2-*methyl*-3-*phenylthiobicyclo*[3.3.0]-*octa*-2,7-*diene* (**27**).—A solution of 2-trimethylsilyl-1,3-dithiane (85 mg, 0.43 mmol) in THF (2 ml) was cooled to 0 °C under

nitrogen and treated with butyl-lithium (1.48M solution in hexane; 0.31 ml, 0.45 mmol). The mixture was stirred at 0 °C for 15 min after which it was diluted with dry hexane (3.5 ml) and cooled to −78 °C. The enone (**22**) (100 mg, 0.41 mmol) in hexane–THF (1.8:1; 3 ml) was added, and stirring was continued at −78 °C for 2 h. Saturated brine was added to the reaction mixture and it was then extracted with ether. The extract was dried ($MgSO_4$), evaporated, and the residue subjected to column chromatography with light petroleum to give the product (**27**) as a white solid (83 mg, 58%) which turned brown after a few days at room temperature; $\nu_{max.}$(KBr) 1 645 and 1 585 cm^{-1}; δ_H 1.90 (3 H, br s, MeC=C), 2.00—2.50 (2 H, m), 2.35—2.50 (1 H, m), 2.70—3.20 (5 H, series of m), 3.45—3.80 (1 H, m), 3.80—4.05 (1 H, m), 6.27 (1 H, dd, *J* 6 Hz, 2.5 Hz), 6.55 (1 H, dd, *J* 6 Hz, 2 Hz), and 7.20 (5 H, s, SPh).

6-*Methyl*-7-*methylthiobicyclo*[3.3.0]*octa*-2,6-*diene*-2-*carbonitrile* (**29**).—A solution of the ketone (**17**) (495 mg, 2.69 mmol) in ethanol (10 ml) was cooled in ice and treated with powdered sodium cyanide (784 mg, 16 mmol) and acetic acid (0.5 ml). The mixture was stirred at 0 °C for 30 min and then at 40—50 °C for 4 h. Concentrated HCl (3 drops) was added to the reaction mixture which was then left for 10 min. The mixture was then diluted with water extracted with ether; the extracts were washed with dilute HCl, dried ($MgSO_4$), and evaporated to give the crude cyanohydrin which was used directly in the next stage.

The crude cyanohydrin mixture from above was dissolved in pyridine (5 ml) and treated with $POCl_3$ (1 ml). The mixture was stirred at 50 °C for 3 h, cooled, and poured into ice–water containing concentrated HCl. The aqueous mixture was extracted with ether and the extract washed successively with water, saturated aqueous sodium hydrogen carbonate, and brine. It was then dried ($MgSO_4$) and evaporated to give a brown oil. Column chromatography with ethyl acetate–light petroleum (5:95) gave the product (**29**) as a white solid (358 mg, 69%), m.p. 68—70.5 °C (ether) (Found: C, 69.3; H, 6.8; N, 7.3. $C_{11}H_{13}NS$ requires C, 69.06; H, 6.85; N, 7.32%); $\nu_{max.}$(KBr) 2 220, 1 633, and 1 617 cm^{-1}; δ_H 1.68 (3 H, br s, MeC=C), 2.12 (3 H, s, SMe), 2.45—2.90 (4 H, series of m, allylic CH_2's), 3.20—3.65 (2 H, broad unresolved signal, angular CH's), and 6.50 (1 H, m, vinyl C*H*).

Methyl exo-6-*Methyl*-7-*oxobicylo*[3.3.0]*oct*-2-*ene*-2-*carboxylate* (**30**).—To a solution of the nitrile (**29**) (358 mg, 1.87 mmol) in methanol (5 ml) was added concentrated H_2SO_4 (2 ml). The mixture was refluxed for 8 h, cooled, poured into water, and extracted with ether. Washing of the combined organic extracts with saturated aqueous sodium hydrogen carbonate, drying ($MgSO_4$), and solvent removal gave the crude product. Column chromatography of this with ethyl acetate–light petroleum (10:90) gave the product (**30**) as an oil (175 mg, 48%) [Found: *m/z* 194.0950 (M^+). $C_{11}H_{14}O_3$ requires 194.0943]; $\nu_{max.}$ 1 740, 1 715, and 1 630 cm^{-1}; δ_H 1.10 (3 H, d, *J* 6 Hz, MeCCO), 1.75—2.20 (1 H, m), 2.25—3.10 (5 H, series of m), 3.50 (1 H, broad unresolved signal), 3.75 (3 H, s, OMe), and 6.80 (1 H, m, vinyl CH).

