CHEMISTRY OF HETEROANALOGS OF ISOFLAVONES.

16.* BENZTHIAZOLE ANALOGS OF ISOFLAVONES

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The reaction of α-(2-benzthiazolyl)-2,4-dihydroxy-5-alkylacetophenones with anhydrides and chlorides of carboxylic acids yielded 3-(2-benzthiazolyl)chromones with electron-acceptor and electron-donor substituents, as well as chromones unsubstituted in the 2-position. Their acylation, alkylation, and aminoacylation reactions and their interaction with electrophilic and nucleophilic reagents were studied.

The great attention paid in recent years to heterocyclic analogs of isoflavonoids is explained by the presence of general and specific types of biological activity. In view of the importance and insufficient study of azole analogs of isoflavones as potential physiologically active substances, methods have been developed for the synthesis of imidazole [2], pyrazole [3], and isoxazole [4] analogs of isoflavones. Pharmacological tests have shown that some of these compounds exhibit high hypolipidemic, anti-inflammatory, and sugar-lowering activity.

Continuing investigations in the field of the chemistry and pharmacology of chromones with nitrogen-containing heterocycles, in this work we synthesized and studied certain properties of benzthiazole analogs of isoflavones (see scheme), among which only two representatives have been described [5].

The starting materials for the synthesis of new 3-(2-benzthiazolyl)-chromones were α-(2-benzthiazolyl)-2,4-dihydroxy-6-propylacetophenone (Ia) and α-(2-benzthiazolyl)-2,4-dihydroxy-6-hexylacetophenone (Ib), produced by condensation of 2-benzthiazolylacetonitrile with 4-alkylresorcinols under modified conditions of the Hoesch reaction.
The ketones Ia,b are high-boiling yellowish crystalline substances, which give a colored chelate complex with an alcohol solution of ferric chloride. The dark-green color of this complex suggested the presence of tautomeric equilibrium between the ketone and enol forms for compounds Ia,b in solution. In an analysis of the PMR spectra of compound Ia in various deuter solvents, we found that in nonpolar solvents, such as chloroform and benzene, it exists exclusively in the ketone form, whereas in the more polar acetone a certain amount of the enol form is observed. In dimethyl sulfoxide, the ketone Ia is 80% enolized, as indicated by the doubled number of signals of the protons of the hydroxyl groups and a consideration of the integral intensity of nonexchangeable aromatic protons of the phenolic portion, as well as a decrease in the intensity of the peak of the protons of the methylene unit, the appearance and increase in the intensity of the signal of the methine proton of the olefinic fragment of the molecule (see Fig. 1). The ketone Ib is 85% enolized in dimethyl sulfoxide. The greater content of the enol form may be associated with its stabilization by the intermolecular hydrogen bond that arises between the enol hydroxyl and dimethyl sulfoxide.

As a result of the reaction of the ketone Ia with trifluoroacetic anhydride or ethoxalyl chloride in pyridine in the cold, the chromones II and III, containing trifluoromethyl and ethoxycarbonyl groups in the 2-position, respectively, were obtained. The reaction of acetic anhydride with the same ketone proceeds in pyridine medium at room temperature with the formation...