## A Novel and Convenient Synthesis of 3-Phenylcoumarins

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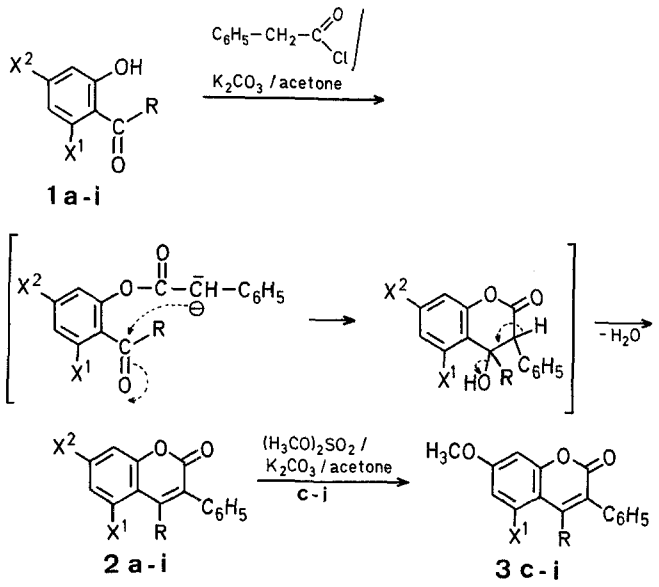
The Perkin reaction[1], as modified by Oglialoro[2] and Bargellini[3] for the synthesis of 3-phenylcoumarins, involves the condensation of 2-hydroxyarylcarbonyl compounds (**1**) with a mixture of phenylacetic acid or sodium phenylacetate and acetic anhydride; other mixtures later recommended as condensing agents are sodium phenylacetate/phenylacetic anhydride[4] and phenylacetic acid/potassium acetate/acetic anhydride[5]. Due to the high temperatures (~180°C) required by these methods, the yields are low. We now report a new and facile method for the synthesis of 3-phenylcoumarins (**2**) in high yields (~98% of crude product) which consists of the condensation of 2-hydroxybenzaldehyde (**1a**) or 2-hydroxyphenyl ketones (**1b–i**) with phenylacetyl chloride in acetone in the presence of anhydrous potassium carbonate; in the case of ketones **1c–i** which possess additional hydroxy groups, the reaction leads to *O*-phenylacetyl derivatives of products **2c–i** which have to be hydrolyzed to the free hydroxycoumarins **2c–i** by heating in methanolic 2% potassium hydroxide. The hydroxycoumarins **2c–i** were *O*-methylated with dimethyl sulfate to give the methoxycoumarins **3c–i**.




The I.R.- and U.V.-spectral data of all compounds **2** and **3** prepared are characteristic of 3-phenylcoumarins[6]. The $^1$H-N.M.R. and mass spectra of compounds **2a, b** and **3c–i** are consistent with the assigned structures. Compounds **2b**[8] and **2c**[9] were further identified by comparison with authentic samples. The structures of the new compounds **2f, 3d, f, h** were proven by microanalysis and spectral data.

In the reaction **1**→**2**, *O*-acylation by phenylacetyl chloride appears to take place readily under the mild conditions used (potassium carbonate, low temperature) so that *C*-acylation, which is regarded as an intermediate step in the Perkin reaction[1], does not interfere.

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**Table 1.** 3-Phenylcoumarins **(2a, b)**, 7-Hydroxy-3-phenylcoumarins **(2c, e, g, i)**, and 5,7-Dihydroxy-3-phenylcoumarins **(2d, f, h)**

| 2 | R | X¹ | X² | Yield[a] [%] | m.p. [°C] | Lit. m.p. [°C] or Molecular formula |
|---|---|---|---|---|---|---|
| a | H | H | H | 90 | 142° | 141°[7] |
| b | $CH_3$ | H | H | 88 | 156° | 153°[8] |
| c | $CH_3$ | H | OH | 85 | 230° | 228°[9] |
| d | $CH_3$ | OH | OH | 76 | 285° | 282°[10] |
| e | $C_2H_5$ | H | OH | 80 | 270° | 268°[11] |
| f | $C_2H_5$ | OH | OH | 75 | 278° | $C_{17}H_{14}O_4$[b] (282.3) |
| g | $C_6H_5$ | H | OH | 81 | 290° | 286°[12] |
| h | $C_6H_5$ | OH | OH | 70 | 260° | 255°[3] |
| i | $-CH_2-C_6H_5$ | H | OH | 78 | 238° | 232°[4] |

[a] Yield of recrystallized product (from methanol).

