

## The Influence of Substituents on Spectral Properties of Radical-Cations and Dications Derived from Certain Phenothiazines (1a)

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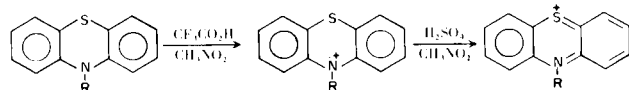
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During the course of our investigation of the mechanism of the bromination of 10-substituted phenothiazines, it became necessary that the spectral properties of the corresponding radical-cations and dications be determined for use in kinetic studies and product identification. Shine (2) has prepared these ionic species of 10-methylphenothiazine and has qualitatively studied them spectrophotometrically in 96% sulfuric acid. However, this medium could not be used in this study because initially prepared solutions of the radical-cations are partially converted to dicationic species and many of the 10-substituted phenothiazines dissolved much too slowly. Therefore, other solvent systems had to be found.

### Results.

#### Radical-Cation Study.

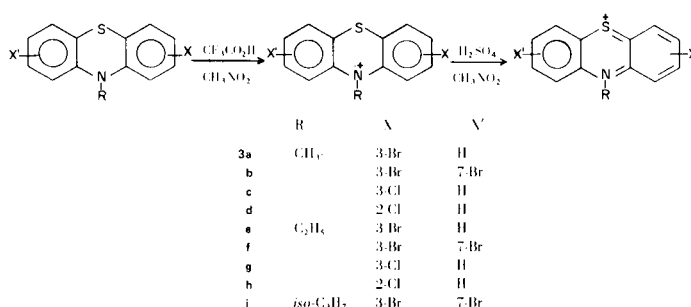
Of the several solvent systems studied, 50% solutions (v/v) of trifluoroacetic acid in nitromethane were found to convert 10-alkyl-(1), 10-aryl-(2), and C-halo-10-alkyl-(3)-phenothiazines to the corresponding radical-cations. The solutions were prepared by initially dissolving the appropriate phenothiazine in nitromethane followed by the addition of trifluoroacetic acid immediately before spectrophotometric scanning. Raymond and Fraenkel (3) have generated radical-cations of aromatic hydrocarbons in this medium. Radical-cations of **1**, **2**, and **3** were stable in this solution for periods up to at least 4 hours, *i.e.* they did not convert to dicationic species; however, isobestic points could not be obtained since the phenothiazine compounds and solvent absorbed in the ultraviolet region. The pertinent spectral data are listed in Table 1.



1 or 2

1a CH<sub>3</sub>  
b C<sub>2</sub>H<sub>5</sub>  
c *i*-C<sub>3</sub>H<sub>7</sub>  
d *n*-C<sub>3</sub>H<sub>7</sub>  
e C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>

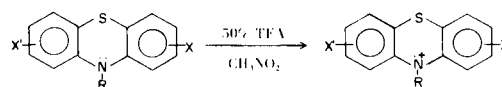
2a C<sub>6</sub>H<sub>5</sub>  
b *p*-ClC<sub>6</sub>H<sub>4</sub>  
c *o*-ClC<sub>6</sub>H<sub>4</sub>  
d *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>  
e *p*-CH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>



The most striking feature of the data is that the absorption maximum (510-515 nm) for the radical cations of the 10-alkyl compounds, (1) and phenothiazine are

