51-1; Me-IV, 15038-69-4; Bz-IV, 15038-70-7; Me-VIII, 15038-71-8; Bz-VIII, 14897-54-2; Me-IX, 14897-55-3; Bz-IX, 14897-56-4; Bz-X, 15038-75-2; Me-XI, 15038-72-9; XI, 15038-73-0; benzyl β-D-galactopyranoside, 14897-46-2.

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Chlorination of Unsymmetrical Benzylic Sulfides with N-Chlorosuccinimide[1]

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The chlorination of eight unsymmetrical benzylic sulfides with N-chlorosuccinimide has been investigated. The resulting mixtures of α-chloro sulfides have been analyzed using nmr spectrometry. The results of these internal competitions are correlated by the Hammett treatment: ρ for the reaction is 1.05 ± 0.04.

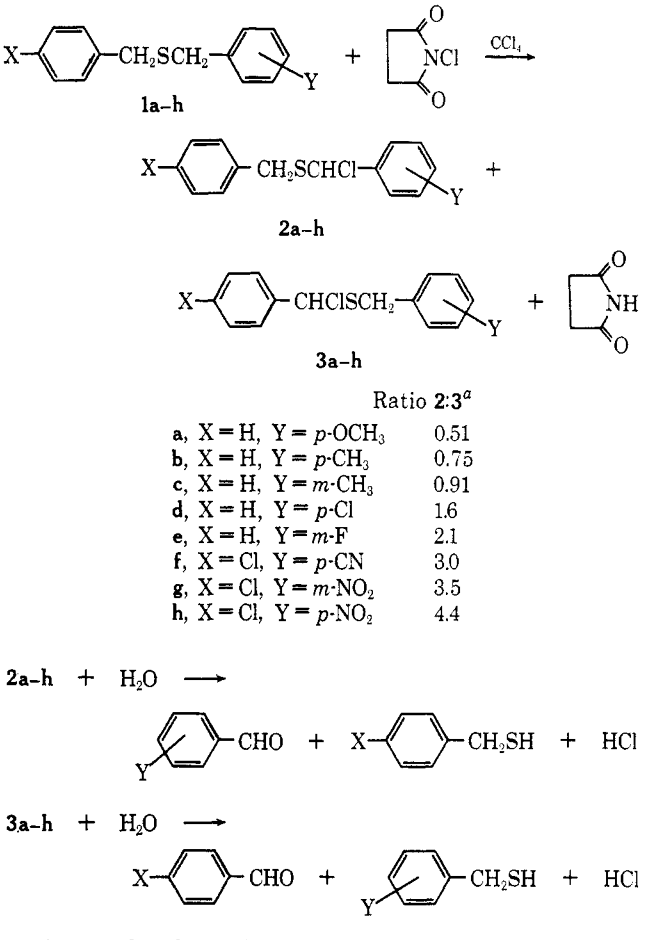
The reaction between benzylic sulfides and N-chlorosuccinimide (NCS) in carbon tetrachloride has previously been shown[2,3] to yield α-chloro sulfides, with no cleavage or ring halogenation. Chlorination of benzyl p-chlorobenzyl sulfide (**1d**) with NCS produced a mixture of the two α-chloro sulfides, benzyl α,p-dichlorobenzyl sulfide (**2d**) and α-chlorobenzyl p-chlorobenzyl sulfide (**3d**); the major component of the mixture was chloro sulfide **2d**. A more complete study of such internal competitive chlorination has now been performed on a series of unsymmetrical benzylic sulfides.

Sulfides **1a–h** were synthesized from the appropriate benzylic halides and potassium mercaptides in ethanol. Nmr spectra of the sulfides were consistent with their structure; satisfactory elemental analyses were obtained on those which have not been previously reported.

Chlorination of each of the sulfides with NCS at room temperature in carbon tetrachloride afforded a mixture of α-chloro sulfides **2** and **3** (Scheme I). The nmr spectra of these mixtures displayed in addition to aromatic multiplets two singlets corresponding to the methinyl hydrogens. The methylene protons of the α-chloro sulfide products are rendered nonequivalent by the asymmetric center at the site of chlorination; they appear in these spectra as two doublets of doublets.

