Studies on Organic Semiconductors. XII. Syntheses and Purifications of Phenazine Derivatives

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Syntheses and Purifications of Phenazine Derivatives

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In order to study the effect of the substituent on the electrical conductivity, 14 substituted phenazines are prepared and pruified by recrystallization, sublimation and chromatography to obtain the conductive purity. These details are described.

1. Introduction

Although the electrical conductivities of organic compounds having some substituents have been frequently measured, the effect of the substituent on the electrical conductivity has been scarcely studied systematically. Therefore, we aimed to make clear the effect of the substituent on the electrical conductivity by measuring the resistances of various kinds of phenazine derivatives. As the conductivity is influenced remarkably by the impurity, the history of the processes of the preparations and purifications is of importance. The present paper describes the preparation and purification methods of 14 phenazine derivatives used as the materials.

2. Results

The preparations of the substituted phenazines were carried out by four methods involving in the modification of the methods described in the literatures*, as shown in scheme I (they must be the best synthetic methods to obtain the pure materials); phenazine,[1] 1,6-dimethoxyphenazine,[2] 2,7-dimethoxyphenazine,[3] 1-chlorophenazine,[4] 1,6-dichlorophenazine[5], 2,7-dichlorophenazine,[4,6] and 2,7-dibromophenazine[4,6] were prepared by the method A, 1,6-dinitrophenazine[7,8] and 1,6-diaminophenazine[7,8] by the method B, 2-chlorophenazine[9] and 2-methoxyphenazine[4] by the method C, and 1-methoxyphenazine[10] by the method D. 1,6-(or 2,7-)Di-*tert*-butylphenazine**, which

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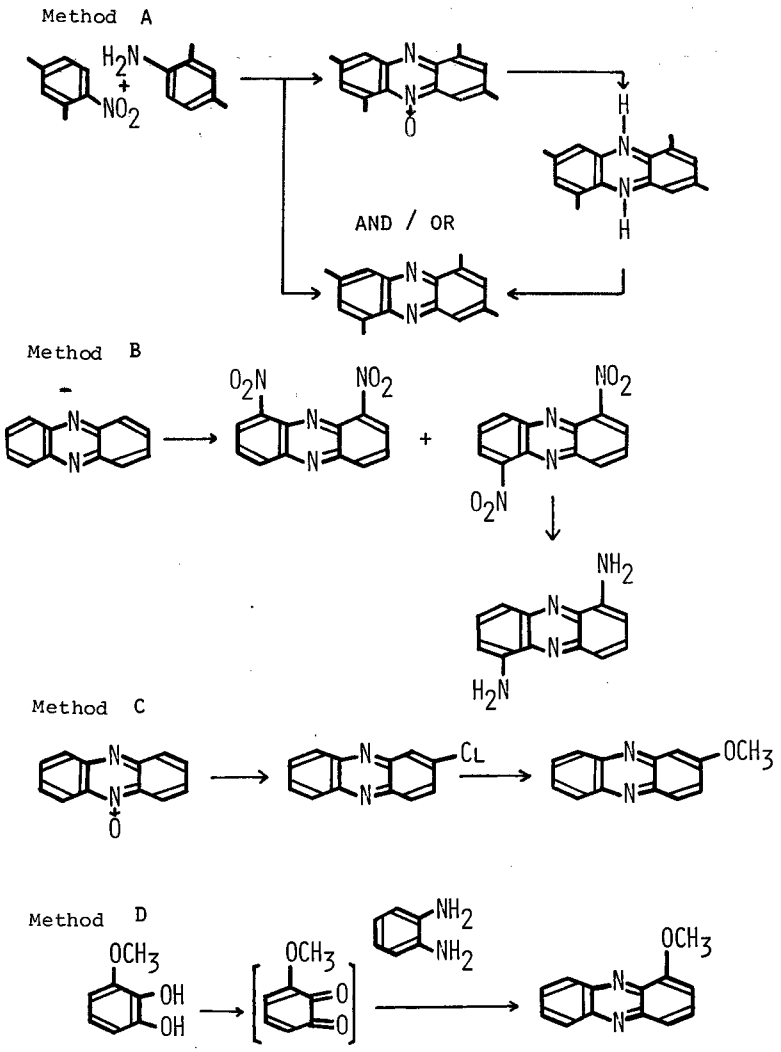
* Melting points of all phenazines are uncorrected. Their IR absorption spectra are agreed with those described in IRDC card published by Nankodo Co., Tokyo.

