

LXXX.—*The Nitration of Benzylpyridines and the Oxidation of Benzylpiperidines.*

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THE nitration of the 2-, 3-, and 4-benzylpyridines was undertaken as a sequel to the nitration of the 2-, 3-, and 4-phenylpyridines (Forsyth and Pyman, J., 1926, 2912), and it was found that the proportion of the meta-isomeride produced (in the case of the 2- and 4-substituted compounds) was greatly diminished in the benzylpyridines as compared with the phenylpyridines, the yields of the nitro-compounds (or oriented degradation products) being as follows :—

Yields (%) of Nitration Products.

	Phenylpyridines.			Benzylpyridines.		
	2-.	3-.	4-.	2-.	3-.	4-.
<i>o</i>	5.1	—	12.7	—	—	—
<i>m</i>	34.9	—	28.5	10.4	—	4.8
<i>p</i>	42.3	64.3	38.0	66.7	63.1	70.2

These results harmonise with Goss, Hanhart, and Ingold's observations (J., 1927, 250) that β -phenylethylamines yield a much smaller proportion of the *m*-nitro-substituted compounds (12% in the case of β -phenylethylamine) than do the benzylamines (49% in the case of benzylamine).

Since we were in possession of quantities of the 2- and 4-benzylpyridines, it appeared to us to be of interest to determine whether their reduction products, the 2- and 4-benzylpiperidines, and also 2-benzyl-1-methylpiperidine, underwent the same type of fission on oxidation with sulphuric acid and manganese dioxide as the 1-benzyltetrahydroisoquinolines or 1-benzyl-2-methyltetrahydroisoquinolines (Pyman, J., 1909, 95, 1266, 1738). This, however, proved not to be the case.

EXPERIMENTAL.

The 2- and 4-benzylpyridines were prepared by the action of benzyl chloride on pyridine, and separated either by fractionation of the picrates (Tschitschibabin's method, *J. Russ. Phys. Chem. Soc.*, 1901, 33, 249; 1915, 47, 1297) or by fractional distillation under atmospheric pressure. These bases, their reduction products, the 2- and 4-benzylpiperidines, and the picrates of each had the b. p.'s or m. p.'s recorded by Tschitschibabin. The following new derivatives were prepared:

1-Benzenesulphonyl-2-benzylpiperidine, prisms from ligroin, m. p. 65° (corr.) (Found: C, 68.2; H, 6.9; S, 9.8. $C_{18}H_{21}O_2NS$ requires C, 68.6; H, 6.7; S, 10.2%).

1-Benzoyl-2-benzylpiperidine, microscopic needles from ligroin, m. p. 68° (corr.) (Found: C, 81.5; H, 7.7; N, 4.8. $C_{19}H_{21}ON$ requires C, 81.7; H, 7.5; N, 5.0%).

1-Benzenesulphonyl-4-benzylpiperidine, needles from alcohol, m. p. 118° (corr.) (Found: C, 68.6; H, 6.7; S, 9.9. $C_{18}H_{21}O_2NS$ requires C, 68.6; H, 6.7; S, 10.2%).

2-Benzyl-1-methylpiperidine could not be prepared by the reduction of 2-benzylpyridine metho-salts, but was obtained in poor yield (12%) by heating 2-benzylpiperidine (6 g.) with methyl iodide (5 g.) for 10 hours at 130°, 2-benzylpiperidine being removed from the tertiary bases obtained as the benzoyl derivative. The picrate crystallised from alcohol in yellow prisms, m. p. 181° (corr.) (Found: N, 13.1. $C_{19}H_{22}O_7N_4$ requires N, 13.4%). The base regenerated from the picrate had b. p. 305–310°/740 mm.

Nitration of 2-Benzylpyridine.—2-Benzylpyridine nitrate [anhydrous prisms from dilute nitric acid, m. p. 116° (corr.) (Found: C, 61.7; H, 5.2. $C_{12}H_{11}N, HNO_3$ requires C, 62.1; H, 5.2%)] (10 g.) was added to concentrated sulphuric acid (20 c.c.), cooled in ice,

during $\frac{1}{2}$ hour. The mixture was warmed at 50° for 5 minutes, poured on ice, and precipitated fractionally by ammonia, giving first 2-*p*-nitrobenzylpyridine (5.42 g.; m. p. $76-78^\circ$), then an oil (3.72 g.). Attempts to separate this oil by fractional precipitation of the base from a salt, or by fractional crystallisation of various salts, were unsuccessful, but on oxidation in neutral suspension with potassium permanganate (5 g.) in water (400 c.c.), it gave a mixture of nitrobenzoylpyridines (3.3 g., m. p. $85-100^\circ$). When this was treated with a limited quantity of water, 2-*m*-nitrobenzoylpyridine (1.05 g.; m. p. $117-120^\circ$) remained undissolved; the solution deposited 2-*p*-nitrobenzoylpyridine (0.8 g.; m. p. 105°). The yields of nitration products isolated are thus para 66.7, and meta 10.4% of the theoretical.

2-*p*-Nitrobenzylpyridine had m. p. 81° (T.,* 81°); its picrate, m. p. $185-187^\circ$ (T., 185°); nitrate, m. p. 132° (corr.); and hydrochloride, m. p. 190° (corr.). It gave on oxidation 2-*p*-nitrobenzoylpyridine, m. p. 105° (T., 103°), giving a hydrochloride, m. p. 187° (Koenigs, *Ber.*, 1926, **59**, 1717, gives m. p. 173°).

