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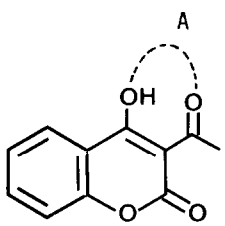
4-OXO-*1H*-AND-*2H*-[1]BENZOPYRANO[4,3-c]PYRAZOLES. PREPARATION FROM 4-HYDROXYCOUMARIN OR 3-CHROMONECARBOXYLIC ACID DERIVATIVES.

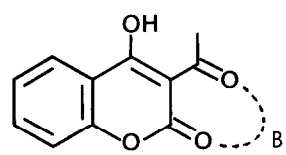
Bernard Chantegrel, Abdel-Ilah Nadi and Suzanne Gelin†

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

Summary : The conversion of 3-acyl-4-hydroxycoumarins to either 4-oxo-1-phenyl-1H-[1]benzopyrano[4,3-c]pyrazoles 2 or 4-oxo-2-phenyl-2H-[1]benzopyrano[4,3-c]pyrazoles 3 is described. The product obtained from the reaction of phenylhydrazine with 3-chromonecarboxylic acid 6a has been established not to be such 2-phenyl[1]benzopyrano[4,3-c]pyrazol-3-2H-one 7 as previously reported but to be 4-oxo-1-phenyl-1H[1]benzopyrano[4,3-c]pyrazole 2a. Our results showed evidence that the method precedently described as yielding 2a, from 4-chloro-3-formyl-coumarin was an implausible one.

Coumarins are well-known for their biological properties[1] as well as their utility in heterocyclic synthesis[2]. In this regard, 3-acyl-4-hydroxycoumarins would be suited for preparing fused-ring systems, according to their cyclization of type A or B with phenylhydrazine as the nucleophile.

