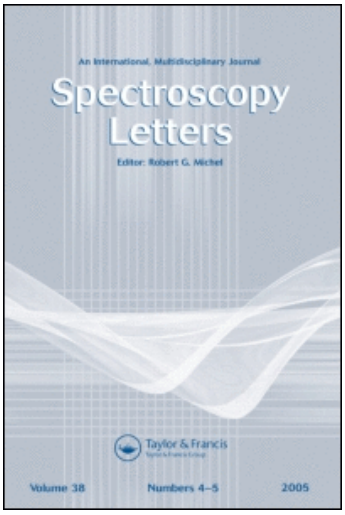

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[a] Division of Material Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa, Japan [b] Graduate School of Natural Sciences, Nagoya City University, Mizuho-ku, Nagoya, Japan

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Crystal Structures and Conformations of 5-Benzyl-2-thiohydantoin and Its 1-Acetylated Derivative

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[1]Division of Material Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa, Japan
[2]Graduate School of Natural Sciences, Nagoya City University, Mizuho-ku, Nagoya, Japan

ABSTRACT The crystal structures of 5-benzyl-2-thiohydantoin (5-BTH) and 1-acetyl-5-benzyl-2-thiohydantoin (1-Ac-5-BTH) have been determined by X-ray diffraction. In the 5-BTH crystals, the enantiomeric (*R*)- and (*S*)-5-BTH molecules are connected to form cyclic dimers *via* the hydrogen bonds of the thioamide and the amide moieties. On the other hand, the intermolecular hydrogen bonds in 1-Ac-5-BTH crystals form an infinite chain. These differences in the hydrogen bond pattern are also discussed in the IR and Raman spectra. The *ab initio* molecular orbital calculations (Gaussian 03) with 6-31G(d,p) basis set were carried out for 5-BTH and 1-Ac-5-BTH to get the preferred conformation.

KEYWORDS *ab initio* MO calculation, 1-acetyl-5-benzyl-2-thiohydantoin, 5-benzyl-2-thiohydantoin, crystal structure, molecular conformation, vibrational spectra

INTRODUCTION

Hydantoins (imidazolidine-2,4-diones), which have a 5-membered ring containing a reactive cyclic urea core, form a wide range of biologically active compounds.[1–4] Their 2-thioxo analogues, 2-thiohydantoins (2-thioxo-imidazolizin-4-ones), also display significant biological activities and are employed as established drugs, fungicides, or herbicides.[5,6] Both compounds are considered as useful intermediates in peptide synthesis and structure determination of polypeptides.[7] Because their biological activities and physicochemical properties are closely related to the electronic structure, conformation, and intermolecular interactions, experimental data pertaining to these features are therefore very important. Furthermore, the 2-thiohydantoin furnishes an interesting feature in structural chemistry. This compound carries a thioamide and an amide group in a molecule, which provide equal numbers of proton donor (D) and acceptor (A) in a D-A-D-A sequence. Because of this unique structural feature, 2-thiohydantoins are expected to form intricate hydrogen bonding networks in crystals. However, there have been few reports on molecular and crystal structures of 2-thiohydantoins compared with that for hydantoins.[8]

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Address correspondence to Ko-Ki Kunimoto, Division of Material Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-92, Japan. E-mail: kunimoto@sgkit.ge.kanzawa-u.ac.jp

In this work, we have studied the crystal structures and conformations of 5-benzyl-2-thiohydantoin (5-BTH) and 1-acetyl-5-benzyl-2-thiohydantoin (1-Ac-5-BTH). The D-A-D-A hydrogen bonding motif of 5-BTH is modified by acetylation of the NH group in 1-Ac-5-BTH. Differences in IR and Raman spectra between the two compounds were interpreted in terms of changes in the molecular structure and the hydrogen bonding. The theoretical molecular conformations were obtained by *ab initio* molecular orbital (MO) calculation and compared with the experimental data.

