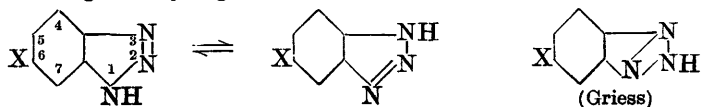


CCCLIV.—*Triazole Compounds. Part III. The Alkylation of Nitro-1:2:3-benztriazoles.*

By OSCAR L. BRADY and CEDRIC V. REYNOLDS.

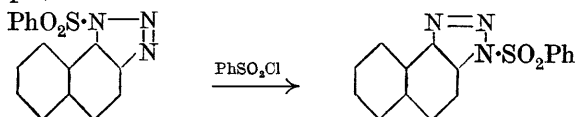
THE alkylation of amidines has been studied in detail by Pyman and his co-workers (J., 1923, **123**, 3359; 1924, **125**, 1431; 1925, **127**, 573, etc.). An investigation of the methylation of some nitrohydroxybenztriazoles led to results which compelled us to study the alkylation of the nitrobenztriazoles themselves: these we found to behave similarly to the glyoxalines and the indazoles studied by Pyman and by Auwers and Duesberg (*Ber.*, 1920, **53**, 1179) respectively.

The benztriazoles containing a substituent in the benzene ring are now generally regarded as tautomeric substances,



the formula of Griess (*Ber.*, 1882, **15**, 1878) failing to account for the existence, in some cases, of two isomeric derivatives (Zincke and Helmert, *J. pr. Chem.*, 1896, **53**, 91).

Morgan and his co-workers (J., 1910, **97**, 1702; 1913, **103**, 1391; 1914, **105**, 117) showed that, under favourable conditions, substituted benzotriazoles on acylation give a mixture of two isomerides and in certain cases one of these may be converted into the other by treatment with excess of a reagent containing a reactive group, preferably the same as that already present in the triazole ring; for example,



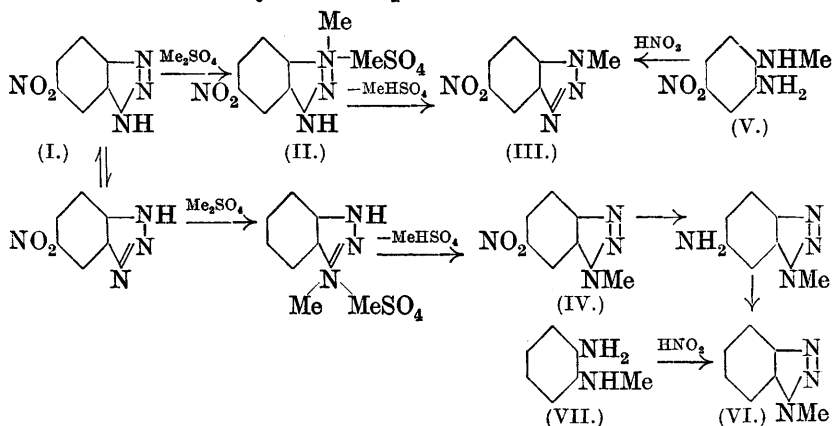
No case was known of two isomerides being produced by the direct alkylation of a substituted benzotriazole, but Zincke and Helmert (*loc. cit.*) obtained 1- and 3-phenyl-6-ethoxy-1:2:3-benzotriazoles by indirect means and we have prepared, similarly, 1:6- and 3:6-dimethyl-1:2:3-benzotriazoles (J., 1928, 193).

Zincke and Helmert, by heating 6-nitro-1:2:3-benzotriazole (I) with methyl iodide, obtained a methiodide which gave only 6-nitro-3-methyl-1:2:3-benzotriazole (III) on being heated. We have confirmed this result and have found that the action of methyl sulphate on the product gives 6-nitro-1:3-dimethylbenzotriazolinium methyl sulphate (XIV), which, when heated as such or, better, after conversion into the *chloride* (XV), gives only 6-nitro-3-methyl-1:2:3-benzotriazole (III).

