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Abstract

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INDOLIC CYCLIZATION OF AZOBENZENE WITH CYCLOHEXANONE

In studying the decomposition reaction of phenyldiazonium borofluoride in various ketones, we established that in acetophenone, diethyl ketone, methyl butyl ketone, dipropyl ketone, and acetoacetic ester the decomposition proceeds readily, with evolution of nitrogen. Reactions in tetralone and cyclopentanone led to almost complete liberation of nitrogen from phenyldiazonium, but in this case traces of aniline and ammonium borofluoride were also detected.

The decomposition reaction of phenyldiazonium in cyclohexanone and its methyl homologs proceeds in an entirely different manner. In this case no evolution of nitrogen occurs. Phenyldiazonium is reduced to phenylhydrazine, which forms the phenylhydrazone of cyclohexanone, cyclizing to tetrahydrocarbazole. The reaction is accompanied by the liberation of ammonium borofluoride; that is, ordinary indolic cyclization takes place here.

In our previous work it was shown that azobenzene is reduced to hydrazobenzene by the hydridic hydrogen of ketones and many other organic compounds (1). When azobenzene interacts with cyclohexanone, surprisingly, as in the case of phenyldiazonium, indolic cyclization likewise occurs: tetrahydrocarbazole is formed and aniline, rather than ammonia as in the classical Fischer–Arbuzov synthesis, is liberated. A complex of boron trifluoride with anisole was used as the catalyst.

The use of boron trifluoride as a condensing agent in the Fischer synthesis of indoles has been described previously (2). Among the reaction products of azobenzene with cyclohexanone, phenylisonitrile (2%) was also detected. Phenylisonitrile is obtained in insignificant amounts (2%) also upon interaction of phenyldiazonium borofluoride with cyclohexanone and acetone. Apparently, a new rearrangement takes place here, the nature of which remains to be clarified.

The formation of indole derivatives from azobenzene and phenyldiazonium borofluoride evidently includes an initial stage of reduction, respectively to hydrazobenzene and phenylhydrazine. If hydrazobenzene is used instead of azobenzene in the reaction with cyclohexanone, tetrahydrocarbazole is formed in the same yield as in the case of azobenzene. It is interesting to note that, despite the presence of boron trifluoride as catalyst, no benzidine rearrangement occurs here. In a blank experiment, in the absence of cyclohexanone, hydrazobenzene in ethereal solution is instantly rearranged to benzidine upon addition of the complex of boron trifluoride with anisole. Apparently, in cyclohexanone the rate of the Fischer indole rearrangement is much greater than that of the benzidine rearrangement. In the case of azobenzene in such ketones as α-tetralone, dipropyl ketone, acetophenone, and cyclopentanone, only benzidine is obtained; no indole derivatives were detected. If in the reaction of azobenzene with cyclohexanone BF_3 is replaced by sulfuric acid, then in cyclohexanone as well only the benzidine rearrangement occurs.

When boron trifluoride is replaced by cuprous chloride (Arbuzov indole synthesis), disproportionation of hydrazobenzene takes place, with formation of azobenzene and aniline, and the reaction proceeds no further.

The mechanism of reduction of phenyldiazonium borofluoride and azobenzene in cyclohexanone and in *p*- and *o*-methylcyclohexanones is probably the same. Reduction occurs by hydride hydrogen abstracted from cyclohexanone or its methyl homologs. The hydrazobenzene formed reacts with the ketone, giving the corresponding enehydrazine.

$$\text{cyclohexanone}+\mathrm{C_6H_5NH{-}NHC_6H_5} \longrightarrow \text{cyclohexenyl hydrazine derivative} \longrightarrow \mathrm{N{-}}\text{phenylindoline hydrazone}+$$

Diphenylcyclohexenylhydrazine cyclizes with formation of tetrahydrocarbazole according to the mechanism proposed by J. and R. Robinsons ([3]) and demonstrated by A. E. Arbuzov, Yu. P. Kitaev ([4,5]) and N. N. Suvorov with co-workers ([6]),

$$\text{diphenylcyclohexenylhydrazine} \longrightarrow \text{tetrahydrocarbazole} + \mathrm{C_6H_5NH_2}$$

Evidently, in this case, as in the Fischer reaction ([11]), the nitrogen directly attached to the cyclohexane ring is eliminated.

Experimental Part

Interaction of phenyldiazonium borofluoride with ketones

With cyclohexanone. 10 g (0.052 mole) of phenyldiazonium borofluoride in 50 ml of cyclohexanone were stirred for one hour at 40-50° (until a negative test with β-naphthol), then for another hour at 110-120°. After cooling, the reaction mixture was diluted with ether and filtered; the precipitate of ammonium borofluoride was washed with ether. Yield 2.8 g (51.8%, calculated on the phenyldiazonium taken for the reaction). The ether-cyclohexanone solution was washed with dilute hydrochloric acid to remove aniline. The aniline was isolated as the benzoyl derivative; yield 0.8 g, m.p. 160-162°. Ether and cyclohexanone were distilled off, the residue was distilled in vacuo, and two fractions were isolated: b.p. 95-104° (3 mm), weight 9 g, a thick oil with the odor of isonitrile; b.p. 105-155° (3 mm), weight 2.1 g, a thick oil which solidified to a white crystalline mass.

