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Solid-State Thiotropolone: An Extremely Rapid Intramolecular Proton Transfer

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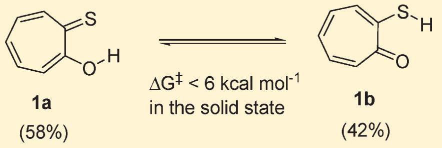
ABSTRACT: Through variable-temperature solution-state NMR and molten- and solid-state CP/MAS ^{13}C NMR spectra, thiotropolone is found to exist as two rapidly equilibrated tautomeric structures, thione and enethiol, even in the solid state far below the melting point. The crystal structure shows an almost perpendicular packing, suggesting that the intramolecular hydrogen bond is dominant.



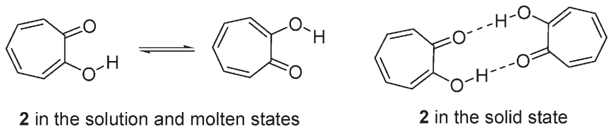
We report herein unprecedented solid-state properties of thiotropolone (**1**, melting point = 54−55 °C).[1] This sulfur analogue **1** of tropolone (**2**) behaves entirely different from the solid state **2**.

Organic compounds with undegenerate tautomeric systems have been reported to exist as mixtures of unequivalent forms in a different ratio at a given temperature in both the solution and solid states. Such temperature dependence may be called "thermodynamic solid state effect (TSSE)". On the other hand, it has been known that in organic crystals the rate of the intermolecular proton-transfer reaction[2] decreases dramatically by lowering the temperature due to a kinetic solid state effect (KSSE).[3] In a typical KSSE, solid-state tropolone[4] (2-hydroxytropone) (**2**) freezes the tautomerism within the NMR time scale, resonating in seven individual carbons ($\Delta G^{\ddagger} = 26 \pm 5$ kcal mol^{-1}) in the ^{13}C CP/MAS NMR.[4] In the solution[5] and molten[4] states, however, **2** has been known as a fast equilibrium system showing the averaged four signals in the NMR (Scheme 1).

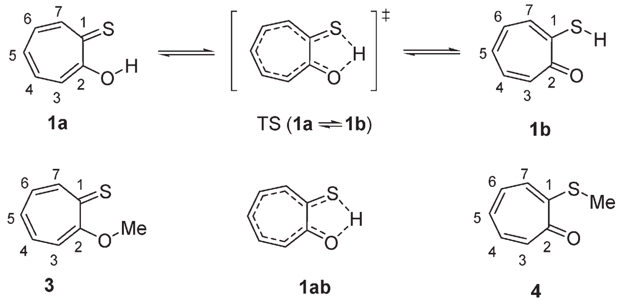
The solid-state **1** is a *crystallographically isolated* system displaying an extremely fast equilibrium even at low temperature without temperature dependence. This would be a novel example of an undegenerate tautomeric system exhibiting neither TSSE nor KSSE.

The thiotropolone **1** contains the two unequivalent tautomeric forms of the thione (**1a**, 2-hydroxy-2,4,6-cycloheptatriene-1-thione) and enethiol (**1b**, 2-sulfanyl-2,4,6-cycloheptatrien-1-one). In fact, the solid-state IR spectrum of **1** indicated both the stretching vibration of C═S (1102 cm^{-1}) of **1a** and that of C═O (1568 cm^{-1}) of **1b**. This assignment is based on wave numbers of two reference compounds **3**[1] [ν(C═S) = 1100 cm^{-1}] and **4**[1] [ν(C═O) = 1547 cm^{-1}] for the methyl-group fixed forms of **1a** and **1b**, respectively (Scheme 2).[6]

Scheme 1. Intramolecular and Intermolecular Proton Transfers of Tropolone (2)



Scheme 2. Solid-State Thiotropolone (1) Exists in an Extremely Fast Equilibrium between Two Unequivalent Tautomeric Structures of the Thione (1a) and Enethiol (1b) Forms, As if It Were a 10 π Aromatic System 1ab[a]



[a] Compounds 2-methoxytropothione (**3**) and 2-(methylthio)tropone (**4**) are used here as the reference fixed forms of the thione **1a** and enethiol **1b** tautomers, respectively.

