CLXVIII.—*Triazole Compounds. Part IV. The Constitution of the Methyl*-1 : 2 : 3-*benztriazole* N-*Oxides and the Action of Methyl Sulphate on Nitro*-1-*hydroxy*-1 : 2 : 3-*benztriazoles.*

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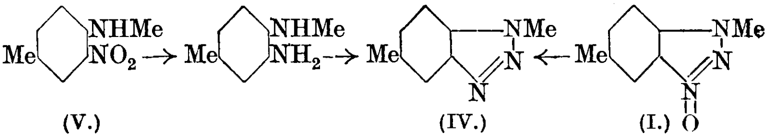
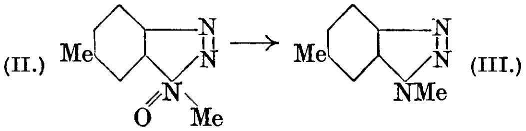
In Part II (J., 1928, 193) a choice was made between the alternative formulæ (I) and (II) for the product of methylation of, *e.g.*, 1-hydroxy-6-methyl-1 : 2 : 3-benztriazole, in which the alkyl group was attached to nitrogen.


(V.) (IV.) (I.)


(II.) (III.)

As the result of the reduction of the *N*-oxide (II) by means of hydriodic acid and red phosphorus it was stated that 1 : 6-dimethyl-

1 : 2 : 3-bentriazole (III) was obtained, and consequently the structure (II) was assigned to it. Further work to be described below led us to doubt the correctness of those results, so the reduction was twice repeated with the original specimen of *N*-oxide (I) or (II). There is no doubt that our previous statement was incorrect, as reduction under the same conditions as before (under which the 1 : 6- and the 3 : 6-dimethyl compound are not interconvertible) gave 3 : 6-dimethyl-1 : 2 : 3-benztriazole (IV), m. p. 50°, unchanged by recrystallisation or admixture with an authentic specimen, (m. p. 50°) synthesised from 3-nitromethyl-*p*-toluidine (V) but melting below 40° in admixture with the 1 : 6-dimethyl compound (III; m. p. 75°). The former error probably arose from confusion of a specimen of the reduction product with one of synthetic 1 : 6-dimethyl-1 : 2 : 3-benztriazole which was being prepared at about the same time. Unfortunately the original reduction product is no longer available. The methyl-*N*-oxides described in Parts I and II (J., 1923, **123**, 2258; *loc. cit.*) are therefore really 3-methyl-1-oxides (I).

The methylation of 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole (VI) in aqueous sodium hydroxide with methyl sulphate gave only an *O*-methyl ether (Part I), whereas other similar compounds such as 6-nitro-1-hydroxy-5-methyl-1 : 2 : 3-benztriazole and 1-hydroxy-1 : 2 : 3-benztriazole gave a mixture of *O*-ether and *N*-oxide (as I). In Part II it was concluded that the behaviour of these compounds on methylation was similar to that of the oximes and that the formation of *O*-ether was favoured by conditions promoting ionisation of the sodium salt, and the *N*-oxide by the reverse (compare Brady and Goldstein, J., 1926, 2403). The fact that 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole is a comparatively strong acid would accordingly favour the production of the *O*-ether on methylation of its sodium salt in aqueous solution. It was also shown that 1-hydroxy-1 : 2 : 3-benztriazole heated with methyl sulphate alone gave 3-methyl-1 : 2 : 3-benztriazole 1-oxide (as I) and none of the *O*-ether.