Table 1

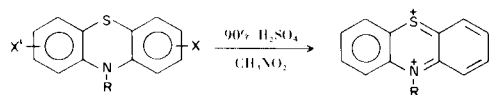
Radical-Cation Spectral Data



R	X	X'	λ max (nm)	ε (l x 10 <sup>-3</sup> )
H	H	H	513	10.3
CH <sub>3</sub>	H	H	513	9.7
C <sub>2</sub> H <sub>5</sub>	H	H	512	9.4
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H	H	512	9.2
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	H	H	521	8.7
C <sub>6</sub> H <sub>5</sub> -CH <sub>2</sub>	H	H	510	8.5
C <sub>6</sub> H <sub>5</sub>	H	H	511	10.0
<i>p</i> -CH <sub>3</sub> -O-C <sub>6</sub> H <sub>4</sub>	H	H	510	10.1
<i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	H	H	511	9.6
<i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub>	H	H	510	10.3
<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	H	H	512	12.3
<i>o</i> -CH <sub>3</sub> -O-C <sub>6</sub> H <sub>4</sub>	H	H	509	-
CH <sub>3</sub>	3-Br	H	540	12.0
	3-Br	7-Br	572	13.5
	2-Cl	H	525	12.2
	3-Cl	H	535	9.7
C <sub>2</sub> H <sub>5</sub>	3-Br	H	538	9.8
	2-Cl	H	524	12.6
	3-Br	7-Br	566	13.0
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	3-Br	7-Br	572	-

Table 2

## Dication Spectral Data



R	X	X'	$\lambda$ max (nm)	isobestic point (nm)
H	H	H	460	487
CH <sub>3</sub>	H	H	460	487
CH <sub>3</sub>	3-Br	7-Br	500	-
C <sub>2</sub> H <sub>5</sub>	H	H	458	484
C <sub>2</sub> H <sub>5</sub>	3-Br	7-Br	500	484
<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H	H	457	483
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	H	H	454	-
<i>i</i> -C <sub>3</sub> H <sub>7</sub>	3-Br	7-Br	501	484
C <sub>6</sub> H <sub>5</sub>	H	H	461	484
<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	H	H	467	485
<i>p</i> -CH <sub>3</sub> -O-C <sub>6</sub> H <sub>4</sub>	H	H	464	486

very similar to those (510-514 nm) of the 10-aryl compounds (2). The absorption maximum of 521 nm exhibited by 10-isopropylphenothiazine (1c) is the only exception.

Bathochromic shifts, however, are observed in all cases when a halogen atom is substituted on the ring. For example, the maximum absorption values of 539 and 572 nm for the radical-cations of the mono and dibromo derivatives of 10-methylphenothiazine, **3a** and **3b**, respectively, represent bathochromic shifts of 26 and 59 nm for the substitution of a bromine atom in the 3 and 3,7 positions of the ring. Similar shifts (22 and 56 nm) are also observed for the 3 and 3,7-bromine substituted 10-ethyl compounds, **3e** and **3f**, respectively, and 3,7-dibromo-10-isopropyl compound **3i**.

## Dication Study.

Solutions of 90% sulfuric acid/10% nitromethane (v/v) were satisfactory for the quantitative formation of dications of **1**, **2**, and **3**. The initial spectrum of a freshly prepared solution revealed the two maximum absorption peaks corresponding to a radical-cation and dication species, the radical-species absorbing at the higher wavelength. The absorption maximum of the radical cations occurred at the same wavelength in 90% sulfuric acid-nitromethane solutions as those observed in 50% trifluoroacetic acid-nitromethane solutions. The lower wavelength absorbing species has previously been identified in the case of **1a** as the dication species (2). As the spectrum of each compound was scanned periodically, the absorbance of the radical-cation decreased in intensity and that of the dication increased. These series of curves depicting

the change with time in the visible spectrum revealed in all cases except 10-isopropylphenothiazine a sharp isobestic point. Eventually, a spectrum was obtained in which the conversion to the dication appeared to be quantitative. The quantitative conversion of these compounds to dication allowed calculation of their molar absorptivities. Table 2 lists the characteristic spectral data.

The absorption maximum of the various dications indicate that the interactions between the substituents and the dications are generally similar to those previously observed in the radical-cation study. For example, the absorption maximum of the dications of 10-alkyl- and 10-aryl compounds **1** and **2** are fairly constant, including that of 10-isopropylphenothiazine whereas bathochromic shifts are observed for the C-halo-10-alkylphenothiazines (3).

