Radical-mediated cyclisation of ω-aryl-β-dicarbonyl compounds to tetrahydrobenzocyclohepten-6-ones, hexahydrobenzocycloocten-6-ones and naphthalen-2(1*H*)-ones

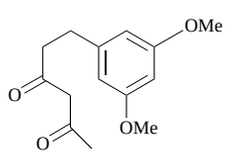
Joanne F. Jamie and Rodney W. Rickards *

Research School of Chemistry, Australian National University, Canberra, ACT 0200, Australia

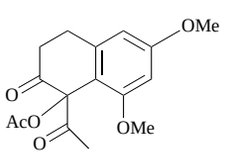
Manganese(III) acetate in acetic acid promotes efficient radical-mediated oxidative cyclisation of ε-aryl-β-dicarbonyl and *Z*-γ,δ-unsaturated δ-aryl-β-dicarbonyl compounds carrying electron-releasing groups in the aromatic ring, forming 6,7,8,9-tetrahydro-5*H*-benzocyclohepten-6-ones and naphthalen-2(1*H*)-ones, respectively. The process is accompanied by secondary acetoxylation at the activated benzylic position of the initial cyclisation products, and is exemplified by the conversions of the ε- and δ-aryl-β-dicarbonyl compounds 6 and 11 into the benzocycloheptenone 18 and the naphthalenone 21, respectively. Application of the oxidation to the formation of 8-membered hexahydro- and tetrahydro-benzocyclo-octen-6-ones 19 and 22 from ζ-aryl-β-dicarbonyl and *Z*-γ,δ-unsaturated ζ-aryl-β-dicarbonyl compounds is limited by low reactivity, and in the latter case, by radical rearrangement followed by cyclisation to a tetralin.

Introduction

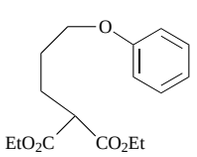
We have recently described the radical-mediated oxidative cyclisation of δ-aryl-β-dicarbonyl compounds to β-tetralones.[1] The annulation proceeds with both β-diketones and β-keto esters, but requires the presence of electron-releasing groups on the aromatic ring for efficiency. It is promoted by four equivalents of manganese(III) acetate in acetic acid at room temperature, and is accompanied by secondary oxidation resulting in acetoxylation at the benzylic α-position of the initially formed β-tetralone, as illustrated by the overall conversion of the diketone **1** into the tetralone **2**. Other authors have reported



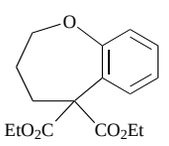
1



2



3



4

similar 5- and 6-membered ring closures of acyclic β-keto esters,[2] malonates[3] and two carbocyclic β-diketones[4] directly onto aromatic rings. These processes constitute extensions of the more familiar cyclisations of olefinic β-keto esters,[5,6] olefinic malonates[7] and several olefinic β-diketones[5c,6] with this one-electron oxidant. The full capabilities of this reagent have been comprehensively reviewed.[8]

We now examine the further extension of this process to the oxidative formation of benzo-fused 7- and 8-membered cycloalkenones from ε- and ζ-aryl-β-dicarbonyl compounds, and the effect on the cyclisation of incorporating a *Z*-γ,δ-olefinic bond into δ-, ε- and ζ-aryl-β-dicarbonyl compound substrates. All the substrates examined incorporate two electron-releasing ether groups *meta* to the dicarbonyl substituent on the benzene ring, in order to increase the reactivity of the aromatic ring towards the initially-formed electrophilic β-dicarbonyl radical.[1] Whilst the manganese(III)-based oxidative cyclisation of olefinic ε- and ζ-unsaturated β-keto esters to cycloheptenones and cyclooctenones has been reported to occur in moderate to good yields,[9,10] the only attempts at 7-membered ring closure of ω-aryl-β-dicarbonyl compounds to our knowledge are those of Citterio *et al.*[3] Oxidation of the phenoxypropyl-substituted malonate ester **3** provided a 15% yield of the benzoxepin **4**, together with a significant amount of the dimerised malonate. In contrast, the phenylbutyl-substituted carbon analogue gave no cyclisation, but only benzylic acetoxylation resulting from an intramolecular 1,5-hydrogen shift of the initially formed malonyl radical.

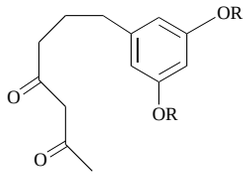
Results and discussion

Synthesis of the ω-aryl-β-dicarbonyl compounds

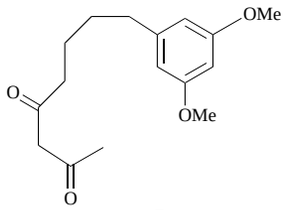
The ε-aryl β-diketones **5** and **6** were synthesised by alkylation of the dilithioenolate of pentane-2,4-dione with 3,5-dibenzyloxy- and 3,5-dimethoxy-phenethyl bromides. The yields were only moderate, and in the former but not the latter case were reduced by competing base-promoted dehydrobromination to the corresponding styrene. The homologous ζ-aryl β-diketone **7** was obtained in 86% yield by alkylation of the same dilithio enolate with 1-bromo-3-(3,5-dimethoxyphenyl)propane. This bromide was prepared from 3,5-dimethoxybenzaldehyde by Perkin condensation with acetic anhydride to give the cinnamic acid, reduction of both carboxy and olefinic groups with lithium aluminium hydride,[11] and bromination of the resulting alcohol. ^{1}H and ^{13}C NMR spectroscopy indicated that the diketones **5**, **6** and **7** all existed predominantly in H-bonded enolic forms in $CDCl_3$ solutions.

The *E*-γ,δ-unsaturated δ-(3,5-dimethoxyphenyl) β-diketone **8** was prepared by dehydration of the corresponding δ-hydroxy diketone[1] with methanesulfonyl chloride in pyridine. Irradiation of solutions of this *E*-isomer, λ_{max} 344 nm, with 350 nm ultraviolet light or with 240–400 nm light from a high pressure mercury lamp, effected no isomerisation to the *Z*-isomer. (*E*)-3′,5′-dimethoxycinnamic acid† was readily isomerised with high pressure mercury radiation, however, to give a 4:1 mixture of *Z*:*E* isomers. Condensation of the derived acid chloride with the lithium enolate of acetone under the conditions of Seebach *et al.*,[12] but in minimal light, gave a 56% yield of a 3:2 mixture

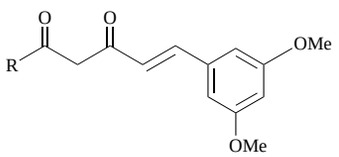
† The IUPAC name for this compound (see Experimental section) is (*E*)-3-(3,5-dimethoxyphenyl)propenoic acid.



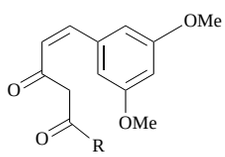
5 R = Bn
6 R = Me



7

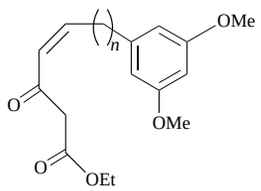


8 R = Me
9 R = OEt

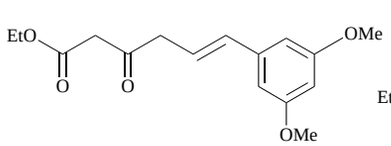


10 R = Me
11 R = OEt

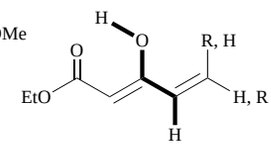
12



13 *n* = 1
14 *n* = 2



15



16

of the *Z*- and *E*-enediones **10** and **8**. The predominant *Z*-γ,δ-unsaturated δ-(3,5-dimethoxyphenyl) β-diketone component **10** of the mixture was stable indefinitely in the dark. Exposure to laboratory or ultraviolet light, however, caused complete conversion within hours into the pure *E*-isomer **8**, in agreement with the observed stability of the *E*-isomer to photoisomerisation. Both *E*- and *Z*-isomers **8** and **10** existed in $CDCl_3$ solutions as single H-bonded enolic forms, most likely the extended conjugated tautomers as observed for the related non-aromatic hex-1-ene-3,5-dione.[13]

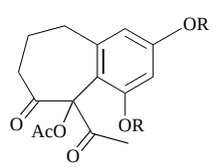
Treatment of 3,5-dimethoxybenzaldehyde with the anion[14] of the ylide **12** afforded, in 90% yield, a mixture of the *E*- and *Z*-γ,δ-unsaturated δ-(3,5-dimethoxyphenyl) β-keto esters **9** and **11** corresponding to the β-diketones **8** and **10**. Even under minimal light the expected[14] *E*-product **9** as measured by ^{1}H NMR spectroscopy dominated in a ratio of 9:1, which was unaltered by lowering the reaction temperature from ambient to 0 °C and acidifying with carbon dioxide instead of mineral acid. This indicates that the favoured formation of *E* products from aromatic aldehydes in such reactions, in contrast to *Z* products from aliphatic aldehydes, is inherent in the reaction itself and not the result of subsequent light- or acid-catalysed isomerisation.[14,15] The required *Z*-β-keto ester **11**, which existed as a 4:1 mixture of keto and enol forms in $CDCl_3$ solution, was separated by chromatography from the *E*-β-keto ester **9**, a 1:1 mixture of keto and enol forms.

The synthesis of the *Z*-γ,δ-unsaturated ε-(3,5-dimethoxyphenyl) β-keto ester **13** was initially hampered by the instability of the starting material 3,5-dimethoxyphenylacetaldehyde, which was prone to oxidation and polymerisation. It was ultimately negated by the facility with which the primary condensation product of this aldehyde and the anion of ylide **12**, presumably a mixture of the *E*- and *Z*-γ,δ-unsaturated β-keto ester **13**, isomerised to the *E*-δ,ε-unsaturated β-keto ester **15**. This rearrangement parallels the known isomerisation of (*E*)-5-phenylpent-3-en-2-one to the thermodynamically favoured (*E*)-5-phenylpent-4-en-2-one.[16] Unlike the conjugated β-keto esters **9** and **11**, the product **15**, like most saturated β-keto esters,[17] existed solely in the keto form in $CDCl_3$. Its structure followed from comparison of its ^{1}H NMR spectrum with those of the above 5-phenylpenten-2-ones,[16] and from its UV absorption in basic ethanol, λ_{max} 280 nm, which resembled that of the enolate of the ethyl acetoacetate, λ_{max} 275 nm.[18]

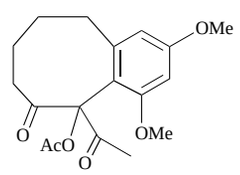
Similar condensation of 3-(3,5-dimethoxyphenyl)propionaldehyde with the anion of ylide **12** in the presence of sodium hydride and 1 drop of water gave a 63% yield of the *Z*-γ,δ-unsaturated ζ-(3,5-dimethoxyphenyl) β-keto ester **14**, as expected with a saturated aldehyde.[14] ^{1}H and ^{13}C NMR spectroscopy of this product in $CDCl_3$ showed a 7:3 equilibrium ratio of keto and enol forms, increasing to 6:1 and 8:1 in CD_3CN and $(CD_3)_2SO$ respectively. The presence of long-range coupling (^4J 1.6 Hz), verified by decoupling experiments, between the enol proton and the γ-olefinic proton confirmed the γ,δ-position of the olefinic group. Similar long-range coupling was observed in enol forms of the *E*- and *Z*-γ,δ-unsaturated β-keto esters **9** and **11**, and is attributed to W-coupling in the thermodynamically preferred s-*trans* conformation **16** of the H-bonded enol tautomers. The fact that the base peak at *m*/*z* 177 in the mass spectrum of the β-keto ester **14** corresponded to the 3′,5′-dimethoxycinnamyl ion is attributed to migration of the olefinic bond under electron-impact ionisation.[19]