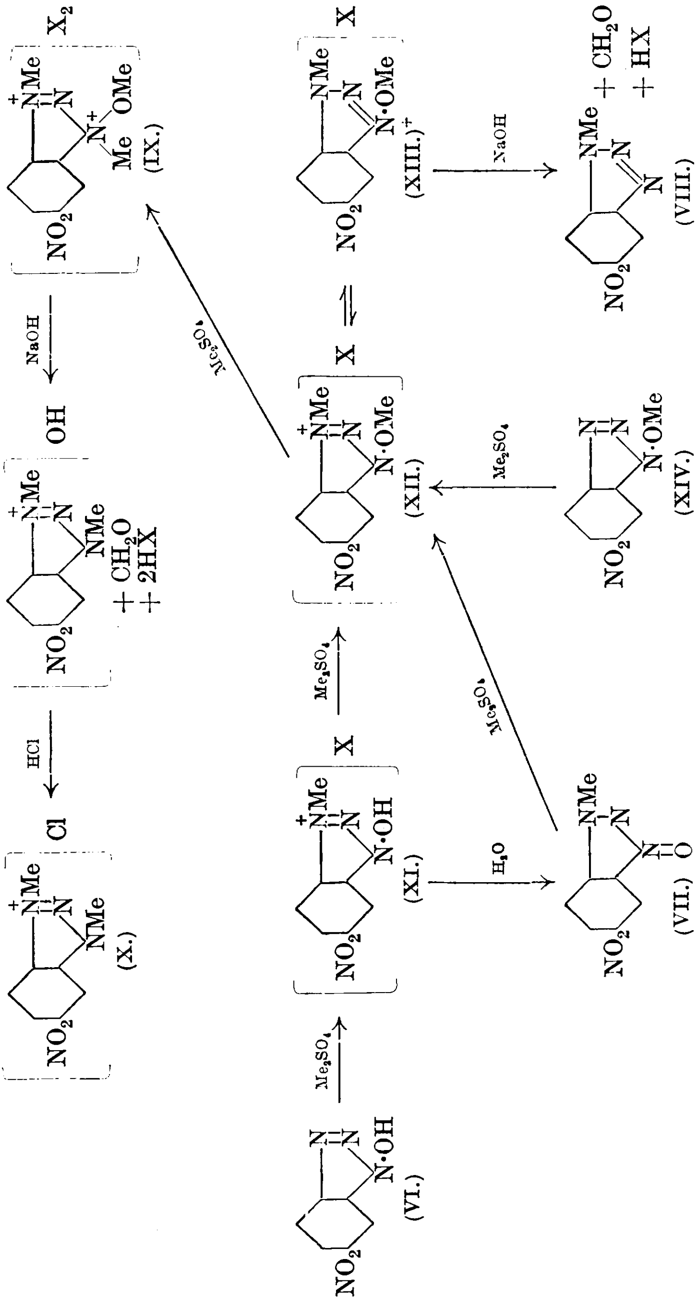
Unsuccessful attempts have now been made to obtain the *N*-oxide from 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole by alkylation in sodium hydroxide solution in presence of much sodium chloride and sulphate to suppress ionisation. When 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole was heated with methyl sulphate alone, a complicated series of reactions occurred. When the amounts of the reactants were kept constant and the time of heating was varied, or the time was constant and the proportions varied, it was found that in the early part of the reaction water-soluble compounds were formed : one of these soon decomposed in aqueous solution, giving a precipitate of *6-nitro-3-methyl-*1 : 2 : *3-benztriazole* 1*-oxide* (VII); another was decomposed by alkali, giving formaldehyde and 6-nitro-3-methyl-1 : 2 : 3-benztriazole (VIII); and a third gave no insoluble product on such treatment. The last, which was subsequently isolated direct from the reaction mixture after prolonged heating, appears to be *6-nitro-*1*-methoxy-*1 : *3-dimethyl-*1 : 2 : *3-benztriazolinium methyl sulphate* (IX), formed by addition of two molecular proportions of methyl sulphate to 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide. The alkali treatment employed for the isolation of the other products decomposed this compound and it was isolated from the mother-liquors, after they had been boiled with hydrochloric acid, as 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium chloride (X), m. p. 136° (decomp.) (Part III, J., 1930, 2672).

The yield of the first compound increased rapidly to a maximum after a very short time of heating and then decreased; the amount of the second product also increased, but more slowly, to a maximum with the time of heating. Finally, prolonged heating gave an increasing yield of the third product.

Increasing the proportion of methyl sulphate from slightly more than one to ten molecular proportions caused very rapid diminution of the amount formed of the progenitor of 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide, a slower diminution of that of 6-nitro-3-methyl-1 : 2 : 3-benztriazole, and an increasing yield of 6-nitro-1-methoxy-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate (IX).

6-Nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide (VII) and 6-nitro-1-methoxy-1 : 2 : 3-benztriazole (XIV), when treated with methyl sulphate, rapidly gave a water-soluble product which with alkalis gave 6-nitro-3-methyl-1 : 2 : 3-benztriazole and formaldehyde.

