

The Preparation of Substituted Pyridyl Tetrazines and Pyridazines Containing the Ferroin Group (1)

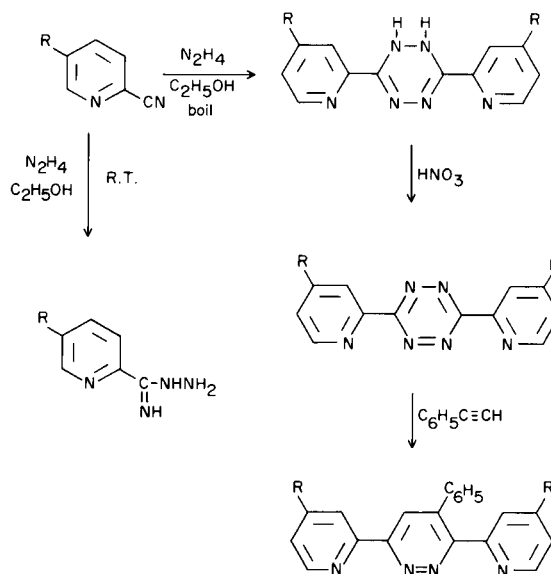
Francis H. Case

Department of Chemistry, Temple University

In previous communications (2,3) were described the preparations of carboximide acid hydrazides (hydrazidines) prepared by treating various cyanopyridine derivatives with 95% hydrazine in ethanol at room temperature. It has been shown (4,5) that 2-cyanopyridine treated with the same reagents, but at a refluxing temperature, yields 3,6-bis(2-pyridyl)dihydro-1,2,4,5-tetrazine, which on mild oxidation is converted to 3,6-bis(2-pyridyl)-1,2,4,5-tetrazine, and further (5,6), that the latter compound when refluxed with phenyl acetylene in toluene is converted to 3,6-bis(2-pyridyl)-4-phenylpyridazine.

In an attempt to provide compounds with possible chelating capability for metal ions, 4-methyl-, 4-ethyl- and 4-phenyl-2-cyanopyridines have been converted to the corresponding dihydrotetrazines and tetrazines, the latter being deep red-colored compounds. From the methyl- and phenylpyridyltetrazines, the corresponding phenylpyridazines were prepared. All of these compounds contain the ferroin group, (=N-C(=)-C(=)N=).

Attempts to make dihydrotetrazines from cyanopyrazine, 6-cyano-2,2'-bipyridine, and 2-cyano-1,10-phenanthroline (whose hydrazidines had been prepared) were unsuccessful.



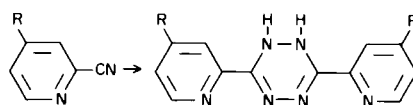
EXPERIMENTAL

Preparation of 3,6-bis(4-alkyl-2-pyridyl)dihydro-1,2,4,5-tetrazines.

A mixture of 0.05 mole of 4-alkyl-2-cyanopyridine, 7 ml. of 95% hydrazine and 25 ml. ethanol was heated at reflux for 5 hours.

TABLE I

3,6-Bis(4-alkyl-2-pyridyl)dihydro-1,2,4,5-tetrazines



R	Yield %	M.P. (°C)	Cryst'n Solvent	Formula	Analysis					
					Calcd. %			Found %		
					C	H	N	C	H	N
CH ₃	59.2	210-211	dimethyl formamide	C ₁₄ H ₁₄ N ₆	63.14	5.30	31.56	63.28	5.50	31.76
C ₂ H ₅	53.0	134-135	ethanol	C ₁₆ H ₁₈ N ₆	65.29	6.16	28.55	65.00	6.24	28.95
C ₆ H ₅	48.7	189-190	dimethyl formamide	C ₂₄ H ₁₈ N ₆	73.83	4.65	21.52	73.79	4.92	21.75

The contents of the flask were then poured into water, the precipitate removed by filtration and crystallized from the solvent indicated in Table I.

