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155. Masatomo Hamana, Bunsuke Umezawa, and Shoichi Nakashima : Studies on Tertiary Amine Oxides. XIV. Reactions of N-(*p*-Dimethylaminophenyl)nitrones having Pyridine, Quinoline or its N-Oxide, as α-Substituent with Carbon Disulfide.

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In the course of the study of infrared spectra of nitrones (group A and B : α-arylnitrones have been, previously, classified into two groups[1]), Shindo[*2] found an interesting phenomenon that nitrone group B and trimethylamine N-oxide, when dissolved in carbon disulfide, showed a characteristic and intensive absorption at 2045 cm^{-1}, which was not observed in carbon tetrachloride. This fact suggested that a certain reaction had taken place between either nitrones or tertiary amine oxide and the solvent. Therefore, the reaction of N,α-diphenylnitrone (I) with carbon disulfide was investigated at first spectrophotometrically. A sample of (I) was dissolved in carbon disulfide and its infrared spectra in the same solution were measured every twenty minutes to check the band at 2045 cm^{-1}. Even at the very beginning, the band appeared in a considerable intensity and the maximum was attained around sixty minutes (Fig. 1).

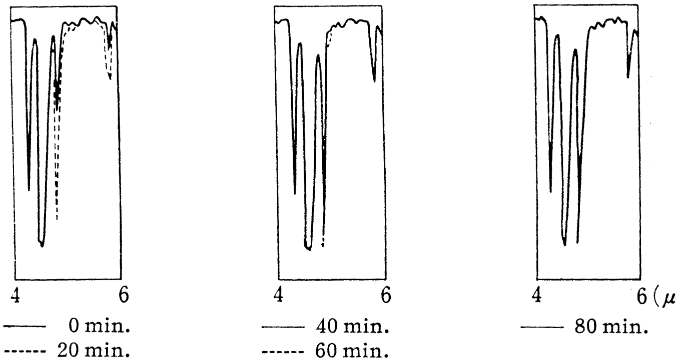

Fig. 1.

With a hope to obtain the compound showing the band at 2045 cm^{-1}, a solution of (I) in carbon disulfide was kept standing overnight at room temperature and the solvent was distilled off cautiously under reduced pressure. In spite of the careful treatment of the product, however, any expected compound could not be obtained but a compound of m.p. 48°, together with an appreciable amount of sulfur was afforded. The compound had no band at 2045 cm^{-1} which was finally identified as N-benzylideneaniline, m.p. 50~51°, by a mixed fusion. Accordingly, (I) was deoxygenated with carbon disulfide, and the reaction proceeded in the following process.

The reaction would have been initiated by the nucleophilic attack of the oxygen atom of carbon disulfide (Ia) and have proceeded through the electron back-shift to leave sulfur and carbonyl sulfide as shown in Chart 1.

To verify the assumption, the infrared spectrum of carbonyl sulfide in carbon disulfide was measured and the band at 2045 cm^{-1} was confirmed to be actually due to carbonyl sulfide as expected. The combination of bands of carbonyl sulfide and N-ben-

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[*2] The authors express their hearty thank to Dr. E. Shindo for his kind information.

1) B. Umezawa : This Bulletin, 8, 967 (1960).

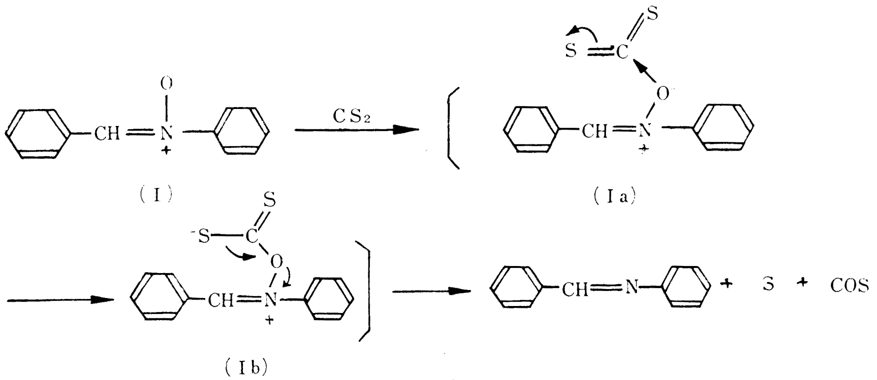


Chart 1.

