2-Benzopyran-3-ones Stabilised by Alkoxy Substituents

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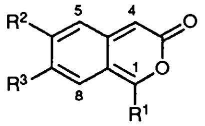
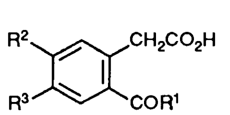
In contrast to the corresponding compounds lacking alkoxy substituents, the 2-benzopyran-3-ones **5, 6, 7** and **9** are stable and easily isolated. In contrast to the 6-methoxy derivative **7**, the 7-methoxy isomer **8** cannot be isolated; the stabilising effect of the 6,7-methylenedioxy group in **5** and **9** is therefore due to the alkoxy group at C-6. This is consistent with a donor–acceptor interaction involving the C-6 alkoxy group and the pyrone carbonyl which decreases reactivity towards nucleophilic attack by water.

2-Benzopyran-3-one **1** is a reactive intermediate responsible for the yellow colour produced by heating *o*-formylphenylacetic acid **11** in acetic anhydride.[1] The pyrone **1** is present in minute concentration in such solutions but has been characterised by trapping, in high yield, with conventional dienophiles[1] and simple olefins.[2] Photolysis of the bis-lactone **18** at low temperature in a matrix serves to further characterise the pyrone **1**;[3] **1** cannot be isolated, probably due to easy hydration back to acid **11**.[1] The 1-methyl derivative **2** and the 1-phenyl derivative **3** also resisted isolation.[1] It was therefore an agreeable surprise to find that the pyrone **4**, used in our podophyllotoxin synthesis,[4] was a stable crystalline compound of good shelf life. Herein we report the attempted preparation of a number of new 2-benzopyran-3-ones the properties of which serve to identify the main stabilising effect in **4**.

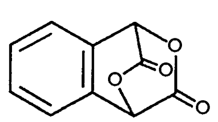
Preparation of o-*Acylphenylacetic Acids.*—The keto-acids **12**–**14** and **16** all carry an alkoxy group *para* to the oxo group and were readily prepared from the corresponding methyl alkoxyphenylacetates by Friedel–Crafts acylation ($R^1COCl/SnCl_4/CH_2Cl_2$/20 °C) followed by ester hydrolysis. The



1 $R^1 = R^2 = R^3 = H$
2 $R^1 = Me, R^2 = R^3 = H$
3 $R^1 = Ph, R^2 = R^3 = H$
4 $R^1 = 3,4,5\text{-}(MeO)_3C_6H_2; R^2, R^3 = OCH_2O$
5 $R^1 = Ph; R^2, R^3 = OCH_2O$
6 $R^1 = Ph, R^2 = R^3 = OMe$
7 $R^1 = Ph, R^2 = OMe, R^3 = H$
8 $R^1 = Ph, R^2 = H, R^3 = OMe$
9 $R^1 = Me; R^2, R^3 = OCH_2O$
10 $R^1 = H; R^2, R^3 = OCH_2O$



11 $R^1 = R^2 = R^3 = H$
12 $R^1 = Ph; R^2, R^3 = OCH_2O$
13 $R^1 = Ph, R^2, R^3 = OMe$
14 $R^1 = Ph; R^2 = OMe; R^3 = H$
15 $R^1 = Ph; R^2 = H; R^3 = OMe$
16 $R^1 = Me; R^2, R^3 = OCH_2O$
17 $R^1 = H; R^2, R^3 = OCH_2O$



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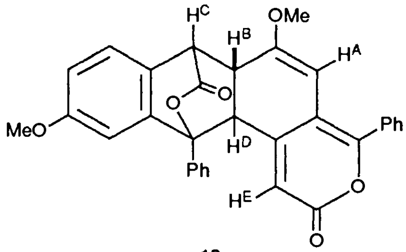
oxo acid **15** was obtained from 5-methoxy-3-phenylindene by ozonisation followed by oxidative work-up ($NaOH/H_2O_2/H_2O/MeOH$). The aldehydo acid **17** was prepared from 6,7-methylenedioxyisochroman-3-one[5] *via* opening of the lactone ring (NaOH, H_2O, EtOH), acidification at 0 °C and rapid esterification of the unisolated and freshly extracted hydroxy acid. Swern oxidation of the product and ester hydrolysis gave **17**.

