A STUDY OF VARIOUS ALIPHATIC SULFONYL COMPOUNDS

by

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I wish also to thank the Office of Naval Research for a fellowship from July, 1951, to October, 1954.

M. S. H.

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INTRODUCTION

A concerted study of aliphatic compounds was initiated in this Laboratory in 1949, because of the paucity of published information regarding their behavior. At that time the primary purpose was to determine the steric requirements of several branched chain sulfonyl chlorides so that they could be compared with analogously branched primary alkyl halides in order to test the assumption that a sulfonyl group may be considered as a pseudo-methylene group from a mechanistic viewpoint. As is true with most research, this investigation since has been broadened to include studies of other types of sulfonyl compounds; namely, polyfunctional sulfonyl chlorides and sulfonic acid esters.

This dissertation is presented on a study the primary purposes of which were:

1. To synthesize 2,3-dimethylbutane-1-sulfonyl chloride and the ethyl ester of the corresponding sulfonic acid in order to determine the shielding effect of a beta methyl group.
2. To synthesize the tertiary sulfonyl chloride, 2,3-dimethylbutane-2-sulfonyl chloride, in order to compare it with the primary isomer, 2,3-dimethylbutane-1-sulfonyl chloride.
3. To investigate a claim that teritary sulfonyl chlorides can be prepared by photochemical chlorosulfonylation.
4. To investigate the reaction mechanism for sulfonyl chloride formation by the chlorosulfonylation of Grignard reagents.

FORMATION OF ALIPHATIC SULFONYL CHLORIDES

There are four general methods for preparing aliphatic sulfonyl chlorides. The oldest of these is the reaction between inorganic acid chlorides and sulfonic acids or their salts. A later preparation is by the action of sulfuryl chloride on Grignard compounds. More recently it was found that sulfonyl chlorides result when aliphatic sulfur bodies are oxidized with chlorine in aqueous media. About the same time photochemical chlorosulfonylation of paraffinic hydrocarbons was discovered. For this study, the sulfonyl chlorides were prepared by chlorosulfonylation of hydrocarbons and Grignard reagents; therefore a detailed discussion follows for only these two methods. A review of the other two methods mentioned above is adequately reported by Scott.[1]

Sulfonyl Chloride Formation by Chlorosulfonylation of Aliphatic Hydrocarbons

With the advent of a unique reaction, which bears the discoverer's name, Reed opened the door to a simple way of preparing aliphatic sulfonylchlorides from hydrocarbons.[2] Because sulfur dioxide has a spare pair of valence electrons about the sulfur atom, this compound is capable of entering into the chain reaction occurring during photochemical chlorination of hydrocarbons, particularly when the hydrocarbon is in the liquid phase. Thus, when a straight chain

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[1] R. B. Scott, Jr., Ph. D. Dissertation, 1949, University of Virginia, Charlottesville, Virginia.

[2] C. F. Reed, U.S.P. 2,046,090; Ref. cit. C.A., 30, 5593 (1936).

hydrocarbon is subjected to the conjoint action of sulfur dioxide and chlorine gases in the presence of actinic light, the only sulfonyl chlorides obtained are primary and secondary ones. If the hydrocarbon is branched and contains tertiary hydrogen atoms as well, there is also the theoretical possibility of forming tertiary sulfonyl chlorides.

The reaction which takes place can be best explained by a free radical mechanism[3] some of which may be represented as follows:

$$Cl_2 + h\nu \longrightarrow 2\ Cl\cdot$$

$$R\text{-}H + Cl\cdot \longrightarrow R\cdot + HCl$$

$$R\cdot + SO_2 \rightleftarrows R\text{-}SO_2\cdot$$

$$R\text{-}SO_2 + Cl_2 \longrightarrow R\text{-}SO_2\text{-}Cl + Cl\cdot$$

The Reed reaction is applicable, of course, to all saturated hydrocarbons above methane in the liquid phase; however, only a small number of these give individual sulfonyl chlorides that can be isolated readily. Short chain hydrocarbons such as propane and butane yield an easily separable mixture of primary and secondary isomers.[4] Some branched chain simple hydrocarbons such as isobutane[5] and neopentane[6] yield only one mono substituted product; this being true also for alicyclic hydrocarbons such as cyclopentane[7] and

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[3] J. Stauff, Z. Electrochem, 48, 550 (1942).

[4] F. Asinger and F. Ebeneder, Ber., 75, 344 (1942).

[5] Ibid.

[6] H.L. McLeod, M.S. Thesis 1951, University of Alabama, University, Alabama.

[7] J.P. Stutts, M.S. Thesis 1954, University of Alabama, University, Alabama.

cyclohexane.[8] A mixture of products results when long chain hydrocarbons are used, and separation of isomers is usually very difficult and impracticable. Chlorosulfonylation of such a hydrocarbon takes place in a statistical manner[9] reminiscent of that occurring in the chlorination process. It is of interest to note that when di- and polysubstitution occurs, the positions substituted are at least three carbon atoms apart.

Chlorosulfonylation of a hydrocarbon is very simple to carry out. A mixture of chlorine and sulfur dioxide gases is passed into a hydrocarbon in the liquid phase in the presence of actinic light, normally gaseous hydrocarbons being dissolved in a solvent such as carbon tetrachloride since the reaction takes place only very slowly in the vapor phase.[10] During the reaction it is essential that an excess of sulfur dioxide be present and that reaction take place at relatively low temperatures (ca. 10-30°) in order to suppress chlorination of the hydrocarbon.

Lockwood[11] points out that when 10 to 20 per cent of the hydrocarbon is chlorosulfonylated, about 90 per cent of the chlorosulfonylation product is the mono and 10 per cent the disulfonyl chloride. With a 50 per cent conversion, about 70 per cent is present as the mono sulfonyl chloride, while with a 70 per cent conversion, about

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[8] A. L. Fox, U. S. P. 2, 174,509, Sept. 26, 1939; Ref. cit. W. H. Lockwood, Chem. Ind., 62-63, 760 (1948).

[9] Lockwood, Ibid.

[10] Asinger and Ebeneder, loc. cit.

[11] Lockwood, loc. cit.

equal amounts of mono- and disulfonyl chlorides are present. Based on these data, the optimum conversion of a hydrocarbon to the mono sulfonyl chloride is about 60 per cent if unreacted hydrocarbon is not recovered.

A modification of the Reed process, developed by Kharasch,[12] consists in the treatment of a paraffinic hydrocarbon with sulfuryl chloride in the presence of an antichlorination catalyst, such as pyridine or stearamide, and actinic light. In this case considerably more chlorination occurs as it is necessary that the sulfuryl chloride reflux (79°).

Sulfonyl Chloride Formation by Chlorosulfonylation of Grignard Reagents

A comparatively little used method of preparing sulfonyl chlorides is the reaction of Grignard reagents with sulfuryl chloride. Early studies concerning the interaction of these two reagents were directed toward the preparation of sulfones.[13] It was found that the action of two moles of Grignard reagent on one mole of sulfuryl chloride gives sulfinic acids instead of the expected sulfones. Later Cherbuliez[14] found that by reversing the usual order of addition by adding the Grignard reagents to an excess of sulfuryl chloride,

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[12] M. S. Karasch and A. T. Read, J. Am. Chem. Soc., 61, 3089 (1939).

[13] Oddo, Atti. accad. Lincei, (5) 14, I, 169 (1905); Gazz, chim Ital., 35, 136 (1905); Ref. cit. E. Cherbuliez, and O. Schnauder, Helv. chim. acta., 6, 249 (1923).

[14] Cherbuliez and Schnauder, ibid.

sulfonyl chlorides are obtained in conversions of twenty-five to thirty-five per cent.

In order to account for by-product alkyl chloride formation, Cherbuliez proposed a mechanism for the reaction occurring in the inverse addition which was based on dissociation of an assumed intermediate complex between sulfuryl chloride and the Grignard reagent. To verify this mechanism, he showed that the distribution of products is a function of temperatures, the optimum for sulfonyl chloride formation being 10° C. Scott[15] found that the yield of octane-2-sulfonyl chloride is not appreciably influenced by variation in the temperature over the range -40° to 10°, thereby suggesting, at least in this instance, that the Cherbuliez mechanism is not operative to an appreciable extent.

In view of the fact that the reaction of Grignard reagents with sulfuryl chloride results in sulfonyl chloride yields generally of the order of 30 per cent and in the formation of considerable by-product alkyl chloride, it is believed that the chloromagnesium salt of the sulfinic acid is an intermediate. The chlorinating action of sulfuryl chloride on the Grignard reagent results in the formation of by-product alkyl chloride, and this chlorinating action on the sulfinic acid salt forms the sulfonyl chloride. The proposed mechanism may be illustrated as follows:

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15. R. B. Scott, Jr. and R. E. Lutz, _J. Org.Chem._, _19_, 830 (1954).

$$\begin{tikzcd}
\text{R-MgCl} \arrow[r, "SO_2Cl_2"] \arrow[d, "SO_2"] & \text{R-Cl} + MgCl_2 + SO_2 \\
RSO_2MgCl \arrow[r, "SO_2Cl_2"] & RSO_2Cl + MgCl_2 + SO_2
\end{tikzcd}$$

This mechanism has been verified by reacting the Grignard compound obtained from benzyl chloride[16] and that from the primary chloride of diisopropyl with sulfur dioxide gas, and then treating the resultant products with a suitable chlorinating agent. In each case, yeilds of sulfonyl chloride were about twice as great as those obtained with the single operation procedure. A paper describing the improved method is in press (September 1955 issue of the *Journal of Organic Chemistry*), a copy of which appears in Appendix II. Further considerations regarding these reactions appear therein.

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[16] J. B. Gayle, Ph. D. Dissertation, 1953, University of Alabama, University, Alabama.

TERTIARY SULFONYL CHLORIDES

In this Laboratory much interest has been focused on tertiary sulfonyl chlorides due to the fact that the literature contains certain discrepancies regarding preparation and properties of them. In the sections following, a general review of tertiary sulfonyl chlorides is given.

Stability of Tertiary Sulfonyl Chlorides

It is generally known that the stability of aliphatic sulfonyl chlorides decreases in the following order:

$$\text{primary} > \text{secondary} > \text{tertiary}$$

Thus, probably all primary sulfonyl chlorides are stable at room temperature, whereas some secondary and probably all tertiary products decompose on standing.

The instability of a tertiary sulfonyl chloride is probably due to the structure of the molecule. There are three side chain alkyl groups attached to the carbon atom carrying the cholorsulfonyl group. This arrangement of the carbon skeleton gives rise to considerable B-strain; much more than that present in either the secondary or the primary sulfonyl chlorides, and undoubtedly contributes to instability of the tertiary sulfonyl chloride.

One possible course for the decomposition of a tertiary sulfonyl chloride is shown by the following reaction scheme:

$$RSO_2Cl \longrightarrow RSO_2^{+1} + Cl^{-1}$$

$$RSO_2^{+1} \longrightarrow R^{+1} + SO_2$$

$$R^{+1} + Cl^{-1} \longrightarrow RCl$$

In explanation this mechanism becomes quite apparent. The carbon-sulfur and the sulfur-chlorine bonds are weaker in a tertiary sulfonyl chloride than in either the secondary or the primary, partailly because of the B-strain and partially because of the inductive effect occasioned by the side chain alkyl groups. This might result, then, in the tertiary sulfonyl chloride having a low ionization potential. Such an ionization would lead to formation of sulfonylium ion to form a carbonium ion, thereby exhibiting an interesting difference from a carbonium ion which is incapable of losing a neutral moiety. This might be followed by neutralization of the electron deficiency of the carbonium ion either by attachment of a chloride ion to form an alkyl chloride, or by loss of a proton to form an olefin. In certain cases rearrangement of the carbonium ion might occur to form a less strained system.

It may be possible that tertiary sulfonyl chlorides decompose by a free-radical mechanism, especially in view of the fact that secondary sulfonyl chlorides have been shown to decompose by this mechanism.[17] However, this type of decomposition usually is induced by heat, or peroxides, or ultraviolet light, or other free radical initiators. Thus, if chlorine is removed from the chlorosulfonyl group as a chlorine atom, sulfur dioxide can be liberated, accompanied by the formation of an alkyl free-radical. The next step is the obvious formation of alkyl chloride. These transformations can be shown by the following reaction scheme:

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[17] M. A. Smook, E. T. Pieski, and C. F. Hammer, Ind. Eng. Chem., 45, 2731 (1953).

$$RSO_2Cl \longrightarrow RSO_2\cdot + Cl\cdot$$

$$RSO_2\cdot \longrightarrow R\cdot + SO_2$$

$$R\cdot + Cl\cdot \longrightarrow RCl$$

Although this mechanism might be operative during decomposition of a tertiary sulfonyl chloride, some free radical initiator has to be present in order to start the chain reaction.

Regardless of the mechanism of decomposition, the fact remains that a tertiary sulfonyl chloride is not stable. This has been shown by Frye,[18] who studied the rate of decomposition of the only known tertiary sulfonyl chloride, 2-methylpropane-2-sulfonyl chloride. The results of this work are discussed in the section entitled "Tertiary Isobutanesulfonyl Chloride."

Tertiary Sulfonyl Chloride Synthesis

Of the four general methods for preparing sulfonyl chlorides, only chlorosulfonylation of a Grignard reagent appears likely to lead to the formation of a tertiary sulfonyl chloride. From the following brief discussion of each method, this generalization seems justifiable.

Method 1: Action of Inorganic Chlorides on Sulfonic Acids or their Salts

The following reaction schemes are illustrative of this process.

1) Formation of an intermediate:

a) $RSO_2OH + SOCl_2 \longrightarrow RSO_2\text{-}O\text{-}SO\text{-}Cl + HCl$

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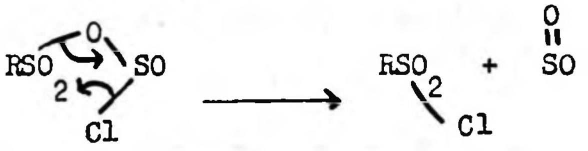
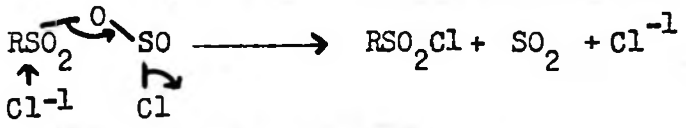
[18] M. K. Frye, M. S. Thesis, 1951, University of Alabama, University, Alabama.

2) Decomposition of the intermediate by one of three routes to form the sulfonyl chloride:

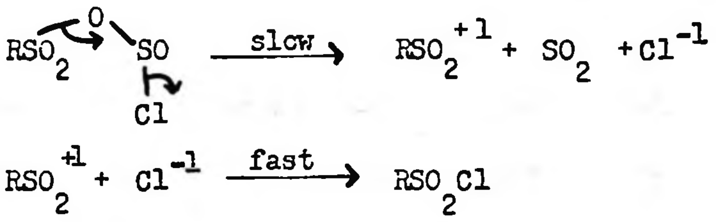
a) with retention of configuration about the sulfur ation (S_Ni mechanism),



b) with inversion of configuration about the sulfur atom (S_N2 mechanism),



c) with racemization of configuration about the sulfur atom (S_N1 mechanism),



This process is quite satisfactory for relatively unhindered sulfonic acids such as pentane-1- and 3-methylbutane-1-sulfonic acids. The reactions probably proceed by a bimolecular attack (S_N2) at the rear face of the sulfur atom. However, a tertiary sulfonic acid would be somewhat analogous to neopentyl alcohol and hindrance afforded by the two alpha methyl groups would be sufficient to force the reaction through the unimolecular reaction (S_N1). Thus a sulfonylium ion is a probable intermediate which could decompose, according to the previously-discussed ionic mechanism, to give sulfur dioxide and either an alkyl chloride or an olefin. Therefore this process is not likely to yield a tertiary sulfonyl chloride.

Method 2: Oxidative Chlorination of Various Sulfur Bodies

Many different types of sulfur bodies can be converted successfully to sulfonyl chlorides by this method. Yields are good if the sulfur atom is attached to a primary carbon atom but are only fair if attached to a secondary one. However, no sulfonyl chloride at all is obtained when the sulfur atom is attached to a tertiary carbon atom; the sulfur being oxidized completely to sulfuric acid.[19] It is possible that a transitory tertiary sulfonyl chloride is formed which is so unstable under conditions of the reaction that it decomposes; the water present enhancing ionization to a sulfonylium ion which could undergo the above-discussed transformations.

Method 3: Chlorosulfonylation of Hydrocarbons

As mentioned earlier, a tertiary sulfonyl chloride may be formed, theoretically, by this reaction. However, a tertiary sulfonyl chloride is a relatively unstable compound, and, if formed, its isolation would be most difficult. Asinger[20] claims that a tertiary sulfonyl chloride is not formed during this reaction, his reason being that there is too much steric hindrance at the tertiary carbon for an attack by a relatively large chlorosulfonyl free radical. It should be noted that Asinger's reasoning is not in accord with the free radical mechanism previously discussed. Helberger and co-workers,[21] in marked disagreement with Asinger, claim to have prepared tertiary

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[19] J. M. Sprague and T. B. Johnson, J. Am. Chem. Soc., 59, 1837 (1937).

[20] Asinger and Ebeneder, loc. cit.

[21] J. Helberger, G. Manecke, and H. Fischer, Ann., 562, 23 (1949).

sulfonyl chlorides by the Reed reaction. Shortly it will be shown that Helberger is in error.

It may be possible that tertiary sulfonyl chlorides are formed during chlorosulfonylation of a hydrocarbon; however, they never had been isolated. This fact may be due to competition of several of the reactions which take place during cholorsulfonylation. For instance,

1) $3^{o}\ R\cdot + Cl_2 \longrightarrow 3^{o}R\text{-}Cl + Cl\cdot$

may be more favored than

2) $3^{o}R\cdot + SO_2 \rightleftarrows 3^{o}RSO_2\cdot$

In the first case a neutral molecule is formed and further reaction at the tertiary position is arrested. Furthermore, collision need not be selective, either chlorine atom being available. In the second, a free radical is formed which could dissociate to the original alkyl free radical and sulfur dioxide, and the effective collision must be with only the sulfur atom. In addition to this the steric requirements of sulfur dioxide obviously are greater than those of chlorine.

It seems likely, then, that if tertiary sulfonyl chlorides are formed they may be present in only small amounts, and due to the relative instability of these compounds, their isolation would be difficult.

Method 4: Sulfonylation of Grignard Reagents

Preparation of sulfonyl chlorides by this method has been shown to proceed through a chloromagnesium salt of the sulfinic acid.[22] As expected, these salts derived from saturated Grignard reagents are

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[22] R. B. Scott, J. B. Gayle, M. S. Heller, and R. E. Lutz, J. Org. Chem., 20, 0000 (1955) (See Appendix II).

not subject to molecular rearrangements. Also, they may be considered somewhat analogous to Grignard reagents, if the sulfinyl group is considered as a pseudo methylene group. Chlorination of Grignard reagents is known to give the corresponding alkyl chloride. Similarly, chloromagnesium sulfinates give the corresponding sulfonyl chloride. The Grignard route, then, is believed to be the only suitable method for tertiary sulfonyl chloride formation.

Tertiary Isobutanesulfonyl Chloride

Asinger[23] claims to have prepared t-isobutanesulfonyl chloride by reacting the potassium salt of t-isobutanesulfonic acid with phosphorous pentachloride; a detailed description of the reaction conditions being omitted in the publication. The product which he obtained is a stable liquid boiling at 80°/15 mm and readily forms a cyclohexylamine derivative melting at 61.5°. Frye[24] made several unsuccessful attempts to duplicate Asinger's work. However, she did prepare t-isobutanesulfonyl chloride in a manner which is considered unequivocal by reacting t-butylmagnesium chloride with sulfuryl chloride. This sulfonyl chloride melts at 89-91° in conformity with expectations based on its symmetrical structure. Attempts to prepare solid derivatives of this sulfonyl chloride failed. Like neopentyl halide, a tertiary sulfonyl chloride would not be expected to be derivatized readily.

The sulfonyl chloride prepared by Frye is relatively unstable.

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[23] Asinger and Ebeneder, loc. cit.

[24] Frye, loc. cit.

It decomposes into t-butyl chloride and sulfur dioxide by first order kinetics and has a half-life of 240, 34, and 6 hours at, respectively, 25°, 35°, and 50°. These characteristics are in accord with the belief that a tertiary sulfonyl chloride should be relatively unstable.

