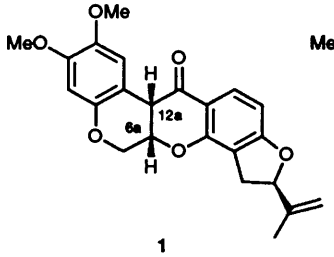
Novel and Efficient Synthesis of Rotenoids *via* Intramolecular Radical Arylation

S. Asiah Ahmad-Junan, Peter C. Amos and Donald A. Whiting*
Chemistry Department, The University, Nottingham, NG7 2RD, UK

Treatment of the iodoarylchromenes **22** with palladium acetate gave the tetracyclic compounds **23** *via* a formal but stereochemically disallowed Heck reaction; a crystalline intermediate palladium species **25** (X-ray analysis) was isolated. The method was employed to synthesise the natural rotenoid (±)-munduserone **29**. Related reductive radical cyclisation of enol acetate **31** gave the (±)-6aα,12α,12aα-chromenochromenol acetate **32** (R = Ac), representing the core structure of the insecticidal rotenoid **2**, in a 5 step (15% overall) route from 2-methylthiomethylchromone **17**. The *cis,cis*-geometry is obtained stereospecifically through an intramolecular 6-*exo* addition mode.

Natural rotenone **1** and its relatives show various biological activities, the best known of which is insecticidal action.[1] The physiological basis of this activity has been much studied,[2] and shown to involve antagonism of NADH-ubiquinone reductase in Complex I of mitochondria, inhibiting electron transport.



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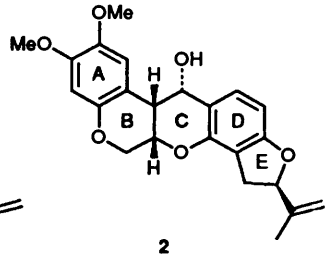

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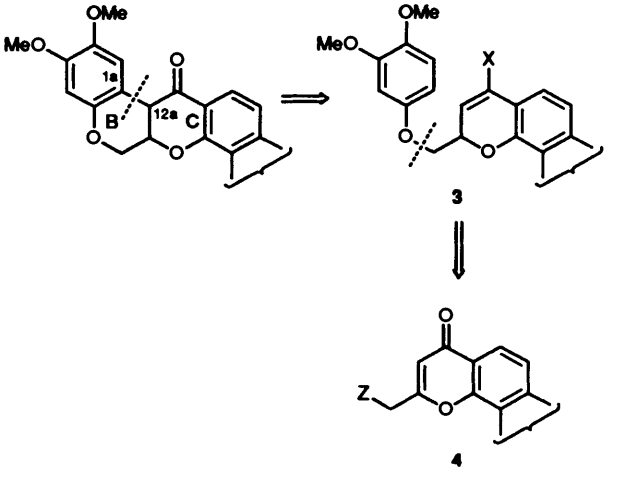
Antifeedant[3] and piscidal[4] activities are also known, the latter valued in fish farming and aquatic conservation; rotenone also blocks microtubule formation.[5] Rapid oxidative detoxification reduces environmental hazards. Structure–activity relationships have been investigated,[6] but have been largely confined to compounds obtained through manipulation of the natural products. The intact A/B/C/D ring system appears to be necessary. Synthetic studies[7] on this distinctive ring system have continued for many years in a search for an approach which would be sufficiently brief and effective to allow more thorough study of the structural requirements for activity.

Previous, relatively lengthy, syntheses have depended on thermodynamic control to attain the *cis*-B/C junction, which is preferred in 12a-epimerisation of the 12-ketones.[8] We wished to obtain the *cis*-geometry by a kinetically preferred process, dispensing with the necessity of the carbonyl function. We chose as target the core tetracycle **32** of the (12*S*)-alcohol **2**, known to be particularly active in *in vitro* studies of electron transport inhibition. In this paper we report a brief, good yielding, and stereoselective synthesis of tetracycle **32**, which has potential for development as an enantioselective route; a synthesis is also described of (±)-munduserone **29**,[9] the simplest natural rotenoid.

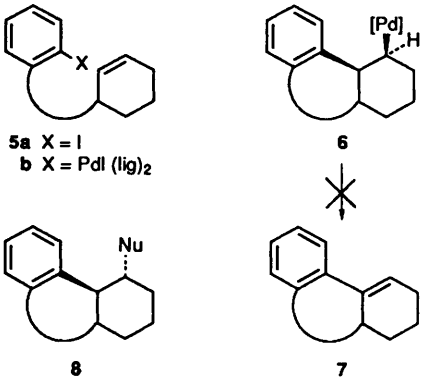
The essential disconnections for the route selected as shown in Scheme 1. The key bond forming step for the closure of ring B is seen as intramolecular arylation of an alkene or enolate, and the intermediate chromenes **3** are to be derived from well known chromones **4**. In the event, we found that the 1a-12a linkage could be achieved in several ways, but at the start of our work we concentrated on an approach using additions of aryl palladium species.

Aryl iodides of general type **5a** would, under the conditions of the Heck reaction, be expected to generate an aryl palladium



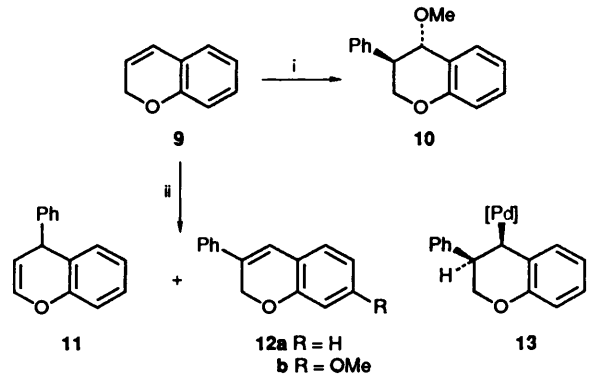
Scheme 1

species **5b**, leading on through *syn* addition to an intermediate **6**. This intermediate would lack the *syn* Pd–H stereochemistry considered necessary for elimination to an alkene **7**, but could yield a substitution product **8** by reaction with a suitable nucleophile (Scheme 2). Intermolecular reactions[10] following



Scheme 2

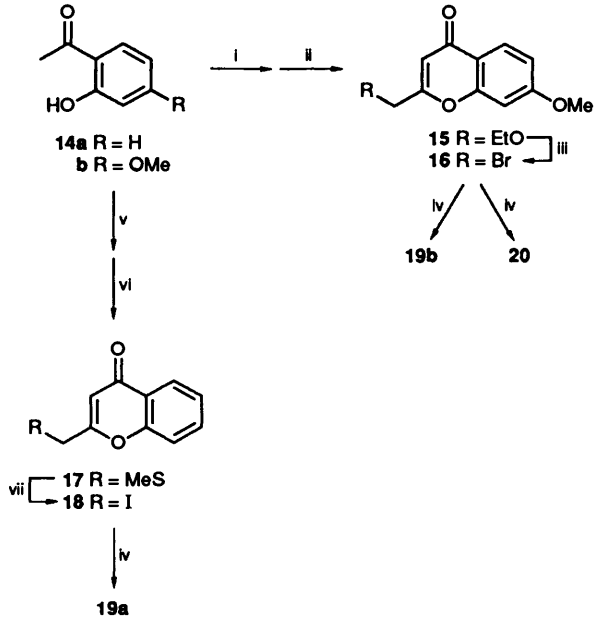
such a course are known and in agreement we have observed that treatment of 2*H*-chromene **9** with phenylmercury(II) chloride and dilithium palladium tetrachloride in methanol gives the methoxy adduct **10** (Scheme 3). In contrast, however, 2*H*-chromene **9** reacted with iodobenzene and palladium acetate in acetonitrile–methanol[11] to give 4-phenyl-4*H*-chromene **11** and, unexpectedly, 3-phenyl-2*H*-chromene **12a** (Scheme 3). Chromenes **12a** and **11** were obtained in 54 and 1%