Dehydration of o-*Acylphenylacetic Acids.*—The foregoing acids were heated in boiling acetic anhydride in an inert atmosphere (2 h) and the product isolated by evaporation of acetic anhydride on a steam-bath under a water-pump vacuum. The residue was triturated with ether and the product purified as detailed in the Experimental section. The stability of **4** was shared by the 1-phenyl substituted 6,7-methylenedioxypyrone **5** and the 1-phenyl substituted 6,7-dimethoxypyrone **6** showing that oxygen substituents in the 1-aryl ring have little influence on stability. This would be expected since the central methoxy in 1,2,3-trimethoxybenzenes does not conjugate efficiently with the aromatic ring,[6] and conjugation of the aryl group with the pyrone ring in **4** will be diminished by steric effects.[7] The stability of the dimethoxy compound **6** rules out any special influence of the methylendioxy group.†

That the C-6, rather than the C-7 alkoxy group, was responsible for stability was shown by comparing the properties of **7** and **8**. The pyrone **7** shared the special stability of **4, 5** and **6** but the 7-methoxypyrone **8** was nonisolable; chromatography of the residue after removal of acetic anhydride gave two compounds tentatively assigned as the *endo* and *exo*-isomers corresponding to structure **19**. These structures show a peri- and regio-selectivity not previously encountered in our work with 2-benzopyran-3-ones. 2-Benzopyran-3-one itself dimerises inefficiently to *syn*- and *anti*-dimers of the gross structure **20**,[3] and its 7-methoxy derivative forms the dimers **21** in good yield.[8] The structure of the *endo*-isomer of **19** was supported by the observation of carbonyl absorption at 1765 and 1722 cm^{-1}. The NOESY spectrum showed a nuclear Overhauser effect between H^A and the methyl group of the enol ether in **19** thus identifying H^A as a broadened singlet at δ 5.37. Double irradiation of H^A caused disappearance of a fine splitting in the signal at 3.67 δ (ddd, J 9, 4 and *ca.* 1 Hz) due to H^B, indicating allylic coupling between H^A and H^B and the regio-isomer depicted in **19**. Similarly, irradiation of the signal at δ 4.98 (H^E) led to loss of allylic coupling in the signal due to H^D at δ 3.62 (d, J 9 and < 1 Hz). Dehydration of **15** in the presence of *N*-phenylmaleimide

† The stability of methylenedioxy groups attached to aromatic rings under strongly acidic conditions is truly remarkable.



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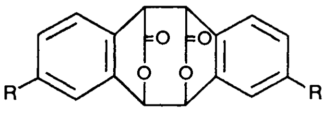
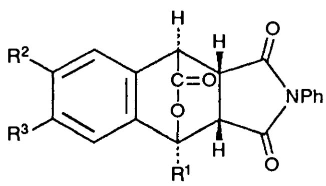
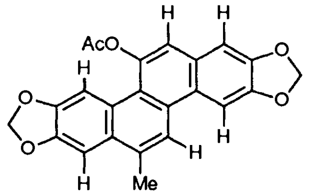


20 R = H
21 R = OMe



22 R^1 = Ph, R^2 = H, R^3 = OMe
23 R^1 = Me; R^2, R^3 = OCH_2O
24 R^1 = H; R^2, R^3 = OCH_2O



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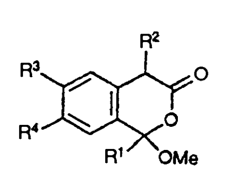
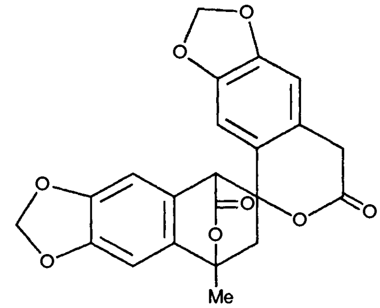


26 R^1 = R^2 = Ph; R^3 = R^4 = H
27 R^1 = Me, R^2 = H; R^3, R^4 = OCH_2O



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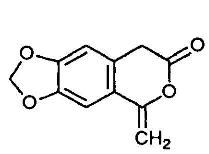

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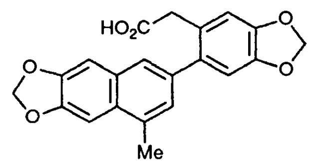

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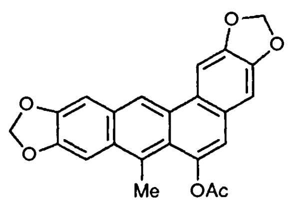

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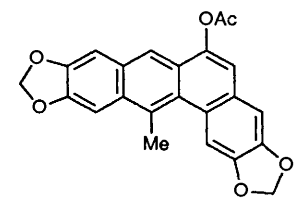

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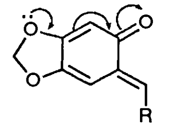
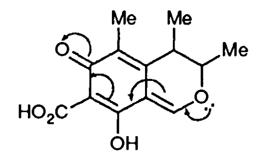


33 R = *E*-CH=CHPh
34 R = 4-$MeOC_6H_4$



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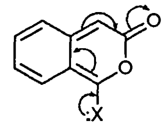

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gave the adduct **22** of the pyrone **8** in 74% yield showing that the pyrone **8** is produced efficiently by acetic anhydride dehydration but fails to survive under the reaction conditions.

