Total Synthesis of the Antileukaemic Lignan (±)-Steganacin [1]

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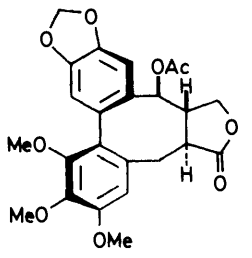
A synthetic route to the antileukaemic lignan (±)-steganacin (1) is described from the readily available piperonal and 3,4,5-trimethoxyphenylacetic acid. Diastereoisomerism encountered in a number of precursors has been ascribed unambiguously to the presence of the bridged biphenyl system (atropisomerism).

In 1973 Kupchan and his co-workers [2] reported the isolation of four related lignans from *Steganotaenia araliacea* Hochst. Two of them, termed steganacin (1) and steganangin, were shown to be respectively the *O*-acetyl and *O*-angelyl derivatives of the third constituent, the β-alcohol steganol. The fourth compound was shown to be the corresponding ketone steganone (2) by reduction with sodium borohydride, which pro-

[1] Preliminary communications, D. Becker, L. R. Hughes, and R. A. Raphael, *J.C.S. Chem. Comm.*, 1974, 430; L. R. Hughes and R. A. Raphael, *Tetrahedron Letters*, 1976, 1543.

[2] S. M. Kupchan, R. W. Britton, M. F. Ziegler, C. J. Gilmore, R. J. Restivo, and R. F. Bryan, *J. Amer. Chem. Soc.*, 1973, **95**, 1335.

duced a 1 : 1 mixture of steganol and episteganol. These natural products were identified as members of the rare group[3] of dibenzocyclo-octene lignans by *X*-ray crystallographic analysis of episteganol, which established the *trans*-fused γ-lactone system (1) as representing the structure and probable absolute configuration of steganacin. The significant antileukaemic activity reported[2] for steganacin and steganangin has aroused interest in the synthesis of these lignans in order to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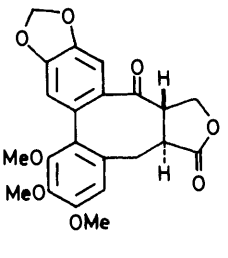
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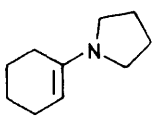
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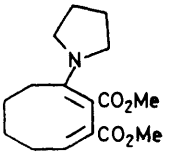
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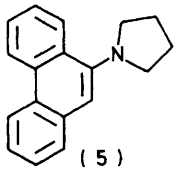
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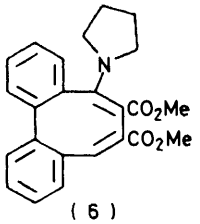
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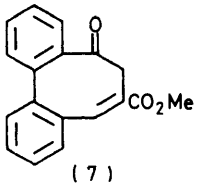
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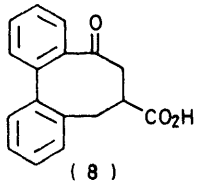
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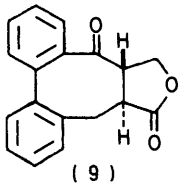
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supplement their natural availability for further pharmacological study. We now report the efficient synthesis of (±)-steganacin from the readily available piperonal and 3,4,5-trimethoxyphenylacetic acid. After this work had been completed a preliminary communication appeared reporting another synthesis of (±)-steganacin by a completely different approach.[4]

The primary synthetic target was steganone (2), from which the other lignans are readily derivable. The nub of any synthetic plan logically centred on the establishment of an efficient process for constructing the highly functionalised eight-membered carbocycle. One such procedure which has been used in monocyclic examples entails the double ring expansion of an enamine.[5] Thus 1-pyrrolidinocyclohexene (3), by reaction with dimethyl but-2-ynedioate, gives by way of a bicyclo[4.2.0]octene intermediate the highly functionalised cyclo-octadiene (4). This structure contains a latent γ-oxo-acid functionality of precisely the type required for elaboration to the oxo-γ-lactone feature contained in steganone. Extension of this process to the required steganone synthesis would require as starting material a dibenzo-fused enamine, *i.e.* a suitably substituted 9-pyrrolidinophenanthrene. Because of the ethylenic properties of the 9,10-double bond of phenanthrenes it appeared that their 9-pyrrolidino-derivatives might exhibit enamine-like properties and undergo an analogous double ring expansion.

To test this hypothesis a model compound, 9-pyrrolidinophenanthrene (5) itself, was synthesised and treated with dimethyl but-2-ynedioate. This led in high yield to the required doubly ring-expanded product (6). Hydrolysis of this product with methanolic hydrochloric acid was accompanied by decarboxylation to give the unsaturated oxo-ester (7). Catalytic hydrogenation over Raney nickel gave the saturated oxo-ester which was hydrolysed to the oxo-acid (8). Treatment of this product with aqueous formaldehyde and potassium hydroxide not only brought about the anticipated aldol hydroxymethylation and concomitant γ-lactonisation, but also effected a cross-Cannizzaro reduction of the carbonyl group. The resulting hydroxy-lactone was readily oxidised by Jones reagent to give the oxo-lactone (9) in high overall yield. Only one homogeneous racemate * was obtained and, as base-catalysed epimerisation can readily take place at both chiral centres of structure (9), the product represents the thermodynamically more stable of the two modes of fusion of the γ-lactone. That this was in fact the desired *trans*-fused diastereoisomer (9) was strongly indicated by the close correspondence, in the relevant non-benzenoid regions, between the n.m.r. spectra of (9) and steganone itself; both in chemical shift position and complexity of the splitting patterns of the six protons concerned there was essential identity. For example the two diastereotopic protons of the γ-lactone methylene group were readily distinguishable as the AB part of an ABX system with J_{AB} 9.5, J_{AX} 9.5, J_{BX} 7.0 Hz; these values were identical with those of the corresponding system in steganone.

After the success of the model sequence the next synthetic goal was the establishment of an efficient

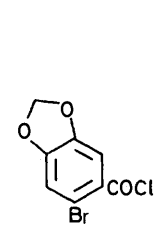
* Racemates are illustrated as one enantiomer throughout.

[3] N. K. Kochetkov, A. Khorlin, O. S. Chizhov, and V. I. Sheichenko, *Tetrahedron Letters*, 1961, 730; 1962, 361; Y. P. Chen, R. Liu, H. Y. Hsu, S. Yamamura, Y. Shizuri, and Y. Hirata, *ibid.*, 1973, 4257; Y. Ikeya, H. Taguchi, and Y. Litaka, *ibid.*, 1976, 1359.

[4] A. S. Kende and L. S. Liebeskind, *J. Amer. Chem. Soc.*, 1976, **98**, 267; A. S. Kende, L. S. Liebeskind, C. Kubiak, and R. Eisenberg, *ibid.*, p. 6389; see also R. E. Damon, R. H. Schlessinger, and J. F. Blount, *J. Org. Chem.*, 1976, **41**, 3772.

