263. *Studies in the Indole Series. Part II. Derivatives of 2-Phenylindole.*

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Nitrous acid is shown to form with 2-phenylindole, not only the 3-oximino-compound, but also 3-nitro-2-phenylindole and a dinitroindole identical with that formed by the direct nitration of 2-phenylindole; the second nitro-group is shown to be in the 5-position. Attempts to prepare a trinitro-2-phenylindole were unsuccessful.

The properties of 3-nitroso-2-phenyl-1-methylindole have been further investigated. An easy method for preparing 2′- and 4′-nitrodeoxybenzoins has been obtained, and the reduction of these compounds studied. An improved method for the preparation of *p*-nitrobenzil is given.

Campbell and Cooper (J., 1935, 1208) suspected that, when an excess of nitrous acid acts upon 2-phenylindole, it not only forms the 3-oximino-compound but also oxidises the latter to the corresponding nitro-compound and effects nitration of the benzene ring. We have now shown that nitrous acid readily accomplishes the oxidation, and when in large excess it forms the dinitro-2-phenylindole first obtained by Angeli and Angelico (*Gazzetta*, 1900, **30**, 268), though their method of preparation is much superior. The m. p. of this dinitro-2-phenylindole was given as "above 280°," and no definite structure was assigned to it. We have obtained the compound in the pure state with a definite m. p. of 312°, and have proved it to be 3 : 5-dinitro-2-phenylindole (I) by oxidation with potassium permanganate in glacial acetic acid to *5-nitro-*N*-benzoylanthranilic acid*. This nitration of the benzene ring in position 5 is paralleled by the nitration of 2 : 3-dimethylindole (Bauer and Strauss, *Ber.*, 1932, **65**, 308; Plant and Tomlinson, J., 1933, 955). By analogy, the dinitro-2-methylindole of Walther and Clemen (*J. pr. Chem.*, 1900, **61**, 249) is probably the 3 : 5-dinitro-compound.

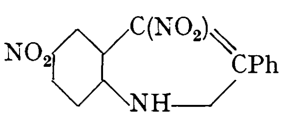
Since Mathur and Robinson (J., 1934, 1415) nitrated dinitro- to a trinitro-2-methylindole, we attempted to prepare trinitro-2-phenylindole by the same method. From the reaction mixture, however, only unchanged dinitro-2-phenylindole was obtained, whilst with stronger nitrating agents oxidation occurred, giving acidic compounds containing 5-nitro-*N*-benzoylanthranilic acid.

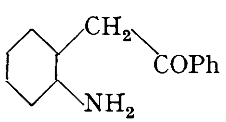
The properties of 3-nitroso-2-phenyl-1-methylindole have been further investigated. Although this is a true nitroso-compound, many of its properties are anomalous. All attempts to oxidise it to the corresponding nitro-compound failed. With alkaline permanganate, oxidation did occur, but the product was a colourless acid, and hence ring fission had taken place. It had been noted earlier that it did not condense with aniline (Campbell and Cooper, *loc. cit.*) : this work has been repeated with aniline, *p*-nitroaniline, and *p*-bromoaniline, but in all cases only the unchanged compound was obtained. Further, the nitroso-compound gave no colour with glacial acetic acid and diphenylamine (nitrosobenzene gives a pink coloration), formed no dye with hydroxylamine hydrochloride and α-naphthol, and liberated iodine from acidified aqueous-alcoholic potassium iodide much less readily than nitrosobenzene. Both in appearance and in some of its chemical properties, 3-nitroso-2-phenyl-1-methylindole resembles *p*-nitrosodimethylaniline rather than nitrosobenzene, for the former gives no colour with glacial acetic acid and diphenylamine, and liberates iodine from potassium iodide solution more slowly than does the latter.

With certain nitroso-compounds it is not possible to carry out the Liebermann reaction owing to sulphuric acid itself producing a coloration, and this also applies to the Angeli–Castellana reaction (*Atti R. Accad. Lincei*, 1905, **141**, 669), but the latter may be modified by using acetic acid instead of sulphuric acid. *C*-Nitroso-compounds such as nitrosobenzene give a pink coloration after a few minutes.

In the course of these investigations we have repeatedly attempted to prepare 2-phenylindole by the reduction of 2′-nitro- (so-called *o*-nitro-)deoxybenzoin with zinc dust and ammonia, as recorded by Pictet (*Ber.*, 1886, **19**, 1064) and List (*Ber.*, 1893, **26**, 2451), but no appreciable quantity of that compound could be isolated, the product being a crystalline compound of sharp m. p. which we believe to be *2′-aminodeoxybenzoin* (II).

(I.)





(II.)

The nitrodeoxybenzoin used by Pictet was a crude oily product (yield not quoted) which List showed to contain 25—30% of 2′-nitrodeoxybenzoin. We obtained the pure compound by nitrating deoxybenzoin with Menke's reagent (*Rec. Trav. chim.*, 1925, **44**, 141, 269), the resulting mixture of 2′- and 4′-isomers being easily separated into its constituents with ether. The reduction of both compounds yielded the corresponding aminodeoxybenzoins, though the 2′-compound afforded a trace of 2-phenylindole and in certain conditions larger quantities were obtained.

