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Title: **Anomalous planar structure observed in**
(*E*)-10-(1,2-dibromoprop-1-en-1-yl)-10*H*-phenothiazine

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Abstract

Both *Z* and *E* isomers of 10-(1,2-dibromoprop-1-en-1-yl)-10*H*-phenothiazine were given by bromine addition to 10-(prop-1-yn-1-yl)-10*H*-phenothiazine with little stereoselectivity. The crystal structure of the *Z* isomer showed a usual butterfly structure, while that of the *E* isomer afforded an anomalous planar structure which was usually observed in positively charged phenothiazines. The reason for the planar structure was concluded to originate in intermolecular charge transfer interaction through the C-Br $\cdots\pi$ halogen bonds.

1. Introduction

Phenothiazines, which are classified into an important class of tricyclic nitrogen-sulfur heterocycles [1-2], are known to have good electron donating property, and have been used to make charge transfer complexes [3-12]. Phenothiazines also attracted interest from the viewpoints of photoinduced electron transfer (PET) [13] or pharmacology [14, 15]. Hence much attention has been paid to correlation between their properties and structures.

Generally, phenothiazines are known to have a butterfly structure. In contrast, they have a planar structure when they have positive charges. A recent report also indicated planarity of phenothiazine rings increases in their excited state [16]. According to Cambridge Structural Database (CSD) [17], 26 structures of planar phenothiazines have been reported, including those of 22 charged phenothiazines. In the remaining four compounds [18-20], they have no charges on phenothiazine rings, and the reason for planarity was interpreted as stabilization by intramolecular charge transfer interaction.

We wish to report herein the fifth anomalous planar phenothiazine compound, (*E*)-10-(1,2-dibromoprop-1-en-1-yl)-10*H*-phenothiazine, which was obtained by bromine addition to 10-(prop-1-yn-1-yl)-10*H*-phenothiazine.

2. Experimental Part

2-1. General procedure

All chemicals were purchased from Kanto Chemical Co. Ltd. and were used without further purification. Preparation of 10-(prop-1-yn-1-yl)-10*H*-phenothiazine was carried out according to the literature [21, 22]. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECA-400 spectrometer in chloroform-*d* with tetramethylsilane as an internal standard. All ^{13}C NMR spectra were obtained with a complete proton decoupling. Elemental analysis was performed on a J-SCEINCE LAB MICRO CORDER JM10.

2-2. Single crystal XRD

X-ray crystallographic data were collected at -180 °C on a RIGAKU Saturn 724+ CCD device with using multi-layered mirror monochromatic Mo $K\alpha$ radiation. The structures were solved by a direct method (SIR92) [23], and were refined by full-matrix least squares method (Shelxl97) [24]. The positions of non-H atoms were obtained from difference Fourier maps and were refined anisotropically. The C-bound H atoms except

for disordered methyl protons were obtained by calculation and were refined as riding on their parent C atoms. $U_{\text{iso}}(\text{H})$ values of the H atoms were set at $1.2U_{\text{eq}}$.

2-3. DFT calculations

DFT calculations were performed on the GAMESS software [25,26] with B3LYP 6-31G (*d,p*) level. The geometrical optimization was carried out with C1 symmetry, where the initial structures for calculations were set at those obtained by single crystal XRD or by calculations of RHF 6-31G(*d*) level.

2-4. Materials

Bromine addition to 10-(prop-1-yn-1-yl)-10H-phenothiazine

A bromine solution in benzene (0.100 M, 1.00 mL) was added to a solution of 10-(prop-1-yn-1-yl)-10H-phenothiazine (23.8 mg, 0.100 mmol) in benzene (2.00 mL) at 5-10 °C and the solution was stirred for 1 hours. It was poured into a saturated sodium thiosulfate solution. The organic layer was washed with water and dried over anhydrous sodium sulfate. After removal of sodium sulfate, it was concentrated by a rotary evaporator. Judged by the ^1H NMR spectrum and yield of the residue, conversion of the addition was 90 %, and the *Z/E* ratio was estimated to be 40/60. The residue was

purified by column chromatography on an alumina with hexane as an eluent to give the *Z* and *E* isomers of 10-(1,2-dibromoprop-1-en-1-yl)-10*H*-phenothiazine in 9.90 mg (yield 24.9 %) as a white powder and 5.39 mg (yield 13.6 %) as a pale yellow powder, respectively.

