

# A Novel Tetracyclic Ring System. 10*H*-Tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole

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Received April 19, 1980

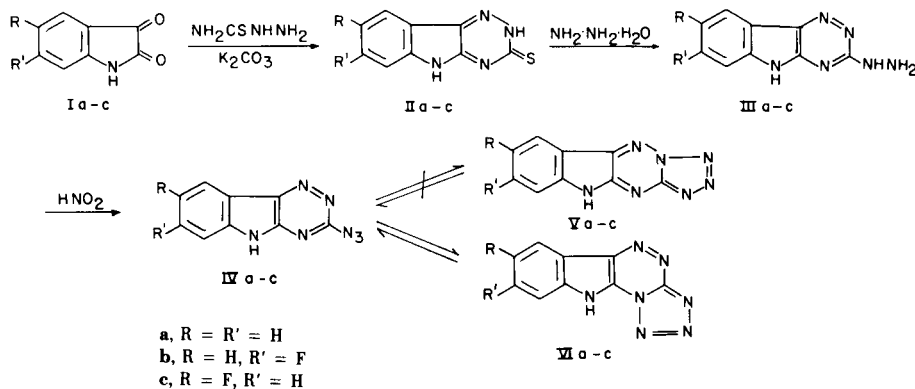
The reaction of 3-hydrazino-1,2,4-triazino[5,6-*b*]indole with nitrous acid affords a novel tetracyclic ring system: 10*H*-tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole. The mode of cyclization has been discussed.

*J. Heterocyclic Chem.*, 17, 1783 (1980).

The reactions of hydrazino compounds with nitrous acid are well known (1,2). However, in some of these reactions, it cannot be predicted with certainty whether the final product would involve the formation of a tetrazole ring system or an azido derivative (3-6). Further, there is some controversy about the structure of the final product when 3-hydrazino-1,2,4-triazine derivatives are cyclized with nitrous acid because the chances of cyclization are equal both at *N*-2 and at *N*-4. Paudler, *et al.* (7), have reported the cyclization at *N*-2, while Messmer, *et al.* (8,9), at *N*-4. In view of this, the reaction of 3-hydrazino-1,2,4-triazino[5,6-*b*]indole with nitrous acid was investigated as it was likely to lead to a new heterocycle.

Indole-2,3-diones (Ia-c), obtained from appropriate anilines, were allowed to react with thiosemicarbazide to afford three different 1,2,4-triazino[5,6-*b*]indole-3-thiones (IIa-c) (10). The latter, on refluxing with hydrazine hydrate, afforded the corresponding 3-hydrazino-1,2,4-triazino[5,6-*b*]indoles (IIIa-c) (11). Reactions of these hydrazino derivatives with nitrous acid give rise to azido derivatives (IVa-c), which may further cyclize either at *N*-2 or *N*-4, leading to the formation of tetrazolo[1',5':2,3]-[1,2,4]triazino[5,6-*b*]indoles (Va-c) or tetrazolo[5',1':3,4]-[1,2,4]triazino[5,6-*b*]indoles (VIa-c), respectively.

The compounds, isolated from the reactions of 3-hydrazino derivatives (IIIa-c) with nitrous acid do not exhibit an azide band at 2150  $\text{cm}^{-1}$  in the ir spectra, thus ruling out the existence of 3-azido derivatives (IVa-c). The characteristic absorptions in the ir spectra (potassium bromide) are at 1180-1220 (tetrazole ring), 1580-1620 ( $\text{N}=\text{N}$ -,  $>\text{C}=\text{N}$ -) and 2780-3080  $\text{cm}^{-1}$  ( $>\text{NH}$ , aromatic  $\geq\text{CH}$ ). The pmr spectra (DMSO) exhibit resonance signals at  $\delta$  8.5 ( $>\text{NH}$ ) and 7.6-8.0 ppm (aromatic protons). The mass spectrum of the final product, where  $\text{R} = \text{R}' = \text{H}$ , has shown  $\text{M}^+$  at *m/e* 211. Now the question arises, whether the cyclization takes place at *N*-2 or *N*-4. It is well known from the literature that the formation of a more benzenoid structure is favoured in similar cases (12) and on this basis, the formation of angular structure VI should be favoured in comparison to the planar structure V, because the  $10\pi$  electron system (aromatic character) of the indole ring is preserved in the former VI (high resonance energy). This view has been supported by isotope labelling studies done by Messmer, *et al.* (8) on benzo-*as*-triazines. On the basis of these observations, the cyclization should take place at *N*-4 and the compounds obtained are identified as 10*H*-tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indoles (VI).



