STUDY OF THE TAUTOMERISM OF 4-CYANO-3-THIOPHANONE AND 4-CYANO-5-METHYLTETRAHYDRO-3-FURANONE

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The Meyer equation is satisfied for the 4-cyano-3-thiophanone-4-cyano-5-methyltetrahydro-3-furanone pair in acetonitrile, alcohols, and aqueous dioxane. The Meyer equation is not satisfied for 4-cyano-3-thiophanone and 4-cyano-5-methyltetrahydro-3furanone paired with β -dicarbonyl compounds in acetonitrile, alcohols, and aqueous dioxane.

In a study of the tautomerism of 1-alkyl-3-carbomethoxy-4-piperidones, we demonstrated [1, 2] that these compounds do not obey the Meyer equation when paired with acetoacetic ester or esters of cyclohexanone-2-carboxylic acid. The Meyer equation is satisfied for tautomers of a single chemical type if the difference in the solvation of identical fragments of their forms is absent, and the solvation of different fragments of the tautomeric forms is independent of the structures of the identical fragments [3]. The nonsatisfaction of the Meyer equation for 1-alkyl-3-carbomethoxy-4-piperidones paired with acetoacetic ester and esters of cyclohexanone-2-carboxylic acid was therefore explained by the difference in the solvation of the nitrogen atoms in the keto and enol forms of the nitrogen-containing heterocyclic β -keto esters as a consequence of the difference in the conformations of the forms.

A similar phenomenon can be observed for 4-cyano-3-thiophanone (I) and 4-cyano-5-methyltetrahydro-3-furanone (II) paired with a cyano ketone that does not contain heteroatoms.

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It is known [4] that the >S and >O groups are well solvated by solvents. The conformations of the keto and enol forms of I and II differ substantially. Different solvation of the heteroatoms in the keto and enol forms of I and II and a change in solvation on passing from solvent to solvent are therefore possible. However, deviation from the Meyer equation is also possible for the I, II pair if the differences in the solvation of the heteroatoms of the tautomeric forms and the changes in them with solvent are different for I and II. It seemed that this condition would be satisfied for I, II, since the lengths and angles of the C-S and C-O bonds and the solvation capacities of the >S and >O groups [4] are extremely different. A study of the character of the deviations from the Meyer equation of the heteroatoms of I and II. In this paper, we have therefore studied the effect of solvents on the equilibria of I and II. It is known [6] that when the conditions enumerated above are satisfied for two β -cyano ketones, they obey the Meyer equation.

The conditions for the satisfaction of the Meyer equation that are presented above are ideal ones. They specify satisfaction of the equation for the case when the differences in the solvation of the forms of

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Solvent	λ _{r,} , nm	e _{T,S}	λ _{τ,} , nm	ϵ_{T_2S}	M _{T,S}	M _{T₂S}	M_{T_1S}/M_{T_2S}
Water Acetonitrile Methanol Ethanol Isobutanol Digxane 50% aqueous digyane	240 235 235 235 235 235 235 240	$\begin{array}{c} 2100\pm 50\\ 2600\pm 100\\ 5400\pm 200\\ 6500\pm 100\\ 7000\pm 100\\ 1940\pm 20\\ 3900\pm 200\\ \end{array}$	245 235 235 235 235 235 235 240	$\begin{array}{c} 730 \pm 40 \\ 830 \pm 20 \\ 3100 \pm 200 \\ 4600 \pm 100 \\ 5400 \pm 70 \\ 740 \pm 10 \\ 1600 \pm 200 \end{array}$	$\begin{array}{c} 1,400\pm0,013\\ 1,300\pm0,014\\ 1,125\pm0,005\\ 1,102\pm0,002\\ 1,094\pm0,002\\ 1,447\pm0,006\\ 1,182\pm0,011 \end{array}$	$\begin{array}{c} 1,252\pm0,241\\ 1,215\pm0,006\\ 1,050\pm0,004\\ 1,033\pm0,002\\ 1,028\pm0,002\\ 1,248\pm0,004\\ 1,101\pm0,012\\ \end{array}$	$\begin{array}{c} 1,118\pm0,033\\ 1,070\pm0,017\\ 1,072\pm0,008\\ 1,067\pm0,003\\ 1,064\pm0,003\\ 1,159\pm0,009\\ 0,073\pm0,022 \end{array}$

