Determination of Structure and ^{13}C Chemical Shift Assignments of the Nitration Products of 2-Chloro-10-methylphenothiazine. X-Ray Molecular Structure of 2-Chloro-7-nitro-10-methylphenothiazine 5-Oxide [1]

Misa V. Jovanovic [2a], Patrice de Meester [2b],
Edward R. Biehl* [2a], and Shirley S. C. Chu [2b]

Department of Chemistry and School of Engineering and Applied Sciences,
Southern Methodist University, Dallas, Texas 75275

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Nitration of 2-chloro-10-methylphenothiazine, **1**, yields two mono-nitro compounds identified as sulfoxide **2** and sulfone **3**. The nmr analyses of the ^{13}C spectra of **2** and **3** establish unequivocally that in both compounds substitution has occurred at the seven position. This is supported by the X-ray crystal structure of one of the compounds 2-chloro-7-nitro-10-methylphenothiazine 5-oxide, **2**, which also shows that the sulfoxide group is in the "pseudo-axial" configuration. Crystals of **2** are monoclinic, space group $P2_1/n$, $a = 11.606(4)$, $b = 13.970(4)$ Å, $c = 9.837(2)$, $\beta = 127.49(2)°$ and $Z = 4$. The structure has been refined by full-matrix least-squares to $R = 0.033$ and $R_w = 0.035$, using 1704 observed reflections.

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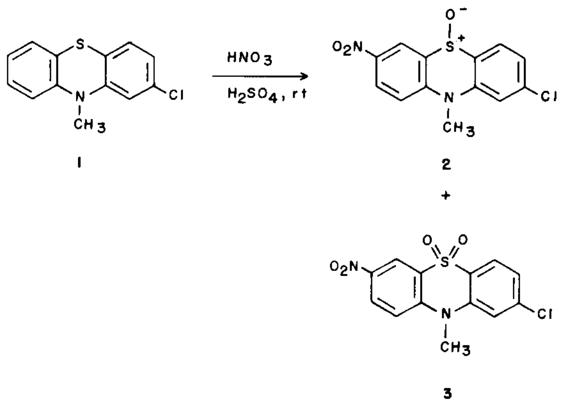
Introduction.

This paper reports on the nitration of 2-chloro-10-methylphenothiazine, **1**. Our interest in studying this reaction was prompted by the following observations. First, although the reaction of 10-substituted phenothiazines with electrophilic reagents has been studied extensively [3], this reaction has been virtually unexplored with benzo-substituted phenothiazines. Since the benzo rings in title compound, **1**, are not equivalent, information on the orienting effect of 2-chloro substituent would be of interest on both theoretical and synthetic grounds. Second, during our studies of the bromination with bromine in acetic acid of various 10-substituted phenothiazines, 5-sulfoxides as well as brominated products were obtained [4,5]. Thus, the nitration of **1** with a stronger oxidizine mixture of nitric acid and sulfuric acid as compared to bromine in acetic acid, should result in both nitration and sulfoxide formation.

Results and Discussion.

2-Chloro-10-methylphenothiazine, **1**, was nitrated at room temperature with concentrated nitric acid/sulfuric acid mixture to produce 2-chloro-7-nitro-10-methylphenothiazine 5-oxide, **2**, and 2-chloro-7-nitro-10-methylphenothiazine 5,5-dioxide, **3**. These products were identified on the basis of elemental analysis, infrared, ^{13}C-nmr and mass spectroscopy. The structure of **2** was also confirmed by x-ray spectroscopy. The x-ray and ^{13}C-nmr analyses are described later in the text. Interestingly, nitration did not occur on the chloro-substituted ring indicating that the chlorine substituent is a stronger deactivating group in the phenothiazine system than in the benzene series. Steric factors may also be involved because of the size of the 2-chloro substituent which may prevent nitration at C_3. We are exploring the influence of other substituents on the orientation of electrophiles to the benzo-portion of the phenothiazine ring.

Equation I



^{13}C NMR Analysis.

The application of ^1H nmr spectroscopy for structural identification of phenothiazines has been modestly successful [3,6,7]. The ^1H nmr spectra of symmetrically substituted phenothiazines can be easily interpreted but become very complex for non-symmetrical phenothiazines. In many instances, their interpretation at best is tedious and time consuming [8]. The ^{13}C nmr spectra provide the means for faster and unambiguous structural assignments of phenothiazine derivatives as we have shown in a previous report [9].

One of the important tools used in the assignment of ^{13}C-nmr signals is the use of SCS (substituent chemical shift) additivity parameters of substituted benzenes. However, application of these SCS additivity parameters to other polycyclic or heterocyclic systems is inappropriate unless the reliability of SCS for a particular substituent has been demonstrated. Many errors in the literature are a result of such comparisons [10,11]. We have shown recently [12] that SCS effects of the chlorine and sulfoxy groups in chlorpromazine and chlorpromazine 5-oxide are small (± 1-2 ppm) and approach the experimental error of the nmr measurement and could not be used in assigning ^{13}C chemical shifts of these chloro derivatives.

