A Novel Synthesis of Cyclopenta- and Cyclohexa-[*d*]xanthones from the Reaction between Cycloalkyl Enamines and 2-Hydroxyphenylpentene-1,3-diones, and their Rearrangement to Cyclopenta- and Cyclohexa-[*a*]xanthones

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Treatment of (*E*)-5-substituted-1-(2-hydroxyphenyl)pent-4-ene-1,3-diones **1** with alicyclic ketone enamines **2** rapidly gives the cycloalkano[*d*]xanthones **3**, but on longer treatment or on reaction of **3** with base, cycloalkano[*a*]xanthones **4** are obtained; their structures, including stereochemistry, were determined from spectroscopic data and, in the case of **3aB**, from X-ray diffraction analysis.

We have reported[1] that reaction of 2-styrylchromones **5** with the enamine **2A** gives substituted 2,3,3a,4-tetrahydrocyclopenta[*a*]xanthen-11(5*H*)-ones **4a**. The 2-styrylchromones **5** are readily obtained by acid catalysed cyclisation of the corresponding (*E*)-5-substituted-1-(2-hydroxyphenyl)-pent-4-ene-1,3-diones **1**.[2]

We have now observed that the reaction of the diones **1** with the enamines **2** in boiling ethanol leads to the cyclopenta- and cyclohexa-[*a*]xanthones **4** in good yield after one day. A ready explanation for this reaction might appear to involve the initial cyclisation of **1** to give **5** which then reacts with the enamine as reported.[1] That this is not the case, however, is indicated by the fact that the yields of **4** in the reactions involving **1** are appreciably higher than those found in the conversion of the chromone **5** to **4**,[1] and furthermore, we have been unable to convert the hydroxydione **1** into **5** under basic conditions.

In an endeavour to investigate the reactions of **1a** and **1b** with **2A** and **2B** more closely, their progress was monitored using TLC. In each case it was found that a new nitrogen-free product, different from **4**, formed rapidly with the reaction being complete in 0.5–5 min (see Table 1). All the products were found to have the same stoichiometric formula, *viz*. (**1** + **2** − C_4H_9N), but their structures could not be readily deduced from spectroscopy. A single crystal X-ray crystallographic analysis of the product from **1a** and **2B** showed the structure to be **3aB**.† Bond distances and angles clearly show the presence of an enol and one ketone carbonyl group. A comparison of the spectra (IR, UV, ^{1}H and ^{13}C NMR, mass spectra) of **3aA**, **3bA** and **3bB** with those of **3aB** revealed a close structural relationship, from which the remaining structures were deduced.‡ The stereochemistry of the latter three products is probably the same as in **3aB** as the spectra are similar, and furthermore this is by far the most stable stereochemical arrangement. All the products **3** were isolated as stable crystalline compounds. The cyclopenta[*d*]xanthone ring system, *e.g.* **3A**, has not hitherto been reported; there are several examples of compounds with a cyclohexa[*d*]xanthene ring, however, which are either naturally occurring sesquiterpenoids[3,4] or products of acid-catalysed rearrangements of