The relative amounts of **2** and **3** in these mixtures was generally assessed by evaluation of the relative areas of the methinyl hydrogen singlets. These peaks appear in the region of 5.65–5.8 ppm and are shifted downfield by 2.2–2.3 ppm relative to the methylene groups of the starting sulfides.[4] The methinyl singlets of the products resulting from the chlorination of **1a** and **1b** were not resolved by the 60-Mc spectrometer employed. The relative amounts of chloro sulfides in these product mixtures was determined by evaluation of the relative areas of the singlets due to the methyl groups.

SCHEME I



	Ratio 2:3[a]
a, X = H, Y = p-OCH_3	0.51
b, X = H, Y = p-CH_3	0.75
c, X = H, Y = m-CH_3	0.91
d, X = H, Y = p-Cl	1.6
e, X = H, Y = m-F	2.1
f, X = Cl, Y = p-CN	3.0
g, X = Cl, Y = m-NO_2	3.5
h, X = Cl, Y = p-NO_2	4.4

[a] Averaged values of several traces of the nmr spectra. Peak areas were determined using a Keuffel and Esser planimeter, Model 620005.

The identity of the predominant component of each mixture of α-chloro sulfides was established by hydrolysis. Aldehydes, produced in the hydrolyses, were identified by examination of the nmr spectra and augmentation with authentic samples. The predom-

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(1) Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Louisville, Ky., Oct 1966.

(2) D. L. Tuleen and T. B. Stephens, *Chem. Ind.* (London), 1555 (1966).

(3) D. L. Tuleen and V. C. Marcum, *J. Org. Chem.*, **32**, 204 (1967).

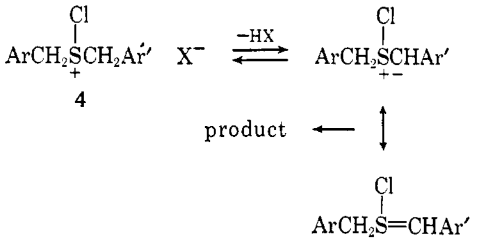
(4) A shielding constant of 2.53 for chlorine has been reported for disubstituted methylenes: R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1964, p 87.

inant aldehyde corresponds to the benzylic moiety which is preferentially chlorinated (Scheme I).

The results of these internally competitive chlorinations are summarized in Scheme I. The relative reactivities are expressed as the ratios of chloro sulfides obtained in the halogenations. Correlation of these data by the Hammett σp treatment[5] affords a ρ value of 1.05 ± 0.04, determined by the method of least squares (Figure 1).[6]

The data presented are consistent with mechanisms previously proposed for the chlorination of sulfides with sulfuryl chloride[7,8] and for the chlorination of benzylic sulfides by NCS.[3] The directive effects are readily interpreted in terms of the preferential abstraction of the more acidic hydrogen from an intermediate chlorosulfonium salt, **4**, by an anionic species, X^- (Scheme II). The base, X^-, could conceivably be the succinimidyl anion, if NCS were the species which donated a chloronium ion to the sulfide. The base could also be chloride ion, if the chlorination proceeded by an ionic chain mechanism involving a continously regenerated small concentration of molecular chlorine.[9]

SCHEME II



Experimental Section[10]

Reagents.—N-Chlorosuccinimide was recrystallized from eight times its weight of hot water and dried in air. Spectrograde carbon tetrachloride, obtained from Matheson Coleman and Bell, was used without further purification. The thiols, benzylic halides, and aldehydes were all commercially available and were used as received.

