

Department of Chemistry, Texas Technological College

Ion Radicals. XIII. Spectroscopic and Cryoscopic Characterization of Ions and Ion Radicals from Phenothiazine and *N*-Methylphenothiazine in Sulfuric Acid Solutions (1,2).

H. J. Shine, D. R. Thompson, and C. Veneziani (3)

The formation and interconversion of the *N*-methylphenothiazine cation radical and the *N*-methylphenothiazine dication from both *N*-methylphenothiazine and *N*-methylphenothiazine *S*-oxide in sulfuric acid solutions have been demonstrated with e.s.r. and absorption spectroscopy. Cryoscopic measurements have shown that in slightly aqueous sulfuric acid *N*-methylphenothiazine *S*-oxide is converted to the *N*-methylphenothiazine dication and, analogously, phenothiazine *S*-oxide is converted to the protonated phenazathionium ion (the phenothiazine dication).

N-Methylphenothiazine (I) and *N*-Methylphenothiazine *S*-Oxide (II).

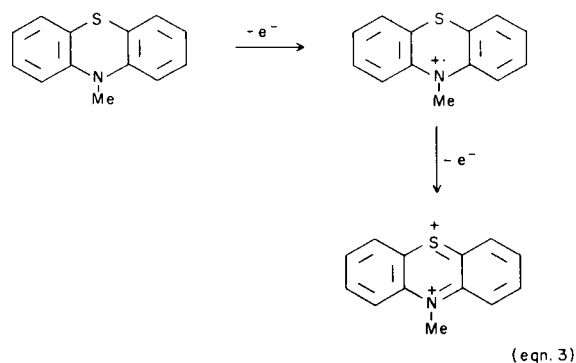
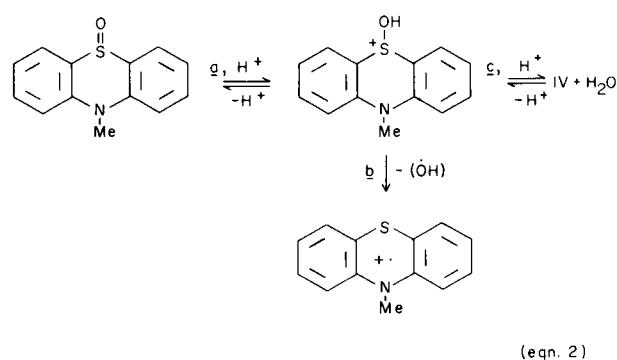
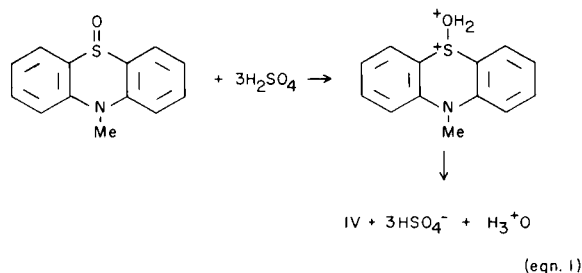
In an earlier paper we have described the reactions of phenothiazine and phenothiazine 5-oxide in acid solutions, and have discussed in detail the relationships between these compounds as they are converted to the phenothiazine cation radical and the phenazathionium ion (4). The compounds *N*-methylphenothiazine (I) and *N*-methylphenothiazine *S*-oxide (II) have now been studied. Our results, obtained with e.s.r. and absorption spectroscopy and *i*-factor measurements, enable us to characterize the *N*-methylphenothiazine cation radical (III) and the *N*-methylphenothiazine dication (IV), and to follow their formation from I and II in acid solutions. The relevant absorption maxima are given in Table I.

A dilute solution of II in 96% sulfuric acid had absorption maxima at 290 and 464 $m\mu$. The *i*-factor of solutions of II in almost 100% sulfuric acid was close to five (Table II), from which we conclude that the *N*-methylphenothiazine dication was formed, as shown in equation 1. With this result in mind we attribute the absorption maxima at 290 and 464 $m\mu$ to the dication (IV).

