Reactions of fused and unfused α-pyrones with magnesium alkoxide, sodium alkoxide and water as the nucleophile: effects of chelation

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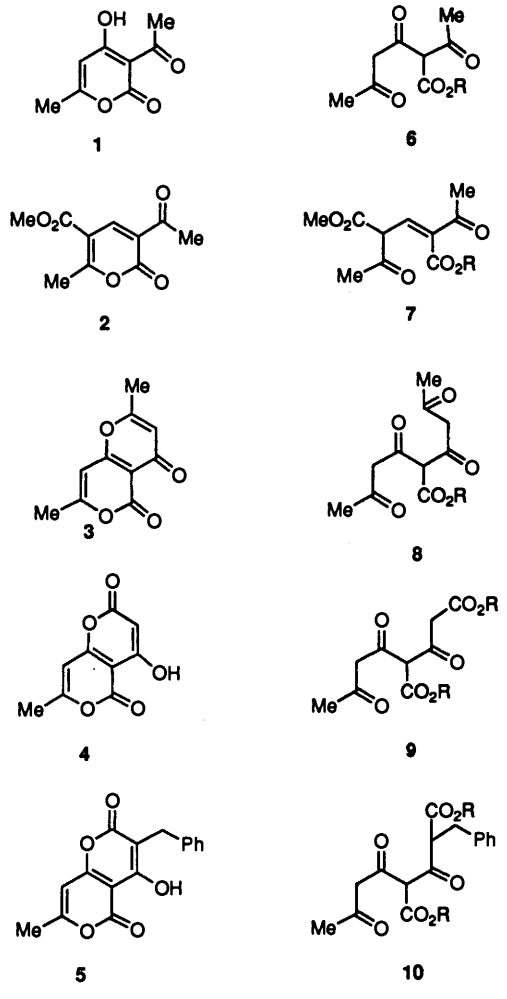
The reactions between a series of α-pyrones (two mono- and three fused) and the non-chelating base sodium alkoxide, the chelating base magnesium alkoxide and water as the nucleophile, have been studied. Aromatic and other products formed reflect the points of attack on the pyrone systems and when sodium methoxide is used the ensuing cyclisation is preferentially by aldol mechanisms. The employment of excess magnesium methoxide or ethoxide gives magnesium-chelated precursors and the nature of products now depends on these intermediates, and the protection afforded by such magnesium chelation to the reaction products. In the case of structures containing chelated β-keto ester features the chelates are screened from attack as aldol acceptors, but are effective Claisen acceptors. In such chelates an adjacent methylene is activated by further magnesium alkoxide to act as an aldol or Claisen donor. These contrasting aldol/ Claisen reactivities, as between a non-chelating and a chelating base, are illustrated in the ensuing chemistry of the pyrones. Treatment with water releases the main carbon chain with decarboxylation, from which new products may form.

Pyrone systems have long been of interest in connection with their relationship to poly-β-ketides which form the structural basis for a large class of natural compounds.[1,2] However, pyrones are not necessarily satisfactory surrogates for poly-β-ketides as they are a source of in-chain pendant carboxylate, as well as terminal carboxylate or acetyl groupings. Such pendants, forming β-keto ester units, are capable of magnesium chelation[3–6] thereby reshaping the geometry of the chain as well as altering its chemical reactivity: it is this area which is of interest in the present paper. In our earlier work we have found that magnesium chelation provides new chemical opportunities and can stabilise products, and that reactions customarily studied using sodium alkoxide as the base may follow a different course when magnesium alkoxide is used. In the present work we report a study of the products, many aromatic, arising from treatment of five pyrones **1–5** with excess (*e.g.* >4 mol equiv.) sodium alkoxide and with excess (*e.g.* >4 mol equiv.) magnesium alkoxide. In addition we report results using hot water as the nucleophile. The pyrones selected for study are shown, along with their reactive formal hydrolysis or alcoholysis products **6–10** (R = H or alkyl).



Pyrones and hydrolysed 'equivalents' studied

Dehydroacetic acid 1

Treatment of dehydroacetic acid **1** with refluxing magnesium ethoxide (10 mol equiv.) in ethanol gave ethyl triacetate[7] **11** (R = Et) (82% yield), formed by ring ethanolysis and deacylation of **6** (R = Et). In a similar way, as reported by Batelaan,[8] methyl triacetate **11** (R = Me) is obtained using magnesium methoxide in methanol. On the other hand, refluxing sodium methoxide (10 mol equiv.) in methanol under similar conditions gave only a rather low yield of methyl triacetate (18%) along with some triacetic lactone **12** (7%) and methyl acetoacetate **13** (16%). In this case deacylation is accompanied by substantial retro-Claisen chain degradation. It is suggested that in the magnesium methoxide example a chelate, probably having the α-pyrone already methanolised,[8] is formed and deacylated. The alkyl triacetate produced can be held in unreactive form as a chelate **14** greatly enhancing the yield. Trione **15** provides an analogous case of unreactivity towards excess magnesium methoxide. Although formally capable of aldol cyclisation, if

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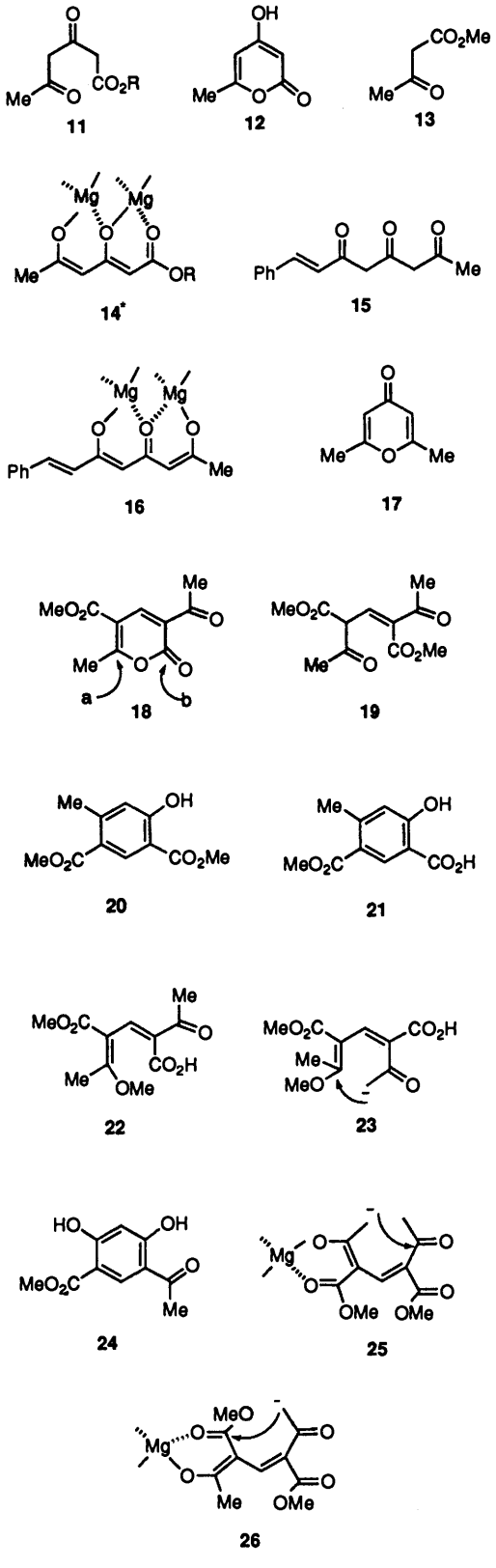


* Unmarked magnesium ligands are OMe and MeOH throughout

refluxed for 24 h with the magnesium reagent in methanol it is recovered quantitatively unchanged. The functionality is presumed to be screened towards further alkoxide attack as in **16**. Collie's classic experiment,[1] heating dehydroacetic acid with syrupy caustic soda to form orcinol, involves of course basic conditions much more drastic than those considered here.

Dehydroacetic acid is fairly resistant to boiling with water for shorter periods but prolonged treatment (60 h) gives 2,6-dimethyl-4-pyrone **17** (78% yield) showing that opening of the 2-pyrone and decarboxylation has occurred, with the trione becoming stabilised as the 4-pyrone under neutral conditions.

3-Acetyl-5-methoxycarbonyl-6-methylpyrone 18 (= 2)

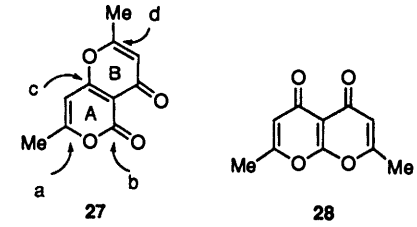
This pyrone was studied in our earlier work[9] and can be made by treating the tautomeric glutaconic ester **19** with sodium methoxide. Treatment with a larger excess of sodium methoxide (12 mol) gives, in 61% yield, a mixture of the *o*-hydroxy ester **20** and its acid **21**.[9] The origins of the former are ascribed to the aldol cyclisation of the geometrically labile glutaconate **19** equilibrating with the pyrone. There are two points of interest for nucleophilic attack by methoxide ion on pyrone **18**, one 'b' leading back to **19** and hence to **20**, the other 'a' to the carboxylic acid **22** which can, by Michael condensation **23**, lead to the half ester **21**. By contrast, when treated with excess magnesium methoxide (4 mol equiv.) the pyrone–glutaconate system **18–19** gives a mixture of the isophthalate aldol product **20** (75%) and the resorcinol Claisen product **24** (25%).[9] None of the latter is formed in the sodium methoxide reaction and neither appears until >1 mol equiv. of magnesium methoxide is present, confirming that the first mol equiv. is used for chelate complexing. Two pathways leading to aromatic products are now open. The complexed glutaconate is capable of aldol condensation to give **20** *via* **25**. On the other hand, the alternative anion **26** undergoes Claisen condensation to give **24**, with the chelate system providing screening against an aldol acceptor reaction. Both are in evidence.