METERIALS AND METHODS

Materials

5-BTH was prepared from l-phenylalanine *via* acid hydrolysis of 1-Ac-5-BTH by the thiocyanate method.[9] 5-BTH and 1-Ac-BTH were obtained as racemic crystals due to racemization of a reaction intermediate.[10] l-Phenylalanine and ammonium thiocyanate were purchased from Tokyo Kasei Co., Tokyo, Japan. Other chemicals were commercial products and used without further purification. l-Phenylalanine (5.03 g, 30.0 mmol) was allowed to react with a mixture of ammonium thiocyanate (2.7 g, 35.4 mmol), acetic anhydride (30 mL, 317 mmol), and acetic acid (3.9 mL) at 100°C for 1 h according to the reported procedure.[9] A white precipitate of 1-Ac-5-BTH was formed by adding 100 mL distillated water, subsequent cooling of the solution in a refrigerator, and recrystallization from methanol. The 1-Ac-5-BTH obtained was dissolved in 12 M hydrochloric acid and heated at 60°C for 1 h to yield 5-BTH. The crude product was washed with cold water several times and purified by repeated crystallization from methanol. The purities of these compounds were checked by the elemental analyses and ^{1}H NMR spectra. 1-Ac-5-BTH: Yield 83%; m.p. 178–180°C; Found: C, 58.32%; H 4.82%; N, 13.59%. Calcd. for $C_{12}H_{12}N_2O_2S$: C, 58.23%; H, 4.89%; N, 13.59%. ^{1}H NMR (270 MHz, DMSO-d_6): δ 2.69 (s, 3H, -CH_3), 3.12 (dd, 1H, J = 13.5 Hz, 2.7 Hz, -CH_2-), 3.38 (dd, 1H, J = 13.5 Hz, 2.7 Hz, -CH_2-), 4.98 (dd, 1H, J = 13.5 Hz, 2.7 Hz, -CH-), 6.96–6.99 (m, 2H, -Ph), 7.23–7.31 (m, 3H, -Ph), 12.41 (s, 1H, -NH-). 5-BTH: Yield 43%; m.p. 171–174°C; Found: C, 57.83%; H, 4.87%; N, 11.12%. Calcd. for $C_{10}H_{10}N_2OS$: C, 58.05%; H, 4.87%; N, 11.28%. ^{1}H NMR (270 MHz, DMSO-d_6): δ 2.98 (d, 2H, J = 5.4 Hz, Hz, -CH_2-), 4.56 (t, 1H, J = 5.4 Hz, -CH-), 7.15–7.31 (m, 5H, -Ph), 10.06 (s, 1H, -C(=S)-NH-), 11.43 (s, 1H, -C(=O)-NH-). The *N*-deuterated 5-BTH and 1-Ac-5-BTH (5-BTH-Nd_2 and 1-Ac-5-BTH-Nd_2) were obtained by exchange reaction with methanol-Od_1 (Merck, 99% atom D).

Spectral Measurements

The IR spectra were recorded on a Perkin-Elmer 1650 FT-IR spectrometer as KBr disks, and Nujol and hexachlorobutadiene mulls by averaging 64 scans with a resolution of 4 cm^{-1}. The FT-Raman spectra were obtained on a Perkin-Elmer 2000 R spectrometer as powder sealed in a capillary tube. The 1064-nm line of an Elforlight Model L04-2000S Nd:YAG laser was used as the exciting source with an output power of about 200 mW at the sample position. All spectra were accumulated for 60 scans with a resolution of 4 cm^{-1}.

X-ray Crystal Structure Analysis

Single crystals of 5-BTH and 1-Ac-5-BTH suitable for X-ray diffraction analysis were grown by slow evaporation from chloroform and hexane/ethanol solutions, respectively, at room temperature. X-ray diffraction data were obtained on a Rigaku/MSC Mercury CCD diffractometer with a graphite-monochromated Mo Kα radiation (λ = 0.7107 Å). The crystal sample was cooled under a cold nitrogen stream at −150 ± 1°C during X-ray exposure to enhance data quality. The data were corrected for both Lorentz and polarization effects. Table 1 summarizes the crystal data and experimental conditions for the crystal structure determination.

The 5-BTH and 1-Ac-5-BTH structures were solved by direct methods using SIR92[11] and SIR88,[12] respectively. Crystal structure analysis was performed by using the *teXsan* crystallographic software package.[13] The nonhydrogen atoms were refined anisotropically. All the H-atom positions were found from a difference Fourier map and refined isotropically. ORTEP diagrams were created using the program ORTEP-3.[14]

