[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE RICE INSTITUTE]

THE EFFECT OF STRUCTURE OF ORGANIC HALIDES ON THEIR RATE OF REACTION WITH INORGANIC HALIDES. II. THE EFFECT OF THE METHYLTHIO GROUP. A NEW VESICANT[1]

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A study of the effect of a sulfur atom on the reactivity of an ω-chlorine atom which is in the same molecule and separated by one, two or three methylene groups should be of interest in connection with the "acid theory" for the mechanism of skin vesication of mustard gas proposed by Lynch, Smith and Marshall[2] and contradicted by later work of Peters and Walker.[3]

To make the conditions for this investigation as simple as possible it was proposed to synthesize a series of sulfur-halogen compounds each of which contained but one chlorine atom; this avoided complications such as the reciprocal induced effect of one chlorine atom on another which might occur if more than one chlorine atom is present in the molecule. The series selected was the ω-chloroalkyl methyl sulfides, CH_3SCH_2Cl, $CH_3SCH_2CH_2Cl$ and $CH_3SCH_2CH_2CH_2Cl$. In these compounds the sulfur atom is attached on one side to the simplest alkyl radical and the chlorine atom is separated from the sulfur atom by one, two and three carbon atoms, respectively. The synthesis of the first member, unfortunately, was not successful; the reactivity of the second and third members was measured using the procedure which has been previously described.[4]

The following table contains the data obtained from the reaction velocity measurements.

TABLE I

REACTION VELOCITY DATA

Compound	K_{50}	K_{60}	A	Relative reactivity at 50°, *n*-butyl chloride taken as unity
n-C_4H_9Cl	0.0415	0.1189	4920	1.00
$CH_3SCH_2CH_2Cl$	.0629	.1666	4540	1.52
$CH_3SCH_2CH_2CH_2Cl$	.1044	.2373	3830	2.52

The above results illustrate still another case in which the γ-halogen compound is more reactive than the β, the ratio being 1.66:1.00 at 50° and 1.42:1.00 at 60°.[5] Although the first member of the series is missing it seems safe to predict that the α-compound would be more reactive than

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[1] Presented before the Detroit meeting of the American Chemical Society, September, 1927.

[2] Lynch, Smith and Marshall, *J. Pharmacol.*, **12**, 282 (1919).

[3] Peters and Walker, *Biochem. J.*, **17**, 260 (1923).

[4] Conant and Kirner, THIS JOURNAL, **46**, 232 (1924).

[5] Conant and Kirner, *ibid.*, **46**, 232 (1924); **47**, 488 (1925); Kirner, *ibid.*, **48**, 2745 (1926).

the β- and γ-compounds inasmuch as in all of the various homologous series which have been measured by this method the α-halogen compounds of a given series possess, without exception, a very much greater reactivity than any other member. Also, chlorodimethyl ether, CH_3OCH_2Cl, the oxygen analog of the missing sulfur compound, was found to possess a very reactive chlorine atom.[6] This is corroborated by the work of Kilpi[7] and Palomaa,[8] who measured the velocity of hydrolysis of various groups, such as Cl, COOR, OCOR, $CONH_2$ and CN when influenced by the presence of an alkyloxy group such as CH_3O, separated from each other by one, two or three methylene groups. In every case they found the order of reactivity to be $\alpha > \gamma > \beta$. Therefore, the evidence points to the existence in the series of ω-halogen alkyl methyl sulfides of a definite, though weak, alternation in reactivity of the chlorine atom through a saturated carbon chain as the chlorine atom is moved further and further from the activating methylthio group.