Methyl 7-endo-*Hydroxy*-6-exo-*methylbicyclo*[3.3.0]*oct*-2-*ene*-2-*carboxylate* (**31**).—A solution of ketone (**30**) (610 mg, 3.14 mmol) in methanol (10 ml) was cooled in an ice–salt bath and sodium borohydride (178 mg, 4.72 mmol) was added. After the reaction mixture had been stirred for 10 min it was poured into ether–2M-HCl and extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (20:80) gave the product (**31**) as a colourless oil (505 mg, 82%) (Found: C, 67.05; H, 8.5. $C_{11}H_{16}O_3$ requires C, 67.32; H, 8.22%); $\nu_{max.}$ 3 450, 1 710, and 1 630 cm^{-1}; δ_H 1.06 (3 H, d, *J* 6 Hz, Me), 1.15—1.65 (2 H, m), 1.95 (1 H, s, O*H*), 2.00—2.95 (4 H, series of m), 3.00—3.35 (1 H, m), 3.45—3.85 (1 H, m), 3.73 (3 H, s, OMe), and 6.65 (1 H, vinyl C*H*).

6-*Methoxycarbonyl*-exo-2-*methylbicyclo*[3.3.0]*oct*-6-*en*-exo-3-*yl Acetate* (**32**).—To a solution of alcohol (**31**) (409 mg, 2.09 mmol) in pyridine (5 ml) was added methanesulphonyl chloride (0.244 ml, 3.13 mmol). The mixture was stirred at room temperature for 1 h and poured into ether–0.5M-HCl. The aqueous layer was extracted with ether and the combined extracts were washed with 0.5M-HCl (×3) and brine, dried ($MgSO_4$), and evaporated to give the crude mesylate (539 mg) which was used directly in the next stage.

To a solution of the crude mesylate (539 mg, 1.97 mmol) in dry acetone (10 ml) under nitrogen was added tetrabutylammonium acetate (1.8 g, 6 mmol), and the mixture was refluxed overnight. The acetone was removed on a rotary evaporator and the residue was partitioned between ether and water. The aqueous layer was extracted with ether, and the combined extracts were washed successively with water and brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (5:95) gave the product (**32**) as a colourless oil (368 mg, 74%) (Found: C, 65.7; H, 8.0. $C_{13}H_{18}O_4$ requires C, 65.53; H, 7.61%); $\nu_{max.}$ 1 740, 1 720, and 1 635 cm^{-1}; δ_H 0.98 (3 H, d, *J* 7 Hz, Me), 1.45—2.90 (6 H, series of m), 2.05 (3 H, s, MeC=O), 3.30—3.60 (1 H, m), 3.72 (3 H, s, OMe), 5.02 (1 H, m, C*H*OAc), and 6.64 (1 H, m, vinyl CH).

6-*Methoxycarbonyl*-exo-2-*methylbicyclo*[3.3.0]*oct*-7-*en*-exo-3-*yl Acetate* (**22**).—A solution of di-isopropylamine (187 mg, 0.259 ml, 1.85 mmol) in THF (5 ml) was cooled to 0 °C under nitrogen and treated with butyl-lithium (1.28 ml of a 1.44M solution in hexane, 1.85 mmol). After being stirred at 0 °C for 15 min the mixture was cooled to −78 °C and added *via* a cannula to a solution of the ester (**32**) (110 mg, 0.46 mmol) and HMPA (331 mg, 0.332 ml, 1.85 mmol) in THF (3 ml) also maintained at −78 °C. The resulting yellow solution was stirred at −78 °C for 10 min and quenched by addition of methanol (1 ml) and stirring for a further 15 min at −78 °C. The reaction mixture was poured into water and extracted with ether. The organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (5:95) gave the product (**22**) as an oil (43 mg, 39%), a 1:5 mixture of starting material:product. Data for product: $\nu_{max.}$ 1 740 and 1 640 cm^{-1}; δ_H 0.99 (3 H, d, *J* 7 Hz, Me), 1.35—2.30 (3 H, series of m), 2.02 (3 H, s, MeC=O), 2.70—2.90 (3 H, series of m), 3.68 (3 H, s,OMe), 5.13 (1 H, q, C*H*OAc), 5.62 (1 H, m), and 5.81 (1 H, m).

