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Structural Parallels Between the Cardiotonic Steroids and the *Erythrophleum* Alkaloids - I. Synthesis of Phenanthrenone Precursors to Novel *Erythrophleum* Alkaloid Analogues

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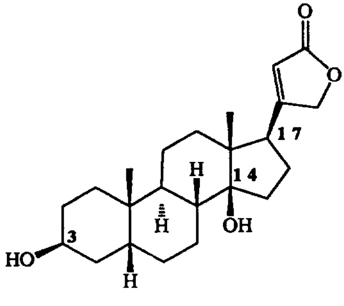
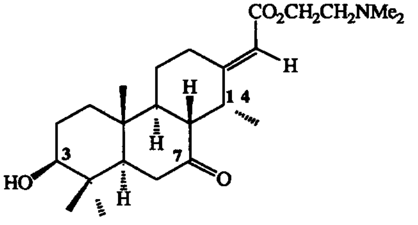
Abstract (4a*R**,10*R**,10a*R**)-10-Hydroxy-7-methoxy-3,4,4a,9,10,10a-hexahydrophenanthren-2(1*H*)-one (3) has been synthesised with the key step involving intramolecular electrophilic alkylation of the aromatic ring, *via* a Pummerer rearranged intermediate, to complete the B-ring of the phenanthrene nucleus Phenanthrenones (4) and (5), bearing a 1-methyl or 1-ethyl group in an axial configuration, have also been prepared by a parallel route· during the cyclisation reaction the 1-alkyl group, lying α to a 1,3-dioxolane protecting group, underwent acid-catalysed epimerisation to give a preponderance of the desired axial epimer

The positive inotropic effect on the heart produced by cardiotonic steroids such as digitoxigenin (1) has been postulated to result from inhibition of membrane-bound Na^+/K^+-dependent adenosine 5'-triphosphatase (Na^+,K^+-ATPase) [1] *Erythrophleum* diterpene alkaloids related to cassaine (2) have an intense action on the heart similar to that produced by the cardiotonic steroids[2] and are also inhibitors of Na^+,K^+-ATPase [3] The available biochemical evidence [3] strongly suggests that the cardiotonic steroids and the *Erythrophleum* alkaloids share the same binding site on Na^+,K^+-ATPase



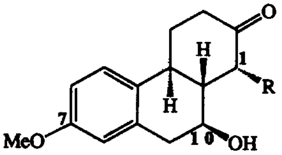
(1)



(2)

Based on superficial inspection of the structural formulae of the cardiotonic steroids and the *Erythrophleum* alkaloids, Thorp and Cobbin[4] have suggested three possible structural parallels between the two classes of compounds which could account for their comparable biological activity the unsaturated ester side-chain of the alkaloids occupies a similar position to the unsaturated lactone side-chain of the steroids; the C-3 oxygenation of both groups of compounds are in similar positions; and the 14α-methyl group of the alkaloids may be homologous to C-15 of the *cis*-fused D-ring of the steroids.

Previous structure-activity studies of the *Erythrophleum* alkaloids[5] have shown the importance of the unsaturated ester grouping and an electronegative grouping at C-3 for cardiotonic activity, but have not given clear insights into the role of the phenanthrene skeleton The influence on activity of the 14α-methyl group has been largely ignored, undoubtedly owing to the synthetic difficulties involved in establishing the axial configuration of this group In view of the possible structural correlation of the 14α-methyl group with the D-ring of the cardiotonic steroids, we were encouraged to undertake the synthesis of analogues of the *Erythrophleum* alkaloids bearing a 14α-methyl group. Our initial observations comparing the Na^+,K^+-ATPase inhibitory activity of analogues with and without the methyl substituent (presented in the accompanying paper[6]) encouraged us to also examine the influence of an ethyl substituent Oxygenation at the 7-position (functionality present in all the *Erythrophleum* alkaloids) was retained in our analogues, however, for ease of synthesis we chose to have an aromatic A-ring In this paper we report the synthesis of the precursor phenanthrenones (3), (4) and (5).[7]

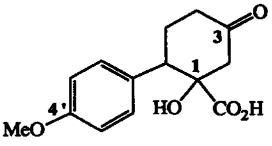


(3) R =H (4) R =Me (5) R = Et

In the reported approaches to the total synthesis of cassaine (2)[8,9] and the synthesis of methyl-(-)-4-epi-cassamate from abietic acid,[10] introduction of the oxygenation at C-7 was accomplished after construction of the tricyclic skeleton In our approach this functionality was to be introduced as a direct consequence of the procedure used in forming the B-ring The methodology involves a Pummerer rearrangement of a β-ketosulphoxide intermediate followed by an intramolecular alkylation of the aromatic ring, and is based on earlier reports of such cyclisations in the formation of phenanthren-2-ones,[11] β-tetralones[12] and some heterocyclic compounds [13]

Ziegler and Condon[14] have reported a facile method for preparing the cyclohexanecarboxylic acid (8) from *p*-methoxyphenylpyruvic acid in good yield This method proved to be well-suited to our needs for the synthesis of (3) Condensation of *p*-methoxyphenylpyruvic acid with methyl vinyl ketone in the presence of sodium hydroxide furnished the hydroxy acid (6) (of undetermined stereochemistry) which on heating to its melting point spontaneously dehydrated to the enone (7) Reduction of (7) with zinc in wet acetic acid then afforded (8) Esterification of (8) (methanol/sulphuric acid) and protection of the ketone as the 1,3-dioxolane (ethylene glycol/*p*-toluenesulphonic acid) gave the *cis*-ester (9) Heating a solution of (9) in methanolic sodium methoxide under reflux gave the *trans*-ester (10) in an overall yield of 78% from the known acid (8) The ester (10) was then converted to the β-ketosulphoxide (11) in quantitative yield by reaction with sodium dimsyl [15]

This product consisted of a 1:1 mixture of diastereomers, epimeric at the sulphur centre, as evidenced in the ^1H n m r spectrum.



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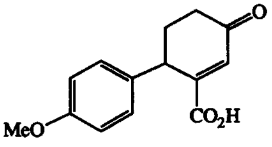

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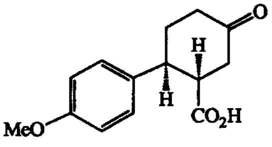

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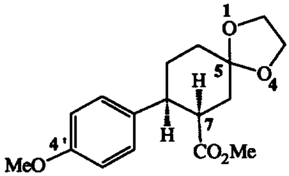

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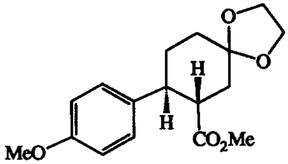
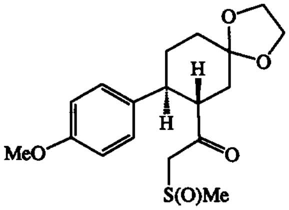
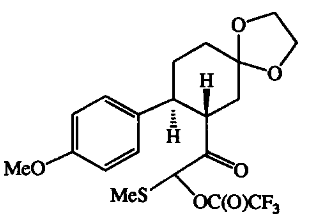


(10)

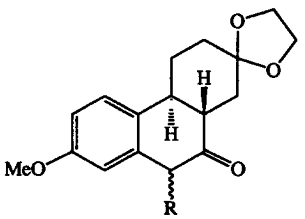


(11)

When the β-ketosulphoxide (**11**) was treated with trifluoroacetic anhydride, according to the general procedure of Mander *et al* ,[11] Pummerer rearrangement occurred to give (**12**) as a mixture of epimers at the methylthio substituted centre After stirring the reaction mixture at room temperature for several hours, there was no evidence of further transformation of this substance to cyclised products However, when several equivalents of anhydrous trifluoroacetic acid were included with the trifluoroacetic anhydride, the desired cyclisation to (**13**) was achieved after stirring for *ca* twenty hours at room temperature This is consistent with Mander's observation[11] of catalysis of the cyclisation of their Pummerer rearranged intermediates by the trifluoroacetic acid formed during the initial Pummerer rearrangement and subsequent cyclisation, and it encouraged us to examine the use of a stronger protic acid Indeed, by using 0 5 equivalents of trifluoromethanesulphonic acid, cyclisation of the Pummerer rearranged intermediate occurred in only 45 minutes at -10°, giving smoother conversion of (**11**) to (**13**)

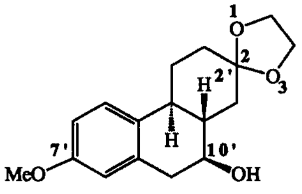


(12)



(13) R = SMe (14) R = H

The ^1H n m r spectrum of the crude cyclisation product displayed two signals for the methylthio group, suggesting that the phenanthrene (**13**) consisted of a mixture of methylthio epimers In addition, (**13**) and the product of the next step (**14**) were found to undergo aerial oxidation with considerable ease, hence purification of these intermediates was not attempted. The sensitivity of compounds similar to (**13**) and (**14**) to aerial oxidation, and the products of oxidation, have been previously commented on ^{11,16} Thus, the crude cyclisation product (**13**) was desulphurised with W2 Raney nickel in acetone at room temperature to obtain the parent phenanthrenone (**14**), which was immediately treated with lithium aluminium hydride to effect reduction of the ketone functionality The desired alcohol (**15**) was thus obtained in 41% overall yield of from the β-ketosulphoxide (**11**) and was concluded to have the equatorial configuration of the hydroxyl group after consideration of the ^{1}H n m r spectral data (it should be noted that within the *Erythrophleum* group of alkaloids approximately half of the isolated compounds have the C-7 oxygenation as a carbonyl group while the other half have an equatorial β-hydroxyl group^8)



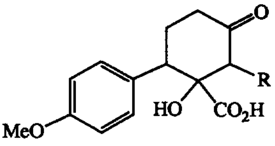
(**15**)

