XXII.—*Nitration of 2'- and 4'-Nitro-1-phenylpiperidines.*

By Raymond James Wood Le Fèvre.

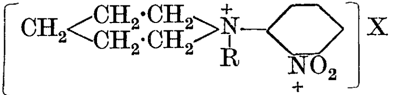
Ordinary nitric acid (*d* 1·4) nitrates 4'-nitro-1-phenylpiperidine quantitatively in the 2'-position, but dissolves the 2'-nitro-isomeride unchanged. By the most extreme conditions of nitration under which the latter remains unaffected the former is destroyed.

Similar but less pronounced differences have been observed in the nitrations of 1 : 4-*di*(2′- and 4′-*nitrophenyl*)*piperazines*.

No such disparity is recorded in the literature concerning the conditions requisite for the production, by nitration of the corresponding mononitro-compounds with nitric acid of density not less than 1·42, of 2 : 4-dinitrodimethyl- or 2 : 4-dinitrodiethylaniline. An observation by Pinnow (*Ber.*, 1899, **32**, 1667), that dimethylaniline gave 95% of its weight of 2 : 4-dinitrodimethylaniline and 50% of its weight of 2-nitrodimethylaniline when treated with dilute sulphuric and nitric acids (see also Schuster and Pinnow, *Ber.*, 1896, **29**, 1053), would seem to indicate, however, that, of the initially formed *o*- and *p*-mononitro-compounds, only the latter underwent further nitration. Even were this so, the deductions from the present work would be unaffected, since the weakest nitrating acid used in the experiments on the nitrophenylpiperidines was ordinary nitric acid (*d* 1·42). For comparison, it is now shown that the interaction of this reagent with 2-nitrodimethylaniline at room temperature leads to high yields of 2 : 4 : 6-trinitrophenylmethylnitroamine, and the observation of Weber (*Ber.*, 1877, **10**, 763), that by nitration of dimethylaniline with a solution of nitric acid in glacial acetic acid complete 2 : 4-dinitration is readily effected, has been verified experimentally.

Moreover, with regard to Pinnow's results, from general principles it would be expected that progressive dilution of the attacking reagent would render any slight difference in reactivity of two positions in a substituted benzene nucleus increasingly obvious, and the experiments of Clemo and Smith (J., 1928, 2414) have shown that dilution of the nitrating acids with *water* is, in the case of certain dimethylanilines, a change of experimental conditions likely to lead to fundamentally different results.

The tendency of 2′- and 4′-nitro-1-phenylpiperidines to undergo salt formation is apparently strong; combination of either with mineral acid was violent (much more so than the analogous reactions with the nitrodimethylanilines) and each gave a stable *perchlorate*, *ferrichloride*, and mercurichloride.

An explanation of the present observations must therefore be sought in the relatively (to dialkyl) rigid structure of the piperidine ring, which, in the case, for example, of the *o*-nitro-compound, would more effectively (*a*) *spread* the area of direct influence of the two positive charges  (I) by its spatial interactions with the bulky *o*-nitro-group and (*b*) prevent the nearer approach of the negative anion $\bar{X}$ and consequent reduction of the strong inductive and direct effects set up by the positive poles indicated in (I) (compare Pollard and Robinson, J., 1927, 2770).

EXPERIMENTAL.

Action of Nitric Acid on 2′-*Nitro*-1-*phenylpiperidine*.—(*a*) When the nitro-compound (2 g.) was added cautiously and in portions to 10 c.c. of fuming nitric acid at the ordinary temperature, it dissolved with a hissing noise (addition of too large a portion caused inflammation). After 5 minutes, dilution with water and basification with ammonia gave nearly 2 g. of a bright red solid, m. p. 76—77° (alone, or mixed with authentic 2′-nitro-1-phenylpiperidine). (*b*) The nitro-compound (2 g.), after being dissolved in 10 c.c. of sulphuric acid, treated with 10 c.c. of fuming nitric acid, and heated on the water-bath for 15 minutes, was largely recovered unchanged; considerable decomposition, however, occurred.

Action of Nitric Acid on 4′-*Nitro*-1-*phenylpiperidine*.—The nitro-compound gave an uncrystallisable red oil under conditions (*a*) and was destroyed under conditions (*b*). When a solution of the nitro-compound (2 g.) in ordinary nitric acid (*d* 1·4) at 0° was left for 1 minute, then diluted with water and made alkaline, an almost quantitative yield of 2′ : 4′-dinitro-1-phenylpiperidine, m. p. 92°, was obtained.