[5] G. A. Berchtold and G. F. Uhlig, *J. Org. Chem.*, 1963, **28**, 1459; K. C. Brannock, R. D. Burpitt, V. W. Goodlett, and J. G. Thweatt, *ibid.*, p. 1464; C. F. Huebner, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, and P. Strachan, *ibid.*, p. 3134.

route to the cognate precursor for steganone, 2,3,4-trimethoxy-6,7-methylenedioxy-9-pyrrolidinophenanthrene (15). The readily available 6-bromopiperonal was oxidised to the corresponding acid, which was converted into the acid chloride (10). Condensation of this latter with the lithio-derivative of t-butyl 3,4,5-trimethoxyphenylacetate furnished the β-oxo-ester (11), which was readily hydrolysed and decarboxylated to the ketone (12) by heating with degassed aqueous dimethyl sulphoxide. Acid-catalysed treatment with pyrrolidine converted the ketone (12) into a homogeneous enamine (13). Assignment of the *E*-stereochemistry shown was



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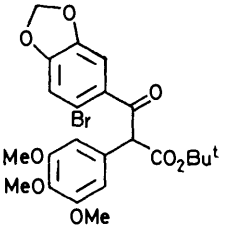

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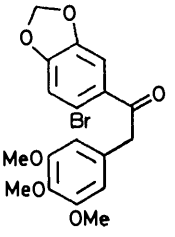

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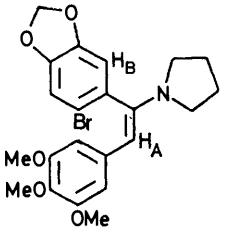

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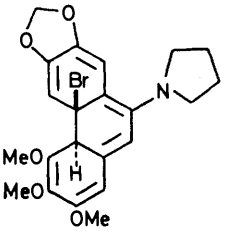

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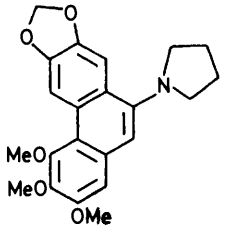


(15)

made on the basis of intramolecular nuclear Overhauser effects. Irradiation at the resonance frequency of the α-protons of the pyrrolidine ring (τ 6.9) caused an enhancement of 18% in the intensity of the resonances of H_A and H_B relative to those of the remaining benzenoid protons. On the basis of analogy in the field of aporphine synthesis [6] it was hoped that irradiation of the stilbene (13) would effect a conrotatory cyclisation to the *trans*-bromodihydrophenanthrene (14), whence ready *trans*-elimination of hydrogen bromide should give the required phenanthrene (15). In spite of the precedent, irradiation of a solution of the enamine (13) in benzene–t-butyl alcohol in the presence of potassium t-butoxide gave no trace of the required phenanthrene. The only process ensuing was the photo-oxidative cleavage [7] of (13) to produce 3,4,5-trimethoxybenzaldehyde and *N*-(6-bromo-3,4-methylenedioxybenzoyl)-pyrrolidine. This difficulty was overcome by carrying out the irradiation on a suspension of the enamine (13) and potassium t-butoxide in refluxing liquid ammonia; [8] the phenanthrene (15) was produced in 65% yield. This profound influence of liquid ammonia as solvent raises the question as to whether the process is a simple electrocyclisation as shown or a free radical process initiated by photochemical homolysis of the carbon–bromine bond.

Heating a solution of the phenanthrene (15) in dioxan with dimethyl but-2-ynedioate gave the desired ring-expanded product (16) in high yield. Treatment of this enamine diester with methanolic hydrochloric acid transformed it into the unsaturated oxo-ester (17), which was converted into a homogeneous saturated oxo-ester (18) by catalytic hydrogenation. The assignment of the position of the double bond in (17) was based on a spectroscopic comparison with the hydrogenated product (18). Thus the benzylic carbonyl band at 1 680 cm^{-1} for (17) was shifted to a *lower* value of 1 660 cm^{-1} for the saturated oxo-ester (18), the reverse of that expected if the double bond of (16) had been conjugated with the ketone. Molecular models show that this shift is explicable in terms of the greater degree of coplanarity of the ketone carbonyl group and its conjugated benzene ring in the saturated oxo-ester (18). A further pointer to the structure (17) was the very low field position of the vinylic proton (τ 2.2). Room temperature hydrolysis of the oxo-ester (18) with lithium hydroxide gave the corresponding oxo-acid. This was then subjected to treatment with aqueous formaldehyde–potassium hydroxide followed by Jones oxidation. This procedure gave a product termed isosteganone (19), which was isomeric with and possessed all the detailed functionality of steganone, but differed considerably in its spectroscopic properties from the natural product. Particularly striking was the difference in the i.r. spectrum; the benzylic ketone carbonyl band of isosteganone appeared at 1 710 cm^{-1} whereas that for steganone occurred at the expected 'conjugated' value of 1 665 cm^{-1}. It was then found that heating isosteganone in xylene effected a quantitative isomerisation to (±)-steganone, which was chromatographically and spectroscopically identical (apart from rotation) with authentic natural (−)-steganone (2). The overall yield of (±)-steganone from the acid chloride (10) by the above ten-step process was 23%.

Reduction of (±)-steganone with sodium borohydride gave the expected 1 : 1 mixture of (±)-steganol

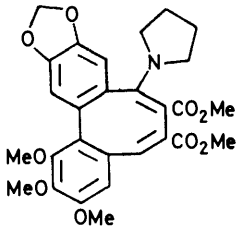
[6] S. M. Kupchan and P. F. O'Brien, *J.C.S. Chem. Comm.*, 1973, 915; M. P. Cava, P. Stern, and K. Wakisaka, *Tetrahedron*, 1973, **29**, 2245.

[7] C. S. Foote, A. A. Dzakpasa, and J. W. P. Lin, *Tetrahedron Letters*, 1975, 1247.

[8] *Cf.* M. F. Semmelhack, B. P. Chong, R. D. Stauffer, T. D. Rogerson, A. Chong, and L. D. Jones, *J. Amer. Chem. Soc.*, 1975, **97**, 2507; R. Rossi and J. F. Bunnett, *J. Org. Chem.*, 1973, **38**, 1407.

and (±)-episteganol, but use of the bulkier lithium tri-t-butoxyaluminium hydride improved the proportion of (±)-steganol to 5 : 2. Acetylation of this alcohol gave (±)-steganacin, identical spectroscopically with the natural antileukaemic lignan (1).

The ready thermal isomerisation of isosteganone (19) to steganone (2) suggested that we had encountered a case of hindered biphenyl isomerism.[9] This prompted us to examine the thermal lability of the homogeneous oxo-ester (18) and the corresponding acid. Heating either compound in xylene produced a 1 : 1 mixture of the starting material and a readily separable isomer. Subjection of the new isomeric oxo-acid to the above formaldehyde-oxidation sequence gave exclusively steganone. Unequivocal confirmation of the nature of the isomerism was provided by an *X*-ray crystallographic examination[10] of the highly crystalline, thermally stable (±)-isosteganol (20), the exclusive product from reduction of (±)-isosteganone with sodium



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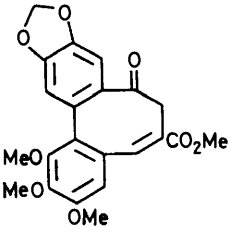

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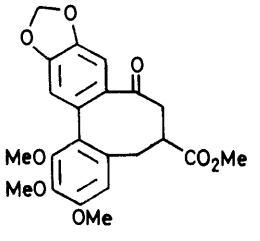

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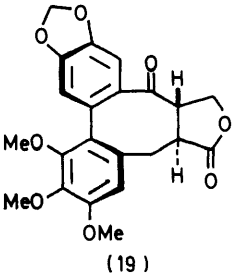