Sulfides 1a–h.—The method employed for the synthesis of the unsymmetrical benzylic sulfides is illustrated for benzyl *p*-methoxybenzyl sulfide (**1a**). Nmr spectra of sulfides **1a–h** were consistent with the assigned structures. To a solution of potassium hydroxide (3.3 g, 0.059 mole) in 80 ml of 95% ethanol was added *p*-methoxy-α-toluenethiol (9.0 g, 0.058 mole). The solution was stirred at room tempetature while a solution of benzyl chloride (7.5 g, 0.059 mole) was slowly added. After the addition was complete, the mixture was refluxed for 1 hr before it was cooled. Water was added and the sulfide was extracted into ether. The ether extracts were washed with water, dried over sodium sulfate, evaporated, and the residue was recrystallized from methanol to afford benzyl *p*-methoxybenzyl sulfide, 10.9 g (77%), mp 40–45°. Further recrystallization gave material of mp 46–47°.

Anal. Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60. Found: C, 73.92; H, 6.74.

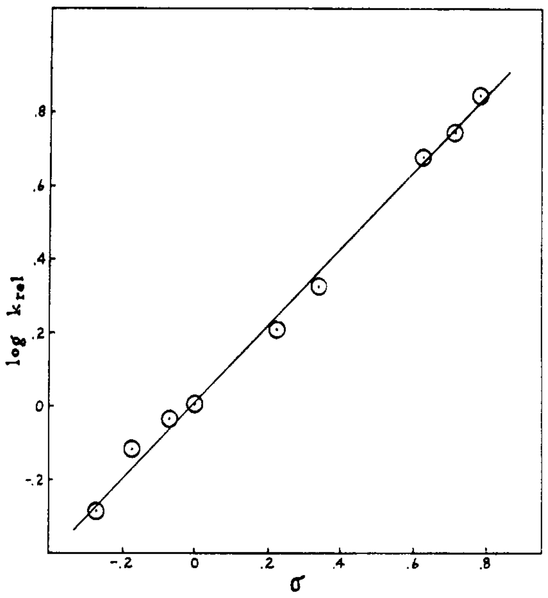


Figure 1.—Correlation of log k_{rel} for chlorination of unsymmetrical benzylic sulfides with N-chlorosuccinimide *vs.* σ.

Benzyl *p*-methylbenzyl sulfide (**1b**), mp 28–31° was synthesized in 53% yield from benzyl mercaptan and α-chloro-*p*-xylene. Recrystallization from methanol afforded material of mp 29–31°.

Anal. Calcd for $C_{15}H_{16}S$: C, 78.85; H, 7.06. Found: C, 78.86; H, 6.95.

Benzyl *m*-methylbenzyl sulfide (**1c**), prepared in 54% yield from benzyl mercaptan and α-chloro-*m*-xylene, was purified by distillation: bp 140–141° (1 mm), $n^{27}\text{D}$ 1.5941 (lit.[11] bp 193–196° (15 mm)).

Anal. Calcd for $C_{15}H_{16}S$: C, 78.85; H, 7.06. Found: C, 78.96; H, 7.10.

Benzyl *p*-chlorobenzyl sulfide (**1d**) was prepared as described previously,[3] bp 144–145° (0.1 mm), $n^{26}\text{D}$ 1.6089.

Anal. Calcd for $C_{14}H_{13}ClS$: C, 67.59; H, 5.27. Found: C, 68.17; H, 5.20.

Benzyl *m*-fluorobenzyl sulfide (**1e**) was prepared from benzyl mercaptan and *m*-fluorobenzyl chloride in 53% yield, bp 134–135° (1 mm) (lit.[12] bp 140–142° (0.2 mm)).

p-Chlorobenzyl *p*-cyanobenzyl sulfide (**1f**) was synthesized in 73% yield from *p*-chlorobenzyl mercaptan and α-chloro-*p*-tolunitrile, mp 76–78°. Recrystallization from methanol afforded material of mp 77–78°.

Anal. Calcd for $C_{15}H_{12}ClNS$: C, 65.80; H, 4.42. Found: C, 65.69; H, 4.56.

p-Chlorobenzyl *m*-nitrobenzyl sulfide (**1g**) was synthesized in 75% yield from *p*-chlorobenzyl mercaptan and *m*-nitrobenzyl chloride. Recrystallization from methanol gave material of mp 52–53.5°.