Scheme 3 *Reagents:* i, PhHgCl, Li_2PdCl_4, MeOH; iii, PhI, $Pd(OAc)_2$, MeCN–MeOH

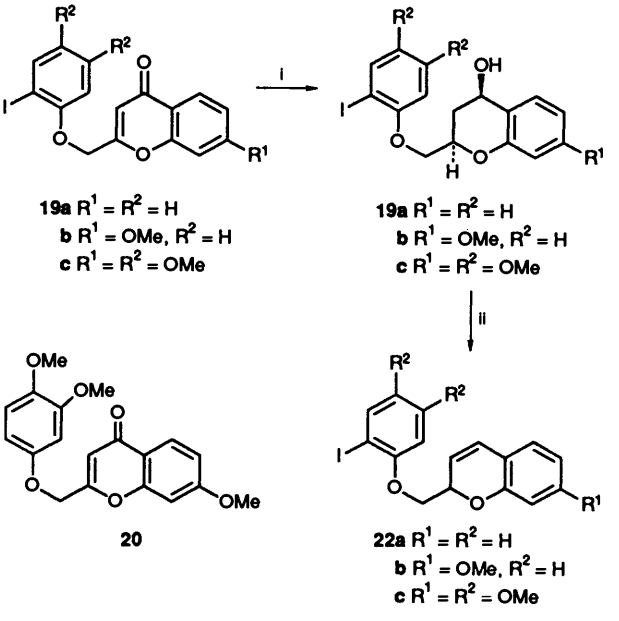
yield respectively, using 50 mol% palladium acetate; at 100 mol% the yields were 23 and 10%. The former could arise by *syn*-addition/*syn*-elimination, but the latter must arise by a different mechanism, since *syn*-elimination from an intermediate **13** is not possible. No methoxy-containing products were observed.

We then proceeded to examine intramolecular cases. For this purpose we needed the aryloxymethylchromenes **22**. These were obtained from the corresponding chromones as follows. 2-Bromomethylchromones have been prepared by the action of *N*-bromosuccinimide on the 2-methylchromones,[12,13] but yields were poor, and in our hands separation of the mono-, di- and non-brominated products proved difficult. Alternatively, condensation of 2-hydroxy-4-methoxyacetophenone **14b** with ethyl ethoxyacetate, and acid-catalysed cyclisation, gave 2-ethoxymethyl-7-methoxychromone **15** (53%), which was converted into the desired bromo compound **16** (53%) by treatment with hydrogen bromide,[13] in fair yield, albeit under rather severe conditions (Scheme 4). A mild and more



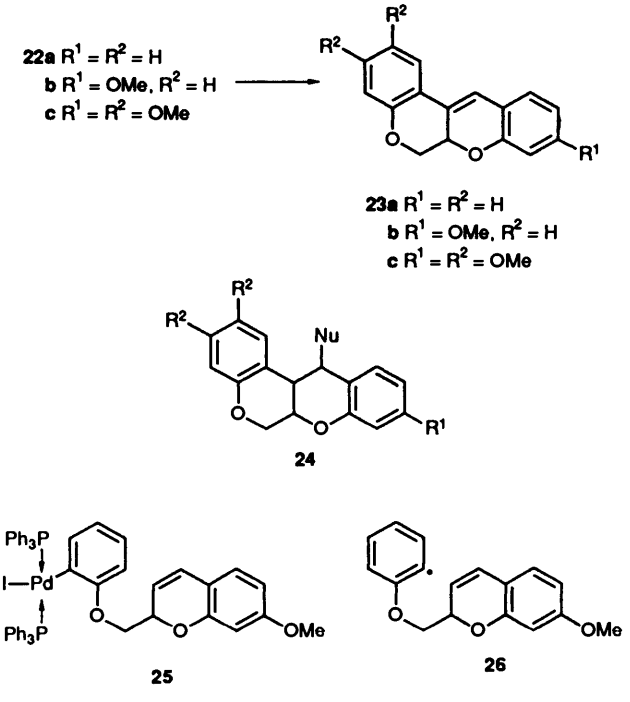
Scheme 4 *Reagents and conditions:* i, $EtOCH_2CO_2Et$, NaH, THF; ii, H_2SO_4, EtOH; iii, HBr; iv, ArOH, K_2CO_3, dry Me_2CO, reflux; v, $MeSCH_2CO_2Et$, NaH, THF; vi, HCl, MeOH; vii, MeI, CH_2Cl_2, reflux

satisfactory route followed *via* condensation of 2-hydroxyacetophenone **14a** with ethyl methylthioacetate which, after ring closure of the intermediate diketone in acid, afforded the methylthiomethylchromone **17** (44%). Transformation of this product to 2-iodomethylchromone **18** (72%) was slowly but smoothly effected by reaction with methyl iodide.[14] The iodide **18** reacted with 2-iodophenol to provide 2-aryloxymethylchromone **19a** (57%), while similar treatment of **16** gave **19b** (66%). To obtain the (2-iodo-3,4-dimethoxyphenoxy)chromone **19c**, the bromide **16** was treated with 3,4-dimethoxyphenol to provide chromone **20** (79%), which was iodinated (iodine–mercuric oxide) to afford **19c** (61%). The chromones **19** underwent conjugate reduction with sodium borohydride to yield the chromanols **21** (67–99%), which readily dehydrated in toluene with toluene-*p*-sulfonic acid to the required chromenes **22** (76–95%) (Scheme 5).



Scheme 5 *Reagents:* i, $NaBH_4$, THF, reflux; ii, PTSA, Toluene, reflux

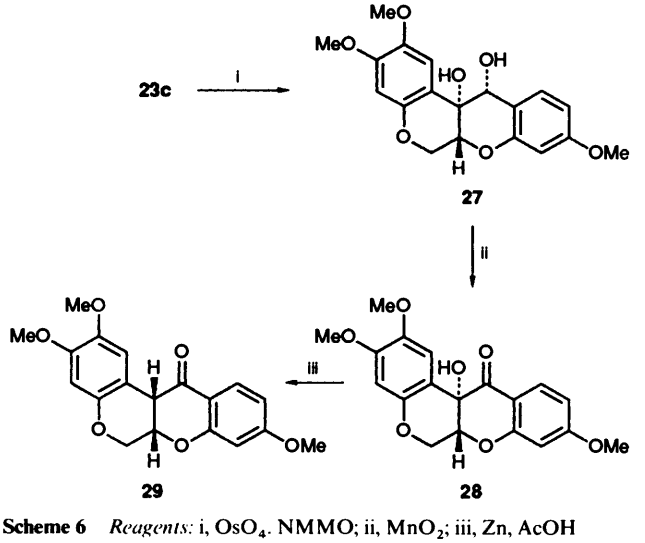
Treatment of the iodoarylchromene **19a** with palladium acetate in acetonitrile–methanol then formed the tetracyclic compound **23a** (58%), m.p. 109–110 °C. The analogous transformations of the iodides **19b** and **19c** to the crystalline compounds **23b** and **23c** also proceeded readily. In the case of the cyclization of **19b** at slightly lower temperature, a second



crystalline product was obtained. Mass spectrometry indicated that this product contained palladium (distinctive isotope pattern), and the compound was examined by single-crystal X-ray analysis,[15] revealing structure **25**, *i.e.* the product of oxidative palladium insertion into the Ar–I bond. This compound decomposed quantitatively in refluxing toluene to tetracyclic compound **23b** and elemental palladium. No products were observed of type **24**, which would result from displacement of palladium from the benzylic site after cyclisation.