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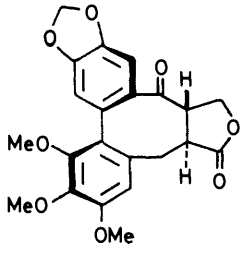

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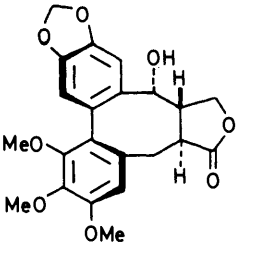
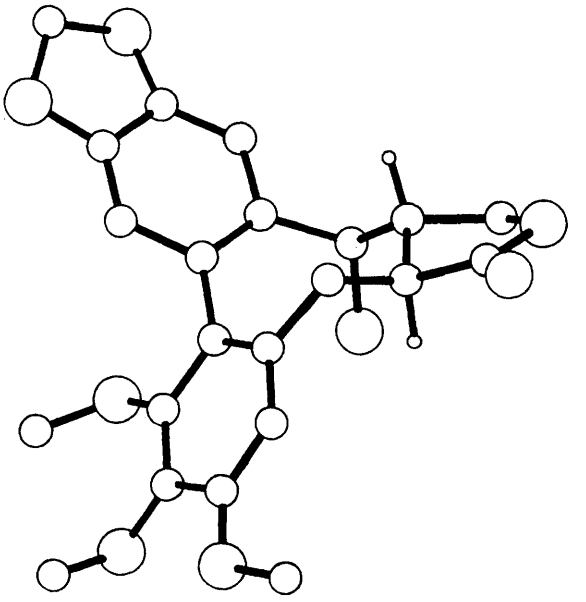


(20)

borohydride. The structure thus revealed (Figure) for the enantiomer corresponding to the natural series showed the retention of the *trans*-fusion of the γ-lactone ring but the skewing of the biphenyl system was revealed to be in the sense *opposite* to that of the natural lignans. The corresponding structure derived from the Figure for isosteganone (19) has the plane of the benzylic carbonyl group almost orthogonal to that of the adjacent benzene ring and thus accounts for the seemingly anomalous 'unconjugated' frequency already noted for this ketone. The attainment of true conjugation in steganone provides a plausible driving force for the completeness of the rearrangement of isosteganone to steganone. This



Crystal structure of isosteganol

molecular shape also explains the stereoselective reduction of isosteganone (19) to the single product isosteganol (20), as one face of the carbonyl group is seen to be highly sheltered by the trimethoxylated benzene ring. Finally the thermal inertness of isosteganol as compared with isosteganone may be plausibly rationalised[4] by postulating that the *trans*-fused γ-lactone 'locks' the molecule and prevents rotation of the aryl–aryl bond. In isosteganone (19) this hindrance may be removed by a β-elimination process, biphenyl isomerisation of the resulting methylene-oxo-acid, and relactonisation to steganone. Such a pathway is not available for isosteganol (20).

EXPERIMENTAL

M.p.s were recorded on a Kofler hot-stage apparatus. T.l.c. was carried out on Merck plates precoated with Kieselgel 60 F_{254}. Preparative thick-layer chromatography (p.l.c.) was carried out on plates (20 × 20 cm; 1.3 mm thick) coated with Kieselgel PF_{254}. Mass spectra were determined on A.E.I. MS 9, MS 30, and MS 902 instruments. U.v. absorption spectra were measured with a Unicam SP 1800 instrument. I.r. spectra were determined on a Perkin-Elmer 257 spectrometer. ^1H N.m.r. spectra were run on a Perkin-Elmer R12B or R24A or a Varian HA-100 spectrometer, with tetramethylsilane as internal standard. Extracts were dried over magnesium sulphate. Light petroleum refers to that fraction of boiling range 60—80 °C.

9-Pyrrolidinophenanthrene (5).—A solution of n-butyl-

[9] *Cf.* L. V. Dvorken, R. B. Smyth, and K. Mislow, *J. Amer. Chem. Soc.*, 1958, **80**, 486.

[10] S. E. Hull, L. R. Hughes, O. Kennard, and R. A. Raphael, in preparation.

lithium (15% in hexane; 36 ml) was added dropwise to stirred pyrrolidine (15 ml) under nitrogen at 0 °C. To this was slowly added a solution of 9-bromophenanthrene [11] (5 g) in pyrrolidine (10 ml) and the mixture was heated under reflux overnight. Cooling, addition of water, extraction with chloroform, drying, evaporation, and crystallisation from ethanol gave pale yellow needles of *9-pyrrolidinophenanthrene* (3.5 g, 75%), m.p. 68—69° (Found: C, 87.5; H, 6.75; N, 5.95. $C_{18}H_{17}N$ requires C, 87.4; H, 6.9; N, 5.65%), $\nu_{max.}$ ($CHCl_3$) 1 620, 1 600, 1 450, 1 390, 1 330, 1 120, and 870 cm^{-1}, $\lambda_{max.}$ ($CHCl_3$) 312 (log ε 3.92), 258infl (4.47), and 247 nm (4.54), τ ($CDCl_3$) 1.30—1.50 (2 H, m, ArH), 1.67—1.78 (1 H, m, ArH), 2.22—2.58 (5 H, m, ArH), 2.80 (1 H, s, H-10), 6.58—6.70 (4 H, m, N·CH_2·CH_2·N), and 7.90—8.02 (4 H, m, C·CH_2·CH_2·C), *m/e* 247 (100%, M^+), 218 (16), 204 (16), 191 (16), 127 (16), and 88 (21).

Dimethyl 5-Pyrrolidinodibenzo[a,c]*cyclo-octene-6,7-dicarboxylate* (6).—Dimethyl but-2-ynedioate (2 ml) was added dropwise at 0 °C to a stirred solution of 9-pyrrolidinophenanthrene (3.4 g) in dioxan (50 ml) under nitrogen. The mixture was heated under reflux for 2 days, cooled, and evaporated under reduced pressure. Crystallisation from ethyl acetate gave pale yellow needles of the *enamine* (4.41 g, 82%), m.p. 155—156° (Found: C, 74.3; H, 6.25; N, 3.9. $C_{24}H_{23}NO_4$ requires C, 74.0; H, 5.95; N, 3.6%), $\nu_{max.}$ ($CHCl_3$) 1 715, 1 680, 1 620, 1 440, 1 260, and 1 130 cm^{-1}, $\lambda_{max.}$ (EtOH) 340 (log ε 3.73), 306 (3.95), and 230 nm (4.31), τ ($CDCl_3$) 2.72br (9 H, s, ArH), 6.32 and 6.42 (6 H, 2 s, CO_2Me), 6.80—7.15 (2 H, m, N·CH_2), 7.25—7.50 (2 H, m, N·CH_2), and 8.2—8.8 (4 H, m, C·CH_2·CH_2·C), *m/e* 389 (100%, M^+), 374 (58), 358 (16), 330 (11), 218 (16), and 118 (37).