TABLE 1. UV Absorption and MTS Values and Their Ratios for I and II in Solutions

the two tautomers in each solvent are identical. However, the Meyer equation can also be satisfied when these differences are not identical but change identically on passing from one solvent to another. This will be observed for two tautomers in a series of monotypic solvents when the character of the solvation of the corresponding forms of the tautomers is identical. Moreover, the tautomers may not even be of the same chemical type. Thus the pairs of tautomers of β -keto esters and β -diketones obey the Meyer equation [7], although, strictly speaking, they cannot be assigned to the same chemical type. In contrast to β -keto esters and β -diketones, the enol form of β -cyano ketones does not have a strong chelate ring. β -Cyano ketones and β -dicarbonyl compounds therefore pertain to different chemical types. However, in connection with what was stated above, the Meyer equation can be satisfied for the β -cyano ketone- β -dicarbonyl compound pair in a series of monotypic solvents. The literature contains data to the effect that, although the Meyer dependence is not maintained for this pair over an extensive number of solvents, it is retained in a series of alcohols [8]. In the present paper, we verified the satisfaction of the Meyer equation for I, II paired with β -dicarbonyl compounds.

The tautomerism of I and II was studied by IR and UV spectroscopy. Cyanothiophanone I is a crystalline substance. There is only one intense band at 1750 cm⁻¹ in its IR spectrum. The C=N absorption band lies at 2243 cm⁻¹. Thus, judging from the IR spectrum, solid I exists in the keto form. Cyanotetrahydrofuranone II was obtained as a liquid. There is an intense band at 1780 cm⁻¹ and a weak band at ~1650 cm⁻¹ in its IR spectrum at 1600-1800 cm⁻¹. The C=N absorption band lies at 2250 cm⁻¹. Thus, judging from the IR spectrum, liquid II is the keto form with a small admixture of the enol form. According to the literature, the absorption bands of the C=O and C = N groups of the keto form are found at 1739 and 2237 cm⁻¹, respectively, for 2-cyano-1-cyclopentanone [9] and at 1739 and 2257 cm⁻¹, respectively, for 2-cyano-1-cyclohexanone [10].

Only the enol form absorbs in the UV spectra of neutral solutions of I and II at 220-340 nm. The ketenimine form does not exist in neutral solutions [8]. In neutral solutions, I and II form a tautomeric system of two forms, of which only one is active in the spectrum. For the quantitative study of tautomerism of this type by IR and UV spectroscopy, we have proposed [11] Eq. (1), which is equivalent to the Meyer equation, and Eq. (2):

$$\frac{\varepsilon_{T_1S_n}}{\varepsilon_{T_1S_n}-\varepsilon_{T_1S_1}} = \operatorname{const} \frac{\varepsilon_{T_2S_n}}{\varepsilon_{T_2S_n}-\varepsilon_{T_2S_1}}, \qquad (1)$$

$$\varepsilon_{0T_{1}} = \frac{\varepsilon_{T_{2}S_{2}} \cdot \varepsilon_{T_{2}S_{1}} (\varepsilon_{T_{1}S_{1}} - \varepsilon_{T_{1}S_{2}}) + n \cdot \varepsilon_{T_{1}S_{1}} \varepsilon_{T_{2}S_{1}} \varepsilon_{T_{2}S_{2}} - \varepsilon_{T_{2}S_{1}})}{n(\varepsilon_{T_{1}S_{1}} \cdot \varepsilon_{T_{2}S_{2}} - \varepsilon_{T_{2}S_{1}} \cdot \varepsilon_{T_{2}S_{2}})},$$
(2)