The relative order of reactivity of the first two members of the series confirms that of Peters and Walker[3] who found that the α,α'-dichlorodimethyl sulfide was hydrolyzed more rapidly than the β,β'-dichlorodiethyl sulfide. The relative reactivity of the β- and γ-chloro-alkyl methyl sulfides toward potassium iodide has recently been confirmed, quantitatively, by Bennett and Berry[9] in a study of the β- and γ-chloro-alkyl phenyl sulfides; they found that the γ-compound reacts about 3.5 times as fast as the β. The order was just reversed, however, when their reactivity was measured by hydrolysis in a 50% aqueous alcoholic solution according to the procedure of Olivier.[10] Although Bennett and Berry state that this method is "likely to be free from the defects of subsidiary reactions," Olivier has shown that the hydrolysis of benzyl chloride under the conditions of the experiment yields benzyl ethyl ether as well as benzyl alcohol, that is, both constituents of the solvent react with the halogen. The results obtained by Olivier on the reactivity of benzyl chloride and various substitution products do not agree with those of Franzen,[11] who carried out his measurements using sodium ethylate and thus worked in an alkaline solution.

The order of reactivity of the ω-chloro-alkyl methyl sulfides toward potassium iodide in absolute acetone solution is undoubtedly $\alpha > \gamma > \beta$; this is not in agreement with the order given by Bennett and Hock[12] for

[6] Conant, Kirner and Hussey, THIS JOURNAL, **47**, 489 (1925).

[7] Kilpi, *Z. physik. Chem.*, **80**, 165 (1912); **86**, 641 (1914).

[8] Palomaa, *Dissertation*, Helsingfors, **1908**; *Chem. Zentr.*, **83**, II, 595 (1912); **84**, II, 1956 (1913).

[9] Bennett and Berry, *J. Chem. Soc.*, **1927**, 1677.

[10] Olivier, *Rec. trav. chim.*, **41**, 301, 646 (1922); **42**, 516 (1923).

[11] Franzen, *J. prakt. Chem.*, **205**, 61 (1918); Franzen and Rosenberg, *ibid.*, **209**, 333 (1920); see von Braun and Engel, *Ann.*, **436**, 319 (1924).

[12] (a) Bennett and Hock, *J. Chem. Soc.*, **1927**, 478; (b) *ibid.*, **127**, 2676 (1925).

the rate of hydrolysis of the ω,ω'-dichlorodialkyl sulfides which they list as: $\alpha,\alpha' > \beta,\beta' > \gamma,\gamma' < \eth,\eth'$. *But, the order in which the* α,α' *and* β,β' *appear was taken from the paper of Peters and Walker, while the position of the* β,β' *was determined relative to the* γ,γ' *by comparative hydrolysis in an alcoholic alkaline solution. The* $\eth,\eth'$ *compound was not isolated and its reactivity was estimated from the reactivity of the corresponding dihydroxy compound.*

It should be pointed out that the hydrolysis of these dihalogen compounds has been quite well established as a two stage reaction,[13] a fact which may vitiate any conclusions which are drawn, since the reactivity of the two chlorine atoms will be different because the activating group in the first stage is quite different from that in the second. Still more important is the fact that Bennett and Hock measured the hydrolysis of the β,β'- and γ,γ'-dichlorodialkyl sulfides in a nearly $N/5$ alcoholic solution of sodium hydroxide. Although they assume the reaction to be one of simple replacement, it has been shown[14] that treatment of mustard gas with sodium ethylate yields vinyl sulfide as the main product. Even the slow hydrolysis of mustard gas by alkali in 50% alcohol in the cold does not yield thiodiglycol, but a substance which seems to be a polymer of vinyl sulfide. It is evident, therefore, that this reaction is not a simple replacement of the chlorine atom by the hydroxyl group but involves the elimination of hydrogen chloride from the β-chlorine and the rather reactive α-hydrogen atom. These observations were confirmed by Bales and Nickelson.[15]

The hydrolysis of the α,α'- and γ,γ'-compounds appears to proceed normally since, in the former, the halogens are attached to the same carbon atoms holding the active α-hydrogens and, in the latter, the halogens are removed a sufficient distance from the active α-hydrogens so that there is no tendency for the elimination of hydrogen chloride in either case. Bloch and Höhn[16] were able to substitute the two halogens in the α,α'-compound by methoxy groups using a methyl alcohol solution of potassium hydroxide or ammonium hydroxide; some dihydroxy compound was also formed which then decomposed into formaldehyde, thioformaldehyde and water. Bennett and Hock[12b] prepared the diphenoxy compound from the γ,γ'-dihalide and, although they do not report their yield, neither do they mention any of the difficulties which are expressed by Helfrich and Reid in the corresponding reaction on the β,β'-compound.