Oxidative cyclisation of the ε- and ζ-aryl β-diketones

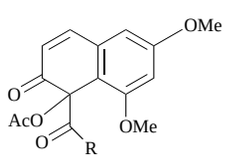
Treatment of the ε-(3,5-dialkoxy-substituted)aryl β-diketones **5** and **6** with 4.2 equiv. of anhydrous manganese(III) acetate in acetic acid at 60 °C for 22 h under argon afforded the acetoxylated tetrahydrobenzocycloheptenones **17** and **18**. The



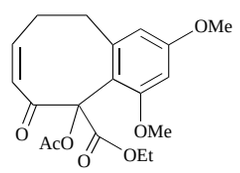
17 R = Bn
18 R = Me



19



20 R = Me
21 R = OEt



22

yields of 76 and 66%, respectively, are equivalent to those previously obtained for the 6-membered ring closure of similarly substituted δ-aryl β-diketones to acetoxylated β-tetralones, *e.g.* **1** to **2**, 71% yield.[1] In contrast to the previous cyclisations, however, the present reactions do not proceed at room temperature, but require warming. At ambient temperature for the same period, starting materials were recovered together with small amounts of the corresponding 4-arylbutanoic acids arising from cleavage of the β-dicarbonyl system. The homologous ζ-aryl β-diketone **7** behaved similarly at ambient temperature, and after 22 h at 60 °C gave a considerable quantity of 5-(3,5-dimethoxyphenyl)pentanoic acid accompanied by the desired acetoxylated hexahydrobenzocyclooctenone **19** in only 4% yield. We attribute this result to the expected combination of adverse entropic and enthalpic factors associated with the formation of an 8-membered ring.

The structures of all reaction products were defined by their

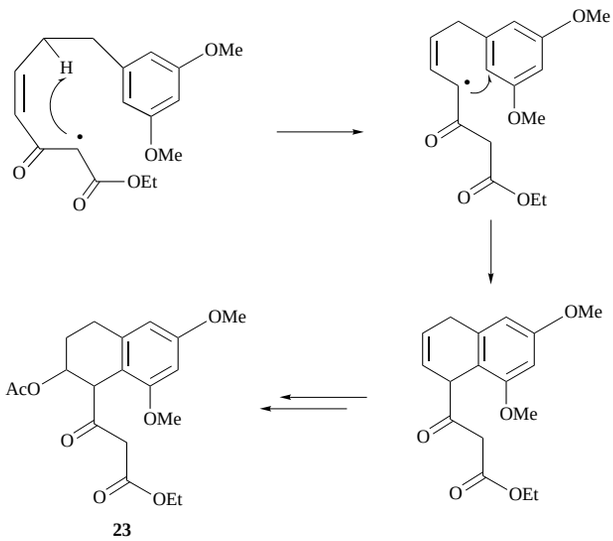
mass and NMR spectra. Mass spectra of the acetoxylated tetra- and hexa-hydrobenzocycloalkenones showed molecular ions, together with characteristic daughter ions corresponding to the loss of ketene followed both by loss of a further ketene fragment and of acetyl and carbonyl fragments.

Oxidative cyclisation of the γ,δ-unsaturated δ- and ζ-aryl-β-dicarbonyl compounds

The pure *E*-γ,δ-unsaturated δ-(3,5-dimethoxyphenyl) β-diketone **8** was stable towards anhydrous manganese(III) acetate in acetic acid at room temperature under argon. Accordingly, the 3:2 mixture of *Z*- and *E*-γ,δ-unsaturated δ-(3,5-dimethoxyphenyl) β-diketones **10** and **8** was treated with 4.2 equiv. of oxidant at room temperature for 22 h, excluding light to avoid *Z* to *E* photoisomerisation. The anticipated acetoxylated naphthalenone **20** was formed in 73% yield based upon the *Z*-β-diketone **10** content of the mixture, accompanied by recovered *E*-β-diketone **8**. The *Z*-β-keto ester **11** corresponding to the *Z*-β-diketone **10** similarly afforded the acetoxylated naphthalenone **21** in 68% yield.

The *Z*-γ,δ-unsaturated ζ-(3,5-dimethoxyphenyl) β-keto ester **14** was stable to laboratory light. Furthermore, it was hoped that the incorporation of a sterically constraining *Z*-alkene in the cyclising chain might compensate for the difficulties encountered earlier in forming an 8-membered hexahydrobenzocyclooctenone ring. Oxidation with manganese(III) acetate under the normal conditions at room temperature for 22 h failed to yield the acetoxylated tetrahydrobenzocyclooctenone **22**, however, giving instead a 13% yield of the tetralin **23** together with 50% recovery of the *Z*-substrate. Raising the reaction temperature to 40 °C for 22 h, or to 80 °C for 1 h, reduced the amount of residual starting material and increased the yield of the tetralin to 20 and 25% respectively, with formation of considerable quantities of a complex mixture.

The tetralin **23** had the molecular formula $C_{19}H_{24}O_7$, containing two hydrogen atoms more than the desired tetrahydrobenzocyclooctenone **22**, and indicating that only one rather than two oxidation steps had occurred despite the obvious addition of acetic acid. The oxidation step clearly involved cyclisation to the aryl ring, since NMR spectroscopy showed that only two *meta*-coupled aromatic protons remained. In contrast to the other benzocycloalkenones described here, this product retained both methylene protons of the parent β-keto ester, but as an AB system (*J* 15.7 Hz) centred at δ 3.65, suggesting the presence of a nearby stereogenic centre. A mutually coupled doublet at δ 4.07 and multiplet at δ 5.21 were assigned to 1-H and 2-H of the tetralin, geminal to the keto ester chain and acetate ester respectively.[20] The methylene protons 3-H_2 and 4-H_2 of the tetralin ring resonated as multiplets at δ 2.10–1.80 and 2.80–2.70.[20] COSY data, decoupling experiments and computer simulations confirmed these assignments, and gave coupling constants of $J_{1,2}$ 4.4, $J_{2,3}$ 6.6 and $J_{2,3'}$ 2.6 Hz. These values indicate, but are not sufficiently definitive to establish, *pseudo*-axial and -equatorial configurations for the keto ester and acetate substituents,[21] although the compound is clearly a single diastereomer. The mass spectrum of the product also contrasted with those of the benzocycloalkenones, and was in agreement with the tetralin structure **23**. The molecular ion at *m*/*z* 364 gave rise to strong fragment ions at *m*/*z* 304 and 249 corresponding to losses of acetic acid and the keto ester chain, and a base peak at *m*/*z* 207 reflecting further loss of ketene from the latter fragment. This tetralin probably arises by initial formation of the β-keto ester radical, which abstracts the ε-hydrogen in a 1,5-hydrogen shift to give the keto allyl radical (Scheme 1). This electrophilic radical could then cyclise to the aromatic ring, regio- and stereo-specific addition of acetic acid to the alkene bond (possibly after migration to the conjugated enone) then yielding the product **23**.



23

Scheme 1 Formation of the tetralin **23**

Conclusions

The previously reported[1] oxidative cyclisation with manganese(III) acetate in acetic acid of δ-aryl-β-dicarbonyl compounds bearing electron-releasing groups on the aromatic ring to α-acetoxylated α-acyl- and α-alkoxy-carbonyl-β-tetralones is equally efficient for the oxidation of the homologous ε-aryl-β-dicarbonyl compounds to α-acetoxylated tetrahydrobenzocycloheptenones, although a higher reaction temperature is necessary. The formation of 8-membered hexahydrobenzocyclooctenone rings by this procedure, however, is inefficient.

The introduction of conjugated unsaturation does not compromise the efficiency of the oxidation of *Z*-γ,δ-unsaturated δ-aryl-β-dicarbonyl compounds to acetoxylated naphthalenones, but *E*-isomers do not react. The homologous *Z*-γ,δ-unsaturated ε-aryl-β-dicarbonyl compounds, even if they could be reasonably obtained, are unlikely to be suitable substrates for the process in view of their facile isomerisation to the *E*-δ,ε-unsaturated isomers. Oxidation of the corresponding bis-homo *Z*-γ,δ-unsaturated ζ-aryl β-keto ester to a tetrahydrobenzocyclooctenone was precluded by the intervention of a radical rearrangement and subsequent cyclisation to a tetralin.

Experimental

General procedures

Details of spectrometry, chromatography, solvents and reagents, and the preparation of dilithio enolates have been provided.[1] Irradiations employed a Philips HPK 125 W water-jacketed high pressure mercury lamp operated at 1.15 A and 125 V.

3,5-Dibenzyloxybenzyl cyanide

The cyanide was prepared by the method of Friedman and Shechter.[22] To a stirred suspension of sodium cyanide (0.62 g, 12.7 mmol) in dry dimethyl sulfoxide (30 cm^3) at 35–40 °C was added 3,5-dibenzyloxybenzyl bromide[1] (4.4 g, 11.5 mmol) so as to maintain this temperature. The reaction was then kept at 35–40 °C for 1.5 h before diluting with water and extracting with diethyl ether. The extracts were washed with hydrochloric acid (5%) and water, dried and evaporated to yield 3,5-dibenzyloxybenzyl cyanide (3.6 g, 95%) as white crystals, mp 84–85 °C (lit.,[23] 85.0–85.5 °C), with IR and ^{1}H NMR spectral data identical to those of Meltzer *et al.*[23]

3,5-Di(benzyloxy)phenylacetic acid

3,5-Di(benzyloxy)phenylacetic acid was prepared from the cyanide by the method of Meltzer *et al.*[23] as white crystals, mp

105–106 °C (lit.,[24] 108 °C), with ^{1}H NMR spectral data identical to those published.[23]

2-(3,5-Dibenzyloxyphenyl)ethanol

3,5-Di(benzyloxy)phenylacetic acid (3.0 g, 8.6 mmol) in dry THF (60 cm^3) was added dropwise to an ice-cold suspension of lithium aluminium hydride (0.9 g, 24 mmol) in THF (60 cm^3). The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The suspension was cooled in ice and quenched by addition of ethyl acetate, then ice. The aqueous layer was extracted with ethyl acetate, and the extracts washed with brine, dried and evaporated. Dry flash chromatography (dichloromethane–ethyl acetate, 2:1) afforded 2-(3,5-dibenzyloxyphenyl)ethanol (2.7 g, 94%) as white crystals, mp 78–80 °C (lit.,[25] 83–84 °C), with IR and ^{1}H NMR spectral data identical to those of Comber *et al.*[25]