The minor influence that 10-aryl groups exert on the spectra of radical cations and dications might indicate that the aryl group is twisted with respect to the ring resulting in the prevention of mutual-electronic interaction. Indeed, one could invoke an argument based on unfavorable steric interaction between the aryl group and the 1,9-peri hydrogen atoms to account for this twisting. Similar effects have been observed in 10-phenylacridine (4). However, the spectral data are not necessarily valid for interpreting the effect of *N*-substituents on charge delocalization. It has been suggested by one of the referees that the data may show only that the polarization moment for  $\lambda$  max does not lie along the 5, 10 axis, but along a horizontal axis. It is possible that even if the polarization moment is along the horizontal axis, the fact that both *N*-alkyl and *N*-aryl substituents do not affect  $\lambda$  max would suggest that there is not any delocalization into the *N*-substituent. Therefore, conclusions on the effect of substituents on the spectral properties of radical-cation and dication cannot be assessed at present. We currently are investigating the possibility that these ionic species might luminesce in order to measure polarization moments.

## EXPERIMENTAL

All melting points were taken on a Fischer Melting Block and are uncorrected. The visible spectra were recorded with a Cary Model 118 Spectrophotometer.

## Materials.

Nitromethane, spectrophotometric grade, was purchased from Aldrich Chemical Company, Inc. and was stored under nitrogen. Trifluoroacetic acid of highest purity was obtained from PCR, Inc., and was distilled prior to use. Phenothiazine was obtained from Aldrich Chemical Company, Inc., and was recrystallized from toluene before use.

## 10-Alkylphenothiazines.

These compounds were prepared by the reaction of the appropriate alkyl halide and the sodium salt of phenothiazine (prepared by the action of sodamide and phenothiazine in liquid ammonia) according to the method of Gilman (5).

## 10-Methylphenothiazine.

This compound had m.p. 98° [lit. (5) 99°].

## 10-Ethylphenothiazine.

This compound had m.p. 101° [lit. (5) 103-104°].

10-*n*-Propylphenothiazine.

This compound had m.p. 49° [lit. (5) 49-50°].

## 10-isoPropylphenothiazine.

This compound had m.p. 59-60° [lit. (5) 59-60°].

## 10-Benzylphenothiazine.

This compound had m.p. 90-91° [lit. (6) 90.5-91.5°].

## Halogen-substituted 10-Alkylphenothiazines.

Some of these halogen derivatives were prepared by the low temperature bromination of the corresponding 10-alkylphenothiazine using pyridinium hydrobromide perbromide according to the method of Biehl (7).

## 3-Bromo-10-methylphenothiazine.

This compound had m.p. 112-112.5° [lit. (7) 112-112.5°].

## 3,7-Dibromo-10-methylphenothiazine.

This compound had m.p. 151-152° [lit. (7) 151-152°].

## 3-Bromo-10-ethylphenothiazine.

This compound had m.p. 123-124° [lit. (8) 123-124°].

## 3,7-Dibromo-10-isopropylphenothiazine.

This compound was an oil which could not be purified satisfactorily for elemental analysis.

The following compound was prepared by reductive dehalogenation of 10-methylphenothiazine 5-oxide according to the procedure of Gilman (8).

## 3-Chloro-10-methylphenothiazine.

This compound had m.p. 106-107° [lit. (9) 107°].

The following compound was synthesized by methylating 2-chlorophenothiazine according to the method of Jones (10).

## 2-Chloro-10-methylphenothiazine.

This compound had m.p. 82-83° [lit. (10) 81-83°].

## 10-Arylphenothiazines.

The 10-arylphenothiazines were prepared by coupling phenothiazine with the appropriate aryl halide in the presence of copper bronze and potassium carbonate in the manner described by Gilman (6).

## 10-Phenylphenothiazine.

This compound had m.p. 89-90° [lit. (11) 89-90°].