In order to assign ^{13}C chemical shifts of compound **2**, SCS parameters for a series of model phenothiazines and their corresponding 5-oxides were ascertained. These parameters as well as evaluation of their coupled and decoupled spectra aided the assignment of ^{13}C chemical shifts of compound **1**.

Table 1

^{13}C Chemical Shifts of 2-chloro-10-methylphenylthiazine, **1**, and its 5-Oxide, **4**, in Deuteriochloroform at Ambient Temperature (28°) [a]

Resonance	**1** [b]	**4** δ Calcd. [c]	**4** ^{13}C Obsvd. [d]	Δ >$\overset{+}{S}$-$\overset{-}{O}$ (ppm [e]
C_1	114.2	115.4	115.7 (+0.3)	+1.5
C_2	133.1	139.1	139.3 (+0.2)	+6.2
C_3	122.0	122.2	121.9 (−0.3)	−0.1
C_4	127.3	132.2	132.1 (−0.1)	+4.8
C_{4a}	121.7	124.3	124.5(−0.2)	+2.8
C_{5a}	122.9	122.5	122.5 (0)	+0.4
C_6	127.4	133.5	133.0 (+0.5)	+5.6
C_7	122.6	122.6	122.4 (−0.2)	−0.2
C_8	126.9	130.9	130.9 (0)	+4.0
C_9	114.1	115.3	115.7 (+0.4)	+1.6
C_{9a}	144.8	139.1	138.8 (−0.3)	−6.0
C_{10a}	146.7	140.2	140.7 (+0.5)	−6.0
CH_3	35.1	—	35.4 (−)	+0.3

[a] Reported in δ ppm downfield from TMS and using deuteriochloroform signal as a double reference standard (77.0 ppm). [b] Taken from reference [9]. [c] Calculated from substituent chemical shifts (SCS) of chloropromazine and chlorpromazine sulfoxide [10]. [d] △ = ^{13}C Observed - ^{13}C calculated is indicated in parentheses. [e] By definition in footnote [d]. △ Values in this column represent the difference between the experimentally observed chemical shifts of **1** and its 5-oxide **4** and are included to demonstrate the $>S^+\text{-}O^-$ substituent effects on this particular compound. They are not to be used for routine calculations of ^{13}C chemical shifts. Hybrid substituent chemical shift parameters (SCS) used to calculate the chemical shifts of **4** (second column) were derived by two independent methods. We generated this set of numbers from ^{13}C chemical shifts of chlorpromazine and its sulfoxide [10]. Differences between the corresponding chemical shifts were added to the chemical shifts of compound **1**. Alternatively, we derived the same set of numbers by adding the differences in chemical shifts of all three substituents: 10-methyl group (phenothiazine, **6**, -10-methylphenothiazine, **7**, [9]), 2-chloro substituent (**6** -2-chlorophenothiazine, **8**, [9]), and sulfoxide group (**6**, -phenothiazine 5-oxide, **9**, [25])and added them to the ^{13}C chemical shifts of the parent phenothiazine, **6**. The ^{13}C chemical shifts of **4** derived by this method matched closely (±0.2 ppm) the chemical shifts derived directly from chlorpromazine.

Table 2

^1H -^{13}C Spin-spin Coupling Constants of 2-Chloro-10-methylphenothiazine Sulfoxide, **4** (in Hz)

Carbon	$^1J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
C_1	$C_1H_1 = 166.14$		$C_1H_3 = 4.69$ [a]
C_2		$C_2H_1 = 4.45$ $C_2H_3 = 4.45$	$C_2H_4 = 11.87$
C_3	$C_3H_3 = 170.12$		$C_3H_1 = 4.67$
C_4	$C_4H_4 = 163.73$		
C_{4a}			$C_{4a}H_3 = 8.68$ [b] $C_{4a}H_1 = 5.85$ [b]
C_{5a}			$C_{5a}H_7 = 6.26$ $C_{5a}H_9 = 6.26$
C_6	$C_6H_6 = 163.38$		$C_6H_8 = 8.45$
C_7	$C_7H_7 = 164.76$		$C_7H_9 = 7.28$
C_8	$C_8H_8 = 162.40$		$C_8H_6 = 8.82$
C_9	$C_9H_9 = 164.25$		$C_9H_7 = 7.53$ [c]
C_{9a}			$C_{9a}H_6 = 8.45$ $C_{9a}H_8 = 8.45$
C_{10a}			$C_{10a}H_4 = 7.38$

[a] Estimated value due to the partial overlap with C_9 resonance. [b] Two couplings were distinguished from each other by partial decoupling of benzenoid protons. [c] Estimated value due to the partial overlap with C_1 resonance.

