Synthesis of 3-(2-Hydroxyaryl)-1-methyl-2-pyrazolin-5-ones from 4-Hydroxycoumarins and their Conversion to 2-Methyl-1-benzopyrano[4,3-*c*]pyrazol-3(2*H*)-one Derivatives

Bernard CHANTEGREL, Suzanne GELIN

Laboratoire de Chimie Organique, Institut National des Sciences Appliquées F-69621 Villeurbanne Cedex, France

Although the 2-pyrazolin-5-one ring system has been extensively studied[1], only one report describes the synthesis of 3-(2-hydroxyphenyl)-2-pyrazolin-5-one by reaction of 4-hydroxycoumarin (**1a**) with hydrazine hydrate[2]. It is also known that **1a** on reaction with phenylhydrazine leads to 4-benzeneazo-3-(2-hydroxyphenyl)-1-phenyl-2-pyrazolin-5-one[3].

We have now found that the reaction of 4-hydroxycoumarins **1a–f** with an excess of methylhydrazine (**2**) gives regioselectively the hitherto unknown 3-(2-hydroxyaryl)-1-methyl-2-pyrazolin-5-ones **3a–f**. When 4,7-dimethoxycoumarin is used in place of 4-hydroxy-7-methoxycoumarin (**1f**), the

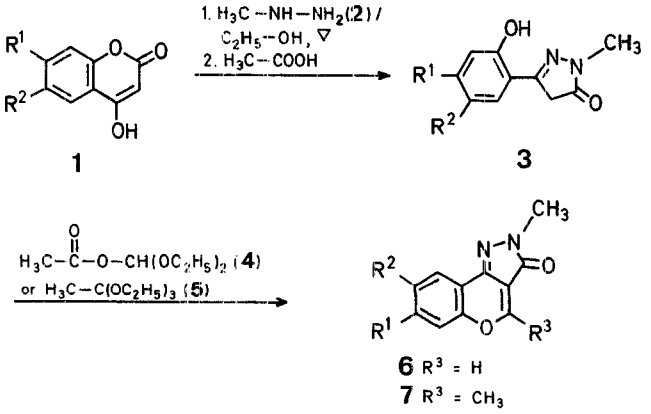


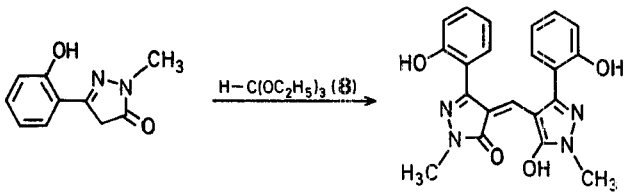
Table. Compounds **3**, **6** and **7** prepared