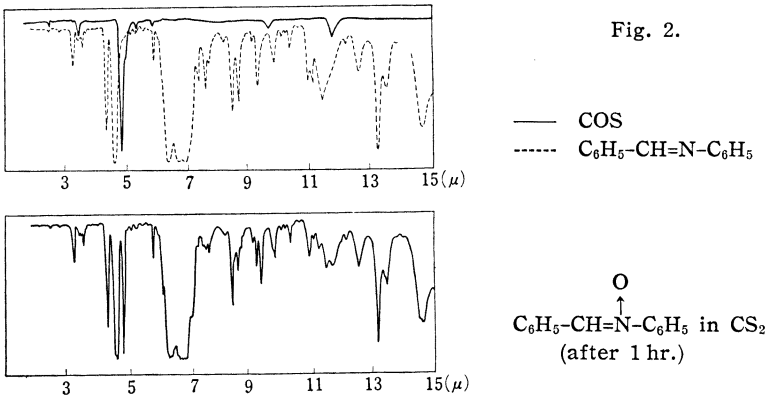


Fig. 2.

zylideneaniline in carbon disulfide was quite similar to that of the reaction mixture of (I) with an excess of carbon disulfide (Fig. 2).

Initiation of the reaction might depend upon the character of N-O bond. Decreasing order of the strength of N-O bond was shown below.

aromatic N-oxide > nitrone group A > group B > ali. tert. amine oxide

Therefore, it was expected that aromatic N-oxide and nitrone group A might be unaffected by carbon disulfide, whereas, nitrone group B and tertiary amine oxide might easily be deoxygenated and that some of nitrones group B might be rearranged by the carbonyl sulfide secondary formed just in the same manner as in sulfur dioxide (Chart 2).

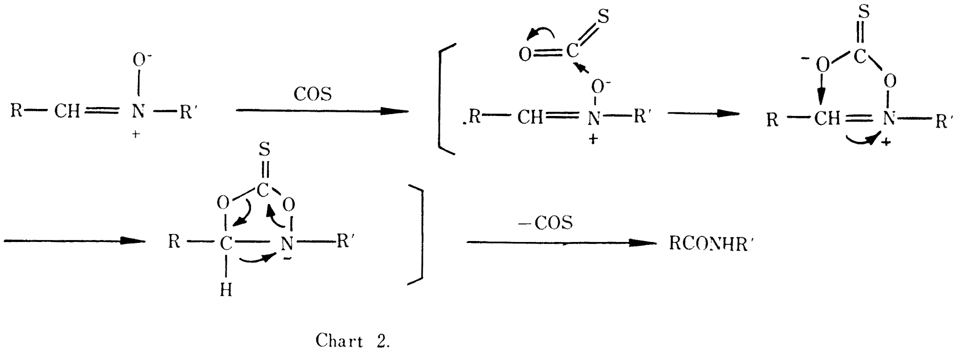
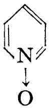
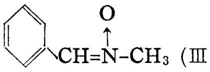
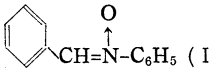
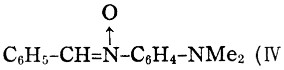
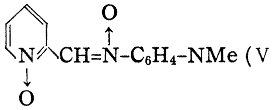
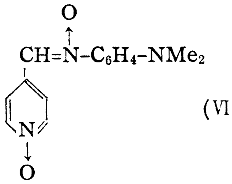
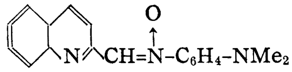
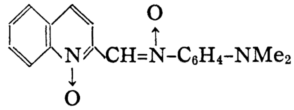
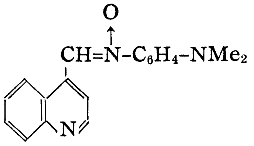
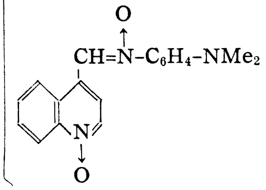
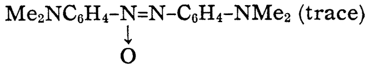
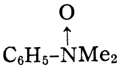


Chart 2.

