Phenothiazine Derivatives. IV[1]*. Reactions of Thionyl Chloride with Some Substituted Diphenylamines and with Naphthylphenylamines*

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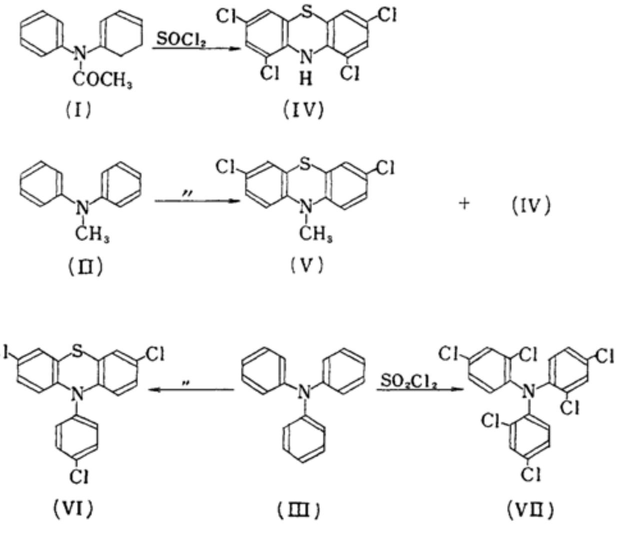
In part III[1] of this series, the reaction of thionyl chloride with diphenylamine was investigated in detail. The present paper describes similar reactions of thionyl chloride with some substituted diphenylamines and with naphthylphenylamines.

***N*-Substituted Diphenylamines.** — *N*-Acetyldiphenylamine (I), methyldiphenylamine (II), and triphenylamine (III) were treated with thionyl chloride with results represented schematically in Chart I. While *N*-acetyldiphenylamine (I) was completely transformed into 1, 3, 7, 9-tetrachlorophenothiazine (IV), methyldiphenylamine (II) gave 7% of 3, 7-dichloro-10-methylphenothiazine (V)[2] besides 89% of the same tetrachlorophenothiazine (IV). It appears that the substituents on the nitrogen atom exerted some steric hindrance on the *ortho* positions to the nitrogen atom, and they were either removed to give way to chlorine atoms entering these positions or retained to hinder chlorination in these positions. With thionyl chloride, triphenylamine (III) gave a nearly quantitative yield of a product $C_{18}H_{10}NCl_3S$, which is probably 3, 7-dichloro-10-(4′-chlorophenyl)phenothiazine (VI) considered on the basis of the orienting and the steric effects, but with sulfuryl chloride it gave a hexachlorotriphenylamine in a high yield, which is supposed to be 2, 4, 2′, 4′, 2″, 4″-hexachlorotriphenylamine (VII) from a similar consideration.

CHART I



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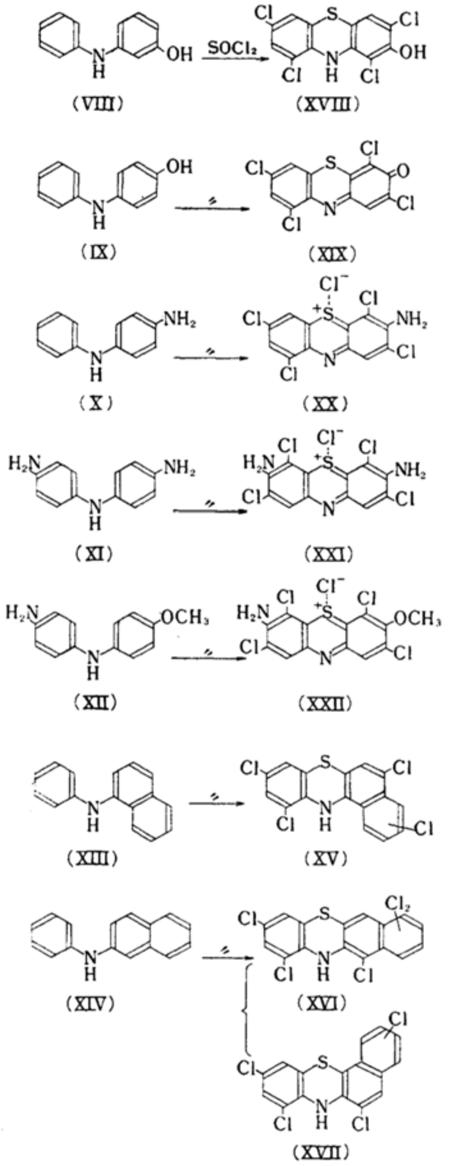
[1] Part III: This Bulletin, **32**, 294 (1959).

