Configurational Relationships among Some Sulfoxides[1]

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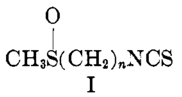
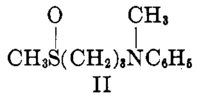
The configuration of sulfur in (−)-N-methyl-N-[3-(methylsulfinyl)propyl]aniline relative to some alkyl aryl sulfoxides and some (−)-menthyl (−)-arylsulfinates was determined using a synthetic procedure which should have general applicability. (−)-N-Methyl-N-[3-(methylsulfinyl)propyl]aniline was chosen as an optical analog of some naturally occurring levorotatory (−)-ω-(methylsulfinyl)alkyl isothiocyanates in an attempt to determine the latter's absolute configuration. While the relative configuration of these compounds was established, their absolute configuration remains uncertain.

Numerous naturally occurring sulfoxides have been isolated in recent years; most of these have in common an optically active methylsulfinyl group.[2a] The absolute configuration about sulfur was established for one of these sulfoxides, (+)-3-(methylsulfinyl)-alanine,[2b] using X-ray methods; in all of the other cases, the configuration is unknown. This article reports the results of experiments designed to determine the configuration of some isothiocyanate sulfoxides (I), where *n* varies from 3 to 10, which have been investigated very extensively by Kjaer and coworkers. Klyne, Day, and Kjaer[3] demonstrated that



$CH_3\overset{O}{\overset{|}{S}}(CH_2)_nNCS$

I

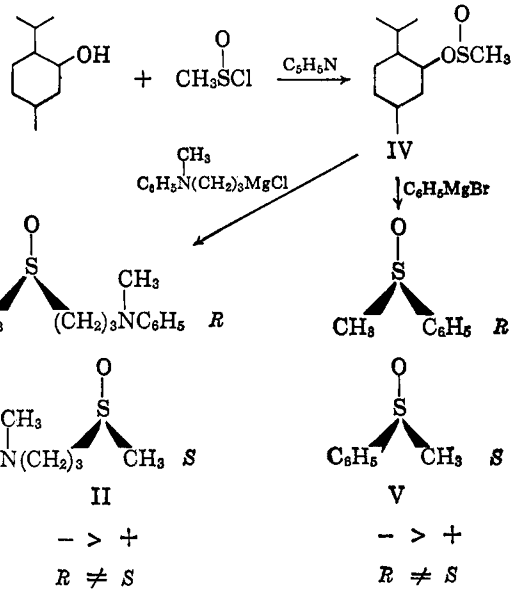


$CH_3\overset{O}{\overset{|}{S}}(CH_2)_3\overset{CH_3}{\overset{|}{N}}C_6H_5$

II

various phenylurea, phenylthiourea, and thiourea derivatives of these naturally occurring sulfoxides all gave negative plain optical rotatory dispersion (O.R.D.) curves between 600 and 300 mμ which were very similar and in some cases almost superimposable. This was interpreted to mean that the absolute configurations were identical for all of these compounds. Since a change in the value of *n* does not affect the sign and scarcely affects the shape of the O.R.D. curves, the functional groups at the terminal position of the alkyl chain must have very little if any influence on the sulfoxide chromophore. N-Methyl-N-[3-(methylsulfinyl)propyl]aniline (II), for this reason, should be a suitable optical analog of these naturally occurring sulfoxides. If the absolute configuration of II could be determined, a comparison of its O.R.D. curve with those obtained by Klyne, Day, and Kjaer would permit an assignment of configuration to the (−)-ω-(methylsulfinyl)alkyl isothiocyanates (I).

In order to determine the absolute configuration of the model compound II, its configuration was related to that of (−)-menthyl (−)-*p*-toluenesulfinate (III). In one of a series of important articles, Herbrandson[4] tentatively assigned the *S*-configuration[5] to sulfur in (−)-menthyl (−)-*p*-iodobenzenesulfinate. Both of these sulfinate esters should have the same absolute configurations. The validity of Herbrandson's assignment will be assumed for the moment. The synthetic procedure used to relate the N-methyl-N-[3-(methylsulfinyl)propyl]aniline (II) to (−)-menthyl (−)-*p*-toluenesulfinate (III) is shown below.



