A New Fused Tetrazole Ring System: Tetrazolo[1,5-*b*]isoquinoline

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Tetrazolo[1,5-*a*]isoquinoline (**5b**), the linear benzologue of tetrazolopyridine, has been prepared. In contrast to the angular isomers (**1b** and **2**) the linear system exists in solution predominantly in the tautomeric azido-form (**5a**) and even in the crystalline state contains a certain amount of 3-azidoisoquinoline (**5a**). The tautomeric equilibrium in solution was studied by nmr spectroscopy.

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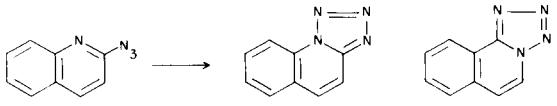
The angular benzologues of tetrazolopyridine: tetrazolo[1,5-*a*]quinoline (**1b**) was described earlier (1) and recently, tetrazolo[5,1-*a*]isoquinoline (**2**) has been reported (2). The third possible isomer, the linearly arranged tetrazolo[1,5-*b*]isoquinoline (**5b**) has, however, not yet been isolated.



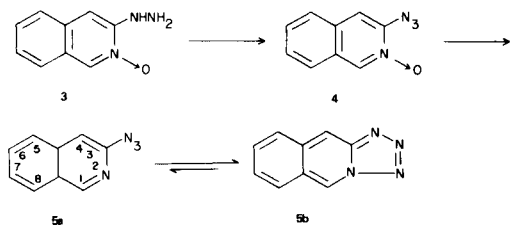
1a **1b** **2**

The former two compounds (**1b** and **2**) can be easily obtained by automatic electrocyclic ring closure of the corresponding azido substituted quinoline and isoquinoline derivatives (*e.g.*, **1a** → **1b**). The chemistry of the azido-tetrazole equilibrium has recently been reviewed by Tisler, *et al.*, (3). Only in some special cases is it possible to isolate both azido and tetrazole compounds in crystalline form (4).

Attempts at the preparation of 3-azidoisoquinoline (**5a**), the precursor of the desired tetrazolo[1,5-*b*]isoquinoline (**5b**), by a common procedure (*via* nucleophilic displacement of the 3-halo substituted isoquinoline) have failed probably due to the extraordinary stability of the halogen atom in position 3 of isoquinoline (5).

In order to obtain 3-azidoisoquinoline (**5a**), 3-chloroisoquinoline was first converted to its *N*-oxide derivative, by the procedure of Robinson *et al.*, (6). This compound resulted in 3-hydrazinoisoquinoline *N*-oxide (**3**) (7) with hydrazine hydrate.

The treatment of 3-hydrazinoisoquinoline *N*-oxide (**3**) with nitrous acid led to the rather unstable 3-azidoisoquinoline *N*-oxide (**4**) as brilliant crystals.



3 **4** **5a** **5b**

In order to remove the oxygen of the *N*-oxide group, the 3-azido *N*-oxide compound (**4**) was treated with phosphorus trichloride in chloroform. The reaction product (**5**) showed a strong azide band in the ir in chloroform solution; in the ir spectrum recorded in solid phase, however, only a very weak but distinct azide band could be found which did not disappear even after several recrystallizations.

Thus, the 3-azidoisoquinoline (**5a**) formed seems to be rather stable in solution but during crystallization an electrocyclization takes place, resulting in a solid containing predominantly the new linear tetrazolo[1,5-*b*]isoquinoline (**5b**) together with a small amount of unchanged 3-azidoisoquinoline (**5a**).

Comparison of the nmr spectra of **1b** and **2** with that of **5** shows a remarkable difference. Proton 3 of the isoquinoline part of the tetrazolo[5,1-*a*]isoquinoline (**2**) appears in DMSO at δ 8.9-9.0 ppm and in deuteriochloroform at δ 8.5-8.6 ppm, respectively, in both solvents as an *ortho* coupled doublet. Appearance of only one doublet points to the fact that even in solution only one species of the two possible tautomeric forms is present. Similar behaviour has been detected in the case of compound **1b**

In contrast to these experiences, proton 1 of the isoquinoline part of tetrazolo[1,5-*b*]isoquinoline (**5**) results in two singlets of different intensities depending on the solvents applied. In DMSO the values of the chemical shifts are δ 9.6 and 9.1 ppm and the ratio of intensities 1:4. In deuteriochloroform the shifts are δ 10.2 and 9.2 ppm and the ratio is 3:2; in both solvents the sum of the integrals of the singlets corresponds to one proton. As shown in the literature (8,9), the signal of the proton adjacent to the tetrazole ring is shifted to higher δ values. Thus, we may conclude that the new tetrazole compound (**5b**) is present in about 80% in DMSO and 40% in deuteriochloroform.