Methyl 4,7,7-*Trimethyl*-8-*oxo*-3-*phenylthiobicyclo*[3.3.0]*oct*-3-*ene*-1-*carboxylate*.—To a stirred suspension of potassium t-butoxide (3.42 g, 30.5 mmol) in THF (20 ml) at −78 °C under nitrogen was added a solution of the ketone (**6**) (4 g, 13.3 mmol) in THF (60 ml). The deep yellow solution was stirred at −78 °C for 10 min, after which time iodomethane (18.5 g, 130 mmol) was added *via* a syringe, and stirring continued at 0 °C for 1 h. The reaction mixture was poured into a separating funnel containing ether–saturated aqueous ammonium chloride. The ether layer was separated, dried ($MgSO_4$), and evaporated to give the crude product which by column chromatography with ethyl acetate–light petroleum (5:95) as eluant provided the product as a colourless oil (3.62 g, 83%) [Found: *m/z* 330.1279 (M^+). $C_{19}H_{22}O_3S$ requires 330.1289]; $\nu_{max.}$ 1 740, 1 730, and 1 587 cm^{-1}; δ_H 1.04 (3 H, s, Me), 1.19 (3 H, s, Me), 1.87 (3 H, br s, MeC=C), 2.00—2.42 (2 H, m), 2.57—3.26 (2 H, m), 3.40—3.65 (1 H, m, allylic CH), 3.69 (3 H, s, OMe), and 7.22 (5 H, s, SPh).

3,3,6-*Trimethyl*-7-*phenylthiobicyclo*[3.3.0]*oct*-6-*en*-2-*one*.—To a stirred solution of powdered sodium cyanide (1.47 g, 30 mmol) in HMPA (120 ml) at 75 °C under nitrogen was added a solution of methyl 4,7,7-trimethyl-8-oxo-3-phenylthiobicyclo[3.3.0]oct-3-ene-1-carboxylate (4.67 g, 14.2 mmol) in HMPA (30 ml). The mixture was stirred at 75 °C for 2 h, cooled, and poured into a separating funnel containing 2M-HCl (500 ml). The product was extracted into carbon tetrachloride and the organic extracts were thoroughly washed with 2M-sodium hydroxide (×2), dried ($MgSO_4$), and evaporated. The residue subjected to column chromatography with ethyl acetate–light petroleum (10:90) gave the product as an oil (3.31 g, 86%) [Found: *m/z* 272.1228 (M^+). $C_{17}H_{20}OS$ requires 272.1235]; $\nu_{max.}$ 1 730 and 1 580w cm^{-1}; δ_H 1.02 (3 H, s, Me), 1.10 (3 H, s, Me), 1.75—2.10 (5 H, m, MeC=C at 1.87), 2.50—3.10 (3 H, series of m), 3.14—3.55 (1 H, br unresolved signal, allylic CH), and 5.21 (5 H, s, SPh).

2,7,7-*Trimethyl*-3-*phenylthiobicyclo*[3.3.0]*oct*-2-*ene* (**33**).—3,3,6-Trimethyl-7-phenylthiobicyclo[3.3.0]oct-6-en-2-one (3.20 g, 11.8 mmol), potassium hydroxide (1.99 g, 35.4 mmol), and hydrazine hydrate (1.18 g, 23.6 mmol) were refluxed together in diethylene glycol (20 ml). After 1 h the condenser was removed and the reaction temperature was allowed to reach 200 °C. Refluxing was continued for a further 3 h. The cooled reaction mixture was acidified with concentrated HCl and extracted with benzene. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (10:90) gave the product (**33**) as a colourless oil (2.85 g, 94%) (Found: C, 78.85; H, 8.6. $C_{17}H_{22}S$ requires C, 79.01; H, 8.58%); $\nu_{max.}$ 1 590, 1 475, and 1 450 cm^{-1}; δ_H 0.98 (3 H, s, Me), 1.05 (3 H, s, Me), 1.0—2.30 (8 H, series of m), MeC=C at 1.80, 2.49—2.90 (2 H, m), 2.95—3.40 (1 H, m, allylic CH), and 7.22 (5 H, s, SPh).

2,7,7-*Trimethyl*-3-*phenylsulphonylbicyclo*[3.3.0]*oct*-2-ene (**34**).—To a stirred solution of the sulphide (**33**) (2.77 g, 10.7 mmol) in dichloromethane (80 ml) at −78 °C was added *m*-chloroperbenzoic acid (95%, 4.88 g, 26.8 mmol). The reaction mixture was stirred at −78 °C for 15 min and at 0 °C for 2 h, and was then poured into a separating funnel containing 10% aqueous sodium sulphite. The aqueous layer was extracted with ether, and the combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (20:80) gave the product (**34**) as a colourless oil (3.05 g, 98%) (Found: C, 70.4; H, 7.75; $C_{17}H_{22}O_2S$ requires C, 70.30; H, 7.64%); $\nu_{max.}$ 1 630, 1 304, and 1 150 cm^{-1}; δ_H 0.90 (3 H, s, Me), 0.98 (3 H, s, Me), 1.0—1.90 (4 H, series of m), 2.12 (3 H, br s, MeC=C), 2.20—2.90 (3 H, series of m), 3.0—3.35 (1 H, m, allylic CH), and 7.40—7.97 (5 H, m, SO_2Ph).