The stability of 1-aryl-6,7-methylenedioxy-2-benzopyran-3-ones encouraged efforts to produce the corresponding 1-methyl derivative. The acid **16** when heated in acetic anhydride produced a deep yellow colour which disappeared upon addition of *N*-phenylmaleimide with formation of the adduct **23** and a product subsequently identified as **25** and discussed below. After the acid **16** had been heated in acetic anhydride (2 h) attempted isolation of **9** by chromatography at 20 °C failed. Chromatography at −20 °C allowed separation of **9** from **25** and minor by-products and gave **9** as bright yellow crystals (52%) characterised by IR, UV, mass and 400 MHz ^1H NMR spectroscopy. Crystalline **9** is unchanged after storage for *ca.* 1 month at −40 °C. The strong resistance to nucleophilic attack conferred by the methylenedioxy group in **9** is evident on comparing the reaction of **9** and 1,4-diphenyl-2-benzopyran-3-one with boiling methanol. The latter was completely converted into a *cis–trans* mixture of the pseudo-esters **26** within 1 h. After 11 h the pyrone **9** gave the pseudo-ester **27** (59%) with 23% recovered **9**.

It is likely that **25** originates from the Diels–Alder adduct **28** of **9** with its tautomer **29**. Decarboxylation and β-elimination in **28** would lead to **30** which, in boiling acetic anhydride, could undergo intramolecular Friedel–Crafts acylation and acetylation to give **25**. Different structures for this product arising *via* alternative regioselectivity in either the Diels–Alder or the Friedel–Crafts reaction are **31** and **32** respectively. However only structure **25** would be expected to show the observed NOE between an aromatic methyl and *two* aromatic protons one of which shows a further NOE with a third aromatic proton (see Experimental section). ^1H NMR monitoring of the pyrone **9** when it was heated at 150 °C (15 min) showed its partial conversion (27%) into a product tentatively identified as the tautomer **29**. Upon continued heating the ^1H NMR signals associated with **29** disappeared and the spectrum indicated a mixture of unidentified products.

The stabilising effect of the methylenedioxy group appears insufficient to render isolable the 2-benzopyran-3-one **10** which lacks a substituent at C-1. Although the acid **17** when heated in boiling acetic anhydride in the presence of *N*-phenylmaleimide gave the adduct **24** in good yield, in the absence of the trap an initial yellow colour tentatively assigned to **10** was rapidly replaced by an insoluble (polymeric?) product. 2-Benzopyran-3-one gives a similar product when generated in a high concentration by thermolysis of **18**.[3]

Simple Hückel calculations for **1** and its 6- and 7-alkoxy derivatives predict LUMO energies of −0.41, −0.46 and −0.42 β units respectively. The more pronounced raising of the LUMO energy of **1** by a 6- compared with a 7-alkoxy group is in accord with the importance of the former in stabilising 2-benzopyran-3-ones towards nucleophilic attack. The exceptional stability of the quinone methide **33** was attributed[9] to 'the extended conjugation of the quinoid nucleus with the cinnamylidene group'. The results reported in the present paper suggest that the stability of **33** as well as **34** is to a greater extent determined by push-pull resonance, *e.g.* **33** (arrows).[10] It should be noted that the donor–acceptor interaction in the pyrones described in this work as well as that in **33** and **34** does not tend to restore the aromaticity of the system as it does in citrinin **35** and related compounds.[11] This suggests that 1-donor substituted pyrones **36** should be particularly stable and **36** (X = NMe_2) an appealing target for synthesis. Our results also suggest that appropriately placed donor groups could stabilise other *o*-quinonoid system such as inden-2-ones and 2,3-naphthoquinones.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. Unless otherwise stated, IR spectra refer to Nujol mulls, UV spectra to ethanol solutions, and ^1H NMR spectra to solutions in deuteriochloroform measured at 90 MHz with a Perkin-Elmer R32 or a JEOL FX 90Q instrument. 400 MHz Spectra were obtained on a Bruker WH-400 instrument. *J* values are given in Hz. Low resolution mass spectra were obtained with a Kratos MS25 instrument and accurate mass measurements were made using a Kratos MS25 instrument and accurate mass measurements were made using a Kratos MS 9150 instrument. Where mass spectral measurements were used to establish molecular formulae the purity of the sample was checked by TLC in more than one solvent system as well as by NMR measurements, and for crystalline material by crystallisation to constant m.p. Chromatography on silica refers to short-column chromatography over Kieselgel G(Merck).[12] Ether refers to diethyl ether and light petroleum to the fraction b.p. 60–80 °C. All reactions were conducted under dry, oxygen-free nitrogen.

