

DIFFERENTIATION EFFECT OF SOLVENTS ON THE KETO-ENOL
EQUILIBRIUM OF HETEROCYCLIC β -DICARBONYL COMPOUNDS

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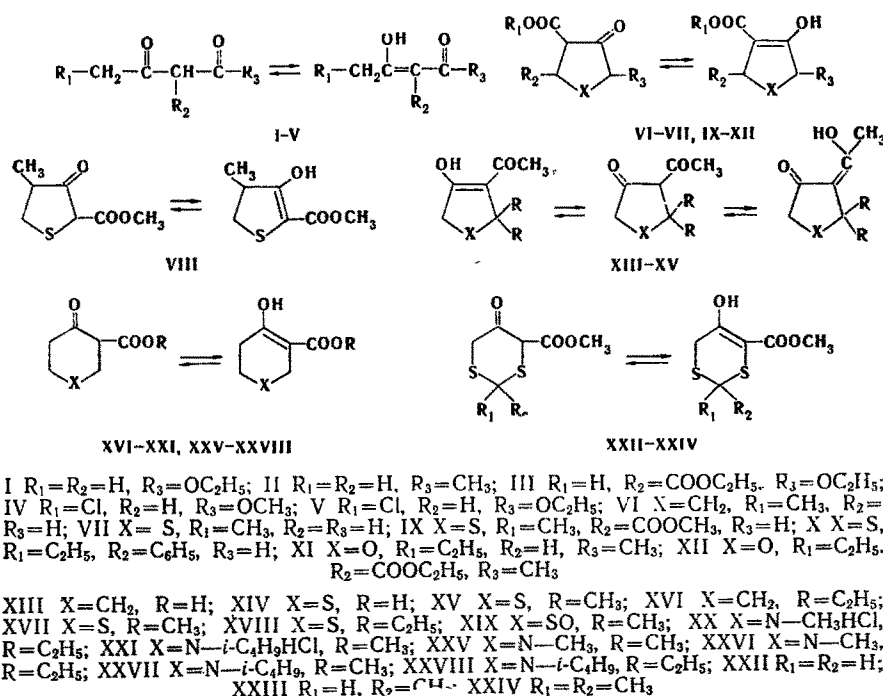
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The differentiation effect of a solvent on the equilibrium of five- and six- membered heterocyclic β -keto esters and β -diketones containing =O, =S, =SO, =NR, =NRHCl, and $-S-C(R)_2-S-$ fragments and, for comparison, on the equilibrium of aliphatic and carbocyclic β -keto esters and β -diketones was studied. The differentiating effect of a solvent is explained by different kinds of solvation of the heteroatomic fragments in the ketone and enol forms of heterocyclic β -dicarbonyl compounds.

The position of the equilibrium of different groups of substances depends in different ways on the nature of the solvent. On passing from solvent to solvent, because of a change in the specific solvation, substances are divided into reaction series, for each of which an equation (1) peculiar to it is satisfied:

$$\ln K_{TS} = \alpha \ln K_{T_2S} + \beta \quad (1)$$

In this equation, K_{TS} is the equilibrium constant of T in solvent S, β is a free term that characterizes the differentiation effect of a solvent on different reaction series, and α is a coefficient that describes the differentiating effect of a solvent within a single reaction series [1].



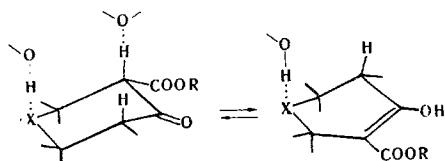
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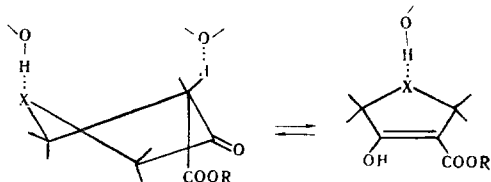
It is assumed that satisfaction of Eq. (1) is determined by the structure of the solvated complexes with respect to the functional groups, which change during the establishment of equilibrium, and it should be satisfied for a group of substances of identical nature [2]. However, cases in which satisfaction of Eq. (1) is due to finer structural peculiarities than affiliation with a group of substances of identical nature are known [3-5].

In the present research we studied the differentiating effect of solvents on the equilibria of aliphatic, carbocyclic, and heterocyclic β -dicarbonyl compounds. In the case of heterocyclic β -dicarbonyl compounds, satisfaction of Eq. (1) may depend on nonidentical hindrances to solvation of the heteroatom fragments in the ketone and enol forms.