** Recently 2,7-di-*tert*-butylphenazine was prepared by Mazitova et al. from 3-amino-4-methoxy-*tert*-butylbenzene, mp 215.5–216°C. F.N. Mazitova, R.R. Shagidullen and V.V. Abushaeva, *Zh. Org. Khim.*, **3**, 878 (1967), *Chem. Abstr.*, **67**, 43137 a (1967).

SCHEME I



has not been described in the literature, was prepared from *o*-(or *p*-)amino-*tert*-butylbenzene and *o*-(or *p*-)nitro-*tert*-butylbenzene according to the method A, and identified by measuring their IR, UV and nmr spectra and their elementary analyses, which showed a distinct difference from those of their corresponding azobenzenes obtained as their by-products during the reactions (Fig. 1, 2 and 3).

The purification of all materials prepared was performed by the combination of vacuum sublimation, recrystallization and liquid-phase chromatography. The purity of them was estimated by measuring their melting points, their UV and IR spectra, and their electrical conductivities in each step of the purification process. Generally***, the purification was repeated until the activation energy ΔE of the electrical conductivity of

*** As far as the cases that the measurements of the conductivities are possible.

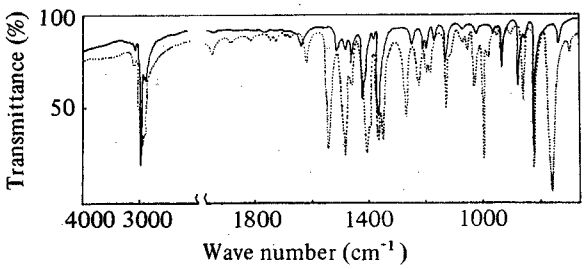


Fig. 1. IR absorption spectra of 1,6-(broken line) and 2,7-(solid line) di-*tert*-butylphenazine (KBr).

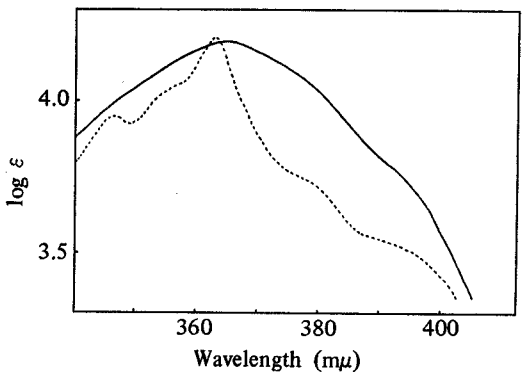


Fig. 2. Absorption spectra of 1,6-(broken line) and 2,7-(solid line) di-*tert*-butylphenazines in benzene.

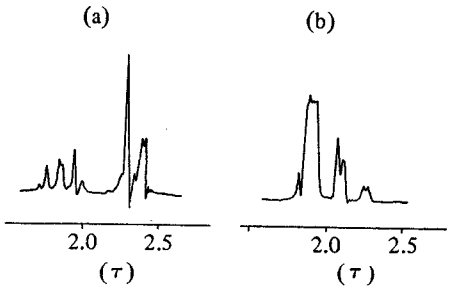


Fig. 3. The nmr spectra of 1,6-di-*tert*-butylphenazine (a) and 2,7-di-*tert*-butylphenazine (b) in CCl_4 (only aromatic protons).

