Synthesis of Some 1-Aryl-4-(2-hydroxybenzoyl)-pyrazol-5-one and 1-Aryl[1]benzopyrano[2,3-*c*]pyrazol-4(1*H*)-one Derivatives from 3-Acyl-4-hydroxycoumarins

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4-Hydroxycoumarins are versatile intermediates for the synthesis of various heterocyclic compounds. The chemistry of coumarins with 3:4 fused ring systems has recently been reviewed[1]. The formation of phenylhydrazones **3** via the 3-acylcoumarins **1** and a phenylhydrazine **2** is well established[2,3,4]. The cyclodehydration of **3** to **4** occurs in boiling xylene with a small amount of *p*-toluenesulfonic acid[3,4].

We now describe a new type of ring transformation of the phenylhydrazones **3** which opens a general route to new 1-aryl-4-(2-hydroxybenzoyl)-pyrazol-5-ones **5**. 4-Aroylpyrazol-5-one derivatives[5,6] are important compounds because of their antibacterial, herbicidal[7], and chelating properties[8]. When the hydrazones **3** are refluxed in acetic acid, they are transformed into the pyrazol-5-one derivatives **5** by a nucleophilic attack at the C-2 lactone carbonyl group with ring opening. The reaction can be achieved in a one step synthesis without isolation of the hydrazone **3**, merely by refluxing the acylcoumarins **1** and the phenylhydrazine **2** in acetic acid.

Compounds **5** are easily converted into the substituted 1-aryl[1]benzopyrano[2,3-*c*]pyrazol-4-(1*H*)-ones **6**. The melting points of compounds **6a** and **6f** are in agreement with those prepared by an alternate route[9]. The previously reported syntheses of this class of compounds involve the cyclization of substituted 1-phenyl-4-phenoxypyrazole-4-carboxylic acids[10,11] or 1-aryl(or alkyl)-3-alkyl-4-(*o*-hydroxybenzoyl)-5-chloropyrazoles[10] or 1-phenyl(or methyl)-3-methyl-4-(*o*-chlorobenzoyl)-pyrazol-5-ones[12] as precursors.

The structures of **5** are established by microanalysis, I.R., ^{1}H-N.M.R., and mass spectra (for **5a**), and by chemical evidence.

3-Acetyl-, 3-propanoyl-, 3-butanoyl-, and 3-benzoyl-4-hydroxycoumarins (**1a, b, c** and **d**) are prepared according to Ref.[2] and Ref.[13]; 6-methyl- and 6-chloro-3-acetyl-4-hydroxycoumarins (**1f, g**) are prepared according to Ref.[14] and Ref.[15].

3-Benzoyl-4-hydroxy-6-chlorocoumarin (**1h**) is prepared from ethyl benzoylacetate and 2-acetoxy-5-chlorobenzoyl chloride by the method of Anschütz[16]; yield: 30%; m.p. 174 °C.

$C_{16}H_9ClO_4$	calc.	C 63.90	H 3.01	Cl 11.79
(300.7)	found	64.06	2.99	11.78

I.R. (KBr): $\nu = 1745$ cm^{-1} (C=O).

1-Aryl-3-alkyl-4-(2-hydroxybenzoyl)-pyrazol-5-ones (5); General Procedure:

Method A: 3-Acyl-4-hydroxycoumarin **1** (0.01 mol) and phenylhydrazine **2** (0.01 mol) in acetic acid (50 ml) are heated under reflux for 1 h (or 6 h in the case of **5e**). Acetic acid is evaporated in vacuo and the residue is dissolved in 10% aqueous potassium carbonate solution (200 ml). The solution is extracted with chloroform (2 × 50 ml) and the aqueous layer is acidified to pH 1 with 5 normal hydrochloric acid. The precipitate is collected by suction, washed with water (10 ml), and dried in the air to give **5**, which is recrystallized from ethanol (or acetic acid in the case of **5e**).

Method B: The phenylhydrazone **3a, b,** or **c** (prepared according to Ref.[2]; 0.01 mol) in acetic acid (50 ml) is heated under reflux for 1 h and worked up as described in Method A. The compounds **5a, b,** and **c** are obtained in 71%, 67%, and 65% overall yield, respectively.