In conformity with the literature data on the conformations of six- and five-membered rings with atoms and groupings that lower the barrier to rotation about the bonds [6, 7], the β -keto esters with six-membered rings under consideration should have preferred "chair" conformations for the keto form and "half-chair" conformations for the enol form. Hindrance to solvation of the heteroatomic fragment on the part of the two β -axial hydrogen atoms, one of which has acidic character and is solvated by solvent molecules, is possible in the keto form. Hindrance on the part of only one nonacidic β -quasi-axial hydrogen atom is possible in the enol form [8].



The examined β -keto esters with five-membered rings should have preferred "half-chair" conformations for the keto form and "envelope" conformations for the enol form. Hindrance to solvation of the heteroatomic fragment on the part of the acidic β -quasi-axial hydrogen atom is possible in the keto form. Quasi-axial hydrogen atoms are absent in the enol form.



Somewhat different factors are operating in esters of 1,3-dithia-5-cyclohexanone-4-carboxylic acid. Here the sulfur atoms themselves hinder axial solvation of one another in the keto form. This hindrance should be less in the enol form. The resulting difference in solvation will lead to a shift in the position of the equilibrium to favor the enol. The magnitude of the shift depends on the peculiarities of the solvation of the heteroatomic fragment. The nitrogen atom in amines forms strong hydrogen bonds [9] and is solvated only from the axial position in a six-membered ring. Equation (1) which differs markedly from the equation for aliphatic and carbocyclic β -dicarbonyl compounds, should therefore be satisfied for N-alkyl-3-carbalkoxy-4-piperidones. The sulfur atom has two electron pairs, one of which occupies an axial position in a six-membered ring, the other of which occupies the equatorial position. Under certain conditions, only axial solvation may be realized [10]. In the general case, solvation occurs alternately from both positions. Hindrance to axial solvation should affect the entropy factor. The greater hindrance to solvation of the axial electron pair in the keto form as compared with the enol form will change this factor in favor of the enol form. A hydrochloride group in the six-membered ring is solvated only from the axial position, whereas a sulfoxide group is solvated from both positions [11]. Great hindrance to solvation in the keto form is possible for β -keto esters with these groups, and as a result of this a shift in the position of the equilibrium to favor the enol form is also possible. However, the hydrogen bonds of sulfides are weaker than those of amines [12]. In sulfoxide and hydrochloride groups the atom bonded to them rather than the heteroatom itself is solvated. Equation (1), which differs from the equations for aliphatic and carbocyclic β -dicarbonyl compounds and N-alkyl-3-carbalkoxy-4-piperidones, should therefore be satisfied for six-membered β -keto-esters with $-S-$, $-S-C(R)_2-S-$, $-NRHCl-$, and $-SO-$ fragments. Solvation of the oxygen atom is realized in the same way as

TABLE 1. Correlation Coefficients α , Free β Terms, Numbers of Correlated Values (n), Correlation Coefficients (r), and Standard Deviations (s) in the Correlation of $\ln M$ and $\ln K$ of I-XXVIII in Dioxane and Alcohols

Correlation parameters	I-VI, XVI $\ln M$			VI-X $\ln M$			XVI-XXI $\ln M$			VI-X $\ln K$		
	CH ₃ OH	C ₂ H ₅ OH	i-C ₄ H ₉ OH	CH ₃ OH	C ₂ H ₅ OH	i-C ₄ H ₉ OH	CH ₃ OH	C ₂ H ₅ OH	i-C ₄ H ₉ OH	CH ₃ OH	C ₂ H ₅ OH	i-C ₄ H ₉ OH
α	0.96	0.97	1.00	1.26	1.24	1.21	0.95	1.21	1.27	0.88	0.86	0.88
β	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.02	0.01	0.00	0.00	0.28
n	7	7	7	5	5	5	8	9	9	5	5	5
r	0.998	0.999	0.999	0.998	0.997	0.998	0.998	0.997	0.998	0.995	0.994	0.996
s	0.011	0.006	0.005	0.004	0.005	0.004	0.005	0.006	0.006	0.07	0.07	0.07

A linear dependence of the complex equilibrium constants of the tautomers in two solvents is observed in the case of a linear dependence of the equilibrium constants of the tautomers in these solvents. One need only accurately select the fixed states. In conformity with the principle of multilinearity [16], the fixed states are selected in the general case in such a way that the dependence of the complex equilibrium constants on the structural parameters and the conditions under which the reactions occur does not have discontinuities in the region under consideration and additional steepness as compared with the dependence of the equilibrium constants on the structural parameters and the conditions under which the reactions occur.