An epimeric mixture of (−)-menthyl (±)-methanesulfinate (IV) was prepared from (−)-menthol and racemic methanesulfinyl chloride. The equilibrium ratio of the amounts of the two epimers, which differ in configuration at sulfur, is not known, but probably is only a few per cent from unity. Herbrandson[4] found a 59:41 equilibrium epimer ratio for the (−)-menthyl (±)-*p*-iodobenzenesulfinates in nitrobenzene. The n.m.r. spectrum of the ester mixture included two partially separated, very sharp signals of about equal intensity. These were assigned to the protons of the two methanesulfinyl groups although long-range splitting by the axial proton has not been ruled out. This point is being investigated. Attempts to separate the two epimers by fractional distillation and by vapor phase chromatography were unsuccessful.

Addition of catalytic amounts of hydrogen chloride to the epimeric mixture should lead to equilibration of the two epimers as described by Herbrandson[4] for similar compounds. When this was done, scarcely

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[1] This research was supported in part by the Public Health Service under Grant No. GM 10800.

[2] (a) B. W. Christensen and A. Kjaer, *Acta Chem. Scand.*, **17**, 846 (1963), and references cited therein; (b) R. Hine, *Acta Cryst.*, **15**, 635 (1962.)

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

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

[5] A referee has suggested that the sulfinyl oxygen in sulfinate esters be assigned a sequence number of 32 rather than 16 since the SO bond presumably has partial double bond character. We do not agree with such a change. Both the author[6] and C. J. M. Stirling [*J. Chem. Soc.*, 5741 (1963)] have followed Herbrandson's original assignment[4] based on the concept of octet valency structures. Any change at this point would lead to confusion in the literature. In addition, configurational assignment to molecules such as sulfinyl fluorides, RS(O)F, would be confusing. Conceivably oxygen could be assigned a value of 16 or 32 and fluorine values of 19 or 38 depending on the amount of double-bonded character. We strongly urge future authors to assign configurations to tri- and tetrasubstituted sulfur on the basis of the most stable octet valency structure and not on the basis of structures involving an expanded octet for sulfur.

any change in rotation was observed. Apparently, the esters were already at or close to equilibrium. An attempt to enrich the ester mixture in the concentration of one of the epimers was undertaken successfully by adding a menthol–pyridine solution in ether to a 3 M excess of methanesulfinyl chloride. The ester rotation became less negative indicating enrichment in the concentration of the epimer containing the dextrorotatory sulfinate group. Mutarotation occurred, however, and over a period of a few days the equilibrium rotation was attained. This mutarotation was probably catalyzed by chloride on the laboratory glassware.[4]

The important point, however, is that the addition of an ether solution of phenylmagnesium bromide to an equilibrium mixture of esters or to a mixture slightly more dextrorotatory than the equilibrium rotation always gave methyl phenyl sulfoxide (V) in which the dextrorotatory isomer predominated over the levorotatory isomer.[6,7] Addition of the Grignard reagent prepared from N-methyl-N-(3-chloropropyl)aniline to the ester mixture always resulted in N-methyl-N-[3-methylsulfinyl)propyl]aniline (II) in which the levorotatory isomer predominated over the dextrorotatory isomer.

The reaction of the Grignard reagent with the esters is rapid compared with the rate of addition of the Grignard solution to the ester solution. A Gilman test[8] on the reaction mixture immediately after the addition of some Grignard reagent was negative; this means that a drop of added Grignard reagent was consumed before the next drop was added. The Grignard reagent possibly could react more rapidly with one epimer than another, although both epimers react rapidly compared with the rate of addition of the Grignard solution.

If the more stable epimer (present in largest concentration) reacts most rapidly, then the per cent of ester mixture which reacts has no influence on the sign of rotation of the product. If the least stable epimer reacts most rapidly, the sign of rotation of the product would depend on the per cent of reaction completed. After a certain per cent of the ester mixture had reacted, one sulfoxide enantiomer could predominate while further along toward 100% reaction the concentration of the other enantiomer formed from the less reactive but predominant epimer could overtake the originally predominant sulfoxide. Perhaps, although this seems unlikely, the relative reactivity of the epimeric esters is reversed depending on the Grignard reagent used.