the material becomes practically a constant. It is quite difficult, however, to attain a constant values of ΔE, because of being impossible to form the cells under the same condition. According to Brown and Aftergut,[11] an active impurity results in two or three linear lines of $\ln \rho$ against $1/T$ plot. Therefore, the purification procedures were repeated till the straight line was observed. As an example, the procedure of the purification for 1,6-dinitrophenazine, which was the most difficult among them, is described below. 1,6-Dinitrophenazine was purified by two methods, in which the method I has the procedures

SCHEME II

Precipitate from the reaction mixture

Method I	Method II
Chromatography*	Fractional crystallization**
Recrystallization***	Chromatography*
Vacuum sublimation****	Recrystallization*** (Step 1)
Recrystallization***	Chromatography*
	Recrystallization*** (Step 2)
	Two times recrystallization*** (Step 3)

* Chromatography over silicagel in the dark.
** Fractional crystallization from gracial acetic acid.
*** Recrystallization from benzene.
**** Vacuum sublimation under the pressure of 10^{-4}mmHg.

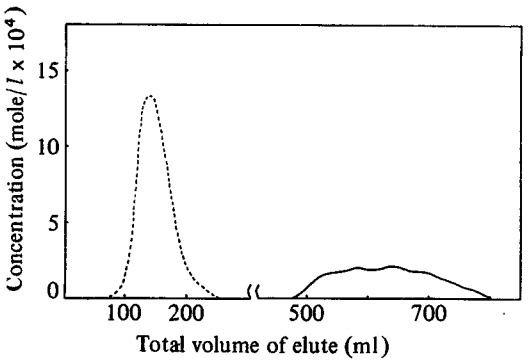


Fig. 4. Separation of dinitrophenazine by chromatography, 1,6-dinitrophenazine (broken line) and 1,9-dinitrophenazine (solid line).

consisting of chromatography, recrystallization, and vacuum sublimation, and the method II has those consisting of the repeated chromatography and recrystallization. A by-product, 1,9-dinitrophenazine could be removed by means of the chromatography, as Fig. 4 shows. The activation energy (ΔE) of the electrical conductivity of 1,6-dinitrophenazine, however, changed even after 1,9-dinitrophenazine was removed: the value of ΔE of the material in the method I and in each step of 1, 2 or 3 of the method II in Scheme II was 1.7 and 1.6-1.7, 2.1 or 2.0 eV, respectively. That is,the value of ΔE reached to a constant value in the step of 2 or 3. This means that the material purified through the step 3 of the method II has the conductive purity.

The other materials were purified and estimated by the method similar to the case of 1,6-dinitrophenazine.

For 1,6-diaminophenazine, the purification method by vacuum sublimation was effective for removing a trace of zinc dust used as the reducing agent. Furthermore, it was again sublimated before its electrical conductivity is measured, because of being unstable in relation to air.

3. Experimental

Phenazine was prepared by reduction of phenazine-5-oxide[1] with sodium dithionite according to the method reported by Scholl and Neuberger[6], then by oxidizing the resulting 5,10-dihydrophenazine with air. The purification was carried out by chromatography over alumina, then recrystallization from ethanol.

1,6-*Dinitrophenazine.*[7,8] Method I. To a solution of 10 g of phenazine in 200 m*l* of concentrated sulfuric acid, 50 m*l* of fuming nitric acid(d=1.50) was added dropwise at the temperature below 75°C. The reaction mixture was kept at 75°C for 8 hr, and added to a large amount of ice-water. A precipitate obtained was collected by filtration, dried and submitted to the purification described above. A typical example of chromatography was made as follows.

