

## CRYSTAL STRUCTURE OF POTASSIUM 2-THIOBARBITURATE

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The crystal and molecular structure of potassium thiobarbiturate  $C_4H_3KN_2O_2S$  ( $C_4H_4N_2O_2S$ -2-thiobarbituric acid,  $H_2TBA$ ) is determined. Crystallographic data for KHTBA are as follows:  $a = 11.2317(17)$  Å,  $b = 3.8687(6)$  Å,  $c = 14.557(2)$  Å,  $\beta = 97.448(4)^\circ$ ,  $V = 627.18(17)$  Å<sup>3</sup>, space group  $P2/c$ ,  $Z = 4$ . Each potassium ion is linked with four oxygen atoms and two S atoms forming a distorted octahedron.  $N-H\cdots O$  and  $C-H\cdots S$  hydrogen bonds form a branched three-dimensional network. The structure is also stabilized by the  $\pi-\pi$  interaction of heterocyclic  $HTBA^-$  ions.

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2-Thiobarbituric acid (4,6-dihydroxy-2-mercaptopyrimidine,  $C_4H_4N_2O_2S$ ,  $H_2TBA$ ) and several of its derivatives have been long used due to their pharmaceutical properties [1]. The complex of  $H_2TBA$  with tin(IV) exhibits anticancer activity [2].  $H_2TBA$  is used as an analytical reagent to detect malonic dialdehyde being a product of peroxidation of lipids [3], palladium, ruthenium, and bismuth [4-6].

2-Thiobarbituric acid is a dibasic acid. By the literature data, in  $H_2TBA$ , the  $pK_{a1}$  values vary in a range of 2.10-2.25, and  $pK_{a2}$  from 10.55 to 10.72 [7]. It has not yet been clearly identified, which forms are included in the equilibrium in both cases. According to one interpretation, a smaller  $pK_{a1}$  value is related to the dissociation of the N-protonated  $H_3TBA^+$  cationic form to  $H_2TBA$ , and  $pK_{a2}$  is related to the dissociation of the uncharged  $H_2TBA$  form to a  $HTBA^-$  anion [7, 8]. Another interpretation associates  $pK_{a1}$  with proton abstraction from the OH group of the neutral  $H_2TBA$  molecule in the enol form, and  $pK_{a2}$  is associated with the equilibrium between singly charged  $HTBA^-$  and doubly charged  $TBA^{2-}$  anionic forms [9, 10]. In order to determine the nature of acid-base equilibria existing in thiobarbituric acid solutions, it seems important to accumulate data on the structure of the products of its interaction with inorganic bases, e.g., alkali metal hydroxides and acids. In the Cambridge Crystallography Data Center (CCDC), the data on the salts of thiobarbituric acid with alkali metal ions or on its compounds with acids are almost absent, except for two potassium compounds [11].

Here, the product of KOH interaction with thiobarbituric acid is obtained and its structure is determined.

## EXPERIMENTAL

In the work,  $C_4H_4N_2O_2S$  thiobarbituric acid (chemically pure), KOH (chemically pure), and KBr (chemically pure) were used.

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**TABLE 1.** Main Crystallographic Characteristics of KHTBA and Parameters of the Experiment

Crystallographic data	
Chemical formula	C <sub>4</sub> H <sub>3</sub> KN <sub>2</sub> O <sub>2</sub>
<i>M<sub>r</sub></i>	182.24
Space group, <i>Z</i>	<i>P</i> 2/ <i>c</i> , 4
<i>a</i> , <i>b</i> , <i>c</i> , Å; β, deg	11.2317(17), 3.8687(6), 14.557(2); 97.448(4)
<i>V</i> , Å <sup>3</sup>	627.18(17)
<i>d</i> , g/cm <sup>3</sup>	1.930
μ, mm <sup>-1</sup>	1.11
Data collection parameters	
Number of measured / indep. reflections, <i>N</i> <sub>1</sub>	8110 / 1919
Number of reflections with <i>I</i> > 2σ( <i>I</i> ), <i>N</i> <sub>2</sub>	1255
Absorption	Multiscanning
<i>R</i> <sub>int</sub>	0.070
2θ <sub>max</sub> , deg	61
<i>h</i> , <i>k</i> , <i>l</i>	-15 → 16, -5 → 5, -20 → 20
Refinement results	
<i>R</i> [over <i>N</i> <sub>1</sub> reflections]	0.0813
<i>R</i> [over <i>N</i> <sub>2</sub> reflections]	0.0402
<i>wR</i> ( <i>F</i> <sup>2</sup> ) [over <i>N</i> <sub>1</sub> reflections]	0.0939
<i>S</i>	1.002
Weight scheme	$w = 1/[\sigma^2(F_0^2) + (0.0387P)^2]$ , where $P = \max(F_0^2 + 2F_c^2)/3$
(Δσ) <sub>max</sub>	<0.007
Δρ <sub>max</sub> /Δρ <sub>min</sub> , e/Å <sup>3</sup>	0.33/-0.38
Extinction coefficient (SHELX97)	<0.0004 was not introduced

