1,2,3-Triazole Analogues of 2-Aminobenzylamine

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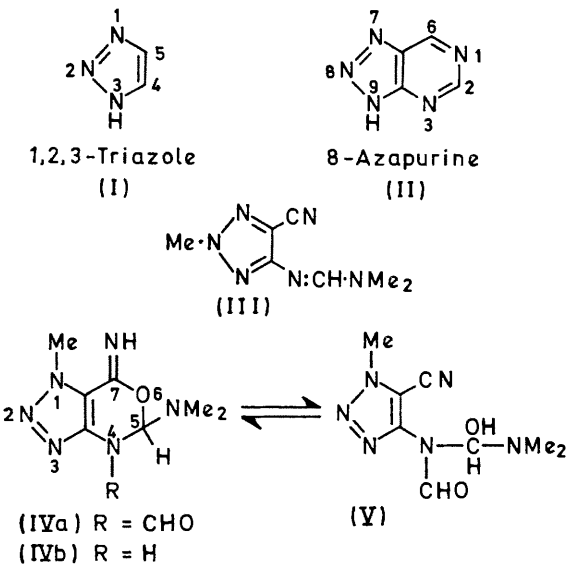
Summary 4-Amino-5-aminomethyl-1,2,3-triazoles, further substituted in the 1-, 2-, or 3-position by a methyl- or benzyl-group, were made by reducing the corresponding 4-amino-5-cyanotriazoles, obtained by the reaction of 4-amino-1,2,3-triazole-5-carboxamides with phosphoryl chloride in dimethylformamide [4-dimethylaminomethyleneamino-analogues, *e.g.* (III), were isolated as intermediates].

ALTHOUGH several reactions are known[1] for converting derivatives of 1,2,3-triazoles (I) into 8-azapurin-6-ones, a need exists for 1,2,3-triazoles capable of giving 8-azapurines (II) (variously substituted in the 2-position) with a free 6-position. Hence the preparation was attempted of 1-, 2-, and 3-methyl, and 3-benzyl, 4-amino-5-aminomethyl-1,2,3-triazoles. Attempted reduction of the corresponding 4-amino-1,2,3-triazole-5-carboxamides[1] by lithium aluminium hydride was only destructive, but the required compounds were obtained by hydrogenating the corresponding aminonitriles, obtained from the above aminoamides as follows.



Each amide, warmed in dimethylformamide with phosphoryl chloride, gave an excellent yield of the amidinonitrile, *e.g.* (III). The m.p.s. for the 1-methyl-, 2-methyl-, 3-methyl-, and 3-benzyl-analogues were, respectively, 99, 92, 131, and 118°. I.r. and n.m.r. spectra were compatible with the given structure. Short boiling with N-HCl converted these amidines, in excellent yields, into the corresponding amines, *e.g.* 4-amino-5-cyano-2-methyl-1,2,3-triazole, from the amidine (III). The m.p.s. (same order as above) were 187, 115, 229—230, and 182°, and all compounds had prominent C:N-stretching bands near 2200 cm^{-1}.

Reduction of these nitriles to the corresponding 5-aminomethyl-derivatives was accomplished in good yields by hydrogenation (Raney nickel, 75°, 4 atmos.) in the presence of ammonia. The products were best purified as the phosphates; the free bases, liberated by aqueous sodium hydroxide, were extracted into chloroform. A typical example, 4-amino-5-aminomethyl-3-benzyl-1,2,3-triazole had m.p. 105°, λ_{max} 244 nm (log ϵ 3·70 at pH 11 and 6); pK_a 8·85; τ [$(CD_3)_2SO$] 2·67 (5H, C_6H_5), 4·54 (2H, 4-NH_2, exchangeable D_2O), 4·62 (2H, $PhCH_2$), 6·30 (2H, CH_2 of CH_2NH_2), 8·13 (2H, NH_2 of CH_2NH_2, exchangeable). Both NH_2 signals were sharp, due to mutual hydrogen bonding. It was stable to boiling with 1N-NaOH, and to storage at 0°. It gave monoformyl- (m.p. 151°) and monoacetyl- (m.p. 199°) derivatives, of which the low pK_a values (*ca.* 1) showed that the aminomethyl group was acylated. When condensed with triethyl orthoacetate, the diamine gave 3-benzyl-1,6-dihydro-2-methyl-8-azapurine, m.p. 194°, reminiscent of the similar formation of 2-methyl-3,4-dihydropteridine from 2-amino-3-aminomethylpyrazine.[2]

An unusual by-product, obtained in the above preparation of the 1-methyl-amidine, incorporated the elements of the latter and formic acid. It was assigned the structure 1*H*,7H-5-dimethylamino-4-formyl-4,5-dihydro-7-imino-1-methyl-[1,2,3]-triazolo[4,5-*d*]-[1,3]-oxazine (IVa), apparently in ring–chain tautomerism with the triazole (V). The latter form was favoured in $CDCl_3$ and showed a doublet in the n.m.r. spectrum at 0·5 (1H) and an OH signal at −1·7; the latter was exchangeable with D_2O which caused the doublet (*J* 11) at 0·5 to collapse to a singlet; other signals were at 1·36 (1H, CHO), 5·71 (3H, Me), and 6·8 (NMe_2). The n.m.r. spectrum in Me_2SO was more characteristic of structure (IVa), and the solid state showed no C:N stretching band near 2200 cm^{-1}. When heated just above its melting point, this substance was quantitatively changed to 7-methyl-8-azapurin-6-one.[1] When set aside in cold 0·5N-NaOH, compound (IVa) was deformylated to (IVb), which gave the same azapurinone when melted.

In the preparation of the 2-methyl-amidine (III), a similar by-product was obtained which showed comparable ring–chain tautomerism, produced 8-methyl-8-azapurin-6-one[1] when melted, and was similarly deformylated to an analogue of compound (IVb). There are many examples in the literature[3] of oxazines being converted into pyrimidines under mild conditions; but the present compounds are unusual in losing dimethylformamide (or dimethylamine) as C-7 rotates during the rearrangement.

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[2] A. Albert and K. Ohta, *Chem. Comm.*, 1969, 1168; *J. Chem. Soc.* (*C*), in the press.
[3] D. J. Brown, "The Pyrimidines," Wiley–Interscience, New York, vols. 1 (1962) and 2 (1970).