[2] A. C. Schmalz and Burger, *J. Am. Chem. Soc.*, **76**, 5458 (1954).

Diphenylamines Substituted in the Benzene Nuclei.—2-, 3- and 4-nitrodiphenylamines were found inert to thionyl chloride, and likewise, phenyl-(2-, 3-, and 4-)tolylamines did not give the corresponding phenothiazines. On the other hand, 3-hydroxy- (VIII), 4-hydroxy- (IX), 4-amino- (X), 4,4′-diamino- (XI) and 4-amino-4′-methoxy- (XII) diphenylamines reacted normally, as shown in Chart II. Assignment of the structures to the products is discussed below.

CHART II



As observed previously1), the reaction of unsubstituted diphenylamine with thionyl chloride proceeds through the formation of the intermediate phenazationium chloride and subsequent chlorination to give 1,3,7,9-tetrachlorophenothiazine, which shows that positions 1,3,7 and 9 of the intermediate phenazathionium chloride are rendered reactive in the chlorination by the effect of the nitrogen atom (position 10). 3-Hydroxydiphenylamine (VIII) is expected to produce 2-hydroxyphenazathionium chloride as the intermediate, in which the hydroxyl group will favor chlorination in positions 1 and 3. Thus, the product $C_{12}H_5ONCl_4S$ from 3-hydroxydiphenylamine (VIII) and thionyl chloride is assumed to be 1,3,7,9-tetrachloro-2-hydroxyphenothiazine (XVIII). Nevertheless, in the redundant 3-substituted phenazathionium intermediates from 4-hydroxy- (IX) and 4-amino- (X) diphenylamines, the hydroxyl group and the amino group in position 3 will orient chlorination to positions 2 and 4. As the hydroxyl group and the amino group have stronger orienting effects than the imino group, it is expected that positions 2, 4, 7 and 9 of the 3-substituted phenazathionium intermediates are reactive toward chlorination. Thus, the phenothiazone $C_{12}H_3ONCl_4S$ obtained from 4-hydroxydiphenylamine (IX) is assumed to be 2,4,7,9-tetrachloro-3-phenothiazone (XIX), and the phenazathionium chloride $C_{12}H_5N_2Cl_5S$ obtained from 4-aminodiphenylamine (X) to be 3-amino-2,4,7,9-tetrachlorophenazathionium chloride (XX). For similar reasons, the product $C_{12}H_6N_3Cl_5S$ from 4,4′-diaminodiphenylamine (XI) and thionyl chloride is supposed to be 3,7-diamino-2,4,6,8-tetrachlorophenazathionium chloride (XXI), and the product $C_{13}H_7ON_2Cl_5S$ from 4-amino-4′-methoxydiphenylamine (XII) and thionyl chloride to be 3-amino-2,4,6,8-tetrachloro-7-methoxyphenazathionium chloride (XXII). 2-Hydroxydiphenylamine gave exceptionally only an unpurifiable black tarry mass.

Naphthylphenylamines. — α-Naphthylamine (XIII) reacted normally with thionyl chloride to form a single product $C_{16}H_7NCl_4S$, probably x,5,9,11-tetrachlorobenzo[a]phenothiazine3) (XV). There are two possibilities for the positions of cyclization in β-naphthylphenylamine (XIV), and in fact two products with formulae $C_{16}H_6NCl_5S$ and $C_{16}H_7NCl_4S$, respectively, were separated chromatographically from the reaction mixture of β-naphthylphenylamine (XIV) and thionyl chloride (Chart II). The product $C_{16}H_6NCl_5S$ obtained in a larger amount is supposed to be the linearly cyclized compound, 1,3,x,x′,11-pentachlorobenzo[b]phenothiazine[3] (XVI). It melts at 147～149°C, and gives dark blue coloration with sulfuric acid. Then the minor product $C_{16}H_7NCl_4S$ may be x,6,8,10-tetrachlorobenzo[c]phenothiazine[3] (XVII). It melts at 217～219°C (decomp.) and produces dark green color with sulfuric acid. These two benzophenothiazines could not be distinguished from each other in the ultraviolet and infrared absorption spectra.

