Biomimetic Syntheses of Polyketide Aromatics from Pyrylium Salts[1]

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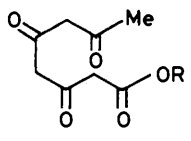
Following attack by nucleophiles, various methoxypyrylium compounds derived from 2*H*-pyran-2-ones and 4*H*-pyran-4-ones react either to produce a linear β-polycarbonyl derivative in which one or more carbonyl groups is derivatised in the form of an enol ether or to form a methylene-2*H*-pyran. The linear polycarbonyl derivatives can undergo biomimetic cyclisation to generate polyketide aromatic systems; syntheses of the following benzene derivatives are described: ethyl 2,4-dimethoxy-6-methylbenzoate (**29**), 2,4-dimethoxy-6-methylbiphenyl (**31**), and 6-(2,4-dimethoxy-6-methylphenyl)-4-methoxy-2*H*-pyran-2-one (**34**).

A wide range of polyketide aromatic systems is produced in living organisms by cyclisation of β-polyketones.[2] Judged from the synthetic standpoint, the approach is remarkable for its versatility, which rests on the facts that polyketone chains of various lengths can be formed, and that a chain of a particular length can cyclise to give more than one type of aromatic system, depending on the regiochemistry of the cyclisation process. Thus even the simple triketo ester (**1**) can form (**2**) *via* an aldol reaction or (**3**) *via* a Claisen condensation, and the number of possible aromatic cyclisation products increases rapidly with increasing chain length. The success of the synthetic strategy *in vivo* is critically dependent on the enzymes which control the regiochemistry of cyclisation, and so ensure that only one of the potential aromatic products is formed.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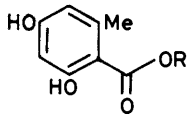
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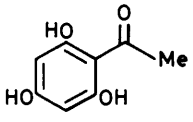
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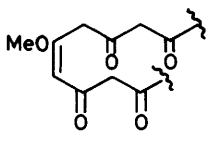
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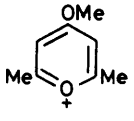
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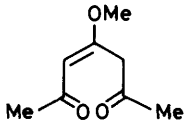
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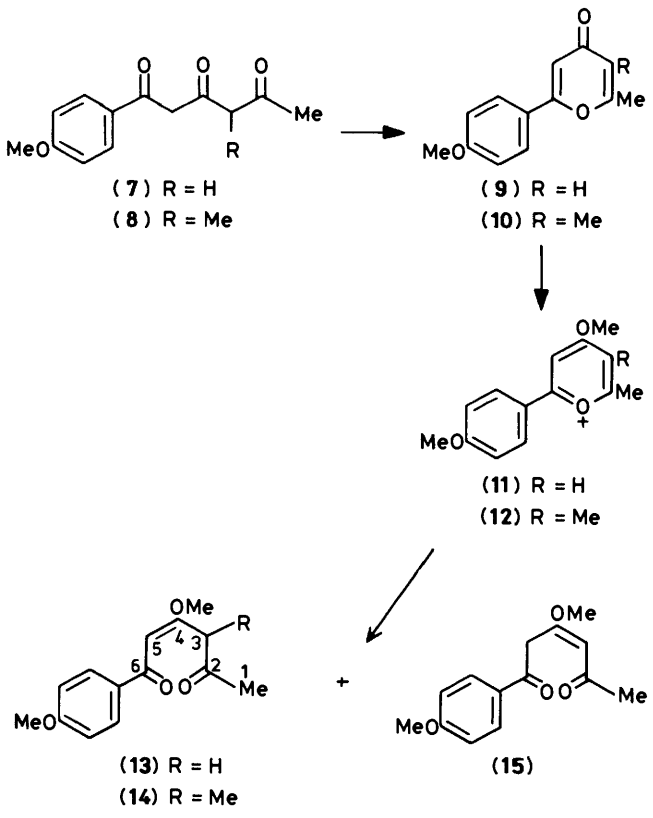
Considerable progress has been made in earlier attempts to mimic the synthetic strategy *in vitro*, particularly in the production of polyketones, either by direct synthesis, or indirectly by hydrolysis of pyrones.[3] There has been less success, however, in model experiments which have attempted to duplicate enzymic control over the steps of cyclisation and aromatisation. Typically, in a synthetic model experiment, the polyketone chain cyclises to give a complex mixture of phenolic compounds, in which no one product is present in high yield. In favourable cases a useful degree of control has been achieved empirically by careful control of such reaction conditions as solvent or pH. More direct control has been achieved either by preparing polyketones in which one or more key carbonyl groups are derivatised as an acetal[4] or an enol ether,[5] or by carrying out the cyclisation in the presence of a suitable cation which can chelate with an enol derivative of the polyketone chain,[6] and so influence its folding prior to cyclisation.

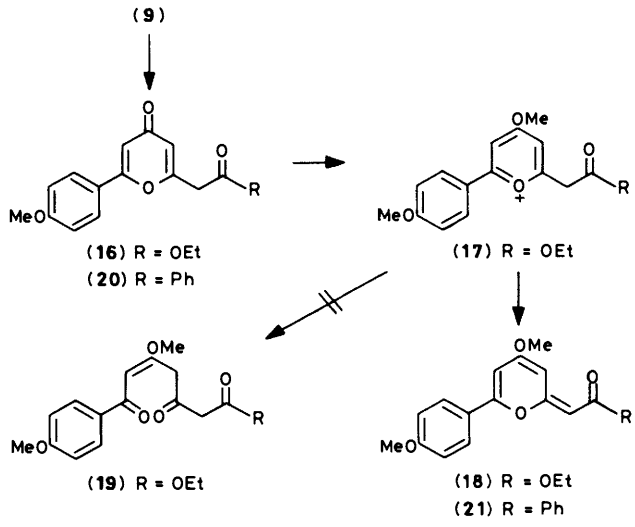
We now describe a biomimetic strategy in which one of the carbonyl groups of the polyketone chain is selectively derivatised as an enol ether. As long as the key double bond at the chain-folding site has the *E*-configuration, as indicated in (**4**), the chain will be folded back on itself so as to bring potential sites of reaction flanking the carbon–carbon double bond in close proximity. It was hoped that this would result in certain modes of cyclisation being favoured over others.[7] It might then be possible to direct the cyclisation towards a particular aromatic system by suitable choice of enol ether.

Enol ethers with the desired stereochemistry are potentially available from hydrolytic cleavage of 4-methoxypyrylium salts, as in the conversion of (**5**) into (**6**). As early as 1906, Baeyer[8] had investigated this reaction and suggested structure (**6**) for the product, but with the techniques at his disposal he was not able to substantiate the proposal. In the present work two analogous pyrylium salts (**11**) and (**12**), prepared as indicated in Scheme 1, were investigated. The triketones (**7**) and (**8**), made by reaction of methyl 4-methoxybenzoate with the dilithium salt of pentane-2,4-dione or its 3-methyl derivative, were cyclised in acid to form the γ-pyrones (**9**) and (**10**) respectively. The corresponding pyrylium salts, (**11**) and (**12**), prepared by treatment with methyl fluorosulphonate, did not undergo the desired ring opening on treatment with aqueous magnesium carbonate or aqueous sodium acetate, but underwent demethylation to regenerate the pyrones (**9**) and (**10**) instead. This undesired reaction was avoided in aqueous 2,6-lutidine, and products were obtained with spectroscopic properties consistent with enol ether formation. The product from (**12**) appeared to be a single tautomer (**14**), but from (**11**) a mixture of both tautomers (**13**) and (**15**) was obtained. These open-chain derivatives are unstable, readily reverting to pyrylium salts on mild treatment with acid or even on silica gel, but, after purification by chromatography on alumina, they can be stored for several weeks at −15 °C.