These reactions can be formulated by supposing that in the first instance methyl sulphate is added to the 3-N atom, giving (XI), which with water loses methyl hydrogen sulphate to give 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide (VII). The action of more methyl sulphate methylates the hydroxyl group, giving (XII), which is tautomeric with (XIII); this is decomposed by alkali to give 6-nitro-3-methyl-1 : 2 : 3-benztriazole (VIII) and formaldehyde, a reaction similar to the behaviour of the amine oxides with alkyl iodides (Dunstan and Goulding, J., 1896, **69**, 839; 1899, **75**, 792; Meisenheimer, *Ber.*, 1908, **41**, 3966; 1913, **46**, 1148; *Annalen*, 1913, **397**, 273). Finally, more prolonged action of methyl sulphate gives 6-nitro-1-methoxy-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate (IX). In the following scheme X is the $MeSO_4$ anion.


(VI.)
(VII.)
(VIII.)
(IX.)
(X.)
(XI.)
(XII.)
(XIII.)
(XIV.)
Me2SO4
H2O
NaOH
HCl
+ CH2O + 2HX
+ CH2O + HX

We have discarded a mechanism based on the assumption that hydroxybenztriazoles can behave as tautomeric compounds (compare Nietzki and Braunschweig, *Ber.*, 1894, **27**, 3381; Hunter, J., 1930, 128), principally in view of the ease with which methyl sulphate reacts with 6-nitro-1-methoxy-1 : 2 : 3-benztriazole (XIV) to give the progenitor of 6-nitro-3-methylbenztriazole (XII).

When 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide is reduced, and the amino-group replaced by hydrogen, 3-methyl-1 : 2 : 3-benztriazole 1-oxide is obtained, identical with the compound formed by the alkylation of 1-hydroxy-1 : 2 : 3-benztriazole with methyl sulphate in aqueous alkali (Part II). The methyl group in the lätter compound has been shown not to be in the 2-position, and the choice between the 1- and the 3-position is determined by analogy with the methylation product of 1-hydroxy-6-methyl-1 : 2 : 3-benztriazole prepared under similar conditions. Moreover, it is impossible to find a reasonable mechanism for the alkylation of 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole unless the methyl group in 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide is in the position here assigned to it. It is this difficulty which led us to suspect an error in our former work.

6-Nitro-1-hydroxy-5-methyl-1 : 2 : 3-benztriazole reacts with methyl sulphate in a similar way to 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole, giving 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole 1-oxide, identical with the compound obtained by alkylation in aqueous alkali (Part I), and then 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole. The constitution of 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole 1-oxide was established by converting it into 3 : 5-dimethyl-1 : 2 : 3-benztriazole, whose constitution is known (Part II) : this further supports the new structure for these oxides. 6-Nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole was synthesised for comparison purposes from 4 : 6-dinitromethyl-*m*-toluidine (Brady, Day, and Reynolds, J., 1929, 2265).

The mechanism of alkylation of these 1-hydroxy-1 : 2 : 3-benztriazoles is similar to that suggested for the nitrobenztriazoles (Part III, *loc. cit.*) and seems to be the only one consistent with the experimental facts.

EXPERIMENTAL.

Methylation of 6-*Nitro*-1-*hydroxy*-1 : 2 : 3-*benztriazole*.—The solution obtained by warming the benztriazole (10 g.) and methyl sulphate (20 c.c.) on the water-bath (10 mins.) was cooled and poured into ether (100 c.c.) with thorough shaking. The precipitated oil was separated, washed twice by decantation with ether (25 c.c.), freed from the last trace of this by a current of warm dry air, and dissolved in water (100 c.c.). After 15 minutes, the solid (A) which had separated was collected, and the filtrate made strongly alkaline with 2*N*-sodium hydroxide. After a short time, the precipitate (B) was collected and the filtrate was made strongly acid with hydrochloric acid and evaporated as completely as possible on the water-bath. The residue was extracted with absolute alcohol, dry ether added to the solution, and the crude material thus precipitated purified by repeated solution in alcohol and precipitation with ether; 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium chloride was then obtained (J., 1930, 2672). Heated to its melting point, this compound lost methyl chloride and gave 6-nitro-3-methyl-1 : 2 : 3-benztriazole.

The material A (2 g.), when crystallised from benzene or alcohol, gave 6-*nitro*-3-*methyl*-1 : 2 : 3-*benztriazole* 1-*oxide* in pale yellow needles, m. p. 196° (decomp.) (Found : N, 29·2. $C_7H_6O_3N_4$ requires N, 28·9%). These changed at 100° into bright yellow prisms, and this form was also obtained from a hot benzene solution of the oxide on addition of hot light petroleum.