The formation of 2-phenylindole establishes the orientation of the 2′-amino-compound, and presumably the so-called *p*-isomer is the 4′-compound (Beilstein nomenclature). This was confirmed by the fact that 4′-nitrodeoxybenzoin, prepared as above, was identical with the nitrodeoxybenzoin prepared from *p*-nitrophenylacetyl chloride and benzene by the Friedel–Crafts reaction (Petrenko-Kritschenko, *Ber.*, 1892, **25**, 2242). The 4′-aminodeoxybenzoin was shown to be identical with that prepared by Golubew (*Ber.*, 1873, **6**, 1252) by reduction of *p*-nitrobenzil, though the mixed m. p. determination was not completely satisfactory, for the amino-compounds decompose on standing owing, possibly, to the condensation of the carbonyl group of one molecule with the amino-group of another.

We have improved Chattaway and Coulson's preparation of *p*-nitrobenzil (J., 1928, 1080).

EXPERIMENTAL.

The m. p.'s recorded were obtained with Kofler's micro-apparatus (" Mikroskopische Methoden in der Mikrochemie ") and calibrated thermometers. In agreement with his claims, the apparatus was found to be much more satisfactory than the ordinary capillary m. p. apparatus. Most of the analyses were done by Dr. Weiler, Oxford, and Mr. W. Brown, Edinburgh. 2-Phenylindole and 3-oximino-2-phenylindole were prepared by the procedure reported by Campbell and Cooper (*loc. cit.*).

Action of Nitrous Acid on 3-Oximino- and 3-Nitro-2-phenylindole.—The oximino-compound (1 g.) was suspended in boiling glacial acetic acid (15 c.c.) and treated with sodium nitrite (0·35 g.; 1 equiv.). The resulting precipitate crystallised from alcohol in yellow needles, and was shown by m. p. and mixed m. p. (236—238°, lit., 238°) to be 3-nitro-2-phenylindole; yield quantitative.

3-Nitro-2-phenylindole (2 g.), when treated in boiling glacial acetic acid with a large excess of sodium nitrite (5 g.), yielded a mixture of unchanged compound and a small amount (0·3 g.) of a yellow crystalline substance which was insoluble in alcohol and cold acetic acid and melted at 312° (decomp.). It was identified as 3 : 5-dinitro-2-phenylindole (I), and shown (mixed m. p.) to be identical with the dinitro-2-phenylindole prepared by Angeli and Angelico (*loc. cit.*). It was best prepared as follows. 2-Phenylindole (10 g.) was mixed with concentrated nitric acid (100 c.c.), and after a brisk reaction the dinitro-compound separated; it was purified by dissolution in dilute sodium hydroxide and precipitation with nitric acid, and crystallised in yellow plates (glacial acetic acid), m. p. 312°.

Oxidation of 3-Oximino-, 3-Nitro-, and 3 : 5-Dinitro-2-phenylindole.—Many oxidising agents were used, but the most satisfactory was potassium permanganate in glacial acetic acid. 3-Oximino- or 3-nitro-2-phenylindole (0·4 g.) was dissolved in glacial acetic acid and heated under reflux with powdered potassium permanganate (1 g.) for 3 hours, and the product poured into water. After decolorisation of the solution by sulphurous acid, a creamy precipitate of benzoylanthranilic acid was obtained, which was crystallised from alcohol, m. p. 179—181° (lit., 181°); yield 0·2 g. The compound was purified by dissolving it in dilute sodium hydroxide, removing any insoluble matter, and reprecipitating with dilute sulphuric acid. 3 : 5-Dinitro-2-phenylindole by the same treatment yielded 5-nitro-*N*-benzoylanthranilic acid, m. p. 257—258°, identical with an authentic specimen prepared as described below.

*5-Nitro-*N*-benzoylanthranilic Acid.*—5-Nitroanthranilic acid (Bogert and Scatchard, *J. Amer. Chem. Soc.*, 1919, **41**, 2066) could not be benzoylated in benzene by benzoyl chloride, but in pyridine *5-nitro-*N*-benzoylanthranil* was easily obtained, m. p. 178—180° (Found: C, 62·8; H, 3·3; N, 10·4. $C_{14}H_8O_4N_2$ requires C, 62·7; H, 3·0; N, 10·4%). By hydrolysis with boiling hydrochloric acid, *5-nitro-*N*-benzoylanthranilic acid* was obtained, m. p. 257—260° (Found: C, 59·3; H, 4·1; N, 9·6. $C_{14}H_{10}O_5N_2$ requires C, 58·8; H, 3·5; N, 9·8%).

Attempted Nitration of 3 : 5-Dinitro-2-phenylindole.—3 : 5-Dinitro-2-phenylindole (2 g.) was boiled with concentrated nitric acid (10 c.c.) for 15 minutes, and the solution cooled. The colourless solid so obtained was obviously a mixture, but after several crystallisations from aqueous alcohol a small amount of 5-nitro-*N*-benzoylanthranilic acid was obtained.