Reactions in which the esters were added to the Grignard reagent rule out the last two possibilities. As each drop of ester solution was added to the Grignard solution, it reacted before the next drop was added. The configuration of the sulfoxide enantiomer predominating in the product isolated reflects the configuration of the predominant ester in the epimeric starting material. Significantly, the specific rotation at the sodium D-line of the methyl phenyl sulfoxide (V) formed in this way was +19° compared to +23° when formed by addition of the Grignard reagent to the esters. The specific rotation of II prepared in this way was −11° compared to −12° when formed by addition of the Grignard reagent to the esters.

An estimate of the optical purity of the products II and V is possible. The almost superimposable O.R.D. curves[3] give the value of 250° for the molecular rotations at the sodium D-line for a series of sulfoxides structurally analogous to II. Sulfoxide II is estimated to be 10% optically pure. An estimate of the optical purity of V is somewhat more speculative in the absence of extensive data. A comparison of the molecular rotation of V with that of optically pure ethyl *p*-tolyl sulfoxide[9] gives a value of 9% optical purity for V.

Thus, the configuration of the two predominating enantiomers, (+)-methyl phenyl sulfoxide and (−)-N-methyl-N-[3-(methylsulfinyl)propyl]aniline, must be the same since they both result from the predominant epimer of the ester mixture.

In an earlier paper,[6] the *R*-configuration was assigned to (+)-ethyl *p*-tolyl sulfoxide prepared from optically pure (−)-menthyl (−)-*p*-toluenesulfinate (III). Mislow, Ternay, and Melillo[10] demonstrated that several alkyl *p*-tolyl sulfoxides prepared from III were all dextrorotatory and gave similar O.R.D. curves; therefore, all (+)-alkyl *p*-tolyl sulfoxides are expected to have the same configuration. This means that (+)-methyl phenyl sulfoxide has the same configuration as the (+)-alkyl *p*-tolyl sulfoxides; the absence of the *para* methyl group should not influence the sign of rotation. Assuming the validity of the *S*-configurational assignment to sulfur in (−)-menthyl (−)-*p*-toluenesulfinate (III), then both (+)-methyl phenyl sulfoxide and (−)-N-methyl-N-[3-(methylsulfinyl)propyl]aniline should be of configuration *R*.

A plain O.R.D. curve between 700 and 300 mμ was obtained for N-methyl-N-[3-(methylsulfinyl)propyl]-aniline (II). If the choice of II as a model compound for the (−)-ω-(methylsulfinyl)alkyl isothiocyanates (I) was a good one, then their configurations should also be *R*.

Several of the assumptions made in this argument should now be examined since Mislow, Ternay, and Melillo[10] pointed out that recent work by Cram and Pine[11] is in conflict with an *R* assignment to (+)-ethyl *p*-tolyl sulfoxide. Cram and Pine assigned the *S*-configuration to sulfur in (+)-2-octyl phenyl sulfoxide. The first assumption concerns the validity of Herbrandson's tentative assignment while the second assumption concerns the validity of supposing that inversion at sulfur occurs when a Grignard reagent reacts with a sulfinate ester. Johnson's[12] elegant work on the inversion of sulfoxides *via* intermediate alkoxysulfonium salts is additional evidence, besides that cited earlier,[6,10] for inversion in the Grignard reaction. This leaves the first assumption as the most probable source of the conflict. While one could make

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(6) K. K. Andersen, *Tetrahedron Letters*, **No. 3**, 93 (1962).

(7) H. Gilman, J. Robinson, and N. H. Beaber, *J. Am. Chem. Soc.*, **48**, 2715 (1926); H. Gilman and J. D. Robinson, *Bull. soc. chim. France*, [4]**45**, 636 (1929).

(8) H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

(9) Unpublished results of N. Papanikolaou and J. W. Foley indicate that the method in ref. 6 leads to optically pure sulfoxides, if optically pure sulfinate esters are used as starting materials.