The ^{13}C NMR (CDCl$_3$) chemical shift of the thiocarbonyl carbon C(1) (δ 183.42) in **1** is situated midway between those of two reference compounds, **3** and **4** (Table 1). The ^{17}O NMR chemical shift (δ 211.7) of **1** is also situated midway between that (δ 36.8)[6] of the hydroxy oxygen in **2** and that (δ 458.2) of the carbonyl oxygen in **4**. From the ^{13}C and ^{17}O shifts, **1** is estimated to exist in a rapid equilibrium mixture of **1a** and **1b** in the ratio of 58:42.[6] The ^{1}H NMR simulation analysis of **1** eventually yields appreciable coupling constants. Table 1 summarizes the result. They appear to be averaged between **1a** and **1b** in the ratio of 58:42 based on coupling constants of **3** and **4**.[6] The averaged structure due to the $^{3}J_{\mathrm{H-H}}$ of **1** is consistent with a rapid

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equilibrium causing the coupling constants with the formal C−C and C═C bonds averaged on the NMR time scale. Variable-temperature ^{13}C and ^{17}O NMR spectra of **1** [binary solvent system of $CD_2Cl_2-CS_2$ (1:1)] do not show a significant difference at all in each chemical shift ($\Delta\delta_C < 0.021$, $\Delta\delta_O <$ 0.22 ppm K^{-1}) at the measured temperature between 27 and −100 °C. This result in **1** demonstrates a very fast equilibrium between the **1a** and **1b** forms. The activation Gibbs free energy $\Delta G^{\ddagger}$ of the interconversion is estimated to be less than 6.8 and 6.2 kcal mol^{-1} from the ^{13}C and ^{17}O NMR, respectively.[6]

Figure 1 shows that ^{13}C CP/MAS (cross-polarization/magic angle spinning) NMR spectroscopy of **1** resonates in individual seven carbons in both the molten (60 °C) and solid states (temperature range between 27 and −130 °C[7]). All the ^{13}C NMR signals in those states are equal to those in solution. The compound **1** is found to be interconverted very rapidly between two tautomeric structures, **1a** and **1b**, *even in the solid state* in the ratio of 58:42 without temperature dependence.[6] $\Delta G^{\ddagger}$ is estimated to be less than 6 kcal mol^{-1}. A very fast equilibrium between the **1a** and **1b** forms was also supported by comparison of observed IR spectrum of **1** with calculated IR spectra of **1a** and **1b** by the DFT method.[6]

This extremely rapid solid-state proton migration also differs entirely from that in thione-enethiol tautomerism[8] reported so far. The former may originate from dissimilarity of C−S and C−O bond distances in exocyclic positions and/or from the packing arrangement of the crystalline structure. In Figure 2, the X-ray diffraction analysis[9] (performed at −150 °C) shows that the crystals of **1** have novel stacking interactions that are arranged nearly perpendicularly (79°) toward the neighboring molecules. This arrangement is in sharp contrast to a parallel stacking in **2**.[10] Table 2 shows bond lengths of the carbon ring in **1** and indicates a well-delocalized structure even in the solid state.[11] The geometry of **1** demonstrates that the solid-state **1** equilibrates between the tautomeric structures of **1a** and **1b** by the intramolecular proton transfer.

Table 1. Coupling Constants ($^3J_{H-H}$ in Hz) by Simulation Analyses and ^{13}C Shifts (in δ) of the Carbon C(1) Involved in the C−S Bond for 1 and Two Reference Compounds (3 and 4).[a]

compd	$^3J_{3,4}$	$^3J_{4,5}$	$^3J_{5,6}$	$^3J_{6,7}$	$\delta_{(C\text{-}1)}$
3	9.89	10.11	8.10	11.74	200.41
1[b]	10.73	9.27	9.09	10.74	183.42
1[c]	(10.73)	(9.27)	(9.09)	(10.74)	(183.47)
4	11.90	8.11	10.45	9.37	160.07

[a] Atom numbers of hydrogen and carbon are those in Scheme 2. [b] Simulation was performed with the Bruker package PANIC. [c] Calculated values based on the observed ones by NMR (for *J*) of **3** and **4** in the ratio of 58:42.

The facile proton transfer in **1** was examined with ab initio G2(MP2)[12] calculations,[13] which were also used in theoretical studies of intramolecular hydrogen bonds of thiomalonaldehyde[14] and β-calcogenovinylaldehydes.[15] Three species, **1a**, TS (**1a** ⇄ **1b**), and **1b**, were confirmed to be planar, and TS has a sole imaginary frequency, $\nu^{\ddagger} = 1914.03i$ cm^{-1}. At −35 °C (the mean value of the present measurement, −130 and 60 °C), the changes of free energies are 0 (**1a**), +5.02 (TS), and +0.79 kcal mol^{-1} (**1b**).[6] The energy order of **1a** and **1b** is consistent with that deduced experimentally,[16] and the small activation Gibbs free energy agrees with that (<6 kcal mol^{-1}) derived experimentally. For TS, the decrease in the activation energy (=0.80 kcal mol^{-1}) due to the tunnel effect was estimated by the Wigner's correction.[17]

