Synthesis of 3-(1-Acyloxybenzyl)-2-oxo-2*H*-1-benzopyrans and 3-(1-Acylaminobenzyl)-2-oxo-2*H*-1-benzopyrans

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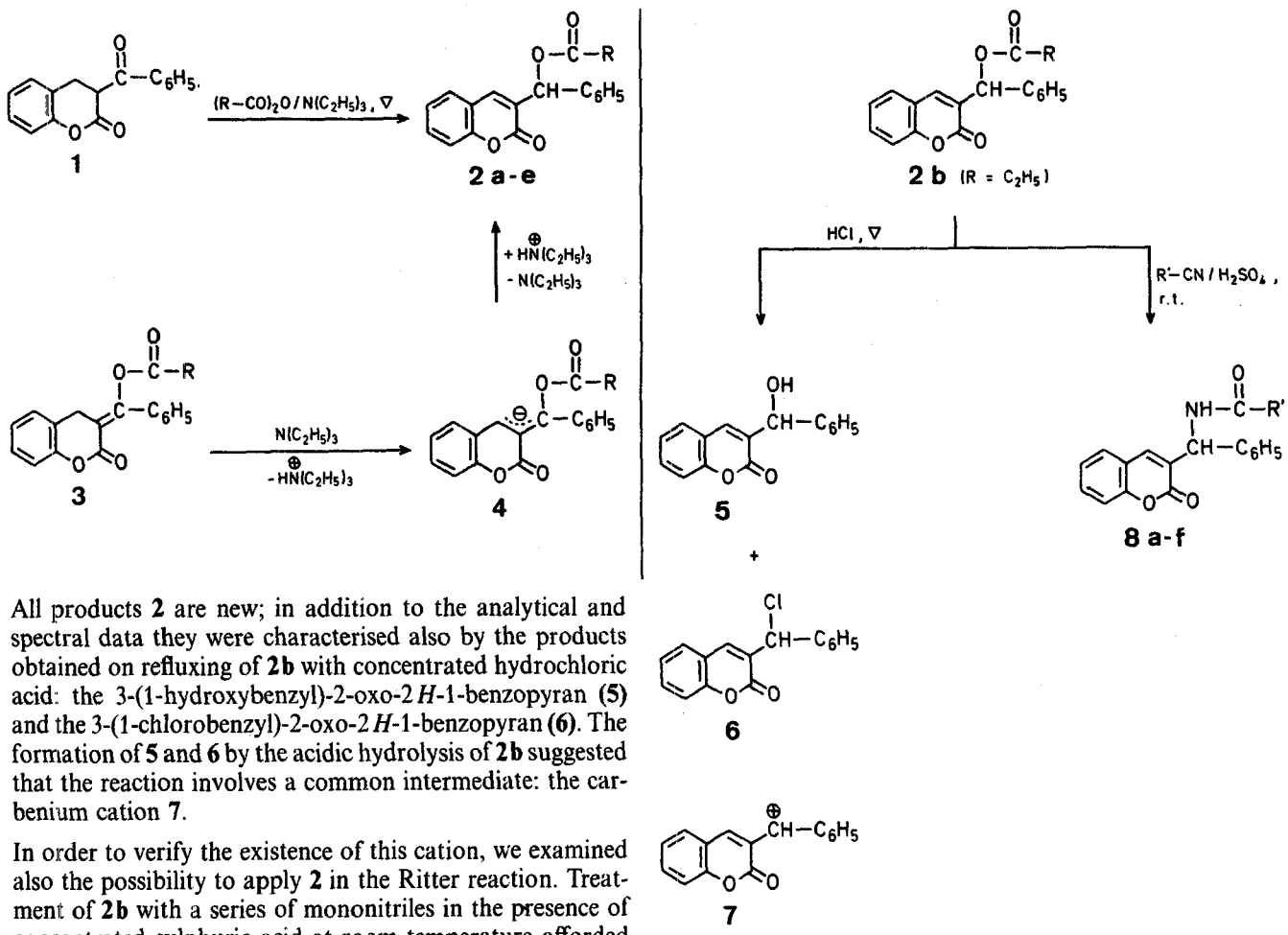
It is known that, under the action of acyl chlorides or acid anhydrides in the presence of a base (usually pyridine), β-ketoesters undergo transformation into esters of their enol forms. Up to now, however, a similar conversion of α-acylated lactones like the 3-acyl-2-oxochromanes (structural analogues of β-ketoesters) has not been described. In the course of our studies on the 3-substituted 2-oxo-2*H*-1-benzopyrans[1,2], we found that by heating of 3-benzoyl-2-oxochromane **(1)** with acid anhydrides in the presence of triethylamine the 3-(1-acyloxybenzyl)-2-oxo-2*H*-1-benzopyrans **2a–e** were formed.



All products **2** are new; in addition to the analytical and spectral data they were characterised also by the products obtained on refluxing of **2b** with concentrated hydrochloric acid: the 3-(1-hydroxybenzyl)-2-oxo-2*H*-1-benzopyran (**5**) and the 3-(1-chlorobenzyl)-2-oxo-2*H*-1-benzopyran (**6**). The formation of **5** and **6** by the acidic hydrolysis of **2b** suggested that the reaction involves a common intermediate: the carbenium cation **7**.