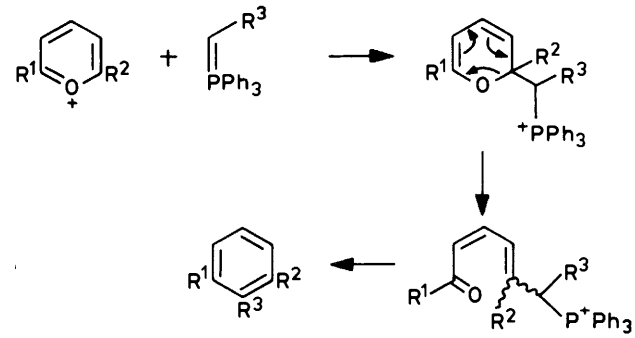
Following these successful pilot studies, the pyrylium salt (**17**) was prepared according to Scheme 2. Thus the carbanion generated by deprotonation of the methyl group of (**9**), using trityl-lithium in tetrahydrofuran, was treated with ethyl chloroformate to give the acylated product (**16**). This exhibited interesting prototropic behaviour, being released as an enol tautomer on acidification of the reaction mixture; the enol slowly being converted into the carbonyl form shown with time. Methylation of this γ-pyrone with methyl fluorosulphonate proceeded as expected to give a solid product which exhibited



Scheme 1.



Scheme 2.



Scheme 3.

spectroscopic properties consistent with the pyrylium salt (**17**). However, this failed to undergo hydrolytic cleavage to form the desired enol ether (**19**) on treatment under standard conditions with a mixture of water and 2,6-lutidine. Instead, as had been observed for other pyrylium salts, a proton was removed from the acidic methylene to produce the methylenepyran derivative (**18**).[9] A wide range of mild hydrolysis conditions were investigated without changing the outcome. More vigorous treatment resulted in loss of the methoxy and ethoxy groups followed by further decomposition. A variety of aqueous acidic conditions also resulted in slow decomposition rather than the production of (**19**).

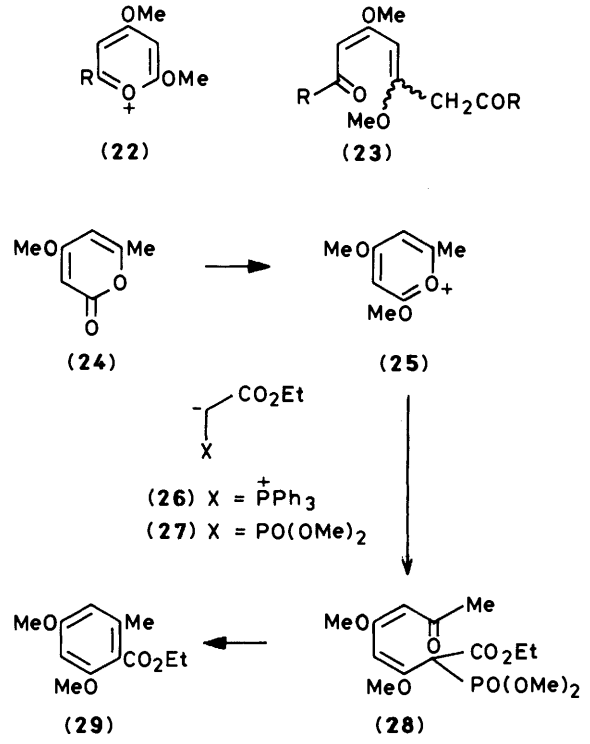
Attention was then turned to the analogous series in which a ketonic carbonyl group took the place of the ester residue of (**16**). A suitable ketone (**20**) was readily prepared by benzoylation of (**9**) using trityl-lithium and benzoic anhydride. On methylation with either dimethyl sulphate or diazomethane, this gave the methylenepyran (**21**). Like (**18**), this resisted base-catalysed hydrolysis of the heterocyclic ring; also the methine proton exchanged readily with D_2O, presumably *via* formation of a pyrylium salt analogous to (**17**).

In view of the marked reluctance of the heterocyclic rings of (**18**) and (**21**) to undergo hydrolytic cleavage, a different approach to enol ether derivatives of linear polyketones was explored. This is based on a standard reaction of simple pyrylium salts, which are known to be susceptible to ring cleavage following attack by certain classes of carbon nucleophile.[10] Of particular relevance is the reaction with Wittig reagents, which typically follows the steps illustrated in Scheme 3 leading ultimately to the formation of a new aromatic ring.[11,12] By analogy, it seemed likely that attack of suitable enolate derivatives on pyrylium salts of general structure (**22**) might generate the interesting selectively protected polyketone system (**23**). Although two keto groups are now derivatised as enol ethers, rather than one as orginally envisaged in (**19**), a compound such as (**23**) could open the way to an interesting variation of the proposed synthetic strategy.

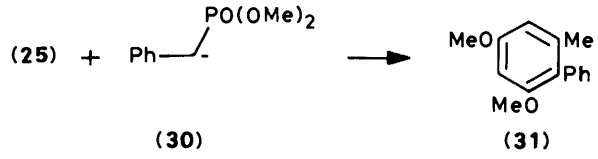
2-Alkoxypyrylium salts such as (**22**) can be considered to be derivatives of an α-pyrone rather than a γ-pyrone, and they were inaccessible to early workers because the available alkylating agents were not sufficiently powerful to alkylate the relatively weakly basic α-pyrone carbonyl. However, more powerful modern alkylating agents are effective; successful conversions have been reported using trimethoxonium tetrafluoroborate,[13] methyl iodide in the presence of silver tetrafluoroborate,[14] and in the present investigation methyl fluorosulphonate.[1]

The readily available methyl ether (**24**)[15] of triacetic lactone has an array of functional groups appropriate for the proposed biomimetic strategy. On treatment with methyl fluorosulphonate in chloroform solution (Scheme 4) it forms the desired pyrylium salt (**25**) as an insoluble crystalline derivative in high yield. The salt is labile and tends to decompose when recrystallised; when heated, methyl fluorosulphonate is evolved, and the parent 4-methoxypyrone regenerated. The solid compound can however be stored for prolonged periods in a cool dry atmosphere.

