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The Crystal Structure of *N*-Methylphenothiazine

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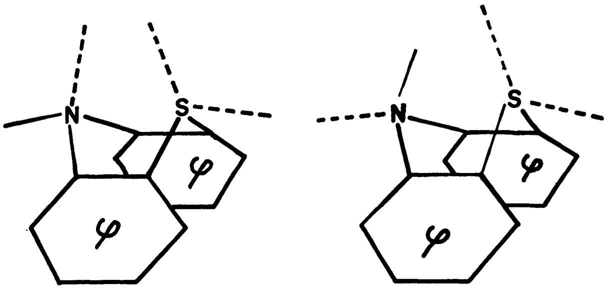
Phenothiazine derivatives are used widely in medical practice. Their actions change entirely with the side chains attached to the phenothiazine nucleus. *N*-substituted phenothiazine can take two different forms, quasi-equatorial and quasi-axial (Fig. 1). According to the calculation based on the molecular orbital theory by Malrieu and Pullman,1) the electronic states of the two forms are different. The energy state and ionization potential of the quasi-equatorial form are lower than those of the quasi-axial one, the former being more reactive towards electrophilic reagents since the nitrogen lone pair electrons participate in the conjugated electronic system. The N–H bond of phenothiazine (PT) has been found to have a quasi-equatorial orientation by X-ray structure analysis.2) PT has a



(a) (b)

Fig. 1. Configuration of *N*-substituted phenothiazine derivatives.
(a) quasi-equatorial form (b) quasi-axial form

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1) J. P. Malrieu and B. Pullman, *Theor. Chim. Acta*, **2**, 293 (1964).

2) J. D. Bell, J. F. Blount, O. V. Briscoe, and H. C. Freeman, *Chem. Commun.*, **1968**, 1656; C. J. Fritchie, Jr., and B. L. Trus, *ibid.*, **1968**, 833; C. J. Fritchie, Jr., *J. Chem. Soc.*, *A*, **1969**, 1328.

0.24—0.34 eV lower ionization potential[3] and is more reactive[4] towards electrophilic reagents than *N*-substituted derivatives which are supposed to take a quasi-axial form because of the steric hindrance of a large substituent.

We report the configuration of *N*-Methylphenothiazine (NMPT) which is regarded as a model substance of *N*-substituted phenothiazine. NMPT has a 0.15 eV higher ionization potential in the acetonitrile solution[5] and is less reactive towards electrophilic reagents than PT. NMPT cation was reported to take a quasi-axial form from the spin densities obtained from ESR measurement.[1] A single crystal, colorless and a prismatic needle in shape, was prepared by evaporation at room temperature from its benzene solution.

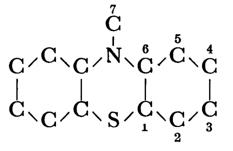
Crystallographic data are as follows:

$C_{13}H_{11}NS$
Orthorhombic: $a=14.9$, $b=11.4$, $c=6.79$Å
Density observed: 1.17_2 g·cm^{-3}
Density calculated: 1.18_2 g·cm^{-3}
Four formula units per unit cell
Space group: $Cmc2_1$

A set of intensity data was collected up to 5th layer around the *c*-axis, and up to 8th layer around the *b*-axis with a Weissenberg camera using Cu*K*α radiation. In total, 383 independent reflections were observed from 755 possible reflections, the rest being too weak to be observed. The intensities were estimated visually and corrected for Lorenz and polarization factors. The scale factor of each layer was determined by the least square method. From the space group $Cmc2_1$, the nitrogen, sulfur atoms and the carbon atom of the methyl group should be on the mirror plane perpendicular to the *b*-axis. The structure was solved by the Patterson and Fourier methods, and refined by diagonal, isotropic least squares. The final *R* factor was 0.135. The final atomic parameters are given in Table 1. The arrangement of the molecules in the crystal is shown in Figure 2. The bond lengths are C–N 1.43Å (0.026) and C–S 1.82Å (0.017). Bond angles are C–S–C 97° (0.77) and C–N–C 120° (2.5). The figure in parenthesis shows the value of standard deviation. The mean bond length of C–C is 1.41Å (0.033) and the mean bond angle of C–C–C is 120° (2.0). The plane equation of a benzene ring is $0.766x+0.294y+0.572z+4.72=0$. The N and S atoms deviate significantly from the planes of the benzene rings (N; 0.07, S; 0.18Å). The dihedral angle of the two benzene rings is 151° which is as large as that of PT. The configuration of the bonds about the nitrogen atom is a flattened tetrahedron, as is also the case with PT. Thus NMPT is determined to take a quasi-equatorial form in the crystal. This is not strange if we consider the fact that the steric effect of the methyl group is small and the molecule with this form is flattened and can be packed well. However, the present result contradicts the presumption based on the similarity of the chemical property to the other *N*-substituted derivatives. It is interesting to study whether the conversion from a quasi-axial form to a quasi-equatorial one happens in crystallization or not. Measurement of the ionization potential of the crystal of PT and NMPT is in progress to explain the difference in electronic state and structure between PT and *N*-substituted derivatives. All calculations were performed with the use of UNICS programs.

TABLE 1. ATOMIC PARAMETERS

Atom	*x/a*	*y/b*	*z/c*	B
C(1)	0.1840	0.1193	0.5745	2.076
C(2)	0.1869	0.2182	0.4662	3.153
C(3)	0.1368	0.3250	0.5426	3.773
C(4)	0.0845	0.3117	0.6961	4.169
C(5)	0.0762	0.2072	0.8039	2.464
C(6)	0.1296	0.1085	0.7469	2.647
C(7)	0.0852	0.0000	1.0485	5.935
N	0.1291	0.0000	0.8541	2.315
S	0.2584	0.0000	0.5033	2.422



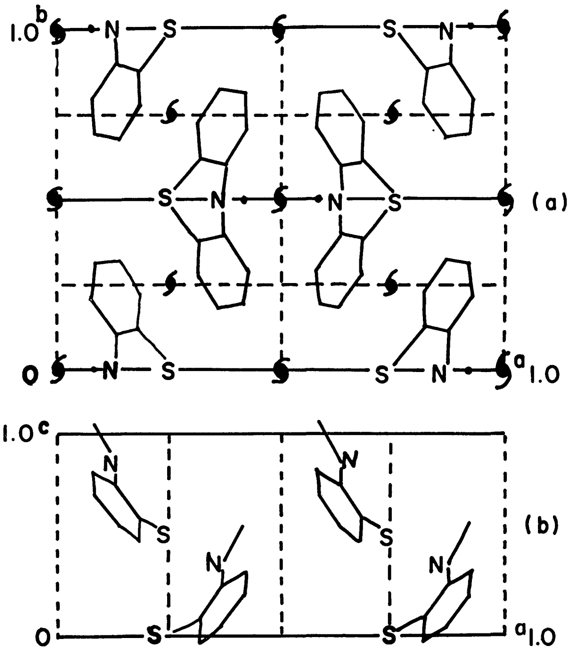


Fig. 2. Arrangement of the molecule in the crystal.
(a) Projection along the *c*-axis
(b) Projection along the *b*-axis

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[4] C. Bodea and I. Silberg, *Advan. Heterocyclic Chem.*, **9**, 433 (1968).

[5] J. P. Billon, G. Cauquis, and J. Combrisson, *J. Chim. Phys.*, **61**, 374 (1964).