Methyl 7,8-Dihydro-8-oxodibenzo[a,c]*cyclo-octene-6-carboxylate* (7).—A solution of the enamine (6) (4.4 g) in tetrahydrofuran (100 ml) was heated under reflux with hydrochloric acid (5%; 150 ml) under nitrogen for 5 h. The solvent was removed under reduced pressure and the residue dissolved in chloroform; the solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. Crystallisation from methanol gave prisms of the *oxo-ester* (7) (2.5 g, 79%), m.p. 149—152° (Found: C, 77.9; H, 4.95. $C_{18}H_{14}O_3$ requires C, 77.7; H, 5.05%), $\nu_{max.}$ ($CHCl_3$) 1 715, 1 680, 1 640, 1 600, 1 440, 1 280, and 1 090 cm^{-1}, $\lambda_{max.}$ (EtOH) 271 (log ε 3.94) and 250 nm (4.2), τ ($CDCl_3$) 2.12 (1 H, s, =CH), 2.16—2.25 (1 H, m, ArH), 2.50—2.80 (6 H, m, ArH), 2.94—3.04 (1 H, m, ArH), 6.28 (3 H, s, CO_2Me), 6.28 (1 H, d, *J* 16 Hz, H_A of CO·CH_AH_B), and 6.76 (1 H, d, *J* 16 Hz, H_B of CO·CH_AH_B), *m/e* 278 (13%, M^+), 246 (26), 218 (73), 189 (100), 165 (61), and 152 (12).

5,6,7,8-Tetrahydro-8-oxodibenzo[a,c]*cyclo-octene-6-carboxylic Acid* (8).—A solution of the unsaturated oxo-ester (7) (750 mg) in ethyl acetate (5 ml) was added to a pre-reduced suspension of Raney nickel (7 g; grade W4) in ethyl acetate (20 ml) and the mixture was stirred overnight under hydrogen (1 atm). Filtration and removal of solvent gave the saturated hydroxy-ester. This oil was dissolved in acetone and Jones reagent added to the stirred solution at 0 °C until the orange colour persisted. The colour was discharged with isopropyl alcohol and the solution filtered and set aside over solid sodium hydrogen carbonate. Evaporation gave the saturated oxo-ester (667 mg) (Found: M^+, 280.1099. Calc. for $C_{18}H_{16}O_3$: *M*, 280.1110), $\nu_{max.}$ ($CHCl_3$) 1 735, 1 670, 1 600, 1 440, and 1 130 cm^{-1}, τ ($CDCl_3$) 1.72—3.0 (8 H, m, ArH), 6.32 (3 H, s, CO_2Me), and 6.7—7.52 (5 H, m, aliphatic ring). To a solution of this product (520 mg) in methanol (50 ml) was added potassium hydroxide solution (10%; 70 ml) and the resulting solution was heated under reflux for 90 min under nitrogen. Removal of solvent and acidification with concentrated hydrochloric acid precipitated a solid, which was extracted with chloroform and washed with water. Drying and evaporation gave the *oxo-acid* (8) (450 mg, 91%), which crystallised from benzene–light petroleum in needles, m.p. 149—152° (Found: C, 76.3; H, 5.5. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%), $\nu_{max.}$ ($CHCl_3$) 2 800—3 300, 1 710, 1 665, 1 660, 1 290, and 1 120 cm^{-1}, $\lambda_{max.}$ (EtOH) 300 (log ε 3.09), 255 (3.52), and 231 nm (3.87), τ ($CDCl_3$) 0.7br (1 H, s, CO_2H), 1.72—2.85 (8 H, m, ArH), and 6.6—7.5 (5 H, m, aliphatic ring), *m/e* 266 (77%, M^+), 221 (10), 194 (100), and 165 (65), *m** 186 ($M^+ \longrightarrow$ 221) and 142 ($M^+ \longrightarrow$ 194).

trans-*7,8,9,10-Tetrahydro-7-hydroxymethyl-8-oxodibenzo*[a,c]*cyclo-octene-6-carboxylic Acid Lactone* (9).—A solution of the oxo-acid (8) (100 mg) in aqueous potassium hydroxide (5%; 10 ml) was treated with aqueous formaldehyde (37%; 1 ml), stirred under nitrogen for 30 min, and acidified with concentrated hydrochloric acid. The precipitate was extracted with chloroform. Washing (brine), drying, and evaporation gave a crude hydroxy-lactone which was oxidised with Jones reagent as above. Crystallisation from 95% ethanol gave the *oxo-lactone* (9) (75 mg, 71%) as needles, m.p. 162—164° (Found: C, 77.9; H, 5.3. $C_{18}H_{14}O_3$ requires C, 77.7; H, 5.05%), $\nu_{max.}$ ($CHCl_3$) 1 775, 1 675, 1 600, 1 145, 1 125, and 1 020 cm^{-1}, $\lambda_{max.}$ (EtOH) 295 (log ε 3.36), 245 (3.95), and 227 nm (4.19), τ ($CDCl_3$) 1.90 (1 H, dd, *J* 7 and 2 Hz, ArH), 2.30—2.84 (7 H, m, ArH), 5.49 (1 H, 't,' H_A of ABX, $J_{AB} = J_{AX} = 9.5$ Hz, CH_2·O), and 5.69 (1 H, dd, H_B of ABX, J_{AB} 9.5, J_{BX} 7 Hz, CH_2·O), and 6.50—7.30 (4 H, m, remaining aliphatic protons), *m/e* 278 (44%, M^+), 194 (100), 180 (17), 166 (59), 165 (77), and 152 (13).

The spectroscopic evidence that the oxo-lactone (9) was a single compound was substantiated by careful chromatographic examination. T.l.c. showed a single spot with a variety of solvents on both alumina and silica plates. High pressure liquid–solid chromatography on a 10 ft × 1/8 in Chlorosil column with a range of heptane–chloroform mixtures confirmed the homogeneity. G.l.c. on a 3% silicone oil on Gas Chrom-R 1/8 in column at a variety of temperatures showed only a single peak.

2-Bromo-4,5-methylenedioxybenzoyl Chloride (10).—Bromine (20 ml) was added dropwise to a stirred solution of piperonal (55 g) in glacial acetic acid (120 ml) and the solution was left overnight at room temperature. The deposited solid was filtered off and the filtrate evaporated under reduced pressure to give a solid mass. The combined solids were crystallised from 95% ethanol to give needles of 6-bromopiperonal [12] (40 g), m.p. 127—129°. Aqueous potassium hydroxide (6%; 500 ml) was added dropwise to a stirred suspension of 6-bromopiperonal (20 g) in ethanol (500 ml) containing silver nitrate solution (36.4 g in 40 ml of water). After 2 h stirring the precipitated salts were filtered off and washed with aqueous potassium hydroxide (1%). Neutral material was removed from the combined filtrates by extraction with ether and

[11] C. A. Dornfield, J. E. Callan, and G. H. Coleman, *Org. Synth.*, Coll. Vol. 3, 1955, p. 134.

