We have previously [1] described some simple structural analogs of the antibiotic griseofulvin, namely enol ethers of 1,3-cyclohexanediione and tetrahydrochromans, e.g., (I) and (II).

In continuation of these investigations in the present work we synthesized the 2-p-halophenyl-7,8-dihydro-5(6H)-chromanones (III) and (IV) and also the bicyclic enol ethers (V)-(X). By the method developed earlier the Mannich ketones (XI) and (XII) were brought into condensation with 1,3-cyclohexanediione, and the resulting triketones (XIII) and (XIV) were reduced with sodium tetrahydroborate with subsequent cyclization into the required compounds (III) and (IV):

For the synthesis of the bicyclic diketones (V)-(VIII) we used the Claisen condensation of the benzoic esters (XV)-(XVIII) with the methyl enol ether of 1,3-cyclohexanediione (3-methoxy-2-cyclohexen-1-one) in an ether medium in presence of 3-4 equivalents of sodium. The position of the benzoyl group was assumed on analogy with the formyl [2, 3] and esterified oxalo [3] derivatives (XIX) and (XX), prepared by the same method. The 3,5-dibromo-2,4-dimethoxybenzoic ester (XXI) did not undergo Claisen reaction under the usual conditions, probably because of the weaker electrophilic character of its carbonyl group. In the acid hydrolysis of the enol ethers (V) and (VI) we isolated the corresponding triketones (XXII) and (XXIII), which with excess of diazomethane in ether formed mixtures of the isomeric enol ethers (V) and (IX) and (VI) and (X). The enol ethers (IX) and (X) have almost the same UV absorption maxima as their isomers (V) and (VI), and, like the latter, they are readily hydrolyzed by hydrochloric acid to the triketones (XXII) and (XXIII). The formation of the third theoretically possible isomers (XXIV) and (XXV) from the triketones (XXII) and (XXIII) must be regarded as not very likely, mainly because these should have marked acidic properties and should be methylated by excess of diazomethane to the diethers (XXVI) and (XXVII). The structures of the enol ethers (V), (VI) and (IX), (X) were confirmed by their IR spectra, in which frequencies corresponding to conjugated carbonyl groups were present.
The simple griseoflavin analogs which we prepared showed tuberculostatic and fungistatic activity, which varies over a fairly wide range depending on the structures of the substances and attained maximum values in the case of the halogen-containing dihydro-5-(6H)-chromanones (III) and (IV) (table).

**EXPERIMENTAL**

**Preparation of 4'-Bromo-3-(dimethylamino)propiophenone Hydrochloride** (XI). A mixture of 20 g of 4'-bromoacetophenone, 8.1 g of dimethylamine hydrochloride, 3.6 g of paraform, and 100 ml of isopropyl alcohol was boiled for six hours, and the precipitate which formed on cooling was filtered off. We obtained 15.6 g (53%) of (XI), m.p. 180-181° (isopropyl alcohol). Found %: N 5.01, 4.99. C₁₁H₁₅ONBrCl. Calculated %: N 5.79.

**Preparation of 2-(2-p-Bromobenzoylethyl)-1,3-cyclohexanedione (XIII).** 15.6 g of the amine hydrochloride (XI) was added to a solution of 5.6 g of 1,3-cyclohexanedione and 2 g of sodium hydroxide in 80 ml of water, and the mixture was refluxed for 90 min. The mixture was cooled, treated with sodium carbonate, and extracted with ether and chloroform to remove impurities of a neutral character. From the alkaline layer, after filtration and acidification, we isolated 3.3 g (20%) of (XIII), m.p. 176-177° (isopropyl alcohol). Found %: C 55.59, 55.59; H 4.74, 4.66; Br 24.91, 24.72. C₁₅H₁₅O₃Br. Calculated %: C 55.67; H 4.68; Br 24.76.

**Preparation of 2-p-Bromophenyl-7,8-dihydro-5(6H)-chromanone (III).** 0.11 g of sodium tetrahydroborate was added to a solution of the sodium derivative of 2-(2-p-bromobenzoyl ethyl)-1,3-cyclohexanedione (prepared from 3.2 g of the β-diketone and 0.4 g of sodium hydroxide) in 30 ml of water. After about 20 h the mixture was acidified with hydrochloric acid, and the precipitate formed was extracted with chloroform. The extract was washed with sodium hydroxide solution and water and was dried over magnesium sulfate. On evaporation we obtained 1.8 g (58%) of (III), m.p. 89-92° (ether). Found %: C 58.22, 58.34; H 5.08, 4.90; Br 25.94, 26.00. C₁₅H₁₄BrO₂. Calculated %: C 58.68; H 4.92; Br 26.02.

**Preparation of 4'-Chloro-3-(dimethylamino)propiophenone Hydrochloride** (XII). By the procedure used for (XI), from 15.4 g of 4'-chloroacetophenone, 8.2 g of dimethylamine hydrochloride, and 3 g of paraform in 75 ml of isopropyl alcohol we obtained 23.8 g (95%) of the hydrochloride (XII), m.p. 170-171° (methanol). Found %: N 5.83, 5.89. C₁₁H₁₅ONCl₂. Calculated %: N 5.62.

**Preparation of 2-p-Chlorophenyl-7,8-dihydro-5(6H)-chromanone (IV).** A mixture of 7 g of 1,3-cyclohexanedione, 12.4 g of (XII), 2.2 g of sodium hydroxide, and 100 ml of water was boiled for seven hours, and we isolated 7.2 g of unpurified 2-(2-p-chlorobenzoyl ethyl)-1,3-cyclohexanedione, m.p. 157-160°. 3.6 g of the triketone obtained was dissolved in 75 ml of 1% sodium hydroxide, 1.92 g of sodium tetrahydroborate was added, and after about 20 h the mixture was acidified. After the usual treatment we isolated 2 g of oil, which was chromatographed on alumina (activity II). Elution with ether gave 0.82 g of (IV), m.p. 77-78° (hexane). Found %: C 68.43, 68.25; H 5.82, 5.68; Cl 13.44, 13.07; C₁₅H₁₄O₂Cl. Calculated %: C 68.56; H 5.76; Cl 13.50.