[b] calc. C 72.35 H 4.96
found 72.12 4.78

**Table 2.** 7-Methoxy- and 5,7-Dimethoxy-3-phenylcoumarins **(3)**

| 3 | R | X¹ | Yield[a] [%] | m.p. [°C] | Lit. m.p. [°C] or Molecular formula[b] |
|---|---|---|---|---|---|
| c | $CH_3$ | H | 86 | 109° | 108°[9] |
| d | $CH_3$ | $OCH_3$ | 89 | 129° | $C_{18}H_{16}O_4$ (296.3) |
| e | $C_2H_5$ | H | 80 | 120° | 115°[11] |
| f | $C_2H_5$ | $OCH_3$ | 85 | 131° | $C_{19}H_{18}O_4$ (310.3) |
| g | $C_6H_5$ | H | 75 | 180° | 177°[12] |
| h | $C_6H_5$ | $OCH_3$ | 80 | 162° | $C_{23}H_{18}O_4$ (358.4) |
| i | $-CH_2-C_6H_5$ | $OCH_3$ | 78 | 180° | 183°[4] |

[a] Yield of recrystallized product (from methanol).

[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.22; H, ±0.15.

**Table 3.** I.R.- and U.V.-Spectral Data of Compounds **2a, 2b,** and **3c–i**

| Compound | I.R. ($CHCl_3$) $\nu_{C=O}$ [$cm^{-1}$] | U.V. (methanol) $\lambda_{max}$ [nm] (log ε) |
|---|---|---|
| **2a** | 1710 | 245 (4.0); 325 (4.22) |
| **2b** | 1710 | 240 (3.86); 325 (4.16) |
| **3c** | 1700 | 245 (3.94); 330 (4.45) |
| **3d** | 1700 | 247 (4.0); 325 (4.40) |
| **3e** | 1700 | 245 (3.97); 325 (4.22) |
| **3f** | 1706 | 245 (3.90); 325 (4.15) |
| **3g** | 1710 | 250 (3.86); 335 (4.35) |
| **3h** | 1710 | 250 (3.80); 335 (4.35) |
| **3i** | 1700 | 245 (3.95); 330 (4.35) |

Attempts to prepare 3-alkylcoumarins following the above method were unsuccessful. Thus, refluxing of 2-hydroxyacetophenone **(1b)** with propanoyl chloride in acetone containing potassium carbonate for 6 h and work-up as for products **2a, b** did not afford 3,4-dimethylcoumarin; instead, most of the starting material **1b** was recovered.

**3-Phenylcoumarins (2); General Procedure:**

A solution of the 2-hydroxyphenylcarbonyl compound **1** (0.02 mol) and phenylacetyl chloride (0.04 mol) in acetone (200 ml) is refluxed with anhydrous potassium carbonate (10 g) for 6 h on a water bath. Then, acetone is removed under reduced pressure and cold water (100 ml) is added to the mixture. The solid product thus formed is isolated by suction and washed with cold water (2 × 50 ml).

Products **2a** and **2b** are directly obtained in this manner. The products obtained from **1c–i** are the *O*-phenylacetyl derivatives of the hydroxycoumarins **2c–i**. These products are hydrolyzed to give the free hydroxycoumarins **2c–i** by refluxing in methanolic 2% potassium hydroxide (100 ml) for 15 min. Methanol is then removed under reduced pressure and the mixture neutralized with ice-cold dilute hydrochloric acid. The pale-yellow product which separates is isolated by suction, washed with cold water (2 × 60 ml), and recrystallized from methanol.

**7-Methoxy- and 5,7-Dimethoxy-3-phenylcoumarins (3c–i); General Procedure:**

To a solution of the hydroxycoumarin (**2c–i**; 5 mmol) in acetone (100 ml), anhydrous potassium carbonate (5 g) and dimethyl sulfate (1.9 g, 15 mmol) are added and the mixture is refluxed for 6 h. Potassium carbonate is then filtered off, the filtrate is evaporated, and ice-cold water (100 ml) is added to the residue. The colorless solid which separates is isolated by suction and recrystallized from methanol.

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