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

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Z. Naturforsch. 40b, 636–638 (1985); received December 30, 1984

2-Dimethyl-2H-Chromenes, Coumarin Derivatives, Phase-Transfer Catalysis

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-yne and 3-chlorobut-1-yne respec-
tively, both reactions progressing via the phase-transfer catalysis.

The pyrano ring is found to be common in a con-
siderable 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 pre-
paration of compounds with the pyrano ring include:
1: Preparation of the dimethylpropargyl ether fol-
lowed by condensation [2] or 2: condensation of the
hydroxy compound with isoprene and dehydrogena-
tion of the chroman ring [3]. These available
methods lengthen the synthetic path ways. A one
step synthesis of the pyrano ring is therefore desir-
able for the formation of relevant natural products.

A simple and efficient procedure has been de-
veloped 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-yne at room temperature, in
the presence of the phase-transfer catalyst tetrabutyl-
ammoniumbromide 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 furano-
xanthones in the same reaction led us to consider its
mechanism.

The synthesis of the pyranocoumarin (2) and the
furanocoumarin (3) indicated that the stereochemis-
try of the reactants may be playing a considerable
role in this mechanism. While the reaction of 4-hy-
droxycoumarin with 3-chloro-3-methylbut-1-yne 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-yne under identical conditions
gave the furanocoumarin (3) as the major product.

* Part 97 in the series “Natural Product Chemistry”. For
Part 96 see J. Reisch and A. S. El-Sharaky, Sci.
Pharm., in press.
** Reprint request to Prof. Dr. Dr. J. Reisch.
Verlag der Zeitschrift für Naturforschung, D-7400 Tübingen
0340–5087/85/0500–0636/$ 01.00/0
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 closure to give the furanocoumarin (3) (Scheme 1) [8]. The results indicate that electrophilic substitution is favoured in these types of reactions.

The pyranocoumarin (2) was synthesised by treating the 4-hydroxycoumarin with 2-methyl-3-butin-2-ol in the presence of phosphorus oxychloride. This reaction suggests the possibility of the formation of ether (1A) by the elimination of water molecule from two hydroxy groups.

### Experimental

M.ps were determined with Kofler hot stage apparatus. IR spectra were recorded on a Pye Unicam SP3-200 spectrometer. $^1$H NMR spectra were recorded on Bruker WM 300 MHz or Varian 60 MHz spectrometers, with TMS as the internal standard. Mass spectra were recorded with an MAT 44 S mass spectrometer. UV spectra of methanol solutions were recorded on a Carl Zeiss DMR 21 spectrometer.

#### 2,2-Dimethyl-5H-pyranocoumarin (2)

a) A mixture of 50 ml dichloromethane, 50 ml water, 1.0 g (6 mmoles) 4-hydroxycoumarin, 1.08 g (12 mmoles) 3-chloro-3-methylbut-1-yne, 0.48 g (12 mmoles) sodium hydroxide, 80 mg Tetrabutylammoniumbromide and 3 mg of potassium iodide was stirred at 50 °C for 24 h. Then the aqueous layer was acidified with diluted hydrochloric acid and extracted the reaction mixture with dichloromethane. 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 CHCl$_3$) to give 0.60 g (60%) of the major product. M.p. 92–94 °C; $\lambda_{max}$ (MeOH) 335.5 (log $\varepsilon$ 4.5728), 340.0 (4.5858), 345.3 (4.6177) and 207.1 (4.6649) nm; $\nu_{max}$ (neat) 3000, 1715, 1640, 1605, 1565, 1495, 1460, 1415, 1360, 1330, 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%); $\delta_{H}$ 60 MHz (CDCl$_3$) 7.78 (1H, m, 1H), 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(CH$_3$)$_3$).

C$_{14}$H$_{12}$O$_2$ 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, $^1$H NMR, m.p., UV.)

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

Same reaction (a) was carried out for 2$\times$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-ynene, 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. (CHCl$_3$) to give 90 mg of the major product. M.p. 89–93 °C; $\lambda_{max}$ (MeOH) 330.5 (log $\varepsilon$ 3.4765), 315 (3.7283), 258.2 (3.5608), 249.2 (3.609), 229.6 (sh-3.7195) and 205.63 (4.1433) nm; $\nu_{max}$ (CHCl$_3$) 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%); $\delta_{H}$ 300 MHz (CDCl$_3$) 7.72 (1H, m, 9H), 7.59 (1H, m, Ar–H), 7.41–7.26 (2H, m, Ar–H), 5.0 ($1H$, t, $J = 3.2$ and 6.0 Hz C=C–H), 4.57 ($1H$, t, $J = 3.3$ and 5.6 Hz C=C–H), 4.10 ($1H$, d, $J = 7.0$ Hz 3H) and 1.55 (3H, d, $J = 7.0$ Hz 3C–CH$_3$).

C$_{15}$H$_{10}$O$_2$ m/z requires 214.0630, found 214.0628.

The financial support of the Minister für Wissenschaft und Forschung des Landes Nordrhein-Westfalen is gratefully acknowledged. H. R. W. D. thanks the DAAD for the award of a fellowship.
[6] a) J. Reisch, Arch. Pharm. (Weinheim) 299, 798, 806 (1966);
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