As this nominal 'intramolecular Heck reaction' is stereochemically disallowed, an alternative mechanism must apply. Since our preliminary communication,[16a] two groups have reported similar 'disallowed' intramolecular Heck reactions,[16b,c] and it has been noted that palladium occupies the benzylic site in such reactions, and either facile stereomutation occurs, or a *trans*-elimination.[16c] In view of the simple thermolytic cyclisation of the palladium species **25** in hydrocarbon solvent, we felt that a homolytic process *via* **26** must be considered. We were thus prompted to investigate a different method for cyclisation, generally considered to proceed through a radical mechanism. Iodide **19a** was treated with cobalt(I) salen, and the resulting aryl cobalt intermediate was photolysed;[17] compound **23a** was obtained in 40% yield, providing some circumstantial support for a radical Heck process. Whatever the mechanism, the reaction offered a simple entry into the tetracyclic system **23**, and we then explored conversion of this system to a natural rotenoid.

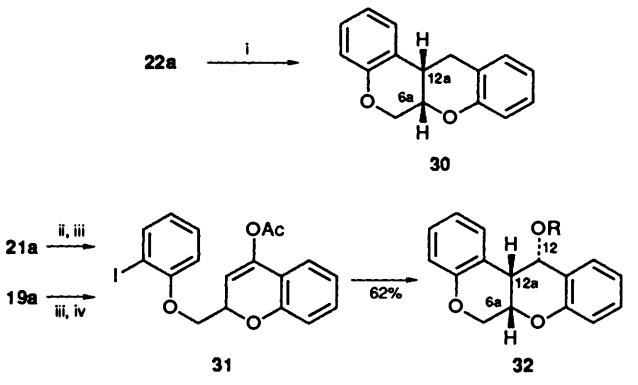
Reaction of compound **23c** with borane–dimethyl sulfide was disappointingly unspecific, giving stereoisomers of both 12- and 12a-alcohols, while bulkier boranes failed to react. To overcome the regiospecificity problem, the tetracyclic compound was treated with osmium tetraoxide–*N*-methylmorpholine *N*-oxide, to yield the diol **27**; oxidation to the rotenolone **28** was followed by zinc effected deoxygenation, to afford (±)-munduserone **29**[9] (Scheme 6) (20% over 3 steps from **23c**), identified by ^{1}H NMR



Scheme 6 *Reagents*: i, OsO_4. NMMO; ii, MnO_2; iii, Zn, AcOH

comparison with other rotenoids.[18] The stereochemistry of **27** and **28** followed by comparison with the parallel chemistry of natural rotenone and isorotenone.[19] The *cis*-B/C-fusion apparent in munduserone is the thermodynamically favoured geometry.[8]

At this stage, the potential of radical addition for attaining both the desired stereochemistry and placing a 12-oxygen substituent had become apparent to us. We first treated the chromene **22a** with tributyltin hydride in refluxing benzene, using AIBN (azoisobutyronitrile) initiator, and were pleased to obtain the tetracycle **30** (74%) as a single stereoisomer. The *cis*-geometry was demonstrated by ^{1}H NMR spectroscopy ($J_{6a,12a}$ 4.4 Hz, *cf.* $J_{6a,12a}$ 4.8 Hz in the parallel *cis*-compound derived from natural rotenone, with $J_{6a,12a}$ 9.5 Hz for its *trans*-counterpart).[20] 12-Oxygenation was introduced by oxidation of the alcohol **21a** to the corresponding chromanone and formation of the enol acetate **31** using isopropenyl acetate. Alternatively, chromone **19a** underwent efficient (85%) conjugate reduction with diisopinocampheyl borane to the saturated ketone, to give a shorter route to the enol acetate **31**. Under the conditions used, a low optical rotation was recorded for the product ketone, but the m.p. was, within experimental error, the same as that of the racemic material. Reaction of the enol ester **31** gratifyingly afforded the acetate **32** (R = Ac) (62%), showing $J_{6a,12a}$ 5.1 Hz, and $J_{12,12a}$ 5.3 Hz, demonstrating the all-*cis* arrangement of hydrogen atoms at the contiguous chiral centres. Alkaline hydrolysis gave the alcohol **32** (R = H) (Scheme 7), which has been oxidised previously[21] to the core tetracycle of the rotenoids.



Scheme 7 *Reagents and conditions*: i, Bu_3SnH, AIBN, benzene, reflux; ii, PCC; iii, isopropenyl acetate, H^+; iv, $(IPC)_2BH$

Thus the parent *cis,cis*-A/B/C/D system of the rotenoid alcohol **2** has been prepared in five steps from the chromone **17**, with an overall yield 15%. This is a marked improvement in efficiency over previous routes. In addition, chiral conjugate reduction of the chromone could open the way to an enantiospecific sysnthesis. This awaits further work.

Experimental

General.—For experimental generalisations, see *J. Chem. Soc., Perkin Trans. 1*, 1991, 1901.

trans-4-*Methoxy*-3-*phenylchroman* **10**.—2*H*-Chromene (0.25 g), lithium chloride (0.17 g), palladium(II) chloride (0.35 g), and phenyl mercuric chloride (0.5 g) were stirred together in dry methanol (20 cm^3) under nitrogen at room temperature for 12 h. The solution was diluted with aq. sodium chloride and extracted with benzene (3 × 50 cm^3). The dried extracts were evaporated and the residue was chromatographed on silica (cyclohexane–ether, 10:1) to yield the *title compound* as a pale yellow gum (0.13 g, 28%) (Found: C, 79.85; H, 6.75%; M^+, 240. $C_{16}H_{16}O_2$ requires C, 79.97; H, 6.71%; *M*, 240); ν_{max}/cm^{-1} 3060, 3040, 2940, 2820, 1610, 1590, 1120 and 1010; δ_H 3.35 (1 H, ddd, *J* 3.6, 5.4, 5.6, 3-H), 3.36 (3 H, s, OMe), 4.30 (1 H, dd, *J* 5.6, 11.2, 2-Ha), 4.44 (1 H, dd, *J* 3.6, 11.2, 2-Hb), 4.51 (1 H, d, *J* 5.4, 4-H), 6.85–6.96 (2 H, m, ArH) and 7.17–7.32 (7 H, m, ArH).