The differentiating effect of a solvent on the equilibria of I-XVIII on passing from dioxane to alcohols was studied. The graph of the dependence of $\ln M$ in dioxane on $\ln M$ in methanol, ethanol, and 2-butanol is presented in Fig. 1. The α and β values, the numbers of experimental points (n) used in the derivation of Eq. (1), the correlation coefficients (r), and the standard deviations with allowance for the Student distribution (s) for three groups of substances [aliphatic and carbocyclic β -dicarbonyl compounds, β -keto esters with five-membered rings and =CH₂ and =S fragments, and β -keto esters with six-membered rings and =S, =SO, =NRHC1, and -S-C(R)₂-S- fragments] are given in Table 1. For comparison, the α , β , n , r , and s values for β -keto esters with five-membered rings and =CH₂ and =S fragments in the correlation of $\ln K$ are given in Table 1. As seen from Table 1, a linear correlation of $\ln M$ is observed in the case of a linear correlation of $\ln K$.

Table 1 and Fig. 1 show that I-XXVIII break down into six reaction series. Aliphatic and carbocyclic β -dicarbonyl compounds I-VI and XVI form one series. β -Diketones XIII-XV, β -keto esters VI-X, and β -keto esters XVI-XXIV comprise three other series. Another two series are formed by β -keto esters VI, XI, XII, and XXV-XXVIII. Thus the observed pattern is in agreement with the above examination of steric hindrance to solvation in the ketone and enol forms of heterocyclic β -dicarbonyl compounds and the peculiarities of solvation of heteroatomic fragments.

EXPERIMENTAL

The UV spectra of solutions (10^{-2} - 10^{-3} mole/liter) of the compounds were recorded with an SF-4A spectrophotometer at a layer thickness of 0.02-0.05 cm. No concentration dependence was observed. The absorption maximum of the enol form was observed at 245-260 nm for β -keto esters with one heteroatom and without a heteroatom, at 270-280 nm for β -diketones, and at 310-315 nm for β -keto esters with two heteroatoms and for 4-methyl-2-carbomethoxy-3-thiophanone. The molar extinction coefficients of I-XXVIII were presented in [17-23]. They were used for the determination of the complex constants from equation (4). The absorption of I in the standard state was assumed to be 100. The absorptions of the remaining compounds in the standard state were calculated from the equation presented in [17] and the assigned absorption of I.

The $\ln M$ values of I-XXVIII are presented in Table 2. The maximum mean square deviation was 0.005. The $\ln K$ values are given in Table 3. The maximum mean square deviation was 0.05. The α coefficients of Eq. (1), which are presented in Table 1, have two significant digits and one doubtful digit. Free term β of Eq. (1) in this table has one significant digit and one doubtful digit.

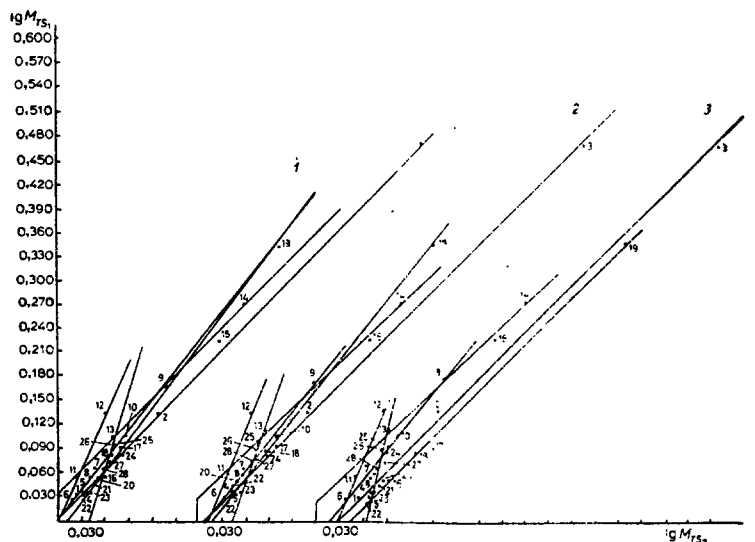


Fig. 1. Graph of the dependence of the logarithms of the complex constants in two solvents: 1) in dioxane and 2-butanol; 2) in dioxane and ethanol; 3) in dioxane and methanol.

solvation of the sulfur atom and affects the entropy factor. Hydrogen bonds with ethers are much stronger than hydrogen bonds with sulfides [9]. As a result of this, Eq. (1), which differs from the equations enumerated above, should be satisfied for 4-carbalkoxy-3-thiophanones and 4-carbalkoxytetrahydro-3-furanones. The satisfaction of Eq. (1) itself for 4-acetyl-3-thiophanones may be due to enolization at the noncyclic carbonyl group [13].