Therefore, the order of reactivity which is given by Bennett and Hock

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[13] Russell, Report to American Chemical Warfare Section; Wilson, Fuller and Schur, This Journal, **44**, 2762, 2867 (1922).

[14] Helfrich and Reid, This Journal, **42**, 1219, 1224 (1920).

[15] Nickelson, *J. Chem. Soc.*, **121**, 2137 (1922).

[16] Bloch and Höhn, *Ber.*, **55B**, 55 (1922).

is not derived from a study of the rate at which a given, clearly defined reaction proceeds, but instead is obtained from several reactions which differ in mechanism.

Vesicant Action

A drop of β-chloro-ethylmethyl sulfide from a 4mm. glass rod was applied to the skin on the left forearm and a similar drop of γ-chloropropylmethyl sulfide was applied to the right forearm. The liquid disappeared in the course of a few minutes. In the case of the β-chloroethyl compound a well defined blister, 1 cm. × 0.8 cm. and about 3 mm. high, had developed after about twenty hours and was surrounded by a reddened area about 2 cm. × 1.3 cm. The blister was punctured aseptically and pressed dry, but filled again. A brownish scar was still plainly evident ten months after the substance had been applied. Judging from war reports (for example, The American University Experiment Station Monograph on Dichlorodiethyl Sulfide) concerning the vesicant action of mustard gas, the above substance seems to act as rapidly and in precisely the same manner as does mustard gas. In fact, the description and photographs given by Warthin and Weller[17] concerning the action of mustard gas on a patient's forearm coincide exactly with the observations made by the author in an experiment performed on himself. The γ-chloropropylmethyl sulfide was found to possess no vesicant properties whatsoever.

It is quite apparent that *only when the halogen is in the β-position with respect to the sulfur atom will the resulting compound possess vesicant properties*. A search of the literature has revealed no case where an α-, γ- or ∂-halogenalkyl sulfide is reported and confirmed as a vesicant compound. There seems to be no obvious relationship between the reactivity of the chlorine atom (at least in replacement reactions) and vesicant action.

Experimental

A. Preparation of an Aqueous Solution of Potassium Methyl Mercaptide

Methyl mercaptan was prepared according to the directions of Klason (or Claesson)[18] who methylated sodium hydrosulfide with methyl sodium sulfate. The mercaptan was absorbed in a 50% solution of potassium hydroxide and the resulting solution was treated with a saturated solution of lead acetate until a filtered test portion yielded a brilliant yellow precipitate of lead methyl mercaptide uncontaminated with any black lead sulfide; this insured an aqueous solution of potassium methyl mercaptide free from potassium sulfide or hydrosulfide.

B. Preparation of an Anhydrous Ethereal Suspension of Sodium Methyl Mercaptide

An anhydrous ethereal solution of methyl mercaptan was prepared and converted into an anhydrous ethereal suspension of the sodium salt according to Klason.[19] The

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[17] Warthin and Weller, *J. Lab. Clin. Med.*, **3**, 454–459 (1917–1918).

[18] Klason, *Ber.*, **20**, 3408 (1887).

[19] Klason, *J. prakt. Chem.*, **15**, 196 (1877).

absence of water was imperative in the reaction with chloromethyl acetate since it is hydrolyzed readily, particularly in alkaline solution. Higher yields were obtained using the anhydrous suspension of the sodium mercaptide rather than the aqueous alkaline solution in the reactions with the chlorohydrins.