3-(3-*Bromopropyl*)-7,7-*dimethyl*-2-*methylene*-3-*phenylsulphonylbicyclo*[3.3.9]*octane* (**36**).—To a solution of the vinyl sulphone (**34**) (0.500 g, 1.72 mmol) in THF (10 ml) at −78 °C under nitrogen was added butyl-lithium (1.57M solution in hexane; 1.21 ml, 1.90 mmol). The deep orange anion was stirred at −78 °C for 15 min and 1,3-dibromopropane (695 mg, 0.35 ml, 3.44 mmol) was added *via* a syringe. The mixture was stirred at −78 °C for 2 h and poured into a separating funnel containing saturated aqueous ammonium chloride and ether. The aqueous layer was extracted with ether and the combined organic layers were dried ($MgSO_4$) and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (10:90) as eluant gave the product (**36**) as a white solid (588 mg, 83%) which appeared to be a 7:1 mixture of isomers by n.m.r., m.p. 85—87 °C (ether) (Found: C, 58.5; H, 6.75. $C_{20}H_{27}BrO_2S$ requires C, 58.38; H, 6.62%); $\nu_{max.}$(KBr) 1 643w, 1 583w, 1 290, and 1 138 cm^{-1}; δ_H 0.86 (6 H, s, Me), 0.60—2.80 (11 H, series of m), 2.90—3.30 (1 H, m, allylic CH), 3.37 (2 H, t, *J* 5 Hz, CH_2Br), 5.23 (1 H, d, *J* 2 Hz, vinyl CH), 5.50 (1 H, d, *J* 2 Hz, vinyl CH), 7.35—8.05 (5 H, m, SO_2Ph), and small signals at 4.74 and 5.16 for vinyl CH of minor isomer.

3-(3-*Iodopropyl*)-7,7-*dimethyl*-2-*methylene*-3-*phenylsulphonylbicyclo*[3.3.0]*octane*.—The bromide (**36**), (350 mg, 0.852 mmol) and sodium iodide (645 mg, 4.3 mmol) were refluxed in dry acetone (6 ml) for 2.5 h. The acetone was removed on the rotary evaporator and the residue was partitioned between ether and water. The aqueous layer was extracted with ether and the combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (10:90) as eluant gave the iodide as a white solid (337 mg, 86%), which appeared to be a 7:1 mixture of isomers by n.m.r., m.p. 103—104 °C (ether) (Found: C, 52.55; H, 5.95. $C_{20}H_{27}IO_2S$ requires C, 52.40; H, 5.94%); $\nu_{max.}$(KBr) 1 635w, 1 575w, 1 289, and 1 132 cm^{-1}; δ_H 0.60—2.90 (18 H, series of m, gem Me at 0.85), 3.15 (2 H, t, *J* 5 Hz, CH_2I), 5.25 (1 H, d, *J* 1 Hz, vinyl CH), 5.51 (1 H, d, *J* 1 Hz, vinyl CH), 7.35—8.00 (5 H, m, SO_2Ph), and small signals at 4.70 and 5.15 for vinyl CH of minor isomer.

7,7-*Dimethyl*-2-*methylene*-3-(3-*nitropropyl*)-3-*phenylsulphonylbicyclo*[3.3.0]*octane* (**37**).—The above iodide (336 mg, 0.734 mmol) in dry ether (5 ml) was added dropwise to a stirred suspension of silver nitrite (282 mg, 1.83 mmol) in ether (3 ml) at 0 °C in a flask which was protected from the light. The mixture was stirred at 0 °C for 16 h, and at room temperature for 2 days; further silver nitrite (141 mg, 0.91 mmol) was then added. Stirring of the mixture was continued for a further 3 days at room temperature, after which it was filtered and evaporated to give the crude product. Column chromatography of the latter with ethyl acetate–light petroleum (20:80) gave the product (**37**) as two isomers, major (low R_F, 90 mg, 33%) and minor (high R_F, 11 mg, 4%); $\nu_{max.}$ major isomer 1 555, 1 450, 1 390, 1 370, 1 310, and 1 148 cm^{-1}; minor isomer 1 558, 1 455, 1 390, 1 375, 1 300, and 1 145 cm^{-1}; δ_H for mixture; 0.84 (6 H, s, gem Me), 0.60—3.40 (12 H, series of m), 4.39 (2 H, t, *J* 3 Hz, CH_2NO_2), 5.26 (1 H, d, *J* 1 Hz, vinyl CH), 5.55 (1 H, d, *J* 1 Hz, vinyl CH), 7.40—8.00 (5 H, m, SO_2Ph), and small signals at 4.75 and 5.15 for vinyl CH of minor isomer.