Table 3

^{13}C Chemical Shifts of 3-Nitro-10-methylphenothiazine, **6**, and Its 5-oxide, **7**, in Deuteriochloroform at Ambient Temperature (28°) [a]

Resonance	**6** [b]	**7**	△ $>S^+\text{-}O^-$ (ppm) [c]
C_1	116.3	115.9	−0.4
C_2	124.2	127.5	+3.3
C_3	142.3	141.4	−0.9
C_4	127.2	127.5	+0.3
C_{4a}	119.5	124.8	+5.3
C_{5a}	123.7	125.3	+1.6
C_6	133.4	133.4	0
C_7	122.7	123.9	+1.2
C_8	130.5	130.9	+0.4
C_9	116.9	116.3	−0.6
C_{9a}	140.5	138.6	−1.9
C_{10a}	145.4	143.7	−1.7
CH_3	36.0	36.1	+0.1

[a] Reported in δ ppm (δ) downfield from TMS and using deuteriochloroform as a double reference standard at 77.0 ppm. [b] Taken from ref [9]. [c] For the interpretation of this column, see footnote [e] in Table 1.

Table 4

^1H -^{13}C Spin-spin Coupling Constants of 3-Nitro-10-methylphenothiazine Sulfoxide, **7** (in Hz)

Carbon	$^1J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
C_1	$C_1H_1 = 165.42$		
C_2	$C_2H_2 = 169.44$		$C_2H_4 = 5.30$
C_3		$C_3H_4 = 5.26$ [a]	$C_3H_1 = 9.62$
C_4	$C_4H_4 = 170.06$		$C_4H_2 = 4.68$
C_{4a}			$C_{4a}H_1 = 5.79$
C_{5a}			$C_{5a}H_7 = 6.96$ $C_{5a}H_9 = 6.96$
C_6	$C_6H_6 = 163.62$		$C_6H_8 = 8.72$
C_7	$C_7H_7 = 166.38$		$C_7H_9 = 7.96$
C_8	$C_8H_8 = 165.30$		$C_8H_6 = 7.30$
C_9	$C_9H_9 = 162.54$		$C_9H_7 = 6.97$
C_{9a}			$C_{9a}H_6 = 8.31$ $C_{9a}H_8 = 8.31$
C_{10a}			$C_{10a}H_4 = 10.78$ [b] $C_{10a}H_2 = 9.37$ [b]

[a] May represent $^2J_{C_3H_3}$ which could be confirmed by spin population transfer at a field strength sufficient to give a first order spectrum for the benzoid protons. [b] The two couplings were distinguished from each other by partial decoupling of benzoid protons.

Table 1 lists the ^{13}C chemical shifts of 2-chloro-10-methylphenothiazine, **1**, and its 5-oxide, **4**. The sulfoxide chemical shift changes ($\triangle > S^+\text{-}O^-$) are similar to those reported for chlorpromazine and chlorpromazine sulfoxide [12]. Also, the calculated ^{13}C chemical shifts for **4** are in good agreement (within ±0.5 ppm) with those observed, substantiating the validity of SCS additivities in this system.

The change in chemical shifts induced by the introduction of the sulfoxy group ($\triangle > S^+\text{-}O^-$) in compound **4** are consistent with those observed for parent phenothiazines [13]. The atoms most affected are carbon atoms *ortho/para* to the sulfoxide functionality. For instance, $\triangle$ C_4, C_6, and C_8 for **4** are +4.8, +5.6 and +4.0 ppm, respectively, as compared to $\triangle$ $C_4(C_6)$ of +5.2 and $\triangle$ $C_2(C_8)$ of +3.7 ppm for 10-methylphenothiazine sulfoxide, **5**. The only other carbons significantly affected by the introduction of the sulfoxy group are those of the center ring. Quaternary carbon atoms adjacent to sulfur are slightly shielded whereas those next to nitrogen are deshielded by 6.0 ppm. This compares favourably with $\triangle C_4(C_{5a})$ of +1.6 and $\triangle$ $C_{9a}(C_{10a})$ of −6.0 ppm for **5**. The fact that $\triangle$ C values remain essentially the same and are independent of ring substitution or N_{10} substitution demonstrates the great utility of SCS additivity parameters once correctly established for a particular ring system. Comparison of SCS additivities of diphenyl sulfoxides with those of phenothiazine sulfoxides would have led to incorrect assignments [10,11].

The ^1H-^{13}C coupling constants of **4** are presented in Table 2. The most important feature is the increase in magnitude of $^1J_{CH}$ of carbons adjacent to chloro group (C_1, C_3) and the decrease of the long range coupling (^3J C_1H_3 and ^3J C_3H_1, allylic coupling) across the chlorine bearing carbon, C_2. The two bond couplings ^2J C_2H_1 and ^2J C_2H_3 are indicative of halogen substitution [14,15] and are a criterion used for distinguishing C_2 from other quaternary resonances.

In order to assess the effect of a nitro group on the carbon resonances, we prepared 3-nitro-10-methylphenothiazine, **6**, and 3-nitro-10-methylphenothiazine sulfoxide, **7**. The ^{13}C chemical shifts are shown in Table 3.