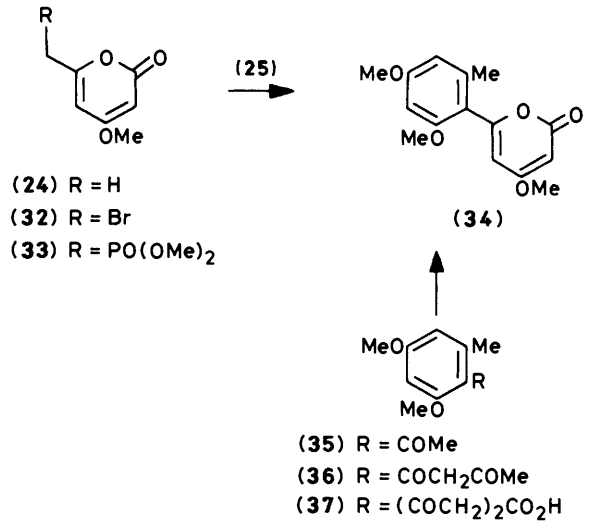
Treatment of the pyrylium salt (**25**) in benzene with ethyl bromoacetate and zinc, under standard conditions for the Reformatsky reaction, resulted mainly in demethylation to regenerate (**24**). Reaction with the phosphorane (**26**) in benzene or tetrahydrofuran was similarly unsuccessful. The desired nucleophilic addition did occur when the phosphonoacetate anion (**27**) was added to a suspension of the pyrylium salt in tetrahydrofuran. The product isolated was the benzene derivative (**29**), and it was obtained in good yield in the presence of an



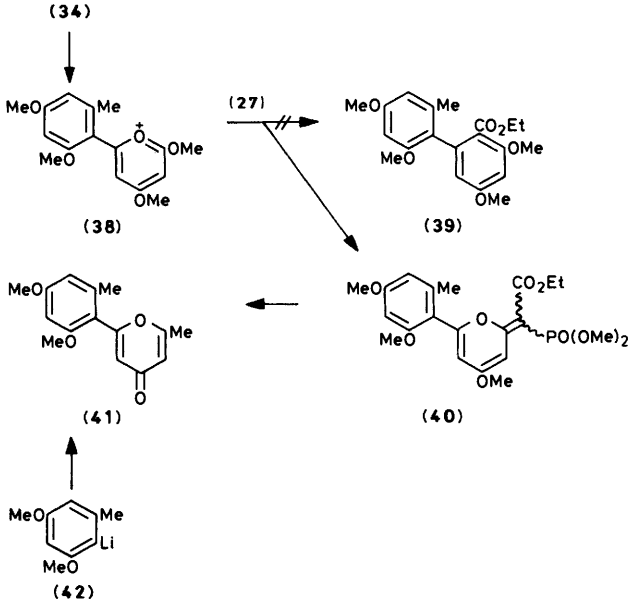
Scheme 4.



Scheme 5.



Scheme 6.



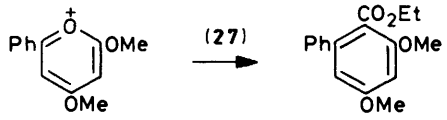
Scheme 7.

extra equivalent of base (NaH). It was not possible to isolate or detect the presumed intermediate (**28**); presumably the initial nucleophilic addition is the rate-limiting step of the overall process by which (**29**) is formed. If the extra mole of NaH is omitted, the anion required for the Wittig step, (**28**) to (**29**), is generated by proton transfer from (**28**) to the starting anion (**27**), and the result is a mixture of (**29**) and unchanged starting materials. The analogous methyl ester was prepared using the methoxycarbonyl analogue of (**27**).

Following this successful precedent, further examples were investigated to test the scope of the reaction. First the pyrylium salt (**25**) was treated with the benzyl phosphonate anion (**30**) (Scheme 5). The expected biphenyl (**31**) was formed, but again no intermediates could be isolated. The yield was low but not optimised. Next the phosphonate (**33**) was prepared from the pyrone (**24**) *via* (**32**), following the method of Bloomer.[16] Reaction of the anion derived from (**33**) with the pyrylium salt (**25**) afforded the 6-arylpyrone (**34**) (Scheme 6). This pyrone is a polyketide system which forms the nucleus of the recently isolated natural product aloenin.[17] The novel synthetic approach described here, in which the carbon skeleton is wholly derived from two molecules of the pyrone (**24**), is a good alternative to the classical approach *via* (**35**), (**36**), and (**37**).[17]

The product of Scheme 6 is another α-pyrone which can be used to investigate the scope of the biomimetic reaction. On treatment with methyl fluorosulphonate, (**34**) was converted into a crystalline pyrylium salt (**38**) (Scheme 7). When this was treated with the anion of methyl phosphonoacetate the desired product (**39**) was not formed. Instead nucleophilic addition was followed by loss of methoxide to give the methylenepyran (**40**). Like the analogues (**18**) and (**21**) described earlier, this was extremely resistant to reactions designed to open the heterocyclic ring. Normally (**40**) was recovered unchanged, but on vigorous treatment with methoxide both the carboxylate and phosphonate groups were removed to leave the γ-pyrone (**41**). The structure of this product was confirmed by an independent synthesis in which the phenyl-lithium derivative (**42**) (prepared by reaction of butyl-lithium with the corresponding bromo compound[18]) was treated with triacetic lactone methyl ether (**24**).

Steric hindrance from the heavily substituted aryl ring at C-6 is presumed to be the factor which caused (**38**) in its reaction with the Wittig reagent to take a path different from that followed by (**25**). The result contrasts with the outcome of the equivalent reaction involving the closely related 6-arylpyrylium salt (**43**). In this case the reaction did follow the normal course



(43) (44)

Scheme 8.

to produce a biphenyl (**44**) rather than a methylenepyran. Clearly the determining factor in the anomalous behaviour of (**38**) is not the aromatic character of the substituent at C-6 of the pyrylium ring. 2,4-Dimethoxypyrylium salts are therefore potentially versatile synthons for the preparation of polyketide aromatic systems. Further examples of the synthetic strategy are presented in a following paper.[19]

Experimental

Solutions were dried over sodium sulphate (anhydrous). Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Unless otherwise stated, i.r. spectra were recorded with a Perkin-Elmer 257 spectrophotometer for solutions in chloroform; u.v. spectra were recorded on a Unicam SP 800 or SP 8000 instrument for solutions in 95% ethanol; mass spectra were recorded on an AEI MS 12 or MS 30 mass spectrometer; ^{1}H n.m.r. spectra were run on a Varian HA 100 or a Perkin-Elmer R12B instrument, for solutions in deuteriochloroform, using Si_4Me as internal standard. Preparative t.l.c. was carried out on glass plates coated with Merck Kieselgel GF_{254}.

Trityl-lithium.—A solution of triphenylmethane (24 g, 0.1 mmol) in dry tetrahydrofuran (150 ml) was flushed with nitrogen gas and cooled to 0 °C in a sealed flask. A solution of butyl-lithium in hexane (15% w/w; 65 ml) was injected. The resulting solution was stable for weeks at −15 °C.

1-(p-*Methoxyphenyl*)*hexane*-1,3,5-*trione* (**7**).—Trityl-lithium in tetrahydrofuran (see above) was injected into pentane-2,4-dione (0.52 ml, 5 mmol) under nitrogen at −15 °C. When the red colour persisted methyl *p*-methoxybenzoate (0.8 g, mmol) in dry tetrahydrofuran (10 ml) was injected. The solution was stirred at −15 °C and trityl-lithium solution added to just maintain the red colour. When this colour persisted Amberlite IRC 120 (H) ion-exchange resin was added until the solution was neutral to moist indicator paper. The resin was filtered off and washed with tetrahydrofuran. Filtrate and washings were passed down a column of Amberlite IRA 400 (OH) ion-exchange resin. The column was washed several times with tetrahydrofuran then eluted with dilute sulphuric acid (2%)–ethanol (2:1). The eluate was diluted with water to three times its volume and extracted four times with diethyl ether. The ether solution was shaken with water, dried over sodium sulphate and evaporated under reduced pressure to give the triketone (0.81 g), which was purified by sublimation to give pale yellow crystals, m.p. 80—81 °C (lit.,[20] 81 °C); $\lambda_{max.}$ 287 and 338 nm; $\nu_{max.}$ 1 710m, 1 600s, 1 260s, and 1 175s cm^{-1}; δ (several tautomers) 8.15—7.65 (2 H, m), 6.92 (2 H, d, *J* 9.3 Hz), 6.15 (s), 5.73 (s), 5.61 (s), 5.27 (s) (total 1 H), 3.89 (s), 3.50 (s) (total 2 H), 3.84 (3 H, s), 2.29 (s), 2.01 (s), and 1.99 (s) (total 3 H); *m/z* 234 (M^+) and 135.

