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A NOVEL CONVERSION REACTION OF 4-OXO-4H-1-BENZOPYRAN-3-CARBOXALDEHYDES TO 3-SUBSTITUTED-5-(2-HYDROXYBENZOYL)-2(1H)-PYRIDONES

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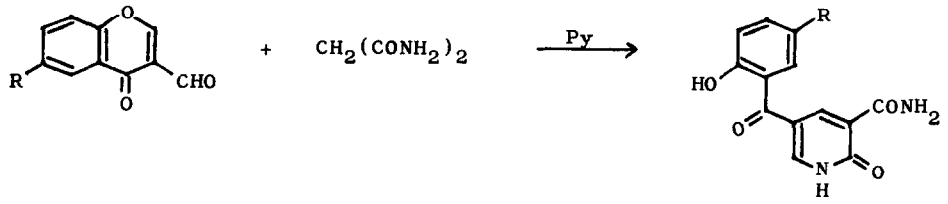
It is well known that the pyrone ring of chromones is cleaved at C-2 by base such as hydroxide anion or amines[1]. We have found that 4-oxo-4H-1-benzopyran-3-carboxaldehydes I[2], which are able to function as β-dialdehyde compounds, are attacked by amide group in some cases to afford 2(1H)-pyridone derivatives, after condensations with malonic acid derivatives. As the preparations of 5-aroyl-2(1H)-pyridones are little known[3,4] until now, we wish to report a novel conversion reaction of I to 3-substituted-5-(2-hydroxybenzoyl)-2(1H)-pyridones and its mechanism.

Condensation reaction of Ia[2] (1eq.) with malonodiamide (1eq.) in pyridine afforded 3-carbamoyl-5-(5-ethyl-2-hydroxybenzoyl)-2(1H)-pyridone IIa; nmr (d_6-DMSO) δ 12.85 (1H, br., OH), 9.98 (1H, s, NH), 8.75 (1H, br., NH), 8.65 (1H, d, J=2.5Hz, pyridone H_4), 8.00 (1H, d, J=2.5Hz, pyridone H_6), 7.63 (1H, br., NH), 7.07-7.37 (2H, m, benzene $H_{4,6}$), 6.87 (1H, d, J=8Hz, benzene H_3), 2.57 (2H, q, J=7Hz, CH_2), 1.18 (3H, t, J=7Hz, CH_3). Similarly, IIb and IIc were obtained from Ib[2,5] and Ic[2], respectively (Table I).

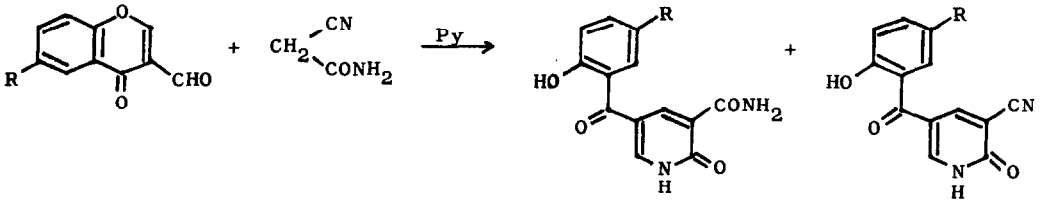


Ia-c IIa-c

Table I

I	Reaction	II	
R	Conditions	Yield (%)	Mp (°C)
a; Et	120° 8 hr	71	245 - 247
b; H	120° 10 hr	62	266 - 267 (dec.)
c; NO_2	120° 12 hr	69	311 - 312 (dec.)

