

## The Preparation of Diazine Derivatives Containing the Ferroin Group (1)

Francis H. Case

Department of Chemistry, Temple University

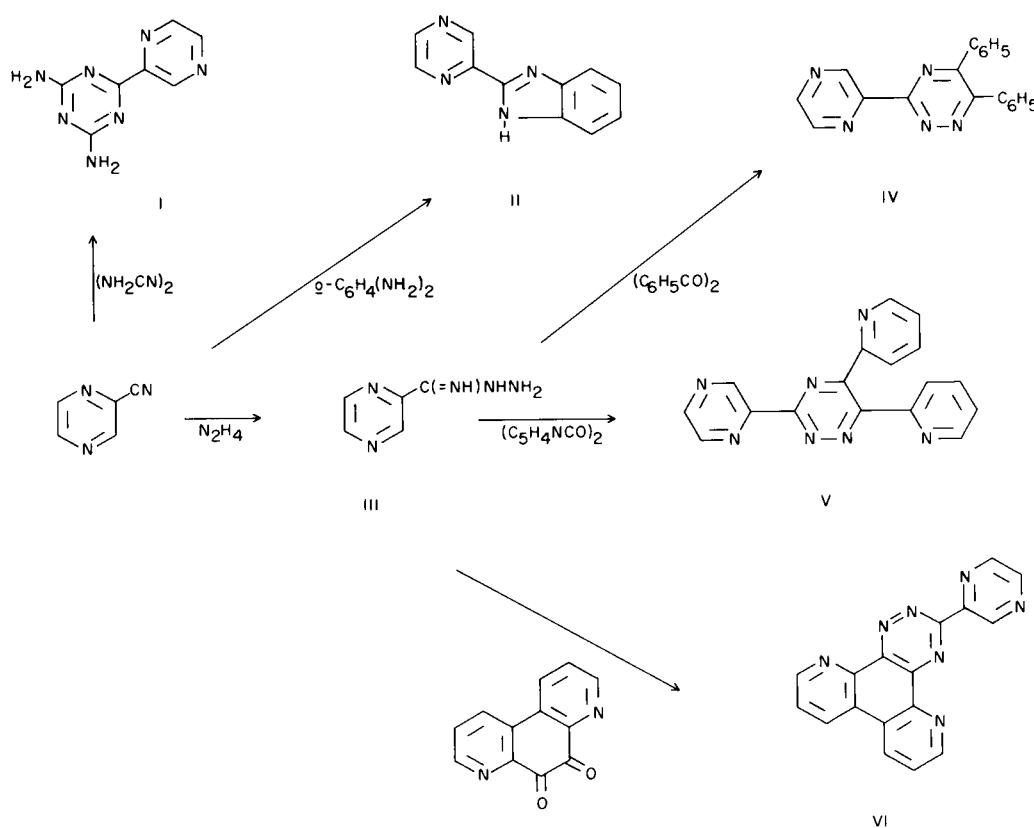
With the idea of providing new compounds capable of chelation with metal ions, certain derivatives of diazines, containing the ferroin ( $=\text{N}-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{N}=\text{O}$ ) group have been prepared.

Starting from cyanopyrazine and using methods previously described for 6-cyano-2,2'-bipyridine (2,3) and cyanoisoquinoline (4) derivatives, there was synthesized 2,4-diamino-6-pyrazyl-1,3,5-triazine (I) by the action of dicyanodiamide; 2-pyrazylbenzimidazole (II) by the action of *o*-phenylenediamine in presence of polyphosphoric acid; and pyrazine carboximidic acid hydrazide (III) (the hydrazidine) on treatment with hydrazine in ethanol.

From the last mentioned compound were prepared 3-pyrazyl-5,6-diphenyl-*as*-triazine (IV) using benzil, 3-pyrazyl-5,6-bis(2-pyridyl)-*as*-triazine (V) using pyridil, and 3-pyrazyl-*as*-triazino[5,6-*f*][4,7]phenanthroline (VI) using 4,7-phenanthroline-5,6-dione.

The five analogous compounds were prepared from 3-cyanopyridazine. From 2-cyanopyrimidine, 2,4-diamino-6-(2-pyrimidyl)-1,3,5-triazine and 2-(2-pyrimidyl)benzimi-

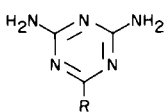
Reactions of Cyanopyrazine.



The formulas for the derivatives of the other diazines differ only in the positions of the nitrogen atoms in the diazine ring.