One hundred milligrams of the precipitate was dissolved in 100 m*l* of benzene, and the resulting solution was chromatographed over silicagel (2.5×30 cm^3. Wakogel Q-12) in the dark. The column was developed by eluting with benzene at a rate of about 1 m*l*/min. Consequtive 5 m*l* fractions were collected. The UV spectrum of each fraction was measured. The absorption at 369 mμ appeared in the fractions of 75–250 m*l* and 500–800 m*l*. IR spectrum of the residues after distilling out benzene in each fraction showed that 1,6-dinitrophenazine is present in the 75–250 m*l* portions and 1,9-dinitrophenazine is contained in 500–800 m*l* fractions. The concentrations of 1,6- and 1,9-dinitrophenazine in each fraction were calculated from the optical densities of their UV absorptions at 369 mμ (the UV spectra of both compounds are almost identical, although the IR spectra of them are distinguishable). The plot of the concentration of 1,6- and 1,9-dinitrophenazine against each portion is shown in Fig. 4. The fractions containing 1,6-dinitrophenazine were mixed, and benzene was distilled out. Recrystallization of the residue from benzene gave a yellow plate, mp 335–336°C (lit[7] 343°C). Yield, 43 mg (Found: C, 53.57; H, 2.20; N, 20.79%). From the 500–800 m*l* portions, 1,9-dinitrophenazine of 39 mg was obtained as yellow needle, mp 263–265°C (decomp.). 1,6-Dinitrophenazine obtained by chromatography was submitted to the next procedure of the purification. That is, this compound was sublimed under the reduced pressure of 10^{-4} mmHg at about 150°C, and then recrystallized from benzene. The value of ΔE of 1,6-dinitrophenazine was 1.7 eV.

Method II. Ten grams of the precipitate were recrystallized from glacial acetic acid to give about 3 g of a yellow plate, mp about 300°C. The yellow plate obtained was chromatographed and recrystallized by the method similar to the method I. The spectrometrical and conductive purity of the material obtained corresponded to that in the step I of the method I. The material was again submitted to chromatography and recrystallization. Although the UV and IR spectra of the material did not change by the procedure of twice chromatography and recrystallization, the value of ΔE increased from 1.7 to 2.0 eV.

1,6-*Diaminophenazine.*[7,8] Zinc dust (2.8 g) in limited amount was added to a solu-

tion of 1.24 g of 1,6-dinitrophenazine in 350 m*l* of 90% (V/V) acetic acid-water at 100°C for about 1.5 hr. After keeping to reflux for an hour, the reaction mixture was filtered off at hot. The filtrate was cooled with ice-water and made alkaline with ammonium hydroxide. The precipitate was collected by filtration and dissolved in 400 m*l* of 2% (V/V) hydrochloric acid. After a small amount of an active carbon was added into the acidic solution, the solution was refluxed for 2 hr, filtered at hot, cooled with ice-water and made alkaline with ammonium hydroxide. The precipitate was recrystallized from ethanol to give red needles, 0.76 g (80%), mp 260–261°C (lit 254[8], 265[7]°C). (found: C, 68.94; H, 4.59; N, 26.30%).

The red needles was chromatographed over cellulose powder, sublimated under a reduced pressure of 10^{-4} mmHg at 130°C, and recrystallized from benzene.

1,6-*Di-tert-butylphenazine*. A mixture of 3 g of *o*-amino-*tert*-butylbenzene, 7 g of *o*-nitro-*tert*-butylbenzene and 20 g of powdered potassium hydroxide in 50 m*l* of anhydrous benzene was vigorously stirred on a steam bath for 6 hr. After the reaction, the reaction mixture was submitted to steam distillation and cooled. The drak brown solid deposited was collected by filtration, washed with water and dried over calcium chloride. The solid was submitted to chromatography over alumina with elution of n-hexane. 1,6-Di-*tert*-butylphenazine was contained in the first fraction of yellow band. The evaporation of n-hexane under a reduced pressure and recrystallization of the residue from benzene gave a yellow prism, mp 195–196°C. Yield, 0.3 g.