**Synthesis of C<sub>4</sub>H<sub>3</sub>KN<sub>2</sub>O<sub>2</sub> (I).** 0.2 g of thiobarbituric acid (H<sub>2</sub>TBA) were dissolved in 2-3 ml of 1-2 M KOH. A white scaly polycrystalline precipitate formed was filtered, washed with acetone, and left to dry in the air until reaching a constant weight. Product yield 89%. White single crystals of the compound were isolated by evaporation of the filtrate. The X-ray diffraction pattern of the polycrystalline substance coincided with that calculated from the crystallographic data for a single crystal, which indicates one phase.

**Single crystal X-ray diffraction study.** The intensities of X-ray reflections from the 0.21×0.20×0.05 mm crystal were measured at 298 K on a single crystal SMART APEX II diffractometer with a CCD detector (Bruker AXS), MoK<sub>α</sub> radiation, λ = 0.7106 Å. The orientation matrix and unit cell parameters were determined and refined using 1919 reflections. The cell corresponds to the monoclinic symmetry. Main crystallographic characteristics and parameters of the experiment are listed in Table 1.

X-ray absorption by the crystal was taken into account based on the analysis of the intensities of equivalent reflections. After this, the intensities of equivalent reflections were averaged, and subsequently only independent reflections were used.

The model was determined using the SHELXS software [12] by direct methods. As a result, the coordinates of all non-hydrogen atoms were found. The structure was refined by the least-squares technique using the SHELXL97 software [13]. The thermal parameters of all non-hydrogen atoms were refined anisotropically. From difference electron density maps, the maxima corresponding to all hydrogen atoms were determined. The coordinates of all hydrogen atoms were further idealized, and for all of them the isotropic thermal parameter was refined. Eventually, the refinement was stopped at *R* = 4.02% for 1255 strong reflections with *F*<sup>2</sup> > 2σ(*F*<sup>2</sup>). The extinction coefficient was not refined due to its low value. Graphical representation of all crystal structures and molecules was made using the DIAMOND software [14]. The structure was deposited with the Cambridge Crystallographic Data Centre under No. 878424. The data can be obtained via the following website [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

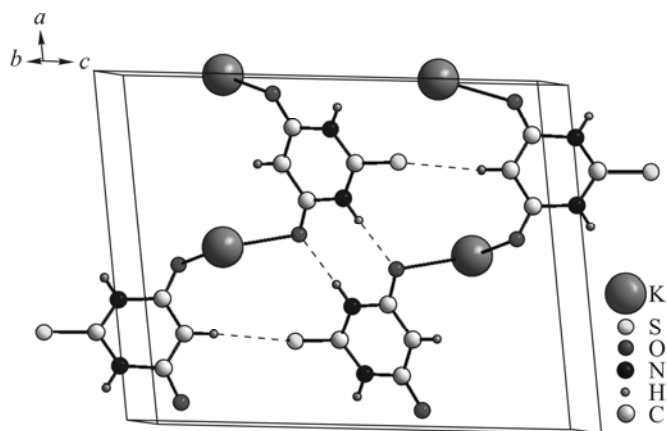
## RESULTS AND DISCUSSION

The structure of **I** is presented in Fig. 1. The asymmetric part of the unit cell contains one HTBA<sup>-</sup> ion and two independent potassium ions (K1 and K2) occupying special sites (Fig. 2). Thus, the cell contains four K<sup>+</sup> and four HTBA<sup>-</sup>. Each potassium ion is linked with four oxygen atoms and two S atoms forming a distorted octahedron (Fig. 3), with the S atoms being in *trans*-position to each other.