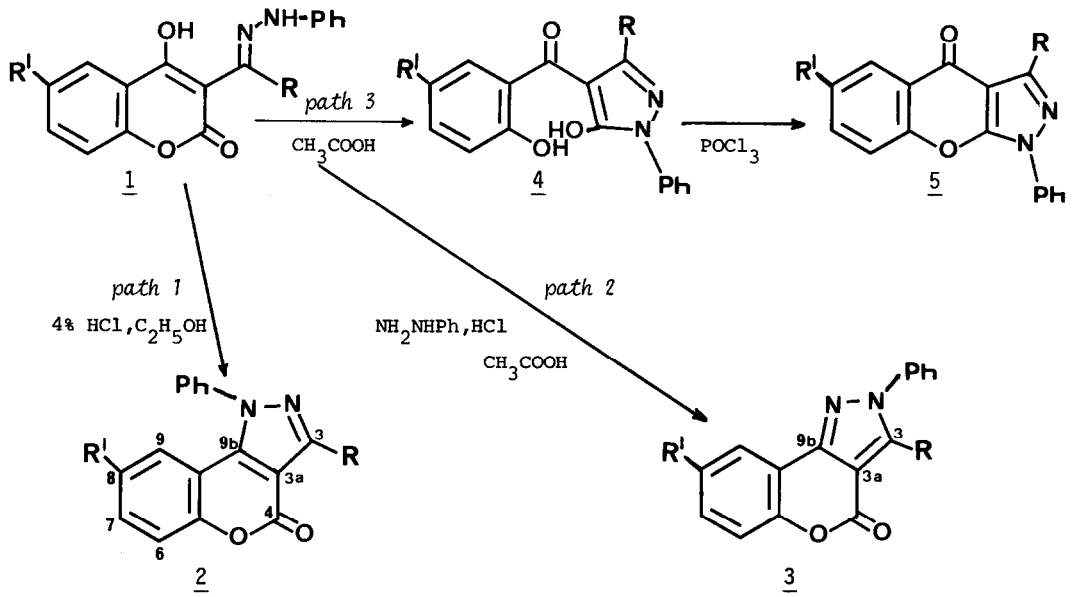




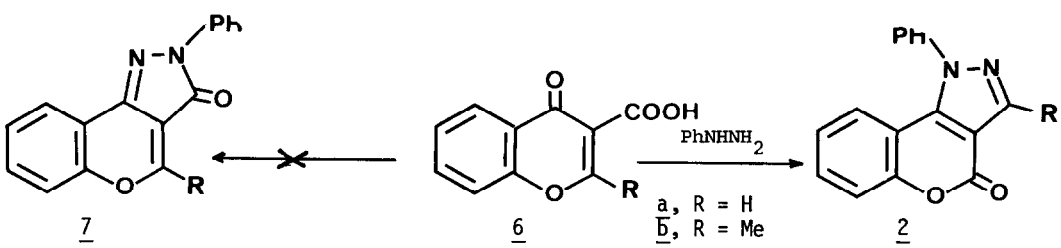
Prior to our work, synthetic studies in this area were limited to the construction of 4-oxo-1-phenyl-*1H*-[1]benzopyrano[4,3-c]pyrazoles 2 by cyclodehydration of the hydrazones 1[3,4](path 1). A recent communication from this laboratory described a B-type ring transformation to give the products 4 and 5 (path 3)[5].

We now report a successful almost regiocontrolled conversion of the hydrazones 1 into the new 4-oxo-2-phenyl-*2H*-[1]benzopyrano[4,3-c]pyrazoles 3 (path 2), by reaction with phenylhydrazinium chloride in refluxing acetic acid. Treatment of the hydrazones 1 with 4% ethanolic hydrogen chloride afforded the compounds 2 , identical with those prepared by using p-toluenesulfonic acid in refluxing xylene for the cyclodehydration[3,4]. The aldehydic hydrazone 1a failed to give the cyclization to 2a or 3a. Proof of the structures 2 and 3 was obtained from their physical and spectral data. The ^{13}C-NMR spectra of 2b and 3b, clearly demonstrated their structures, by comparison of the C-3, C-3a, C-9b and CH_3 signals.

It is known that a carbon adjacent to a sustituted nitrogen (pyrrole-like) resonates upfield of the signal of that same carbon in the other isomer (pyridine-like) in isomeric pyrazoles[6 9]. Additionnal support for the assignments was provided by the ^{1}H-NMR and UV spectra of each isomer pair. Our results are presented in the tables 1-3.



On the other hand, compounds 2a,b were obtained from the reaction of the corresponding 3-chromonecarboxylic acids 6a,b, by reaction with phenylhydrazine, in accordance with the known nucleophilic rearrangement of these substances[10]. However, condensation of 6a with phenylhydrazine has been described as leading to 7[11]. This alternative structure is ruled out by the observation that the substance shows the characteristic IR band at 1745 cm^{-1} (ν CO lactone), as all the other analogous compounds 2. The correct structure 2a was also established by its spectrum, compared to the series of 1-phenyl derivatives 2b-e. In the ^{13}C-NMR spectra, the downfield shift (11 ppm), due to the methyl effect, observed for the C-3 carbon atom in going from 2a to 2b is in accord with the literature data on related structures[6].



Condensation of phenylhydrazine with 4-chloro-3-formylcoumarin has been reported as yielding 2a (mp 221°C), without any spectral data[12]. The melting point of 2a is in fact 191°C. We were unable to reproduce the claimed synthesis of 4-chloro-3-formylcoumarin from 4-hydroxycoumarin, N,N-dimethylformamide and phosphorus oxychloride ; instead, 4-hydroxycoumarin was mostly recovered, along with tricoumarol, which was precedently reported as the result of this reaction[13]. It is concluded that the series of the reported products such as 2 (R = H), was not in fact obtained.