On the other hand, the reaction of Ia with cyanoacetamide in pyridine afforded the desired 3-cyanopyridone IIIa; nmr (d_6-DMSO) δ 13.00 (1H, br.) 10.03 (1H, br.s), 8.40 (1H, d, J=2.5Hz), 8.08 (1H, d, J=2.5Hz), 7.1-7.4 (2H, m), 6.92 (1H, d, J=8Hz), 2.53 (2H), 1.18 (3H, t, J=7Hz); ir (KBr) 2250 (CN) cm^{-1}, together with IIa. Similarly IIIb and IIb were obtained from Ib. In the case of Ic, only IIc was isolated. (Table II)



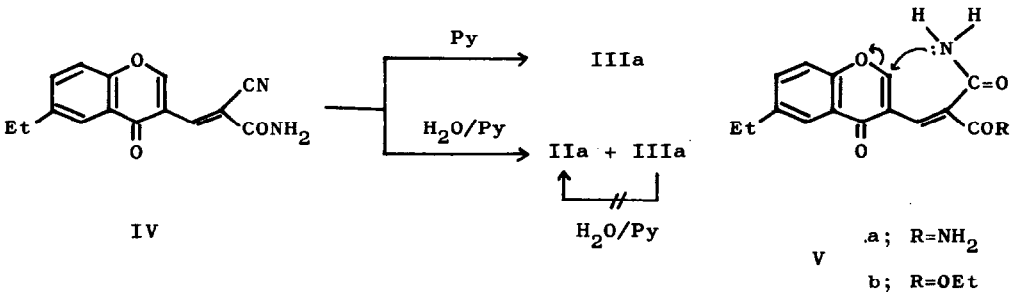
Ia-c IIa-c IIIa,b

Table II

I	Reaction	Yield (%)		III
R	Conditions	II	III	Mp (°C)
a; Et	Reflux 1 hr	23	22	238-240 (dec.)
b; H	Reflux 1 hr	20	21	266-268 (dec.)
c; NO_2	Reflux 5 min	57	--	--

The reaction of Ia with cyanoacetamide in pyridine in a short time (reflux, 5 min) afforded 2-cyano-3-(6-ethyl-4-oxo-4H-1-benzopyran-3)acrylamide IV, mp 201-203° (dec.); nmr (d_6-DMSO) δ 9.05 (1H, s, chromone H_2), 8.10 (1H, s, acrylamide H_3), 7.5-8.0 (5H, m), 2.77 (2H, q), 1.25 (3H, t, J=7Hz); ir (KBr) 2225 (CN) cm^{-1}, in 42% yield. IV may be the initial product of this condensation reaction. In an attempt to study the mechanism of isomerization of IV, IV was employed as a starting material. Whereas IV was transformed to IIIa in 60% yield by heating in pyridine, IV was converted to both IIa and IIIa (1:1) by the similar condition in the presence of water. As IIIa and cyanoacetamide are not converted to IIa and malonodiamide each other by the same condition, the hydrolysis of nitrile to amide can only progress on IV. This fact suggests the intermediary formation of 2-carbamoyl-3-(6-ethyl-4-oxo-4H-1-benzopyran-3)acrylamide Va.

The reaction of Ia with ethyl cyanoacetate in pyridine at room temperature afforded ethyl 2-cyano-3-(6-ethyl-4-oxo-4H-1-benzopyran-3)acrylate VI, mp 87-88°, 75%, and ethyl 5-(5-ethyl-2-hydroxybenzoyl)-2(1H)-pyridone-3-carboxylate VII, mp 222-224° (4%). Similarly VI was transformed to VII by heating in pyridine in the presence of water. This fact also supports that Va and Vb are formed intermediary in this conversion reaction.



The structure of IIb was confirmed by the following reactions. IIb was hydrolyzed and decarboxylated to afford 5-(2-hydroxybenzoyl)-2(1H)-pyridone, mp 170.5-171.5°, nmr (d_6-DMSO) δ 12.00 (1H, br.), 10.15 (1H, br. s), 7.80 (1H, dd, J=9 and 2.5Hz), 7.70 (1H, d, J=2.5Hz), 7.2-7.5 (2H, m), 6.7-7.1 (2H, m), 6.40 (1H, d, J=9Hz), which was converted to the known 6-hydroxy-nicotinic acid[6] upon Dakin oxidation.

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