To exemplify the above consideration, reactions of pyridine N-oxide (II), N-methyl-α-phenylnitrone (III),[2] N-(*p*-dimethylaminophenyl)-α-phenylnitrone (IV),[3] N-(*p*-dimethylaminophenyl)-α-(1-oxido-2-pyridyl)nitrone (V),[4] N-(*p*-dimethylaminophenyl)-α-(1-oxido-4-pyridyl)nitrone (VI), N-(*p*-dimethylaminophenyl)-α-(2-quinolyl)nitrone (VII),

Table I. Reactions of Nitrones and N-Oxides (ar. or ali.) with CS_2 and COS

		CS_2	COS	
	 (II)	recovery (quantitatively)		
Nitrone group A	 (III)	recovery (88%)		
Nitrone group B	 (I)	anil (13.6%)+S	recovery (83.3%)	
	 $C_6H_5\text{-}CH{=}\overset{\overset{O}{\uparrow}}{N}\text{-}C_6H_4\text{-}NMe_2$ (IV)	anil (61.4%)	anil (74.3%)	
	 (V)	anil (6.7%) anilide (18%)	(standing for 30 min.) (V) (24%) anilide (6%)	(standing overnight) anilide (12%) $ONC_6H_4\text{-}NMe_2$ (small)
	 (VI)	anil (42.2%)+S	anil (5.3%) $ONC_6H_4\text{-}NMe_2$ (small)	
	 (VII)	anil (63.5%)	anil (37%)	
	 (VIII)	anil (53%)	(VIII) (60%) anil (5%)	
	 (IX)	anil (53%) anilide (trace)	(IX) (64%) anil (trace)	(standing overnight) (IX) (trace) anil (16.9%) anilide (trace)
	 (X)	anilide (6.6%) anil (63.4%) S	(X) (14%) anilide (10%) anil (2.1%)	
	$Et_3N{\to}O$ (XI)	Et_3N (2.5%)	 $Me_2NC_6H_4\text{-}\underset{\underset{O}{\downarrow}}{N}{=}N\text{-}C_6H_4\text{-}NMe_2$ (trace)	
	 $C_6H_5\text{-}\overset{\overset{O}{\uparrow}}{N}Me_2$ (XII)	$C_6H_5NMe_2$ (30.8%)		

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[2] O.L. Brady, F.P. Dunn, R.F. Goldstein : J. Chem. Soc., **1926**, 2386.

[3] F. Kröhnke : Ber., **71**, 2583 (1938).

[4] M. Hamana, B. Umezawa, Y. Gotoh, K. Noda : This Bulletin, 8, 692 (1960).

N-(*p*-dimethylaminophenyl)-*α*-(1-oxido-2-quinolyl)nitrone (VIII), N-(*p*-dimethylaminophenyl)-*α*-(4-quinolyl)nitrone (IX), N-(*p*-dimethylaminophenyl)-*α*-(1-oxido-4-quinolyl)nitrone (X), triethylamine N-oxide[5)](XI) and N,N-dimethylaniline N-oxide[5)](XII) were carried out and the results were shown in Table I.

By carbon disulfide, (II) and (III) were recovered unchanged in higher yields, on the other hand, (XI) and (XII) were smoothly deoxygenated in lower yields. The prolonged reaction period of time with (XI) was undesirable to give no identifiable product (unpleasant odor). Therefore, lower yield might be caused by the instability of (XI) toward carbon disulfide or carbonyl sulfide. Nitrone group B (I, IV, V, VI, VII, VIII, IX, and X) could be readily deoxygenated in various yields with occasional formation of sulfur. And further, in the cases of (V), (IX), and (X), the corresponding anilides could be obtained as anticipated. Any formation of thioanilides was not observed. Therefore the reagent which caused the rearrangement might be carbonyl sulfide and reactions of nitrone group B with the reagent were investigated as shown in Table I.

The fact that by carbonyl sulfide (I) was recovered unchanged in better yield appeared to show the entity leading to deoxygenation to be by no means carbonyl sulfide but carbon disulfide itself. In some cases, however, corresponding anils were obtained in lower yields than that in the reaction with carbon disulfide. From the occasional detection of N,N-dimethyl-*p*-phenylenediamine, 4,4′-bis(dimethylamino)azoxybenzene or benzaldehyde, it would be suggested that the anils might be formed through hydrolysis of the starting nitrones followed by the recombination of the resulting aldehydes and N,Ndimethyl-*p*-phenylenediamine (Chart 3).