An investigation currently is being carried out to determine precisely the structure of Asinger's stable "sulfonyl chloride." It is believed that the compound prepared by him is not a sulfonyl chloride.

A Claim to Preparing Tertiary Sulfonyl Chlorides by the Reed Reaction

It was mentioned earlier that a tertiary sulfonyl chloride may be formed, theoretically, by the Reed reaction, but, even if formed, its isolation would be most difficult. However, Helberger and co-workers[25] claim to have prepared several tertiary sulfonyl chlorides of alkyl chlorides by this route.

In view of the instability of the sulfonyl chloride obtained when t-butylmagnesium chloride is reacted with sulfuryl chloride and failure to obtain a tertiary sulfonyl chloride when either isobutane[26] or diisopropyl[27] is chlorosulfonylated, it seemed doubtful that the sulfonyl chlorides prepared by Helberger upon chlorosulfonylating several branched alkyl chlorides are tertiary. Although Helberger

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25. Helberger, Manecke, and Fisher, loc. cit.

26. Asinger and Ebeneder, loc. cit.

27. See page 19.

claimed that these are tertiary, no proof of structure was presented, and the reasoning offered for concluding such structure is unsound.

Helberger reasoned that since a sultone did not result when the acid from hydrolysis of chlorosulfonylated isobutyl chloride was heated under reduced pressure, the sulfo group must be attached to the tertiary carbon atom, on the assumption that the five-membered ring sultone would have formed if the sulfo group were attached to the primary carbon atom. Therefore, he reasoned, a tertiary sulfonyl chloride must have been obtained in the reaction. From this he concluded that, if a tertiary sulfonyl chloride results in this case, then one also should result on chlorosulfonylating either isoamyl chloride or 4-chloro-2-methylpentane. He further reasoned that since sultones are obtained from the sulfonyl chlorides obtained in these last two cases, they must be sultones of tertiary sulfonic acids. This, therefore, renders these sultones five-membered ring esters. It should be pointed out here that Asinger[28] reports the product from chlorosulfonylating isobutyl chloride as being the chloro primary sulfonyl chloride from which a five-membered ring sultone was obtained by hydrolysis and heating under reduced pressure.

When 4-chloro-2-methylpentane is subjected to the Reed reaction there is the possibility of forming a mixture of chlorosulfonyl chlorides; however, only two of these are capable of being transformed into sultones, only five- and six-membered ring sultones being known.

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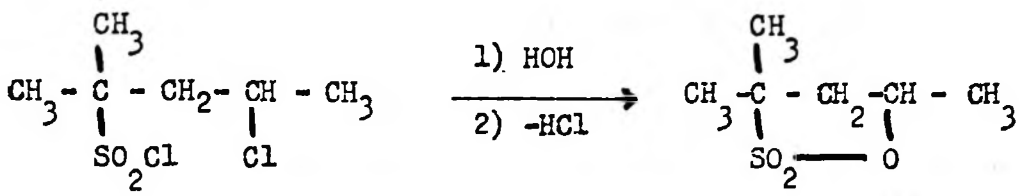
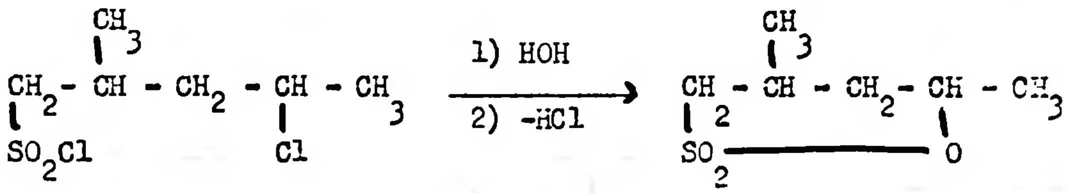
28. F. Asinger, F. Ebeneder, and H. Eckholt, U.S. Office of Publication Board, P.B. 70183, Frame 892-894.

These are:



$$CH_3-\underset{SO_2Cl}{\overset{CH_3}{C}}-CH_2-\underset{Cl}{CH}-CH_3 \xrightarrow[2)\ -HCl]{1)\ HOH} CH_3-\overset{CH_3}{C}-CH_2-CH-CH_3 \quad (C{-}SO_2{-}O{-}CH)$$

I II

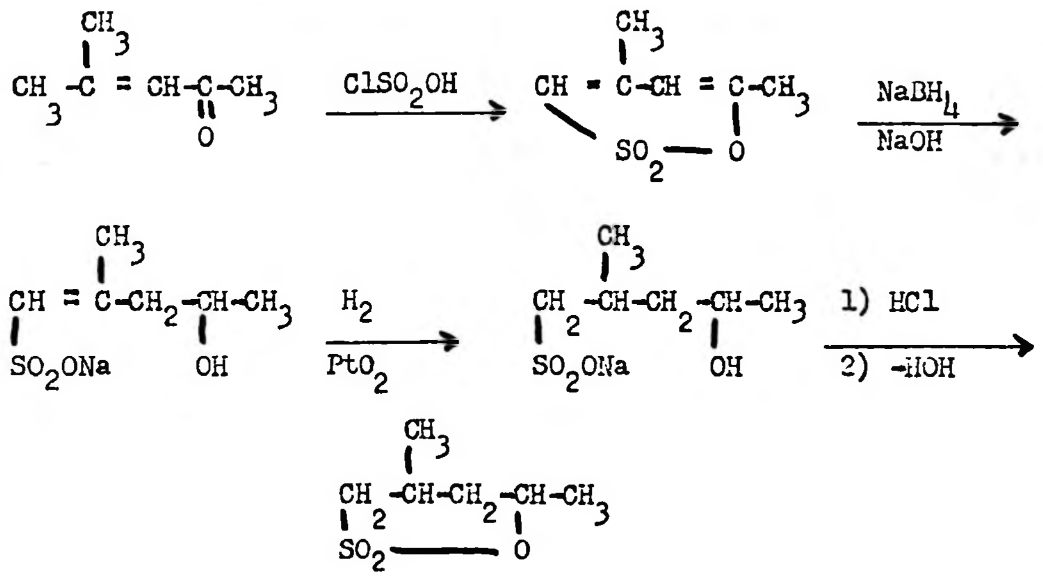


$$\underset{SO_2Cl}{CH_2}-\overset{CH_3}{CH}-CH_2-\underset{Cl}{CH}-CH_3 \xrightarrow[2)\ -HCl]{1)\ HOH} CH_2-\overset{CH_3}{CH}-CH_2-CH-CH_3 \quad (CH_2{-}SO_2{-}O{-}CH)$$

III IV

Although Helberger recognized these two possibilities, he designated the chlorosulfonyl chloride (I) as being the main reaction product from chlorosulfonylation, and the sultone (II) as being the subsequent reaction product.

It was proved in an unequivocal manner that the actual reaction products isolated from the reaction represented above are the chloro primary sulfonyl chloride (III) and the six-membered sultone (IV). This was shown by preparing 4-hydroxy-2-methylpentane-1-sulfonic acid sultone by the following sequence of reactions represented:



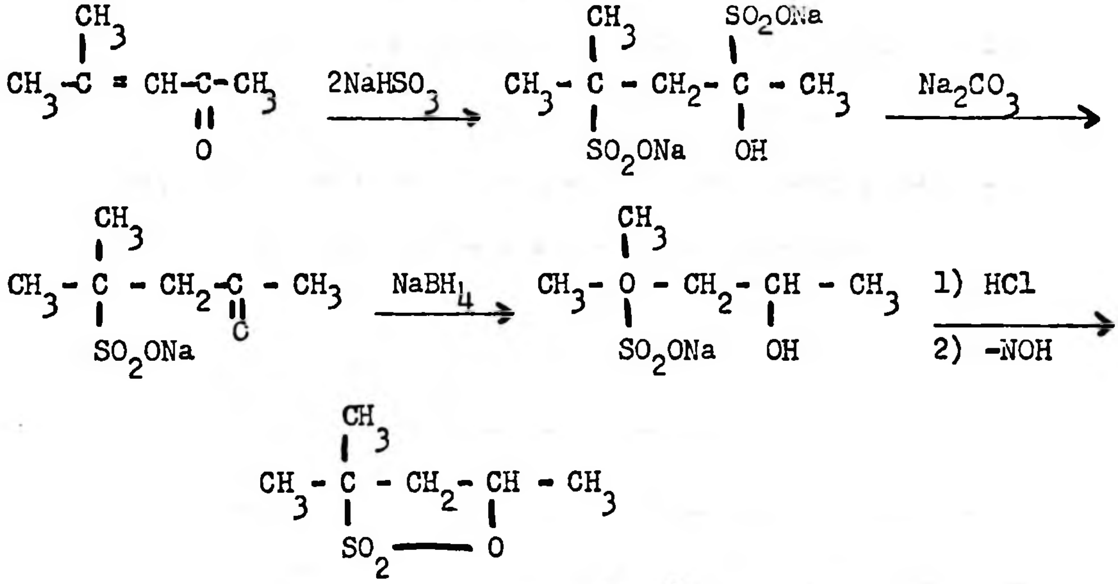
$$CH_3-\overset{CH_3}{C}=CH-\underset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{ClSO_2OH} CH=\overset{CH_3}{C}-CH=C-CH_3 \quad (CH{-}SO_2{-}O{-}C) \xrightarrow[NaOH]{NaBH_4}$$

$$\underset{SO_2ONa}{CH}=\overset{CH_3}{C}-CH_2-\underset{OH}{CH}-CH_3 \xrightarrow[PtO_2]{H_2} \underset{SO_2ONa}{CH_2}-\overset{CH_3}{CH}-CH_2-\underset{OH}{CH}-CH_3 \xrightarrow[2)\ -HOH]{1)\ HCl}$$

$$CH_2-\overset{CH_3}{CH}-CH_2-CH-CH_3 \quad (CH_2{-}SO_2{-}O{-}CH)$$

The sultone from each preparation has a melting point of 46.5-47.0° (Helberger reported 45°) and mixtures from the two preparations show no depression in melting point.

Synthesis of the sultone Helberger claimed to have prepared, 4-hydroxy-2-methylpentane-2-sulfonic acid sultone, was then accomplished by the reactions represented:



This sultone has a melting point of 49.5-50.0°.

Mixtures of these six-membered (m.p. 46.5-47°) and the five-membered (m.p. 49.5-50°) ring sultones resulted in the formation of a liquid. Thus, the reaction product obtained by chlorosulfonylating 4-chloro-2-methylpentane clearly is a chloro primary sulfonyl chloride which leads to a six-membered ring sultone. Undoubtedly the same is true in the case of isoamyl chloride.

SYNTHESIS OF SULFONYL CHLORIDES OF DIISOPROPYL

Only one primary and one tertiary mono sulfonyl chloride derivative is possible in the diisopropyl (2,3,-dimethylbutane) system; namely, 2,3-dimethylbutane-1- and 2,3-dimethylbutane-2-sulfonyl chlorides. The primary isomer contains an asymmetric carbon atom, and, therefore has a dextro, a levo, and a racemic form. Due to the methods of synthesis, this sulfonyl chloride undoubtedly was obtained as the racemate, and no attempts were made to resolve it into enantiomorphs. Attempts to prepare the tertiary isomer were unsuccessful. Methods of synthesis are presented in the sections which follow.

2,3-Dimethylbutane-1-sulfonyl Chloride

This primary sulfonyl chloride was prepared by photochemical chlorosulfonylation of diisopropyl, according to Reed,[29] in a conversion of 21 per cent. Fractional distillation of the chlorosulfonylated mass yielded only one mono sulfonyl chloride, the primary one. That a tertiary isomer was not obtained confirms the findings of Asinger[30] on chlorosulfonylation of isobutane. The primary sulfonyl chloride of diisopropyl has the following properties: b.p. 61°/1 mm., n_D^{25} 1.4607, d_4^{25} 1.4524 and M_D 44.0 (theory, 44.3).

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[29] Reed, <u>loc. cit.</u>

[30] Asinger and Ebeneder, <u>loc. cit.</u>

This sulfonyl chloride was shown to be the primary isomer by an independent synthesis through reaction of the Grignard reagent from 1-chloro-2,3-dimethylbutane with sulfuryl chloride, according to Cherbuliez,[31] in a 33 per cent yield. The yield subsequently was increased to 70 per cent when the modified Cherbuliez process was used.[32] The properties of the sulfonyl chloride prepared by this route are in agreement with those of the product obtained by the Reed process, b.p. 71°/1.8 mm., n_D^{25} 1.4608, d_4^{25} 1.4528, and M_D 43.9.

The sulfonyl chlorides from either process yields a benzylamide melting at 81-82°. A mixture of the benzylamides derived through the two methods shows no depression in melting point. The unsubstituted amide also was prepared as a characterizing derivative (m.p. 48-49°).

The primary chloride of diisopropyl, prepared by photochemical chlorination of diisopropyl and used in preparing the corresponding sulfonyl chloride by the Cherbuliez and its modified process, was separated from its tertiary isomer by fractional distillation. To make certain which was the primary chloride, each isomer was derivatized, especially since no refractive index is recorded in the literature for the primary one. The tertiary isomer (b.p. 55°/108 mm., 111-112°/754, n_D^{25} 1.4171; literature 67.6-70.0°/108 mm., n_D^{25} 1.4162,[33] and b.p. 110°/750 mm., n_D^{25} 1.4178[34]) formed a solid dibromide,

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31. Cherbuliez and Schnauder, loc. cit.

32. See Appendix II.

33. H.C. Brown and R.S. Fletcher, J. Amer. Chem. Soc., 71, 1845 (1949).

34. V. J. Shiner, J. Amer. Chem. Soc., 76, 1603 (1954).

2,3-dibromo-2,3-dimethylbutane, which melted in agreement with this lone derivative reported in the literature.[35]

According to the literature, the primary isomeric chloride of diisopropyl (b.p. 65°/108 mm., 122.5-123°/754, n_D^{25} 1.4201; literature[36] b.p. 122°) has never been derivatized directly; however a single derivative of the related 3,4-dimethylvaleric acid was found. Unfortunately melting points reported for this derivative, the anilide, are widely divergent; Huston[37] claiming that it melts at 67°, Detling[38] mentioning 110.0-110.5°. In order to rectify this situation, the anilide of 3,4-dimethylvaleric acid was prepared by reacting the Grignard reagent of the primary chloride with phenyl isocyanate; it melts at 109.5-110.5°, in agreement with Detling.

The tertiary isometic chloride of diisopropy was similarly derivatized to obtain the anilide of 2,2,3-trimethylbutyric acid, which melts at 78.5-79.0°. This latter anilide also was prepared from the chloride derived from 2,3-dimethyl-2-butanol obtained by reacting methyl (isopropyl) ketone with methylmagnesium iodide. It melts at 77.5-78°. A mixture of this anilide and the isomeric anilide from the primary chloride melted at 63.5-68.5°.

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[35] A. V. Grosse and V. N. Ipatieff, J. Org. Chem., 8, 438 (1943).

[36] Schorlemmer, Ann., 144, 18 (1867); Ref. cit., G. Egloff, R. E. Schaad, and C. D. Lowry, Chem. Rev., 8, 1 (1931).

[37] R. C. Huston and A. H. Agett, J. Org. Chem., 6, 123 (1941).

[38] K.D. Detling, C. C. Crawford, D. L. Yabroff, and W. H. Peterson, British patent 591,632, Aug. 25, 1947; Ref. cit., C.A. 42, 1948.

Upon examining the supporting dissertations of Agett[39] and Guile,[40] it became quite clear that Huston is in error regarding the structure of the anilide he reported as derived from 3,4-dimethylvaleric acid. Guile thought that he had prepared sec.-isoamyl bromide by reacting the corresponding alcohol with phosphorous tribromide. However, he makes no mention of conditions, physical properties of the product, or derivatization of the product. Except possibly under conditions unknown at that time,[41] rearrangement should occur during this reaction. Agett later used Guile's bromide, without characterizing it, in the preparation of what he thought was 3,4-dimethyl-1-pentanol by reacting the Grignard compound of the uncharacterized bromide with ethylene oxide. In order to establish the structure of the product alcohol, Agett oxidized the alcohol to the acid, which he derivatized as the anilide. He then proceeded to synthesize this acid from malonic ester with the same uncharacterized bromide obtained from sec.-isoamyl alcohol, and from it to prepare the anilide. The only thing he established is that either route leads to the same acid.

2,3-Dimethylbutane-2-sulfonyl Chloride

Attempts to prepare the tertiary sulfonyl chloride of diisopropyl by the modified Cherbuliez process were unsuccessful. However, it is believed that the desired product was formed during the reaction but

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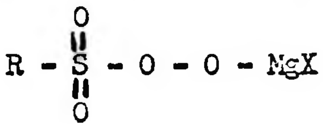
[39] A. H. Agett, Ph. D. Dissertation, 1940, Michigan State College, East Lansing, Michigan.

[40] R. L. Guile, Ph. D. Dissertation, 1938, Michigan State College, East Lansing, Michigan.

[41] L. H. Sommers, J. Am. Chem. Soc., 73, 3542 (1951).

that it was decomposed by a free-radical mechanism during the chlorination step to give a complex mixture of polychlorinated diisopropyl. That polychloro compounds are formed is not surprising, especially in view of the fact that they also are obtained when the Grignard compound corresponding to 2-chloro-2-methylheptane is chlorosulfonylated.[42]

The reasons offered in assuming that a free-radical mechanism is operative during chlorination of chloromagnesium 2,3-dimethylbutane-1-sulfinate are given as follows: 1) Sulfinic acids and their salts are known to be readily oxidized by air. Once started, the autooxidation process might be operative during the chlorination of the sulfinic acid salt. This might result, then, in the formation of either alkyl hydroperoxides, the tertiary hydrogen atoms of the diisopropyl group being attacked more readily than the primary ones, or persulfonic acid salts possibly having a structure represented by



$$R - \overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}} - O - O - MgX$$

Either of these oxidizing agents could start the same type of chain reaction that occurs during the earlier-described, free radical induced decomposition of a sulfonyl chloride and thereby cause chlorination of the alkyl halide from the sulfonyl chloride.

Because it is believed that the tertiary sulfonyl chloride was formed during the attempted preparations, the procedure used is outlined. 2,3-Dimethyl-2-butanol, prepared by the condensation of methylmagnesium iodide and methyl isopropyl ketone, was treated with concentrated hydrochloric acid to give the corresponding alkyl chloride. The Grignard

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[42] Scott, loc. cit.

reagent was then prepared and treated with sulfur dioxide until all of it was converted into the yellow chloromagnesium sulfinate. Chlorine was bubbled into a suspension of this salt in carbon tetrachloride. After the solvent had been removed in vacuo, the residual liquid was distilled under reduced pressure to give the following fractions:

Fraction	B. P.	n_D^{25}
1	48-58°/0.7 mm.	1.4795
2	58-68°/0.7 mm.	1.4887
3	68-78°/0.7 mm.	1.5051
4	78-90°/0.7 mm.	1.5149
5	90-100°/0.7 mm.	1.5242
6	100-107°/0.7 mm.	1.5337
7	107-113°/0.7 mm.	1.5377

The material from each fraction contains chlorine, but does not contain sulfur. Some of the chlorine atoms are on vicinal carbon atoms, some are on primary carbon atoms, some on tertiary ones. It should be noted that on one occasion when chlorination of the salt, suspended in ether, was near completion, an explosion occurred, indicative of peroxide formation, and about 98 per cent of the products was lost.

A fraction of high boiling polychlorides (boiling range 40° /2 mm. to 70° /2 mm.), obtained from photochemical chlorination of diisopropyl, was further chlorinated and distilled under reduced pressure to give seven fractions of material, the properties of which compare well with those obtained by chlorination of the chloromagnesium tertiary sulfinate. The distillation results are as follows:

Fraction	B. P.	n_D^{25}
1	45-55°/1.5 mm.	1.4836
2	55-65°/1.5 mm.	1.4897
3	65-70°/1.5 mm.	1.4935
4	70-82°/1.5 mm.	1.5058
5	82-92°/1.5 mm.	1.5118
6	92-100°/1.5 mm.	1.5167
7	100-105°/1.5 mm.	1.5212

Based on this comparison, it is believed that the products isolated during attempted preparations of 2,3-dimethylbutane-2-sulfonyl chloride are complex mixtures of polychlorinated diisopropyl. For subsequent preparations of sulfonyl chlorides by the procedure outlined above, it is suggested that a peroxide inhibitor be used such as hydroquinone or sodium diethyldithiocarbamate. Or possibly a trace of the latter might stabilize the tertiary sulfonyl chloride once it is isolated.