where ε_{TS} is the molar extinction coefficient of tautomer T in solvent S, ε_{0T} is the molar extinction coefficient of the absorbing form of tautomer T, which is independent of the solvent, and n is from $\varepsilon_{0T} = n \cdot \varepsilon_{0T_1}$. Equation (1) makes it possible to solve the problem of the satisfaction of the Meyer equation when the molar extinction coefficients of the absorbing forms of the tautomers are unknown. The satisfaction of (1) means the satisfaction of the Meyer equation. Equation (2) makes it possible to find the molar extinction coefficients of the absorbing forms of the tautomers, even when none of them is known. Equations (1) and (2) were verified in the case of β -keto esters [7]. In the present paper, they were used for the study of the tautomerism of I and II by UV spectroscopy.

The UV spectra of I, II in water, acetonitrile, alcohols, dioxane, and 50% aqueous dioxane were recorded (Table 1). In addition, the UV spectra of I and II in ethanol in the presence of NaOH were recorded. In alkaline solution, I absorbs at 263 nm ($\epsilon_{\rm TS}$ 17,000), while II absorbs at 265 nm ($\epsilon_{\rm TS}$ 11,000). These results are in good agreement with the literature data for model compounds. Thus, in neutral solution, 2cyano-1-cyclopentanone absorbs at 235 nm ($\epsilon_{\rm TS}$ 2400) but absorbs at 262 nm ($\epsilon_{\rm TS}$ 16,840) in alkaline so-

FABLE 2.	M_{TS}	Values	of I	and II a	\mathbf{and}	Their	Ratios	in	Solutions
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Solvent	M _{T,S}	M _{T,S}	M _{T,S} /M _{T₂S}
Water Acetonitrile Methanol Ethanol Isobutyl alcohol Dioxane 50% aq. dioxane	$\begin{array}{c} 1,351\pm0,11\\ 1,265\pm0,012\\ 1,112\pm0,004\\ 1,092\pm0,002\\ 1,084\pm0,001\\ 1,391\pm0,006\\ 1,162\pm0,009 \end{array}$	$\begin{array}{c} 1,222\pm0,014\\ 1,191\pm0,006\\ 1,045\pm0,003\\ 1,030\pm0,001\\ 1,025\pm0,001\\ 1,219\pm0,004\\ 1,091\pm0,011 \end{array}$	$\begin{array}{c} 1,105\pm0,013\\ 1,062\pm0,018\\ 1,064\pm0,007\\ 1,060\pm0,003\\ 1,058\pm0,001\\ 1,141\pm0,008\\ 1,065\pm0,019\\ \end{array}$

TABLE 3. M_{TS} Ratios of I and III-VI in Various Solvents

Solvent	M_{T_1S}/M_{T_3S}	M_{T_1S}/M_{T_4S}	M_{T_1S} / M_{T_5S}	M_{T_1S} / M_{T_6S}
Acetonitrile Methanol Ethanol Isobutyl alcohol Dioxane	$\begin{array}{c} 1,010\pm0,012\\ 1,033\pm0,006\\ 1,016\pm0,003\\ 0,975\pm0,001\\ 0,780\pm0,005\end{array}$	$\begin{array}{c} 1,269 \pm 0,031 \\ 1,290 \pm 0,11 \\ 1,269 \pm 0,009 \\ 1,239 \pm 0,012 \\ 0,990 \pm 0,010 \end{array}$	$\begin{array}{c} 0,981 \pm 0,16 \\ 0,985 \pm 0,006 \\ 0,985 \pm 0,003 \\ 0,959 \pm 0,002 \\ 0,766 \pm 0,004 \end{array}$	$\begin{array}{c} 1,089 \pm 0,014 \\ 1,114 \pm 0,014 \\ 1,077 \pm 0,007 \\ 1,052 \pm 0,005 \end{array}$

