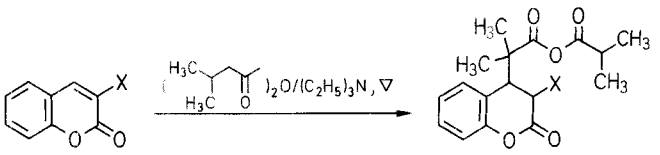
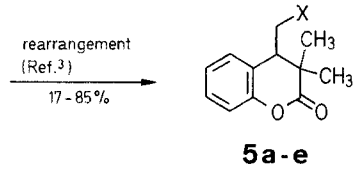


4a-e

| 4,5 | X |
|---|---|
| a | –C≡N |
| b | –COOCH$_3$ |
| c | –COOC$_2$H$_5$ |
| d | –COOC$_4$H$_9$-*t* |
| e | –COO–C$_6$H$_5$ |



5a-e

## Synthesis of the Nitrile and Some Esters of 3,3-Dimethyl-2-oxochroman-4-acetic Acid

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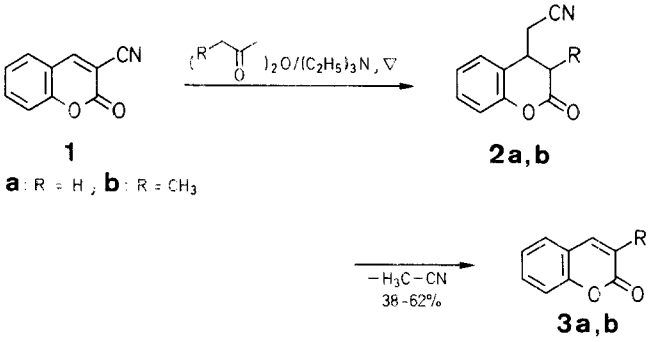
It is shown that the previously found rearrangement can be applied on the nitrile **4** (X = CN) when the anhydride used possesses only one α-hydrogen atom. Refluxing of this nitrile with isobutyric anhydride in the presence of triethylamine leads to the expected rearrangement product **5** (X = CN). Making use of the same anhydride, the esters **4** (X = COOR) are converted into esters **5** (X = COOR).

In earlier publications[1,2] we described a new molecular rearrangement, consisting in transformation of the esters of 2-oxo-2*H*-1-benzopyran-3-carboxylic acid, when heated with acetic, propionic, or butyric anhydride and triethylamine, into esters of 2-oxochroman-4-acetic acid, respectively, alkylated or not, in position 3.

Now we report the results of our investigation on the possibility to realize the same rearrangement with the nitrile of 2-oxo-2*H*-1-benzopyran-3-carboxylic acid (**1**). Using acetic anhydride we found that in this case instead of the expected nitrile **2a**, 2-oxo-2*H*-1-benzopyran (**3a**) was obtained. When the anhydride of propionic acid was employed 3-methyl-2-oxo-2*H*-1-benzopyran (**3b**) and very small amount (7%) of the nitrile **2b** were isolated.



**1** **2a,b**

**a**: R = H; **b**: R = CH$_3$



**3a,b**

According to our previously observations[1] these facts could be explained with an elimination of acetonitrile from the initially formed rearrangement products **2a** and **2b**. Therefore we checked to stop the conversion at the nitrile stage by carrying it out with an anhydride, containing only one α-hydrogen atom. Refluxing a mixture of **1** and isobutyric anhydride in the presence of triethylamine, we obtained with fairly good yield (58%) the expected 3,3-dimethyl-2-oxochroman-4-acetonitrile (**5a**) together with negligible amounts of nonidentified side products. This result prompted us to prepare also some esters of the unknown 3,3-dimethyl-2-oxochroman-4-acetic acid. Starting from the corresponding ester of 2-oxo-2*H*-1-benzopyran-3-carboxylic acid and following the same procedure we have obtained the methyl and the ethyl esters (**5b** and **5c**) with very good yields. The yields of the *t*-butyl and the phenyl ester (**5d** and **5e**) were, however, considerably lower.

**Rearrangement of 1; General Procedure:**

A mixture of **1**[4] (1.71 g; 10 mmol), triethylamine (1.4 ml, 10 mmol), and the corresponding anhydride (10 ml) is refluxed for 10 h. The excess of anhydride is distilled in vacuo and to the residue water (50 ml) is added. The resulting emulsion is extracted with chloroform (3 × 50 ml). The extract is washed with dilute sodium hydrogen carbonate solution (3 × 50 ml), then with water, and dried with sodium sulfate. The residue after removal of the solvent is purified by column chromatography over silica gel (eluent: hexane/ethyl acetate with gradually increasing of polarity).

The results obtained with the employed anhydrides are given below.

(a) With *acetic anhydride*: The chromatography gives **3a**; yield: 0.55 g (38%), m.p. 67–69°C (Ref.[5], m.p. 67–67.5°C); mixture m.p. with an authentic sample is not depressed.