The precipitate B after crystallisation from alcohol was found to be 6-nitro-3-methyl-1 : 2 : 3-benztriazole by comparison with a specimen prepared by the action of nitrous acid on 4-nitro-2-aminomethylaniline (Pinnow and Koch, *Ber.*, 1897, **30**, 2851); the amines obtained by reduction of the two specimens were also identical.

A similar experiment, in which, however, the reaction mixture was heated on the water-bath for 3 hours, gave a water-soluble product which was not decomposed until sodium hydroxide was added; 6-nitro-3-methyl-1 : 2 : 3-benztriazole was then precipitated. If freshly prepared moist silver oxide was substituted for the sodium hydroxide, the same compound was obtained and it was possible to detect formaldehyde in the solution by the usual tests.

6-Nitro-1-hydroxy-1 : 2 : 3-benztriazole (10 g.), in a tube with a graduation mark indicating 25 c.c., was mixed with methyl sulphate so that the level of the liquid was somewhat below the mark. The tube was heated on the water-bath with continual agitation and just before complete solution was effected the liquid was made up to the mark with hot methyl sulphate and thoroughly stirred. Samples (5 c.c.) were taken from time to time and examined by the method described in the preliminary methylation above. Complete solution occurred after 10 minutes and a sample taken at once gave 0·35 g. of 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide (A), 1·3 g. of 6-nitro-3-methyl-1 : 2 : 3-benztriazole (B), and 0·5 g. of 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium chloride (C). After 15 minutes, A = 0·25 g., B = 1·35 g., C = 0·5 g.; after 30 minutes, A = 0·1 g., B = 1·5 g., C = 0·75 g.; after 60 minutes, A = 0, B = 1·3 g., C = 1·0 g.; after 180 minutes, A = 0, B = 1·0 g., C = 2·0 g. These figures are the means obtained in a number of experiments; the values for C are only approximate.

In another experiment a number of mixtures of 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole (2 g.) and methyl sulphate (4 c.c.) were heated on the water-bath for given periods and then examined as before. The following yields of the various products were obtained: after 10 minutes, A = 0·35—0·38 g., B = 1·25—1·35 g., C = 0·5 g.; after 15 minutes, A = 0·23—0·25 g., B = 1·3—1·35 g., C = 0·5 g.; after 30 minutes, A = 0·1—0·15 g., B = 1·4—1·5 g., C = 0·75 g.; after 1 hour, A = 0, B = 1·3—1·35 g., C = 1·0 g.; after 3 hours, A = 0, B = 0·8—1·0 g.; C = 2·0 g.; after 8 hours, A = 0, B = 0·5 g., C = 3·0 g.

6-Nitro-1-hydroxy-1 : 2 : 3-benztriazole (2 g.) was heated at 100° for 8 hours with methyl sulphate (5 c.c.). Addition of excess of ether (dried over sodium) to the cooled product precipitated an oil, which was washed with dry ether by decantation. The oil was dissolved in absolute alcohol and precipitated with ether, but would not crystallise. After being freed from solvent in an evacuated desiccator, it gave analytical results corresponding with 6-*nitro*-1-*methoxy*-1 : 3-*dimethyl*-1 : 2 : 3-*benztriazolinium methyl sulphate* (IX) (Found: N, 12·5; S, 14·7. $C_{11}H_{18}O_{11}N_4S_2$ requires N, 12·6; S, 14·4%).

Action of Methyl Sulphate on 6-*Nitro*-3-*methyl*-1 : 2 : 3-*benztriazole* 1-*Oxide and on* 6-*Nitro*-1-*methoxy*-1 : 2 : 3-*benztriazole*.—The oxide (0·5 g.) was heated on the water-bath for 5 minutes with methyl sulphate (2 c.c.) and, after cooling, excess of dry ether added. The precipitated oil was dissolved in water and warmed with moist silver oxide; 6-nitro-3-methyl-1 : 2 : 3-benztriazole was then obtained, and formaldehyde detected in the solution; 2*N*-sodium hydroxide gave a precipitate of the above compound in the cold after a short time. In a second experiment 1 g. was heated for an hour with methyl sulphate (5 c.c.) and treated with ether. The precipitated oil was purified by repeated solution in absolute alcohol and precipitation with ether. The product behaved similarly to the 6-nitro-1-methoxy-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium methyl sulphate described above. Alkalis gave formaldehyde but no insoluble compound; neither ether nor chloroform extracted anything from the alkaline solution. The alkaline solution was acidified with 2*N*-hydrochloric acid and boiled, the sulphuric acid removed with barium chloride, and the filtrate concentrated at 60°. The residue, on crystallisation from alcohol and ether, gave 6-nitro-1 : 3-dimethyl-1 : 2 : 3-benztriazolinium chloride.

