

Department of Chemistry, Temple University

The Preparation of Triazines and Benzimidazoles
From 1- and 3-Cyanoisoquinolines (1)

Francis H. Case and Lloyd Kennon

The preparation from 1- and 3-cyanoisoquinolines of certain benzimidazoles and symmetrical triazines containing the ferrioin group is described; also that of certain unsymmetrical triazines from 3-cyanoisoquinoline.

In previous communications (2,3) were described triazine and benzimidazole derivatives related to 6-cyano-2,2'-bipyridine. The present work deals with similar derivatives of 1- and 3-cyanoisoquinolines. These all contain a ferrioin (=N-C(=)-C(=)-N=) group and hence have the possibility of chelating metal ions.

By the action of an ethanol solution of hydrazine, 3-cyanoisoquinoline was converted into 3-isoquinoline-carboximidic acid hydrazide (I). Refluxing of the latter with an ethanol solution of benzil yielded 3-(3-isoquinolyl)-5,6-diphenyl-*as*-triazine (II). Similar treatment with α -pyridyl afforded 3-(3-isoquinolyl)-5,6-bis(2-pyridyl)-*as*-triazine (III). Reaction of 4,7-phenanthroline-5,6-dione with I yielded 3-(3-isoquinolyl)-*as*-triazino-[5,6-*f*][4,7]phenanthroline (IV).

From 1-cyanoisoquinoline we were unable to prepare the carboximidic hydrazide, and hence the analogues of the above *as*-triazines were not forthcoming.

Treatment of 3-cyanoisoquinoline with dicyanodiamide in the presence of alkali yielded 2,4-diamino-6-(3-isoquinolyl)-1,3,5-triazine (V). Reaction of V with guanidine

hydrochloride in presence of sodium ethoxide produced 2-amino-4,6-bis-(3-isoquinolyl)-1,3,5-triazine (VI). Analogous symmetrical triazines were produced by treating 1-cyanoisoquinoline with the same reagents.

Attempts to trimerize the two cyanoisoquinolines to 2,4,6-tris(3-isoquinolyl)-1,3,5-triazines by the use of sodium hydride, as had been done in the case of 6-cyano-2,2'-bipyridine (2) were unsuccessful.

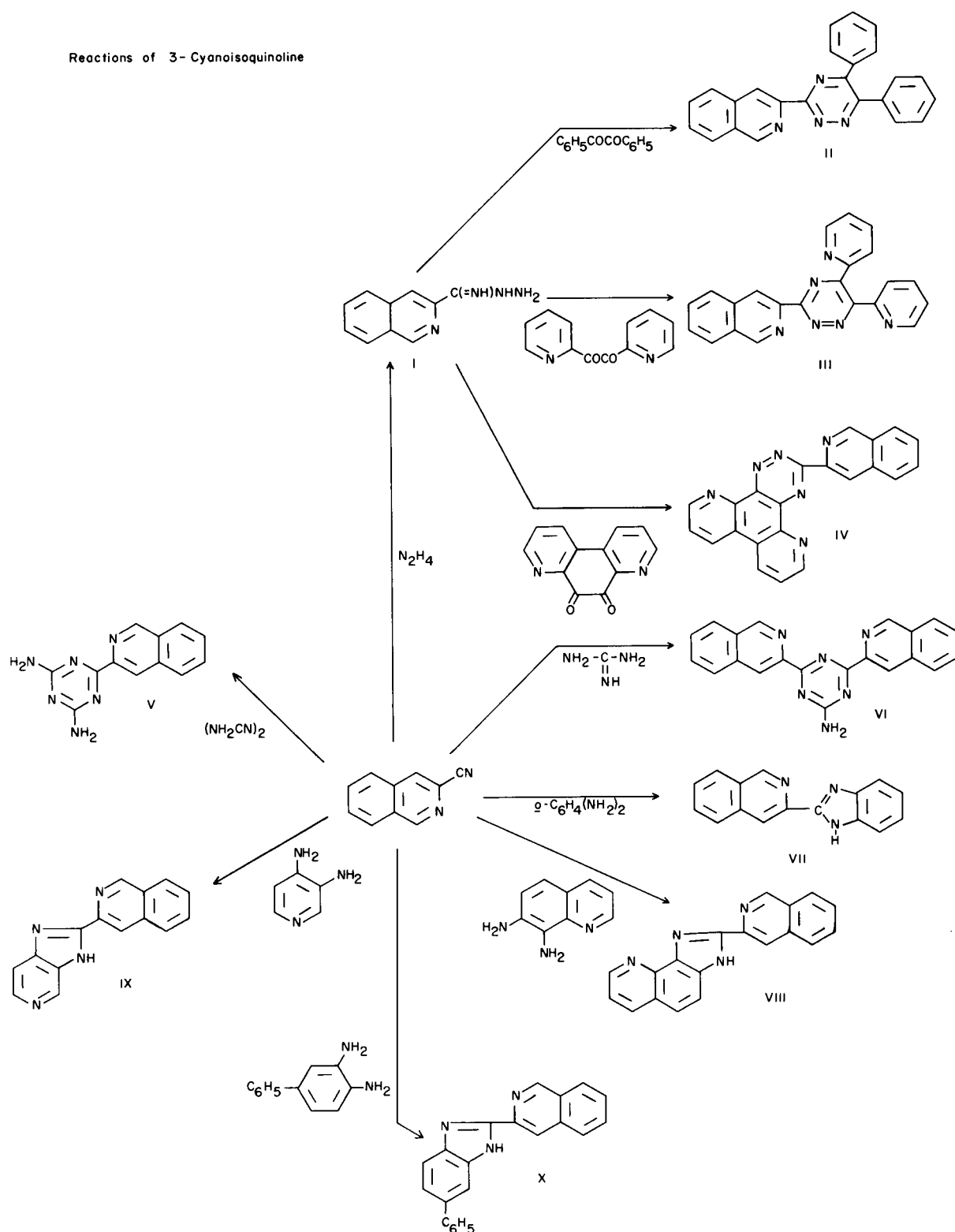
The preparation of 2-substituted benzimidazoles by the action of *o*-phenylenediamine with nitriles in presence of polyphosphoric acid at 250° has been described by Hein, Alheim and Leavitt (4). Using this procedure, and varying the diamine we have prepared the following compounds from 3-cyanoisoquinoline: 2-(3-isoquinolyl)benzimidazole (VII) (from *o*-phenylenediamine), 3*H*-imidazo[4,5-*h*]-quinoline (VIII) (from 7,8-diaminoquinoline), 1*H*-imidazo[4,5-*c*]pyridine (IX) (from 3,4-diaminopyridine) and 2-(3-isoquinolyl)-5(6)-phenylbenzimidazole (X) (from 3,4-diaminobiphenyl). The four analogous 1-isoquinolyl compounds were prepared in a similar manner. The properties and analyses of these compounds are recorded in Table I.