The assignments were straightforward since we have already established that carbon resonances of the unsubstituted benzene ring of monosubstituted phenothiazines are

Table 5

^{13}C Chemical Shifts of 2-Chloro-7-nitro-10-methylphenothiazine Sulfoxide, **2**, and the Corresponding Sulfone, **3**, in Hexadeuteriomethyl Sulfoxide at Ambient Temperature (28°) [a]

Resonance	**2**	**3**	$\triangle$ SO - > SO_2 (ppm)
C_1	117.0	117.6	+0.6
C_2	138.0	138.8	+0.8
C_3	123.3	118.7	−4.6
C_4	132.1	124.3	−7.8
C_{4a}	123.3	122.1	−1.2
C_{5a}	124.1	122.8	−1.3
C_6	127.5	123.6	−3.9
C_7	140.9	141.0	+0.1
C_8	126.7	128.0	+1.3
C_9	117.5	118.4	+0.9
C_{9a}	142.9	145.2	+3.3
C_{10a}	139.2	141.6	+2.4
CH_3	36.2	36.7	+0.5

[a] δ ppm downfield from TMS and using solvent as a double reference standard (d_6-DMSO = 39.5 ppm).

Table 6

^1H -^{13}C Spin-spin Coupling Constants of 2-Chloro-7-nitro-10-methylphenothiazine Sulfoxide, **2**, and Corresponding Sulfone **3** (in Hz)

Compound **2**

Carbon	$^1J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
C_1	C_1H_1 = 169.51		C_1H_3 = 4.08
C_2		C_2H_1 = 5.70	C_2H_4 = 14.15
		C_2H_3 = 5.70	
C_3	C_3H_3 = 175.77		C_3H_1 = 3.84
C_4	C_4H_4 = 166.43		
C_{4a}			$C_{4a}H_3$ = 8.25 [a]
			$C_{4a}H_1$ = 6.18 [a]
C_{5a}			$C_{5a}H_9$ = 5.50
C_6	C_6H_6 = 170.05		C_6H_8 = 5.23
C_7		C_7H_6 = 6.93 [b]	C_7H_9 = 10.67
C_8	C_8H_8 = 169.93		C_8H_6 = 4.21
C_9	C_9H_9 = 168.31		
C_{9a}			$C_{9a}H_6$ = 10.69
			$C_{9a}H_8$ = 10.69
C_{10a}			$C_{10a}H_4$ = 7.88
Compound 3			
C_1	C_1H_1 = 170.31		C_1H_3 = 3.77
C_2		C_2H_1 = 5.65	C_2H_4 = 13.84
		C_2H_3 = 5.65	
C_3	C_3H_3 = 171.95		C_3H_1 = 4.38
C_4	C_4H_4 = 169.96		
C_{4a}			$C_{4a}H_3$ = 8.75 [a]
			$C_{4a}H_1$ = 6.05 [a]
C_{5a}			$C_{5a}H_9$ = 5.65
C_6	C_6H_6 = 169.00		C_6H_8 = 3.80
C_7		C_7H_6 = 3.64	C_7H_9 = 8.60
		C_7H_8 = 3.64	
C_8	C_8H_8 = 170.94		C_8H_6 = 4.37
C_9	C_9H_9 = 170.05		
C_{9a}			$C_{9a}H_6$ [c]
			$C_{9a}H_8$ [c]
C_{10a}			$C_{10a}H_4$ = 6.45

[a] Two couplings were distinguished from each other by partial decoupling of benezenoid protons. [b] May represent $^2J_{C_7H_8}$ which could be confirmed by spin population transfer at a field strength sufficient to give a first order spectrum for the benezonoid protons. [c] $^3J_{CH}$ coupling not observed due to the ^{14}N quadrupole broadening of C_{10a} resonance.

Table 7

Crystal and Experimental Data of 2-Chloro-7-nitro-10-methylphenothiazine 5-Oxide

Chemical formula	$C_{13}H_9O_3N_2SC\ell$
Formula weight	308.74
Crystal system	Monoclinic
Space group	Ps_1/n
Unit-cell dimensions	a = 11.606(4)Å b = 13.970(4) c = 9.837(2) β = 127.49(2)° V = 1265.5(6)Å^3
Number of molecules per unit cell	4
Density (calculated)	1.620 g.cm^{-3}
X-radiation used for data collection	λ(MoKα) = 0.71069Å
Linear absorption coefficient	μ(MoKα) = 4.16 cm^{-1}
Total number of independent reflections with 2θ < 50°	2253
Number of observed reflections with I < 3σ(I)	1704
Maximum residue electron density	0.24 e$^-$/Å^3
Residual R-factors for observed reflections R	0.033
R_w	0.035
Crystal size	0.42 × 0.24 × 0.15 mm

very similar to those of the parent phenothiazine [9].