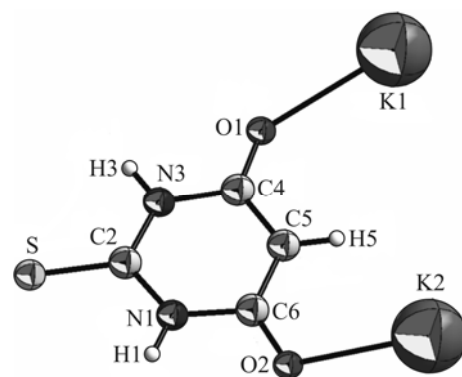
The K–O distances in the compound vary from 2.7307(19) Å to 3.097(2) Å, they are in good agreement with the distances for this bond in the CCDC (2.7–3.2 Å). The lengths of two K–S bonds are in a range from 3.2352(9) Å to 3.2415(8) Å; this corresponds to the normal lengths of such bonds (3.2–3.3 Å) given in the CCDC. The other K1–S distances being 3.6750(9) Å indicate the absence of interaction. In **I**, a small increase in the S–C4 distance to 1.680(2) Å as compared to free H<sub>2</sub>TBA (1.629 Å [11]) is observed, which is explained by sulphur atom interaction with the potassium ion. Apparently, it is primarily ion-dipole in nature.

Commercially available H<sub>2</sub>TBA is a thione-enol tautomer [15].

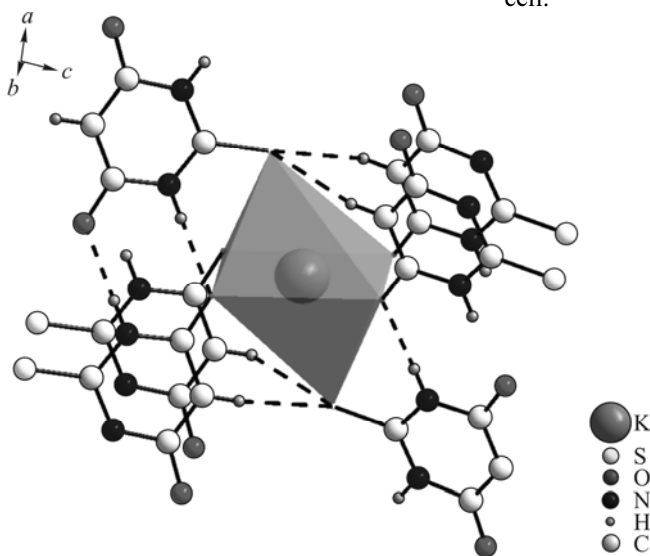
The main bands in the IR spectrum of **I** in KBr, which are typical of the H<sub>2</sub>TBA thione-enol tautomer, give evidence of a similar structure of the thiobarbiturate ion in KHTBA and are consistent with the results of the single crystal X-ray diffraction



**Fig. 1.** Structure of **I**. Hydrogen bonds are denoted by dashed lines.



**Fig. 2.** Asymmetric part of the HTBA unit cell.



**Fig. 3.** Coordination environment of the K1 ion. Intermolecular hydrogen bonds are denoted by dashed lines.

**TABLE 2.** Hydrogen Bonds D–H···A (Å, deg) in the Structure of **I**

D–H···A	D–H	H···A	D···A	D–H···A
N1–H1···O2 <sup>2</sup>	0.86	1.96	2.814 (3)	175
N3–H3···O1 <sup>3</sup>	0.86	1.99	2.845 (3)	175
C5–H5···S <sup>1</sup>	0.93	2.85	3.416 (2)	120

Symmetry operations: <sup>1</sup>  $x, -y+2, z-1/2$ ; <sup>2</sup>  $-x+2, -y+2, -z+1$ ; <sup>3</sup>  $-x+1, -y+1, -z+1$ .