2-*m*-Nitrobenzoylpyridine crystallises from alcohol in prisms or from water in needles, m. p. 122° (corr.) (Found: C, 63.0; H, 3.5. $C_{12}H_8O_3N_2$ requires C, 63.2; H, 3.5%). Its orientation was determined by oxidation with permanganate, *m*-nitrobenzoic acid (m. p. 140° alone or mixed with a known specimen) being isolated in 14% yield.

Nitration of 3-Benzylpyridine.—3-Benzylpyridine nitrate [anhydrous prisms from dilute nitric acid, m. p. 140° (corr.) (Found: C, 61.8; H, 5.0%)] (3 g.) was added slowly to concentrated sulphuric acid (10 c.c.) cooled in ice. The mixture was warmed at 50° for 5 minutes, poured on ice, and fractionally precipitated with ammonia. The first two crops (1.52 g.) became crystalline and after recrystallisation from alcohol gave pure 3-*p*-nitrobenzylpyridine (1.44 g.; m. p. 88°). Later crops (1.30 g.) were oily and were converted into nitrate; when this was crystallised from a large volume of aqueous alcohol, the nitrate of the *p*-isomeride separated (0.14 g., m. p. 157°). Previous attempts to effect the further separation of similar mixtures of nitro-3-benzylpyridines either as such or as the nitrobenzoylpyridines having proved fruitless, on this occasion the mixture was oxidised with permanganate; a mixture of nitrobenzoic acids (0.23 g.) was then obtained from which 0.09 g. of *p*-nitrobenzoic acid (m. p. 234°) and a trace of *m*-nitrobenzoic acid (m. p. $118-125^\circ$) were isolated.

The yields of nitration products are thus para, 63.1%; meta, trace.

* T = Tschitschibabin.

3-*p*-Nitrobenzylpyridine crystallises from alcohol in small colourless prisms, m. p. 88° (corr.) (Found : C, 67·5; H, 4·8. $C_{12}H_{10}O_2N_2$ requires C, 67·3; H, 4·7%). It is sparingly soluble in water, but readily soluble in alcohol or ether. The picrate crystallises from alcohol as a flocculent mass of needles, m. p. 145—146° (corr.) (Found : N, 15·4. $C_{12}H_{10}O_2N_2 \cdot C_6H_3O_7N_3$ requires N, 15·8%). The nitrate forms clusters of needles, m. p. 157° (corr.), from water or alcohol.

3-*p*-Nitrobenzylpyridine was prepared by heating the above base (1·4 g.) with potassium permanganate (7 g.) in 3% aqueous solution for $\frac{1}{2}$ hour, destroying the excess of permanganate with alcohol, and filtering the solution; it separated, on cooling, in needles, m. p. 106° (corr.), the yield being 1·0 g. (Found : C, 62·9; H, 3·6. $C_{12}H_8O_3N_2$ requires C, 63·2; H, 3·5%). Its picrate crystallised from alcohol in glistening plates, m. p. 185—187° (corr.). The final mother-liquor from the permanganate oxidation was acidified and gave *p*-nitrobenzoic acid (0·21 g., m. p. 235°; mixed m. p. 235°), whence the orientation of the nitro-group in the above bases is known.

Nitration of 4-Benzylpyridine.—4-Benzylpyridine nitrate [anhydrous prisms, m. p. 110° (corr.), from dilute nitric acid (Found : C, 62·3; H, 5·1%)] (16 g.) was added to concentrated sulphuric acid (30 c.c.), cooled with ice, in the course of $\frac{1}{2}$ hour. The mixture was warmed at 50° for 5 minutes, poured on ice, basified with ammonia, and extracted with ether. The extract gave an oil (15·6 g.) which crystallised on keeping, and after recrystallisation from alcohol gave 4-*p*-nitrobenzylpyridine (9·9 g., m. p. 74°). The alcoholic mother-liquor left an oil, which was oxidised with permanganate and gave a mixture of nitro-4-benzoylpyridines (3·1 g., m. p. 80—100°). This material was converted into hydrochlorides and crystallised fractionally from alcohol, giving first 4-*m*-nitrobenzoylpyridine hydrochloride (0·87 g., m. p. 245°; giving with ammonia the base, m. p. 129°), then the hydrochloride (0·9 g., m. p. 198°) of the para-isomeride, which gave with ammonia pure 4-*p*-nitrobenzoylpyridine (0·5 g., m. p. 121°). The final liquor was concentrated and basified, and the precipitate crystallised to constant m. p. from water; a substance (0·34 g.) of m. p. 75° was then obtained which is presumably 4-*o*-nitrobenzoylpyridine. The yields of nitration products isolated are thus para 70·2, meta 4·8%.

4-*p*-Nitrobenzylpyridine had m. p. 74° (T., 74°); its picrate, m. p. 168° (T., 167°). 4-*p*-Nitrobenzoylpyridine had m. p. 121° (T., 123°).

4-*m*-Nitrobenzoylpyridine crystallises from water in needles, m. p. 129° (corr.) (Found : C, 62·8; H, 3·9. $C_{12}H_8O_3N_2$ requires C, 63·2; H, 3·5%). On oxidation with potassium permanganate

it gave *m*-nitrobenzoic acid (m. p. 140°; mixed m. p. 140°) in 25% yield.

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