Acid-base properties and complex-forming ability of 4,6-dimethyl-2-(1*H*)-pyrimidinone (thione)

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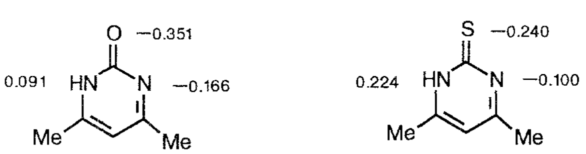
Complex formation of 4,6-dimethyl-2-(1*H*)-pyrimidinone (thione) with dysprosium(III) tris(acetylacetonate), Dy(acac)$_3$, in 80 % (v/v) aqueous methanol was investigated by pH-metric titration and paramagnetic birefringence. Due to its higher basicity and lower acidity, 4,6-dimethyl-2-(1*H*)-pyrimidinone is coordinated by Dy(acac)$_3$ without deprotonation, whereas its thio analog is coordinated in the deprotonated form. Due to the higher acidity of 4,6-dimethyl-2-(1*H*)-pyrimidinethione, the complex of its anion with Dy(acac)$_3$ is much more stable than that derived from the oxo analog, as inferred from the comparison of the stability constants.

Key words: 4,6-dimethyl-2-(1*H*)-pyrimidinone, 4,6-dimethyl-2-(1*H*)-pyrimidinethione, dysprosium tris(acethylacetonate), complex formation; stability constants.

The physical and chemical properties of pyrimidine derivatives are known to vary over a wide range depending on the nature of their substituents.[1] The purpose of the present work is to perform a comparative evaluation of the acid-base properties and the complex-forming ability of 4,6-dimethyl-2-(1*H*)-pyrimidinone (**1**) and 4,6-dimethyl-2-(1*H*)-pyrimidinethione (**2**) (Scheme 1). The acid-base properties were examined by pH-metric titration. The ability to form complexes was evaluated using Dy^{3+} tris(acetylacetonate) in aqueous methanol by the method of paramagnetic birefringence (PBR).

Scheme 1



1 **2**

Experimental

Compounds **1** and **2** were prepared according to known procedures[2,3] and purified by recrystallization. Methanol was purified by distillation according to a standard procedure.[4] The p*K* values for dissociation of compounds **1** and **2** were estimated by pH-metric titration. The data were processed using the CPESSP[5] mathematical simulation program.

All of the measurements were carried out at 25 °C in 80 % (v/v) aqueous methanol. The activity of protons was determined with an accuracy of 0.05 pH units on an I-130 pH-meter, which was adjusted using standard aqueous buffer solutions. To measure the pH of water-organic solutions, an electrode was preliminarily steeped in the corresponding aqueous organic solvent for ~24 h. The pH values of solutions were determined from the relationship:

$$\mathrm{pH} = \mathrm{pH}_{\mathrm{meas}} - \Delta\mathrm{pH},$$

where pH$_{\mathrm{meas}}$ is the pH value experimentally determined in a mixed solvent and ΔpH is the difference between the activity of protons in water and that in the organic solvent—water mixture estimated according to the previously described procedure.[6]

Quantum-chemical calculations were carried out by the MNDO—PM3[7] method with full optimization of the geometry using the AMPAC program.

Results and Discussion

The p*K* values for the equilibrium dissociation of compounds **1** and **2** in aqueous methanol are given in Table 1. Compound **1** is more basic than pyrimidine: p*K* of its protonated form (equilibrium (1)) is 3.35, whereas p*K* of pyrimidine is 1.3 (*cf.* Ref. 8).

$$[\mathrm{H_2L}]^+ \leftrightarrow \mathrm{H}^+ + \mathrm{HL} \qquad (1)$$

The acidity of compound **1** (p*K* = 10.7) is noticeably lower than that of its thio analog **2** (see Table 1). The charge distribution in molecules **1** and **2** shown in

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Table 1. The p*K* values for dissociation of compounds **1** and **2** in 80 % aqueous methanol