A dilute solution of II in 45% sulfuric acid (Figure 1) initially had a spectrum like that of II in ethanol. In time this spectrum disappeared and was replaced by one which we attribute to the cation radical (III). The reaction occurring in this solution is described by the paths (a) and (b) of equation 2.

The oxide (II) was not detectable as II in 78% sulfuric acid. Instead it was converted quickly to the *N*-methylphenothiazine dication (IV) which in time disappeared and was replaced by the cation radical (III) (Figure 2). This transformation is believed to go through the intermediate protonated oxide as shown by paths (b) and (c) of equation 2.

These reactions are entirely similar to those which have been observed with phenothiazine 5-oxide (4). We are now



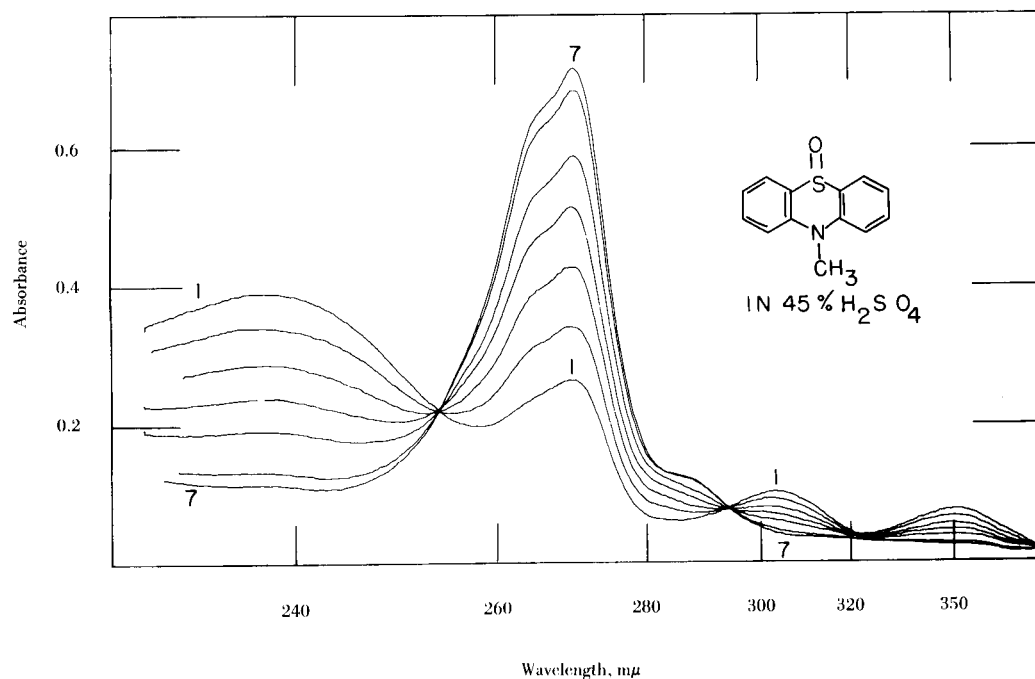


Figure 1. The change with time in the ultraviolet spectrum of a $1.5 \times 10^{-5} M$ solution of *N*-methylphenothiazine *S*-oxide in 45% sulfuric acid. Scan 1 was recorded after 5 minutes in solution and scan 7 after 2 hours.