To the best of our knowledge, this is the first evidence of a linearly arranged, fused, three-membered tetrazole system. Interestingly, however, while the two angular condensed isomers (**1b** and **2**) exist only in the tetrazole form either in the solid phase or in solution, in our case (**5a** and **5b**) the equilibrium is less favourable to the closed tetrazole compound, and even the crystallized product contains some of the open-chain azido isomer. This observation may be due to the fact that the linearly fused system (**5b**) is less aromatic than the angular ones (**1b** and **2**).

EXPERIMENTAL

Infrared spectra were recorded on a Unicam Sp 200 instrument. Nmr spectra were obtained with a Varian XL-100 spectrometer. Melting points were determined on a Büchi apparatus and are uncorrected.

Tetrazolo[1,5-*a*]quinoline and tetrazolo[5,1-*a*]isoquinoline were prepared from 2-chloroquinoline and 1-chloroisoquinoline, respectively, by the method described by Kadaba (10).

3-Hydrazinoisoquinoline 2-Oxide (**3**).

3-Chloroisoquinoline 2-oxide (**6**) (3.0 g., 1.7 mmoles) was suspended in a mixture of methanol-hydrazine hydrate 1:1 (30 ml.) and refluxed for 10 minutes. After cooling, the precipitated pale yellow crystalline product was filtered and recrystallized from acetonitrile to give 2.0 g. (66%) of product; M.p. 208-210°. Reference 7 gives a different m.p. value of 148° which seems to be, however, a misprint.

Anal. Calcd. for $C_9H_9N_3O$: N, 23.98. Found: N, 23.82.

3-Azidoisoquinoline 2-Oxide (**4**).

3-Hydrazinoisoquinoline 2-oxide (**3**) (0.3 g., 1.7 mmoles) was dissolved in glacial acetic acid (3 ml.) and a solution of sodium nitrite (0.15 g.) in water (3 ml.) was added dropwise so that the mixture was kept below 5°. The dark brown reaction mixture was neutralized with 10 ml. of sodium hydroxide solution (10%) and extracted with chloroform. After evaporation of the chloroform phase, the residue was treated with water. The resulting solid was recrystallized from ethyl acetate to give 0.18 g. (57%) of brilliant crystals, m.p. 113-115°; ir (potassium bromide): 2120 cm^{-1}, azide.

Anal. Calcd. for $C_9H_6N_4O$: N, 30.09. Found: N, 29.80.

Tetrazolo[1,5-*b*]isoquinoline (**5**).

3-Azidoisoquinoline 2-oxide (**4**) (0.4 g., 2.1 mmoles) was dissolved in 4 ml. of chloroform, and 4 ml. of phosphorus trichloride was added carefully. The resulting suspension was refluxed in a 70° oil bath for three hours. The almost homogeneous mixture was then evaporated *in vacuo*, and the residue treated with water. The crude product was recrystallized from 20% methanol-water to give 0.25 g. (53%), m.p. 122°; ir (potassium bromide): 2150 cm^{-1}, weak azide band; (chloroform): 2150 cm^{-1}, strong azide band.

Anal. Calcd. for $C_9H_6N_4$: N, 32.92. Found: N. 32.56. Mol. wt. (mass spectrum): Calcd.: 170. Found: 170.

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REFERENCES AND NOTES

(1) W. Marckwald and E. Meyer, *Chem. Ber.*, **33**, 1885 (1900).
(2) H. Reimlinger, *ibid.*, **103**, 1900 (1970).
(3) M. Tisler, *Synthesis*, 123 (1973).
(4) A. Messmer, Gy. Hajós, P. Benkó and L. Pallos, *J. Heterocyclic Chem.*, **10**, 575 (1973).
(5) W. J. Gensler, "Heterocyclic Compounds", Vol. 4, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, 1952, p. 409.
(6) M. M. Robinson and B. J. Robinson, *J. Am. Chem. Soc.*, **80**, 3443 (1958).
(7) M. Bellas and H. Suschitzky, *J. Chem. Soc.*, 4561 (1964).
(8) T. Sasaki, K. Kanematsu and M. Murata, *J. Org. Chem.*, **36**, 446 (1971).
(9) C. Temple and J. A. Montgomery, *ibid.*, **30**, 826 (1965).
(10) P. K. Kadaba, *Synthesis*, 71 (1973).