3-(7,7-*Dimethyl*-2-*methylene*-3(*phenylsulphonylbicyclo*-[3.3.0]*octan*-3-*yl*)*propanal Ethylene Acetal* (**40**).—To a solution of vinyl sulphone (**34**) (843 mg, 2.91 mmol) in THF (15 ml) at −78 °C under nitrogen was added butyl-lithium (1.58M solution in hexane; 2.03 ml, 3.20 mmol). The deep orange solution was stirred at −78 °C for 15 min and then quenched with 2-(2-iodoethyl)-1,3-dioxolane (1.06 g, 4.66 mmol) in THF (5 ml). The reaction mixture was stirred at −78 °C for 1.5 h after which it was poured into a separating funnel containing ether-saturated aqueous ammonium chloride. The aqueous layer was extracted with ether and the combined organic layers were dried ($MgSO_4$) and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (20:80) as eluant gave the product (**40**) as a white solid (873 mg, 77%), m.p. 121.5—122 °C (ether) (Found: C, 67.85; H, 7.9. $C_{22}H_{30}O_4S$ requires C, 67.78; H, 7.74%); $\nu_{max.}$(KBr) 1 640w, 1 585w, 1 285, and 1 138 cm^{-1}; δ_H 0.89 (6 H, s, Me), 0.60—1.95 (6 H, series of m), 1.95—2.78 (5 H, series of m), 2.85—3.40 (1 H, m, allylic CH), 3.70—4.05 (4 H, m, OCH_2CH_2O), 4.84 (1 H, t, *J* 4 Hz, OCHO), 5.25 (1 H, s, vinyl CH), 5.51 (1 H, s, vinyl CH), and 7.32—8.10 (5 H, m, SO_2Ph).

3-(2,7,7-*Trimethylbicyclo*[3.3.0]*oct*-2-*en*-3-*yl*)*propanal Ethylene Acetal* (**42**).—To a mixture of sulphone (**40**) (820 mg, 2.1 mmol) and disodium hydrogen phosphate (1.21 g, 8.5 mmol) in dry methanol (20 ml) at 0 °C was added 6% sodium amalgam (4.2 g). The mixture was stirred at 0 °C for 1.5 h after which more 6% sodium amalgam (2.5 g) was added, and stirring continued at 0 °C for a further 1.5 h. The reaction mixture was poured into water, extracted with ether and the combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (10:90) gave the product (**42**) as a colourless oil (476 mg, 90%) (Found: C, 76.7; H, 10.5; $C_{16}H_{26}O_2$ requires C, 76.75; H, 10.47%); $\nu_{max.}$ 2 950, 2 860, and 1 135 cm^{-1}; δ_H 0.92 (3 H, s, Me), 1.02 (3 H, s, Me), 0.75—1.20 (2 H, m), 1.55 (3 H, br s, MeC=C), 1.40—1.92 (4 H, series of m), 1.92—2.26 (3 H, series of m), 2.30—2.80 (2 H, m), 2.82—3.25 (1 H, m, allylic CH), 3.75—4.05 (4 H, m, OCH_2CH_2O), and 4.83 (1 H, t, *J* 5 Hz, OCHO).

3-(2,7,7-*Trimethylbicyclo*[3.3.0]*oct*-2-*en*-3-*yl*)*propanal* (**43**).—The acetal (**42**) (538 mg, 2.14 mmol), pyridinium toluene-*p*-sulphonate (320 mg, 1.28 mmol), and water (2 ml) were refluxed together in acetone (10 ml) for 40 h. The acetone was removed on the rotary evaporator and the residue was dissolved in ether and the solution washed with saturated aqueous sodium hydrogen carbonate. The ether layer was dried ($MgSO_4$) and evaporated and the residue subjected to column chromatography with ether–light petroleum (3:97) as eluant to give the product (**43**) as a sweet smelling oil (334 mg, 75%), together with recovered starting material (48 mg); yield based on recovered starting material 83%; $\nu_{max.}$ 2 930, 2 850, 2 710, and 1 722 cm^{-1}; δ_H 0.92 (3 H, s, Me), 1.00 (3 H, s, Me), 0.80—1.32 (2 H, m), 1.54 (3 H, br s, MeC=C), 1.50—1.90 (2 H, m), 1.92—2.13 (1 H, m), 2.15—2.80 (6 H, series of m), 2.85—3.28 (1 H, m, allylic C*H*), and 9.75 (1 H, s, C*H*O).

