Crystal Structure Determination of 2'-Nitro-10-Phenylphenothiazine

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The structure of the titled compound, **4**, has been solved by x-ray analysis. One of the important structural features of **4** is that the 2'-nitrophenyl group is in the plane bisecting the phenothiazine ring which is in contrast to that of 10-(2'-pyrazyl)phenothiazine of 4'-nitro-10-phenylphenothiazine in which the 10-aryl group is perpendicular to the plane bisecting the phenothiazine ring. The structure of **4** is in agreement with its ^1H and ^{13}C nmr data which indicate that resonance interactions between the 2'-nitrophenyl group and the lone pair of electrons on N_{10} are hindered sterically by the 2'-nitro group.

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Recently, we have described the syntheses of some novel phenothiazines, heteroarylphenothiazines and their pyridobenzothiazine analogs [1]. ^{13}C nmr spectroscopy revealed that strong electonic interactions between the 10-aryl group and the phenothiazine ring were present in some of those compounds. For example, the carbon chemical shifts of the phenothiazine ring carbon atoms in 4'-nitrophenylphenothiazine, **1**, were significantly different from those of the corresponding atoms in 10-phenylphenothiazine, **2**, whereas no such difference was observed between 4'-methoxy-10-phenylphenothiazine, **3**, and the 10-phenyl compound, **2**, [2]. We attributed those chemical shift changes in **1** to direct resonance interactions between the 4'-nitrophenyl group and the lone pair of electrons on N_{10}.

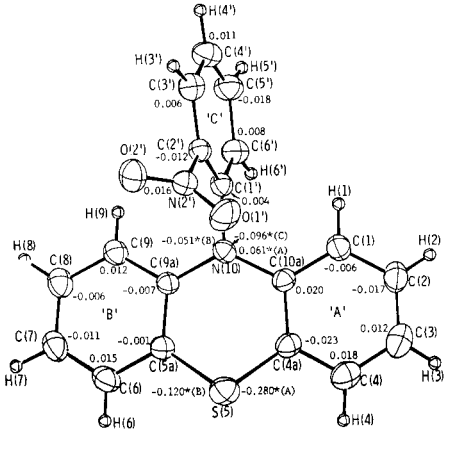


Figure 1

ORTEP drawing of a molecule of **4** with the deviations of atoms from the least-squares planes shown in Å units. The equations for the planes are:

Plane 'A' $-0.7240(9)x-0.605(1)y+0.425(1)z = 5.16(3)$

Plane 'B' $-0.629(1)x-0.368(1)y+0.7629(9)z = 12.74(2)$

Plane 'C' $0.569(1)x+0.457(1)y+0.602(1)z = 15.74(2)$

where x, y, and z are in Å. Dihedral angles between 'A' and 'B' 154.8(1)°, 'A' and 'C' 117.5(1)°, 'B' and 'C' 86.7(1)°. An asterisk indicates atoms excluded from the calculation of the least-squares planes. The lettering in parentheses indicates the plane that the deviation is from.

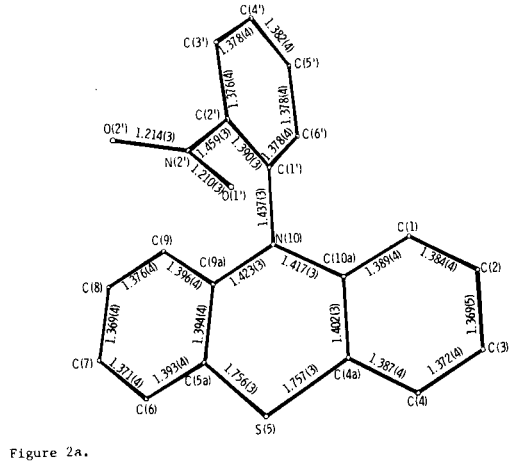


Figure 2a.