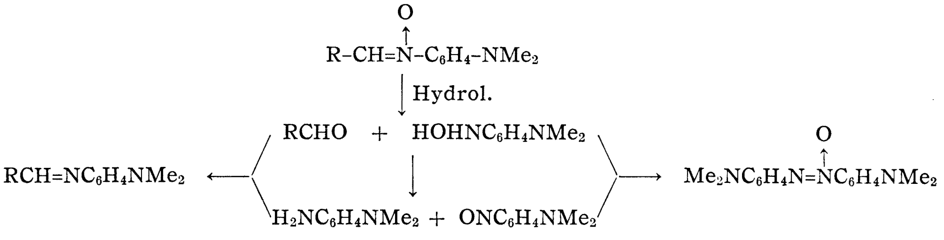

Chart 3.

A treatment of (V) with carbonyl sulfide, followed by standing for 30 minutes at room temperature, gave 6% of the corresponding anilide together with a recovery of (V) in 24% and a yield of anilide could be raised to 12% by standing overnight. Therefore, it would be clear that the rearrangement might be due to carbonyl sulfide as shown before. The fact that a trace of sulfur was produced by the reaction of (X) with carbonyl sulfide would be due to hydrogen sulfide, which was a decomposed product of the reagent in the presence of moisture as shown below.

$$COS+H_2O \xrightarrow{\text{slowly}} CO_2+H_2S$$

Previously, N-oxide group was found to be favorable for the rearrangement of nitrone and another evidence for the fact appeared to be presented : namely, (X) was more easily rearranged than (IX) in the reaction with carbon disulfide. The following facts may, therefore, be concluded.

1. Aromatic N-oxide and nitrone group A were stable toward carbon disulfide. However, nitrone group B and tertiary amine oxide were smoothly deoxygenated to the corresponding anil and tertiary amine respectively. Therefore, the classification of nitrones into group A and B seemed to be reasonable.

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5) R. Huisgen, F. Bayerlein, W. Heydkamp : Chem. Ber., **92**, 3223 (1959).

2. Some of nitrone group B were confirmed to be rearranged by carbonyl sulfide. Although the latter seemed not so effective as sulfur dioxide, the fact that the rearrangement could be caused by the reagent containing carbon atom at the center instead of sulfur seemed to be of much interest.

3. Another proof was given to the suggestion that N-oxide group would accelerate the rearrangement of nitrone.

Experimental[*3]

Reaction of Pyridine 1-Oxide (I) with CS_2——A mixture of 500 mg. of (I) in 20 cc. of $CHCl_3$ and 10 cc. of CS_2 was allowed to stand for two days at room temperature. Evaporation of the solvent and later distillation gave the product (I) quantitatively, picrate, m.p. 180$\sim$181° (from MeOH).

Reaction of N-Methyl-α-phenylnitrone (II) with CS_2——After the similar treatment with 500 mg. of (II), 400 mg. of (II), starting material m.p. 81$\sim$82° (from benzene and petr. ether), was recovered unchanged.

Reactions of N,α-Diphenylnitrone (III)——a) with CS_2: To a solution of 400 mg. of (III) in 10 cc. of $CHCl_3$ was added 5 cc. of CS_2 and the solution was kept standing overnight at room temperature. On evaporation of the solvent and crystallization of the product from a mixture of Et_2O and hexane, gave ca. 30 mg. of S. Treatment of the mother liquor gave N-benzylideneaniline, m.p. 48° (from aq. MeOH), 50 mg. (13% yield). b) with COS: COS was passed through a solution of 300 mg. of (III) in 15 cc. of $CHCl_3$. On usual treatment, (III), m.p. 113$\sim$114° (from a mixture of benzene and petr. benzin), 280 mg., (93.3% yield) was recovered unchanged.

Reactions of N-(*p*-Dimethylaminophenyl)-α-phenylnitrone (IV)——a) with CS_2: Similar treatment with 200 mg. of (IV) and chromatography of the product gave yellow crystals of N-benzylidene-N',N'-dimethyl-*p*-phenylenediamine, m.p. 99$\sim$100° (from petr. benzin), 120 mg., (64.2% yield). b) with COS: After passing COS through a solution of 200 mg. of (IV) in 20 cc. of $CHCl_3$, the solution gradually turned dark red and was maintained overnight in a refrigerator. During the course of the treatment, a smell of benzaldehyde was noticed. Chromatographic purification gave N-benzylidene-N',N'-dimethyl-*p*-phenylenediamine, m.p. 99$\sim$100°, 70 mg. (37.4% yield).