5-*Iodopent*-2-*yne*.—A mixture of pent-3-yn-1-ol (2 g, 23.8 mmol) and triethylamine (4.33 g, 6.0 ml, 42.8 mmol) in dry dichloromethane (100 ml) was cooled in an ice–salt bath and treated dropwise with methanesulphonyl chloride (3.28 g, 2.23 ml, 28.6 mmol). After being stirred at −10 °C for 2 h the reaction mixture was washed successively with ice–water, cold 2M-HCl, saturated aqueous sodium hydrogen carbonate, and brine. The organic layer was dried ($MgSO_4$) and evaporated to give the crude pent-3-ynyl mesylate (3.74 g). To a solution of the crude mesylate (3.74 g, 23.1 mmol) in dry acetone (40 ml) was added sodium iodide (10.8 g, 72 mmol). The mixture was stirred overnight at room temperature, refluxed for 2 h, and then evaporated on a rotary evaporator; the residue was then partitioned between ether and water. The aqueous layer was extracted with ether and the combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ether–light petroleum (10:90) gave the product as an oil (3.44 g, 75%); $\nu_{max.}$ 1 438, 1 255, and 1 177 cm^{-1}; δ_H 1.79 (3 H, t, *J* 3 Hz, Me), 2.50—2.90 (2 H, m), and 3.20 (2 H, t, *J* 6 Hz).

7,7-*Dimethyl*-2-*methylene*-3-*pent*-3-*ynyl*-3-*phenylsulphonylbicyclo*[3.3.0]*octane* (**44**).—To a solution of the vinyl sulphone (**34**) (779 mg, 2.69 mmol) in THF (10 ml) at −78 °C under nitrogen was added butyl-lithium (1.60M solution in hexane; 1.85 ml, 2.95 mmol). The orange–red solution was stirred at −78 °C for 15 min after which 5-iodopent-2-yne (784 mg, 4.04 mmol) in THF (5 ml) was added *via* a cannula. After being stirred at −78 °C for 1.5 h the reaction mixture was poured into saturated aqueous ammonium chloride. The aqueous layer was extracted with ether and the combined organic extracts were dried ($MgSO_4$) and evaporated. Column chromatography of the residue with ether–light petroleum (15:85) gave the product (**44**) as a white solid (678 mg, 72%) which appeared to be a 5:1 mixture of isomers from n.m.r.; m.p. 92—94 °C (ether) (Found: C, 74.05; H, 8.05. $C_{12}H_{28}O_2S$ requires C, 74.12; H, 7.92%); $\nu_{max.}$(KBr) 1 640w, 1 585w, 1 290, and 1 144 cm^{-1}; δ_H 0.88 (6 H, s, Me), 0.65—1.90 (9 H, series of m, MeC=C at 1.75), 1.95—3.40 (6 H, series of m, sharp signal at 2.21), 5.24 (1 H, d, *J* 1 Hz, vinyl CH), 5.48 (1 H, d, *J* 1 Hz, vinyl CH), 4.43, 5.65 (small doublets, vinyl CH's of minor isomer), and 7.35—8.00 (5 H, m, SO_2Ph).

2,7,7-*Trimethyl*-3-*pent*-3-*ynylbicyclo*[3.3.0]*oct*-2-*ene* (**45**).—To a mixture of sulphone (**44**) (475 mg, 1.33 mol) and disodium hydrogen phosphate (758 mg, 5.34 mmol) in dry methanol (10 ml) at 0 °C was added 6% sodium amalgam (4.0 g). The mixture was stirred at 0 °C for 1.5 h and then poured carefully into water. The product was extracted into ether and the combined ether extracts were washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ethyl acetate–light petroleum (5:95) as eluant gave the product (**45**) as a clear oil (250 mg, 87%) (Found: C, 89.15; H, 11.2. $C_{16}H_{24}$ requires C, 88.82; H, 11.18%); $\nu_{max.}$ 2 920, 2 825, 1 573, and 1 440 cm^{-1}; δ_H 0.92 (3 H, s, Me), 1.01 (3 H, s, Me), 0.70—1.34 (2 H, m), 1.55 (3 H, s, MeC=C), 1.76 (3 H, s, MeC=C), 1.50—1.93 (2 H, m), and 1.95—3.35 (8 H, series of m, sharp signal at 2.17); δ_C 3.4, 12.4, 17.4, 27.5, 28.3, 29.0, 38.7, 40.8, 41.7, 46.1, 49.8, 55.4, 75.3, 79.3, 130.9, and 135.8.

