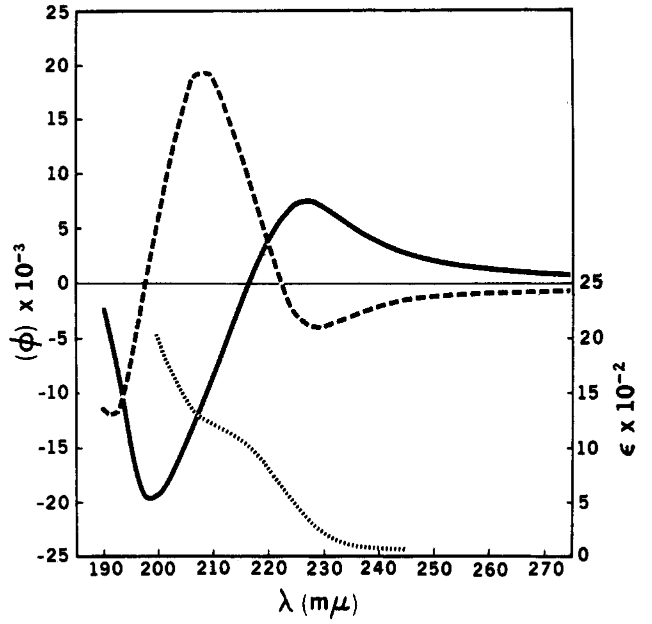

Figure 1.—Optical rotatory dispersion of (+)-3-(*n*-propylsulfinyl)alanine (———) and (−)-3-(*n*-propylsulfinyl)alanine (– – – –); ultraviolet spectrum (''''''''''''''').

with the 4-(methylsulfinyl)-α-amino-*n*-butyric acids. Another possible explanation is that the levorotatory isomers might be showing Cotton effects due to both chromophores, the sulfoxide group giving rise (see Figure 1) to the negative Cotton effect centered at 218 mμ and the amino acid chromophore being centered about the descending limb of the curve at 200 mμ. However, none of the levorotatory isomers gave a shoulder on the ascending limb of the negative Cotton effect to add support to this proposal. Such shoulders have been observed[6] in certain polypeptides and proteins when two opposed Cotton effects occur in close proximity. The difference in absolute amplitudes for the isomeric 3-(methylsulfinyl)alanines (see Table I) is about 11,000. Using α-amino-*n*-butyric acid as a model compound without the sulfoxide group, one obtains a difference of (2 × 3800[5])7600. That the combination of sulfoxide and amino acid chromophores is possibly an additive feature is suggested by this example but further confirmatory evidence is desirable.

The absolute configuration about sulfur has been established by Hine[7] for (+)-3-(methylsulfinyl)alanine by X-ray analysis. Klyne, Day, and Kjaer[8] have recorded O.R.D. curves for a series of derivatives of some naturally occurring isothiocyanate sulfoxides. Negative plain curves which were very similar and nearly superimposable were obtained in the wave-length region of 300–600 mμ. These results indicate that the sulfoxides studied are of similar configuration. Variation in the number of methylene groups between the sulfoxide chromophore and the functional group on the terminal carbon atom did not effect either the sign or the shape of the O.R.D. curve.

The results obtained in the present study also indicate that the asymmetric α-carbon atom and its attached functional groups have little influence on the asymmetrically perturbed sulfoxide chromophore. Therefore, since Hine assigned[7] (+)-3-(methylsulfinyl)-alanine the (*S*)-configuration, the dextrorotatory alkyl sulfinyl amino acids described in Table I may be assigned the (*S*)-configuration about sulfur and the levorotatory isomers the (*R*)-configuration.

These conclusions may be extended to similar alkyl sulfinyl amino acids and possibly to the isothiocyanate sulfoxides.[8] The domination of the rotatory dispersion curve by the sulfoxide chromophore should permit determination of absolute configuration of dialkyl sulfoxides by observing the sign of rotation at the sodium line.

Andersen[9] recently proposed a method for assigning relative and absolute configurations to asymmetric sulfoxides. He noted[9] that Herbrandson and Cusano's[10] assignment of the (*S*)-configuration about sulfur in (−)-menthyl (−)-*p*-iodobenzenesulfinate is consistent with Hine's[7] assignment to (+)-3-(methylsulfinyl-alanine. More recently, Fleischer, Axelrod, Green, and Mislow[11] have unequivocally established the absolute configurations of (−)-menthyl (−)-*p*-iodobenzenesulfinate and of (−)-menthyl (−)-*p*-toluenesulfinate using X-ray and chemical methods. The absolute configuration about the sulfur atom is (*S*) in both cases,[11] as had been suggested previously.[10,12] The results obtained in this important paper[11] are mutually compatible with configurational assignments made by Andersen[12] and by Montanari, *et al.*,[13] to some aryl alkyl sulfoxides and also with the assignments made in this paper concerning alkyl sulfinyl amino acids.