(10) K. Mislow, A. L. Ternay, Jr., and J. T. Melillo, *J. Am. Chem. Soc.*, **85**, 2329 (1963).

(11) D. J. Cram and S. H. Pine, *ibid.*, **85**, 1096 (1963).

(12) C. R. Johnson, and J. B. Sapp, Abstracts of Papers, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963, p. 23Q; C. R. Johnson, *J. Am. Chem. Soc.*, **85**, 1020 (1963).

a choice between Herbrandson's assignment and Cram and Pine's assignment by contemplating molecular models, the uncertainty in bond angles, bond lengths, and van der Waals radii make such an endeavor speculative. For this reason, the configurational relationships assigned in this paper must be considered relative.

It should be noted that Hine[2b] assigned the *S*-configuration to the dextrorotatory methylsulfinyl group in (+)-3-(methylsulfinyl)alanine.[13] The assignment of the *R*-configuration to (−)-N-methyl-N-[3-(methylsulfinyl)propyl]aniline is consistent with Hine's assignment, and then, of course, with Herbrandson's assignment, but such a configurational comparison is based on the very questionable assumption that the asymmetric carbon atom and its attached functional groups do not greatly influence the more powerfully rotating asymmetrically perturbed sulfoxide chromophore in this amino acid.

On the other hand, the work of Phillips[14] on the inversion of sulfinate esters seems to favor Cram's assignment. When 1 mole of racemic ethyl *p*-toluenesulfinate was treated with 0.5 mole of (−)-(*R*)-2-octanol, 2-octyl *p*-toluenesulfinate predominating in the levorotatory epimer was formed. The unchanged portion of the ethyl ester was also levorotatory. Similar results were obtained using *n*-butyl *p*-toluenesulfinate; a levorotatory ester predominated in the unchanged enantiomeric ester mixture. Upon treatment with *n*-butyl alcohol, the levorotatory ethyl ester was converted to the *n*-butyl ester in which the dextrorotatory isomer predominated. These ester interchange reactions are best explained as proceeding by nucleophilic attack by the alcohol on the sulfur atom with inversion and displacement of an alkoxy group. Application of Cram's rule[15] to S$_N$2-type transition states involving the (−)-(*R*)-2-octanol and the (*R*)- and (*S*)-alkyl *p*-toluenesulfinates leads one to predict that the transition state involving the octanol and the (*S*)-ester has a lower energy than the transition state involving the octanol and the (*R*)-ester. In these transition states, the CO bonds of entering and leaving alkoxy groups are considered to lie on a line passing through the sulfur atom and perpendicular to a plane containing the *p*-toluenesulfinyl group. Arrangement of the *p*-tolyl group of the ester is considered to be *trans* or *anti* to the *n*-hexyl group of the 2-octanol. The levorotatory ethyl and *n*-butyl esters which predominate in the unchanged portion of the esters should be the least reactive ones and so of configuration *R*. It is significant that Phillips' work suggests that alkyl *p*-toluenesulfinates of the same sign of rotation have the same configuration. This is supported by Mislow's conclusion that the *p*-toluenesulfinyl group is a dissymmetric chromophore whose sign of rotation is not changed by alkyl groups as in alkyl *p*-tolyl sulfoxides. Neither do alkoxy groups seem to influence this chromophore's sign of rotation. To be consistent with the previous argument, (−)-menthyl (−)-*p*-toluenesulfinate should also be of configuration *R* about sulfur and not *S* as tentatively suggested by Herbrandson. It should be emphasized that this application of Cram's rule is speculative; further research is needed to establish the validity of the preceding analysis.

In spite of the present confusion concerning their absolute configurations, the relative configurations of several sulfoxides have been assigned using a method capable of extension to other sulfoxides and sulfinate esters.