10-*p*-Tolylphenothiazine.

This compound had m.p. 135-136° [lit. (6) 135-136°].

10-(*o*-Methoxyphenyl)phenothiazine.

This compound had m.p. 111.5-112.5°.

*Anal.* Calcd. for C<sub>19</sub>H<sub>15</sub>NO<sub>2</sub>: C, 74.72; H, 4.95; N, 4.58. Found: C, 74.84; H, 4.96; N, 4.26.

10-(*p*-methoxyphenyl)phenothiazine.

This compound had m.p. 173-174°.

*Anal.* Calcd. for C<sub>19</sub>H<sub>15</sub>NO<sub>2</sub>: C, 74.72; H, 4.95; N, 4.59. Found: C, 74.70; H, 4.93; N, 4.47.

10-(*p*-Nitrophenyl)phenothiazine.

This compound had m.p. 158-159°.

*Anal.* Calcd. for C<sub>18</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>S: C, 67.48; H, 3.78; N, 8.74. Found: C, 67.19; H, 3.85; N, 8.74.

## Radical-Cation Spectral Studies.

Solutions for radical-cation studies were prepared by initially dissolving accurately weighed quantities of the phenothiazine derivatives in sufficient volumes of nitromethane to produce 2 x 10<sup>-4</sup> M stock solutions. A 0.5-ml. aliquot of the stock solution was placed in a 1-cm pathlength cell and diluted with an equal volume of trifluoroacetic acid to a final concentration of 1 x 10<sup>-4</sup> M before scanning. Molar absorptivities were obtained by recording the absorbance over a period of 1 hour at the λ max corresponding to the particular radical-cation species. The curves revealed that in each case a maximum value of the absorbance was reached within 15 minutes which remained constant for at least 45 minutes.

## Dication Spectral Studies.

Solutions for the dication studies were prepared by initially dissolving accurately weighed amounts of the phenothiazine derivatives in sufficient volumes of nitromethane to produce 8 x 10<sup>-4</sup> M stock solutions. A 0.2-ml. aliquot of the stock solution was placed in a 1-cm pathlength cell and was diluted with 1.8 ml. of 96% sulfuric acid to produce a final concentration of 8 x 10<sup>-5</sup> M before scanning.

## REFERENCES

- (1a) Sponsored in part by grants from the Robert A. Welch Foundation, Houston, Texas; Gulf Oil Corporation; and Sherwin-Williams Paint Company; (b) Robert A. Welch Predoctoral Fellow; (c) Gulf Oil and Sherwin-Williams Scholar.
- (2) H. J. Shine, D. R. Thompson, and C. Veneziani, *J. Heterocyclic Chem.*, **4**, 517 (1967).
- (3) A. Reymond and G. K. Fraenkel, *J. Phys. Chem.*, **71**, 4570 (1967).
- (4) C. W. N. Cumper, R. F. A. Ginman, and A. I. Vogel, *J. Chem. Soc.*, 4525 (1962).
- (5) H. Gilman, R. K. Ingham, J. G. Champaigne, Jr., J. W. Diehl, and R. O. Ranck, *J. Org. Chem.*, **19**, 560 (1964).
- (6) H. Gilman, R. D. Nelson, and J. G. Champaigne, *J. Am. Chem. Soc.*, **74**, 4205 (1952).
- (7) E. R. Biehl, T. Daniel, P. C. Reeves, and S. Lapis, *J. Heterocyclic Chem.*, **10**, 247 (1974).
- (8) H. Gilman and J. Eisch, *J. Am. Chem. Soc.*, **77**, 3862 (1955).
- (9) A. C. Schmalz and A. Burger, *ibid.*, **76**, 5455 (1954).
- (10) D. H. Jones, *J. Chem. Soc. (C)*, 132 (1971).
- (11) H. Gilman, P. R. Van Ess and D. A. Shirley, *J. Am. Chem. Soc.*, **66**, 1215 (1944).