For the preparation of the anhydrous ethereal suspension of sodium methyl mercaptide the aqueous solution of the potassium salt was treated with 1:1 hydrochloric acid and the liberated methyl mercaptan was dried by passing it through a tower containing anhydrous potassium carbonate and then condensed by passing through a coil maintained at −20° and collected in anhydrous ether. The anhydrous ethereal solution thus obtained was placed in a large bottle; metallic sodium, in large pieces, was added and the bottle stoppered and protected from moisture by a calcium chloride tube; it was then placed in an ice-bath and allowed to stand overnight. The sodium did not react with the dissolved mercaptan, only a small amount of grayish sediment being present which was shown to be flakes of metallic sodium. When a little absolute methyl or ethyl alcohol was added to the ethereal solution the reaction started immediately with rapid evolution of hydrogen even at 0° and with the formation of a large amount of a beautiful white flaky precipitate.

The ether used as the solvent had been dried over calcium chloride, then over sodium and finally distilled from phosphorus pentoxide so that it was free from water and alcohol. Apparently a small amount of alcohol is necessary to catalyze the reaction between the sodium and the mercaptan. The mercaptan may be too weak an acid to react with the sodium directly though it reacts with either sodium methylate or ethylate. The following equations represent the probable mechanism of the reaction

$$CH_3SH + Na = \text{No reaction} \qquad (1)$$
$$2CH_3CH_2OH + 2Na = 2\,CH_3CH_2ONa + H_2 \qquad (2)$$
$$CH_3SH + CH_3CH_2ONa = CH_3SNa + CH_3CH_2OH \qquad (3)$$

The alcohol regenerated in Reaction 3 then reacts with more sodium and the cycle repeats until no more mercaptan remains. The non-reactivity of the alcohol-free ethereal solution of mercaptan was not due to the amount of surface exposed by the sodium because sodium wire was also used, which presented a much greater surface than the sticks of sodium originally used. There was no reaction in this case either until a small amount of alcohol was added.

On treating the total ethereal solution with absolute ethyl alcohol (12.5 cc. of alcohol per liter of the ethereal solution), cooling in an ice-bath and allowing the reaction to proceed overnight, it was found that the reaction took place readily and that next morning the bottle was over half full of a white fluffy precipitate of sodium methyl mercaptide. More sodium was added until the reaction was complete; any unreacted sodium was removed and the mercaptide allowed to stand under the ether until ready for use.

C. Preparation of Methylthio Methyl Acetate, $CH_3SCH_2OCOCH_3$

The reactions which were expected to result in the formation of the first member of the series follow.

$$\text{Anhydrous } CH_3SNa + ClCH_2OCOCH_3 = CH_3SCH_2OCOCH_3 + NaCl \qquad (1)$$
$$CH_3SCH_2OCOCH_3 + H_2O = CH_3SCH_2OH + CH_3COOH \qquad (2)$$
$$CH_3SCH_2OH + SOCl_2 = CH_3SCH_2Cl + HCl + SO_2 \qquad (3)$$

Reaction 1 proceeded smoothly and the new compound, methylthio methyl acetate was obtained. Hydrolysis, however, did not yield the expected products.

Chloromethyl acetate was made, using the directions of L. Henry,[20] by chlorination

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[20] Henry, *Ber.*, 6, 740 (1873).

of methyl acetate in the sunlight at 0–5°. A given weight of chloromethyl acetate was added dropwise to about a 10% excess of the ethereal suspension of sodum mercaptide in a flask fitted with a reflux condenser. It was found advisable to use an excess of the mercaptide because the final purification by fractional distillation was greatly simplified. An approximately determined weight of the mercaptide was obtained by shaking the ethereal suspension and pipetting off a definite volume, filtering and weighing the solid. From this weight the volume of suspension to be used in an experiment was determined.