Removal of the 1,3-dioxolane protecting group of (**15**) (wet acetone/pyridinium *p*-toluenesulphonate) gave the ketone (**3**) in 77% yield The ^{1}H n m r spectrum of (**3**) displayed a signal attributable to H-10a which was not observable in the spectrum of (**15**) due to overlapping The signal appeared at δ 1 79 and showed three large axial-axial coupling constants ($J_{10,10a}$ 10 Hz, $J_{1ax,10a}$ 14 Hz, $J_{4a,10a}$ 10 Hz) and a small axial-equatorial coupling ($J_{1eq,10a}$ 4 Hz), confirming the *trans* stereochemistry of the ring junction

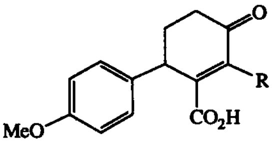
A parallel pathway was used for the preparation of the methyl- and ethyl-substituted phenanthrenones (**4**) and (**5**) Sodium methoxide catalysed condensation of *p*-methoxyphenylpyruvic acid with ethyl vinyl ketone or propyl vinyl ketone (generated *in situ* from 1-chloro-3-pentanone and 1-chloro-3-hexanone respectively) gave the hydroxy acids (**16**) and (**17**) in 50% and 62% yield respectively

The ^{1}H n m r. and ^{13}C n.m r spectra of the products indicated that they were diastereomerically pure, however, the stereochemistry has not been determined Heating (**16**) and (**17**) to their melting points to effect dehydration furnished the enones (**18**) and (**19**) in 91% and 88% yield respectively Treatment of the enones (**18**) and (**19**) with zinc in wet acetic acid to effect reduction of the double bond gave the ketoacids (**20**) and (**21**), as mixtures of diastereomers, in 85% and 95% yield respectively H p l c analysis of the methylated (diazomethane) ketoacid mixture (**20**) indicated the presence of three components in a ratio of 33 11 56, (**21**) consisted of four components in the ratio 10 37 4 49 The two major diastereomers in each case, (**20a**)/(**20b**) and (**21a**)/(**21b**), were isolated in pure form using a combination of radial chromatography and fractional crystallisation, with the assigned stereochemistries readily following from examination of the ^{1}H n m r and ^{13}C n m r spectra of the isomers

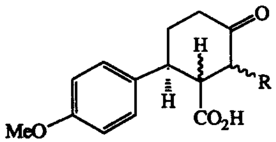
The ketoacid mixtures (**20**) and (**21**) were then esterified (methanol/sulphuric acid) and the ketone groups protected as the 1,3-dioxolanes (ethylene glycol/*p*-toluenesulphonic acid) to give the esters (**22**) and (**23**) in 76% and 83% overall yield respectively The ^{1}H n m r spectra of (**22**) and (**23**) indicated that each consisted of three of the four possible diastereomers with isomer distributions somewhat altered from those of (**20**) and (**21**) As will be discussed later, an equatorial configuration of the methyl or ethyl group is not necessarily preferred when it lies α to a 1,3-dioxolane group, and is subject to epimerisation under the reaction conditions employed Heating solutions of (**22**) and (**23**) in methanolic sodium methoxide under reflux in order to epimerise the methoxycarbonyl group exclusively into an equatorial disposition gave the esters **(24)** and **(25)** in 98% and 88% yield respectively. The ^{1}H n.m.r. spectra of **(24)** and **(25)** indicated that each consisted of a mixture of two diastereomers in a ratio of 4:1. The isomers were not chromatographically separable, however, the major diastereomers **(24a)** and **(25a)** could be isolated in pure form by fractional crystallisation and were shown to have the all *trans* stereochemistry (6*R**,7*S**,8*R**) based on their ^{1}H n.m.r. spectra. The minor diastereomers present in the mixtures **(24)** and **(25)** presumably have the (6*R**,7*R**,8*S**) configuration, where the methyl or ethyl group is axially oriented.



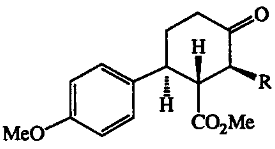
(16) R = Me **(17)** R = Et



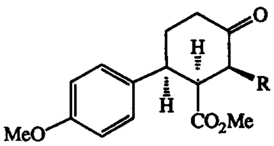
(18) R = Me **(19)** R = Et



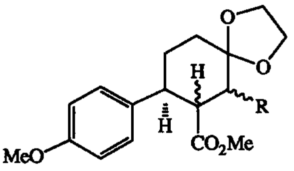
(20) R = Me **(21)** R = Et



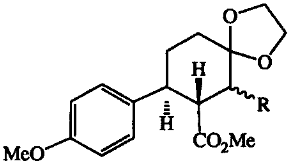
(20a) R = Me
(21a) R = Et



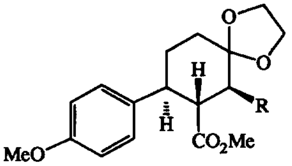
(20b) R = Me
(21b) R = Et



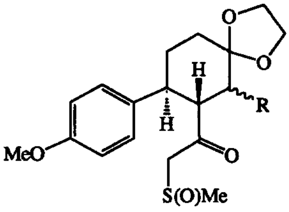
(22) R = Me
(23) R = Et



(24) R = Me **(25)** R = Et



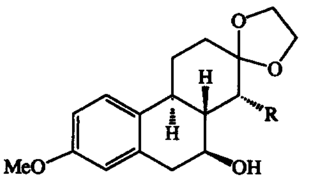
(24a) R = Me **(25a)** R = Et



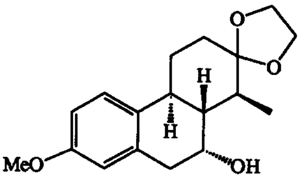
(26) R = Me **(27)** R = Et

Reaction of the ester mixtures **(24)** and **(25)** with sodium dimsyl afforded the β-ketosulphoxides **(26)** and **(27)** as mixtures epimeric at the sulphur centre in addition to the methyl or ethyl substituted centre, in 94% and 92% yield respectively. Subjecting the methyl-substituted β-ketosulphoxide mixture **(26)** to the same series of reactions as detailed for **(11)** above, *i.e.* Pummerer rearrangement with trifluoroacetic anhydride, cyclisation with trifluoromethanesulphonic acid (the cyclisation proceeding more slowly in this case), desulphurisation with W2 Raney nickel and reduction with lithium aluminium hydride, gave the desired phenanthrene **(28)** in 28% overall yield from **(26)**.

The structure of **(28)** followed from analysis of its ^{1}H n.m.r. spectrum. The signals for H-9'$_{eq}$ (δ 3.12, dd, $J_{9'eq,9'ax}$ 16 Hz, $J_{9'eq,10'}$ 6 Hz) and H-9'$_{ax}$ (δ 2.82, dd, $J_{9'eq,9'ax}$ 16 Hz, $J_{9'ax,10'}$ 10 Hz) established that the 10' hydroxyl group was equatorial (H-10' was obscured by other signals). Taken together with the signal at δ 1.91, assigned to H-10a', with two large axial-axial couplings ($J_{4a',10a'}$ 12 Hz, $J_{10',10a'}$ 11 Hz) and a small axial-equatorial coupling ($J_{1',10a'}$ 4 Hz), the configurations at C1', C4a', C10' and C10a' were established. In the ^{13}C n.m.r spectrum of (**28**), the γ-effect [17] of the axial 1'-methyl group shielded C3' (7 3 p.p m), C4a' (7 2 p p.m) and C10' (3 4 p.p m) in (**28**) when comparing the chemical shifts for these carbons in the des-methyl phenanthrene (**15**)



(**28**) R = Me (**29**) R = Et



(**30**)

In addition to (**28**), a slightly higher R_f component was isolated, in 20% yield by weight from (**26**), which proved to be an inseparable mixture of two compounds The high field ^1H n m.r spectrum of the mixture indicated the presence of a phenanthrene, thought to have structure (**30**), together with an unidentified component, in a ratio of *ca* 3 1 The mixture was sufficiently enriched in (**30**) to allow some meaningful decoupling experiments to be carried out, identifying key signals for the assignment of structure The establishment of the axial configuration of the 10'-hydroxyl group of (**30**) followed from assignment of the signals for H-10' (δ 4 32, broad singlet, $W_{h/2}$ 9 Hz), H-9'$_{eq}$ (δ 3.08, dd, $J_{9'eq,9'ax}$ 16 Hz, $J_{9'eq,10'}$ 3 Hz) and H-9'$_{ax}$ (δ 2 89, dd, $J_{9'eq,9'ax}$ 16 Hz, $J_{9'ax,10'}$ 2 Hz) H-10a' appeared at δ 1 51 with a small coupling to H-10' ($J_{10',10a'} \approx 2$ Hz) and two large couplings ($J_{1',10a'} \approx J_{4a',10a'} \approx 11$ Hz) to H-1' and H-4a', thus establishing the configurations at C1', C4a', C10' and C10a'.

The results of the cyclisation sequence suggest that the two phenanthrenones leading to (**28**) and (**30**) are formed in an estimated ratio of *ca* 3 2, with the axial epimer predominating, and that lithium aluminium hydride reduction of these takes place in a thermodynamically preferred direction (the resulting hydroxyl group avoiding an unfavourable 1,3-interaction with the methyl group) Since the starting β-ketosulphoxide (**26**) had a preponderance of the equatorial methyl epimer (*ca* 4 1), epimerisation at the methyl-substituted centre appeared to have occurred during cyclisation Approximately the same product distribution was found when the β-ketosulphoxide derived from (**24a**), and thus having only the equatorial methyl configuration, was used for the conversion Epimerisation of the methyl group is assumed to occur during the cyclisation reaction through acid-catalysed opening of the 1,3 dioxolane ring reversibly forming an enol-ether species The preference for the axial configuration of the methyl group may be the result of an unfavourable steric interaction between the 1,3-dioxolane ring and the methyl group when in an equatorial configuration in the tricyclic product The observed epimerisation of the methyl group and the direction of hydride reduction has some precedence in the work of Turner *et al* [9]

Removal of the 1,3-dioxolane group of (**28**) using the weak acid catalyst, 2,6-dimethylpyridinium *p*-toluenesulphonate[18] in wet acetone, cleanly afforded the desired phenanthrenone (**4**) in 90% yield, with no evidence of epimerisation of the methyl group The use of stronger acids, or exposure of (**4**) to base, readily formed a 1 1 mixture of the epimeric 1-methylphenanthren-2-ones The fact that the methyl group of (**4**) remained axial followed from the ^1H n m r spectrum, where the H-10a signal appeared at δ 1 88 with two large axial-axial couplings ($J_{4a,10a}$ 11 Hz, $J_{10,10a}$ 10 Hz) and a small axial-equatorial coupling ($J_{1,10a}$ 4 Hz) Comparison of the ^{13}C n.m r. spectrum of (4) with that of (3) indicated shielding of C3 (6.3 p.p m), C4a (6.5 p p m) and C10 (4 1 p.p.m), as expected for an axial configuration of the 1-methyl group.