Equilibrium	p*K*	
	1	**2**
(1)	3.35±0.05	—
(2)	—	1.5±0.1
(3)	10.7±0.1	6.3±0.1

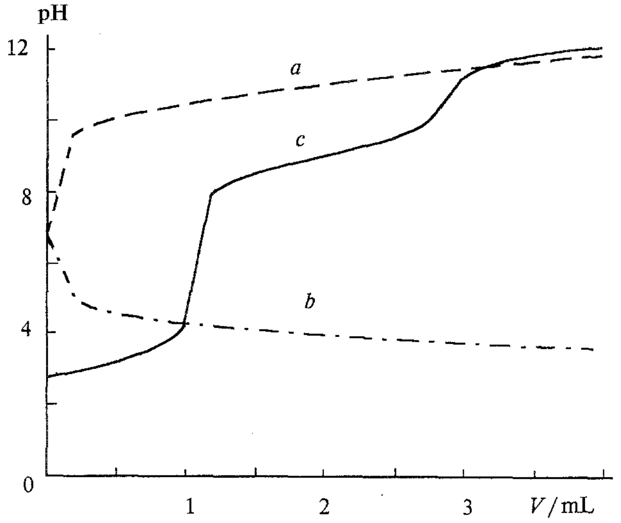

Fig. 1. The curves of pH-metric titration of compounds **1** (*a*, *b*) and **2** (*c*):
a, C_1 = 0.028 mol L^{-1}, C_{KOH} = 0.088 mol L^{-1};
b, C_1 = 0.028 mol L^{-1}, C_{HCl} = 0.04 mol L^{-1};
c, C_2 = 0.021 mol L^{-1}, C_{KOH} = 0.088 mol L^{-1}.

Scheme 1, obtained by the MNDO—PM3 method, is in agreement with the acid-base properties of these compounds. Because the polarizability of the C=S bond is higher than that of C=O bond, the p(N)—π*(C=S) conjugation is stronger and, therefore, the proportion of bipolar forms is higher. This favors an increase in acidity and a characteristic charge separation in molecule **2**.

However, whereas the shape of the titration curve of compound **1** is typical of a bipolar form in the pH region where it exists (5—9 pH units), the curve of thio analog **2** with two pH jumps is characteristic of weak acids (Fig. 1). Mathematical processing of the titration data with the CPESSP program allows one to conclude that the first and the second jumps are caused by equilibria (2) and (3), respectively.

$$2HL \leftrightarrow [HL_2]^- + H^+ \qquad (2)$$

$$HL \leftrightarrow L^- + H^+ \qquad (3)$$

Therefore it is reasonable to assume that the absence of the jump normal for bipolar systems in the beginning of the titration of compound **2** occurs as a result of equilibrium (2), and not because the proportion of the bipolar form is too low.

The above-considered distinctions between the acid-base properties of substituted pyrimidines **1** and **2** are the main reasons for their different abilities to form complexes. In addition, the vacant d-AO with π-symmetry of the sulfur atom can overlap with the π-system of the aromatic ring,[9] thus increasing the stability of the corresponding complex. However, this factor is only essential in the case when π-symmetry orbitals participate noticeably in the coordination bond. The ability of compounds **1** and **2** to form complexes was estimated using $Dy(acac)_3$, which has an ionic coordination bond.[10] In aqueous methanol, at concentrations above 80 % (v/v), the two molecules of water incorporated in the first coordination sphere of Dy^{3+} are replaced by methanol molecules, and the latter, in turn, may be replaced by molecules of a base.