Found: C, 81.92; H, 8.13; N, 9.50%. Calcd for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58%. Mass, parent peak at m/e 292. The nmr spectrum (Fig. 3) of the yellow prism in carbon tetrachloride solution showed a quartet signal centered at 1.90τ which is attributable to the protons of 4-and 9-positions, and two doublet signals at 2.38τ and 2.28τ which are attributable to the protons of 2-, 3-, 7- and 8-positions. These values of τ corresponded to those of phenazine having 1.87τ for 1-, 4-, 6- and 9-protons and 2.33τ for the other protons.[12] The signal ascribed to protons of *tert*-butyl group appeared at 8.25τ. The visible light absorption spectrum of this compound was similar to that of phenazine.

From the second fraction of yellow band, a yellow plate, mp 202–203.5°C, was obtained (about 10 mg). This was assigned to be 1,6-di-*tert*-butylphenazine-5-oxide by IR spectrum.

2,7-Di-*tert*-butylphenazine was prepared and purified by the method similar to the case of 1,6-di-*tert*-butylphenazine; *p*-amino-*tert*-butylbenzene and *p*-nitro-*tert*-butylbenzene were used as the starting materials. The crude material was obtained as the mixture of 2,7-di-*tert*-butylphenazine and its N-oxide. Although the mixture could be separated by the repeated chromatography over alumina, the amount of the N-oxide became large in comparison with that of 2,7-di-*tert*-butylphenazine. Therefore, the mixture was reduced by sodium dithionite without the separation of the two compounds, followed by the oxidation of the resulting dihydrophenazine with air. The recrystalliza-

tion from n-hexane or ethanol gave a yellow plate, mp 217–217.5°C. Yield, 0.3 g.

Found: C, 82.22, H, 8.29; N, 9.53%. Calcd for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58%. Mass, parent peak at m/e 292. The nmr spectrum (Fig. 3) of this compound showed a quartet signal centered at 1.88τ which is attributable to the protons of 1-, 4-, 6- and 9-positions, two doublet ones at 2.09τ and 2.26τ which are due to the protons of 3- and 8-positions and a signal of *tert*-butyl protons at 8.52τ. The nmr spectrum of 2,7-di-*tert*-butylphenazine-5-oxide showed four quartet signals at 1.52τ, 1.98τ, 2.16τ and 2.32τ, and singlet signal at 8.54τ. These signals were assigned to be the protons of 4- and 6-, of 1- and 9-, of 8-, and 3-positions, and of *tert*-butyl group, respectively.

2,7-*Dichlorophenazine*-5-*oxide*.[4,6] To a mechanically stirred solution of the mixture of 59.8 g of *p*-chloronitrobenzene and 20.4 g of *p*-chloroaniline in 150 m*l* of a dried benzene was added 49.4 g of powdered potassium hydroxide. The reaction was allowed to reflux under stirring for 8 hr. Benzene, the starting materials and some by-products were removed by steam distillation. After cooling, the solid deposited was filtered off and washed sequentially with water and benzene. The resulting brown solid was dissolved in benzene, and chromatographed over alumina. Elution with benzene gave 3.5 g of yellow powder. Recrystallization from benzene gave 2,7-dichlorophenazine-5-oxide of yellow needles, mp 231°C (Decomp.) (lit 236°C decomp.).

2,7-*Dichlorophenazine*.[4,6] To a hot solution of 1 g of 2,7-dichlorophenazine-5-oxide in a minimum amount of ethanol was added under stirring vigorously 300 m*l* of 6% (wt.) sodium hydroxide solution containing 20 g of sodium dithionite, and the reaction mixture was refluxed for 2 hr. After cooling, a large amount of water was added to the reaction mixture. A white precipitate was collected by filtration, washed with water, and dried over calcium chloride. After dispersing the precipitate in benzene, and filtering off, the filtrate was diluted with the same amount of ethanol to that of benzene. The diluted solution was stirred under the atmosphere of air until the color of the solution turned to light yellow. After distilling out benzene and ethanol in *vacuo*, the yellow residue was chromatographed over alumina. Elution with benzene gave 2,7-dichlorophenazine of yellow needles, mp 260–261°C (lit 265.5[13]). Yield, 60%. (Found: C, 57.83; H, 2.48; N, 11.48%).

