α,β-Unsaturated ketones of the imidazo[1,2-a]benzimidazole series were synthesized from 3-formyl- and 3-acetyl-substituted imidazo[1,2-a]benzimidazoles by crotonic condensation in the presence of alkaline catalysts. The α,β-ununsaturated ketones can also be obtained by direct acylation of 3-unsubstituted imidazo[1,2-a]benzimidazoles with the chlorides of unsaturated acids. The properties and pharmacological activity of the ketones obtained were studied.

Chalcones contain a reactive α,β-unsaturated ketone grouping, which, as assumed in [2], is responsible for their antibacterial and fungicidal activity. The analogs of chalcones of some nitrogen heterocycles, namely, benzimidazole [3], pyridine [4], pyrimidine, etc., display a broad spectrum of pharmacological activity, including hypotensive and diuretic activity. In order to study the effect of this sort of keto group on the biological properties of imidazobenzimidazoles, we obtained α,β-unsaturated ketones III-VII from 3-acetyl- and 3-formyl-2,9-disubstituted imidazo[1,2-a]benzimidazoles (I and II).

Despite the strong electron-donor character of the system, I and II quite readily undergo crotonic condensation under alkaline conditions. Condensation of I with aldehydes does not take place in the presence of acid catalysts. This is probably explained by the sharp decrease in the nucleophilicity of the acetyl group upon protonation of the nitrogen atom in the 1 position of the heteroring. In this case only the salts of the starting imidazobenzimidazoles were isolated from the reaction mixture. Analogs of chalcones containing a nitrofuryl grouping, which is very sensitive to alkaline agents [5], therefore cannot be obtained by means of this condensation. Compounds of this type can be obtained by direct acylation of 3-unsubstituted imidazo[1,2-a]benzimidazoles with chlorides of unsaturated acids [6]. The reaction takes place when the reagents are heated without a solvent or in pyridine. α,β-Ununsaturated ketones of the imidazo[1,2-a]pyridine series, the acetyl-substituted derivatives of which are unstable in acidic media [7], were also synthesized by this method. Nitration of ketone IVf in acetic anhydride also leads to nitrofuryl-substituted IVg, but the yield of the latter is considerably lower in this case.

*See [1] for communication XIII.

All of the α,β-unsaturated ketones obtained by us are characterized by a trans orientation of the substituents attached to the double bond, as attested to by the presence in their IR spectra of intense absorption bands of out-of-plane and in-plane deformation vibrations of the hydrogen atoms of the vinyl group at 980-1000 and 1290-1310 cm⁻¹, respectively [8]. The stretching vibrations of the C=C and C=N bonds appear in the form of two intense bands at 1580-1620 cm⁻¹. A weak band of carbonyl group absorption is observed in the spectra of ketones VI and VII at 1650-1660 cm⁻¹, whereas in the spectra of ketones III and IV it is shifted to the lower-frequency region (1635-1645 cm⁻¹); this can be explained by simultaneous conjugation of the C=O group with the electron-donor imidazobenzimidazole ring and the ethylene bond. The low intensity of the absorption band of the carbonyl group as compared with the band of the stretching vibrations of the C=C bond indicates their s-cis-orientation relative to one another [9, 10].

The electronic spectra of IIIa and IVa are characterized by two absorption bands of approximately equal intensity (log ε 4.25-4.4) at 300 and 366-370 nm due to π-electron transitions in the conjugated system of bonds. The long-wave band in the spectra of ketones VIa and VIIa is shifted to 415-420 nm, evidently due to lengthening of the conjugation chain. The introduction of a nitro group in the para position of the phenyl ring or replacement of the phenyl group by an electron-donor furyl grouping in ketones III, IV, and VII leads to a bathochromic shift of the long-wave band of 15-20 nm. Halochromic properties are characteristic for III-VII: The absorption maxima of the long-wave bands of sulfuric acid solutions of these compounds are shifted by 100-150 nm to the red region as compared with the spectra of alcohol solutions.

Ketones III and IV undergo characteristic reactions involving addition to the double bond to give γ-nitro ketones VIII and morpholides IX. Treatment of them with an alkaline solution of hydrogen peroxide leads to keto oxides X.

\[
\text{VIII} \quad \text{IX} \quad \text{X}
\]

The reaction of ketones III and IV with hydrazines is hindered; this can be explained by the combined effect of electronic and steric factors. No reaction occurs with phenylhydrazine even under the most severe conditions. We were able to isolate the corresponding hydrazones in low yields when IIIa and IVa were refluxed for a long time with the more reactive 2,4-dinitrophenylhydrazine. The absorption bands of CH=CH and CO groups vanish in the IR spectra of the hydrazones; the vibrations of ring C=C and C=N bonds appear at 1600 and 1620 cm⁻¹, the nitro groups give doublet absorption bands at 1318, 1340 and 1510, 1525 cm⁻¹, and a νNH band at 3280 cm⁻¹ and a band of medium intensity at 1680 cm⁻¹, which is characteristic for the vibrations of the out-of-plane C=N bond of α,β-unsaturated compounds [8], appear in the spectra.

Heating ketones IIIa, IVa, VIa, and VIIa with hydrazine hydrate leads to pyrazoline derivatives XI and XII. It was noted that the formation of the latter occurs more readily in the case of ketones VI and VII, in which the electron-donor imidazobenzimidazole ring has a lesser effect on the carbonyl group. Bands of vibrations of ring C=C and C=N bonds at 1610 and 1628 cm⁻¹ are observed in the IR spectra of XI and XII, and the stretching vibrations of the NH group appear at 3200-3250 cm⁻¹.

Tests of the substances obtained in this research for fungicidal activity did not give interesting results.

The effect of some of the chalcone analogs (IVa, b, f, V, and VII) on the arterial pressure level was studied in experiments on Numbutan-narcotized rats. The systemic arterial pressure was recorded in the carotid by the usual method. Since the investigated compounds are insoluble in water, they were administered intravenously in the form of alcohol solutions. The investigation showed that all of the compounds have a clearly expressed hypotensive effect (Table 1). Ketone IVf, which markedly lowered the blood pressure in doses of 2.5 mg/kg, was found to be the most active compound. A hypotensive effect of IVb and VIIa was noted in the case of administration of large doses (10 mg/kg) than for ketone IVf. Ketones IVa and V displayed the lowest activity.