Preparation of 1 : 4-*Di*(2′- *and* 4′-*nitrophenyl*)*piperazines*.—Equal weights of the appropriate chloronitrobenzene and piperazine hydrate were gently boiled together for 15 minutes. The product was extracted repeatedly with boiling alcohol, and the residue crystallised. 1 : 4-*Di*(2′-*nitrophenyl*)*piperazine* separated in orange plates, m. p. 193—194°, from much glacial acetic acid (Found : N, 17·2. $C_{16}H_{16}O_4N_4$ requires N, 17·1%), and the corresponding 4′-*nitro*-compound as a microcrystalline red powder, m. p. 263—264°, from phenol–nitrobenzene although the crude substance was yellow (Found : N, 17·2%).

Nitration of 1 : 4-*Di*(2′- *and* -4′-*nitrophenyl*)*piperazines*.—1 G. of each compound was dissolved in separate equal large volumes of hot acetic acid and 5 c.c. of nitric acid (*d* 1·5) were added. The production of 1 : 4-di(2′ : 4′ : 6′-trinitrophenyl)piperazine (Le Fèvre and Turner, J., 1927, 113) from the former compound was complete after the mixture had been kept at the ordinary temperature for 12 hours; in the case of the 4′-nitro-compound, 10 minutes were sufficient.

Action of Nitric Acid on 2-*Nitrodimethylaniline*.—This substance was prepared in good yield by 8 hours' boiling of a mixture of *o*-chloronitrobenzene (15 g.), 30% dimethylamine solution (35 g.), and sufficient alcohol to produce a homogeneous solution. The product, after dilution with water, was extracted with benzene, and the extract washed with water and finally with dilute sulphuric acid. The acid solution was basified and again shaken with benzene. 2-Nitrodimethylaniline distilled at 145—155°/*ca.* 30 mm. as a clear red oil.

By addition of 1 g. to 15 c.c. of nitric acid (*d* 1·42) at the ordinary temperature, followed after 15 minutes' solution by precipitation by dilution with water, a cream-coloured crystalline product was obtained, brief treatment of which with hot aqueous-alcoholic ammonia gave picramide, m. p. 188—189° (alone or mixed with an authentic specimen). Crystallisation of the nitration products from alcohol afforded cream plates, m. p. 131° (alone or mixed with authentic 2 : 4 : 6-trinitrophenylmethylnitroamine). Since 2 : 4-dinitrodimethylaniline is undoubtedly a precursor of "tetryl" in its direct formation from dimethylaniline, it is obvious that the 4-mononitration of 2-nitrodimethylaniline is a readily effected process and that 2-nitrodimethylaniline differs markedly from 2′-nitro-1-phenylpiperidine in this respect.

Dinitration of Dimethylaniline.—Dimethylaniline (12 g.; 1 mol.), dissolved in glacial acetic acid (80 g.), was slowly treated at 0—5° with fuming nitric acid (15 g.; 2 mols.) diluted with an equal volume of acetic acid. The resulting mixture was left until its temperature had risen to 15°; it was then diluted with much water. The yellow crystalline precipitate obtained, after drying, had m. p. *ca.* 75° (after two crystallisations from carbon disulphide the m. p. was 78·5—79·5°) and its weight (19 g.) corresponded to a 90% yield of 2 : 4-dinitrodimethylaniline.

Complex Salts from 2′- *and* 4′-*Nitro*-1-*phenylpiperidines.*—The two nitro-compounds dissolved readily in concentrated hydrochloric acid. To the solutions, slightly diluted with water, concentrated ferric chloride solution was added slowly. After filtration and crystallisation from acetic acid, 2′-*nitro*-1-*phenylpiperidinium ferrichloride*, dark yellow needles, m. p. 147—148° (Found: N, 7·0. $C_{11}H_{15}O_2N_2Cl_4Fe$ requires N, 6·9%), and 4′-nitro-1-phenylpiperidinium ferrichloride, straw-yellow needles, m. p. 130—135°, were obtained. No ferrichloride formation could be observed with 2′ : 4′-dinitro-1-phenylpiperidine.

Addition of aqueous mercuric chloride to the above hydrochloric acid solutions gave the corresponding mercurichlorides, which formed cream-coloured plates, m. p. 170—175°, and bright yellow plates, m. p. 70—80°, respectively.

Addition of aqueous perchloric acid to mineral acid solutions of 2′-nitro-1-phenylpiperidine precipitated a white microcrystalline *perchlorate* which, after crystallisation from glacial acetic acid, had

m. p. 240—243° (decomp.) (Found : N, 9·3. $C_{11}H_{15}O_6N_2Cl$ requires N, 9·15%). The corresponding 4′-nitro-1-phenylpiperidinium perchlorate was apparently soluble in water, since a hydrochloric acid solution of 4′-nitro-1-phenylpiperidine could, after addition of aqueous perchloric acid, be diluted with a large excess of water without any precipitation occurring.

UNIVERSITY COLLEGE, LONDON. [*Received, November* 14*th*, 1929.]