TABLE I

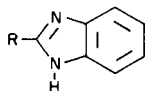
## 2,4-Diamino-6-diazyl-1,3,5-triazines



R	Yield %	M.P. (°C)	Crystallization Solvent	Formula	Analysis					
					Calcd. %			Found %		
					C	H	N	C	H	N
Pyrazyl (I)	77.8	344-345	dimethyl formamide	C <sub>7</sub> H <sub>7</sub> N <sub>7</sub>	44.44	3.73	51.83	44.11	3.75	51.59
3-Pyridazyl	75.0	310-311	dimethyl formamide-water	C <sub>7</sub> H <sub>7</sub> N <sub>7</sub>	44.44	3.73	51.83	44.35	3.98	51.91
2-Pyrimidyl	40.7	355-356	water	C <sub>7</sub> H <sub>7</sub> N <sub>7</sub>	44.44	3.73	51.83	44.22	3.70	52.10
4-Pyrimidyl	38.8	298-299	water	C <sub>7</sub> H <sub>7</sub> N <sub>7</sub>	44.44	3.73	51.83	44.90	3.96	51.60

TABLE II

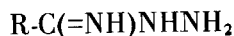
## 2-Diazyl Benzimidazoles



R	Yield %	M.P. (°C)	Crystallization Solvent	Formula	Analysis					
					Calcd. %			Found %		
					C	H	N	C	H	N
Pyrazyl (II)	22.2	235-236	benzene	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub>	67.34	4.11	28.55	67.63	4.27	28.33
3-Pyridazyl	16.7	270-271	benzene-ethanol	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub>	67.34	4.11	28.55	67.47	4.28	28.96
2-Pyrimidyl	50.8	299-300	ethanol	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub>	67.34	4.11	28.55	67.77	4.34	28.81

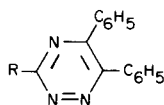
TABLE III

## Diazyl Hydrazidines



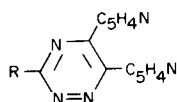
R	Yield %	M.P. (°C)	Crystallization Solvent	Formula	Analysis					
					Calcd. %			Found %		
					C	H	N	C	H	N
Pyrazyl (III)	82.6	123-124	benzene	C <sub>5</sub> H <sub>7</sub> N <sub>5</sub>	43.79	5.14	51.07	44.15	5.26	51.07
3-Pyridazyl	77.0	164-165	ethanol	C <sub>5</sub> H <sub>7</sub> N <sub>5</sub>	43.79	5.11	51.07	43.87	5.39	50.91
4-Pyrimidyl	30.8	146-147	benzene	C <sub>5</sub> H <sub>7</sub> N <sub>5</sub>	43.79	5.11	51.07	43.91	5.12	50.79

TABLE IV

3-Diazyl-5,6-diphenyl-*as*-triazines

R	Yield %	M.P. (°C)	Crystallization Solvent	Formula	Analysis					
					Calcd. %			Found %		
					C	H	N	C	H	N
Pyrazyl (IV)	75.8	179-180	ethanol	C <sub>19</sub> H <sub>13</sub> N <sub>5</sub>	73.30	4.21	22.49	73.65	4.44	22.44
3-Pyridazyl	74.8	215-216	ethanol	C <sub>19</sub> H <sub>13</sub> N <sub>5</sub>	73.30	4.21	22.49	72.93	4.54	22.25
4-Pyrimidyl	76.9	180-181	ethanol	C <sub>19</sub> H <sub>13</sub> N <sub>5</sub>	73.30	4.21	22.49	73.55	4.44	22.74

TABLE V

3-Diazyl-5,6-bis(2-pyridyl)-*as*-triazines

R	Yield %	M.P. (°C)	Crystallization Solvent	Formula	Analysis					
					Calcd. %			Found %		
					C	H	N	C	H	N
Pyrazyl (V)	46.7	191-192	dimethyl formamide	C <sub>17</sub> H <sub>11</sub> N <sub>7</sub>	65.14	3.54	31.32	65.35	3.71	30.96
3-Pyridazyl	40.0	206-207	ethanol	C <sub>17</sub> H <sub>11</sub> N <sub>7</sub>	65.14	3.54	31.32	65.52	3.94	31.44
4-Pyrimidyl	53.3	198-199	dimethyl formamide-water	C <sub>17</sub> H <sub>11</sub> N <sub>7</sub>	65.14	3.54	31.32	65.50	3.68	31.17

All three of the above triazines gave a deep blue or purple color with Fe(II).

dazole were prepared, but the hydrazidine could not be prepared and hence its derivatives were not forthcoming.

From 4-cyanopyrimidine were prepared 6-(4-pyrimidyl)-1,3,5-triazine, 4-pyrimidyl carboximidic acid hydrazide, 3-(4-pyrimidyl)-5,6-diphenyl-*as*-triazine and 3-(4-pyrimidyl)-5,6-bis(2-pyridyl)-*as*-triazine by similar methods. The preparation of the various cyanodiazines was effected for the most part according to one of the procedures outlined by Robba (5).