[12] A. modification of the process of A. H. Parijs, *Rec. trav. Chim.*, 1930, **49**, 27.

the solution acidified with concentrated hydrochloric acid. Extraction with chloroform (4 × 500 ml), washing (water), drying, and evaporation gave 2-bromo-4,5-methylenedioxybenzoic acid (20 g), m.p. 198—201° (lit.,[13] 200—202°). To this acid (10 g) was added a solution of thionyl chloride (29.4 ml) in benzene (50 ml) and the resulting solution was heated under reflux for 30 min. Removal of solvents under reduced pressure, dissolution of the residue in chloroform, washing with saturated sodium hydrogen carbonate solution and brine, drying, and evaporation gave the *acid chloride* (10 g, 94%), which was used for the next stage as soon as possible. A portion crystallised from benzene–light petroleum in prisms, m.p. 89—91° (Found: C, 36.7; H, 1.65. $C_8H_4ClBrO_3$ requires C, 36.4; H, 1.5%), $\nu_{max.}$ (CCl_4) 1 800, 1 770, 1 615, 1 485, 1 250, 1 115, 1 045, and 985 cm^{-1}, τ ($CDCl_3$) 2.45 and 2.95 (2 H, 2 s, ArH), and 3.90 (2 H, s, O·CH_2·O), *m/e* 264/262 (38%, M^+), 229/227 (100), 201/199 (46), 181 (31), and 143 (28).

t-Butyl 3,4,5-Trimethoxyphenylacetate.—3,4,5-Trimethoxyphenylacetic acid was obtained by hydrolysis (aqueous sodium hydroxide) of the corresponding nitrile, produced most conveniently from 2,6-dimethoxyphenol.[14] The acid (9 g), isobutene (22 ml), ether (20 ml), and concentrated sulphuric acid (1 ml) were sealed in a pressure bottle and shaken at room temperature for 24 h. More isobutene (22 ml) and concentrated sulphuric acid (1 ml) were added and the mixture was shaken for a further 24 h. The bottle was cooled to −5 °C and the contents poured into chilled aqueous sodium hydroxide (7%; 100 ml). Extraction with ether, washing with sodium hydrogen carbonate solution, drying (potassium carbonate), and evaporation gave the *ester* (10.4 g, 93%), crystallising from light petroleum in needles, m.p. 66—67° (Found: C, 64.0; H, 7.8. $C_{15}H_{22}O_5$ requires C, 63.8; H, 7.85%), $\nu_{max.}$ (CCl_4) 1 730, 1 580, 1 460, 1 320, 1 230, and 1 130 cm^{-1}, τ (CCl_4) 3.57 (2 H, s, ArH), 6.24 (6 H, s, 2 OCH_3), 6.30 (3 H, s, OCH_3), 6.66 (2 H, s, $ArCH_2$), and 8.56 (9 H, s, CMe_3), *m/e* 282 (34%, M^+), 226 (47), 211 (19), 181 (100), 165 (25), and 137 (19).

t-Butyl α-(2-Bromo-4,5-methylenedioxybenzoyl)-α-(3,4,5-trimethoxyphenyl)acetate (11).—To a stirred solution of di-isopropylamine (10 ml) in dry tetrahydrofuran at 0 °C under nitrogen, n-butyl-lithium (1.86M in hexane; 38 ml) was added dropwise. After 10 min the mixture was cooled to −78 °C and a solution of the above t-butyl ester (10 g) in tetrahydrofuran (150 ml) was added slowly. After further stirring at −78 °C for 3 h a solution of the acid chloride (10) (9.34 g) in tetrahydrofuran was added dropwise and the stirring was continued at −78 °C for 1 h. The mixture was allowed to warm slowly to room temperature and poured into hydrochloric acid (20 ml of concentrated acid in 250 ml of ice–water). Extraction with ether, washing with dilute hydrochloric acid (2%) and brine, drying (Na_2SO_4), and evaporation gave the product (11) as an oily solid which was used directly for the next stage. A sample was crystallised from 95% ethanol to give the *oxo-ester* (11) as needles, m.p. 97—99° (Found: C, 54.0; H, 5.0; Br, 15.7. $C_{23}H_{25}BrO_8$ requires C, 54.2; H, 4.9; Br, 15.7%), $\nu_{max.}$ ($CHCl_3$) 1 630, 1 600, 1 580, 1 480, 1 370, 1 340, 1 230, and 1 130 cm^{-1}, $\lambda_{max.}$ (EtOH) 298 (log ε 3.93) and 236infl nm (4.22), τ ($CDCl_3$) 3.10 (1 H, s, H-6 of ArCO), 3.53 (1 H, s, H-3 of ArCO), 3.66 (2 H, s, H-2 and -6 of ArCH), 4.12 (2 H, s, O·CH_2·O), 6.23 (3 H, s, OCH_3), 6.31 (6 H, s, 2 OCH_3), and 8.50 (9 H, s, CMe_3), *m/e* 510 and 508 (13%, M^+), 373 (18), 355 (100), 284 (28), 229/227 (82), and 208 (84).

2′-Bromo-4′,5′-methylenedioxy-2-(3,4,5-trimethoxyphenyl)-acetophenone (12).—A solution of the crude β-oxo-ester (11) in aqueous dimethyl sulphoxide (3 : 1; 240 ml) was degassed by bubbling nitrogen through for 2 h. The solution was then heated under reflux under nitrogen for 2.5 h and the solvents were removed under reduced pressure. Crystallisation of the residue from 95% ethanol gave the *ketone* (12) [10.79 g, 74% based on acid chloride (10)] as needles, m.p. 111—112° (Found: C, 52.9; H, 4.4; Br, 19.3. $C_{18}H_{17}BrO_6$ requires C, 52.8; H, 4.2; Br, 19.6%), $\nu_{max.}$ ($CHCl_3$) 1 695, 1 595, 1 510, 1 480, 1 240, 1 135, and 1 040 cm^{-1}, $\lambda_{max.}$ (EtOH) 303 (log ε 3.64), 278 (3.66), and 225infl nm (4.35), τ ($CDCl_3$) 2.99 (1 H, s, H-6′), 3.16 (1 H, s, H-3′), 3.58 (2 H, s, H-2 and -6), 4.00 (2 H, s, O·CH_2·O), 5.87 (2 H, s, $ArCH_2$), and 6.19 (9 H, s, 3 OCH_3), *m/e* 410/408 (30%, M^+), 329 (23), 229/227 (67), and 181 (100).

2-Bromo-3′,4′,5′-trimethoxy-4,5-methylenedioxy-α-pyrrolidinostilbene (13).—Pyrrolidine (6.4 ml) and toluene-*p*-sulphonic acid (100 mg) were added to a solution of the ketone (12) (10.5 g) in degassed benzene (125 ml) and the mixture was heated under nitrogen in a Dean–Stark apparatus. After 6 h more pyrrolidine (6.4 ml) was added and heating continued for a further 10 h. The solvents were then removed under reduced pressure and the solid residue was crystallised from 95% ethanol to give needles of the *enamine* (13) (10.4 g, 88%), m.p. 148—149° (Found: C, 57.0; H, 5.25; Br, 17.2; N, 3.25. $C_{22}H_{24}BrNO_5$ requires C, 57.1; H, 5.2; Br, 17.4; N, 3.05%), $\nu_{max.}$ ($CHCl_3$) 1 600, 1 500, 1 480, 1 230, 1 135, and 1 040 cm^{-1}, $\lambda_{max.}$ (EtOH) 310 (log ε 4.29) and 238 nm (4.14), τ ($CDCl_3$) 2.90 (1 H, s, H-3), 3.16 (1 H, s, H-6), 4.00 (2 H, s, H-2′ and -6′), 4.03br (2 H, d, *J* 2 Hz, O·CH_2·O), 4.79 (1 H, s, ArCH=), 6.26 (3 H, s, OCH_3), 6.40 (6 H, s, 2 OCH_3), 6.68—7.00 (4 H, m, N·CH_2), and 8.00—8.20 (4 H, m, C·CH_2·CH_2·C), *m/e* 463 and 461 (100%, M^+), 449/447 (69), 381 (8), 350 (10), and 248 (12), *m** 431 ($M^+ \longrightarrow$ 448). The nuclear Overhauser experiment establishing this enamine as having the *E*-configuration is described in the main text.