1-(p-*Methoxyphenyl*)-4-*methylhexane*-1,3,5-*trione* (**8**).—This was prepared from 3-methylpentane-2,4-dione[21] (0.59 ml, 5 mmol) following the procedure described for (**7**). The product (0.9 g) gave an oil which sublimed to form yellow crystals of the *trione*, m.p. 56—57 °C (Found: M^+, 248.1052. $C_{14}H_{16}O_4$ requires M^+, 248.1048); $\lambda_{max.}$ 330 nm; $\nu_{max.}$ 1 721s, 1 603s, 1 260s, and 1 178s cm^{-1}; δ 7.86 (2 H, d, *J* 9.3 Hz), 6.93 (2 H, d, *J* 9.3 Hz), 6.13 (1 H, s), 3.86 (3 H, s), 3.51 (1 H, q, *J* 7.3 Hz), 2.23 (3 H, s), and 1.38 (3 H, d, *J* 7.3 Hz); *m/z* 248 (M^+), 177, and 135.

2-(p-*Methoxyphenyl*)-6-*methyl*-4H-*pyran*-4-one (**9**).—1-(*p*-Methoxyphenyl)hexane-1,3,5-trione (100 mg, 0.43 mmol) was dissolved in trifluoroacetic acid (2 ml) at −15 °C. The solution was stirred at −15 °C, and after 10 min trifluoroacetic anhydride (0.5 ml) was added. After 30 min the solution was evaporated under reduced pressure. The residue was recrystallised twice from tetrahydrofuran–di-isopropyl ether to give the *pyrone* (83 mg), m.p. 143—144 °C (Found: C, 72.25; H, 5.3. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%); $\lambda_{max.}$ 301 nm; $\nu_{max.}$ 1 660s and 1 604s cm^{-1}; δ 7.70 (2 H, d, *J* 9.3 Hz), 6.97 (2 H, d, 9.3 Hz), 6.59 (1 H, d, *J* 2.7 Hz), 6.23 (1 H, d, *J* 2.7 Hz), 3.86 (3 H, s), and 2.36 (3 H, s); *m/z* 216 (M^+), 188, and 173.

2-(p-*Methoxyphenyl*)-5,6-*dimethyl*-4H-*pyran*-4-*one* (**10**).—This was prepared from 1-(*p*-methoxyphenyl)-4-methylhexane-1,3,5-trione (100 mg) following the procedure described for (**9**). The product was purified by sublimation at 110 °C and 0.01 mmHg to give the *pyrone* (85 mg), m.p. 123—124 °C (Found: C, 73.05; H, 6.3. $C_{14}H_{14}O_3$ requires C, 73.03; H, 6.13%); $\lambda_{max.}$ 296 nm; $\nu_{max.}$ 1 650s and 1 605s cm^{-1}; δ 7.72 (2 H, d, *J* 9 Hz), 6.99 (2 H, d, *J* 9 Hz), 6.63 (1 H, s), 3.87 (3 H, s), 2.39 (3 H, s), and 2.00 (3 H, s); *m/z* 230 (M^+) and 187.

4-*Methoxy*-2-(p-*methoxyphenyl*)-6-*methylpyrylium Fluorosulphonate* (**11**).—Methyl fluorosulphonate (40 mg, 0.35 mmol) in dry chloroform (2 ml) was shaken with anhydrous potassium carbonate (100 mg) to remove traces of acid. The clear solution was added to 2-(*p*-methoxyphenyl)-6-methyl-4*H*-pyran-4-one (50 mg, 0.23 mmol) in dry chloroform (1 ml). After being stirred under nitrogen for 3 h the solution was cooled to 0 °C. The product was filtered off and washed with dry chloroform. The filtrate and washings were evaporated under reduced pressure, and the residue triturated with dry tetrahydrofuran–di-isopropyl ether. The resulting crystals were collected, washed with dry chloroform, combined with the first crop, and dried to give the *pyrylium salt* (72 mg), m.p. 128—129 °C; $\lambda_{max.}$ 251 and 362 nm; $\nu_{max.}$ (Nujol) 1 628m and 1 601m cm^{-1}; δ(CD_3CN) 8.19 (2 H, d, *J* 9 Hz), 7.69 (1 H, d, *J* 3 Hz), 7.20 (1 H, d, *J* 3 Hz), 7.18 (2 H, d, *J* 9 Hz), 4.29 (3 H, s), 3.93 (3 H, s), and 2.75 (3 H, s).

4-*Methoxy*-2-(p-*methoxyphenyl*)-5,6-*dimethylpyrylium Fluorosulphonate* (**12**).—This was prepared from 2-(*p*-methoxyphenyl)-5,6-dimethyl-4*H*-pyran-4-one (55 mg, 0.24 mmol) following the procedure described for (**11**) to give the *pyrylium salt* (64 mg). m.p. 151—152 °C; $\lambda_{max.}$ 263 and 362 nm; $\nu_{max.}$ (Nujol) 1 628m and 1 601m cm^{-1}; δ(CF_3CO_2H) 8.14 (2 H, d, *J* 9 Hz), 7.66 (1 H, s), 7.25 (2 H, d, *J* 9 Hz), 4.46 (3 H, s), 4.06 (3 H, s), 2.86 (3 H, s), and 2.35 (3 H, s).

4-*Methoxy*-6-(p-*methoxyphenyl*)*hexene*-2,6-*diones* (**13**) + (**15**).—4-Methoxy-2-(*p*-methoxyphenyl)-6-methylpyrylium fluorosulphonate (50 mg, 0.15 mmol) was dissolved in methanol (2 ml). Water (10 ml) and 2,6-lutidine (20 mg, 0.19 mmol) were added and the solution stirred for 8 h. Water (50 ml) was added and the solution extracted with diethyl ether (4 × 20 ml). The ether solution was dried, evaporated under reduced pressure, and the residue purified by p.l.c. on alumina with diethyl ether as eluant. Recovery from the band of R_F 0.9 gave a mixture of the *diones* as a colourless oil (31 mg, 83%); $\lambda_{max.}$ 284 nm; $\nu_{max.}$ 1 722m, 1 675m, 1 656m, 1 600s, 1 584s, and 1 169s cm^{-1}; δ (1st isomer, 40%) 7.95 (2 H, d, *J* 9 Hz), 6.90 (2 H, d, *J* 9 Hz), 5.46 (1 H, s), 4.38 (2 H, s), 3.90 (3 H, s), 3.85 (3 H, s), 2.18 (3 H, s), (2nd isomer, 60%) 7.87 (2 H, d, *J* 9 Hz), 6.90 (2 H, d, *J* 9 Hz), 6.28 (1 H, s), 3.85 (3 H, s), 3.81 (3 H, s), 3.70 (2 H, s), and 2.29 (3 H, s); *m/z* 248 (M^+), 205, and 135.