1-Bromo-2-(3,5-dibenzyloxyphenyl)ethane

Bromination of 2-(3,5-dibenzyloxyphenyl)ethanol was effected by the method of Kuchar *et al.*[26] Phosphorus tribromide (168 μl, 1.8 mmol) was added to the alcohol (1.2 g, 3.6 mmol) and pyridine (24 μl) in dry diethyl ether (10 cm^3) at −5 °C. The mixture was warmed to room temperature and stirred for 24 h before quenching with ice and extracting with diethyl ether. The extracts were washed with both saturated aqueous sodium hydrogen carbonate and water, dried and evaporated. Flash chromatography (hexane–dichloromethane, 1:1) gave 1-*bromo*-2-(3,5-*dibenzyloxyphenyl*)*ethane* (800 mg, 57%) as white needles, mp 33–34 °C (Found: C, 66.2; H, 5.3; Br, 20.0. Calc. for $C_{22}H_{21}BrO_2$: C, 66.5; H, 5.3; Br, 20.1%); ν_{max}(melt)/cm^{-1} 1594, 1452, 1160, 1057, 697; δ_H(300 MHz)‡ 7.47–7.35 (m, 10 H, 2 × OCH$_2$*Ph*), 6.57 (br s, 1 H, Ar 4-H), 6.50 (br s, 2 H, Ar 2-H and Ar 6-H), 5.06 (s, 4 H, 2 × OC*H*$_2$Ph), 3.58 (t, *J* 7.7, 2 H, CH$_2$), 3.13 (t, *J* 7.7, 2 H, CH$_2$); δ_C(75.5 MHz) 160.1 (ArC-3 and ArC-5), 141.2 (ArC-1), 136.8 (Ph), 128.6 (Ph), 128.0 (Ph), 127.6 (Ph), 107.9 (ArC-2 and ArC-6), 100.4 (ArC-4), 70.1 (2 × O*C*H$_2$Ph), 39.7 (CH$_2$), 32.6 (CH$_2$); *m*/*z* 398 (M$^+$, 1%), 396 (M$^+$, 1), 91 (C_7H_7, 100).

1-(3,5-Dibenzyloxyphenyl)heptane-4,6-dione 5

1-Bromo-2-(3,5-dibenzyloxyphenyl)ethane (470 mg, 1.2 mmol) in dry THF (9 cm^3) was added to 1,3-dilithiopentane-2,4-dione (1.3 mmol) in THF (4 cm^3) (prepared from lithium 2,2,6,6-tetramethylpiperidide and pentane-2,4-dione) at −20 °C under argon. The solution was allowed to equilibrate to room temperature and after 10 h was quenched with 20% aqueous sodium dihydrogen orthophosphate and extracted with ethyl acetate. The extracts were washed with saturated aqueous ammonium chloride, dried and concentrated to an oil. Chromatography (hexane–ethyl acetate, 2:1) provided 3,5-*dibenzyloxystyrene* (4 mg, 11%) (Found: M$^+$, 316.1464. Calc. for $C_{22}H_{20}O_2$: *M*, 316.1463); δ_H(300 MHz) 7.50–7.30 (m, 10 H, 2 × OCH$_2$*Ph*), 6.69 (d, *J* 2.2, 2 H, Ar 2-H and Ar 6-H), 6.62 (dd, *J* 17.6, 11.0, 1 H, =CH), 6.57 (t, *J* 2.2, 1 H, Ar 4-H), 5.73 (d, *J* 17.6, 1 H, =CH$_2$), 5.26 (d, *J* 11.0, 1 H, =CH$_2$), 5.06 (s, 4 H, 2 × OC*H*$_2$Ph); δ_C(75.5 MHz) 160.1 (ArC-3 and ArC-5), 139.7 (ArC-1), 136.9 (=CH or Ph), 136.8 (Ph or =CH), 128.6 (Ph), 128.0 (Ph), 127.5 (Ph), 114.4 (=CH$_2$), 105.6 (ArC-2 and ArC-6), 101.7 (ArC-4), 70.1 (2 × O*C*H$_2$Ph); *m*/*z* 316 (M$^+$, 3%), 91 (C_7H_7, 100).

Further elution gave 1-(3,5-*dibenzyloxyphenyl*)*heptane*-4,6-*dione* **5** (200 mg, 41%) as a colourless oil (Found: C, 77.9; H, 6.9. Calc. for $C_{27}H_{28}O_4$: C, 77.9; H, 6.8%); ν_{max}(film)/cm^{-1} 1716 (m), 1594 (br), 1453, 1158, 737, 699; δ_H(300 MHz) 15.5 (br s, 0.9 H, OH), 7.50–7.30 (m, 10 H, 2 × OCH$_2$*Ph*), 6.49 (br s, 1 H, Ar 4-H), 6.46 (br s, 2 H, Ar 2-H and Ar 6-H), 5.48 (s, 0.9 H, 5-H, enolic form), 5.03 (s, 4 H, 2 × OC*H*$_2$Ph), 3.52 (s, 0.2 H, 5-H$_2$, keto form), 2.60 (t, *J* 7.1, 2 H, 1-H$_2$ or 3-H$_2$), 2.28 (t, *J* 7.1, 2 H, 3-H$_2$ or 1-H$_2$), 2.22 (s, 0.3 H, COCH$_3$, keto form), 2.06 (s, 2.7 H, COCH$_3$, enolic form), 2.00–1.85 (m, 2 H, 2-H$_2$); δ_C(75.5 MHz) 193.9 (CO), 191.2 (CO), 159.9 (ArC-3 and ArC-5), 143.9 (ArC-1), 136.9 (Ph), 128.5 (Ph), 127.9 (Ph), 127.5 (Ph), 107.7 (ArC-2 and ArC-6), 99.9 (ArC-4 or C-5), 99.6 (C-5 or ArC-4), 70.0 (2 × O*C*H$_2$Ph), 37.5 (CH$_2$), 35.4 (CH$_2$), 26.8 (CH$_2$), 24.9 (CO*C*H$_3$); *m*/*z* 416 (M$^+$, 1%), 91 (C_7H_7, 100).

3,5-Dimethoxybenzyl cyanide

Treatment of 3,5-dimethoxybenzyl bromide (3.8 g, 16.5 mmol) with sodium cyanide in the same manner as for 3,5-dibenzyloxybenzyl bromide[22] yielded 3,5-dimethoxybenzyl cyanide (2.9 g, 100%) as white crystals, mp 53–54 °C (lit.,[27] 53–54 °C).

3,5-Dimethoxyphenylacetic acid

Hydrolysis of 3,5-dimethoxybenzyl cyanide (2.85 g, 16 mmol) as for 3,5-dibenzyloxybenzyl cyanide[23] gave 3,5-dimethoxyphenylacetic acid (3.1 g, 98%) as white crystals, mp 103–104 °C (lit.,[28] 103.5–104.5 °C).

2-(3,5-Dimethoxyphenyl)ethanol

Reduction of 3,5-dimethoxyphenylacetic acid (2.8 g, 14.3 mmol) with lithium aluminium hydride as for 3,5-dibenzyloxyphenylacetic acid afforded after dry flash chromatography (hexane–ethyl acetate, 1:1) 2-(3,5-dimethoxyphenyl)ethanol[29] (2.6 g, 100%) as a pale yellow oil.

1-Bromo-2-(3,5-dimethoxyphenyl)ethane

Bromination of 2-(3,5-dimethoxyphenyl)ethanol (2.2 g, 12 mmol) with phosphorus tribomide, employing the procedure of Bhati,[29] gave after dry flash chromatography (hexane–ethyl acetate, 3:1) 1-bromo-2-(3,5-dimethoxyphenyl)ethane[30] as a pale yellow oil (1.57 g, 53%), with ^{1}H NMR spectral data identical to those of Crombie *et al.*[30]

1-(3,5-Dimethoxyphenyl)heptane-4,6-dione 6

1-Bromo-2-(3,5-dimethoxyphenyl)ethane (50 mg, 0.20 mmol) in dry THF (1.6 cm^3) was added to 1,3-dilithiopentane-2,4-dione (0.44 mmol) in THF (1.4 cm^3) (prepared from lithium 2,2,6,6-tetramethylpiperidide and pentane-2,4-dione) at −20 °C under argon. The reaction mixture was allowed to warm to room temperature, and after 3 h was worked-up as for the diketone **5**. Purification of the crude product by chromatography (hexane–ethyl acetate, 1:1) gave 1-(3,5-*dimethoxyphenyl*)-*heptane*-4,6-*dione* **6** (26 mg, 48%) as a pale yellow oil (Found: C, 68.4; H, 7.5. Calc. for $C_{15}H_{20}O_4$: C, 68.2; H, 7.6%); ν_{max}(film)/cm^{-1} 1726 (m), 1706 (m), 1600 (br), 1462, 1429, 1206, 1152; δ_H(300 MHz) 15.50 (br s, 0.9 H, OH), 6.35 (m, 3 H, Ar 2-H, Ar 4-H and Ar 6-H), 5.49 (s, 0.9 H, 5-H, enolic form), 3.79 (s, 6 H, 2 × OCH$_3$), 3.55 (s, 0.2 H, 5-H$_2$, keto form), 2.60 (t, *J* 7.5, 2 H, 1-H$_2$ or 3-H$_2$), 2.30 (t, *J* 7.5, 2 H, 3-H$_2$ or 1-H$_2$), 2.23 (s, 0.3 H, COCH$_3$, keto form), 2.06 (s, 2.7 H, COCH$_3$, enolic form), 2.00–1.90 (m, 2 H, 2-H$_2$); δ_C(75.5 MHz) (enolic form) 193.8 (CO), 191.3 (CO), 160.8 (ArC-3 and ArC-5), 143.9 (ArC-1), 106.5 (ArC-2 and ArC-6), 99.9 (ArC-4 or C-5), 98.0 (C-5 or ArC-4), 55.2 (2 × OCH$_3$), 37.5 (CH$_2$), 35.5 (CH$_2$), 26.9 (CH$_2$), 24.9 (CO*C*H$_3$); *m*/*z* 264 (M$^+$, 24%), 165 (ArCH$_2$CH$_2^+$, 67), 164 (100), 152 (83), 113 (36), 100 (34), 85 (CH$_3$COCH$_2$CO$^+$, 70).