Product	R^1	R^2	Yield [%]	m.p. [°C]	Molecular Formula[a]	I.R. [cm^{-1}] ν_{OH}	$\nu_{C=O}$	^{1}H-N.M.R. (Solvent) δ [ppm]
3a	H	H	65	152–153°	$C_{10}H_{10}N_2O_2$ (190.2)	3230 3300–2400	1710 ($CHCl_3$) 1710 (KBr)	($CDCl_3$) 3.42 (s, 3H); 3.67 (s, 2H); 6.8–7.5 (m, 4H); 10.0 (br. s, 1H). ($DMSO$-d_6) 3.58 (s, 3H); 5.95 (s, 1H); 6.6–7.4 (m, 3H); 7.4–7.8 (m, 1H); 11.3 (br. s, 2H)
3b	CH_3	H	54	150–151°	$C_{11}H_{12}N_2O_2$[b] (204.2)	3240 3600–2400	1710 ($CHCl_3$) 1715 (KBr)	($CDCl_3$) 2.35 (s, 3H); 3.40 (s, 3H); 3.59 (s, 2H); 6.75 (d, 1H, J = 8 Hz); 6.85 (s, 1H); 7.04 (d, 1H, J = 8 Hz); 9.91 (s, 1H) ($DMSO$-d_6) 2.12 (s, 3H); 3.58 (s, 3H); 5.88 (s, 1H); 6.5–6.9 (m, 2H); 7.48 (d, 1H, J = 8 Hz); 10.7–11.8 (m, 2H)
3c	H	CH_3	76	169–170°	$C_{11}H_{12}N_2O_2$ (204.2)	3230 3300–2400	1710 ($CHCl_3$) 1710 (KBr)	($CDCl_3$) 2.27 (s, 3H); 3.37 (s, 3H); 3.60 (s, 2H); 6.6–7.3 (m, 3H); 9.90 (s, 1H) ($DMSO$-d_6) 2.18 (s, 3H); 3.57 (s, 3H); 5.90 (s, 1H); 6.6–7.2 (m, 2H); 7.42 (s, 1H); 10.8 (br. s, 1H); 11.4 (br. s, 1H)
3d	CH_3	CH_3	68	227–228°	$C_{12}H_{14}N_2O_2$ (218.2)	3400–2400	1700 (KBr)	($DMSO$-d_6) 2.17 (s, 6H); 3.62 (s, 3H); 5.90 (s, 1H); 6.70 (s, 1H); 7.34 (s, 1H); 10.7 (br. s, 1H); 11.2 (br. s, 1H)
3e	OH	H	50	266–267°	$C_{10}H_{10}N_2O_3$ (206.2)	3400–2400	1670 (KBr)	($DMSO$-d_6) 3.60 (s, 3H); 5.80 (s, 1H); 6.2–6.5 (m, 2H); 7.37 (d, 1H, J = 8 Hz); 9.5 (br. s, 1H); 11.0 (br. s, 1H)
3f	OCH_3	H	54	165–166°	$C_{11}H_{12}N_2O_3$ (220.2)	3200 3400–2400	1700 ($CHCl_3$) 1700 (KBr)	($CDCl_3$) 3.32 (s, 3H); 3.55 (s, 2H); 3.77 (s, 3H); 6.3–6.6 (m, 2H); 7.07 (d, 1H, J = 8 Hz); 10.30 (s, 1H)
6a	H	H	60	229–230°	$C_{11}H_8N_2O_2$ (210.3)		1680 (KBr)	($CDCl_3$) 3.57 (s, 3H); 7.4–7.7 (m, 3H); 8.0–8.3 (m, 1H); 8.47 (s, 1H)
6b	CH_3	H	90	209–210°	$C_{12}H_{10}N_2O_2$[c] (214.2)	3540, 3480	1675 (KBr)	–[d]
6c	H	CH_3	80	228–229°	$C_{12}H_{10}N_2O_2$ (214.2)		1680 (KBr)	($CDCl_3$) 2.40 (s, 3H); 3.53 (s, 3H); 7.42 (s, 2H); 7.90 (s, 1H); 8.40 (s, 1H)
6d	CH_3	CH_3	80	289–291°	$C_{13}H_{12}N_2O_2$ (228.2)		1670 (KBr)	–[d]
6e	OH	H	90	335–338°	$C_{11}H_8N_2O_3$ (216.2)	3400–2800	1680 (KBr)	–[d]
6f	OCH_3	H	57	211–212°	$C_{12}H_{10}N_2O_3$ (230.2)		1680 (KBr)	($CDCl_3$) 3.53 (s, 3H); 3.87 (s, 3H); 6.9–7.2 (m, 2H); 8.03 (d, 1H, J = 8 Hz); 8.38 (s, 1H)
7a	H	H	70	174–175°	$C_{12}H_{10}N_2O_2$ (214.2)		1680 (KBr)	($CDCl_3$) 2.81 (s, 3H); 3.60 (s, 3H); 7.4–7.6 (m, 3H); 7.9–8.2 (m, 1H)
7b	CH_3	H	59	136–137°	$C_{13}H_{12}N_2O_2$ (228.2)	3540, 3480	1675 (KBr)	($CDCl_3$) 2.49 (s, 3H); 2.78 (s, 3H); 3.59 (s, 3H); 7.1–7.4 (m, 2H); 8.00 (d, 1H, J = 8 Hz)
7c	H	CH_3	71	147–148°	$C_{13}H_{12}N_2O_2$[c] (228.2)		1680 (KBr)	($CDCl_3$) 2.40 (s, 3H); 2.70 (s, 3H); 3.52 (s, 3H); 7.33 (s, 2H); 7.82 (s, 1H)
7d	CH_3	CH_3	73	209–210°	$C_{14}H_{14}N_2O_2$ (242.3)		1690 (KBr)	–[d]
7e	OH	H	85	350–354°	$C_{12}H_{10}N_2O_3$ (230.2)	3250–2400	1680 (KBr)	–[d]
7f	OCH_3	H	60	166–168°	$C_{13}H_{12}N_2O_3$ (244.2)		1700 (KBr)	($DMSO$-d_6) 2.63 (s, 3H); 3.33 (s, 3H); 3.83 (s, 3H); 6.9–7.2 (m, 2H); 7.87 (d, 1H, J = 8 Hz)

