of methanol containing 1 ml. of concd. sulfuric acid was added with good agitation to avoid any rise of temperature. The insoluble picrolonic acid was filtered. The methanolic solution of the base was cooled to 0°, and 150 mg. of sodium nitrite, dissolved in 10 ml. of methanol, was slowly added. After leaving overnight at 5°, 300 mg. of catalytic copper powder were added when a fast evolution of nitrogen took place. After 1 hr. the suspension was boiled for 30 min., the copper filtered, one volume of water added, and the acidic solution extracted with ether, the extract being discarded. It was then made alkaline with concd. ammonia and extracted again with ether until a negative Mayer reaction was obtained.

The ether extract containing the basic substances was evaporated, and the well dried residue (355 mg.) was dissolved in the minimum amount of benzene and submitted to chromatography on a column of 23 g. of alumina (Woelm, grade III). The elution was carried out with benzene containing increasing amounts of ethanol. With benzene–0.2% ethanol, the initial fractions eluted contained a substance giving a positive alkaloid reaction, with R_f 0.59 and a green fluorescence in the ultraviolet. In the medium fractions another basic product with R_f 0.32 and violet fluorescence was detected, and in the last fractions, a substance also with R_f 0.32 but with a pale blue fluorescence was present. By increasing the concentration of ethanol to 0.4% and then to 1%, elution of the same substances went on, until another one with R_f 0.07 and green fluorescence appeared in the last collected fractions.

Only the fractions containing the products with R_f 0.32 and a violet fluorescence and with R_f 0.07 were worked, as a preliminary hydrolysis with acid showed on paper chromatography that they were related to (±)-isocorydine and (±)-laudanidine.

(±)-*Isocorydine hydrochloride.* Evaporation of the fractions containing the product with R_f 0.32 with violet fluorescence yielded 13 mg. of a crude product, that was boiled for 40 min. with 1 ml. of 20% hydrochloric acid. After cooling, the solution was extracted with ethyl ether, made basic with ammonia, and extracted again with ether. The ether extract gave on evaporation an oily residue of 7.5 mg. Seventy-five milligrams of this crude residue, obtained from several preparations totaling 10 g. of the picrolonate, was dissolved in benzene and chromatographed employing a column of 8 g. of alumina. After washing the column with benzene, it was eluted with benzene–0.1% ethanol. All fractions containing the substance giving R_f 0.32 and violet fluorescence were united and evaporated. The dried residue (35 mg.) was dissolved in absolute ether and hydrogen chloride passed through the solution. A white solid precipitated, that was centrifuged, dried, dissolved in warm absolute ethanol, and ether added to turbidity. By staying at 0° overnight, crystals were formed that were collected had a m.p. 211–212° (35 mg.).

Recrystallization from absolute ethanol–ether, gave small prisms, m.p. 211–212° (Vacuum) λ_{max} 220 mμ (log ε 4.65); 267 mμ (4.18); 303 mμ (3.81). The ultraviolet spectrum and the usual color reactions were identical to those obtained with (−)-isocorydine hydrochloride, m.p. 215–218°.

Anal. Calcd. for $C_{20}H_{23}NO_4 \cdot HCl$: C, 63.57; H, 6.40; N, 3.71; Cl, 9.39. Found: C, 63.69; H, 6.46; N, 3.61; Cl, 9.67.

(±)-*Isocorydine* (II). A solution of 30 mg. of the former hydrochloride in 2 ml. of water was made alkaline with sodium hydrogen carbonate solution and extracted with ether, until the Mayer reaction was negative. The ethereal extract was well dried, and the ether evaporated off. The oily residue crystallized when a small amount of absolute ether was added. After recrystallization from acetone–absolute ether, a m.p. of 150–152° was obtained; λ_{max} 267 mμ (log ε 4.10), 302 mμ (3.58) (Ethanol) [identical with the ultraviolet spectrum of a sample of natural (±)-isocorydine]. The infrared spectra in chloroform were also identical except for a shoulder at 8.25 μ in the spectrum of the racemic compound. The m.p. of (±)-isocorydine is in agreement with that given by Kikkawa (m.p. 151–152°). Go[5] gave a m.p. 185° for a (±)-isocorydine that he prepared by racemization of the natural base.

(±) *Laudanidine* (*Laudanine*) (V). The fractions containing the substance with R_f 0.07 were united and evaporated giving 130 mg. of an oily residue that was boiled for 40 min. with 10 ml. of 20% hydrochloric acid. The acidic solution was extracted with ether, made alkaline with ammonia, and exhaustively extracted with ether. This ethereal solution was evaporated and the residue (51 mg.) dissolved in 0.5 methanol. By staying at 5° (±)-laudanidine crystallized; that recrystallized from methanol gave 7 mg. of prisms m.p. 164–165°, λ_{max} 284 mμ (log ε 3.78) giving no depression in m.p. with an authentic sample of (±)-laudanidine (m.p. 163–164°).

When the eluted fractions containing the substance with R_f 0.07 from several preparations representing in total 10 g. of picrolonate were worked as described, 90 mg. of (±)-laudanidine, m.p. 163–165°, were obtained.

Acknowledgment. We thank Dr. R. H. F. Manske, Gelph, Ontario, for a sample of (±)-isocorydine, Dr. P. A. Plattner, Hoffmann-La Roche, Bassel, for a generous gift of isovanilline, and to Mr. J. F. Alicino and Dr. N. H. Coy, the Squibb Institute for Medical Research, New Brunswick, N. J., for the microanalysis and the infrared spectra.