3-*Phenyl*-2H-*chromene* **12a** *and* 4-*Phenyl*-4H-*chromene* **11**.—2*H*-Chromene (0.25 g), iodobenzene (1.81 g), palladium(II) acetate (0.3 g) and triphenylphosphine (0.6 g) were dissolved in dry acetonitrile (4 cm^3), triethylamine (1.7 cm^3) and methanol

(2 cm^3), and the mixture was heated at 80 °C under argon for 12 h. The solution was then evaporated and the residue was chromatographed on silica (light petroleum–ether, 8:1) to yield first *3-phenyl-2H-chromene* (0.1 g, 25%), m.p. 91–91.5 °C (Found: C, 86.35; H, 5.9%; M^+, 208. $C_{15}H_{12}O$ requires C, 86.51; H, 5.81%; *M*, 208.089); ν_{max}/nm (ε) 241 (4.27), 247infl (4.21), 293 (4.08), 303infl (4.05) and 329 (4.09); ν_{max}/cm^{-1} 3000, 2980, 1600 and 1120; δ_H 5.20 (2 H, d, *J* 1, 2-H_2), 6.86 (1 H, t, *J* 1, 4-H), 6.91–7.45 (4 H, m, ArH) and 7.47 (5 H, PhH), followed by *4-phenyl-4H-chromene* (0.04 g, 10%), as a gum (Found: M^+, 208.088); δ_H 4.69 (1 H, dd, *J* 2, 4, 4-H), 5.04 (1 H, dd, *J* 4, 6, 3-H), 6.68 (1 H, dd, *J* 2, 6, 2-H), 6.90–7.26 (4 H, m, ArH) and 7.32 (5 H, PhH).

In a repeat reaction using palladium(II) acetate (0.22 g), the yields of chromenes **12a** and **11** were 54 and 1% respectively.

7-Methoxy-3-phenyl-2H-chromene **12b**.—7-Methoxy-2*H*-chromene (0.2 g), palladium(II) acetate (0.28 g), triphenylphosphine (0.6 g) and iodobenzene (0.2 cm^3) were added to dry acetonitrile (4 cm^3) containing triethylamine (1.3 cm^3), and the mixture was heated at 80 °C for 12 h. The product was evaporated and the residue was filtered through alumina (grade III, chloroform elution). Evaporation and chromatography on silica using light petroleum–ether, 7:1, afforded the *title compound* as cream crystals (0.1 g, 35%), m.p. 95–96 °C (Found: C, 80.2; H, 5.9%; M^+, 238. $C_{16}H_{14}O_2$ requires C, 80.65; H, 5.92%; *M*, 238); ν_{max}/cm^{-1} 2900, 2830, 1610, 1120 and 970; δ_H 3.80 (3 H, s, OMe), 5.14 (2 H, d, *J* 1, 2-H_2), 6.46 (1 H, d, *J* 2, 8-H), 6.48 (1 H, dd, *J* 2, 8, 6-H), 6.79 (1 H, t, *J* 1, 4-H), 7.02 (1 H, d, *J* 8, 5-H) and 7.27–7.46 (5 H, m, PhH).

2-Methylthiomethylchromen-4-one **17**.—2-Hydroxyacetophenone (28.7 g) and ethyl 2-(methylthio)acetate (56.5 g) in dry tetrahydrofuran (THF) (50 cm^3) were added dropwise under nitrogen to a slurry of sodium hydride (40 g, 60% oil dispersion) in THF (50 cm^3), over 45 min. The mixture was stirred during addition with occasional ice cooling. When addition was complete, the mixture was refluxed on steam for 30 min, cooled, quenched with water, and washed with ether. The aqueous phase was diluted with methanol, acidified with conc. hydrochloric acid (*ca.* 150 cm^3), and refluxed for 30 min. The cooled product was extracted with chloroform. The dried extracts were evaporated, and the residue was chromatographed on silica (ethyl acetate–hexane, 1:1), to yield the *title compound* (19.2 g, 44%), m.p. 89–90 °C (Found: C, 64.15; H, 4.7%; M^+, 206.037. $C_{11}H_{10}O_2S$ requires C, 64.06; H, 4.89%; *M*, 206.040); ν_{max}/cm^{-1} 1643 and 1610; δ_H 2.20 (3 H, s, Me), 3.59 (2 H, s, CH_2), 6.35 (1 H, s, 3-H), 7.41–7.68 (3 H, m, Ar-H) and 8.25 (1 H, dd, *J* 3, 8, 5-H).

2-Iodomethylchromen-4-one **18**.—2-Methylthiomethylchromen-4-one (10.0 g) was refluxed in dichloromethane (10 cm^3) with methyl iodide (200 g) for 3 d, when the mixture was cooled and filtered. The filtrate was concentrated and set aside at room temperature when the *title compound* (11.2 g, 72%) crystallised out as yellow needles, m.p. 140–142 °C (Found: C, 41.7; H, 2.45%; M^+, 285.949. $C_{10}H_7IO_2$ requires C, 41.99; H, 2.47%; *M*, 285.949); ν_{max}/cm^{-1} 1640 and 1610; δ_H 4.38 (2 H, s, CH_2), 6.45 (1 H, s, 3-H), 7.36–7.76 (3 H, m, ArH) and 8.24 (1 H, dd, *J* 3, 8, 5-H).

2-Ethoxymethyl-7-methoxychromen-4-one **15**.—Sodium (2.5 g) was added slowly to a cooled solution of 2-hydroxy-4-methoxyacetophenone (5 g) and ethyl ethoxyacetate (10 cm^3) in dry ether (250 cm^3). More ethyl ethoxyacetate (9 cm^3) and sodium metal (2.5 g) were then added. The mixture was stirred for 24 h and refluxed for 1 h when it was cooled, washed with water, acidified with acetic acid, and extracted with ether. The ether extracts were washed with aq. sodium hydrogen carbonate, dried and evaporated. The residual oil was dissolved in ethanol (125 cm^3) with conc. sulfuric acid (1 cm^3), and the solution was refluxed for 30 min. Benzene was added and the mixture was distilled to remove solvent (150 cm^3). The cooled solution was diluted with ether and washed with aq. sodium hydroxide and water and dried. Evaporation and crystallization of the residue from light petroleum gave the title compound (3.5 g, 53%), m.p. 69–70 °C (lit.,[13] m.p. 70–71 °C) (Found: C, 66.8; H, 6.25%; M^+, 234. Calc. for $C_{13}H_{14}O_4$: C, 66.81; H, 6.02%; *M*, 234); δ_H 1.25 (3 H, t, *J* 7, Me), 3.59 (2 H, q, *J* 7, CH_2), 3.94 (3 H, s, OMe), 4.24 (2 H, s, OCH_2), 6.12 (1 H, s, 3-H), 6.69 (1 H, d, *J* 3, 8-H), 6.84 (1 H, dd, *J* 3, 9, 6-H) and 7.94 (1 H, d, *J* 9, 5-H).

2-Bromomethyl-7-methoxychromen-4-one **16**.—2-Ethoxymethyl-7-methoxchromen-4-one (3 g) was dissolved in 48% hydrogen bromide in glacial acetic acid (20 cm^3), and the solution was heated at 50 °C for 24 h. Solvent (10 cm^3) was distilled off, and the residue was diluted with water to yield the title compound (1.4 g, 53%), m.p. 141–142 °C from ethanol (lit., m.p. 141–142 °C) (Found: C, 48.9; H, 3.5%; M^+, 268, 270. Calc. for $C_{11}H_9BrO_3$: C, 49.10; H, 3.37%; *M*, 268, 270); δ_H 3.94 (3 H, s, OMe), 4.29 (2 H, s, CH_2Br), 6.28 (1 H, s, 3-H), 6.97 (1 H, d, *J* 7, 8-H), 7.01 (1 H, dd, *J* 2, 9, 6-H) and 8.13 (1 H, d, *J* 9, 5-H).