2,3,4-Trimethoxy-6,7-methylenedioxy-9-pyrrolidinophenanthrene (15).—A three-necked straight-sided vessel was employed, equipped with a central quartz immersion well in which was located a 125 W Hanovia medium-pressure mercury lamp cooled by a surrounding jacket of dry air. The other two necks were provided with inlets for nitrogen and ammonia and a condenser cooled with solid carbon dioxide. The vessel was charged with the enamine (15) (5 g), potassium t-butoxide (12 g), and a magnetic stirrer. The apparatus was thoroughly flushed with dry nitrogen and cooled to −78 °C, and dry ammonia was admitted (*ca.* 700 ml) with continuation of the nitrogen stream. The temperature was then allowed to rise to the b.p. of ammonia and kept at that level by external cooling. The u.v. lamp was switched on and the reactants dispersed by vigorous stirring. After 6 h irradiation aqueous sodium carbonate (10%; 150 ml) and methanol (150 ml) were added slowly and the ammonia was allowed to evaporate overnight. Extraction with ether, washing (brine), drying (Na_2SO_4) and evaporation gave a semi-solid residue, which was crystallised from 95% ethanol to give the *phenanthrene* (15) (2.7 g, 65%) as pale yellow rhombs, m.p. 133—135° (Found: C, 69.3; H, 6.25; N, 3.9. $C_{22}H_{23}NO_5$ requires C, 69.3; H, 6.1; N, 3.65%), $\nu_{max.}$ (CCl_4) 1 630, 1 600, 1 490, 1 465,

[13] K. Böttcher, *Ber.*, 1909, **42**, 265.

[14] J. H. Short, D. A. Dunnigan, and C. W. Ours, *Tetrahedron*, 1973, **29**, 1931.

1 240, 1 100, and 1 050 cm^{-1}, $\lambda_{max.}$ (EtOH) 362 (log ε 3.07), 344 (3.45), 319infl (3.97), 289 (4.50), 261 (4.60), and 253 nm (4.58), τ ($CDCl_3$) 1.01 (1 H, s, ArH), 2.34, 2.90, and 3.06 (3 H, 3 s, 3 ArH), 3.94 (2 H, s, O·CH_2·O), 6.03 (9 H, s, 3 OCH_3), 6.68—6.82 (4 H, m, N·CH_2), and 7.90—8.06 (4 H, m, C·CH_2·CH_2·C), *m/e* 381 (100%, M^+), 366 (75), 323 (21), 252 (11), 190 (14), and 183 (11), *m** 351 ($M^+ \longrightarrow$ 366).

Dimethyl 1,2,3-*Trimethoxy*-10,11-*methylenedioxy*-8-*pyrrolidinodibenzo*[a,c]*cyclo-octene*-6,7-*dicarboxylate* (16).—A solution of the phenanthrene (15) (600 mg) and dimethyl but-2-ynedioate (0.2 ml) in dry dioxan (5 ml) was heated under reflux under nitrogen for 48 h. More acetylenic ester (0.2 ml) was added and the heating was continued for 48 h. Removal of the solvent under reduced pressure and crystallisation from ethanol gave pale yellow needles, m.p. 226—228°, of the *diester* (16) (750 mg, 91%) (Found: C, 64.0; H, 5.7; N, 2.55. $C_{28}H_{29}NO_9$ requires C, 64.2; H, 5.6; N, 2.7%), $\nu_{max.}$ ($CHCl_3$) 1 715, 1 675, 1 485, 1 450, 1 335, 1 250, 1 105, and 1 045 cm^{-1}, $\lambda_{max.}$ (EtOH) 344 (log ε 4.21), 302 (4.62), and 248infl nm (4.74), τ ($CDCl_3$) 2.77 (1 H, s, CH=), 3.30 (1 H, s, ArH), 3.46 (2 H, s, ArH), 4.01br and 4.03br (2 H, 2 s, O·CH_2·O), 6.14, 6.16, and 6.17 (9 H, 3 s, 3 OCH_3), 6.31 and 6.42 (6 H, 2 s, 2 CO_2Me), 6.60—6.90 (2 H, m, N·CH_2), 7.16—7.40 (2 H, m, N·CH_2), and 8.16—8.80 (4 H, m, C·CH_2·CH_2·C), *m/e* 523 (100%, M^+), 508 (70), 493 (11), 406 (11), 262 (14), and 241 (11), *m** 494 ($M^+ \longrightarrow$ 508).

Methyl 7,8-*Dihydro*-1,2,3-*trimethoxy*-10,11-*methylenedioxy*-8-*oxodibenzo*[a,c]*cyclo-octene*-6-*carboxylate* (17).—A solution of the enamine diester (16) (700 mg) in methanol (25 ml) was heated under reflux with hydrochloric acid (5%; 30 ml) under nitrogen for 3 h. Removal of methanol under reduced pressure, extraction with ether, washing with sodium hydrogen carbonate solution and brine, drying, evaporation and crystallisation from methanol gave plates m.p. 144—145°, of the unsaturated *oxo-ester* (17) (500 mg, 90%) (Found: C, 64.0; H, 4.95. $C_{22}H_{20}O_8$ requires C, 64.1; H, 4.9%), $\nu_{max.}$ (CCl_4) 1 725, 1 680, 1 485, 1 400, 1 250, and 1 120 cm^{-1}, $\lambda_{max.}$ (EtOH) 320 (log ε 3.72), 274 (4.14), and 240 nm (4.40), τ ($CDCl_3$) 2.20 (1 H, s, CH=), 2.78 (1 H, s, H-9), 3.44 and 3.54 (2 H, 2 s, H-4 and -12), 3.97 and 4.01 (2 H, 2 d, *J* 2 Hz, O·CH_2·O), 6.10 (6 H, s, 2 OCH_3), 6.26 (3 H, s, OCH_3), 6.36 (1 H, d, *J* 15 Hz, H_A of CO·CH_AH_B), 6.52 (3 H, s, CO_2Me), and 6.75 (1 H, d, *J* 15 Hz, H_B of CO·CH_AH_B), *m/e* 412 (78%, M^+), 384 (100), 370 (33), 349 (53), 322 (15), and 294 (13).

Methyl 5,6,7,8-*Tetrahydro*-1,2,3-*trimethoxy*-10,11-*methylenedioxy*-8-*oxodibenzo*[a,c]*cyclo-octene*-6-*carboxylate* (18).—A solution of the unsaturated oxo-ester (17) (650 mg) in methyl acetate was reduced with hydrogen at 1 atm for 12 h over Raney nickel (grade W 4; 2 g). Filtration and evaporation left a residue which was dissolved in acetone (15 ml), treated with Jones reagent and worked up as in the cognate experiment described previously (with some batches of Raney nickel this subsequent oxidation was unnecessary). Crystallisation of the product from chloroform–di-isopropyl ether gave prisms, m.p. 127—129°, of the saturated *oxo-ester A* (18) (605 mg, 93%) (Found: C, 63.8; H, 5.4. $C_{22}H_{22}O_8$ requires C, 63.8; H, 5.35%), $\nu_{max.}$ (CCl_4) 1 735, 1 660, 1 480, 1 405, 1 365w, 1 340w, 1 240, 1 165, and 1 120 cm^{-1}, $\lambda_{max.}$ (EtOH) 320 (log ε 3.68), 275 (4.05), and 237 nm (4.39), τ (CCl_4) 2.56 (1 H, s, H-9), 3.45 and 3.56 (2 H, 2 s, H-4 and -12), 3.98 and 4.00 (2 H, 2 d, *J* 2 Hz, O·CH_2·O), 6.16, 6.20, and 6.37 (9 H, 3 s, 3 OCH_3), 6.47 (3 H, s, CO_2Me), and 7.10—7.72 (5 H, m, aliphatic ring), *m/e* 414 (100%, M^+), 383 (12), 371 (8), 328 (18), 313 (16), and 285 (16).