(*E*)-3-(3,5-Dimethoxyphenyl)propenoic acid

The acid was prepared by Perkin condensation.[31] A mixture of 3,5-dimethoxybenzaldehyde (4.0 g, 24 mmol), acetic anhydride (3.5 cm^3, 35 mmol) and freshly fused potassium acetate (1.4 g) was stirred under argon at 160 °C for 1 h and then at 170–180 °C for 3 h. The mixture was cooled to 80–100 °C and hot water (~80 °C, 12 cm^3) was added with stirring, followed by saturated aqueous sodium carbonate until alkaline. After 3 h, the mixture was washed with chloroform and acidified with concentrated hydrochloric acid. The organic material was

‡ *J* Values are given in Hz.

extracted with chloroform, dried, evaporated and recrystallised from water–ethanol (3:1), to give (*E*)-3-(3,5-dimethoxyphenyl)propenoic acid (3.6 g, 72%) as pale yellow crystals, mp 174–175 °C (lit.,[32] 174–175 °C), with ^{1}H NMR spectral data in agreement with those published.[32]

3-(3,5-Dimethoxyphenyl)propan-1-ol

(*E*)-3-(3,5-Dimethoxyphenyl)propenoic acid was reduced using the procedure of Nystrom and Brown for sparingly diethyl ether-soluble compounds.[33] To a suspension of lithium aluminium hydride (4.0 g, 0.1 mol) in anhydrous diethyl ether (180 cm^3) at reflux was added (*E*)-3-(3,5-dimethoxyphenyl)-propenoic acid (3.0 g, 14 mmol) *via* a Soxhlet apparatus. After 22 h the reaction mixture was cooled in ice and the excess of reducing agent destroyed by the addition of ethyl acetate (30 cm^3), followed by ice. Sulfuric acid (1 M) was added until the aqueous layer became clear. The aqueous layer was extracted with ethyl acetate and the extracts dried, evaporated, and subjected to dry flash chromatography (increasing polarity from dichloromethane to dichloromethane–ethyl acetate, 1:1) to afford 3-(3,5-dimethoxyphenyl)prop-2-en-1-ol (80 mg, 3%) as white needles, mp 51–52 °C (lit.,[34] 54–55 °C), with ^{1}H NMR spectral data consistent with those of Klemm *et al.*[34]

Further elution provided 3-(3,5-dimethoxyphenyl)propan-1-ol (2.1 g, 74%) as a pale yellow viscous oil, with ^{1}H NMR data consistent with values published by Klemm *et al.*[34]

1-Bromo-3-(3,5-dimethoxyphenyl)propane

A mixture of 3-(3,5-dimethoxyphenyl)propan-1-ol (400 mg, 2.0 mmol), carbon tetrabromide (1.35 g, 4.0 mmol) and triphenylphosphine (1.0 g, 4.0 mmol) in acetonitrile (6 cm^3) was stirred at 80 °C for 1.5 h. The acetonitrile was removed under vacuum and the residue purified by dry flash chromatography (hexane–dichloromethane, 1:1) to afford 1-*bromo*-3-(3,5-*dimethoxyphenyl*)*propane* (508 mg, 96%) as a colourless oil (Found: C, 51.1; H, 6.1; Br, 30.9. Calc. for $C_{11}H_{15}BrO_2$: C, 51.0; H, 5.8; Br, 30.8%); ν_{max}(film)/cm^{-1} 2938, 1596, 1462, 1429, 1355, 1295, 1206, 1161, 1068, 830; δ_H(300 MHz) 6.36 (d, *J* 2.2, 2 H, Ar 2-H and Ar 6-H), 6.32 (t, *J* 2.2, 1 H, Ar 4-H), 3.78 (s, 6 H, 2 × OCH_3), 3.40 (t, *J* 6.5, 2 H, CH_2Br), 2.72 (t, *J* 7.3, 2 H, 3-H_2), 2.25–2.10 (m, 2 H, 2-H_2); δ_C(75.5 MHz) 161.1 (ArC-3 and ArC-5), 143.1 (ArC-1), 106.6 (ArC-2 and ArC-6), 98.0 (ArC-4), 55.1 (2 × OCH_3), 34.0 (CH_2), 33.7 (CH_2), 32.9 (CH_2); *m*/*z* 260 (M^+, 8%), 258 (M^+, 8), 179 (M^+ − Br, 7), 152 (100).

1-(3,5-Dimethoxyphenyl)octane-5,7-dione 7

1-Bromo-3-(3,5-dimethoxyphenyl)propane (410 mg, 1.6 mmol) in dry THF (8 cm^3) was added dropwise to 1,3-dilithiopentane-2,4-dione (3.2 mmol) in THF (20 cm^3) (prepared from lithium 2,2,6,6-tetramethylpiperidide and pentane-2,4-dione) at −20 °C under argon. The reaction mixture was slowly warmed to room temperature and stirred for 20 h. Work-up as for the diketone **5** followed by dry flash chromatography (hexane–ethyl acetate, 1:1), afforded 1-(3,5-*dimethoxyphenyl*)*octane*-5,7-*dione* **7** (377 mg, 86%) as a colourless oil (Found: C, 69.0; H, 7.9. Calc. for $C_{16}H_{22}O_4$: C, 69.0; H, 8.0%); ν_{max}(film)/cm^{-1} 2938, 1726 (m), 1705 (m), 1600 (br), 1462, 1429, 1349, 1323, 1293, 1205, 1151, 1070, 1059, 831; δ_H(300 MHz) 13.30 (br s, 0.9 H, OH), 6.34 (br s, 2 H, Ar 2-H and Ar 6-H), 6.31 (br s, 1 H, Ar 4-H), 5.48 (s, 0.9 H, 6-H, enolic form), 3.79 (s, 6 H, 2 × OCH_3), 3.56 (s, 0.2 H, 6-H_2, keto form), 2.60–2.50 (m, 2 H, 1-H_2 or 4-H_2), 2.35–2.25 (m, 2 H, 4-H_2 or 1-H_2), 2.24 (s, 0.3 H, $COCH_3$, keto form), 2.05 (s, 2.7 H, $COCH_3$, enolic form), 1.70–1.60 (m, 4 H, 2-H_2 and 3-H_2); δ_C(75.5 MHz) (enolic form) 194.3 (s, CO), 192.0 (s, CO), 161.0 (s, ArC-3 and ArC-5), 144.9 (s, ArC-1), 106.6 (d, ArC-2 and ArC-6), 99.9 (d, ArC-4 or C-6), 97.7 (d, C-6 or ArC-4), 55.1 (q, 2 × OCH_3), 37.9 (t, CH_2), 35.8 (t, CH_2), 30.5 (t, CH_2), 25.1 (t, CH_2), 24.8 (q, $COCH_3$); *m*/*z* 278 (M^+, 17%), 165 (M^+ − $CH_3COCH_2COCH_2CH_2$, 26), 152 (100), 85 ($CH_3COCH_2CO^+$, 27), 43 (CH_3CO^+, 65).

(*Z*)-3-(3,5-Dimethoxyphenyl)propenoic acid

Isomerisation of the (*E*)-acid was effected by the method of Lindenfors.[35] (*E*)-3-(3,5-Dimethoxyphenyl)propenoic acid (180 mg, 0.86 mmol) in spectroscopic grade ethanol (200 cm^3) in a quartz tube was irradiated at room temperature with a water-cooled high pressure mercury lamp for 2 h. The solvent was removed under vacuum in the absence of light and heat to give a mixture of (*Z*)- and (*E*)-3-(3,5-dimethoxyphenyl)propenoic acids (180 mg, 100%; *Z*:*E* 4:1); δ_H(300 MHz) (*Z* isomer) 6.98 (d, *J* 12.7, 1 H, =CH), 6.80 (d, *J* 2.3, 2 H, Ar 2-H and Ar 6-H), 6.46 (t, *J* 2.3, 1 H, Ar 4-H), 5.97 (d, *J* 12.7, 1 H, =CH), 3.80 (s, 6 H, 2 × OCH_3); δ_C(75.5 MHz) 170.3 (CO), 160.3 (ArC-3 and ArC-5), 145.4 (=C), 136.1 (ArC-1), 118.9 (=C), 107.8 (ArC-2 and ArC-6), 101.9 (ArC-4), 55.4 (2 × OCH_3).

(*Z*)-3-(3,5-Dimethoxyphenyl)propenoyl chloride

To the mixture of (*Z*)- and (*E*)-3-(3,5-dimethoxyphenyl)-propenoic acids (180 mg, 0.86 mmol; *Z*:*E* 4:1) in dry dichloromethane (9.0 cm^3) under argon in the dark was added oxalyl chloride (87 µl, 1.0 mmol). The solution was stirred in the dark for 3 h, then evaporated to dryness to provide a mixture of (*Z*)- and (*E*)-3-(3,5-dimethoxyphenyl)propenoyl chlorides (*Z*:*E* 4:1); δ_H(300 MHz) 7.76 (d, *J* 15.2, ~0.2 H, =CH, *E*), 6.88 (d, *J* 12.4, ~0.8 H, =CH, *Z*), 6.81 (d, *J* 2.1, ~1.6 H, Ar 2-H and Ar 6-H, *Z*), 6.69 (d, *J* 2.1, ~0.4 H, Ar 2-H and Ar 6-H, *E*), 6.61 (d, *J* 15.2, ~0.2 H, =CH, *E*), 6.57 (t, *J* 2.1, ~0.2 H, Ar 4-H, *E*), 6.53 (t, *J* 2.1, 0.8 H, Ar 4-H, *Z*), 6.24 (d, *J* 12.4, ~0.8 H, =CH, *Z*), 3.83 (s, ~1.2 H, 2 × OCH_3, *E*), 3.81 (s, ~4.8 H, 2 × OCH_3, *Z*); δ_C(75.5 MHz) 166.2 (CO), 164.3 (CO), 161.2 (ArC-3 and ArC-5, *E*), 160.6 (ArC-3 and ArC-5, *Z*), 150.8 (=C, *E*), 146.8 (=C, *Z*), 134.9 (ArC-1, *Z*), 134.8 (ArC-1, *E*), 124.2 (=C, *Z*), 122.9 (=C, *E*), 108.2 (ArC-2 and ArC-6, *Z*), 106.9 (ArC-2 and ArC-6, *E*), 104.3 (ArC-4, *E*), 103.5 (ArC-4, *Z*), 55.5 (2 × OCH_3, *Z*), 55.4 (2 × OCH_3, *E*); *m*/*z* 228 (M^+, 7%), 226 (M^+, 21), 191 (M^+ − Cl, 100).

(*Z*)- and (*E*)-1-(3,5-Dimethoxyphenyl)hex-1-ene-3,5-diones 10 and 8

The enediones **10** and **8** were synthesised using a modification of the procedure of Seebach *et al.*[12] *n*-Butyllithium (0.61 cm^3, 1.4 M, 0.86 mmol) was added dropwise to a solution of 2,2,6,6-tetramethylpiperidine (145 µl, 0.86 mmol) in dry THF (2.2 cm^3) at −50 °C under argon. The pale yellow solution was stirred at room temperature for 30 min, then cooled to −78 °C. To this was rapidly added dry acetone (63 µl, 0.86 mmol). The colourless solution was stirred for 30 min at −78 °C, then cooled to −90 °C and slowly transferred (*via* Teflon tubing) to a solution of (*Z*)- and (*E*)-3-(3,5-dimethoxyphenyl)propenyol chlorides (0.86 mmol; *Z*:*E* 4:1) in THF (2.2 cm^3) in the dark at −90 °C. The resulting bright orange solution was stirred for 1 h at −90 °C, then worked up as for the diketone **5**, except that light was rigorously excluded. Dry flash chromatography (hexane–ethyl acetate, 2:1) of the crude product, with exclusion of light, provided the (*Z*)- and (*E*)-1-(3,5-*dimethoxyphenyl*)*hex*-1-*ene*-3,5-*diones* **10** and **8** (120 mg, 56% based on the starting cinnamic acid mixture; *Z*:*E* 3:2 from ^{1}H NMR spectroscopy) as a bright yellow solid; *m*/*z* 248 (M^+, 45%), 205 (M^+ − CH_3CO, 77), 191 (M^+ − CH_3COCH_2, 80), 170 (32), 148 (30), 141 (40), 91 (20), 85 ($CH_3COCH_2CO^+$, 21), 77 (100). The sample did not isomerise significantly to the (*E*)-isomer if kept in the dark.