REACTIONS OF ALIPHATIC SULFONYL COMPOUNDS

Ethanolysis of Sulfonyl Chlorides

Early studies[43] concerning the solvolysis of aromatic sulfonyl chlorides have shown that the reaction is essentially first order when carried out with a large excess of alcohol. Recently, Tommila[44] found that solvolysis of these compounds takes place by a bimolecular (S_N2) mechanism.

In this Laboratory a number of non-aromatic sulfonyl chlorides have been studied under essentially the same conditions of ethanolysis by refluxing a mixture of the sulfonyl chloride and ethanolic hydrogen chloride. Hydrogen chloride was incorporated into the alcohol in order to minimize a possible variable since it is formed during the reaction. It was found that the sulfonyl chlorides disappear by a first order solvolytic attack to form esters which in turn react with the chloride ions or solvent molecules to form, respectively, alkyl chlorides and ethers. These reactions may be represented as follows:

$$RSO_2Cl + EtOH \longrightarrow RSO_2OEt + HCl$$

$$RSO_2OEt + HCl \longrightarrow RSO_2OH + EtCl$$

$$RSO_2OEt + EtOH \longrightarrow RSO_2OH + EtOEt$$

The bimolecular (S_N2) nature of ethanolysis also was demonstrated in the case of aliphatic sulfonyl chlorides paralleling the findings of Tommila.

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43. M. R. Gouban, Chem. Zentr., II 18 (1911).

44. E. T. Tommila and P. Hirsjarvi, Acta. Chem. Scand., 5, 659 (1951).

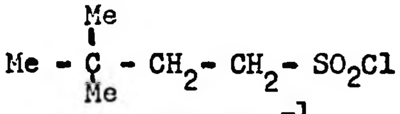
In order to learn the effect of a beta methyl group on the rate of ethanolysis of an aliphatic sulfonyl chloride, 2,3-dimethylbutane-1-sulfonyl chloride was chosen for such an investigation. Figure I illustrates ethanolysis of this sulfonyl chloride and consecutive conversion of the resultant ester into the sulfonic acid. Table I presents the rate constant and the half-life during ethanolysis of this sulfonyl chloride, and for comparison also includes some data obtained for several other sulfonyl chlorides studied under essentially the same conditions of reaction.

From a consideration of the rate constants presented in Table I for all the sulfonyl chlorides except those of dl-camphor-10- and 2-propene-1-sulfonyl chloride, the differences and similarities must be due to the steric requirements of each sulfonyl chloride for ethanol. A comparison of rate constants for octane-1- (I), neopentylmethane- (II), and butane-1-sulfonyl chloride (III) reveals that the

$C_5H_{11}-CH_2-CH_2-CH_2-SO_2Cl$

k = 0.089 min.$^{-1}$

I



$Me-\underset{Me}{\overset{Me}{C}}-CH_2-CH_2-SO_2Cl$

k = 0.092 min.$^{-1}$

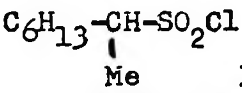
II

$CH_3-CH_2-CH_2-CH_2-SO_2Cl$

k = 0.085 min.$^{-1}$

III

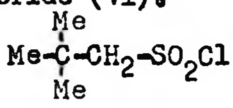
steric requirements for ethanol are substantially the same but significantly less than those of octane-2- (IV), neopentane- (V), and camphane-10-sulfonyl chloride (VI).



$C_6H_{13}-\underset{Me}{CH}-SO_2Cl$

IV

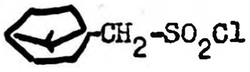
k = 0.014 min.$^{-1}$



$Me-\underset{Me}{\overset{Me}{C}}-CH_2-SO_2Cl$

V

k = 0.016 min.$^{-1}$



VI

k = 0.018 min.$^{-1}$

Table 1: Rates of Ethanolysis of Aliphatic Sulfonyl Chlorides

Sulfonyl Chloride	Reference	k min.$^{-1}$	$t_{\frac{1}{2}}$ mins.
dl-Camphor-10-	1	0.171	4
2-Propene-1-	2	0.102	7
Neopentylmethane-	3	0.092	8
Octane-1-	4	0.089	8
Butane-1-	3	0.085	8
α-toluene-	1	0.063	11
2,3-Dimethylbutane-1-	--	0.047	15
Camphane-10-	1	0.018	39
Neopentane-	3	0.016	43
Octane-2-	4	0.014	50
Cyclopentane-	5	0.003	231

References:

1. J. B. Gayle, Ph. D. Dissertation, 1953, University of Alabama, University, Alabama.
2. J. Preston, M. S. Thesis, 1954, University of Alabama, University, Alabama.
3. Paper presented by R. B. Scott, Jr., at the Southeastern Regional Meeting of the American Chemical Society in Birmingham, Alabama, October 21, 1954.
4. R.B. Scott, Jr. and R. E. Lutz, "A Study of Aliphatic SulfonylCompounds, I. Octane-1- and -2-sulfonyl Chlorides," J. Org. Chem., 19, 830 (1954).
5. J. P. Stutts, M. S. Thesis, 1954, University of Alabama, University, Alabama.

Note: Each "k" value is the average of the results obtained for four separate determinations.

Figure I

Distribution of Products for the Reaction of 2,3-Dimethylbutane-1-sulfonyl Chloride with Boiling Ethanolic Hydrogen Chloride

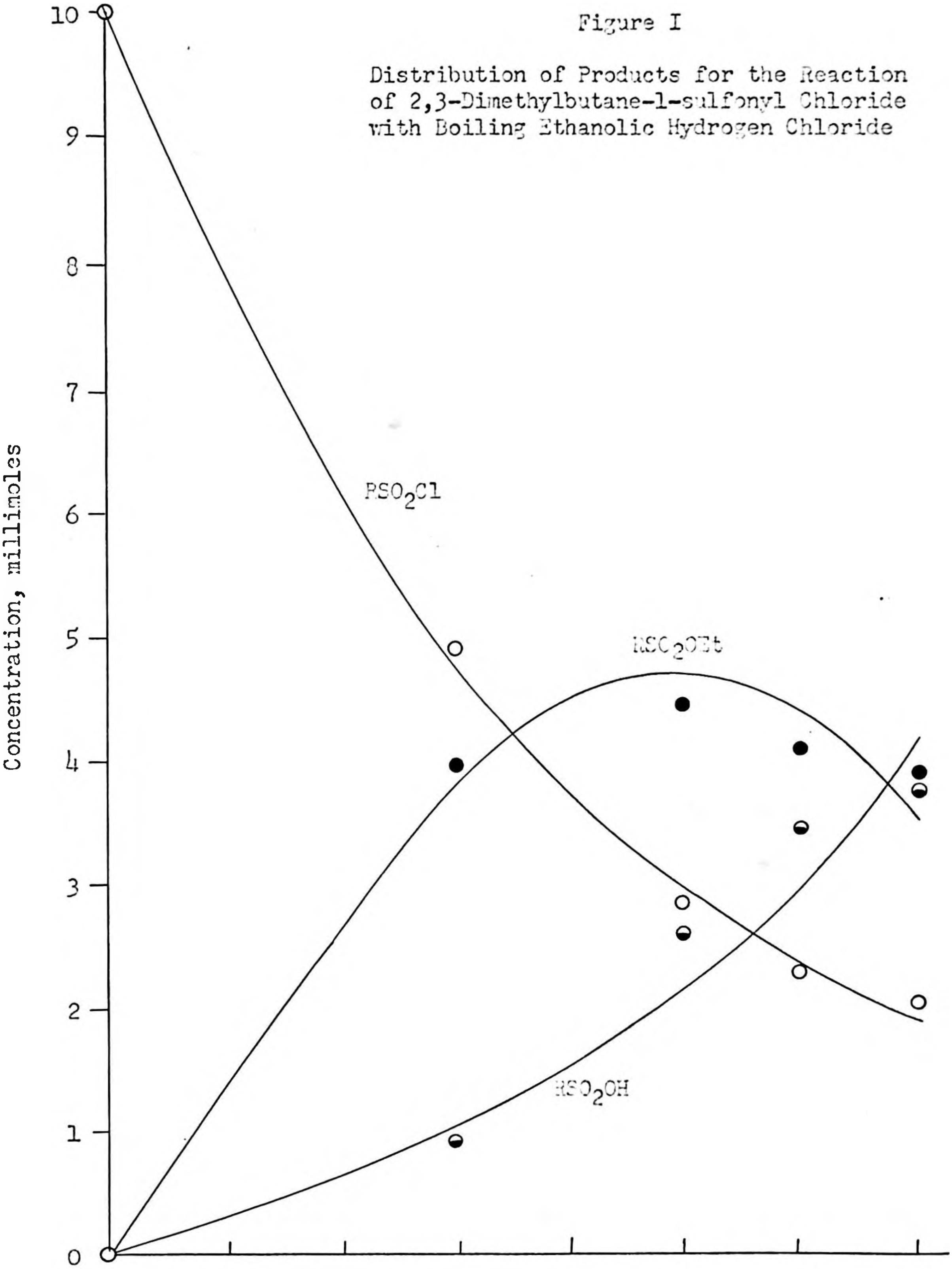
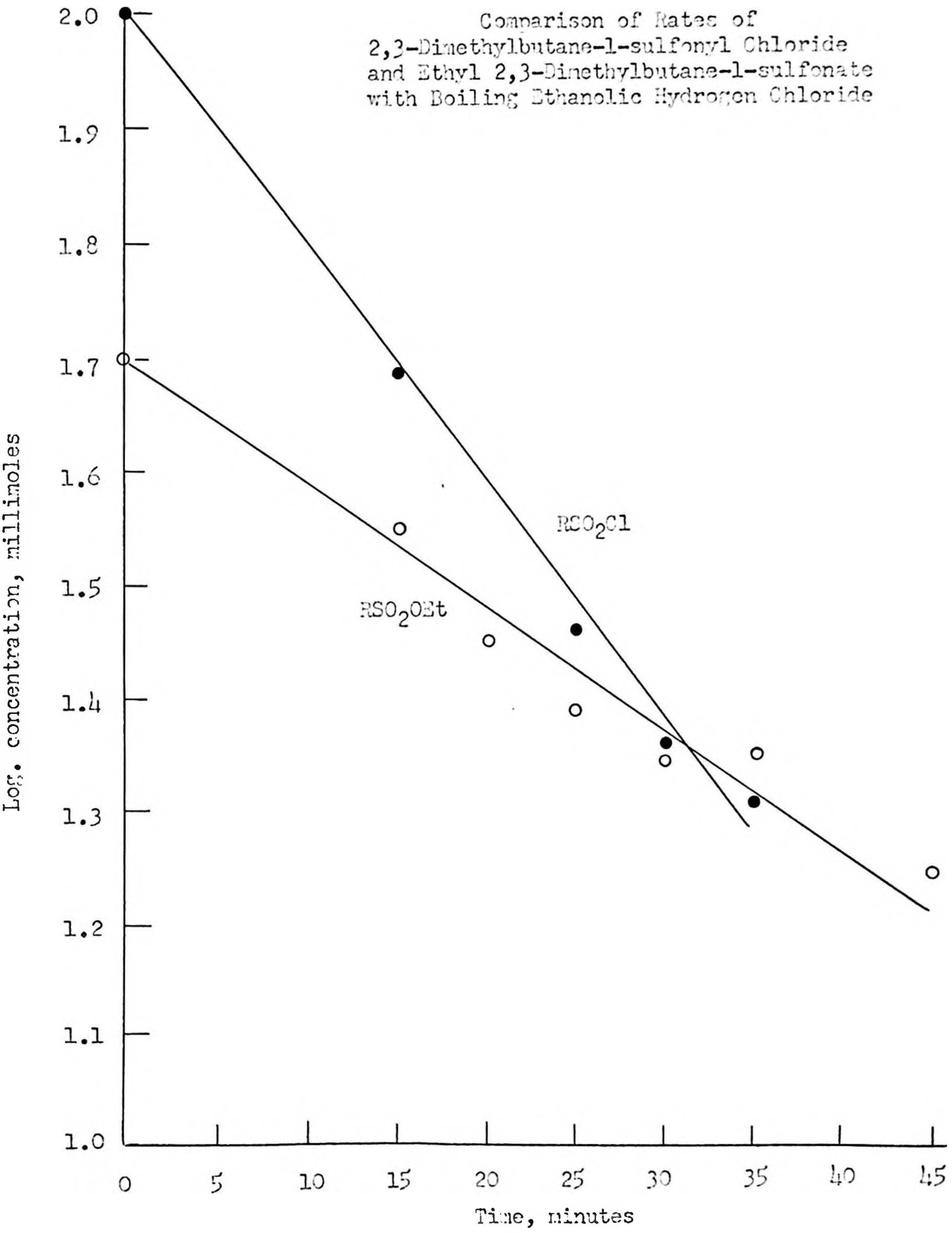
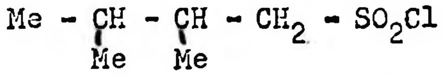


Figure II



Comparison of Rates of
2,3-Dimethylbutane-1-sulfonyl Chloride
and Ethyl 2,3-Dimethylbutane-1-sulfonate
with Boiling Ethanolic Hydrogen Chloride

The last three sulfonyl chlorides, like the first three, have similar steric requirements. Putting it another way, one alpha methyl group provides as much hindrance to ethanolysis as two beta methyl groups or two rigidly fixed beta methylene groups, and two gamma methyl groups afford no hindrance during the reaction. A comparison of rate constants of 2,3-dimethylbutane-1-sulfonyl chloride (VII) with octane-10 (I) and neopentylmethanesulfonyl chloride (II)



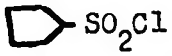
$$\underset{\text{Me}}{\text{Me}-\text{CH}}-\underset{\text{Me}}{\text{CH}}-\text{CH}_2-\text{SO}_2\text{Cl}$$

VII

$k = 0.047 \text{ min.}^{-1}$

indicates that one beta methyl group is moderately effective in hindering the reaction.

Cyclopentanesulfonyl chloride (VIII) reacts much more slowly than any of the above mentioned sulfonyl chlorides.

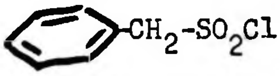


VIII

$k = 0.003 \text{ min.}^{-1}$

This may be due to the large steric requirements of the five-membered ring.

Due to the withdrawal inductive effect of the phenyl group in α-toluenesulfonyl chloride (IX),

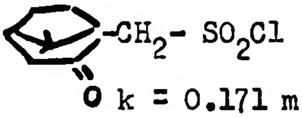


IX

$k = 0.063 \text{ min.}^{-1}$

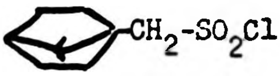
one would expect its rate of ethanolysis to be considerably faster than octane-1-sulfonyl chloride (k 0.089 min.^{-1}); however, this is not the case. The slight decrease can be accounted for by assuming that the planar phenyl group sterically hinders ethanolysis to an extent of the order of that of a beta methyl group, the enhancing polar effect offsetting this to some extent.

A comparison of rate constants for dl-camphor-10-sulfonyl chloride (X) with that of camphane-10-sulfonyl chloride (VI)



$k = 0.171\ \text{min.}^{-1}$

X



$k = 0.018\ \text{min.}^{-1}$

VI

indicates that the keto group has a strong polar effect, since both sulfonyl chlorides have essentially the same steric requirements.

Similarly, the data for 2-propene-1-sulfonyl chloride (X) and octane-1-sulfonyl chloride (I)

$CH_2 = CH - CH_2 - SO_2Cl$

$k = 0.102\ \text{min.}^{-1}$

XI

$C_5H_{11} - CH_2 - CH_2 - CH_2 - SO_2Cl$

$k = 0.089\ \text{min.}^{-1}$

I

reveals the polar effect of the double bond. As in the case of α -toluenesulfonyl chloride (IX), the effect does not appear to be sufficiently great to assign to this compound a homoallylic character, however.

From the above considerations, it is evident that the mechanism of reaction for sulfonyl chlorides is different from that of the carboxylic acid analogs. While the sulfur-oxygen bonds of the sulfonyl group generally are considered to be resonant between a covalent bond and a single bond, additions to them have never been clearly reported, although the analogous carboxylic acid chlorides are attacked by primary addition to the carbonyl group followed by elimination through a triad system.[45] Therefore, an attack on the sulfonyl group takes place by either a unimolecular (S_N1) or bimolecular (S_N2) displacement.

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[45] E. R. Alexander, "Ionic Organic Reactions," p. 231.

Unimolecular displacement (S_N1) of the chlorine from sulfonyl chlorides occurs when the sulfur-chlorine bond is activated to such an extent that ionization takes place in solution. The solvated sulfonylium ion then may be attacked by a solvent molecule or by a solvated negative ion to complete the reaction. Since ionization is the slowest of the three possible steps, it is the rate determining one and the rate of the reaction is dependent on the concentration of only the sulfonyl chloride. Therefore the displacement is said to be unimolecular (S_N1).

Bimolecular displacement (S_N2) of the chlorine occurs when the energy of activation is reduced below that necessary for ionization of the sulfur-chlorine bond. The attack by either a solvent molecule or a negative ion takes place at the rear face of the tetrahedral sulfur atom and results in an inversion of configuration about the sulfur atom in a manner similar to the well-known Walden inversion.

Recently, Gayle[46] has reasoned that both unimolecular and bimolecular displacement mechanisms are operative during ethanolysis of sulfonyl chlorides with the bimolecular one being responsible for approximately eighty-six per cent of the products for the more highly hindered displacements and approximately ninety-eight per cent for the relatively unhindered ones.

It is mentioned above that the sulfonyl chlorides cannot be compared with the carboxylic acid chlorides. Instead, their reaction mechanisms are similar to compounds that undergo displacement reactions

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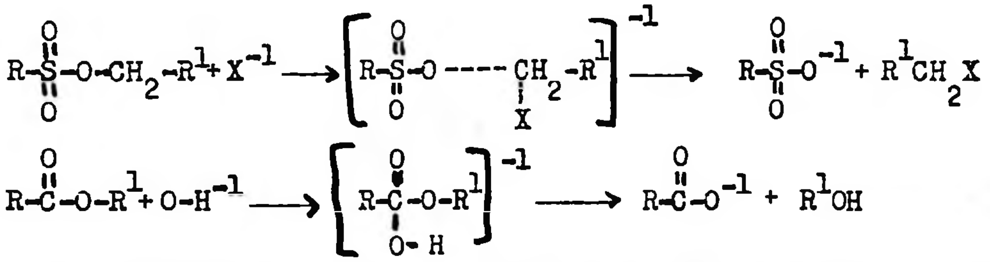
[46] Gayle, loc. cit.

such as the alkyl halides; therefore, their reactions are subject to the same sorts of steric effects. It should be pointed out that although there is less hindrance in displacement at the sulfur atom than in displacement at the carbon atom, the analogy with alkyl halides still holds, especially if a sulfonyl group is considered as the equivalent of a methylene group except about a third larger.

Alkylation of Ethanolic Hydrogen Chloride by Ethyl Alkanesulfonates

Some years ago, Ferns and Lapworth[47] showed that sulfonic acid esters behave differently from their carboxylic acid analogs in that the former esters act as alkylating agents whereas the latter ones usually do not. Due to this alkylating action, sulfinic esters more nearly resemble alkyl halides than they do carboxylic ester, if the acid moiety is considered the analog of the halide. Here, the resemblance to alkyl halides is in a different sense from that used when comparing sulfonyl chlorides to the latter. More recently, Tommila[48] studied the mechanisms of reaction of both sulfonic and carboxylic esters with nucleophilic reagents. These mechanisms are represented by the following schemes:



$$R-\overset{O}{\underset{O}{S}}-O-CH_2-R^1+X^{-1}\longrightarrow\left[R-\overset{O}{\underset{O}{S}}-O----\underset{X}{CH_2}-R^1\right]^{-1}\longrightarrow R-\overset{O}{\underset{O}{S}}-O^{-1}+R^1CH_2X$$

$$R-\overset{O}{C}-O-R^1+O-H^{-1}\longrightarrow\left[R-\underset{O-H}{\overset{O}{C}}-O-R^1\right]^{-1}\longrightarrow R-\overset{O}{C}-O^{-1}+R^1OH$$

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[47] J. Ferns and A. Lapworth, *J. Chem. Soc.*, *101*, 273 (1912).

[48] E. Tommila and M. Lindholm, *Acta. Chem. Scand.*, *5*, 647 (1951).