Anal. Calcd for $C_{14}H_{12}ClNO_2S$: C, 57.24; H, 4.12. Found: C, 56.95; H, 4.04.

p-Chlorobenzyl *p*-nitrobenzyl sulfide (**1h**) was prepared from *p*-chlorobenzyl mercaptan and *p*-nitrobenzyl bromide.[13] Recrystallization from methanol afforded 57% of the sulfide, mp 91–93°. Further recrystallization gave material of mp 91.5–93°.

Anal. Calcd for $C_{14}H_{12}ClNO_2S$: C, 57.24; H, 4.12. Found: C, 56.98; H, 4.19.

Chlorination of Sulfides.—To a solution of a known quantity of sulfide (about 1 g)[14] in 10 ml of spectrograde carbon tetrachloride was added an equimolar amount of N-chlorosuccinimide. The temperature was maintained at 20–25° as the mixture was stirred magnetically for 30–45 min. Succinimide

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(5) K. B. Wiberg, "Physical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1964, p 403.

(6) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

(7) W. E. Truce, G. H. Birum, and E. T. McBee, *J. Am. Chem. Soc.*, **74**, 3594 (1952).

(8) F. G. Bordwell and B. M. Pitt, *ibid.*, **77**, 572 (1955).

(9) J. Adams, P. A. Gosselain, and P. Goldfinger, *Bull. Soc. Chim. Belges*, **65**, 523 (1956).

(10) Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are corrected. Analyses were performed by the Galbraith Laboratories, Knoxville, Tenn. Nmr spectra were recorded on a Varian Associates A-60 spectrometer, employing tetramethylsilane as an internal reference. The nmr spectrometer was purchased with a grant from the National Science Foundation (GP 1683).

(11) H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **26**, 185 (1901).

(12) J. V. Braun and A. Friedsam, *Ber.*, **63B**, 2407 (1930).

(13) This benzylic halide is sparingly soluble in ethanol; the solid was added directly to the ethanolic solution of the potassium mercaptide.

(14) *p*-Chlorobenzyl *p*-nitrobenzyl sulfide was much less soluble in carbon tetrachloride than the other compounds studied; in this case a solution of 0.8 g of the sulfide in 20 ml of solvent was chlorinated.

was removed by filtration and the filtrate was analyzed by nmr spectrometry. The spectra were run at minimum sweep width (50 cps); low radio frequency field use minimized saturation.

Hydrolysis of the Chloro Sulfides.—Each of the product mixtures was combined with 50 ml of water and stirred overnight. The layers were separated, the aqueous phase was extracted once with carbon tetrachloride, and the combined organic phase was washed once with water and dried over calcium chloride. Examination of the aldehydic region of the nmr spectra of the hydrolysates and augmentation indicated that predominant chlorination had occurred as indicated in Scheme I. The yields of aldehyde appeared to be essentially quantitative. The aldehydic proton of *m*-fluorobenzaldehyde appeared as two peaks, as noted by Klinck and Stothers.[15]

Acknowledgment.—Acknowledgment is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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[15] R. E. Klinck and J. B. Stothers, *Can. J. Chem.*, **40**, 1071 (1962).

The Chlorination of Aldehydes by Cupric Chloride

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Butyraldehyde and isobutyraldehyde undergo α chlorination in almost quantitative yield on refluxing with $CuCl_2$ in aqueous isopropyl alcohol or aqueous acetone (which is not attacked). A kinetic study of the isobutyraldehyde reaction in aqueous acetone shows a process first order in both aldehyde and copper, catalyzed by both acid and chloride ion and retarded by CuCl. Comparison with literature data indicates that the chlorination is more rapid than acid-catalyzed enolization and possible reaction paths are discussed.

The chlorination of acetone by cupric chloride was first observed by Kohlschütter,[2] and the kinetics of the reaction were studied by Kochi,[3] who also showed[4] its significance in the Meerwein reaction between diazonium salts and olefins. More recently Kosower[5] has reported that the reaction, conducted in dimethylformamide solvent, is a good general procedure for ketone halogenation, and both he[5,6] and Castro[7] have examined the reactions of cupric chloride with a number of other substrates and have reviewed the older literature in detail.