Cyclisation of the ethyl-substituted β-ketosulphoxide mixture (27) gave the axial 1-ethyl phenanthrene (29) in 27% overall yield from (27) The stereochemical assignment of (29) followed from its ^{1}H n m r and ^{13}C n m r spectra, which were analogous to those of the corresponding 1-methylphenanthrene (28) The other major component from the reaction sequence (isolated in 11% overall yield by weight from (27)) proved to be an inseparable 1 1 mixture The ^{1}H n m r. spectrum of the mixture was too complex to completely confirm the formation of an equatorial ethyl-substituted phenanthrene analogous to (30), however, a broad singlet at δ 4 31 ($W_{h/2} \approx 10$ Hz) attributable to H-10' and a broad doublet at δ 3 08 ($J \approx 16$ Hz) attributable to H-9'$_{eq}$ suggested its presence Removal of the 1,3-dioxolane protecting group from (29) (2,6-dimethylpyridinium *p*-toluenesulphonate/wet acetone) then gave the ketone (5) in 98% yield.

The phenanthrenones (3), (4) and (5) are thus readily available in multigram quantities using the methodology described, and have been converted into analogues of the *Erythrophleum* alkaloids for structure-activity studies, as detailed in the accompanying paper

Experimental

General Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Microanalyses were performed by either the Australian Microanalytical Service (Melbourne) or MHW Laboratories, Phoenix, Arizona ^{1}H n m r spectra were recorded using the following instruments: 80 MHz, Bruker WP80, 90 MHz, Bruker HX90, 300MHz, Bruker AM300. Spectra were recorded with $CDCl_3$ or d_4-MeOH solutions with either trimethylsilane as internal standard (δ 0.00), or referenced using residual $CHCl_3$ (δ 7 26) or residual CHD_2OD (δ 3 30) The multiplicities of the signals are described as either s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet, $W_{h/2}$ = width at half-height) or br (broad). ^{13}C n m.r spectra were recorded using either a Bruker WP80 (20 1 MHz) or a Bruker AM 300 (75 5 MHz) instrument Chemical shifts were measured relative to $CDCl_3$ (δ 77 0) or d_4-MeOH (δ 49 0) Assignments were made with the aid of SFORD and DEPT techniques Assignments marked with an asterisk are interchangeable Mass spectra (*m/z*) were recorded with a Hewlett-Packard 5986 GC/MS system using a direct insertion mode (ionization energy 35 eV) and are described in terms of m/z (% of base peak) Optical rotations ($[\alpha]_D$) were measured using a Perkin-Elmer 141 Polarimeter at ambient temperature Concentrations are quoted in g/100 ml High pressure liquid chromatography (h p l c) was carried out on a Waters Associates Liquid Chromatograph equipped with a model 6000A solvent delivery system, a model 440 absorbance detector (operating at 254 and 280 nm), and using a 10 μ μ-Porasil Radial-Pak Column installed in a Waters Z-module Radial Compression Separation System. Radial chromatography was carried out with a Harrison Research Chromatotron using glass plates spread with either 1, 2 or 4 mm layers of Merck Keiselgel 60PF$_{254}$ (Art 7749) Analytical thin layer chromatography (t l c) was carried out using Merck (Art 5554) silica gel 60 PF$_{254}$, precoated aluminium sheets Organic materials were visualised by spraying the plates with 6% $CeSO_4$ in 2N H_2SO_4 after which they were warmed at 100° for 5 min Alumina refers to Fluka, 507c, neutral alumina, and was adjusted to activity II by the addition of 3% (v/w) of water

Materials 1-Chloro-3-pentanone was prepared from propionyl chloride and ethylene according to the procedure of Woodward *et al* [19] 1-Chloro-3-hexanone was prepared from butyryl chloride and ethylene according to the procedure of Bowden *et al* [20] Pyridinium *p*-toluenesulphonate was prepared from pyridine and *p*-toluenesulphonic acid monohydrate according to the procedure of Grieco *et al* [21] The same procedure was adapted for the preparation of 2,6-dimethylpyridinium *p*-toluenesulphonate *p*-Methoxyphenylpyruvic acid and *cis*-6-(4'-methoxyphenyl)-3-oxocyclohexanecarboxylic acid (8) were prepared according to the procedures of Ziegler and Condon [14] All other reagents were obtained from commercial sources Light petroleum (petrol) refers to the fraction boiling at 40-60° Anhydrous tetrahydrofuran (thf) and anhydrous ether were obtained by distillation from sodium benzophenone ketyl Other solvents were purified and dried (where necessary) by methods described in the literature [22]

Methyl cis-*8-(4'-Methoxyphenyl)-1,4-dioxaspiro[4.5]decane-7-carboxylate* (9) A solution of the acid (8) (26 0 g, 105 mmol) and concentrated sulphuric acid (5 ml) in methanol (250 ml) was heated under reflux for 12 hrs The solution was cooled, poured into water and extracted with CH_2Cl_2 The extract was washed with sat

r, dried ($MgSO_4$) and the solvent was removed *in vacuo*. The product was dissolved in benzene
)-toluenesulphonic acid (100 mg) and ethylene glycol (40 g) and the mixture was heated under
)tropic removal of water for 20 hrs. The solution was cooled, washed with water, dried ($MgSO_4$)
it was removed *in vacuo* The *ester* (**9**) (27.6 g, 87% over two steps) crystallised from
m p. 106-7°; Found C, 66 70; H, 7.32% $C_{17}H_{22}O_5$ requires C, 66 65, H, 7 24%, ^{1}H n m r
Cl$_3$) δ 1 56-2 44 (m, 6H, {H-6}$_2$, {H-9}$_2$, {H-10}$_2$), 2 94-3 28 (m, 2H, H-7, H-8), 3 50 (s,
72 (s, 3H, OMe), 3 92 (br s, 4H, {H-2}$_2$, {H-3}$_2$), 6.72-7.33 (AA'BB', J_{AB} 9 Hz, 4H, ArH),
1 MHz, $CDCl_3$): See Table 1, *m/z*. 306 (24%, M$^+$), 192 (32), 159 (21), 157 (43), 149 (19),
100), 99 (94), 86 (14)

-*(4'-Methoxyphenyl)-1,4-dioxaspiro[4.5]decane-7-carboxylate* (**10**). The ester (**9**) (25.0 g, 82
olved in methanolic sodium methoxide (200 ml, 0.2 *M*) and the solution was heated under reflux
solution was cooled, poured into 5% aqueous NH_4Cl solution and extracted with CH_2Cl_2 The
shed with water, dried ($MgSO_4$) and the solvent was removed *in vacuo*. The *ester* (**10**) (22.5 g,
ed from benzene/petrol, m p 88-9°, Found C, 66 87, H, 7 32% $C_{17}H_{22}O_5$ requires C, 66 65,
n m.r (90 MHz, $CDCl_3$). δ 1 61-2 11 (m, 6H, {H-6}$_2$, {H-9}$_2$, {H-10}$_2$), 2.56-3 00 (m, 2H,
(s, 3H, CO_2Me), 3 73 (s, 3H, OMe), 3.95 (br s, 4H, {H-2}$_2$, {H-3}$_2$), 6 72-7 26 (AA'BB',
ArH), ^{13}C n.m.r (20 1 MHz, $CDCl_3$)· See Table 1, *m/z* 306 (19%, M$^+$), 192 (38), 157 (37),
11), 134 (100), 99 (62)

hoxyphenyl)-1,4-dioxaspiro[4 5]decan-7-yl Methylsulphinylmethyl Ketone (**11**) A solution of
, prepared from NaH (1 54 g of 55% dispersion, 35 mmol) and DMSO (20 ml),^{15} was diluted
) and cooled to 0° under an atmosphere of Ar. A solution of the ester (**10**) (5 0 g, 16 mmol) in thf
n added dropwise and the mixture was stirred for 0.5 hrs The reaction mixture was poured onto
ished ice (200 g) and concentrated HCl (5 ml) and was then extracted with CH_2Cl_2 The CH_2Cl_2
shed with 5% aqueous $NaHCO_3$, water, dried ($MgSO_4$) and the solvent was removed *in vacuo*
as dissolved in a small volume of CH_2Cl_2 and was triturated with petrol to give the
) as a colourless, amorphous solid (5.75 g, 100%), ^{1}H n.m r. (90 MHz, $CDCl_3$)· δ 1.56-2 00
2, {H-9}$_2$, {H-10}$_2$), 2.26 (s, 1 5H, S(O)Me of one diastereoisomer), 2.33 (s, 1.5H, S(O)Me
oisomer), 2 44-2 89 (m, 1H, H-7), 3 06 (A part of ABq, *J* 17 Hz, 0.5H, COC($\underline{H}$)HS(O) of one
r), 2.94-3.29 (m, 1H, H-8), 3 37 (s, 1H, COC$\underline{H_2}$S(O) of one diastereoisomer), 3 68 (B part of
0 5H, COC(H)$\underline{H}$S(O) of one diastereoisomer), 3 76 (s, 3H, OMe), 3 98 (br s, 4H, {H-2}$_2$,
7 26 (AA'BB', J_{AB} 9 Hz, 4H, ArH)