The addition of each drop of chloromethyl acetate caused the ether to boil; the addition was regulated so that the ether slowly refluxed. When the addition was complete the mixture was refluxed three hours and allowed to stand overnight. Next morning the sodium chloride and unchanged mercaptide were filtered off and washed with ether, the filtrate transferred to a flask and the ether distilled off from a water-bath. The residue was placed in a Claissen fractionating flask and fractionated in vacuum. After three complete fractionations a product boiling at 53–55° at 11 mm. was obtained; this fraction was used for analysis. The boiling point at 20 mm. was 60–62°; yield, 38%. The yield could undoubtedly be improved, for the reaction was carried out with sodium mercaptide residues which contained about 10% of metallic sodium. The substance was analyzed by weighing it into a thin walled glass bulb which was sealed and heated to redness in a Parr sulfur bomb with 3 g. of sodium peroxide; the sulfur was determined as barium sulfate in the usual manner.

Anal. Subs., 0.1097: $BaSO_4$, 0.2155. Calcd. for $C_4H_8O_2S$: S, 26.7. Found: 27.0.

D. Attempt to Prepare Hydroxydimethyl Sulfide. Hydrolysis of Methylthio Methyl Acetate

The acetate described above was hydrolyzed using a 2.5% solution of hydrogen chloride in absolute methanol. The reaction mixture separated into two layers one of which was insoluble in ether and contained no sulfur and the other was soluble in ether. The latter, after two fractionations, boiled at 70–71° at 48 mm., and contained sulfur but gave a negative Beilstein test. Two analyses gave, respectively, 52.65 and 52.16% S. Calcd. for C_2H_6OS, 41.05. Obviously, some substance other than that desired was produced in the hydrolysis. In view of the instability of the dihydroxydimethyl sulfide prepared by Bloch and Höhn,[16] it is questionable whether the hydroxymethyl methyl sulfide is capable of existence. It probably decomposes readily into methyl mercaptan and formaldehyde.

E. Preparation of β-Hydroxyethyl Methyl Sulfide, $CH_3SCH_2CH_2OH$

The sodium methyl mercaptide was filtered from the ether in which it was suspended, dried on filter paper and its weight determined; 88 g. (1.26 moles) was used. This was placed in a one liter flask fitted with a stirrer and reflux condenser. Three hundred and fifty cc. of dry ether (the same ether from which the mercaptide had been filtered) was added and 101 g. (1.26 moles) of ethylene chlorohydrin was added dropwise. No reaction took place at first, so the flask was warmed in a water-bath until the ether started refluxing and on continued addition of the chlorohydrin enough heat was liberated by the reaction to keep the ether gently boiling. After all of the chlorohydrin was added the mixture was refluxed for three and one-half hours and allowed to stand overnight.

The precipitate of sodium chloride and unreacted mercaptide was filtered off and the ether distilled through a Glinsky column. The residue was transferred to a 300cc. Claissen fractionating flask and twice fractionated in vacuum; 90 g. of a product boiling from 62–70° at 16 mm. was obtained (the main portion boiled at 68–70°), which corresponds to a 78% yield. The product was a water white liquid of rather unpleasant odor, quite soluble in water and extremely soluble in alcohol and ether. Its boiling point at 30 mm. was 80.5–81°; $d_{20°}^{20°}$ = 1.0640; $n_D^{30°}$ = 1.4867.

Anal. Subs., 0.0725, 0.0743: $BaSO_4$, 0.1829, 0.1870. Calcd. for C_3H_8OS: S, 34.79. Found: 34.66, 34.58.

Using an aqueous alkaline solution of potassium methyl mercaptide in the reaction with ethylene chlorohydrin, similar to the method employed by Demuth and Meyer,[21] for the preparation of β-hydroxyethyl ethyl sulfide, the yield was but 33%.