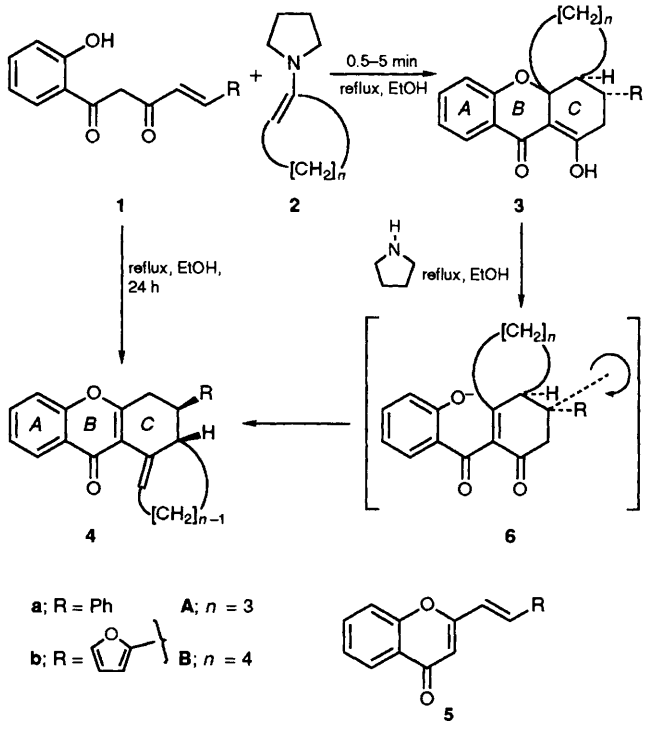

Table 1 Data for the cyclopenta- and cyclohexa-[*d*]xanthones **3**

Reactants	Reaction time/min	Product	Yield (%)
1a + **2A**	0.5	**3aA**	65
1a + **2B**	5	**3aB**	62
1b + **2A**	0.5	**3bA**	70
1b + **2B**	5	**3bB**	60

† *Crystal data* for **3aB**: $C_{23}H_{22}O_3$, crystallised from 95% ethanol, M = 346.15, monoclinic, space group $P2_1/n$, a = 14.686(6), b = 11.244(3), c = 21.789(4) Å, β = 98.29(2)°, U = 3560(1) Å^3, Z = 8, $F(000)$ = 1464, D_c = 1.289 g cm^{-3}, μ = 0.79 cm^{-1} (Mo-Kα). Intensities were recorded for 3714 unique reflections ($2\theta_{max}$ 40°) on an Enraf-Nonius CAD-4 diffractometer with ω-scan angle (0.60 + 0.344 tanθ)° at a scan speed of 0.75 to 8.24° min^{-1} using Mo-Kα radiation (graphite crystal monochromator, λ = 0.71073 Å) at 296 K. Intensity data were corrected for Lorentz and polarization effects, but no correction was made for absorption. The structure was solved by direct methods and refined by full-matrix least-squares on F, using the Enraf-Nonius SDP-1985 programs. Only isotropic thermal vibration was considered for non-H atoms in the fused ring system but the two exocyclic O atoms and six phenyl C atoms were refined anisotropically. The hydroxy H-atom, located in the difference Fourier, and all other H atoms in calculated positions, were not refined. Convergence for 289 variables, when $\Sigma w(|F_o|-|F_c|)^2$ was minimized, was reached at R = 0.067 and R_w = 0.060 with $w = 4F_o^2/\sigma^2(F_o^2)$, where $\sigma^2(F_o^2) = [\sigma^2(I) + (0.04F_o^2)^2]$ for the 1577 reflections with $I \geq \sigma(I)$. The final Δρ values were +0.26 and −0.24 e Å^{-3}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

‡ All new compounds were racemic but only one enantiomer is depicted for clarity. All new substances had spectroscopic data (IR, UV, NMR and mass spectrum) consistent with the assigned structure. Satisfactory combustion and/or high resolution mass spectral analytical data were obtained for all new compounds. *Typical data* for 1,2,3,3a,4,5-hexahydro-4-(2-furyl)-6-hydroxycyclopenta[*d*]xanthen-7-one **3bA**: colourless plates, m.p. 112–114 °C; ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 181.0, 179.9, 158.6, 155.5, 121.1 and 106.3 (6 × sp^2 quaternary C), 141.6, 135.1, 126.6, 121.5, 118.3, 110.1 and 106.2 (7 × sp^2 CH), 88.9 (sp^3 C, C-12a), 47.5 and 36.7 (2 × CH, C-3a and C-4), 37.7, 35.9, 27.9 and 21.5 (4 × CH_2); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.86 (dd, *J* 7.7 and 1.8 Hz, 1H), 7.52–7.33 (m, 2H), 7.26–6.84 (m, 2H), 6.30 (dd, *J* 3.1 and 1.8 Hz, 1H), 6.12 (d, *J* 3.1 Hz, 1H), 3.13–2.16 (m, 6H) and 1.95–1.24 (m, 4H); MS *m/z*, 322 (M$^+$, 43%), 293 (44), 280 (63) and 279 (100); IR (Nujol) ν/cm^{-1} 1602; UV (EtOH) λ_{max}/nm 218 (ε 40 000), 262 (10 000), 308 (16 000) and 355 (12 000).

