SUMMARY

1. The relative acidities (pK_a values) of 17 hydroxycoumarins in water, methanol, acetone, dimethylformamide, and dimethyl sulfoxide have been determined.

2. Linear equations have been derived for the relationship between $pK_a^{H_2O}$ and pK_a in acetone, dimethylformamide, and dimethyl sulfoxide.

3. On the basis of the titration constants (pK_t), the shapes of the curves, and sizes of the potential jumps, acetone has been proposed as the optimum solvent for performing potentiometric analysis.

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BASICITY CONSTANTS OF NATURAL ISOFLAVONOIDS

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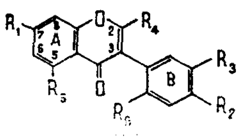
The basicities (pK_{BH^+}) of 13 natural isoflavones have been determined spectrophotometrically in sulfuric acid solutions. It has been shown that the change of basicity in this series of compounds depends on the geometry of the molecules and on intramolecular effects.

Quantitative information on the basicities of natural flavonoids is not only of interest for judging their electronic structure but may also have practical use, for example, in pharmaceutical analysis. At the present time, the basicities of the flavonones and flavonols have been studied in fairly great detail [1-4], but there is almost no such information on isoflavonoid compounds.

We have determined the basicities of a number of natural isoflavonoids possessing valuable pharmacological properties — in particular, pronounced antiatherosclerotic activity [5] — by a spectrophotometric method.

Structures of the compounds studied:



I. $R_1=R_2=R_3=R_4=R_5=R_6=H$
II. $R_1=OH$; $R_2=R_3=R_4=R_5=R_6=H$
III. $R_1=R_2=OH$; $R_3=R_4=R_5=R_6=H$
IV. $R_1=OH$; $R_2=OCH_3$; $R_3=R_4=R_5=R_6=H$
V. $R_1=R_2=OCH_3$; $R_3=R_4=R_5=R_6=H$
VI. $R_1=OH$; $R_2=R_3=OCH_3$; $R_4=R_5=R_6=H$
VII. $R_1=R_2=R_3=OCH_3$; $R_4=R_5=R_6=H$
VIII. $R_1=OH$; $R_4=CH_3$; $R_2=R_3=R_5=R_6=H$
IX. $R_1=R_2=OCH_3$; $R_5=OH$; $R_3=R_4=R_6=H$
X. $R_1=R_2=R_5=OH$; $P_3=R_4=R_6=H$

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XI. $R_1=OCH_3$; $R_5=OH$;
$R_3=R_4=R_6=H$;
$R_2=$ glucopyranosyl
XII. $R_1=$ glucosyl
$R_2=OCH_3$; $R_3=R_4=R_5=R_6=H$

XIII. $R_1=OH$; $R_6=OCH_3$;
$R_2=R_3=-O-CH_2-O-$;
$R_4=R_5=H$
XIV. $R_1=$ glucopyranosyl
$R_2=R_3=-O-CH_2-O-$;
$R_6=OCH_3$;
$R_4=R_5=H$

As can be seen from the facts given (Table 1), isoflavone and its derivatives are weaker bases than, for example, chromone or flavone [1, 6]. An exception is compound (VIII), the basicity of which is close to that of chromone (pK_{BH^+} for chromone = −2.0). This result does not contradict the work of Tolmachev et al. [6] according to which alkyl or phenyl groups introduced into position 2 of chromone derivatives increase the basicity of the compounds. This increase in basicity can be explained by the electron-donating nature of the substituents.

A phenyl group introduced into position 3 of the chromone molecule (isoflavone and its derivatives) decreases its basicity. The low basicity of the isoflavones as compared with chromones of flavones is explained both by steric hindrance in protonation and by a decrease in the conjugation of the π-system of ring B with the remaining π-system of the molecule through a disturbance of coplanarity [7]. We may also mention that voluminous substituents such as glycosyl or glucopyranosyl introduced even into position 7 affect the basicities of the compounds studied in the direction of a decrease, apparently by disturbing the coplanarity of the molecule (Table 1, compounds (V) and (XII)).