However, there is need for further work in establishing absolute configurations of asymmetric sulfoxides. The application of O.R.D. in relating these substances will very likely prove as fruitful as it has with other chromophores.

Experimental

Materials.—The alkyl sulfinyl amino acids were obtained as described by Carson and Wong.[14] O.R.D. measurements were carried out on a Cary[15] Model 60 spectropolarimeter and ultraviolet spectra were determined on a Cary[15] 14 spectrophotometer.

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(6) E. R. Blout, I. Schmier, and N. S. Simmons, *J. Am. Chem. Soc.*, **84**, 3193 (1962).

(7) R. Hine, *Acta Cryst.*, **15**, 635 (1962).

(8) W. Klyne, J. Day, and A. Kjaer, *Acta Chem. Scand.*, **14**, 215 (1960).

(9) K. K. Andersen, *J. Org. Chem.*, **29**, 1953 (1964).

(10) H. F. Herbrandson and C. M. Cusano, *J. Am. Chem. Soc.*, **83**, 2124 (1961).

(11) E. B. Fleischer, M. Axelrod, M. Green, and K. Mislow, *ibid.*, **86**, 3395 (1964).

(12) K. K. Andersen, *Tetrahedron Letters*, 93 (1962).

(13) A. Mayr, F. Montanari, and M. Tramontini, *Gazz. chim. ital.*, **90**, 739 (1960); A. Maccioni, F. Montanari, M. Secci, and M. Tramontini, *Tetrahedron Letters*, 607 (1961).

(14) J. F. Carson and F. F. Wong, *J. Org. Chem.*, **26**, 4997 (1961).

(15) Reference to a product or company name does not imply endorsement by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

Chlorination of Aromatic N-Sulfinylamines

GERHARD OTTMANN AND HAYWOOD HOOKS, JR.

Olin Mathieson Chemical Corporation, Chemicals Division, New Haven, Connecticut

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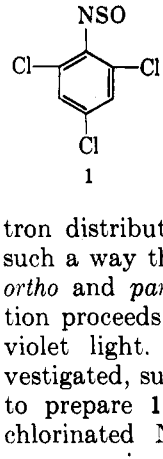
The chlorination of aromatic N-sulfinylamines has received little attention in the past. It is presently accepted that the chlorination proceeds under rupture of the N═SO bond to the corresponding amine hydrochlorides.[1] Thus, Michaelis[2] obtained 2,4,6-trichloroaniline hydrochloride in an undisclosed yield by chlorination of N-sulfinylaniline. The formation of chlorination products which have retained their –NSO groups was apparently not observed in this reaction. In our search for preparative methods for polychlorinated aromatic mono- and diamines we have investigated the chlorination of some aromatic N-sulfinylamines.

Exhaustive chlorination of N-sulfinylaniline in carbon tetrachloride at 20 and 75° afforded 2,4,6-trichloroaniline hydrochloride in only 28% yield, and a small amount of a mixture of chlorinated N-sulfinylanilines. A dark, undistillable tar was the dominating reaction product. In a striking contrast to the complete conversion of N-sulfinylaniline, N,N′-disulfinyl-*p*-phenylenediamine failed to react with chlorine in carbontetrachloride, as well as in a CCl$_4$–SOCl$_2$ mixture, and was recovered quantitatively.

We have now found that aromatic N-sulfinylamines can be readily chlorinated to N-sulfinylpolychloroarylamines in pure thionyl chloride as solvent. This method is also applicable to sulfinylamines, such as N,N′-disulfinyl-*p*-phenylenediamine, which do not react with chlorine in an indifferent solvent or in a SOCl$_2$–solvent mixture. By this method, we have synthesized N-sulfinyl-2,4,6-trichloroaniline (**1**), N,N′-disulfinyl-2,4,6-trichloro-*m*-phenylenediamine (**2**), and N,N′-disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine (**3**) in good yields and high purity. It is assumed that the chlorination-promoting effect of the thionylchloride results from an interaction of the polar SOCl$_2$[3] with the N-sulfinylamines whereby the electron distribution of the –NSO group is polarized in such a way that electrophilic attack of the chlorine in *ortho* and *para* position is facilitated. The chlorination proceeds in absence of both a catalyst and ultraviolet light. Among other chlorination agents investigated, sulfuryl chloride was successfully employed to prepare **1**, **2**, and **3** from the corresponding unchlorinated N-sulfinylamines. Slightly lower yields were experienced in the SO$_2$Cl$_2$ chlorinations.



