EQUILIBRIUM NH ACIDITIES OF ACRIDAN, PHENANTHRIDONE, 9-ACRIDONE, AND SUBSTITUTED 9-ACRIDONES

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The equilibrium NH acidities of acridan, phenanthridone, 9-acridone, and 2-substituted 9-acridones (substituents: Me_2N, MeO, F, Br, I, and NO_2) were measured by transmetallation in dimethyl sulfoxide (DMSO). The role of conjugation and the aromatic character of the heterocyclic ring in stabilization of the anions is discussed. The energies of deprotonation of phenanthridone and 9-acridone were estimated by the CNDO/2 (complete neglect of differential overlap) method; it is shown that the difference between them is in agreement with the experimental results. The dependence $pK = 16.2 - 3.37\sigma_I - 1.84\sigma_R$ (s 0.23, r 0.989) was obtained for the 2-substituted 9-acridones.

9-Acridone and the related heterocyclic compounds play an important role in the chemistry of luminophores [1], and their spectral properties have recently been studied intensively [2], whereas relatively little is known regarding the structural principles of the reactivities of these compounds. This gap has been filed to a certain extent by the results of the present research, which is devoted to a study of their equilibrium NH acidities. The results obtained also are of general significance; in combination with similar data for other NH acids they give an idea of the effect of a number of structural factors on the equilibrium NH acidities of organic compounds.

The equilibrium constants of the reactions of acridan, phenanthridone, 9-acridone, and a series of 2-substituted 9-acridones with the potassium derivatives of CH or NH indicators were determined in dimethyl sulfoxide (DMSO) by spectrophotometry, and the pK values of the investigated compounds (Table 1) were calculated on the basis of these constants.

Since most of them, inasmuch as they are carbonyl-containing amino compounds, are capable of a tautomeric lactam—lactim transformation [7], a question relative to the nature of the acidities (NH or OH forms of the acids) characterized by the measured pK values (pK_{meas}) naturally arises. These values, the corresponding pK values of both forms (pK_{NH} and pK_{OH}) and the tautomeric equilibrium constants (K_T = [OH forms]/[NH forms]) are interrelated by the expression $pK_{meas} = pK_{NH} + \log(1 + K_T) = pK_{OH} + \log(1 + 1/K_T)$. It follows from this expression that when $K_T \leq 0.25$, the difference between pK_{meas} and pK_{NH} lies within the limits of the accuracy of the method (0.1 pK unit), and pK_{meas} in these cases can therefore be related to the NH acidity.

It is known that in aqueous solution 9-acridone (III) exists in the NH form [7]. The transition to aprotic DMSO is evidently accompanied by a certain shift of the equilibrium to favor the OH form. However, considering the high polarity of the solvent — a factor that favors stabilization of the lactam — and the magnitude of the K_T value in water (10^{-7} [7]), it it may be assumed that the concentration of the form in a solution of 9-acridone remains virtually unchanged in this case. In the case of 2-substituted VI-IX, which contain electron-acceptor substituents, the equilibrium may still be shifted to favor the OH form. Thus the introduction of a chlorine atom into the α position relative to the NH group of 4-pyridone increases the K_T value by three orders of magnitude [7]. However, in VI-IX the substituents are separated from the heteroatom by a benzene ring, and their effect on the position of the

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TABLE 1. Equilibrium NH Acidities (pK_{NH}) of the Investigated Heterocyclic Compounds in DMSO

Compound	Name	pK_{NH}	Indicator[a]	K[b]	λ_{max}[c], nm
I	Acridan	25,2	AMP	0,21±0,03 (5)	390
II	Phenanthridone	18,3	PF	2,2±0,2 (3)	—
III	9-Acridone	16,4	PBI	0,65±0,06 (6)	352, 432, 456
IV	2-Dimethylamino-9-acridone	16,5	BI	2,0±0,2 (4)	460
V	2-Methoxy-9-acridone	16,4	PBI	0,6±0,1 (3)	375, 440
VI	2-Fluoro-9-acridone	15,4	PBI	6,1±0,7 (3)	351, 437, 462
VII	2-Bromo-9-acridone	15,2	PBI	9,3±0,9 (3)	357, 438, 464
VIII	2-Iodo-9-acridone	15,0	CBA	0,7±0,2 (3)	359, 415, 440
IX	2-Nitro-9 acridone	12,9	CAE	9,0±0,5 (4)	378, 408