In this Laboratory a number of ethyl esters of sulfonic acids have been studied under conditions similar to those used for ethanolysis of the previously described sulfonyl chlorides. It was found that reaction of the esters was bimolecular (S_N2), thus agreeing with the findings of Tommila.

Attack on ethyl 2,3-dimethylbutane-1-sulfonate by ethanolic hydrogen chloride under conditions similar to those used for ethanolysis of 2,3-dimethylbutane-1-sulfonyl chloride and the ethanolysis of the ester in the absence of hydrogen chloride were studied. The data follows in Table 2. These are compared in Table 3 with those of the ethyl esters of sulfonic acids which have been studied under similar conditions in this Laboratory.

Table 2

Rate of Attack of Ethanolic Hydrogen Chloride on Ethyl 2,3-Dimethylbutane-1-sulfonate at Reflux

Reflux Time Mins.	RSO_2OEt Initial Mg.-Moles	RSO_2OEt Final Mg.-Moles	$k^{a,b}$ $Min.^{-1}$
15	5.00	3.53	0.023
20	5.00	2.81	0.029
25	5.00	2.43	0.029
30	5.00	2.22	0.027
35	5.00	2.27	0.023
45	5.00	1.76	0.023

[a] Average k 0.026 $min.^{-1}$ [b] $t_{\frac{1}{2}}$ = 27 min.

The rate constants for the reactions of the ethyl sulfonates with enthanolic hydrogen chloride represent the combined rates for the following two reactions:

1. $RSO_2OEt + HCl \longrightarrow RSO_2OH + EtCl$
2. $RSO_2OEt + EtOH \longrightarrow RSO_2OH + EtOEt$

The rate of the first reaction is not necessarily the difference between the rate of attack by ethanolic hydrogen chloride and the rate of ethanolysis because of the possibility of a "salt effect" from the hydrogen chloride.

From data similar to those in Table 3 and those obtained for several primary sulfonyl chlorides (see Table I, page 28), it has been suggested by Gayle[49] that the rates of ethanolysis of saturated primary sulfonyl chlorides are directly proportional to the rates of attack of ethanolic hydrogen chloride of the corresponding ester. This is seen readily in Figure III. Thus, it has been demonstrated that the steric requirements of the ethyl esters of primary sulfonic acids are related in some anomalous way to those of the alkyl halides having structures analogous to the sulfonic acid moiety. This relationship does not exist in the case of ethyl esters of secondary sulfonic acids. From these observations, then, it appears that the beta methyl group of ethyl 2,3-dimethylbutane-1-sulfonate only moderately hinders reactions of the ester, in conformity with its effect on the corresponding sulfonyl chloride. Studies of esters which are hindered in the alcohol moiety are being contemplated with the hope that this will lead to information from which a more nearly quantitative evaluation of steric effects eventually can be made.

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[49] J. B. Gayle, Unpublished work at the University of Alabama, University, Alabama.

Table 3: Rates of Reaction of Sulfonic Acid Esters

Sulfonic acid, Ethyl esters	Reference	Specific Rate Constants, k, $min.^{-1}$ EtOH-HCl	k, $min.^{-1}$ Abs. EtOH
Neopentylmethane-	1	0.051	0.003
Octane-1-	2	0.051	0.004
Octane-2-	2	0.041	0.003
2-Propene-1-	3	0.039	----
2,3-Dimethylbutane-1-	--	0.026	0.003
Cyclopentane-	4	0.022	0.002
Camphane-10-	5	0.016	0.001
Neopentane-	1	0.011	0.002

References:

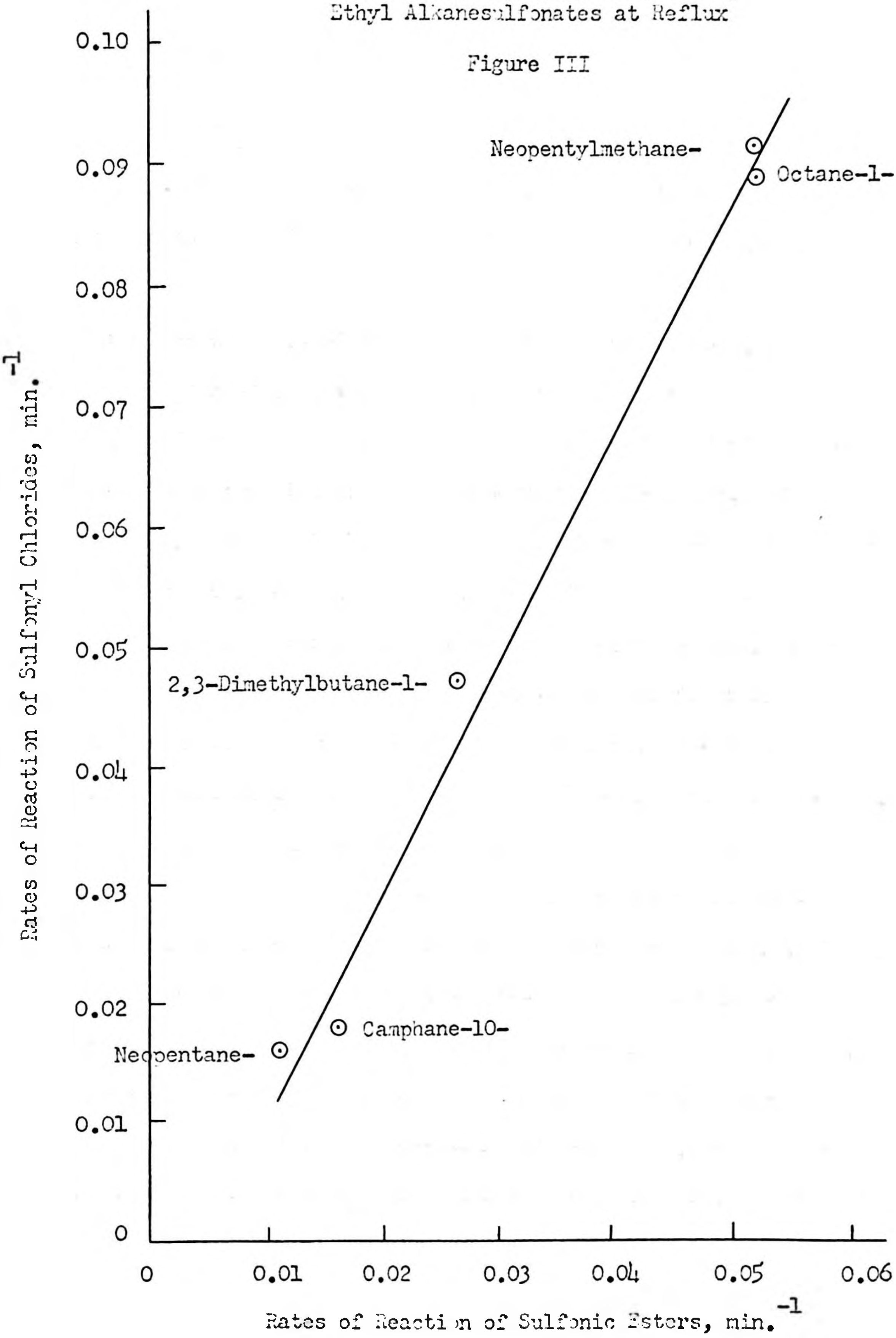
1. Paper presented by R. B. Scott, Jr., at the Southeastern Regional Meeting of the American Chemical Society in Birmingham, Alabama, October 21, 1954.
2. R. B. Scott, Jr., and R. E. Lutz, "A Study of Aliphatic Sulfonyl Compounds, I. Octane-1- and -2-sulfonyl Chlorides," *J. Org. Chem.* *19*, 830 (1954).
3. J. Preston, M. S. Thesis, 1954, University of Alabama, University, Alabama.
4. J. P. Stutts, M. S. Thesis, 1954, University of Alabama, University, Alabama.
5. J. B. Gayle, Ph. D. Dissertation, 1953, University of Alabama, University, Alabama.

Note:

Each "k" value is the average of the results obtained for four separate determinations.

Rates of Ethanolysis of Sulfonyl Chlorides vs. Rates of Alkylation of Ethanolic Hydrogen Chloride by Ethyl Alkanesulfonates at Reflux

Figure III



EXPERIMENTAL

Preparation of 1- and 2-Chloro-2,3-dimethylbutane

1- and 2-Chloro-2,3-dimethylbutane from Diisopropyl (H-I-32, 33, 34, and 129). Diisopropyl was photochemically chlorinated in the liquid phase on several occasions. A typical procedure (H-I-33) is described.

Four moles (345 g.) of diisopropyl (2,3-dimethylbutane, Phillips Petroleum, pure grade) in a two-liter, three-necked, round-bottomed flask equipped with gas inlet tube, reflux condenser, and stirrer was chlorinated over a period of two hours with one mole (71 g.) of chlorine (U.S. Army surplus). The reaction was activated by the light from two 150-watt General Electric Par 38 Projector Flood lamps and maintained between 0° and 10° with a carbon ice-acetone bath. After the reaction period, the chlorinated mass was washed first with 500 cc. of water, next three times each with 500-cc. portions of 10% sodium bicarbonate solution and, finally with three 500-cc. portions of water. After drying over anhydrous calcium chloride for one hour and then with anhydrous potassium carbonate overnight, the reaction mass was fractionally distilled through an adiabatically heated 106-cm. x 17-mm. column packed with 1/8" glass Pyrex single-turn "helices" and equipped with electronically activated magnetic total-condensation still head. Potassium carbonate was used as a distilland stabilizer. There were obtained 49 g. (0.4 mole, 10% conversion) of 2-chloro-2,3-dimethylbutane, b. p. 55°/108 mm., n_D^{25} 1.4171, and 51 g. (0.4 mole, 10% conversion) of 1-chloro-2,3-dimethylbutane, b. p. 65°/108 mm., n_D^{25} 1.4201.

In another preparation (H-I-129) a 250-watt unfiltered infrared lamp was used instead of the projector flood lamps. In this case, nine moles (774 g.) of diisopropyl was chlorinated over a period of four and one-half hours with 4.5 moles (320 g.) of chlorine. The temperature was maintained between 20° and 30° as no reaction occurred at lower temperatures. Fractional distillation of the crude mixture of alkyl chlorides through the previously described column yielded 212 g. (1.8 mole, 20% conversion) of 2-chloro-2,3-dimethylbutane, b. p. 61°/ca. 108 mm., n_D^{25} 1.4171 and 121 g. (1.0 mole, 9% conversion) of 1-chloro-2,3-dimethylbutane, b. p. 71°/ca. 108 mm., n_D^{25} 1.4201.

2-Chloro-2,3-dimethylbutane from the Corresponding Alcohol (H-II-133, 141, and 148). 2,3-Dimethyl-2-butanol was prepared and converted into the corresponding chloride on several occasions according to Shiner.[50] A typical procedure (H-II-133) is described.

57 G. (0.4 mole) of methyl iodide (Allied Chemical and Dye Corp.), diluted with about 60 cc. of dry ether, was added, dropwise, and with stirring, during ten hours to 9.6 g. (0.4 mole) of magnesium turnings (Eastman Kodak, Grignard Reagent grade) in a 200-cc., three-necked, round-bottomed flask fitted with a tantalum wire Hershberg-type stirrer, reflux condenser vented through a drying tube containing calcium chloride, and dropping funnel. After the Grignard reagent had been stirred for an additional two hours, it was transferred to a 500-cc., three-necked flask fitted as above and 60 cc. of dry ether was added. The resulting mixture was cooled to salt-ice temperatures

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[50] Shiner, loc. cit.

and 31 g. (0.36 mole) of methyl isopropyl ketone (Eastman Kodak, 3146), diluted with about 75 cc. of dry ether, was added, with stirring, during one and one-quarter hours. While stirring was continued for another three hours, the mixture was allowed to warm to room temperature. The reaction mass was poured carefully onto a slurry of crushed ice in 300 cc. of 10% sulfuric acid. The ether layer was separated and the aqueous layer was extracted with three portions each of 30 cc. of ether. The combined ether layers were dried over anhydrous magnesium sulfate overnight. After the ether had been removed by evaporation, the residual tertiary alcohol was fractionally distilled four times from a small Claisen-type distilling flask having a Vigreaux side-arm. There was collected 12.0 g. (0.12 mole, 30% yield based on methyl iodide) of 2,3-dimethyl-2-butanol, b. p. 116°, n_D^{25} 1.4141 (literature,[51] b. p. 117°/750 mm., n_D^{25} 1.4155).

The freshly distilled, tertiary alcohol was shaken with 32 cc. of concentrated hydrochloric acid (C. P. 38%) in a 150-cc. separatory funnel. After the mixture had settled, the lower aqueous layer was drawn off. The organic layer was diluted with 40 cc. of ether, washed with six portions each of 30 cc. of water, and dried over calcium chloride. After the ether had been removed by evaporation, the crude halide was distilled from the Claisen-type distilling flask into three fractions of n_D^{25} 1.4160, 1.4164, 1.4166, respectively, the combined weight being 9.5 g (0.08 mole, 67% yield based on 2,3-dimethyl-2-butanol).

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[51] Shiner, loc. cit.

Derivatives of 1- and 2-Chloro-2,3-dimethylbutane

N-Phenyl 3,4-Dimethylvaleramide (H-I-36). In a test tube were placed 0.3 g. (12 mg.-moles) of magnesium turnings (Eastman Kodak, Grignard Reagent grade) and a small crystal of iodine. After the iodine had been sublimed throughout the magnesium, 1.07 g. (9 mg.-moles) of 1-chloro-2,3-dimethylbutane (n_D^{25} 1.4201) dissolved in about 15 cc. of dry ether was poured onto the magnesium, and the mixture then was stirred during one-half hour.

To the chilled Grignard compound was added, dropwise, a solution containing 0.95 g. (9 mg.-moles) of phenyl isocyanate (Eastman Kodak, P 553) and 15 cc. of dry ether. The resulting mixture was decomposed by pouring it into 25 cc. of dilute hydrochloric acid. The ether layer was separated and then evaporated to dryness to give a solid mixture of anilide and diphenylurea. The anilide was extracted with several portions of hot carbon tetrachloride and recrystallized from isooctane (2,2,3-trimethylpentane, pure grade) until a constant melting point of 109.5-110.5° (literature, 110-110.5°[52] and 67°[53]) resulted. 1.03 G. (5 mg.-moles, 55% yield based on alkyl chloride) of pure N-phenyl 3,4-dimethylvaleramide was collected.

N-Phenyl 2,3,3-Trimethylbutryamide from 2-Chloro-2,3-dimethylbutane Derived from Chlorination of Diisopropyl (H-I-37). 6.0.G.

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52. Detling, et al., loc. cit.

53. Huston and Agett, loc. cit.

(0.25 mole) of magnesium turnings (Eastman Kodak, Grignard Reagent grade) and several small crystals of iodine were placed in a half-liter, three-necked, round-bottomed flask fitted with an efficient stirrer, reflux condenser, and dropping funnel. The flask was heated with a flame from a micro-burner until the iodine sublimed throughout the magnesium. It was then allowed to cool. 27.3 G. (0.23 mole) of 2-chloro-2,3-dimethylbutane (n_D^{25} 1.4171), obtained from photochemical chlorination of diisopropyl, was diluted with 35 cc. of dry ether. About 6 cc. of the ether-halide solution and a drop of methyl iodide were added directly into the reaction flask. After vigorous stirring for a few minutes, the reaction started. Approximately 20 cc. of dry ether was added directly to the flask after the reaction had been allowed to proceed for a short time. With rapid stirring, about 30 cc. of ether-halide solution was added at a rate slightly less than one drop a second. The remaining ether-halide solution was diluted with about 20 cc. more of dry ether and then added at the same rate. Periodically, dry nitrogen was passed over the reactants. Total time of reaction was three hours.

Titration for yield of Grignard compound was carried out as follows: A 1.402-g. aliquot of Grignard compound was decomposed by pouring it into 30 cc. of distilled water in an Erlenmeyer flask. The mixture was heated on a hot plate for a few minutes and then allowed to cool. To this 31.00 cc. of 0.1248 N sulfuric acid was added and the acidified sample titrated with 1.51 cc. of 0.1555 N sodium hydroxide to the phenolphthalein end-point. The total weight of Grignard compound was 38.5 g. Calculation indicates a 44% yield based on the amount of tertiary chloride used.

To 1.4 g. (9.7 mg.-moles) of this tertiary Grignard reagent 1.7 g. (16.5 mg.-moles) of phenyl isocyanate dissolved in about 15 cc. of dry ether was added, dropwise, over a period of about five minutes at room temperature. The resulting mixture was decomposed by pouring into 25 cc. of dilute hydrochloric acid. The solid residue obtained from evaporating the ether layer was extracted with hot carbon tetrachloride. By cooling the extract 0.45 g. (2.2 mg.-moles, 22% conversion based on Grignard reagent) of crude N-phenyl 2,2,3-trimethylbutyramide was obtained. It was recrystallized from dilute ethanol to yield a product melting at 78.5-79°.

N-Phenyl 2,2,3-Trimethylbutyramide from 2-Chloro-2,3-dimethylbutane Derived from 2,3-Dimethyl-2-butanol (H-II-139). The Grignard reagent from 2-chloro-2,3-dimethylbutane was prepared in the usual manner from 9.5 g. (0.08 mole) of the tertiary alkyl chloride (n_D^{25}1.4160-1.4166), obtained from 2,3-dimethyl-2-butanol, dissolved in 25 cc. of dry ether and 2.0 g. (0.08) of magnesium turnings. The reaction period was two hours. To the Grignard reagent 6.2 g. (0.05 mole) of freshly distilled phenyl isocyanate dissolved in 40 cc. of dry ether was added, dropwise, during one-half hour. The resulting product was decomposed and the anilide was separated from diphenylurea as described above. 2.9 G. (0.014 mole, 18% conversion based on alkyl chloride) of crude N-phenyl 2,2,3-trimethylbutyramide was obtained. It was recrystallized from neohexane until a constant melting point of 77.5-78° resulted.

Anal.[54] Calc'd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33.

Found: C, 76.11; H, 9.36.

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[54] Clark Microanalytical Laboratory, Urbana, Ill., reference number 24348.

A mixture of this anilide and the isomeric anilide derived from the primary chloride melted at 63.5-68.5°.

2,3-Dibromo-2,3-dimethylbutane (H-I-35). According to the method of Grosse and Ipatieff,[55] 1.57 g. (13 mg.-moles) of 2-chloro-2,3-dimethylbutane (n_d^{25} 1.4171) was photochemically brominated in the liquid phase by adding, dropwise, liquid bromine (Coleman and Bell Co.) to the tertiary alkyl chloride in a test tube while irradiating the reaction zone with light from a 150-watt General Electric Par 38 Projector Flood lamp. After each addition, the tube was shaken until the characteristic bromine color was discharged. Reaction was accompanied by copious evolution of hydrogen bromide. Bromine was added until almost all the alkyl chloride was converted to a white, solid, dibromo compound, the tertiary chlorine atom having been displaced. This crude derivative, representing a 77% conversion (10 mg.-moles, 2.47 g.) to 2,3-dibromo-2,3-dimethylbutane was recrystallized seven times from ether as silky needles. It sublimed without melting in an open capillary melting point tube at 164-168° (literature,[56] 165-175°).

An authentic sample of the dibromo derivative prepared from the hydrocarbon, diisopropyl, following the same procedure outlined above, sublimed without melting in an open capillary at 163-170°. Mixtures of the alkyl dibromide derived from the differently-prepared samples showed no depression in sublimation point.

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[55] Grosse and Ipatieff, *loc. cit.*

[56] *Ibid.*

Preparation of 2,3-Dimethylbutane-1-sulfonyl Chloride

2,3-Dimethylbutane-1-sulfonyl Chloride from Chlorosulfonylation of Diisopropyl (H-I-39, 67, 80, and 88). Diisopropyl was photochemically chlorosulfonylated on several occasions. A typical procedure (H-I-88) is described.

One and one-half moles (129 g.) of diisopropyl (Phillips Petroleum, pure grade), diluted with an equal volume of carbon tetrachloride, in a 500-cc., three-necked, round-bottomed flask equipped with a gas inlet tube, reflux condenser, and stirrer was chlorosulfonylated with a mixture of 0.8 mole (57 g.) of chlorine, and 1.5 moles (96 g.) of sulfur dioxide over a period of one hour. The reaction was activated by light from a 150-watt General Electric Par 38 Projector Flood lamp and maintained at 0° to 10° with a salt-ice bath. The residue, from removal under reduced pressure of unreacted hydrocarbon, diluent, and by-product alkyl chlorides, was distilled through a 36-cm. x 16-mm. Vigreaux column fitted with a partial condensation still head to yield 60 g. (0.32 mole) boiling at $61^{\circ}/1$ mm. n_D^{25} 1.4607, d_4^{25} 1.1524, M_D 44.0 (theory 44.3).