F. Preparation of γ-Hydroxypropyl Methyl Sulfide, $CH_3SCH_2CH_2CH_2OH$

The procedure used was exactly the same as described above for the lower homolog. One hundred and five grams (1.5 moles) of dry sodium methyl mercaptide in suspension in 360 cc. of ether and 141.8 g. (1.5 moles) of trimethylene chlorohydrin were used. Two fractionations yielded 120 g. of a product boiling from 90–97° at 17 mm., the bulk of the material distilling from 93–94°; yield, 76%. The product was a water white liquid of unpleasant odor. It was fairly soluble in water and very soluble in alcohol and ether; boiling point at 30 mm., 105–105.5°; $d_{20°}^{20°}$ = 1.0314; $n_D^{30°}$ = 1.4832.

Anal. Subs., 0.0888: $BaSO_4$, 0.1973. Calcd. for $C_4H_{10}OS$: 30.2. Found: 30.53.

Using an aqueous alkaline solution of the potassium salt gave a yield of 54.5%.

G. Preparation of β-Chloro-ethyl Methyl Sulfide, $CH_3SCH_2CH_2Cl$

This substance was prepared by treatment of the corresponding hydroxy compound with thionyl chloride, using chloroform as the solvent according to the procedure of Steinkopf, Herold and Stöhr.[21b] The entire reaction was carried out in the same flask from which the product was finally distilled. This precaution was taken because of the similarity in structure of this substance to mustard gas and to β-chloro-ethyl ethyl sulfide (which Meyer[22] states is poisonous, but less so than mustard gas).

Fifty grams (0.54 mole) of β-hydroxyethyl methyl sulfide was dissolved in 100 g. of dry chloroform and placed in a 300-cc. Claissen fractionating flask which was fitted with a thermometer in place for distillation, with a dropping funnel, and with its side arm protected by a calcium chloride tube; 83.3 g. (0.7 mole) of thionyl chloride dissolved in 200 g. of dry chloroform was placed in the dropping funnel and added dropwise. Each drop produced an evolution of sulfur dioxide and hydrogen chloride and the mixture warmed up and so was cooled at intervals by immersion in ice water. Vigorous shaking was maintained.

After a small amount of thionyl chloride had been added, each additional drop produced a local turbidity which finally resulted in the separation of a layer on the surface of the chloroform. About one hour was required for the addition of the thionyl chloride. The mixture was allowed to stand at room temperature for one and one-half hours and then the chloroform was distilled off from a boiling water-bath. During this process the upper oily layer disappeared and the solution became homogeneous. The residue was systematically fractionated in vacuum. After two fractionations a product boiling at 55–56° at 30 mm. was obtained. The yield in a number of experiments varied between 70 and 80%.

The product was a water white liquid with an odor resembling that of mustard gas. The boiling point at 20 mm. was 44°; $d_{20°}^{20°}$ = 1.1245; $n_D^{30°}$ = 1.4902.

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[21] (a) Demuth and Meyer, *Ann.*, **240**, 310 (1887). (b) See also Steinkopf, Herold and Stöhr, *Ber.*, **53B**, 1010 (1920).

[22] Meyer, *Ber.*, **20**, 1729 (1887).

Anal. Subs., 0.1653, 0.1974: $BaSO_4$, 0.3526, 0.4221. Calcd. for C_3H_7SCl: 28.99. Found: 29.30, 29.37.

An unsuccessful attempt was made to prepare the Grignard reagent of this substance, using the ordinary technique and also Baeyer's activated magnesium. This inactivity is analogous to that experienced by Reid and Helfrich[14] in attempting to prepare the Grignard reagent from mustard gas, and to Hamonet's attempts to obtain the magnesium compound of the corresponding oxygen ethers of the type $ROCH_2CH_2Cl$.[23]

H. Preparation of γ-Chloropropyl Methyl Sulfide, $CH_3SCH_2CH_2CH_2Cl$

This substance was made by exactly the same procedure as described above. In this case the addition of the thionyl chloride produced practically no heat and no layers formed during the reaction. After two fractional vacuum distillations a fraction boiling at 62–65° at 21 mm. was obtained. The yields varied between 70 and 75%. The substance was a water white liquid with an odor resembling that of the β compound. The boiling point of the product used for analysis was 71.2° at 29 mm.; $d_{20°}^{20°} = 1.0863$; $n_D^{30°} = 1.4833$.

