REFERENCES

1. E. G. Tomich, B. Basil, and B. Davis, Brit. J. Pharmacol., 8, 166, 1953.
2. H. Bojarska-Dahlig, Roczn. chim., 29, 119, 1955.
3. H. Bojarska-Dahlig, Przem. chem., 9, 34, 1953; 10, 266, 1954.
4. British patent no. 836960, 1960; C. A., 54, 24810, 1960.
5. British patent no. 517382, 1940; C. A., 35, 7124, 1941.
6. N. G. Polyanskii, Usp. khim., 31, 1046, 1962.
7. V. I. Isagulyants and K. S. Shanazarov, Khim. prom., 1, 67, 1964.
8. M. Dohrn and P. Diedrich, Ann., 494, 284, 1932.

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THE AUTOXIDATION OF Δ^{10}-DODECAHYDROACRIDINE

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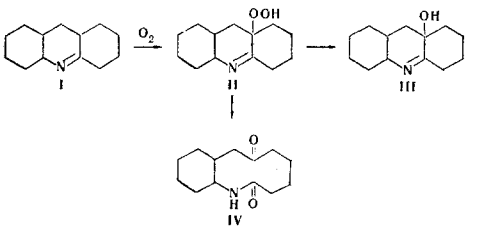
The autoxidation of Δ^{10}-dodecahydroacridine in heptane in an atmosphere of oxygen has given 12-hydroperoxy-Δ^{10}-dodecahydroacridine, which has been reduced to 12-hydroxy-Δ^{10}-dodecahydroacridine and has been converted into 5-azabicyclo[8, 4, 0]tetradecane-6, 11-dione. The two latter compounds were also isolated when Δ^{10}-dodecahydroacridine underwent autoxidation in air in the absence of a solvent.

Preparation of Δ^{10}-dodecahydroacridine has been reported previously [1]. Like its bicyclic analogs—$\Delta^{1,9}$-octahydroquinoline and $\Delta^{1,8}$-hexahydropyrindene [2]—the imine I proved to have an extremely high tendency to autoxidation both in a solvent and without a solvent.

When a solution of the imine I in heptane was stirred in an atmosphere of oxygen, about 1 mole of O_2 was absorbed; an unstable crystalline hydroperoxide—12-hydroperoxy-Δ^{10}-dodecahydroacridine (II)—deposited.

By a known method for the reduction of hydroperoxides [3], on treatment with sodium hydrosulfite the hydroperoxide II formed 12-hydroxy-Δ^{10}-dodecahydroacridine (III). In aqueous dioxane in the presence of a small amount of hydrochloric acid, the hydroperoxide II underwent rearrangement. Judging from the IR spectrum, the rearrangement product was a macrocyclic ketolactam—5-azabicyclo[8, 4, 0]tetradecane-6, 11-dione (IV). The formation of similar products by the rearrangement of hydroperoxides of cyclic imines has been mentioned in the literature [4, 5]. In the rearrangement of the hydroperoxide of $\Delta^{1,9}$-octahydroquinoline [2], the corresponding 10-membered ketolactam could not be isolated, since it underwent transannular cyclization (interaction of the keto and N—H groups across the ring). In our case, according to its IR spectrum, the product contained both a keto group and a —CONHR group—i.e., no cyclization took place.

The autoxidation of Δ^{10}-dodecahydroacridine on standing in the air without a solvent led to the formation of a mixture of oxidation products from which compounds III and IV were isolated. The formation of the first of them can be explained by the interaction of the hydroperoxide formed initially with the unoxidized imine. Similar reactions have been described in the literature [6]. Rearrangement of the hydroperoxide took place simultaneously, leading to the formation of compound IV.



I II III IV

EXPERIMENTAL

12-Hydroperoxy-Δ^{10}-dodecahydroacridine (II). A solution of 4 g of freshly distilled I in 80 ml of heptane was stirred in a flask connected with a burette filled with oxygen. In the first 7 min, 172 ml of O_2 was absorbed, and then the rate of absorption fell. Only after 1 hr 40 min had 392 ml of O_2 (84% by theory) been absorbed. The precipitate of hydroperoxide that had separated was filtered off with suction, washed with heptane, and kept at 0° C over paraffin wax until it had reached constant weight. Yield 3.9 g (83.5%). Mp 96° C (decomp.). The sub-

stance vigorously liberates iodine from a solution of sodium iodide in acetic acid. Found, %: C 70.17, 70.00; H 10.02, 10.26; N 6.42, 6.47. Calculated for $C_{13}H_{21}NO_2$, %: C 69.96; H 9.42; N 6.30. The somewhat high analytical results are possibly due to the presence of a small amount of **III** in the hydroperoxide. The hydroperoxide can be stored at 0° C for 10 days with no change in the melting point.