3,6-Bis(4-methyl-2-pyridyl)-1,2,4,5-tetrazine.

To a solution of 1 g. of the corresponding dihydrotetrazine in 5 ml. of acetic acid was added, with cooling, 0.8 ml. of concentrated nitric acid. After standing one hour at room temperature, the mixture was poured into cold water and made alkaline by addition of sodium carbonate solution. The resulting precipitate was washed with water, dried, and crystallized from ethanol, yielding 0.5 g. (50.5%) of product melting at 244-245°.

Anal. Calcd. for $C_{14}H_{12}N_6$: C, 63.64; H, 4.55; N, 31.81. Found: C, 63.46; H, 4.64; N, 31.86.

3,6-Bis(4-phenyl-2-pyridyl)-1,2,4,5-tetrazine.

A solution of 1.2 g. of the dihydrotetrazine in 5 ml. of acetic acid was treated with 0.7 ml. of concentrated nitric acid and the solution treated as above. The resulting dried precipitate was crystallized from dimethylformamide, yielding 0.9 g. (75.0%) of pure product melting at 247-248° dec.

Anal. Calcd. for $C_{24}H_{16}N_6$: C, 74.23; H, 4.13; N, 21.64. Found: C, 73.89; H, 4.25; N, 21.73.

3,6-Bis(4-ethyl-2-pyridyl)-1,2,4,5-tetrazine.

(In this case a milder procedure was necessary.) To a solution of 1 g. of the corresponding dihydro compound in 40 ml. of acetic acid was added, with cooling, 4 ml. of 5 N nitric acid. After one-hour's standing at room temperature, the mixture was poured into water and neutralized with sodium carbonate solution. The resulting precipitate was crystallized from benzene-petroleum ether, yielding 1.7 g. (56.7%) of pure product melting at 134-135°.

Anal. Calcd. for $C_{16}H_{16}N_6$: C, 65.73; H, 5.52; N, 28.75. Found: C, 65.28; H, 5.58; N, 29.08.

3,6-Bis(4-methyl-2-pyridyl)-4-phenylpyridazine.

A mixture of 1.1 g. of 3,6-bis(4-methyl-2-pyridyl)-1,2,4,5-tetrazine, 25 ml. of toluene and 0.5 g. of phenylacetylene was heated at reflux for 5 hours. After removal of the toluene *in vacuo*, the solid residue was crystallized from benzene-petroleum ether, yielding 0.5 g. (31.2%) of pure product melting at 160-161°.

Anal. Calcd. for $C_{22}H_{18}N_4$: C, 78.08; H, 5.36; N, 16.56. Found: C, 78.10; H, 5.34; N, 16.52.

3,6-Bis(4-phenyl-2-pyridyl)-4-phenylpyridazine.

A toluene solution (25 ml.) of 0.6 g. of 3,6-bis(4-phenyl-2-pyridyl)-1,2,4,5-tetrazine and 0.4 g. of phenylacetylene was heated at reflux for 7 hours. Removal of the toluene *in vacuo* yielded 0.5 g. (70.4%) of a solid which after crystallization from benzene-petroleum ether melted at 140-141° dec.

Anal. Calcd. for $C_{32}H_{22}N_4$: C, 83.09; H, 4.79; N, 12.11. Found: C, 82.90; H, 5.13; N, 12.36.

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.*, **30**, 93 (1965).
- (3) F. H. Case, *J. Heterocyclic Chem.*, **5**, 223 (1968).
- (4) F. Dallacker, *Monatsh. Chem.*, **91**, 302 (1960).
- (5) W. A. Butte and F. H. Case, *J. Org. Chem.*, **26**, 4690 (1961).
- (6) R. A. Carboni and R. V. Lindsey, *J. Am. Chem. Soc.*, **81**, 4342 (1959).

Received April 15, 1968

Philadelphia, Pa. 19122