Tetrahedron Letters No.44, pp. 5369-5373, 1966. Pergamon Press Ltd.
Printed in Great Britain.

3-AMINO-s-TETRAZINES FROM THE THERMAL DECOMPOSITION OF 4-AMINO-3-AZIDO-s-TRIAZOLES

H. H. Takimoto and G. C. Denault
Aerospace Corporation, El Segundo, California 90245

(Received 19 August 1966)

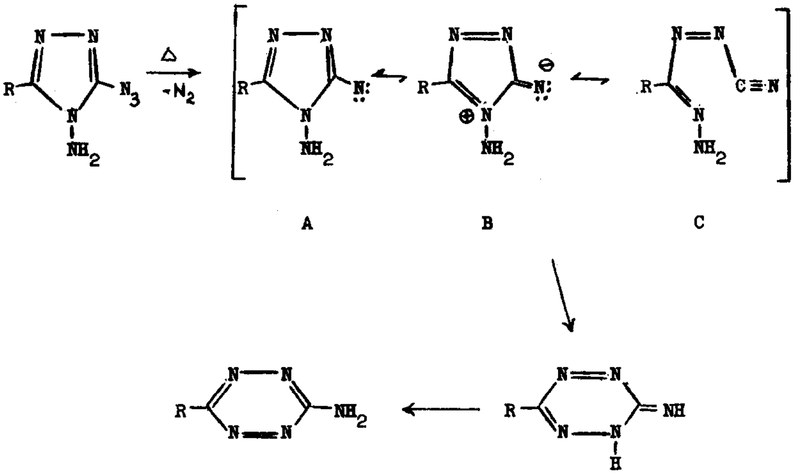
The chemistry of nitrene intermediates, which are generally obtained by a loss of nitrogen from an azide, has been the subject of considerable interest in recent years (1). The present report describes the thermolytic decompositions of 4-amino-3-azido-s-triazoles to yield 3-amino-s-tetrazines. This decomposition reaction is a convenient route for the synthesis of 3-amino-s-tetrazines whose usual methods of preparation have inherent limitations.

The treatment of 4-amino-3-hydrazino-5-methyl-s-triazole hydrochloride (2) with nitrous acid produced 4-amino-3-azido-5-methyl-s-triazole, (3), Ia, m.p. 84-86° dec.; ν_{max}^{KBr} 2150 cm^{-1}(N_3). Anal. Calcd. for $C_3H_5N_7$: C, 25.90; H, 3.63; N, 70.48. Found: C, 25.78; H, 3.90; N, 70.31. The structure of this compound was established by reduction with thiophenol to the known 3,4-diamino-5-methyl-s-triazole (4). Heating Ia in chlorobenzene at 110° smoothly liberated a mole of nitrogen to yield the bright red 3-amino-6-methyl-s-tetrazine, IIa, 95% yield, (m.p. 171-173°). Anal. Calcd, for $C_3H_5N_5$: C, 32.43; H, 4.54; N, 63.04; mol. wt., 111. Found: C, 32.51; H, 4.47; N, 63.10; mol. wt., 116 (5). Its infrared spectrum (KBr) exhibited strong absorptions at 3325, 3160, 1625, and 1515 cm^{-1}. Compound IIa showed a maximum ($\lambda_{max}^{p\text{-diox.}}$ 530 mμ, ϵ 735) in the visible which is characteristic of s-tetrazines (6). The proton n.m.r. spectrum (7) in acetone-d_6 showed a broad peak at 6.90 (amino) and a second peak at 2.73 p.p.m. (methyl) from tetramethylsilane in the ratio of 2:3 respectively. Catalytic hydrogenation resulted in a rapid disappearance of the bright red color to form the 3-amino-6-methyl-1,2-dihydro-*s*-tetrazine, IIIa, which was readily oxidized (8) back to IIa or was thermally rearranged to 3,4-diamino-5-methyl-*s*-triazole (4). IIa is readily acetylated and this product undergoes a 1,4-addition with styrene with a loss of nitrogen to yield IIIa and 3-acetamido-6-methyl-4(or 5)-phenylpyridazine, (9) m.p. 155-158°. *Anal*. Calcd. for $C_{13}H_{13}N_3O$: C, 68.71; H, 5.76; N, 18.49. Found: C, 68.66; H, 6.01; N, 18.33. With cyclohexene, the tetrazine yielded IIIa and a tetrahydrophthalazine derivative, m.p. 204-206°. *Anal*. Calcd. for $C_{11}H_{15}N_3O$: C, 64.36; H, 7.37; N, 20.48. Found: C, 64.12; H, 7.42; N, 20.70. The reaction of acetylated IIa with olefins initially forms the dihydropyridazines, which undergo a redox reaction with the unreacted tetrazine, thereby, producing a mixture of dihydrotetrazine and pyridazines.