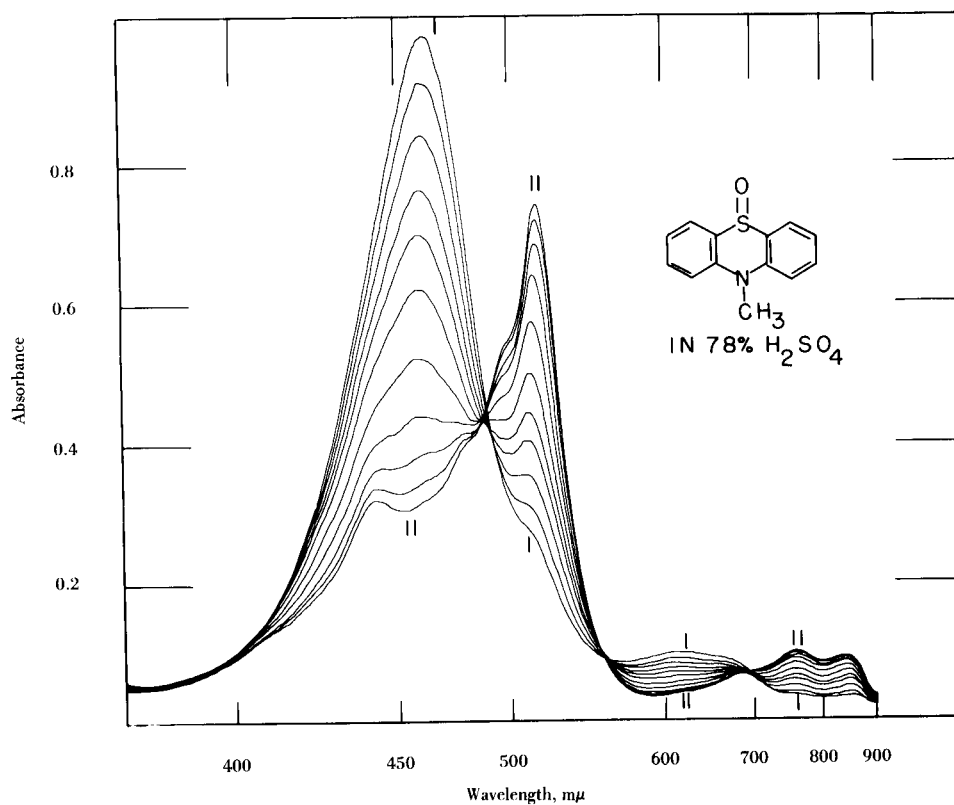


Figure 2. The change with time in the visible spectrum of a $7.5 \times 10^{-5} M$ solution of *N*-methylphenothiazine *S*-oxide in 78% sulfuric acid. Scan 1 was recorded after 4 minutes in solution and scan 11 after 4.5 hours.

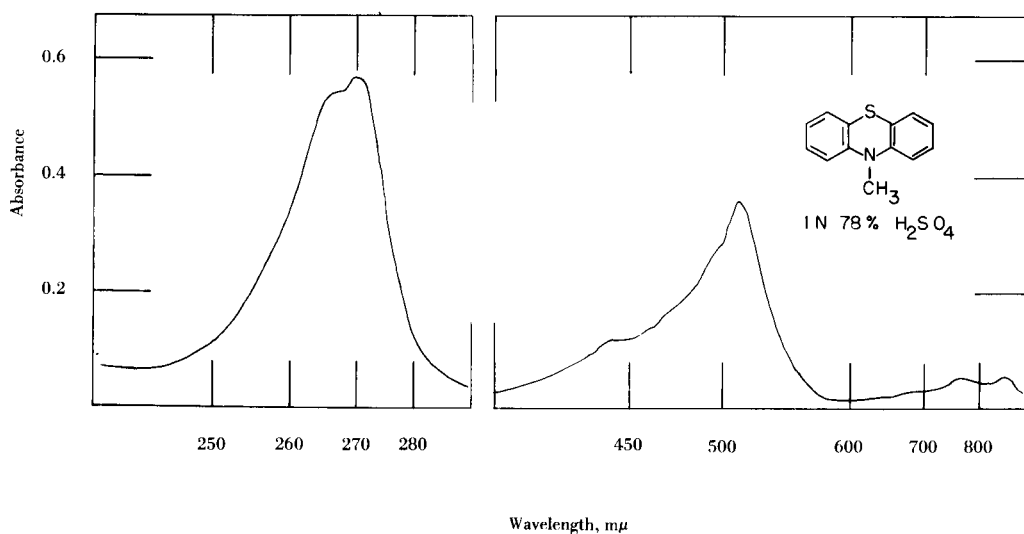


Figure 3. The absorption spectra of solutions of *N*-methylphenothiazine (I) in 78% sulfuric acid. Ultraviolet: 1.5×10^{-5} *M* I, and recorded after 6.5 hours; visible: 1.5×10^{-4} *M* I, and recorded after 32 hours.