TABLE I

2-Substituted Benzimidazole Derivatives

2-Substituted Compound	Isoquinolyl Group	Yield, %	M.P. (°C)	Cryst'n Solvent	Formula	Analysis			
						Calcd. % C	H	Found % C	H
Benzimidazole	1-	45.8	211-212	benzene	C ₁₆ H ₁₁ N ₃	78.35	4.52	78.68	4.69
	3- (VII)	79.2	176-177	benzene				78.19	4.67
3-H Imidazo[4,5- <i>h</i>]quinoline	1-	52.6	219-220	benzene	C ₁₉ H ₁₂ N ₄	77.01	4.08	76.91	4.16
	3- (VIII)	36.8	235-236	benzene				77.40	4.24
1-H Imidazo[4,5- <i>c</i>]pyridine	1-	35.0	221-222	benzene	C ₁₅ H ₁₀ N ₄	73.16	4.09	72.83	4.31
	3- (IX)	44.0	278-279	ethanol				73.08	4.23
5(6)-Phenylbenzimidazole	1-	23.8	163-164	methanol	C ₂₂ H ₁₅ N ₃	82.22	4.70	82.63	4.83
	3- (X)	64.5	189-190	benzene				82.40	4.70

Reactions of 3-Cyanoisoquinoline



The reactions of 1-cyanoisoquinoline were analogous except that 1-isoquinolinecarboximidic acid hydrazide and hence its derivatives could not be prepared.

EXPERIMENTAL

3-Isoquinolinecarboximidic acid hydrazide (I).

A mixture of 2.6 g. of 3-cyanoisoquinoline, 5 ml. of 95% hydrazine and 3 ml. of ethanol was stirred at room temperature until complete solution resulted (7 hours). On cooling the hydrazidine separated out and was crystallized from benzene. The yield was 2.3 g. (74.2%) of product melting at 122-123°.

Anal. Calcd. for $C_{10}H_{10}N_4$: C, 64.47; H, 5.42. Found: C, 64.68; H, 5.65.

3-(3-Isoquinolyl)-5,6-diphenyl-*as*-triazine (II).

A mixture of 1 g. of the above hydrazidine and 1.1 g. of benzil in 25 ml. of ethanol was allowed to stand overnight. The precipitate was separated by filtration and crystallized from dimethyl formamide-water. The yield was 1.5 g. (78.9%) of material melting at 198-199°.

Anal. Calcd. for $C_{24}H_{16}N_4$: C, 79.98; H, 4.48. Found: C, 79.84; H, 4.56.