'*0a'R*)-10'-Hydroxy-7'-methoxy-3',4',4a',9',10',10a'-hexahydrospiro[1,3-dioxolane-*
anthrene] (**15**) To a stirred solution of the sulphoxide (**11**) (10.0 g, 28 mmol) in dry CH_2Cl_2
° under an atmosphere of Ar was added dropwise trifluoroacetic anhydride (4.4 ml, 31 mmol),
fluoromethanesulphonic acid (1 2 ml, 14 mmol) The solution was stirred at -10° for 0.75 hrs
ie (7 ml) was then added in a rapid stream The solution was washed with dilute HCl, water,
and the solvent was removed *in vacuo* The product was dissolved in acetone (300 ml) and was
Raney nickel (40 g) for 2 hrs at room temperature under an atmosphere of Ar. The mixture was
ough Celite, the nickel was washed with CH_2Cl_2, and the solvent was removed from the filtrate *in*
ion of the product in dry ether (200 ml) was added dropwise to $LiAlH_4$ (2 g) in ether (100 ml) at
nosphere of Ar and the mixture was then stirred for 0.5 hrs Saturated aqueous Na_2SO_4 was
to the mixture until coagulation occurred, the mixture was filtered through Celite, the solids were
her and the solvent was removed from the filtrate *in vacuo* The product was applied to a pad of
l, activity II, 200 g) and was eluted with 30% EtOAc/petrol to give the desired *phenanthrene* (**15**)
small amount of another substance which is assumed to be the 10'*S** isomer (t l c analysis)
from CH_2Cl_2/petrol gave the pure *phenanthrene* (**15**) (3 34 g, 41% over three steps), m p 168-
, 70.30, H, 7 40 % $C_{17}H_{22}O_4$ requires C, 70 32, H, 7 64%, ^{1}H n m r. (300 MHz, $CDCl_3$) δ
5, 12.5 Hz, 1H, H-1'$_{ax}$), 1 45-1 61 (m, 1H, H-4'$_{ax}$), 1.63-1 77 (m, 2H, H-3'$_{ax}$, H-10a'), 1 91
, 13 Hz, 1H, H-4'$_{eq}$), 2.27-2 46 (m, 3H, H-3'$_{eq}$, H-4a', H-1'$_{eq}$), 2.79 (dd, *J* 10, 16 Hz, 1H, H-
J 6, 16 Hz, 1H, H-9'$_{eq}$), 3 71 (ddd, *J* 6, 10, 10 Hz, 1H, H-10'), 3 77 (s, 3H, OMe), 3 90-4 06
}$_2$, {H-5}$_2$), 6 62 (d, *J* 2 5 Hz, 1H, H-8'), 6 74 (dd, *J* 2 5, 8 5 Hz, 1H, H-6'), 7 18 (d, *J* 8 5
^{13}C n m r (75 5 MHz, $CDCl_3$) See Table 2, *m/z* 290 (11%, M$^+$), 272 (14), 188 (46), 186
171 (12), 145 (12), 128 (15), 99 (100)

0aR)-10-Hydroxy-7-methoxy-3,4,4a,9,10,10a-hexahydrophenanthren-2(1H)-one* (**3**) A
1,3-dioxolane (**15**) (7 80 g, 27 mmol) and pyridinium *p*-toluenesulphonate (2 0 g, 8 mmol) in
0 ml) was heated under reflux for 20 hrs The acetone was removed *in vacuo* and the residue was
H_2Cl_2 The CH_2Cl_2 solution was washed with water, dried ($MgSO_4$) and the solvent was

removed *in vacuo*. The *ketone* (**3**) (5.10 g, 77%) crystallised from CH_2Cl_2/petrol, m.p. 140-2°; Found: C, 72.91; H, 7.34 %. $C_{15}H_{18}O_3$ requires C, 73.15, H, 7.37%, ^{1}H n.m.r. (300 MHz, $CDCl_3$): δ 1.66 (dddd, *J* 6, 12, 12, 12 Hz, 1H, H-4$_{ax}$), 1.79 (dddd, *J* 4, 10, 10, 14 Hz, 1H, H-10a), 2.23 (dd, *J* 14, 14 Hz, 1H, H-1$_{ax}$), 2.49-2.57 (m, 2H, H-3$_{ax}$, H-4$_{eq}$), 2.69-2.88 (m, 3H, H-3$_{eq}$, H-4a, H-9$_{ax}$), 2.96 (ddd, *J* 2, 4, 14 Hz, 1H, H-1$_{eq}$), 3.17 (dd, *J* 6, 16 Hz, 1H, H-9$_{eq}$), 3.78 (s, 3H, OMe), 3.84 (ddd, *J* 6, 10, 10 Hz, 1H, H-10), 6.64 (d, *J* *J* 2.5 Hz, 1H, H-8), 6.76 (dd, *J* 2.5, 8.5 Hz, 1H, H-6), 7.21 (d, *J* 8.5 Hz, 1H, H-5); ^{13}C n.m.r. (75.5 MHz, $CDCl_3$): See Table 2; *m/z*: 246 (100%, M$^+$), 228 (16), 189 (46), 186 (26), 175 (22), 174 (22), 173 (22), 172 (48), 171 (66), 161 (38), 159 (17), 158 (20), 146 (16), 145 (24), 115 (25), 91 (19).

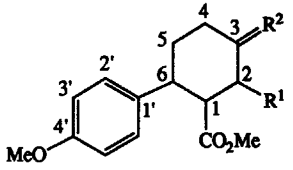
1-Hydroxy-6-(4'-methoxyphenyl)-2-methyl-3-oxocyclohexanecarboxylic Acid (**16**). *p*-Methoxyphenylpyruvic acid (160 g, 0.825 mol) was added in portions to a stirred solution of sodium methoxide (117 g, 2.17 mol) in methanol (1 l), maintaining the temperature of the mixture below 10°. 1-Chloro-3-pentanone (115 g, 0.96 mol) was then added dropwise and the mixture was stirred at room temperature for 20 hrs. The reaction mixture was then poured into 5% HCl (2 l) and the precipitated product was collected. The *acid* (**16**) (115 g, 50%) crystallised from MeOH/EtOAc, m.p. 170-5° (dec), Found: C, 64.82, H, 6.57%. $C_{15}H_{18}O_5$ requires C, 64.75, H, 6.47%. ^{1}H n.m.r. (300 MHz, d_4-MeOH) δ 0.93 (d, *J* 6.5 Hz, 3H, Me-2), 1.95 (m, W$_{h/2}$ 26 Hz, 1H, H-5$_{eq}$), 2.37-2.55 (m, 2H, H-4$_{eq}$, H-5$_{ax}$), 2.67 (m, W$_{h/2}$ 35 Hz, 1H, H-4$_{ax}$), 3.12 (dq, *J* 1, 6.5 Hz, 1H, H-2), 3.57 (dd, *J* 4, 13 Hz, 1H, H-6), 3.73 (s, 3H, OMe), 6.76-6.81/7.25-7.30 (AA'BB', *J*$_{AB}$ 9 Hz, 4H, ArH), ^{13}C n.m.r. (75.5 MHz, d_4-MeOH): δ 8.8 (Me-2), 30.1 (C-5), 41.9 (C-4), 50.3* (C-6), 52.2* (C-2), 55.6 (OMe), 83.9 (C-1), 114.4 (C-3', C-5'), 130.8 (C-2', C-6'), 133.4 (C-1'), 160.2 (C-4'), 175.7 (CO_2H), 212.0 (C-3), *m/z* 278 (12%, M$^+$), 147 (17), 135 (11), 134 (100).

6-(4'-Methoxyphenyl)-2-methyl-3-oxo-1-cyclohexenecarboxylic Acid (**18**). The acid (**16**) (100 g, 0.360 mol) was heated at 190° (bath), under a stream of Ar, until the solid had completely melted. The oil was mechanically stirred for 10 min, and was then diluted with toluene (150 ml). On cooling to room temperature the *unsaturated acid* (**18**) (85 g, 91 %) was collected, m.p. 150-3°, Found: C, 69.38, H, 6.34%. $C_{15}H_{16}O_4$ requires C, 69.22, H, 6.20%, ^{1}H n.m.r. (300 MHz, d_4-MeOH) δ 1.95 (d, *J* 2 Hz, 3H, Me-2), 2.10 (m, W$_{h/2}$ 35 Hz, 1H, H-5$_{ax}$), 2.28-2.53 (m, 3H, {H-4}$_2$, H-5$_{eq}$), 3.74 (s, 3H, OMe), 4.07 (ddq, *J* 5, 5, 2 Hz, 1H, H-6), 6.82-6.87/7.12-7.17 (AA'BB', *J*$_{AB}$ 9 Hz, 4H, ArH), ^{13}C n.m.r. (75.5 MHz, d_4-MeOH) δ 13.1 (Me-2), 32.6 (C-5), 36.2 (C-4), 44.1 (C-6), 55.7 (OMe), 115.0 (C-3', C-5'), 130.3 (C-2', C-6'), 134.2 (C-1'), 136.0 (C-2), 150.4 (C-1), 160.2 (C-4'), 171.1 (CO_2H), 201.4 (C-3), *m/z* 260 (86%, M$^+$), 242 (22), 215 (12), 200 (15), 187 (10), 186 (22), 173 (31), 172 (100), 171 (11), 159 (26), 144 (11), 134 (12), 128 (14), 121 (10), 116 (11), 115 (21), 108 (22).

