The Cation Radical Salts of Phenothiazine and Related Compounds[1]

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The cation radical salts of phenothiazine bromide, phenothiazine bisulfate monohydrate, and phenothiazine picrate were prepared. The absorption spectra in a dilute hydrochloric acid solution and the solid-state spectra of the salts were examined. The solid-state spectra showed a strong charge-transfer band and blue-shifts of the high-energy bands, unlike the absorption spectra in solution. The magnetic susceptibilities of these salts were measured at room temperature. They were found to be diamagnetic, with values almost corresponding to those of the diamagnetic contribution of the salts, except for that of the picrate. These spectroscopic and magnetic properties were discussed on the basis of the charge-transfer interaction between the phenothiazine cation radicals. The properties of the usual phenothiazine-picric acid charge-transfer complex and the holoquinoid phenothiazine perchlorate were investigated in association with those of the cation radical salts.

In 1913 the cation radical salts of phenothiazine were first prepared by Pummerer and Gassner, and then in 1915 they were prepared again by Kehrmann and Diserens.[2,3] In their articles, however, these cation radical salts were described as "semiquinoid phenazathionium salts," because the concept of "the cation radical salts" had not yet been established.

Much attention has been paid to the cation radical salts of phenothiazine and its derivatives, since (1) the tranquilizer drug, chloropromazine, is a substituted phenothiazine and (2) many dyestuffs, such as methylene blue, are oxidation products of substituted phenothiazines. Although many papers have been written on the ESR of the radical cations of phenothiazine and its derivatives in solution,[4] few attempts have been made to investigate the solid-state properties of the phenothiazine cation radical salts.[5]

In general, solid ion-radical salts have been a matter of great interest, because the ion-radical molecules form, in themselves, a plane-to-plane stacking into columns so as to make a large overlap between their half-filled molecular orbitals.[6] Much knowledge regarding the mutual charge-transfer interaction has been accumulated by measuring the solid-state spectra and the magnetic susceptibilities.[7-10] Hence, the purpose of the present paper is to apply these physical methods to the solid phenothiazine cation radical salts. We shall examine how the charge-transfer interaction contributes to the solid-state properties of these cation radical salts.

On the other hand, the phenothiazine-picric acid charge-transfer complex and the holoquinoid phenothiazine perchlorate were also prepared, since the properties of these compounds are interesting in comparison with those of the phenothiazine cation radical salts.

Experimental

Materials. The cation radical salts of phenothiazine bromide, phenothiazine bisulfate monohydrate,[11] and phenothiazine picrate were prepared according to the methods of Pummerer and Gassner[2] and of Kehrmann and Diserens.[3] Although Pummerer and Gassner reported two polymorphic forms for the picrate,[2] no such polymorphism was found in the present preparation.

The phenothiazine-picric acid charge-transfer complex was precipitated from a benzene solution containing nearly equivalent amounts of phenothiazine and picric acid. The holoquinoid phenothiazine perchlorate was prepared from phenothiazine *S*-oxide, which had been made through the oxidation of phenothiazine with hydrogen peroxide.[3]

The synthetic schemes of these compounds are illustrated in Fig. 1.

Measurements. The absorption spectra of the cation radical salts were measured in a 4.2% aqueous hydrochloric acid solution, while that of the holoquinoid phenothiazine perchlorate was measured in an acetonitrile solution. All the measurements of the absorption spectra were made at room temperature by means of a Beckman DK-2A spectrophotometer.

The diffuse reflection spectra were recorded on a Beckman DK-2A spectroreflectometer in the range from 4.0 to 30.8 kK at room temperature. The solid-state spectra were then obtained by plotting the diffuse reflection spectra using the Kubelka-Munk equation, $f(R)=(1-R)^2/2R$, in which R is the reflectance. The experimental details were the same as those in previous papers.[8-10]

The magnetic susceptibility measurements were made by the Gouy method at room temperature. Water was used in calibrating the cell constant.

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[1] This work was presented at the Symposium on Molecular Structure, Tokyo, October, 1968.

[2] R. Pummerer and S. Gassner, *Ber.*, **46**, 2310 (1913).