According to the present NMR, IR and X-ray analyses and ab initio calculations, the crystal structure of thiotropolone has a specific intramolecular hydrogen bond to preclude the intermolecular one. The S···O bond distances (2.85 Å in **1a**, 2.69 Å in

Table 2. Ring C−C, C−O and C−S Distances (*r* in Å) by X-Ray Analysis for 1 and Two Reference Compounds (3 and 4)[a]

compd	$r_{1,2}$	$r_{2,3}$	$r_{3,4}$	$r_{4,5}$	$r_{5,6}$
3	1.432(7)	1.362(7)	1.429(7)	1.369(8)	1.400(8)
1	1.433(2)	1.381(2)	1.395(2)	1.377(2)	1.380(2)
1[b]	(1.456)	(1.393)	(1.397)	(1.390)	(1.380)
4	1.490(6)	1.436(6)	1.353(6)	1.420(7)	1.352(6)

compd	$r_{6,7}$	$r_{1,7}$	$r_{C(1)\text{-}S}$	$r_{C(2)\text{-}O}$
3	1.366(7)	1.442(7)	1.692(5)	1.365(6)
1	1.376(2)	1.421(2)	1.698(1)	1.345(2)
1[b]	(1.383)	(1.418)	(1.708)	(1.316)
4	1.407(6)	1.384(6)	1.731(4)	1.249(5)

[a] Atom numbers of hydrogen and carbon are those in Scheme 2 and Figure 2. [b] Calculated values based on the observed ones by X-ray analyses (for *r*) of **3** and **4** in the ratio of 58:42.

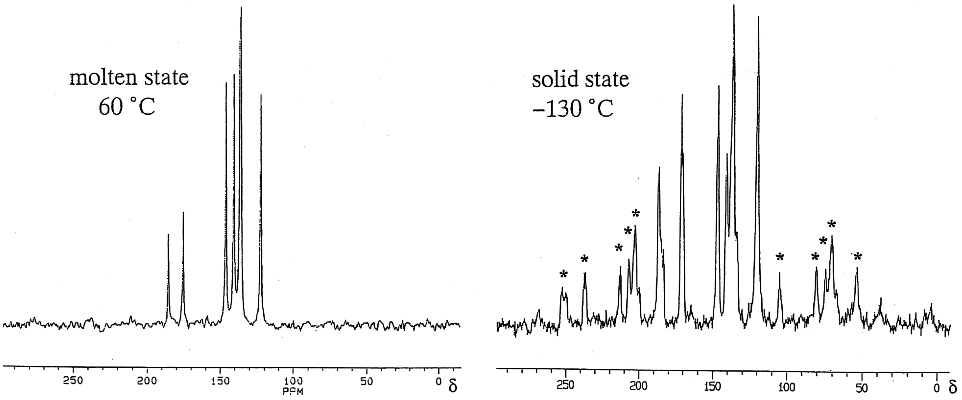

Figure 1. Temperature independence of the CP/MAS ^{13}C NMR spectra (67.8 MHz) of thiotropolone (**1**). (Left) Molten state at 60 °C. (Right) Solid state at −130 °C. Asterisk (*) denotes spinning sideband (spinning speed is 4.5 kHz).