4-Methoxy-6-(p-methoxyphenyl)-3-methylhex-4-ene-2,6-dione (**14**).—This prepared from 4-methoxy-2-(*p*-methoxyphenyl)-5,6-dimethylpyrylium fluorosulphonate (50 mg, 0.15 mmol), and purified by p.l.c. following the procedure described for (**13**) + (**15**). Recovery from the band of R_F 0.8 gave the *dione* as a colourless oil (31 mg, 81%) which was homogeneous by t.l.c.; $\lambda_{max.}$ 301 nm; $\nu_{max.}$ 1 726m, 1 652m, 1 602s, 1 586s, and 1 171s cm^{-1}; δ 7.90 (2 H, d, *J* 9 Hz), 6.81 (2 H, d, *J* 9 Hz), 6.23 (1 H, s), 4.98 (1 H, q, *J* 7 Hz), 3.85 (3 H, s), 3.81 (3 H, s), 2.30 (3 H, s), and 1.29 (3 H, d, *J* 7 Hz); *m/z* 262 (M^+), 247, 219, and 135.

2-Ethoxycarbonylmethyl-6-(p-methoxyphenyl)-4H-pyran-4-one (**16**).—Trityl-lithium in tetrahydrofuran was injected into 2-(*p*-methoxyphenyl)-6-methyl-4*H*-pyran-4-one (44 mg, 0.20 mmol) in dry tetrahydrofuran (5 ml) under nitrogen at −30 °C until the red colour persisted. Ethyl chloroformate (150 mg, 1.38 mmol) was immediately injected and the reaction mixture stirred for 15 min at −30 °C. Glacial acetic acid was added until the solution was neutral to moist indicator paper. The solution was evaporated under reduced pressure, and the residue triturated with diethyl ether–acetone. The lithium acetate was filtered off and washed with diethyl ether. The filtrate and washings were evaporated under reduced pressure, and the residue purified by p.l.c. on silica gel with ethyl acetate. Recovery from the band of R_F 0.3—0.5 gave the *pyrone* as a colourless oil (37 mg, 63%) which was homogeneous by t.l.c. (Found: M^+, 288.1003. $C_{16}H_{16}O_5$ requires M^+, 288.0997); $\lambda_{max.}$ 307 nm; $\lambda_{max.}$ 1 736s, 1 659s, and 1 605s cm^{-1}; δ 7.68 (2 H, d, *J* 9 Hz), 6.95 (2 H, d, *J* 9 Hz), 6.61 (1 H, d, *J* 3 Hz), 6.25 (1 H, d, *J* 3 Hz), 4.23 (2 H, q, *J* 7 Hz), 3.84 (3 H, s), 3.60 (2 H, s), 1.29 (3 H, t, *J* 7 Hz); *m/z* 288 (M^+), 187, and 153.

2-Ethoxycarbonylmethyl-4-methoxy-6-(p-methoxyphenyl)-pyrylium Fluorosulphonate (**17**).—Methyl fluorosulphonate (20 mg, 0.18 mmol) in dry chloroform (1 ml) was shaken with anhydrous potassium carbonate (50 mg) to remove traces of acid. The clear solution was added to 2-ethoxycarbonylmethyl-6-(*p*-methoxyphenyl)-4*H*-pyran-4-one (30 mg, 0.10 mmol) and stirred under nitrogen at 40 °C until the u.v. spectrum showed the reaction to be complete. The solution was evaporated under reduced pressure and the residue triturated with diethyl ether–acetone. The crystals were collected, washed with a little acetone, then diethyl ether, and dried under reduced pressure to give the *pyrylium salt* (34 mg), which decomposed slowly above 60 °C; $\lambda_{max.}$ (MeOH) 253 and 367 nm; $\nu_{max.}$ (Nujol) 1 737m, 1 630m, and 1 600 cm^{-1}; δ(CF_3CO_2H) 8.07 (2 H, d, *J* 10 Hz), 7.57 (1 H, d, *J* 3 Hz), 7.27 (1 H, d, *J* 3 Hz), 7.17 (2 H, d, *J* 10 Hz), 4.35 (3 H, s), 4.35 (2 H, q, *J* 7 Hz), 4.20 (2 H, s), and 1.36 (3 H, t, *J* 7 Hz).

2-Ethoxycarbonylmethylene-4-methoxy-6-(p-methoxyphenyl)-2H-pyran (**18**).—Water (10 ml) and 2,6-lutidine (0.5 ml) were added to 2-ethoxycarbonylmethyl-4-methoxy-6-(*p*-methoxyphenyl)pyrylium fluorosulphonate (45 mg) in methanol (2 ml), and the solution was stirred for 3 h. Water (30 ml) was added and the solution extracted with diethyl ether (3 × 25 ml). The ethereal solution was dried, and evaporated under reduced pressure. The residue was purified by p.l.c. on alumina with diethyl ether. Recovery from the band of R_F 0.9 gave the *pyran* as a yellow oil (31 mg) which was homogeneous by t.l.c. (Found: M^+, 302.1163. $C_{17}H_{18}O_5$ requires M^+, 302.1154); $\lambda_{max.}$ 276, 310sh, 322, and 394 nm; $\nu_{max.}$ 1 665s, 1 544s, and 1 129s cm^{-1}; δ 7.58 (2 H, d, *J* 10 Hz), 7.10 (1 H, d, *J* 3 Hz), 6.87 (2 H, d, *J* 10 Hz), 6.00 (1 H, d, *J* 3 Hz), 5.11 (1 H, s, slowly exchanges with D_2O), 4.12 (2 H, q, *J* 8 Hz), 3.81 (6 H, s), and 1.27 (3 H, t, *J* 8 Hz); *m/z* 302 (M^+), 259, 185, and 135.

2-(p-Methoxyphenyl)-6-phenacyl-4H-pyran-4-one (**20**).—Trityl-lithium in tetrahydrofuran was injected into 2-(*p*-methoxyphenyl)-6-methyl-4*H*-pyran-4-one (46 mg, 0.21 mmol) at −15 °C until the red colour persisted. Benzoic anhydride (130 mg, 0.66 mmol) was injected, and after 3 min more trityl-lithium in tetrahydrofuran was added until the red colour reappeared. The solution was stirred at −15 °C for 10 min, then glacial acetic acid was added until the solution was neutral to moist indicator paper. The solution was evaporated under reduced pressure, and the residue dissolved in ethyl acetate (25 ml), which was shaken with saturated aqueous sodium hydrogen carbonate (3 × 20 ml). The organic layer was dried and evaporated under reduced pressure. The residue was purified on silica gel with ethyl acetate. Recovery from the band of R_F 0.3 gave an oil which crystallised from ethyl acetate to give the *pyrone* (45 mg), m.p. 200 °C (decomp.) which was homogeneous by t.l.c. (Found: M^+, 320.1058. $C_{20}H_{16}O_4$ requires M^+, 320.1048); $\lambda_{max.}$ 244 and 304 nm; $\nu_{max.}$ 1 690m, 1 661s, and 1 606s cm^{-1}; δ 8.03 (2 H, d, *J* 9 Hz), 7.8—7.4 (5 H, m), 6.93 (2 H, d, *J* 9 Hz), 6.61 (1 H, d, *J* 3 Hz), 6.29 (2 H, d, *J* 3 Hz), 4.36 (2 H, s), and 3.82 (3 H, s); *m/z* 320 (M^+), 216, 119, and 105.