After washing with petroleum ether, crystalline tetrahydrocarbazole was filtered off; yield 1.2 g (13%), m.p. 114–115°, literature data ([8]): m.p. 114°. A mixed sample with authentic tetrahydrocarbazole melted without depression. Tetrahydrocarbazole picrate had m.p. 132–133°; literature data ([8]): m.p. 132°.

The first fraction and the filtrate from the second fraction were combined, washed with 10% sulfuric acid, the sulfurous acid extracts were distilled, and formic acid was determined in the distillate by boiling with mercuric chloride ([9]). Yield 2%, calculated on the phenyldiazonium taken for the reaction.

With *o*-methylcyclohexanone*. From the reaction mixture there were isolated 5.25 g (96.9%) of ammonium borofluoride and 0.2 g of *N*-benzoylaniline. Distillation in vacuo gave 3 g of a light-yellow oil containing nitrogen (Lassaigne test), b.p. 132–150° (15 mm). The oil was dissolved in alcohol. From the alcoholic solution there were obtained 2.4 g of the yellow picrate of 11-methyl-

* The reaction was carried out under the conditions described in the experiment with cyclohexanone.

tetrahydrocarbazole with m.p. 168–169°; literature data [10]: m.p. 169°.

Found, %: C 55.07; 55.17; H 4.46; 4.27; N 13.62; 13.72
$C_{19}H_{18}N_4O_7$. Calculated, %: C 55.07; H 4.32; N 13.53

From the mother liquor, 0.64 g of 1-methyltetrahydrocarbazole picrate was isolated, m.p. 145° (dark-brown needles); literature data [10]: m.p. 145°.

Found, %: C 55.25; H 4.56; N 13.85;

The overall yield of methyltetrahydrocarbazoles was 0.0073 mole (14%, calculated on the borofluoride of phenyldiazonium taken into the reaction).

With **n-methylcyclohexanone**.* 3.8 g of ammonium borofluoride (70.3%) and 0.5 g of N-benzoylaniline were obtained. On vacuum distillation, 3.3 g of a thick nitrogen-containing oil was isolated, b.p. 150–180° (4 mm). From 1.1 g of this oil, 0.7 g of 3-methyltetrahydrocarbazole picrate was obtained, m.p. 127–128°, crystallized from a petroleum ether–benzene mixture (1:1).

Found, %: N 13.77; 13.67

The overall yield of 3-methyltetrahydrocarbazole was 9.7% of theory.

With **cyclopentanone**.* Almost all of the phenyldiazonium borofluoride decomposed with evolution of nitrogen. Only 0.2 g of NH_4BF_4 and 0.3 g of N-benzoylaniline were isolated.

Reaction of Azobenzene with Ketones

With **cyclohexanone**. To 10 g (0.0549 mole) of azobenzene in 60 ml of cyclohexanone was added 10 ml of anisole containing 3 g (0.044 mole) of boron trifluoride. The mixture was heated at 100–110° for 2.5 h, then diluted with ether and washed with 5% hydrochloric acid. From the hydrochloric-acid extracts, 6.1

g (0.065 mole) of aniline was obtained, b.p. 175–180°. Cyclohexanone and its condensation products were distilled off from the organic layer under vacuum, and the residue was subjected to steam distillation. From the distillate, 3.3 g (35.1%) of tetrahydrocarbazole was isolated.

With **n-methylcyclohexanone**.* From the hydrochloric-acid aqueous extracts, 0.7 g of benzidine sulfate and 2 g (0.0204 mole) of aniline were isolated. From the organic layer, methylcyclohexanone and its condensation products were distilled off under vacuum; azobenzene was removed from the residue by steam distillation. The weight of the remaining oil was 2.2 g. From 0.5 g of this oil, 0.25 g of 3-methyltetrahydrocarbazole picrate was obtained, m.p. 127–128°; a mixed sample with 3-methyltetrahydrocarbazole picrate melted without depression. The overall yield of picrate was 1.1 g (0.00265 mole; 4.8%, calculated on the initial azobenzene).

With α**-tetralone**.* From the reaction mixture, only 3.2 g (59.7%) of benzidine sulfate was isolated, calculated on the azobenzene that entered into the reaction. 6.55 g of azobenzene was recovered from the reaction.

With **dipropyl ketone**.* From the reaction mixture, 1.3 g of the sulfate salt of benzidine (22.6%) was obtained. 6.31 g of azobenzene was recovered from the reaction.

Reaction of Hydrazobenzene with Cyclohexanone

5 g (0.0271 mole) of hydrazobenzene (m.p. 122–123°), 50 ml of cyclohexanone, and 6 ml of anisole containing 1.6 g of boron trifluoride were boiled for 2.5 h in a stream of nitrogen and worked up in the same way as in the experiment with cyclohexanone. From the hydrochloric-acid extracts, aniline was isolated, which, after diazotization, coupled with β-naphthol. Yield of the azo dye: 1.6 g (0.0064 mole), m.p. 130–131°; literature data (^{11}): m.p. 131°. From the organic layer, by distillation with superheated steam, 1.4 g of tetrahydrocarbazole was isolated (0.0082 mole; 30.2% of theory).

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* The reaction was carried out under the conditions described in the experiment with cyclohexanone.

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