Z isomer: ^1H NMR (400 MHz, CDCl_3): 2.39 (s, 3H, CH_3); 6.94 (dt, $^3J=7.4$ Hz and $^4J=1.2$ Hz, 2H); 6.99 (m, 4H); 7.09 (dt, $^3J=7.7$ Hz and $^4J=1.7$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): 25.01; 116.20; 120.41; 122.85; 124.07; 126.75; 127.39; 132.68; 139.22. Anal. Calc. for $\text{C}_{15}\text{H}_{11}\text{N}_1\text{O}_1\text{S}_1\text{Br}_2$: C, 45.37; H, 2.79; N, 3.53. Found; C, 45.28; H, 2.68; N, 3.55.

E isomer: ^1H NMR (400 MHz, CDCl_3): 2.61 (s, 3H); 6.92-6.96 (m, 4H); 6.99 (dd, $^3J=8.0$ Hz and $^4J=1.8$ Hz, 2H); 7.07 (dt, $^3J=7.6$ Hz and $^4J=1.8$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): 27.59; 116.21; 119.74; 120.50; 123.52; 124.07; 126.71; 127.21; 138.19. Anal. Calc. for $\text{C}_{15}\text{H}_{11}\text{N}_1\text{O}_1\text{S}_1\text{Br}_2$: C, 45.37; H, 2.79; N, 3.53. Found; C, 45.15; H, 2.80; N, 3.51.

3. Results and Discussion

3-1 Bromine addition to 10-(prop-1-yn-1-yl)-10*H*-phenothiazine

Bromine addition to an ynamine compound of 10-(prop-1-yn-1-yl)-10*H*-phenothiazine in benzene gave both *Z* and *E* isomers as shown in Scheme 1. The configuration of both isomers was determined by single crystal XRD. (*vide infra*) The ratio of the *Z* and *E* isomers was estimated to be 40 : 60 judged by the integration of the NMR signals, but the isolated yields of both isomers are 24.9 % and 13.6 % respectively because of their instability for column chromatography.

This result indicates that the addition to the ynamine has little stereoselectivity as similar to previous reports [27], and suggests either bromination proceeds without formation of a bridged bromonium ion owing to conjugation with lone pair of the nitrogen atom or the bromonium ion has little steric hindrance.

3-2 Crystal structures of the *Z* and *E* isomers

Single crystals of the *Z* and *E* isomers with sufficient quality for X-ray analysis were obtained by slow concentration from toluene solutions. Crystal data and geometric parameters of both isomers are summarized at Table 1 and Table 2, respectively.

Figure 1 shows the crystal structure of the *Z* isomer. In the *Z* isomer, the phenothiazine moiety has a butterfly structure, and the central six-membered ring has a boat conformation. The dihedral angle between two benzene rings is $31.11(14)^\circ$. The structure around the nitrogen atom is pyramidal, where the N atom locates upward at $0.128(3)$ Å from the plane formed by three adjacent carbon atoms (plane N). The dihedral angle between plane N and N1/C13/C14/C15/Br1/Br2 (r.m.s. deviation = 0.0206 Å) is $87.88(3)^\circ$, indicating the phenothiazine moiety doesn't conjugate with the dibromopropenyl group. Intramolecular contact can be detected at C_{sp3}-H $\cdots$ N1 and Br1 $\cdots$ H11 where the distances are $2.480(5)$ Å and $2.7759(9)$ Å, respectively.