Analysis of the mixture gave the following data for the (*Z*)-enedione **10**; δ_H(300 MHz) 15.5 (br s, 1 H, OH), 6.80 (d, *J* 12.7, 1 H, =CH), 6.68 (d, *J* 2.2, 2 H, Ar 2-H and Ar 6-H), 6.45 (t, *J* 2.2, 1 H, Ar 4-H), 5.93 (d, *J* 12.7, 1 H, =CH), 5.57 (s, 1 H, 4-H), 3.78 (s, 6 H, 2 × OCH_3), 2.08 (s, 3 H, $COCH_3$); δ_C(75.5 MHz) 195.6 (CO), 180.5 (CO), 160.3 (ArC-3 and ArC-5), 140.3 (=C), 137.4 (ArC-1), 125.3 (=C), 107.6 (ArC-2 and ArC-6), 102.3 (ArC-4 or C-4), 101.3 (C-4 or ArC-4), 55.5 (2 × OCH_3), 26.3 ($COCH_3$); and for the (*E*)-enedione **8**; δ_H(300 MHz) 9.90 (br s, 1 H, OH), 7.50 (d, *J* 15.8, 1 H, 1-H or 2-H), 6.65 (d, *J* 2.2,

2 H, Ar 2-H and Ar 6-H), 6.47 (t, *J* 2.2, 1 H, Ar 4-H), 6.42 (d, *J* 15.8, 1 H, 2-H or 1-H), 5.65 (s, 1 H, 4-H), 3.81 (s, 6 H, 2 × OCH_3), 2.16 (s, 3 H, $COCH_3$); δ_C(75.5 MHz) 198.2 (C-5), 176.5 (C-3), 161.0 (ArC-3 and ArC-5), 139.7 (=C), 136.9 (ArC-1), 123.2 (=C), 105.8 (ArC-2 and ArC-6), 102.1 (ArC-4 or C-4), 101.3 (C-4 or ArC-4), 55.4 (2 × OCH_3), 27.2 ($CO\mathit{C}H_3$).

Ethyl (*E*)- and (*Z*)-5-(3,5-dimethoxyphenyl)-3-oxopent-4-enoates 9 and 11

The isomeric β-keto esters **9** and **11** were prepared by modification of the procedure of Pietrusiewicz and Monkiewicz.[14] To a stirred solution of the ylide[36] **12** (0.47 g, 1.2 mmol) in THF (9 cm^3) was added sodium hydride (100 mg, 60% dispersion in oil, 2.4 mmol) followed by 3,5-dimethoxybenzaldehyde (200 mg, 1.2 mmol). The flask was covered in aluminium foil and 1 drop of water was added. After 40 min, ethyl acetate (2.5 cm^3) was added to the clear orange solution, followed by water saturated with carbon dioxide (2.5 cm^3). Solid carbon dioxide was then added until the pH of the aqueous layer was 6–7. The aqueous layer was extracted with ethyl acetate and the extracts were dried and evaporated. Dry flash chromatography (dichloromethane) of the crude material afforded *ethyl* (*E*)-5-(3,5-*dimethoxyphenyl*)-3-*oxopent*-4-*enoate* **9** (260 mg, 78%) as a pale yellow solid (Found: C, 64.8; H, 6.8. Calc. for $C_{15}H_{18}O_5$: C, 64.7; H, 6.5%); ν_{max}(film)/cm^{1} 1598, 1460, 1427, 1238, 1206, 1157; δ_H(300 MHz) 12.0 (d, *J* 1.4, ~0.5 H, OH), 7.49 (d, *J* 16.1, ~0.5 H, 5-H, keto form), 7.34 (d, *J* 15.8, ~0.5 H, 5-H, enolic form), 6.75 (d, *J* 16.1, ~0.5 H, 4-H, keto form), 6.68 (d, *J* 2.2, ~0.5 H, Ar 2-H and Ar 6-H), 6.63 (d, *J* 2.2, ~0.5 H, Ar 2-H and Ar 6-H), 6.51 (t, *J* 2.2, ~0.5 H, Ar 4-H), 6.44 (t, *J* 2.2, ~0.5 H, Ar 4-H), 6.39 (dd, *J* 15.8, 1.4, ~0.5 H, 4-H, enolic form), 5.16 (s, ~0.5 H, 2-H, enolic form), 4.22 (q, *J* 7.1, ~1 H, $OC\mathit{H}_2CH_3$), 3.80 (s, 6 H, 2 × OCH_3), 3.69 (s, ~1 H, 2-H_2, keto form), 1.31 (t, *J* 7.1, ~1.5 H, $OCH_2C\mathit{H}_3$), 1.28 (t, *J* 7.1, ~1.5 H, $OCH_2C\mathit{H}_3$); δ_C(75.5 MHz) 192.0 (CO), 172.8 (CO), 168.9 (CO), 167.3 (CO), 161.0 (ArC-3 and ArC-5), 160.9 (ArC-3 and ArC-5), 144.6, 137.2, 136.7, 135.8, 125.6 (=C), 122.3 (=C), 106.3 (ArC-2 and ArC-6), 105.4 (ArC-2 and ArC-6), 103.1 (ArC-4), 101.6 (ArC-4), 92.1 (C-2, enolic form), 61.4 ($O\mathit{C}H_2CH_3$), 60.2 ($O\mathit{C}H_2CH_3$), 55.4 (2 × OCH_3), 55.3 (2 × OCH_3), 47.5 (C-2, keto form), 14.2 ($OCH_2\mathit{C}H_3$), 14.1 ($OCH_2\mathit{C}H_3$); *m*/*z* 278 (M^+, 28%), 204 (29), 191 (100).

Further elution afforded *ethyl* (*Z*)-5-(3,5-*dimethoxyphenyl*)-3-*oxopent*-4-*enoate* **11** (30 mg, 9%) as a pale yellow solid (Found: M^+, 278.1155. Calc. for $C_{15}H_{18}O_5$ *M*, 278.1154); δ_H(300 MHz) 12.1 (d, *J* 1.0, ~0.2 H, OH), 6.92 (d, *J* 12.6, ~0.8 H, 5-H, keto form), 6.71 (d, *J* 12.9, ~0.2 H, 5-H, enolic form), 6.69 (d, *J* 2.1, ~1.6 H, Ar 2-H and Ar 6-H, keto form), 6.63 (d, *J* 2.3, ~0.2 H, Ar 2-H and Ar 6-H, enolic form), 6.47 (t, *J* 2.1, ~0.8 H, Ar 4-H, keto form), 6.41 (t, *J* 2.3, ~0.2 H, Ar 4-H, enolic form), 6.22 (d, *J* 12.6, ~0.8 H, 4-H, keto form), 5.88 (dd, *J* 12.9, 1.0, ~0.2 H, 4-H, enolic form), 5.14 (s, ~0.2 H, 2-H, enolic form), 4.20 (q, *J* 7.2, ~0.8 H, $OC\mathit{H}_2CH_3$, enolic form), 4.17 (q, *J* 7.1, ~3.2 H, $OC\mathit{H}_2CH_3$, keto form), 3.80 (s, ~4.8 H, 2 × OCH_3, keto form), 3.78 (s, ~1.2 H, 2 × OCH_3, enolic form), 3.48 (s, ~1.6 H, 2-H_2, keto form), 1.28 (t, *J* 7.2, ~0.6 H, $OCH_2C\mathit{H}_3$, enolic form), 1.25 (t, *J* 7.1, ~2.4 H, $OCH_2C\mathit{H}_3$, keto form); δ_C(75.5 MHz) 194.5 (CO), 172.8 (CO), 169.8 (CO), 167.3 (CO), 160.6 (ArC-3 and ArC-5, keto form), 160.2 (ArC-3 and ArC-5, enolic form), 141.8, 138.0, 136.6, 127.9, 123.6, 107.5 (ArC-2 and ArC-6, enolic form), 107.4 (ArC-2 and ArC-6, keto form), 102.1 (ArC-4, keto form), 100.7 (ArC-4, keto form), 93.2 (C-2, enolic form), 61.3 ($O\mathit{C}H_2CH_3$, keto form), 60.2 ($O\mathit{C}H_2CH_3$, enolic form), 55.4 (2 ×OCH_3), 49.6 (C-2, keto form), 14.3 ($OCH_2\mathit{C}H_3$, enolic form), 14.1 ($OCH_2\mathit{C}H_3$, keto form); *m*/*z* 278 (M^+, 22%), 204 (26), 191 (100).

3-(3,5-Dimethoxyphenyl)propanal

3-(3,5-Dimethoxyphenyl)propan-1-ol (1.0 g, 5.1 mmol) was oxidised following the procedure of Omura and Swern[37] to afford 3-(3,5-*dimethoxyphenyl*)*propanal* in quantitative yield as a colourless oil (Found: C, 68.1; H, 7.2. Calc. for $C_{11}H_{14}O_3$: C, 68.0; H, 7.3%); ν_{max}(film)/cm^{-1} 1724, 1597, 1206, 1151; δ_H(300 MHz) 9.83 (s, 1 H, CHO), 6.35 (br s, 2 H, Ar 2-H and Ar 6-H), 6.32 (br s, 1 H, Ar 4-H), 3.78 (s, 6 H, 2 × OCH_3), 2.90 (t, *J* 6.6, 2 H, CH_2), 2.77 (t, *J* 6.6, 2 H, CH_2); δ_C(75.5 MHz) 201.5 (CO), 161.0 (ArC-3 and ArC-5), 142.8 (ArC-1), 106.4 (ArC-2 and ArC-6), 98.2 (ArC-4), 55.3 (2 × OCH_3), 45.1 (C-2), 28.4 (C-3); *m*/*z* 194 (M^+, 21%), 166 ($M^+ - CO$, 100), 151 ($M^+ - CH_2$-CHO, 34).

