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A NOVEL REACTION OF 6-NITROQUINOLINE WITH ACTIVE METHYLENE COMPOUNDS IN THE PRESENCE OF POTASSIUM CYANIDE

Yukihiko Tomioka, Akihumi Mochiike, Junko Himeno, and
Motoyoshi Yamazaki*
Faculty of Pharmaceutical Sciences, Fukuoka University,
Nanakuma, Nishi-ku, Fukuoka, Japan

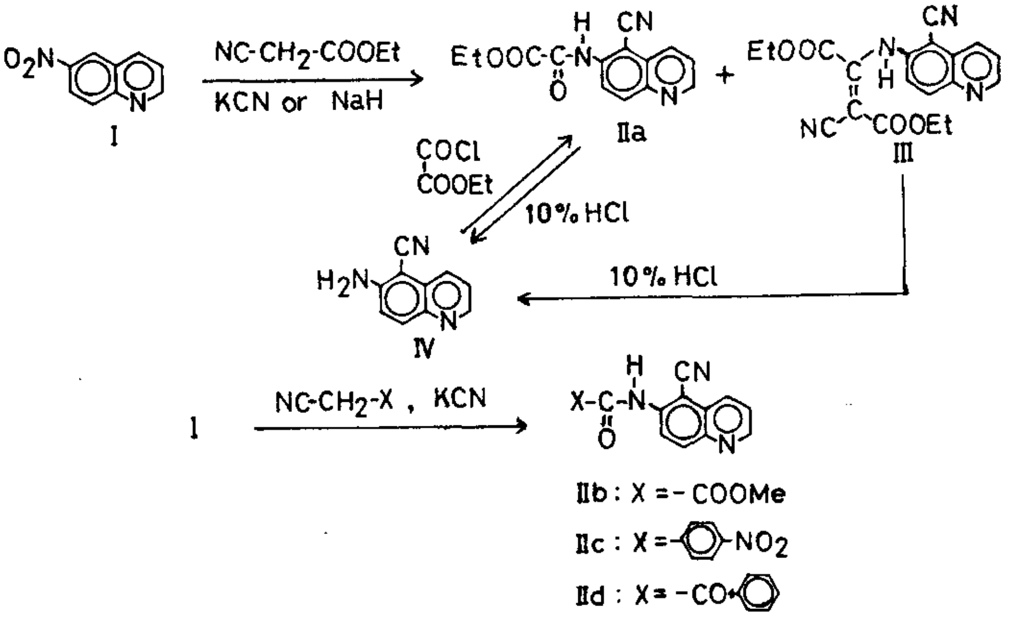
6-Nitroquinoline (I) reacts with ethyl cyanoacetate in the presence of potassium cyanide or sodium hydride to produce 6-ethoxalylaminoquinoline-5-carbonitrile (IIa) and diethyl 2-cyano-3-(5-cyano-6-quinolylamino)-fumalate (III). Reactions with some other active methylene compounds in the presence of potassium cyanide also afforded respective products corresponding to IIa (IIb, IIc and IId).

A previous paper from our laboratory has described that 4-nitroquinoline 1-oxides react with some nucleophiles in the presence of potassium cyanide to give the corresponding 4-substituted quinoline-3-carbonitriles.[1] As an extension of this study, we examined reactions of 6-nitroquinoline with compounds containing cyanomethylene group in the presence of potassium cyanide and found another novel reaction.

A solution of 6-nitroquinoline (I) (1.74 g, 0.01 mole) in DMF

(20 ml) was added to a stirred suspension of ethyl cyanoacetate (3.39 g, 0.03 mole) and potassium cyanide (1.92 g, 0.03 mole) in DMF (10 ml), and the whole was stirred at room temperature for another 30 min. Successive treatment of the reaction mixture with ice-water and 10% hydrochloric acid afforded 6-ethoxalylaminoquinoline-5-carbonitrile (IIa) (colorless needles, mp 182°C) and diethyl 2-cyano-3-(5-cyano-6-quinolylamino)fumalate (III) (yellow prisms, mp 184°C) in 56.0 and 6.3% yields, respectively. Apparently III would be formed from IIa through condensation with another mole of cyanoacetate, and both IIa and III were hydrolyzed by heating with 10% hydrochloric acid to the same compound, 6-aminoquinoline-5-carbonitrile (IV), which was prepared from 6-amino-5-bromoquinoline[2] and cuper(I) cyanide.

