One-pot Synthesis of 4-Phenylcoumarins†

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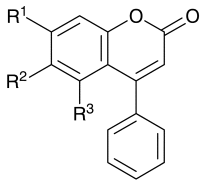
A one-pot synthesis of 4-phenylcoumarins in good yield was achieved by the interaction of phenylpropiolic acid with phenols in polyphosphoric acid in the presence of $Tl(OAc)_3$.

We have reported the reaction of phenylpropiolic acid (ØPA) with phenols in presence of polyphosphoric acid (PPA) as a viable method for the synthesis of flavones, though concomitant formation of some 4-phenylcoumarins could not be totally suppressed.[1] Continued investigations of this reaction has now made it possible for us to divert this reaction towards the exclusive formation of 4-phenylcoumarins.

These compounds have earlier been prepared by exploiting the von-Pechmann[2] and Perkin reactions.[3] More recently the technique of coupling preformed coumarins with phenyl units employing aryl stannates[4] or aryl triacetates[5] has been reported. A multistage synthesis starting with aryl Grignard reagents is also on record.[6]

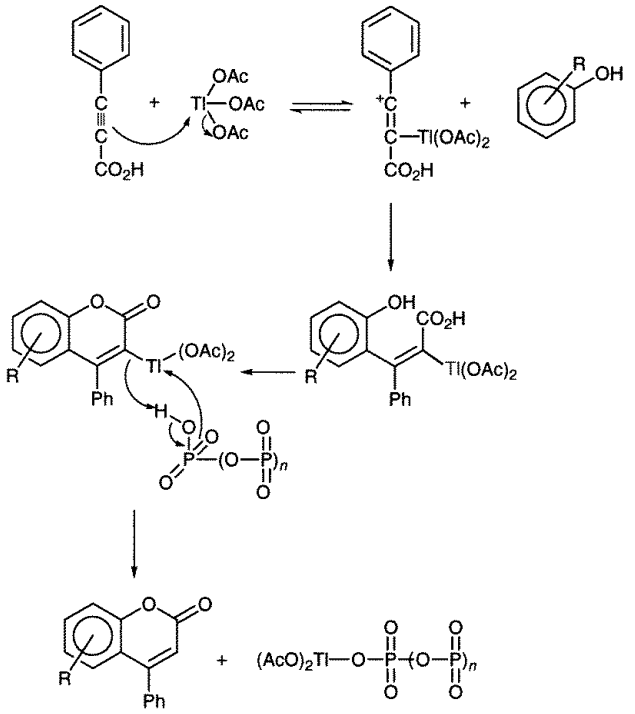
I **II**

In the PPA-mediated reaction of ØPA with phenol the exclusive formation of 4-phenylcoumarins would require the preferential formation of the vinyl cation **I** *vis-à-vis* the acylium cation **II**. Thallium(III) species have been reported to oxidise various organic substrates, including acetylenes, through a two-electron process.[7] Assuming such a process to favour the formation of **I** [R = $Tl(OAc)_3$] at the expense of **II**, the reaction was conducted in the presence of $Tl(OAc)_3$, and as expected 4-phenylcoumarins were formed with total exclusion of flavones. Details of the reactants, products and yields are provided in Table 1.



III R^1 = OH; R^2, R^3 = H
IV R^1, R^3 = OH; R^2 = H
V R^1 = OH; R^2 = H; R^3 = Me
VI R^1 = R^2 = Me; R^3 = H
VII R^2 = *n*-C_6H_{13}; R^1 = OH; R^3 = H

Mechanistically this reaction, akin to the Friedel and Crafts cycloalkylation, requires elaboration on the mode of expulsion of the thallium subsequent to the generation of the vinyl cation **I** [R = $Tl(OAc)_3$]. Uemera *et al.*[18] invoked a six-membered transition state to explain the expulsion of Tl^{3+} in a similar protodethallation sequence. In the current instance PPA can be assumed to play a role in the protodethallation step and the overall mechanism can be pictured as in Scheme 1.



Scheme 1

The following information of diagnostic value could be gleaned from the spectral data of the compounds prepared. (a) In the NMR spectra ($CDCl_3$) the 3-H of the 7-hydroxy-4-phenylcoumarins and their derivatives resonates at different values: 7-OH; δ 5.75–6.1; 7-OMe, δ 6.0–6.2 and 7-OAc; δ 6.2–6.3. (b) Identical substituents when present at the 5 and 7 positions show divergence in their chemical shifts, the 5-substituents being considerably shielded. Shielding constants [$\Delta\delta$ (ppm)] observed are: OMe, 0.45–0.5; OAc, 1.0 and Me, 0.6. (c) In the IR spectra the carbonyl stretching frequency (cm^{-1}, KBr) vary considerably; 7-OH, 1685; 7-OAc, 1730–1740 and 7-Me, 1710.

The method being reported is simple and involves very little time. Inputs of doubtful purity do not hamper the reaction or affect the yield and no protection of the reagents is required. Isolation of the products and their purification is possible through precipitation, filtration and crystallisation and secondary methods like chromatography, *etc.* are not necessary. This method holds the promise of developing into a general one of wide applicability. However, *ortho*- and *para*-dihydric phenols, because of their propensity to be oxidised to the corresponding quinones,[9] may not be employed. Of the different regioisomeric products possible in the case of resorcinol and the three alkylated phenols, only one each is obtained, and the products formed are those predictable on electronic grounds, substitution taking place at the maximum activated positions. Additional selec-

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Table 1 Products and yields

Reactants; ØPA+	Product	mp/°C	Yield (%)
Resorcinol	7-hydroxy-4-phenylcoumarin (**III**)	240	85
Phloroglucinol	5,7-dihydroxy-4-phenylcoumarin (**IV**)	252	75
Orcinol	7-hydroxy-5-methyl-4-phenylcoumarin (**V**)	226	60
3,4-Dimethylphenol	6,7-dimethyl-4-phenylcoumarin (**VI**)	148	45
4-Hexylresorcinol	6-Hexyl-7-hydroxy-4-phenylcoumarin (**VII**)	192	60

tivity imposed due to steric effects explains the formation of single products. The physical constants and spectral characteristics of compounds **III**,[2] **IV**[2] and **V**[10] (see below) are compatible with those reported, while **VI** and **VII** are reported for the first time.