Reactions of N-(*p*-Dimethylaminophenyl)-α-(1-oxido-2-pyridyl)nitrone (V)——a) with CS_2: Standing a solution of 500 mg. of (V) overnight in 15 cc. of $CHCl_3$ and 10 cc. of CS_2 at room temperature and chromatography of the product gave 4'-dimethylaminopicolinanilide 1-oxide, m.p. 219° (from MeOH), 90 mg., (18% yield) and 2-(dimethylaminophenyliminomethyl) pyridine 1-oxide, m.p. 144° (from a mixture of benzene and petr. benzin), 30 mg. (6.7% yield). b) with COS: After passing COS through a solution of 500 mg. of (V) in 20 cc. of $CHCl_3$, the solution was allowed to stand for 0.5 hr. at room temperature (red coloration). Chromatography and fractional recrystallization of the product afforded 4'-dimethylaminopicolinanilide 1-oxide, m.p. 217°, 30 mg. (6% yield) and (V), m.p. 160$\sim$161° (from AcOEt), 120 mg. (24% recovery). When another reaction mixture of 500 mg. of (V) was kept overnight in a refrigerator and worked up as above, 60 mg. (12% yield) of 4'-dimethylaminopicolinanilide 1-oxide and a small amount of *p*-nitrosodimethylaniline were obtained.

Reactions of N-(*p*-Dimethylaminophenyl)-α-(1-oxido-4-pyridyl)nitrone (VI)——a) with CS_2: Chromatography of the reaction product of 500 mg. of (VI) with 20 cc. of CS_2 in 30 cc. of $CHCl_3$ gave 4-(*p*-dimethylaminophenyliminomethyl)pyridine 1-oxide, m.p. 205$\sim$206° (from AcOEt), 200 mg. (42.2% yield) and S, m.p. 120$\sim$121. b) with COS: Passing COS through a solution of (VI) in 20 cc. of $CHCl_3$, standing of the solution overnight at room temperature and working up as usual gave 4-(*p*-dimethylaminophenyliminomethyl)pyridine 1-oxide, m.p. 207°, 10 mg. (5.3% yield) and 10 mg. of *p*-nitrosodimethylaniline.

Reactions of N-(*p*-Dimethylaminophenyl)-α-(2-quinolyl)nitrone (VII)——a) with CS_2: Usual treatment of 300 mg. of (VII) with 5 cc. of CS_2 gave 2-(*p*-dimethylaminophenyliminomethyl)quinoline, m.p. 142$\sim$143° (from MeOH), 180 mg. (63.5% yield). b) with COS: Chromatography of the reaction product of 200 mg. of (VII) afforded 4'-dimethylaminophenyliminoquinaldine, m.p. 145$\sim$146°, 70 mg. (37% yield).

[*3] All melting points are uncorrected and all products or, in some cases, their picrates are identified with the authentic specimens by mixed fusion respectively. Unless otherwise mentioned, chromatography was carried out over alumina (elution with $CHCl_3$ and a mixture of $CHCl_3$ and a small amount of MeOH), and reaction mixtures with CS_2 or COS were allowed to stand overnight at room temperature or treated immediately after passing through the gas respectively. COS was generated by adding a saturated solution of NH_4SCN in 20 cc. of H_2O to an ice cooled dil. H_2SO_4 (208 g. of conc. H_2SO_4 in 100 cc. of H_2O). Under carefully controlled conditions, an evolution of the gas lasted for 1.5 to 2 hr.

Reactions of N-(*p*-Dimethylaminophenyl)-α-(1-oxido-2-quinolyl)nitrone (VIII)——a) with CS$_2$: Treating usually of 200 mg. of (VIII) in 20 cc. of CHCl$_3$ and 5 cc. of CS$_2$ gave 2-(*p*-dimethylaminophenyliminomethyl)quinoline 1-oxide, m.p. 213~214° (from MeOH), 100 mg. (53% yield). b) with COS: Usual treatment of 200 mg. of (VIII) with COS and chromatography of the product gave (VIII) m.p. 205~206° (from MeOH), 120 mg. (60% recovery) and 2-(*p*-dimethylaminophenyliminomethyl)quinoline 1-oxide, m.p. 214~215°, 10 mg. (5% yield).

