Triazoles. Part V. Derivatives of 3-Amino-1 : 2 : 4-triazole.*

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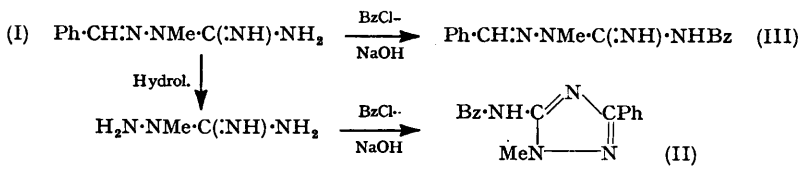
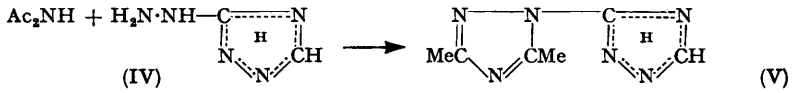
Three 3-amino-5-R-1 : 2 : 4-triazoles are prepared from aminoguanidine and the appropriate organic acid. 1-Benzylideneamino-1-methylguanidine hydriodide is benzoylated but not cyclised by benzoyl chloride; 1-amino-1-methylguanidine is both benzoylated and cyclised. 3-Amino-5-methyl-1 : 2 : 4-triazole is monoacetylated by diacetimide, but 3-hydrazino-1 : 2 : 4-triazole gives 3 : 5-dimethyl-1-(1 : 2 : 4-triazol-3-yl)-1 : 2 : 4-triazole. The ultra-violet absorption spectra of some triazoles are recorded.

Reaction of aminoguanidine with organic acids has been used to yield 3-amino-1 : 2 : 4-triazole (Manchot and Noll, *Annalen*, 1905, **343**, 1) and some of its 5-alkyl derivatives (Reilly and Madden, *J.*, 1929, 815). 3-Amino-5-phenyl-1 : 2 : 4-triazole is obtained from aminoguanidine and benzoic acid only in poor yields unless the reaction is carried out in concentrated hydrochloric or hydrobromic acid; salicylic acid fails to react under these conditions, but 3-amino-5-pyridyl-1 : 2 : 4-triazoles are obtained by using pyridine-2- and 3-carboxylic acid. In the last case an equimolar adduct of the reactants is formed under the conditions used by Reilly and Madden, but this cyclises in boiling hydrobromic acid.

In attempts to prepare 1-methyl-3-phenyl-1 : 2 : 4-triazole or its simple derivatives by an unambiguous method (cf. Part III, *J.*, 1954, 3319) 1-benzylideneamino-1-methylguanidine hydriodide (as I) (Finnegan, Henry, and Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 2981) was hydrolysed and then cyclised with benzoyl chloride to 5-benzamido-1-methyl-3-phenyl-1 : 2 : 4-triazole (II). Without previous hydrolysis Schotten–Baumann treatment with benzoyl chloride gives 1-benzylideneamino-3-benzoyl-1-methylguanidine (III).



3-Amino-5-methyl-1 : 2 : 4-triazole with diacetimide gives a monoacetyl derivative (cf. Birkhofer, *Ber.*, 1943, **73**, 769); it is not cyclised although Bülow and Haas (*Ber.*, 1909, **42**, 4638) observed pyrazole formation in the somewhat analogous reaction of diacetimide with 1 : 3-diketones. 3-Hydrazino-1 : 2 : 4-triazole hydrochloride (as IV) (Manchot and Noll, *loc. cit.*) and diacetimide afford 3 : 5-dimethyl-1-(1 : 2 : 4-triazol-3-yl)-1 : 2 : 4-triazole (V) in a low yield.



The aliphatic derivatives of 3-amino-1 : 2 : 4-triazole in ethanol show no absorption bands above 215 mμ. The triazole (V) has a band similar to that of acetyldimethyltriazole (Part IV, *loc. cit.*). The absorption spectra of 3-amino- and 3-hydroxy-5-phenyl-1 : 2 : 4-triazole are similar. The cation of the former has practically the same $\lambda_{max.}$ as the neutral compound but its extinction is increased (Fig. 1). The aminopyridyl-1 : 2 : 4-triazoles absorb at longer wave-lengths, but with lower extinction, than 3-amino-5-phenyl-1 : 2 : 4-triazole. Their cations show two bands. The effect of excess of hydrogen chloride on

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these bands is illustrated for 3-amino-5-3′-pyridyl-1 : 2 : 4-triazole in Fig. 2. The spectra of the neutral aminopyridyltriazoles may be compared with those of 2 : 2′- and 3 : 3′-dipyridyl (Spiers and Wibaut, *Rec. Trav. chim.*, 1937, **56**, 573). In both series the 2-pyridyl derivatives absorb at higher wave-lengths and with greater intensity.

FIG. 1. FIG. 2.