The effect of a decrease in basicity due to noncoplanarity under the influence of a voluminous substituent can fully compete with the analogous effect caused by the formation of an intramolecular hydrogen bond, and also through the dipole—dipole repulsive interaction of the dipole of an OH group and the dipole of the OH formed on the protonation of a carbonyl group [4]. An intramolecular H bond in the isoflavonoids is possible only for compounds having a 5-hydroxy group. In this case, as in that of the 5-hydroxyflavones [8], in the 1600-1700 cm^{-1} region of the IR spectra the $\nu_{C=O}$ band of the 5-hydroxyisoflavone derivatives is located at lower frequencies than the $\nu_{C=C}$ band of the heterocyclic fragment (Table 1).

In the series studied, compounds (XIII) and (XIV) had the lowest basicities. In their molecules, ring B is apparently isolated from conjugation by the methylenedioxy and methoxy groups to the greatest extent, as is confirmed by the high values of $\nu_{C=O}$; the 6'-methoxy group also exerts steric hindrance on protonation. The sugar residue in position 7 of compound (XIV) lowers the basicity by approximately half an order of magnitude, as also in the case of compounds (V) and (XII) (Table 1).

TABLE 1. Protonation Constants of the Isoflavonoids (pK_{BH^+}) in Aqueous Solutions of Sulfuric Acid at 25°C, and Absorption Frequencies of the C=O and C=C Bonds (in KBr tablets and in tetrahydrofuran), cm^{-1}

Compound	$-pK_{BH^+}$	$\nu_{C=O}$	$\nu_{C=C}$
I	2,50 [7]	1652 (KBr) [9]	1652 (KBr) [9]
II	2,57	1656 (THF)	1633 (THF)
III	2,66	1630 (KBr)	1630 (KBr)
IV	2,72	1638 (KBr)	1638 (KBr)
V	2,96	1640 (KBr)	1640 (KBr)
VI	2,83	1632 (KBr)	1632 (KBr)
VII	2,60	1635 (KBr)	1635 (KBr)
VIII	2,04	1643 (KBr)	1623 (KBr)
IX	3,57	1615 (KBr) 1625 (THF)	1660 (KBr) 1663 (THF)
X	2,91	1628 (KBr) 1630 (THF)	1658 (KBr) 1663 (THF)
XI	3,57	1624 (KBr) 1630 (THF)	1663 (KBr) 1665 (THF)
XII	3,54	1643 (KBr) 1655 (THF)	1626 (KBr) 1630 (THF)
XIII	4,50	1665 (KBr)	1600 (KBr)
XIV	4,96	1690 (KBr)	1615 (KBr)

It is known that in a series of ketones of similar structure there is a direct relationship between their basicities and the frequencies of the stretching vibrations of the carbonyl group [9]. However, for our compounds, as follows from Table 1, no correlation is observed between $\nu_{C=O}$ and basicity. We consider that the absence of such a relationship is due to spatial factors and, in particular, to the different degrees of solvation of the cyclic oxygen atom [6]. We propose subsequently to seek correlations of the basicity—biological activity type [10].

EXPERIMENTAL

The compounds studied were isolated from plants of the Leguminosae family or were obtained synthetically [5]. Basicities (pK_{BH^+}) were measured on a Specord UV-VIS spectrophotometer in aqueous sulfuric acid solutions using Hammet's acidity function H_0 [11]. The values of H_0 were taken from the literature [12]. As the pK values were taken the values of H_0 were used at the point of half-protonation. IR spectra were measured on UR-20 and Shimadzu IR-27G spectrophotometers in KBr tablets and in tetrahydrofuran (THF).

SUMMARY

1. The basicities (pK_{BH^+}) of 13 natural isoflavonoids have been measured spectrophotometrically in aqueous sulfuric acid solutions.

2. Using the results of IR spectroscopy it has been shown that the change in basicity in this series of compounds depends on the geometry of the molecules and on intramolecular effects.

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