TABLE 1 Crystal Data and Structure Refinement

Compound	5-BTH	1-Ac-5-BTH
Color/shape	Colorless/prism	Colorless/prism
Chemical formula	$C_{10}H_{10}N_2OS$	$C_{12}H_{12}N_2O_2S$
Formula weight	206.26	248.30
Temperature, K	123	123
Crystal system	Monoclinic	Monoclinic
Space group	$C2/c$ (C_{2h}^6)	$P2_1/c$ (C_{2h}^5)
Unit cell dimensions	$a = 13.368(3)$Å	$a = 11.508(2)$Å
	$b = 5.7553(8)$Å	$b = 13.396(3)$Å
	$c = 25.882(5)$Å	$c = 7.714(2)$Å
	$\beta = 96.1840(9)^\circ$	$\beta = 95.380(4)^\circ$
Volume, Å^3	1979.6(6)	1184.1(4)
Z	8	4
Density (calculated), mg/m^3	1.384	1.393
Absorption coefficient, mm^{-1}	0.293	0.264
Diffractometer	Rigaku/MSC Mercury CCD	Rigaku/MSC Mercury CCD
Θ range for data collection, deg	4.8–55.0	15.4–55.0
Reflections measured	7262	123–29
Independent reflections	2052 ($R_{int} = 0.043$)	2742 ($R_{int} = 0.034$)
Observed reflections	1700 [$I > 1.20\sigma(I)$]	2270[$I > 1.20\sigma(I)$]
Data/restraints/parameters	1700/0/167	2270/0/202
Goodness of fit	1.46	1.21
Final R indices [$I > 1.20\sigma(I)$]	$R = 0.040$, $wR = 0.051$	$R = 0.035$, $wR = 0.044$
Largest diff. peak and hole, e/Å^3	0.34 − 0.16	0.26 − 0.14

Quantum Mechanical Calculation

Semiempirical and *ab initio* MO calculations were carried out using the CAChe MOPAC[15] and the Gaussian 03 set programs,[16] respectively. The starting structures of 5-BTH and 1-Ac-5-BTH were taken from the crystal structure coordinates obtained in this work. The low-energy conformers were searched for the rotation about the C-benzyl bond using the MOPAC AM1 Hamiltonian. In all cases, the PRICISE option was used to provide higher accuracy within this calculation. The low-energy conformers were extracted from the MOPAC AM1 calculations, and their molecular structures were further optimized by the *ab initio* calculation at the HF level using 6-31G(d,p) basis set.

RESULTS AND DISCUSSION

Crystal Structures of 5-BTH and 1-Ac-5-BTH

The final positional and thermal parameters of 5-BTH and 1-Ac-5-BTH for non-H atoms are presented in Table 2. Table 3 summarizes the selected structure parameters and the hydrogen bonding geometries. As given in Table 1, 5-BTH and 1-Ac-5-BTH

TABLE 2 Fractional Atomic Coordinates and Equivalent Isotropic Thermal Parameters for Non-hydrogen Atoms

Atom	X	Y	Z	B_{eq}/Å^2
5-BTH				
S1	0.13862(3)	−0.08450(7)	−0.05987(1)	1.961(10)
O1	0.05475(9)	0.5058(2)	0.07014(4)	2.24(2)
N1	0.08229(9)	0.2576(2)	0.00265(5)	1.77(2)
N2	0.1906(1)	0.0132(3)	0.04177(5)	2.23(3)
C1	0.1381(1)	0.0588(3)	−0.00386(6)	1.76(3)
C2	0.0951(1)	0.3381(3)	0.05290(6)	1.94(3)
C3	0.1734(.1)	0.1803(3)	0.08240(6)	1.98(3)
C4	0.1385(1)	0.0660(3)	0.13036(6)	2.03(3)
C5	0.2198(1)	−0.0878(3)	0.15807(5)	1.98(3)
C6	0.1917(1)	−0.2970(3)	0.17868(6)	2.30(3)
C7	0.2622(2)	−0.4430(3)	0.20537(6)	2.66(3)
C8	0.3626(1)	−0.3810(3)	0.21165(7)	2.69(8)
C9	0.3930(1)	−0.1743(4)	0.19102(7)	2.85(4)
C10	0.3213(1)	−0.0264(3)	0.16435(6)	2.48(3)
1-Ac-5-BTH				
S1	0.84753(3)	0.03491(3)	0.12011(4)	1.454(8)
O1	0.88337(10)	−0.25409(7)	−0.2655(1)	1.54(2)
O2	0.8813(1)	0.11039(8)	−0.4531(1)	2.04(2)
N1	0.8638(1)	−0.12893(9)	−0.0683(2)	1.13(2)
N2	0.8535(1)	0.00571(8)	−0.2336(.1)	1.11(2)
C1	0.8542(.1)	−0.02630(10)	−0.0636(2)	1.06(2)
C2	0.8721(1)	−0.16623(10)	−0.2307(2)	1.12(3)
C3	0.8589(1)	−0.07901(10)	−0.3551(2)	1.14(3)
C4	0.7470(1)	−0.0898(1)	0.4802(2)	1.45(3)
C5	0.6393(1)	−0.1080(1)	−0.3873(2)	1.54(3)
C6	0.5963(2)	−0.2041(1)	−0.3703(3)	2.58(4)
C7	0.4970(2)	−0.2206(2)	−0.2839(3)	3.71(5)
C8	0.4404(2)	−0.1424(2)	−0.2135(3)	3.14(4)
C9	0.4820(1)	−0.0462(2)	−0.2286(2)	2.51(4)
C10	0.5806(1)	−0.0293(1)	−0.3155(2)	1.94(3)
C11	0.8601(1)	0.1030(1)	−0.3020(2)	1.42(3)
C12	0.8408(2)	0.1914(1)	−0.1900(2)	1.84(3)