lution [9]. 2-Cyano-1-cyclohexanone in neutral solution absorbs at 236 nm (ϵ_{TS} 4800) but at 264 nm (ϵ_{TS} 11,800) in alkaline solution [10]. The rate of establishing equilibrium in solutions of I and II is very high. The pure compounds exist in the keto form, but, according to the UV spectra, in solution, even in isobutyl alcohol, there is a large amount of the enol form in solution 5 min after dissolving. However, I and II decompose in solution on standing. The maximum molar extinction coefficients of I and II in each solvent were therefore taken as the equilibrium values, and the decrease in the molar extinction coefficient in the course of 30 min was taken as the error in their determination if it exceeded the limits of the apparatus error. The molar extinction coefficients of I and II 5 min after preparation of the solutions are presented in Table 1. In determining the percentage of enol in the β -cyano ketones from the UV spectra, it is always assumed that the molar extinction coefficients of enols are independent of the nature of the solvent [12]. We used this assumption on the basis of our own data [13].

For work with Eq. (1), it was necessary to select a standard state. The $M_{TSn} = \epsilon_{TSn}/(\epsilon_{TSn} - \epsilon_{TS_1})$ value contains a difference. When the difference is small, the error in its determination may be very large. The standard state should therefore be selected in such a way that the difference is as large as possible while maintaining M_{TS} at a value other than unity. Considering this, we took the absorption of I in the standard state as equal to 600 and calculated the absorption of II in the standard state from the equation presented in [7]. The following values were obtained for pairs of solvents: acetonitrile-methanol 145, aceto-nitrile-ethanol 149, acetonitrile-isobutyl alcohol 151, and acetonitrile-50% aqueous dioxane 143. The average value of the molar extinction coefficient of II in the standard state was taken as equal to 147. The standard state enters into all of the M_{TS} values, and a small error in its determination does not affect the satisfaction of Eq. (1).

The M_{TS} values for I and II and their ratios in different states (Table 1) were calculated. The M_{TS} ratios of I and II, which are the constants of Eq. (1), are extremely close in acetonitrile, alcohols, and aqueous dioxane. The satisfaction of Eq. (1) is characterized by the maximum deviation of the equation constant from the average value in a number of states. The maximum deviation of the equation constant for the I, II pair does not exceed the limits of the error in the determination of this constant. Thus Eq. (1) and the Meyer equation are satisfied for I, II in the given solvents. The solvents are of different chemical types, and the most probable reason for the satisfaction of the Meyer equation for the I, II pair is therefore identical solvation of the heteroatoms of the keto and enol forms. This fact seems of definite interest. It is unlikely that identical obstacles to solvation of the heteroatom in the keto and enol forms of I, II exist. It is most likely that the heteroatom, for example, oxygen, forms a hydrogen bond with the most favorably disposed electron pair, and the obstacles to its solvation are insignificant in both forms.

Equations (2) were written for I, II for different combinations of states. Pairs from the solvent and the standard state were considered. Compound I was taken as tautomer T_1 , and II was taken as T_2 . Equations of the (2a) type were obtained:

$$c_{0T_1} = -B \frac{1}{n} + A.$$
(2a)

The A and B coefficients for combinations of the standard state with various solvents are as follows: 9200 and 2100 for acetonitrile, 9000 and 2050 for methanol, 9600 and 2200 for ethanol, 10,000 and 2300 for isobutyl alcohol, 8800 and 2000 for 50% aqueous dioxane, 4350 and 900 for dioxane, and 5700 and 1200 for water. If, in accordance with Table 1, the last two values are discarded, $A = 9400 \pm 600$, and $B = 2150 \pm 150$. Equations of this type make it possible to determine the molar extinction coefficient of tautomer T for small B values if n is fixed within certain limits [7]. The B coefficient decreases as the difference between the molar extinction coefficients of two tautomers in monotypic states increases. Unfortunately, we do not yet have other β -cyano ketones at our disposal, and we cannot compile pairs of tautomers with the desirable molar extinction coefficients. The B value in the equation is too high for the I-II pair. In this case, however, n cannot be less than one, since ε_{0T} cannot be less than 7000. For this reason, n should in all likelihood lie between one and two. When this value is substituted into Eq. (2a), we obtain a ε_{0T} value of 7750 \pm 750.