A chain structure along the *c* axis (Figure 2) is formed by C13–Br1 $\cdots$ S1ⁱ [symmetry code: (i) *x*, -*y*+2, *z*+1/2.] halogen bonds whose distance is $3.430(15)$ Å (Table 3), indicating 6 % shrinkage compared with the sum of van der Waals radii of Br and S atoms. The angle of C13–Br1 $\cdots$ S1ⁱ is $162.48(9)^\circ$.

In the *E* isomer, the phenothiazine moiety has an anomalous planar structure (Figure 3) in which the dihedral angle between two benzene rings is $2.40(11)^\circ$. The vinylic part is found to be disordered (Form A and B = 50/50). The structure around the nitrogen atom is pyramidal, where the N atom locates upward at $0.138(3)$ Å in disordered form A and $0.123(3)$ Å in disordered form B from the plane formed by corresponding three adjacent carbon atoms (plane N_A and N_B). The dihedral angles of the vinyl plane with the plane N_A and N_B are $87.714(12)^\circ$ and $86.708(13)^\circ$ respectively, indicating the phenothiazine moiety doesn't conjugate with the dibromopropenyl group. The significant differences in molecular structure between the *Z* and *E* isomers are observed in the central six-membered ring. In comparison of the *E* isomer with the *Z* isomer, tendency in shrinkage of bond distances and expansion of C6-S1-C7 and C1-N1-C12 angles is recognized in the central six-membered ring (Table 2). Intramolecular C_{sp3}-H...N and Br...H interactions become disappeared which were detected in the *Z* isomer.

Figure 4 indicates the crystal packing structure of the *E* isomer. Intermolecular Br2...C10ⁱ and Br2...H4ⁱⁱ [symmetry codes: (i) $x, -y+3/2, z+1/2$ (ii) $-x+2, y-1/2, -z+3/2$.] distances are $3.355(4)$ Å (Table 3) and $2.8588(8)$ Å, shrinking by 5 % and 6 % respectively compared with the sum of van der Waals radii of Br with C or H atoms.

Intermolecular $\text{Br2}\cdots\text{C10}^{\text{i}}$ contact gives a chain structure along the c axis, and $\text{Br2}\cdots\text{H4}^{\text{ii}}$ affords another chain along the b axis.

3-3 DFT calculations

DFT calculations of the Z and E isomers were performed on the GAMESS software with B3LYP 6-31G (d,p) level. Selected geometric parameters are listed in Table 2. Concerning for the Z isomer, two kinds of folded conformers, $Z1$ and $Z2$ (Figure 5), were afforded, whose structural difference is relative orientation of the $\text{C}=\text{C}$ bond to upward ($Z1$) or downward ($Z2$) to the phenothiazine unit. The conformer $Z1$ is estimated to be more stable by 5.3 kJ mol^{-1} than $Z2$. It is consistent with the structure in the crystal having $Z1$ conformation. The origin in this stabilization is considered to be intramolecular $\text{C}_{\text{sp}3}\text{-H}\cdots\text{N}$ (2.502 Å) and $\text{C}_{\text{sp}2}\text{-H}\cdots\text{Br}$ (2.780 and 2.790 Å) interactions. The dihedral angle of phenothiazine unit in $Z1$ is calculated to 28.2° which is very similar to the observed value of $31.11(14)^\circ$. When the optimization was carried out with the crystal structure as an initial structure, the final structure converged to $Z1$.

On optimization of the E isomer, two kinds of folded conformers, $E1$ and $E2$, were

also given as shown in Figure 5. The dihedral angles in *E1* and *E2* are 26.3° and 25.4° respectively which are significantly different from the observed angle of 2.40(11)°. The energy difference between *E1* and *E2* was estimated to 3.0 kJ mol^{-1} which also originated probably into $\text{C}_{\text{sp}2}\text{-H}\cdots\text{Br}$ hydrogen bonds. It is thought to decrease with decreasing the dihedral angles and the *E* isomer afforded the structural disorder. When the optimization was carried out with both disordered forms in the crystal structure as an initial ones, both structures converged to the meta stable structure *E2*, indicating that a potential surface around the planar structure is very complicated. The significant difference between the calculated and observed structures is considered that the molecule essentially has a butterfly structure and that destabilization with decreasing a dihedral angle is overcome by the stabilization from intermolecular interactions.