1-(2,10,10-*Trimethyl*-cis,anti,cis-*tricyclo*[6.3.3.0^{2,6}]*undecan*-3-*ylidene*)*ethyl Formate* (**46**).—The acetylene (**45**) (81 mg, 0.037 mmol) was vigorously stirred with dry formic acid (1 ml) (2 phase system) at 50 °C for 16 h. The cooled reaction mixture was poured into ether–water and the aqueous layer was extracted with ether. The combined ether extracts were dried ($MgSO_4$) and evaporated. Column chromatography of the residue with ether–light petroleum (5:95) gave the enol formate (**46**) as an oil (55 mg, 56%) (Found: C, 77.9; H, 10.15. $C_{17}H_{26}O_2$ requires C, 77.81; H, 99.9%); $\nu_{max.}$ 2 970, 2 890, 1 760, 1 740, and 1 700 cm^{-1}; δ_H 0.70—2.90 (25 H, series of m, sharp signals at 0.94, 1.07, 1.12, 1.52, and 1.93), and 8.00 (1 H, s, OCHO).

2,10,10-*Trimethyl*-cis,anti,cis-*tricyclo*[6.3.3.0^{2,6}]*undecan*-3-*one* (**49**).—To a stirred suspension of $RuO_2 \cdot xH_2O$ (Aldrich, 0.2 g), in carbon tetrachloride (25 ml) at 0 °C was added sodium periodate (1.6 g) in water (25 ml). After being stirred at 0 °C for 1 h the mixture was filtered into a separating funnel and the aqueous layer was discarded. The yellow CCl_4 layer, containing the ruthenium tetraoxide, was shaken with a fresh solution of sodium periodate (0.5 g) in water (25 ml), and the two phase mixture was stored in the refrigerator.

A stirred solution of enol formate (**46**) (54 mg, 0.21 mmol) in CCl_4 (6 ml) was covered with water (*ca.* 1 ml) and treated with the ruthenium tetraoxide solution (CCl_4 layer) at room temperature until t.l.c. indicated consumption of starting material (*ca.* 10 ml). Excess of ruthenium tetraoxide was destroyed by the addition of a few drops of isopropyl alcohol. The mixture was filtered into a separating funnel and the organic layer was washed with water, dried ($MgSO_4$), and evaporated. Column chromatography of the residue with ether–light petroleum (5:95) gave the product (**49**) as an oil which gradually crystallised (17 mg, 42%), m.p. 42—43 °C (light petroleum) (lit.,[40] 43—44 °C); $\nu_{max.}$ 2 940, 2 860, 1 735, 1 470, and 1 370 cm^{-1}; δ_H 0.90 (3 H, s), 0.93 (3 H, s), 1.03 (3 H, s), 0.84—1.50 (5 H, m), 1.53—1.80 (3 H, m), 1.90—2.60 (4 H, m), and 2.73—2.86 (1 H, m).

Methyl 7-*Nitromethyl*-1,4-*dioxaspiro*[4.4]*nonane*-6-*carboxylate* (**52**).—To a solution of the unsaturated ester (**11**) (2.44 g, 13.3 mmol) in nitromethane (3.5 ml, 66 mmol) was added

tetramethylguanidine (0.340 ml, 2.7 mmol). The deep orange solution was stirred under nitrogen for 3 days at room temperature after which it was acidified to pH 6 with 2M-HCl and extracted with ether. The organic extracts were dried ($MgSO_4$) and evaporated to give the crude product which was purified by column chromatography with ethyl acetate–light petroleum (20:80) as eluant to give the product (**52**) as a colourless oil (2.30 g, 71%) (Found: C, 48.95; H, 6.05; N, 6.15. $C_{10}H_{15}NO_6$ requires C, 48.97; H, 6.17; N, 5.71%); $\nu_{max.}$ 1 740, 1 560, and 1 380 cm^{-1}; δ_H 1.15—2.25 (4 H, series of m), 2.69 (1 H, d, *J* 7 Hz, $CHCO_2Me$), 2.90—3.35 (1 H, m, $CHCH_2NO_2$), 3.62 (3 H, s, OMe), 3.7—3.92 (4 H, m, OCH_2CH_2O), and 4.30 (2 H, d, *J* 7 Hz, CH_2NO_2); *m/z* 245 (M^+), 186 ($M - CO_2Me$); and the *trans* isomer (210 mg, 6%); $\nu_{max.}$ 1 735, 1 560, and 1 380 cm^{-1}; δ_H 1.05—2.30 (4 H, series of m), 2.70—3.00 (1 H, m), 3.05—3.25 (1 H, m), 3.58 (3 H, s), 3.70—3.95 (4 H, m), and 4.0—4.55 (2 H, m).