In order to solve the problem of the satisfaction of the Meyer equation for I, $II-\beta$ -dicarbonyl compound pairs, we found the molar extinction coefficients of I, II in the standard state corresponding to the standard state of acetoacetic ester with a molar extinction coefficient of 100. The following values were obtained for various solvent pairs: 461 and 110 for acetonitrile-methanol, 527 and 130 for acetonitrileethanol, and 648 and 159 for acetonitrile-isobutyl alcohol, respectively, for I and II. The average values of 545 and 133 were taken for I and II, respectively. The M_{TS} values for I and II in solutions were calculated by means of these values.

In this case, the standard state is determined with a large error. However, as we have previously noted [7], the error in the determination of the standard state is introduced identically over all M_{TS} values and does not affect the satisfaction of Eq. (1). In fact, the M_{TS} ratios for I and II, which are presented in Table 2, are equal, within the limits of experimental error, in acetonitrile, alcohols, and aqueous dioxane. The maximum deviation in the constant of Eq. (1) from the average value in the series of solvents does not exceed the limits of the error in the determination of the constant. The ratios of the MTS values of I to those of acetoacetic ester (III), acetylacetone (IV), and the ethyl esters of cyclopentanone-2-carboxylic acid (V) and cyclohexanone-2-carboxylic acid (VI) are presented in Table 3. The M_{TS} values of III and IV were taken from [7]. The standard states of IV and VI are presented relative to the standard state of III with a molar extinction coefficient of 100. It is apparent from Table 3 that the differences between the constants of Eq. (1) in various states far exceed the limits of the experimental error. The deviation is particularly high in dioxane. This indicates poor satisfaction of the Meyer equation for I in pairs with β -dicarbonyl compounds, even in monotypic solvents. The character of the solvation, respectively, of the keto and enol forms of I, as well as II and β -dicarbonyl compounds, apparently differs markedly. However, this does not exclude the possibility of the satisfaction of the Meyer equation for other β -cyano ketones- β -dicarbonyl compound pairs in other sets of monotypic solvents.

EXPERIMENTAL

<u>4-Cyano-3-thiophanone (I)</u>. Ethyl thioglycolate [7 g (0.06 mole)] was added to a solution of 24 g (0.35 mole) of sodium ethoxide in 50 ml of absolute benzene, and 3 g (0.06 mole) of acrylonitrile was then added slowly dropwise with stirring. At the end of the addition, the reaction mixture was heated to 60°, allowed to stand for 1 h, and then poured into 50 ml of ice water containing 8 ml of concentrated hydrochloric acid. The benzene layer was separated and washed. The benzene was removed in vacuo, and the residue was distilled to give 42% of a product with bp 125° (1 mm), mp 71°, and nD²³ 1.5118. Found: C 47.0; H 4.2; N 10.8%. C₅H₅NOS. Calculated: C 47.2; H 3.9; N 11.0%.

<u>4-Cyano-5-methyltetrahydro-3-furanone (II)</u>. Ethyl lactate [10.3 g (0.09 mole)] was added to 2.3 g (0.1 g-atom) of powdered sodium metal in 60 ml of ether, and the mixture was allowed to stand until the reaction was complete. The ether was removed in vacuo, and 50 ml of benzene was added. Acrylonitrile [15 g (0.28 mole)] was then added slowly with stirring, and the mixture was heated to 60° and allowed to stand for 1 h. The mixture was then poured into 50 ml of ice water containing 5 ml of concentrated hydro-chloric acid, and the benzene layer was separated and washed. The benzene was removed in vacuo, and the residue was distilled to give a product with bp 52° (1.5 mm), n_D^{18} 1.4580, and d_4^{18} 1.1459. Found: C 57.3; H 5.6; N 11.3%; MRD 29.76. $C_6H_7NO_2$. Calculated: C 57.6; H 5.6; N 11.2%. MRD 29.19 ketone, 30.69 enol.

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