Proceeding from all of these considerations, we calculated the α coefficient and the free β term in Eq. (1) for aliphatic and carbocyclic β -dicarbonyl compounds I-VI and XVI, for β -keto esters with five-membered rings and $=\text{CH}_2$ and $=\text{S}$ fragments (VI-X), and for β -keto esters with six-membered rings and $=\text{CH}_2$, $=\text{S}$, $=\text{SO}$, $=\text{NRHCl}$, and $-\text{S}-\text{C}(\text{R})_2-\text{S}-$ fragments (XVI-XXIV). Because of the small number of cyclic β -diketones and cyclic β -keto esters with an $=\text{O}$ fragment in the five-membered ring and cyclic β -keto esters with an $=\text{NR}$ fragment in the six-membered ring, the α coefficient and the free β term in Eq. (1) were not calculated for them. However, an idea of the differentiation effect of solvents on these groups of substances can be obtained from graphical analysis.

Complex constants were used for the characteristics of the position of the equilibria of I-XXVIII in place of the equilibrium constants. Complex constants of the form

$$M_{\text{TS}} = \frac{K_{\text{TS}}(1+K_{\text{TS}_1})}{K_{\text{TS}}-K_{\text{TS}_1}} \quad (2)$$

$$M_{\text{TS}} = \frac{(1+K_{\text{TS}_1})(K_{\text{TS}}-K_{\text{TS}_2})}{(1+K_{\text{TS}_2})(K_{\text{TS}}-K_{\text{TS}_1})} \quad (3)$$

where M_{TS} is the complex equilibrium constant of keto enol T in solvent S, K_{TS} is the equilibrium constant of keto enol T in solvent S, and S_1 and S_2 are standard solvents, are determined from spectral data only through the molar extinction coefficient of the keto enol (ϵ_{TS}) both when only one of the tautomeric forms (4) absorbs and when both forms absorb and their absorptions overlap (5).

$$M_{\text{TS}} = \frac{\epsilon_{\text{TS}}}{\epsilon_{\text{TS}_1} - \epsilon_{\text{TS}}} \quad (4)$$

$$M_{\text{TS}} = \frac{\epsilon_{\text{TS}} - \epsilon_{\text{TS}_2}}{\epsilon_{\text{TS}_1} - \epsilon_{\text{TS}}} \quad (5)$$

Expressions (4) and (5) were derived under the assumption that the molar extinction coefficients of the absorbing forms are independent of the nature of the solvent. This assumption is well satisfied for keto enols with an intramolecular hydrogen bond (IHB) in the enol [14, 15].

TABLE 2. Logarithms of the Complex Constants of I-XXVIII in Solutions

Compound	CH ₃ OH	C ₂ H ₅ OH	<i>i</i> -C ₄ H ₉ OH	C ₆ H ₅ O ₂	Compound	CH ₃ OH	C ₂ H ₅ OH	<i>i</i> -C ₄ H ₉ OH	C ₆ H ₅ O ₂
I	0,061	0,045	0,025	0,033	XV	0,230	0,220	0,200	0,230
II	0,160	0,140	0,130	0,140	XVI	0,093	0,072	0,057	0,053
III	0,520	0,500	0,460	0,470	XVII	0,150	0,100	0,079	0,093
IV	0,072	0,049	0,033	0,033	XVIII	0,130	0,086	0,068	0,086
V	0,068	0,041	0,033	0,033	XIX	0,400	0,300	0,280	0,350
VI	0,041	0,033	0,017	0,025	XX	0,086	0,053	0,049	0,053
VII	0,076	0,057	0,045	0,064	XXI	0,083	0,049	0,045	0,045
VIII	0,072	0,057	0,041	0,057	XXII	0,068	0,037	0,033	0,025
IX	0,160	0,150	0,140	0,170	XXIII	0,076	0,049	0,041	0,037
X	0,110	0,100	0,088	0,110	XXIV	0,096	0,086	0,083	0,086
XI	0,049	0,033	0,025	0,053	XXV	0,093	0,076	0,072	0,097
XII	0,086	0,064	0,061	0,140	XXVI	0,083	0,072	0,068	0,090
XIII	0,093	0,083	0,072	0,110	XXVII	0,090	0,072	0,064	0,076
XIV	0,270	0,260	0,240	0,270	XXVIII	0,076	0,064	0,057	0,064

TABLE 3. Logarithms of the Equilibrium Constants of VI-X in Solutions

Compound	CH ₃ OH	C ₂ H ₅ OH	<i>i</i> -C ₄ H ₉ OH	C ₆ H ₅ O ₂
VI	1,45	1,08	1,35	1,29
VII	0,24	0,15	0,06	0,13
VIII	0,30	0,08	0,18	0,12
IX	0,54	0,90	0,67	0,44
X	0,32	0,69	0,40	0,32

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