[a] Satisfactory microanalysis obtained: C ±0.33, H ±0.20, N ±0.24.
[b] This compound crystallizes with water in the molar ratio 3:1.
[c] This compound crystallizes with water in the molar ratio 1:1.
[d] This compound is too insoluble to allow N.M.R.-measurements.

starting material is recovered unchanged. From this, it appears that the 4-hydroxy group is essential for the ring transformation. The possible isomeric 3-pyrazolones are ruled out on the basis of spectroscopic data. Compounds **3a–c** and **f** are soluble in chloroform and their I.R. spectra exhibit strong carbonyl absorptions at 1700 cm^{-1} when measured in this solvent. This is only consistent with the 5-pyrazolone structure[4a] since the isomeric 3-pyrazolones show no carbonyl absorptions in chloroform solution[4b].

The ^{1}H-N.M.R. data reveal that these products exist in the 5-pyrazolone form in chloroform solution and predominantly as the 5-hydroxy tautomer in dimethyl sulfoxide solution. This is in accord with previous work concerning the tautomerism of 1-substituted 2-pyrazolin-5-one derivatives[5].



3a **9**

Compounds **3** serve as educts for the new 2-methyl-1-benzopyrano[4,3-*c*]pyrazol-3(2*H*)-one derivatives **6** and **7**, respectively, which are obtained by reaction with diethoxymethyl acetate **(4)** and triethyl orthoacetate **(5)**, respectively. An attempt to replace diethoxymethyl acetate by triethyl orthoformate **(8)** led to the formation of **9** from **3a**. This type of reaction is known for 5-pyrazolone derivatives[6].

The starting compounds **1a**[7], **1b**[8], **1c, d**[9], **1e, f**[10] are prepared as described in the literature.

3-(2-Hydroxyaryl)-2-pyrazolin-5-ones 3; General Procedure:
A solution of **1** (10 mmol) and methylhydrazine (1.38 g, 30 mmol) in ethanol (75 ml) is refluxed for 8 h. After cooling and acidification with glacial acetic acid (5 ml), ethanol is evaporated in vacuo. Water (50 ml) is added. In the case of **3d** and **3e**, the precipitate is collected by filtration, washed with water, and recrystallized from glacial acetic acid. In the case of **3a, b, c, f**, chloroform (100 ml) is added to the residue. The organic phase is separated, dried with sodium sulfate, and evaporated to a solid residue which is purified by column chromatography on silica gel, eluting with ether for **3a** and **3c** and ethyl acetate for **3b** and **3f**. Analytical samples are obtained by recrystallization from acetonitrile (Table).

2-Methyl-1-benzopyrano[4,3-*c*]pyrazol-3(2*H*)-ones 6 and 7; General Procedure:
A mixture of **3** (5 mmol) and diethoxymethyl acetate[11] (**4**; 2.64 g, 15 mmol) or triethyl orthoacetate **5**; 2.43 g, 15 mmol) is heated at 130–135 °C for 10 min. The reaction mixture is cooled. The precipitated solid is filtered and washed with anhydrous ether to give yellow crystals of **6** or **7** Analytical samples are obtained by sublimation (Table).

4-[5-Hydroxy-3-(2-hydroxyphenyl)-1-methyl-4-pyrazolylmethylene]-3-(2-hydroxyphenyl)-1-methyl-2-pyrazolin-5-one (9):
This compound is prepared from **3a** (0.95 g, 5 mmol) and triethyl orthoformate (**8**; 2.22 g, 15 mmol) in a manner analogous to that described for the preparation of **7**; yield: 0.8 g (82%). Analytical sample is obtained by recrystallization from glacial acetic acid; m. p. 210–211 °C.

$C_{21}H_{18}N_4O_4$	calc.	C 64.60	H 4.65	N 14.35
(390.4)	found	64.54	4.72	14.51

I.R. (KBr): ν = 3300–2400 (OH); 1580 cm^{-1} (C=O).
^{1}H-N.M.R. ($CDCl_3$): δ = 3.70 (s, 6H); 6.7–7.5 (m, 9H); 8.07 (s, 1H); 9.41 ppm (s, 2H).

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