The Reactions of 4-Hydroxy-2-pyrones With 2-Hydroxybenzaldehydes. A Note of Warning

P. de March, M. Moreno-Mañas* and J. L. Roca

Departamento de Química Orgánica, Facultad de Ciencias,
Universidad Autónoma de Barcelona, Bellaterra, Barcelona, Spain

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The reaction between 2-hydroxybenzaldehyde and 4-hydroxy-6-methyl-2-pyrone (triacetic acid lactone) affords 3-acetoacetyl-2-chromenone, **7**, instead of 3-(2-hydroxybenzylidene)-6-methyl-3,4-dihydro-2*H*-pyran-2,4-dione, **6**. The structures previously reported in the literature for the products formed in the reactions of 4-hydroxy-2-chromenone with 2-hydroxybenzaldehydes in a molar ratio 1:1 are considered erroneous. Thus, the previously reported 3-(2-hydroxybenzylidene)chroman-2,4-dione, **10**, should be formulated as 3-(2-hydroxybenzoyl)-2-chromenone, **11**.

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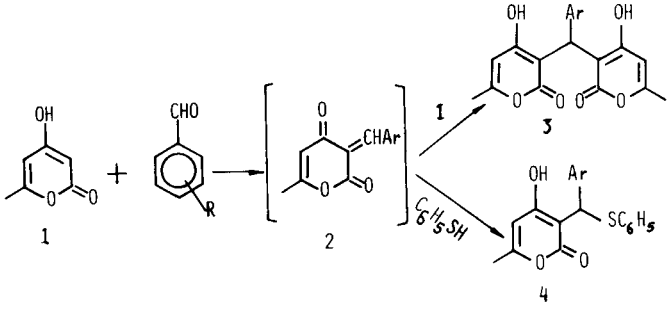
The reactions between aromatic aldehydes and 4-hydroxy-6-methyl-2-pyrone, **1**, (triacetic acid lactone), afford arylbis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methanes, **3**. The postulated intermediates, 3-arylmethylene-6-methylpyran-2,4-dione, **2** have never been isolated. However, they can be trapped by thiophenol to afford aryl(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)phenylthiomethanes **4** [1,2] (Scheme 1).

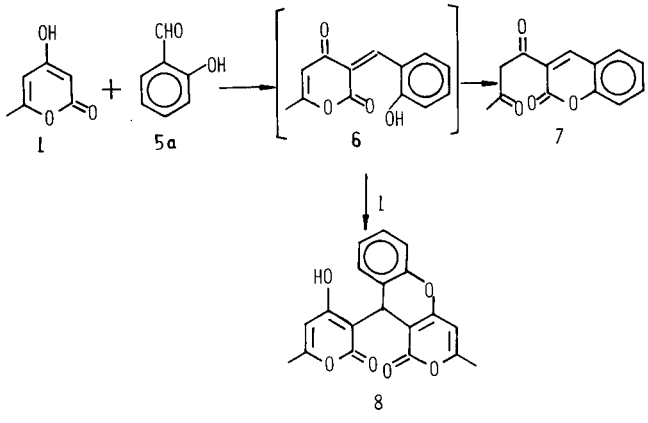
Scheme 1



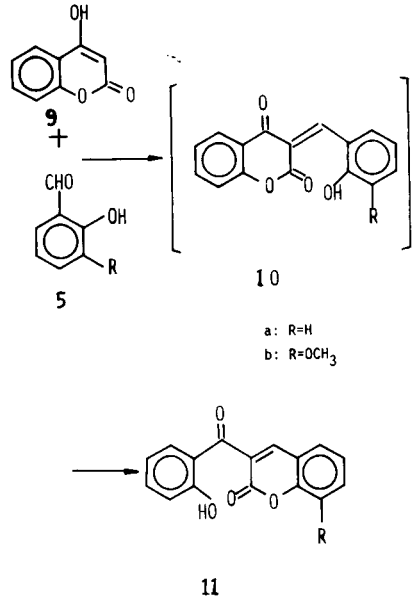
However, when the lactone **1** was treated with 2-hydroxybenzaldehyde, **5a**, in refluxing ethanol in the absence of catalyst, a product arising from condensation of the starting materials in a 1:1 ratio was isolated, in addition to the not unexpected 10-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-3-methyl-1*H*,10*H*-pyrano[4,3-*b*]chromen-1-one, **8**, (Scheme 2). The 1:1 condensation product was not 3-(2-hydroxybenzylidene)-6-methylpyran-2,4-dione, **6**, but 3-acetoacetyl-2-chromenone, **7**, formed by intramolecular translactonization. This was demonstrated by comparison with an authentic specimen of **7**, kindly supplied by Professor F. M. Dean, prepared by acetylation of 3-acetyl-2-chromenone [3,4]. Particularly relevant was the mass spectrum of **7** [4], which presented the base peak at m/e 173 ($M^+ - CH_2COCH_3$) not compatible with structure **6**.