The formation of adducts between $Dy(acac)_2$ and compounds **1** and **2** was studied by PBR.[12] The search for the model of complex formation and the evaluation of the corresponding constants were based on the dependence of the magneto-optical data on the concentrations of compounds **1** and **2** at a constant concentration of $Dy(acac)_3$ (Table 2). As can be seen from Table 2, an increase in the concentration of compound **2** results in a considerable decrease in pH, owing to the high acidity of **2**, and this may cause partial decomposition of $Dy(acac)_3$. Therefore, the correct evaluation of the complex-formation constants in the $Dy(acac)_3$—**2** system requires a magneto-optical study of the equilibria in the Dy^{3+}—Hacac system as its pH is varied. Based on the pH dependence of the magneto-optical data at Dy^{3+} : Hacac ratios of 1 : 1, 1 : 2, 1 : 3, and 1 : 4.5 and taking into account the dissociation constant of Hacac (p*K* = 9.76±0.05) determined by pH-metric titration, we found, after processing the results by the CPEESP program, the equilibrium constants for reactions (4)—(6) and the PBR ($_mP$) constants for complexes $[Dy(acac)]^{2+}$, $[Dy(acac)_2]^+$, and $Dy(acac)_3$ (Table 3).

$$Dy^{3+} + Hacac \leftrightarrow [Dy(acac)]^{2+} + H^+ \qquad (4)$$

$$[Dy(acac)\ ]^{2+} + Hacac \leftrightarrow [Dy(acac)_2]^+ + H^+ \qquad (5)$$

$$[Dy(acac)_2]^+ + Hacac \leftrightarrow [Dy(acac)_3] + H^+ \qquad (6)$$

The validity of the model suggested for the formation of the complex between Dy^{3+} and acetylacetone is indirectly supported by the fact that the $_mP$ value for $Dy(acac)_3$ (see Table 3) coincides with the PBR constant ($_mP = -40 \cdot 10^{-15}$ emu) obtained for dissolution of $Dy(acac)_3 \cdot 3H_2O$ synthesized by the known procedure[13] in methanol. The experimental dependence of the magneto-optical characteristics for compound **1** on the con-

Table 2. The dependences of the magneto-optical parameters of the complexes on the pH and concentrations of the components

Dy(acac)$_3$—**1**				Dy(acac)$_3$—**2**			
pH	$C_{\text{acac}}\cdot10^3$ /mol L^{-1}	$C_1\cdot10^2$ /mol L^{-1}	$\frac{\Delta\varphi}{C_{\text{acac}}}$ /deg L mol^{-1}	pH	$C_{\text{acac}}\cdot10^3$ /mol L^{-1}	$C_2\cdot10^{-2}$ /mol L^{-1}	$\frac{\Delta\varphi}{C_{\text{acac}}}$ /deg L mol^{-1}
8.15	3.95	36.79	18.5	8.71	23.46	0.0	−1.6
8.17	3.95	32.19	17.7	8.10	23.46	1.07	1.5
8.30	3.95	22.99	17.0	7.94	23.60	1.55	2.5
8.40	3.90	18.42	16.0	7.75	23.46	2.14	4.3
8.45	3.95	13.80	15.7	7.63	23.60	2.59	5.1
8.51	3.90	11.51	15.3	7.44	23.46	3.21	7.0
8.55	3.90	9.21	14.9	7.38	23.60	3.63	8.5
8.63	3.90	4.60	4.9	7.14	23.46	4.27	9.2
8.63	15.70	4.60	0.6	6.96	23.60	5.18	12.3
8.63	15.70	2.30	0.5	6.70	11.73	3.21	13.0
—	—	—	—	5.90	11.73	4.27	12.8
—	—	—	—	5.26	11.73	5.34	13.0

Note: $\Delta\varphi$ is the angle of rotation of the polarization plane.