6-(4'-Methoxyphenyl)-2-methyl-3-oxocyclohexanecarboxylic Acid (**20**). To a solution of the unsaturated acid (**18**) (80 g, 0.308 mol) in glacial acetic acid (1 l) was added water (100 ml) and zinc dust (115 g) and the mixture was then heated under reflux. After 24 hrs additional zinc dust (115 g) was added and refluxing was continued for a further 24 hrs. The solution was decanted from the residual zinc while still hot and the solvent was then removed *in vacuo*. The residue was partitioned between dilute HCl and EtOAc, and the aqueous phase was then extracted further with EtOAc. The combined organic extracts were washed with sat. NaCl, dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the *acid* (**20**) (68 g, 85%) as a solid. H.p.l.c. analysis (10% EtOAc/petrol, 2.0 ml min^{-1}) of the methylated (diazomethane) acid (**20**) indicated the presence of two major diastereomers (R$_t$ 8.5 min, 33%, R$_t$ 16.5 min, 56%) and one minor isomer (R$_t$ 14.2 min, 11%). The major isomers were isolated by radial chromatography (30% EtOAc/petrol). The (1*R**,2*S**,6*S**) isomer (**20a**) (R$_t$ 8.5 min) eluted first and crystallised from CH_2Cl_2/petrol, m.p. 90-2°, Found: C, 69.39, H, 7.43%. $C_{16}H_{20}O_4$ requires C, 69.55, H, 7.30%, ^{1}H n.m.r. (300 MHz, $CDCl_3$). δ 1.01 (d, *J* 6.5 Hz, 3H, Me-2), 1.99 (dddd, *J* 5, 13, 13, 13 Hz, 1H, H-5$_{ax}$), 2.17 (dddd, *J* 3, 3, 6, 13 Hz, 1H, H-5$_{eq}$), 2.48-2.67 (m, 3H, H-1, {H-4}$_2$), 2.84 (dq, *J* 12, 6.5 Hz, 1H, H-2), 3.29 (ddd, *J* 3, 13, 13 Hz, 1H, H-6), 3.41 (s, 3H, CO_2Me), 3.78 (s, 3H, OMe), 6.80-6.85/7.08-7.13 (AA'BB', *J*$_{AB}$ 9 Hz, 4H, ArH), ^{13}C n.m.r. (75.5 MHz, $CDCl_3$) See Table 1, *m/z* 276 (25%, M$^+$), 217 (14), 216 (14), 203 (11), 200 (26), 192 (11), 174 (15), 161 (17), 159 (11), 148 (10), 147 (31), 135 (21), 134 (100), 128 (12), 121 (18), 91 (11).

The (1*R**,2*R**,6*R**) isomer (**20b**) (R$_t$ 16.5 min) crystallised from CH_2Cl_2/petrol, m.p. 128-30°, Found: C, 69.57, H, 7.25%. $C_{16}H_{20}O_4$ requires C, 69.55, H, 7.30%, ^{1}H n.m.r. (300 MHz, $CDCl_3$) δ 1.03 (d, *J* 6.5 Hz, 3H, Me-2), 2.07 (ddddd, *J* 2, 2, 5, 6, 12 Hz, 1H, H-5$_{eq}$), 2.50 (dddd, *J* 1, 6, 13, 14 Hz, 1H, H-4$_{ax}$), 2.60-2.80 (m, 3H, H-2, H-4$_{eq}$, H-5$_{ax}$), 3.22 (ddd, *J* 2, 5, 5 Hz, 1H, H-1), 3.43 (ddd, *J* 5, 5, 13 Hz, 1H, H-6), 3.45 (s, 3H, CO_2Me), 3.79 (s, 3H, OMe), 6.83-6.87/7.09-7.12 (AA'BB', *J*$_{AB}$ 9 Hz, 4H, ArH), ^{13}C n.m.r. (75.5 MHz, $CDCl_3$) See Table 1, *m/z* 276 (34%, M$^+$), 216 (10), 200 (11), 174 (10), 161 (14), 148 (16), 147 (53), 135 (17), 134 (100), 129 (30), 121 (25), 119 (11), 101 (15), 91 (12).

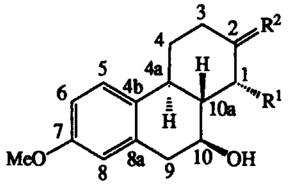
Table 1



R^1 = H, Me, Et; R^2 = O, OCH_2CH_2O

Carbon	(9)#	(10)#	(20a)	(20b)	(24a)#	(21a)	(21b)	(25a)#
1	40.7	45.0	58.5	56.8	55.5	58.5	54.4	54.6
2	33.1	35.1	46.5*	45.9	42.0	52.8	52.8	47.9
3	108.5	108.0	210.1	209.3	109.3	209.8	208.9	110.3
4	35.3	38.0	41.3	40.4	34.9	41.8	40.7	34.9
5	27.2	31.6	33.9	27.3	31.2	34.0	27.4	31.0
6	44.7	48.2	46.0*	44.2	45.9	46.3	44.2	46.4
1'	134.9	135.7	133.6	133.7	135.3	133.6	133.6	135.3
2'	129.2	128.3	128.1	127.9	128.1	128.1	127.8	128.2
3'	113.6	113.9	114.0	113.9	113.6	113.9	113.8	113.6
4'	158.1	158.4	158.6	158.6	158.1	158.6	158.4	158.1
OMe	55.2	55.2	55.2	55.2	55.0	55.2	55.1	55.1
$CO_2\underline{C}H_3$	51.2	51.4	51.6	51.3	51.0	51.6	51.2	51.0
$CH_2\underline{C}H_3$	-	-	-	-	-	11.7	11.7	13.2
$\underline{C}H_2CH_3$	-	-	-	-	-	20.5	19.8	20.6
Me-2	-	-	12.4	12.3	11.5	-	-	-
$O\underline{C}H_2\underline{C}H_2O$	64.5	64.6	-	-	65.1 65.3	-	-	64.6 64.8
$\underline{C}O_2CH_3$	173.8	174.8	173.4	172.7	174.6	173.5	172.5	174.7

Table 2



R^1 = H, Me, Et, R^2 = O, OCH_2CH_2O

Carbon	(15)#	(3)	(28)#	(4)	(29)#	(5)
1	35.0	39.8	36.2	44.3	43.6	52.1
2	108.8	210.7	111.0	215.0	111.6	214.3
3	37.2	43.6	29.9	37.3	30.8*	37.7
4	28.4	30.9	29.1	31.8	29.6*	32.4
4a	41.1	40.7	33.9	34.2	34.9	35.0
4b	130.8	129.2	131.1	129.6	131.1	129.8
5	126.6	126.7	127.0	127.4	127.2	127.3
6	112.3	112.6	112.3	112.7	112.4	112.7
7	158.1	158.1	157.6	158.0	157.6	158.0
8	113.8	113.7	113.5	113.6	113.4	113.6
8a	136.1	135.8	135.6	135.5	135.6	135.5
9	40.0	40.9	40.5	40.4	40.5	40.6
10	71.2	70.9	67.8	66.8	67.4	66.9
10a	45.2	47.8	47.3	49.7	48.5	50.7
OMe	55.2	55.2	55.2	55.2	55.1	55.2
Me-1	-	-	9.2	11.5	-	-
$CH_2\underline{C}H_3$	-	-	-	-	15.7	11.7
$\underline{C}H_2CH_3$	-	-	-	-	18.8	18.8
$O\underline{C}H_2\underline{C}H_2O$	64.4	-	64.2	-	64.1 64.3	-

\# Numbering system altered for purpose of table

***Methyl 8-(4'-Methoxyphenyl)-6-methyl-1,4-dioxaspiro[4.5]decane-7-carboxylate* (22)** A solution of the acid (**20**) (60 g, 0.229 mol) and concentrated sulphuric acid (10 ml) in methanol (600 ml) was heated under reflux for 25 hrs The solution was cooled, poured into water and extracted with CH_2Cl_2. The extract was washed with sat $NaHCO_3$, water, dried ($MgSO_4$) and the solvent was removed *in vacuo* The product was dissolved in benzene (500 ml) with *p*-toluenesulphonic acid (100 mg) and ethylene glycol (50 g) and the mixture was heated under reflux with azeotropic removal of water for 24 hrs. The solution was cooled, washed with water, dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the *ester* (**22**) (56 g, 76% over two steps) as a semi-solid; ^{1}H n m.r (80 MHz, $CDCl_3$, partial spectrum): δ 0.85 (d, *J* 6.5 Hz, 0.73H, Me-6), 1 00 (d, *J* 7 Hz, 1 72H, Me-6), 1.11 (d, *J* 6.5 Hz, 0.55H, Me-6), 3.37 (s, 0.73H, CO_2Me), 3 40 (s, 1 72H, CO_2Me), 3 43 (s, 0 55H, CO_2Me), 3 76 (s, 3H, OMe), 3.84-4.09 (m, 4H, $\{H\text{-}2\}_2$, $\{H\text{-}3\}_2$)

***Methyl (6R*S*,7R*,8S*)-8-(4'-Methoxyphenyl)-6-methyl-1,4-dioxaspiro[4.5]decane-7-carboxylate* (24)** The ester (**22**) (50 g, 0.156 mol) was dissolved in methanolic sodium methoxide (500 ml, *ca.* 3 *M*) and the solution was heated under reflux for 24 hrs The solution was cooled, poured into 5% aqueous NH_4Cl solution and extracted with CH_2Cl_2 The extract was washed with water, dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the *ester* (**24**) (49 g, 98%) as a solid, ^{1}H n m r (80 MHz, $CDCl_3$, partial spectrum) δ 0 85 (d, *J* 6 5 Hz, 2 45H, Me-6), 1 03 (d, *J* 7 Hz, 0.55H, Me-6), 3 37 (s, 2 45H, CO_2Me), 3 46 (s, 0.55H, CO_2Me), 3 76 (s, 3H, OMe), 3 98 (br s, 4H, $\{H\text{-}2\}_2$, $\{H\text{-}3\}_2$) A portion of the *ester* (**24**) was recrystallised twice from CH_2Cl_2/petrol to give the (6*R**,7*S**,8*R**) isomer (**24a**), m p 105-7°, Found C, 67 56; H, 7 70% $C_{18}H_{24}O_5$ requires C, 67 48, H, 7 55%; ^{1}H n m r (300 MHz, $CDCl_3$) δ 0 84 (d, *J* 6 5 Hz, 3H, Me-6), 1.60 (m, $W_{h/2}$ 33 Hz, 1H, H-10$_{ax}$), 1 75-1.91 (m, 3H, $\{H\text{-}9\}_2$, H-10$_{eq}$), 2.12 (dq, *J* 11, 6 5 Hz, 1H, H-6), 2 60 (dd, *J* 11, 11 Hz, 1H, H-7), 2 80 (ddd, *J* 5, 11, 11 Hz, 1H, H-8), 3 36 (s, 3H, CO_2Me), 3.74 (s, 3H, OMe), 3 90-4 02 (m, 4H, $\{H\text{-}2\}_2$, $\{H\text{-}3\}_2$), 6.75-6 80/7 06-7.10 (AA'BB', J_{AB} 9 Hz, 4H, ArH), ^{13}C n m r (75 5 MHz, $CDCl_3$) See Table 1, *m/z* 320 (8%, M$^+$), 171 (12), 134 (54), 100 (10), 99 (100).

