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Reactions of 4-Oxo-4*H*-1-benzopyran-3-carboxaldehydes with Pentane-2,4-dione in Acidic Medium—a New Route to Dihydroxybenzophenone Derivatives†

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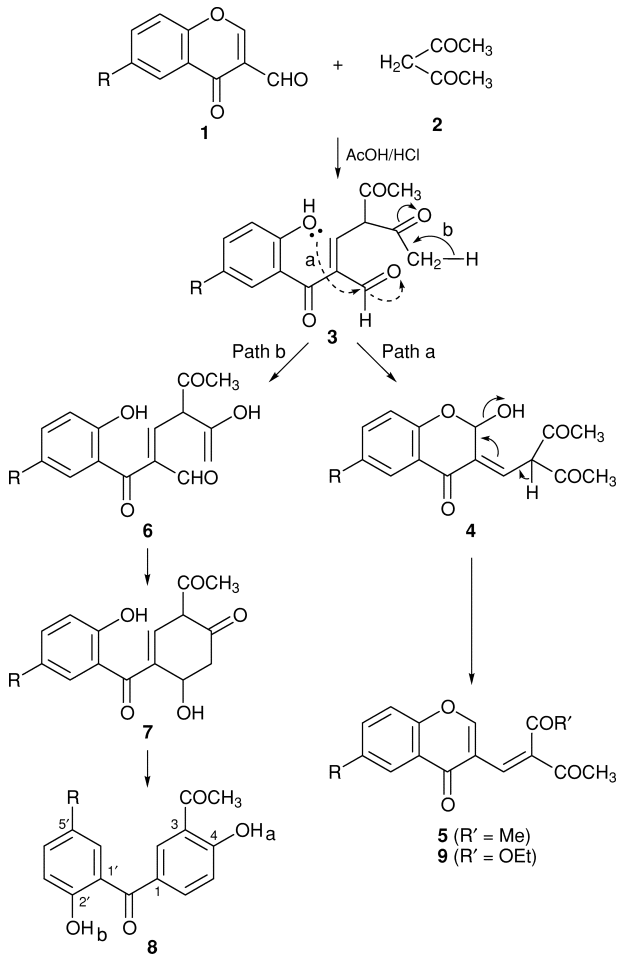
Reaction of the title aldehyde **1** with acetylacetone **2** gives benzophenone **8** along with the Knoevenagel-type product **5** under acidic conditions.

Aldehyde **1** reacts with various active methylene compounds[1] in basic media to produce mainly Knoevenagel-type condensation products. With **1**, malonamide or cyanoacetamide produces pyridone derivatives[2] which are assumed to form *via* the Knoevenagel-type condensation product. Similarly, compound **5** or **9** or a mixture of **1** and **2** or **1** and ethyl acetoacetate produces pyridine derivatives[3] when treated with ammonium acetate in ethanol. A benzophenone derivative is produced when **9a** is treated with ethyl acetoacetate in piperidine–ethanol or from **1a** in one-pot using the same reaction conditions but with excess ethyl acetoacetate.[4]

Recapitulating the mechanism of the base catalysed condensation of **1** and **2**—attack of the nucleophile at the 2-position of pyran ring, followed by ring opening and recyclisation to **4** and subsequent elimination of water to **5** (Scheme 1, path a),[1] the ring opened intermediate phenoxide of **3** may follow an alternative route (Scheme 1, path b) where the enolate of **6** can cyclise and could ultimately form **8**. But no **8** was obtained under basic conditions. The phenoxide ion is probably nucleophilic enough to favour path a. The reaction sequence may follow path b at least to some extent if the nucleophilic character of the phenoxide ion is decreased somehow. This is indeed achieved by carrying out the reaction in an acidic medium. In fact, **8** was obtained in low to moderate (15–30%) yield along with **5** (30–40%) when a solution of **1** in acetic acid is added to a preheated (70–80 °C) mixture of **2** in acetic acid containing a catalytic amount of HCl. Compound **5**[4] fails to give **8** when heated in HCl–AcOH at 70–80 °C, which rules out the possibility of formation of **8** *via* **5**. Various other attempts, *e.g.* stirring **5** at room temperature with Al_2O_3–DMF, $AlCl_3$–CS_2, H_2SO_4 or PPA (DMF = dimethylformamide; PPA = polyphosphoric acid) heating with $AlCl_3$ in the solid phase at 120 °C or refluxing with K-10 montmorillonite in benzene or toluene, were made to form **8**, but all failed. Hence, formation of **8** is rationalised as follows—1,4-addition of the enol form of **2** to **1** followed by ring opening generates **3** which then enolises to **6**. Compound **8** is obtained from **6** by cyclisation (→7) and subsequent dehydration and tautomerisation (Scheme 1, path b). A relatively high yield of **8d** also supports the proposed mechanism. The presence of a nitro group at the *para* position of the hydroxy group in **3** decreases the nucleophilicity of the hydroxy group and path b becomes the preferred one. **5d** could not be isolated from the reaction mixture of **1d** and **2**. So it is obvious that path a is less favourable here.