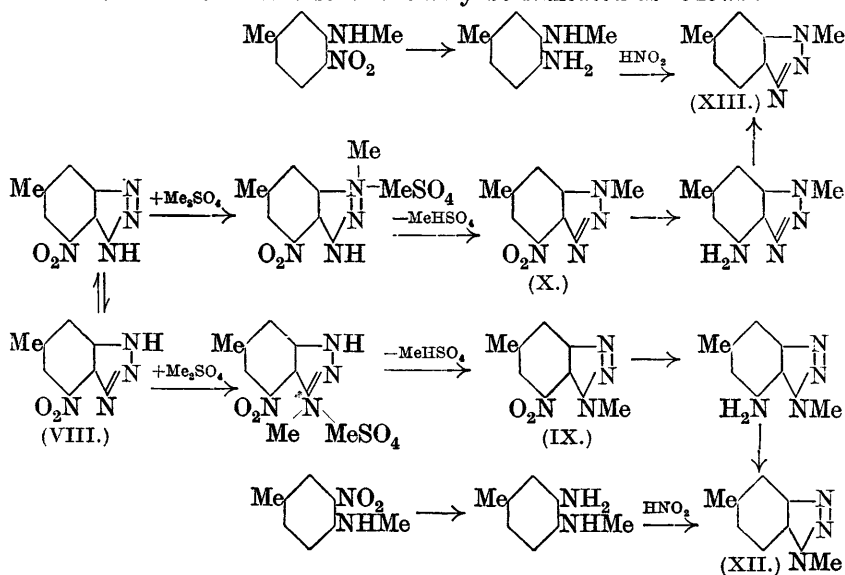
When, however, alkylation is carried out with methyl sulphate in aqueous sodium hydroxide, a mixture of 6-nitro-1-methyl-(IV) and a slightly smaller quantity of 6-nitro-3-methyl-benzotriazole (III) results. The position of the methyl group in 6-nitro-3-methyl-1:2:3-benzotriazole is fixed by its synthesis from 4-nitro-2-amino-methylaniline (V), and it is shown that the methyl group in 6-nitro-1-methyl-1:2:3-benzotriazole cannot be in the 2-position by its conversion into 1-methyl-1:2:3-benzotriazole (VI), which can be synthesised from methyl-*o*-phenylenediamine (VII).

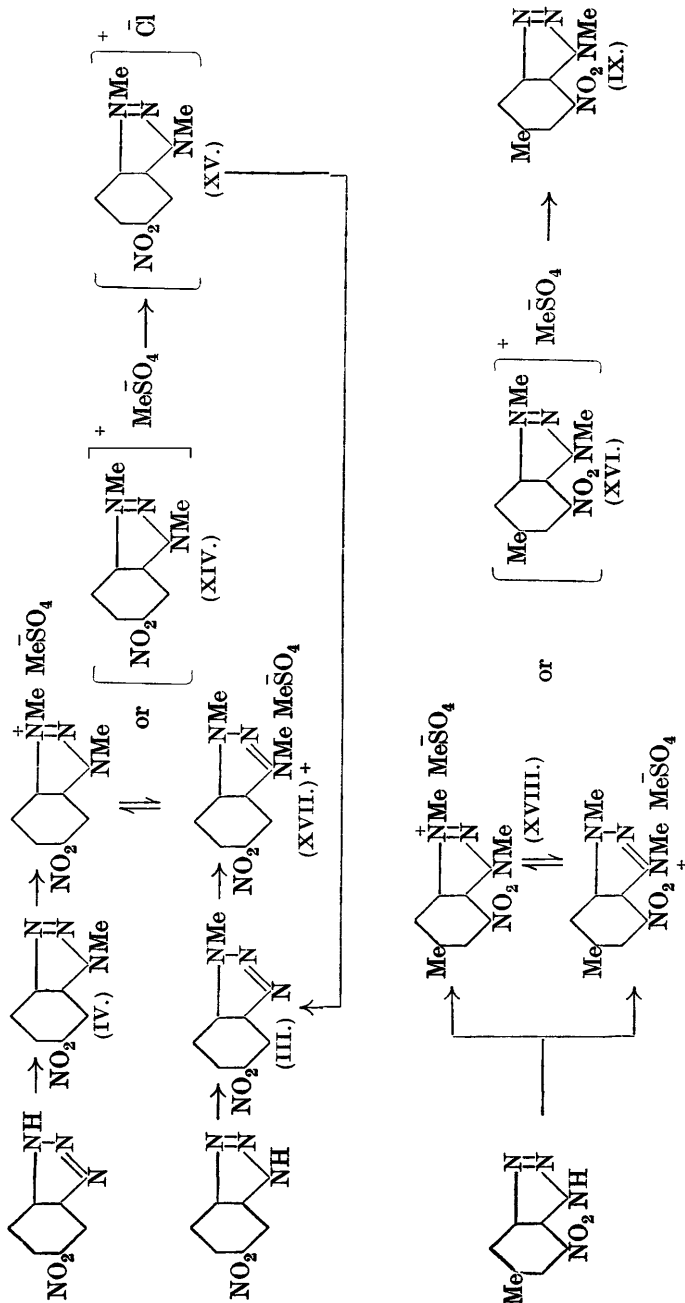
We suggest that the benzotriazoles consist of equilibrium mixtures of the two tautomeric forms, the proportion of each tautomeride depending on external conditions. Methylation in aqueous alkali takes place by the addition of methyl sulphate to the nitrogen atom in the triazole ring remote from the imino-group, followed by elimination of methyl hydrogen sulphate across the ring (compare Pyman, J., 1922, **121**, 2619, and Auwers, *Ber.*, 1925, **58**, 2081, who suggest similar mechanisms for the alkylation of 4-nitro-5-methyl-

glyoxaline and the acetylation of indazoles respectively). The above reactions may then be represented as follows :