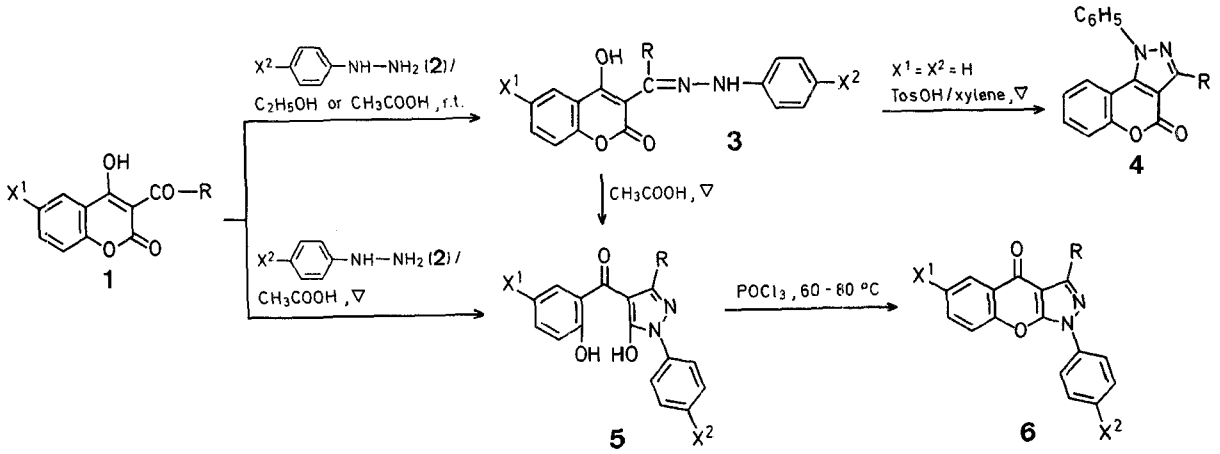

Table 1. 1-Aryl-3-alkyl-4-(2-hydroxybenzoyl)-pyrazol-5-ones **5**

Product	R	X^1	X^2	Yield[a] [%]	m.p.[b] [°C]	Molecular Formula[c]	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6) δ [ppm]
5a[d]	CH_3	H	H	68	198–199°	$C_{17}H_{14}N_2O_3$ (294.3)	1630	2.05 (s, 3H); 6.9–7.2 (m, 2H); 7.3 (m, 7H); 9.80 (br. s, 2H)
5b	C_2H_5	H	H	65	146–147°	$C_{18}H_{16}N_2O_3$ (308.3)	1630	1.10 (t, 3H, J=8 Hz); 2.52 (q, 2H, J=8 Hz); 6.8–7.1 (m, 2H); 7.1–8.2 (m, 7H); 10.12 (br. s, 2H)
5c	*n*-C_3H_7	H	H	78	160–161°	$C_{19}H_{18}N_2O_3$ (322.3)	1625	0.80 (t, 3H, J=8 Hz); 1.52 (sext, 2H, J=8 Hz); 2.50 (t, 2H, J=8 Hz); 6.7–7.1 (m, 2H); 7.1–7.8 (m, 7H); 10.77 (br. s, 2H)
5d	C_6H_5	H	H	60	125–126°	$C_{22}H_{16}N_2O_3$ (356.4)	1630	6.6–7.0 (m, 2H); 7.0–7.7 (m, 10H); 7.7–7.95 (m, 2H); 8.45 (br. s, 2H)
5e	CH_3	H	NO_2	62	254–255°	$C_{17}H_{13}N_3O_5$ (339.3)	1630	2.10 (s, 3H); 6.8–7.05 (m, 2H); 7.3–7.7 (m, 2H); 8.14 (d, 2H, J=9 Hz); 8.38 (d, 2H, J=9 Hz); 10.62 (br. s, 2H)
5f	CH_3	CH_3	H	67	164–165°	$C_{18}H_{16}N_2O_3$ (308.3)	1635	2.12 (s, 3H); 2.25 (s, 3H); 6.85 (d, 1H, J=8 Hz); 7.1–7.7 (m, 5H); 7.7–7.9 (m, 2H); 8.32 (br. s, 2H)
5g	CH_3	Cl	H	70	192–193°	$C_{17}H_{13}ClN_2O_3$ (328.7)	1635	6.18 (s, 3H); 6.93 (d, 1H, J=8 Hz); 7.1–7.6 (m, 5H); 7.6–7.85 (m, 2H); 10.40 (br. s, 2H)
5h	C_6H_5	Cl	H	80	172–173°	$C_{22}H_{15}ClN_2O_3$ (390.8)	1625	6.70 (d, 1H, J=9 Hz); 7.3–7.7 (m, 5H); 7.7–7.9 (m, 2H); 9.27 (br. s, 2H)

[a] Method A.
[b] Recrystallized from ethanol (acetic acid in the case of **5e**).
[c] The microanalyses were in satisfactory agreement with the calculated values (C ±0.28, H ±0.21, N ±0.29, Cl ±0.34).
[d] M.S.: *m/e* (relative intensity) = 294 (M^+, 35); 200 (15); 121 (100).