The SCS additivity parameters are much larger for the nitro group and are more useful in assigning carbon chemical shifts. The △ >S^+-O^- values for **7** are slightly deceptive since they are the result of the combined effects of the sulfoxy and nitro groups (Table 3). Henceforth, △ C_2 and C_4 represent the shielding effect of nitro group (−5.3 ppm [16]) and the deshielding of the sulfoxy substituent. The opposite is true for quaternary carbons adjacent to N_{10} where the deshielding effect of the nitro substituent (+6.0 ppm [16]) masks the shielding effect of the sulfoxide moiety.

Carbon resonances of C_1 and C_{4a} of compound **7** were assigned partially on the basis of ^{13}C-^1H couplings which are summarized in Table 4. The signal at δ 115.9 ppm was assigned to C_1 on the basis of the absence of a three bond coupling due to the substituted C_3 position. The signal at δ 116.3 ppm exhibited the three bond coupling and was thus assigned to C_9, on the basis of symmetry. Similarly, the quaternary carbon *meta* to the nitro group (C_{4a}) appears as a narrow doublet and is easily distinguished from

Table 8

Fractional atomic coordinates and thermal parameters (× 10_4) for non-hydrogen and (× 10^3) for hydrogen atoms. (The estimated standard deviations are given in parentheses and refer to the last positions of respective values.)

The expression for the thermal parameters with U values in Å^2 is:

$$T = \mathrm{expl}-2\pi^2(U_{11}h^2a^{*2}+U_{22}k^2b^{*2}+U_{33}\ell^2c^{*2}+2U_{12}hka^*b^*+2U_{13}h\ell a^*c^*+2U_{23}k\ell b^*c^*)$$

Atom	x	y	z	Ull	U22	U33	U12	U13	U23
C(1)	3319(3)	5776(2)	−414(3)	612(16)	410(14)	449(14)	72(12)	326(13)	−28(11)
C(2)	1981(3)	5519(2)	−1875(3)	593(16)	547(15)	398(13)	186(14)	237(13)	−25(11)
CL(2)	1087(1)	6323(1)	−3581(1)	963(6)	675(5)	459(4)	323(4)	192(4)	56(3)
C(3)	1335(3)	4655(2)	·2050(3)	493(16)	749(20)	420(14)	74(15)	166(13)	−95(14)
C(4)	2080(3)	4033(2)	−712(3)	495(15)	597(17)	475(14)	−96(13)	248(13)	−108(13)
C(4A)	3452(2)	4254(2)	786(3)	447(14)	490(13)	382(12)	−48(11)	251(11)	−58(10)
S(5)	4372(1)	3293(0)	2197(1)	632(4)	422(3)	377(3)	−182(3)	241(3)	−38(2)
O(5)	5216(2)	2806(1)	1716(2)	960(14)	401(9)	487(10)	116(9)	356(10)	−35(8)
C(5A)	5605(2)	3990(1)	4044(3)	423(12)	382(12)	372(11)	−40(10)	248(11)	−47(9)
C(6)	6242(3)	3508(2)	5582(3)	520(14)	384(13)	431(13)	4(11)	319(12)	−25(10)
C(7)	7385(2)	3915(2)	7070(3)	463(13)	409(13)	362(12)	86(10)	247(11)	7(10)
N(7)	8114(2)	3378(2)	8671(2)	671(15)	475(13)	400(11)	172(11)	315(12)	32(9)
O(71)	7488(2)	2675(1)	8683(2)	1005(16)	512(11)	550(11)	37(11)	456(11)	84(9)
O(72)	9317(2)	3643(1)	9908(2)	637(12)	786(13)	371(9)	128(10)	146(10)	4(9)
C(8)	7895(3)	4812(2)	7086(3)	446(14)	449(14)	376(13)	22(11)	186(12)	−77(11)
C(9)	7233(3)	5305(2)	5573(3)	477(14)	348(13)	437(13)	−41(11)	244(12)	−61(10)
C(9A)	6076(2)	4907(1)	4004(3)	395(12)	379(11)	355(11)	4(9)	239(10)	−45(9)
N(10)	5429(2)	5410(1)	2492(2)	474(11)	340(9)	381(10)	−33(8)	256(9)	−25(8)
C(10)	6068(3)	6327(2)	2545(4)	688(20)	450(14)	480(15)	−150(14)	357(15)	−44(12)
C(10A)	4089(2)	5148(1)	973(3)	431(13)	412(12)	345(11)	34(10)	246(10)	−38(9)
H(1)	374(2)	636(2)	−37(3)						
H(3)	39(3)	450(2)	−307(3)						
H(4)	172(3)	341(2)	−80(3)						
H(6)	592(3)	289(2)	558(3)						
H(8)	867(2)	509(2)	811(3)						
H(9)	757(2)	591(2)	564(3)						
H(101)	588(3)	649(2)	145(4)						
H(102)	713(3)	630(2)	328(3)						
H(103)	570(3)	682(2)	289(3)						

