1,2,3-Triazolo[1,5-c]pyrimidine, a Novel Heterocycle in the Polyazaindolizine Series

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The synthesis and structural properties of the novel heterocycle 1,2,3-triazolo[1,5-c]pyrimidine are described. No evidence of a triazole-diazoalkylideneazine valence tautomerism process was observed at room temperature.

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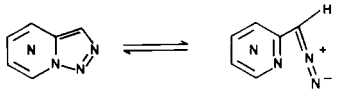
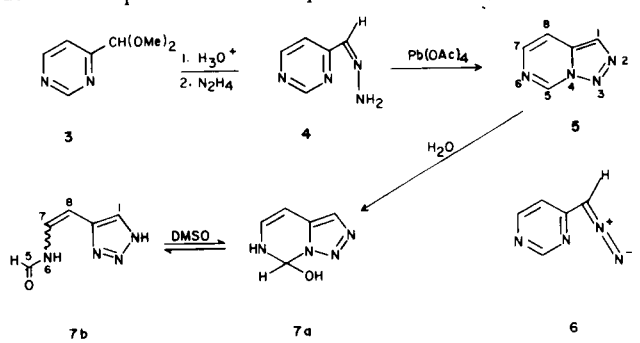
1,2,3-Triazoloazines with a bridgehead nitrogen (**1**) are scarcely known in the literature (1). In particular the possible existence of a diazo tautomer **2** has been investigated only in the 1,2,3-triazolo[1,5-*a*]pyrimidine series (2). As part of a study to evaluate the influence of the nature of the azine on the equilibrium **1** ⇌ **2** we wish to report the synthesis and some properties of 1,2,3-triazolo[1,5-c]pyrimidine, a previously unknown polyazaindolizine heterocycle.



1 **2**

As the precursor of the desired heterocycle we used 4-pyrimidinecarboxaldehyde dimethylacetal (**3**) prepared from 1,1-dimethoxy-4-dimethylaminobut-3-enone and formamidine acetate according to Bredereck, *et al.*, (3). Contrary to the diethylacetal (3), the hydrolysis of compound **3** with aqueous sulfuric acid proved difficult and attempts to isolate the aldehyde resulted in its decomposition. Nevertheless, the hydrazone **4** has been prepared in acceptable yields without isolating the aldehyde.

By treatment with lead tetracetate in benzene at room temperature, the hydrazone **4** reacted to completion almost immediately giving a new compound fluorescent in the uv light. The product, namely **5**, was identified by elemental and spectral analysis. The uv absorptions and nmr data obtained in various solvents are consistent with a polyazaindolizine structure (1). In particular, the observed long range coupling constant between H-1 and H-5 (4) also exists in an homologous series, *e.g.* imidazo[1,5-*a*]pyrimidines (5) and pyrrolo[1,2-*a*]pyrazines (6). The mass spectrum of compound **5** is easily interpreted assuming the initial loss of a nitrogen molecule from the molecular ion and the subsequent loss of HCN from the resulting fragment. Ir spectra in chloroform solution or in the solid state show no absorption between 2000 and 2200 cm^{-1} thus ruling out the presence of tautomer **6** under these conditions.



3 **4** **5** **7b** **7a** **6**

Trifluoroacetic acid is known to favor the open-chain tautomer in the azidoazine-tetrazoloazine isomerization which is similar to the equilibrium **1** ⇌ **2** (7). However, upon addition of traces of trifluoroacetic acid to a solution of compound **5** in dimethylsulfoxide or in chloroform a covalent hydrate **7** was formed instead of the expected diazo tautomer **6**. The covalent hydrate structure was assigned on the basis of the elemental analysis, the tendency of azolo[c]pyrimidines to be covalently hydrated at position 5 (8,9), and the profound differences observed between the ir, uv and pmr spectra of compounds **6** and **7**. Thus, most of the pmr signals of the hydrate **7** are shifted to higher fields indicating a loss of aromaticity. The complexity of the pmr spectra also suggests the presence of several tautomers among which open-chain structures **7b** seem to dominate (10) contrary to one report concerning the closely related tetrazolo[1,5-c]-pyrimidine series (8).

EXPERIMENTAL

Melting points are uncorrected. The pmr spectra were taken on a Perkin Elmer R-12 B instrument (60 MHz) and were compared with TMS as an internal standard. Infrared spectra were determined on a Perkin Elmer 577 spectrometer and uv spectra on a Hitachi-Perkin Elmer 124 instrument. The purity of all compounds prepared has been systematically checked by tlc.

1,1-Dimethoxy-4-dimethylaminobut-3-enone (3).

To a solution of 14.7 g. (0.1 mole) of dimethylformamide diethylacetal in 100 ml. of 2-butanol was added 14.6 g. (0.12 mole) of methylglyoxal dimethylacetal. The mixture was heated to reflux for 20 hours. Removal of the solvent left a dark red oil which was distilled, b.p.$_{0.05}$ = 110-115° (yield, 60%); ir (neat liquid): 1645, 1565 cm^{-1}; pmr (carbon tetrachloride): δ 2.98 (broad s, NMe_2), 3.30 (s, OMe), 4.23 (s, O-CH-O), 5.18 (d, $J_{3,4}$ = 12.5 Hz, H-4), 7.47 (d, H-3).

4-Pyrimidinecarboxaldehyde Dimethylacetal (**3**) (3).

A mixture of 6.24 g. (0.06 mole) of formamidine acetate and 6.92 g. of 1,1-dimethoxy-4-dimethylaminobut-3-enone was heated to 110-120° for 4 hours. After cooling, 20 ml. of water was

added with stirring. The product was extracted with chloroform and purified by distillation, b.p.$_{0.2}$ = 45-50° (yield, 75%); pmr (carbon tetrachloride): δ 3.18 (s, OMe), 5.17 (s, O-CH-O), 7.50 (dd, $J_{2,5}$ = 1.5 Hz, $J_{5,6}$ = 5 Hz, H-5), 8.77 (d, H-6), 9.13 (d, H-2).