Anal.[57] Calc'd for $C_6H_{13}Cl\,O_2S$: C, 39.02; H, 7.10; S, 17.36; Cl, 19.20

Found: C, 39.27; H, 7.06; S, 17.24; Cl, 19.30.

2,3-Dimethylbutane-1-sulfonyl Chloride from the Corresponding Alkyl Chloride (H-I-52). One mole (121 g.) of 1-chloro-2,3-dimethylbutane (n_D^{25} 1.4201), prepared by photochemical chlorination of

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[57] Clark Microanalysis Laboratory, Urbana, Ill., reference number 12912.

2,3-dimethylbutane, was diluted with 125 cc. of dry ether. Approximately 125 cc. of the ether-halide solution was added at a rate of about a drop per second with stirring to one mole (24 g.) of magnesium turnings (Eastman Kodak, Grignard Reagent grade) in a one-liter, three-necked, round-bottomed flask fitted with a tantalum wire, Hershberg-type stirrer, reflux condenser, and dropping funnel. The remaining ether-halide solution was diluted with 75 cc. of dry ether and added at the same rate. After all additions, requiring seven and one-half hours, the charge was stirred for an additional hour and then allowed to settle overnight.

Titration for yield of Grignard compound was carried out as follows: A 3.00-cc. aliquot of clear Grignard reagent was added to about 30 cc. of distilled water in an Erlenmeyer flask. This was heated on a hot plate for a few minutes and then allowed to cool. Then 10.00 cc. of 1.000 N sulfuric acid (Eimer and Amend Volumetric Standard) was added and the acidified sample was titrated with 7.90 cc. of 0.500 N sodium hydroxide (Eimer and Amend Volumetric Standard), to a phenolphthalein end-point. The total volume of the Grignard reagent was about 375 cc. Calculation indicates a 75% yield based on the alkyl chloride used.

In the same apparatus used for preparation of the Grignard reagent and flushed with nitrogen were placed 171 g. (1.2 moles) of sulfuryl chloride (Eastman Kodak, P 322) and 275 cc. of dry ether. To this 0.75 mole of the Grignard reagent from 1-chloro-2,3-dimethylbutane in 375 cc. of ethereal solution was added during one and one-third hours while the sulfuryl chloride solution was continually stirred. A reaction temperature of 0° to 10° was maintained by means of a salt-ice bath. The white, chalky slurry which formed was poured into 1.5 liters of stirred chopped-ice and water. The ether layer was separated, washed, first with three 200-cc. portions of cold water, next with three 250-cc. portions of cold, 5% sodium bicarbonate solution, and finally four times with 250-cc. portions of cold water. The ether solution of sulfonyl chloride was dried over calcium chloride for several hours and then with potassium carbonate overnight. Each drying and subsequent storage took place in a refrigerator. After the ether and other low boiling materials had been removed by evaporation in vacuo, the remaining crude sulfonyl chloride was distilled through the earlier-described 36-cm. x 16-mm. Vigreaux column. 615 G. (0.33 mole, 44% yield based on Grignard reagent or 33% based on alkyl chloride) of pure 2,3-dimethylbutane-1-sulfonyl chloride, b. p. 71°/ 1.8 mm., n_D^{25} 1.4607, d_4^{25} 1.1528, was obtained.

In another preparation (H-II-43), the Grignard reagent was prepared in a manner similar to that described above from one mole (121 g.) of 1-chloro-2,3-dimethylbutane dissolved in 300 cc. of dry ether and one mole (24 g.) of magnesium turnings (Eastman Kodak, Grignard Reagent grade). Total time of reaction was ten and one-half hours. A 2.00-cc. aliquot of the 355 cc. of this Grignard reagent solution was added to 50.00 cc. of 0.2172 N nitric acid and the acidified sample was titrated with 12.10 cc. of 0.4626 N sodium hydroxide solution to a phenolphthalein end-point, indicating a 93% yield based on the alkyl chloride used.

Into each of three 250-cc. beakers were placed 50 cc. of dry ether and 25.00 cc. aliquots (65.8 mg.-moles of the reagent) of this Grignard preparation. During one hour, anhydrous sulfur dioxide was bubbled slowly into the solution. Dry ether was added periodically to each beaker because of some volatilization of the solvent.

Into the ether suspension of slightly yellow sulfinic acid salt in one beaker, was bubbled chlorine gas over a period of two hours. After the precipitated magnesium chloride had been dissolved in water, the ethereal solution of sulfonyl chloride was separated and washed, first with several portions of water, then with four portions each of 25 cc. of 5% sodium bicarbonate, and finally again with several portions of water. The ether solution was dried over calcium chloride for one hour, then decanted into a dry Erlenmeyer flask. After almost all of the ether had been removed by evaporation, the remaining liquid was transferred to a tared 50-cc. round-bottomed flask. Evaporation of the solvent, in vacuo, yielded 10.183 g. (55.1 mg.-moles, representing an 84% yield based on Grignard reagent or 76% based on alkyl chloride) of slightly yellow 2,3-dimethylbutane-1-sulfonyl chloride, n_D^{25} 1.4609 (pure, n_D^{25} 1.4607).

The ether was evaporated from the second preparation of sulfinate and the slightly yellow salt was placed in a vacuum oven at 65°. Weight of dry salt was 12.8 g. (61 mg.-moles). To this dry salt suspended in 100 cc. of dry ether was added 30 g. (0.22 mole) of sulfuryl chloride (Eastman Kodak, P 322) in small portions over a period of two minutes. The mixture then was heated gently for ten minutes. A violent hydrolysis of the excess sulfuryl chloride occurred when water was added carefully in small portions to the chilled mixture. The ethereal layer was separated, washed, and dried, and then placed in a tared 50-cc. round-bottomed flask. Evaporation of the solvent under reduced pressure yielded 9.464 g. (51.2 mg.-moles, representing a 78% yield based on

Grignard reagent or 70% based on alkyl chloride) of slightly yellow 2,3-dimethylbutane-1-sulfonyl chloride, n_D^{25} 1.4613.

The ether also was removed from the third preparation, in vacuo, to yield 11.2 g. (54 mg.-moles) of slightly yellow sulfinic acid salt. Into a suspension of the salt in 75 cc. of water was bubbled chlorine gas until all of the solid material disappeared. After the sulfonyl chloride had been dissolved in ether, the ethereal solution was washed with several portions of water and then dried over calcium chloride. It then was placed in a tared 50-cc. round-bottomed flask. Evaporation of the ether under reduced pressure yielded 9.469 g. (51.3 mg.-moles, representing a 78% yield based on Grignard reagent or 70% based on alkyl chloride) of slightly yellow sulfonyl chloride, n_D^{25} 1.4611.

Attempted Preparation of 2,3-Dimethylbutane-2-sulfonyl Chloride

Two attempts to prepare 2,3-dimethylbutane-2-sulfonyl chloride by the modified Cherbuliez procedure were carried out (H-II-141 and 148). One of these procedures (H-II-148) is described.

The Grignard reagent corresponding to 2-chloro-2,3-dimethylbutane was prepared in the usual manner from 41.8 g. (0.35 mole) of the tertiary alkyl chloride (n_D^{25} 1.4162), obtained from the corresponding alcohol, dissolved in 110 cc. of dry ether, and 8.5 g. (0.35 mole) of magnesium turnings (Eastman Kodak, Grignard Reagent grade). Total time of reaction was seven and one-half hours. After the Grignard reagent had been cooled with a salt-ice bath, dry sulfur dioxide gas was bubbled into the stirred ethereal solution during four hours, moisture being excluded from the reaction zone with a tube containing calcium chloride. The reaction mass was removed and placed in a vacuum oven at room temperature. There was obtained 50.4 g. (0.24 mole, 69% conversion based on alkyl halide) of slightly yellow chloromagnesiumsulfinate salt.

A mixture of 33.8 g. of this salt in 100 cc. of carbon tetrachloride (Allied Chemical and Dye Corp., technical grade) was placed in a 250-cc. flask fitted with a gas inlet tube and a tube containing calcium chloride. Into the mixture, after it had been cooled to about 10° with an ice-water bath, was bubbled chlorine gas over a period of four hours. The solution was filtered and then subjected to reduced pressure, thereby removing the solvent. During these operations, a strong odor of sulfur dioxide was noted. The residual liquid was distilled from a Claisen-type flask having a Vigreaux side-arm to give the following fractions:

Fraction	B. P.	n_D^{25}	Approx. Wt. (g.)
1	48-58°/0.7 mm.	1.4795	0.5
2	58-68°/0.7 mm.	1.4887	1.5
3	68-78°/0.7 mm.	1.5051	1.5
4	78-90°/0.7 mm.	1.5149	3.0
5	90-100°/0.7 mm.	1.5242	3.0
6	100-107°/0.7 mm.	1.5337	3.0
7	107-113°/0.7 mm.	1.5377	0.5

The last drop in the condenser had a refractive index of n_D^{25} 1.5372.

The following tests were made on the above-described fractions: 1) A sample of each fraction except fractions 1 and 2 was fused with sodium, and the usual tests for chloride and sulfide ions were carried out. Each experiment gave a negative sulfide ion test and a positive chloride ion test. 2) A precipitate formed immediately when a sample of each fraction was tested with a dilute ethanolic solution of silver nitrate. 3) A precipitate formed in about two minutes and iodine was liberated immediately when a sample of each fraction was tested with a dilute acetone solution of sodium iodide.

In order to further identify the products, 16 g. of high boiling material (boiling range, 40 to 70° /2 mm.) obtained by chlorination of diisopropyl, was chlorinated further in the presence of a 150-watt General Electric Par 38 Projector Flood lamp and at a temperature of about 25° until the weight increased to 21 g. Distillation from the above-mentioned Claisen type distilling flask of the washed and dried liquid gave the following fraction:

Fraction	B. P.	n_D^{25}	Approx. wt. (g.)
1	45-55°/1.5 mm.	1.4836	2.1
2	55-65°/1.5 mm.	1.4897	2.3
3	65-70°/1.5 mm.	1.4935	2.7
4	70-82°/1.5 mm.	1.5058	3.4
5	82-92°/1.5 mm.	1.5118	2.9
6	92-100°/1.5 mm.	1.5167	1.3
7	100-105°/1.5 mm.	1.5212	1.1

The last drop in the condenser had a refractive index of n_D^{25} 1.5233.

Preparation of Ethyl 2,3-Dimethylbutane-1-sulfonate

Ethyl 2,3-Dimethylbutane-1-sulfonate from the Action of Diazoethane on Free Sulfonic Acid (H-I-83). In a 500-cc., three-necked, round-bottomed flask fitted with an efficient stirrer, thermometer, and dropping funnel was placed a solution of 14.4 g. (0.36 mole) of sodium hydroxide in 35 g. of water. The solution was heated to 55° and then 22.2 g. (0.12 mole) of pure 2,3-dimethylbutane-1-sulfonyl chloride was added, with stirring, over a period of thirty-five minutes. Stirring was continued for twenty-five minutes after addition was complete. The mixture was neutralized with dilute hydrochloric acid to the methyl orange end-point. After the water had been evaporated (in vacuo), the sodium sulfonate was extracted with three portions each of 100 cc. of hot absolute ethanol. Evaporation of the solvent gave 22.9 g. (0.12 mole, 100% yield based on sulfonyl chloride) of sodium 2,3-dimethylbutane-1-sulfonate.

This sodium sulfonate was placed into a 500-cc. Erlenmeyer flask and slurried with 400 cc. of dry ether. Dry hydrogen chloride (generated by the action of concentrated sulfuric acid on concentrated hydrochloric acid and dried by passing through a tube containing calcium chloride) was bubbled into the mixture for several hours. Precipitated sodium chloride was removed by filtration and washed with several portions of dry ether. Ether was evaporated from the combined ethereal solutions to yield 20 g. (0.12 mole, 100% yield based on sodium sulfonate) of light brown 2,3-dimethylbutane-1-sulfonic acid.

In a one-liter, round-bottomed flask fitted with a reflux condenser were placed 123 g. (1.5 moles) of ethylamine hydrochloride (Smith, New York), 300 g. (5 moles) of urea (Coleman and Bell Co., C. P.), and 377 g. of water, according to the Organic Syntheses preparation for diazomethane.[58] The solution was boiled gently under reflux for two and three-quarter hours and then vigorously for one-quarter of an hour. After the mixture had been allowed to stand overnight at room temperature, 104 g. (1.5 moles) of sodium nitrite was added, and the resulting solution was cooled to 0°. To a mixture of 600 g. of crushed ice and 100 g. of concentrated sulfuric acid in a five-liter beaker which was surrounded by a chloroform-carbon tetrachloride-dry ice freezing mixture, was added the cold ethylurea-nitrite solution at such a rate that the reaction temperature did not rise above 0°. Time for addition was one hour. The nitrosoethylurea, which rose to the surface of the liquid, was filtered with suction and pressed well on the filter. About 50 cc. of ice water was stirred with the slightly orange crystals to form a paste which then was sucked as dry as possible. 107 G (0.91 mole, 61% yield based on ethylamine hydrochloride) of nitrosoethylurea was obtained. Into a one-liter beaker were charged 120 cc. of a 50% potassium hydroxide solution and 500 cc. of ether. The contents were cooled to below 5° and the ether was kept blanketed with an atmosphere of nitrogen as 56.8 g. (0.4 mole) of nitrosoethylurea was added in small increments. A deep orange color, characteristic of diazoethane, formed in the ether layer.

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58. A. H. Blatt, "Organic Syntheses," Collective Vol. II (2nd Edition), p. 165.

About 400 cc. of the ether solution of diazoethane was decanted into a 500-cc. distillation flask from which all but about 75 cc. of the solution was distilled into a cold (5°) solution of 16.6 g. (0.1 mole) of 2,3-dimethylbutane-1-sulfonic acid in 400 cc. of dry ether, the distillate first being condensed. More ethereal diazoethane was prepared and distilled into the sulfonic acid solution until a golden yellow color persisted, indicative of an excess of the diazo hydrocarbon. To minimize loss of diazoethane the receiving flask was vented through a reflux condenser. In all, about 1600 to 1800 cc. of the ethereal diazoethane solution was distilled, the ethylnitrosourea used amounting to one mole (117 g.).

Although the ether solution containing the sulfonic ester was golden yellow, it was strongly acidic, indicating the presence of some sulfonic acid, persistence of the yellow color proving to be an undependable indicator. The solution was concentrated to about 75 cc. and then was washed with three portions each of about 75 cc. of water. The water washings were combined and the solvent was evaporated, in vacuo, to give 10.2 g. (0.061 mole) of unreacted 2,3-dimethylbutane-1-sulfonic acid.

The ether solution containing the ester was dried over calcium chloride for three hours and then with magnesium sulfate overnight. After the ether had been removed by evaporation, the crude ester was distilled under reduced pressure from a Claisen-type distilling flask to give 6.7 g. (0.035 mole, 90% conversion based on recovered sulfonic acid) of ethyl 2,3-dimethylbutane-1-sulfonate (n_D^{25} 1.4373).

The sweet smelling ester was redistilled from the previously-described 36-cm. x 16-mm. Vigreaux column, b. p. 82° /0.8 mm., n_D^{25}

1.4377, d_4^{25} 1.0437, M_D 48.8 (theory 49).

Anal.[59] Calc'd for $C_8H_{18}O_3S$: C, 49.45; H, 9.34

Found: C, 49.46; H, 9.32

Ethyl 2,3-Dimethylbutane-1-sulfonate from Alkyl Halide and Silver Sulfonate (H-I-110, 111, and 134). Ethyl 2,3-dimethylbutane-1-sulfonate was prepared according to the method of Rheinbolt[60] on several occasions. A typical procedure (H-I-110) is described.

Into a 250-cc., round-bottomed flask fitted with a reflux condenser was charged a mixture of 18.5 g. (0.1 mole) of 2,3-dimethylbutane-1-sulfonyl chloride (n_D^{25} 1.4612) and 70 cc. of 10% ethanolic hydrogen chloride solution. After the mixture had been refluxed for five and one-quarter hours, the reaction products were dissolved in ether and washed with four portions each of 500 cc. of water. The water washings were combined and then placed in a vacuum oven, at 60°, until all of the water and hydrogen chloride were removed, leaving 2,3-dimethylbutane-1-sulfonic acid as a dark brown liquid. Moist silver oxide, obtained by the interaction of silver nitrate and 20% sodium hydroxide solution then was added to a dilute aqueous solution of the sulfonic acid until an excess of silver oxide was present. The resulting solution was filtered and then evaporated to dryness, yielding 20.1 g. (0.073 mole) of silver sulfonate.

A mixture of 19.1 g. (0.07 mole) of the dry silver sulfonate and about 20 cc. of dry ether was placed in a ground-glass stoppered bottle.

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[59] Clark Microanalytical Laboratory, Urbana, Ill., reference number 16477.

[60] H. Reinbolt, J. Mott, and E. Motzkus, J. prakt. chem., 134, 267 (1932); Ref. cit. C. A., 26, 5544 (1932).

To this mixture was added 10.9 g. (0.07 mole) of freshly distilled ethyl iodide (Columbia Organic Chemical Co.). Formation of silver iodide (yellow) took place rather slowly apparently being completed in about five minutes; the reaction mixture then was allowed to stand overnight. The crude ester left upon evaporating the ether solution was distilled from the 36-cm. x 16-mm. Vigreaux column into four fractions of ethyl 2,3-dimethylbutane-1-sulfonate with n_D^{25} 1.4378, 1.4389, 1.4387, and 1.4377, respectively, the combined weight being 10.9 g. (0.06 mole, 86% conversion based on silver sulfonate).

Reaction Rate Studies on 2,3-Dimethylbutane-1-sulfonyl Chloride

Four separate reaction rate determinations (H-I-100,101, and 102) were carried out by refluxing mixtures containing 1.8469 g. (0.0100 mole) of 2,3-dimethylbutane-1-sulfonyl chloride, 0.50 g. (0.014 mole) of hydrogen chloride, and 8.4 g. (0.18 mole) of dry ethanol for varying periods. A first order reaction rate constant was determined for each, and an average of 0.047 min.$^{-1}$ at a reflux temperature of 83-84^{0} was calculated ($t_{\frac{1}{2}}$ = 15 min.). The data are recorded in Table 5.

The ethyl alcohol used in these studies was absolute alcohol which had been dried over calcium hydride for twenty-four hours and distilled from a moisture free distillation apparatus. Hydrogen chloride, generated by the action of concentrated sulfuric acid on concentrated hydrochloric acid, was passed through sulfuric acid, a trap of glass-wool, and a tube containing calcium chloride, and absorbed in the alcohol until the desired concentration of alcoholic-hydrogen chloride was obtained. The solution was stored in a glass stoppered bottle in a desiccator containing calcium chloride.

The analytical method used to estimate the composition of sulfonyl chloride-ester mixture after each reaction test was similar to that reported by Scott.[61] Known amounts of sulfonyl chloride and ester were mixed thoroughly and the refractive index of each mixture recorded. These results are given in the following table:

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61. Scott, loc. cit.

