

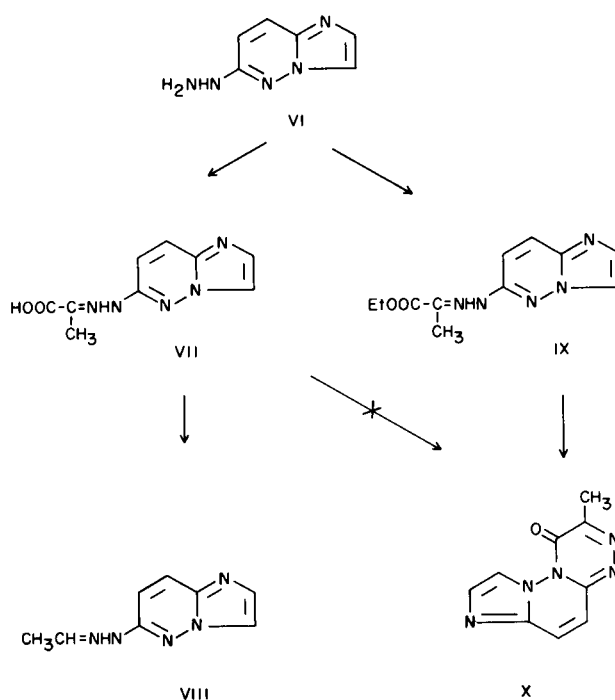
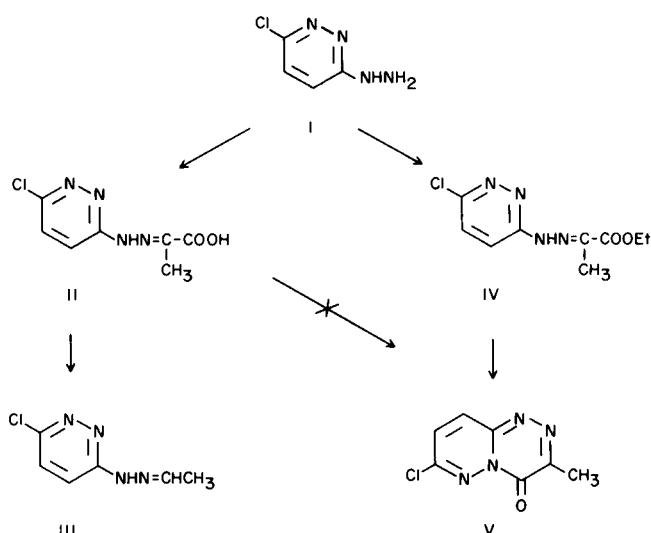
Synthesis of Pyridazine Derivatives. XXVII.  
The Formation of 4*H*-Pyridazino[6,1-*c*]-*as*-triazine and  
1*H*-Imidazo(1',2':2,3)pyridazino[6,1-*c*]-*as*-triazine Ring System

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In a continuing investigation of bi- and polycyclic heterocycles, based on pyridazine we have examined the possibility of forming the hitherto unknown bicycle, 4*H*-pyridazino[6,1-*c*]-*as*-triazine. A feasible approach to this system seemed to be from hydrazinopyridazines as starting material. Thus, 6-chloro-3-hydrazinopyridazine (I) when condensed with pyruvic acid afforded the hydrazone (II) which we attempted to thermally cyclize. However heating it at 175-180° for 30 minutes did not afford the bicycle and, instead, decarboxylation to the already known ethylidene derivative (III) (I) took place. Even heating with polyphosphoric acid at elevated temperature was not successful and the unchanged starting acid could be recovered.

We have found that the cyclization proceeded successfully if 3-( $\alpha$ -carbethoxyethylidenehydrazino)-6-chloropyridazine (IV), prepared from 6-chloro-3-hydrazinopyridazine (I) and ethyl pyruvate, was used. After heating with polyphosphoric acid at 140° for 1 hour the bicycle, 7-chloro-3-methylpyridazino[6,1-*c*]-*as*-triazine-4-one (V) was formed in moderate yield. The structure of V is substantiated by infrared and nmr spectroscopic evidence.



In an analogous way we tried to form the triazine ring starting with 6-hydrazinoimidazo[1,2-*b*]pyridazine (VI). Again, we were able to establish that the condensation product (VII) with pyruvic acid did not cyclize in the presence of hot polyphosphoric acid, whereas heating the compound alone caused decarboxylation to the known 6-ethylidenehydrazinoimidazo[1,2-*b*]pyridazine (VIII) (2). In a similar way, as above, the use of the corresponding ester (IX) and heating in the presence of polyphosphoric acid yielded a representative (X) of the hitherto unknown 1*H*-imidazo[1',2':2,3]pyridazino[6,1-*c*]-*as*-triazine system.

#### EXPERIMENTAL (3)

3-( $\alpha$ -Carbethoxyethylidenehydrazino)-6-chloropyridazine (IV).

To a solution of 1.44 g. of 6-chloro-3-hydrazinopyridazine (I) in 25 ml. of hot ethanol were added 1.16 g. of ethyl pyruvate and

0.5 ml. of glacial acetic acid. The reaction mixture was heated to boiling for a few minutes and allowed to cool slowly to room temperature. After cooling on ice the formed precipitate was collected by filtration, washed with ethanol and crystallized from the same solvent. Yield 2.1 g. (87%); m.p. 184°; infrared (Nujol), 3175 (NH) and 1706 cm<sup>-1</sup> (COOEt); NMR (deuteriochloroform),  $\tau$  2.19 (d, H<sub>4</sub>), 2.60 (d, H<sub>5</sub>), 8.62 (t, CH<sub>3</sub> of ethyl group), 5.66 (q, CH<sub>2</sub> of ethyl group), 7.77 (s, CH<sub>3</sub> group); J = 9.5 cps (H<sub>4</sub>, H<sub>5</sub>), J = 7 cps (CH<sub>2</sub>, CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>9</sub>H<sub>11</sub>ClN<sub>4</sub>O<sub>2</sub>: C, 44.55; H, 4.57; N, 23.10. Found: C, 45.10; H, 4.68; N, 23.32.