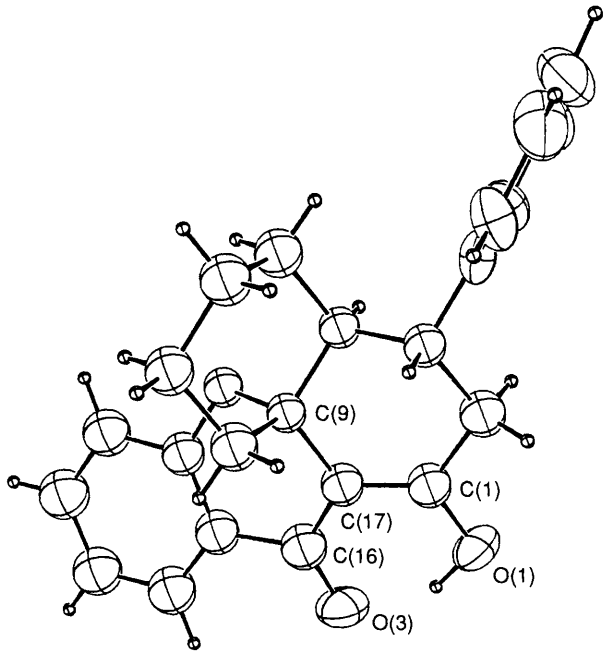

Fig. 1 ORTEP drawing of one molecule of **3aB** showing non-systematic numbering. Selected interatomic distances (Å) and angles (°) for molecule 1 and [molecule 2]: O(3)–C(16), 1.26(1) [1.27(1)]; O(1)–C(1), 1.330(9) [1.321(9)]; C(1)–C(17), 1.37(2) [1.35(1)]; C(9)–C(17), 1.51(2) [1.50(2)]; C(16)–C(17), 1.40(1) [1.40(1)]; C(16)–C(17)–C(1), 120.5(8) [120.4(8)]; C(9)–C(17)–C(1), 120.1(7) [121.9(8)]; C(9)–C(17)–C(16), 119.5(6) [117.6(6)]. The intramolecular H-bond distances from O(1) and O(3) are 1.01 and 1.61 Å respectively with a bond angle of 147° [1.67, 1.08 Å, and 137°].

1-benzyldecalin derivatives.[5] Compound **3aB** has a *cis*-fused decalin system like aureol[3] and the antifungal, antibacterial compound podosporin A,[4] emphasising the potential of this synthetic route to these interesting natural products and their analogues. This is now being studied. That the cycloalkano[*d*]xanthones **3** are intermediates in the formation of the cycloalkano[*a*]xanthones **4** from **1** and **2** has been confirmed from the fact that on heating **3** in refluxing ethanol and pyrrolidine, a quantitative yield of **4** was obtained in each case.

These results suggest that **3** is formed from the reaction between **1** and **2** by a base-promoted fast reaction beginning with a Michael addition of the enamine to the α,β-unsaturated carbonyl (analogous to that reported[1] for the product isolated from the reaction between a 3-methyl-2-styrylchromone and **2A**), followed by a cyclisation to give ring *C*, and finally by an internal displacement of the pyrrolidine group by phenoxide ion giving ring *B*. The rearrangement of **3** to **4** may be rationalized by a slow base-induced opening of ring *B* to give **6**, which after the rotation shown, recyclises *via* nucleophilic attack of the phenoxide ion at the newly formed ketone, to give a product which on elimination of water gives the stable conjugated chromone system.

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