Table 4

Index of Refraction of Known Mixtures of Sulfonyl Chloride and Ester Mixture

RSO_2Cl gms.	RSO_2Cl mg.-moles	RSO_2OEt gms.	RSO_2OEt mg.-moles	n_D^{25}	RSO_2Cl mole %	RSO_2OEt mole %
0.2638	1.428	0.0623	0.321	1.4560	81.67	18.33
0.1766	0.956	0.0892	0.459	1.4523	67.56	32.44
0.1259	0.682	0.1702	0.876	1.4463	43.77	56.23
0.0586	0.317	0.2888	0.459	1.4410	17.59	82.41

A plot of mole per cent versus refractive index for these mixtures are recorded in Figure IV. From a composition-refractive index graph (see Figure IV), the composition of a mixture of ester and sulfonyl chloride is readily estimated from the weight and refractive index of the mixture. A material balance for each reaction rate determination is recorded in Table 6. A typical reaction rate determination follows. A mixture of 1.8669 g. (0.0100 mole) of 2,3-dimethylbutane-1-sulfonyl chloride (n_D^{25} 1.4707), 0.5 g. (0.014 mole) of hydrogen chloride, and 8.4 g. (0.18) of dry ethanol were placed in a 25-cc. round-bottomed flask and refluxed for 15.0 minutes on a boiling water bath. The initial time, t_1, was taken when reflux started and the final time, t_2, when reflux stopped. After this reaction period, the flask was plunged quickly into a beaker containing chopped ice and water for a few moments, and then the contents were poured into a 200-cc. separatory funnel containing cold water. The reaction flask was washed out with several portions of cold water followed with

Table 5

Ethanolysis of 2,3-Dimethylbutane-1-sulfonyl Chloride[a]

Time Mins.	RSO_2Cl, mg.-moles Obt'd[b]	RSO_2Cl, mg.-moles Calc'd[c]	RSO_2OEt, mg.-moles Obt'd[d]	RSO_2OEt, mg.-moles Calc'd[c]	RSO_2OH[d] mg.-moles	k, min.$^{-1}$
15	4.91	5.00	3.98	4.07	0.93	0.046
25	2.87	2.90	4.46	4.50	2.60	0.050
30	2.29	2.34	4.11	4.21	3.45	.048
35	2.06	2.11	3.92	4.02	3.89	.045
Average						0.047

[a] Mixture of 1.8469 g. of sulfonyl chloride, 0.50 g. of hydrogen chloride, and 8.4 g. of dry ethanol refluxed for the times indicated. [b] Estimated from weight of mixture of sulfonyl chloride and ester after extraction of sulfonic acid and from refractive index of totally distilled mixture. [c] Calculated by stoichiometric difference from amount of sulfonic acid and from refractive index of distilled sulfonyl chloride-ester mixture. [d] Estimated by titration of aqueous extract after expelling hydrogen chloride.

Table 6

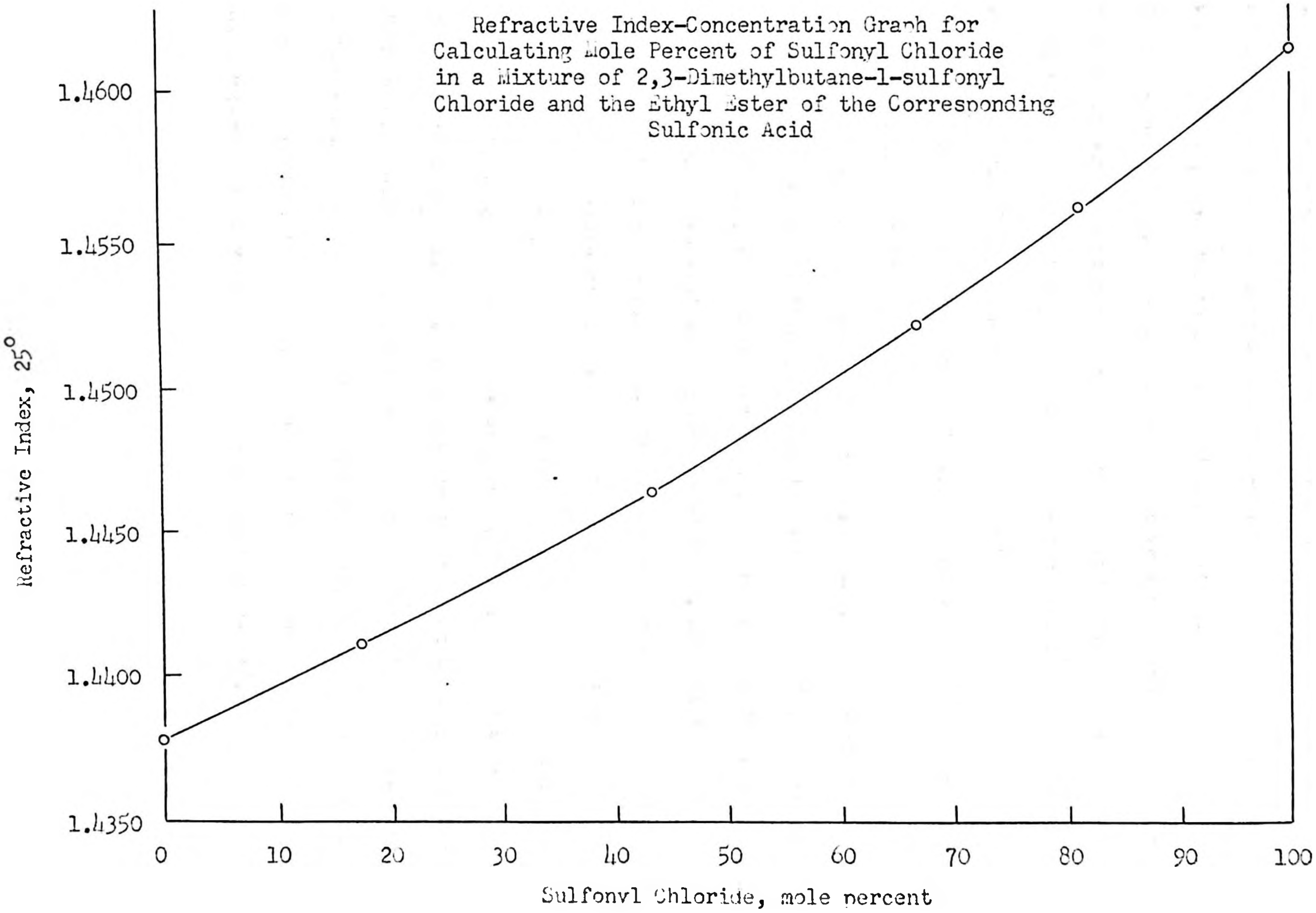
Analytical Data for Ethanolysis of 2,3-Dimethylbutane-1-sulfonyl Chloride

Time Mins.	RSO_2Cl-RSO_2OEt Mixture Wt. (g.)	RSO_2Cl-RSO_2OEt Mixture n_D^{25}[a]	RSO_2Cl Mole % In mixture[b]	Ml of 0.1123 N NaOH to neutralize RSO_2OH	Material Balance %
15	1.6856	1.4490	55.2	8.32	98.2
25	1.3984	1.4454	39.2	23.15	99.3
30	1.2221	1.4447	35.7	30.68	98.5
35	1.1429	1.4444	34.4	34.50	98.5

[a] Refractive index of totally distilled mixture. [b] Estimated from Figure IV.

Figure IV

Refractive Index-Concentration Graph for
Calculating Mole Percent of Sulfonyl Chloride
in a Mixture of 2,3-Dimethylbutane-1-sulfonyl
Chloride and the Ethyl Ester of the Corresponding
Sulfonic Acid



several portions of ether. The ester-sulfonyl chloride mixture was extracted with four 35-cc. portions of ether and the combined ether extracts were then washed with two 35-cc. portions of water (the last washing being neutral to litmus) and dried over magnesium sulfate for twenty-four hours. The aqueous solutions were combined and concentrated under reduced pressure to give dark brown sulfonic acid free from hydrogen chloride (negative chloride ion test). Titration with 8.32 cc. of 0.1123 N sodium hydroxide solution to the phenolphthalein end-point indicated that 0.93 mg,-mole of sulfonic acid was formed during the reaction.

The ether solution was poured into a 250-cc. Erlenmeyer flask, concentrated to about 10 cc. with an infrared lamp, and transferred to a tared 25-cc. round-bottomed flask. The Erlenmeyer flask was washed out with several small portions of ether, and the washings were added to the 25-cc. flask. After most of the ether had been removed by moderate heat, the system was subjected to a reduced pressure of 10 mm. until the residual weight remained constant. The ester-sulfonyl chloride mixture weighed 1.6856 g. and had a refractive index of n_D^{25} 1.4424. This mixture after being totally distilled from a micro-distilling flask had an index of refraction n_D^{25} 1.4490, a trace amount of impurity having been removed. From these data it was estimated that 3.98 mg.-moles of ester had been formed and that 4.91 mg.-moles of sulfonyl chloride was left unreacted.

Reaction Rate Studies on Ethyl 2,3-Dimethylbutane-1-sulfonate

Attack of Ethanolic Hydrogen Chloride on Ethyl 2,3-Dimethylbutane-1-sulfonate (H-I-116 and 117, and H-II-66, 67 and 68). Two sets of experiments, each comprising three determinations, were carried out for the attack of ethanolic hydrogen chloride on the intermediate ester formed during ethanolysis of 2,3-dimethylbutane-1-sulfonyl chloride in a manner similar to that reported for the sulfonyl chloride. A first order reaction rate constant of 0.026 $min.^{-1}$ at a reflux temperature of 83-84° was calculated ($t_{\frac{1}{2}}$ = 27 min.) Results from these experiments are recorded in Tables 7 and 8.

Experiment A was carried out by refluxing for varying times mixtures of 0.915 g. (0.0050 mole) of ester, 0.425 g. (0.0116 mole) of hydrogen chloride, and 6.2 g. (0.14 mole) of dry ethanol; the molar proportions of ester to hydrogen chloride to ethanol being 1:2.3:280. The amount of sulfonic acid formed during the reaction period was determined by titration of the aqueous extract after expelling hydrogen chloride. The amount of unreacted ester was determined by weighing the residual ester obtained upon evaporation of the washed ether extracts.

Experiment B was performed by refluxing for varying times mixtures of 0.915 g. (0.0050 mole) of ester, 1.81 g. (0.0495 mole) of hydrogen chloride, and 24.4 g. (0.53 mole) of ethanol; the molar proportions of ester to hydrogen chloride to ethanol being 1:10:100. In these experiments the unreacted ester was not recovered; however, the amount was estimated by stoichiometric difference from sulfonic acid. The amount of sulfonic acid was estimated by differential titration for total acidity and chloride ion in the reaction product mixture.

Table 7

Ethanolic Hydrogen Chloride Attack on Ethyl 2,3-Dimethylbutane-1-sulfonate at Reflux[a]

Experiment	Time Mins.	RSO_2OH Mg.-moles	RSO_2OEt, mg.-moles Obt'd[b]	Cal'd[c]	k, min.$^{-1}$
A	15	1.47[d]	3.68	3.53	0.023
	35	2.73[d]	2.37	2.27	.023
	45	3.24[d]	1.85	1.76	.023
B	20	2.19[e]		2.81	.029
	25	2.57[e]		2.43	.027
	30	2.78[e]		2.22	.027
Average					0.026

A. Mixture of 0.9715 g. of ester, 0.425 g. of hydrogen chloride, and 6.2 g. of dry ethanol refluxed different times and analyzed.
B. Mixture of 0.9715 g. of ester, 0.81 g. of hydrogen chloride, and 24.4 g. of dry ethanol refluxed different times and analyzed.

[a] Temperature of refluxing mixture was 83-84°. [b] Based on weight of recovered ester. [c] Based on sulfonic acid determination. [d] Based on total acidity after removal of hydrogen chloride. [e] Based on differential titrations for total acidity and chloride ion.

Table 8

Analytical Data for Ethanolic Hydrogen Chloride Attack on Ethyl 2,3-Dimethylbutane-1-sulfonate at Reflux

Experiment A		Experiment B		
Time Mins.	Ml. of 0.1018 N NaOH	Time Mins.	Ml. of 0.333 N NaOH	Ml. of 0.4400 N $AgNO_3$
15	14.40	20	147.85	105.90
35	26.83	25	140.45	99.50
45	31.85	30	139.90	98.60

Solvolysis of Ethyl 2,3-Dimethylbutane-1-sulfonate (H-I-120). One determination was made of the rate of ethanolysis of the ethyl ester by refluxing 0.9715 g. (0.0050 mole) of ethyl 2,3-dimethylbutane-1-sulfonate in 20 cc. of dry ethanol for eight hours. The amount of sulfonic acid formed during this period was found to be 0.0037 mole as determined by titrating the aqueous extract of the reaction mass with 36.00 ml of 0.1013 N sodium hydroxide solution to a phenolphthalein end-point. The first order reaction rate constant is 0.003 min.^{-1} ($t_{\frac{1}{2}}$ = 231 min.).

4-Hydroxy-2-methylpentane-2- and 4-Hydroxy-2-methylpentane-1-sulfonic Acid Sultone

Preparation of 4-Hydroxy-2-methylpentane-2-sulfonic Acid Sultone (H-II-154). In a 250-cc. round-bottomed flask fitted with a reflux condenser was placed a mixture of 9.8 g. (0.1 mole) of mesityl oxide in 35 cc. of ethanol and 22.0 g. (0.21 mole) of sodium bisulfite in 50 cc. of water. After the homogeneous solution had been heated at gentle reflux for about one hour, the sodium bisulfite addition compound began to precipitate. Heating at 85° was continued overnight. Then 13.0 g. (0.12 mole) of sodium carbonate in 25 cc. of water was added with stirring to the cooled mixture. After the resulting solution had been evaporated to dryness and the dry mass had been powdered, the 1-4 bisulfite addition product was extracted with 45-cc. portions of boiling absolute ethanol. On removing the solvent by evaporation, 16.9 g. (0.08 mole) of dry sodium 2-methyl-4-pentanone-2-sulfonate was obtained.

This sodium ketosulfonate, dissolved in 75 cc. of water, was added, with stirring, to a solution of 2.1 g. (0.055 mole) of sodium borohydride (Metal Hydrides) in 25 cc. of water during one-half hour. The reaction was exothermic. The mixture was heated at 75° for three and one-half hours, then cooled, made slightly acid with 10% hydrochloric acid solution, and evaporated to dryness under reduced pressure at 60°. The resultant sodium hydroxysulfonate was separated from the inorganic salts by extracting with five 35-cc. portions of boiling absolute ethanol. On combining the extracts and evaporating the solvent, 16.2 g. (0.08 mole) of sodium 2-hydroxy-2-methylpentane-1-sulfonate was obtained. This sodium sulfonate is a gummy, colorless mass that has to be frozen prior to powdering.

A mixture of this sodium hydroxysulfonate and 150 cc. of dry ether was placed into a 250-cc. Erlenmeyer flask fitted with a gas inlet tube and a drying tube containing calcium chloride. Dry hydrogen chloride was bubbled into this mixture during three and one-half hours. The sodium chloride which formed was filtered off and washed with small portions of dry ether. After combining the ethereal solutions, the solvent was evaporated to give 10.7 g. (0.06 mole) of dark brown 4-hydroxy-2-methylpentane-2-sulfonic acid. This sulfonic acid was heated under 5 mm. pressure in a Claisen-type distilling flask having a Vigreaux side-arm (the pot bath temperature was kept between 190° and 195°) to distill off 7.9 g. (0.05 mole) of solid 4-hydroxy-2-methylpentane-2-sulfonic acid sultone boiling at 135-140° /5 mm. This product was recrystallized from an isooctane-carbon tetrachloride mixture until a constant melting point of 49.5-50.0° resulted.

Anal.[62] Calc'd for $C_6H_{12}O_3S$: C, 43.88; H, 7.37

Found: C, 44.08; H, 7.59.

A betaine derivative was prepared by heating a mixture of 0.5 g. (3 mg.-moles) of 4-hydroxy-2-methylpentane-2-sulfonic acid sultone and 1.2 g. (16 mg.-moles) of dry pyridine on a steam bath for one hour. After the excess pyridine had been removed by evaporation in vacuo, 0.7 g. (2.5 mg.-moles) of white derivative was obtained. This product was recrystallized from ethanol until a constant melting point of 140.5-

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[62] Clark Microanalytical Laboratory, Urbana, Ill., reference number 26999.

141.0° resulted. It has not yet been analyzed.

Preparation of 4-Hydroxy-2-methylpentane-1-sulfonic Acid Sultone (H-II-166). 4-Hydroxy-2-methyl-1,3-pentadiene-1-sulfonic acid sultone was prepared according to Eastman and Gallup[63] on several occasions (H-II-161, 166, and 167). A typical procedure (H-II-161) follows: In a 500-cc., three-necked, round-bottomed flask fitted with a mechanical stirrer, thermometer, and dropping funnel was placed a mixture of 39.3 g. (0.4 mole) of mesityl oxide (Matheson, technical grade) and 80 g. of acetic anhydride. The mixture was then cooled to -3° by means of a salt-ice bath. To this cool, stirred solution was added cautiously 48 g. (0.41 mole) of chlorosulfonic acid (Eastman Kodak, P 669) over a period of one hour. The reaction temperature was not allowed to exceed 3°. The resulting dark, orange-red colored solution was stirred one hour at 0°, an additional hour at room temperature, and then poured onto about 600 cc. of crushed ice and water. The sand colored crystals which formed were washed with several portions of water and then dried, 33.5 g. (0.21 mole, 53% yield based on mesityl oxide) of crude sultone being obtained. Four crystallizations from a carbon tetrachloride isooctane mixture yielded 26.8 g. (0.17 mole, 43% yield based on mesityl oxide) of light grey 4-hydroxy-2-methyl-1,3-pentadiene-1-sulfonic acid sultone melting at 70.0-70.5° (literature,[64] 70.5-71.0°).

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63. R. H. Eastman and D. Gallup, J. Am. Chem. Soc., 70, 864 (1949).

64. Th. Morel and P. E. Verkade, Rec. trav. chem., 68, 619 (1949).

33.4 G. (0.21 mole) of this crude, dry unsaturated sultone was mixed with 50 cc. of water and 4.6 g. (0.11 mole) of sodium hydroxide pellets dissolved in 20 cc. of water. The solution was heated to 70°, and added, with stirring, to a warm solution of 4.0 g. (0.11 mole) of sodium borohydride (Metal Hydrides) dissolved in 80 cc. of water during 24 minutes. After standing at room temperature for one and one-half hours, the mixture was made slightly acid with 10% hydrochloric acid, and then evaporated to dryness, in vacuo, at 60°. The unsaturated hydroxysulfonate was separated from the inorganic salts by extracting it with six 40-cc. portions of boiling absolute ethanol. On combining the extracts and evaporating the solvent, 15 g. (0.07 mole) of slightly yellow, hygroscopic sodium 4-hydroxy-2-methyl-1-pentane-1-sulfonate was obtained.

Into a 40-cm. x 25-mm. glass tube externally fitted at the middle of one side with a small capillary tube as a gas inlet was placed 6.5 g. (0.03 mole) of the unsaturated hydroxysulfonate dissolved in 80 cc. of distilled water and 0.1 g. of platinum oxide (Baker and Co.). After the tube had been placed in a Burgess-Parr reduction apparatus, the mixture was shaken in an atmosphere of hydrogen under an initial pressure of 515 lb. per sq. in. at 75° for three hours and then overnight at room temperature. The reaction tube was emptied and the catalyst removed by filtration, both tube and catalyst being rinsed with small portions of water. The combined aqueous solutions were evaporated to dryness under diminished pressure on a steam bath. The resulting dry sodium 4-hydroxy-2-methylpentane-1-sulfonate was slurried in 75 cc. of dry ether in a 125-cc. round-bottomed flask and dry hydrogen chloride was bubbled into the suspension during four hours. The sodium chloride which formed was separated by filtration and washed with small portions of dry ether. The ether solutions were combined and evaporated, and the resulting dark brown sulfonic acid was placed in a vacuum oven at 60° overnight, 4.6 g. (0.025 mole) of 4-hydroxy-2-methylpentane-1-sulfonic acid being collected. This sulfonic acid was heated under 4 mm. pressure, the pot bath temperature being kept between 180° and 195°, to distill off 1.2 g. (0.007 mole, 28% based on free sulfonic acid) of 4-hydroxy-2-methylpentane-1-sulfonic acid sultone boiling at 135-142° /4 mm. The oily distillate was washed with water and then allowed to stand in the open at room temperature for 1.5 days, after which time it solidified. Recrystallization from a carbon tetrachloride-isooctane mixture yielded white needles melting at 46.5-47.0°.

Approximately equal amounts of this saturated sultone and the five membered ring isomer, 4-hydroxy-2-methylpentane-2-sulfonic acid sultone, were mixed to give a wax-like product which slowly liquified.

<u>4-Hydroxy-2-methylpentane-1-sulfonic Acid Sultone from Chlorosulfonylation of 4-Chloro-2-methylpentane</u> (H-II-175). A mixture of 204 g. (2 moles) of 4-methyl-2-butanol (Eastman Kodak, P 3607) and 450 cc. of C. P. concentrated hydrochloric acid (s.g. 1.18-1.19) was placed in a one-liter, round-bottomed flask fitted with a reflux condenser through which extended a glass stirring rod connected to a mechanical stirrer. The homogeneous solution was then heated with stirring on a steam bath for six hours. At the end of this reaction period, two layers had formed. The upper layer was decanted into a separatory funnel, washed

with seven portions each of about 75 cc. of water and dried with calcium chloride overnight. Distillation of this mixture through a small Vigreaux-type column gave 135.4 g. (1.1 moles, 55% conversion) of 4-chloro-2-methylpentane, b. p. 112-113°, n_D^{20} 1.4111 (literature,[65] b. p. 111-112° /733 mm., n_D^{20} 1.4113).