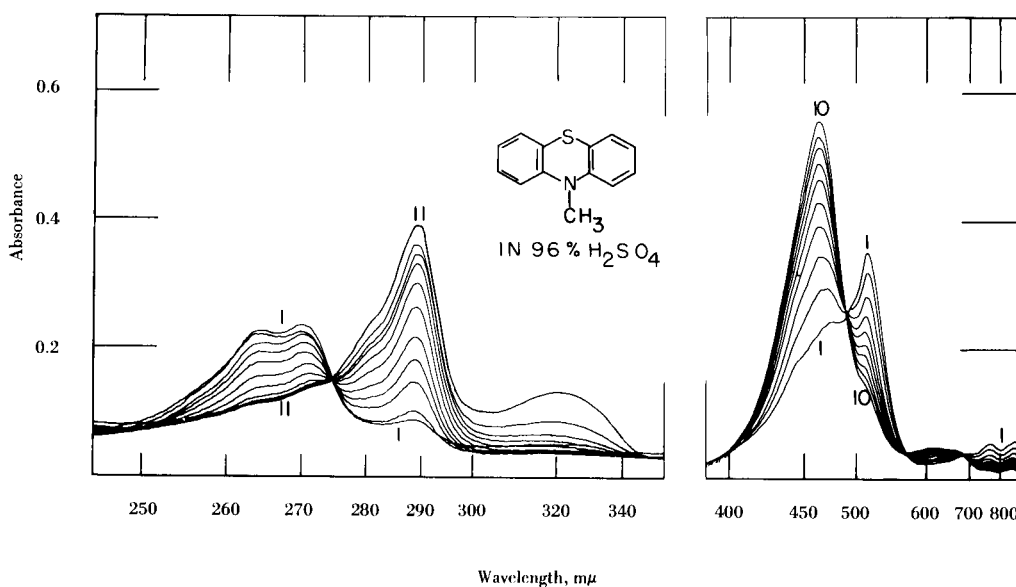


Figure 4. The changes with time in the absorption spectra of solutions of *N*-methylphenothiazine (I) in 96% sulfuric acid. The solutions were made directly in the spectrophotometer cell from a crystal of the I; therefore, the concentrations were unknown. For the ultraviolet spectra scan I was recorded after 1 minute and scan II after 70 minutes. For the visible spectra scan I was recorded after 1 minute and scan 10 after 75 minutes.