The reactions between 4-hydroxy-2-chromenone (4-hydroxycoumarin), **9**, and several 2-hydroxybenzaldehydes, **5**, have been reported to afford 1:1 condensation products in addition to the usual 2:1 products [5,6]. Since the 3-(2-hydroxybenzylidene)chroman-2,4-dione structures, **10**, (Scheme 3) were attributed to the 1:1 condensation products, we suspected these assignments to be in error and decided to reexamine two of these products.

Scheme 2

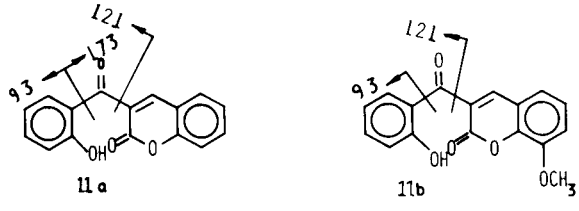


Scheme 3



When salicylaldehyde (**5a**, R = H) reacted with **9** under the experimental conditions already described [5,6], a 1:1 condensation product, mp 177-179° (lit [5,6] mp 175°) was isolated. It exhibited the following spectroscopic behaviour; ir (potassium bromide): 1710, 1620, 1600, 1585 cm^{-1}; pmr (deuteriochloroform): δ 7.5-8.35 (m, 8H), 8.5 (s, 1H), 11.7 (s, 1H); cmr (deuteriochloroform): δ 196.2, 163.3, 157.8, 154.7, 143.9, 137.8, 133.5, 132.5, 129.0, 126.7, 125.0, 119.1, 118.6, 118.0, 116.9; ms: 266 (M^+, 36), 265 (100), 249 (17), 173 (8), 121 (41), 120 (18), 118 (8), 93 (12), 92 (9), 89 (11), 65 (18). Particularly relevant are the pmr and ms data. Thus, coumarin itself presents two doublets at δ 6.4 and 7.75 due to the olefinic moiety. Although it is difficult to predict where the olefinic proton of **10** would appear, it is reasonable to assume that a chemical shift at δ 8.5 is compatible with structure **11** taking into account the effect of the magnetic anisotropy of its ketone group. Moreover, structure **11a** can account for the peak at m/e 121 (41), which can not be easily accomodated by structure **10a** (Scheme 4).

Scheme 4



11a 11b

Similarly, the reaction between **9** and **5b** gave a 1:1 condensation product, mp 194-196° (lit [6] mp 198°) which presented the following spectroscopic behaviour: ir (potassium bromide): 1705, 1615, 1600, 1580 cm^{-1}; pmr (d_6-dimethyl sulfoxide): δ 4.0 (s, 3H), 6.9-7.9 (m, 7H), 8.4 (s, 1H); ms: 297 (14), 296 (M^+, 64), 295 (100), 280 (12), 279 (41), 265 (33), 176 (21), 148 (11), 121 (75), 93 (16), 89 (11), 76 (10), 65 (18). Comments similar to those formulated for **11a** apply here. Particularly relevant is the peak at 121 (75) which is attributed to the 2-hydroxybenzoyl moiety present in structure **11b**, but not in **10b**.