One mole (102 g.) of the freshly prepared 2-chloro-4-methylpentane was mixed with 60 cc. of carbon tetrachloride and chlorosulfonylated, according to Helberger[66] in a manner similar to that described earlier for diisopropyl, with one mole of sulfur dioxide and 0.5 mole of chlorine gases during one hour. The reaction mass was washed, first with five 100-cc. portions of water, then with six 100-cc. portions of 5% sodium bicarbonate solution, finally with seven 100-cc. portions of water, and then dried over calcium chloride for four hours. After this drying period, a strong odor of sulfur dioxide and hydrogen chloride was noted being emitted from the solution; therefore, in order to prevent further decomposition, the solvent was evaporated, and the resulting mixture of products divided into two equal parts. One portion was placed in a 250-cc. flask and refluxed for 30 hours with a mixture of 110 cc. of ethanol and 10 cc. of concentrated hydrochloric acid. This was cooled and added to 100 cc. of water and the resulting solution was shaken with several portions of ether to remove alkyl chlorides, and the combined ether extracts were washed with successive portions of water. The aqueous solutions were combined and

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[65] F. C. Whitmore and F. Johnston, J. Am. Chem. Soc., 60, 2265 (1938).

[66] Helberger, Menecke, and Fisher, loc. cit.

concentrated under reduced pressure at 60° to give 15.2 g. of a mixture of dark brown sulfonic acids which then was distilled under reduced pressure from a Claisen-type distilling flask having a Vigreaux side-arm to give 3.9 g. (0.024 mole) of slightly acidic, crude, liquid 4-hydroxy-2-methylpentane-1-sulfonic acid sultone boiling at 140-145° /5 mm. The crude sultone was dissolved in about 35 cc. of ether and washed with five portions each of 35 cc. of water to remove the free acid. On evaporating the solvent, after the solution had been dried overnight with calcium chloride, the residual slightly colored, crude sultone was crystallized by cooling with dry ice. Recrystallization from carbon tetrachloride-isooctane mixture gave a product melting at 46.5-47.0°. A mixture of this sultone and the sultone derived from sodium 4-hydroxy-2-methyl-1,3-pentadiene-1-sulfonic acid sultone, showed no depression in melting point. A liquid resulted when equal portions of this sultone and the five membered ring isomer were mixed.

The other portion was hydrolyzed by adding it to an agitated solution of 10% sodium hydroxide at 60° over half an hour, and then the mixture was evaporated in vacuo, to dryness. No further work was done with these salts since the desired sultone was obtained from the first portion as described above.

SUMMARY

The steric effect of a beta methyl group on the rate of ethanolysis of an aliphatic sulfonyl chloride, and on the rate of alkylation with the ethyl ester of the corresponding sulfonic acid has been demonstrated.

2,3-Dimethylbutane and the ethyl ester of the corresponding sulfonic acid have been prepared. The sulfonic acid has been characterized as the amide and the benzylamide.

The chlorosulfonylation of Grignard reagents with sulfuryl chloride proceeds by way of a sulfinic acid salt. This resulted in development of a modified procedure for preparing sulfonyl chlorides which gives increased yields and minimizes by-product formation.

Attempts to prepare the tertiary sulfonyl chloride, 2,3-dimethylbutane-2-sulfonyl chloride, were unsuccessful. Instead of the desired product, a complex mixture of polychlorinated diisopropyl was obtained upon chlorination of the sulfinic acid salt.

Tertiary sulfonyl chlorides are not prepared from hydrocarbons or alkyl chlorides when these classes of compounds are photochemically chlorosulfonylated. The sultones related to the sulfonyl chlorides obtained upon chlorosulfonylation of 4-chloro-2-methylpentane and, undoubtedly, 1-chloro-3-methylbutane are those of delta hydroxysulfonic acids, not those of gamma hydroxysulfonic acids as claimed in the literature.

As a new characterizing derivative of the tertiary chloride of diisopropyl, the anilide of 2,2,3-trimethylbutyric acid has been prepared. Discrepancies regarding the reported melting point of the anilide of 3,4-dimethylvaleric acid have been uncovered and rectified.

CONCLUSIONS

1. The steric effect of a beta methyl group on the rate of ethanolysis of an aliphatic sulfonyl chloride and on the rate of alkylation with the ethyl ester of the corresponding sulfonic acid is only moderate.
2. Tertiary sulfonyl chlorides are not obtained from hydrocarbons or from alkyl halides when these classes of compounds are photochemically chlorosulfonylated. The sultone related to the sulfonyl chloride obtained upon chlorosulfonylation of 4-chloro-2-methylpentane is that of the delta hydroxysulfonic acid, not that of the gamma hydroxysulfonic acid as claimed in the literature.
3. Chlorosulfonylation of a Grignard reagent with sulfuryl chloride proceeds through an intermediate sulfinic acid salt which is subsequently chlorinated to yield a sulfonyl chloride. Preparation of the sulfinic acid salt as a separate operation obviates by-product alkyl chloride and sulfone formation, thereby enhancing yields of sulfonyl chloride.
4. The melting point of the anilide of 3,4-dimethylvaleric acid is 110-110.5° and not 67° as reported in the literature.

APPENDIX I

The original report covering the study of 2,3-dimethylbutane-1-sulfonyl chloride will be published in the following form in the Journal of Organic Chemistry, Vol. 20, September, 1955:

(Contribution from the Chemistry Laboratory of the University of Alabama)

A STUDY OF ALIPHATIC SULFONYL COMPOUNDS. II. 2,3-DIMETHYLBUTANE-1-SULFONYL CHLORIDE[1]

Robert B. Scott, Jr. and Morgan S. Heller

Recently the bimolecular nature of the alcoholysis of sulfonyl chlorides was confirmed by comparing the rates of ethanolysis of octane-1- and -2-sulfonyl chlorides (1). As the steric requirements of a sulfonyl chloride are increased by an alpha methyl group it became desirable to learn if a beta methyl group is appreciably effective, especially as the alpha methyl shielding effect on the sulfur atom is considerably less than that of the analogously situated beta methyl group on the halogeno carbon atom of 1-bromo-2-methylbutane (2). 2,3-Dimethylbutane-1-sulfonyl chloride, the primary sulfonyl chloride from diisopropyl, was chosen for such an investigation.

This sulfonyl chloride was prepared by chlorosulfonylation (3)

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1. From a part of the research of Morgan S. Heller to be incorporated in his dissertation in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Alabama. Carried out as a part of project NR 055 222 under contract N9onr 961(00) between the Office of Naval Research and the University of Alabama. Rights reserved for reproduction in whole or in part for any purpose of the United States Government.

of 2,3-dimethylbutane. Fractional distillation yielded only one sulfonyl chloride; this was shown to be the primary isomer by independent synthesis through sulfonylation of the Grignard reagent (4) from 1-chloro-2,3-dimethylbutane with sulfuryl chloride, while the tertiary sulfonyl chloride was not found to be present.[2] Although this new sulfonyl chloride has an asymmetric center, no attempts have been made yet to resolve it into enantiomorphs.

2,3-Dimethylbutane-1-sulfonyl chloride undergoes alcoholysis in excess boiling ethanolic hydrogen chloride at a rate ($k = 0.047$ min.$^{-1}$) intermediate between that for octane-1-sulfonyl chloride ($k = 0.089$ min.$^{-1}$) and that for octane-2-sulfonyl chloride ($k = 0.014$ min.$^{-1}$) (1). From this comparison it is evident that a beta methyl group is moderately effective in hindering the attack on the sulfo group by ethanol. The distribution of products, as reaction progresses successively from sulfonyl chloride to ester to sulfonic acid, is illustrated in Fig. 1.

The attack on ethyl 2,3-dimethylbutane-1-sulfonate, prepared from the free sulfonic acid with diazoethane and from its silver salt with ethyl iodide, by boiling ethanolic hydrogen chloride ($k = 0.026$ min.$^{-1}$) is considerably slower than that on ethyl octane-1-sulfonate ($k = 0.051$ min.$^{-1}$) (1). This substantiates the conclusion that the steric requirements of ethyl octane-2-sulfonate are greater than those of its normal isomer (1), although it is difficult

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[2] This is consistent with the findings of Asinger (5), who obtained only the primary sulfonyl chloride on chlorosulfonylation of isobutane.

to visualize a relationship between the steric requirements of a sulfonyl chloride and the correspondent sulfonic ester when the reaction centers are quite different.[3]

It was shown that solvolysis probably contributes little to the ester attack, a single determination of the rate of ethanolysis ($k = 0.003$ min.$^{-1}$) being made at reflux.

EXPERIMENTAL

2,3-Dimethylbutane-1-sulfonyl chloride by chlorosulfonylation of 2,3-dimethylbutane. One and one-half moles (129 g.) of 2,3-dimethylbutane, diluted with an equal volume of carbon tetrachloride, was chlorosulfonylated (3) at 0° to 10° over a period of one hour with a mixture of 0.8 mole of chlorine and 1.5 moles of sulfur dioxide in the light from a 150-watt General Electric Par 38 Projector Flood lamp. The residue from removal under reduced pressure of unreacted hydrocarbon, diluent, and byproduct alkyl chlorides was distilled through a 36 cm. x 16 mm. Vigreaux column fitted with a partial condensation still head to yield 60 g. (0.32 mole) of sulfonyl chloride boiling at 61°/1 mm., n_D^{25} 1.4607, d_4^{25} 1.1524, M_D 44.0. The distilland was stabilized with potassium carbonate.

Anal. Calc'd for $C_6H_{13}O_2SCl$: C, 39.02; H, 7.10;
S, 17.36; Cl, 19.20.
Found: C, 39, 27; H, 7.06; S, 17.24; Cl, 19.30.

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[3] However, if such a relationship does exist, the rate constant for ethyl octane-2-sulfonate ($k = 0.041$ min.$^{-1}$) might be expected to be lower than that for ethyl 2,3-dimethylbutane-1-sulfonate. This seeming discrepancy might be attributed to a difference in reactivities between esters of primary and secondary sulfonic acids.

Chlorination of 2,3-dimethylbutane. For an unequivocal synthesis of 2,3-dimethylbutane-1-sulfonyl chloride by the method of Cherbuliez (4), commercial diisopropyl was photochemically chlorinated and the primary and tertiary chlorides were separated by fractional distillation through an adiabatically heated 106 cm. x 17 mm. column packed with 1/8-inch Pyrex single-turn helices and equipped with electronically actuated magnetic total-condensation still head. Potassium carbonate was used as distilland stabilizer. Fractionation into the two isomers was efficient, based on observation of two successive, clearly defined refractive index plateaus, each associated with a characteristic distillation temperature. As insufficient or conflicting information for identifying these alkyl chlorides is to be found in the literature each of the two principal fractions was characterized. From four mole (345 g.) of the hydrocarbon reacted at 0° to 10° over a period of two hours with one mole of chlorine there was obtained 49 g. (0.4 mole) of 2-chloro-2,3-dimethylbutane, b. p. 55°/108 mm.[4], 111-112 /754 mm., n_D^{25} 1.4171, and 51 g. (0.4 mole) of 1-chloro-2,3-dimethylbutane, b. p. 65°/106 mm., 122.5-123°/754 mm., n_D^{25} 1.4201 (index not found in literature).

Identification of the isomeric chlorides from 2,3-dimethylbutane. The higher boiling fraction separated from the crude chlorinated diisopropyl was identified as 1-chloro-2,3-dimethylbutane through conversion into the anilide of 3,4-dimethylvaleric acid by reacting the Grignard reagent of the chloride with phenyl isocyanate. The anilide

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[4] Uncorrected pressure calibration.

melting point of 109.5-110.5° is in agreement with that reported by Detling (6) but in marked disagreement with the 67° reported by Huston (7). Examination of the supporting dissertation of Agett (8) and Guile (9) showed the latter melting point to be questionable.

Because of confusing or inadequate reports of physical properties and derivatives of the isomeric chlorides, the tertiary chloride, identified by photochemical bromination to 2,3-dibromo-2,3-dimethylbutane (sublimed 164-168°) which was identical to that prepared directly from the hydrocarbon in agreement with Grosse (10), was similarly converted into 2,2,3-trimethylbutyranilide, the melting point, 78.5-79°, of which is significantly different from either of the literature values for the isomeric anilide.[5]

<u>Anal.</u> Calc'd for $C_{13}H_{19}ON$: C, 76.05; H, 9.33

Found: C, 76.11; H, 9.36

<u>2,3-Dimethylbutane-1-sulfonyl chloride from 1-chloro-2,3-dimethylbutane.</u> One mole (121 g.) of 1-chloro-2,3-dimethylbutane was converted into the Grignard reagent (75% yield) which was slowly added at 10° to a vigorously stirred ether solution containing 171 g. (1.27 moles) of sulfuryl chloride. Fractional distillation of the residue from evaporation of the washed ether solution through a 36 cm. x 16 mm. Vigreaux column fitted with partial condensation still head yielded

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[5] The anilide from the tertiary chloride also was prepared from the chloride derived from 2,3-dimethyl-2-butanol obtained by reacting methyl i-propyl ketone with methylmagnesium iodide (11). It melted at 77.5-78°. A mixture of this anilide and the isomeric anilide from the primary chloride melted at 63.5-68.5°.

61.5 g. (0.33 mole) of 2,3-dimethylbutane-1-sulfonyl chloride, b. p. 71°/1.8 mm., n_D^{25} 1.4608, d_4^{25} 1.1528, M_D 44.0. These physical properties are in close agreement with those for the chlorosulfonylation product. Again the distilland was stabilized with potassium carbonate.

Characterizing derivatives of 2,3-dimethylbutane-1-sulfonic acid. The benzylamide prepared from the chlorosulfonylated diisopropyl and recrystallized to constant melting point from 2,2,4-trimethylpentane melted without depression at 31-32° when mixed with that prepared from the sulfonyl chloride derived from the Grignard reagent.

Anal. Calc'd for $C_{13}H_{21}O_2NS$: C, 61.14; H, 6.29.
Found: C, 61.09; H, 8.21.

The *amide*, prepared by treating the sulfonyl chloride with excess ammonium hydroxide, was recrystallized to a constant melting point of 48-49° from 2,2,4-trimethylpentane containing a little chloroform. It is soluble in aqueous ammonia.

Anal. Calc'd for $C_6H_{15}O_2NS$: C, 43.61; H, 9.15.
Found: C, 43.96; H, 9.12.

Ethyl 2,3-dimethylbutane-1-sulfonate. The free sulfonic acid obtained by alcoholysis of 2,3-dimethylbutane-1-sulfonyl chloride was converted in 90% yield into the ethyl ester with diazoethane. The ester also was prepared in 80% by reacting ethyl iodide with the dried silver salt obtained from moist silver oxide and the free sulfonic acid. The sweet-smelling product was fractionally distilled in the same manner as for the sulfonyl chloride, b. p. 82°/0.8 mm., n_D^{25} 1.4377, d_4^{25} 1.0437, M_D 48.8.

Anal. Calc'd for $C_8H_{18}O_3S$: C, 49.45; H, 9.34.
Found: C, 49.46; H, 9.32.

Ethanolysis of 2,3-dimethylbutane-1-sulfonyl chloride. Mixtures containing 1.8469 g. (0.0100 mole) of 2,3-dimethylbutane-1-sulfonyl chloride, 0.50 g. (0.014 mole) of hydrogen chloride, and 8.4 g. (0.18 mole) of dry ethanol were refluxed (83-84°) for varying periods. Composition of the mixture of sulfonyl chloride and ester remaining after aqueous extraction of the sulfonic acid was estimated from the weight of the mixture and from the refractive index of the totally distilled mixture. The amount of sulfonic acid in the aqueous extract was determined by titration after expelling hydrogen chloride (negative chloride test) by concentration under vacuum. The results are recorded in Table I.

Action of alcoholic hydrogen chloride on ethyl 2,3-dimethylbutane-1-sulfonate. Rate of attack on the intermediate ethyl ester formed during ethanolysis of 2,3-dimethylbutane-1-sulfonyl chloride was determined in a manner somewhat like that described for the sulfonyl chloride. Mixtures of 0.9715 g. (0.0050 mole) of ethyl 2,3-dimethylbutane-1-sulfonate, 0.425 g. (0.0116 mole) of hydrogen chloride, and 6.2 g. (0.14 mole) of dry ethanol were refluxed for various periods. Composition of the reaction product was estimated by weighing the unreacted ester recovered by partitioning it from the sulfonic acid with ether and water, and by titrating the sulfonic acid in the aqueous layer (after expelling the hydrogen chloride). Mixtures containing approximately four times as much alcoholic hydrogen chloride (1.808 g., 0.0495 mole of hydrogen chloride; 24.4 g., 0.53 mole of ethanol) were similarly treated except that unreacted ester was not recovered and the sulfonic acid was estimated by differential titrations for total acidity and chloride ion. The first order rate constants were based on sulfonic acid determinations. The results are recorded in Table II.

Solvolysis of ethyl 2,3-dimethylbutane-1-sulfonate. The rate of ethanolysis of the intermediate ethyl sulfonate was estimated by refluxing a mixture of 0.9715 g. (0.0050 mole) of ethyl 2,3-dimethylbutane-1-sulfonate and 20 ml. of dry ethanol for 8.00 hours. Titration of the aqueous solution after ether extraction of unreacted ester indicated that 0.0037 mole of 2,3-dimethylbutane-1-sulfonic acid had been formed, showing that solvolysis had progressed 74% ($k = 0.003$ min.^{-1}).

SUMMARY

The steric effect of a beta methyl group on the rate of ethanolysis of an aliphatic sulfonyl chloride, and the effect of that group on the rate of alkylation with the ethyl ester of the corresponding sulfonic acid has been demonstrated.

2,3-Dimethylbutane-1-sulfonyl chloride and the ethyl ester of the corresponding sulfonic acid have been prepared. The sulfonic acid has been characterized as the amide and the benzamide.

As a new characterizing derivative of the tertiary chloride of diisopropyl, the anilide of 2,2,3-trimethylbutyric acid has been prepared.

ACKNOWLEDGMENT

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TABLE I

Ethanolysis of 2,3-Dimethylbutane-1-sulfonyl Chloride[a]

Time Mins.	RSO_2Cl, mg.-moles		RSO_2OEt, mg.-moles		RSO_2OH[d] mg.-moles	Material Balance %	k, min.$^{-1}$
	Obt'd[b]	Calc'd[c]	Obt'd[b]	Calc'd[c]			
15	4.91	5.00	3.98	4.07	0.93	98.2	0.046
25	2.87	2.90	4.46	4.50	2.60	99.3	0.050
30	2.29	2.34	4.11	4.21	3.45	98.5	0.048
35	2.06	2.11	3.92	4.02	8.87	98.5	0.045
Average						98.6	0.047

[a] Mixtures of 1.8469 g. of sulfonyl chloride, 0.50 g. of HCl, and 8.4 g. of dry ethanol refluxed for times indicated.

[b] Estimated from weight of mixture of sulfonyl chloride and ester after extraction of sulfonic acid and from refractive index of distilled mixture.

[c] Calculated by stoichiometric difference from amount of sulfonic acid and from refractive index of distilled sulfonyl chloride-ester mixture.

[d] Estimated by titration of aqueous extract after expelling HCl.

