TABLE I

PROPERTIES OF CARBINOLS AND HYDROCARBONS

Substance	M. p., °C.	Empirical formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
XVI, R = C_6H_5	233–234 d.[a]	$C_{39}H_{30}O$	91.1	5.8	91.0	5.9
XVII, R = CH_3	180[c]	$C_{34}H_{26}$	94.0	6.0	93.6	6.0
XVII, R = C_6H_5	227[a]	$C_{39}H_{28}$	94.4	5.6	94.1	5.6
XVII, R = α-$C_{10}H_7$	244[b]	$C_{43}H_{30}$	94.5	5.5	94.2	5.6
XVIII	159[c]	$C_{45}H_{34}O_2$	89.1	5.6	88.9	5.7

[a] Prisms. [b] Needles. [c] Tiny rods.

2-benzoyl-4,5-diphenylbenzoic acid VIII[8] with phenylmagnesium bromide, decomposing the complex with ammonium chloride, and recrystallizing from acetic acid. It forms rods; m. p. 180°.

Anal. Calcd. for $C_{32}H_{22}O_2$: C, 87.7; H, 5.0. Found: C, 87.7; H, 4.9.

(b) **From the Acid X.**—An intimate mixture of 15 g. of the acid and 2 g. of copper carbonate was heated at 260–265° for a half hour, and the cooled melt extracted with hot benzene; it was filtered from metallic copper and diluted with ligroin. The lactone was deposited in a yield of 20%. From the filtrate 3,4-diphenylbenzhydrylbenzene XI crystallized in a 30% yield. It forms needles and rods from acetic acid, m. p. 143°.

Anal. Calcd. for $C_{31}H_{24}$: C, 93.9; H, 6.1. Found: C, 93.9; H, 6.0.

The hydrocarbon XI was also synthesized from 3,4-diphenylbenzophenone and phenylmagnesium bromide; the oily carbinol was reduced by zinc and acetic acid.

The lactone is unaffected by bromine, acetyl chloride and chromic acid. It is reduced to the acid X by zinc and acetic acid.

2-Bromo-3,3,5,6-tetraphenylindenone, XV, was obtained when the dibromoketone XIV[1] was treated with excess phenylmagnesium bromide in the usual manner. It separates in needles from benzene, m. p. 240°. The yield was 60%. Repetition of the treatment on this bromoketone gave the indanone II.

Anal. Calcd. for $C_{33}H_{23}OBr$: C, 76.9; H, 4.5; Br, 15.5. Found: C, 76.7; H, 4.4; Br, 15.4.

The carbinols, XVI, were secured by the usual procedure, decomposing the organometallic complex with ammonium chloride. The corresponding hydrocarbons XVII were produced by refluxing 4 g. of the carbinols in 50 cc. of 2% sulfuric acid in acetic acid for a half hour. Their properties are collected in Table I.

The glycol, 1,2,3,3,5,6-hexaphenylindandiol-1,2, XVIII, was prepared from the diketone IX and an excess of phenylmagnesium bromide in butyl ether for six hours at 100°.

Summary

The bimolecular product, formed by the action of acidic dehydrating agents on anhydracetonebenzil, forms a peroxide, upon treatment with alkaline hydrogen peroxide. This substance loses its oxygen and gives an isomer in acetic acid solution. The isomer affords a previously described indanone on decarbonylation.

The indanone has been degraded to known products, the syntheses of two of which are described. It has also been converted into a carbinol and hydrocarbon isomeric with some closely related substances.

ROCHESTER, N. Y. RECEIVED JULY 6, 1942

(8) Allen, A. C. Bell, A. Bell and VanAllan, THIS JOURNAL, **62**, 656 (1940).

[CONTRIBUTION FROM THE NICHOLS CHEMISTRY LABORATORY OF NEW YORK UNIVERSITY]

Deamination of 5-Amino-8-nitroisoquinoline[1]

BY BERTRAM KEILIN AND W. E. CASS[2]

In an attempt to prepare 8-nitroisoquinoline, 5-acetylaminoisoquinoline[3] was nitrated and the resulting acetylaminonitroisoquinoline hydrolyzed to an aminonitroisoquinoline. When the aminonitroisoquinoline was diazotized in hydrochloric acid solution and treated with hypophosphorous acid,[4] there was obtained 8-chloroisoquinoline, identified by analysis and by comparison with a known sample of 8-chloroisoquinoline.[5]

In the preceding diazotization-deamination, the nitro group was displaced by chlorine, nitrous acid being evolved. This displacement of the nitro group possibly occurred during diazotization,

(1) Constructed, in part, from the B.A. research paper of Bertram Keilin, New York University, University College, 1942.