The α,γ-bispyrone 27 (= 3)

The bispyrone was made by Praill's method.[10] Treatment of dehydroacetic acid with perchloric acid in acetic acid gives the perchlorate of a bis-γ-pyrone **28** which rearranges to the required α,γ-bispyrone **27** on treatment with potassium acetate. When refluxed with sodium methoxide (10 mol equiv.) in methanol for 18 h, the α,γ-bispyrone gave the aliphatic cleavage product methyl triacetate **11** (R = Me) as the major product (52% yield), together with further degradation products. This is consistent with opening of the A-ring at 'b' and the B-ring at 'd' followed by retro-Claisen degradation as indicated in **29**. There was very little cyclised material though two minor resorcinol-based aromatic products were also isolated and are of some interest. These were resorcylic ester **30** (2%) and its acetyl relative **31** (1%) and their formation can be explained as follows. Attack by methoxide ion at 'b' and 'c' in **27** leads to **32** which by aldol condensation between 'e' and 'f' gives **31**, whilst **30** is its deacylation product. A specimen of the latter was synthesised for comparison (see Experimental section).

On the other hand the products isolated from refluxing the α,γ-bispyrone **27** with excess magnesium methoxide were all aromatic—the acetylresorcinol **33** (23%) and the three minor products **34** (3%), **35** (2%) and **31** (3%), all based on a resorcinol pattern of oxygenation. The chain cleavage reaction product **11** (R = Me) is not now in evidence, the major product **33** being the decarboxylation product of **34** which itself originates from methoxide attack at 'b' and 'd' of **27**. There are three possible monochelation sites in **29**, and **36** is an attractive candidate for cyclisation *via* Michael reaction, followed by aromatisation, though the bis-chelate **37** is also a possibility. Such chelated species protect the chain from cleavage in the sense **29** and account for the absence of methyl triacetate among the products. As indicated above, **31** probably originates from the 'b'–'c' cleavage forming **32** which cyclises to give **31** and its acid **35**. The latter on treatment with diazomethane gives **31**.

Refluxing the α,γ-bispyrone **27** with water for 50 h gave 2-acetyl-3,5-dihydroxytoluene **33** in a clean reaction in 62% yield. Such treatment of the bispyrone would be expected to release, by nucleophilic attack by water at 'b' and 'd' in **27**, the easily decarboxylated chain **38**, cyclised by aldol condensation and aromatisation to give **33**.



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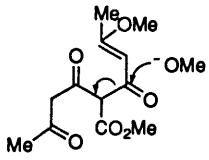

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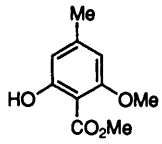

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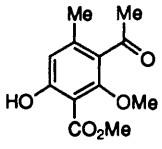

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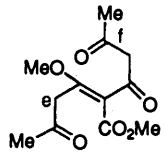

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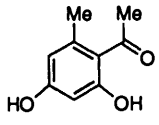

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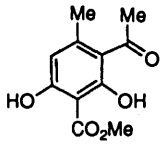

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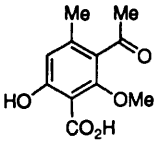

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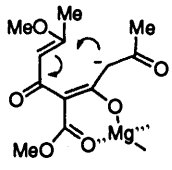

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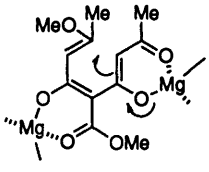

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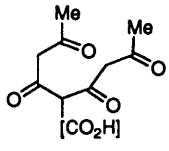

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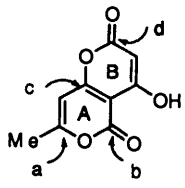

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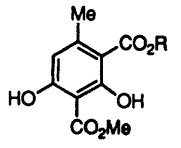

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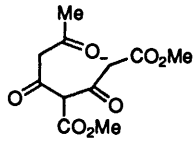

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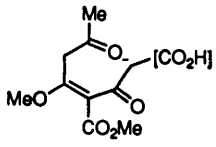

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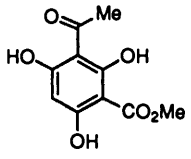

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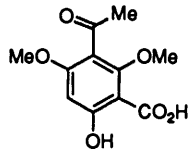

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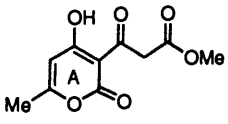

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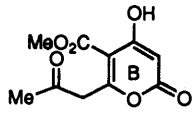

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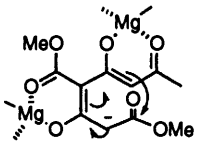

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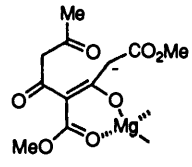

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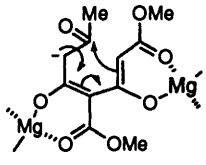


48a

The α,α′-bispyrone 39 (= 4)

The bispyrone was made from triacetic lactone and malonyl dichloride in the presence of trifluoroacetic acid, according to the method of Money *et al.*[11] When treated with sodium methoxide (10 mol) under reflux, the main product was the resorcylic diester **40** (R = Me) (46%), together with the resorcylic methoxy ester **30** (8%). The first of these is the product of attack at the carbonyl positions 'b' and 'd' of the bispyrone **39**. Such attack leads to the carbon chain **41** which undergoes aldol cyclisation and aromatisation to give **40** (R = Me). On the other hand attack at 'b' and 'c' in **39** leads to chain **42**. Decarboxylation of the latter, together with aldol cyclisation and aromatisation accounts for **30**. The aldol cyclisations as indicated in **41** and **42** are clearly more rapid than the chain degradation process analogous to **29**, no methyl triacetate being observed. Money *et al.* and Scott *et al.*[11,12] report that treatment of **39** with aqueous or alcoholic potassium hydroxide, also gives, by aldol condensation, resorcinol derivatives similar to those obtained by us with sodium methoxide in methanol.

By contrast with sodium methoxide, treatment of the α,α′-bispyrone **39** with refluxing magnesium methoxide (10 mol) gives, as the major product (55%), the Claisen-derived phloroglucinol ester **43** (also obtained by Douglas and Money[12d] in a similar experiment, though the amount of reagent used is not stated). We additionally found the resorcinol dicarboxylic ester **40** (R = Me) (21%) identical with that obtained from the methanolic sodium methoxide treatment above together with a trace of the phloroglucinol carboxylic acid **44**. Interestingly, if the amount of magnesium methoxide was reduced (2.66 mol equiv.), a new compound identified as the α-pyrone **45** was additionally obtained in 44% yield whilst the erstwhile major product **43** declined to 41%. The α-pyrone **45**, probably stabilised as a bis-chelate prior to work-up, is formed by methanolysis of ring B at 'd' and is clearly different from the isomeric A-ring-cleaved (at 'b') α-pyrone **46** obtained by Scott *et al.*[12e] by hydrolysis of **39** with 2 M aqueous potassium hydroxide, followed by esterification. As expected, treatment of α-pyrone **45** with 10 mol equiv. of magnesium methoxide gave methyl 2,4,6-trihydroxy-3-acetylbenzoate **43** and 2,4-dimethoxycarbonyl-

3,5-dihydroxytoluene **40** (R = Me). As in the sodium methoxide case, magnesium methoxide attack on the bispyrone **39** is assumed to give the same formal chain **41** but this is now in magnesium complexed form. Structure **47** is a possible intermediate to give the major product **43** by Claisen condensation. A mono-complex **48** of chain **41**, or a bis-complex **48a**, might account for **40** (R = Me), the acetyl group not now being protected as a carbonyl acceptor by chelation. On boiling with water for 3 h the B-ring of the bispyrone **39** was opened with decarboxylation, and dehydroacetic acid **1** (see above) was isolated in 96% yield.

The benzyl substituted bispyrone 49 (= 5)

This bispyrone was made by the method of Ziegler and Junek[13] in which triacetic lactone and bis(2,4-dichlorophenyl) benzylmalonate are heated at 250 °C and the product is crystallised from nitrobenzene. When treated with sodium ethoxide (10 mol), the A-ring lactone was ethanolysed giving the pyrone **50** (R = Et) in 96% yield. It is the A-ring that is hydrolysed by methanolic potassium hydroxide in the case of bispyrone **39**[12e] and the preference seems accentuated in this alkoxide reaction by steric effects from the benzyl substituent.