Friedel–Crafts Acylation of Methyl Alkoxyphenylacetates.—The methyl ester (10 mmol) in CH_2Cl_2 (30 ml) was cooled to 0–5 °C and stannic chloride (16.5 mmol) was added. The acid chloride (13.2 mmol) in CH_2Cl_2 (30 ml) was added over 15 min. The ice-bath was removed and the mixture stirred (24 h). The product was poured into water, isolated in ether in the usual way and purified as indicated.

Methyl 2-Benzoyl-4,5-methylenedioxyphenylacetate was purified by chromatography on silica in ether–benzene (1:99) (31% yield) (Found: M^+, 298.0836. $C_{17}H_{14}O_5$ requires M^+, 298.0841); ν_{max}/cm^{-1} 1729 and 1652; δ_H(90 MHz) 7.85–7.48 (5 H, m), 6.9 (1 H, s), 6.86 (1 H, s), 6.03 (2 H, s), 3.82 (2 H, s) and 3.61 (3 H, s).

Methyl 2-benzoyl-4,5-dimethoxyphenylacetate was purified by chromatography on silica in ethyl acetate–light petroleum (1:2) (58% yield), m.p. 100–102 °C (from ethyl acetate–light petroleum) (Found: C, 68.9; H, 5.8. $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.8%); ν_{max}/cm^{-1} 1729 and 1639; δ_H(90 MHz) 7.87–7.32 (5 H, m), 6.97 (1 H, s), 6.89 (1 H, s), 3.97 (3 H, s), 3.86 (2 H, s), 3.80 (3 H, s) and 3.62 (3 H, s).

Methyl 2-benzoyl-5-methoxyphenylacetate was purified by crystallisation from ethyl acetate–light petroleum (1:2) (71% yield), m.p. 69–70 °C (Found: C, 72.0; H, 5.7. $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.7%); ν_{max}/cm^{-1} 1732 and 1647; δ_H(90 MHz) 7.86–6.87 (8 H, m), 3.96 (2 H, s), 3.88 (3 H, s) and 3.62 (3 H, s).

Methyl 2-acetyl-4,5-methylenedioxyphenylacetate was purified by chromatography on silica in ethyl acetate–light petroleum (33:67) (49% yield), m.p. 117–117.5 °C (Found: C, 61.1; H, 5.1. $C_{12}H_{12}O_5$ requires C, 61.0; H, 5.1%); ν_{max}/cm^{-1} 1719 and 1659; δ_H(90 MHz) 7.28 (1 H, s), 6.7 (1 H, s), 6.01 (2 H, s), 3.84 (2 H, s), 3.68 (3 H, s) and 2.51 (3 H, s).

o-Acylalkoxyphenylacetic Acids.—The ester (2.5 mmol), ethanol (5 ml) and 2M sodium hydroxide solution (5 ml) were boiled under reflux (1 h). The crude acid was isolated in the usual way and purified as indicated.

2-Benzoyl-4,5-methylenedioxyphenylacetic acid was recrystallised from MeOH (40% yield), m.p. 182–184 °C (Found: C, 67.6; H, 4.25. $C_{16}H_{12}O_5$ requires C, 67.6; H, 4.3%); ν_{max}/cm^{-1} 3198br, 1713 and 1650; δ_H[$CDCl_3$ and 10% $(CD_3)_2SO$] (90 MHz) 7.85–7.45 (5 H, m), 6.90 (1 H, s), 6.85 (1 H, s), 6.05 (2 H, s) and 3.75 (2 H, s).

2-Benzoyl-4,5-dimethoxyphenylacetic acid was purified by recrystallisation from ethyl acetate (80% yield), m.p. 162–163 °C (Found: C, 68.2; H, 5.35. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.4%); ν_{max}/cm^{-1} 3198–2380, 1707 and 1652; δ_H(90 MHz) 11.26 (1 H, br s), 7.92–7.32 (5 H, m), 6.98 (2 H, s), 3.97 (3 H, s) and 3.80 (5 H, apparent s, OMe and CH_2).

2-Benzoyl-5-methoxyphenylacetic acid was purified by recrystallisation from ether (50% yield), m.p. 130–131 °C (Found: C, 70.8; H, 5.0. $C_{16}H_{14}O_4$ requires C, 71.1; H, 5.2%); ν_{max}/cm^{-1} 3210–2380br, 1713 and 1644; δ_H(90 MHz) 10.74 (1 H, s), 7.77–6.74 (8 H, m), 3.70 (3 H, s) and 3.69 (2 H, s).

2-Acetyl-4,5-methylenedioxyphenylacetic acid was recrystallised from methanol (71% yield), m.p. 171–174 °C (Found: C, 59.4; H, 4.5. $C_{11}H_{10}O_5$ requires C, 59.5; H, 4.5%); ν_{max}/cm^{-1} 3350–2450, 1707 and 1664; δ_H[$(CD_3)_2CO$] (90 MHz) 7.41 (1 H, s), 6.87 (1 H, s), 6.09 (2 H, s), 3.87 (2 H, s) and 2.52 (3 H, s).