2-(2′-Iodophenoxymethyl)chromen-4-one **19a**.—2-Bromomethylchromen-4-one (1 g), 2-iodophenol (1.3 g) and potassium carbonate (0.9 g) were refluxed together in dry acetone (10 cm^3) for 5 h. Water was added and the mixture was extracted with chloroform. The extracts were washed with aq. sodium hydroxide and water, and dried. Evaporation of the solvent gave a solid which crystallised from methanol to yield the *title compound* (0.9 g, 57%), m.p. 148–149 °C (Found: C, 50.6; H, 3.05%; M^+, 377.976. $C_{16}H_{11}IO_3$ requires C, 50.82; H, 2.93%; *M*, 377.975); ν_{max}/cm^{-1} 3200infl, 3000, 1660 and 1620; δ_H 5.12 (2 H, s, CH_2), 6.81 (1 H, s, 3-H), 6.88–7.08 (2 H, m, 6′-H, 8-H), 7.34–7.89 (4 H, m, ArH), 7.98 (1 H, dd, *J* 2, 8, 3′-H) and 8.37 (1 H, dd, *J* 2, 8, 5-H).

A very similar preparation from 2-iodomethylchromen-4(4*H*)-one gave identical material in 74% yield.

2-(2′-Iodophenoxymethyl)-7-methoxychromen-4-one **19b**.—2-Bromomethyl-7-methoxychromen-4-one (0.4 g) and 2-iodophenol (0.38 g) were refluxed in acetone (20 cm^3) over anhydrous potassium carbonate (0.3 g) for 12 h. The mixture was diluted with water and extracted with chloroform. Evaporation of the dried organic extracts gave a solid which crystallised from methanol to yield the *title compound* (0.4 g, 66%), as brown crystals, m.p. 157–158 °C (Found: C, 49.85; H, 3.4%; M^+, 408. $C_{17}H_{13}IO_4$ requires C, 50.03; H, 3.19%; *M*, 408); ν_{max}/cm^{-1} 3060, 1650, 1610 and 1510; δ_H 3.95 (3 H, s, OMe), 5.03 (2 H, s, CH_2), 6.65 (1 H, s, 3-H), 6.74–7.01 (3 H, m, ArH), 7.04 (1 H, dd, *J* 3, 9, 6-H), 7.26–7.51 (1 H, m, 5′-H), 7.88 (1 H, dd, *J* 2, 8, 3′-H) and 8.17 (1 H, d, *J* 9, 5-H).

2-(3′,4′-Dimethoxyphenoxymethyl)-7-methoxychromen-4-one **20**.—2-Bromomethyl-7-methoxychromen-4-one (0.9 g) and 3,4-dimethoxyphenol (0.6 g) were refluxed in acetone (30 cm^3) over anhydrous potassium carbonate (0.8 g) for 48 h. The solution was filtered and the filtrate was evaporated. The residue was chromatographed on a short silica column (chloroform) to yield the *title compound* (0.9 g, 79%), m.p. 133–135 °C (Found: C, 66.4; H, 5.4%; M^+, 342. $C_{19}H_{18}O_6$ requires C, 66.66; H, 5.30%; *M*, 342); ν_{max}/cm^{-1} 1650, 1610 and 1020; δ_H 3.85, 3.88 and 3.91 (each 3 H, s, OMe), 4.90 (2 H, s, CH_2), 6.45 (1 H, dd, *J* 3, 9, 6′-H), 6.46 (1 H, s, 3-H), 6.61 (1 H, d, *J* 3, 2′-H), 6.78 (1 H, d, *J* 9, 5′-H), 6.87 (1 H, d, *J* 2, 8-H), 6.98 (1 H, dd, *J* 2, 8, 6-H) and 8.10 (1 H, d, *J* 8, 5-H).

2-(2′-*Iodo*-4′,5′-*dimethoxyphenoxymethyl*)-7-*methoxychromen*-4-*one* **19c**.—2-(3′,4′-Dimethoxyphenoxymethyl)-7-methoxychromen-4-one (0.6 g) in ethanol (4 cm^3) at 50 °C under nitrogen was treated with yellow mercuric oxide (0.4 g) followed by iodine (0.4 g). After 30 min the mixture was filtered through Kieselguhr and evaporated. The residue was eluted with chloroform through a short silica column to yield the *title compound* (0.5 g, 61%), as orange cubic crystals, m.p. 186–187 °C from ethanol (Found: C, 49.0; H, 3.65; I, 27.09%; M^+, 468. $C_{19}H_{17}IO_6$ requires C, 48.74; H, 3.66; I, 27.1%; *M*, 468); ν_{max}/cm^{-1} 3080, 1650, 1600 and 1020; δ_H 3.77, 3.78 and 3.84 (each 3 H, s, OMe), 4.85 (2 H, d, *J* 0.8, CH_2), 6.48 (1 H, s, 6′-H), 6.51 (1 H, t, *J* 0.8, 3-H), 6.78 (1 H, d, *J* 2, 8-H), 6.92 (1 H, dd, *J* 2, 9, 6-H), 7.13 (1 H, s, 3′-H) and 8.03 (1 H, d, *J* 9, 5-H).

2-(2′-*Iodophenoxymethyl*)*chroman*-4-*ol* **21a**.—2-(2′-Iodophenoxymethyl)chromen-4-one (1 g) in THF (35 cm^3) was treated with sodium borohydride (0.5 g) in ethanol–water (1:1, 18 cm^3). The reaction mixture was refluxed for 1.5 h, cooled, and THF was evaporated off. Ether (20 cm^3) was added and the mixture was washed with brine. The organic layer was dried and evaporated to yield the *title compound* (1 g, 99%), m.p. 137–138 °C from ethanol (Found: C, 50.65; H, 4.35%; M^+, 382. $C_{16}H_{15}IO_3$ requires C, 50.28; H, 3.96%; *M*, 378); ν_{max}/cm^{-1} 3400, 3000, 1615 and 1580; δ_H(400 MHz) 1.86 (1 H, d, *J* 7.8, OH), 2.13 (1 H, ddd, *J* 9.8, 10.3, 13.2, 3-Ha), 2.61 (1 H, ddd, *J* 2.2, 5.8, 13.2, 3-Hb), 4.22 (1 H, dd, *J* 5.4, 9.8, 9-Ha), 4.32 (1 H, dd, *J* 5.1, 9.8, 9-Hb), 4.61 (1 H, dddd, *J* 2.2, 5.1, 5.4, 10.3, 2-H), 5.04 (1 H, m, 4-H), 6.74 (1 H, m), 6.87 (2 H, m), 6.98 (1 H, m), 7.20 (1 H, m), 731 (1 H, m), 7.49 (1 H, d, *J* 7.6, 5-H) and 7.78 (1 H, d, *J* 7.8, 3′-H).

2-(2′-*Iodophenoxymethyl*)-7-*methoxychroman*-4-*ol* **21b**.—2-(2′-Iodophenoxymethyl)-7-methoxychromen-4-one (2.2 g) was reduced with sodium borohydride (1.1 g) as in the preceding experiment, to yield the *title compound* (1.5 g, 67%), m.p. 64–67 °C from ethanol (Found: C, 49.05; H, 4.6%; M^+, 412. $C_{17}H_{17}IO_4$ requires C, 49.53; H, 4.16%; *M*, 412); ν_{max}/cm^{-1} 3580, 3050 and 1580; δ_H(250 MHz) 1.79 (1 H, bd, *J* 7.6, OH), 2.11 (1 H, ddd, *J* 9.3, 10.0, 13.2, 3-Ha), 2.56 (1 H, ddd, *J* 2.5, 6.0, 13.3, 3-Hb), 3.78 (3 H, s, OMe), 4.21 (1 H, dd, *J* 5.3, 9.8, 9-Ha), 4.31 (1 H, dd, *J* 5.1, 9.8, 9-Hb), 4.61 (1 H, dddd, *J* 2.5, 5.1, 5.3, 10.0, 2-H), 4.98 (1 H, bm, 4-H), 6.41 (1 H, d, *J* 2, 5, 8-H), 6.56 (1 H, dd, *J* 2.5, 8.5, 6-H), 6.74 (1 H, ddd, *J* 1.3, 7.3, 7.8, 4′-H), 6.86 (1 H, dd, *J* 1.3, 8.3, 6′-H), 7.30 (1 H, ddd, *J* 1.6, 7.3, 8.3, 5′-H), 7.39 (1 H, dd, *J* 0.7, 8.5, 5-H) and 7.78 (1 H, dd, *J* 1.6, 7.8, 3′-H).