### 3-( $\alpha$ -Carboxyethylidenehydrazino)-6-chloropyridazine (II).

This compound was prepared in essentially the same way as described above for compound IV in 82% yield, m.p. 234° (from ethanol). Infrared (Nujol), 3215 (NH), broad bands at 2427 and 1887 (strong hydrogen bonding) and 1704 cm<sup>-1</sup> (COOH).

*Anal.* Calcd. for C<sub>7</sub>H<sub>7</sub>ClN<sub>4</sub>O<sub>2</sub>: C, 39.25; H, 3.29; N, 26.11. Found: C, 39.47; H, 3.53; N, 26.22.

### 7-Chloro-3-methylpyridazino[6,1-c]-as-triazin-4-one (V).

A mixture containing 2.42 g. of 3-( $\alpha$ -carboxyethylidenehydrazino)-6-chloropyridazine (IV) and 30 g. of polyphosphoric acid was heated at 140° for 1 hour. At the end of the reaction, the mixture was cooled on ice and 100 g. of crushed ice and solid sodium bicarbonate (until pH 4 was reached) were added. The separated product was collected by filtration, washed with cold water, dried and crystallized from ethanol, yield 0.72 g. (36%). The compound has no definite melting point and decomposes between 150 and 153°. Infrared (Nujol), 1712 cm<sup>-1</sup> (CO); NMR (deuteriochloroform),  $\tau$  2.63 (d, H<sub>8</sub>), 2.07 (d, H<sub>9</sub>), 7.30 (s, CH<sub>3</sub>); J = 10 cps (H<sub>8</sub>, H<sub>9</sub>).

*Anal.* Calcd. for C<sub>7</sub>H<sub>5</sub>ClN<sub>4</sub>O: C, 42.77; H, 3.23; N, 28.49. Found: C, 42.74; H, 3.23; N, 28.31.

If, instead of the ester, the free acid (II) was heated in the presence of polyphosphoric acid at 135-140° for 1 hour and then at 160° for 10 minutes, no changes were observed and the starting compound could be isolated. However, heating of 100 mg. of the acid in a tube at 175-180° for 30 minutes and then connecting the tube to a vacuum caused accumulation of the pure 3-ethylidenehydrazino-6-chloropyridazine (ca. 10 mg.) on the cool part of the tube. A mixed melting point with an authentic specimen (1) was undepressed.

### 6-( $\alpha$ -Carboxyethylidenehydrazino)imidazo[1,2-b]pyridazine (IX).

A solution containing 1.50 g. of 6-hydrazinoimidazo[1,2-b]pyridazine (2) in 30 ml. of hot ethanol was treated with 1.16 g. of ethyl pyruvate and 1 ml. of glacial acetic acid. The reaction mixture was heated under reflux for a few minutes and upon cooling the separated product was collected by filtration, washed with ethanol and dried. Upon crystallization from ethanol, the pure compound (IX) was obtained in 78% yield (1.95 g.), m.p. 189-190°.

*Anal.* Calcd. for C<sub>11</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>: C, 53.43; H, 5.30; N, 28.33. Found: C, 53.58; H, 5.63; N, 28.56.

### 6-( $\alpha$ -Carboxyethylidenehydrazino)imidazo[1,2-b]pyridazine (VII).

This compound was obtained in essentially the same manner as described for compound IX. From 1.49 g. of 6-hydrazinoimidazo[1,2-b]pyridazine and 1 g. of pyruvic acid were obtained 1.05 g. of the product. Crystallization from ethanol and water (1:1) gave the pure compound, m.p. 178-179°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>9</sub>N<sub>5</sub>O<sub>2</sub>: C, 49.31; H, 4.14; N, 31.95. Found: C, 49.64; H, 4.07; N, 32.04.

The compound when heated at about 180° was decarboxylated into the known 6-ethylidenehydrazinoimidazo[1,2-b]pyridazine, m.p. 172° (2).

### 2-Methylimidazo[1',2':2,3]pyridazino[6,1-c]-as-triazine (X).

6-( $\alpha$ -Carboxyethylidenehydrazino)imidazo[1,2-b]pyridazine (X) (1.24 g.) and 20 g. of polyphosphoric acid were heated at 150-160° for 1.5 hours until foaming of the reaction mixture had stopped. The reaction mixture was cooled on ice, 70 g. of crushed ice were added and the pH of the mixture was brought to 4 with sodium bicarbonate. The separated product was collected by filtration, washed with iced water and dried. Yield of the crude product was 0.24 g. (25%). Crystallization from ethanol and water (1:1) gave the pure compound, m.p. 160-162°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>7</sub>N<sub>5</sub>O: C, 53.73; H, 3.51; N, 34.81. Found: C, 53.90; H, 3.85; N, 34.98.

## REFERENCES

- (1) A. Pollak and M. Tisler, *Tetrahedron*, **22**, 2073 (1966).
- (2) B. Stanovnik and M. Tisler, *ibid.*, **23**, 387 (1967).
- (3) All melting points were taken on a Kofler melting point apparatus. The infrared spectra were recorded on a Perkin-Elmer Model 137 Spectrophotometer. For the determination of NMR spectra a Varian A-60 Spectrometer was used (TMS as internal standard).

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