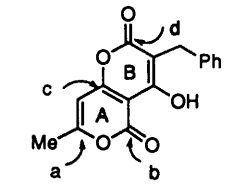
Refluxing bispyrone **49** with 1 mol equiv. of magnesium ethoxide in ethanol caused no observable change, but with 2 mol equiv., four new products were observed and after refluxing with 10 mol equiv. of magnesium ethoxide these four products were isolated in a total yield of 44%. They included the pyrone **50** (R = H) (22%) and the ester of its retro-Claisen companion **51** (R = Et) (3%). On treatment with acetic anhydride and pyridine the carboxylate **50** (R = H) recyclised to give **52**, the acetate of **49**. It is clear that with both sodium and magnesium alkoxides the benzyl substituent exerts a considerable steric screening effect on the B-ring during ethanolysis of the bispyrone **49**. Claisen products **53** (13%) and **54** (6%) however show that ethanolysis of both rings does occur, releasing a full chain which is probably magnesium complexed. The deacylated phloroglucinol **54** is deacylated before aromatic cyclisation since it was not formed by refluxing **53** with excess magnesium ethoxide. A benzyl hindered bis-chelate **55** may be involved as in the case of **47** where an α-anion is formed. Alternatively, ionisation of the chelate ring as in **56** (known to occur from deuteriation experiments[6]) could initiate the aromatisation process. No aldol material was found.

Nucleophilic attack by water on the bispyrone **49** required sterner conditions than mere refluxing. It was therefore autoclaved with water at 250 °C. Two products were formed. One was the resorcinol **57** (35%), the other benzylacetone **58** (60%). Clearly under these conditions the hydroloysed chain (attack at 'b' and 'd' in **49**) is released and decarboxylated. The decarboxylated chain undergoes aldol cyclisation giving **57** or alternatively the chain is degraded by retro-Claisen reaction to give benzylacetone **58** and acetoacetic acid which decarboxylates to acetone (see **59**).

The reaction of the styrylpyrone **60** with magnesium methoxide in methanol was also examined during the investigation. Despite the apparent potential reactivity of the system, refluxing with the reagent for 24 h merely methanolysed the pyrone ring and the triketo ester **61** was isolated in 93% yield. It is presumed that the product is held in the protected magnesium bis-chelate form **62** until work up. Although theoretically capable of anion formation at the terminal methyl group,[14] the complex is geometrically unsuitable for cyclisation.

Conclusion

This investigation, using a series of pyrones, provides examples further to those derived from xanthophanic–glaucophanic enol chemistry, and turns on contrasts and comparisons between the action of magnesium alkoxide, sodium alkoxide and water. Magnesium chelation of β-keto ester or β-diketone systems provides geometrical constraints on initial or intermediate



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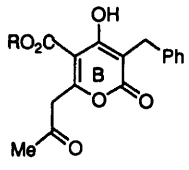

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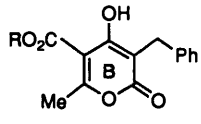

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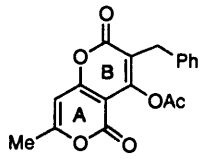

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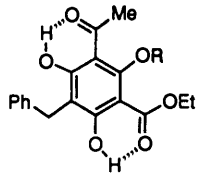

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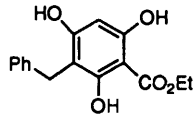

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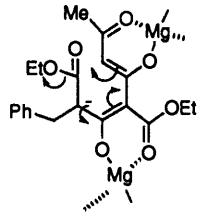

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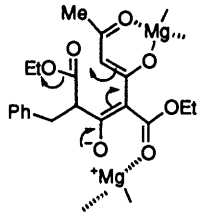

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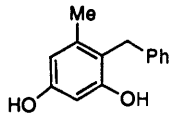

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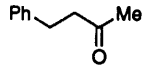

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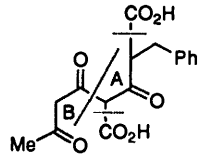

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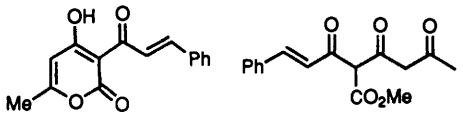
structures, as well as altering reactivities. Such chelation can stabilise final structures by their protective action, or through precipitation from solution, and on occasion a previously unrecognised kinetic product may be sequestered as a magnesium chelate[6] and hence isolated. A chelated β-keto ester system is protected in an aldol electron acceptor situation, where there is reversibility, but is effective in corresponding Claisen reactions where there is a displacement reaction. An anion formed adjacent to the chelate ring however, is effective in initiating both aldol and Claisen condensations of other unchelated groups, and aromatisation is a frequent driving force impelling the reaction forward.

Experimental

Melting points were determined using an electrically heated block apparatus. Ultraviolet spectroscopic data were obtained in ethanol using a Unicam SP800 spectrophotometer and infrared data on a Unicam SP 200G instrument in chloroform or as



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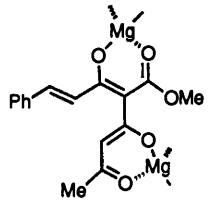

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a mull. Routine NMR spectra were determined at 60 or 100 MHz in deuteriochloroform: exchangeable hydrogens were located by D_2O shake. *J* Values are given in Hz. Evaporation signifies evaporation under reduced pressure. Light petroleum refers to the fraction with bp 60–80 °C.

Treatment of dehydroacetic acid 1 (1 mol equiv.) with magnesium ethoxide (10 mol equiv.)

Dehydroacetic acid (3-acetyl-4-hydroxy-6-methyl-2-pyrone) **1** (0.336 g) in benzene (20 cm^3) was refluxed for 18 h with magnesium ethoxide solution prepared from magnesium (0.486 g) and ethanol (40 cm^3). After cooling, water (40 cm^3) was added and the mixture was acidified with 4 M hydrochloric acid and extracted with benzene. After washing with water and drying (Na_2SO_4) the benzene layer was evaporated to yield ethyl triacetate **11** (ethyl 3,5-dioxohexanoate) (R = Et) (0.280 g, 82%), bp 70–75 °C (bath)/0.1 mmHg (lit.,[7] 130–140 °C/20 mmHg), n_D^{18} 1.4695 (Found: C, 55.85; H, 7.15%; M^+, 172. Calc. for $C_8H_{12}O_4$: C, 55.8; H, 7.05%; *M*, 172); $\nu_{max}(CHCl_3)/cm^{-1}$ 1743 (ester carbonyl), 1620 (chelated carbonyl); λ_{max}(0.01 M ethanolic KOH)/nm 288 (ε/dm^3 mol^{-1} cm^{-1} 10 550); λ_{max}(0.02 M ethanolic H_2SO_4)/nm 273 (ε 4150); $\delta_H(CCl_4)$ 1.28 (3 H, t, *J* 7, *Me*CH_2O), 2.05 (3 H, s, MeCO), 3.24 (2 H, s, CH_2), 4.16 (2 H, q, *J* 7, MeCH_2), 5.58 (1 H, s, =CH). The compound, which gave a dark red ferric chloride reaction, was identical with an authentic specimen made by heating triacetic lactone (4-hydroxy-6-methyl-2-pyrone) **12** in ethanol in a sealed tube for 48 h at 110 °C. The blue copper chelate was made by adding the ester (35 mg) in ethanol (250 mm^3) to copper(II) acetate (20 mg) in ethanol (500 mm^3) containing one drop of ammonia (*d* 0.880). It had mp 181–183 °C (decomp.) (lit.,[7] 183–184 °C).

Treatment of dehydroacetic acid 1 (1 mol equiv.) with magnesium methoxide (10 mol equiv.)

Dehydroacetic acid (3.36 g) in benzene (200 cm^3) was refluxed for 18 h with magnesium methoxide solution prepared from magnesium (4.86 g) and methanol (400 cm^3). Work up as above gave methyl triacetate **11** (R = Me) (2.01 g, 64%), bp 62–64 °C/0.1 mmHg, n_D^{18} 1.4740 (Found: C, 53.05; H, 6.2%; M^+, 158. Calc. for $C_7H_{10}O_4$: C, 53.15; H, 6.35%; *M*, 158). The parent M^+ was obtained using an inlet temperature of 130 °C: at inlet temperatures of 210 °C and 160 °C a molecular ion of *m/z* 280 was measured indicating dimerisation and elimination of two molecules of water. ν_{max}(film)/cm^{-1} 1743 (ester), 1615 (chelated carbonyl); $\delta_H(CCl_4)$ 2.05 (3 H, s, CH_3CO), 3.25 (2 H, s, CH_2), 3.68 (3 H, s, ester Me), 5.56 (1 H, s, =CH), 14.58 (1 H, br s, chelated OH). Blue copper(II) chelate mp 200 °C (decomp.). When warmed at 80 °C with a little conc. sulfuric acid, and then diluted with water, triacetic lactone **12**, mp and mixed mp 189–190 °C, was obtained.

At a magnesium methoxide:substrate ratio of 0.5:1 no methyl triacetate formed and only unchanged starting material was recovered. At a 1:1 ratio both dehydroacetic acid and methyl triacetate were present. At ratios between 2:1 and 10:1 only methyl triacetate could be detected by TLC and IR.

Treatment of dehydroacetic acid 1 (1 mol equiv.) with sodium methoxide (10 mol equiv.)