2-(2′-*Iodo*-4′,5′-*dimethoxyphenoxymethyl*)-7-*methoxychroman*-4-*ol* **21c**.—2-(2′-Iodo-4′,5′-dimethoxyphenoxymethyl)-7-methoxychromen-4-one (0.5 g) was reduced with sodium borohydride (0.25 g) as in the preceding experiment, to yield the *title compound* (0.43 g, 83%), m.p. 93–95 °C from ethanol (Found: C, 48.7; H, 4.85; $M - H^+$, 471. $C_{19}H_{21}IO_6$ requires C, 48.32; H, 4.48; *M*, 472); ν_{max}/cm^{-1} 3580, 3440 and 1610; δ_H(400 MHz) 1.80 (1 H, bd, *J* 7.5, OH), 2.00 (1 H, ddd, *J* 9.6, 9.6, 13.3, 3-Ha), 2.48 (1 H, ddd, *J* 2.4, 5.8, 13.3, 3-Hb), 3.70, 376 and 3.79 (each 3 H, s, OMe), 4.09 (1 H, dd, *J* 5.0, 9.9, 9-Ha), 4.20 (1 H, dd, *J* 5.4, 9.9, 9-Hb), 4.51 (1 H, dddd, *J* 2.4, 5.0, 5.4, 9.6, 2-H), 4.90 (1 H, bm, 4-H), 6.33 (1 H, d, *J* 2.4, 8-H), 6.49 (1 H, dd, *J* 2.4, 8.6, 6-H), 6.50 (1 H, s, 6′-H), 7.11 (1 H, s, 3′-H) and 7.29 (1 H, d, *J* 8.6, 5-H).

2-(2′-*Iodophenoxymethyl*)-2H-*chromene* **22a**.—2-(2′-Iodophenoxymethyl)chroman-4-ol (1.1 g) was refluxed in toluene (70 cm^3) with toluene-*p*-sulfonic acid (PTSA) (0.1 g) for 10 min. The cooled solution was washed with aq. sodium hydrogencarbonate, dried and evaporated to afford the *title compound* (0.8 g, 76%), as an oil (Found: M^+, 363.995. $C_{16}H_{13}IO_2$ requires *M*, 363.996); ν_{max}/cm^{-1} 3000infl, 1610 and 1570; δ_H 4.10 (1 H, dd, *J* 6, 10, 9-Ha), 4.27 (1 H, dd, *J* 5, 10, 9-Hb), 5.33 (1 H, ddd, *J* 3, 5, 6, 2-H), 5.89 (1 H, dd, *J* 3, 10, 3-H), 6.56 (1 H, d, *J* 10, 4-H) and 6.71–7.40 (7 H, Ar-H).

2-(2′-*Iodophenoxymethyl*)-7-*methoxy*-2H-*chromene* **22b**.—2-(2′-Iodophenoxymethyl)-7-methoxychroman-4-ol (1 g) was stirred in acetyl chloride (8 cm^3) for 30 min. After evaporation of the acid chloride, benzene was added and the mixture was refluxed for 1 h. The product solution was cooled and filtered through a charcoal–Kieselguhr column. Evaporation gave the *title compound* (0.9 g, 95%) as an oil (Found: C, 51.85; H, 4.2%; M^+, 394. $C_{17}H_{15}IO_3$ requires C, 51.80; H, 3.84%; *M*, 394); ν_{max}/cm^{-1} 3000, 1615 and 1580; δ_H 3.73 (3 H, s, OMe), 4.06 (1 H, dd, *J* 5, 10, 9-Ha), 4.25 (1 H, dd, *J* 6, 10, 9-Hb), 5.30 (1 ddd, *J* 4, 5, 6, 2-H), 5.80 (1 H, dd, *J* 4, 10, 3-H), 6.35–7.20 (6 H, Ar-H, 4-H), 7.15–7.30 (1 H, m, 5′-H) and 7.69 (1 H, dd, *J* 2, 7, 3′-H).

2-(2′-*Iodo*-4′,5′-*dimethoxyphenoxymethyl*)-7-*methoxy*-2H-*chromene* **22c**.—2-(2′-Iodo-4′,5′-dimethoxyphenoxymethyl)-7-methoxychroman-4-ol (0.7 g) was dehydrated as in the preceding experiment, to yield the *title compound* (0.6 h, 88%) as an oil (Found: M^+, 454.029. $C_{19}H_{19}IO_5$ requires *M*, 454.028); ν_{max}/cm^{-1} 3000 and 1610; δ_H(250 MHz) 3.75, 3.81 and 3.82 (each 3 H, s, OMe), 4.05 (1 H, dd, *J* 4.8, 10.0, 9-Ha), 4.21 (1 H, dd, *J* 6.6, 10.0, 9-Hb), 5.28 (1 H; ddd, *J* 3.6, 4.8, 6.6, 2-H), 5.70 (1 H, dd, *J* 3.6, 10.0, 3-H), 6.40 (1 H, d, *J* 2.5, 8-H), 6.43 (1 H, dd, *J* 2.5, 8.0, 6-H), 6.49 (1 H, d, *J* 10.0, 4-H), 6.53 (1 H, s, 6′-H), 6.90 (1 H, d, *J* 8.0, 5-H) and 7.17 (1 H, s, 3′-H).

6,6a-*Dihydrorotoxen* **23a**.—(*a*) 2-(2′-Iodophenoxymethyl)-2*H*-chromene (0.8 g), palladium(II) acetate (0.4 g), triphenylphosphine (0.8 g), and triethylamine (2.3 cm^3) were heated at 80 °C in dry acetonitrile (10 cm^3) with stirring under argon for 12 h. The solvent was evaporated off and the residue was eluted with chloroform through a short alumina (grade 3) column. The eluate was evaporated and the product was chromatographed on silica using cyclohexane–ether (9:1), to afford the *title compound* (0.3 g, 58%) as needles from methanol, m.p. 109–110 °C (Found: C, 80.95; H, 5.3%; M^+, 236. $C_{16}H_{12}O_2$ requires C, 81.37; H, 5.08%; *M*, 236); ν_{max}/cm^{-1} 3040infl, 3000infl, 1600, 1570 and 1120; λ_{max}/nm (ε) 211 (4.34), 236infl (3.95), 244 (4.09), 252 (4.08), 286infl (3.71), 296 (3.84), 307 (3.79), 332infl (4.01), 346 (4.18) and 362 (4.05); δ_H(250 MHz) 4.18 (1 H, dd, *J* 10.0, 10.9, 6-Ha), 4.61 (1 H, dd, *J* 5.4, 10.0, 6-Hb), 5.37 (1 H, ddd, *J* 2.3, 5.4, 10.9, 6a-H), 6.83 (1 H, d, *J* 2.3, 12-H), 6.84–7.27 (7 H, ArH) and 7.64 (1 H, dd, *J* 1.5, 7.9, 1-H).