7-Nitromethyl-1,4-dioxaspiro[4.4]*nonan-6-ylmethanol* (**53**).—A suspension of lithium aluminium hydride (104 mg, 2.75 mmol) in dry ether (5 ml) was stirred at 0 °C under a nitrogen atmosphere and anhydrous aluminium chloride (122 mg, 0.92 mmol) was added. The mixture was stirred at room temperature for 30 min and then cooled to 0 °C. The nitro ester (**52**) (300 mg, 1.22 mmol) in ether (5 ml) was added to the solution dropwise *via* a cannula. Stirring was continued at 0 °C for 30 min after which the reaction mixture was poured into water, and the pH adjusted to 6 with 2M-HCl. The aqueous layer was extracted with ethyl acetate and the combined organic extracts were washed with water and brine, dried ($MgSO_4$) and evaporated to give the crude product. This was purified by column chromatography with ethyl acetate–light petroleum (40:60) as eluant to give the product (**53**) as an oil (227 mg, 85%) (Found: C, 49.95; H, 7.2; N, 6.95. $C_9H_{15}NO_5$ requires C, 49.76; H, 6.95; N, 6.45%); $\nu_{max.}$ 3 500br, 1 562, and 1 395 cm^{-1}; δ_H 1.20—2.25 (5 H, series of m), 2.45—2.90 (2 H, m, OH at 2.67), 3.52 (2 H, d, *J* 5 Hz, CH_2OH), 3.78 (4 H, s, OCH_2CH_2O), and 4.20—4.70 (2 H, m, CH_2NO_2).

7-Nitromethyl-6-tetrahydropyranyloxymethyl-1,4-dioxaspiro[4.4]*nonane* (**54**).—A mixture of the alcohol (**53**) (423 mg, 1.95 mmol), dihydropyran (491 mg, 5.85 mmol), and pyridinium *p*-toluenesulphonate (98 mg, 0.39 mmol) was stirred in dichloromethane (6 ml) for 4 h at room temperature. The mixture was diluted with ether (20 ml), washed once with brine, dried ($MgSO_4$), and then evaporated. Column chromatography of the residue with ethyl acetate–light petroleum–triethylamine (30:70:1) as eluant gave the product (**54**) as an oil (447 mg, 79%) (Found: C, 55.6; H, 7.8; N, 4.85. $C_{14}H_{23}NO_6$ requires C, 55.80; H, 7.69; N, 4.65%); $\nu_{max.}$ 1 720, 1 555, and 1 390 cm^{-1}; δ_H 1.25—1.90 (10 H, series of m), 2.20—2.90 (2 H, m), 3.15—3.80 (8 H, series of m, sharp signal at 3.73), and 4.05—4.90 (3 H, m, CH_2NO_2 and OCHO); *m/z* 301 (M^+), 200.

6-Tetrahydropyranyloxymethyl-1,4-dioxaspiro[4.4]*nonane-7-carboxylic Acid* (**51**).—The nitro compound (**54**) (245 mg, 1 mmol) was added to a vigorously stirred solution of KOH (560 mg, 10 mmol) in water (100 ml). Stirring was continued until the nitro compound had dissolved (*ca.* 1 h) and $MgSO_4$ (5.5 g) in water (15 ml) was then added. The reaction mixture was cooled in ice and treated with potassium permanganate (316 mg, 2 mmol) dissolved in the minimum amount of water. Stirring was continued for a further 5 h at room temperature. The reaction mixture was acidified to pH 6 and extracted with ether. The ether extracts were washed with saturated aqueous sodium hydrogen carbonate. The aqueous layer was reacidified and extracted with ether. The combined organic layers were dried ($MgSO_4$) and evaporated to give (**51**) as a white solid (116 mg, 50%), m.p. 68—70 °C (ether) (lit.,[9] 69—71 °C); $\nu_{max.}$(KBr) 3 050br, 1 735, and 1 710 cm^{-1}; δ_H 1.35—2.25 (10 H, series of m), 2.50—3.00 (2 H, m), 3.25—4.15 (8 H, m, singlet at 3.92), 4.65 (1 H, s), and 9.0 (1 H, br s).

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