Dehydroacetic acid (3.36 g) in benzene (200 cm^3) was refluxed for 18 h with sodium methoxide solution prepared from sodium (4.6 g) and methanol (400 cm^3). The product was cooled and water and 4 M hydrochloric acid were added. Extraction with benzene, followed by drying (Na_2SO_4) and evaporation gave a pale yellow liquid (940 mg) which was shown to be a mixture of methyl acetoacetate and methyl triacetate and estimated quantitatively by NMR. Further extraction of the aqueous layer gave a solid, shown to be triacetic lactone **12** (0.17 g). The methyl acetoacetate and methyl triacetate were separated by fractional distillation. Methyl acetoacetate (376 mg, 16%) had bp 50 °C/7.5 mmHg, n_D^{16} 1.4208 (lit.,[15] 73–74 °C/12 mmHg, n_D^{19} 1.4190). It was spectroscopically identical with authentic material and gave a 2,4-dinitrophenylhydrazone, mp 119–200 °C (lit.,[15] 119 °C). Methyl triacetate (564 mg, 18%) had bp 111 °C/7.5 mmHg, n_D^{16} 1.4718 and was identical with an authentic specimen (TLC, IR, UV and NMR). It formed a copper(II) chelate, mp and mixed mp with an authentic specimen 200 °C (decomp.).

Triacetic lactone **12** (170 mg, 7%) was recrystallised from methanol–benzene to give prismatic crystals, mp and mixed mp with an authentic specimen 186–188 °C (lit.,[16] 186–187 °C) (Found: C, 56.85; H, 4.75%; M^+, 126. Calc. for $C_6H_6O_3$: C, 57.15; H, 4.8%; *M*, 126); $\nu_{max}(CHCl_3)/cm^{-1}$ 1705 (2-pyrone carbonyl), 1650, 1580; λ_{max}(EtOH)/nm 207 (ε/dm^3 mol^{-1} cm^{-1} 10 950), 284 (6850); $\delta_H([^2H_6]DMSO)$ 2.08 (3 H, s, Me), 5.70 (1 H, s, =CH at C-3), 6.04 (1 H, s, =CH at C-5), 11.87 (1 H, s, OH). It gave no colouration with neutral ethanolic ferric chloride.

As judged by TLC and NMR, methyl acetoacetate, methyl triacetate and triacetic lactone were not formed until the molar ratio of sodium methoxide to dehydroacetic exceeded 1:1. At a 2:1 ratio all three were present, and so also was some unchanged dehydroacetic acid. At ratios of 4:1 to 10:1 the latter had disappeared.

Treatment of dehydroacetic acid 1 with boiling water

Dehydroacetic acid (500 mg) was refluxed with water (25 cm^3) for 12 h. It was mainly recovered unchanged mp 105 °C by benzene extraction. However, longer reflux (60 h) yielded 2,6-dimethyl-4-pyrone **17** (78%).

The Praill α,γ-bispyrone (2,7-dimethyl-4,5-dioxo-4-*H*,5*H*-pyrano[4,3-*b*]pyran)

Dehydroacetic acid (8.4 g) in acetic anhydride (50 cm^3) was slowly added to an ice-cold solution of perchloric acid (72%; 6.9 g) in acetic anhydride (50 cm^3) and the orange solution was stirred for 5 h at 0 °C. (**WARNING**: Although we have experienced no difficulties with this preparation, perchloric acid and perchlorates are explosive and dangerous materials.) The solution was kept overnight at 0 °C when the pale yellow crystals (8.5 g), mp 220 °C (lit.,[10] 223 °C), were filtered off. They are reported to be the perchlorate of bis-pyrone **28**. The perchlorate (9 g) was treated with potassium acetate (3 g) in ethanol (30 cm^3) at 70 °C for 10 min and the potassium perchlorate was filtered off before cooling. The required Praill bispyrone **27** (3 g) then crystallised, and was recrystallised from ethanol as pale orange needles, mp 180 °C (lit.,[10] 183–184 °C) (Found: C, 62.6; H, 4.1%; M^+, 192. Calc. for $C_{10}H_8O_4$: C, 62.5; H, 4.2%; *M*, 192); $\nu_{max}(CHCl_3)/cm^{-1}$ 1762 (2-pyrone carbonyl), 1675 (4-pyrone carbonyl), 1642, 1565; λ_{max}(EtOH)/nm 239 (ε/dm^3 mol^{-1} cm^{-1} 15 350), 298 (8450); $\delta_H(CDCl_3)$ 2.35 (6 H, s, 2 × pyrone Me), 6.18, 6.24 (2 H, s, 2 × pyrone =CH). The compound gave no colour with ferric chloride.

Treatment of the Praill α,γ-bispyrone 27 (1 mol equiv.) with magnesium methoxide (10 mol equiv.)

The bispyrone (3.84 g) in benzene (50 cm^3) and methanol (50 cm^3) was refluxed for 18 h with magnesium methoxide solution

prepared from magnesium (4.86 g) and methanol (400 cm^3). It was cooled, diluted with water (0.5 dm^3), acidified with 4 M hydrochloric acid, and extracted with benzene. The benzene extracts were washed, dried (Na_2SO_4) and evaporated to give a yellow oil (2.95 g) which partially crystallised. The pale yellow crystals (D) were filtered off (a previous experiment showed that this was difficult to isolate by column chromatography). The filtered oil was chromatographed on silica gel and elution with benzene gave compound (A), elution with benzene–chloroform (B) and elution with chloroform (C). Final elution with chloroform–methanol gave only gummy material.

Compound A was *methyl 2-hydroxy-4-methyl-6-methoxybenzoate* **30** (116 mg, 3%), mp 94–95 °C from light petroleum (Found: C, 61.35; H, 6.35%; M^+, 196. $C_{10}H_{12}O_4$ requires C, 61.2; H, 6.2%; *M*, 196); $\nu_{max}(CHCl_3)/cm^{-1}$ 1658 (chelated ester carbonyl), 1625, 1580; λ_{max}(EtOH)/nm 216 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 17 000), 258 (10 200), 314 (3100); $\delta_H(CDCl_3)$ 2.26 (3 H, s, aromatic Me), 3.80 (3 H, s, MeO), 3.89 (3 H, s, MeO), 6.20 (1 H, s, aryl H), 6.40 (1 H, s, aryl H), 11.48 (1 H, s, OH). As expected the compound did not react with diazomethane but gave a violet ferric chloride reaction and a positive Gibbs reaction. It was identical with the synthesised specimen below.

Compound B was methyl 2,6-dihydroxy-3-acetyl-4-methylbenzoate **34** (139 mg, 3%), crystals, mp 96–97 °C from light petroleum (lit.,[12b] 96–98 °C) (Found: C, 58.65; H, 5.45%; M^+, 224. Calc. for $C_{11}H_{12}O_5$: C, 58.9; H, 5.4%; *M*, 224); ν_{max}-$(CHCl_3)/cm^{-1}$ 3440 (OH), 3200 (OH), 1683 (chelated ester carbonyl), 1642 (chelated acetyl carbonyl), 1575; λ_{max}(EtOH)/nm 218 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 10 250), 248 (18 100), 324 (4800); δ_H 2.31 (3 H, s, aromatic Me), 2.53 (3 H, s, MeCO), 4.04 (3 H, s, MeO), 6.33 (1 H, s, ArH), 10.09 and 11.34 (2 × OH). The compound gave a purple ferric chloride reaction and a positive Gibbs reaction.

Compound C was 2-acetyl-3,5-dihydroxytoluene **33** (775 mg, 23%) and formed needles from chloroform or water, mp 159 °C (lit.,[17] 159 °C) (Found: C, 64.8; H, 6.05%; M^+, 166. Calc. for $C_9H_{10}O_3$: C, 65.05; H, 6.05%; *M*, 166); $\nu_{max}(CHCl_3)/cm^{-1}$ 3580 (aryl OH), 3268 (chelated OH), 1625 (chelated acetyl carbonyl); λ_{max}(EtOH)/nm 211infl (ε 9300), 222 (12 100), 230infl (8500), 282 (10 400), 308infl (5250); $\delta_H([^2H_6]DMSO)$ 2.23 (3 H, s, aromatic Me), 2.46 (3 H, s, MeC=O), 6.20 (2 H, *J* 2, 2 × aryl H), 9.85 (1 H, s, OH), 10.85 (1 H, s, chelated OH). The compound gave a red ferric chloride reaction and a positive Gibbs test.

Compound D was *2-methoxy-3-acetyl-4-methyl-6-hydroxybenzoic acid* **35** (81 mg, 2%), crystallising from benzene as colourless plates, mp 186–187 °C (Found: C, 58.6; H, 5.3%; M^+, 224. $C_{11}H_{12}O_5$ requires C, 58.9; H, 5.4%; *M*, 224); there was loss of CO_2 in the mass spectrum (intense 44 peak); ν_{max}-$(CHCl_3)/cm^{-1}$ 3260 (OH), 1695 (carboxylic acid), 1685 (acetyl carbonyl); λ_{max}(EtOH)/nm 214 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 11 200), 240 (16 000), 266infl (8550), 320 (5050); δ_H 2.34 (3 H, s, Ar-Me), 2.55 (3 H, s, MeC=O), 4.09 (3 H, s, OMe), 6.36 (1 H, s, Ar-H), 11.23 (1 H, br s, carboxy), 12.74 (1 H, s, chelated OH). The phenol gave a dark red ferric chloride reaction and dissolved in aqueous ethanolic sodium hydrogen carbonate with effervescence. The phenol gave a negative Gibbs test. It reacted with diazomethane to give a methyl ester, mp 117–118 °C, identical with the specimen described below.