12-Hydroxy-Δ^{10}-dodecahydroacridine (III). A mixture of 2.8 g of the hydroperoxide **II**, 50 ml of ether, 50 ml of 1N KOH solution, and 6 g of sodium hydrosulfite was stirred at room temperature until the qualitative reaction for hydroperoxide was negative. The reaction product was separated off, washed with water, and dried. Yield 0.97 g (37.5%). Rods, soluble in acetic acid and dioxane, sparingly soluble in ethanol and benzene, insoluble in water, petroleum ether, and diethyl ether. Mp 191–192° C (from aqueous ethanol). Found, %: C 75.56, 75.63; H 10.14, 10.06; N 7.03, 6.90. Calculated for $C_{13}H_{21}NO$, %: C 75.40; H 10.14; N 6.76. IR spectrum (in CCl_4), ν, cm^{-1}: 1670 (C=N), 3620 (O–H). Picrate, mp 140–140.5° C (from aqueous ethanol). Found, %: N 12.88, 12.73. Calculated for $C_{13}H_{21}NO \cdot C_6H_3N_3O_7$, %: N 12.83.

5-Azabicyclo[8, 4, 0]tetradecane-6, 11-dione (IV). A mixture of 2.2 g of the hydroperoxide **II**, 20 ml of water, 20 ml of dioxane, and 5 drops of concentrated HCl were stirred at 32–37° C until the almost complete disappearance of the qualitative reaction for hydroperoxide (this required about 10 hr). The mixture was neutralized with a few drops of ammonia solution, and the dioxane and water were distilled off under reduced pressure. The residue was treated with 15 ml of cold acetone, and the rearrangement product was filtered off with suction and then separated from mineral impurities by dissolution in chloroform. This gave 0.9 g (41%) of the product. After two recrystallizations from acetone, mp 146–148° C. Chromatographic purification of the product on a column of Al_2O_3 (elution with chloroform), and subsequent recrystallization from dioxane gave a sample with mp 157.5–158° C. Hexagonal plates, soluble in ethanol, benzene, chloroform, and ethyl acetate, less readily in acetone and dioxane, and sparingly in heptane. Found, %: C 70.23, 70.26; H 10.07, 9.98; N 6.31, 6.38. Calculated for $C_{13}H_{21}NO_2$, %: C 69.96; H 9.42; N 6.30. IR spectrum (in KBr), ν, cm^{-1}: 3280, 3100, 1660, 1580 (–CONHR), 1720 (C=O).

Autoxidation of Δ^{10}-dodecahydroacridine in the absence of a solvent. Compound I (1.4 g) was spread in a thin layer on the bottom of a Petri dish and left in the air for 25 days. The crystalline mass obtained was triturated with heptane, and the crystals were filtered off and washed with hot water. The substance (0.51 g), insoluble in water, was identified as **III**. Evaporation of the aqueous extract yielded 0.63 g of **IV**.

REFERENCES

1. V. A. Kaminskii and M. N. Tilichenko, KhGS [Chemistry of Heterocyclic Compounds], **3**, 708, 1967.

2. L. A. Cohen and B. Witkop, J. Am. Chem. Soc., **77**, 6595, 1955.

3. R. J. S. Beer, T. Broadhurst, A. Robertson, and L. McGrath, J. Chem. Soc., 4351, 1952.

4. B. Witkop and I. B. Patrik, J. Am. Chem. Soc., **73**, 2196, 1951.

5. B. Witkop, I. B. Patrik, and M. Rosenblum, J. Am. Chem. Soc., **73**, 2641, 1951.

6. R. F. Parcell and F. P. Hauck, J. Org. Chem., **28**, 3468, 1963.

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ANALOGS OF PYRIMIDINE NUCLEOSIDES

IV. The Silyl Method of Obtaining N_1-(α-Tetrahydrofuryl) and N_1-(α-Tetrahydropyranyl) Derivatives of Uracils and 6-Azauracil*

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N_1-(α-Tetrahydrofuranyl)- and N_1-(α-tetrahydropyranyl)uracils and the corresponding 6-azauracils have been obtained by the condensation of bistrimethylsilyl derivatives of uracils and 6-azauracils with α-chlorotetrahydrofuran and α-chlorotetrahydropyran. The superiority of the "silyl" method over the "mercury" method used previously has been demonstrated.

We have previously obtained N_1-(α-tetrahydrofuryl)-uracils (**IVa–f**) by the condensation of mercury derivatives of the pyrimidine bases with α-chlorotetrahydrofuran (CTHF) [1], and one of these compounds, **IVc**, is of value as an agent for the treatment of some types of malignant tumors. However, the proposed method of synthesizing compounds IV proved to be unsuitable: the yields were only about 40%, and the process of purification of the end product from traces of mercury proved to be extremely laborious.

In view of the desirability of developing a technologically convenient method, we have studied the possibility of obtaining compounds **IVa–f** by condensing bistri-

*For part III, see [9].