In the course of an investigation aimed at generating radicals *via* redox processes we have found that aldehydes are also cleanly halogenated by cupric chloride in partially aqueous systems *via* the reaction shown in eq 1.

$$R_2CHCHO + 2CuCl_2 \rightarrow R_2CClCHO + HCl + 2CuCl \quad (1)$$

Since reaction of aldehydes with inorganic oxidizing agents leads in general to either formation of acids or extensive degradation, this little known reaction is both striking and of potential synthetic value. As far as we are aware, its only mention in the literature is a brief observation by Castro[7] and a description of a high temperature continuous process in the patent literature for the chlorination of isobutyraldehyde.[8]

General Characteristics of the Reaction.—The products of reaction between aldehydes and cupric chloride depend markedly on reaction conditions. In nonaqueous solvents the copper is reduced, but either HCl produced or copper salts acting as Lewis acids lead to extensive acid-catalyzed reactions. Thus refluxing *n*-butyraldehyde with a small amount of $CuCl_2$ either alone or in acetonitrile yields chiefly 2-ethyl-2-hexenal, while in isopropyl alcohol the major products are acetals. In contrast, refluxing equimolar quantities of $CuCl_2$ and butyraldehyde (1.02 *M* in 3:1 isopropyl alcohol–water) for 1 hr gives 90% α-chlorobutyraldehyde by gas–liquid partition chromatography (glpc) on the basis of eq 1 with the balance of the aldehyde remaining unchanged. The reaction also proceeds in aqueous *t*-butyl alcohol and aqueous acetone, with, in the last case, negligible chlorination of solvent.

Isobutyraldehyde is chlorinated even more rapidly and in refluxing 4:1 isopropyl alcohol–water gives 95% α-chloroisobutyraldehyde in 5 min. In aqueous acetone the yield is 96%, again without chlorination of solvent. When cupric acetate was used in place of $CuCl_2$, no reaction was detected.

The reaction of acetaldehyde is much more sluggish and the products were not investigated, while no reduction of copper was observed on heating $CuCl_2$ in aqueous isopropyl alcohol with either benzaldehyde or pivalaldehyde. Reactions of other metal halides were not investigated in detail, but ferric chloride, which is not reduced by refluxing aqueous acetone, was observed to react slowly with added isobutyraldehyde, giving α-chloroisobutyraldehyde in 77% yield based on iron reduced. The effects of some other variables on the $CuCl_2$ reaction are discussed below, but, in summary, the reaction appears a remarkably clean and simple route for the chlorination of aldehydes possessing reactive α-hydrogen, perhaps taking advantage of the catalysis by acid and chloride ion mentioned below.

Kinetics.—Since the reaction in aqueous solvents closely follows the stoichiometry of eq 1, kinetics were followed by consumption of cupric ion, determined by iodometric titration, using, in general, excess aldehyde to maintain essentially constant aldehyde concentrations. No attempt was made to ensure constant ionic strength, since only gross effects were investigated.

Although cuprous chloride is insoluble in aqueous acetone or isopropyl alcohol, a significant quantity remains in solution at the end of the reaction, apparently solubilized by chloride ion from the HCl pro-

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[1] Postdoctoral Fellow on leave from Montecatini Edison S.p.A., Bollate (Milano), Italy. Support of this work by Montecatini Edison S.p.A. is gratefully acknowledged.

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[4] J. K. Kochi, *ibid.*, **77**, 5090 (1955).

[5] E. M. Kosower, W. J. Cole, G. S. Wu, D. E. Cardy, and G. Meisters, *J. Org. Chem.*, **28**, 630 (1963).

[6] E. M. Kosower and G. S. Wu, *ibid.*, 633 (1963).

[7] C. E. Castro, E. J. Gaughan, and D. C. Owsley, *ibid.*, **30**, 587 (1965).

[8] Farbewerke Hoechst A. G., French Patent 1,369,565 (Aug 14, 1964); *Chem. Abstr.*, **62**, 10340 (1965).