(*b*) Triphenylphosphine(salen)cobalt(III) bromide (0.67 g) was dissolved in dry THF (15 cm^3) under a stream of nitrogen, and freshly prepared sodium amalgam (1%; 0.02 mol sodium) was added. The mixture was stirred until the colour changed from dark brown through red to deep green. The solution was transferred *via* a catheter to a dry flask in the dark under nitrogen and 2-(2′-iodophenoxymethyl)-2*H*-chromene (0.36 g) in THF (2 cm^3) was added. The mixture was stirred at ambient temperature for 24 h. The solvent was then evaporated. The residue was dissolved in dichloromethane (10 cm^3) and irradiated and refluxed with a tungsten lamp (500 W). The solvent was evaporated, and the product chromatographed as above to yield the title compound (0.11 g, 48%), as yellow needles from methanol, m.p. 109–110 °C, spectroscopically identical with the above sample.

9-*Methoxy*-6,6a-*dihydrorotoxen* **23b**.—2-(2′-Iodophenoxymethyl)-7-methoxy-2*H*-chromene (0.9 g), palladium(II) acetate (0.3 g), triphenylphosphine (1 g), and triethylamine (2.5 cm^3) were heated at 70 °C in dry acetonitrile (20 cm^3) with stirring under argon for 12 h. The solvent was evaporated off and the residue was eluted with chloroform through a short alumina

(grade 3) column. The eluate was evaporated and the product was chromatographed on silica using cyclohexane–ether (9:1), to afford two products. The first eluted was the *title compound* (0.15 g, 25%), m.p. 138–139 °C from methanol (Found: C, 76.8; H, 5.4%; M^+, 266. $C_{17}H_{14}O_3$ requires C, 76.68; H, 5.30%; *M*, 266); ν_{max}/cm^{-1} 3000, 1620 and 1580; λ_{max}/nm 214 (4.37), 242infl (4.08), 250 (4.23), 258 (4.19), 291infl (3.57), 300infl (3.72), 313 (3.88), 339infl (4.25), 350 (4.27) and 365 (4.27); δ_H(250 MHz) 3.79 (3 H, s, OMe), 4.17 (1 H, dd, *J* 10.1, 10.8, 6-Ha), 4.61 (1 H, dd, *J* 5.4, 10.1, 6-Hb), 5.33 (1 H, ddd, *J* 2.5, 5.4, 10.8, 6a-H), 6.42 (1 H, d, *J* 2.5, 8-H), 6.49 (1 H, dd, *J* 2.5, 8.3, 10-H), 6.80 (1 H, d, *J* 2.3, 12-H), 6.88 (1 H, dd, *J* 1.2, 8.5, 4-H), 6.98 (1 H, ddd, *J* 1.2, 7.4, 8.0, 2-H), 7.01 (1 H, d, *J* 8.3, 11-H), 7.16 (1 H, ddd, *J* 1.6, 7.4, 8.5, 3-H) and 7.62 (1 H, dd, *J* 1.6, 8.0, 1-H).

The second compound eluted crystallised from light petroleum–ether to yield brownish cubic crystals of the *bis(triphenylphosphine)palladium*(II) *intermediate* **25** (0.6 g, 26%), the structure of which was determined by X-ray crystallography.[15] Heating this compound in toluene gave a quantitative yield of the dihydro-rotoxen **23b**, identical with the above sample.

2,3,9-*Trimethoxy*-6,6a-*dihydrorotoxen* **23c**.—2-(2′-Iodo-4′,5′-dimethoxyphenoxymethyl)-7-methoxy-2*H*-chromene (0.5 g), palladium(II) acetate (0.15 g), triphenylphosphine (0.45 g), and triethylamine (1.2 cm^3) were heated at 80 °C in dry acetonitrile (10 cm^3) with stirring under argon for 12 h. Product isolation as in the previous experiments afforded the *title compound* (0.2 g, 56%), m.p. 135–136 °C (Found: C, 70.1; H, 5.7%; M^+, 326. $C_{19}H_{18}O_5$ requires C, 69.93; H, 5.56%; *M*, 326); ν_{max}/cm^{-1} 3030infl, 1610 and 1575; λ_{max}/nm 214 (4.25), 243infl (4.03), 250 (4.13), 259 (4.07), 311infl (3.74), 344infl (4.24), 358 (4.45) and 376 (4.37); δ_H(250 MHz) 3.79, 3.86 and 3.91 (3 H, s, OMe), 4.14 (1 H, dd, *J* 9.9, 10.9, 6-Ha), 4.57 (1 H, dd, *J* 6.0, 9.9, 6-Hb), 5.30 (1 H, ddd, *J* 2.3, 6.0, 10.9, 6a-H), 6.42 (1 H, s, 1-H), 6.43 (1 H, d, 2.5, 8-H), 6.49 (1 H, dd, *J* 2.5, 8.3, 10-H), 6.61 (1 H, d, *J* 2.3, 12-H), 7.00 (1 H, d, *J* 8.3, 11-H) and 7.01 (1 H, s, 4-H).

Dihydroxylation of 2,3,9-*Trimethoxy*-6,6a-*dihydrorotoxen* **23c**.—Compound **23c** (50 mg) and osmium tetroxide (5 mg) in *tert*-butyl alcohol (0.5 cm^3), were stirred together in acetone (10 cm^3) and water (2 cm^3) at room temperature for 14 d. Excess of aq. sodium metabisulphite was added and the mixture was extracted with ethyl acetate. The organic extracts were filtered through Kieselguhr–magnesium sulfate, and evaporated, to yield the *diol* **27** (52 mg, 92%), m.p. 223–225 °C from methanol (Found: M^+, 360.121. $C_{19}H_{20}O_7$ requires *M*, 360.121); ν_{max}(mull)/cm^{-1} 3380infl and 1630; δ_H(250 MHz) 2.41 (1 H, s, 12a-OH), 2.77 (1 H, d, *J* 11.6, 12-OH), 3.79, 3.84 and 3.88 (each 3 H, s, OMe), 4.34 (3 H, m, 6-H_2, 6a-H), 4.94 (1 H, d, *J* 11.6, 12-H), 6.41 (1 H, s, 4-H), 6.44 (1 H, d, *J* 2.5, 8-H), 6.66 (1 H, dd, *J* 2.5, 8.7, 10-H), 7.49 (1 H, d, *J* 8.7, 1-H) and 7.84 (1 H, s, 1-H).

(±)-*Munduserone* **29**.—The diol **27** (10 mg) was stirred in dry dichloromethane (10 cm^3) with activated manganese dioxide (0.3 g) for 12 h at room temperature. The mixture was filtered through Kieselguhr and evaporated. The product was refluxed in acetic acid (1 cm^3) with activated zinc powder (0.3 g). The solvent was evaporated off, and the residue, in chloroform, was filtered through Kieselguhr. After evaporation the final product was purified by HPLC (reverse phase, C8, methanol–water, 3:1), to afford the *title compound* (2 mg, 21%) (Found: M^+, 342.111. $C_{19}H_{18}O_6$ requires *M*, 342.110); δ_H(250 MHz) 3.77, 3.80 and 3.81 (each 3 H, s, OMe), 3.85 (1 H, d, *J* 4.1, 12a-H), 4.19 (1 H, bd, *J* 12.1, 6-Ha), 4.64 (1 H, dd, *J* 3.1, 12.1, 6-Hb), 4.95 (1 H, dd, *J* 3.1, 4.1, 6a-H), 6.43 (1 H, d, *J* 2.4, 8-H), 6.47 (1 H, 4-H), 6.58 (1 H, dd, *J* 2.4, 8.8, 10-H), 6.76 (1 H, d, *J* 0.8, 1-H) and 7.87 (1 H, d, *J* 8.8, 11-H).