Table 1 - Preparation of Compounds 2 and 3

Compd	R	R'	Molecular formula[a]	Procedure	Yield	M.p. (°C)[b]	I.R. (KBr) ν(C=O) cm^{-1}	U.V. (EtOH) λ max (nm) ε.10^{-3}
2a	H	H	$C_{16}H_{10}N_2O_2$	(A)	80	191	1745	307 (5.9); 297 (6.6); 270 (11.7); 260 (11.5).
2b	Me	H	$C_{17}H_{12}N_2O_2$	(A) (B)	60 54	220[3]	1745	308 (6.6); 298 (7.4); 272 (12.3); 261 (12.2).
2c	Et	H	$C_{18}H_{14}N_2O_2$	(B)	60	160[3]	1750	308 (7.3); 299 (8.1); 272 (13.2); 261 (12.9).
2d	Me	Me	$C_{18}H_{14}N_2O_2$	(B)	71	264	1745	308 (6.7); 272 sh.(8.7); 260 sh.(17.2).
2e	Me	Cl	$C_{17}H_{11}ClN_2O_2$	(B)	72	290	1755	310 (6.9); 273 (11.8); 262 (11.8).
3b	Me	H	$C_{17}H_{12}N_2O_2$	(C)	43[c]	180	1750	299 (7.6); 282 sh. (10.6).
3c	Et	H	$C_{18}H_{14}N_2O_2$	(C)	48	144	1750	299 (6.9); 286 sh.(8.7); 273 sh.(10); 259 sh.(16).
3d	Me	Me	$C_{18}H_{14}N_2O_2$	(C)	50[c]	198	1745	305 (6.7); 272 sh.(8.7); 260 sh. (17.2).
3e	Me	Cl	$C_{17}H_{11}ClN_2O_2$	(C)	64[c]	170	1760	309 (6.7); 298 (7.2); 260 sh. (14.4).

a, All products gave satisfactory microanalyses. b, recrystallized from ethanol. c, isolated yield by column chromatography.

(A) A mixture of 3-chromonecarboxylic acid (0.01 mol)[10] and phenylhydrazine (0.01 mol), in acetic acid (50 ml) was heated under reflux for 4 h. The solvent was removed and the residue was recrystallized to give 2a or 2b.

(B) 3-Acyl-4-hydroxycoumarin phenylhydrazone 1 (0.01 mol) was added to 4% ethanolic hydrogen chloride. The mixture was refluxed for 6 h. After elimination of the solvent, the residue was recrystallized to give 2.

(C) A mixture of 3-acyl-4-hydroxycoumarin phenylhydrazone 1 (0.01 mol) and phenylhydrazine hydrochloride (1.4 g, 0.01 mol) in acetic acid (100 ml) was heated under reflux for 2 h. After elimination of the solvent, the residue was dissolved in dichloromethane (100 ml). The dichloromethane solution was successively washed with 10% aqueous potassium carbonate solution (3 X 50 ml) and then water. The dry solution was concentrated to 5 ml and chromatographed over silica gel (80 g) using dichloromethane as eluent, to give first 3 as the main product and then 2 (7-11%) as the minor product.

Table 2 - Selected ^{13}C-NMR spectral data of compounds 2a,b and 3b δ ppm ($CDCl_3$).

Compound	C-3	C-3a	C-4	C-9b	CH_3
2a	139.5	108.3	157.0	140.9	
2b	150.5	106.2	157.6	141.4	12.8
3b	144.2	106.2	158.4	148.3	12.0

The carbon shifts were assigned from the multiplicity in the off-resonance decoupled spectr and examination of the coupled spectra, general chemical shift argument and literature data on related pyrazoles [6-9] and coumarins[14,15].

Table 3 - 80 MHz-^1H-NMR spectral data of substances 2 and 3 δ ppm ($CDCl_3$), J(Hz).

Compound	R	H-6	H-7	R'	H-9	C_6H_5
2a	8.35 (s,1H)	7.0-7.25 (2H)		7.40-7.50 (2H)		7.61 (s)
2b	2.75 (s,3H)	7.0-7.40 (2H)		7.50-7.70 (2H)		7.76 (s)
2c	1.42 (t,3H)	6.90-7.20 (2H)		7.35-7.50 (2H)		7.62 (s)
	3.12 (q,2H)					
2d	2.66 (s,3H)	7.27 (s,2H)		2.17 (s,3H)	6.86 (s)	7.61 (s)
2e	2.66 (s,3H)	7.33 (s,2H)			7.0 (d) J=1	7.40-7.72
3b	2.72 (s,3H)	7.10-7.50 (3H)			8.06 (d/d) J=7/1	7.51 (s)
3c	1.28 (t,3H)	7.10-7.50 (3H)			8.07 (d/d) J=7/1	7.51 (s)
	3.08 (q,2H)					
3d	2.73 (s,3H)	7.25 (s,2H)		2.41 (s,3H)	7.87 (s)	7.57 (s)
3e	2.70 (s,3H)	7.17 (d) J=9	7.32 (d/d) J=9/2		7.92 (d) J=2	7.52 (s)

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