Nitration of Deoxybenzoin.—Deoxybenzoin (10 g.) was dissolved in acetic anhydride (50 c.c.), and cupric nitrate (15 g.) added slowly, the mixture being continuously stirred and the temperature maintained at 25—30°. The mixture was then kept for an hour at room temperature, and poured into water (300 c.c.). The resulting solid (10 g.) was extracted with cold ether (100 c.c.), the 2′-compound dissolving and the 4′-isomer remaining. The nitro-compounds were purified by crystallisation first from benzene–light petroleum (b. p. 60—80°) (1 : 1), and then from alcohol: 2′-compound, m. p. 72—74° (lit., 73—74°), yield 6 g.; 4′-compound, m. p. 138—140° (lit., 141—142°), yield 2 g. Quantities up to 35 g. of deoxybenzoin have been nitrated by this method, but the temperature must be maintained between 25° and 30°: below 25° nitration does not occur, and above 30° oxidation to benzils takes place. Both compounds were identified by oxidation to the corresponding nitrobenzoic acids, and by their oximes and dinitrophenylhydrazones. *2′-Nitrodeoxybenzoin-2 : 4-dinitrophenylhydrazone*, prepared by Brady's method (J., 1931, 756), was obtained in orange prisms (from tetralin), m. p. 219—221° (Found: N, 16·5. $C_{20}H_{15}O_6N_5$ requires N, 16·6%), and the *4′-isomeride* was similarly obtained as orange-red prisms, m. p. 233—234° (Found: N, 17·0%). 4′-Nitrodeoxybenzoin was shown to be identical with the compound prepared as below.

Preparation of 4′-Nitrodeoxybenzoin.—Petrenko-Kritschenko's method (*loc. cit.*) was used with the following modifications. After the brisk reaction with aluminium chloride, the mixture was heated on the water-bath for an hour and then poured on ice and concentrated hydrochloric acid. The benzene layer was separated, more benzene being added if necessary to dissolve any remaining solid, and the solution was heated for an hour under reflux with good animal charcoal. The solution was filtered, an equal volume of light petroleum (b. p. 60—80°) added, and the mixture kept for 2 hours. The resulting precipitate was crystallised repeatedly from alcohol (charcoal); m. p. 141—142°, yield poor.

Reduction of 2′- and 4′-Nitrodeoxybenzoins.—In our hands the method of Pictet (*loc. cit.*) and List (*loc. cit.*) afforded a dark tarry product, which gave a definite pine-splint reaction but yielded only a very small amount of 2-phenylindole by tedious treatment with ligroin. A more satisfactory result was obtained when 2′-nitrodeoxybenzoin (5 g.) was treated with excess zinc dust in concentrated ammonia (25 c.c.). After reduction was complete, the mixture was filtered, and on neutralisation with dilute sulphuric acid yielded yellow crystalline *2′-aminodeoxybenzoin* (II) (3 g.), which after crystallisation from alcohol melted at 170° (Found: C, 80·7; H, 5·2; N, 6·7. $C_{14}H_{13}ON$ requires C, 80·0; H, 6·2; N, 6·6%). The compound dissolved in hydrochloric acid, and decomposed on standing; a solution in acetic anhydride, after being kept at room temperature for several days, gave the pine-splint test, but no 2-phenylindole could be isolated. 4′-Nitrodeoxybenzoin, when reduced in a similar manner, gave 4′-aminodeoxybenzoin, m. p. 94—96° (lit., 95—96°), identical with the amine formed in very poor yields by reduction of *p*-nitrobenzil (Golubew, *loc. cit.*). Attempts to prepare picrates and acetyl and benzoyl derivatives of the amines were unsuccessful.

2-Phenylindole (1 g.) was obtained by reducing 2′-nitrodeoxybenzoin (6 g.) with zinc dust and glacial acetic acid, 4 g. of the nitro-compound being recovered unchanged.

Preparation of p-*Nitrobenzil.*—Pure benzoin (200 g.) was suspended in acetic anhydride (1000 c.c.), and the mixture cooled in ice. Concentrated sulphuric acid (200 c.c.) was added, and the mixture stirred and cooled to 0°. Potassium nitrate (110 g.) was added in small quantities, and the mixture then kept for 2 days at room temperature before being poured into water. The oil which separated was washed with water, extracted with ether, and the ether evaporated, leaving an oil which soon solidified and was crystallised twice from alcohol or acetone; m. p. 127—128° (lit., 125°), yield 60%. The compound was shown to be identical with the acetyl derivative of *p*-nitrobenzoin obtained by Francis and Keene (J., 1911, **99**, 344). *p*-Nitrobenzil was obtained by heating the acetyl compound (5 g.) with concentrated nitric acid (14 c.c.) on the water-bath for 1 hour and pouring the solution into water. The resulting precipitate was crystallised three times from glacial acetic acid; m. p. 142° (lit., 142°), yield 4 g.

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