1-*Chlorophenazine*-5-*oxide*.[4] One hundred gram of a powdered potassium hydroxide was added to a solution of the mixture of 100 g of *o*-chloroaniline and 280 g of nitrobenzene in 400 m*l* of a dried benzene. The solution was refluxed under stirring for 8 hr, then cooled, and poured into 1 liter of water. The benzene layer was extracted several times with 500 m*l* portion of 6 N hydrochloric acid. The by-products were contained in the first extraction. The next extraction contained 1-chlorophenazine-5-oxide. After the repeated extractions, the hydrochloric acid solution collected was neutralized with the concentrated ammonium hydroxide. A precipitate was collected by filtration and chromatographed on alumina. The column was developed by eluting with benzene.

After distilling out benzene, the recrystallization of the residue from ethanol gave 1-chlorophenazine-5-oxide of yellow needles, mp 155.5–156°C (lit 159–160°C). Yield, 6%.

1-*Chlorophenazine*.[4] A mixture of 3.9 g of 1-chlorophenazine-5-oxide and 50 m*l* of aniline was boiled under reflux for 6 hr. After the reaction, the unreacted aniline was removed by steam distillation. The residual solid was collected by filtration, dissolved in benzene, and submitted to chromatography on alumina. Elution with benzene gave yellow needles, mp 121.5–122.5°C (lit 122–123°C). Yield, 82% (Found: C, 67.29; H, 3.20; N, 12.96%.)

The yellow needles were chromatographed on alumina again, and recrystallized from ethanol.

2,7-*Dibromophenazine*.[4,6] According to the method of the preparation of 2,7-dichlorophenazine, 2,7-dibromophenazine was prepared form *p*-bromoaniline and *p*-bromonitrobenzene. Yield, 55% (from 5-oxide), mp 245–245.5°C (lit 244.5–245[13]°C). (Found: C, 42.45; H, 1.68; N, 8.03%).

1,6-*Dichlorophenazine*[5]. By the method described in the literature, 1,6-dichlorophenazine was prepared, mp 267–268°C (lit 266–267°C). (Found: C, 58.08; H, 2.36; N, 11.05%). It was purified by means of chromatography over alumina and recrystallization from benzene.

2-*Chlorophenazine*.[9] A solution of 10 g of phenazine-5-oxide in 100 m*l* of phosphorous oxychloride was refluxed for 7 hr. The reaction mixture was poured into 1 kg of ice-water. The precipitate was collected by filtration, washed with water and dried over calcium chloride. The precipitate was dissolved in benzene and chromatographed over alumina. Elution with benzene gave 2.82 g of 2-chlorophenazine, pale yellow needles, mp 138–138.5°C (lit 138°C). (Found: C, 67.36; H, 3.82; N, 12.84%). The pale yellow needles were again chromagotraphed over alumina, sublimated in *vacuo* and recrystallized from methanol.

2-*Methoxyphenazine*.[2,4] A solution of the mixture of 2.65 g of 2-chlorophenazine and 10.0 g of potassium hydroxide in 300 m*l* of anhydrous methanol was refluxed on a water bath for 6 hr. After the reaction, the solution was poured into 1 liter of water. The precipitate was filtered off, dried over calcium chloride, chromatographed over alumina, sublimated in *vacuo*, and recrystallized from methanol-water to give pale yellow needles, mp 122.5–123°C (lit 123–124°C). Yield 90%. (Found: C, 74.52; H, 4.86; N, 13.82%).

1-Methoxyphenazine,[10] mp 167.5–168.5°C (lit 167–169°C), 1,6-dimethoxyphenazine,[2] mp 249°C (lit 249–250°C), and 2,7-dimethoxyphenazine,[3] mp 246°C (lit 246°C), were prepared by the method described in the literatures.

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