(b) With *propionic anhydride*: By working up of the fractions 15–21 **3b** is obtained; yield: 1.0 g (62%); m.p. 90–91°C (Ref.[6], m.p. 91°C). The substance is identified and by comparing its I.R. and N.M.R. spectra with those of the authentic sample. After supplementary purifying of fractions 60–67 over silica gel and recrystallisation of the obtained product from ethanol **2b** is isolated; yield: 0.15 g (7%); m.p. 138–148°C (a mixture of diastereoisomers).

$C_{12}H_{11}NO_2$ (201.2) calc. C 71.62 H 5.51 found 71.98 5.71

I.R. ($CHCl_3$): $\nu$ = 1780; 2260 cm$^{-1}$.

$^1$H-N.M.R. ($CDCl_3$): $\delta$ = 1.40 (dd, 3H, $CH_3$); 2.17–2.90 (m, 2H, $CH_2$); 3.04–3.41 (m, 2H, H-3 and H-4); 7.04–7.42 ppm (m, 4H$_{arom}$).

(c) With *isobutyric anhydride*: The chromatography fractions 45–55 give **5a**; yield: 1.25 g (58%); m.p. 85–87°C.

$C_{13}H_{13}NO_2$ (215.2) calc. C 72.54 H 6.09 found 72.36 6.05

I.R. ($CHCl_3$): $\nu$ = 1765; 2250 cm$^{-1}$.

$^1$H-N.M.R. ($CDCl_3$): $\delta$ = 1.24 and 1.42 [two s, 6H, $C(CH_3)_2$]; 2.17–3.07 (m, 3H, $CH_2$ and H-4); 7.00–7.42 ppm (m, 4H$_{arom}$).

**Preparation of 5b–e:**

Using the corresponding ester of 2-oxo-2*H*-1-benzopyran-3-carboxylic acid **4** (5 mmol), isobutyric anhydride (5 ml) and triethyl-

amine (5 mmol), the above described general procedure is followed. The isolation of the reaction products, however, is performed by extraction with ether (3 × 50 ml), removal of the solvent, and column chromatography of the residue (silica gel; ethyl acetate/hexane 1:19 and 1:9). The yields and the physical and spectral data of the obtained substances are given in the Table.

**Table.** Esters of 3,3-Dimethyl-2-oxochroman-4-acetic Acid **5**

| **5** | Yield [%] | m.p. [°C] | Molecular Formula[a] | $^1$H-N.M.R. ($CDCl_3$)[b] $\delta$ [ppm] |
|---|---|---|---|---|
| **b** | 85 | 58–60° | $C_{14}H_{16}O_4$ (248.3) | 1.23 and 1.39 [two s, 6H, $C(CH_3)_2$]; 2.2–3.0 (m, 2H, $CH_2$); 3.12–3.32 (m, 1H, H-4); 3.60 (s, 3H, $OCH_3$); 7.00–7.32 (m, 4$H_{arom}$) |
| **c** | 80 | liquid | $C_{15}H_{18}O_4$ (262.3) | 1.15 (t, 3H, $CH_2\underline{CH}_3$); 1.19 and 1.32 [two s, 6H, $C(CH_3)_2$]; 2.10–2.87 (m, 2H, $CH_2$); 3.07–3.27 (m, 1H, H-4); 4.02 (q, 2H, $CH_2$); 6.90–7.25 (m, 4$H_{arom}$) |
| **d** | 17 | liquid | $C_{17}H_{22}O_4$ (290.3) | 1.2 (s, 3H, $CH_3$); 1.36 [s, 12H, $CH_3 + C(CH_3)_3$]; 2.26 (q, 1H, $CH_2$, $J_{AB}$ = 15.2 Hz, $J_{AX}$ = 9.3 Hz); 2.65 (q, 1H, $CH_2$, $J_{BX}$ = 5.3 Hz); 3.16 (q, 1H, H-4); 7.00–7.11 (m, 2H, H-6 + H-8, $H_{arom}$); 7.21–7.30 (m, 2H, H-5 + H-7, $H_{arom}$) |
| **e** | 29 | 81–83° | $C_{19}H_{18}O_4$ (310.3) | 1.26 and 1.47 [two s, 6H, $C(CH_3)_2$]; 2.42–3.00 (m, 2H, $CH_2$); 3.17–3.42 (m, 1H, H-4); 6.87–7.37 (m, 9$H_{arom}$) |

[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.24%, H ±0.19%).

[b] Spectra were recorded on Tesla BS-487 C or Bruker 250 MHz with TMS as internal standard. I.R. ($CHCl_3$) of **5b–d**: $\nu$ = 1745 (COOR), 1765 $cm^{-1}$ (C=O, $\delta$-lactone). For the same carbonyl groups in the I.R. spectrum of **5e** there is only one absorption at 1765 $cm^{-1}$.

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