TABLE II

Attack of Ethanolic Hydrogen Chloride on Ethyl 2,3-Dimethylbutane-1-sulfonate

Experiment	Time Mins.	RSO_2OH mg.-moles	RSO_2OEt, mg.-moles Recovered	RSO_2OEt, mg.-moles Calc'd[a]	k, $min.^{-1}$
A	15	1.47[b]	3.68	3.53	0.023
	35	2.73[b]	2.37	2.27	.023
	45	3.24[b]	1.85	1.76	.023
B	20	2.19[c]		2.81	.029
	25	2.57[c]		2.43	.029
	30	2.78[c]		2.22	.027
Average					0.026

A. Mixtures of 0.9715 g. of ester, 0.425 g. of HCl, and 6.2 g. of ethanol refluxed for times indicated.

B. Mixtures of 0.9715 g. of ester, 1.81 g. of HCl, and 24.4 g. of ethanol refluxed for times indicated.

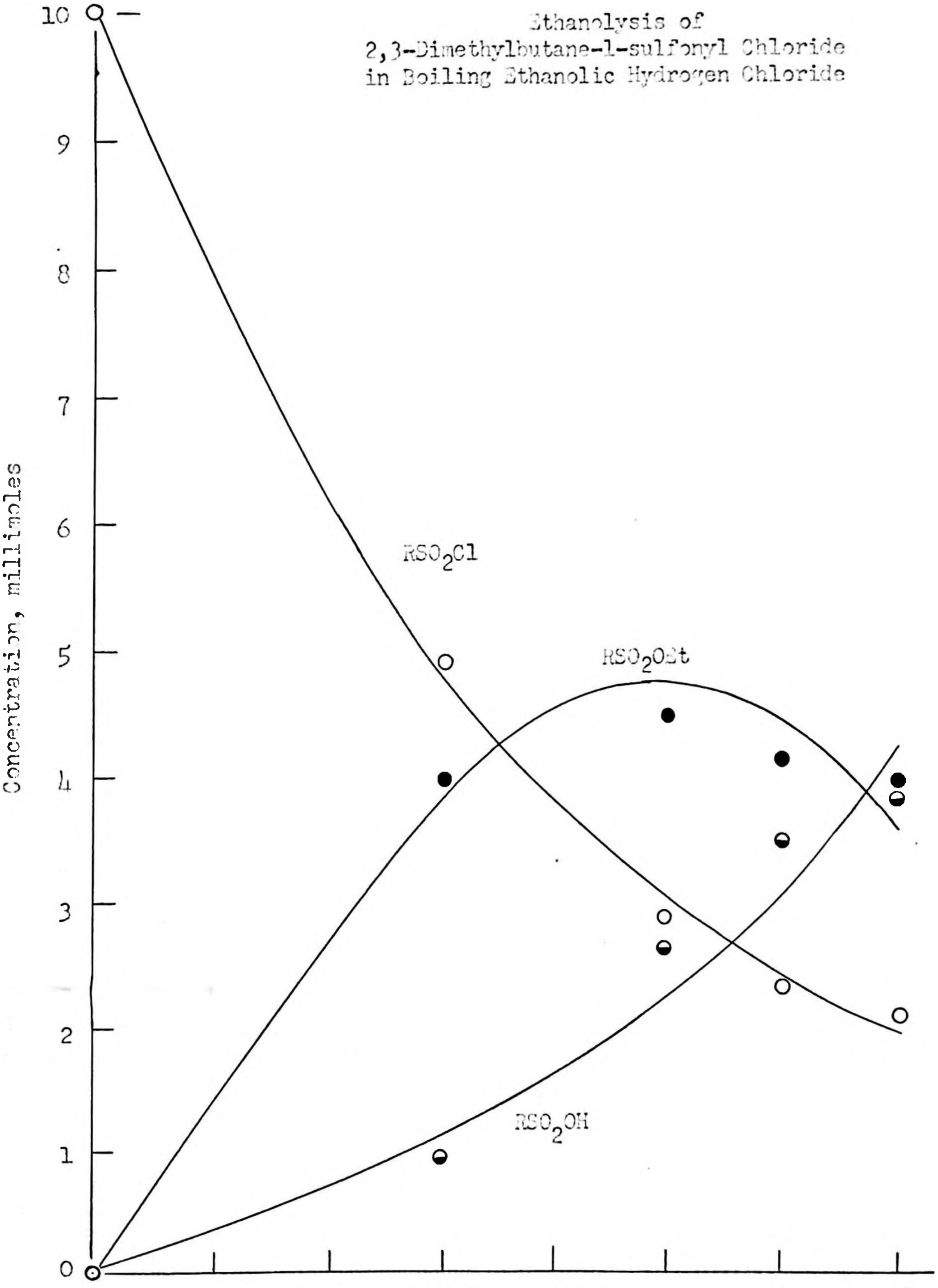
[a] Based on sulfonic acid determination.

[b] Based on total acidity after expelling HCl.

[c] Based on differential titrations for total acidity and chloride ion.

Figure I

Ethanolysis of
2,3-Dimethylbutane-1-sulfonyl Chloride
in Boiling Ethanolic Hydrogen Chloride



APPENDIX II

The original report covering sulfonyl chloride formation from Grignard reagents will be published in the following form in the <u>Journal of Organic Chemistry</u>, Vol. 20, September, 1955:

(Contribution from the Chemistry Laboratories of the Universities of Alabama and Virginia)

A STUDY OF ALIPHATIC SULFONYL COMPOUNDS. III. SULFONYL CHLORIDE FORMATION FROM GRIGNARD REAGENTS[1]

Robert B. Scott, Jr., John B. Gayle,[2]
Morgan S. Heller, and Robert E. Lutz

Probably the most generally applicable method for preparation of aliphatic sulfonyl chlorides is that of Cherbuliez (1), wherein organomagnesium chlorides are added to sulfuryl chloride. In spite of the general utility of this process it has not been widely used, perhaps because of the relatively low conversions, which are usually less than 35% based on the alkyl chloride from which the Grignard reagent is prepared.

In order to account for the formation of alkyl chlorides and

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[1] Partially from the dissertation presented by Robert B. Scott, Jr. at the University of Virginia (1949), partially from that presented by John B. Gayle at the University of Alabama (1954), and partially from material to be incorporated in the dissertation of Morgan S. Heller at the University of Alabama, in partial fulfillment for the Doctor of Philosophy degree at the respective universities.

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other by-products in this process, Cherbuliez suggested a mechanism based on dissociation of an assumed intermediate complex between sulfuryl chloride and the Grignard reagent. His observation that the distribution of products is a function of temperature and that alkyl chloride formation is favored by low temperatures was cited as confirmation of the mechanism he proposed.

Our finding that the yield of octane-2-sulfonyl chloride is not significantly influenced by variations in temperature over the range -40° to 10° suggests that in this instance the mechanism proposed by Cherbuliez is not operative to an appreciable extent, and the results of subsequent experiments with other sulfonyl chlorides suggest that the following equations better account for production of sulfonyl chloride and alkyl chloride, principally, and of a small amount of sulfone (2).[3]

(1)[4] $RMgCl + SO_2Cl_2 \rightarrow RCl + MgCl_2 + SO_2$

(2) $RMgCl + SO_2 \longrightarrow RSO_2MgCl$

(3)[4] $RSO_2MgCl + SO_2Cl_2 \longrightarrow RSO_2Cl + MgCl_2 + SO_2$

(4)[5] $RSO_2MgCl + RCl \longrightarrow RSO_2R + MgCl_2$

Formation of by-products according to equations 1 or 4 is probably responsible to a considerable extent for the low yields obtained with

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[3] In order to account for the sulfinic acids he obtained, Oddo (3) takes the opposite view, that the sulfonyl chloride is the primary reaction product which then reacts with the Grignard reagent to produce equivalent amounts of alkyl chloride and sulfinate.

[4] It is possible that chlorination follows dissociation of sulfuryl chloride.

[5] The possibility of $RMgCl + RSO_2Cl \rightarrow RSO_2R + MgCl_2$ was rejected in view of the low yields of sulfone and of the failure of ethyl chlorosulfonate to react with Grignard reagents to yield esters of sulfonic acids (4).

this process. Since these particular reactions are not essential to the formation of sulfonyl chlorides, it is evident that a modification of the Cherbuliez process consisting of successive operations in which Grignard reagents are reacted with anhydrous sulfur dioxide to give sulfinic acid salts which in turn are reacted with a suitable chlorinating agent, should result in increased yields of sulfonyl chlorides. In comparable experiments with α-toluene- and 2,3-dimethylbutane-1-sulfonyl chlorides, this modification gave yields nearly twice as great as those obtained with the singly operation procedure, thereby suggesting that the modified procedure deserves consideration as a general method.

Besides giving increased yields, exceptionally pure products are obtained by the modified process. Also, the relatively slight heats of reaction, compared with those of the Cherbuliez process, make for greater ease in handling.

Another advantage lies in the flexibility of the process, which permits various chlorinating agents to be used as a matter of convenience. For instance, the use of gaseous chlorine, although slow, is of some advantage in that it does not appear to react with the ether under the conditions used, whereas sulfuryl chloride is apt to do so. Also, with chlorine, there is no excess to be decomposed or otherwise removed.

A further advantage is that it is a simple matter to free the sulfinic acid from halide ions derived from the original alkyl halide, thereby permitting preparation of sulfonyl chlorides from alkyl bromides, a possibility not realized with the Cherbuliez process.

Conversion of sulfinic acid salts to sulfonyl chlorides by treatment with sulfuryl chloride or chlorine is of interest in that it represents a variation of the well-known process for preparing sulfonyl chlorides by chlorinative oxidation of various sulfur bodies in aqueous medium (5). Use of an anhydrous medium with the sulfinate is feasible only because this sulfur body already possesses the requisite number of oxygen atoms and is therefore not dependent on the solvent or on the chlorinating agent as an oxygen donor.[6]

EXPERIMENTAL

Effect of temperature on yield by the Cherbuliez method. Each of three preparations of the Grignard reagent from 2-octyl chloride was slowly added to a cold ethereal solution containing a

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[6] Of interest from a theoretical viewpoint is the seeming resemblance of the modified process to the reaction of halogens with silver salts of carboxylic acids wherein an intermediate product of the reaction has been shown to be the acyl hypohalite, RCO-O-X (6). Although admittedly speculative, an analogous sulfinyl hypohalite might have a real existence and may even be a common intermediate in some of the several methods for preparation of sulfonyl chlorides represented by the following equations:

$$\left.\begin{array}{l}
\mathrm{RMgX} \xrightarrow{SO_2} \mathrm{RSO\text{-}O\text{-}MgX} \xrightarrow{Cl_2} [\mathrm{RSO\text{-}O\text{-}Cl}] \\
\mathrm{RSH} \xrightarrow{Cl_2,\ HOH} \mathrm{RSO\text{-}O\text{-}H} \xrightarrow{Cl_2} [\mathrm{RSO\text{-}O\text{-}Cl}] \\
\mathrm{RH} \xrightarrow{Cl\cdot} \mathrm{R}\cdot \xrightarrow{SO_2} \mathrm{RSO\text{-}O}\cdot \xrightarrow{Cl_2} [\mathrm{RSO\text{-}O\text{-}Cl}] \\
\mathrm{RSO_2\text{-}O^-\ Na^+} \xrightarrow{PCl_5} \mathrm{RSO_2\text{-}O\text{-}PCl_4} \xrightarrow{-POCl_3} [\mathrm{RSO\text{-}O\text{-}Cl}]
\end{array}\right\} \xrightarrow{S_Ni} \mathrm{RSO_2Cl}$$

While formation of a sulfinyl hypochlorite may be considered to be less probable in the last case, such a retrogressive step might be favored by the disposition of the atoms concerned in a pseudo five membered ring.

5% excess of sulfuryl chloride based on the octyl chloride used. The reactions were carried out at -40° to -30°, at 0° to 5°, and at 5° to 10°, respectively. The amounts of octane-2-sulfonyl chloride (2) obtained represent conversions based on 2-octyl chloride of 28%, 33%, and 31%, respectively, the differences being no greater than might be expected without varying the temperature.

α-Toluenesulfonyl chloride by the proposed modification. Over a period of 4 hrs. anhydrous sulfur dioxide was bubbled into a dilute ethereal solution of the Grignard reagent from 52 ml. (0.45 mole) of benzyl chloride. Chlorine then was bubbled into the resulting ethereal suspension of sulfinic acid salt over a period of six hours. After the suspension had been filtered to remove inorganic salts, the ether was evaporated, and 46 g. (0.24 mole) of relatively pure[7] α-toluenesulfonyl chloride (m. p. 83-88°) was obtained for a conversion of 53% based on benzyl chloride used. Cherbuliez obtained a 34% yield of this sulfonyl chloride by reacting the Grignard compound with sulfuryl chloride.

In a similar experiment the intermediate sulfinic acid salt was converted to the free sulfinic acid which then was treated in ether solution with sulfuryl chloride to obtain the sulfonyl chloride. While in this instance the yield was not determined it appeared to be at least as great as in the previously described experiment.

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7. A simple wash with 2,2,4-trimethylpentane occasions no noticeable loss and raises the melting point to 90-92° compared to an ultimate 92-94° by repeated crystallizations.

Direct comparison of the proposed modification and the Cherbuliez procedure. One mole (127 g.) of benzyl chloride was converted into the Grignard reagent which then was diluted with ether to approximately 400 ml. A 25-ml. aliquot (representing 0.063 mole of benzyl chloride) was added slowly with stirring to a cooled solution of 12 ml. (0.15 mole) of sulfuryl chloride in 25 ml. of ether. Upon working up in the usual manner, 3.72 g. (0.020 mole, 32% conversion based on benzyl chloride) of α-toluenesulfonyl chloride was obtained.

A second 25-ml. aliquot of the Grignard reagent was treated similarly except that only 6 ml. (0.07 mole) of sulfuryl chloride was used and the order of addition was reversed. The yield of sulfonyl chloride was 3.74 g. (0.020 mole, 32% conversion based on benzyl chloride).

A third 25-ml. aliquot was further diluted to 50 ml. with dry ether and a slow stream of anhydrous sulfur dioxide was directed at the surface of the solution. A solid film formed at the surface of the solution and was broken up by swirling. After about an hour the ether had evaporated, leaving a residue of solid sulfinic acid salt. The residue then was broken up, ether was added, and chlorine was bubbled into the suspension for about two hours. The yield of sulfonyl chloride isolated was 6.64 g. (0.035 mole, 57% conversion based on benzyl chloride). This is approximately 1.8 times as great as that obtained using sulfuryl chloride with the Grignard reagent (1.7 times that reported by Cherbuliez).

2,3-Dimethylbutane-1-sulfonyl chloride. Scott and Heller (7) converted 1-chloro-2,3-dimethylbutane into the Grignard reagent (yield 75% by titration) which then was reacted with sulfuryl chloride by the Cherbuliez method. To obtain pure 2,3-dimethylbutane-1-sulfonyl chloride it was necessary to distill the residue from evaporation of the water-washed ether solution of the resulting mixture of products. Conversion was 33% based on the original alkyl chloride, 44% based on the Grignard reagent.

The Grignard reagent (yield 90%) was prepared from one mole (121 g.) of 1-chloro-2,3-dimethylbutane, the final volume of solution being approximately 340 ml. Over a period of an hour anhydrous sulfur dioxide was bubbled slowly into three 25-ml. aliquots (65.8 mg.-moles of Grignard reagent by titration) each of which had been diluted further with 75 ml. of ether. The ether suspension of sulfinate from one aliquot was treated with chlorine as described in the case of α-toluenesulfonyl chloride. That from a second aliquot was treated instead with 30 g. (0.22 mole) of sulfuryl chloride. The ether was evaporated from the third aliquot, the residue was suspended in 100 ml. of water and chlorine was bubbled in as in the case of the ether suspension. On working up the products from these three experiments, yields of 2,3-dimethylbutane-1-sulfonyl chloride were obtained amounting, in the order described, to 84%, 78%, and 78%, respectively, based on the Grignard reagent, or to 76%, 70%, and 70%, respectively, based on alkyl chloride, which is about twice as great as that obtained by the Cherbuliez procedure. The undistilled product, although slightly discolored, had the same refractive index (n_D^{25} 1.4607) as previously determined for the distilled compound (7).

SUMMARY

It is shown that sulfinic acid salts are probable intermediates during the reaction of Grignard reagents with sulfuryl chloride to form sulfonyl chlorides. A modified procedure for producing sulfonyl chlorides from Grignard reagents has been developed which gives increased yields and minimizes byproduct formation.

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APPENDIX III

Miscellaneous Preparation

Attempted Preparation of 4-Hydroxy-2-methylpentane-2-sulfonic Acid Sultone(H-II-116). In a 200-cc., three-necked, round-bottomed flask fitted with a reflux condenser, stirrer, and dropping funnel were placed 4.9 g. (0.5 mole) of mesityl oxide and a few milligrams of dibenzoyl peroxide. After the mixture had been heated to 40°, 44 g. (0.6 mole) of thioacetic acid was added to the stirred mesityl oxide solution during three-quarters of an hour. A reaction temperature of from 42° to 48° was maintained. After all additions, the reaction mass was heated to 60° and stirred for an additional two hours. The resulting yellow liquid was distilled under reduced pressure from a Claisen-type distilling flask to give 69.6 g. (0.4 mole, 80% yield based on mesityl oxide) of colorless 4-acetylthio-4-methyl-2-pentanone; b. p. 83°/4 mm., n_D^{20} 1.4779-1.4785 (literature,[1] b. p. 84-86°/6 mm.)

A mixture of 17.4 g. (0.1 mole) of the 1-4 addition product and 50 cc. of dry ether was added slowly during two hours to a slurry of 5.7 g. (0.15 mole) of lithium aluminum hydride (Metal Hydrides) in a 200-cc., three-necked, round-bottomed flask fitted with an efficient stirrer, reflux condenser vented through a tube containing calcium chloride, and a dropping funnel. After all of the ethereal solution had been added, the resulting mixture was stirred for an

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[1] R. Brown, W. E. Jones, and A. R. Pinder, J. Chem. Soc., 1951, 2123.

additional two hours. About 25 cc. of cold water then was added, cautiously, in order to decompose excess reducing agent. The reaction products were poured slowly onto a mixture of 500 cc. of 10% sulfuric acid and crushed ice. The ether layer was separated and dried first over calcium chloride for several hours and then over potassium carbonate for one hour. After the ether had been removed by evaporation, the residual liquid was distilled under reduced pressure from a Claisen-type distilling flask to give 10.6 g. (0.18 mole, 79% yield based on thioacetic acid) of 4-hydroxy-2-methyl-2-pentanethiol; b. p. 79-80°/9 mm., n_D^{25} 1.4703. This material gave a positive test for a thiol group (lead acetate) and a negative test for a keto group (phyenylhydrazine). Although the product appears to be a new composition of matter, it was not analyzed. This hydroxy mercaptan also was prepared on several other occasions (H-II-122, 124, and 127) by the procedure just outlined. In each case, the yields and properties of the product were essentially the same.

17.7 G. (0.14 mole) of hydroxy mercaptan (n_D^{25} 1.4702-1.4714) was placed into a 150-cc. Erlenmeyer flask and then cooled to about -10°. To this agitated liquid was added, dropwise, 14.0 g. (0.05 mole) of phosphorous tribromide. After all additions, the mixture was stirred for an additional one-half hour and then allowed to stand in the cold (ca. 0°) for six hours and at room temperature overnight. The reaction mass then was poured into 150 cc. of cold water. After the mixture had been allowed to stand for several minutes, two layers formed. The organic layer was dissolved in ether, and the ethereal solution dried over calcium chloride. After the solvent had been evaporated, the residual liquid was distilled under reduced pressure from a Claisen-type distilling flask having a Vigreaux side-arm to give the following fractions:

Fraction	B. P.	n_D^{25}	wt. (g.)
1	55-58°/17 mm.	1.4915	0.9
2	57-59°/16 mm.	1.4932	3.5
3	60°/20 mm.-75°/10 mm.	1.4959	0.7
4	75-85°/10 mm.	1.4962	1.8
5		1.4939	1.1

The material from each fraction gave a positive test for a thiol group and a positive test for a halogen group.

To a warm (ca. 60°), stirred, solution of 1.2 cc. of 30 per cent hydrogen peroxide and 4 cc. of glacial acetic acid was added, dropwise, 3.6 g. (0.02 mole) of bromo mercaptan (fractions 3, 4, and 5) during one-quarter of an hour. The mixture was then stirred for an additional half-hour. On cooling the solution, two layers formed. The upper layer was dissolved in ether, and the ethereal solution was washed with several small portions of water and then dried. After the ether had been removed by evaporation, 2.1 g. of unreacted bromo mercaptan was obtained. Evaporation of the acetic acid solution, and the combined water washings did not yield the desired bromo sulfonic acid.

Miscellaneous Reaction Rate Study

Neutral Chloride Ion Attack on Ethyl 2,3-Dimethylbutane-1-sulfonate (H-I-143 and 144). A mixture of 0.9715 g. (0.0500 mole) of ethyl 2,3-dimethylbutane-1-sulfonate, 1.06 g. (0.025 mole) of lithium chloride, and 12.9 g. (0.28 mole) of dry ethanol was refluxed for varying times. The amount of unreacted ester was determined by weighing the residual ester obtained upon evaporation of the washed ether extracts. The data obtained are presented as follows:

Time Mins.	RSO_2OEt, mg.-moles Initial	Final	k $Min.^{-1}$
15	5.00	0.32	0.183
20	5.00	0.33	0.136
25	5.00	0.11	0.153

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