Although products **11a** and **11b** have not been in our hands amenable to X-ray analysis, we consider that the available spectroscopic evidence strongly favours the structures of 3-(2-hydroxybenzoyl)-2-chromenone, **11a**, and 3-(2-hydroxybenzoyl)-8-methoxy-2-chromenone, **11b**, for the 1:1 condensation products arising from the reactions of 4-hydroxy-2-chromenone with salicylaldehyde, **5a**, and with 2-hydroxy-3-methoxybenzaldehyde, **5b**, respectively.

EXPERIMENTAL

The ir spectra were recorded on a Perkin-Elmer 1310 spectrophotometer. The pmr and cmr spectra were recorded on a Brucker WP80SY spectrometer. The ms were run on a Hewlett-Packard 5985-B spectrometer; only peaks with intensity higher than 20% are given.

Reaction Between 2-Hydroxybenzaldehyde, **5a**, and 4-Hydroxy-6-methyl-2-pyrone, **1**.

The aldehyde **5a** (1.43 g, 0.012 mole) in ethanol (6 ml) was added to the lactone **1** (1.25 g, 0.01 mole) in ethanol (13 ml). The mixture was refluxed for 10 minutes and upon standing for 2 hours a yellow precipitate (0.16 g) of 3-acetoacetyl-2-chromenone, **7**, appeared. It was filtered off. The solution, left overnight at 0°, produced a mixture (0.35 g) of **7** and 10-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-3-methyl-1*H*,10*H*-pyrano[4,3-*b*]chromen-1-one, **8**. Addition of **5a** (0.01 mole) to the residual solution afforded a new crop of **7** (0.89 g overall, 39%) and mixtures of **7** and **8**. Pure samples of **7** were produced by recrystallization in methanol. The chromenone **7** had mp 150-152° (lit [3], mp 152-153°); ir (potassium bromide): 1725, 1605, 1580 cm^{-1}; pmr (deuteriochloroform): δ (enol form) 2.24 (s, 3H), 7.0 (s, 1H), 7.2-7.8 (m, 4H), 8.63 (s, 1H), small peaks at 2.32 and 4.20 due to the keto form were detected; cmr (d_6-dimethyl sulfoxide): δ 198.4, 173.3, 153.9, 145.9, 134.3, 130.2, 125.0, 124.9, 118.2, 116.0, 115.9, 100.9, 26.7; the mass spectrum was identical to that described [4]: 230 (M^+, 38), 229 (20), 187 (23), 173 (100).

Anal. Calcd. for $C_{13}H_{10}O_4$: C, 67.82; H, 4.38. Found: C, 67.60; H, 4.35.

Product **8** had mp 250° dec; ir (potassium bromide): 3300-2800 (broad), 1705, 1655-1645 (broad), 1615, 1590, 1565 cm^{-1}; pmr (d_6-dimethyl sulfoxide): δ 2.1 (s, 3H), 2.2 (s, 3H), 5.2 (s, 1H), 6.0 (s, 1H), 6.2 (s, 1H), 6.9-7.2 (m, 4H); cmr (d_6-dimethyl sulfoxide): δ 165.0, 163.0, 161.8, 160.9, 160.8, 149.1, 128.3, 127.7, 124.7, 122.9, 115.6, 104.2, 99.8, 98.5, 97.5, 26.8, 19.0; ms: 338 (M^+, 59), 268 (23), 267 (94), 253 (92), 226 (37), 213 (100), 171 (49), 115 (23), 69 (31), 43 (56).

Anal. Calcd. for $C_{18}H_{14}O_6$: C, 67.45; H, 4.17. Found: C, 67.24; H, 4.24.

A better synthesis of **7** was as follows: to a solution of the lactone **1** (1.23 g, 0.0098 mole) in absolute ethanol (11 ml), molecular sieves and **5a** (1.45 g, 0.012 mole) in ethanol (7 ml) were added. The mixture was refluxed for 10 minutes. A precipitate (1.23 g) of **7** appeared overnight. It was filtered off and more **5a** (1.3 g, 0.01 mole) was added to the solution. Upon standing overnight a new crop of **7** (0.8 g) was produced. The overall yield of **7** was 89%.

Acknowledgements.

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