Alkoxy-substituted 2-Benzopyran-3-ones.—The pyrones **5**, **6** and **7** were prepared by the general procedure involving the *o*-acylphenylacetic acid (100 mg) and acetic anhydride (4–5 ml), heating under reflux (2 h) and evaporation at 100 °C in a high vacuum. The pyrones were generally obtained in pure form by trituration with ether.

6,7-Methylenedioxy-1-phenyl-2-benzopyran-3-one. (56% yield), m.p. 165–168 °C (Found: C, 72.2; H, 3.7. $C_{16}H_{10}O_4$ requires C, 72.2; H, 3.8%); ν_{max}/cm^{-1} 1692; $\lambda_{max}(CH_3CN)$/nm 265, 320sh and 445 (ε 34 057, 3230 and 6525); δ_H(90 MHz) 7.75–7.27 (5 H, m), 6.75 (1 H, s), 6.40 (1 H, s), 6.17 (1 H, s) and 5.93 (2 H, s).

6,7-Dimethoxy-1-phenyl-2-benzopyran-3-one. (91% yield), m.p. 123–125 °C (Found: C, 72.2; H, 5.0. $C_{17}H_{14}O_4$ requires C, 72.3; H, 5.0%); ν_{max}/cm^{-1} 1691; $\lambda_{max}(CH_3CN)$/nm 261 and 322 (ε 36 742 and 3768); δ_H(90 MHz) 7.88–7.40 (5 H, m), 6.71 (1 H, s), 6.46 (1 H, s), 6.17 (1 H, s), 3.98 (3 H, s) and 3.80 (3 H, s).

6-Methoxy-1-phenyl-2-benzopyran-3-one. (59% yield), m.p. 94–96 °C (Found: C, 76.2; H, 4.8. $C_{16}H_{12}O_3$ requires C, 76.2; H, 4.8%); ν_{max}/cm^{-1} 1695; $\lambda_{max}(CH_3CN)$/nm 268 and 320sh (ε 26 370 and 4466); δ_H(90 MHz) 7.79–7.22 (6 H, m), 6.50 (1 H, dd, *J* 9 and 2), 6.31 (1 H, d, *J* 2), 6.14 (1 H, s) and 3.90 (3 H, s).

2-Benzoyl-4-methoxyphenylacetic Acid.—3-Phenyl-5-methoxyindene (409 mg, 1.845 mmol) in dry dichloromethane (24 ml), was cooled to −78 °C and ozonised oxygen bubbled through at 0.1 dm^3 min^{-1} and 0.34 kg cm^{-3} pressure for 5 min. The solvent was evaporated to small volume at 20 °C and the residue stirred vigorously with 2M sodium hydroxide (16 ml), hydrogen peroxide (30%; 1.6 ml), methanol (16 ml) and ether (16 ml). After 20 min the mixture was poured into 2M hydrochloric acid (45 ml) and the aqueous phase extracted with ethyl acetate. The organic layer was washed with saturated brine, dried ($MgSO_4$) and evaporated. The crude product crystallised from methanol to give the oxo acid **15** as pale yellow needles (301 mg, 60%); m.p. 159–161 °C; ν_{max}/cm^{-1} 1700 and 1650; δ_H($CDCl_3$ + 10% [$^2H_6$]DMSO) (90 MHz) 7.92–6.82 (9 H, m, ArH and CO_2H), 3.77 (3 H, s, OMe), 3.68 (2 H, s); *m/z* 226 (M − CO_2) 209, 181, 165, 105, 77, 51 and 44 (72.2, 15.0, 14.8, 22.1, 39.6, 100, 40.1 and 17.3%).

The N-*Phenylmaleimide Adduct of the Pyrone* **8**.—The foregoing oxo acid (68.0 mg) and *N*-phenylmaleimide (87 mg) in acetic anhydride (4 ml) were boiled under reflux (2 h). The acetic anhydride was removed under a water pump vacuum while the mixture was heated on a boiling water-bath, and the resulting crude product was chromatographed on silica (35 g). Elution with ether–dichloromethane (5:95) gave the *title compound* **22** (79 mg, 74%), m.p. 194–195 °C (from ethanol) (Found: C, 73.1; H, 4.6; N, 3.2. $C_{26}H_{19}NO_5$ requires C, 73.4; H, 4.5; N, 3.3%); ν_{max}/cm^{-1} 1768 and 1715; δ_H(90 MHz) 8.05–6.37 (13 H, m), 4.50 (1 H, d, *J* 9), 4.51 (1 H, d, *J* 2), 3.82 (1 H, dd, *J* 9 and 2) and 3.68 (3 H, s, OMe); *m/z* 381 (M − CO_2) 234, 189, 165, 119, 91, 77 and 44 (39.2, 100.0, 21.7, 7.1, 8.7, 5.6, 8.4 and 12.4%).