Experimental

Thionyl chloride (10 ml.) was added dropwise to 1.0 g. of the compound to be treated with the reagent, and the mixture was gently heated under reflux for 30 min., when hydrogen chloride and sulfur dioxide were evolved. The cooled mixture was poured onto ice, and the product was collected and dried. The following substances were obtained, depending upon the starting materials.

1,3,7,9-Tetrachlorophenothiazine (IV) and 3,7-Dichloro-10-methylphenothiazine (V).—The mixed product, obtained from methyldiphenylamine (II) as the starting material, was recrystallized from a mixture of ethanol and benzene. 1,3,7,9-Tetrachlorophenothiazine (IV), m.p. 235～236°C, crystallized out in yellow needles in a yield of 89%. The mother liquor was evaporated, and the residue was recrystallized from 50% aqueous ethanol. 3,7-Dichloro-10-methylphenothiazine (V), m.p. 129～130°C, was obtained in yellowish-green needles in a yield of 7%. The two substances were identified with authentic samples[1,2], respectively. The former IV was also obtained quantitatively from *N*-acetyldiphenylamine (I).

3,7-Dichloro-10-(4′-chlorophenyl)phenothiazine (VI).—Obtained from triphenylamine (III). Yellow fine crystals from benzene, m.p. 131～132°C. Yield, 91%. The substance shows indigo-blue coloration with sulfuric acid.

Anal. Found: C, 57.54; H, 2.89; N, 4.16. Calcd. for $C_{18}H_{10}NCl_3S$: C, 57.09; H, 2.66; N, 3.70%.

1,3,7,9-Tetrachloro-2-hydroxyphenothiazine (XVIII).—Obtained from pure 3-hydroxydiphenylamine (VIII), and recrystallized from chloroform-ethanol. Fine powder with chocolate color, m.p. 202～203°C (decomp.). Yield, 92%. The substance is soluble in 10% aqueous caustic soda, and produces blue-violet color with sulfuric acid.

Anal. Found: C, 40.49; H, 1.54; N, 4.03. Calcd. for $C_{12}H_5ONCl_4S$: C, 40.82; H, 1.43; N, 3.97%.

2,4,7,9-Tetrachloro-3-phenothiazone (XIX).—Derived from freshly distilled 4-hydroxydiphenylamine (IX). White crystals with pinkish tinge from ethanol-benzene, m.p. 145～146°C. Yield, nearly quantitative. It gives cobalt-blue coloration with sulfuric acid.

Anal. Found: C, 41.11; H, 1.01; N, 4.00. Calcd. for $C_{12}H_3ONCl_4S$: C, 41.06; H, 0.86; N, 3.99%.

3-Amino-2,4,7,9-tetrachlorophenazathionium Chloride (XX).—Obtained from freshly rectified 4-aminodiphenylamine (X). Reddish-violet fine powder from chloroform, m.p. 185～186°C. Yield, 86%. It gives reddish-violet coloration with sulfuric acid.

Anal. Found: C, 37.40; H, 1.10; N, 7.30. Calcd. for $C_{12}H_5N_2Cl_5S$: C, 37.28; H, 1.30; N, 7.25%.

3,7-Diamino-2,4,6,8-tetrachlorophenazathionium Chloride (Tetrachlorothionine) (XXI).—From pure 4,4′-diaminodiphenylamine. Bluish-purple fine powder from methanol, m.p. over 360°C. Yield, 94%. It gives dark green coloration with sulfuric acid.

Anal. Found: C, 36.13; H, 1.78; N, 10.46. Calcd. for $C_{12}H_6N_3Cl_5S$: C, 35.90; H, 1.51; N, 10.47%.

3-Amino-2,4,6,8-tetrachloro-7-methoxyphenazathionium Chloride (XXII).—Obtained from 4-amino-4′-methoxydiphenylamine (XII). Bluish-violet fine powder from methanol, m.p. 281～284°C (decomp.). Yield, 82%. Its color in sulfuric acid is bluish violet.