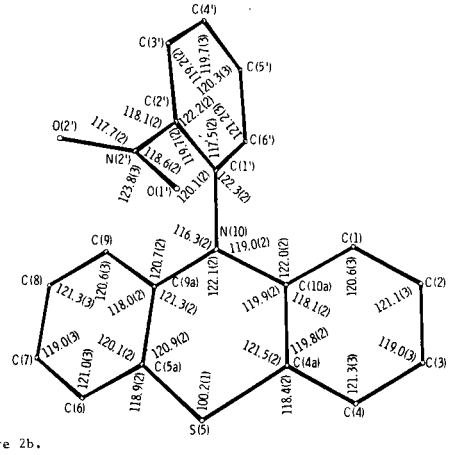


Figure 2b.

Figure 2.

Bond lengths (Å)(a) and bond angles (°)(b) of **4** with e.s.d.'s in parentheses.

Table 1

Crystal and Experimental Data of 2′-nitro-10-phenylphenothiazine

Chemical formula	$C_{18}H_{12}O_2N_2S$
Formula weight	320.4
Crystal system	Monoclinic
Space Group	$P2_1/c$
Unit cell dimensions	a = 8.681(a)Å
	b = 7.340(1)
	c = 23.632(3)
	β = 97.69(1)°
	V = 1492.3(4)Å^3
Number of molecules per unit cell	4
Density (calculated)	1.426 g cm^{-3}
X-radiation used for data collection	$\lambda(CuK_\alpha)$ = 1.5418Å
Linear absorption coefficient	$\mu(CuK_\alpha)$ = 19.05 cm^{-1}
Total number of reflections with $2\theta < 130°$	2489
Number of reflections with $I > 3\sigma(I)$	1785
Maximum residue electron density	0.15 e Å^{-3}
Disagreement index, R for 1785 observed reflections	0.039
Weighted disagreement index, R_w for 1785 observed reflections	0.048
Crystal size	0.42 × 0.12 × 0.05 mm

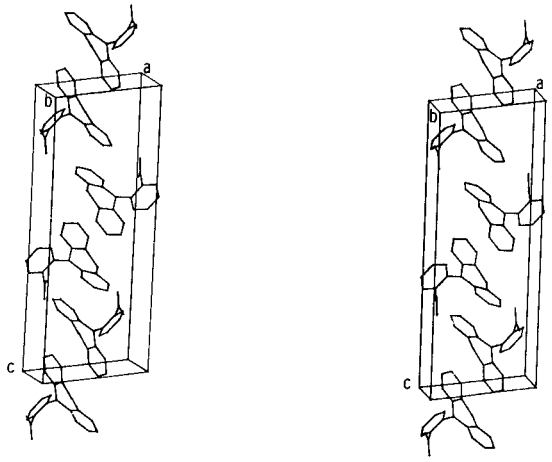


Figure 3

Stereoscopic drawing of molecular packing of **4**, excluding hydrogen atoms, in the unit cell.

However, the ^{13}C nmr spectrum of 2′-nitro-10-phenylphenothiazine, **4**, showed that the phenothiazine ring carbon chemical shifts were approximately the same as those of the 10-phenyl compound, **2**, indicating that resonance interaction between the pi electrons of the 2′-nitrophenyl group and the lone pair of electrons on N_{10} in compound **4** is inhibited. For resonance to occur between those two electronic systems, the 10-phenyl ring must be perpendicular to the plane bisecting the phenothiazine ring. Construction of a Drieding Model reveals such a structure for **4** is prevented by the steric effect of the 2′-nitro group. The crystal structure for 2′-methoxy-10-phenylphenothiazine, **5** has been reported [3] and it shows that the 2′-methoxy group does exhibit such a sterric effect, that is, the 2′-methoxyphenyl ring is not perpendicular to but is in the plane bisecting the phenothiazine ring. This paper reports on the structure determination of the 2′-nitro compound, **1**, which was carried out to see if the 2′-nitro group exhibited a steric effect similar to that of the 2′-methoxy derivative.

EXPERIMENTAL

The crystals of 2′-nitro-10-phenylphenothiazine are transparent brown elongated needles. A crystal was cut to 0.42 × 0.12 × 0.05 mm in dimensions and was used for the determination of unit cell parameters and the intensity measurements. The unit cell parameters were obtained from a least-squares analysis of 15 reflections with 2θ values measured on a Syntex $P2_1$ automatic diffractometer with graphite monochromatized CuKα radiation. The crystal data are summarized in Table 1. The intensity data were collected with the $\theta/2\theta$ scanning mode. A total of 2489 independent reflections were measured with 2θ values below 130°, of which 1785 reflections were considered as observed by the criterion $I > 3\sigma$ (I), where σ(I) was determined from counting statistics. The intensity data were reduced to structure amplitudes by the application of Lorentz and polarization factors, and no absorption corrections were applied.