[3] F. Kehrmann and L. Diserens, *ibid.*, **48**, 318 (1915).

[4] G. Vincow, "Radical Ions," ed. by E. T. Kaiser and L. Kevan, Interscience Publishers, New York (1968), p. 188, and the references cited therein.

[5] Y. Sato, M. Kinoshita, M. Sano, and H. Akamatu, This Bulletin, **40**, 2539 (1967); **42**, 548 (1969).

[6] G. R. Anderson and C. J. Fritchie, Jr., Second National Meeting, Society for Applied Spectroscopy, San Diego, October, 14, Paper 111 (1963); C. J. Fritchie, Jr., *Acta Crystallogr.*, **20**, 892 (1966); C. J. Fritchie, Jr., and P. Arthur, Jr., *ibid.*, **21**, 139 (1966); P. Goldstein, K. Seff, and K. N. Trueblood, *ibid.*, **B24**, 778 (1968); J. Tanaka and N. Sakabe, *ibid.*, **B24**, 1345 (1968).

[7] R. G. Kepler, *J. Chem. Phys.*, **39**, 3528 (1963).

[8] Y. Iida and Y. Matsunaga, This Bulletin, **41**, 2615 (1968).

[9] Y. Iida, *ibid.*, **42**, 71, 637 (1969).

[10] Y. Iida, *ibid.*, **43**, 2772 (1970).

[11] This compound, although Kehrmann and Diserens described it as phenothiazine sulfate,[3] was found to be bisulfate monohydrate on the basis of our elemental analysis (Calcd for $C_{12}H_{12}NO_5S_2$: C, 45.9; H, 3.9; N, 4.5%. Found: C, 46.7; H, 4.0; N, 5.3%) and the value of the molar extinction coefficient of the absorption spectrum in solution.

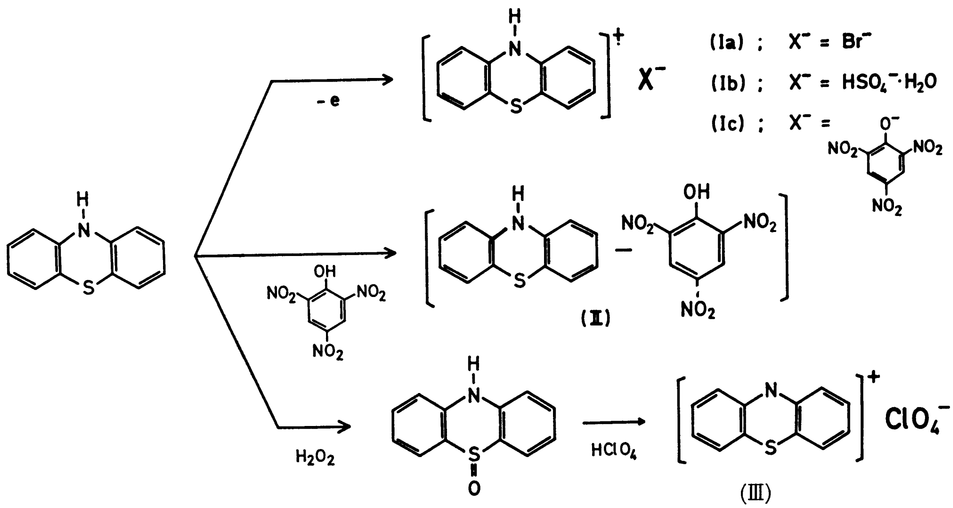

Fig. 1. The synthetic scheme of the compounds used in this study; (Ia) the cation radical salt of phenothiazine bromide, (Ib) the cation radical salt of phenothiazine bisulfate monohydrate, (Ic) the cation radical salt of phenothiazine picrate, (II) the phenothiazine-picric acid charge-transfer complex, and (III) the holoquinoid phenothiazine perchlorate.

The Absorption Spectra in Solution

In order to characterize the solid-state spectra of the phenothiazine cation radical salts, it is necessary to compare them with the absorption spectra of the salts in solution; therefore, we will examine the spectra in this section.

