180. *Preparation and Dinitration of* 1-*Phenylpiperidine.*

By Raymond James Wood Le Fèvre.

Pinnow (*Ber.*, 1899, **32**, 1667; see also Schuster and Pinnow, *ibid.*, 1896, **29**, 1053), using dilute nitric and sulphuric acids, has shown that 4-nitrodimethylaniline is more easily substituted in the 2-position than is 2-nitrodimethylaniline in the 4-position. Stronger reagents overcome and mask this evidently fine difference of reactivity (Le Fèvre, J., 1930, 147). A more marked contrast exists between the 2′- and 4′-nitro-1-phenylpiperidines, 4′-nitro-1-phenylpiperidine being easily mononitrated, even by nitric acid of *d* 1·42, to yield 2′ : 4′-dinitro-1-phenylpiperidine, whereas 2′-nitro-1-phenylpiperidine is unaffected by nitric acid of *d* 1·5.

By implication, then, the dinitration of 1-phenylpiperidine should lead to a mixture of 2′-nitro- and 2′ : 4′-dinitro-1-phenylpiperidines. 1-Phenylpiperidine was accordingly added to nitric acid at − 10°.

The product consisted of slightly impure 2′ : 4′-dinitro-1-phenylpiperidine (yield, *ca.* 90%), and the solids obtained by the evaporation of the alcoholic mother-liquors from its crystallisation contained no 2′-nitro-1-phenylpiperidine—a fact indicated both by the non-precipitation of the perchlorate of this substance when excess of perchloric acid was added to a hydrochloric acid solution of the crude material and by mixed m. p. determinations.

Since production of the dinitro-compound can only be consistently viewed as proceeding *via* the 4′-nitro-derivative, this experiment indicates that the piperidino-radical possesses an abnormally strong *p*-orienting influence.

Further proof that dinitration proceeds wholly through the 4′-mononitro-compound consisted in the isolation of only 4′-nitro-1-phenylpiperidine from the regulated mononitration of the base in acetic acid–anhydride solution.

These, like the similar results reported for various phenylglyoxalines (Forsyth and Pyman, J., 1930, 397; compare also the *p*-nitration of *tert.*-butylbenzene studied by Malherbe, *Ber.*, 1919, **52**, 319, and the low *o*/*p* ratio found for phenyl*cyclo*hexane by Mayes and Turner, J., 1929, 500), are probably due to steric hindrance accentuated by the structurally rigid heterocyclic nuclei.

Examination of Alternative Preparations of 1-*Phenylpiperidine.*—The method of von Braun (*Ber.*, 1904, **37**, 3212) is costly. Other obvious preparative methods have therefore been explored.

(*a*) Both 2′- and 4′-nitro-1-phenylpiperidine were conveniently reduced by the iron–water process (Lellmann and Just, *Ber.*, 1891, **24**, 2103), and diazotisation, etc., of the 2′-amino-compound gave 1-phenylpiperidine in yields of about 50%, but deamination of 4′-amino-1-phenylpiperidine was unsatisfactory.

(*b*) Phenylation was not effected by boiling piperidine with the phenyl esters of *p*-toluenesulphonic, phosphoric, acetic, and benzoic acids or with potassium phenyl sulphate.

(*c*) *o*- and *p*-Nitrophenyl *p*-toluenesulphonates, which interact with aniline with production of *o*- and *p*-nitrodiphenylamine, respectively (Ullmann and Nadai, *Ber.*, 1908, **41**, 1872), react with piperidine (the *m*-nitrophenyl ester is resistant) to give *o*- and *p*-nitrophenol, respectively, and *p*-toluenesulphonylpiperidide (compare Groves, Turner, and Sharp, J., 1927, 512; Turner and Fox, J., 1930, 1853; Henley and Turner, *ibid.*, p. 928).

(*d*) Interaction between iodobenzene and piperidine under pressure (see Lellmann and Geller, *Ber.*, 1888, **21**, 2279) and the thermal decomposition of benzeneazopiperidide (Wallach, *Annalen*, 1886, **235**, 242) in high-boiling solvents gave unsatisfactory or negative results.

(*e*) Attempts to produce sodium piperidide by treating piperidine in boiling xylene with powdered sodamide were partly successful and the mixture gave a small yield of 1-phenylpiperidine when heated with iodobenzene.

(*f*) From the violent interaction between ethereal phenylmagnesium iodide or bromide and 1-chloropiperidine, only diphenyl and small quantities of basic oils were obtained.

EXPERIMENTAL.