4-Methoxy-6-(p-methoxyphenyl)-2-phenacylidene-2H-pyran (**21**).—(*a*) Diazomethane (large excess) in diethyl ether (10 ml) was added to 2-(*p*-methoxyphenyl)-6-phenacyl(4*H*-pyran-4-one (15 mg) in methanol (2 ml). After 2 h, excess of diazomethane was removed in a stream of nitrogen, and the solution evaporated under reduced pressure to give a yellow oil (16 mg, 100%), which was identical with the product of the following reaction.

(*b*) 2-(*p*-Methoxyphenyl)-6-phenacyl-4*H*-pyran-4-one (25 mg, 0.078 mmol), anhydrous potassium carbonate (40 mg), and dimethyl sulphate (40 mg, 0.32 mmol) were heated at reflux in dry acetone (2 ml) for 16 h. The solution was filtered and the residue purified by p.l.c. on alumina with ether. Recovery from the band of R_F 0.8—0.9 gave the *pyran* as a yellow oil which was homogeneous by t.l.c. (21 mg) (Found: M^+, 334.1196. $C_{21}H_{18}O_4$ requires M^+, 334.1205); $\lambda_{max.}$ 257, 294, and 430 nm; $\nu_{max.}$ 1 650s, 1 602s, and 1 483s cm^{-1}; δ 8.1—7.7 (2 H, m), 7.72 (2 H, d, *J* 9 Hz), 7.6—7.1 (3 H, m), 6.95 (2 H, d, *J* 9 Hz), 6.89 (1 H, d, *J* 3 Hz), 6.36 (1 H, s, slowly exch. with D_2O), 6.24 (1 H, d, *J* 3 Hz), 3.94 (3 H, s), and 3.85 (3 H, s); *m/z* 334 (M^+), 257, 165, 135, and 105.

2,4-Dimethoxy-6-methylpyrylium Fluorosulphonate (**25**).—Methyl fluorosulphonate (1 ml, 12 mmol) in dry chloroform (5 ml) was shaken with anhydrous potassium carbonate (1 g) to remove traces of acid. The clear solution was added to triacetic lactone methyl ether (1.4 g, 10 mmol) in dry chloroform (20 ml), and the resulting solution heated at reflux under nitrogen for 8 h. It was then concentrated under reduced pressure to one third its volume, and cooled to −15 °C. The product was filtered off, washed with cold chloroform and then pentane, and dried under reduced pressure to give the *pyrylium salt* (2.3 g), m.p. 87—89 °C (decomp.) (Found: C, 37.0; H, 4.3. $C_8H_{11}FO_6S$ requires C, 37.80; H, 4.36%); $\lambda_{max.}$ 258 nm; $\nu_{max.}$ (CH_3CN) 1 674s, 1 667s, 1 284s, and 1 256s cm^{-1}; δ(CD_3CN) 6.93 (1 H, d, *J* 3 Hz), 6.59 (1 H, d, *J* 3 Hz), 4.29 (3 H, s), 4.14 (3 H, s), and 2.58 (3 H, s).

Ethyl 2,4-Dimethoxy-6-methylbenzoate (**29**).—Oil-free sodium hydride (31 mg, 1.3 mmol) was added to ethyl dimethylphosphonoacetate (250 mg, 1.3 mmol) in dry tetrahydrofuran (20 ml) under nitrogen, and the solution stirred at 0 °C for 3 h in a flask sealed from the atmosphere. Powdered 2,4-dimethoxy-6-methylpyrylium fluorosulphonate (300 mg, 1.2 mmol) was added, followed, 2 h later, by oil-free sodium hydride (31 mg, 1.3 mmol). The solution was stirred at room

temperature for 18 h and then added to dilute sulphuric acid (2%; 200 ml). The aqueous solution was extracted with ethyl acetate (4 × 50 ml), and the combined organic layers were shaken with water (200 ml), dried, and evaporated under reduced pressure. The residue was purified by p.l.c. with diethyl ether as eluant. Recovery from the band of R_F 0.9 gave the ester as a colourless oil which was homogeneous by t.l.c. (172 mg) (Found: M^+, 224.1053. $C_{12}H_{16}O_4$ requires M^+, 224.1048); $\lambda_{max.}$ 249 and 282 nm; $\nu_{max.}$ 1 710s, 1 605s, 1 589s, 1 490m, 1 268s, 1 159s, 1 097s, and 1 049s cm^{-1}; δ 6.29 (2 H, s), 4.34 (2 H, q, *J* 7 Hz), 3.77 (6 H, s), 2.29 (3 H, s), and 1.35 (3 H, t, *J* 7 Hz); *m/z* 224 (M^+), 179, and 178.

Methyl 2,4-Dimethoxy-6-methylbenzoate.—This was prepared in essentially the same way as the ethyl ester above but on a larger scale using oil-free sodium hydride (1.2 g, 50 mmol) in dry tetrahydrofuran (150 ml) with methyl dimethylphosphonoacetate (3.8 g, 21 mmol), followed by addition of pyrylium salt (**25**) (5.08 g, 20 mmol). The product was distilled at 90—100 °C/0.01 mmHg, and was crystallised (2.03 g), m.p. 43 °C (lit.,[22] 44—45 °C); $\lambda_{max.}$ 282 nm; $\nu_{max.}$ 1 715s, 1 600s, and 1 500m cm^{-1}; δ 2.24 (3 H, s), 3.76 (6 H, s), 3.85 (3 H, s), and 6.29 (2 H, s); *m/z* 210 (M^+) and 179.

2,4-Dimethoxy-6-methylbenzoic Acid.—Ethyl 2,4-dimethoxy-6-methylbenzoate (29 mg) in aqueous sulphuric acid (70%; 5.6 ml) was stirred for 15 h and then poured into water (150 ml). The aqueous solution was extracted with ethyl acetate (3 × 50 ml) and the combined organic layers shaken with water (2 × 100 ml), dried, and evaporated under reduced pressure. Recrystallisation of the crude product from carbon tetrachloride gave the acid (18 mg), m.p. 146—147 °C (lit.,[23] 147 °C); $\lambda_{max.}$ 281 nm; $\nu_{max.}$ 2 964m, 1 721s, 1 320s, and 1 159s cm^{-1}; δ 6.38 (2 H, s), 3.92 (3 H, s), 3.80 (3 H, s), and 2.55 (3 H, s); *m/z* 196 (M^+), 179, and 178.

2,4-Dimethoxy-6-methylbiphenyl (**31**).—n-Butyl-lithium in hexane (15% w/w; 0.25 ml, 0.39 mmol) was injected into dimethyl benzylphosphonate (78 mg, 0.39 mmol) in dry tetrahydrofuran (5 ml) under nitrogen and the solution stirred for 30 min. Powdered 2,4-dimethoxy-6-methylpyrylium fluorosulphonate (95 mg, 0.37 mmol) was added, followed, after 3 h, by oil-free sodium hydride (10 mg, 0.42 mmol). The solution was stirred for 22 h and then poured into dilute sulphuric acid (2%; 25 ml). The aqueous solution was extracted with diethyl ether (3 × 10 ml) and the ethereal solution shaken with water (30 ml), dried over magnesium sulphate, and evaporated under reduced pressure. The residue was purified by p.l.c. with benzene as eluant. Recovery from the band of R_F 0.6 gave the product, which was further purified by sublimation at 120 °C and 0.02 mmHg, to give the *biphenyl* (40 mg), m.p. 71.5—72.5 °C (Found: C, 78.7; H, 7.2. $C_{15}H_{16}O_2$ requires C, 78.92; H, 7.06%); $\lambda_{max.}$ 245 and 282 nm; $\nu_{max.}$ 1 607s, 1 585m, 1 480m, and 1 156s cm^{-1}; δ 7.4—6.9 (5 H, m), 6.26 (2 H, s), 3.76 (3 H, s), 3.62 (3 H, s), and 2.02 (3 H, s); *m/z* 228 (M^+), 212, 197, 169, and 149.