Similarly, the thermal decomposition of 4-amino-3-azido-5-phenyl-*s*-triazole, Ib, yielded 3-amino-6-phenyl-s-tetrazine, IIb (96%) [m.p. 226-228°, $\lambda_{max}^{C_2H_5OH}$ 530 mμ (ε 506)]. [Lit. value (10): m.p. 226-227°, $\lambda_{max}^{C_2H_5OH}$ 530-535 mμ, ε 513]. *Anal*. Calcd.for $C_8H_7N_5$: C, 55.48; H, 4.08; N, 40.44. Found: C, 55.58; H, 4.26; N, 40.39. The dihydrotetrazine, IIIb, formed by the reduction of IIb with thiophenol, was rearranged by heat to the 3, 4-diamino-5-phenyl-*s*-triazole (4). IIb after acetylation reacted with styrene to produce IIIb and 3-acetamido-4(or 5), 6-diphenylphridazine, (9) m.p. 264-266°. *Anal*. Calcd. for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.22; N, 14.52. Found: C, 74.61; H, 5.44; N,14.67.

The facile thermal isomerization of dihydrotetrazines to triazoles has been well established (8). In fact the compounds reported to have been the dihydro derivatives in early reports have later been proven to be the triazoles. Furthermore, the reactions of s-tetrazines with olefins to yield dihydropyridazines have been described by Carboni and Lindsey (11). These workers reported that unsaturated compounds having electron-donating groups reacted more readily with 3,6-bis-(polyfluoralkyl)-*s*-tetrazines. In the case of II, decreasing the electron-density of the *s*-tetrazine (the diene portion) by acetylation of the 3-amino group facilitated the reaction. The above results are consistent with the assignment of the s-tetrazine structure for II.

The decomposition of 4-amino-3-azido-s-triazoles may proceed via two possible mechanisms. In one process, nitrogen is eliminated from the azido group to form the nitrene intermediate (12) for which several canonical forms may be written in analogy to the thermolysis product of 5-azido-1, 4-diaryl-*v*-triazoles described by Smith, Krbechek, and Resemann (1h). The amino group in structure C adds across the nitrile forming an imino compound which readily tautomerizes to yield II.



(a) $R = CH_3$ (b) $R = C_6H_5$

An alternative mechanism involves a concerted process in which the nitrogen elimination and the rearrangement occur simultaneously. The 4-amino group on the starting azidotriazole would then be expected to assist the removal of the nitrogen. However, the fact that 4-acetamido-3-azido-5-methyl-*s*-triazole also decomposed at 110° tends to favor the nitrene mechanism. In a concerted process this compound would require a higher thermolysis temperature due to the decreased nucleophilicity of the 4-amino group by acetylation. Further study is required before the mechanism of the decomposition of 4-amino-3-azido-*s*-triazoles is established.

In addition, 3-amino-*s*-tetrazine and 3-amino-6-ethyl-*s*-tetrazine have also been prepared from the corresponding azidotriazoles. Detailed work on the thermolyses and reactions of the tetrazines will be reported later.

Acknowledgment - The authors are indebted to Dr. L. Schieler for his helpful interest in this work. The authors are also grateful to Mr. S. Hotta for infrared and ultraviolet spectral measurements and assistance in the laboratory.

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