$B_{eq} = (8/3)\pi^2 \ (U_{11} \ (aa^*)^2 + U_{22} \ (bb^*)^2 + U_{33} \ (cc^*)^2 + 2U_{12} \ aa^*bb^*\cos\gamma + 2U_{13} \ aa^*cc^*\cos\beta + 2U_{23} \ bb^*cc^*\cos\alpha)$

TABLE 3 Selected Bond Lengths (Å), and Bond and Torsion Angles (°) for 5-BTH and 1-Ac-5-BTH

	5-BTH	1-Ac-5-BTH
Bond lengths		
S1-C1	1.666(1)	1.645(2)
O1-C2	1.214(2)	1.217(2)
N1-C1	1.386(2)	1.380(2)
N1-C2	1.374(2)	1.360(2)
N2-C1	1.334(2)	1.380(2)
N2-C3	1.462(2)	1.477(2)
C2-C3	1.527(2)	1.510(2)
N2-C11		1.415(2)
O2-C11		1.214(2)
C11-C12		1.494(2)
Bond angles		
C1-N1-C2	112.3(1)	113.8(1)
C1-N2-C3	113.5(1)	111.6(1)
S1-C1-N1	124.0(1)	122.0(1)
S1-C1-N2	128.9(1)	131.9(1)
N1-C1-N2	107.1(1)	106.1(1)
O1-C2-N1	126.9(1)	125.2(1)
O1-C2-C3	126.7(1)	127.9(1)
N1-C2-C3	106.4(1)	106.8(1)
N2-C3-C2	100.6(1)	101.5(1)
N2-C3-C4	112.8(1)	112.7(1)
C2-C3-C4	114.3(1)	110.7(1)
C3-C4-C5	111.7(1)	113.2(1)
O2-C11-N2		117.0(1)
N2-C11-C12		119.7(1)
O2-C11-C12		123.2(1)
Torsion angles		
S1-C1-N1-C2	178.5(1)	−178.0(1)
S1-C1-N2-C3	179.2(1)	−178.8(1)
O1-C2-N1-C1	−178.7(2)	178.6(1)
O1-C2-C3-N2	179.0(2)	−178.0(1)
O1-C2-C3-C4	57.9(2)	62.1(2)
N1-C1-N2-C3	−0.1(2)	1.9(1)
N1-C2-C3-N2	−3.1(2)	4.6(1)
N1-C2-C3-C4	−124.2(1)	−115.2(1)
N2-C1-N1-C2	−2.2(2)	1.4(2)
N2-C3-C4-C5	66.1(2)	−60.7(2)
C1-N1-C2-C3	3.4(2)	−4.0(2)
C1-N2-C3-C2	1.9(2)	−4.0(1)
C1-N2-C3-C4	124.1(1)	114.4(1)
C2-C3-C4-C5	−179.8(1)	52.2(2)
O2-C11-N2-C1		165.9(1)
C3-N2-C11-C12		172.3(1)

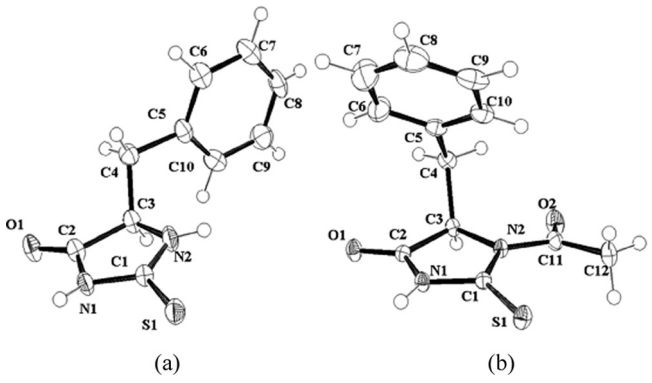
D-H···A	D-H (Å)	H···A (Å)	D···A (Å)	D-H···A(°)
5-BTH				
N2-H···S1^{i}	0.80(2)	2.58(2)	3.375(2)	179(2)
N1-H···O1^{ii}	0.78(2)	2.07(2)	2.831(2)	165(2)
1-Ac-5-BTH				
N1-H1···O1^{iii}	0.80(2)	2.00(2)	2.804(2)	179(2)

Symmetry codes: (i) $x-1/2$, $y+1/2$, z (ii) $x-1/2$, $y-1$, z (iii) $-x$, $y+1/2$, $-z+1/2$.