Preliminary tests have shown that the 3-diazyl-5,6-bis(2-pyridyl)-*as*-triazines and 3-diazyl-*as*-triazino[5,6-*f*][4,7]-phenanthrolines give deep purple solutions in presence of Fe(II).

## EXPERIMENTAL

## Cyanopyrazine.

The procedures referred to by Robba (5) were used, starting with pyrazine-2,3-dicarboxylic acid. In the dehydration of the

amide to the nitrile the use of phosphorus pentoxide was found to be more reliable than phosphorus oxychloride.

## 3-Cyanopyridazine.

The procedures referred to by Robba were used, starting with furfuryl acetate. After oxidation of the 3-hydroxymethylpyridazine to the acid the ethyl ester was prepared (6) and converted to the amide. Dehydration to the nitrile followed Robba's procedure.

## 2-Cyanopyrimidine.

The method of Case and Koft (7) was used.

## 4-Cyanopyrimidine.

4-Methylpyrimidine was prepared from 3-ketobutyraldehyde dimethyl acetal and formamide (8). After oxidation to the acid the ethyl ester (9) was made and the amide and nitrile by Robba's method. The nitrile was used without purification.

## Preparation of 2,4-Diamino-6-diazyl-1,3,5-triazines.

A mixture of 1 g. of cyanodiazine, 0.75 g. of dicyanodiamide, 0.075 g. of potassium hydroxide and 5 ml. of methyl cellosolve

was heated at reflux for 3 hours and then poured into water. The resulting precipitate was crystallized from the solvent indicated in Table I.

#### Preparation of 2-Diazybenzimidazoles.

A mixture of 1.0 g. each of cyanodiazine and *o*-phenylenediamine and 20 g. of polyphosphoric acid was heated 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 II.

#### Preparation of Hydrazidines of Cyanodiazines.

A mixture of 2 g. of cyanodiazine, 4 ml. of ethanol and 6 ml. of 95% hydrazine was allowed to stand at room temperature for two hours, and then overnight at 0°. In the case of cyanopyrazine the crude hydrazidine was isolated by evaporation of the solvent *in vacuo* at 50°. In the other two cases the hydrazidine precipitated and was dried and crystallized from the solvent indicated in Table III. No hydrazidine could be obtained from 2-cyanopyrimidine.

#### Preparation of 3-Diazy-5,6-diphenyl-*as*-triazines.

A mixture of 0.65 g. of cyanodiazine hydrazidine, 1 g. of benzil and 10 ml. of ethanol was heated at reflux for 1 hour. On cooling the triazine precipitated and was crystallized from ethanol.

#### Preparation of 3-Diazy-5,6-bis(2-pyridyl)-*as*-triazines.

The quantities and procedure were the same as in the case of the 5,6-diphenyl-*as*-triazines except that  $\alpha$ -pyridil was substituted for benzil. The crystallization solvents are indicated in Table V.

#### 3-Pyrazyl-*as*-triazino[5,6-*f*][4,7]phenanthroline (VI).

A mixture of 1 g. of the hydrazidine of cyanopyrazine, 1.5 g. of 4,7-phenanthroline-5,6-dione, and 25 ml. of ethanol was

heated at reflux for one hour. The precipitate obtained on cooling was then crystallized from dimethyl formamide. The yield was 1.2 g. (53.1%), m.p. 361-362°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>9</sub>N<sub>7</sub>: C, 65.57; H, 2.92; N, 31.51. Found: C, 65.60; H, 3.15; N, 31.70.

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

The previous quantities and procedure were used, substituting the hydrazidine of 3-cyanopyridazine. The yield of pure product melting at 380° after crystallization from dimethyl formamide was 1.9 g. (83.7%).

*Anal.* Calcd. for C<sub>17</sub>H<sub>9</sub>N<sub>7</sub>: C, 65.57; H, 2.92; N, 31.51. Found: C, 65.90; H, 3.10; N, 31.55.

Both the above compounds gave a deep purple color with Fe (II).

#### 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) F. H. Case and L. Kennon, *ibid.*, **4**, 483 (1967).
- (5) M. Robba, *Ann. Chim. (Paris)*, **5**, 531 (1960).
- (6) W. Leanza, M. Becker, and E. Rogers, *J. Am. Chem. Soc.*, **75**, 4086 (1953).
- (7) F. H. Case and E. Koft, *ibid.*, **81**, 905 (1959).
- (8) H. Brederick, R. Gompper, and G. Morlock, *Chem. Ber.*, **90**, 942 (1957).
- (9) K. Shirakawa, S. Bau, and M. Yoneda, *J. Pharm. Soc. Japan*, **73**, 598 (1953); *Chem. Abstr.*, **48**, 9362f (1954).

Received December 26, 1967

Philadelphia, Pa. 19122