Table 2. 1-Aryl-3-alkyl[1]benzopyrano[2,3-*c*]pyrazol-4(1*H*)-ones **6**

Product	R	X^1	X^2	Yield [%]	m.p.[a] [°C]	Molecular Formula[b] or Lit. m.p. [°C]	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]	U.V. (C_2H_5OH) λ_{max} [nm] (ε)	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
6a	CH_3	H	H	78	172–173°	168–170°[9]	1670	242 (28400); 264 (16800)	2.70 (s, 3H); 7.2–7.7 (m, 6H); 7.85 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.33 (dd, 1H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz)
6b	C_2H_5	H	H	60	140–141°	$C_{18}H_{14}N_2O_2$ (290.3)	1665	242 (27000); 264 (15900)	1.43 (t, 3H, J=8 Hz); 3.10 (q, 2H, J=8 Hz); 7.2–7.7 (m, 6H); 7.20 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.35 (dd, 1H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz)
6c	*n*-C_3H_7	H	H	67	125–126°	$C_{19}H_{16}N_2O_2$ (304.3)	1670	242 (27900); 264 (16800)	1.07 (t, 3H, J=8 Hz); 1.92 (sext, 2H, J=8 Hz); 3.06 (t, 2H, J=8 Hz); 7.3–7.8 (m, 6H); 7.90 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.34 (dd, 1H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz)
6d	C_6H_5	H	H	63	176–177°	$C_{22}H_{14}N_2O_2$ (338.3)	1670	242 (32500); 262 (25300)	7.2–7.8 (m, 9H); 7.93 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.2–8.5 (m, 3H)
6e	CH_3	H	NO_2	52	270–271°	$C_{17}H_{11}N_3O_4$ (321.3)	1680	218 (36200); 290 (22400)	2.68 (s, 3H); 7.3–7.8 (m, 3H); 7.3–7.8 (m, 3H); 8.13 (d, 1H, J=9 Hz); 8.2–8.4 (m, 1H); 8.35 (d, 1H, J=9 Hz)
6f	CH_3	CH_3	H	63	152–153°	149–150°[9]	1685	240 (28800); 264 (17100)	2.47 (s, 3H); 2.70 (s, 3H); 7.4–7.7 (m, 5H); 7.90 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.13 (s, 1H)
6g	CH_3	Cl	H	70	150–151°	$C_{17}H_{11}ClN_2O_2$ (310.7)	1670	242 (25200); 264 (14500)	2.65 (s, 3H); 7.3–7.7 (m, 5H); 7.83 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.22 (d, 1H, $J_{1,2}$=2 Hz)
6h	C_6H_5	Cl	H	80	215–216°	$C_{22}H_{13}ClN_2O_2$ (372.8)	1665	242 (29700); 260 (25000)	7.3–7.7 (m, 8H); 7.88 (dd, 2H, $J_{1,2}$=8 Hz, $J_{1,3}$=2 Hz); 8.3–8.5 (m, 3H)

[a] Recrystallized from ethanol.
[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.25, H ±0.29, N ±0.23, Cl ±0.20); exception **6e** (C, −0.53).

1-Aryl-3-alkyl[1]benzopyrano[2,3-*c*]pyrazol-4-(1*H*)-ones (6); General Procedure:

A stirred mixture of **5** (0.01 mol) and phosphoryl chloride (15 ml) is heated in a water bath to 60–70 °C (80 °C in the case of **5e**) for 20 min. The mixture is poured into ice/water (400 ml) and extracted with chloroform (3 × 100 ml). The extracts are washed successively with 1 normal aqueous sodium hydroxide (3 × 100 ml), water (2 × 20 ml), and dried with sodium sulfate. The solvent is evaporated under reduced pressure and the residual crude compound **6** is recrystallized from ethanol.

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