[a]The indicators were as follows (the pK values are indicated in parentheses): AMP is 4-amino-6-methoxypyrimidine (24.5 [3]), PF is 9-phenylfluorene (18.5 — standard acid [4]), PBI is 2-phenylbenzimidazole (16.2 [5]), BI is benzimidazole (16.8 [5]), CBA is 2-cyanobenzanilide (14.8 [6]), and CAE is cyanoacetic ester (13.8 [4]). [b]The equilibrium constant of the reaction of the potassium derivative of the indicator with the investigated NH acid (the number of determinations is given in parentheses). [c]For the anions of the investigated compounds.

tautomeric equilibrium should therefore be much weaker than in 4-pyridone. It therefore seemed unlikely to us that the K_T values of 2-substituted 9-acridones in DMSO reach the limit indicated above (0.25), i.e., it may be assumed that the pK values presented in Table 1 characterize the NH acidities.

As one should have expected, the NH acidity of acridan (I) is substantially lower than the acidities of the remaining investigated compounds, in which the carbonyl group has a strong acidifying effect on the N—H bond. At the same time, its acidity is close to that of diphenylamine (pK 25.1 [8]), from which it differs only with respect to the o,o'-methylene bridge between the phenyl groups. It is interesting to note that the UV spectra of the two compounds in DMSO are essentially identical (a broad band with a maximum at 285-290 nm is observed), while the positions of the maxima in the spectra of the anions differ appreciably: 365 nm for the diphenylamine anion [9] and 390 nm for the acridan anion. In this connection, the assumption that conjugation of the unshared pair of the nitrogen atom with the π system is stronger in the acridan anion suggests itself, and the acridan anion should be thermodynamically more stable than the diphenylamine anion (the decrease in the electron density on the nitrogen atom promotes a decrease in the energy of the σ orbital occupied by the second electron pair that is liberated in the ionization of the N—H bond). However, measurements of the acidities do not reveal the proposed difference. It is possible that the contribution of $p-\pi$ conjugation to stabilization of the amide anions is generally relatively small and, in a quantitative respect, is expressed weakly here. In addition, it may be compensated to a certain extent by the positive inductive effect of the methylene group. Moreover, one cannot exclude the possibility that the differences in the solvation of the two NH acids and the conjugate bases in DMSO are also significant.

Replacement of the methylene bridge in acridan by a C—C bond between the phenyl rings, i.e., transition to the carbazole structure (pK 19.6 [5]), is accompanied by an increase in the NH acidity by almost six orders of magnitude. It is natural to link this effect with further involvement of the unshared pair of the nitrogen atom in $p-\pi$ conjugation in the formation of the aromatic π systems of the heterocyclic ring. The latter probably plays an important role in stabilization of the anion. Its disruption on passing from the pyrrole structure of the heteroring to a pyridone structure, although it is accompanied by an increase in the NH acidity, nevertheless results in a change that is smaller than one might have expected upon introduction of a carbonyl grup into the α position relative to the acidic center. Thus it is apparent from a comparison of the pK values of diphenylamine (see above) and benzanilide (19.3 [6]) that the NH acidity here increases by more than five pK units, whereas in the case of a similar structural change in the carbazole molecule the NH acidity

increases by only 1.3 pK units [compare with phenanthridone (II)]. Judging from the crystallographic data [10], the molecule retains its planar configuration in this case, i.e., there is no steric inhibition of conjugation, but the aromatic character of the heterocyclic ring vanishes, which leads to a substantial decrease in the acidifying effect of the carbonyl group.

The effect of "dearomatization" of the heteroring is smaller if the carbonyl group is introduced into carbazole as an o,o' bridge between the phenyl rings: 9-Acridone (III) is a stronger NH acid than phenanthridone (II), despite weakening of the inductive effect of the CO group on the N—H bond. The unusual character of this result compelled us to compare the experimental data with the results of quantum-chemical calculations. The calculated [by the CNDO/2 (complete neglect of differential overlap) method] energy of deprotonation of 9-acridone (16.03 eV) is less than that for phenanthridone (16.23 eV), i.e., even according to the calculations, the acidity of III should be higher than that of II (by 3.3 pK units). The qualitative agreement with the experimental results (1.9 pK units) makes it possible to assume that the difference in the strengths of the two NH acids observed in DMSO is not due to solvation effects but rather to purely structural factors. However, it is not yet possible to express a definite judgment regarding the reasons for the lower stability of the anion of II.