The structure was solved by the application of direct methods with the weighted multisolution tangent-refinement program, MULTAN 78 [4]. The E map showed the positions of all non-hydrogen atoms. The refinements were carried out by full-matrix least-squares method using the SHELX system of programs [5]. The anisotropic temperature factors were used for non-hydrogen atoms. All hydrogen atoms were located in a difference Fourier synthesis and the isotropic temperature factors were used for hydrogen atoms in the refinement. All the reflections were used in the refinement and the weight the reflection was assigned as $1/[\sigma(F)]^2$, where σ(F) was calculated from counting statistics. The quantity $\Sigma w||F_o|-|F_c||/\Sigma|F_o|$ was minimized. The final R index, $\Sigma||F_o|-|F_c||/\Sigma|F_o|$, was 0.039 and the weighted disagreement index was 0.048 for 1785 observed reflections. The final difference Fourier synthesis showed a maximum residue of electron density of 0.15 e Å^{-3}. The atomic scattering factors used for sulfur, nitrogen, carbon, and hydrogen were those from International Tables for X-ray Crystallography [6]. The final atomic parameters are given in Table 2.

Results and Discussion.

The identification of the atoms and the configuration of the molecule, **4**, are shown in ORTEP [7] drawing in Figure 1. The bond lengths and bond angles, with their standard deviations, are shown in Figure 2. The configuration of the phenothiazine ring system and the conformation of the 10-phenyl ring are similar to those found in 2′-methoxy-10-phenylphenothiazine, **5**, [5] and 4′-bromo-10-phenylphenothiazine, **6**, [8]. These can be shown by comparing the bond lengths and the bond angles of the phenothiazine ring and the folding angles of the ring systems. The mean values of the C-S bond lengths and the C-N bond lengths within the central ring are 1.757(3) and 1.420(3)Å, 1.757(2) and 1.419(2)Å, and 1.762(4) and 1.421(5)Å, in **4**, **5**, and **6**, respectively. The C-S-C and

Table 2

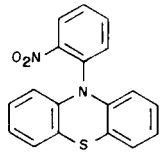
Fractional Atomic Coordinates and Thermal Parameters (X 10^4) for Non-hydrogen and X 10^3) for Hydrogen Atoms. (The estimated standard deviations are given in parentheses and refer to the last positions of respective values).

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

$$T = \exp\{-2\pi^2(U_{11}h^2a^{*2} + U_{22}k_2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*\}$$