In order to verify the existence of this cation, we examined also the possibility to apply **2** in the Ritter reaction. Treatment of **2b** with a series of mononitriles in the presence of concentrated sulphuric acid at room temperature afforded the expected, new 3-(1-acylaminobenzyl)-2-oxo-2*H*-1-benzopyrans **8a–f** in high yields (75–96%). Attempts to hydrolyse some of them to the free amine by boiling with an acid, however, failed.

As far as the mechanism of the transformation of **1** into **2** is concerned, it is very probable that firstly the esters **3** are formed. As fairly strong carbon acids (active methylene groupe in position 4) they easily isomerise then to **2**. The isomerisation, involving deprotonation of **3** and reprotonation of the generated anion **4** is favoured, obviously, by the formation of the more stable 2-pyranone ring of **2**.

3-(1-Acyloxybenzyl)-2-oxo-2*H*-1-benzopyrans 2a–e; General Procedure:

A mixture of 3-benzoyl-2-oxochromane (**1**; 1.26 g, 5 mmol), triethylamine (0.7 ml, 5 mmol), and the appropriate anhydride (5 ml) is refluxed for 10 h. The excess of anhydride is removed under reduced presure and water (50 ml) is added. The mixture is extracted with benzene (3 × 50 ml) and the combined extracts are washed with dilute sodium hydrogen carbonate solution, then with water (50 ml), and dried with sodium sulphate. After evaporation of the solvent, the residue is purified by the column chromatography (on silica gel with 1:4 ethyl acetate/hexane as eluent) to give pure **2a–e** (Table 1).

Table 1. 3-(1-Acyloxybenzyl)-2-oxo-2*H*-1-benzopyrans (**2a–e**)

Product **2**	R	Yield [%]	m.p. [°C]	Molecular formula[a,b]	^{1}H-N.M.R. ($CDCl_3$)[c] δ [ppm]
a	CH_3	85	136–138°	$C_{18}H_{14}O_4$ (294.3)	2.22 (s, 3H, CH_3); 6.95 (s, 1H, CH); 7.25–7.50 (m, 9H_{arom}); 7.75 (s, 1H, H-4)
b	C_2H_5	91	110–112°	$C_{19}H_{16}O_4$ (308.3)	1.19 (t, 3H, CH_3); 2.50 (q, 2H, CH_2); 6.95 (s, 1H, CH); 7.25–7.50 (m, 9H_{arom}); 7.71 (s, 1H, H-4)
c	*n*-C_3H_7	93	72–74°	$C_{20}H_{18}O_4$ (322.3)	0.97 (t, 3H, CH_3); 1.41–2.00 (m, 2H, $CH_2CH_2CH_3$); 2.47 (t, 2H, $CH_2CH_2CH_3$); 6.95 (s, 1H, CH); 7.25–7.50 (m, 9H_{arom}); 7.71 (s, 1H, H-4)
d	*i*-C_3H_7	81	105–106°	$C_{20}H_{18}O_4$ (322.3)	1.19, 1.29 [d, 6H, $CH(CH_3)_2$]; 2.55–2.90 [m, 1H, $CH(CH_3)_2$]; 6.96 (s, 1H, CH); 7.25–7.50 (m, 9H_{arom}); 7.72 (s, 1H, H-4)
e	H_3C—CH=CH	59	118–120°	$C_{20}H_{16}O_4$ (320.3)	1.94 (dd, 3H, CH_3, $J_{H_\alpha,CH_3} \approx 1.5$ Hz); 5.59 (dd, 1H, H-α, $J_{H_\alpha,H_\beta} \approx 16$ Hz); 6.97 (s, 1H, CH); 7.12–7.50 (m, 9H_{arom} + H); 7.75 (s, 1H, H-4)

[a] Satisfactory microanalyses obtained: C ±0.19, H ±0.20; exception: **2e**, C – 0.49; analyses performed in the Laboratory of Elemental Analysis at Sofia University.

[b] I.R. ($CHCl_3$): **2a–d** $\nu_{C=O}$ = 1740, 1720 cm^{-1}; **2e** $\nu_{C=O}$ = 1735, 1715 cm^{-1}.

[c] Recorded on a Tesla BS-487 C spectrometer.