Table 9

Bond Lengths (Å) and Bond Angles(°) with Estimated Standard Deviations in Parentheses

a) Bond lengths

C(1)	- C(2)	1.374(4)
C(1)	- C(10A)	1.395(4)
C(2)	- CL(2)	1.742(3)
C(2)	- C(3)	1.375(4)
C(3)	- C(4)	1.360(4)
C(4)	- C(4A)	1.395(4)
C(4A)	- S(5)	1.751(3)
C(4A)	- C(10A)	1.405(4)
S(5)	- O(5)	1.487(2)
S(5)	- C(5A)	1.770(3)
C(5A)	- C(6)	1.388(4)
C(5A)	- C(9A)	1.403(3)
C(6)	- C(7)	1.365(4)
C(7)	- N(7)	1.462(4)
C(7)	- C(8)	1.382(4)
N(7)	- O(71)	1.226(3)
N(7)	- O(72)	1.224(3)
C(8)	- C(9)	1.374(4)
C(9)	- C(9A)	1.404(4)
C(9A)	- N(10)	1.382(3)
N(10)	- C(10)	1.465(4)
N(10)	- C(10A)	1.399(3)

b) Bond angles

C(2)	- C(1)	- C(10A)	120.13(27)
C(1)	- C(2)	- CL(2)	118.06(24)
C(1)	- C(2)	-C(3)	122.89(29)
CL(2)	- C(2)	- C(3)	119.05(24)
C(2)	- C(3)	- C(4)	117.55(29)
C(3)	- C(4)	- C(4A)	121.70(28)
C(4)	- C(4A)	- S(5)	114.90(21)
C(4)	- C(4A)	- C(10A)	120.42(25)
S(5)	- C(4A)	- C(10A)	124.01(20)
C(4A)	- S(5)	- O(5)	107.50(13)
C(4A)	- S(5)	- C(5A)	96.54(13)
O(5)	- S(5)	- C(5A)	107.51(12)
S(5)	- C(5A)	- C(6)	114.42(20)
S(5)	- C(5A)	- C(9A)	123.99(18)
C(6)	- C(5A)	- C(9A)	121.02(23)
C(5A)	- C(6)	- C(7)	119.48(27)
C(6)	- C(7)	- N(7)	119.29(25)
C(6)	- C(7)	- C(8)	121.34(27)
N(7)	- C(7)	- C(8)	119.34(25)
C(7)	- N(7)	- O(71)	117.62(22)
C(7)	- N(7)	- O(72)	118.54(22)
O(71)	- N(7)	- O(72)	123.83(23)
C(7)	- C(8)	- C(9)	119.27(28)
C(8)	- C(9)	- C(9A)	121.49(27)
C(5A)	- C(9A)	- C(9)	117.33(23)
C(5A)	- C(9A)	- N(10)	121.92(21)
C(9)	- C(9A)	- N(10)	120.75(22)
C(9A)	- N(10)	- C(10)	118.33(21)
C(9A)	- N(10)	- C(10A)	122.62(19)
C(10)	- N(10)	- C(10A)	118.45(21)
C(1)	- C(10A)	- C(4A)	117.27(23)
C(1)	- C(10A)	- N(10)	120.94(22)
C(4A)	- C(10A)	- N(10)	121.78(21)

the ^{13}C signal of C_{5a} which in the ^{1}H-coupled spectrum of **7** appears as a narrow "triplet" due to the two equivalent allylic couplings (H_7 and H_9).

Table 10

Torsion Angles, Ring Puckering Parameters and Least-squares Planes

a) Torsion angles (°) around the central phenothiazine ring

C(4A)	- S(5)	- C(5A)	- C(9A)	−28.2(2)
S(5)	- C(5A)	- C(9A)	- N(10)	11.0(3)
C(5A)	- C(9A)	- N(10)	- C(10A)	14.2(3)
C(4A)	- C(10A)	- N(10)	- C(9A)	−13.2(3)
S(5)	- C(4A)	- C(10A)	- N(10)	−13.2(4)
C(5A)	- S(5)	- C(4A)	- C(10A)	29.1(3)

b) Puckering parameters of central phenothiazine ring

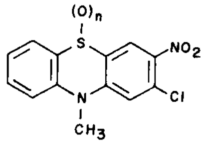
Central ring		Ideal boat conformation	
Q =	0.352 Å		
q_2	0.329	q_2	= 0
q_3	−0.125	q_3	= 0
θ	110.88°	θ	= 90
ϕ_2	358.28	ϕ_2	= 360

c) Least-squares planes

Deviations (Å) of atoms from least-squares planes (* refers to atoms not included in the least-squares plane calculation.)