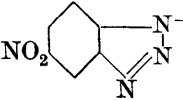
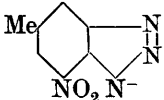


The methylation of 7-nitro-5-methyl-1 : 2 : 3-benzotriazole (VIII) in aqueous sodium hydroxide gave a mixture of 7-nitro-1 : 5-dimethyl-1 : 2 : 3-benzotriazole (IX) and 7-nitro-3 : 5-dimethyl-1 : 2 : 3-benzotriazole (X), the latter preponderating. The orientations of these compounds were established by reduction to the amino-compounds and replacement of the amino-group by hydrogen to give 1 : 5-dimethyl- (XII) and 3 : 5-dimethyl-1 : 2 : 3-benzotriazole (XIII) respectively, these compounds having been synthesised for purposes of identification. The reactions may be indicated as follows :





The mechanism here adopted seems preferable to simple metathesis or addition of methyl sulphate at the imino-group. Current polarity views would indicate that in the two tautomeric systems the nitro-group would favour the existence in alkaline solution of

the ions  and , yet in the methyl-

ations the compounds in which the methyl group is attached to the nitrogen atom in the *m*-position to the nitro-group preponderate. The proportions in which the two methyl derivatives are formed are not likely to indicate the true relative amounts of the tautomerides at equilibrium, since some of the compound formed in smaller yield may be produced by metathesis.

As with 6-nitro-1 : 2 : 3-benzotriazole, so 7-nitro-5-methyl-1 : 2 : 3-benzotriazole (VIII), after heating with methyl sulphate alone and decomposition of the methosulphate obtained, gives only 7-nitro-1 : 5-dimethyl-1 : 2 : 3-benzotriazole (IX).

The formation of only one methyl derivative under these conditions is not surprising, since 6-nitro-1-methyl-1 : 2 : 3-benzotriazole (IV) and 7-nitro-3 : 5-dimethyl-1 : 2 : 3-benzotriazole (X) behave in a similar way to the acyl derivatives of Morgan and the alkyl indazoles of Auwers and Duesberg (*Ber.*, 1920, **53**, 1179) and, when heated with methyl sulphate, give methosulphates which yield 6-nitro-3-methyl-1 : 2 : 3-benzotriazole and 7-nitro-1 : 5-dimethyl-1 : 2 : 3-benzotriazoles, respectively, on being heated.

In the presence of the excess of methyl sulphate the two methyl derivatives first formed are converted into methosulphates, which are electromerides and interconvertible and may be regarded as 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benzotriazolium methyl sulphate (XIV).

The position of the nitro-group would favour the elimination of Me_2SO_4 from the 1-N atom in (XIV) or (XV) and from the 3-N atom in (XVI) or, from another point of view, would tend to favour the forms (XVII) and (XVIII) respectively; consequently, on heating, only (III) and (IX) are produced.

EXPERIMENTAL.

6-Nitro-1 : 3-dimethyl-1 : 2 : 3-benzotriazolium Methyl Sulphate (XIV).—6-Nitro-3-methyl-1 : 2 : 3-benzotriazole (1 g.), prepared by the action of nitrous acid upon 4-nitro-2-aminomethylaniline (Brady, Day, and Reynolds, *J.*, 1929, 2264; Pinnow and Koch, *Ber.*, 1897, **30**, 2851), and methyl sulphate (5 c.c.) were warmed together on the water-bath for an hour. After cooling, the product was poured

into excess of ether and the precipitated oil was purified by repeated precipitation from absolute alcohol by dry ether and finally crystallised from a mixture of alcohol and ether; 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate was then obtained in colourless prisms, m. p. 110° (decomp.) (Found : N, 18.6; S, 10.6. $C_9H_{12}O_6N_4S$ requires N, 18.4; S, 10.5%).

This compound, when heated, regenerates some 6-nitro-3-methyl-1 : 2 : 3-benztriazole, but this is best recovered after conversion of the methyl sulphate into the chloride. The methyl sulphate was dissolved in boiling 2*N*-hydrochloric acid, the sulphuric acid removed by addition of barium chloride in slight excess, the filtrate concentrated under reduced pressure, and the residue made faintly acid with hydrochloric acid and dissolved in absolute alcohol. To the filtered solution, a large excess of dry ether was added; the precipitate obtained gave, after repeated precipitation from alcohol by ether, 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium chloride, m. p. 136° (decomp.) (Found : N, 24.7; Cl, 15.6. $C_8H_9O_2N_4Cl$ requires N, 24.5; Cl, 15.5%). The iodide prepared by Zincke and Helmert (*J. pr. Chem.*, 1896, **53**, 98) was obtained from the methyl sulphate in an analogous way.