All four compounds A–D were formed in similar 18 h reflux reactions using ratios of magnesium methoxide to bispyrone **27** of 2:1 to 10:1, no pyrone **27** remaining. At a ratio of 0.5:1 compound D **35** had formed, and there were traces of A **30** and B **31**, but no pyrone **27** remained. At a ratio of 1:1 A and D were present along with a trace of B but no pyrone **27** remained. Product examinations were by TLC developing with chloroform–methanol, visualising with UV light and iodine.

Synthesis of Compound A 30

Hydrated orcinol (3,5-dihydroxytoluene) (11.45 g), potassium hydrogen carbonate (20 g) and glycerol (20 g) were heated together under carbon dioxide at 115–120 °C for 6 h. The product was cooled and treated with water and hydrochloric acid to give *p*-orsellinic acid (2,6-dihydroxy-4-methylbenzoic acid), mp 165–166 °C (lit.,[18] 165–166 °C) which was methylated with diazomethane to give methyl *p*-orsellinate as long needles from diethyl ether, mp 96–97 °C (lit.,[15] 98–99 °C). Further methylation could not be achieved using diazomethane. Methyl *p*-orsellinate was now methylated using dimethyl sulfate and alkali and the product, methyl 2-hydroxy-4-methyl-6-methoxybenzoate **30**, had mp 96 °C after chromatography on silica eluting with light petroleum:benzene (1:1) (lit.,[15] 95–97 °C). It was identical with compound A obtained from the Praill bispyrone **27** above.

Treatment of the Praill α,γ-bispyrone 27 (1 mol equiv.) with sodium methoxide (10 mol equiv.)

The bispyrone **27** (1.92 g) in benzene (25 cm^3) and methanol (25 cm^3) was refluxed for 18 h with sodium methoxide solution prepared from sodium (2.3 g) and methanol (200 cm^3). The product was acidified with 4 M hydrochloric acid, diluted with water and extracted with benzene. The benzene extracts were washed, dried and evaporated to give a pale yellow liquid (1.09 g). TLC indicated the presence of one major compound A with trace amounts of two others B and C. The bulk of A was distilled off at 88 °C/0.7 mmHg and the remaining material was chromatographed on silica eluting with light petroleum–benzene and then benzene.

Compound A was methyl triacetate **11** (R = Me) (0.823 g, 52%), n_D^{17} 1.4700. It was identical with the material obtained above as shown by UV, IR and NMR spectra. It gave a copper chelate, mp and mixed mp 200 °C (decomp.).

Compound B was methyl 2-hydroxy-4-methyl-6-methoxybenzoate **30** (43 mg, 2%), mp and mixed mp 95 °C with the specimen above. Spectral data were also the same.

Compound C proved to be *methyl 2-methoxy-3-acetyl-4-methyl-6-hydroxybenzoate* **31** (25 mg, 1%) and formed long colourless needles from light petroleum, mp 117–118 °C (Found: C, 60.25; H, 5.8%; M^+, 238. $C_{12}H_{14}O_5$ requires C, 60.5; H, 5.9%; *M*, 238); $\nu_{max}(CHCl_3)/cm^{-1}$ 1732 (small), 1693 (chelated ester carbonyl), 1660 (acetyl carbonyl), 1618, 1517; λ_{max}(EtOH)/nm 215infl ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 9450), 245 (14 250), 265infl (9600), 320 (4550); $\delta_H(CDCl_3)$ 2.33 (3 H, s, Ar-Me), 2.53 (3 H, s, MeC=O), 3.87, 3.93 (6 H, 2 × s, 2 × OMe), 6.28 (1 H, s, Ar-H), 12.35 (1 H, s, chelated OH). The compound gave a dark red ferric chloride reaction and a negative Gibbs reaction. It was identical with the product obtained by treatment of the acid **35** with diazomethane.

A series of similar reactions covering sodium methoxide:pyrone ratios between 0.5:1 to 10:1 showed that at all ratios the major product was compound A, with traces of B and C, no unchanged pyrone remaining.

Treatment of the Praill α,γ-bispyrone 27 (1 mol equiv.) with boiling water

The bispyrone **27** (500 mg) was refluxed with water (25 cm^3) for 50 h and the crystals which formed on cooling were extracted with diethyl ether and crystallised from chloroform to give 2-acetyl-3,5-dihydroxytoluene **33** (265 mg, 62%), mp 159 °C. Identity with the specimen above was confirmed by mixed mp and spectroscopic characteristics.

The Scott α,α′-bispyrone (7-methyl-2,5-dioxo-2*H*,5*H*-pyrano-[4,3-*b*]pyran) 39

Triacetic lactone **12** (6.3 g, 1 mol), malonyl dichloride (7.05 g, 1 mol) and trifluoroacetic acid (7 g) were heated at 100 °C for 5 h. HCl was evolved and the mixture solidified. Trifluoroacetic acid was removed under vacuum and the residue was triturated with diethyl ether and filtered off. It was then titurated with methanol to remove unchanged triacetic lactone. The product was dissolved in chloroform and decolourised with activated char-

coal. The recovered bispyrone **39** (5.2 g, 53%) crystallised from nitrobenzene, mp 231–232 °C (lit.,[12c] 232 °C) (Found: C, 55.4; H, 3.2%; M^+, 194. Calc. for $C_9H_6O_5$: C, 55.7; H, 3.1%; *M*, 194); $\nu_{max}(CHCl_3)/cm^{-1}$ 1750 (2-pyrone carbonyl), 1710 (2-pyrone carbonyl), 1640, 1630, 1565; λ_{max}(EtOH)/nm 213 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 13 250), 270 (12 950), 329 (8400); $\delta_H([^2H_6]DMSO)$ 2.35 (3 H, s, MeC=), 5.47 (1 H, pyrone =CH), 6.62 (1 H, s, pyrone CH). It gave a red colour with ferric chloride.

Treatment of the Scott α,α′-bispyrone 39 (1 mol equiv.) with magnesium methoxide (10 mol equiv.)

The bispyrone **39** (1.94 g) in benzene (300 cm^3) was refluxed for 18 h with magnesium methoxide solution prepared from magnesium (2.43 g) and methanol (200 cm^3). It was cooled, diluted with water (0.5 dm^3), acidified with 4 M hydrochloric acid and extracted with benzene. The benzene extracts were washed, dried (Na_2SO_4) and evaporated to give a white solid (2.05 g) shown by TLC to consist of two major products (A and B) together with a trace of a third product (C). The solid was chromatographed on silica gel, eluting with light petroleum–benzene, then benzene. Compound C was not present in sufficient quantity for isolation, but was obtained from an experiment using a lower ratio of magnesium methoxide.

Compound A was shown to be *methyl* 2,4,6-*trihydroxy*-3-*acetylbenzoate* **43** (1.24 g, 55%), needles, mp 136–137 °C from light petroleum (Found: C, 53.0; H, 4.4%; M^+, 226. $C_{10}H_{10}O_6$ requires C, 53.1; H, 4.45%; *M*, 226); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430 (OH), 1670 (chelated ester carbonyl), 1645, 1635 (chelated acetyl carbonyl); λ_{max}(EtOH)/nm 208 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 17 000), 256 (68 400), 277infl (31 150), 318 (8000); $\delta_H(CDCl_3)$ 2.69 (3 H, s, MeC=O), 4.09 (ester OMe), 5.98 (1 H, s, ArH), 10.34 (1 H, br s, free OH), 12.90 (1 H, br, OH chelated to Me ester), 14.35 (1 H, sharp s, OH chelated to acetyl C=O). The compound gave a dark red ferric chloride reaction, a positive Gibbs reaction, and was unchanged when boiled with further magnesium methoxide solution.

Compound B was 2,4-*bis*(*methoxycarbonyl*)-3,5-*dihydroxytoluene* **40** (R = Me) (500 mg, 21%), mp 109–110 °C from light petroleum (Found: C, 54.75; H, 4.95%; M^+, 240. Calc. for $C_{11}H_{12}O_6$: C, 55.0; H, 5.05%; *M*, 240); $\nu_{max}(CHCl_3)/cm^{-1}$ 1725 (small), 1667 (chelated ester carbonyl), 1663 (chelated ester carbonyl), 1653, 1645, 1615, 1575; λ_{max}(EtOH)/nm 233 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 16 850), 250 (15 450), 316 (4950); $\delta_H(CDCl_3)$ 2.47 (3 H, s, Ar-Me), 3.97, 4.05 (6 H, 2 × s, 2 × ester OMe), 6.40 (1 H, s, ArH), 11.73 (1 H, br s, chelated OH), 12.76 (1 H, br s, chelated OH). The compound was unchanged on further reluxing with magnesium or sodium methoxide solution. It gave a dark red colour with ferric chloride, a positive Gibbs test, and was identical with the specimen described below (spectral and mixed mp criteria).

Treatment of the Scott α,α′-bispyrone 39 (1 mol equiv.) with magnesium methoxide (2.33 mol equiv.)