3-(3-Isoquinolyl)-5,6-bis(2-pyridyl)-*as*-triazine (III).

A mixture of 1 g. of the above hydrazidine and 1.1 g. of pyridil in 25 ml. of ethanol was heated at reflux for 1 hour. After cooling, the solid separating was removed by filtration and crystallized from ethanol. The yield was 1.5 g. (79.0%) of product melting at 221-222°. A deep purple color was obtained on treatment with Fe (II).

Anal. Calcd. for $C_{22}H_{14}N_6$: C, 72.93; H, 3.87. Found: C, 72.74; H, 4.19.

3-(3-Isoquinolyl)-*as*-triazino[5,6-*f*][4,7]phenanthroline (IV).

A mixture of 1 g. of the above hydrazidine, 1 g. of 4,7-phenanthroline-5,6-dione and 25 ml. of ethanol was heated at reflux for 4.5 hours. After cooling, the resulting precipitate was separated by filtration and crystallized from dimethyl formamide, yielding 0.9 g. (47.4%) of product melting at 350-351°.

Anal. Calcd. for $C_{22}H_{12}N_6$: C, 73.30; H, 3.36. Found: C, 73.00; H, 3.53.

2,4-Diamino-6-(1-isoquinolyl)-1,3,5-triazine.

A mixture of 2.5 g. of 1-cyanoisoquinoline, 1.7 g. of dicyanodiamide, 0.1 g. of potassium hydroxide and 8 g. of methyl cellosolve was heated at reflux for 4 hours. After cooling, water was added and the resulting precipitate separated by filtration and dried. Crystallization from methyl cellosolve yielded 3.6 g. (92.0%) of product melting at 251-253°. This proved to be a hemihydrate, which retained water of hydration on heating at 110°.

Anal. Calcd. for $C_{12}H_{10}N_6 \cdot \frac{1}{2}H_2O$: C, 58.29; H, 4.48. Found: C, 58.27; H, 4.38.

2,4-Diamino-6-(3-isoquinolyl)-1,3,5-triazine (V).

In this preparation the reagents and quantities were the same as

in the preceding experiment, except that 3-cyanoisoquinoline was substituted for the 1-isomer. The yield of crude product, melting at 344-352°, was 3.4 g. (88.0%). An analytical sample, crystallized from methyl cellosolve, melted at 354° dec.

Anal. Calcd. for $C_{12}H_{10}N_6$: C, 60.49; H, 4.23. Found: C, 60.51; H, 4.29.

2-Amino-4,6-bis(1-isoquinolyl)-1,3,5-triazine.

To a cooled solution of 1.3 g. of guanidine hydrochloride in 20 ml. of absolute ethanol was added 0.32 g. of sodium. After solution was complete, the precipitated sodium chloride was removed and washed with 7 ml. of absolute ethanol. 1-Cyanoisoquinoline (3.6 g.) was then added and the mixture heated at reflux for 15 hours. After cooling, the precipitate was collected and crystallized from dimethylformamide. The yield of product melting at 286-288° was 1.0 g. (26.0%). After drying at 110° it still retained $\frac{1}{2}$ mole of water of hydration.

Anal. Calcd. for $C_{21}H_{14}N_6 \cdot \frac{1}{2}H_2O$: C, 70.18; H, 4.21. Found: C, 70.25; H, 3.90.

2-Amino-4,6-bis(3-isoquinolyl)-1,3,5-triazine (VI).

The procedure was similar to that above except that 3-cyanoisoquinoline (2.7 g.) was substituted for 1-cyanoisoquinoline. Proportional amounts of the other ingredients were used. Crystallization of the precipitated product from dimethylformamide yielded 1.3 g. (42%) of product melting at 385°.

Anal. Calcd. for $C_{21}H_{14}N_6$: C, 71.99; H, 4.03. Found: C, 71.78; H, 4.25.

General Procedure for the Action of Diamines with Cyanoisoquinolines.

Equimolecular amounts of nitrile and diamine (not to exceed 0.01 mole of each) were mixed with 20 g. of polyphosphoric acid and the mixture maintained at 250° for 4 hours. It was then poured into water and neutralized with ammonium hydroxide. The resulting precipitate was dried and crystallized from the solvent indicated in Table I.

REFERENCES

- (1) This work was supported by a grant from the Committee on Research and Publications of Temple University.
- (2) F. H. Case, *J. Org. Chem.*, **31**, 2398 (1966).
- (3) F. H. Case, *J. Heterocyclic Chem.*, **4**, 157 (1967).
- (4) P. W. Hein, R. G. Alheim, and J. J. Leavitt, *J. Am. Chem. Soc.*, **79**, 427 (1957).

Received May 8, 1967

Philadelphia, Pa. 19122