Atom	X	Y	Z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	7895(3)	-388(4)	9896(1)	491(15)	665(18)	501(15)	-23(13)	56(12)	-89(14)
C(2)	7873(4)	731(5)	10366(1)	647(19)	887(23)	499(16)	-134(16)	102(15)	-284(18)
C(3)	6827(4)	2130(5)	10359(1)	796(22)	807(22)	635(19)	-283(18)	359(18)	-340(19)
C(4)	5816(4)	2443(4)	9871(1)	621(17)	480(15)	815(22)	-122(15)	344(16)	-117(14)
S(5)	4740(1)	2093(1)	8747(0)	740(5)	435(3)	811(5)	46(3)	93(4)	91 (3)
C(6)	3127(3)	-218(5)	7987(1)	436(15)	762(21)	643(17)	188(16)	78(13)	58(15)
C(7)	2902(3)	-1783(5)	7670(1)	466(15)	961(25)	551(16)	-68(17)	50(13)	-113(16)
C(8)	3942(3)	-3182(5)	7778(1)	486(16)	819(23)	591(16)	-205(16)	118(13)	-121(15)
C(9)	5208(3)	-3037(4)	8193(1)	447(14)	562(16)	527(14)	-83(12)	92(12)	-10(13)
N(10)	6834(2)	-1251(3)	8918(1)	395(11)	462(11)	482(11)	-68(9)	29(9)	20(9)
C(4a)	5851(3)	1389(3)	9386(1)	491(14)	425(13)	604(15)	-63(12)	203(12)	-111(12)
C(5a)	4420(3)	-15(4)	8400(1)	446(13)	505(14)	493(13)	79(11)	137(11)	-12(12)
C(9a)	5487(3)	-1433(3)	8507(1)	365(12)	508(13)	407(12)	35(11)	126(10)	-22(11)
C(10a)	6863(3)	-105(3)	9402(1)	430(13)	443(13)	486(13)	-58(11)	140(11)	-105(11)
C(1')	7983(3)	-2662(3)	8922(1)	392(12)	436(12)	453(12)	-26(11)	40(10)	-19(11)
C(2')	9060(3)	-2604(3)	8537(1)	387(11)	410(12)	456(12)	-20(10)	62(10)	-23(10)
C(3')	10092(3)	-4001(4)	8490(1)	516(15)	522(15)	602(15)	-101(13)	165(13)	-5(12)
C(4')	10107(3)	-5475(4)	8852(1)	529(15)	436(15)	853(19)	-51(14)	76(14)	68(13)
C(5')	9046(4)	-5565(4)	9238(1)	625(18)	497(16)	757(18)	152(15)	85(15)	8(13)
C(6')	7989(3)	-4179(4)	9266(1)	516(15)	512(15)	638(16)	83(13)	162(14)	4(12)
N(2')	9098(3)	-1035(3)	8160(1)	484(12)	542(13)	536(12)	42(10)	123(10)	-1(10)
O(1')	9263(3)	466(3)	8371(1)	1208(20)	463(11)	825(14)	60(11)	185(14)	-120(12)
O(2')	8981(3)	-1320(3)	7650(1)	870(16)	948(17)	502(11)	109(11)	166(10)	58(13)
H(1)	867(4)	-132(4)	991(1)	76(9)					
H(2)	855(4)	49(4)	1068(1)	69(9)					
H(3)	676(4)	288(5)	1065(1)	81(10)					
H(4)	507(3)	338(4)	982(1)	44(7)					
H(6)	250(3)	76(4)	792(1)	53(7)					
H(7)	203(4)	-195(5)	737(2)	94(11)					
H(8)	380(4)	-432(5)	756(1)	74(10)					
H(9)	584(4)	-402(4)	826(1)	61(9)					
H(3')	1074(4)	-395(4)	820(1)	62(8)					
H(4')	1084(3)	-646(4)	882(1)	60(7)					
H(5')	903(4)	-652(4)	951(1)	66(8)					
H(6')	730(3)	-423(4)	954(1)	49(7)					

C-N-C bond angles within the central ring are 100.2(1) and 122.2(2)°, 100.7(1) and 122.5(1)°, and 99.0(2) and 120.4(3)°, in **4**, **5**, and **6**, respectively. The least-squares planes of the phenyl ring and the two benzo rings, together with the deviations of the atoms from the plane are shown in Figure 1. The folding angle between the planes of the two benzo rings is 154.8(1)° in **4** as compared to the 157.5° in **5** and 147.9° (mean value of two crystallographically independent molecules) in **6**. The decrease in puckering of the dihedral angle in **4** and **5** has been attributed to the ortho effect of the 2'-substituents [3]. The dihedral angles between the plane of the phenyl ring and the two planes of the benzo rings are 117.5(1) and 86.7(1)°, which indicates that the phenyl ring is not as nearly bisecting the dihedral angles of the phenothiazine ring as observed in **5** and **6**. Nonetheless, the 2'-nitro group does exert a steric effect similar to that of the 2'-methoxy group which prevents the 10-phenyl ring and the lone pair of electrons on N_{10} from achieving the conformation necessary for mutual resonance interac-



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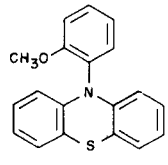

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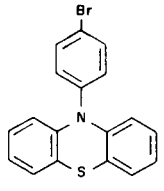

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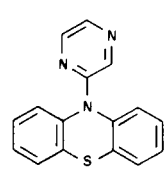

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Table 3

Torsion Angles and Ring Puckering Parameters.