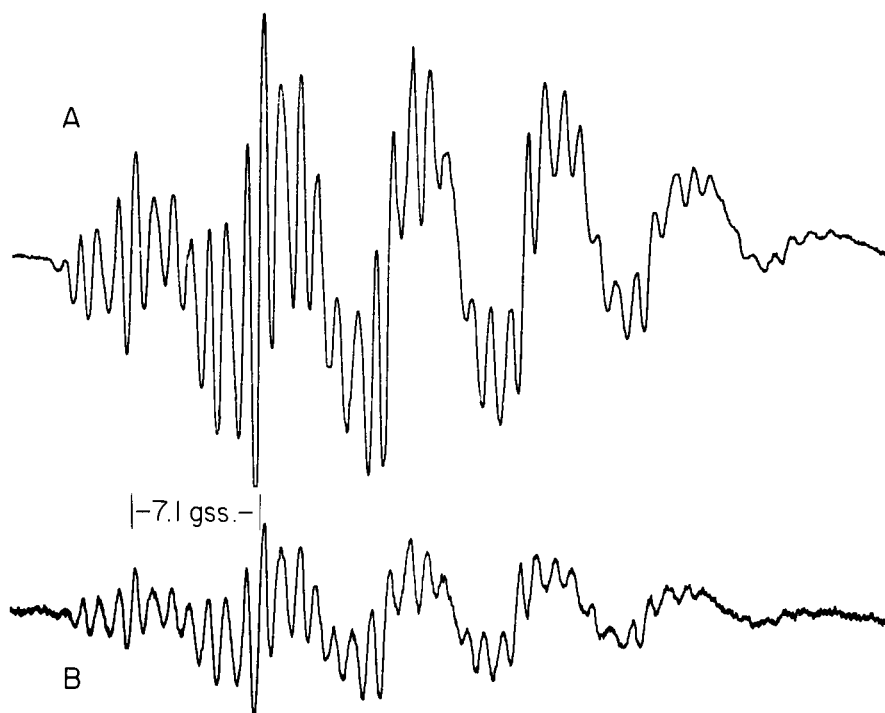


Figure 5. The e.s.r. spectra of 1 hour-old, 10^{-3} M solutions of (A) *N*-methylphenothiazine and (B) *N*-methylphenothiazine *S*-oxide in 96% sulfuric acid. The field increases from left of the spectra to the right.

able to add to those observations the *i*-factor result with phenothiazine 5-oxide (Table II) which shows that the protonated phenazathionium ion exists in slightly aqueous sulfuric acid, and supports the earlier proposal for the participation of the dication in the phenothiazine reactions (4).

Kehrmann and Sandoz (5) recorded a λ max of 460 $m\mu$ for a solution of II in concentrated sulfuric acid. The spectrum was attributed to the diacid phenazathionium salt, which is what we describe as the ion (IV). On diluting the diacid-salt solution Kehrmann and Sandoz noted a change in the spectrum to one with a λ max of 515 $m\mu$, and formulated the change, not without some question, as going to the monoacid salt with the same oxidation state as the diacid salt. It is recognizable now that the change was to the cation radical (III).

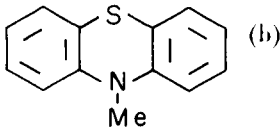
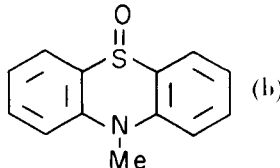
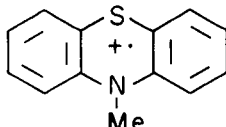
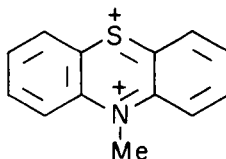
N-methylphenothiazine (I) in 78% sulfuric acid was readily oxidized to the phenothiazine cation radical. The radical was detected by e.s.r. spectroscopy. Its ultraviolet and visible spectra are recorded in Figure 3. The radical was formed very rapidly from I in 96% sulfuric acid, and soon underwent further oxidation to the dication (IV) as

shown by the absorption maxima at 290 and 464 $m\mu$ (Figure 4 and equation 3). The two-stage oxidation of I has been carried out anodically by Billon (6,7) but under the conditions used the second-stage dication existed apparently only as the protonated *S*-oxide. There is a second reaction which I (or III) undergoes in 96% sulfuric acid, and which caused the growth of a broad band at 320 $m\mu$ (Figure 4). We have not pursued this reaction; it does not appear to end in a radical species, since the e.s.r. spectrum of a solution of I in 96% sulfuric acid (Figure 5) changed with time only in intensity and not in character. This second reaction does not occur when I is dissolved in 30% fuming sulfuric acid, the spectrum of the solution being cleanly that of the dication (IV).

Figure 5 shows the e.s.r. spectrum of the cation radical (III) obtained with both I and II in 96% sulfuric acid. The detection of the radical in the solution of II does not contradict the deduction from the absorption spectra of dilute solutions that II is converted to the dication (IV) in 96% sulfuric acid. The concentration of the cation radical in the initially 10^{-3} M solution of II, which was used for e.s.r. spectroscopy, was low. If the cation radical was

TABLE I

Major Absorption Maxima

	Species	Maxima, $m\mu$ (a)		
I	 (b)	253	307	
II	 (b)	233	272	297
III		265 (s)	270	513
IV		282 (s)	290	464

(a) (s) denotes shoulder. (b) solvent: 95% ethanol.

present in the more dilute solutions (10^{-6} to 10^{-5} M) its concentration was too low for it to be detected in their absorption spectra.