Estimated standard deviations in the least significant figure are given in parentheses.

were crystallized in the monoclinic forms with eight and four molecules, respectively, in a unit cell. The thiohydantoin unit is nearly planar in both molecules, with maximum deviations from planarity of 0.036 and 0.052 Å, respectively, for 5-BTH and 1-Ac5-BTH. As shown in Fig. 1a, the benzyl moiety of 5-BTH takes the extended conformation with respect to the thiohydantoin ring [C2-C3-C4-C5, −179.8(1)°; N2-C3-C4-C5, 66.1(2)°]. The thiohydantoin ring geometries of 5-BTH are comparable with those reported for 2-thiohydantoin and 5,5-diphenyl-2-thiohydantoin.[17–19] Thus, the C2-O1 and C2-N1 [1.214(2) and 1.374(2) Å] bond distances are in the range observed for the normal *cis*-amide moiety. The C1-S1 bond distance [1.666(2) Å] is intermediate between those of a C-S bond (1.82 Å) and a C=S bond (1.56 Å), and the C1-N2 distance [1.334(2) Å] is between those of a C-N bond (1.47 Å) and a C=N bond (1.27 Å).[20]

In contrast with the 5-BTH case, a folded conformation with the aromatic ring over the thiohydantoin ring was found for 1-Ac-5-BTH as shown in Fig. 1b [C2-C3-C4-C5, 52.2(2)°; N2-C3-C4-C5, −60.7(2)°]. Overall molecular geometries of 1-Ac-5-BTH are similar to those in 1-acetyl-2-thiohydantoin.[21] The acetyl group on the N2 atom is rotated 11.78(6)° out of plane from the least square plane of the thiohydantoin ring, and the C11-O2 bond is oriented *trans* to the N2-C1 bond. The bond angle C1-N2-C11 [130.3(1)°] is wider than that of C3-N2-C11 [117.7(1)°], resulting from the repulsion between the S1 atom and the methyl group. The C1-S1 [1.645(1) Å] and C1-N2 [1.380(2) Å] bond distances of 1-Ac-5-BTH are significantly shorter and longer,



(a) (b)

FIGURE 1 ORTEP drawings of (a) 5-BTH and (b) 1-Ac-BTH. The *R*-antipode of a racemic pair is shown with the atom numbering.

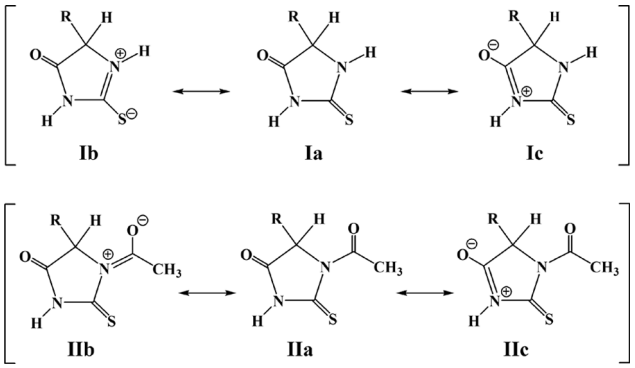


FIGURE 2 Resonance structures related to the thioamide group in BTH (Ia, Ib, Ic) and 1-Ac-5-BTH (IIa, IIb, IIc).

respectively, than those of 5-BTH [1.666(2) and 1.334(2) Å]. Differences in the C1-S1 and C1-N2 bond lengths between 5-BTH and 1-Ac-5-BTH can be rationalized by differences in the resonance structure, as shown in Fig. 2. In the structure of 5-BTH, the zwitterionic canonical forms, Ib and Ic, contribute together with the neutral canonical form Ia to the resonance structure. As a result, the C1-S1 and C1-N2 bonds have single- and double-bond characters, respectively. On the other hand, in the case of 1-Ac-5-BTH, the canonical structures, IIb and IIc, contribute to the resonance structure.