(2) Present address: Research Laboratory, General Electric Company, Schenectady, New York.

(3) Craig and Cass, THIS JOURNAL, **64**, 783 (1942).

(4) Adams and Kornblum, *ibid.*, **63**, 188 (1941).

(5) Pomeranz, *Monatsh.*, **18**, 1 (1897), prepared, but did not analyze, 8-chloroisoquinoline by ring closure of *o*-chlorobenzalaminoacetal.

because it was noted that an excess of nitrous acid was always present in the diazotized solution, even when less than the theoretical amount of sodium nitrite had been added. Since the replacement of the nitro group by chlorine resulted in the formation of 8-chloroisoquinoline, the structure, 5-amino-8-nitroisoquinoline, was assigned to the starting material. Other examples of the displacement of a nitro group, labilized by the diazonium group, have been observed in the case of dinitroanisidines[6] and 1-nitro-2-aminonaphthalene.[7]

Several further attempts to prepare 8-nitroisoquinoline from 5-amino-8-nitroisoquinoline were made without success. Diazotization in dilute or concentrated sulfuric acid and deamination with alcohol or hypophosphorous acid failed to lead to 8-nitroisoquinoline. The use of acetic and sulfuric acids as a diazotization medium[8] and alcohol deamination likewise failed, possibly as a result of the low solubility of 5-amino-8-nitroisoquinoline in glacial acetic acid.

Experimental

All melting points are corrected.

5-Acetylamino-8-nitroisoquinoline.—Finely powdered and thoroughly dried 5-acetylaminoisoquinoline[9] (18.6 g., 0.1 mole) was added slowly with mechanical stirring to 100 cc. of concentrated sulfuric acid maintained at 0–10°. When all of the acetylaminoisoquinoline had dissolved, a cool solution of 11.1 g. (0.11 mole) of potassium nitrate in 40 cc. of concentrated sulfuric acid was added with constant stirring during the course of forty-five minutes, the mixture being maintained at 15–20°. After the addition of the potassium nitrate–sulfuric acid was complete, the reaction mixture was allowed to stand at 15–20° for an additional forty-five minutes and then poured onto excess cracked ice. The acid solution was neutralized with ammonium hydroxide, more ice being added as necessary to keep the solution cool. The precipitated crude product was filtered and recrystallized from alcohol, using decolorizing charcoal, as yellow-brown needles; yield, 11.2 g; m. p. 225–227°. By concentration of the mother liquor, an additional 5.2 g. of substance of m. p. 224–226° was recovered, making the total yield 16.4 g. (71%). Further recrystallizations from alcohol gave yellow needle clusters of m. p. 226–228°.

Anal. Calcd. for $C_{11}H_9O_3N_3$: C, 57.14; H, 3.92; N, 18.18. Found: C, 57.3; H, 3.8; N, 18.1.

5-Amino-8-nitroisoquinoline Hydrochloride.—A solution of 15 g. of 5-acetylamino-8-nitroisoquinoline in 150 cc. of 20% hydrochloric acid was boiled under reflux for twenty-five minutes. The reaction mixture was cooled and the orange-red crystalline precipitate filtered. This substance proved to be the monohydrate of 5-amino-8-nitroisoquinoline hydrochloride. The crude yield was 15.6 g. (97%). The substance was recrystallized from water plus a small amount of hydrochloric acid as orange needles, m. p. 288–290° (dec.). On standing in a vacuum desiccator over sulfuric acid, the product became orange-red in color and lost its water of hydration. (This color change was also observed during the melting point determination for the hydrated salt.) The anhydrous salt melted at 289–291° (dec.).

Anal. Calcd. for $C_9H_8O_2N_3Cl \cdot H_2O$: H_2O, 7.39. Found: H_2O, 7.3, 7.4. Calcd. for $C_9H_8O_2N_3Cl$: N, 18.63; Cl, 15.71. Found: N, 18.5; Cl, 15.7.