Experimental

To an equimolar mixture of phenylpropiolic acid (1.46 g, 0.01 mol) and resorcinol (1.10 g, 0.01 M) was added sufficient PPA to obtain a paste of thin consistency. This mixture was heated on a water-bath for 1 h with stirring using a glass rod. The contents were then diluted with MeOH (30 ml) refluxed for 1 h and the product precipitated by addition to crushed ice and extracted with diethyl ether. The ether solution was washed with aq. $NaHCO_3$ and water, dried over Na_2SO_4 and the ether recovered to yield compound **III** (2.03 g); mp. 240 °C (lit.,[2] 230–235 °C); UV, λ_{max} 238, 333 nm; IR 3150 and 1685 cm^{-1}; δ_H ([$^2H_6$]DMSO) 6.07 (1 H, s, H-3) 6.70 (1 H, dd, *J* 2.5 and 8, H-6), 6.81 (1 H, d, *J* 2.5, H-8), 7.26 (1 H, d, *J* 8 Hz, H-5), 7.5 (5 H, br s). Acetate: mp 124 °C; IR 1730, 1765 cm^{-1}; δ_H ([$^2H_6$]DMSO) 2.33 (3 H, s, OAc), 6.37 (1 H, s, H-3), 7.01 (1 H, dd, *J* 2.5, 8, H-6); 7.24 (1 H, d, *J* 2.5, H-8), 7.53 (1 H, d, *J* 8 Hz, H-5), (7.52 5 H, br s). Methyl ether: mp 111 °C; δ_H 3.83 (3 H, s, OMe), 6.18 (1 H, s, H-3), 6.75 (1 H, dd, *J* 2.5, 8, H-6), 6.83 (1 H, d, *J* 2.5, H-8), 7.33 (1 H, d, *J* 8-Hz, H-5), 7.45 (5 H, br s).

IV: mp 232 °C (lit.,[2] 234–235 °C); λ 262, 334 nm; IR 3150, 1685 cm^{-1}; δ_H 5.76 (1 H, s, H-3), 6.23, 6.33 (1 H each, d, *J* 2.5 Hz, H-8, H-6), 7.33 (5 H, br s). Acetate: mp 185 °C; IR 1740, 1765 cm^{-1}; δ_H ($CDCl_3$) 1.30, 2.30 (3 H each, s, 2 × OAc), 6.2 (1 H, s, H-3), 6.76, 7.1 (1 H each, d, *J* 2.5 Hz, H-8, H-6), 7.4 (5 H, br s). Methyl ether: mp 172 °C; δ_H 3.4, 3.84 (3 H each, 2 × OMe), 6.0 (1 H, s, H-3), 6.23, 6.53 (1 H each, d, *J* 2.5 Hz, H-8, H-6), 7.30 (5 H, br s).

V: mp 226 °C (lit.,[10] 226 °C); λ 232, 324 nm; IR 3150, 1680 cm^{-1}; δ_H 1.70 (3 H, s, Me), 5.86 (1 H, s, H-3), 6.48, 6.61 (1 H each, d, *J* 2.5 Hz, H-8, H-6), 7.33 (5 H, br s). Acetate: mp 158 °C; IR 1730, 1765 cm^{-1}; δ_H ($CDCl_3$) 1.80 (3 H, s, Me), 2.23 (3 H, s, OAc), 6.2 (1 H, s, H-3), 6.80, 7.1 (1 H each, d, *J* 2.5 Hz, H-8, H-6), 7.43 (5 H, br s). Methyl ether: mp 128 °C; δ_H 1.76 (3 H, s, Me), 3.8 (3 H, s, OMe), 6.07 (1 H, s, H-3), 6.6, 6.78 (1 H each, d, *J* 2.5 Hz, H-8, H-6), 7.36 (5 H, br s).

VI: mp 148 °C; λ 288, 324 nm; IR 1710 cm^{-1}; δ_H ($CDCl_3$) 2.25, 2.35 (3 H each, s, 2 × Me), 6.31 (1 H, s, H-3), 7.22 (1 H, s, H-8), 7.30 (1 H, s, H-5), 7.52 (5 H, br s).

VII: mp 192 °C; IR 3200, 1710 cm^{-1}; δ_H, hexyl side chain, 0.88 (3 H, t, *J*, Me), 1.35 (8 H, m, 4 × CH_2), 2.6 (2 H, t, *J* 8 Hz, $ArCH_2$); 6.07 (1 H, s, H-3), 6.9 and 7.1 (1 H each, H-8, H-5), 7.46 (5 H, br s). Acetate: mp 152 °C; IR 1735, 1770 cm^{-1}; δ_H ($CDCl_3$), hexyl side chain, 0.9 (3 H, t, *J* 7 Hz, Me) 1.35 (8 H, m, 4 × CH_2), 2.36 (2 H, m, $ArCH_2$); 2.4 (3 H, s, OAc), 6.26 (1 H, s, H-3), 7.11 and 7.30 (1 H each, s, H-8, H-5), 7.5 95 H, br s).

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