Attempted Preparation of 7-*Methoxy*-1-*phenyl*-2-*benzopyran*-3-*one*.—The oxo acid **15** (99.6 mg) in acetic anhydride (4 ml) was boiled under reflux (2 h). The dark red solution was evaporated to dryness under a water pump vacuum whilst the mixture was heated on a boiling water-bath. During evaporation the intensity of the red colour decreased. The residue was chromatographed on silica in ether–dichloromethane (1:19) to give the *endo-dimer* **19** (18.6 mg, 10%), m.p. 133–135 °C (from ethanol) (Found: C, 75.9; H, 4.6. $C_{32}H_{24}O_6$ requires C, 76.2; H, 4.8%); ν_{max}/cm^{-1} 1765 and 1722; δ_H(400 MHz) 7.52–7.35 (10 H, m), 7.25 (1 H, d, *J* 8), 6.99 (1 H, d, *J* 2), 6.90 (1 H, dd, *J* 8 and 2), 5.37 [1 H, s, with further fine splitting (wffs)], 4.98 (1 H, s, wffs), 4.50 (1 H, d, *J* 4), 3.71 (3 H, s), 3.67 (1 H, dd, *J* 9 and 4, wffs), 3.62 (1 H, d, *J* 9 wffs) and 3.42 (3 H, s, OMe); *m/z* 460 (M − CO_2), 458, 325, 252, 224, 105, 83, 69 and 44 (21.3, 45.4, 20.2, 27.3, 35.4, 60.7, 36.5, 49.3 and 100%).

The eluate obtained immediately before elution of the compound **19** gave a small quantity of a compound tentatively assigned as the *exo*-isomer **19** (6.3 mg, 4%), m.p. 212–215 °C (from ethanol); ν_{max}/cm^{-1} 1765 and 1722; δ_H(400 MHz) 7.65–7.39 (11 H, m,), 6.94 (1 H, dd, *J* 2 and 8), 6.85 (1 H, d, *J* 2), 5.73 (1 H, s), 5.37 (1 H, s), 4.46 (1 H, d, *J* 2), 3.74 (3 H, s), 3.72 (1 H, d, *J* 10), 3.65 (3 H, s) and 3.17 (1 H, dd, *J* 10 and 2); 3.73 (1 H, dd, *J* 10 and 1) (partly overlapped by OMe resonance).

1-*Methyl*-6,7-*methylenedioxy*-2-*benzopyran*-3-*one*.—2-Acetyl-4,5-methylenedioxyphenylacetic acid (45 mg, 0.202 mmol) and acetic anhydride (3 ml, freshly distilled from quinoline) were boiled under reflux (2 h). The acetic anhydride was removed under a water pump vacuum over a steam bath and the residue triturated with ether (2 × 0.5 ml). The solid product was chromatographed on silica (30 g) in ether–dichloromethane (1:9) at −21 °C. The yellow band gave the crystalline pyrone **9** (22 mg, 52%); ν_{max}/cm^{-1} 1693; $\lambda_{max}(CH_3CN)$/nm 281sh and 406 nm (ε 2947 and 4080); δ_H(400 MHz) 6.45 (1 H, s), 6.36 (1 H, s), 6.04 (1 H, s), 5.96 (2 H, s) and 2.55 (3 H, s); *m/z* 204 (M$^+$), 176 (M − CO), 147 (M − CO − HCO), 133 (M − CO − MeCO), 118, 89, 75, 63 and 50 (58.9, 100.0, 49.7, 19.8, 11.7, 25.9, 30.4, 21.2 and 19.7%). The least polar fraction from the above chromatography (19 mg) was the polynuclear aromatic compound **25**, m.p. 263–265 °C (from ethyl acetate); ν_{max}/cm^{-1} 1753; δ_H(400 MHz) 2.53 (3 H, s), 2.76 (3 H, br s), 6.11 (2 H, s), 6.12 (2 H, s), 7.17 (1 H, s), 7.40 (1 H, s), 7.45 (1 H, s), 8.03 (1 H, s), 8.22 (1 H, br s) and 8.60 (1 H, s); a NOESY spectrum showed the lower field methyl group correlated with the signals at δ 7.45 and 8.22 and that δ 7.45 correlated with no other proton and δ 8.22 correlated with δ 8.02 only. The signals at 7.17 and 7.40 correlated with one another and that at δ 8.60 correlated with no other proton; $\lambda_{max}(CH_3CN)$/nm 277 (100, 233) with much weaker peaks at 296, 308, 323, 336, 354 and 374 nm; *m/z* 388 (M$^+$), 346 (M − CH_2CO), 317, 260, 231, 200 and 43 (30.5, 100, 14.4, 7.0, 3.9, 17.9 and 63.1%).