Table 3. Equilibrium constants (β), stability constants (β_{stab}), and PBR constants ($_mP_i$) of Dy^{3+} acetylacetonates in 80 % aqueous methanol

Equilibrium	logβ	Complex	logβ_{stab}	$_mP_i\cdot10^{15}$ /emu
(4)	−2.0±0.1	[Dy(acac)]$^{2+}$	7.7	276±40
(5)	−2.5±0.2	[Dy(acac)$_2$]$^+$	14.9	590±100
(6)	−2.4±0.2	[Dy(acac)$_3$]	22.4	−39±3

Table 4. Constants (β) for the equilibria occurring in the Dy(acac)$_3$—L systems and stability constants (β_{stab}), and PBR constants ($_mP_i$) of the resulting complexes

L	Equilibrium	logβ	Complex	logβ_{stab}	$_mP_i\cdot10^{15}$ /emu
1	(7)	−1.0±0.1	[Dy(acac)$_3$HL]	23.4	600±100
2	(8)	−2.4±0.06	[Dy(acac)$_3$L]$^-$	26.9	−299±30
2	(9)	4.2±0.1	[Dy(acac)$_2$L$_2$]$^-$	28.1	563±70
2	(10)	2.9±0.1	[Dy(acac)L$_3$]$^-$	28.1	500±90
Py	(7)	1.0±0.1	[Dy(acac)$_3$L]	23.4	−75±6
bipy	(7)	1.8±0.1	[Dy(acac)$_3$L]	24.2	−1950±90
phen	(7)	2.4±0.1	[Dy(acac)$_3$L]	24.8	−3580±150

centration and pH (see Table 2) is adequately described by the assumption of equilibrium (7). The constant for this equilibrium is given in Table 4.

$$\text{Dy(acac)}_3 + \text{HL} \leftrightarrow [\text{Dy(acac)}_3\text{HL}] \quad (7)$$

However, an adequate description of the similar experimental data for thio analog **2** requires that equilibria (8)—(10) be included in the model of complex formation:

$$\text{Dy(acac)}_3 + \text{HL} \leftrightarrow [\text{Dy(acac)}_3\text{L}]^- + \text{H}^+ \quad (8)$$

$$[\text{Dy(acac)}_3\text{L}]^- + \text{HL} \leftrightarrow [\text{Dy(acac)}_2\text{L}_2]^- + \text{Hacac} \quad (9)$$

$$[\text{Dy(acac)}_2\text{L}_2]^- + \text{HL} \leftrightarrow [\text{Dy(acac)L}_3]^- + \text{Hacac} \quad (10)$$

Thus, compound **2** coordinates with Dy(acac)$_3$ with the abstraction of a H$^+$, which is in agreement with its higher acidity. The [Dy(acac)$_3$L]$^-$ complex (HL is compound **2**) is much more stable than its analog derived from compound **1**, which may be due to the ionic constituent of the coordination bond. As the concentration of compound **2** increases, its anion displaces acetylacetonate from the coordination sphere of Dy^{3+} (see equilibria (9) and (10)).

The stability constant of the [Dy(acac)$_3$HL] complex (HL is compound **1**) is practically identical to that of the pyridine-containing complex, [Dy(acac)$_3$Py], which we determined previously, in spite of the considerably lower basicity of compound **1** compared with that of pyridine.[7] The increase in the adduct-formation constant for compound **1** is probably due to the character of its bidentate coordination.[14,15] Anion **2** is coordinated to give an adduct that is more stable than the corresponding adducts of bidentate bases such as 2,2′-bipyridyl (bipy) and 1,10-phenanthroline (phen) (see Table 4). This seemingly correlates with the ionic constituent of the coordination bond. However, the increase in the stability on going from [Dy(acac)$_3$L]$^-$ to [Dy(acac)$_2$L$_2$]$^-$ and [Dy(acac)L$_3$]$^-$ does not agree with the fact that the basicity of the anion of **2** is lower than that of acac$^-$ (p*K* of Hacac and compound **2** are 9.76 and 6.86, respectively).

Thus, the comparative analysis of the acid-base properties of compounds **1** and **2** in 80 % (v/v) aqueous methanol carried out by pH-metric titration has shown that compound **1**, which has lower acidity, combines with Dy(acac)$_3$ without the abstraction of a proton, whereas its thio analog **2** coordinates in the deprotonated form. The acidity of compound **2** does not agree with the high stability of its complexes.

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