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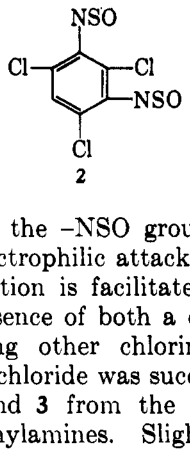

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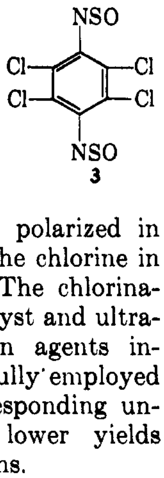

3

The preparations of compounds **1**, **2**, and **3** from the corresponding amines do not require the isolation of the unchlorinated sulfinylamines but can conveniently be done as one-step reaction by dissolving the amine in excessive SOCl$_2$ and chlorinating the reaction mixture in the same reactor at a reaction temperature of between 50 and 60°.

Strong absorptions in the infrared spectra of compounds **1**, **2**, and **3** at 1195, 1191, and 1174 cm.$^{-1}$, respectively, are tentatively assigned to the –NSO group vibration which in case of N-sulfinylaniline has a band at 1160 cm.$^{-1}$.[4] Another strong infrared absorption of N-sulfinylaniline at about 1300 cm.$^{-1}$ had been associated with the –NSO group. We have observed absorptions at 1300 cm.$^{-1}$ in case of **1**, at 1284 cm.$^{-1}$ in case of **2**, and at 1250 cm.$^{-1}$ in case of **3**. In addition, N,N′-disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine has a medium-to-strong band at 1228 cm.$^{-1}$, which is missing in the other three sulfinylamines.

Compounds **1**, **2**, and **3** are more stable to moisture and dilute mineral acids than their parent compounds. For instance, pure N,N′-disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine (**3**) did not show a very appreciable degree of decomposition upon storage for several months; under the same environmental conditions, N,N′-disulfinyl-*p*-phenylenediamine decomposed completely within a few hours.

Compounds **1**, **2**, and **3** are quantitatively converted to 2,4,6-trichloroaniline (**4**), 2,4,6-trichloro-*m*-phenylenediamine (**5**), and 2,3,5,6-tetrachloro-*p*-phenylenediamine (**6**), respectively, by treatment with aqueous alkali at room temperature or with boiling, dilute mineral acids. The amines **4**, **5**, and **6** were identified by melting point and elemental analysis. The structure of compound **5** was confirmed by n.m.r. spectroscopy.[5]

In summary, the chlorination of aromatic amines in thionyl chloride to form polychlorinated aromatic N-sulfinylamines is a convenient method for the preparation of polychlorinated aromatic amines which are otherwise not easily accessible, such as compound **6**.[6]

Experimental

Melting points and boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer 137B.

N-Sulfinyl-2,4,6-trichloroaniline (1).—To 400 ml. (655 g.) of thionyl chloride was added 93 g. (1.0 mole) of aniline dropwise and with stirring at 50 to 60°. The reaction is accompanied by heavy HCl evolution and formation of a precipitate. After complete addition, the mixture was stirred for additional 2 hr., and then 742 g. of sulfuryl chloride was added over a period of 5 hr. while the reaction temperature was maintained at 50–60°. After the heavy HCl evolution had ceased, thionyl chloride was removed from the clear but dark solution by distillation *in vacuo*, and the resulting oil was allowed to crystallize upon standing overnight. The precipitate was separated by filtration and afforded, after recrystallization from *n*-pentane, 130 g. (54% yield) of pure N-sulfinyl-2,4,6-trichloroaniline, m.p. 52.5–53.5°.

Anal. Calcd. for C$_6$H$_2$Cl$_3$NOS: Cl, 43.90; N, 5.77. Found: Cl, 43.80; N, 5.82.

A sample of 5 g. of compound **1** was treated with 50 ml. of 2 *N* aqueous sodium hydroxide affording 3.8 g. (95% yield) of 2,4,6-trichloroaniline, m.p. 77–78°.

