A Convenient Synthesis of the 2-Dimethyl-2H-Chromene-System*

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2,2-Dimethyl-5H-pyrano(3,2-c)-1-benzopyrano-5-one(2) and 4H-2,3-dihydro-3-methyl-2-methylene-furan-1-benzopyran-4-one (3), two new coumarin derivatives were synthesised from 4-hydroxycoumarin by treating with 3-chloro-3-methylbut-1-yn-1-ene and 3-chlorobut-1-yn-1-ene respectively, both reactions progressing via the phase-transfer catalysis.

The pyrano ring is found to be common in a considerable number of natural products [1], particularly in coumarins, xanthones, flavonoids and some of the alkaloids. In the synthesis of these natural products, the formation of the pyrano ring is an important step. Most of the commonly used methods in the preparation of compounds with the pyrano ring include: 1: Preparation of the dimethylpropargyl ether followed by condensation [2] or 2: condensation of the hydroxy compound with isoprene and dehydrogenation of the chroman ring [3]. These available methods lengthen the synthetic pathway ways. A one step synthesis of the pyrano ring is therefore desirable for the formation of relevant natural products.

A simple and efficient procedure has been developed for the preparation of the pyrano ring based on the principle of phase-transfer catalysis. Ethers of both simple and highly hindered phenols prepared by similar methods have been previously described [4].

The reaction of 2,5-dihydroxybenzoic acid with 3-chloro-3-methylbut-1-yn-1-ene at room temperature, in the presence of the phase-transfer catalyst tetrabutylammoniumbromide under alkaline conditions gave 2,2-dimethyl-6-hydroxybenzopyran-5-carboxilic acid (80%) [5]. This one step reaction was found to be successful in the synthesis of some pyranoxanthones while furanoxanthones were yielded as by-products [5]. The formation of pyranoxanthones and furanoxanthones in the same reaction led us to consider its mechanism.

The synthesis of the pyranocoumarin (2) and the furanocoumarin (3) indicated that the stereochemistry of the reactants may be playing a considerable role in this mechanism. While the reaction of 4-hydroxycoumarin with 3-chloro-3-methylbut-1-yn-1-ene in the presence of tetrabutylammoniumbromide under alkaline conditions gave the pyranocoumarin (2) as the major product the reaction of the same coumarin with 3-chlorobut-1-yn-1-ene under identical conditions gave the furanocoumarin (3) as the major product.


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C-Alkylation by way of an SN-2 reaction to form pyrano rings has been described in literature [6]. However, in the synthesis of the pyranocoumarin (2), steric hinderance of the two methyl groups prevents the electrophilic substitution of the tertiary carbonium ion at the position three of the 4-hydroxycoumarin. The formation of the ether (1A) and the subsequent sigmatropic rearrangement paved way for the final electrocyclic ring closure, to give the pyranocoumarin (2) [7]. In the case of the second reaction, sterically less hindered secondary carbonium ion easily attack at position three of the 4-hydroxycoumarin. Thus, it can be explained that electrophilic substitution leads to a nucleophilic ring opening. The organic layer was washed with water and dried over anhydrous sodium sulphate to give crude product. The crude product was subjected to preparative t.l.c. (1% MeOH in CHCl₃) to give 0.60 g (60%) of the major product. M.p. 92–94 °C; λ_max (MeOH) 335.5 (log ε 4.5728), 340.0 (4.5858), 345.3 (4.6177) and 207.1 (4.6649) nm; ν_max (neat) 3000, 1715, 1640, 1605, 1565, 1495, 1460, 1415, 1360, 1330, 1300, 1280, 1250, 1215, 1195, 1160, 1115, 1040, 990, 910, 865, 760, 720 and 660 cm⁻¹; MS 288 M⁺ (15%), 213 (100%), 185 (21%), 181 (5%), 169 (5%), 141 (5%), 128 (16%), 121 (21%), 115 (9%), 107 (15%), 93 (16%), 79 (16%), 69 (46%), 65 (22%), 51 (24%); δ_H 60 MHz (CDCl₃) 7.78 (1H, m, 1H, m, 10H), 7.57–7.05 (3H, m, 7.8 and Ar–H), 6.55 (1H, d, J = 10 Hz, 4H), 5.54 (1H, d, J = 10 Hz, 3H) and 1.57 (6H, s, 2C(CH₃)₂).

C₁₃H₁₂O₂ m/z requires 228.0792, found 228.0786.

b) 4.05 g (25 mmoles) of 4-hydroxycoumarin was refluxed for 4 d with 5.25 g (62.5 mmoles) of 2-methyl-3-butin-2-ol, 0.65 ml (2.5 mmoles) phosphorous oxychloride and 100 ml of chloroform. Reaction mixture was cooled in an ice bath and precipitate was filtered to get 2.573 g of the starting material. Weight of the filtrate was 1.506 g and it gave 0.127 g of the pyranocoumarin (2) (3%). (IR, ¹H NMR, m.p., UV.)

4H-2,3-Dihydro-3-methyl-2-methylene-furan-(3,2-c)-1-benzopyran-4-one (3)

Same reaction (a) was carried out for 24 × 4 h using following reagents: 50 ml dichloromethane, 50 ml water, 1.0 g (6 mmoles) 4-hydroxycoumarin, 1.08 g (12 mmoles) 3-chlorobut-1-yn-1, 0.48 g (12 mmoles) sodium hydroxide, 80 mg tetrabutylammoniumbromide and 3 mg potassium iodide.

The crude product was subjected to preparative t.l.c. (CHCl₃) to give 90 mg of the major product (9%); m.p. 99–103 °C; λ_max (MeOH) 330.5 (log ε 3.4765), 315 (3.7283), 258.2 (3.5608), 249.2 (3.609), 229.6 (sh-3.7195) and 205.63 (4.1433) nm; ν_max (CHCl₃) 2970, 1720, 1680, 1610, 1570, 1500, 1440, 1405, 1280, 1145, 1100, 1075, 1030, 985, 910 and 845 cm⁻¹; MS 214 M⁺ (72%), 199 (100%), 186 (12%), 171 (91%), 158 (5%), 121 (17%), 115 (17%), 100 (9%), 92 (13%), 85 (10%), 79 (12%), 65 (19%), 58 (19%) and 51 (12%); δ_H 300 MHz (CDCl₃) 7.72 (1H, m, 9H), 7.59 (1H, m, Ar–H), 7.41–7.26 (2H, m, Ar–H), 5.0 (1H, t, J = 10 Hz C=CH₃), 4.10 (1H, d, J = 7.0 Hz 3H) and 1.55 (3H, d, J = 7.0 Hz 3C–CH₃).

C₁₃H₁₂O₂ m/z requires 214.0630, found 214.0628.

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