6-(2,4-Dimethoxy-6-methylphenyl)-4-methoxy-2H-pyran-2-one (**34**).—Oil-free sodium hydride (5 mg, 0.21 mmol) was added to 6-(dimethylphosphonomethyl)-4-methoxy-2*H*-pyran-2-one (**33**)[16] (50 mg, 0.20 mmol) in dry tetrahydrofuran (15 ml). The solution was stirred under nitrogen for 30 min, and then powdered 2,4-dimethoxy-6-methylpyrylium fluorosulphonate (54 mg, 0.21 mmol) was added, followed, after 1 h, by oil-free sodium hydride (5 mg, 0.21 mmol). The solution was stirred for 13 h then added to dilute sulphuric acid (2%; 100 ml). The aqueous solution was extracted with ethyl acetate (3 × 50 ml), and the ethyl acetate solution shaken with water (100 ml), dried, and evaporated under reduced pressure. The residue was purified by p.l.c. with diethyl ether as eluant. Recovery from the band R_F 0.6 gave the product (23 mg), which was recrystallised from light petroleum (b.p. 60—80 °C) to give the *pyrone* as needles, m.p. 132—133 °C (Found: C, 65.1; H, 5.95. $C_{15}H_{16}O_5$ requires C, 65.21; H, 5.8%); $\lambda_{max.}$ 298 nm; $\nu_{max.}$ 1 709s, 1 647s, 1 609m, 1 571s, 1 492m, and 1 161s cm^{-1}; δ 6.36 (2 H, s), 5.99 (1 H, d, *J* 3 Hz), 5.50 (1 H, d, *J* 3 Hz), 3.85 (3 H, s), 3.81 (3 H, s), 3.76 (3 H, s), and 2.27 (3 H, s); *m/z* 276 (M^+), 248, and 205.

1-(2,4-Dimethoxy-6-methylphenyl)butane-1,3-dione (**36**).—Sodium ethoxide was prepared free of ethanol by treating sodium with an excess of ethanol and evaporating the solution to dryness under reduced pressure. The resultant solid was ground to a powder, and dried under high vacuum. A solution of 2,4-dimethoxy-6-methylacetophenone (**35**)[24] (1.49 g, 10 mmol) in dry ethyl acetate (5 ml) was injected into a sealed flask containing dry sodium ethoxide (2 g, 30 mmol). The mixture was stirred for 15 h at room temperature, and then poured into dilute sodium hydroxide (30 ml) and extracted with diethyl ether (2 × 20 ml). The ethereal extracts were re-extracted with dilute aqueous sodium hydroxide (15 ml). The combined aqueous extracts were acidified with hydrochloric acid (3 M) and extracted with diethyl ether (3 × 20 ml). The ethereal layers were dried over magnesium sulphate and evaporated to dryness to yield the butanedione (2.2 g), m.p. 77—78 °C (lit.,[17,25] 72—73 °C and 74—76 °C); spectral data were identical with those reported.[17]

5-(2,4-Dimethoxy-6-methylphenyl)-3,5-dioxopentanoic Acid (**37**).—n-Butyl-lithium (1.7 M in hexane; 11.2 ml, 19 mmol) was injected into a flask containing di-isopropylamine (2.02 g, 20 mmol) and dry tetrahydrofuran (25 ml), under an atmosphere of nitrogen, cooled to 0 °C. The solution was stirred for 20 min, and then a solution of 1-(2,4-dimethoxy-6-methylphenyl)-butane-1,3-dione (**36**) (1.88 g, 8 mmol) in dry tetrahydrofuran (15 ml) was injected. The mixture was stirred for 2 h, then solid carbon dioxide was added until the mixture had cooled to −78 °C. After warming to 0 °C it was poured onto a mixture of ice (40 g) and hydrochloric acid (5 ml; 10 M). The mixture was extracted with diethyl ether (3 × 5 ml) and then the combined ethereal extracts were extracted with sodium hydrogen carbonate (0.5 M; 3 × 15 ml). The alkaline solution was acidified and then extracted with diethyl ether (3 × 15 ml). The ethereal extracts were dried and evaporated to dryness under reduced pressure to give the diketo acid (**37**) (2.01 g) which was used in the next step without further purification; $\nu_{max.}$ 3 500—2 500, 1 625, 1 600, and 1 325 cm^{-1}; δ 6.33 (2 H, s), 5.85 (1 H, s), 3.80 (6 H, s), 3.47 (2 H, s), and 2.33 (3 H, s).

4-Methoxy-6-(2,4-dimethoxy-6-methylphenyl)-2H-pyran-2-one (**34**).—The foregoing acid (**37**) (2.0 g, 7.2 mmol) was dissolved in dry diethyl ether (12 ml), cooled to −15 °C, and trifluoroacetic anhydride (5 ml, 35 mmol) was added. The mixture was stirred for 1 h and then evaporated to dryness under reduced pressure. The residual solid was kept in contact with water overnight and then collected by filtration; it was washed with water and then diethyl ether to yield the hydroxypyrone (1.68 g), m.p. 197 °C, which was used in the next step without further purification; $\nu_{max.}$ (Nujol) 1 655, 1 630, 1 570, and 1 335 cm^{-1}; $\lambda_{max.}$ (MeOH) 293 nm; δ(CD_3COCD_3) 6.50 (2 H, s), 6.10 (1 H, d, *J* 2 Hz), 5.43 (1 H, d, *J* 2Hz), 3.83 (3 H, s), 3.78 (3 H, s), and 2.24 (3 H, s); *m/z* 262 (M^+, 1%), 244 (6%), 218 (84%), and 203 (100%). A mixture of the hydroxy pyrone (2.33 g, 8.9 mmol), dimethyl sulphate (1.17 g, 9.3 mmol), anhydrous potassium carbonate (3.7 g), and redistilled acetone (60 ml) was heated at reflux with stirring for 18 h, and then cooled, filtered, and washed with acetone. The combined filtrate and washings were evaporated to dryness to yield the methyl

ether (**34**) (2.45 g), which was identical with that prepared above, m.p. 132—133 °C.

2,4-*Dimethoxy*-6-(2,4-*dimethoxy*-6-*methylphenyl*)*pyrylium Fluorosulphonate* (**38**).—Methyl fluorosulphonate (0.3 ml) was added to the foregoing methoxypyrone (**34**) (55 mg, 0.2 mmol). As the solid pyrone dissolved it was replaced by crystals of the pyrylium salt. After 30 min the mixture was filtered and the crystals washed with hexane to yield the *pyrylium salt* (**38**) which was pure by n.m.r. (57 mg), m.p. 99—100 °C (decomp.); $\lambda_{max.}$ 262 and 348 nm; δ(CD_3CN) 7.12 (1 H, d, *J* 2 Hz), 6.70 (1 H, d, *J* 2 Hz), 6.53 (2 H, s), 4.27 (3 H, s), 4.20 (3 H, s), 3.84 (3 H, s), 3.80 (3 H, s), and 2.30 (3 H, s).

