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A NOVEL SYNTHESIS OF s-TRIAZOLOAZINES FUSED AT THE N_2-C_3 BOND OF THE TRIAZOLE RING

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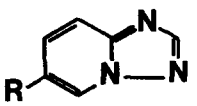
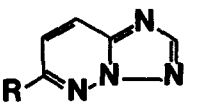
So far, there is no simple and general synthetic method for the preparation of 2-unsubstituted s-triazoloazines with bridgehead nitrogen and where the triazole ring is fused to the azine ring through the N_2-C_3 bond. Several synthetic approaches were employed for building such heterocyclic systems. Thus, the corresponding s-triazolo(1,5-a)pyridines (I),[1] s-triazolo-(2,3-b)pyridazines (II),[2] and s-triazolo(1,5-a)pyrazines (III)[3] were prepared by oxidative cyclization of the corresponding 2-azinylamidines.



I



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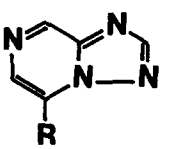
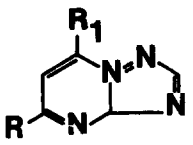
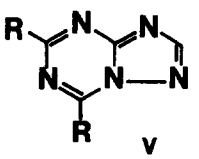


III

On the other hand, the s-triazolo(2,3-a)pyrimidine system (IV) is formed when 3-amino-1,2,4-triazoles are condensed with 1,3-dicarbonyl compounds The reaction may lead also to the isomeric s-triazolo(4,3-a)pyrimidines. Moreover, isomerization of s-triazolo(4,3-a)pyrimidines into s-triazolo-(2,3-a)pyrimidines can occur in a thermal, acid or base catalyzed reaction.[4] s-Triazolo(2,3-a)triazines (V) were obtained in a similar manner, either from 3-amino-s-triazole [5] or 2-hydrazino-1,3,5-triazin-4-one derivatives. [6]



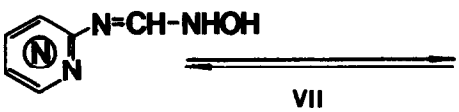
IV

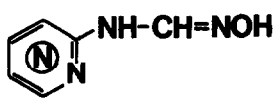


V

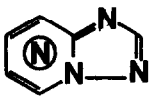
We here give an account of a versatile synthesis of these heterocyclic systems, starting from the corresponding aminoazines. With N,N-dimethylaminoformamide dimethylacetal these were transformed into N,N-dimethylaminomethylene derivatives (VI) and further transformation with hydroxylamine yielded VII. Cyclization to VIII could be achieved with polyphosphoric acid or, in

VI





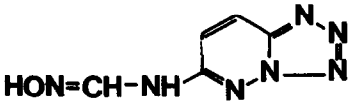
VII



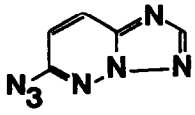
VIII

the case of II (R=Cl), by heating the corresponding oxime over its melting point (Table I).

In addition, the s-triazolo(2,3-b)pyridazine system could be synthesized from 6-aminotetrazolo(1,5-b)pyridazine by converting this compound successively into its N,N-dimethylaminomethylene derivative and further into IX, which upon cyclization underwent spontaneous opening of the tetrazole ring to give X. This represents another case of the azido-tetrazolo



IX



X

isomerization which we have observed previously with related systems.[7]

Table I

Compound[a]	M.p. (°C)	Nmr data (in $CDCl_3$): τ (multiplicity, proton), J
I, R=NO_2	204-208	1.62 (s, H_2), 0.50 (d, H_5), 1.82 (dd, H_7), 2.30 (dd, H_8); $J_{5,7}$ = 2.0, $J_{7,8}$ = 9.0 Hz
II, R=H	138-142	1.62 (s, H_2), 1.56 (dd, H_6), 2.58 (dd, H_7), 1.92 (dd, H_8); $J_{6,7}$ = 4.2, $J_{7,8}$ = 8.9, $J_{6,8}$ = 1.8 Hz
II, R=Cl	135-138	1.58 (s, H_2), 2.63 (dd, H_7), 1.93 (dd, H_8); $J_{7,8}$ = 9.0 Hz
II, R=N_3	158-162	1.75 (s, H_2), 3.10 (d, H_7), 2.08 (d, H_8); $J_{7,8}$ = 9.0 Hz
III, R=H	127	1.50 (s, H_2), 1.42 (dd, H_5), 1.81 (d, H_6), 0.63 (d, H_8); $J_{5,6}$ = 4.5, $J_{5,8}$ = 1.5 Hz
III, R=Cl	108-110	1.50 (s, H_2), 1.80 (s, H_6), 0.82 (s, H_8)
IV, R=R_1=H	140-141[b]	1.48 (s, H_2), 1.13 (dd, H_6), 2.83 (dd, H_7), 1.05 (dd, H_8); $J_{6,7}$ = 4.8, $J_{6,8}$ = 1.0, $J_{7,8}$ = 6.9 Hz
V, R= morpholino	218-222	2.20 (s, H_2), 5.75 and 6.25 (m, morpholino)

[a] For all compounds satisfactory analytical data were obtained.

[b] Lit.[8] gives m.p. 140-142°.

In the case of 2-amino-4-methylpyrimidine as starting compound, cyclization can involve either N_1 or N_3 atom of the pyrimidine ring. In fact, both isomers (IV, R = Me, R_1 = H, and R = H, R_1 = Me) were formed in ratio of 1:5.

Finally, it should be mentioned that when the described reaction sequence was applied to 2-aminopyridine, instead of the bicyclic derivative pyridylurea was isolated, indicating that a Beckmann rearrangement took place.

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REFERENCES

1. J. D. Bower and G. R. Ramage, J. Chem. Soc., 4506 (1957).
2. M. Zupan, B. Stanovnik, and M. Tišler, Tetrahedron Letters, 4179 (1972).
3. T. Okamoto, Y. Torigoe, M. Sato, and Y. Isogai, Chem. Pharm. Bull., 16, 1154 (1968).
4. W. L. Mosby: Heterocyclic Systems with Bridgehead Nitrogen Atoms, Part II p. 878, Interscience, 1961.
5. E. C. Taylor, R. W. Hendess, J. Amer. Chem. Soc., 87, 1980 (1965).
6. J. Kobe, B. Stanovnik, and M. Tišler, Tetrahedron, 26, 3357 (1970).
7. B. Stanovnik, M. Tišler, and B. Stefanov, J. Org. Chem., 36, 3812 (1971), and previous papers cited therein.
8. C. F. H. Allen, H. R. Beilfuss, D. M. Burness, G. A. Reynolds, J. F. Tinker, and J. A. Van Allan, J. Org. Chem., 24, 796 (1959).