In addition, the energy difference between the stable conformers of *Z1* and *E1* is 0.9 kJ mol^{-1} . This similar stability may be one of the important factors for little stereoselectivity in the addition.

3-4 Correlation between molecular structure and intermolecular interactions

Four planar phenothiazines have already been reported, two of which are phenothiazine 5,5-dioxides [20]. The remaining two molecules are phenothiazines with electron withdrawing substituents [18,19]. The planarity of these phenothiazines is well explained by the effect of charge transfer interactions. Although intramolecular charge transfer interactions were carefully considered on *Z*1 and *E*1, any strong reasons for stabilization of a planar structure could not be found out from the DFT calculations. (*see* ESI)

In the crystal structures of both *Z* and *E* isomers, they have intermolecular halogen bonds between C-Br bond and phenothiazine π system. According to the DFT calculations of both isomers, the HOMOs and the LUMOs delocalize on the phenothiazine π -system and dibromovinyl unit, respectively. However the HOMO-LUMO gap of *E*1 is relatively smaller than that of *Z*1, which is thought to make the intermolecular $\pi \cdots \sigma^*_{\text{C-Br}}$ charge transfer interactions effective. Increase of planarity in phenothiazine units makes instability of the HOMO level, which also works effectively to the intermolecular charge transfer interactions and then colors the crystals. The larger crystal density of the *E* isomer than that of *Z* isomer in spite of the structural disorder also supports tight crystal packing owing to intermolecular interactions.

4. Summary

We examined bromine addition to 10-(prop-1-yn-1-yl)-10*H*-phenothiazine and the reaction gave two kinds of mono adducts in almost the same yield, which were characterized to be the *Z* or *E* isomers of 10-(1,2-dibromoprop-1-en-1-yl)-10*H*-phenothiazine. This result means that there is little stereoselectivity in bromine addition to the ynamine compound and suggests that the bromination proceeds without formation of a bridged bromonium ion.

The crystal structure of the *Z* isomer showed a usual butterfly structure. However that of the *E* isomer afforded an anomalous planar structure which was usually observed in charged phenothiazines. DFT calculations of both isomers afforded a butterfly structure as the optimized structures. The little energy difference between the isomers is thought to cause little stereoselectivity for the addition. The reason for the planar structure was concluded to originate in intermolecular charge transfer interactions through C–Br $\cdots\pi$ halogen bonds.

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Scheme 1. A result of bromine addition to 10-(prop-1-yn-1-yl)-10*H*-phenothiazine.

Figure 1. The asymmetric unit of the *Z* isomer with atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres.

Figure 2. Crystal packing structure of the Z isomer. [symmetry codes: (i) $x, -y+2, z+1/2$; (ii) $x, -y+2, z-1/2$.]

Figure 3. The asymmetric unit of the *E* isomer with atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres. Disordered atoms are discriminated with A/B notation, and the disordered forms are drawn as solid and open bonds, respectively.

Figure 4. Crystal packing structure of the *E* isomer. [symmetry codes: (i) $x, -y+3/2, z+1/2$; (ii) $-x+2, y-1/2, -z+3/2$; (iii) $x, -y+3/2, z-1/2$.]

Z1 (0.9 kJ mol^{-1})
Dihedral angle: 28.2°

Z2 (6.2 kJ mol^{-1})
Dihedral angle: 24.5°

E1 (0.0 kJ mol^{-1})
Dihedral angle: 26.3°

E2 (3.0 kJ mol^{-1})
Dihedral angle: 25.4°

Figure 5. Optimized structures for the *Z* and *E* isomers. Energy differences from the most stable *E1* are written in the parenthesis. Intramolecular C-H $\cdots$ Br and C-H $\cdots$ N interactions are drawn in red and blue dashed lines, respectively.