N,N′-Disulfinyl-2,4,6-trichloro-*m*-phenylenediamine (2).—An amount of 21.6 g. (0.2 mole) of *m*-phenylenediamine was added in small increments to 120 ml. (196 g., 1.6 moles) of thionyl chloride with stirring but without external cooling. When the exothermic reaction had ceased, the mixture was stirred for 15 hr. at room temperature. Then, the reaction mixture was heated to 60–65° while chlorine was passed into it over a period of 6.5 hr. at a rate of 9 g./hr. The precipitate had now dissolved and a dark but clear solution was obtained. After filtration from some solid which had formed upon cooling, thionyl chloride was removed by distillation under atmospheric pressure affording 49 g. (0.16 mole, 80%) of crude N,N′-disulfinyl-2,4,6-trichloro-*m*-phenylenediamine. Distillation *in vacuo* afforded 39 g. (0.13 mole, 65%) of a dark orange-colored oil (b.p. 139–141° at 0.5

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(1) G. Kresze, *et al.*, *Angew. Chem.*, **74**, 139 (1962).

(2) A. Michaelis, *Ann.*, **274**, 201 (1893).

(3) H. Spandau and E. Brunneck, *Z. Anorg. Chem.*, **270**, 201 (1952); **278**, 197 (1955).

(4) G. Kresze and A. Maschke, *Ber.*, **94**, 450 (1961).

(5) N. S. Dokunikhin and M. M. Sergeeva, *Dokl. Akad. Nauk SSSR*, **88**, 987 (1953).

(6) V. S. F. Berkmans and A. F. Holleman, *Rec. trav. chim.*, **44**, 851 (1925); R. Adams and D. S. Acker, *J. Am. Chem. Soc.*, **74**, 3029 (1952).

mm, n^{22}_{D} 1.6835) which solidified upon standing. Recrystallization from hexane afforded pure N,N′-disulfinyl-2,4,6-trichloro-*m*-phenylenediamine, m.p. 54–55°.

Anal. Calcd. for $C_6HCl_3N_2O_2S_2$: C, 23.73; H, 0.33; N, 9.23; S, 21.08. Found: C, 23.84; H, 0.50; N, 9.23; S, 20.86.

Treatment of 16 g. of N,N′-disulfinyl-2,4,6-trichloro-*m*-phenylenediamine with 50 ml. of 20% aqueous sodium hydroxide afforded 10 g. of pure 2,4,6-trichloro-*m*-phenylenediamine,[5] m.p. 140–141° (91% yield).

N,N′-Disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine (3).—An amount of 108 g. (1.0 mole) of *p*-phenylenediamine was added portionwise over a period of 30 min. to 600 ml. (983 g., 8.25 moles) of thionyl chloride with agitation. During the addition, the temperature of the reaction mixture was maintained at 50 to 65° by means of an oil bath kept at 50 to 55°. After stirring for additional 2 hr., an amount of 281 g. (7.92 moles) of chlorine was passed over a period of 4.5 hr. into the reaction mixture at 55 to 65°.

N,N′-Disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine precipitated slowly from the warm reaction mixture and was separated by filtration after the chlorination was completed (indicated by the presence of chlorine gas in the condenser), and the reaction mixture cooled to 0°. Recrystallization from carbon tetrachloride afforded 250 g. (75% yield) of compound **3**, m.p. 171–172°, in form of yellow needles.

Anal. Calcd. for $C_6Cl_4N_2O_2S_2$: C, 21.32; Cl, 42.00; N, 8.29; S, 18.93. Found: C, 21.60; Cl, 42.20; N, 8.20; S, 18.40.

Chlorination of N,N′-disulfinyl-*p*-phenylenediamine with sulfuryl chloride in thionyl chloride afforded compound **3** in a yield of 43%.

A nearly quantitative yield of 2,3,5,6-tetrachloro-*p*-phenylenediamine (**6**), m.p. 224–225°, was obtained by treatment of N,N′-disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine with either 15% aqueous sodium hydroxide at room temperature or with boiling hydrochloric acid.

Acknowledgment.—The authors are indebted to Mr. J. Pregler for technical assistance and to Dr. H. Agahigian for taking the n.m.r. spectra.

The Triacetyl-D-glucal Dichlorides

Morton S. Lefar and C. Edwin Weill

Department of Chemistry, Rutgers, The State University, Newark, New Jersey

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Dihalogen addition products of the glycals and triacetyl glycals are formed quite readily by the direct addition of halogen to the unsaturated linkage. Inspection of I shows that carbon atoms 1 and 2 may become asymmetric and thus afford four different stereoisomers.

