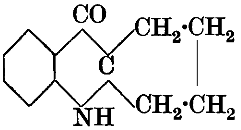
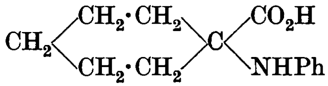
CLXXXIII.—*The Reactions of* 1-*Anilino*cyclo*hexane*-1-*carboxylic Acid. Synthesis of ψ-Indoxyl*spirocyclo*hexane.*

By RAYMOND LIVINGSTON BETTS, RUDOLPH MUSPRATT, and SYDNEY GLENN PRESTON PLANT.

IT was shown by Plant and Facer (J., 1925, **127**, 2037) that the fusion of 1-anilino*cyclo*pentane-1-carboxylic acid with a mixture of potassium hydroxide and sodium ethoxide, under conditions similar to those used by Bucherer and Grolée (*Ber.*, 1906, **39**, 986) for the preparation of 2 : 2-dimethyl-ψ-indoxyl from α-anilino*iso*butyric acid, yielded carbazole and not the expected ψ-indoxyl*spirocyclo*pentane (I). We have now prepared 1-*anilino*cyclo*hexane*-1-*carboxylic acid* (II) by the hydrolysis, first to the *amide*, of 1-anilino-1-cyano*cyclo*hexane, described by Walther and Hübner (*J. pr. Chem.*, 1916, **93**, 124), and we find that this compound differs fundamentally in some of its reactions from the corresponding derivative of *cyclo*pentane. When heated with potassium hydroxide, it gave *ψ-indoxyl*spirocyclo*hexane* (III) in comparatively good yield. ψ-Indoxyl*spirocyclo*pentane has been obtained by a series of reactions from tetrahydrocarbazole (Perkin and Plant, J., 1923, **123**, 676) and, owing to the fact that it gives a number of interesting derivatives, including co-ordinated compounds of the alkali metals (Sidgwick and Plant, J., 1925, **127**, 209), it was hoped to obtain confirmatory evidence for its structure by synthesis from 1-anilino*cyclo*pentane-1-carboxylic acid by the method mentioned above. Although this led to other results, we now find that the reactions of ψ-indoxyl*spirocyclo*hexane are so similar to those observed with ψ-indoxyl*spirocyclo*pentane that they amply confirm the structure assigned to the latter compound. ψ-Indoxyl*spirocyclo*hexane can be acetylated, and is easily nitrated by dilute nitric acid to give 10-*nitro-ψ-indoxyl*spirocyclo*hexane* (IV), which gives a character-

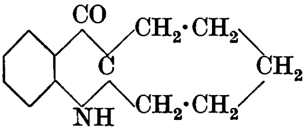
(I.)



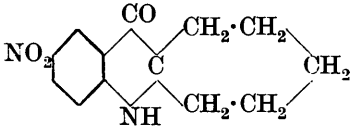


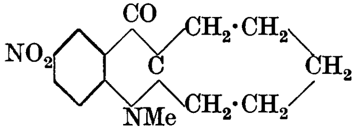
(II.)

(III.)



istic sodium derivative, from which 10-*nitro*-7-*methyl*-ψ-*indoxyl*spirocyclo*hexane* (V) can readily be obtained. The conditions required for these reactions and the characteristic properties of the products are exactly those observed in the corresponding *cyclo*pentane series. Like ψ-indoxyl*spirocyclo*pentane, ψ-indoxyl*spirocyclo*hexane could not be made to give a nitroso-derivative or a semicarbazone. The behaviour of these two compounds towards sodium hydroxide is fundamentally similar. Only on heating with concentrated aqueous sodium hydroxide is a metallic derivative obtained, and, in both cases, water instantaneously brings about hydrolysis of the product, but whilst the sodium derivative of ψ-indoxyl*spirocyclo*pentane can be obtained with a second molecule of ψ-indoxyl*spirocyclo*pentane attached to it by co-ordinate links, similar conditions gave only the simple sodium salt of ψ-indoxyl*spirocyclo*hexane. There is here no fundamental difference between the two compounds, since the isolation of these co-ordinated compounds in this series must depend upon a number of arbitrary factors, such as the melting point.


(IV.)


(V.)

It has been shown (Plant and Facer, *loc. cit.*) that 1-anilino*cyclo*pentane-1-carboxylic acid, on heating, loses aniline and water to give the lactone of 1-1′-hydroxy*cyclo*pentane-1′-carboxylylanilino*cyclo*pentane-1-carboxylic acid. 1-Anilino*cyclo*hexane-1-carboxylic acid does not appear to undergo this reaction, but breaks up into aniline and Δ^1-*cyclo*hexene-1-carboxylic acid.

EXPERIMENTAL.

1-*Anilino*cyclo*hexane*-1-*carboxylic Acid* (II).—1-Anilino-1-cyano*cyclo*hexane was prepared by Walther and Hübner's method (*loc. cit.*). The *nitrosoamine* separated when its solution in alcohol containing hydrochloric acid was treated with concentrated aqueous sodium nitrite, and, after recrystallisation from methyl alcohol, it was obtained in pale yellow prisms, m. p. 70°. When a solution of 1-anilino-1-cyano*cyclo*hexane in concentrated sulphuric acid was kept for 2 days at room temperature and then poured on ice, and the mixture was made alkaline with ammonia, 1-*anilino*cyclo*hexane*-1-*carboxylamide* separated quantitatively in a pure condition. It crystallised from dilute alcohol in colourless plates, m. p. 148°

(Found: N, 12·4. $C_{13}H_{18}ON_2$ requires N, 12·8%). The *nitroso-amine* separated from methyl alcohol in pale yellow prisms, m. p. 172°. This amide was comparatively stable and hydrolysis to the corresponding acid was complete only after prolonged boiling with hydrochloric acid. On rubbing with concentrated hydrochloric acid, the *hydrochloride* of the amide separated; a paste of this was added to an excess of hydrochloric acid, and the mixture was boiled under reflux with continuous stirring for 12 hours and then evaporated to dryness. The residue was heated with an excess of dilute aqueous sodium hydroxide, and the solution was filtered and acidified with glacial acetic acid; 1-*anilino*cyclo*hexane*-1-*carboxylic acid* then separated. After recrystallisation from alcohol, it was obtained in colourless prisms, m. p. 142° (Found: N, 6·2. $C_{13}H_{17}O_2N$ requires N, 6·3%).