***(6R*S*,7R*,8S*)-8-(4'-Methoxyphenyl)-6-methyl-1,4-dioxaspiro[4 5]decan-7-yl Methylsulphinylmethyl Ketone* (26).** The ester (**24**) (20.0 g, 62 5 mmol) was added to a solution of sodium dimsyl, prepared from NaH (6 0 g of 55% dispersion, 0 138 mol) and DMSO (150 ml),[15] and the mixture was stirred at room temperature under an atmosphere of Ar for 20 hrs The reaction mixture was poured onto a mixture of crushed ice (500 g) and concentrated HCl (20 ml) and was then extracted with CH_2Cl_2 The CH_2Cl_2 extract was washed with 5% aqueous $NaHCO_3$, water, dried ($MgSO_4$) and the solvent was removed *in vacuo* to give the *sulphoxide* (**26**) (21.5 g, 94%) as a pale yellow gum; ^{1}H n m r (80 MHz, $CDCl_3$, partial spectrum) δ 0 85 (d, *J* 6.5 Hz, 1 6H, Me-6), 0 92 (d, *J* 7 Hz, 0 5H, Me-6), 0 98 (d, *J* 7 Hz, 0 9H, Me-6), 2 22 (s, 1 6H, S(O)Me), 2 26 (s, 0.5H, S(O)Me), 2 41 (s, 0 9H, S(O)Me), 3 76 (s, 1 0H, OMe), 3 77 (s, 2 0H, OMe), 4 00 (br s, 4H, $\{H\text{-}2\}_2$, $\{H\text{-}3\}_2$)

***(1'R*,4a'S*,10'S*,10a'R*)-10'-Hydroxy-7'-methoxy-1'-methyl-3',4',4a',9',10',10a'-hexahydrospiro[1,3-dioxolane-2,2'(1' H)-phenanthrene]* (28).** To a stirred solution of the sulphoxide (**26**) (21 5 g, 58 7 mmol) in dry CH_2Cl_2 (800 ml) at -10° under an atmosphere of Ar was added dropwise trifluoroacetic anhydride (9 1 ml, 64 4 mmol), followed by trifluoromethanesulphonic acid (2 4 ml, 28 mmol) The solution was stirred at -10° for 1 5 hrs and dry pyridine (15 ml) was then added in a rapid stream The solution was washed with dilute HCl, water, dried ($MgSO_4$) and the solvent was removed *in vacuo* The product was dissolved in acetone (500 ml) and was stirred with W2 Raney nickel (80 g) for 2 hrs at room temperature under an atmosphere of Ar The mixture was then filtered through Celite, the nickel was washed with CH_2Cl_2, and the solvent was removed from the filtrate *in vacuo* A solution of the product in dry ether (300 ml) was added dropwise to $LiAlH_4$ (4 g) in ether (150 ml) at -78° under an atmosphere of Ar and the mixture was then stirred for 0 5 hrs The mixture was then allowed to warm to room temperature over 1 hr, and sat Na_2SO_4 was added dropwise until coagulation occurred The mixture was filtered through Celite, the solids were washed with ether, and the solvent was removed from the filtrate *in vacuo* Radial chromatography (25% EtOAc/petrol) gave two major components, a higher R_f component (4 2 g), followed by the desired *phenanthrene* (**28**) (5 0 g, 28% over three steps) as a gum, Found C, 70 93, H, 7 86% $C_{18}H_{24}O_4$ requires C, 71 03, H, 7 95%, ^{1}H n m r (300 MHz, $CDCl_3$) δ 1 06 (d, *J* 7 Hz, 3H, Me-1'), 1 50 (dddd, *J* 3 5, 13, 13, 13 Hz, 1H, H-4'$_{ax}$), 1 68 (dddd, *J* 2, 3, 3 5, 13 Hz, 1H, H-3'$_{eq}$), 1 89 (ddd, *J* 4, 13, 13 Hz, 1H, H-3'$_{ax}$), 1 91 (ddd, *J* 4, 11, 12 Hz, 1H, H-10a'), 2 26-2.39 (m, 2H, H-1', H-4'$_{eq}$), 2 67 (ddd, *J* 3, 12, 13 Hz, 1H, H-4a'), 2 82 (dd, *J* 10, 16 Hz, 1H, H-9'$_{ax}$), 3 12 (dd, *J* 6, 16 Hz, 1H, H-9'$_{eq}$), 3 77 (s, 3H, OMe), 3 85-4 01 (m, 5H, $\{H\text{-}4\}_2$, $\{H\text{-}5\}_2$, H-10'), 6 60 (d, *J* 2 5 Hz, 1H, H-8'), 6 73 (dd, *J* 2 5, 8 5 Hz, 1H, H-6'), 7 19 (d, *J* 8 5 Hz, 1H, H-5'), ^{13}C n m r (75 5 MHz, $CDCl_3$) See Table 2, *m/z* 304 (7%, M$^+$), 188 (7), 175 (5), 100 (10), 99 (100).

Higher R_f component (mainly compound (**30**)): ^{1}H n m r (300 MHz, $CDCl_3$, partial spectrum) δ 1 03 (d, *J* 6 5 Hz, 2 25H, Me-1'), 1 08 (d, *J* 6 5 Hz, 0 75H, Me-unidentified component), 1 51 (ddd, *J* ≈ 2, 11, 11 Hz, H-10a'), 1 60 (ddd, *J* ≈ 3 5, 13, 13 Hz, H-3'$_{ax}$), 1 97 (dq, *J* ≈ 6 5, 11 Hz, H-1'), 2 42 (m, $W_{h/2}$ 20 Hz, 0 75H, H-4'$_{eq}$), 2.67 (ddd, *J* 3 5, 11, 11 Hz, 0 75H, H-4a'), 2 89 (dd, *J* 2, 16 Hz, 0 75H, H-9'$_{ax}$), 3 08 (dd, *J* 3, 16 Hz, 0 75H, H-9'$_{eq}$), 3 77 (s, 2 25H, OMe), 3.79 (s, 0 75H, OMe-unidentified component), 3 90-4.10 (m, 4H, 1,3-dioxolanes), 4 32 (br s, $W_{h/2}$ 9 Hz, 0.75H, H-10'), 6 61 (d, *J* 2.5 Hz, 0.75H, H-8'), 6 71-6 80 (m, 1 25H, H-6' and ArH unidentified component), 7 09 (d, *J* 8 Hz, 0 25H, ArH unidentified component), 7 23 (d, *J* 8 5 Hz, 0 75H, H-5')

*(1*R**,4aS*,10S*,10a*R**)-10-Hydroxy-7-methoxy-1-methyl-3,4,4a,9,10,10a-hexahydrophenanthren-2(1*H*)-one* (**4**) A solution of the 1,3-dioxolane (**28**) (4 8 g, 15 8 mmol) and 2,6-dimethylpyridinium *p*-toluenesulphonate (1 5 g, 5 4 mmol) in wet acetone (300 ml) was heated under reflux for 70 hrs The acetone was removed *in vacuo* and the residue was dissolved in CH_2Cl_2 The CH_2Cl_2 solution was washed with water, dried ($MgSO_4$) and the solvent was removed *in vacuo*. The *ketone* (**4**) (3 7 g, 90%) crystallised from CH_2Cl_2/petrol, m p 125-6°, Found C, 74 00, H, 7 72 % $C_{16}H_{20}O_3$ requires C, 73 82, H, 7 74%, ^{1}H n m.r (300 MHz, $CDCl_3$) δ 1 25 (d, *J* 7 5 Hz, 3H, Me-1), 1 60 (m, $W_{h/2}$ 44 Hz, 1H, H-4$_{ax}$), 1 88 (ddd, *J* 4, 10, 11 Hz, 1H, H-10a), 2 40 (m, $W_{h/2}$ 26 Hz, 1H, H-3$_{eq}$), 2 62-2 77 (m, 2H, H-3$_{ax}$, H-4$_{eq}$), 2.83 (dd, *J* 10, 16 Hz, 1H, H-9$_{ax}$), 2 97-3 11 (m, 2H, H-1, H-4a), 3.15 (dd, *J* 6, 16 Hz, 1H, H-9$_{eq}$), 3 78 (s, 3H, OMe), 4 00 (m, $W_{h/2}$ 30 Hz, 1H, H-10), 6 63 (d, *J* 2 5 Hz, 1H, H-8), 6 76 (dd, *J* 2 5, 8 5 Hz, 1H, H-6), 7 22 (d, *J* 8 5 Hz, 1H, H-5), ^{13}C n m r (75 5 MHz, $CDCl_3$)· See Table 2, *m/z* 260 (100%, M$^+$), 203 (94), 199 (30), 187 (18), 186 (25), 185 (59), 175 (37), 172 (33), 171 (95), 161 (37), 160 (16), 159 (39), 158 (19), 147 (15), 146 (15), 145 (22), 144 (25), 128 (15), 122 (17), 115 (18), 91 (18)