Torsion angles around the central phenothiazine ring:

C(4a)-S(5)-C(5a)-C(9a)	-28.6(2)°
S(5)-C(5a)-C(9a)-N(10)	2.8(3)
C(5a)-C(9a)-N(10)-C(10a)	29.1(4)
C(9a)-N(10)-C(10a)-C(4a)	-25.2(3)
N(10)-C(10a)-C(4a)-S(5)	-9.6(3)
C(10a)-C(4a)-S(5)-C(5a)	32.3(2)

Torsion angles about the N(10)-C(1') bond:

C(9a)-N(10)-C(1')-C(2')	82.4(3)°
C(9a)-N(10)-C(1')-C(6')	-92.1(3)
C(10a)-N(10)-C(1')-C(2')	-115.5(3)
C(10a)-N(10)-C(1')-C(6')	69.9(3)

Torsion angles about the C(2')-N(2') bond:

C(1')-C(2')-N(2')-O(1')	56.0(3)
C(1')-C(2')-N(2')-O(2')	-124.9(3)
C(3')-C(2')-N(2')-O(1')	-125.0(3)
C(3')-C(2')-N(2')-O(2')	54.1(3)

Puckering parameters:

Central phenothiazine	Ideal boat conformation
Q = 0.437 Å	q_2 = Q
q_2 = 0.429	q_3 = 0
q_3 = 0.084	
θ = 101.1°	θ = 90°
ϕ_2 = 355.3°	ϕ_2 = 360°

tions. The conformation of the 2'-nitrophenyl ring is in contrast to the conformation of the pyrazine ring in 10-(2'-pyrazyl)phenothiazine, **7**, [9], in which the pyrazine ring is perpendicular to the plane bisecting the phenothiazine ring. The structure of 4'-nitro-10-phenylphenothiazine has a similar conformation as that of **7**. In both instances, there is electronic interaction between the phenothiazine ring and the 10-substituent [9,10].

The data in Table 3 reveal several other important structural features of compound **4**. The central ring of the phenothiazine ring system is in a boat conformation as shown from the torsional angles around the central ring and the puckering parameters [11]. As is observed in other 10-substituted phenothiazines, the sum of the three C-N-C-bond angles of 357.4 in **4** indicates the three C-N bonds are approximately planar in configuration. The torsion angles of the nitro group with respect to the phenyl ring shows that the 2'-nitro group is planar and that the plane of the nitro group is tilted from the phenyl ring by 55.6(1)°.

The packing of the molecules in the unit cell is shown in the stereoscopic drawing in Figure 3. The closest intermolecular distances are 3.238 and 3.374 Å, between O(1)---C(4') and O(1)---C(3'), respectively.

Acknowledgement.

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REFERENCES AND NOTES

[1] M. V. Jovanovic and E. R. Biehl, *J. Heterocyclic Chem.*, **20**, 1677 (1983).

[2] M. V. Jovanovic and E. R. Biehl, *Org. Magn. Reson.*, in press (1984).

[3] S. S. C. Chu, H. T. Yang, and D. van der Helm, *Acta Cryst.*, **B32**, 2567 (1976).

[4] P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declerco, and M. M. Woolfson, MULTAN 78, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data 1978, University of York, England, ad Louvain, Belgium.

[5] G. M. Sheldrick, SHELX 76, Programs for Crystal Structure Determination, University of Cambridge, England, 1976.

[6] Internation Tables for X-ray Crystallography, Vol IV, Birmingham: Kynoch Press, 1974.

[7] C. K. Johnson, ORTEP, Report ORNL-3784, Oak Ridge National Laboratory, Tennessee 1965.

[8] S. S. C. Chu and H. T. Yang, *Acta Cryst.* **B33**, 1892 (1977).

[9] M. V. Jovanovic, E. R. Biehl, R. D. Rosenstein, and S. S. C. Chu, *J. Heterocyclic Chem.*, in press (1984).

[10] M. V. Jovanovic, E. R. Biehl, P. de Meester, and S. S. C. Chu, *ibid.*, accepted (1984).

[11] D. Cremer and J. A. Pople, *J. Am. Chem. Soc.*, **97**, 1354 (1975).