Anal. Found: C, 37.22; H, 1.41; N, 6.97. Calcd. for $C_{13}H_7ON_2Cl_5S$: C, 37.47; H, 1.69; N, 6.73%.

x,5,9,11-Tetrachlorobenzo[a]phenothiazine (XV).—One gram of α-naphthylphenylamine (XIII) gave 1.7 g. (96%) of this compound (XV) in reddish-violet fine crystals, which was purified chromatographically, and then recrystallized from benzene, m.p. 266～268°C. Its coloration with sulfuric acid is bluish violet.

Anal. Found: C, 49.43; H, 2.19; N, 3.15. Calcd. for $C_{16}H_7NCl_4S$: C, 49.65; H, 1.82; N, 3.62%.

1,3,x,x′,11-Pentachlorobenzo[b]phenothiazine (XVI) and x,6,8,10-Tetrachlorobenzo[c]phenothiazine (XVII).—One gram of β-naphthylphenylamine (XIV) gave 1.8 g. of a crude crystalline mixture. The mixture was dissolved in 20 ml. of benzene, and passed through a column of alumina. The chromatogram was eluted first with the same solvent and then developed with a mixture of chloroform and ethanol. The first fraction gave a substance in yellow fine crystals, which was assumed to be 1,3,x,x′,11-pentachlorobenzo[b]phenothiazine (XVI). Recrystallized from chloroform-ethanol, it melts at 147～149°C and gives dark blue coloration with sulfuric acid, Yield, 1.2 g. (62%).

Anal. Found: C, 45.32; H, 1.88; N, 3.07. Calcd. for $C_{16}H_6NCl_5S$: C, 45.57; H, 1.43; N, 3.32%.

The second fraction, which was strongly fluorescent in solution, gave another substance in fine yellow crystals, which was assumed to be the other possible product, x,6,8,10-tetrachlorobenzo[c]phenothiazine (XVII). Recrystallized from chloroform-ethanol, it melts at 217～219°C (decomp.). Yield, 0.5 g. (28%). It gives dark green coloration with sulfuric acid.

Anal. Found: C, 49.70; H, 2.04; N, 3.57. Calcd. for $C_{16}H_7NCl_4S$: C, 49.65; H, 1.82; N, 3.62%.

Reaction of Triphenylamine (III) with Sulfuryl Chloride.—Sulfuryl chloride (10 ml.) was added to 1.0 g. of triphenylamine (III), and the mixture was gently refluxed for 30 min., and

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[3] The nomenclature of these benzophenothiazines conforms to the "Ring Index" (1940).

poured onto crushed ice. The precipitate was collected, dried, and recrystallized from ethanol. 2, 4, 2′, 4′, 2″, 4″-Hexachlorotriphenylamine (VII) was obtained in colorless crystals, m.p. 78~79°C. Yield, 92% of the theory. It remains colorless with sulfuric acid.

Anal. Found: C, 47.66; H, 2.44; N, 3.17. Calcd. for $C_{18}H_9NCl_6$: C, 47.83; H, 2.01; N, 3.10%.

Summary

Reactions of thionyl chloride with some substituted diphenylamines and with naphthylphenylamines were studied. *N*-Acetyldiphenylamine gave the known 1, 3, 7, 9-tetrachlorophenothiazine. Methyldiphenylamine gave a small yield of the known 3, 7-dichloro-10-methylphenothiazine besides the same tetrachlorophenothiazine as the main product. The following new compounds were obtained from respective starting materials and their structures were deduced: 3, 7-dichloro-10-(4′-chlorophenyl)-phenothiazine from triphenylamine, 1, 3, 7, 9-tetrachloro-2-hydroxyphenothiazine from 3-hydroxydiphenylamine, 2, 4, 7, 9-tetrachloro-3-phenothiazone from 4-hydroxydiphenylamine, 3-amino-2, 4, 7, 9-tetrachlorophenazathionium chloride from 4-aminodiphenylamine, 3, 7-diamino-2, 4, 6, 8-tetrachlorophenazathionium chloride from 4, 4′-diaminodiphenylamine, 3-amino-2, 4, 6, 8-tetrachloro-7-methoxyphenazathionium chloride from 4-amino-4′-methoxydiphenylamine, x, 5, 9, 11-tetrachlorobenzo[a] phenothiazine from α-naphthylphenylamine, and 1, 3, x, x′, 11-pentachlorobenzo[b] phenothiazine and x, 6, 8, 10-tetrachlorobenzo [c] phenothiazine from β-naphthylphenylamine.

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