Heteroannulation of 4-Oxochromene-3-carbaldehyde Derivatives using Halogenoalkanols and Base

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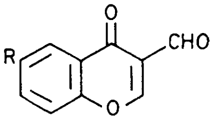
4-Oxochromene-3-carbaldehyde derivatives react with 2-iodoethanol and potassium carbonate in acetone to produce tetrahydrofuro[2,3-*b*][1]benzopyran-4-ones.

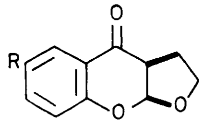
4-Oxochromene-3-carbaldehydes are highly functional molecules, capable of reacting as heterodienes,[1] cuprate acceptors,[2] or dienophiles,[3] and undergoing a variety of rearrangements.[4] Herein we describe a new transformation of these versatile heterocycles, namely their conversion to the hitherto unknown tetrahydrofuro[2,3-*b*][1]benzopyran-4-one system *via* a one-step heteroannulation procedure.

Treatment of 6-hydroxy-4-oxochromene-3-carbaldehyde (**1a**)[5] with 2-iodoethanol under standard alkylation conditions gave a major product, isolated by extraction and crystallisation, of m.p. 174—175 °C (ethyl acetate–light petroleum, 1 : 1). From spectral data ($\nu_{max.}$ 3425 and 1670 cm^{-1}; *m/z* 206) it was apparent that the expected hydroxyethylation had not occurred, but that a chromanone had been formed with concomitant deformylation. The ^{1}H n.m.r. spectrum of the product [δ(CDCl$_3$), 2.0—2.5 (m, 2H), 2.9—3.2 (m, 1H), 4.0—4.4 (m, 2H), 4.9 (s, 1H, D$_2$O exchangeable), 5.9 (d, 1H, *J* 4 Hz), and 6.9—7.3 (m, 3H)] was consistent with the tetrahydrofuro[2,3-*b*][1]benzopyran-4-one structure (**2a**).

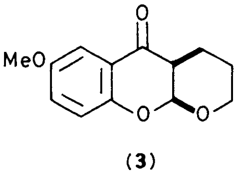
With other derivatives of (**1**)[6,7] analogous results were obtained (Table 1). Each product displayed the spectral signals characteristic of the acetal hydrogen [δ 5.9—6.0 (d, 1H, *J* 4—4.5 Hz)] and chromanone carbonyl group ($\nu_{max.}$ 1680—1695 cm^{-1}). The reaction of the 6-methoxy derivative (**1c**) was also efficient using 2-bromoethanol, but was less so using 3-iodopropanol,[8] which furnished the tetrahydropyrano[2,3-*b*][1]benzopyran-5-one (**3**) in only 25% yield despite more vigorous reaction conditions. The ^{1}H n.m.r. spectrum of the latter [δ 5.5 (d, 1H, *J* 3 Hz)] is consistent with the *cis* arrangement depicted.[9]



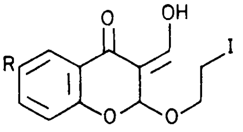
(**1**)



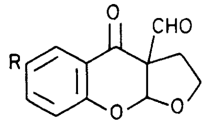
(**2**)



(**3**)



(**4**)



(**5**)

The heteroannulation is probably initiated by addition of the halogenoalkanol to the 2-position of compound (**1**). This

Table 1. Reactions of 4-oxochromene-3-carbaldehyde derivatives (**1**) with halogenoalkanols and base.

Derivative of (**1**)[a]	R	Halogenoalkanol	Product	% Yield[b]
(**1a**)	OH	I[CH$_2$]$_2$OH	(**2a**)	65
(**1b**)	H	I[CH$_2$]$_2$OH	(**2b**)	53[c]
(**1c**)	OMe	I[CH$_2$]$_2$OH	(**2c**)	70
(**1c**)	OMe	Br[CH$_2$]$_2$OH	(**2c**)	60
(**1d**)	NO$_2$	I[CH$_2$]$_2$OH	(**2d**)	40[c]
(**1c**)	OMe	I[CH$_2$]$_3$OH[d]	(**3**)	25[c]

[a] Reaction conditions: compound (**1**) (1 mmol), the halogenoalkanol (3 mmol), and anhydrous potassium carbonate (0.3—0.5 g) were heated in acetone (30 ml) under reflux for 4 h. Products were isolated by evaporation, extraction with ethyl acetate, and crystallisation. [b] Yields refer to isolated chromatographically homogeneous material. All products were characterised by elemental analysis and spectroscopy. [c] Purified by chromatography over silica gel. [d] Using halogenoalkanol (8 mmol) and anhydrous potassium carbonate (2 g) in acetone (30 ml), and heating under reflux for 72 h.

produces an intermediate (**4**) capable of base-induced intramolecular alkylation, which gives (**5**). Subsequent deformylation, also promoted by base, leads to the observed product. This type of reaction sequence should have considerable scope and is under investigation.

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