5-Amino-8-nitroisoquinoline.—Neutralization of a hot aqueous solution of the preceding hydrochloride with ammonium hydroxide caused the formation of a voluminous precipitate of the free base in nearly quantitative yield. The substance crystallized from alcohol as orange needles, m. p. 268–270° (dec.).

Anal. Calcd. for $C_9H_7O_2N_3$: C, 57.14; H, 3.73; N, 22.22. Found: C, 57.3; H, 3.7; N, 22.1.

Treatment of 5-amino-8-nitroisoquinoline with warm dilute hydrochloric acid caused the formation of the hydrate of its hydrochloride salt (m. p. 288–290° (dec.)). Likewise the substance, heated with acetic anhydride, was transformed into 5-acetylamino-8-nitroisoquinoline (m. p. 226–228°).

8-Chloroisoquinoline.—A suspension of 4.88 g. (0.02 mole) of the hydrate of 5-amino-8-nitroisoquinoline hydrochloride in 30 cc. of concentrated hydrochloric acid was cooled to −10–0° and, with stirring, a solution of 1.3 g. (0.019 mole) of sodium nitrite in 10 cc. of water was slowly added. As diazotization proceeded, the color of the solution lightened and the suspended aminonitroisoquinoline hydrochloride dissolved. A starch–iodide test for nitrous acid was at all times positive. After the addition of the nitrite, the solution was stirred and cooled for five minutes and then 20 cc. of ice-cold 50% hypophosphorous acid was added. Nitrogen and some oxides of nitrogen were evolved. The reaction mixture was allowed to stand in an icebox six hours, then overnight at room temperature and finally was poured on ice and made basic with 20% sodium hydroxide solution. Steam distillation of the mixture separated a colorless oil which, on standing in the icebox, crystallized in long fine needles. The crude yield was 2.3 g. (70%); m. p. 54–55°. The substance crystallized from petroleum ether as small, white prisms of m. p. 55.5–56.5° (Pomeranz[5] reported m. p. 55°). The substance showed no depression in a mixed melting point with a sample of 8-chloroisoquinoline, prepared by ring closure, described below.

Anal. Calcd. for C_9H_6NCl: C, 66.07; H, 3.70; N, 8.56; Cl, 21.67. Found: C, 66.0; H, 3.6; N, 8.5; Cl, 21.2.

Picrate.—Recrystallized from alcohol as hair-fine yellow needles; m. p. 189.5–191.5°. No depression was observed

(6) Meldola and Eyre, *J. Chem. Soc.*, **79**, 1076 (1901); **81**, 988 (1902).

(7) Morgan, *ibid.*, **81**, 1376 (1902).

(8) Hodgson and Walker, *ibid.*, 1620 (1933).

(9) In the preparation of large amounts of 5-acetylaminoisoquinoline,[3] it was observed that this substance, recrystallized from dilute alcohol, lost its crystalline appearance on standing in a vacuum desiccator over sulfuric acid. Analysis indicated that the substance crystallized as a hemi-hydrate. *Anal.* Calcd. for $C_{11}H_{10}ON_2 \cdot {}^1/_2H_2O$: H_2O, 4.62. Found: H_2O, 4.6.

in a mixed melting point with the picrate of 8-chloroisoquinoline prepared by ring closure.

Anal. Calcd. for $C_{15}H_9O_7N_4Cl$: N, 14.27. Found: N, 14.0.

o-Chlorobenzalaminoacetal.—Equimolar amounts of *o*-chlorobenzaldehyde and aminoacetal[10] were heated in an oil-bath at 110° until the liberated water was driven off. The product, distilled under reduced pressure, was obtained as an almost colorless oil in 95% yield; b. p. 114–117° (2 mm.) (oil-bath at 150–160°).

Anal. Calcd. for $C_{13}H_{15}O_2NCl$: C, 61.05; H, 7.10; N, 5.48. Found: C, 60.7; H, 7.0; N, 5.3.