Fischer, Bergmann, and Schotte[1] reported that the chlorination of triacetyl-D-glucal (I) afforded a crystalline product of m.p. 92–94°, the optical rotation of which varied with the number of recrystallizations. Danilov and Gakhokidze[2] reported m.p. 89–92° for this material.

The addition of bromine to triacetyl-D-glucal has recently been studied by Lemieux and Fraser-Reid.[3] N.m.r. analysis of the sirupy product showed that it was a mixture of tri-*O*-acetyl-2-bromo-2-deoxyglycopyranosyl bromides containing about 60% and 30% of the compounds with the α-D-*gluco* and α-D-*manno* configurations, respectively.

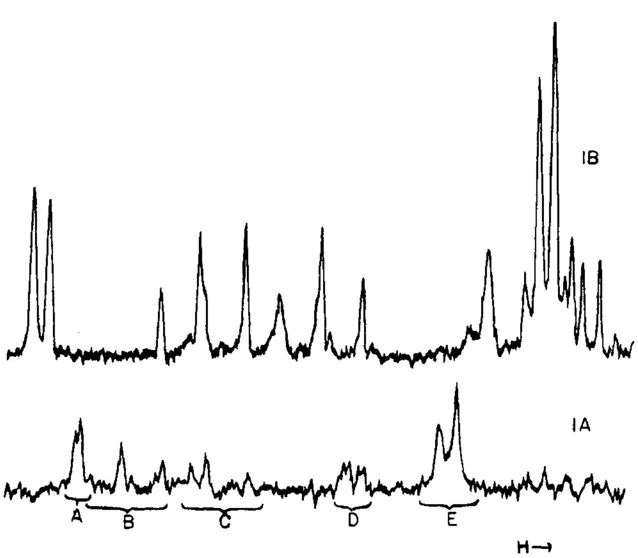
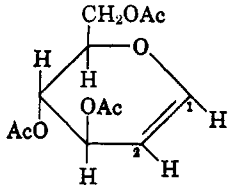


Figure 1.—The n.m.r. spectra of (A) tri-*O*-acetyl-2-chloro-2-deoxy-α-D-mannopyranosyl chloride; and (B) the *gluco* stereoisomer

Experiments in our laboratories have been designed to separate and identify the isomers formed on chlorination of triacetyl-D-glucal. Two such compounds have been separated from the dichloro addition product and, by means of n.m.r. spectroscopy, have been shown to be triacetyl-2-chloro-2-deoxy-α-D-glucopyranosyl chloride (III) and triacetyl-2-chloro-2-deoxy-α-D-mannopyranosyl chloride (II).



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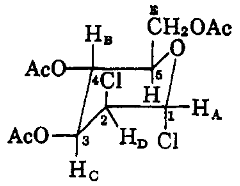

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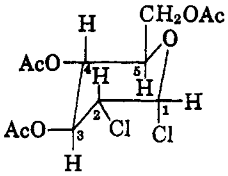

III

The n.m.r. spectra of compound III (Figure 1B) showed a doublet at 6.08 p.p.m. with $J = 3$ c.p.s. and two triplets centered at 5.08 ($J = 8$ c.p.s.) and 5.42 p.p.m. ($J = 8$ c.p.s.).

Lemieux[4] has shown that the coupling constants between the vicinal hydrogen atoms of pyranose monosaccharides in diaxial, diequatorial, and axial-equatorial conformations are *ca.* 7, 3, and 3 c.p.s., respectively. Since the signal at 6.08 p.p.m. is assigned to the anomeric proton, it follows that III has the α-D-*gluco* configuration.

The n.m.r. spectrum of II (Figure 1A) showed a signal at 5.54 p.p.m. (labeled A) which is coupled to a proton whose resonance appears at about 4.52 p.p.m.

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[1] E. Fischer, M. Bergmann, and H. Schotte, *Ber.*, **53**, 509 (1920).

[2] S. N. Danilov and A. M. Gakhokidze, *J. Gen. Chem. USSR*, **6**, 704 (1936); *Chem. Abstr.*, **30**, 633 (1936).

[3] R. U. Lemieux and B. Fraser-Reid, *Can. J. Chem.*, **42**, 532 (1964). This reference contains an excellent discussion of the stereochemical aspects of the halogenation reaction.

[4] R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, **81**, 6098 (1958).