Table 2. 3-(1-Acylaminobenzyl)-2-oxo-2*H*-1-benzopyrans (**8a–f**)

Product **8**	R^1	Yield [%]	m.p. [°C] (solvent)	Molecular formula[a,b]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
a	CH_3	75	168–170° (ethyl acetate)	$C_{18}H_{15}O_3N$ (293.3)	2.61 (s, 3H, CH_3); 6.49 (d, 1H, CH); 7.37–7.75 (m, 9H_{arom}); 8.11 (s, 1H, H-4); 9.09 (d, 1H, NH)
b	$ClCH_2$	96	151–153° (ethyl acetate)	$C_{18}H_{14}O_3NCl$ (327.8)	4.40 (s, 2H, CH_2); 6.44 (d, 1H, CH); 7.37–7.75 (m, 9H_{arom}); 8.12 (s, 1H, H-4); 8.77 (d, 1H, NH)
c	$C_6H_5CH_2$	94	177–179° (ethyl acetate)	$C_{24}H_{19}O_3N$ (369.4)	4.07 (s, 2H, CH_2); 6.42 (d, 1H, CH); 7.25–7.75 (m, 14H_{arom}); 8.00 (s, 1H, H-4); 8.61 (d, 1H, NH)
d	C_6H_5	96	232–235° (ethyl acetate)	$C_{23}H_{17}O_3N$ (355.4)	6.62 (d, 1H, CH); 7.45–7.92 (m, 14H_{arom}); 8.12 (s, 1H, H-4); 8.81 (d, 1H, NH)
e	$H_2C{=}CH$	79	216–218° (ethyl acetate)	$C_{19}H_{15}O_3N$ (305.3)	6.07 (m, 1H, C$\underline{H}$=CH_2); 6.56 (m, 3H, C$\underline{H}$—C_6H_5 + CH=C$\underline{H}_2$); 7.37–7.82 (m, 9H_{arom}); 8.10 (s, 1H, H-4); 8.62 (d, 1H, NH)
f	$C_2H_5OOC{-}CH_2$	82	124–126° (C_2H_5OH)	$C_{21}H_{19}O_5N$ (365.4)	1.32 (t, 3H, CH_3); 3.45 (s, 2H, CH_2); 4.26 (q, 2H, C$\underline{H}_2$$CH_3$); 6.25 (d, 1H, CH); 7.20–7.50 (m, 9H_{arom}); 7.82 (s, 1H, H-4); 8.30 (d, 1H, NH)

[a] All products gave satisfactory microanalyses: C ±0.23; H ±0.21; N ±0.29; exception: **8b**, C +0.42.

[b] I.R. ($CHCl_3$): ν = 1665–1680 (CONH), 1720 (C=O, lactone), 3400–3450 (NH) cm^{-1}.

Hydrolysis of 2b:

A suspension of 3-(1-propanoyloxybenzyl)-2-oxo-2*H*-1-benzopyrane (**2b**; 0.50 g) in concentrated hydrochloric acid (10 ml) is heated under reflux for 6 h. The mixture is cooled to room temperature, poured into water (50 ml), and extracted with ether (3 × 50 ml). The organic extract is washed with dilute sodium hydrogen carbonate solution (30 ml), then with water (30 ml), and dried with sodium sulphate. The solvent is evaporated and the residue is chromatographed on silica gel, using 1:4 ether/heptane as eluent. The fractions 4–8 (5×50 ml), after evaporating the solvent, give pure **6**; yield: 0.23 g, (52%); m.p. 124–126°C.

$C_{16}H_{11}ClO_2$ (270.7) calc. C 70.99 H 4.10 found 71.46 4.16

I.R. ($CHCl_3$): ν = 1723 cm^{-1} (C=O, lactone).

^{1}H-N.M.R. ($CDCl_3$): δ = 6.23 (s, 1H, CH); 7.17–7.55 (m, 9H_{arom}); 7.90 ppm (s, 1H, H-4).

From the fractions 13–17 (5×50 ml) is isolated **5**; yield: 0.18 g (44%), m.p. 119–122°C.

$C_{16}H_{12}O_3$ (252.26) calc. C 76.18 H 4.80 found 76.30 5.01

M.S.: *m/e* = 252 (M^+), 234 ($M^+ - H_2O$), 206 ($M^+ - H_2O, -CO$), 175 ($M^+ - C_6H_5$), 147 ($M^+ - C_6H_5CO$), 118 ($M^+ - C_6H_5CO, -CO, -H$); 105 ($C_6H_5CO^+$).

I.R. ($CHCl_3$): ν = 1715 (C=O, lactone), 3600 cm^{-1} (OH).

^{1}H-N.M.R. ($CDCl_3$): δ = 3.47 (s, 1H, OH; disappeared on addition of D_2O); 5.85 (s, 1H, CH); 7.22–7.55 (m, 9H_{arom}); 7.62 ppm (s, 1H, H-4).

3-(1-Acylaminobenzyl)-2-oxo-2*H*-1-benzopyrans 8a–f; General Procedure:

To a mixture of **2b** (1.54 g, 5 mmol) and appropriate nitrile (5 mmol) is added dropwise conc. sulfuric acid (2 ml) for 5–10 min. The mixture is stirred, allowed to stand at room temperature for 1 h, and then poured into ice/water (50 ml). The resultant white solid is isolated by filtration, washed with sodium hydrogen carbonate solution, and water, and recrystallised (Table 2).

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[1] A. Bojilova, C. Ivanov, *Synthesis* **1976**, 267.
[2] C. Ivanov, A. Bojilova, *Chem. Ber.* **111**, 3755 (1978).