The e.s.r. spectrum of III consists of six major lines (arising from the closely similar *N*-coupling constant and methyl-coupling constant) with overlapping hyperfine ring-proton splitting. The spectrum has been analyzed by Lhoste and Tonnard (8).

EXPERIMENTAL

N-Methylphenothiazine (I) was prepared by the method used by Gilman *et al.* for the *N*-ethyl compound (9). Crystallization from benzene gave m.p. 100-102°; Lit. (5) m.p. 99°. *N*-Methylpheno-

thiazine *S*-oxide was prepared as described by Schmalz and Burger (10). Crystallization from ethanol gave m.p. 194-196°.

Absorption and e.s.r. spectra were recorded as described earlier (4,11).

i-Factor measurements were made as described earlier (12). The data in Table II were obtained in each case with one solution only; an increment of the compound was added after the making of each freezing point measurement, so that the final time recorded represents the time the whole of the material had been in solution (for example, 168 hours with 33.8 *m* phenothiazine 5-oxide). Each freezing point depression recorded in Table II is the average of several depressions measured during the period the solute was in solution. The data obtained with a standard substance (benzoic anhydride) are included for comparison. The molal freezing-point depression constant used was 6.12°.

TABLE II

i-Factor Determinations

Phenothiazine 5-Oxide

Sulfuric acid, 200.2 g.; initial f. pt., 10.095°

Molality x 10 ³	Time in solution, hr.	f. pt. depression	<i>i</i>
5.45	25	0.163	4.87
11.2	50	0.340	4.96
16.6	73	0.509	4.99
22.7	97	0.696	5.01
28.4	145	0.867	4.99
33.8	168	1.04	5.01 Ave: 4.97

N-Methylphenothiazine *S*-Oxide

Sulfuric acid, 199.0 g.; initial f. pt., 10.048°

Molality x 10 ³	Time in solution, hr.	f. pt. depression	<i>i</i>
5.07	25	0.153	4.94
9.93	51	0.300	4.93
14.5	74	0.443	4.97
19.6	98	0.596	4.97
24.5	145	0.738	4.91
29.5	178	0.904	5.01 Ave: 4.95

Benzoic Anhydride

Sulfuric acid, 199.0 g.; initial f. pt., 10.047°

Molality x 10 ³	Time in solution, hr.	f. pt. depression	<i>i</i>
5.34	47	0.068	2.06
11.1	165	0.147	2.17
19.2	192	0.240	2.04
25.2	215	0.324	2.09
29.7	238	0.381	2.13 Ave: 2.08

REFERENCES

(1) Supported by the Directorate of Chemical Science, Air Force Office of Scientific Research, U. S. Air Force under Grant No. AF-AFOSR-975-66.

(2) Part XII, H. J. Shine, M. Rahman, H. Seeger and G.-S. Wu, *J. Org. Chem.*, **32**, 1901 (1967).

(3) Post-doctoral fellow, 1964-1965.

(4) H. J. Shine and E. E. Mach, *J. Org. Chem.*, **30**, 2130 (1965).

(5) F. Kehrmann and M. Sandoz, *Ber.*, **50**, 1673 (1917).

(6) J.-P. Billon, *Ann. Chim.*, **7**, 183 (1962).

(7) J.-P. Billon, G. Cauquis and J. Combrisson, *J. Chim. Phys.*,

61, 374 (1964).

(8) J.-M. Lhoste and F. Tonnard, *ibid.*, **63**, 678 (1966).

(9) H. Gilman, R. K. Ingham, J. F. Champaigne, Jr., J. W. Diehl and R. O. Ranck, *J. Org. Chem.*, **19**, 560 (1954).

(10) A. C. Schmalz and A. Berger, *J. Am. Chem. Soc.*, **76**, 5455 (1954).

(11) H. J. Shine, C. F. Dais and R. J. Small, *J. Org. Chem.*, **29**, 21 (1964).

(12) H. J. Shine and D. R. Thompson, *Tetrahedron Letters*, 1591 (1966).

Received May 29, 1967

Lubbock, Texas 79409