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THE SYNTHESIS OF s-TRIAZOLO/1,5-b/PYRIDAZINE 3-OXIDE DERIVATIVES

J. Bratož-Stres, S. Polanc, B. Stanovnik, and M. Tišler

Department of Chemistry, University of Ljubljana
61000 Ljubljana, Yugoslavia

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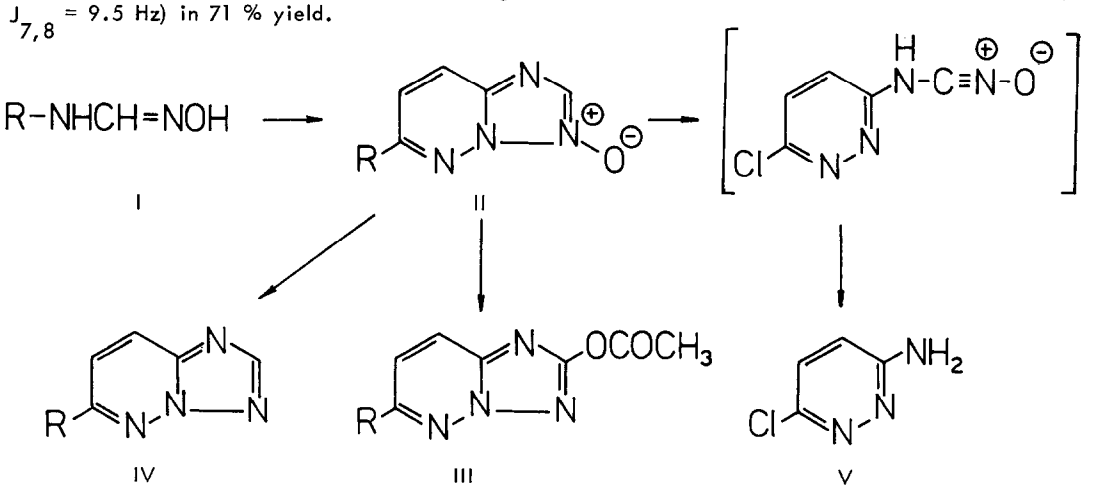
In a recent paper the synthesis of 2-substituted s-triazolo/1,5-a/pyridine 3-oxide and s-triazolo/1,5-a/pyrimidine 3-oxide has been described [1]. To our knowledge, there is no general synthesis for the preparation of 2-unsubstituted s-triazoloazine 3-oxides with bridgehead nitrogen.

We wish to report the synthesis of 6-substituted s-triazolo/1,5-b/pyridazine 3-oxide derivatives from 6-chloro-3-hydroxyiminomethyleneaminopyridazine. It represents a potential method for the preparation of other s-triazoloazine 3-oxides from heterocyclic hydroxyiminomethyleneamino derivatives. These were used as the starting material in a general synthesis of s-triazoloazines with the triazole ring fused to the azine ring through the N_2-C_3 bond [2].

The oxidation of I (R=6-chloropyridazinyl-3-) with bromine in acetic acid in the presence of sodium acetate results in the formation of 6-chloro-s-triazolo/1,5-b/pyridazine 3-oxide (II, R = Cl, m.p. 218°, M^+ = 170, NMR spectrum in $CDCl_3$/TMS: τ = 1.57 (s, H_2), 1.97 (d, H_8), 2.56 (d, H_7), $J_{7,8}$ = 9.5 Hz) in 71 % yield.



The compound II is thermally stable. No deoxygenation was observed in boiling toluen or xylene after 2 hours. In refluxing acetic anhydride it was transformed into 2-acetoxy-6-chloro-s-triazolo /1,5-b/pyridazine (III, R = Cl, m.p. 230°, M^+ = 212, decomp.) in 4 % yield. Nucleophilic substitution of chlorine at position 6 in 6-chloro-s-triazolo/1,5-b/pyridazine 3-oxide is taking place with hydrazine hydrate (98 %) in boiling ethanol giving 6-hydrazino-s-triazolo/1,5-b/pyridazine 3-oxide (II, R = $NHNH_2$ m.p. 230-232°, M^+ = 166, NMR spectrum in d_6-DMSO/TMS: τ = 1.78 (s, H_2), 2.25 (d, H_8), 3.00 (d, H_7), $J_{7,8}$ = 9.5 Hz) in 36 % yield. It was transformed with nitrous acid into 6-azido-s-triazolo /1,5-b/pyridazine 3-oxide (II, R = N_3, m.p. 130-134°, M^+ = 177, NMR spectrum in $CDCl_3$/TMS: τ = 1.45 (s, $H_2$7, 2.0 (d, H_8), 3.02 (d, H_7), $J_{7,8}$ = 9.5 Hz) in 83 % yield, identical with the compound obtained from 6-chloro-s-triazolo/1,5-b/pyridazine 3-oxide and sodium azide in refluxing ethanol in 3,5 % yield.

Hydrogenation of II (R = N_3) in the presence of Pd/C (5 %) in methanol afforded 6-amino-s-triazolo/1,5-b/pyridazine 3-oxide (II, R = NH_2, m.p. 259-263°) in 65 % yield, while in the presence of hydrochloric acid 6-amino-s-triazolo/1,5-b/pyridazines was isolated, identical with an authentic sample prepared according to the lit. [2]. Deoxygenation of II (R = Cl or N_3) was achieved also with PCl_3 in chloroform giving s-triazolo/1,5-b/pyridazine and 6-azido-s-triazolo/1,5-b/pyridazine, respectively, identical with the compounds reported in the lit. [2].

Decomposition of triazole part of the molecule was observed when 6-chloro-s-triazolo /1,5-b/pyridazine 3-oxide (II, R = Cl) was refluxed either in 2 N hydrochloric acid or in 2 N sodium hydroxide solution. 3-Amino-6-chloropyridazine (V) was isolated as the only product. Sodium ethoxide or sodium thiophenolate afforded 3-amino-6-chloropyridazine (V) together with a number of other unidentified products.

Satisfactory analytical data were obtained for all compounds.

References

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