The intermolecular hydrogen bonds that link the molecules are indicated in the molecular packing shown in Figs. 3 and 4. In 5-BTH crystals, the amide and thioamide groups of one molecule form centrosymmetric cyclic dimers with the amide and thioamide groups, respectively, of the adjacent molecules through the intermolecular N-H···O and N-H···S hydrogen bonds [N2···S1($x-1/2$, $y+1/2$, z), 3.375(2) Å, N2-H2···S1($x-1/2$, $y+1/2$, z), 178(2)°, N1···O1(x, y-1, z), 2.831(2) Å, N1-H1···O1(x, $y-1$, z), 165(2)°]. The hydrogen bondings form an infinite sheet. On the other hand, in 1-Ac-5-BTH crystals, the amide N-H of one molecule is hydrogen-bonded to the amide C=O group of another molecule to form an infinite hydrogen bonding chain [N1···O1($-x$, $y+1/2$, $-z+1/2$), 2.804(2) Å, N1-H1···O1($-x$, $y+1/2$, $-z+1/2$), 179(2)°]. The S1 atom does not participate in the hydrogen bond system.

IR and Raman Spectra of 5-BTH and 1-Ac-5-BTH and their *N*-Deuterated Analogues

There are some studies on the IR specta of 2-thiohydantoin derivatives, but no reports have been published on the Raman spectra. Elmore discussed the nature of the thioureide bands,[22] and Poupaert and Bouche studied an IR spectroscopic characterization of these compounds.[23] Lebedev et al. reported vibrational analyses of 2-thiohydantoin and its 1-acetyl derivative.[24]

Figures 5 and 6 show the IR and Raman spectra of 5-BTH and 1-Ac-5-BTH. The differences in intermolecular hydrogen bondings between 5-BTH and 1-Ac-5-BTH crystals are reflected in their IR and Raman spectra. The typical group frequencies are summarized in Table 4. In the Raman spectrum of 5-BTH, νC=O band is observed at 1724 cm^{-1}, a lower frequency by 16 cm^{-1} than that of the corresponding IR band. This frequency difference

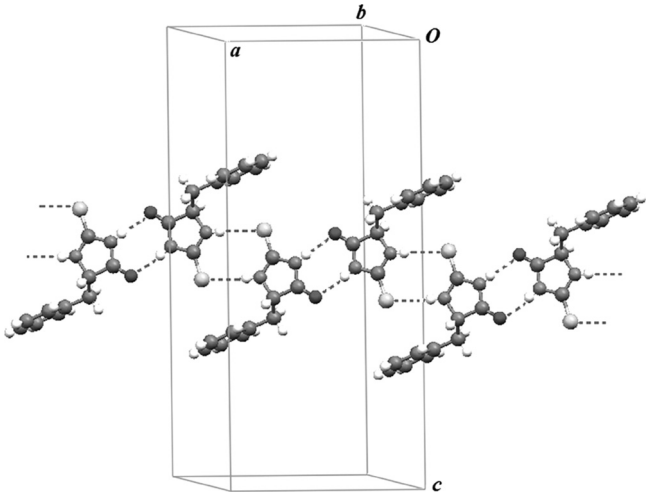


FIGURE 3 Perspective views of intermolecular hydrogen bonds in BTH crystals.

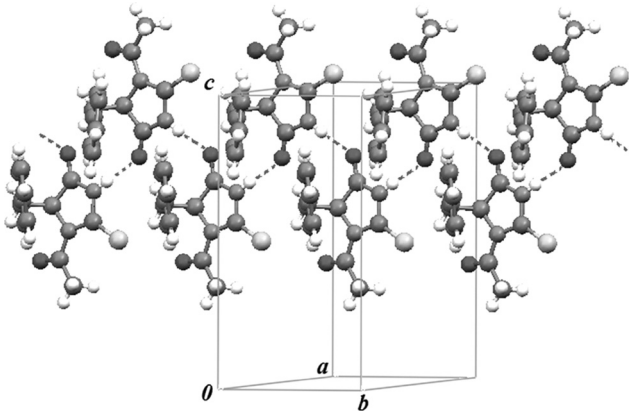


FIGURE 4 Perspective views of intermolecular hydrogen bonds in 1-Ac-BTH crystals.

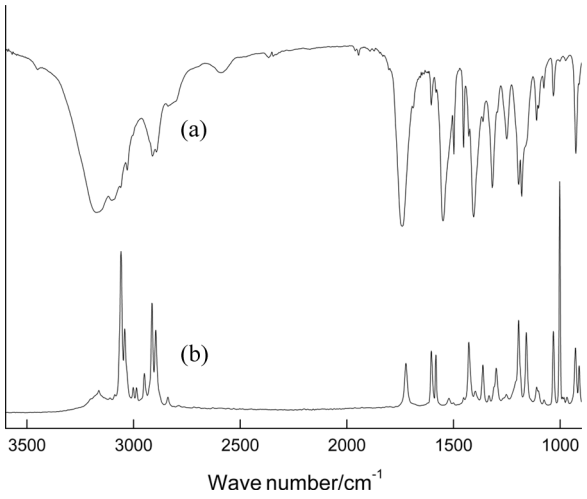


FIGURE 5 **(a) IR and (b) Raman spectra of 5-BTH.**

between the IR and Raman bands is explained in terms of the in-phase and out-of-phase C=O stretchings of the centrosymmetric hydrogen bonding cyclic dimer. Many other IR bands of 5-BTH also have frequencies different from those of the Raman bands, whereas in the 1-Ac-5-BTH spectra the frequency differences are small.

