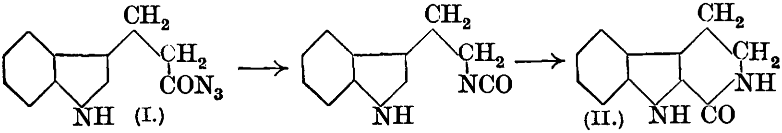
XXXVII.—*The Decomposition of β-3-Indolylpropionic Azide.*

By Richard Helmuth Fred Manske and Robert Robinson.

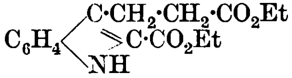
In a recent synthesis of harmaline (Manske, Perkin, and Robinson, this vol., p. 1) advantage was taken of the Japp-Klingemann reaction for the preparation of arylhydrazones of certain α-diketones and α-keto-acids. In continuation of the work, an attempt was made to obtain 3-β-aminoethylindole by applying the Curtius reaction to β-3-indolylpropionic acid. A remarkably satisfactory method of preparation of this acid was devised, but the same process has quite recently (*Ber.*, 1926, **59**, 1858) been placed on record by Kalb, Schweitzer, and Schimpf, so that a detailed description is unnecessary; the chief variations are mentioned in the experimental section. Methyl β-3-indolylpropionate was converted in the normal manner into the related hydrazide and azide (I). The nature of the products obtained on the decomposition of the latter substance varies with the conditions, and in benzene solution, in presence of hydrogen chloride, the carbimide, which is doubtless initially formed, undergoes intramolecular condensation with the formation of 3-keto-3 : 4 : 5 : 6-tetrahydro-4-carboline (II). The constitution of the product is proved by the fact that on distillation with zinc dust in a stream of hydrogen



it gives a small amount of norharman along with indole. The reaction involved is analogous to that occurring in the formation of *iso*quinoline by dehydration of cinnamaldoxime.

EXPERIMENTAL.

Ethyl β-2-*Carbethoxy*-3-*indolylpropionate*,



$$C_6H_4\left\langle\begin{array}{l}C\cdot CH_2\cdot CH_2\cdot CO_2Et\\ \quad\gtrdot C\cdot CO_2Et\\ NH\end{array}\right.$$

—The following process gives excellent results, but it is essential to avoid needless delays. A benzenediazonium chloride solution is prepared from aniline (38 g.), concentrated hydrochloric acid (100 c.c.), sodium nitrite (28 g.), and ice (200 g.); potassium hydroxide (48 g.) is dissolved in water (600 c.c.). One-half of the latter solution is shaken in a separator with ethyl *cyclo*pentanonecarboxylate (63 g.) and a small volume of undissolved oil is taken up in benzene. The aqueous layer is added to crushed ice (400 g.), and the benzene layer shaken with the remainder of the alkali. About half the diazo-solution is then added to the solution of the ester and after a minute the remainder of the alkali is introduced from the tap funnel, followed by the second half of the diazo-solution. After 5 minutes, the solution is acidified with concentrated hydrochloric acid (100 c.c.) and the precipitated mass is washed by decantation and dried. This crude phenylhydrazone of ethyl hydrogen α-ketoadipate (55·6 g.) is refluxed with 98% alcohol (156 c.c.) and concentrated sulphuric acid (40 g.) for 2·5 hours. On addition of water, cooling, and washing with sodium hydrogen carbonate solution, the product is obtained in a granular form. It is dried and purified by distillation in a high vacuum; b. p. 212°/2 mm. (yield, 43 g.; m. p. 94°). The ester crystallises from benzene in large, colourless prisms, m. p. 95—96°. The results of elementary analysis of this ester, the dicarboxylic acid obtained on hydrolysis, and the indolepropionic acid derived by heating the dibasic acid were in satisfactory agreement with theory. *Methyl* β-3-*indolylpropionate* crystallises from methyl alcohol in prisms, m. p. 79—80° (Found: N, 7·1. $C_{12}H_{13}O_2N$ requires N, 6·9%).

β-3-*Indolylpropionhydrazide*, $C_6H_4{:}C_2H_2N\cdot C_2H_4\cdot CO\cdot N_2H_3$, was prepared by the interaction of the methyl ester (40 g.) and hydrazine hydrate (15 g.) (oil-bath at 140°); the product (yield, 39 g.) crystallised from alcohol in colourless, hexagonal prisms or tablets, m. p. 129—130° (Found: N, 19·9, 20·4. $C_{11}H_{13}ON_3$ requires N, 20·8%). This hydrazide is sparingly soluble in cold alcohol and moderately readily soluble in hot water.

3-*Keto*-3 : 4 : 5 : 6-*tetrahydro*-4-*carboline* (II).—Crushed ice (200 g.) was added to a solution of β-3-indolylpropionhydrazide (10 g.) in acetic acid (50 c.c.), and sodium nitrite (4 g.) dissolved in a little water was then introduced. The liquid became milky, and in a few minutes pasty, owing to the separation of the crystalline azide (I). This was collected, washed with water, and drained as far as possible; it was then gradually added to boiling benzene (75 c.c.). Nitrogen was evolved and when this stage was completed a stream of hydrogen chloride was led through the hot solution. The benzene was finally distilled, and the residue washed with dilute hydrochloric acid. The substance (yield, 6—7 g.) crystallises from alcohol (charcoal) in characteristic, colourless, spear-head-shaped, microscopic prisms, m. p. 173—174° (Found: C, 71·1; H, 5·4; N, 15·1. $C_{11}H_{10}ON_2$ requires C, 70·9; H, 5·4; N, 15·0%). This cyclic amide is sparingly soluble in cold alcohol or ether and is readily soluble in hot alcohol. It dissolves in warm concentrated hydrochloric acid, but is precipitated on the addition of water; no indole colour reactions are exhibited. On distillation with zinc dust in a stream of hydrogen the chief product was a neutral compound having the properties of indole, but by extraction of the distillate with dilute hydrochloric acid a small quantity of norharman was obtained. The base was recognised by its appearance and m. p. (198°), and by the blue fluorescence of its aqueous acid solutions.

THE UNIVERSITY, MANCHESTER. [*Received, December 10th,* 1926.]