Reactions of N-(p-Dimetylaminophenyl-α-(4-quinolyl)nitrone (IX)——a) with CS$_2$: Usual treat ment of 300 mg. of (IX) in 20 cc. of CHCl$_3$ and 10 cc. of CS$_2$ gave 4-(*p*-dimethylaminophenyliminomethyl) quinoline, m.p. 155~156° (from MeOH), 150 mg. (53% yield) and a trace of 4′-dimethylaminocinchoninanilide, m.p. 222~223° (from MeOH). b) with COS : Usual treatment of 250 mg. of (IX) and fractional recrystallization gave (IX), m.p. 194~195° (from MeOH), 160 mg. (64% recovery) and a trace of 4-(*p*-dimethylaminophenyliminomethyl)quinoline, m.p. 152~153°. When another reaction mixture of 250 mg. of (IX) was allowed to maintain overnight in a refrigerator and chromatographed, 4-(*p*-dimethylaminophenyliminomethyl)quinoline, m.p. 154~155° (from MeOH), 40 mg. (16.9% yield), trace of both (IX) and 4′-dimethylaminocinchoninanilide, m.p. 221~222° (from MeOH), were obtained.

Reactions of N-(*p*-Dimethylaminophenyl)-α-(1-oxido-4-quinolyl)nitrone (X)——a) with CS$_2$: Usual treatment of 300 mg. of (X) in 10 cc. of CS$_2$ gave S and the solid which was digested in hot benzene. From the insoluble portion, 4′-dimethylaminocinchoninanilide 1-oxide, m.p. 247° (from MeOH), 20 mg. (6.6% yield), was obtained. Chromatography (elution with benzene and a mixture of benzene and a small amount of MeOH) of the soluble portion afforded 4-(*p*-dimethylaminophenyliminomethyl)quinoline 1-oxide, m.p. 176~177° (from a mixture of benzene and petr. benzin), 180 mg. (63.4% yield). b) with COS : Working up of 500 mg. of (X) with COS as usual and crystallization of the product from MeOH gave (X), m.p. 218°, 70 mg. (14% recovery). Chromatography of the residue from the methanolic mother liquor afforded 4′-dimethylaminocinchoninanilide 1-oxide, m.p. 249° (from MeOH), 50 mg. (10% yield), 4-(*p*-dimethylaminophenyliminomethyl)quinoline 1-oxide, m.p. 176° (from MeOH), 10 mg. (2.1% yield), 4,4′-bis(dimethylamino)azoxybenzene (orange yellow), m.p. 245°, less than 10 mg. and trace of S.

Reaction of Triethylamine N-oxide (XI) with CS$_2$——To a solution of 1 g. of (XI) in 20 cc of CHCl$_3$, 5 cc. of CS$_2$ was added dropwise under ice-cooling. After standing at room temperature for 1 hr. the solution was subjected to steam distillation and the distillate was passed into 30 cc. of dil. HCl. Concentration of the HCl solution and addition of Na picrate formed the precipitate of triethylamine picrate, m.p. 170~171° (from MeOH), 70 mg. (2.5% yield).

Reaction of N,N-Dimethylaniline N-oxide (XII) with CS$_2$——To a solution of 550 mg. of (XII) in 20 cc. of dioxane, 5 cc. of CS$_2$ was added dropwise carefully at room temperature. After standing for 1 hr., distilling off the solvent cautiously *in vacuo* and adding 5 cc. of H$_2$O to the residue, the product was extracted with Et$_2$O. Usual treatment of the Et$_2$O layer gave N,N-dimethylaniline, b.p. 205~215°, (bath temperature), 150 mg. (30.8% yield), picrate, 158~160°. Trace of (XII), picrate, m.p. 136~137°, was also obtained from the H$_2$O layer.

The authors are grateful to Mrs. S. Matsuba and Mr. M. Shirozu for elemental analyses, and to Messrs. H. Yano, H. Matsui and K. Hikita for the measurement of infrared and ultraviolet spectra.

Summary

Nitroue group B and tertiary amine oxides were found to be deoxygenated by carbon disulfide and some of the nitrones were rearranged by the carbonyl sulfide secondary formed.

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