Ethyl (*Z*)-7-(3,5-dimethoxyphenyl)-3-oxohept-4-enoate 14

The β-keto ester **14** was prepared similarly to the β-keto ester mixture **9** and **11** by modification of the procedure of Pietrusiewicz and Monkiewicz.[14] To a stirred solution of the ylide[36] **12** (2.0 g, 5.1 mmol) in THF (25 cm^3) was added sodium hydride (420 mg, 60% dispersion in oil, 10 mmol), followed by 3-(3,5-dimethoxyphenyl)propanal (0.98 g, 5.0 mmol) in THF (13 cm^3). The flask was covered in aluminium foil and 1 drop of water was added. After 75 min ethyl acetate (25 cm^3) was added to the orange solution, followed by water saturated with carbon dioxide until the pH of the aqueous layer was 6–7. The mixture was extracted with ethyl acetate, and the extracts dried and concentrated to a yellow oil. Dry flash chromatography (hexane–ethyl acetate, 3:1) gave *ethyl* (*Z*)-7-(3,5-*dimethoxyphenyl*)-3-*oxohept*-4-*enoate* **14** (970 mg, 63%) as a colourless oil (Found: C, 66.5; H, 7.3. Calc. for $C_{17}H_{22}O_5$: C, 66.6; H, 7.2%); λ_{max}(EtOH)/nm 280; λ_{max}(EtOH, apparent pH 10)/nm 310 (log ε 4.32); ν_{max}(film)/cm^{-1} 1740, 1692, 1657, 1596, 1464, 1428, 1315, 1295, 1234, 1206, 1151, 1071, 1035; δ_H(300 MHz) 12.14 (d, *J* 1.6, ~0.3 H, OH), 6.39 (d, *J* 2.3, ~0.6 H, Ar 2-H and Ar 6-H, enolic form), 6.37 (d, *J* 2.2, ~1.4 H, Ar 2-H and Ar 6-H, keto form), 6.35–6.20 (m, ~2.4 H, Ar 4-H, and 4-H and 5-H, keto form), 5.92 (dt, *J* 11.8, 7.4, ~0.3 H, 5-H, enolic form), 5.67 (dm, *J* 11.8, ~0.3 H, 4-H, enolic form), 5.01 (s, ~0.3 H, 2-H, enolic form), 4.21 (q, *J* 7.1, ~0.6 H, $OC\mathit{H}_2CH_3$, enolic form), 4.20 (q, *J* 7.1, ~1.4 H, $OC\mathit{H}_2CH_3$, keto form), 3.78 (s, 6 H, 2 × OCH_3), 3.48 (s, ~1.4 H, 2-H_2, keto form), 3.10–2.90 (m, 2 H, 6-H_2), 2.71 (br t, *J* 7.4, 2 H, 7-H_2), 1.30 (t, *J* 7.1, ~0.9 H, $OCH_2C\mathit{H}_3$, enolic form), 1.28 (t, *J* 7.1, ~2.1 H, $OCH_2C\mathit{H}_3$, keto form); δ_C(75.5 MHz) 192.5 (CO), 173.0 (CO), 171.3 (CO), 167.3 (CO), 160.7 (ArC-3 and ArC-5), 149.7 (=C), 143.3 (ArC-1), 141.9 (=C), 125.8 (=C), 123.4 (=C), 106.4 (ArC-2 and ArC-6), 98.0 (ArC-4, keto form), 97.9 (ArC-4, enolic form), 92.0 (C-2, enolic form), 61.2 ($O\mathit{C}H_2CH_3$, keto form), 60.0 ($O\mathit{C}H_2CH_3$, enolic form), 55.2 (2 × OCH_3), 50.5 (C-2, keto form), 35.8 (CH_2, enolic form), 35.1 (CH_2, keto form), 30.8 (CH_2, enolic form), 30.6 (CH_2, keto form), 14.2 ($OCH_2\mathit{C}H_3$, enolic form), 14.0 ($OCH_2\mathit{C}H_3$, keto form); *m*/*z* 306 (M^+, 4%), 219 (20), 191 (15), 177 (100), 151 (49).

Ethyl (*E*)-6-(3,5-dimethoxyphenyl)-3-oxohex-5-enoate 15

2-(3,5-Dimethoxyphenyl)ethanol (200 mg, 1.1 mmol) in dry dichloromethane (1.6 cm^3) was added rapidly to a suspension of pyridinium chlorochromate (0.34 g, 1.6 mmol) in dichloromethane (2.2 cm^3). After 3 h, ethyl acetate was added, the suspension filtered through Celite, and the filtrate evaporated to provide crude 3,5-dimethoxyphenylacetaldehyde as a viscous brown oil. To this material in THF (5 cm^3) was added the ylide[36] **12** (0.47 g, 1.2 mmol) in THF (4 cm^3), and sodium hydride (100 mg, 60% dispersion in oil, 2.4 mmol). The reaction vessel was covered in aluminium foil and 1 drop of water added. After 35 min the reaction mixture was diluted with ethyl acetate (5 cm^3), and quenched by adding water saturated with carbon dioxide (5 cm^3), followed by solid carbon dioxide. The aqueous layer was extracted with ethyl acetate and the extracts were dried, evaporated, subjected to dry flash chromatography (dichloromethane) to remove salts and then gravity chromatography (hexane–ethyl acetate, 3:1) to give, in order of elution, ethyl (*E*)-5-(3,5-dimethoxyphenyl)-3-oxopent-4-enoate **9** [20 mg, 7% based on the 2-(3,5-dimethoxyphenyl)ethanol]

with spectroscopic data as described above, and *ethyl* (*E*)-6-(3,5-*dimethoxyphenyl*)-3-*oxohex*-5-*enoate* **15** [38 mg, 12% based on the 2-(3,5-dimethoxyphenyl)ethanol] (Found: M^+, 292.1310. Calc. for $C_{16}H_{20}O_5$: *M*, 292.1311); λ_{max}(EtOH)/nm 260; λ_{max}(EtOH, apparent pH 10)/nm 280; δ_H(300 MHz) 6.54 (d, *J* 2.3, 2 H, Ar 2-H and Ar 6-H), 6.45 (d, *J* 15.9, 1 H, 5-H), 6.39 (t, *J* 2.3, 1 H, Ar 4-H), 6.29 (dt, *J* 15.9, 6.6, 1 H, 6-H), 4.22 (q, *J* 7.1, 2 H, OCH_2CH_3), 3.81 (s, 6 H, 2 × OCH_3), 3.53 (s, 2 H, CH_2-2), 3.47 (d, *J* 6.6, CH_2-4), 1.29 (t, *J* 7.1, 3 H, OCH_2CH_3); δ_C(75.5 MHz) 200.8 (CO), 167.1 (CO), 161.0 (ArC-3 and ArC-5), 138.7 (ArC-1), 134.6 (=C), 121.5 (=C), 104.5 (ArC-2 and ArC-6), 100.1 (ArC-4), 61.6 (OCH_2CH_3), 55.4 (2 × OCH_3), 48.9 (CH_2), 46.9 (CH_2), 14.2 (OCH_2CH_3); *m*/*z* 292 (M^+, 14%), 204 (52), 178 (29), 177 ($M^+ - CH_3CH_2OCOCH_2CO$, 100).

Oxidation of 1-(3,5-dibenzyloxyphenyl)heptane-4,6-dione 5 with manganese(III) acetate

The β-diketone **5** (50 mg, 0.12 mmol) and anhydrous manganese(III) acetate (0.5 mmol) were stirred in dry degassed acetic acid (0.9 cm^3) for 22 h at room temperature under argon. The brown suspension was diluted with water and extracted with ethyl acetate. The extracts were dried and evaporated, and the crude product chromatographed (acid-washed silica gel; increasing polarity from hexane–ethyl acetate, 1:1, to ethyl acetate) to give starting material (41 mg, 82% recovery), followed by 4-(3,5-*dibenzyloxyphenyl*)*butanoic acid* (4 mg, 9%) (Found: M^+, 376.1674. Calc. for $C_{24}H_{24}O_4$: *M*, 376.1675); δ_H(300 MHz) 7.50–7.30 (m, 10 H, 2 × OCH_2Ph), 6.48 (br s, 1 H, Ar 4-H), 6.45 (br s, 2 H, Ar 2-H and Ar 4-H), 5.02 (s, 4 H, 2 × OCH_2Ph), 2.62 (t, *J* 7.3, 2 H, 2-H_2 or 4-H_2), 2.36 (t, *J* 7.3, 2 H, 4-H_2 or 2-H_2), 2.00–1.90 (m, 2 H, 3-H_2); δ_C(75.5 MHz) 180.0 (CO), 160.0 (ArC-3 and ArC-5), 143.6 (ArC-1), 136.9 (Ph), 128.6 (Ph), 128.0 (Ph), 127.6 (Ph), 107.8 (ArC-2 and ArC-6), 99.7 (ArC-4), 70.1 (2 × OCH_2Ph), 35.2 (CH_2), 32.8 (CH_2), 29.7 (CH_2); *m*/*z* 376 (M^+, 1%), 91 ($C_7H_7^+$, 100).

5-Acetoxy-5-acetyl-2,4-dibenzyloxy-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-6-one 17

The β-diketone **5** (70 mg, 0.17 mmol) was treated with manganese(III) acetate as above, except that the reaction mixture was maintained at 60–70 °C. Dry flash chromatography of the brown reaction product (hexane–ethyl acetate, 3:1) afforded 5-*acetoxy*-5-*acetyl*-2,4-*dibenzyloxy*-6,7,8,9-*tetrahydro*-5H-*benzocyclohepten*-6-*one* **17** (53 mg, 76%) as pale yellow crystals, mp 157–159 °C (Found: C, 73.4; H, 6.0. Calc. for $C_{29}H_{28}O_6$: C, 73.7; H, 6.0%); ν_{max}(KBr)/cm^{-1} 1746, 1715, 1600, 1156; δ_H(300 MHz) (assignments confirmed with absolute value COSY and filtered double quantum COSY data) 7.50–7.30 (m, 10 H, 2 × OCH_2Ph), 6.55 (d, *J* 2.4, 1 H, 1-H or 3-H), 6.49 (d, *J* 2.4, 1 H, 3-H or 1-H), 5.05 (s, 2 H, 2-OCH_2Ph), 5.01 and 4.85 (each d, *J* 10.8, 1 H, 4-OCH_2Ph, AB system), 3.61 (ddd, *J* ~14, ~14, 6.0, 1 H, 9-H), 3.30 (dd, *J* 21.6, 10.2, 1 H, 7-H), 2.64 (ddd, *J* ~14, 5.5, 2.2, 1 H, 9-H), 2.30 (m, 1 H, 7-H, 2nd order), 2.20–2.00 (m, 2 H, 8-H_2), 2.16 (s, 3 H, $COCH_3$), 1.97 (s, 3 H, $COCH_3$); δ_C(75.5 MHz) 202.9 (CO), 201.3 (CO), 167.9 ($OCOCH_3$), 160.6 (C-2 or C-4), 157.8 (C-4 or C-2), 144.7 (C-4a or C-9a), 136.6 (Ph), 135.6 (Ph), 128.6 (Ph), 128.5 (Ph), 128.4 (Ph), 128.3 (Ph), 128.1 (Ph), 127.6 (Ph), 117.0 (C-9a or C-4a), 108.7 (C-1 or C-3), 99.2 (C-3 or C-1), 97.5 (C-5), 71.0 (OCH_2Ph), 70.1 (OCH_2Ph), 34.2 (CH_2), 32.8 (CH_2), 26.0 ($COCH_3$), 23.2 (CH_2), 21.5 ($COCH_3$); *m*/*z* 472 (M^+, 0.2%), 430 ($M^+ - CH_2CO$, 0.2), 387 ($M^+ - CH_2CO - CH_3CO$, 0.3), 91 ($C_7H_7^+$, 100).

5-Acetoxy-5-acetyl-6,7,8,9-tetrahydro-2,4-dimethoxy-5*H*-benzocyclohepten-6-one 18

(a) The β-diketone **6** (59 mg, 0.22 mmol) in acetic acid (1.6 cm^3) was treated with manganese(III) acetate (0.92 mmol) at room temperature for 22 h as for the diketone **5**. Dry flash chromatography of the brown product (hexane–ethyl acetate, 2:1) afforded starting material (44 mg, 75%) together with more polar material. The latter material was dissolved in diethyl ether and washed twice with saturated aqueous sodium hydrogen carbonate. The ethereal layer was dried and concentrated to afford 5-*acetoxy*-5-*acetyl*-6,7,8,9-*tetrahydro*-2,4-*dimethoxy*-5H-*benzocyclohepten*-6-*one* **18** (2 mg, 3%), with spectroscopic data as in (b). The basic layer was acidified with hydrochloric acid (5%), extracted with diethyl ether, and the dried extracts were evaporated and sublimed (130 °C, 0.2 mmHg) to give 4-(3,5-dimethoxyphenyl)butanoic acid (3 mg, 6%) as white crystals, mp 60–62 °C (lit.,[29] 63–64 °C); δ_H(300 MHz) 6.34 (m, 3 H, Ar 2-H, Ar 4-H and Ar 6-H), 3.78 (s, 6 H, 2 × OCH_3), 2.62 (t, *J* 7.3, 2 H, 2-H_2 or 4-H_2), 2.38 (t, *J* 7.3, 2 H, 4-H_2 or 2-H_2), 2.00–1.90 (m, 2 H, 3-H_2); δ_C(75.5 MHz) 178.4 (CO), 160.8 (ArC-3 and ArC-5), 143.5 (ArC-1), 106.5 (ArC-2 and ArC-6), 97.9 (ArC-4), 55.2 (2 × OCH_3), 35.2 (CH_2), 33.0 (CH_2), 25.9 (CH_2); *m*/*z* 224 (M^+, 27%), 165 ($M^+ - CH_2CO_2H$, 58), 152 (100).

