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N-HETARYLTETRAZOLES - I.
TETRAZOLYLTETRAZOLO/1,5-a/PYRIMIDINES, INTERMEDIATES IN THE FORMATION OF s-TRIAZOLO/4,3-c/TETRAZOLO/1,5-a/PYRIMIDINES [1]

A. Könnecke and E. Lippmann
Sektion Chemie der Karl-Marx-Universität, DDR-701 Leipzig, Liebigstrasse 18

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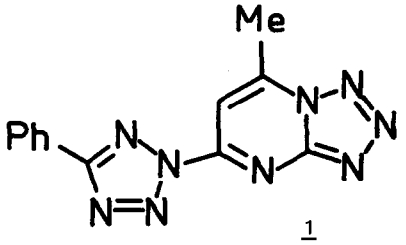
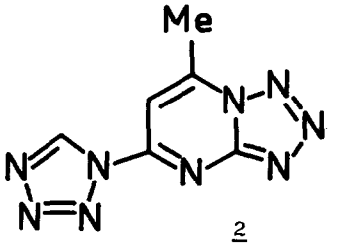
Key intermediates in the one-step synthesis of s-triazolo/4,3-x/azines from 2-chloroazines (cyclic imidoyl chlorides) and 5-substituted tetrazoles are thermal unstable and hitherto unknown 2-(5-R-tetrazol-2-yl)azines. Under the reaction conditions employed functionalized nitrilimines are formed by loss of nitrogen, and recyclization finally yields s-triazoloazines.[2]

This paper describes attempts in preparing these intermediates, a new class of heterocycles, as well as their thermal and acid-catalyzed conversions.

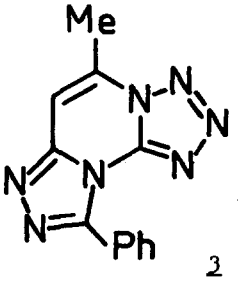
After standing for 1 to 2 days at room temperature in benzene solution, 5-chloro-7-methyltetrazolo/1,5-a/pyrimidine, selected as starting compound because of its very reactive chlorine atom, reacted with 5-phenyltetrazole and tetrazole in the presence of equimolar amounts NEt_3 to give the desired tetrazolyltetrazolo/1,5-a/pyrimidines 1 and 2, respectively, in 91% and 87% yield.



1



2



3

7-Methyl-5-(5-phenyltetrazol-2-yl)tetrazolo/1,5-a/pyrimidine (1) decomposes before melting (above 155°) and finally melts at 242-244° dec. identical with 9-methyl-5-phenyl-s-triazolo/4,3-c/tetrazolo/1,5-a/pyrimidine (3) obtained directly from the chlorotetrazolopyrimidine and 5-phenyltetrazole in boiling chlorobenzene/NEt_3 in 85% yield. Thermolysis of 1 in boiling chlorobenzene or toluene gave 3 in almost quantitative yield. Added dipolarophiles, e.g. 25-fold excess diethyl acetylenedicarboxylate, did not compete with the intramolecular nitrilimine-cyclization and 3 was formed exclusively.

Unexpected, treatment of 1 with TFA at room temperature caused nitrogen evolution. After about 10 min. the reaction was complete and addition of water precipitated 3 (90% yield). This acid-catalyzed conversion represents a new synthetic method and the course of the reaction may be explained as follows: 1 becomes protonated at the tetrazolopyrimidine ring (tetrazoles are of lower basicity[3]) affording an equilibrium mixture of tautomeric 1-cation and 2-azido-4-methyl-6-(5-phenyltetrazol-2-yl)pyrimidinium cation. Due to protonation the electron withdrawal of the pyrimidine part of the molecule strongly enhances and this effects nitrogen extrusion even at room temperature as it is known from 2,5-diaryltetrazoles, that the thermolysis temperatures are lowered by electron accepting substituents at N2 of the tetrazole ring.[4]

Consequently, 1 is a real intermediate in the formation of 3 and therefore has the structure of a 2,5-disubstituted tetrazole.

In the formation of 2 hetarylation occured at N1 of tetrazole. Structure assignment of the resulting 7-methyl-5-(tetrazol-1-yl)tetrazolo/1,5-a/pyrimidine (2), mp. 164-166° dec., is based on its p.m.r. spectrum. In DMSO-d_6 H5' resonates at δ 10.64 ppm clearly indicating 1-substitution.[5] 2 was found to be stable in TFA solution even at elevated temperatures. Hence, 2 is no precursor of compounds of type 3. As shown previously, thermolysis of acylated[6] or trimethylsilylated[7,8] parent tetrazole entirely differs from 5-phenyltetrazole from structural reasons since tetrazole always prefers 1-substitution.[9]

Similar experiments with other chlorotetrazoloazines are in progress and details, along with data on azido-tetrazolo equilibria, will be given in the full paper.

References

1. Tetrazoles XXII; part XXI A. Könnecke and E. Lippmann, Z. Chem. in press.
2. R. Huisgen, H.J. Sturm, and M. Seidel, Chem. Ber. 94, 1555 (1961).
3. A. Könnecke, E. Lippmann, and E. Kleinpeter, Tetrahedron in press.
4. a) S.-Y. Hong and J.E. Baldwin, Tetrahedron 24, 3787 (1968);
   b) T.L. Gilchrist, G.E. Gymer, and C.W. Rees, J.C.S.Perkin I, 1747 (1975);
   c) Review: E. Lippmann and A. Könnecke, Z. Chem. 16, 90 (1976).
5. A. Könnecke, S. Behrendt, and E. Lippmann, J. prakt. Chem. in press.
6. A. Könnecke, E. Lippmann, and E. Kleinpeter, Tetrahedron Lett. 533 (1976).
7. L. Birkhofer, A. Ritter, and P. Richter, Chem. Ber. 96, 2750 (1963).
8. Structures concluded from thermolysis products[7] are consistent with n.m.r. results (to be published).
9. Benzoyltetrazole and arylsulfonyltetrazoles have been reported to be only 1-substituted derivatives: J. Stawinski, T. Hozumi, and S.A. Narang, Chem. Commun. 243 (1976); Can. J. Chem. 54, 670 (1976). See also M.S. Poonian, E.F. Nowoswiat, J.F. Blount, T.H. Williams, R.G. Pitcher, and M.J. Kramer, J. Med. Chem. 19, 286 (1976).