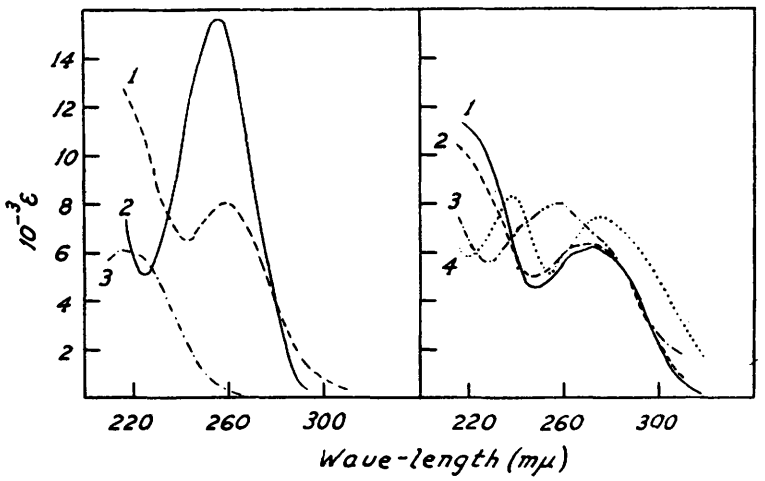

FIG. 1. 1, 3-*Hydroxy-5-phenyl*-1 : 2 : 4-*triazole*. 2, *Cation of* 1. 3, 3 : 5-*Dimethyl*-1-(1 : 2 : 4-*triazol*-3-*yl*)-1 : 2 : 4-*triazole*.

FIG. 2. 1, 3-*Amino-5-3′-pyridyl*-1 : 2 : 4-*triazole*. 2, *Cation of* 1, 85 *molar excess of* HCl. 3, *Cation of* 1, 420 *molar excess of* HCl. 4, *Cation of* 1, 12,300 *molar excess of* HCl.

EXPERIMENTAL

M. p.s are corrected. Absorption spectra were determined for 4—8 × 10^{-5}M-solutions in ethanol. A Unicam spectrophotometer and 10-mm. quartz cells were used.

3-Amino-1 : 2 : 4-triazole (Allen and Bell, *Org. Synth.*, 1946, **26**, 11), and its 5-methyl- (Morgan and Reilly, *J.*, 1916, **109**, 155), 5-ethyl-, 5-propyl-, and 5-*iso*propyl derivatives (Reilly and Madden, *loc. cit.*) were prepared by known methods.

Aminoguanidine sulphate (12·3 g.), heptanoic acid (13·0 g.), water (5 c.c.), and nitric acid (3 drops) were heated at 180° for 2 hr. The product was crushed and treated with a hot solution of sodium carbonate, and the mixture was evaporated to dryness. Extraction with ethyl acetate, evaporation, and recrystallisation from the same solvent gave 3-*amino-5-hexyl*-1 : 2 : 4-*triazole* (6·7 g., 40%), m. p. 131·5° (Found : C, 57·3; H, 9·6. $C_8H_{16}N_4$ requires C, 57·1; H, 9·6%).

Aminoguanidine sulphate (12·3 g.), benzoic acid (12·2 g.), and nitric acid (3 drops) were similarly treated and worked up. No 3-amino-5-phenyl-1 : 2 : 4-triazole was obtained. In a similar experiment the temperature was kept at 120° for 4 hr. Extraction with chloroform followed by recrystallisation from ethyl acetate afforded 3-amino-5-phenyl-1 : 2 : 4-triazole (2·4 g., 14%), m. p. 188°; the picrate had m. p. 218° (decomp.). Benzoic acid (24·6 g.), aminoguanidine sulphate, and 40% hydrobromic acid (40·5 g.) were boiled under reflux for 24 hr. The product was brought to pH 8 with 2N-sodium carbonate and evaporated to dryness. The residue was extracted with dry ethanol–ether (1 : 1; 2 × 100 c.c.). After evaporation of the solvent material containing some inorganic matter was obtained (16·2 g.). 5% of this material was converted into the picrate which was recrystallised from 80% ethanol and gave pure 3-amino-5-phenyl-1 : 2 : 4-triazole picrate (1·16 g., 30%), m. p. and mixed m. p. 219°. The residue of the crude material was treated with concentrated nitric acid. The nitrate was washed with benzene and recrystallised from water [yield 9·35 g., 21%; m. p. 207° (decomp.)]. The experiment was repeated except for the replacement of hydrobromic acid by constant-boiling hydrochloric acid. A 5% aliquot part of the crude product was converted into the picrate (1·24 g., 32%). The bulk was converted into the nitrate (7·97 g., 18%), m. p. 207° (decomp.). Attempts to form a triazole from aminoguanidine with ethyl benzoate or salicylic acid failed.

Aminoguanidine sulphate (34·4 g.) and pyridine-3-carboxylic acid (24·6 g.) in hydrobromic acid (50 g.) were boiled under reflux for 40 hr. The clear solution was neutralised with sodium carbonate and evaporated to dryness. Extraction of the residue with ethyl acetate (Soxhlet) recovered the basic product. Removal of the solvent and recrystallisation from methanol gave *3-amino-5-3′-pyridyl-1 : 2 : 4-triazole* (14·3 g., 44%), colourless needles, m. p. 233° (Found : C, 52·3; H, 4·3; N, 43·5. $C_7H_7N_5$ requires C, 52·2; H, 4·4; N, 43·4%), which had absorption max. at 273 (ε 6300) and 218 mμ (ε 11,300). The *picrate* was precipitated from aqueous solution and crystallised from water as yellow monoclinic needles, m. p. 269° (Found : C, 40·7; H, 2·9. $C_{13}H_{10}O_7N_8$ requires C, 40·0; H, 2·6%).