(b) The β-diketone **6** (40 mg, 0.15 mmol) was treated with manganese(III) acetate as in (a), except that the reaction was maintained at 60–70 °C. Dry flash chromatography (hexane–ethyl acetate, 1:1) provided 5-*acetoxy*-5-*acetyl*-6,7,8,9-*tetrahydro*-2,4-*dimethoxy*-5H-*benzocyclohepten*-6-*one* **18** (32 mg, 66%) as pale yellow crystals, mp 143–145 °C (Found: C, 63.4; H, 6.4. Calc. for $C_{17}H_{20}O_6$: C, 63.7; H, 6.3%); ν_{max}(KBr)/cm^{-1} 1743, 1720, 1206; δ_H(300 MHz) 6.37 (d, *J* 2.4, 1 H, 1-H or 3-H), 6.35 (d, *J* 2.4, 1 H, 3-H or 1-H), 3.80 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.59 (ddd, *J* ~14, ~14, 6.4, 1 H, 9-H), 3.29 (dd, *J* 21.6, 10.1, 1 H, 7-H), 2.61 (ddd, *J* ~14, 5.5, 2.2, 1 H, 9-H), 2.40 (s, 3 H, $COCH_3$), 2.31 (m, 1 H, 7-H, 2nd order), 2.15 (s, 3 H, $COCH_3$), 2.15–1.85 (m, 2 H, 8-H_2); δ_C(75.5 MHz) 203.0 (CO), 201.4 (CO), 168.0 ($OCOCH_3$), 161.3 (C-2 or C-4), 158.8 (C-4 or C-2), 144.5 (C-4a or C-9a), 117.3 (C-9a or C-4a), 107.9 C-1 or C-3), 98.2 (C-3 or C-1), 97.2 (C-5), 55.6 (OCH_3), 55.2 (OCH_3), 34.3 (CH_2), 32.6 (CH_2), 26.0 ($COCH_3$), 23.1 (CH_2), 21.5 ($COCH_3$); *m*/*z* 320 (M^+, 4%), 278 ($M^+ - CH_2CO$, 14), 236 ($M^+ - CH_2CO - CH_2CO$, 77), 235 ($M^+ - CH_2CO - CH_3CO$, 39), 207 (235 − CO, 100).

Oxidation of 1-(3,5-dimethoxyphenyl)octane-5,7-dione 7 with manganese(III) acetate

(a) The β-diketone **7** (50 mg, 0.18 mmol) in acetic acid (1.3 cm^3) was treated with manganese(III) acetate (0.75 mmol) at room temperature for 22 h as for the diketone **5**. The brown mixture was diluted with brine and extracted with chloroform. The extracts were washed with brine, dried and evaporated to provide a crude brown solid. Gravity chromatography (acid washed silica gel; increasing polarity from hexane–ethyl acetate, 1:1, to ethyl acetate) afforded 1,1-*dichloro*-6-(3,5-*dimethoxyphenyl*)*hexan*-2-*one* (2 mg, 4%) (Found: M^+, 304.0633. Calc. for $C_{14}H_{18}{}^{35}Cl_2O_3$: *M*, 304.0633. Found: M^+, 306.0594. Calc. for $C_{14}H_{18}{}^{35}Cl^{37}ClO_3$: *M*, 306.0603); *m*/*z* 308 (M^+, ~0.4%), 306 (M^+, 2.4), 304 (M^+, 3.7), 269 [M^+ (304) − ^{35}Cl, 1], 221 ($M^+ - CHCl_2$, 18), 152 (100), 151 (63). (This ketone is an artifact formed on dilution of the reaction with brine, by manganese(III)-promoted α,α-dichlorination of the starting material followed by retro-Claisen cleavage.)

Further elution afforded starting material (25 mg, 50%), followed by 5-(3,5-*dimethoxyphenyl*)*pentanoic acid* (10 mg, 23%) (Found: M^+, 238.1205. Calc. for $C_{13}H_{18}O_4$: *M*, 238.1205); ν_{max}(film)/cm^{-1} 3600–2500 (br, COOH, C-H), 3000, 2927, 2851, 1708, 1596, 1462, 1429, 1346, 1323, 1292, 1259, 1233, 1205, 1152, 1059; δ_H(300 MHz) 6.36 (d, *J* 2.1, 2 H, Ar 2-H and Ar 6-H), 6.33 (t, *J* 2.1, 1 H, Ar 4-H), 3.80 (s, 6 H, 2 × OCH_3), 2.61 (t, *J* 6.8, 2 H, 2-H_2 or 5-H_2), 2.40 (t, *J* 6.9, 2 H, 5-H_2 or 2-H_2), 1.80–1.65 (m, 4 H, 3-H_2 and 4-H_2); δ_C(75.5 MHz) 178.3 (CO), 160.7 (ArC-3 and ArC-5), 144.4 (ArC-1), 106.4 (ArC-2 and ArC-6), 97.6 (ArC-4), 55.2 (2 × OCH_3), 35.8 (CH_2), 33.6 (CH_2), 30.5 (CH_2), 24.2 (CH_2); *m*/*z* 238 (M^+, 17%), 152 (100).

(b) The β-diketone **7** (100 mg, 0.36 mmol) was treated with manganese(III) acetate as in (a), except that the reaction mixture

was kept at 60 °C. The brown suspension was diluted with water, extracted with chloroform, and the extracts washed with saturated aqueous sodium hydrogen carbonate. Acidification of the aqueous layer with hydrochloric acid (5%) and extraction with chloroform, drying and concentration of the extracts yielded 5-(3,5-*dimethoxyphenyl*)*pentanoic acid* (35 mg, 41%) as a pale yellow viscous oil, with spectroscopic data as in (a). The residual organic layer was dried, concentrated, and subjected to dry flash chromatography (hexane–ethyl acetate, 2:1) to give starting material (20 mg, 20%), followed by 5-*acetoxy*-5-*acetyl*-5,6,7,8,9,10-*hexahydro*-2,4-*dimethoxybenzocycloocten*-6-*one* **19** (5 mg, ~4%) as a pale yellow viscous oil contaminated with a small amount of impurity (Found: M^+, 334.1415. Calc. for $C_{18}H_{22}O_6$: *M*, 334.1416); δ_H(300 MHz) 6.34 (d, *J* 2.4, 1 H, 1-H or 3-H), 6.27 (d, *J* 2.4, 1 H, 3-H or 1-H), 3.79 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 2.90–2.50 (m, 4 H, 7-H_2 and 10-H_2), 2.35 (s, 3 H, $COCH_3$), 2.13 (s, 3 H, $OCOCH_3$), 1.80–1.50 (m, 4 H, 8-H_2 and 9-H_2); *m*/*z* 334 (M^+, 2%), 292 ($M^+ - CH_2CO$, 4), 250 ($M^+ - CH_2CO - CH_2CO$, 21), 249 ($M^+ - CH_3CO - CH_2CO$, 12), 221 (249 − CO, 22), 43 (CH_3CO^+, 100).

1-Acetoxy-1-acetyl-6,8-dimethoxynaphthalen-2(1*H*)-one 20

A mixture of the (*Z*)- and (*E*)-enediones **10** and **8** (105 mg, 0.43 mmol, 3:2) in acetic acid (3.1 cm^3) was treated with manganese(III) acetate (1.8 mmol) under argon in the dark at room temperature for 22 h. The ethyl acetate extract of the reaction, obtained as in the case of the diketone **5**, upon dry flash chromatography (hexane–ethyl acetate, 2:1) afforded the (*E*)-enedione **8** (35 mg, 33%; 80% recovery based on the *E*-starting material), followed by 1-*acetoxy*-1-*acetyl*-6,8-*dimethoxynaphthalen*-2(1H)-*one* **20** (55 mg, 43%; 73% based on the *Z*-starting material) as a yellow oil (Found: M^+, 304.0947. Calc. for $C_{16}H_{16}O_6$: *M*, 304.0947); δ_H(300 MHz, CD_2Cl_2) 7.40 (d, *J* 10.0, 1 H, 3-H or 4-H), 6.55 (br s, 2 H, 5-H and 7-H), 6.17 (d, *J* 10.0, 1 H, 4-H or 3-H), 3.85 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 2.43 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $OCOCH_3$); δ_C(75.5 MHz, CD_2Cl_2) 201.9 (CO), 192.4 (CO), 168.9 ($OCOCH_3$), 161.6 (C-6 or C-8), 158.4 (C-8 or C-6), 145.9 (C-3 or C-4), 133.4 (C-4a or C-8a), 124.9 (C-4 or C-3), 118.1 (C-8a or C-4a), 106.7 (C-5 or C-7), 100.9 (C-7 or C-5), 84.6 (C-1), 55.9 (OCH_3), 55.7 (OCH_3), 26.8 ($COCH_3$), 20.5 ($OCOCH_3$); *m*/*z* 304 (M^+, 1%), 262 ($M^+ - CH_2CO$, 17), 220 ($M^+ - CH_2CO - CH_2CO$, 100), 205 (25).

Ethyl 1-acetoxy-1,2-dihydro-6,8-dimethoxy-2-oxonaphthalene-1-carboxylate 21

The (*Z*)-β-keto ester **11** (23 mg, 0.08 mmol) in acetic acid (0.6 cm^3) was treated with manganese(III) acetate (0.34 mmol) for 22 h at room temperature in the dark as for the mixed *Z*- and *E*-enediones **10** and **8**. Gravity chromatography (hexane–ethyl acetate, 1:1) of the ethyl acetate extracted product gave *ethyl* 1-*acetoxy*-1,2-*dihydro*-6,8-*dimethoxy*-2-*oxonaphthalene*-1-*carboxylate* **21** (19 mg, 68%) as pale yellow crystals, mp 145–147 °C (Found: C, 60.8; H, 5.4. Calc. for $C_{17}H_{18}O_7$: C, 61.1; H, 5.4%); ν_{max}(KBr)/cm^{-1} 1771, 1738, 1671, 1595, 1336, 1247, 1235, 1201, 1164, 1054; δ_H(300 MHz) 7.37 (d, *J* 9.9, 1 H, 3-H or 4-H), 6.51 (br s, 2 H, 5-H and 7-H), 6.29 (d, *J* 9.9, 1 H, 4-H or 3-H), 4.25–4.05 (m, 2 H, OCH_2CH_3, diastereotopic), 3.85 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 2.10 (s, 3 H, $COCH_3$), 1.12 (t, *J* 7.1, 3 H, OCH_2CH_3); δ_C(75.5 MHz) 190.9 (CO), 169.2 (CO), 164.9 (CO), 161.3 (C-6 or C-8), 158.7 (C-8 or C-6), 145.1 (C-3 or C-4), 132.8 (C-4a or C-8a), 125.1 (C-4 or C-3), 116.5 (C-1), 106.6 (C-5 or C-7), 100.6 (C-7 or C-5), 62.2 (OCH_2CH_3), 55.8 (OCH_3), 55.5 (OCH_3), 20.6 ($COCH_3$), 13.8 (OCH_2CH_3); *m*/*z* 334 (M^+, 7.3%), 220 (39), 219 ($M^+ - CH_2CO - CH_3CH_2OCO$, 100).