## EXPERIMENTAL

Melting points are uncorrected. Ir spectra were recorded on Perkin Elmer (model 337) in potassium bromide discs, nmr spectra were recorded at 60 MHz on Perkin Elmer (model RB-12) in DMSO with TMS as external standard.

Indole-2,3-diones (Ia-c).

These compounds were prepared according to literature methods starting from the corresponding anilines (13-15).

1,2,4-Triazino[5,6-*b*]indole-3-thiones (IIa-c).

These compounds were prepared by refluxing the corresponding indole-2,3-dione with thiosemicarbazide in alkaline medium by following the method of Gladych, *et al.* (16).

3-Hydrazino-1,2,4-triazino[5,6-*b*]indole (IIIa).

1,2,4-Triazino[5,6-*b*]indole-3-thione (IIa, 2 g.) was refluxed with hydrazine hydrate (15 ml.) for 4-5 hours. On cooling, crystals separated, which were filtered and washed with ethanol to afford 1.4 g. of the desired compound. It was recrystallized from DMF, m.p. 276-277°, lit. m.p. 278-279° (11).

3-Hydrazino-7-fluoro-1,2,4-triazino[5,6-*b*]indole (IIIb).

Compound IIIb was obtained in 64.6% yield by refluxing IIb with hydrazine hydrate, m.p. 282-283°.

*Anal.* Calcd. for C<sub>8</sub>H<sub>7</sub>FN<sub>6</sub>: C, 49.54; H, 3.21; N, 38.53. Found: C, 49.38; H, 3.22; N, 38.47.

3-Hydrazino-8-fluoro-1,2,4-triazino[5,6-*b*]indole (IIIc).

Compound IIIc was prepared in 65.8% yield from IIc and hydrazine hydrate, m.p. 295-297°.

*Anal.* Calcd. for C<sub>8</sub>H<sub>7</sub>FN<sub>6</sub>: C, 49.54; H, 3.21; N, 38.53. Found: C, 49.43; H, 3.42; N, 38.42.

10*H*-Tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole (VIa).

To a solution of 3-hydrazino-1,2,4-triazino[5,6-*b*]indole (2 g., 0.01 mole) in polyphosphoric acid (15 ml.), was added sodium nitrite solution (0.75 g. in 5 ml. of water, 0.011 mole) at 0-5° during 30 minutes with stirring. The mixture was kept for 2 hours at room temperature, diluted with water and filtered. The yellowish compound was recrystallized from DMF-ethanol, yield 61%, m.p. 292° dec.

*Anal.* Calcd. for C<sub>8</sub>H<sub>5</sub>N<sub>7</sub>: C, 51.18; H, 2.37; N, 46.44. Found: C, 51.12; H, 2.34; N, 46.38.

8-Fluoro-10*H*-tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole (VIb).

Compound VIb was prepared by the same procedure described as for VIa in 58.5% yield from IIIb, m.p. 277° dec.

*Anal.* Calcd. for C<sub>8</sub>H<sub>4</sub>FN<sub>7</sub>: C, 47.16; H, 1.74; N, 42.79. Found: C, 47.11; H, 1.72; N, 42.82.

7-Fluoro-10*H*-tetrazolo[5',1':3,4][1,2,4]triazino[5,6-*b*]indole (VIc).

This compound has also been obtained by a similar method in 59.0% yield from IIIc, m.p. 282° dec.

*Anal.* Calcd. for C<sub>8</sub>H<sub>4</sub>FN<sub>7</sub>: C, 47.16; H, 1.74; N, 42.79. Found: C, 47.13; H, 1.71; N, 42.76.

Acknowledgement.

The authors are thankful to the Council of Scientific and Industrial Research, New Delhi, India for financial assistance.

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