SYNTHESIS OF AN ANALOG OF THE ALKALOID DAURICINE

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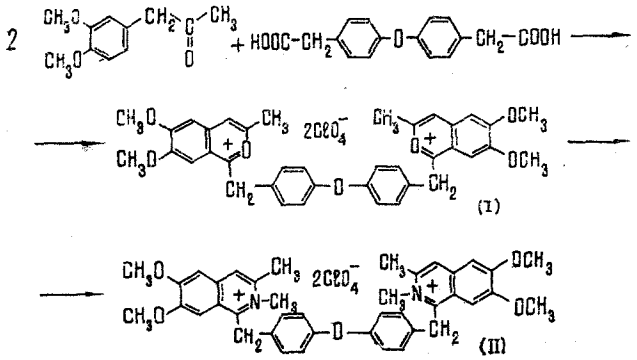
The synthesis of curare analogs possessing a high and specific activity is of undoubted interest from the point of view of isolating the influence of features of the structures of these compounds on their physiological activity.

In order to obtain difficulty accessible bimolecular ether derivatives of isoquinoline we have used 2-genzopyrylium salts, which have been employed previously to obtain isoquinoline bases and analogs of natural alkaloids of the isoquinoline series. We synthesized a structural analog of the alkaloid dauricine in the following way:



The initial bis-2-benzopyrylium salt (I) was obtained by the acylation of 3,4-dimethoxyphenylacetone (0.01 mole) with di(4-carboxymethylphenyl) ether (0.005 mole) in the presence of 21 g of polyphosphoric acid (100°C, 1 h). The hot mixture was poured onto 100 g of ice and was treated with 2 ml of 70% $HClO_4$. The crystals of the diperchlorate of bis[4-(3-methyl-6,7-dimethoxybenzopyrylio-1-methyl)phenyl] ether, $C_{38}H_{36}O_{15}Cl_2$ (I) that deposited were filtered off and were recrystallized from nitromethane. The yield was quantitative, mp 345°C (decomp.); IR spectrum: 1100, 1280, 1570, 1620 cm^{-1}.

The brief heating of a solution of 0.4 g (0.0005 mole) of (I) in acetone with 0.5 ml of a 20% aqueous solution of methylamine led to the formation of the diperchlorate of bis[4-(2,3-dimethyl-6,7-dimethoxyisoquinolinio: 1-methyl)phenyl] ether, $C_{40}H_{42}Cl_2$ (II). The yield was 93%, mp 234°C (from acetic acid). IR spectrum: 1100, 1280, 1600, 1620 cm^{-1}.

The analyses of the compounds obtained corresponded to the calculated figures.

In preliminary trials on cats, after the intravenous administration of substance II in a dose of 3 mg/kg partial curaremimetic effect was observed.

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