In the IR spectrum of 5-BTH, the C=O band is hardly influenced by *N*-deuteration, but in the Raman spectrum, a shift of 18 cm^{-1} to a lower frequency is observed. This shift suggests a possibility that a vibrational coupling with the NH bending within the constituent molecules occurs through the strong hydrogen-bond dimer in the A_g or B_g crystal modes. 5-BTH crystals belong to a space group C_{2h}^6 ($C2/c$); the A_g and B_g crystal modes are Raman-active and the A_u and B_u crystal modes are IR-active. For 1-Ac-5-BTH, the ring νC=O is observed as a doublet (1756 and 1730 cm^{-1}) in the Raman spectrum. This splitting is probably caused by the crystal field; because a space group is C_{2h}^5 ($P2_1/c$), the two crystal modes (A_g and B_g) appear in the Raman spectrum. Although no clear splitting is observed in this region of the IR spectrum, a weak shoulder band occurs at 1735 cm^{-1}, a lower frequency side of the very strong 1748 cm^{-1} band, suggesting the presence of this splitting. In fact, a splitting clearly appears at 1747 and 1720 cm^{-1} in the IR spectrum of 1-Ac-5-BTH-Nd_1, corresponding with the A_u and B_u crystal modes. A lower component of the doublet is shifted by about 15 cm^{-1} in both spectra on *N*-deuteration. This behavior could be attributed to a difference in coupling between the crystal modes.

The νC=O of the acetyl group of 1-Ac-5-BTH is ascribed to the 1705 cm^{-1} band in the IR spectrum and to the 1704 cm^{-1} band in the Raman spectrum. Although the bond length of the acetyl C=O is slightly shorter than that of the ring C=O (Table 3), this assignment is reasonable, as this band is not shifted at all by *N*-deuteration. Contrarily, for 1-acetyl-2-thiohydantoin, Lebedev et al. assigned the bands at 1788 cm^{-1} and 1714 cm^{-1} to the acetyl C=O and the ring C=O band, respectively, stating that the presence of the acetyl group leads to a decrease in the ring νC=O (from 1738 cm^{-1} in thiohydantoin to 1714 cm^{-1} in the acetyl derivative).[25]. However, their assignment should be revised, because the following effects are expected; in such 5-membered ring carbonyl compounds, C=O stretching frequencies increase owing to ring strain, and furthermore in 1-acetyl-2-thiohydantoin, the acetyl group attracts electrons from the ring, so that the ring C=O frequency is higher than that of the acetyl C=O.

Quantum Mechanical Calculation

The molecular conformations of 5-BTH and 1-Ac-5-BTH were searched for the rotation about the C3-C4 bond using the MOPAC AM1 method. The torsion angle (C2-C3-C4-C5) was varied between −180° and 180°. As a result, three local minima were found for 5-BTH, and 1-Ac-5-BTH, which correspond with

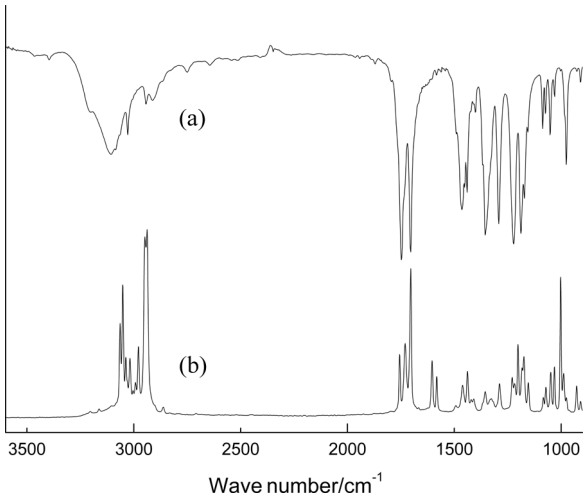


FIGURE 6 **(a) IR and (b) Raman spectra of 1-Ac-5-BTH.**

TABLE 4 Some Characteristic Frequencies of 5-BTH and 1-Ac-5-BTH and Their *N*-Deuterated Compounds