The bispyrone **39** (0.97 g) in benzene (150 cm^3) was refluxed for 18 h with magnesium methoxide solution prepared from magnesium (323 mg) and methanol (100 cm^3). It was worked up as before to give an oil which crystallised (1.07 g) and was chromatographed on silica eluting with benzene and then chloroform. Compounds A and B eluted together and were individually estimated by NMR spectroscopy of the mixture. Compound D followed, then C.

Compound A was methyl 2,4,6-trihydroxy-3-acetylbenzoate **43** (480 mg, 41%).

Compound B was 2,4-bis(methoxycarbonyl)-3,5-dihydroxytoluene **40** (R = Me) (87 mg, 7%).

Compound C was shown to be 2,4-*dimethoxy*-3-*acetyl*-6-*hydroxybenzoic acid* **44** (98 mg, 8%), needles, mp 165–166 °C from light petroleum (Found: C, 54.45; H, 4.95%; M^+, 240.063. $C_{11}H_{12}O_6$ requires C, 55.0; H, 5.05%; *M*, 240.064). The mass spectrum showed a strong peak at *m/z* 44 and a strong $M^+ - 44$ peak. The compound had $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (carboxylic carbonyl), 1660 (free acetyl carbonyl) 1618, 1575; λ_{max}(EtOH)/nm 225 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 17 250), 260 (10 450), 303 (4600); $\delta_H(CDCl_3)$ 2.62 (3 H, s, aryl MeC=O) 3.90, 3.95 (6 H, 2 × s, 2 × OMe), 6.36 (1 H, s, ArH), 10.4 (2 H, br s, OH and carboxy). The compound gave a dark red colour with ferric chloride and a negative Gibbs test. It was acid to litmus and dissolved in sodium hydrogen carbonate solution with effervescence: it was unchanged by further magnesium methoxide treatment.

Compound D was shown to be 3-(2-*methoxycarbonylacetyl*)-4-*hydroxy*-6-*methyl*-2-*pyrone* **45** (500 mg, 44%), mp 89–90 °C from light petroleum (Found: C, 53.1; H, 4.4%; M^+, 226. $C_{10}H_{10}O_6$ requires C, 53.1; H, 4.45%; *M*, 226); $\nu_{max}(CHCl_3)/cm^{-1}$ 1746 (2-pyrone carbonyl), 1733 (ester carbonyl), 1646, 1623 (chelated carbonyl), 1568; λ_{max}(EtOH)/nm 209infl ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 4300), 227 (9100), 313 (12 100); $\delta_H(CDCl_3)$ 2.30 (3 H, s, MeC=), 3.75 (3 H, s, ester OMe), 4.03 (2 H, CH_2), 6.00 (1 H, s, pyrone CH=), 15.70 (1 H, br s, chelated OH). The pyrone gave an orange colour with ferric chloride. When boiled with excess (10 mol equiv.) magnesium methoxide solution there was substantial formation of compounds A and B, together with unchanged D; compound C was not detected by TLC.

A series of 10 × 18 h reflux reactions between magnesium methoxide in methanol–benzene and the Scott bispyrone **39** was studied by TLC using ratios of 0.5, 1.0, 1.5, 2.0, 2.66, 4.0, 5.0, 6.0 and 10.0:1 magnesium methoxide:pyrone. Products A, B and D were not formed until the ratio reached 2.0:1 and C did not emerge clearly until the ratio reached 2.66:1. Relative yields of C and D decreased as magnesium methoxide ratios increased and C was present only in trace amounts at 10 mol equiv., whilst D had disappeared.

2,4-Bis(methoxycarbonyl)-3,5-dihydroxytoluene 40 (R = Me)[19]

Sodium (2.3 g, 0.1 mol) was added in small portions and with vigorous shaking for 1 h to a mixture of dimethyl acetonedicarboxylate (dimethyl 3-oxoglutarate) (17.4 g, 0.1 mol) and methyl acetoacetate (11.6 g, 0.1 mol) which was cooled to room temperature. When all the sodium had dissolved the mixture was heated to 120 °C and finally to 145 °C for a few minutes. On cooling, methanol (75 cm^3) was added and the mixture was acidified with 2 M sulfuric acid, diluted with water and extracted with diethyl ether. Work up of the diethyl ether extracts gave a solid (750 mg) which was chromatographed using preparative layer chromatography (Kieselgel HF_{254} nach Stahl), eluting with chloroform. The top band gave 2,4-dimethoxycarbonyl-3,5-dihydroxytoluene (290 mg), mp 110–111 °C from light petroleum. It was identical (mixed mp and spectral comparison) with the specimen obtained from the Scott bispyrone above.

Treatment of the Scott α,α′-bispyrone 39 (1 mol equiv.) with sodium methoxide (10 mol equiv.)

The bispyrone (388 mg) in benzene (60 cm^3) was kept at 20 °C for 18 h with sodium methoxide solution prepared from sodium (460 mg) and methanol (40 cm^3). (As judged by TLC, refluxing the solution gave a similar result.) It was worked up as before to give an oil which crystallised (280 mg) and was chromatographed on silica, eluting with benzene and then benzene–chloroform, to give compounds A and B. Continued elution with chloroform gave only a little gum.

Compound A was methyl 2-hydroxy-4-methyl-6-methoxybenzoate **30** (32 mg, 8%), needles from methanol, mp 96 °C (lit.,[15] 95–97 °C). It was identical with one of the products (**30**) obtained above from treating the Praill bispyrone **27** with magnesium methoxide (mixed mp and spectral comparison) and remained unchanged on treatment with magnesium methoxide.

Compound B was 2,4-dimethoxycarbonyl-3,5-dihydroxytoluene **40** (R = Me) (220 mg, 40%). It formed needles, mp 109–110 °C, from light petroleum and was identical with the specimen described earlier (TLC, mixed mp and spectral comparison).

A kinetic experiment performed at room temperature under conditions similar to those above showed that compound B appeared after about 15 min and then gradually increased in amount whilst compound A appeared after about 1 h, gradually increasing in amount.

Under conditions similar to the main experiment described above, the ratios of sodium methoxide to bispyrone **39** were changed in a series 0.5, 1, 2, 4, 8, 10:1. Ratios 0.5:1 and 1.0:1 produced no compound A or B but at 2:1 and higher ratios they were both present in quantity with only a trace, or at higher ratios none, of unchanged bispyrone.

Treatment of the Scott α,α′-bispyrone 39 with boiling water

The bispyrone **39** (500 mg) was powdered and refluxed with water (25 cm^3) for 3 h. It dissolved after 30 min to give a clear solution and on cooling crystals formed which were extracted with benzene to give dehydroacetic acid **1** (413 mg, 96%). It had mp and mixed mp 111–112 °C and spectral data were identical with authentic material.

The Ziegler α,α′-bispyrone (3-benzyl-4-hydroxy-7-methyl-2,5-dioxo-2*H*,5*H*-pyrano[4,3-*b*]pyran) 49

Benzylmalonic acid (4.85 g, 1 mol equiv.), 2.4-dichlorophenol (8.15 g, 1 mol equiv.) and phosphorus oxychloride (7.68 g, 2 mol equiv.) were heated together at 145 °C for 30 min. The dark gum which formed crystallised, and on recrystallisation from light petroleum gave colourless needles of the bis(2,4-dichlorophenyl) benzylmalonate (8.75 g), mp 121 °C.

Triacetic lactone **12** (0.63 g, 1 mol) and bis(2,4-dichlorophenyl) benzylmalonate (2.42 g, 1 mol equiv.) were heated together at 250 °C for 20 min. On cooling, the bispyrone **49** formed was triturated with benzene and filtered off and recrystallised from nitrobenzene (1.0 g, 70%), mp 227–228 °C (lit.,[13] 225–226 °C) (M^+, 284. Calc. for $C_{16}H_{12}O_5$: *M*, 284); $\nu_{max}(CHCl_3)/cm^{-1}$ 1740 (2-pyrone carbonyl), 1710 (2-pyrone carbonyl) 1695, 1645, 1633, 1575; λ_{max}(EtOH)/nm 210 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 22 050), 278 (12 050), 336 (9600); $\delta_H([^2H_6]DMSO)$ 2.39 (3 H, s, pyrone MeC=), 3.73 (2 H, s, CH_2), 6.83 (1 H, s, pyrone =CH), 7.31 (5 H, s, ArH). The compound gave a purple colour with ferric chloride.

On treatment with acetic anhydride in pyridine the pyrone gave an *acetate* **52** as needles, mp 164 °C, from methanol (Found: C, 66.05; H, 4.55%; M^+, 326. $C_{18}H_{14}O_6$ requires: C, 66.25; H, 4.3%; *M*, 326); ν_{max}(mull)/cm^{-1} 1782 (acetate), 1748 (pyrone carbonyl), 1725 (pyrone carbonyl), 1646, 1615, 1565; λ_{max}(EtOH)/nm 211 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 11 750), 285 (9200), 338 (13 000); $\delta_H(CDCl_3)$ 2.24 (3 H, s, acetyl Me), 2.42 (3 H, s, pyrone MeC=), 3.85 (2 H, s, CH_2), 6.27 (1 H, pyrone =CH), 7.37 (5 H, s, ArH). The acetate gave no colour with ferric chloride.