Anal. Subs., 0.2094: $BaSO_4$, 0.3930. Calcd. for C_4H_9SCl: 25.73. Found: 25.79.

Reaction Velocity Measurements

Procedure

The purification of the reagents used in the titrations, the concentration, and the method of calculation of the reaction velocity constant *K* and the temperature coefficient

TABLE II

REACTION BETWEEN β-CHLORO-ETHYL METHYL SULFIDE AND POTASSIUM IODIDE

At 50°

Time, hours	Percentage reacted (100z)	*K*
2.0	5.82	0.0654
6.0	14.18	.0562
8.0	20.99	.0654
15.0	35.36	.0657
20.0	41.83	.0617
	Ave. =	.0629

At 60°

Time, hours	Percentage reacted (100z)	*K*
2.0	14.48	0.1725
3.0	16.82	.1357
4.0	27.96	.1835
6.0	37.09	.1748
	Ave. =	.1666

REACTION BETWEEN γ-CHLOROPROPYL METHYL SULFIDE AND POTASSIUM IODIDE

At 50°

Time, hours	Precentage reacted (100z)	*K*
2.0	11.63	0.1359
4.0	18.63	.1127
6.0	25.63	.1102
8.0	31.37	.1057
15.0	46.00	.0940
20.0	53.55	.0857
25.0	60.53	.0869
	Ave. =	.1044

At 60°

Time, hours	Percentage reacted (100z)	*K*
2.0	20.68	0.2571
3.0	24.47	.2085
4.0	34.80	.2413
5.0	40.00	.2320
6.0	47.69	.2478
	Ave. =	.2373

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[23] Wurtz, "Dictionnaire de Chimie," **2**, 751. Compare Bennett and Hock, *J. Chem. Soc.*, **129**, 472 (1927).

A were identical with that previously described.[4] It was necessary to modify slightly the procedure used in making the titration and to employ the method of extraction which was described in the paper just referred to. When the potassium iodate was added to the mixture being titrated, a yellow color developed which persisted long after the theoretically required amount had been added; this yellow color completely covered the end-point. It was shown to be due to the action of the potassium iodate on the organic sulfur chloride or iodide. Preliminary experiments proved that when the organic sulfur compound was extracted with chloroform before addition of the potassium iodate, sharp end-points were observed and consistent results obtained. Only negligible amounts of iodine were liberated during the reaction proper and on addition of the aqueous acid, so that no correction was necessary.

The author is exceedingly grateful to Professor J. B. Conant who suggested this problem and offered much valuable advice during the course of the work.

Summary

1. The method previously developed for determining the effect of structure of organic halides on their rate of reaction with inorganic halides has been extended to include the influence of the methylthio group. This group causes a definite, though weak, alternation in the reactivity of an ω-chlorine atom through at least three carbon atoms in a saturated chain.

2. In an attempt to correlate the structure of ω-halogen alkyl sulfides with vesicant action it was found that only when the halogen atom was in the β-position with respect to the sulfur atom did the resulting compound possess vesicant properties. This appears to be true of β,β′-dihalogen alkyl sulfides also. No apparent relationship exists between vesicant action and the chemical reactivity (at least in replacement reactions) of the halogen atom, a fact which is not in agreement with the acid theory of skin vesication.

3. A new vesicant, β-chloro-ethyl methyl sulfide, has been prepared, which judging from rather crude tests seems to produce the same general effects as mustard gas and at approximately the same rate.

4. The following substances have been prepared and their properties described for the first time: methylthio methyl acetate; β-hydroxyethyl methyl sulfide; β-chloro-ethyl methyl sulfide; γ-hydroxypropyl methyl sulfide; γ-chloropropyl methyl sulfide.

HOUSTON, TEXAS