The N-*Phenylmaleimide Adduct of* 1-*Methyl*-6,7-*methylenedioxy*-2-*benzopyran*-3-*one*.—2-Acetyl-4,5-methylenedioxyphenylacetic acid (100 mg) and acetic anhydride (5 ml) were boiled under reflux (2 h). The acetic anhydride was evaporated by heating on a steam-bath under a water pump vacuum. The product was triturated with ether and dried in a high vacuum. The crude product (94 mg), *N*-phenylmaleimide (94 mg) and benzene (5 ml) were boiled under reflux (30 min). The product was chromatographed on silica in benzene to give the previously described acetate **25** (28 mg) followed by the adduct **23** (30 mg), m.p. 182–183 °C (from ether); δ(90 MHz) 2.19 (3 H, s), 3.56 (1 H, d, *J* 9), 3.7 (1 H, dd, *J* 9 and 2), 4.36 (1 H, d, *J* 2), 6.0 (2 H, AB-system, J_{AB} *ca.* 1), 6.7 (2 H, m), 6.88 (2 H, apparent s) and 7.35 (3 H, m); *m/z* 377 (M$^+$), 333 (M − CO_2), 214, 213, 186, 176, 128, 102, 91, 77, 57 and 44 (0.8, 8.8, 0.6, 0.6, 14.8, 1.2, 5.1, 1.7, 1.4, 2.1, 2.5 and 100%). The acetate **25** was not produced when 2-acetyl-4,5-methylenedioxyphenylacetic acid (50 mg) was heated with acetic anhydride in the presence of *N*-phenylmaleimide (50 mg).

Reaction of 1-*Methyl*-6,7-*methylenedioxy*-2-*benzopyran*-3-*one with Methanol*.—The pyrone (44 mg) in dry methanol (4 ml) was boiled under reflux in a base-washed apparatus (11 h). The 400 MHz ^{1}H NMR spectrum of the evaporated product indicated unchanged starting material (23%), the pseudo-ester **27** (73%) and the related oxo ester (4%). The product was chromatographed on silica at 20 °C in ether–dichloromethane (1:9) to give the *pseudo-ester* **27** (30 mg, 59%), m.p. 102–103 °C (from benzene–light petroleum) (Found: C, 60.8; H, 5.2. $C_{12}H_{12}O_5$ requires C, 61.0; H, 5.1%); ν_{max}/cm^{-1} 1736; δ_H(90 MHz) 6.85 (1 H, s), 6.62 (1 H, s), 5.99 (2 H, s), 3.61 (1 H, d, *J* 19.5), 3.78 (1 H, d, *J* 19.5), 3.34 (3 H, s) and 1.79 (3 H, s); *m/z* 236 (M$^+$), 205, 192, 177, 162, 91, 76 and 43 (22.9, 18.5, 40.0, 100.0, 15.6, 24.0, 20.6 and 43.0%).

Thermal Stability of 1-*Methyl*-6,7-*methylenedioxy*-2-*benzopyran*-3-*one*.—The *title compound* (10 mg) in dry deuteriobenzene (0.4 ml) was placed in a thermolysis tube which fitted snugly inside an NMR tube. After five freeze–pump–thaw cycles the thermolysis tube was heated in a constant temperature bath and removed at intervals for NMR monitoring at 90 MHz. After 15 min at 150 °C peaks attributed to the tautomer **29** at δ 3.71 (2 H, s), 4.90 (2 H, apparent s), as well as 6.0 (2 H, s), 6.56 (1 H, s) and 6.90 (1 H, s) accounted for 27% of the mixture, the remainder being starting material. After the mixture had been heated for 150 min numerous other peaks appeared in its spectrum; the tube was opened, the solvent evaporated and the residue dissolved in $CDCl_3$ and the 400 MHz spectrum obtained. The signal at δ 4.9 due to the exocyclic methylene group now appeared as an AB-system centred at δ 4.93 (J_{AB} 2.5).

2-*Formyl*-4,5-*methylenedioxyphenylacetic Acid*.—4,5-Methylenedioxyisochroman-3-one[5] (300 mg), 2M aqueous sodium hydroxide (5 ml) and ethanol (2 ml) were boiled under reflux (2.5 h). The clear yellow solution was cooled to 20 °C, washed with a little ether, cooled to 0–5 °C and acidified to pH 2 when the hydroxy acid was precipitated. The mixture was quickly extracted with ether (2×) and treated with diazomethane. Evaporation of the dried ($MgSO_4$) ether extract gave the hydroxy ester (230 mg, 71%); δ_H(90 MHz) 2.85 (1 H, br s), 3.65 (3 H, s), 3.70 (3 H, s), 4.55 (2 H, s), 5.95 (2 H, s), 6.72 (1 H, s) and 6.89 (1 H, s); ν_{max}/cm^{-1} 1740, 3170 and 3280. Without delay the hydroxy ester was oxidised by the Swern procedure.