A solution of the oxo-ester A (100 mg) in xylene (5 ml) was heated under reflux under nitrogen for 2 h. Removal of solvent followed by p.l.c. [ethyl acetate–hexane (3 : 7)] gave equal amounts of starting oxo-ester A and a new faster moving isomeric *oxo-ester B*, which crystallised from methanol in prisms, m.p. 133—134° (Found: C, 63.7; H, 5.55%), $\nu_{max.}$ (CCl_4) 1 740, 1 660, 1 480, 1 405, 1 360w, 1 345w, 1 320w, 1 240, and 1 120 cm^{-1}, $\lambda_{max.}$ (EtOH) 326 (log ε 3.75), 276 (4.09), and 241 nm (4.37), τ (CCl_4) 2.44 (1 H, s, H-9), 3.44 and 3.59 (2 H, 2 s, H-4 and -12), 3.97 and 4.01 (2 H, 2 d, *J* 2 Hz, O·CH_2·O), 6.20 (6 H, s, 2 OCH_3), 6.36 (3 H, s, OCH_3), 6.47 (3 H, s, CO_2Me), and 6.86—7.60 (5 H, m, aliphatic ring), *m/e* 414 (100%, M^+), 383 (13), 371 (8), 328 (17), 313 (16), and 285 (13).

5,6,7,8-*Tetrahydro*-1,2,3-*trimethoxy*-10,11-*methylenedioxy*-8-*oxodibenzo*[a,c]*cyclo-octene*-6-*carboxylic Acids A and B*.—Lithium hydroxide (508 mg) was added to a stirred suspension of the oxo-ester A (18) (500 mg) in aqueous methanol (3 : 4; 35 ml) and the mixture was stirred overnight. The resulting clear solution was diluted with lithium hydroxide solution (2%; 15 ml) and extracted with chloroform. The aqueous solution was acidified with dilute hydrochloric acid and extracted with chloroform. The extracts were washed with brine, dried, and evaporated and the residue was crystallised from benzene–light petroleum to give needles, m.p. 144—146°, of the *oxo-acid A* (460 mg, 95%) (Found: M^+, 400.1170. $C_{21}H_{20}O_8$ requires *M*, 400.1156), $\nu_{max.}$ ($CHCl_3$) 2 800—3 200br, 1 710, 1 660, 1 620, 1 600, 1 485, 1 410, 1 365w, 1 345w, 1 240, and 1 120 cm^{-1}, $\lambda_{max.}$ (EtOH) 312 (log ε 3.61), 2.75 (3.98), and 236 nm (4.35), τ ($CDCl_3$) 1.24—1.50br (1 H, CO_2H), 2.49 (1 H, s, H-9), 3.37 and 3.44 (2 H, 2 s, H-4 and -12), 3.94 and 3.97 (2 H, 2 d, *J* 2 Hz, O·CH_2·O), 6.08 (6 H, s, 2 OCH_3), 6.43 (3 H, s, OCH_3), and 7.05—7.70 (5 H, m, aliphatic ring), *m/e* 400 (41%, M^+), 357 (8), 317 (11), 279 (19), 274 (19), and 258 (100).

The oxo-ester B (18) (60 mg) was treated with lithium hydroxide in the same manner to give the *oxo-acid B* (53 mg, 91%), which crystallised from chloroform–light petroleum in needles, m.p. 169—172° (Found: M^+, 400.1165), $\nu_{max.}$ ($CHCl_3$) 2 800—3 200br, 1 705, 1 660, 1 620, 1 600, 1 485, 1 405, 1 365w, 1 345w, 1 315w, 1 240, and 1 115 cm^{-1}, τ ($CDCl_3$) 2.30 (1 H, s, H-9), 3.22 and 3.43 (2 H, 2 s, H-4 and -12), 3.92br and 3.94br (2 H, 2 s, O·CH_2·O), 6.06, 6.15, and 6.40 (9 H, 3 s, 3 OCH_3), and 6.72—7.54 (5 H, m, aliphatic ring), *m/e* 400 (64%, M^+), 357 (11), 328 (14), 279 (21), 274 (25), and 258 (100).

Heating the oxo-acid A in xylene for 3 h gave a *ca.* 1 : 1 mixture of unchanged oxo-acid A and oxo-acid B.

Isosteganone (19).—Aqueous formaldehyde (37%; 0.8 ml) was added to a solution of the oxo-acid A (200 mg) in aqueous potassium hydroxide (5%; 4 ml) and the mixture was stirred under nitrogen at room temperature for 2 h. The solution was acidified with concentrated hydrochloric acid and extracted with chloroform, and the extract was washed with brine and evaporated. The residue was dissolved in acetone (10 ml) and treated at 0 °C with Jones reagent in the usual manner. The product was dissolved in chloroform and washed with aqueous potassium hydroxide (5%). The aqueous extracts were acidified with hydrochloric acid and extracted with chloroform to give unchanged oxo-acid A (50 mg). The initial chloroform

extract was washed with brine, dried, and evaporated to yield a solid. Crystallisation from chloroform–ethanol gave (±)-*isosteganone* (19) (120 mg, 78%) as needles, m.p. 232—234° (thermal isomerisation to steganone had probably taken place during the heating) (Found: C, 64.0; H, 5.1. $C_{22}H_{20}O_8$ requires C, 64.1; H, 4.9%), $\nu_{max.}$ ($CHCl_3$) 1 780, 1 710, 1 590, 1 480, 1 400, 1 260, 1 230, 1 110, and 1 035 cm^{-1}, $\lambda_{max.}$ 284 (log ε 3.69) and 248 nm (4.06), τ ($CDCl_3$) 3.29, 3.37, and 3.44 (3 H, 3 s, 3 ArH), 3.94 (2 H, s, O·CH_2·O), 5.58 (1 H, d, *J* 4 Hz, H_A of C·CH_AH_B·O), 5.66 (1 H, s, H_B of C·CH_AH_B·O), 6.12 (6 H, s, 2 OCH_3), 6.30 (1 H, m), 6.48 (3 H, s, OCH_3), 6.71 (1 H, d, *J* 14 Hz), and 7.29—7.71 (2 H, m), *m/e* 412 (100%, M^+), 328 (21), 313 (9), 285 (13), and 191 (20).

Isosteganol (20).—To a solution of isosteganone (19) (20 mg) in methanol (1 ml) and dichloromethane (0.5 ml) was added sodium borohydride (2 mg). After 1 h a few drops of saturated ammonium chloride solution were added. Extraction with dichloromethane, drying, and evaporation gave a single alcohol, homogeneous by t.l.c., which was crystallised from chloroform–methanol to give (±)-*isosteganol* (20) as prisms, m.p. 240—242° (Found: M^+, 414.1292. $C_{22}H_{22}O_8$ requires *M*, 414.1312). The structure as determined by *X*-ray diffraction is shown in the Figure. It remained unchanged on attempted thermal isomerisation.