Table 1. Crystal data and refinement details for the *Z* and *E* isomers.

Compounds	<i>Z</i> isomer	<i>E</i> isomer
Chemical formula	$\text{C}_{15}\text{H}_{11}\text{N}_1\text{Br}_2\text{S}_1$	
Formula weight	397.13	
Crystal size (mm)	$0.10 \times 0.10 \times 0.05$	$0.30 \times 0.30 \times 0.10$
Crystal system	Monoclinic	Monoclinic
Space group	$C2/c$	$P2_1/c$
<i>Unit cell dimensions</i>		
a (Å)	18.581(6)	10.498(4)
b (Å)	12.322(4)	10.419(4)
c (Å)	13.823(5)	13.008(5)
α (°)	90	90
β (°)	116.448(4)	101.543(5)
γ (°)	90	90
V (Å ³)	2833.4(16)	1394.1(9)
Z	8	4
D_x (Mg/m ³)	1.862	1.892
μ (mm ⁻¹)	5.87	5.97
θ range (°)	2.1 – 31.3	2.0 – 31.2
Index ranges	$-24 \leq h \leq 23$	$-13 \leq h \leq 13$
	$-15 \leq k \leq 13$	$-11 \leq k \leq 13$
	$-17 \leq l \leq 17$	$-15 \leq l \leq 16$
Reflections collected	11219	11130
Independent reflections	3232	3170
Reflections with $I > 2\sigma(I)$	2926	2618
R (int)	0.024	0.025
Refinement method	full-matrix least-squares on F^2	
Goodness-of-Fit on F^2	1.126	0.989
R_1, wR_2	0.0395, 0.0901	0.0331, 0.0912
Refined parameters	173	190
Residual density (eÅ ⁻³)	0.91, -0.74	1.19, -0.44
CCDC deposit no.	1031106	1031107

Table 2. Observed and calculated geometric parameters of the *Z* and *E* isomers (Å, °).

Compounds	<i>Z</i> isomer	<i>Z</i> 1	<i>E</i> isomer	<i>E</i> 1
bond lengths				
S1—C6	1.770(4)	1.779	1.758(3)	1.777
S1—C7	1.770(4)	1.779	1.763(3)	1.778
N1—C1	1.429(5)	1.432	1.430(4)	1.433
N1—C12	1.424(4)	1.433	1.423(4)	1.432
C1—C6	1.399(5)	1.407	1.392(5)	1.406
C7—C12	1.393(5)	1.406	1.386(5)	1.405
bond angles				
C6—S1—C7	99.59(18)	99.4	102.21(14)	99.7
C1—N1—C12	120.8(3)	121.0	124.2(3)	121.4
S1—C6—C1	120.5(3)	120.7	124.0(2)	121.3
S1—C7—C12	120.8(3)	120.8	124.4(2)	121.3
N1—C1—C6	119.9(3)	120.3	122.4(3)	120.5
N1—C12—C7	119.9(4)	120.2	122.4(3)	120.5
dihedral angles				
two benzene rings	31.11(14)	28.2	2.40(11)	26.3
N ^{<i>a</i>} and vinyl planes	87.88(3)	89.8	87.714(12) 86.708(13)	89.5

a: N plane is defined as the plane formed by C1, C12 and C13 atoms.

Table 3. Geometric parameters for the halogen bonds in the *Z* and *E* isomers (Å, °).

	C—Br	Br···X ^a	∠C—Br···X ^a
<i>Z</i> isomer			
C13—Br1···S1	1.941(5)	3.4230(15)	162.48(9)
<i>E</i> isomer			
C14A—Br2···C10	1.948(7)	3.355(4)	164.6(2)
C13B—Br2···C10	1.948(7)	3.355(4)	164.5(2)

^a: X = S1 or C10