2-Ethyl-1-hydroxy-6-(4'-methoxyphenyl)-3-oxocyclohexanecarboxylic Acid (**17**) *p*-Methoxyphenylpyruvic acid (75 g, 0 387 mol) was condensed with 1-chloro-3-hexanone (57 g, 0 43 mol) according to the procedure described for the preparation of (**16**) The *acid* (**17**) (70 g, 62%) crystallised from MeOH/EtOAc, m p 170-4° (dec), Found C, 65 53, H, 6 83% $C_{16}H_{20}O_5$ requires C, 65 74, H, 6 90%; ^{1}H n m r (300 MHz, d_4-MeOH) δ 0 85-1 05 (m, 4H, C($\underline{H}$)HC$\underline{H}_3$), 1 87-2 03 (m, 2H, H-5$_{eq}$, C(H)$\underline{H}$CH$_3$), 2 36-2 57 (m, 2H, H-4$_{eq}$, H-5$_{ax}$), 2 67 (m, $W_{h/2}$ 40 Hz, 1H, H-4$_{ax}$), 2 91 (apparent dd, *J* 1 5, 10 Hz, 1H, H-2), 3 55 (dd, *J* 4, 13 Hz, 1H, H-6), 3 72 (s, 3H, OMe), 6 76-6 81/7 23-7 28 (AA'BB', J_{AB} 9 Hz, 4H, ArH); ^{13}C n m.r (75 5 MHz, d_4-MeOH) δ 13 6 (CH$_2\underline{C}$H$_3$), 18 8 ($\underline{C}$H$_2$CH$_3$), 30 5 (C-5), 42 7 (C-4), 50 6 (C-6), 55 5 (OMe), 59.4 (C-2), 84 7 (C-1), 114 3 (C-3', C-5'), 130 8 (C-2', C-6'), 133 1 (C-1'), 160 1 (C-4'), 175 8 (CO_2H), 211 4 (C-3), *m/z* 292 (5%, M$^+$), 148 (7), 147 (11), 135 (12), 134 (100), 121 (5), 119 (5)

2-Ethyl-6-(4'-methoxyphenyl)-3-oxo-1-cyclohexenecarboxylic Acid (**19**) The acid (**17**) (75 g, 0 257 mol) was converted to (**19**) according to the procedure described for the preparation of (**18**) The *unsaturated acid* (**19**) (62 g, 88%) crystallised from EtOAc, m p 145-8°, Found C, 69 84, H, 6 71% $C_{16}H_{18}O_4$ requires C, 70 06, H, 6 61%, ^{1}H n m r (300 MHz, $CDCl_3$) δ 1 07 (apparent t, *J* 7 5 Hz, 3H, CH$_2$C$\underline{H}_3$), 2 00 (m, $W_{h/2}$ 34 Hz, 1H, H-5$_{ax}$), 2 30-2 62 (m, 5H, {H-4}$_2$, H-5$_{eq}$, C$\underline{H}_2$CH$_3$), 3 77 (s, 3H, OMe), 4 05 (br dd, *J* ≈ 5, 5 Hz, 1H, H-6), 6 82-6 87/7.08-7 13 (AA'BB', J_{AB}9 Hz, 4H, ArH), ^{13}C n m r (75 5 MHz, $CDCl_3$) δ 14 2 (CH$_2\underline{C}$H$_3$), 20 7 ($\underline{C}$H$_2$CH$_3$), 31 2 (C-5), 34 7 (C-4), 42 1 (C-6), 55 2 (OMe), 114 1(C-3', C-5'), 129 0 (C-2', C-6'), 132 0 (C-1'), 143 4 (C-2), 145 2 (C-1), 158 6 (C-4'), 172 3 (CO_2H), 199 2 (C-3), *m/z* 274 (57%, M$^+$), 256 (15), 213 (15), 186 (38), 173 (19), 166 (18), 158 (18), 134 (16), 128 (16), 121 (18), 115 (18), 108 (100)

2-Ethyl-6-(4'-methoxyphenyl)-3-oxocyclohexanecarboxylic Acid (**21**) The unsaturated acid (**19**) (120 g, 0 438 mol) was converted to (**21**) according to the procedure described for the preparation of (**20**) The *acid* (**21**) (115 g, 95%) was obtained as a solid H p l c analysis (10% EtOAc/petrol, 2 0 ml min^{-1}) of the methylated (diazomethane) acid (**21**) indicated the presence of two major diastereomers (R_t 6 9 min, 37%, R_t 12 1 min, 49%) and two minor isomers (R_t 6 3 min, 10%, R_t 9 7 min, 4%) The major isomers were isolated by radial chromatography (20% EtOAc/petrol) The (1*R**,2*S**,6*S**) isomer (**21a**) (R_t 6 9min) eluted first and crystallised from CH_2Cl_2/petrol, m p 82-3°, Found C, 70 37, H, 7 71% $C_{17}H_{22}O_4$ requires C, 70.32, H, 7 64%, ^{1}H n m r (300 MHz, $CDCl_3$) δ 0 89 (dd, *J* 7 5, 7 5 Hz, 3H, C(H)HC$\underline{H}_3$), 1 34 (m, $W_{h/2}$ 38 Hz, 1H, C($\underline{H}$)HCH$_3$), 1 61 (m, $W_{h/2}$ 42 Hz, 1H, C(H)$\underline{H}$CH$_3$), 1 97 (dddd, *J* 5, 13, 13, 13 Hz, 1H, H-5$_{ax}$), 2 15 (dddd, *J* 3, 3, 5 5, 13 Hz, 1H, H-5$_{eq}$), 2 48 (ddd, *J* 3, 5, 13 Hz, 1H, H-4$_{eq}$), 2 58 (ddd, *J* 5 5, 13, 13 Hz, 1H, H-4$_{ax}$), 2 66-2 77 (m, 2H, H-1, H-2), 3 25 (m, $W_{h/2}$ 27 Hz, 1H, H-6), 3 38 (s, 3H, CO_2Me), 3 77 (s, 3H, OMe), 6 79-6 84/7 06-7 11 (AA'BB', J_{AB} 9 Hz, 4H, ArH), ^{13}C n m r (75 5 MHz, $CDCl_3$) See Table 1, *m/z* 290 (24%, M$^+$), 231 (12), 230 (14), 214 (15), 192 (10), 188 (10), 175 (11), 174 (10), 148 (10), 147 (29), 135 (17), 134 (100), 121 (21), 115 (16), 91 (10), 83 (11)

The (1*R**,2*R**,6*R**) isomer (**21b**) (R_t 12 1 min) crystallised from CH_2Cl_2/petrol, m p 103 5-4 5°, Found C, 70 52, H, 7 83% $C_{17}H_{22}O_4$ requires C, 70 32, H, 7 64%, ^{1}H n m r (300 MHz, $CDCl_3$) δ 0 93 (dd, *J* 7 5, 7 5 Hz, 3H, C(H)HC$\underline{H}_3$), 1 08 (ddq, *J* 6, 12, 7 5 Hz, 1H, C($\underline{H}$)HCH$_3$), 1 90 (ddq, *J* 6, 12, 7 5 Hz, 1H, C(H)$\underline{H}$CH$_3$), 2 05 (ddddd, *J* 1 5, 2, 5, 6, 12 Hz, 1H, H-5$_{eq}$), 2 41-2 54 (m, 2H, H-2, H-4$_{ax}$), 2 57-

2 78 (m, 2H, H-4$_{eq}$, H-5$_{ax}$), 3 30 (ddd, *J* 1 5, 5, 5 Hz, 1H, H-1), 3 39 (ddd, *J* 5, 5, 13 Hz, 1H, H-6), 3 43 (s, 3H, CO$_2$Me), 3.78 (s, 3H, OMe), 6.81-6 86/7 07-7 12 (AA'BB', J_{AB} 9 Hz, 4H, ArH); ^{13}C n.m r. (75.5 MHz, CDCl$_3$) See Table 1; *m/z* 290 (27%, M$^+$), 175 (10), 174 (14), 148 (14), 147 (45), 143 (26), 135 (16), 134 (100), 121 (29), 115 (24), 83 (13)

Methyl 6-Ethyl-8-(4'-methoxyphenyl)-1,4-dioxaspiro[4 5]decane-7-carboxylate **(23)**. The acid **(21)** (103 g, 0 373 mol) was converted to **(23)** according to the procedure described for the preparation of **(22)** The *ester* **(23)** (99 g, 83% over two steps) was obtained as a semi-solid, ^{1}H n m r (80 MHz, CDCl$_3$, partial spectrum) δ 3 36 (s, 0 6H, CO$_2$Me), 3 39 (s, 1 5H, CO$_2$Me), 3 49 (s, 0.9H, CO$_2$Me), 3.77 (s, 3H, OMe), 3 88-4 13 (m, 4H, {H-2}$_2$, {H-3}$_2$)

*Methyl (6R*S*,7R*,8S*)-6-Ethyl-8-(4'-methoxyphenyl)-1,4-dioxaspiro[4 5]decane-7-carboxylate* **(25)** The ester **(23)** (99 g, 0 296 mol) was epimerised according to the procedure described for the preparation of **(24)** The *ester* **(25)** (87 g, 88%) was obtained as a solid, ^{1}H n m.r (80 MHz, CDCl$_3$, partial spectrum)· δ 3 35 (s, 2 4H, CO$_2$Me), 3.45 (s, 0 6H, CO$_2$Me), 3 75 (s, 3H, OMe), 3 99 (br s, 4H, {H-2}$_2$, {H-3}$_2$) A portion of the ester **(25)** was recrystallised twice from CH$_2$Cl$_2$/petrol to give the (6*R**,7*S**,8*R**) isomer **(25a)**, m p 101-2°, Found C, 68 13; H, 7 89% C$_{19}$H$_{26}$O$_5$ requires C, 68 24, H, 7 84%; ^{1}H n.m r (300 MHz, CDCl$_3$) δ 0 89 (dd, *J* 7 5, 7 5 Hz, 3H, C(H)HC$\underline{H}_3$), 1.20 (ddq, *J* 4, 14, 7 5 Hz, 1H, C($\underline{H}$)HCH$_3$), 1 51-1 62 (m, 2H, C(H)$\underline{H}$CH$_3$, H-10$_{ax}$), 1.70-1.90 (m, 3H, {H-9}$_2$, H-10$_{eq}$), 1 97 (ddd, *J* 4, 4, 11 Hz, 1H, H-6), 2.69 (dd, *J* 11, 11 Hz, 1H, H-7), 2.79 (ddd, *J* 4, 11, 11 Hz, 1H, H-8), 3 35 (s, 3H, CO$_2$Me), 3 75 (s, 3H, OMe), 3 92-4 05 (m, 4H, {H-2}$_2$, {H-3}$_2$), 6 77-6 81/7 08-7 10 (AA'BB', J_{AB} 9 Hz, 4H, ArH), ^{13}C n m.r (75 5 MHz, CDCl$_3$) See Table 1, *m/z* 334 (5%, M$^+$), 185 (9), 135 (5), 134 (39), 100 (7), 99 (100)