**TABLE 3.** Parameters of the  $\pi$ – $\pi$  Interaction of HTBA<sup>–</sup> Cations in the Crystal of **I**

Cg <sub>i</sub> –Cg <sub>j</sub>	$d(\text{Cg}–\text{Cg}), \text{Å}$	$\alpha, \text{deg}$	$\beta, \text{deg}$	$\gamma, \text{deg}$	Cg <sub>i</sub> –p, Å	Shift, Å
Cg <sub>1</sub> –Cg <sub>1</sub> '	3.8686	0	27.41	27.41	3.4343	1.781

Cg<sub>1</sub> is the N1, C2, N3, C4, C5, C6 ring plane. Cg<sub>1</sub>' is produced by transformation  $[x, y-1, z]$ .

study. The most significant difference is observed in a range of 1100–1720 cm<sup>–1</sup>. Thus, a band at 1720 cm<sup>–1</sup> assigned to  $\nu(\text{C}=\text{O})$  [8] disappears in the H<sub>2</sub>TBA spectrum; instead strong bands at 1610 cm<sup>–1</sup> and 1630 cm<sup>–1</sup> emerge. This confirms the coordination of the ligand to the K<sup>+</sup> ion through the oxygen atom. An intense H<sub>2</sub>TBA absorption band at 1159 cm<sup>–1</sup> assigned to  $\nu(\text{C}=\text{S})$  [8] is absent in the IR spectrum of KHTBA, which agrees with the ligand coordination through the sulfur atom.

In [8], based on the conclusions of [7], the results of the pH study are explained by the dominance of the H<sub>3</sub>TBA<sup>+</sup> cationic form in the aqueous solution at pH < 1, the H<sub>2</sub>TBA neutral form at 3 < pH < 9, and the HTBA<sup>–</sup> anionic form at pH > 12. The produced KHTBA salt appeared to be moderately soluble in water (0.05 M); pH of its saturated solution is 8. When the solution was acidified with HCl, the solubility of **I** decreased. According to the data from [8], at pH 8 the H<sub>2</sub>TBA neutral form is dominant; the formation of the H<sub>3</sub>TBA<sup>+</sup> cationic form on acidifying, on the contrary, should increase its solubility. The attempts to isolate the compounds of thiobarbituric acid with HCl and HClO<sub>4</sub> acids invariably resulted in the production of thiobarbituric acid. The synthesis of a series of metal complexes containing the TBA<sup>2–</sup> anion of doubly deprotonated thiobarbituric acid [9, 10] and our results are in a better agreement with another interpretation of its acid-base equilibria. It associates pK<sub>a1</sub> with proton abstraction from the enol group of the neutral H<sub>2</sub>TBA molecule, and pK<sub>a2</sub> with the equilibrium between singly charged HTBA<sup>–</sup> and doubly charged TBA<sup>2–</sup> anionic forms [9, 10]. This agrees with the finding that the proton of the CH<sub>2</sub> group is the most “acidic” in thiobarbituric acid [8] (C5 in Fig. 2), which, in the free compound, passes to the oxygen atom of the neighboring carbonyl group (enolization). It is the C5–OH group which is the most probable coordination center of the ligand, as in compound **I**.

The analysis of the structure revealed the presence of four intermolecular hydrogen bonds: N–H···O and C–H···S (Table 2), forming a three-dimensional framework. Two N–H···O hydrogen bonds between the HTBA<sup>–</sup> ions close the 8-membered ring corresponding to a supramolecular motif  $R_2^2(8)$  [16]. In addition, six 6-membered rings with the participation of K<sup>+</sup> ions ( $R_1^1(6)$ ) form: four of them close C5–H5···S hydrogen bonds and two close N1–H1···O2 and N3–H3···O1 hydrogen bonds (Fig. 3).

The analysis by the PLATON software of shortened intermolecular contacts [17] showed the presence of  $\pi$ – $\pi$  interaction between the rings of the HTBA<sup>–</sup> ions. Its geometric characteristics are given in Table 3. The HTBA<sup>–</sup> ions have head-to-head packing [16]. The  $\pi$ – $\pi$  interaction was also found in the polymorphic forms of thiobarbituric acid [15].

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