Steganone (2).—(*a*) A solution of isosteganone (120 mg) in dry xylene (5 ml) was heated under reflux under nitrogen for 1 h. Removal of the solvent under reduced pressure and crystallisation from 95% ethanol or chloroform–ethanol gave needles of (±)-*steganone* (2) (116 mg), m.p. 227—229° (Found: C, 63.7; H, 5.05. $C_{22}H_{20}O_8$ requires C, 64.1; H, 4.9%), $\nu_{max.}$ ($CHCl_3$) 1 775, 1 665, 1 610, 1 590, 1 480, 1 405, 1 230, 1 140, 1 120, 1 040, and 1 010 cm^{-1}, $\lambda_{max.}$ (EtOH) 320 (log ε 3.69), 277 (3.93), and 239 nm (4.34), τ ($CDCl_3$) 2.48 (1 H, s, H-9), 3.38 and 3.47 (2 H, 2 s, H-4 and -12), 3.92br (2 H, s, O·CH_2·O), 5.53 (1 H, ' t,' $J_{AB} = J_{AX} = 9.5$ Hz, H_A of CH_X·CH_AH_B·O), 5.67 (1 H, dd, J_{AB} 9.5, J_{BX} 7 Hz, H_B of CH_X·CH_AH_B·O), 6.12 (6 H, s, 2 OCH_3), 6.40 (3 H, s, OCH_3), and 6.70—7.60 (4 H, m, aliphatic ring), *m/e* 412 (100%, M^+), 398 (5), 381 (3), 328 (17), 313 (6), 285 (8), and 176 (6).

The n.m.r. spectrum of the synthetic (±)-steganone was identical with that of authentic naturally occurring (−)-steganone. The synthetic and natural steganone were indistinguishable by t.l.c. on both silica and alumina in a variety of solvent systems.

(*b*) Aqueous formaldehyde (37%; 0.2 ml) was added to a solution of the oxo-acid B (15 mg) in aqueous potassium hydroxide (5%; 1 ml) and the mixture was stirred under nitrogen for 2 h. The product was worked up and oxidised with Jones reagent as for isosteganone. Crystallisation from chloroform–ethanol gave (±)-steganone, identical with the product obtained in (*a*).

Steganol and Epistеganol.—A solution of steganone (125 mg) in dry tetrahydrofuran (3 ml) was added dropwise to a stirred solution of lithium tri-t-butoxyaluminium hydride (115 mg) in tetrahydrofuran (5 ml) at 0 °C under nitrogen. After 15 min saturated ammonium chloride solution was added and the mixture was extracted with ether. Washing with water, rapid drying (Na_2SO_4), and evaporation to 5 ml gave a concentrate which was separated by p.l.c. [ether–light petroleum (4 : 1)] to give (±)-*steganol* (82 mg, 65%) as the slower moving of the two components. It crystallised from methanol as a methanol solvate, needles m.p. 112—114° (Found: C, 61.7; H, 5.7. $C_{23}H_{26}O_9$ requires C, 61.9; H, 5.85%), $\nu_{max.}$ ($CHCl_3$) 3 580, 1 770, 1 590, 1 480, 1 410, 1 230, 1 135, 1 105, 1 035, and 1 010 cm^{-1}, $\lambda_{max.}$ (EtOH) 285 (log ε 3.69) and 253 nm (3.97), τ ($CDCl_3$) 3.24 (1 H, s, H-9), 3.44 and 3.56 (2 H, 2 s, H-4 and -12), 4.00br (2 H, s, O·CH_2·O), 5.42—5.62 (2 H, m, C·CH_2·O), 6.12, 6.15, and 6.28 (9 H, 3 s, 3 OCH_3), 6.10 (1 H, m), 6.56 (3 H, s, CH_3OH), 6.82—7.10 (1 H, m), 7.27—7.76 (3 H, m), and 8.00—8.40br (2 H, s, 2 OH; removed by D_2O), *m/e* 414 (100%), 396 (6), 330 (33), 313 (6), 299 (13), and 282 (4).

The faster moving component gave (±)-*epistеganol* (34 mg, 27%), crystallising from methanol in plates, m.p. 215—217° (Found: C, 63.5; H, 5.45. $C_{22}H_{22}O_8$ requires C, 63.8; H, 5.35%), $\nu_{max.}$ ($CHCl_3$) 3 580, 1 770, 1 590, 1 480, 1 405, 1 330, 1 230, 1 105, 1 035, and 1 110 cm^{-1}, $\lambda_{max.}$ (EtOH) 292 (log ε 3.72) and 253 nm (3.91), τ ($CDCl_3$) 2.92 (1 H, s, H-9), 3.30 and 3.50 (2 H, 2 s, H-4 and -12), 3.94 and 3.99 (2 H, 2 d, *J* 2 Hz, O·CH_2·O), 5.02 (1 H, d, *J* 8 Hz, C*H*OH), 5.68 (1 H, dd, J_{AB} 9, J_{AX} 7 Hz, H_A of CH_X·CH_AH_B·O), 5.93 (1 H, dd, J_{AB} 9, J_{BX} 11 Hz, H_B of CH_X·CH_AH_B·O), 6.12 (6 H, s, 2 OCH_3), 6.39 (3 H, s, OCH_3), 6.66—7.82 (4 H, m), and 8.10br (1 H, s, OH; removed by D_2O), *m/e* 414 (35%, M^+), 394 (100), 330 (20), 305 (12), 303 (14), and 237 (8).

Steganacin (1).—A solution of (±)-steganol (54 mg) in dry pyridine (5 ml) and acetic anhydride (0.033 ml) was stirred under nitrogen for 4 h at room temperature. Saturated sodium hydrogen carbonate solution was then added. Acidification with sulphuric acid (2N), extraction with ether, washing with sulphuric acid (2N) and brine, drying (Na_2SO_4), and evaporation gave a solid which was crystallised from chloroform–ethanol to yield (±)-*steganacin* (1) (54 mg, 98%) as needles, m.p. 214—217° (Found: C, 63.1; H, 5.5. $C_{24}H_{24}O_9$ requires C, 63.2; H, 5.3%), $\nu_{max.}$ 1 770, 1 730, 1 590, 1 480, 1 410, 1 230, 1 140, 1 040, and 1 015 cm^{-1}, $\lambda_{max.}$ (EtOH) 290 (log ε 3.56) and 256 nm (3.89), τ ($CDCl_3$) 3.11 (1 H, s, H-9), 3.41 and 3.56 (2 H, 2 s, H-4 and -12), 4.00br (2 H, s, O·CH_2·O), 4.19br (1 H, d, *J* 8 Hz), 5.62—5.82 (2 H, m, C·CH_2·O), 6.09, 6.14, and 6.28 (9 H, 3 s, 3 OCH_3), 6.10 (1 H, m), 6.82—7.10 (1 H, m), 7.26—7.64 (2 H, m), and 8.12 (3 H, s, OAc), *m/e* 456 (100%, M^+), 414 (12), 398 (11), 396 (7), 366 (11), and 330 (8).

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