1-Anilino*cyclo*hexane-1-carboxylic acid was heated in a distillation flask, and the oily distillate treated with an excess of dilute hydrochloric acid; the undissolved portion then soon solidified. This product melted at 29—31° and was identified as Δ^1-*cyclo*hexene-1-carboxylic acid (compare Aschan, *Annalen*, 1892, **271**, 267). It was readily soluble in dilute aqueous sodium carbonate, from which it was reprecipitated by the addition of hydrochloric acid. Its solution in chloroform, after addition of the calculated amount of bromine, was kept for 2 hours, the solvent removed by evaporation, and the residue recrystallised from benzene–petroleum, from which 1 : 2-dibromo*cyclo*hexane-1-carboxylic acid separated in colourless prisms, m. p. 144° (compare Aschan, *loc. cit.*). That portion of the distillate which dissolved in dilute hydrochloric acid was identified as aniline by conversion into acetanilide.

*ψ-Indoxyl*spirocyclo*hexane* (III).—A mixture of 1-anilino*cyclo*hexane-1-carboxylic acid (35 g.) and potassium hydroxide (90 g.) was heated to 340—350°, maintained at that temperature for ½ hour, allowed to cool, and treated with an excess of water. The insoluble portion was ground with water and dried in a desiccator over sulphuric acid. The crude product (14 g., melting indefinitely at about 80°) was distilled; the yellow, oily distillate solidified on rubbing with petroleum. After recrystallisation from petroleum, the product (m. p. 110—117°) was further purified by boiling it with acetic anhydride (50 c.c.) for an hour, cooling the solution and shaking it with an excess of water, and recrystallising the 7-*acetyl-ψ-indoxyl*spirocyclo*hexane* so obtained from methyl alcohol, from which it separated in large, colourless prisms (6 g.), m. p. 105° (Found: N, 5·7. $C_{15}H_{17}O_2N$ requires N, 5·7%). A solution of the acetyl derivative in alcohol (90 c.c.) and water (60 c.c.), containing potassium hydroxide (18 g.), was boiled for ½ hour and thereafter diluted with water; *ψ-indoxyl*spiro*cyclohexane* (4 g.) then separated in a pure condition. It can be crystallised from petroleum and obtained in colourless prisms, m. p. 124° (Found: C, 77·8; H, 7·5; N, 6·8. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·4; N, 7·0%).

ψ-Indoxyl*spirocyclo*hexane is not altered, even on boiling, by dilute hydrochloric acid or dilute sodium hydroxide solution. When heated in a steel tube at 200—210° with an excess of 20% aqueous sodium hydroxide, it was converted into a *sodium* derivative, which could be removed by filtration through asbestos. The sodium derivative (Found: Na, 9·7. $C_{13}H_{14}ONNa$ requires Na, 10·3%) did not melt up to 350° and was immediately hydrolysed, on grinding with water, to give ψ-indoxyl*spirocyclo*hexane. On warming with dry benzene or toluene, the substance dissolved almost completely, and on filtering and cooling the solution ψ-indoxyl*spirocyclo*hexane separated—which seems to indicate that combined water is present in the sodium derivative.

When a solution of ψ-indoxyl*spirocyclo*hexane in alcohol was treated with a few drops of concentrated hydrochloric acid and a few drops of a concentrated solution of sodium nitrite, kept for 15 minutes, and then diluted with water, the substance was recovered completely unchanged. The substance was also recovered unchanged from attempts to make a semicarbazone.

When ψ-indoxyl*spirocyclo*hexane (3 g.) was heated with a mixture of nitric acid (30 c.c. of *d* 1·4) and water (120 c.c.), the liquid at first became green and a dark green oil separated. The colour rapidly changed to yellow and, after boiling for 3 minutes, the mixture was cooled and the solid recrystallised from dilute alcohol, from which 10-*nitro-ψ-indoxyl*spirocyclo*hexane* separated in pink prisms, m. p. 177—178° (Found: N, 11·3. $C_{13}H_{14}O_3N_2$ requires N, 11·4%). 10-Nitro-ψ-indoxyl*spirocyclo*hexane is soluble in very dilute aqueous sodium hydroxide to give a deep yellow solution, but from more concentrated solutions the sodium salt separates as a yellow solid, which may be dissolved by warming. When an excess of methyl sulphate was shaken with the warm solution in aqueous sodium hydroxide, a yellow product immediately separated, and, after recrystallisation from dilute alcohol, 10-*nitro*-7-*methyl-ψ-indoxyl*spirocyclo*hexane* was obtained in yellow plates, m. p. 129° (Found: N, 10·9. $C_{14}H_{16}O_3N_2$ requires N, 10·8%). No methyl iodide was obtained on heating the substance with hydriodic acid under the usual conditions of a Zeisel experiment, so it is evident that the methyl group is attached to nitrogen and is not present as methoxyl.

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THE DYSON PERRINS LABORATORY,
OXFORD.

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