All of the cation radical salts exhibit a golden yellow color in solution and are quite stable in an acidic solution, such as an acetic acid or a dilute hydrochloric acid solution. In other solvents, however, they rapidly decompose to show a green color, the molecular species of which has not yet been ascertained.

Some of the absorption spectra of these cation radical salts in a 4.2% hydrochloric acid solution are reproduced in Fig. 2. In these measurements, the salts seem to be completely dissociated, because the concentrations are as dilute as of $1-2\times10^{-4}$ mol/*l*. When the counter anions are Br^- and $HSO_4^-\cdot H_2O$, since they have no absorptions in the energy region now under consideration, the absorption spectra of the salts appear to be solely due to the phenothiazine cation radical monomer. The absorption spectrum of the salt of the picrate has extra shoulders around 24.5 kK and 28 kK; these shoulders are assigned to the bands due to the picrate anion.

The monomer spectrum of the phenothiazine cation radical has a weak band around 13.5 kK composed of several vibrational structures at 15.0 kK, 13.5 kK, and 12.2 kK, a strong band at 19.3 kK with a shoulder at 19.9 kK, and a band at 22.8 kK. These features are well in accordance with those of the cation radical reported by Shine and Mach,[12] who dissolved phenothiazine in a sulfuric acid solution and then examined the absorption spectrum. Unfortunately, however, no attempt has been made to account for the electronic transitions by means of molecular orbital calculations.

On the other hand, Kagiya *et al.* reported on the temperature variation of the absorption spectrum of the phenothiazine bromide in an ethanol-ether-sulfuric acid solution.[13] They found that, at low temperatures, the monomer absorptions were diminished, while new bands

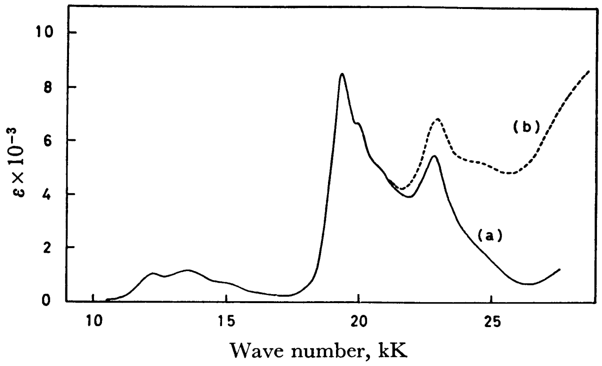

Fig. 2. The absorption spectra of the cation radical salts of (a) phenothiazine bisulfate monohydrate and (b) phenothiazine picrate, in 4.2% aqueous hydrochloric acid solution.

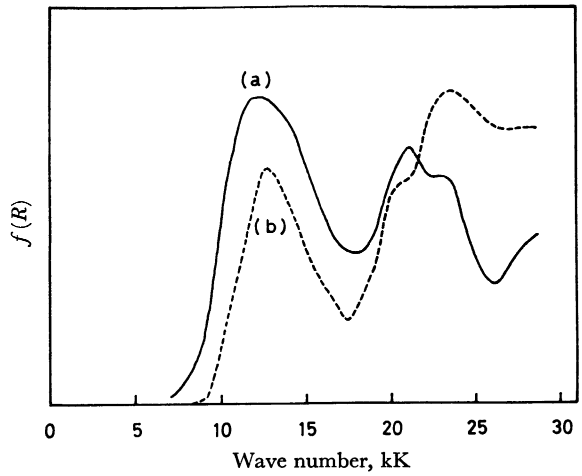

Fig. 3. The solid-state spectra of the cation radical salts of (a) phenothiazine bisulfate monohydrate and (b) phenothiazine picrate.