Treatment of the Ziegler α,α′-bispyrone 49 (1 mol equiv.) with magnesium ethoxide (10 mol equiv.)

The bispyrone **49** (4.26 g) in benzene (300 cm^3) was refluxed for 18 h with magnesium ethoxide solution prepared from magnesium (3.65 g) and ethanol (300 cm^3). It was cooled, diluted with water (0.6 dm^3), acidified with 4 M hydrochloric acid and extracted with benzene. The benzene extracts were washed, dried (Na_2SO_4) and evaporated to give a yellow gum (4.85 g) shown by TLC to consist of unchanged starting bispyrone and four other compounds A–D. The components of the gum were separated on silica gel: elution with light petroleum–benzene gave compound A, with benzene B, with benzene–chloroform C, then unchanged bispyrone, and with chloroform D. Final elution with methanol gave a gum.

Unreacted bispyrone **49** (1.168 g, 28%) crystallised in needles, mp 226 °C, from nitrobenzene and was identical with authentic material (mixed mp and spectral data).

Compound A was *ethyl* 2,4,6-*trihydroxy*-3-*acetyl*-5-*benzylbenzoate* **53** (R = H) (646 mg, 13%), needles mp 93–94 °C, from light petroleum (Found: C, 65.55; H, 5.45%; M^+, 330. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.5%; *M*, 330); $\nu_{max}(CHCl_3)/cm^{-1}$ 3390 (free OH), 1666 (chelated ester carbonyl), 1625 (chelated acetyl carbonyl), 1595; λ_{max}(EtOH)/nm 208 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 38 500), 258 (71 850), 327 (6950); $\delta_H(CCl_4)$ 1.43 (3 H, t, *J* 7, *Me*CH_2O), 2.61 (3 H, s, MeCO), 3.80 (2 H, s, benzyl CH_2), 4.43 (2 H, q, *J* 7 MeCH_2), 7.14 (5 H, s, ArH), 10.03 (1 H, br s, free OH, *p*- to the benzyl group), 12.12 (1 H, br s, OH chelated to Et ester), 14.84 (1 H, sharp s, OH chelated to acetyl). The compound gave a dark red ferric chloride test, a negative Gibbs reaction, and remained unchanged on further treatment with magnesium ethoxide solution. When treated with acetic anhydride and pyridine compound A formed a monoacetate, *ethyl* 2-*acetoxy*-4,6-*dihydroxy*-3-*acetyl*-5-*benzylbenzoate* **53** (R = Ac) which crystallised from light petroleum–benzene, mp 146–147 °C (Found: C, 64.05; H, 5.5%; M^+, 372. $C_{20}H_{20}O_7$ requires C, 64.5; H, 5.4%; *M*, 372); ν_{max}(mull)/cm^{-1} 1770 (acetate), 1650 (chelated ester), 1620 (chelated acetyl), 1597; λ_{max}(EtOH)/nm 213 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 17 800), 239 (19 300), 264 (14 250), 333 (4150); $\delta_H(CDCl_3)$ 1.36 (3 H, t, *J* 7, *Me*CH_2), 2.22 (3 H, s, acetate Me), 2.77 (3 H, s, ArCO*Me*), 3.87 (2 H, s, ArCH_2), 4.41 (2 H, q, *J* 7, CH_3CH_2O), 7.24 (5 H, m, C_6H_5), 13.62 (1 H, sharp, OH chelated to ethyl ester), 14.89 (1 H, OH chelated to acetyl carbonyl).

Compound B was *ethyl* 2,4,6-*trihydroxy*-3-*benzylbenzoate* **54** (241 mg, 6%), mp 152–153 °C, from benzene–light petroleum (Found: C, 66.8; H, 5.9%; M^+, 288. $C_{16}H_{16}O_5$ requires C, 66.65; H, 5.6%, *M*, 288); $\nu_{max}(CHCl_3)/cm^{-1}$ 3580 (free OH), 3425 (free OH), 3220 (broad, chelated OH), 1665 (chelated ester carbonyl), 1645, 1609, 1496; λ_{max}(EtOH)/nm 228 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 21 700), 273 (19 050), 313 (3100); $\delta_H(CDCl_3)$ 1.43 (3 H, t, *J* 7, *Me*CH_2), 3.99 (2 H, s, PhCH_2), 4.53 (2 H, q, *J* 7, CH_3CH_2), 5.79 (1 H, s, free OH *p*- to ester), 5.98 [1 H, s, C(5)H], 7.30 (5 H, s, CH_2*Ph*), 10.00 (1 H, br s, OH *p*- to benzyl), 10.45 (1 H, br s, chelated OH). The compound gave a blue-green ferric chloride reaction, a positive Gibbs test, and was unchanged by further treatment with magnesium ethoxide.

Compound C was 3-*benzyl*-4-*hydroxy*-5-*ethoxycarbonyl*-6-*methyl*-2-*pyrone* **51** (R = Et) (137 mg, 3%), pale yellow needles, mp 204–205 °C, from light petroleum–benzene (Found: C, 66.5; H, 5.6%; M^+, 288.099. $C_{16}H_{16}O_5$ requires C, 66.66; H, 5.6%; *M*, 288.100); $\nu_{max}(CHCl_3)/cm^{-1}$ 1706 (free ester carbonyl), 1690 (pyrone carbonyl), 1684, 1632, 1604, 1574; λ_{max}(EtOH)/nm 218 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 15 300), 271 (8650), 284 (6250), 297infl (4250); $\delta_H(CDCl_3)$ 1.38 (3 H, t, *J* 7, *Me*CH_2), 2.61 (3 H, s, pyrone MeC=), 3.80 (2 H, s, CH_2Ph), 4.44 (2 H, q, *J* 7, MeCH_2), 7.29 (5 H, s, CH_2*Ph*), 11.82 (1 H, s, OH). The compound gave a red ferric chloride reaction and when treated further with magnesium ethoxide compound B was formed as indicated by TLC.

Compound D was 3-*benzyl*-4-*hydroxy*-5-*carboxy*-6-*acetonyl*-2-*pyrone* **50** (R = H) (968 mg, 22%), mp 163 °C, from benzene (Found: C, 63.35; H, 4.45%; M^+, 302.079. $C_{16}H_{14}O_6$ requires C, 63.55; H, 4.65%; *M*, 302.079); there were intense peaks at *m/z* 44 and $M^+ - 44$; $\nu_{max}(CHCl_3)/cm^{-1}$ 1730 (2-pyrone), 1710 (acetonyl carbonyl), 1695 (carboxylic acid) 1645, 1605, 1575; λ_{max}(EtOH)/nm 219 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 15 650), 262 (7000), 301 (4850); $\delta_H(CDCl_3)$ 1.93 (3 H, s, MeCO), 3.49 (2 H, s, acetonyl CH_2), 3.81 (2 H, s, benzyl CH_2), 7.33 (5 H, s, *Ph*CH_2); $\delta_H([^2H_6]DMSO)$ 1.19 (3 H, s, MeCO), 3.71 (2 H, s, acetonyl CH_2), 4.15 (2 H, s, benzyl CH_2), 7.18 (2 H, s, OH and CO_2H), 7.34 (5 H, s, $PhCH_2$). The compound gave a red ferric chloride reaction, was acid to litmus and phenolphthalein, and dissolved in aqueous sodium hydrogen carbonate with effervescence. On further treatment with magnesium ethoxide the compound remained unchanged. Treated with acetic anhydride and pyridine compound D formed an *acetate*, mp 165–166 °C, from methanol (Found: C, 66.0; H, 4.25%. Calc. for $C_{18}H_{14}O_6$: C, 66.25; H, 4.3%). It was identical with the acetate of the Ziegler bispyrone **49** (mixed mp and spectral examination). In a series of experiments in which the ratios of magnesium ethoxide:

substrate were varied between 0.5:1 and 10:1, compounds A–D were not produced until the ratio reached 2:1 and were all still present at 10:1 ratio.

Treatment of the Ziegler α,α′-bispyrone 49 (1 mol equiv.) with sodium ethoxide (10 mol equiv.)

The bispyrone **49** (284 mg) in benzene (20 cm^3) was added to sodium ethoxide solution prepared from sodium (230 mg) and ethanol (20 cm^3) and the mixture was kept at room temperature for 18 h (refluxing the solution gave a similar result). Water was added and the solution was acidified with 4 M HCl and extracted with benzene. Evaporation of the benzene extracts gave a crystalline solid (317 mg, 96%), shown to be 4-*hydroxy*-3-*benzyl*-5-*ethoxycarbonyl*-6-*acetonyl*-2-*pyrone* **50** (R = Et). Colourless needles, mp 115–116 °C, were obtained from light petroleum; mp 116–118 °C from ethanol (Found: C, 65.35; H, 5.4%; M^+, 330. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.5%; *M*, 330); $\nu_{max}(CHCl_3)/cm^{-1}$ 3170 (OH), 1730 (ester carbonyl), 1705 (acetonyl carbonyl), 1695 (pyrone carbonyl), 1650, 1600; λ_{max}(EtOH)/nm 218 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 14 850), 266 (9550), 299 (br, 4250); $\delta_H(CDCl_3)$ 1.13 (3 H, q, *J* 7, *Me*CH_2), 1.70 (3 H, s, acetonyl CH_3CO), 3.06 (2 H, s, acetonyl CH_2), 3.71 (2 H, q, *J* 7, Me*C*H_2), 3.77 (2 H, s, benzyl CH_2), 7.26 (5 H, s, *Ph*CH_2), 10.92 (1 H, s, OH). The compound gave a dark red colour with ferric chloride. Treatment of **50** (R = Et) with excess magnesium ethoxide solution gave compounds (A) **53** (R = H), (B) **54**, (C) **51** (R = Et) and (D) **50** (R = H), along with unchanged pyrone **50** (R = Et) as shown by TLC. Treatment of the pyrone **50** (R = Et) and compound D, **50** (R = H) with diazoethane gave one and the same product (TLC—dark green fluorescence when viewed in UV light). The pyrone **50** (R = Et) was not found at ratios of substrate **49**:sodium methoxide molarities 0.5:1 or 1:1, but it was found between ratios 2:1 and 10:1.