C(1)	−0.002(4) Å	C(5a)	−0.011(4)
C(2)	−0.008)4	C(6)	0.017(4)
C(3)	0.006(4)	C(7)	−0.004(4)
C(4)	0.006(4)	C(8)	−0.009(4)
C(4a)	−0.011(4)	C(9)	0.011(4)
C(10a)	0.010(4)	C(9a)	0.001(4)
Cl(2)*	−0.057(5)	S(5)*	−0.291(4)
S(5)*	−0.309(4)	N(7)*	−0.064(5)
N(10)*	0.063(5)	O(71)*	0.193(5)
		O(72)*	−0.389(5)
		N(10)*	0.012(4)

The structural assignments of compounds **2** and **3** is now possible. Table 5 contains the ^{13}C chemical shifts of compounds **2** and **3** which we have tentatively assigned as the 7-nitro isomers. The other possible products are 2-chloro-3-nitro-10-methylphenothiazine sulfoxide, **8a**, and the corresponding sulfone, **8b**. The chemical shifts of **2** and **3** are in accord with those reported for models **4** and **7**. If the reaction products were the 3-isomers (**8a** and **8b**), the ^{13}C chemical shifts of the unsubstituted benzene ring should be identical to those of 10-methylphenothiazine sulfoxide and 10-methylphenothiazine sulfone [13]) and the chemical shifts of the substituted ring would be markedly different from those of **4** and **7**.



8a n = 1
8b n = 2

The ^{13}C-^{1}H coupling constants confirm our tentative assignment of the nitro isomer. Compounds **8a** and **8b** have only four carbon atoms (C_1, C_4, C_6 and C_9) adjacent to the heteroatom bearing substituents, whereas **2** and **3** have six such carbons (C_1, C_3, C_4, C_6, C_8 and C_9). Table 6 shows that *all ipso* ^{13}C-^{1}H couplings ($^1J_{CH}$) of **2** and **3** are larger in magnitude (~ 170 Hz) than the same C-H couplings for the 10-methylphenothiazine sulfoxide [13] and the carbon atoms *not* adjacent to hetero groups in compounds **1**, **4**, **5** and **7** (Tables 2 and 4 and ref. 13). Thus, structures **2** and **3** depicted as 7-nitro derivatives are the correct representations for our products. Spin-lattice relaxation times, (T_1) for the proton-bearing carbon atoms next to hetero groups are also 10% higher than T_1 for other protonated carbons and can also be used qualitatively for chemical shift assignments when they are available [17].

Similarly, the three-bond allylic couplings across the chloro and nitro groups are much smaller than typical allylic couplings and are in the range of 3.8-5.7 Hz. They could only be present in the 7-nitro isomer ($^3J\ C_1H_3$, $^3J\ C_3H_1$, $^3J\ C_6H_8$, $^3J\ C_8H_6$) since *no* such C-H couplings are possible in **8a** and **8b** where both *meta* positions are blocked by substituents.

X-Ray Analysis.

In order to confirm our results reached by ^{13}C nmr spectroscopy, the x-ray structure of one of our products, **2**, has been determined.

The identification of the atoms and the configuration of the molecule are shown in the ORTEP [18] drawing in Figure 1. The bond lengths and bond angles are listed in Table 9. The torsion angles and the puckering parameters of the central ring, given in Tables 10a and b, show that **2** is in the boat conformation. The methyl group and the sulfonyl oxygen atoms are in equatorial and axial positoins, respectively, relative to the central ring. The planarity of the two benzo rings can be estimated from Table 10c. The folding angle between the two benzo ring planes is 164.5(1)°. The angle between the nitro group and the benzo ring to which it is attached to is 16.0(1)°. The packing of the molecules in the unit cell is shown in Figure 2.

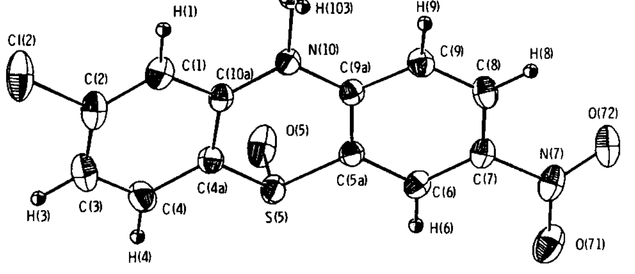


Figure 1. ORTEP drawing of **2**. Thermal ellipsoids are scaled at the 50% probability level. Hydrogen atoms are represented as spheres of arbitrary radii.

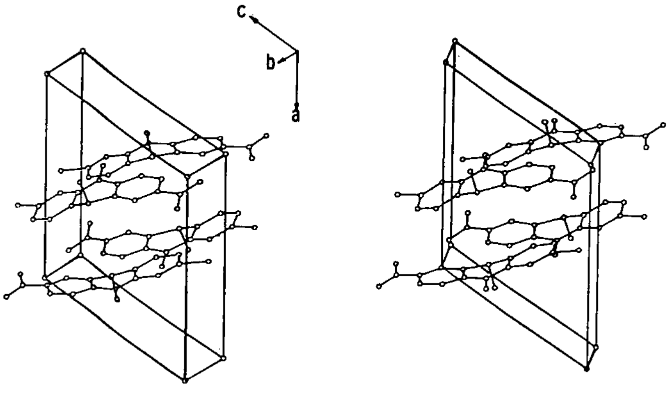


Figure 2. Stereoscopic drawing of the molecular packing in the cell.