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

[13] T. Kagiya, K. Nakai, S. Nakayama, and K. Suzuki, Paper presented at the 23rd Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1970.

appeared at 23.9 kK, 21.3 kK, and 14.5 kK. These bands were assigned to the dimer of the cation radicals on the basis of the concentration dependence on their optical densities. The high-energy bands at 21.3 kK and 23.9 kK seem to be shifted bands of the monomer bands at 19.3 kK and 22.8 kK respectively. On the other hand, the band at 14.5 kK is located in the low-energy region, and it is broad without any vibrational structures. It can not be assigned to the shifted band of the cation radical monomer, since it takes place only when the dimer is formed between the cation radicals. Therefore, the low-energy band at 14.5 kK seems to be attributable to charge-transfer absorption in the dimer.[14]

The Solid-State Spectra

Phenothiazine Bisulfate Monohydrate (Fig. 3, Curve a). The solid-state spectrum of this salt shows a strong low-energy band at 12.0 kK, high-energy bands at 21.1 kK and 23.3 kK, and a shoulder around 28 kK. These spectroscopic features are different from those of the cation radical monomer in solution, but they are similar to those of the cation radical dimer. The high-energy bands at 21.1 kK and 23.3 kK in the solid-state spectrum are coincident with those at 21.3 kK and 23.9 kK respectively in the dimer spectrum. These bands arise mostly from the monomer bands at 19.3 kK and 22.8 kK respectively. This means that in both the solid state and the dimer, when the cation radicals come close enough together for the π orbitals to overlap, the π–π transitions due to the monomer are blue-shifted by the field of the other cation radicals. In accordance with this view, the low-energy band at 12.0 kK of the solid-state spectrum is as much intensified as the charge-transfer band at 14.5 kK of the dimer spectrum.[13] Although the former value is a little bit lower than the latter, the band at 12.0 kK can be assigned to the charge-transfer transition between the phenothiazine cation radicals in the solid state. However, we must keep in mind the fact that the weak absorption due to the monomer spectrum around 13.5 kK should overlap with this charge-transfer band.

Phenothiazine Picrate (Fig. 3, Curve b). The solid-state spectrum of this salt is composed of the charge-transfer band at 12.8 kK and the high-energy bands at 20.7 kK and 23.3 kK. The increased intensity of the absorption at 23.3 kK, compared to that of the bisulfate monohydrate, may arise from the overlap with the band due to the picrate anion. Except for this difference, the situation of the solid state of this salt appears to be very analogous to that of the bisulfate monohydrate.

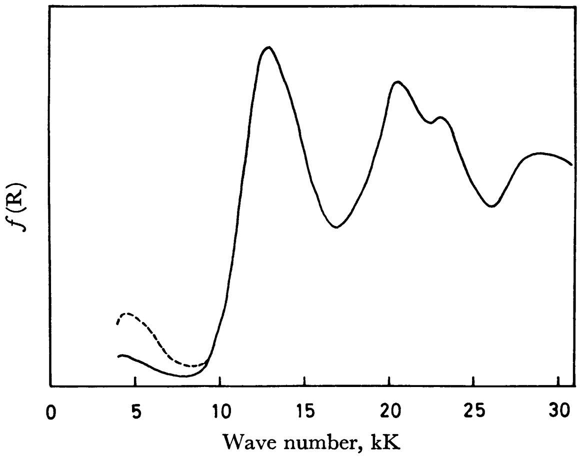

Fig. 4. The solid-state spectrum of the cation radical salt of phenothiazine bromide. The broken line indicates the spectrum of the sample taken from a different batch, as the salt was synthesized repeatedly.

Phenothiazine Bromide (Fig. 4). The solid-state spectrum of this salt shows a weak low-energy band at 4.2 kK, a strong charge-transfer band at 12.9 kK and high-energy bands at 20.5 kK, 23.0 kK, and 28.6 kK. Except for the band at 4.2 kK, these spectroscopic features are quite identical with those for the bisulfate monohydrate. As for the band at 4.2 kK, the intensity, although weak, was found to be not reproducible when the preparation of the salt was repeated. Matsunaga and Shono found that the intensity of this band was very much increased when some iodine was added to this salt.[15] They suggested that the formation of a complex cation radical salt, (Phenothiazine)$^+$ (Phenothiazine)^0 Br_2I^-, might be responsible for the appearance of this band. Therefore, the phenothiazine bromide, which exhibits its band at 4.2 kK, may be contaminated with a small amount of a complex cation radical salt of (Phenothiazine)$^+$ (Phenothiazine)^0 Br_3^-.