Experimental

(−)-Menthyl (±)-Methanesulfinate (IV).—A solution of methanesulfinyl chloride[16] (50.2 g., 0.510 mole) in anhydrous ether (150 ml.) was added dropwise with stirring and cooling in an ice bath to a solution of U.S.P. (−)-menthol (78.1 g., 0.500 mole) and pyridine (40.3 g., 0.510 mole) in ether (50 ml).. After the mixture stood overnight in an ice bath, ether (100 ml.) was added. The mixture was extracted with cold water, cold 10% hydrochloric acid, cold aqueous sodium bicarbonate, and again with cold water, in that order. After drying over sodium sulfate and subsequent removal of the ether *in vacuo*, crude IV (101 g., 0.46 mole, 93% yield) was obtained. Fractionation through a 15-cm. Vigreux column gave pure IV, b.p. 88–89° (0.4 mm.), $[\alpha]^{25}\text{D}$ −99 ± 1° (*c* 2.04, acetone); $\nu_{\max}^{\text{neat}}$ 1137 cm.$^{-1}$; n.m.r. (40% in $CHCl_3$), τ 7.30 and 7.32, peaks assigned to $CH_3S(O)O$– protons on basis of comparison to other alkyl methanesulfinates prepared in this laboratory.

Anal. Calcd. for $C_{11}H_{22}O_2S$: C, 60.51; H, 10.16. Found: C, 60.30; H, 10.10.

Methyl Phenyl Sulfoxide (V).—A Grignard reagent prepared from bromobenzene (31.4 g., 0.200 mole) and magnesium (5.5 g., 0.23 g.-atom) in anhydrous ether (100 ml.) was added at −10° over a 45-min. period with stirring to an ether solution (100 ml.) of (−)-menthyl (±)-methanesulfinate [39.2 g., 0.180 mole, $[\alpha]^{24}\text{D}$ −98 ± 1° (*c* 2.29, acetone)]. After stirring for 10 min. more without cooling, the mixture was hydrolyzed with saturated ammonium chloride. The organic layer was dried over magnesium sulfate, filtered, and concentrated to give an oil. Upon fractional distillation crude menthol (25.5 g., 0.163 mole, 91% yield) and crude methyl phenyl sulfoxide (V, 12.7 g., 0.0907 mole, 50% yield) were obtained. The crude sulfoxide was stirred overnight with dilute sodium hydroxide to hydrolyze traces of unchanged ester. Distillation then gave pure methyl phenyl sulfoxide, b.p. 85° (0.5 mm.), lit.[17] b.p. 139–140° (14 mm.), $[\alpha]^{23}\text{D}$ +23 ± 1° (*c* 2.29, acetone). A vapor phase chromatogram indicated only an insignificant trace of (−)-menthol. The infrared spectrum was identical with that of an authentic sample. Oxidation of the sulfoxide with hydrogen peroxide in glacial acetic acid gave methyl phenyl sulfone, m.p. 86.5–87.5, lit.[17] m.p. 88°, which did not depress the melting point of an authentic sample.

Several repetitions of the above reaction on different samples of ester always gave (+)-methyl phenyl sulfoxide. Addition of the ester to the Grignard solution gave similar results, $[\alpha]^{23}\text{D}$ +19 ± 1° (*c* 2.07, acetone).

N-Methyl-N-[3-(methylsulfinyl)propyl]aniline (II).—A Grignard reagent prepared from N-methyl-N-(3-chloropropyl)aniline[18] (11.1 g., 0.0603 mole) and excess magnesium in an ether–benzene (50:50 ml.) mixture was added over a 30-min. period at 0° with stirring to an ether solution (50 ml.) of (−)-menthyl methanesulfinate (10.9 g., 0.0500 mole). A portion of the same preparation of ester as used in the synthesis of V was used. After standing for 4 hr., the mixture was hydrolyzed with dilute ammonium chloride. The ether layer was separated and extracted twice with 10% hydrochloric acid. The acid extracts were made basic with aqueous sodium hydroxide. The oil which separated was taken up in ether. After drying over magnesium sulfate and removal of the ether, a levorotatory oil (10.8 g.) which crystallized upon standing was obtained. The levorotation was not caused by (−)-menthol since blank experiments showed that a mixture of racemic sulfoxide and (−)-menthol was cleanly separated using the above procedure; the racemic sulfoxide did not show any levorotation due to contaminating (−)-menthol. The infrared spectrum of the crude sulfoxide did not include the

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[13] C. J. Morris and J. F. Thompson, *Chem. Ind.* (London), 951 (1955).