6-Nitro-1-methoxy-1 : 2 : 3-benztriazole (2 g.) was heated for 10 minutes on the water-bath with methyl sulphate (5 c.c.), and the product poured into ether. The precipitated oil was dissolved in water, but no insoluble material was produced until sodium hydroxide was added; 6-nitro-3-methyl-1 : 2 : 3-benztriazole was then precipitated.

6-*Amino*-3-*methyl*-1 : 2 : 3-*benztriazole* 1-*Oxide*.—Solid sodium hydrosulphite in small portions was added to a boiling solution of 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide (2 g.) in 70% alcohol (30 c.c.) until reduction was complete. As much as possible of the alcohol was removed on the water-bath, water (10 c.c.) added, and then 2*N*-sodium hydroxide until the solution was just alkaline. The 6-*amino*-3-*methyl*-1 : 2 : 3-*benztriazole* 1-*oxide* was extracted with chloroform; it crystallised from benzene–light petroleum in colourless prisms, m. p. 225° (decomp.), readily soluble in water and oxidisable in air (Found : N, 34·3. $C_7H_8ON_4$ requires N, 34·1%).

This compound (0·5 g.) was added to a mixture of absolute alcohol (25 c.c.) and fuming sulphuric acid (2 c.c.), the solution heated to boiling, and finely powdered sodium nitrite (2 g.) added in small portions. Most of the alcohol was evaporated and water (10 c.c.) and a slight excess of a saturated solution of sodium carbonate were added; chloroform then extracted 3-methyl-1 : 2 : 3-benztriazole 1-oxide which, after being crystallised twice from benzene–light petroleum, was identified by comparison with another specimen.

Methylation of 6-*Nitro*-1-*hydroxy*-5-*methyl*-1 : 2 : 3-*benztriazole*.—This compound (2 g.) (prepared by the method given in Part I, *loc. cit.*) and methyl sulphate (5 c.c.) were heated at 100° for 10 minutes. The oil precipitated by ether was dissolved in water and after 10 minutes the 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole 1-oxide which separated was crystallised from methyl alcohol : it was identical with the compound obtained by alkylation with methyl sulphate in 2*N*-sodium hydroxide (Part I). When the filtrate from the above was made alkaline with sodium hydroxide, 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole separated : after crystallisation from alcohol, it was found to be identical with the compound obtained by the action of nitrous acid on 6-nitro-4-aminomethyl-*m*-toluidine (Brady, Day, and Reynolds, J., 1929, 2265). The mother-liquor, after removal of the above compound, on treatment with hydrochloric acid and barium chloride to remove sulphate, and evaporation, gave a residue which on extraction with alcohol and precipitation with ether yielded an uncrystallisable oil. This was probably 6-nitro-1 : 3 : 5-trimethyl-1 : 2 : 3-benztriazolinium chloride; on heating, it gave 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole.

Heating a similar mixture of the hydroxytriazole and methyl sulphate for more than 30 minutes and treating the product as before gave none of the 1-oxide but a good yield of 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole; prolonged heating reduced the yield of the latter compound, but a good yield of the triazolinium chloride was then obtained.

Conversion of 6-*Nitro*-3 : 5-*dimethyl*-1 : 2 : 3-*benztriazole* 1-*Oxide into* 3 : 5-*Dimethyl*-1 : 2 : 3-*benztriazole*.—When 6-nitro-3 : 5-dimethyl-1 : 2 : 3-benztriazole 1-oxide was reduced with sodium hydrosulphite similarly to 6-nitro-3-methyl-1 : 2 : 3-benztriazole 1-oxide above, 6-*amino*-3 : 5-*dimethyl*-1 : 2 : 3-*benztriazole* 1-*oxide* was obtained; it formed colourless prisms, m. p. 279° (decomp.), from benzene–light petroleum (Found: N, 31·6. $C_8H_{10}ON_4$ requires N, 31·6%). The amino-group in this compound was removed as before and the product was boiled under reflux for 6 hours with hydriodic acid (*d* 1·7) and red phosphorus. The solution was diluted with water, filtered, made alkaline with sodium hydroxide, and extracted with chloroform. The product, crystallised from light petroleum, gave 3 : 5-dimethyl-1 : 2 : 3-benztriazole, m. p. 75°, which did not depress the melting point of a synthetic specimen.

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[*Received, March* 10*th*, 1931.]