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Reactions of 1-Diazo-3-(*o*-nitrophenyl)-acetone[1]

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Received July 27, 1961

The reaction of *o*-nitro-ω-diazoacetophenone (I) with glacial acetic acid involves ring closure, with formation of *N*-hydroxyisatin (IV).[2] There appears to be no direct evidence for the mechanism of this interesting transformation, but it seems likely that the initial stage is cyclization to a six-membered intermediate (II) which is followed by deprotonation and cleavage to *o*-nitrosophenylglyoxal (III) and finally recyclization to IV. With this possible path in mind the similar treatment of 1-diazo-3-(*o*-nitrophenyl)acetone (V) with acetic acid was examined to see whether a corresponding ring closure to 1,3-dihydroxycarbostyril (VI) would occur, presumably *via* a seven-membered intermediate.

The diazo ketone was prepared in the usual way from *o*-nitrophenylacetyl chloride. This acid chlo-

(1) This work was supported by contract DA 18-108-405-CML-654 with the U. S. Army Chemical Research and Development Command.

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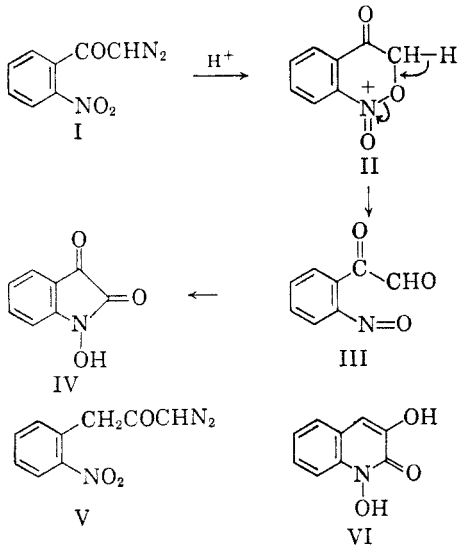

ride has been prepared in impure form by treatment of the acid with phosphorus pentachloride,[3] but it cannot be distilled, and the dark crude product obtained with either phosphorus pentachloride or thionyl chloride gave only dark tar on treatment with diazomethane. On refluxing the acid with oxalyl chloride in ether solution, followed by evaporation and treatment with diazomethane, a crystalline product was obtained in 30% yield based on the acid. This material was shown to be the diazoketone V by reduction with hydriodic acid to *o*-nitrophenylacetone[3b]; this sequence offers a convenient alternative preparation for the latter compound.

The only product isolated from the reaction of V in acetic acid was the normal acetoxymethyl *o*-nitrobenzyl ketone, which after hydrolysis gave positive Tollens and periodate tests. The chloromethyl ketone was obtained in high yield with methanolic hydrochloric acid. There was no evidence in either case of the formation of the hydroxycarbostyril. This finding lends support to the mechanism I → IV suggested for the reaction of the lower homolog, as there are numerous examples[4] of the cyclization of *o*-substituted nitrobenzenes at the γ-carbon atom of the side chain to give 1-hydroxyquinoline derivatives such as VI. If, therefore, the conversion of I to IV occurred by any process involving the direct closure of the N—C-2 bond in IV rather than the intermediate formation of II, the reaction of V would be expected to follow an analogous course to give VI.

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EXPERIMENTAL

1-Diazo-3-(o-nitrophenyl)acetone (V). A solution of 10 g. of *o*-nitrophenyl acetic acid and 14 ml. of oxalyl chloride in 100 ml. of ether was refluxed for 14 hr., filtered to remove a trace of solid, and concentrated. The residue was dissolved in benzene and evaporated *in vacuo*. The resulting orange oil was dissolved in ether and added to a solution of 0.16 moles of diazomethane in 400 ml. of ether. After standing overnight the solution was filtered and evaporated *in vacuo*. The yellow crystals of V which separated on cooling were collected, 3.2 g., m.p. 51–52°. Recrystallization from ether gave bright yellow prisms, m.p. 52°, λ_{KBr} 4.64, 6.12 μ.

Anal. Calcd. for $C_9H_7O_3N_3$: C, 52.68; H, 3.44; N, 20.48. Found: C, 52.64; H, 3.00; N, 20.51.

A solution of 200 mg. of the product in 50 ml. of chloroform was swirled for a few minutes with 10 ml. of 57% hydriodic acid. The deep violet chloroform solution was then washed with saturated potassium iodide solution followed by several portions of 1*N*. sodium thiosulfate solution and then water. The resulting colorless chloroform solution was then evaporated to a thick syrup which crystallized on cooling to 20°. This material was treated with semicarbazide in the usual way to give nearly colorless crystals of the semicarbazone, m.p. 211–212°, 198 mg. (82%) (reported for *o*-nitrophenylacetone[3b]: m.p. 26–27°; semicarbazone, m.p. 213–214°).

1-Acetoxy-3-(o-nitrophenyl)acetone. A solution of 200 mg. of the diazo ketone V in 0.6 ml. of glacial acetic acid was warmed to 90° for 10 min. (until gas evolution had ceased). The solution was then evaporated and the crystalline residue was recrystallized from ether to give 120 mg. of nearly colorless crystals, m.p. 67–68°; infrared (KBr): 5.85–5.9 μ (broad, fused carbonyl peaks), 6.62 μ (NO_2).

Anal. Calcd. for $C_{11}H_{11}O_6N$: C, 55.69; H, 4.67; N, 5.91. Found: C, 55.71; H, 4.71; N, 6.20.

1-Chloro-3-(o-nitrophenyl)acetone. A solution of 200 mg. of V in methanol was treated with three drops of conc. hydrochloric acid. After gas evolution had ceased the solution was evaporated and the crystalline residue was recrystallized from methanol to give glistening white laths; 182 mg., m.p. 97–98°.

Anal. Calcd. for $C_9H_8O_3NCl$: C, 50.60; H, 3.77. Found: C, 50.81; H, 3.83.

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