The structure of IIa was confirmed by direct comparison with the authentic sample prepared from IV and ethoxalyl chloride.



Structure assignment of III was based on the satisfactory elemental analysis $\left[C_{19}H_{16}N_4O_4\right]$ and the spectral data shown in Table.

It was further found that no reaction occured in the absence of potassium cyanide, but significantly the reaction proceeded also with sodium hydride instead of potassium cyanide, producing IIa and III in somewhat lower yields of 36.5 and 1.9%, respectively.

Subsequently, reactions of I with methyl cyanoacetate, p-nitrophenylacetonitrile and ω-cyanoacetophenone were examined similarly in the presence of potassium cyanide to furnish IIb, IIc and IId in 19.6, 50.5 and 22.9%, respectively.

The structures of 6-methoxalylaminoquinoline-5-carbonitrile IIb, pale yellow needles, mp 175°C, and 6-p-nitrobenzoylaminoquinoline-5-carbonitrile IIc, pale yellow plates, mp 240°C, were proved by direct comparison with those of authentic samples obtained from IV through condensation with methoxalyl chloride and p-nitrobenzoyl chloride, respectively. Their spectral properties are found in Table. The structure of 6-phenyloxalylaminoquinoline-5-carbonitrile IId, pale yellow needles, mp 197-199°C, was deduced on the basis of spectral data shown in Table.

Table

Spectral data of 6-substituted quinoline-5-carbonitriles

compd.	ir spectra (ν)			Proton nmr spectra(δ)					
	NH	CN	C=O	C-2	C-3	C-4	C-7	C-8	others
IIa	3358	2205	1731	a) 9.04	7.78	8.48	8.00	8.38	1.36 ($-OCH_2\underline{CH_3}$)
	3130			(4.5)	(9)	(9)	(9)	(9)	4.38 ($-O\underline{CH_2}CH_3$)
				(1)	(4.5)	(1)			11.33 (NH)
IIb	3355	2206	1723	b) 9.08	7.87	8.56	8.29	8.46	4.11 ($-O\underline{CH_3}$)
	3138			(4.5)	(9)	(9)	(9)	(9)	10.23 (NH)
				(1)	(4.5)	(1)			
IIc	3225	2215	1658	a) 9.11	7.83		8.05		8.20-8.80 (6H)
	3110			(4.5)	(9)		(9)		11.40 (NH)
				(1)	(4.5)				
IId	3320	2204	1706	c) 8.97		8.87			7.44-7.74 (4H)
			1658	(4.5)		(9)			8.32-8.48 (4H)
				(1)		(1)			9.85 (NH)
III		2210	1737	b) 9.05	7.79	8.51	7.70	8.37	1.13 ($-OCH_2\underline{CH_3}$)
			1670	(4.5)	(9)	(9)	(9)	(9)	1.35 ($-OCH_2\underline{CH_3}$)
				(1)	(4.5)	(1)			4.28 ($(-O\underline{CH_2}CH_3)_2$)
									11.61 (NH)

a) In $(CD_3)_2SO$. b) In $(CD_3)_2CO$. c) In $CDCl_3$. Coupling constants(Hz) are indicated in parentheses.

Although the details of the reaction mechanism have not been established, the formation of IIa in a moderate yield from the reaction of I with ethyl cyanoacetate in the presence of sodium hydride indicates that the 5-cyano group of IIa may most likely originate from the cyanomethylene group, and potassium cyanide seems to behave only as a base. In order to elucidate the reaction mechanism and also to explore the scope of the reaction, we are now examining the reaction using other aromatic and heteroaromatic nitro compounds and active methylene compounds under various conditions.

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