Magnetic Susceptibilities

It has been well established that the charge-transfer interaction between the ion radicals leads to a marked decrease in the paramagnetic susceptibilities of ion radical salts.[7–10] The charge-transfer interaction is known to stabilize the antiferromagnetic state where the spins associated with the ion radicals are antiparallel. This is also true of the present phenothiazine cation radical salts. Table 1 shows the observed values of the magnetic susceptibilities at room temperature, together with the estimated diamagnetic contribution.

Solid phenothiazine bromide was found to be diamagnetic at room temperature (-147×10^{-6} emu/mol). After correction had been made for the diamagnetism, the paramagnetic contribution of the salt was found to be as small as 13×10^{-6} emu/mol. It is not clear whether this paramagnetic contribution is due to the intrinsic paramagnetism or to an impurity paramagnetism. However, even if it is attributed to the intrinsic paramag-

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[14] According to the Hausser and Murrell theory, the ion-radicals in a dimer may be stacked face-to-face, and the spin exchange interaction leads to a singlet ground state and an excited triplet state. Therefore, we must take into consideration the fact that intermolecular charge-transfer may make a significant contribution to stabilizing the ground singlet state of the dimer. The low-energy charge-transfer absorption characteristic of the dimer arises mostly from a transition from the thus-stabilized ground state to an excited singlet state expressed by a combination of the wave functions for charge-transfer structures, R–R^{2+}. See K. H. Hausser and J. N. Murrell, *J. Chem. Phys.*, **27**, 500 (1957).

[15] Y. Matsunaga and K. Shono, This Bulletin, **43**, 2007 (1970).

Table 1. The data on the static magnetic susceptibilities of the phenothiazine cation radical salts at room temperature (25°C)

Compound	$\chi_{obs}\times10^6$ (emu/mol)	$\chi_{dia}\times10^{6}$ a) (emu/mol)
Phenothiazine Bromide	-147	-160
Phenothiazine Bisulfate Monohydrate	-175	-177
Phenothiazine Picrate	-56	-205
	-33	
	-8	
	$+18$	

a) The values of the calculated diamagnetic contribution of the salts. They were estimated from the value of diamagnetic susceptibility of each component. The experimentally determined value of diamagnetic susceptibility for a neutral phenothiazine was used in place of the cation radical. See Ref. 5.

netism for the bromide, the antiferromagnetic spin exchange interaction between the cation radicals seems to be greater than 0.1 eV. The situation in the bisulfate monohydrate appears to be almost the same as that in the bromide.

In the phenothiazine picrate, the observed value of the magnetic susceptibility was found to increase progressively as the measurements were repeated. This is shown by the multiple values of the susceptibilities listed in Table 1. In this case, the antiferromagnetic spin exchange interaction may be gradually eliminated by the fine pulverization of the sample in the course of the measurements. The population of the free spins may increase accordingly. However, a question still remains of why only the salt of the picrate, as it was ground to a fine powder, shows such a magnetic behavior.

Compounds Related to the Cation Radical Salts

Phenothiazine-Picric Acid Charge-Transfer Complex. The difference in chemical composition between the phenothiazine-picric acid charge-transfer complex and the cation radical salt of the picrate is slight; that is, the former includes the picric acid, while the latter includes the picrate anion. However, there is a marked difference in electronic structure between the two substances. In the cation radical salt, as has been mentioned above, the charge-transfer interaction takes place between the cation radicals, whereas in the charge-transfer complex it takes place between phenothiazine and picric acid. As is shown in the solid-state spectrum (Fig. 5, Curve a), the charge-transfer band in the latter case was found to be located at 18.2 kK.

The magnetic susceptibility for the charge-transfer complex was found to be -197×10^{-6} emu/mol; this value corresponds well to the -205×10^{-6} emu/mol value for the sum of the diamagnetic contribution of the component molecules, and it should be compared with that for the cation radical salt of the picrate.