Another interesting observation is in the mode of addition of reagents. The first mode, which is described in the Experimental section produced compounds **5** and **8**. But in the second mode, when an equimolar amount of **1a** or **1b**, **2** and a catalytic amount of HCl are taken together in acetic acid at room temperature and then heated for 2 h at 70–80 °C, only **5** (40–45%) was obtained along with some unreacted aldehyde (~10%). No trace of **8** was observed even by TLC. This observation may be rationalised by considering the more ready protonation of the aldehydic oxygen of the more basic 3-formylchromone **1** than that of acetylacetone which then undergoes 1,2-addition and finally gives **5** (Scheme 2).



Scheme 1 **a**, R = H; **b**, R = Me; **c**, R = Cl; **d**, R = NO_2

*To receive any correspondence.
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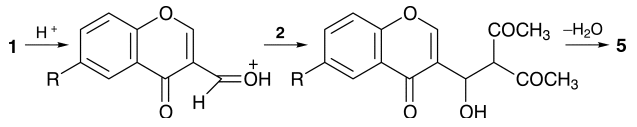

Scheme 2

Experimental

All mp values are uncorrected. IR spectra were recorded on a Perkin Elmer 782 spectrometer as KBr discs. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker AM 300L spectrometer using Me_4Si as internal standard and the coupling constants are expressed in Hz.

General Procedure[5] *for the Formation of* 3-*Acetyl*-2′,4-*dihydroxy*-5′-*substituted Benzophenone* **8**.—Concentrated HCl (2–3 drops) was added to acetylacetone (500 mg, 5 mmol) in acetic acid (5 ml) at 70–80 °C. The reagent mixture was stirred at that temperature for 15 min. A solution of **1** (5 mmol) in acetic acid (15 ml) was added dropwise. The resultant solution was stirred for 2 h at that temperature. The dark-red reaction mixture was cooled and poured on to crushed ice (100 g). The solid deposit was filtered, washed with water and dried. The crude mixture was chromatographed over silica gel (100–200 mesh) using 5% ethyl acetate in light petroleum as eluent to give **8** from the first few fractions and then **5**[3,4] (30–40%) from the later fractions of the same eluent. Compound **5d** could not be isolated from the reaction mixture of **1d** and **2**. Characterisation data of **8** are as follows:

8a: yield 17%; mp 128 °C; δ_H 2.66 ($COCH_3$, s), 6.88–6.96 (H-3′, H-5′, m), 7.12 (H-5, d, *J* 9), 7.44–7.66 (H-4′, H-6′, m), 7.92 (H-6, dd, *J* 9 and 1.8), 8.28 (H-2, d, *J* 1.8), 11.84 (OH_b, exchangeable, s) and 12.72 (OH_a, exchangeable, s); ν_{max}/cm^{-1} 3120–2750, 1650, 1630, 1600 (Found: C, 70.42, H, 4.75. $C_{15}H_{12}O_4$ requires C, 70.30; H, 4.72%).

8b: yield 15%; mp 141 °C; δ_H 2.24 (CH_3, s), 2.64 ($COCH_3$, s), 7.00 (H-3′, d, *J* 9), 7.12 (H-5, d, *J* 9), 7.32–7.44 (H-4′, H-6′, m), 7.88 (H-6, dd, *J* 9 and 1.8), 8.20 (H-2, d, *J* 1.8), 11.60 (OH_b, exchangeable, s) and 12.66 (OH_a, exchangeable, s); ν_{max}/cm^{-1} 3200–2750, 1650, 1640, 1600 (Found: C, 71.09; H, 5.24. $C_{16}H_{14}O_4$ requires C, 71.10; H, 5.22%).

8c: yield 20%; mp 144 °C; δ_H 2.71 ($COCH_3$, s), 7.07 (H-3′, d, *J* 9), 7.12 (H-5, d, *J* 9), 7.48 (H-4′, dd, *J* 9 and 1.8), 7.55 (H-6′, d, *J* 1.8), 7.86 (H-6, dd, *J* 9 and 1.8), 8.20 (H-2, d, *J* 1.8), 11.65 (OH_b, exchangeable, s) and 12.72 (OH_a, exchangeable, s); ν_{max}/cm^{-1} 3300–2750, 1660, 1640, 1600 (Found: C, 62.60; H, 3.87. $C_{15}H_{11}ClO_4$ requires C, 62.40; H, 3.84%).

8d: yield 30%; mp 174 °C; δ_H 2.71 ($COCH_3$, s), 7.18 (H-5, d, *J* 9), 7.21 (H-3′, d, *J* 9), 7.92 (H-6, dd, *J* 9 and 1.8), 8.25 (H-2, d, *J* 1.8), 8.42 (H-4′, dd, *J* 9 and 1.8), 8.62 (H-6′, d, *J* 1.8), 12.49 (OH_a, exchangeable, s) and 12.81 (OH_b, exchangeable, s); ν_{max}/cm^{-1} 3200–2800, 1660, 1640, 1600 (Found: C, 59.81; H, 3.66; N, 4.67. $C_{15}H_{11}NO_6$ requires C, 59.80; H, 3.68; N, 4.65%).

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