Methyl 4-*Methoxy*-6-(2,4-*dimethoxy*-6-*methylphenyl*)*pyran*-2-*ylidenedimethylphosphonoacetate* (**40**):—Sodium hydride (50% dispersion in oil, 38 mg, 0.79 mmol) was added to a solution of methyl dimethylphosphonoacetate (15 mg, 0.85 mmol) dissolved in dry tetrahydrofuran (12 ml) under nitrogen. After 30 min, the foregoing pyrylium salt (**38**) (137 mg, 0.35 mmol) was added. After being stirred overnight, the mixture was poured into sulphuric acid (1M; 25 ml) and extracted with ethyl acetate (3 × 10 ml); the combined extracts were washed with water, dried, and evaporated to dryness under reduced pressure. Purification by p.l.c. (ethyl acetate–acetone, 2:1, R_F 0.4) gave the *pyran* (**40**) as an oil which was homogeneous by t.l.c. (134 mg) (Found: M^+, 440.1252. $C_{20}H_{25}O_9P$ requires M^+, 440.1236); $\nu_{max.}$ 1 740, 1 655, 1 605, 1 325, 1 155, and 1 100 cm^{-1}; $\lambda_{max.}$ (MeOH) 247 and 280sh nm; δ (varied due to traces of acid in the solvent) 6.60 (1 H, t, *J* 2 Hz), 6.37 (2 H, ABq, *J* 2 Hz), 6.30 (1 H, d, *J* 2 Hz), 4.19 (1 H, d, J_{H-P} 24 Hz), 3.9—3.7 (18 H, m), and 2.23 (3 H, s); in trifluoroacetic acid the resonances at 6.60 and 6.30 shift to 7.55 p.p.m., and that at 4.19 shifts to 5.1 p.p.m.; *m/z* 440 (M^+), 426, 309, 289, 259, and 176.

2-(2,4-*Dimethoxy*-6-*methylphenyl*)-6-*methyl*-4H-*pyran*-4-*one* (**41**).—(*a*) *From the pyran* (**40**). Sodium hydride (50% dispersion in oil; 100 mg, 2 mmol) was added to a solution of the pyran (**40**) (140 mg, 0.32 mmol) in dry methanol (5 ml). After being heated at reflux with the exclusion of moisture during 30 h, the mixture was added to sulphuric acid (2%, 40 ml) and then extracted with ethyl acetate (4 × 15 ml). The organic extracts were washed with water, dried, and evaporated under reduced pressure. The residue was purified by p.l.c. (ethyl acetate) to give the *pyrone* (R_F 0.4) (19 mg), m.p. 118—120 °C (Found: M^+, 260.1050. $C_{15}H_{16}O_4$ requires M^+, 260.1049); $\nu_{max.}$ 1 660, 1 605, 1 155, and 1 100 cm^{-1}; $\lambda_{max.}$ 242, 278sh, and 295sh nm; δ 6.38 (2 H, ABq, *J* 2 Hz), 6.27 (1 H, d, *J* 2 Hz), 6.17 (1 H, d, *J* 2 Hz), 3.84 (3 H, s), 3.78 (3 H, s), 2.30 (3 H, s), and 2.25 (3 H, s); *m/z* 260 (M^+), 232, 189, and 176 (100%).

(*b*) *From* (**42**). n-Butyl-lithium (1.7M in hexane; 1.2 ml, 2.04 mmol) was injected slowly into a solution of 2-bromo-3,5-dimethoxytoluene[18] (462 mg, 2 mmol) in dry diethyl ether (4 ml) which was maintained under an atmosphere of nitrogen at −15 °C. After 30 min the methyl ether of triacetic lactone (**24**) (280 mg, 2 mmol) was added, and the mixture was stirred for a further 60 min under the protective atmosphere at −15 °C. Hydrochloric acid (12 M; 10 ml) was then added and the mixture kept overnight. It was then neutralised with aqueous sodium hydrogen carbonate solution (1M) and extracted with ethyl acetate (3 × 15 ml). The combined organic extracts were washed with water, dried, and evaporated under reduced pressure. The residue was purified by chromatography on a column of silica gel (20 g), with ethyl acetate as eluant. The following compounds were obtained in this order: 3,5-dimethoxytoluene (190 mg), triacetic lactone methyl ether (30 mg), and the pyran-4-one (**41**) (111 mg). The latter product was identical with the pyrone produced in the previous experiment.

2,4-*Dimethoxy*-6-*phenylpyrylium Fluorosulphonate* (**43**).—A solution of methyl fluorosulphonate (1 ml, 12 mmol) in chloroform (5 ml) was shaken with anhydrous potassium carbonate (1 g), and then half was removed and added to a solution of 4-methoxy-6-phenyl-2*H*-pyran-2-one[26] (1.03 g, 5 mmol) in chloroform (11 ml). The mixture was heated at reflux under nitrogen for 3 h and then cooled to −15 °C, filtered, washed with cold chloroform, and dried *in vacuo* to yield the *pyrylium salt* (**43**), which was pure by n.m.r. (1.37 g); $\nu_{max.}$ (Nujol) 1 650, 1 540, 1 505m, and 1 414m cm^{-1}; δ(CD_3CN) 7.8—7.7 (2 H, m), 7.45 (1 H, d, *J* 2.5 Hz), 7.25 (3 H, m), 6.50 (1 H, d, *J* 2.5 Hz), 4.35 (3 H, s), and 4.15 (3 H, s).

2-*Methoxycarbonyl*-3,5-*dimethoxybiphenyl* (**44**).—Sodium hydride (50% dispersion in oil, 440 mg, 9.0 mmol) was added to a solution of methyl dimethylphosphonoacetate (1.65 g, 9.07 mmol) in dry tetrahydrofuran (50 ml). The mixture was stirred for 30 min under an atmosphere of dry nitrogen, and then 2,4-dimethoxy-6-phenylpyrylium fluorosulphonate (**43**) (1.37 g, 4.3 mmol) was added. After being stirred for a further 16 h under a nitrogen atmosphere, the mixture was poured into aqueous sulphuric acid (2%, 50 ml), and extracted with ethyl acetate (4 × 25 ml). The organic layers were washed with water, dried, and evaporated to dryness under reduced pressure. The residual oil was purified by chromatography (silica gel) eluting first with light petroleum (b.p. 60—80 °C). Further elution with ethyl acetate–benzene (1:1) yielded an oil which was purified by distillation to give the *biphenyl* (**44**) as an oil (0.76 g), b.p. 130 °C/0.01 mmHg (Found: C, 70.60; H, 6.15. $C_{16}H_{16}O_4$ requires C, 70.58; H, 5.92%); $\lambda_{max.}$ 287 nm; $\nu_{max.}$ (CCl_4) 2 940w, 1 730, 1 600br, 1 350m, and 1 340m cm^{-1}; δ(CCl_4) 7.29 (5 H, s), 6.37 (2 H, s), 3.81 (3 H, s), 3.78 (3 H, s), and 3.46 (3 H, s); *m/z* 272 (M^+) and 241.

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