EXPERIMENTAL

Materials.

Compounds **1** and **6** were available from the previous study [9]. 3-Nitro-10-methylphenothiazine sulfoxide, **7**, [19]; ir (nujol): 1045, 1032 cm^{-1} (SO axial), and 2-chloro-10-methylphenothiazine sulfoxide, **4**, [20] were prepared by literature procedures. Compounds **4** and **7** were also prepared by the method described in ref 13; *i.e.* oxidation of **1** and **6** by sodium nitrite in dichloromethane/acetic acid mixture.

Nitration of 2-Chloro-10-methylphenothiazine, 1.

To a solution of 5 ml of concentrated nitric acid (d = 1.42) was added 2.48 g (10 mmoles) of **1**. After all of **1** dissolved (10 minutes), the mixture was cooled to 15° and to it was added dropwise 2.5 ml of concentrated sulfuric acid. The orange solution immediately turned reddish-brown, was brought to room temperature and left standing for 8 hours. (The external ice-water bath was used throughout the addition of sulfuric acid to maintain the temperature at 25°). After this time, the reaction mixture was poured into 100 ml of ice-cold water, partially neutralized with sodium carbonate and the yellow precipitate collected by filtration. The crude product was washed with additional 10 ml of cold water, air dried and triturated with 100 ml of hot 50:50 benzene-ethanol solution, filtered and mother-liquor evaporated to dryness to yield **2** which was recrystallized twice from hot benzene to yield yellow solid; mp 230-231.5°; ms: (70 ev), m/e 308 (P), 310 (P+2), 292, 294; ir (nujol): 1048, 1030 cm^{-1} (SO axial).

Anal. Calcd. for $C_{13}H_9ClN_2O_3S$: C, 50.57; H, 2.94; N, 9.08. Found: C, 50.36; H, 2.96; N, 8.79.

The remaining solid was washed with additional 25 ml of hot benzene and benzene evaporated *in vacuo* to give 0.6 g more of **2** (overall yield, 1.48 g, 48%). The residual yellow flakes contained almost pure **3**, 1.32 g (41% yield). Small amount of **3** was recrystallized from 2-propanol to yield the analytical sample of **3** as deep yellow needles; mp > 300°; ms: (70 ev), m/e 322 (P), 324 (P+2), 308, 310, 292, 294; ir (nujol): 1350, 1330, 1296, 1167, 1131 cm^{-1} (SO_2).

Anal. Calcd. for $C_{13}H_9ClN_2O_4S$: C, 48.08; H, 2.80; N, 8.63. Found: C, 47.99; H, 2.84; N, 8.67.

Single Crystal Data.

The crystals of **2** are orange prisms. A crystal of size 0.42 × 0.24 × 0.15 mm was selected for the determination of the cell parameters and the intensity measurements. Unit cell parameters were obtained by least-squares fit of 15 reflections centered in the range $19 < 2\theta < 32°$ on a

Syntex $P2_1$ diffractometer with graphite monochromatized MoKα radiation. The space group $P2_1/n$ was determined from the systematic absences $h0\ell$, $h + \ell$ odd and $0k0$, k odd. The pertinent crystal and experimental data are summarized in Table 7. Data were collected at 295 K. The scan speed varied between 2.93 and 14.65°/minute, depending on the intensity of a 2 second free scan. The intensities of three standard reflections (1 0 3, 1 0 −3 and 0 4 0), remeasured every 97 reflections did not vary significantly during data collection. The intensity data were reduced to structure amplitudes by the application of the Lorentz and polarization factors. No absorption correction was applied.

Structure Determination.

The structures was solved by MULTAN78 [21] and refinements were carried out by full-matrix least-squares using SHELX76 [22]. The non-hydrogen atoms were refined with anisotropic temperature factors. All hydrogen atoms were located and refined with isotropic temperature factors. The quantity $\Sigma w2(|F_o|-|F_c|)^2$ was minimized in the least-squares and the weight used was $w = 1/(\sigma F_o^2 + 1.67 \times 10^{-4} F_o^2)$. The final R index, $\Sigma||Fo| - |Fc|| /\Sigma|Fo|$ was 0.033 and the weighted residual R_w was 0.035 for the 1704 observed reflections. Two hundred seventeen variables were used in the least-squares refinements. During the last cycle the maximum $(\triangle/\sigma)$ was 0.30. The R factor for all 2253 independent data was $R = 0.048$ and $R_w = 0.041$. The atomic scattering factors for all atomic species and the real and the imaginary parts of the anomalous dispersion for S and Cl were taken from the International Tables for X-ray Crystalography [23]. Other programs used in this study (bond lengths, torsion angles, *etc.*) were written by Shiono [24] and locally modified for our IBM 3081D. The final atomic coordinates are given in Table 8.

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