BEHAVIOR OF ACRIDINE TOWARD SODIUM AMIDE AND ALKALI

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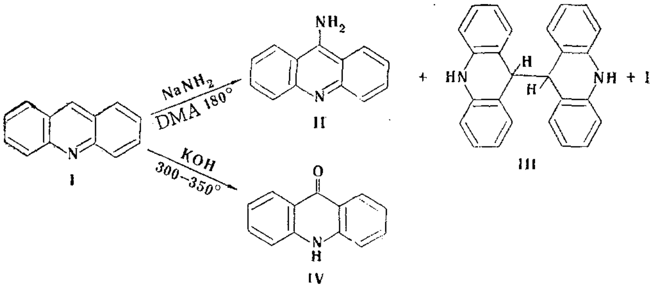
Acridine undergoes the Chichibabin reaction with difficulty in dimethylaniline or xylene at temperatures up to 150-160°, but a mixture of 9-aminoacridine and diacridanyl, with predominance of the latter, is formed at higher temperatures. Fusion of acridine with alkali at 300-350° gives acridone in 28% yield.

According to a communication by Bauer, acridine (I) readily undergoes the Chichibabin reaction to form 9-aminoacridine in 72% yield on reaction with sodium amide in dimethylaniline (DMA) at 150°C [1]. However, in an attempt to reproduce this experiment, we obtained different results – I reacts very slowly with sodium amide in DMA or xylene at temperatures up to 150-160°. Appreciable reaction, accompanied by the formation of a copious dark yellow precipitate, begins in DMA at 180°. When the mixture is heated for 3 h at this temperature, three compounds – the starting acridine (14%), 9-aminoacridine (31%), and a colorless compound, which is insoluble in the ordinary organic solvents and was identified as diacridanyl (III) – are isolated. Structure III was established on the basis of the results of elementary analysis, the IR spectrum, and the similarity between the physical properties of the product and those described in the literature [2]. In addition, the diacridanyl that we obtained by reduction of acridine with zinc dust in acetic acid proved to be completely identical to the sample synthesized via the Chichibabin reaction.



When solid III or a solution of it in nitrobenzene or dimethylformamide (DMF) is heated, it is oxidized by air oxygen to give acridine and traces of acridone (this is apparently one of the reasons for its indistinct melting point). To avoid the oxidation of diacridanyl during amination, the reaction was carried out under nitrogen.

The formation of III is in agreement with our conception of the mechanism of the Chichibabin reaction under heterogeneous conditions [3]. On the one hand, the basicity of acridine (pK_a 5.61) [4] and the magnitude of the effective positive charge (q) on the γ-carbon atom (+0.105), which we calculated by the Hückel MO method with the parameters in [5], are favorable for the Chichibabin reaction. However, the sorption of acridine on the surface of sodium amide crystals through the pyridine nitrogen atom should sharply hinder the reaction because of the remoteness of the C_9 atom from the amide ion in the adsorbed complex. This apparently leads to an increase in the specific weight of the always competitive (with amination) metalation of the heterocyclic ring [3], as a result of which carbanion V is formed and is followed by the production of diacridanyl in accordance with the following scheme:

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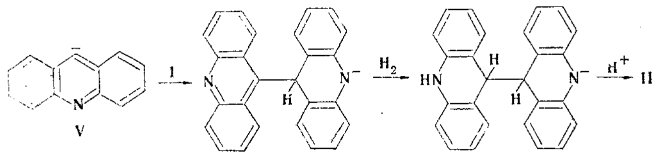

The hydrogenation step necessary for the formation of III explains why almost no hydrogen evolution (a characteristic sign of the Chichibabin reaction) is observed in the amination of I; a small amount of hydrogen (10-15%) is evolved only at the very end of the reaction. Since 1 mole of hydrogen is consumed when two acridine molecules unite to form III, it is clear why the ratio of the yields of II and III is 2 : 3 rather than 1.

We further found that acridine is hydroxylated by potassium hydroxide at 350° to form acridone IV in 28% yield. The evolution of a considerable amount of hydrogen is observed in this reaction, and III is not formed (possibly because of its instability at high temperatures).