[14] H. Phillips, *J. Chem. Soc.*, **127**, 2552 (1925).

[15] F. Q. Abd Elhafez and D. J. Cram, *J. Am. Chem. Soc.*, **75**, 339 (1953); D. J. Cram and F. Q. Abd Elhafez, *ibid.*, **74**, 5828 (1952).

[16] I. B. Douglass and B. S. Farah, *Org. Syn.*, **40**, 62 (1960).

[17] H. Bohme, H. Fischer, and R. Frank, *Ann.*, **563**, 54 (1949).

[18] J. von Braun and G. Kirschbaum, *Ber.*, **52**, 1716 (1919).

very intense and characteristic sulfinate ester stretching band at about 1140 cm.$^{-1}$.

The sulfoxide was recrystallized several times from *n*-hexane to give pure II; m.p. 80.0–80.5°, $\nu_{max}^{CHCl_3}$ 1035 cm.$^{-1}$ (sulfoxide stretching). N.m.r. (25% in $CHCl_3$) is in τ-units: triplet, 6.57, J = 7 c.p.s. (N–CH_2–); singlet, 7.12 (N–CH_3); multiplet, 7.23–7.53 (–CH_2–SO–); singlet, 7.53 (CH_3–SO–); pentuplet, 8.03, J = 7 c.p.s. (–CH_2–CH_2–CH_2–). The n.m.r. assignments were made by comparison with the spectrum of N-methyl-N-propylaniline.

Anal. Calcd. for $C_{11}H_{17}NOS$: C, 62.52; H, 8.11. Found: C, 62.51; H, 8.04.

The rotation went to zero as the recrystallization proceeded while the rotation of the oil from the mother liquors became more levorotatory. A racemic compound preferentially crystallized from the *n*-hexane. To circumvent this problem, the crude sulfoxide (5.5 g.) was distilled through a small Vigreux column. N-Methyl-N-propylaniline (0.9 g.) from the hydrolysis of the Grignard reagent was obtained as the first fraction, b.p. about 60° (0.5 mm.), lit.[19] b.p. 95–98° (10 mm.). The infrared and n.m.r. spectra were identical with those obtained from an authentic sample. The column was removed and the remainder of the material distilled to give II (2.2 g.); b.p. about 180° (0.6 mm); m.p. 75–78°; $[\alpha]^{28}D$ $-12 \pm 1°$ (*c* 2.54, acetone); O.R.D. (*c* 1.85, ethanol) gave a negative plain curve: $[\phi]_{600}$ $-23°$, $[\phi]_{500}$ $-30°$, $[\phi]_{400}$ $-54°$, $[\phi]_{350}$ $-90°$, $[\phi]_{340}$ $-97°$. Addition of gaseous hydrogen chloride to the ethanol solution to form the hydrochloride salt did not change the O.R.D. values indicating that the aniline group probably does not influence the sulfoxide chromophore very much.

The n.m.r. spectrum of the distilled sulfoxide was identical with that obtained from the recrystallized sulfoxide. Addition of 5% of (−)-menthol to the recrystallized sulfoxide gave a mixture whose n.m.r. spectrum clearly revealed the methyl groups of the menthol. In order to have $[\alpha]D$ $-12°$, the distilled sulfoxide would need to be contaminated with 20% (−)-menthol or 10% (−)-menthyl methanesulfinate. The n.m.r. spectrum ruled out such contamination.

Several repetitions of the reaction always gave levorotatory II. Addition of the ester to the Grignard reagent gave identical results: rotation of II, $[\alpha]^{25}D$ $-11 \pm 1°$ (c 2.07, acetone).

Instruments.—The infrared spectra were obtained on Perkin-Elmer Model 21 and Model 337 spectrophotometers, the n.m.r. spectra on a Varian Model A-60 spectrometer, and the O.R.D. curves on a Rudolph Model 260/655/850/810-614 recording spectropolarimeter.

Acknowledgment.—The author is most grateful to Drs. W. Gaffield and G. G. Lyle for obtaining the O.R.D. curves, and to the National Science Foundation for a departmental grant, G-22718, enabling the purchase of an n.m.r. spectrometer.