Methylation of 6-Nitro-1 : 2 : 3-benztriazole.—When 6-nitro-1 : 2 : 3-benztriazole, prepared from 4-nitro-*o*-phenylenediamine (Zincke, *Annalen*, 1900, **311**, 290), was heated with excess of methyl iodide for 2 hours in a sealed tube at 100° , 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium iodide was formed. Similarly, the triazole (2 g.), when heated on the water-bath for 30 minutes with methyl sulphate (5 c.c.), gave 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate. When, however, the triazole (2 g.) in 2*N*-sodium hydroxide (25 c.c.) was methylated with methyl sulphate (4 c.c.), an almost theoretical yield of a solid was obtained which, on fractional crystallisation from alcohol and benzene alternately, gave 6-nitro-1-methyl-1 : 2 : 3-benztriazole as pale yellow needles, m. p. 187° , from alcohol (Found : N, 31.6. $C_7H_6O_2N_4$ requires N, 31.5%), and a somewhat smaller quantity of 6-nitro-3-methyl-1 : 2 : 3-benztriazole.

6-Nitro-1-methyl-1 : 2 : 3-benztriazole (1 g.) was heated with methyl sulphate (5 c.c.) for 30 minutes at 100° , and the product poured into dry ether, 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate being obtained. The iodide also was prepared by means of methyl iodide.

6-Amino-1-methyl-1 : 2 : 3-benztriazole.—A boiling solution of 6-nitro-1-methyl-1 : 2 : 3-benztriazole (2 g.) in alcohol (15 c.c.) was treated with small portions of sodium hydrosulphite until reduction was complete. The solution was made just alkaline with concen-

trated sodium carbonate solution and extracted with chloroform. After removal of the solvent the residue was crystallised from a small amount of boiling water (animal charcoal) and then from benzene-light petroleum; 6-amino-1-methyl-1 : 2 : 3-benztriazole was thus obtained in colourless plates, m. p. 201° (Found : N, 37.7. $C_7H_8N_4$ requires N, 37.9%). This compound (0.5 g.) was dissolved in a mixture of absolute alcohol (25 c.c.) and fuming sulphuric acid (2 c.c.), the solution heated to boiling, and finely powdered dry sodium nitrite (2 g.) added in small portions. Most of the alcohol was removed and water (10 c.c.) and a slight excess of a saturated solution of sodium carbonate were added; chloroform then extracted 1-methyl-1 : 2 : 3-benztriazole, identified by comparison with an authentic specimen.

Methylation of 7-Nitro-5-methyl-1 : 2 : 3-benztriazole.—The triazole (3 g.), prepared by Lindemann and Krause's method (*J. pr. Chem.*, 1927, **115**, 270) from 5-nitro-3 : 4-tolylenediamine (Brady, Day, and Reynolds, *loc. cit.*), was dissolved in *N*/2-sodium hydroxide (400 c.c.) and treated with methyl sulphate (10 c.c.). The solid which separated, on fractional crystallisation from alcohol and benzene alternately, gave 7-nitro-1 : 5-dimethyl-1 : 2 : 3-benztriazole, identified with the compound prepared by Pinnow (*J. pr. Chem.*, 1901, **63**, 360), and a larger amount of 7-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole, which formed pale brown needles, m. p. 196° (Found : N, 29.2. $C_8H_8O_2N_4$ requires N, 29.2%).

7-Amino-3 : 5-dimethyl-1 : 2 : 3-benztriazole, prepared from the corresponding nitro-derivative by reduction with sodium hydro-sulphite as above, formed colourless plates, m. p. 190° (Found : N, 34.6. $C_8H_{10}N_4$ requires N, 34.6%). Removal of the amino-group as before gave 3 : 5-dimethyl-1 : 2 : 3-benztriazole.

Action of Methyl Sulphate on 7-Nitro-5-methyl-1 : 2 : 3-benztriazole and on 7-Nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole.—7-Nitro-5-methyl-1 : 2 : 3-benztriazole (2 g.) was heated on the water-bath for 10 minutes with methyl sulphate (10 c.c.), and the mixture poured into ether. The precipitated methyl sulphate, which could not be induced to crystallise, was converted into the chloride (compare 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate). The chloride gave only 7-nitro-1 : 5-dimethyl-1 : 2 : 3-benztriazole when heated. 7-Nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole and methyl sulphate also gave an uncrystallisable methyl sulphate, which was converted, through the chloride, into 7-nitro-1 : 5-dimethyl-1 : 2 : 3-benztriazole.

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