EXPERIMENTAL

Amination of Acridine. A. A mixture of 3.6 g (0.02 mole) of acridine, 3.2 g (0.065 mole) of technical-grade (80%) finely ground sodium amide, and 14 ml of DMA was stirred at 180° for 3 h. The copious formation of a finely crystalline light green precipitate was observed. Hydrogen was evolved very sluggishly, and 20-30 ml could be collected only at the end of the experiment. The mixture was then cooled and treated cautiously with 20 ml of water. The resulting yellow precipitate was removed by filtration, washed successively with petroleum ether (40 ml), water (100 ml), and petroleum ether (40 ml), and dried at 80° to give 3.4 g of light green crystals. Treatment of the crystals with alcohol in a Soxhlet apparatus gave 1.6 g (44%) of colorless crystals of III, which were insoluble in the ordinary solvents. Compound III melted with decomposition at 195-210°. Found,%: C 86.7; H 6.3; N 7.8. $C_{26}H_{20}N_2$. Calculated,%: C 86.2; H 6.1; N 7.7. IR spectrum (mineral oil): $\nu_{N=H}$ 3378 cm^{-1} (intense sharp peak). Evaporation of the alcohol solution gave 1.8 g of yellow crystals. Recrystallization from benzene gave 1.2 g (31%) of 9-aminoacridine with mp 233-234° (mp 234° [6]). IR spectrum ($CHCl_3$), cm^{-1}: ν_{as} 3530, ν_s 3440, δ 1635 (NH_2). Removal of the benzene from the mother liquor by distillation gave 0.5 g (14%) of acridine with mp 110°. The IR spectrum was identical to the spectrum of a genuine sample of I.

B. A mixture of 1.82 g (0.01 mole) of acridine, 1.6 g (0.032 mole) of 80% sodium amide, and 15 ml of o-xylene was stirred at 150° for 4 h. No hydrogen evolution was observed. The mixture was cooled and treated cautiously with 20 ml of water. The finely crystalline yellow precipitate was removed by filtration, washed successively with water (60 ml), petroleum ether (40 ml), and water (40 ml), and dried at 80°. The product (0.6 g) was recrystallized from benzene, and the insoluble diacridanyl portion (0.018 g) was removed by filtration. The solution was cooled to precipitate 0.2 g (10%) of yellow crystals of 9-aminoacridine with mp 233-234°. The o-xylene yielded 0.92 g (50%) of acridine.

Reduction of Acridine. A 0.36-g (6 mmole) sample of zinc dust was added to a solution of 1 g (5.4 mmole) of acridine in dilute acetic acid (3 ml of the acid and 12 ml of water), and the mixture was refluxed for 10-15 min. The resulting colorless precipitate was removed by filtration, washed successively with water (60 ml), ether (20 ml), and water (60 ml), and dried at 80°, to give 0.95 g (96%) of a product that was insoluble in ordinary solvents and melted at 195-210° (dec.). The IR spectrum at 700-3600 cm^{-1} was identical to the spectrum of III obtained by the amination reaction. On heating, the substance was converted to acridine containing traces of acridone (the formation of the latter was established by thin-layer chromatography on aluminum oxide).

Oxidation of Diacridanyl (III). A mixture of 0.4 g (1.2 mmole) of III and 15 ml of nitrobenzene was heated to the boiling point. The diacridanyl dissolved, and the red solution was refluxed for 40 min. It was then cooled, treated with 10 ml of concentrated HCl, and steam distilled to remove the nitrobenzene. The residual solution was neutralized with ammonium hydroxide to precipitate 0.4 g (100%) of yellow crystals of I, which, according to the IR spectra and melting points, was identical to a genuine sample.

Hydroxylation of Acridine. A mixture of 1.8 g (0.01 mole) of acridine and 3.0 g (0.05 mole) of anhydrous powdered KOH was heated on a metal bath. Uniform hydrogen evolution began only at 300°. A total of 160 ml (72%) of hydrogen was evolved during heating for 1 h at 300-350°. The mixture was cooled, the solid black melt was triturated with concentrated HCl, and the solid (2.05 g) was removed by filtration. The crystals were dissolved in 150 ml of alcohol and boiled three times with activated charcoal. The pinkish solution was treated with water to precipitate 0.55 g (28%) of slightly yellowish crystals of 9-acridone with mp 353-354° (from alcohol), in agreement with the data in [7]. The IR spectrum of the product was identical to the spectrum of a genuine sample.

LITERATURE CITED

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