[19] R. L. Bent, *et. al., J. Am. Chem. Soc.*, **73**, 3100 (1951).

The Chlorination of Active Hydrogen Compounds with Sulfuryl Chloride.

I. Ketones

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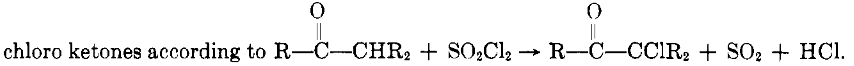
A number of ketones possessing α-hydrogen atoms are readily chlorinated by sulfuryl chloride to yield α-chloro ketones according to  $R-\overset{\overset{O}{\|}}{C}-CHR_2 + SO_2Cl_2 \rightarrow R-\overset{\overset{O}{\|}}{C}-CClR_2 + SO_2 + HCl$. In general, the order of preferred substitution is methine > methylene > methyl. In several cases, α,α-dichloro ketones were the major products. The chlorination is sensitive to steric factors as well as electronic ones; *e.g.*, 1,2,3-triphenylpropanone-1 did not react even when dissolved in an excess of sulfuryl chloride. An acid-catalyzed ionic mechanism is proposed to explain the experimental results.

A few isolated examples of the chlorination of active hydrogen compounds by sulfuryl chloride can be found.[1–7] The compounds studied (and the products obtained) included malonic esters[1,2] (chloromalonates), methyl ethyl ketone[3] (3-chlorobutanone-2), acetone[4] (1-chloropropanone-2 and 1,1-dichloropropanone-2), cyclopentyl phenyl ketone[5] (α-chlorocyclopentyl phenyl ketone), methyl and ethyl levulinate[6] (chlorination of the methylene group α to the keto carbonyl), and β-diketones[7] (2,2-dichloro-1,3-diketones). In all cases but one,[4] a single product was isolated and/or reported even though more than one α-methyl, methylene, or methine group was often present.

In order to gain a better understanding of the scope and limitations of the chlorination of active hydrogen compounds with sulfuryl chloride, a variety of ketones have been subjected to this reaction and the results are reported here.

Results

A total of nine different ketones was used in this investigation and the chlorinated products obtained from them are summarized in Table I. In every case chlorination occurred exclusively in the α-positions.

The "linear" ketones, acetone, methyl ethyl ketone, and diethyl ketone, each gave several products upon treatment with an equimolar amount of sulfuryl chloride. However, the major product[8] from each was the α,α-dichloro derivative [1,1-dichloropropanone-2 (60–70%), 3,3-dichlorobutanone-2 (48%), and 2,2-dichloropentanone-3 (58%), respectively]. The other products from the chlorination of methyl ethyl ketone and diethyl ketone consisted of nearly equal amounts of the α,α'-dichloro and monochloro derivatives. The methylene protons of methyl ethyl ketone were substituted much more readily than the methyl protons. On the other hand, very little 1,3-dichloropropanone-2 was formed

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[1] A. K. Macbeth, *J. Chem. Soc.*, 1116 (1922).

[2] K. G. Naik and N. T. Talati, *J. Indian Chem. Soc.*, **8**, 203 (1931).

[3] E. R. Buchman, A. O. Reims, and H. Sargent, *J. Org. Chem.*, **6**, 764 (1941).

[4] E. R. Buchman and H. Sargent, *J. Am. Chem. Soc.*, **67**, 401 (1945).

[5] G. Cauquil and J. Rouzaud, *Compt. rend.*, **237**, 1720 (1953).

[6] H. Yasuda, *J. Sci. Res. Inst.* (Tokyo), **513**, 32 (1957).

[7] E. Gudriniece, G. Vanags, A. Kurzemnicks, and Z. Grants, *Izv. Vysshikh Uchebn. Zavedenii Khim. i Khim. Tekhnol.*, **3**, 119 (1960); *Chem. Abstr.*, **54**, 17,352.

[8] The per cent yields given, unless otherwise specified, are based upon the relative quantity of chlorinated products which were obtained. The actual yields in terms of conversion of sulfuryl chloride were generally high, *i.e.*, >80%.