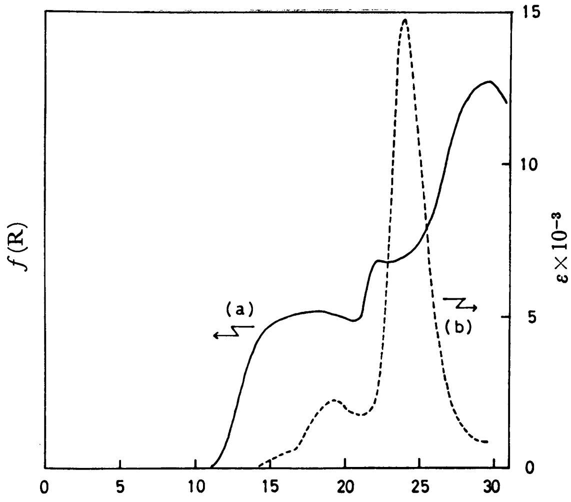

Fig. 5. The solid-state spectrum of the phenothiazine-picric acid charge-transfer complex (a), and the absorption spectrum of the holoquinoid phenothiazine perchlorate in acetonitrile solution (b).

Holoquinoid Phenothiazine Perchlorate. The phenothiazine cation radical is known to undergo both one-electron oxidation and deprotonation to form the holoquinoid cation;[3] this cation has, therefore, a closed electronic shell and is a univalent cation (see Fig. 1). The holoquinoid cation appears yellow in solution and is stable at room temperature. As is shown by Curve b of Fig. 5, the absorption spectrum of the holoquinoid salt of the perchlorate in an acetonitrile solution[16] consists of a weak band at 19.3 kK and a strong absorption at 23.9 kK. This spectrum seems to be solely due to the holoquinoid cation monomer.

Discussion

The above-mentioned results on the solid-state properties of all the phenothiazine cation radical salts clearly indicate the large values both in an antiferromagnetic spin-exchange interaction and in the intensity of the charge-transfer band. This means that a strong charge-transfer interaction takes place between the phenothiazine cation radicals. Therefore, the cation radical molecules may be expected to be stacked in a face-to-face manner and to form, in themselves, linear chain columns; this feature of the crystal structure has been found in a number of other ion radical

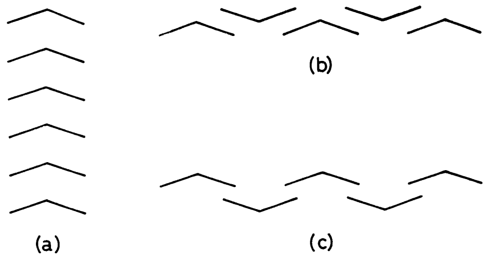

Fig. 6. Three kinds of possible stackings of the phenothiazine cation radical molecules to form linear chain columns in the solid state. A folded figure denotes a phenothiazine cation radical molecule viewed along the direction connecting the nitrogen and sulfur atoms.

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[16] The concentration of the solution was 8.05×10^{-5} mol/l.

salts.[6] In this case, the charge-transfer absorption may be expressed as a transition of the $\{\cdots P^{+}P^{+}P^{+}P^{+}\cdots\} \rightarrow \{\cdots P^{+}P^{2+}P^{0}P^{+}\cdots\}$ type, where P denotes a phenothiazine molecule. As for the spin system, these cation radical salts may be considered to be a linear-chain antiferromagnet.

On the other hand, the molecular structure of neutral phenothiazine is known to be non-planar, but to be of a folded form.[17] It appears that the structure of its cation radical, although it has not yet been ascertained, is also of a folded form. Therefore, unlike planar ion-radical molecules, the stacking manner of the phenothiazine cation radicals seems to be complicated, for the linear chain columns of the cation radicals can be built up not only by the arrangement of (a) but also by that of (b) or (c), as is illustrated in Fig. 6. In this respect, further study of the X-ray diffraction is required to determine by which arrangement the phenothiazine cation radicals are stacked in the present solid salts.

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[17] J. D. Bell, J. F. Blount, O. V. Briscoe, and H. C. Freeman, *Chem. Commun.*, 1656 (1968).