The data on the acidities of 2-substituted 9-acridones (IV-IX) demonstrate the somewhat unusual (for NH acids) regularity of the effect of the substituents in the para position with respect to the acidic center. In such cases the pK values of NH acids (for example, substituted 2-aminopyrimidine [2], benzanilide [5], and N-phenylcarbamate [8]) generally change symbatically with respect to the Hammett σ constants of the para substituents; the σ^- constants are used in the correlations for strong electron acceptors (CN and NO_2 groups), whereas the σ^0 constants are used for electron donors. However, in the examined series of NH acids the σ^0 constants are clearly unsuitable for the description of the effects of the 2-Me_2N and 2-MeO groups, which have almost no effect on the acidity of 9-acridone (compare the pK values of III and IV and V). In addition, the difference in the pK values of 9-acridone and substituted 9-acridones VI and VII does not correspond to the Hammett σ constants of the fluorine and bromine atoms. On the basis of the indicated constants, correlation Eq. (1) therefore does not adequately describe the acidities of 2-substituted 9-acridones, despite the satisfactory correlation coefficient. In particular, one's attention is directed to the appreciable disparity between the pK value of III and the free term of Eq. (1).

$$pK = 15.8 - 2.31\sigma,\ s\ 0.32,\ r\ 0.973. \quad (1)$$

A substantially better result is achieved by means of two-parameter correlation (2) with the use of the inductive (σ_I) and resonance (σ_R) constants of the substituents.

$$pK = 16.2 - 3.37\sigma_I - 1.84\sigma_R,\ s\ 0.23,\ r\ 0.989. \quad (2)$$

It is apparent from the ratio of the ρ_I and ρ_R values (1.75) that the contribution of the resonance effects of the para substituents to the energetics of the acidic ionization of the N—H bond of substituted 9-acridones is almost half the contribution of their inductive effects. As a consequence of this, π-donor groupings do not have the destabilizing effect on the anion that is observed for NH acids that contain an acidic center in the side chain, for which the ratio of the ρ_I and ρ_R values is close to unity (the largest value (1.2) was obtained for 5-substituted 2-aminopyrimidines [2]). In our opinion, the noted peculiarity in the behavior of acridones is associated in part with the presence of a carbonyl group, which plays an important role in stabilization of the anion via a conjugation mechanism. According to the results of calculations by the CNDO/2 method, when the proton of the N—H bond of 9-acridone is detached, the π-electron density on the oxygen atom increases by 0.12 charge units (on the nitrogen atom it decreases by 0.28 charge units). This π acceptor may appreciably weaken the resonance effect of the substituents in the benzene ring of 9-acridone on the unshared pair of the nitrogen atom. On the other hand, the orientation of the electron pair that is liberated upon ionization of the N—H bond in the nodal plane of the π system also hinders the manifestation of resonance effects of the substituents in the rigidly fixed structure of the 9-acridone molecule.

In conclusion, we would like to note that the results obtained in this research are of interest not only as new information regarding the structural principles of the equilibrium NH acidities of organic compounds but also as additional information that is extremely useful for the development of concepts regarding the electronic structures of amide anions. Of course, the reliability of the considerations expressed here depends on how valid our assumptions regarding the nature of the acidities of the investigated compounds are. The possibility that future studies of the tautomeric equilibria for substituted 9-acridones in DMSO will introduce certain corrections into the proposed interpretation of the experimental data is not excluded.

EXPERIMENTAL

The acridan, which was a chemically pure reactive preparation, was purified by sublimation *in vacuo*. The phenanthridone was synthesized from diphenic acid monoamide by treatment with bromine in the presence of alkali [11]. The 9-acridone and the substituted 9-acridones IV-IX were obtained by dehydration of phenylanthranilic acid or the corresponding 4'-substituted compounds by the methods described in [12, 13]. The melting points of the compounds after recrystallization from benzene or toluene were in agreement with the literature values. The pK values were measured by a method that has been previously used frequently [3-6].

X-ray diffraction data on the geometries of the molecules [10, 14, 15] were used in the calculations by the CNDO/2 method of the total energies of the ground electronic states of the molecules and anions of 9-acridone and phenanthridone. It was assumed that the geometry of the anion did not change as compared with the geometry of the starting molecule.

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