*(6R*S*,7R*,8S*)-6-Ethyl-8-(4'-methoxyphenyl)-1,4-dioxaspiro[4 5]decan-7-yl Methylsulphinylmethyl Ketone* **(27)** The ester **(25)** (10 0 g, 30 0 mmol) was converted to **(27)** according to the procedure described for the preparation of **(26)** The *sulphoxide* **(27)** (10 5 g, 92%) was obtained as a gum, ^{1}H n m r (80 MHz, CDCl$_3$, partial spectrum) δ 2.17 (s, 0 72H, S(O)Me), 2 23 (s, 1 42H, S(O)Me), 2 44 (s, 0 86H, S(O)Me), 3 76 (s, 0 72H, OMe), 3 78 (s, 2 28H, OMe), 4 02 (br s, 4H, {H-2}$_2$, {H-3}$_2$)

(1'R,4a'S*,10'S*,10a'R*)-1'-Ethyl-10'-hydroxy-7'-methoxy-3',4',4a',9',10',10a'-hexahydrospiro[1,3-dioxolane-2,2'(1'H)-phenanthrene]* **(29)** The sulphoxide **(27)** (10 0g, 26 3 mmol) was converted to **(29)** according to the procedure described for the preparation of **(28)** Radial chromatography (25% EtOAc/petrol) of the reaction product gave two major components, a higher R$_f$ component (1 1 g), followed by the desired *phenanthrene* **(29)** (2 3 g, 27% over three steps) as a gum, Found C, 71 48, H, 8 20% C$_{19}$H$_{26}$O$_4$ requires C, 71 67, H, 8 23%, ^{1}H n m r (300 MHz, CDCl$_3$) δ 1 11 (apparent t, *J* 7 5 Hz, 3H, CH$_2$C$\underline{H}_3$), 1 40-1 57 (m, 3H, H-4'$_{ax}$, C$\underline{H}_2$CH$_3$), 1 69 (dm, *J* 13 Hz/W$_{h/2}$ 8 Hz, 1H, H-3'$_{eq}$), 1 90 (ddd, *J* 4, 11, 11 Hz, 1H, H-10a'), 1 93 (ddd, *J* 5, 13, 13 Hz, 1H, H-3'$_{ax}$), 2 06 (m, W$_{h/2}$ 14 Hz, 1H, H-1'), 2 30 (m, W$_{h/2}$ 24 Hz, 1H, H-4'$_{eq}$), 2 55 (ddd, *J* 3, 11, 13 Hz, 1H, H-4a'), 2 80 (dd, *J* 10, 16 Hz, 1H, H-9'$_{ax}$), 3 07 (dd, *J* 5, 16 Hz, 1H, H-9'$_{eq}$), 3 76 (s, 3H, OMe), 3 85-4 03 (m, 5H, {H-4}$_2$, {H-5}$_2$, H-10'), 6 58 (d, *J* 2 5 Hz, 1H, H-8'), 6 72 (dd, *J* 2 5, 8 5 Hz, 1H, H-6'), 7 16 (d, *J* 8 5 Hz, 1H, H-5'), ^{13}C n m r. (75 5 MHz, CDCl$_3$) See Table 2, *m/z* 318 (5%, M$^+$), 190 (4), 100 (6), 99 (100)

(1R,4aS*,10S*,10aR*)-1-Ethyl-10-Hydroxy-7-methoxy-3,4,4a,9,10,10a-hexahydrophenanthren-2(1H)-one* **(5)** The 1,3-dioxolane **(29)** (5 4 g, 17 0 mmol) was converted to **(5)** according to the procedure described for the preparation of **(4)** The *ketone* **(5)** (4 6 g, 98%) was obtained as a gum, Found C, 74 52, H, 8 19 % C$_{17}$H$_{22}$O$_3$ requires C, 74 42, H, 8 08%, ^{1}H n m r (300 MHz, CDCl$_3$)· δ 0 90 (dd, *J* 7 5, 7 5 Hz, 3H, C(H)HC$\underline{H}_3$), 1 60 (m, W$_{h/2}$ 48Hz, 1H, H-4$_{ax}$), 1 70 (ddq, *J* 12, 12, 7 5 Hz, 1H, C($\underline{H}$)HCH$_3$), 1 80-1 92 (m, 2H, C(H)$\underline{H}$CH$_3$, H-10a), 2 40 (m, W$_{h/2}$ 20 Hz, 1H, H-3$_{eq}$), 2 61-2 73 (m, 2H, H-3$_{ax}$, H-4$_{eq}$), 2 77-2 88 (m, 2H, H-1, H-9$_{ax}$), 3 07-3 20 (m, 2H, H-4a, H-9$_{eq}$), 3 78 (s, 3H, OMe), 4 05 (m, W$_{1/2}$ 28 Hz, 1H, H-10), 6 62 (d, *J* 2 5 Hz, 1H, H-8), 6 75 (dd, *J* 2 5, 8 5 Hz, 1H, H-6), 7 21 (d, *J* 8 5 Hz, 1H, H-5), ^{13}C n m r (75 5 MHz, CDCl$_3$) See Table 2, *m/z* 274 (100%, M$^+$), 227 (26), 217 (45), 200 (16), 199 (73), 185 (19), 175 (22), 172 (35), 171 (84), 161 (30), 159 (38), 158 (23), 147 (19), 145 (18), 144 (18)

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References

(1) Akera, T , *Science*, **1977**, *198*, 569, Akera, T and Brody, T M., *Pharmacol Rev* , **1978**, *29*, 187; Thomas, R., Brown, L , Boutagy, J. and Gelbart, A., *Circ Res* , Supp I, **1980**, *46*; Akera, T , in *Handbook of Experimental Pharmacology*, Greeff, K , ed., Vol. 56/1, Springer-Verlag Berlin, Heidelberg, New York, 1981, pp. 287-336

(2) Dalma, G., in *The Alkaloids*, Manske, R.H.F. and Holmes, H.L., eds., Vol. IV, Academic Press New York, 1954, pp. 265-73 , McCawley, E.L , in *The Alkaloids*, Manske, R H F , ed., Vol V, Academic Press New York, 1955, pp. 101-4.

(3) Tobin, T , Akera, T , Brody, S L., Ku, D and Brody, T.M., *Eur J Pharmacol* , **1975**, *32*, 133, Akera, T , Fox, A.L. and Greeff, K., in *Handbook of Experimental Pharmacology*, Greeff, K., ed., Vol 56/1, Springer-Verlag Berlin, Heidelberg, New York, 1981, pp 459-86

(4) Thorp, R H and Cobbin, L.B., in *Medicinal Chemistry*, de Stevens, G., ed , Vol 6, Academic Press· New York, 1967, pp. 137-49.

(5) Clarke, R L., Daum, S.J., Shaw, P.E , Brown Jr., T.G , Groblewski, G.E. and O'Conner, W V , *J Med Chem* , **1967**, *10*, 582, Clarke, R.L., Daum, S J., Shaw, P.E., Brown Jr , T.G , Groblewski, G.E. and O'Conner, W V., *J Med Chem* , **1967**, *10*, 593; Daum, S J. and Clarke, R.L , *J Med Chem* , **1968**, *11*, 1069, Daum, S.J. and Clarke, R.L., *J Med Chem* , **1970**, *13*, 320, Cronlund, A , *Acta Pharm Suec* , **1976**, *13*, 27; Cronlund, A., and Sandberg, F., *Acta Pharm Suec* , **1976**, *13*, 35, Cronlund, A , *Acta Pharm Suec* , **1976**, *13*, 175, Hauth, H., *Planta Medica* (Supp 4), **1971**, 40.

(6) Baker, R.W., Knox, J.R , Skelton, B.W and White, A.H , *Tetrahedron*, following paper, this issue.

(7) The structures of digitoxigenin (1) and cassaine (2) represent the single enantiomer; all other structures represent racemic mixtures

(8) Atrache, V., PhD Thesis, University of Western Australia, 1981

(9) Turner, R.B , Buchardt, O., Herzog, E , Morin, R B., Riebel, A and Sanders, J M , *J Am Chem Soc* , **1966**, *88*, 1766

(10) Abad, A , Agullo, C , Arno, M , Domingo, L R. and Zaragoza, R J., *Tetrahedron Lett* , **1986**, *27*, 3289

(11) Blair, I A., Mander, L.N and Mundill, P H.C., *Aust J Chem* , **1981**, *34*, 1235

(12) Oikawa, Y and Yonemitsu, O , *Tetrahedron*, **1974**, *30*, 2653

(13) Oikawa, Y. and Yonemitsu, O , *J Org Chem* , **1976**, *41*, 1118

(14) Ziegler, F E. and Condon, M E , *J Org Chem* , **1971**, *36*, 3707

(15) Corey, E J and Chaykovsky, M., *J Am Chem Soc* , **1965**, *87*, 1345

(16) Valko, J T. and Wolinsky, J., *J Org Chem* , **1979**, *44*, 1502.

(17) Stothers, J B , *Carbon-13 NMR Spectroscopy*, Academic Press New York, 1972, pp 65-7

(18) Paquette, L A , Nitz, T J., Ross, R J. and Springer, J P , *J Am Chem Soc* , **1984**, *106*, 1446

(19) Woodward, R.B , Sondheimer, F., Taub, D , Heusler, K. and McLamore, W M , *J Am Chem Soc* , **1952**, *74*, 4224

(20) Bowden, K , Braude, E A , Jones, E R.H and Weedon, B C L , *J Chem Soc* , **1946**, 45

(21) Miyashita, N., Yoshikoshi, A and Grieco, P.A , *J Org Chem* , **1977**, *42*, 3772

(22) Perrin, D.D , Amarego, W L F and Perrin, D.R , *Purification of Laboratory Chemicals*, 2nd Ed , Pergamon Press Oxford, 1980