6a,12a-cis-6,6a,12,12a-*Tetrahydrorotoxen* **30**.—2-(2-Iodophenoxymethyl)-2*H*-chromene (0.6 g) in dry benzene (20 cm^3) at reflux was treated with a solution of tributyltin hydride (1.1 equiv.) in benzene (0.03 mol dm^{-3}) containing azoisobutyronitrile (AIBN) (0.05 equiv.) over 30 min. The reaction mixture was then refluxed for 7 h, when it was cooled and evaporated. The residue was chromatographed on silica (ethyl acetate–hexane, 1:2) to yield the title compound (0.29 g, 74%), m.p. 145–149 °C (lit.,[22] m.p. 146–148 °C) from methanol (Found: C, 79.05; H, 6.1%; M, 239.093. $C_{16}H_{14}O_2$ requires C, 80.64; H, 5.94%; *M*, 238.099); ν_{max}/cm^{-1} 3030, 1620 and 1580; δ_H(250 MHz), 3.17 (1 H, dd, *J* 6.7, 16.6, 12-Ha), 3.24 (1 H, dd, *J* 5.6, 16.6, 12-Hb), 3.43 (1 H, ddd, *J* 4.4, 5.6, 6.7, 12a-H), 4.29 (1 H, dd, *J* 2.2, 12.1, 6a-H), 4.47 (1 H, dd, *J* 6.3, 12.1, 6-Hb), 4.68 (1 H, bdd, *J* 4.4, 6.3, 6a-H), 6.80–6.90 (4 H, m, ArH), 7.03–7.15 (3 H, m, ArH) and 7.19–7.22 (1 H, m, ArH).

2-(2-*Iodophenoxymethyl*)*chromanone*.—(*a*) 2-(2-Iodophenoxymethyl)chromanol (0.38 g) was added rapidly to a stirred suspension of pyridinium chlorochromate (PCC) (0.32 g) in dichloromethane (2 cm^3). The mixture was stirred for 1 h, diluted with ether, and the solution was decanted from the deposited solids. The organic phase with ether washings was filtered through Florisil and evaporated. The residue crystallised from methanol to yield the *title compound* (0.35 g, 35%), m.p. 85–87 °C (Found: C, 50.55; H, 3.45%; M^+, 379.990. $C_{16}H_{13}IO_3$ requires C, 50.53; H, 3.45%; *M*, 379.991); ν_{max}/ cm^{-1} 3000, 1685, 1612 and 1585; δ_H(400 MHz) 2.90 (1 H, dd, *J* 3.0, 17.0, 3-Ha), 3.20 (1 H, d, *J* 17.0, 3-Hb), 4.30 (1 H, dd, *J* 4.4, 10.2, 9-Ha), 4.36 (1 H, dd, *J* 4.4, 10.2, 9-Hb), 4.85 (1 H, dt, *J* 3.0, 4.4, 2-H), 6.75 (1 H, dd, *J* 1.3, 7.6, Ar-H), 6.90 (1 H, dd, *J* 1.3, 8.2, Ar-H), 7.02–7.09 (2 H, m, Ar-H), 7.32 (1 H, m, Ar-H), 7.51 (1 H, m, ArH), 7.80 (1 H, dd, *J* 1.3, 8.0, Ar-H) and 7.92 (1 H, dd, *J* 1.3, 8.0, 5-H).

(*b*) Borane–THF (25 cm^3, 25 mmol) was added dropwise to (−)-α-pinene (7.8 g) at 0 °C under nitrogen, and the mixture was stirred for 4 h. A solution of 2-(2-iodophenoxymethyl)-chromen-4-(4*H*)-one (1.0 g) in the minimum of THF was added dropwise into the reagent solution. The resulting yellow solution was allowed to warm to room temperature, and then stirred for 15 h. After addition of sufficient water to destroy excess of borane, the mixture was evaporated, and the residue was purified by chromatography on silica (chloroform–cyclohexane, 1:2), to yield the title compound (0.85 g, 85%), m.p. 86–89 °C from methanol, $[\alpha]_D^{20}$ +5.3 (*c* 1.2, chloroform) (Found: C, 50.6; H, 3.4%; M^+, 379.991). The IR and ^{1}H NMR spectra were indistinguishable from those of the above specimen.

4-*Acetoxy*-2-(2-*iodophenoxymethyl*)-2H-*chromene* **31**.—2-(2-Iodophenoxymethyl)chromanone (0.2 g) was dissolved in ispropenyl acetate (10 cm^3) with conc. sulphuric acid (2 drops), and the mixture was refluxed for 3 h, when it was cooled and evaporated. The black residue was chromatographed on Florisil (chloroform–hexane, 1:1) to yield the *title compound* (0.13 g, 61%), as a yellowish oil [Found: C, 51.15; H, 3.55%; M^+, 423 (FAB + ve). $C_{18}H_{15}IO_4$ requires C, 51.18; H, 3.58%; *M*, 422]; ν_{max}/cm^{-1} 1760, 1610 and 1590; δ_H(250 MHz) 4.23 (3 H, s, Me), 4.17 (1 H, dd, *J* 5.3, 9.8, 9-Ha), 4.39 (1 H, dd, *J* 6.0, 9.8, 9-Hb), 5.51 (1 H, ddd, *J* 3.8, 5.3, 6.0, 2-H), 5.69 (1 H, d, *J* 3.8, 3-H) and 6.72–7.77 (8 H, m, ArH).

6a,12a-cis-12,12a-cis-12-*Acetoxy*-6,6a,12,12a-*tetrahydrorotoxen* **32**.—Tributyltin hydride in dry benzene (1.1 equiv., 0.025 mol dm^{-3}) containing AIBN (0.05 equiv.) was added dropwise over 1 h to a solution of the preceding enol acetate (50 mg) in benzene (0.05 mol dm^{-3} solution) at reflux. The reaction mixture was heated at reflux for 3 h, cooled, and evaporated. The residue was chromatographed on silica (ethyl acetate–hexane, 1:4) to afford the *title compound* (43.4 mg, 62%), m.p.

126–129 °C from methanol (Found: C, 72.95; H, 5.4%; M^+, 296.106. $C_{18}H_{16}O_4$ requires C, 72.97; H, 5.41%; *M*, 296.105); ν_{max}/cm^{-1} 1770, 1610 and 1580; δ_H(250 MHz) 1.75 (3 H, s, Me), 3.65 (1 H, dd, *J* 5.1, 5.3, 12a-H), 4.34 (1 H, dd, *J* 5.2, 10.2, 6-Ha), 4.54 (1 H, d, *J* 10.2, 6-Hb), 4.92 (1 H, dd, *J* 5.1, 5.2, 6a-H), 6.38 (1 H, d, *J* 5.3, 12-H), 6.85–6.97 (4 H, m, ArH) and 7.17–7.35 (4 H, m, ArH). Two compounds, m.p. 163 °C and m.p. 147–147.5 °C, of the same structure but of undetermined stereochemistry, has been described in the literature.[23,23] These may be stereoisomers, solvates, or different crystalline forms, a common feature of rotenoid chemistry.

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