4-Pyrimidinecarboxaldehyde Hydrazone (**4**).

A solution of 3.08 g. of acetal **3** and 0.3 ml. of concentrated sulfuric acid in 30 ml. of water was heated to 60-70° for 2 hours during which the solution progressively darkened. After cooling, a solution of 10 ml. of hydrazine hydrate in 20 ml. of water was slowly added and the mixture was allowed to stand at room temperature for 24 hours. The hydrazone was extracted with 150 ml. of chloroform. After removal of the solvent, 1.35 g. of a pale yellow solid was obtained, m.p. 117-118° (*n*-heptane, benzene); pmr (DMSO-d_6): δ 7.57 (s, H-1'), 7.61 (dd, $J_{5,6}$ = 5.6 Hz, $J_{2,5}$ = 1.1 Hz, H-5), 7.94 (s, NH_2), 8.55 (d, H-6), 8.96 (d, H-2); ms: m/e (relative abundance), 123 (M + 1, 52), 122 (M^+, 80), 96 (60), 95 (37), 80 (15), 67 (45), 55 (82), 54 (35), 43 (67), 39 (100), 38 (40).

Anal. Calcd. for $C_5H_6N_4$: C, 49.15; H, 4.95; N, 45.87. Found: C, 49.00; H, 4.89; N, 45.11.

1,2,3-Triazolo[1,5-*c*]pyrimidine (**5**).

The hydrazone **3** (0.122 g., 0.001 mole) was gradually added to a solution of 0.50 g. of lead tetracetate in 25 ml. of anhydrous benzene under vigorous stirring at room temperature. After only 5 minutes, tlc showed that the formation of compound **4** was complete (blue fluorescent spot at 254 nm). After filtration, the solution was evaporated without heating. The crude solid obtained was rapidly chromatographed on neutral alumina (eluent: benzene). It was further purified through sublimation and recrystallization, m.p. 130-131° (benzene, petroleum ether) (yield, 60%); ir (chloroform): 1620 cm^{-1}, no absorption between 2000 and 2200 cm^{-1}; ir (potassium bromide): 1610 cm^{-1}, no absorption between 2000 and 2200 cm^{-1}; uv (*n*-heptane): 266, 273 (i), 294, 301, 309, 323, 340 nm (log ε = 3.75, 3.66, 3.20, 3.21, 3.21, 3.08, 2.65); uv (chloroform): 267, 276 (i), 296 nm (log ε = 3.87, 3.79, 3.38); pmr (deuteriochloroform): δ 7.72 (dd, $J_{7,8}$ = 6.7 Hz, $J_{5,8}$ = 1.6 Hz, H-8), 8.05 (d, H-7), 8.18 (d, $J_{1,5}$ = 0.6 Hz, H-1), 9.68 (dd, H-5); pmr (DMSO-d_6): δ 7.97 (d, $J_{7,8}$ = 7.5 Hz, H-8), 8.00 (d, H-7), 8.39 (H-1), 10.00 (H-5); ms: m/e (relative abundance), 121 (M + 1, 5), 120 (M^+, 47), 92 (24), 66 (12), 65 (100), 64 (27), 38 (97).

Anal. Calcd. for $C_5H_4N_4$: C, 50.00; H, 3.36; N, 46.64. Found: C, 49.71; H, 3.48; N, 46.64.

Covalent Hydrate of Compound **4** (**7**).

1,2,3-Triazolo[1,5-*c*]pyrimidine was covalently hydrated in benzene solution during chromatography on neutral alumina. The same hydrate was obtained by adding a trace of trifluoroacetic acid to a wet solution of **4** in dimethylsulfoxide or chloroform. Finally, compound **4** in the solid state was slowly transformed into the hydrate on standing several weeks at room temperature. The hydrate was a pale yellow solid insoluble in chloroform and not fluorescent in uv light, m.p. 160-161°; ir (potassium bromide): 3300, 3170, 1642, 1525 cm^{-1}; uv (wet methanol): 249 (i), 271 nm (log ε = 4.04, 4.17); pmr (DMSO-d_6): δ (at 30°) 5.75 (d, $J_{7,8}$ = 9.2 Hz, H-8), 7.03 (dd, $J_{6,7}$ = 11.0 Hz, H-7), 7.96 (broad s, H-5), 8.38 (s, H-1), 10.30 (very broad doublet removed if heavy water is added, NH-6), 15.05 (broad s, NH of triazole nucleus), in addition low intensity signals are found at 5.65 (d), 7.93 (s), 8.63 (s); (at 120°) only 5 intense signals are found: 5.70 (d, $J_{7,8}$ = 9.5 Hz, H-8), 6.95 (broad dd, H-7), 7.83 (sharp s, H-5), 8.35 (s, H-1), 10.10 (broad, NH-6).

Anal. Calcd. for $C_5H_6N_4O$: C, 43.48; H, 4.38; N, 40.56. Found: C, 43.36; H, 4.39; N, 40.76.

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(10) The nmr signals are too numerous and some of them too broad or too weak to attempt complete unambiguous assignments. Although we previously favored **7a** as the dominant tautomer we revised our conclusions once variable temperature pmr spectra at 100 MHz were available. Above 90° an averaged spectrum is obtained which is considerably simpler than at 30°. This suggests the existence of an equilibrium between several conformationally mobile tautomers. Therefore, we tentatively propose the open-chain tautomer **7b** as the dominant tautomer. This conclusion is reinforced by the amide absorptions found in the ir spectra.