Dinitration of 1-*Phenylpiperidine.*—Phenylpiperidine (5 g.) was added during 20 minutes to 50 c.c. of nitric acid (*d* 1·5), kept below — 10°. After 10 minutes, the solution was poured over 150 g. of ice, 100 c.c. of water were added, the liquid was decanted, and the solid product extracted with benzene (50 + 50 + 30 c.c.). The extracts were washed with 15 c.c. of water, with 2*N*-caustic soda, and with water (three times with each), dried with sodium sulphate, and evaporated, leaving a residue (4·2 g.), m. p. 80—85°. The decanted aqueous liquid, on dilution, gave 2·5—3 g. of an orange solid, m. p. 89—92°. Recrystallisation of the combined products gave 6 g. of 2′ : 4′-dinitro-1-phenylpiperidine, m. p. 92° (Lellmann and Geller, *Ber.*, 1888, **21**, 2283).

Mononitration of 1-*Phenylpiperidine.*—A solution of phenylpiperidine (3·1 g.) in acetic acid (40 c.c.) and acetic anhydride (10 c.c.) was treated at the ordinary temperature with 1 c.c. of nitric acid (*d* 1·5) in 30 c.c. of acetic acid, and after 10 minutes the mixture was diluted with water. The yellow plates obtained (3·5 g.), m. p. 93—94°, had, after recrystallisation from 95% alcohol, m. p. 102—103° (alone or mixed with authentic 4′-nitro-1-phenylpiperidine). The acid filtrate was made ammoniacal. Yellow needles (and a reddish gum, 0·2 g.) were obtained, m. p. 90—95°, and 101—102° after crystallisation.

Preparation of 1-*Phenylpiperidine.*—2′- and 4′-Nitro-1-phenylpiperidine (51 g.), reduced with iron filings (100 g.), water (150 c.c.), and a trace of hydrochloric acid in the usual way, gave 2′-amino-1-phenylpiperidine (30 g.), b. p. 145°/14 mm., and the 4′-amino-compound (25 g.), m. p. 40°, respectively. Either amino-compound (20 g.) was dissolved in 125 c.c. of concentrated sulphuric acid and diazotised with sodium nitrite (8·2 g.) and the solution was added slowly to 240 c.c. of boiling 95% ethyl alcohol. After the evolution of nitrogen ceased, water was added, and the clear solution made alkaline and extracted with chloroform. The yield of phenylpiperidine, b. p. 245—250°, was 10 g. from the 2′-amino-compound, and but small from the 4′-isomeride.

Interaction of Piperidine and Various Phenyl Esters.—Phenyl *p*-toluenesulphonate and triphenyl phosphate were recovered unchanged after being heated with an equal weight of piperidine for 6 hours at 100°.

A mixture of 10 g. of phenyl acetate and 30 g. of piperidine was left over-night at the ordinary temperature. Distillation yielded phenol and piperidine, 18 g. (up to 200°), and acetylpiperidine, 21 g. (225—230°). Phenyl benzoate, salol, and acetylsalol were observed qualitatively to behave analogously.

Interaction of Piperidine with o-, m-, *and* p-*Nitrophenyl* p-*Toluenesulphonates.*—The *m*-ester (Henley and Turner, *loc. cit.*) (3 g.) was gently boiled with piperidine (2 g.) for 1 hour, and the deep red solution then diluted with water. The precipitate produced (about 2·6 g.) had m. p. 103—104°, and 112° (after one crystallisation from spirit) alone or mixed with *m*-nitrophenyl *p*-toluenesulphonate.

Piperidine (4 g.) and *o*-nitrophenyl *p*-toluenesulphonate were boiled for 1 hour, and the deep red solution was diluted, just acidified with dilute sulphuric acid, and steam-distilled, 1·6 g. of *o*-nitrophenol being obtained (1·75 g. after correction for solubility in water). Crystalline material (2·1 g.; 94% yield), m. p. 100°, obtained from the residual liquor, had m. p. 101—102° (alone or mixed with *p*-toluenesulphonylpiperidide) after one crystallisation from spirit.

The *p*-nitrophenyl ester (2 g.) and piperidine (10 c.c.), after 1 hour's boiling, gave, when diluted and made alkaline, a white solid, m. p. 100°, evidently *p*-toluenesulphonylpiperidide. The alkaline solution on acidification gave *p*-nitrophenol, m. p. 114°.

Preparation of 1-*Chloropiperidine.*—A solution of piperidine (25 g.) in water (25 c.c.) was dropped slowly into a suspension of bleaching powder (200 g.) in 1 l. of water containing 25 g. of potassium hydroxide, a slow current of steam being passed meanwhile. A light yellow oil was obtained with the aqueous distillate; after being washed and dried with calcium chloride, it had b. p. 50—56°/23 mm. (Lellmann and Geller, *Ber.*, 1888, **21**, 1921, give b. p. 52°/25 mm.).

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