8-Chloroisoquinoline.—The method of Tyson,[11] using sulfuric acid and phosphorus pentoxide, was employed for the ring closure of *o*-chlorobenzalaminoacetal. The method of working up the product, however, was modified as follows. The cooled sulfuric acid reaction mixture (from 20 g. of *o*-chlorobenzalaminoacetal) was poured on ice and made basic with ammonium hydroxide. The basic solution was extracted with three 200-cc. portions of ether. The combined ether extracts were then extracted with 100 cc. of 6 *N* hydrochloric acid. The hydrochloric acid solution was evaporated to dryness on the steam-bath, made basic with potassium carbonate solution and steam distilled. There was obtained 8-chloroisoquinoline of m. p. 55–56° in 9% yield. The picrate crystallized from alcohol as very fine yellow needles of m. p. 189.5–191.5°.

(10) Cass, THIS JOURNAL, **64**, 785 (1942).

(11) Tyson, *ibid.*, **61**, 183 (1939).

Summary

1. The preparation of 5-amino-8-nitroisoquinoline has been described.

2. Deamination of 5-amino-8-nitroisoquinoline in hydrochloric acid has been shown to yield 8-chloroisoquinoline.

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[CONTRIBUTION FROM THE NICHOLS CHEMISTRY LABORATORY OF NEW YORK UNIVERSITY]

2-Phenyloxazole; *para*-Substituted Derivatives[1]

BY JEROME J. ROSENBAUM AND W. E. CASS[2]

In an extension of previously reported work[3] on the synthesis of ortho-substituted derivatives of 2-phenyloxazole, *p*-nitrobenzalaminoacetal was treated with sulfuric acid and phosphorus pentoxide. The product isolated from this reaction proved to be 2-(*p*-nitrophenyl)-oxazole. Oxidation of this substance yielded *p*-nitrobenzamide. By reduction of the nitro group there was obtained 2-(*p*-aminophenyl)-oxazole, from which several derivatives were prepared. Deamination of 2-(*p*-aminophenyl)-oxazole resulted in the formation of 2-phenyloxazole, identical with the substance obtained by the deamination of 2-(*o*-aminophenyl)-oxazole.[3] Nitration of 2-phenyloxazole resulted in the formation of 2-(*p*-nitrophenyl)-oxazole.

The preparation of 2-(*p*-nitrophenyl)-oxazole was also accomplished by treatment of *p*-nitrobenzoylaminoacetal with sulfuric acid and phosphorus pentoxide. Unlike the case of the corresponding ortho derivative,[3] this alternate method of preparation gave 2-(*p*-nitrophenyl)-oxazole in yields comparable to those obtained from *p*-nitrobenzalaminoacetal.

Pharmacological tests on 2-(*p*-sulfanilamidophenyl)-oxazole were carried out by the Merck Institute for Therapeutic Research, Rahway, New Jersey. In staphylococcal infections in mice, this compound was not particularly effective in comparison with sulfathiazole. In streptococcal infections, although some activity was shown, the compound was not as effective as sulfanilamide.

Experimental

All melting points are corrected.

***p*-Nitrobenzalaminoacetal.**—Equimolar amounts of *p*-nitrobenzaldehyde and aminoacetal[3] were heated in an oil-bath at 110–120° until the liberated water was driven off. The reaction mixture was allowed to cool somewhat and twice its volume of dry ether was added. Cooling of the ether solution with dry-ice resulted in the precipitation of *p*-nitrobenzalaminoacetal in 80–87% yield. Further recrystallization from ether gave white plates of m. p. 56–57°, b. p. 165–168° (2 mm.) (oil-bath 200–210°).

Anal. Calcd. for $C_{13}H_{15}O_4N_2$: C, 58.62; H, 6.81; N, 10.52. Found: C, 58.7; H, 6.5; N, 10.6.

2-(*p*-Nitrophenyl)-oxazole from *p*-Nitrobenzalaminoacetal.—The reaction of *p*-nitrobenzalaminoacetal with sulfuric acid and phosphorus pentoxide was carried out following the method used in the preparation of 2-(*o*-nitrophenyl)-oxazole.[3] The crude product, however, was not purified by steam distillation but by recrystallization from alcohol, using decolorizing charcoal. 2-(*p*-Nitrophenyl)-oxazole was thus obtained as yellowish needles in 40% yield, m. p. 163.5–164.5°.

(1) Constructed, in part, from the B.A. research paper of Jerome J. Rosenbaum, New York University, University College, June, 1942.

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(3) Cass, THIS JOURNAL, **64**, 785 (1942).