Treatment of the Ziegler α,α′-bispyrone 49 with water at 250 °C/ 40 atm

The bispyrone **5** (0.25 g) was insoluble and unaffected by refluxing with water (25 cm^3) for 18 h. The bispyrone (5.0 g) was finely powdered and heated with water (300 cm^3) for 3 h in an autoclave at 250 °C and 40 atm. Isolation by extraction with diethyl ether gave a brown oil (2.91 g) shown by TLC to consist of two components which were separated by chromatography on silica gel, eluting with chloroform.

The first eluted compound was benzylacetone **58** (1.55 g, 60%), bp 70 °C/0.4 mmHg (lit.,[15] 115 °C/13 mmHg), $n_D^{23.5}$ 1.5098 (lit.,[15] 1.511) (Found: C, 80.95; H, 8.2%; M^+, 148. Calc. for $C_{10}H_{12}O$: C, 81.05; H, 8.15%; *M*, 148); ν_{max}(liquid film)/cm^{-1} 1720 (carbonyl), 1605, 1500; $\delta_H(CCl_4)$ 2.00 (3 H, s, MeCO), 2.72 (4 H, m, CH_2CH_2), 7.14 (5 H, s, ArH). It was spectrally identical with authentic material and formed a 2,4-dinitrophenylhydrazone, mp 130–131 °C (lit.,[15] 131–132 °C).

The second compound was 2-*benzyl*-3,5-*dihydroxytoluene* **57** (1.326 g, 35%), a viscous liquid, bp 205 °C (bath)/0.45 mmHg (Found: C, 78.1; H, 6.75%; M^+, 214. $C_{14}H_{14}O_2$ requires C, 78.45; H, 6.6%; *M*, 214); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600 (OH), 3340 (OH), 1608, 1495; λ_{max}(EtOH)/nm 213 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 16 300), 225infl (9800), 282 (2150); $\delta_H(CHCl_3)$ 2.10 (3 H, s, Ar*Me*), 3.90 (2 H, s, benzyl CH_2), 5.60 (2 H, br, 2 × OH), 6.19, 6.23 [2 H, d, d, *J* 2.5, C(4)H, C(6)H], 7.1 (5 H, s, *Ph*CH_2). The compound gave a dark green colour with ferric chloride and formed a non-crystalline diacetate when treated with acetic anhydride and pyridine at 20 °C for 18 h, ν_{max}(film)/cm^{-1} 1774 (acetates), 1621, 1593, 1496; $\delta_H(CCl_4)$ 2.04 (3 H, Ar-*Me*), 2.16 (6 H, s, 2 × acetate Me), 3.87 (2 H, benzyl CH_2), 6.67, 6.73 (2 H, d, d, *m*-coupled), 7.05 (5 H, s, *Ph*CH_2).

3-Cinnamoyl-4-hydroxy-6-methyl-2-pyrone 60

Dehydroacetic acid (100.8 g, 1 mol equiv.), benzaldehyde (63.6 g, 1 mol) and piperidine (6 cm^3) in anhydrous pyridine (480 cm^3) were warmed to 45 °C for 45 min, then at 100 °C for 15 min. Removal of the solvent under reduced pressure and crystallisation of the residue from benzene gave the 2-pyrone **60** (50 g), mp 130–131 °C, from light petroleum–benzene (lit.,[14] 130–132 °C) (Found: C, 70.55; H, 4.6%; M^+, 256. Calc. for $C_{15}H_{12}O_4$: C, 70.3; H, 4.7%; *M*, 256); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720 (2-pyrone), 1630 (chelated carbonyl), 1550 (broad); λ_{max}(EtOH)/nm 234 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$) 9700), 355 (22 700); $\delta_H(CDCl_3)$ 2.25 (3 H, s, pyrone Me), 5.93 (1 H, s, pyrone =CH), 7.35 (5 H, s, ArH), 7.91 and 8.28 [2 H, 2 × d, *J* 16, (*E*)-CH=CH], 17.86 (1 H, s, chelated OH). The compound gave a red colour, with ferric chloride.

2-Methyl-6-styryl-4-pyrone

A mixture of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrone **60** (18.4 g) in acetic acid (100 cm^3) and concentrated hydrochloric acid (100 cm^3) was heated at 105 °C and then refluxed for 20 min. The solvent was removed under reduced pressure and the crystalline pyrylium salt was diluted with water (40 cm^3) and decomposed with cold sodium hydroxide solution (10%, 400 cm^3). The product was extracted with chloroform and decolourised with alumina to give the 4-pyrone (12.0 g), mp 123 °C, from benzene–light petroleum (lit.,[14] 124–125 °C) (Found: M^+, 212. Calc. for $C_{14}H_{12}O_2$: *M*, 212); $\nu_{max}(CHCl_3)/cm^{-1}$ 1661 (4-pyrone carbonyl), 1636, 1609; $\lambda_{max}(CDCl_3)$/nm 228 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 17 350), 2331 (15 100), 317 (29 550); $\delta_H(CDCl_3)$ 2.33 (3 H, s, pyrone Me), 6.08, 6.19 (2 H, each d, *J* 2.5, 2 × pyrone =CH), 6.64, 7.35 (2 H, each d, *J* 16, 2 × CH=CH), 7.40 (5 H, s, ArH).

8-Phenyloct-7-ene-2,4,6-trione 15

Barium hydroxide (8.0 g) in hot 1:1 aqueous ethanol (80 cm^3) was added to 2-methyl-6-styryl-4-pyrone (6.0 g) and the mixture was heated on a steam bath for 30 min. The yellow barium salt was filtered off, decomposed with dilute hydrochloric acid and extracted with chloroform. Work-up and crystallisation from benzene–light petroleum gave the trione (4.2 g) as bright yellow needles mp 118–119 °C (lit.,[14] 114–115 °C) (Found: M^+, 230. Calc. for $C_{14}H_{14}O_3$: *M*, 230); ν_{max}(mull)/cm^{-1} 1630, 1590, 1579; λ_{max}(EtOH)/nm 228 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 7350), 365 (31 400). The NMR spectrum was complicated by tautomerism: $\delta_H(CDCl_3)$ 1.99 (3 H, s, MeC=O), 2.25 [CHC(O)=], 3.50, 3.62 (CH_2), 5.25, 5.66, 6.27, 6.54 (=CH), 7.38 (ArH), 13.84, 14.40 (2 × chelated OH). The compound gave a dark green colour with ferric chloride.

Treatment of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrone 60 (1 mol equiv.) with magnesium methoxide (10 mol equiv.)

The 2-pyrone (1.28 g) in benzene (50 cm^3) was refluxed for 24 h with magnesium methoxide solution prepared from magnesium (1.216 g) and methanol (100 cm^3). The clear yellow solution was worked up in the usual way. Extraction with benzene gave a yellow oil (1.34 g, 93%), which crystallised giving yellow prisms of 8-*phenyl*-5-*methoxycarbonyloct*-7-*ene*-2,4,6-*trione* **61**, mp 72–74 °C, from methanol (Found: C, 66.6; H, 5.55; M^+, 288. $C_{16}H_{16}O_5$ requires C, 66.65; H, 5.6%; *M*, 288); $\nu_{max}(CHCl_3)/cm^{-1}$ 1715 (ester), 1630 (chelated acetyl carbonyl), 1615, 1580, 1553; λ_{max}(EtOH)/nm 231 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 9800), 347 (24 400). The NMR spectrum was complicated by tautomerism: $\delta_H(CCl_4)$ 1.99, 2.15 (MeC=O), 3.73, 3.79 (*Me* O_2C), 5.68 (=CH), 7.33 (ArH), 7.42 and 7.68 (each d, *J* 16, CH=CH), 13.85, 15.93, 17.74 (chelated OH). The compound gave a dark red colour with ferric chloride.

Treatment of 8-phenyl-5-methoxycarbonyloct-7-ene-2,4,6-trione 61 (1 mol equiv.) with magnesium methoxide (10 mol equiv.)

The trione (230 mg) in benzene (10 cm^3) was refluxed for 24 h with magnesium methoxide solution prepared from magnesium (243 mg) and methanol (20 cm^3). Work up gave completely unchanged trione (230 mg) mp 118–119 °C, mixed mp with authentic material and spectral comparison.

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