Aminoguanidine sulphate (17·2 g.) and pyridine-3-carboxylic acid (12·3 g.) in water (100 c.c.) were boiled under reflux for 24 hr. Neutralisation with sodium carbonate and extraction of the dry residue with chloroform gave colourless crystals (9·0 g.), m. p. 155—158°, which recrystallised from propan-2-ol as prisms, m. p. 165°. The substance appears to be an equimolar *adduct* of the starting materials (Found : C, 43·0; H, 6·0; N, 35·1. $C_7H_{11}O_2N_5$ requires C, 42·6; H, 5·6; N, 35·5%). The substance (1 g.) was boiled with hydrobromic acid (5 g.) for 24 hr. Addition of picric acid to the neutralised aqueous solution of the product gave the picrate of 3-amino-5-3′-pyridyl-1 : 2 : 4-triazole (1·05 g., 53%), m. p. and mixed m. p. 268°.

Aminoguanidine sulphate (17·2 g.) and pyridine-2-carboxylic acid hydrochloride (15·8 g.) in hydrobromic acid (25 g.) were treated as in the preceding experiment, giving *3-amino-5-2′-pyridyl-1 : 2 : 4-triazole* (6·8 g., 42%), colourless prismatic needles, m. p. 217° (Found : C, 52·4; H, 4·4%), which had absorption max. at 283 mμ (ε 8100) in EtOH, or 278 (ε 12,300) and 254·5 mμ (ε 9900) in a 4000-molar excess of HCl. The *picrate* crystallised from ethanol as yellow needles, m. p. 229° (Found : C, 39·4; H, 2·9%).

1-Benzylideneamino-1-methylguanidine hydriodide (30·4 g.) was distilled with steam in the presence of concentrated sulphuric acid (50 c.c.). Iodine, benzaldehyde, and some benzoic acid distilled with about 1500 c.c. of water. The residue was boiled under reflux overnight and distilled with steam again. After the collection of 7000 c.c., benzaldehyde could no longer be detected in the distillate. Half of the residue was made strongly alkaline with 10% aqueous sodium hydroxide, at <30°. Benzoyl chloride (14 g.) was added and the mixture shaken for 1 hr. The product was extracted with chloroform (3 × 75 c.c.), and the solvent removed, leaving 4·6 g., m. p. 125—128°, mixed m. p. with benzamide below 116°. Recrystallisation from benzene gave *5-benzamido-1-methyl-3-phenyl-1 : 2 : 4-triazole* (4 g., 17%), m. p. 134° (Found : C, 69·5; H, 5·3. $C_{16}H_{14}ON_4$ requires C, 69·0; H, 5·1%).

1-Benzylideneamino-1-methylguanidine hydriodide (0·35 g.) was shaken with 20% aqueous sodium hydroxide (5 c.c.) and benzoyl chloride (1·5 c.c.) in acetone (5 c.c.) for 10 min. The product crystallised in colourless needles, which had m. p. 187° after being washed with a little water. Recrystallisation from benzene with the addition of light petroleum (b. p. 40—60°) gave *3-benzoyl-1-benzylideneamino-1-methylguanidine* (0·23 g., 80%), m. p. 187° (Found : C, 68·8; H, 5·7; N, 20·4. $C_{16}H_{16}ON_4$ requires C, 68·5; H, 5·8; N, 20·0%).

3-Amino-5-methyl-1 : 2 : 4-triazole (0·2 g.) and diacetimide (0·2 g.) were heated at 150° for 5 min. The mixture solidified and was rubbed on a porous tile with benzene and light petroleum (b. p. 60—80°), leaving the monoacetyl derivative of the aminotriazole, m. p. 282° (Birkhofer, *loc. cit.*, found 284°).

Diacetimide (6·1 g.) and 3-hydrazino-1 : 2 : 4-triazole hydrochloride (2·7 g.) were heated in acetic acid (1·0 g.) with anhydrous sodium acetate (1·4 g.) at 110—120° for 14 hr. The product was diluted with water (70 c.c.) and extracted continuously with ether for 4 hr. The ether extract was dried and evaporated, leaving a residue which was purified by sublimation at 160°/1 mm. *3 : 5-Dimethyl-1-(1 : 2 : 4-triazol-3-yl)-1 : 2 : 4-triazole* (0·3 g., 9%) was obtained as colourless prisms, m. p. 191° (Found : C, 44·2; H, 5·0; N, 51·3. $C_6H_8N_6$ requires C, 43·9; H, 4·9; N, 51·2%). The same reactants in aqueous acetic acid gave the same triazole in 4% yield.

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