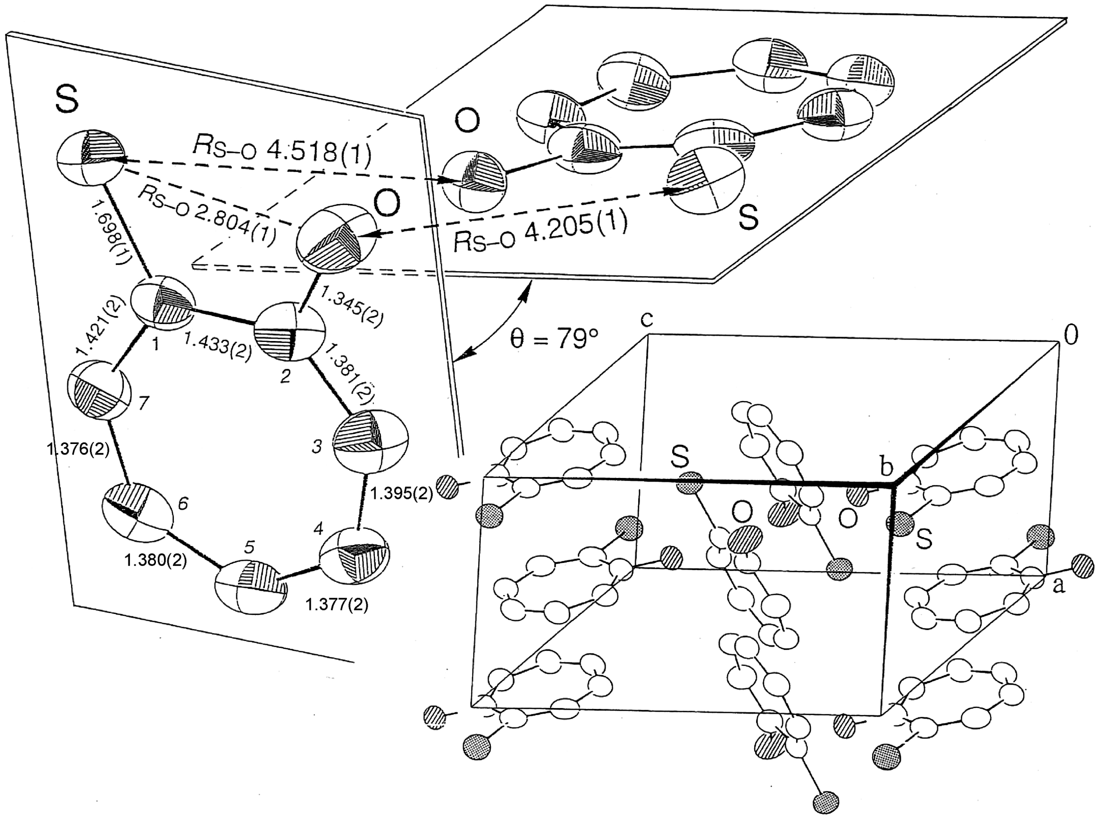

Figure 2. Packing arrangement of the crystals of thiotropolone (**1**). The figures show a large free-space packing to allow an intramolecular transfer by the rapid chelate proton interconversion as well as a novel specific stacking arranged almost perpendicularly (78.84°). Distances are in angstrom.

TS and 2.87 Å in **1b**) are smaller than the sum (3.32 Å) of van der Waals radii. Due to that preclusion and the entropically favorable orientation, the nearly perpendicular and large free-space stacking has been obtained. Each **1** molecule stays as if it were in the gas phase and as if it had a peripheral 10π-electron aromatic system **1ab**[18] (see Scheme 2). In summary, the present thiotropolone **1** is a compound which has a high intrinsic basicity and acidity of the hydrogen-bond acceptor and donor groups[19] along with the resonance assistance.[20]

EXPERIMENTAL SECTION

Crystal data for **1**: crystal dimensions 0.30 × 0.22 × 0.10 mm^3, triclinic, space group *P*1, $a = 7.064(7)$ Å, $b = 8.268(3)$ Å, $c = 11.578(5)$ Å, $\alpha = 75.57(3)$ °, $\beta = 78.55(6)$ °, $\gamma = 87.06(6)$ °, $V = 641.8(7)$ Å^3, $Z = 4$, ρcalcd = 1.430 Mg m^{-3}, 2θmax = 60°, T = 123 K, number of data measured 2657, number of data used in refinement 2199, linear absorption coefficient 0.3873 mm^{-1}, number of parameters 225. All H atoms were refined isotropically, max/min residual electron density 0.31/−0.40 eÅ^3. The data were collected on a Mac Science DIP3000 diffractometer with graphitemonochromated MoKα (ν = 0.71073 Å) radiation. No absorption correction was performed. The structure was solved using SIR92/Crystan. Refinement *R* values: $R = 0.060$, $wR = 0.061$ for $I > 1.5\sigma(I)$.

ASSOCIATED CONTENT

Supporting Information. ^{1}H, ^{13}C and ^{17}O NMR spectra, ^{13}C CP/MAS NMR spectra, IR spectra, ab initio calculations, and the way of calculating the concentration ratio of **1a** and **1b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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and are not calibrated. It is known that under MAS NMR experiments, the increase in sample temperature of several tens of degrees occurs by the sample rotation of the order of kHz and the high-power ^{1}H decoupling. Therefore, the temperatures and the calculated $\Delta G^\ddagger$ value may include some errors. For example, see: Mildner, T.; Ernst, H.; Freude, D. *Solid State NMR* **1995**, *5*, 269.

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