5-BTH		5-BTH-Nd_2		1-Ac-5-BTH		1-Ac-5-BTH-Nd_1		
IR (KBr disk)	Raman	IR (Nujol)	Raman	IR (KBr disk)	Raman	IR (Nujol)	Raman	Assignment
3175 vs	3163 w	2365 s	2376 w					νN–H(N–D), thioamide
3102 s	—	—	—	3106 m	3101 vw	2318 m	2319 vw	νN–H(N–D), amide
1740 vs	1724 w	1738 vs	1706 m	1747 vs	1756 mw	1746 m	1754 mw	νC=O, amide
				1735 sh	1731 mw	1720 w	1717 ms	νC=O, acetyl(νC=O, amide, doublet)
				1704 vs	1704 m	1705 vs	1705 w	νC=O, acetyl
1549 s	1522 vw	1496 m	—	1464 s	1462 w	1419 s	1422 vw	νC-N + δN-H or νC-N (thioureide band)

the I-A, I-B, and I-C conformers for 5-BTH and with II-A, II-B, and II-C conformers for 1-Ac-5-BTH. The molecular structures of these low-energy conformers were further optimized by the *ab initio* calculation at the HF level using 6-31G(d,p) basis set. Table 5 gives selected structural geometries and total energies of these conformers calculated by the *ab initio* MO, together with the X-ray data. The I-B and II-A forms were obtained as the lowest energy conformers for 5-BTH and 1-Ac-5-BTH, respectively, although the energy difference is very small (1.33–2.90 kcal/mol for 5-BTH and 1.86–4.33 kcal/mol for 1-Ac-5-BTH). The I-A, I-B, and I-C forms and the II-A, II-B, and II-C forms have similar bond lengths and bond angles, respectively, but the torsion angles are very different. The I-B form of 5-BTH has an extended conformation with the N2-C3-C4-C5 torsion angle of 65.02°, whereas the II-A form of 1-Ac-5-BTH takes a folded conformation with the N2-C3-C4-C5 torsion angle of –55.92°. These values are close to those obtained by the X-ray analysis [66.1(2)° and –60.7(2)°]. These observations indicate that these molecules take rather relaxed conformations in the crystal phase. For 5-BTH, the calculated C2-O1 (C=O) and C1-N1 bond lengths in the I-B form are shorter than those in the X-ray structure [1.186 and 1.370 Å compared with 1.214 and 1.386 Å, respectively]. 1-Ac-5-BTH in the II-A form also shows similar features [1.186 and 1.361 Å compared with 1.217 and 1.380 Å, respectively]. These differences in the C2-O1 and C1-N1 bond lengths between the experimental and the calculated values can be rationalized by the NH···O intermolecular hydrogen bonds formed both in 5-BTH and 1-Ac-5-BTH crystals.

TABLE 5 Comparison of Structural Parameters and Total Energies Obtained by Ab Initio Mo Calculation and X-Ray Analysis

	Calculated							
	5-BTH				1-Ac-5-BTH			
Parameters	I-A	I-B	I-C	Experimental	II-A	II-B	II-C	Experimental
Bond length (Å)								
S1-C1	1.656	1.656	1.656	1.666(1)	1.651	1.653	1.652	1.645(2)
O1-C2	1.186	1.186	1.186	1.214(2)	1.186	1.186	1.186	1.217(2)
N1-C1	1.369	1.370	1.367	1.386(2)	1.361	1.362	1.359	1.380(2)
N1-C2	1.370	1.373	1.375	1.374(2)	1.370	1.374	1.376	1.360(2)
N2-C1	1.334	1.333	1.334	1.334(2)	1.369	1.365	1.369	1.380(2)
N2-C3	1.448	1.448	1.451	1.462(2)	1.474	1.472	1.476	1.477(2)
C2-C3	1.523	1.523	1.527	1.527(2)	1.511	1.512	1.512	1.510(2)
Torsion angles (°)								
N2-C3-C4-C5	−56.94	65.02	165.60	66.1(2)	−55.92	67.75	177.33	−60.7(2)
C2-C3-C4-C5	58.35	179.04	−80.69	−179.8(1)	65.29	175.72	−84.00	52.2(2)
Total energy (a.u.)	965.84359	965.84571	965.84107		1117.62013	1117.61323	1117.61717	
Energy difference, ΔE (kcal/mol)	1.33	0.00	2.90		0.00	4.33	1.86	

These intermolecular hydrogen bonds in the crystals lead to the electronic redistribution of the 2-thiohydantoin ring, so that the C2-O1 and C1-N1 bond distances become longer than those obtained by the quantum chemical calculations for the isolated molecules. In either compound, there is no significant difference in the C=S bond length.

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