To oxalyl chloride (533 mg) in dichloromethane (9 ml) at −65 °C was added dimethyl sulphoxide (656 mg) in dichloromethane (2.5 ml) slowly with stirring. After the mixture had been stirred for a further 5 min at −65 °C the foregoing hydroxy ester (855 mg) in dichloromethane (5 ml) was added over 5 min and the mixture stirred for 20 min before triethylamine (1.93 g) was added to it. After being stirred for 5 min at −65 °C the mixture was allowed to reach 20 °C over 20 min, iced water (20 ml) added and the phases separated. The organic layer was washed with water (3 ×), dried ($MgSO_4$) and evaporated. The crude product (852 mg) was chromatographed on silica (100 g) in ethyl acetate–light petroleum (1:3) to give *methyl 2-formyl-4,5-methylenedioxyphenylacetate* (596 mg, 70%) (Found: M^+, 222.0526. $C_{11}H_{10}O_5$ requires M^+, 222.0528); ν_{max}/cm^{-1} 1690 and 1740; δ_H(60 MHz) 3.70 (3 H, s), 3.97 (2 H, s), 6.05 (2 H, s), 6.80 (1 H, s), 7.30 (1 H, s) and 10.00 (1 H, s); *m/z* 222 (M^+), 190 (M − MeOH), 163, 162, 149, 135, 134, 105, 77 and 51 (54.3, 46.8, 84.6, 86.6, 22.8, 100.0, 26.3, 26.0, 76.0 and 70.2%).

This ester (150 mg), glacial acetic acid (5 ml), water (5 ml) and concentrated hydrochloric acid were boiled under reflux (1 h). The cooled product was poured into water (50 ml) and extracted into ethyl acetate (2 × 50 ml). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (4 × 15 ml) and the combined aqueous extracts acidified with concentrated hydrochloric acid and extracted with ethyl acetate (2 × 50 ml). The organic extract was washed with water, dried ($MgSO_4$) and evaporated to give *2-formyl-4,5-methylenedioxyphenylacetic acid* **17** (124 mg), m.p. 155–158 °C (from benzene) (Found: M^+, 208.0370. $C_{10}H_8O_5$ requires 208.0372); ν_{max}/cm^{-1} 1600, 1690 and 2400–3400; δ_H(90 MHz) [$(CD_3)CO$] 4.06 (2 H, s), 6.13 (2 H, s), 6.94 (1 H, s), 7.35 (1 H, s), 10.07 (1 H, s); *m/z* 208 (M^+), 190, 164, 163, 162, 149, 135, 105, 77 and 51 (55.4, 17.3, 72.5, 100, 77.7, 14.5, 64.6, 25.9, 82.7 and 74.3%).

Dehydration of 2-Formyl-4,5-methylenedioxyphenylacetic Acid in the Presence of N-*Phenylmaleimide*.—The *title acid* (50 mg) and *N*-phenylmaleimide (50 mg) in acetic anhydride (distilled from 1% quinoline; 3 ml) were boiled under reflux (2 h). The acetic anhydride was removed under a water pump vacuum whilst heating on a steam bath and the residue chromatographed on silica in benzene–ether (95:5) to give the adduct **24** (49 mg), m.p. 230–233 °C (from ether); δ_H(90 MHz) 3.67 (1 H, dd, *J* 8.4 and 3.6), 3.96 (1 H, dd, *J* 8.4 and 4.5), 4.38 (1 H, d, *J* 3.6), 5.90 (1 H, d, *J* 4.5), 6.0 (2 H, AB system, J_{AB} 1, OCH_2O), 6.64 (2 H, m), 6.86 (2 H, apparent s) and 7.35 (3 H, m); *m/z* 363 (M^+), 319, 172, 114, 78, 63 and 44 (13.3, 8.8, 48.1, 14.0, 100, 6.2 and 21.6%).

Attempted Preparation of 6,7-Methylenedioxy-2-benzopyran-3-one.—2-Formyl-4,5-methylenedioxyphenylacetic acid (50 mg) was heated in boiling acetic anhydride (distilled from 1% quinoline; 3 ml) for 2 h. After *ca.* 15 min the solution became cloudy and a precipitate appeared, adhering to the side of the flask. Removal of acetic anhydride by evaporation under a water pump vacuum at 100 °C and trituration of the product with ether afforded no crystalline product although the majority of the product was insoluble in ether (polymeric?). TLC on silica [benzene–ether (3:1)] indicated a complex mixture and very little yellow product. Similar failure resulted from attempted dehydration using dicyclohexylcarbodiimide in boiling benzene (1 h) followed by attempted isolation by chromatography on silica in dichloromethane at −25 °C.

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