Ethyl 3-[1-(2-acetoxy-1,2,3,4-tetrahydro-6,8-dimethoxynaphthyl)]-3-oxopropanoate 23

(a) The β-keto ester **14** (50 mg, 0.16 mmol) in acetic acid (1.1 cm^3) was treated with manganese(III) acetate (0.67 mmol) for 22 h at room temperature as for the diketone **5**. The ethyl acetate extracted product was subjected to dry flash chromatography (increasing polarity from hexane–ethyl acetate, 1:3, to hexane–ethyl acetate, 1:1) to afford, in order of elution, starting material (25 mg, 50%) and the *tetralin* **23** (8 mg, 13%) as a colourless oil (Found: C, 62.6; H, 6.8. Calc. for $C_{19}H_{24}O_7$: C, 62.6; H, 6.6%); ν_{max}(film)/cm^{-1} 1740 (br), 1610, 1239, 1211, 1147; δ_H(500 MHz) (assignments made on the basis of decoupling and COSY data) 6.23 (d, *J* 2.3, 1 H, 5-H or 7-H), 6.22 (d, *J* 2.3, 1 H, 7-H or 5-H), 5.21 (ddd, *J* 6.6, 4.4, 2.6, 1 H, 2-H), 4.17 (q, *J* 7.3, 2 H, OCH_2CH_3), 4.07 (d, *J* 4.4, 1 H, 1-H), 3.72 (s, 3 H, OCH_3), 3.69 and 3.60 (each d, *J* 15.7, 1 H, $COCH_2CO$, AB system), 3.68 (s, 3 H, OCH_3), 2.79 (ddd, *J* ~17, ~9, 5.5, 1 H, 4-H), 2.72 (ddd, *J* ~17, ~7, ~6, 1 H, 4-H), 2.06 (s, 3 H, $COCH_3$), 2.08–2.00 (m, 1 H, 3-H, superimposed by $COCH_3$), 1.86–1.79 (m, 1 H, 3-H), 1.27 (t, *J* 7.3, 3 H, OCH_2CH_3); δ_C(125.7 MHz) 192.0 (CO), 170.6 (CO), 167.3 (CO), 159.7 (C-6 or C-8), 158.0 (C-8 or C-6), 138.6 (C-4a or C-8a), 113.5 (C-8a or C-4a), 104.4 (C-5 or C-7), 96.5 (C-7 or C-5), 69.6 (C-2), 61.1 (OCH_2CH_3), 55.3 (OCH_3), 55.3 (OCH_3), 51.8 (CH_2CO or C-1), 48.8 (C-1 or CH_2CO), 25.5 (C-3 or C-4), 25.1 (C-4 or C-3), 21.2 ($OCOCH_3$), 14.1 (OCH_2CH_3); *m*/*z* 364 (M^+, < 1%), 304 (M^+ − HOAc, 20), 249 ($M^+ - COCH_2CO_2$-CH_2CH_3, 25), 207 (249 − CH_2CO, 100), 189 (21); *m*/*z* (CI) 365 ($[MH]^+$).

(b) The β-keto ester **14** (75 mg, 0.24 mmol) and manganese(III) acetate (1.0 mmol) in acetic acid (1.7 cm^3) were stirred at 40 °C for 22 h under argon. Flash chromatography (hexane–ethyl acetate, 1:1) of the product gave starting material (10 mg, 13%), plus a mixture of more polar compounds. Successive preparative TLC (hexane–ethyl acetate, 1:1) gave the *tetralin* **23** (18 mg, 20%) with spectroscopic data as in (a).

(c) The β-keto ester **14** (40 mg, 0.13 mmol) and manganese(III) acetate (0.55 mmol) in acetic acid (0.97 cm^3) were stirred at 80 °C for 1 h under argon. Work up as above provided, after gravity chromatography (increasing polarity from hexane–ethyl acetate, 1:1, to ethyl acetate), the *tetralin* **23** (12 mg, 25%), followed by a mixture of compounds (25 mg) that were not separated even after further chromatography.

Acknowledgements

The research described was carried out during the tenure of an Australian Postgraduate Research Award and a Kodak Scholarship (J. F. J.). Microanalyses were done by the ANU Microanalytical Service, mass spectra were recorded by Mr M. G. Chapman and Ms J. M. Rothschild, and expert technical assistance was provided by Mr A. J. Herlt.

References

1 J. F. Jamie and R. W. Rickards, *J. Chem. Soc.*, *Perkin Trans. 1*, 1996, 2603.
2 A. Citterio, L. Pesce, R. Sebastiano and R. Santi, *Synthesis*, 1990, 142.
3 A. Citterio, D. Fancelli, C. Finzi, L. Pesce and R. Santi, *J. Org. Chem.*, 1989, **54**, 2713.
4 I. S. Aidhen and N. S. Narasimhan, *Tetrahedron Lett.*, 1989, **30**, 5323; *Indian J. Chem.*, *Sect. B*, 1993, **32**, 222.
5 (*a*) B. B. Snider, R. Mohan and S. A. Kates, *J. Org. Chem.*, 1985, **50**, 3659; (*b*) B. B. Snider, R. Mohan and S. A. Kates, *Tetrahedron Lett.*, 1987, **28**, 841; (*c*) R. Mohan, S. A. Kates, M. A. Dombroski and B. B. Snider, *Tetrahedron Lett.*, 1987, **28**, 845; (*d*) B. B. Snider and M. A. Dombroski, *J. Org. Chem.*, 1987, **52**, 5487; (*e*) B. B. Snider, J. J. Patricia and S. A. Kates, *J. Org. Chem.*, 1988, **53**, 2137; (*f*) J. E. Merritt, M. Sasson, S. A. Kates and B. B. Snider, *Tetrahedron Lett.*, 1988, **29**, 5209; (*g*) P. Jones and G. Pattenden, *Synlett*, 1997, 398.
6 J. R. Peterson, R. S. Egler, D. B. Horsley and T. J. Winter, *Tetrahedron Lett.*, 1987, **28**, 6109.
7 E. J. Corey and M-c. Kang, *J. Am. Chem. Soc.*, 1984, **106**, 5384.
8 G. G. Melikyan, *Synthesis*, 1993, 833; *Org. React.*, 1997, **49**, 427;

J. Iqbal, B. Bhatia and N. K. Nayyar, *Chem. Rev.*, 1994, **94**, 519; B. B. Snider, *Chem. Rev.*, 1996, **96**, 339.
9 J. E. Merritt, M. Sasson, S. A. Kates and B. B. Snider, *Tetrahedron Lett.*, 1988, **29**, 5209.
10 B. B. Snider and J. E. Merritt, *Tetrahedron*, 1991, **47**, 8663.
11 F. A. Hochstein and W. G. Brown, *J. Am. Chem. Soc.*, 1948, **70**, 3484.
12 D. Seebach, T. Weller, G. Protschuk, A. K. Beck and M. S. Hoekstra, *Helv. Chim. Acta*, 1981, **64**, 716.
13 S. Masuda, M. Tanaka and T. Ota, *Chem. Lett.*, 1984, 1327.
14 K. M. Pietrusiewicz and J. Monkiewicz, *Tetrahedron Lett.*, 1986, **27**, 739.
15 B. E. Maryanoff, A. B. Reitz, M. S. Mutter, R. R. Inners and H. R. Almond, Jr., *J. Am. Chem. Soc.*, 1985, **107**, 1068.
16 J. Fayos, J. Clardy, L. J. Dolby and T. Farnham, *J. Org. Chem.*, 1977, **42**, 1349.
17 R. M. Silverstein, G. C. Bassler and T. C. Morrill, *Spectrometric Identification of Organic Compounds*, 4th edn., Wiley, New York, 1981.
18 *Organic Electronic Spectral Data*, ed. O. H. Wheeler and L. A. Kaplan, Wiley, New York, 1966, vol. III, p. 81.
19 J. H. Beynon in *Mass Spectrometry and its Applications to Organic Chemistry*, Elsevier, Amsterdam, 1960, p. 262.
20 F. A. Bovey, in *NMR Data Tables for Organic Compounds*, Wiley, New York, 1967, vol. 1.
21 P. Sohár, in *Nuclear Magnetic Resonance Spectroscopy*, CRC Press, Florida, 1984, vol. III, p. 140.
22 L. Friedman and H. Shechter, *J. Org. Chem.*, 1960, **25**, 877.
23 P. C. Meltzer, H. C. Dalzell and R. K. Razdan, *J. Chem. Soc.*, *Perkin Trans 1*, 1981, 2825.
24 B. Lal, P. Singh, A. P. Bhaduri and K. Kar, *Indian J. Chem.*, 1975, **13**, 898.
25 M. F. Comber, M. V. Sargent, B. W. Skelton and A. H. White, *J. Chem. Soc.*, *Perkin Trans. 1*, 1989, 441.
26 M. Kuchar, B. Brunová, V. Rejholec, Z. Roubal and O. Nemecek, *Collect. Czech. Chem. Commun.*, 1976, **41**, 633.
27 R. Adams, S. MacKenzie, Jr. and S. Loewe, Jr., *J. Am. Chem. Soc.*, 1948, **70**, 664.
28 S. Winstein and R. Heck, *J. Am. Chem. Soc.*, 1956, **78**, 4801.
29 A. Bhati, *Tetrahedron*, 1962, **18**, 1519.
30 L. Crombie, W. M. L. Crombie, S. V. Jamieson, P. Tuchinda and A. J. Whitaker, *J. Chem. Soc.*, *Perkin Trans. 1*, 1982, 1485.
31 B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell in *Vogel's Textbook of Practical Organic Chemistry*, Longman Scientific and Technical, London, 5th edn., 1989.
32 C. J. Pouchert, *The Aldrich Library of NMR Spectra*, Aldrich Chemical Co., USA, 2nd edn., 1983, vol. 2, p. 180.
33 R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, 1947, **69**, 1197.
34 L. H. Klemm, R. A. Klemm, P. S. Santhanam and D. V. White, *J. Org. Chem.*, 1971, **36**, 2169.
35 S. Lindenfors, *Ark. Kemi*, 1958, **12**, 267.
36 (*a*) A. Svendsen and P. M. Boll, *Tetrahedron*, 1973, **29**, 4251; (*b*) F. Serratosa and E. Sole, *An. R. Soc. Esp. Fis. Quim. Ser. B*, 1996, **62**, 431; *Chem. Abstr.*, 1967, **66**, 2623f.
37 K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651.

Paper 7/04869F
Received 8*th July* 1997
Accepted 1*st September* 1997