Nov. 1979 The Chemistry of 2H-3,1-Benzoxazine-2,4(1H)dione (Isatoic Anhydride). 6. Synthesis of Spiro[indoline-2,2'(1'H)quinazolines]

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The reaction of isatoic anhydrides with potassium cyanide is described. The stoichiometry of the reactants and reaction times dictate the formation of either 2-imino-3-indolinones or spiro[indoline-2,2'(1'H)quinazolines]. Some spectral data is also discussed.

J. Heterocyclic Chem., 16, 1501 (1979).

Sir:

In a previous report (1), the reaction of 2H-3,1-benzox-azine-2,4(1H)diones (1, isatoic anhydride) with potassium cyanide to produce 2-imino-3-indolinones (2) was described.

When the reaction was performed employing one half an equivalent of potassium cyanide per one equivalent of isatoic anhydride an entirely different product was formed. Based on the following spectral evidence (for example when R = CH₃), the structure was found to be 1,1'-dimethylspiro[indoline-2,2'(1'H)quinazoline]-3,4'-(3'H)dione (3a), a new ring system. The ir spectrum (nujol) exhibited absorptions at 3180 (N-H), 1715 (C=O), and 1655 cm⁻¹ (amide C=O); nmr (deuteriochloroform + DMSO-d₆): δ 8.7 (s, 1), 7.9-7.3 (m, 4), 6.8 (m, 4), 2.9 (s, 3), 2.6 (s, 3); carbon 13 (DMSO-d₆): 196.4 (C=O), 163.0 (N-C=O), 87.9 (N-C-(NR)₂) ppm; ms: (70 eV) m/e 293 (M⁺ for C₁₂H₁₈N₃O₂).

Apparently, the first step in the reaction is the formation of 2 which, in turn, reacts with another molecule of the isatoic anhydride to give intermediate A. Nucleophic attack on the imino carbon results in the formation of the product (3). The possibility of the structure of the product being A was ruled out because in the nmr, the methyl signal of 3a appears as a sharp singlet ruling out an NHCH₃ grouping and in the C_{13} spectrum, no signal for an imino type carbon was visible. The absorption at 87.9 ppm is consistent for a quaternary spiro carbon.

The experimental procedure for this type of reaction is as follows: A mixture of 0.02 mole of an appropriate isatoic anhydride (2) and 0.01 mole of potassium cyanide in 30.0 ml. of dimethylformamide (3) was placed in an oil bath at 50°. The temperature of the bath was raised to 100° over a period of 15 minutes and the reaction was stirred at 100° for an additional 1 hour. The mixture was poured into cold water and the resulting precipitate was filtered, dried and recrystallized from an appropriate solvent (the results are summarized in Table 1) (4).

Analysis

Table 1

No.	$\mathbf{R}_{\mathbf{i}}$	R ₂	M.p., °C	Yield	Crystallization Solvent	Molecular Formula	Calcd. (Found)			
							3a	CH,	н	251-253
							(69.4	5.5	14.2)	
3b	CH,	Cl	265-268	28	Dichloromethane/	$C_{17}H_{13}CIN_3O_2$	56.4	3.6	11.6	19.6
	•				methanol		(56.2	3.7	11.7	19.5)
3c	CH ₂ CH=CH ₂	Н	63-68	29		$C_{21}H_{19}N_3O_2$	73.0	5.6	12.2	
	. — .						(72.8	5.8	11.9)	
3d	CH2-(-)	Н	173-175	36	Dichloromethane/ether	$C_{29}H_{23}N_3O_2$	78.2	5.2	9.4	
	~					27 20 2	(78.5	5.5	9.5)	

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REFERENCES AND NOTES

- G. M. Coppola, J. Heterocyclic Chem., 16, 827 (1979).
 G. E. Hardtmann, G. Koletar and O. R. Pfister, ibid., 12, 565 (1975).
- (3) Dimethylformamide was freshly distilled over calcium hydride
- prior to every reaction.

 (4) No attempt has been made to optimize the yield of the described reaction.