Sulfinate Esters. II. The Sythetic Utility of Methyl Methanesulfinate[1]

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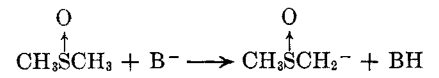
Methyl methanesulfinate can be converted into the *n*-butyl ester by refluxing with 1-butanol in presence of catalytic amounts of sodium methoxide or sulfuric acid. Attempts to form the methoxysulfinyl carbanion and cause it to enter into Claisen-type condensations were unsuccessful. Similarly, no deuterium exchange could be demonstrated when the ester was heated with sodium methoxide in the presence of deuteriomethanol. After saponification of the ester, the resulting solution of sodium methanesulfinate readily reacted with compounds such as benzyl chloride, *n*-butyl bromide, chloroacetone, phenacylbromide, 2,4-dinitrophenyl chloride, and methanesulfenyl chloride forming the expected methylsulfonyl compounds. Saponification of the ester, followed by acidification of the alkaline solution with formic acid and addition of formaldehyde and a nitrogen compound (amine or amide), yielded products formed by Mannich-type reactions. Methylsulfonylmethyl derivatives were prepared from urea, benzamide, acetamide, methanesulfonamide, and *p*-toluidine. Pmr δ shifts are reported for the compounds prepared.

In a previous publication[2] a convenient method for the preparation of alkanesulfinate esters was described. Since these sulfinate esters have excellent stability, if kept away from moisture, they have potential as shelf reagents if their synthetic utility can be demonstrated.

Alcoholysis reactions of sulfinate esters have been utilized by several workers since Phillips[3] first caused ethyl *p*-toluenesulfinate to react with optically active 2-octanol. We find that *n*-butyl methanesulfinate can be formed in excellent yield by the reaction of 1-butanol with methyl methanesulfinate, either in the presence of catalytic amounts of sulfuric acid or sodium methoxide.

On the other hand, repeated attempts to prepare *t*-butyl methanesulfinate by the reaction of *t*-butyl alcohol with methyl methanesulfinate in the presence of catalytic amounts of sulfuric acid, sodium methoxide, or sodium *t*-butoxide all resulted in failure.

Many recent studies have demonstrated that dimethyl sulfoxide will react with strong bases to form the methylsulfinyl carbanion.[4] It seemed possible that methyl methanesulfinate, $CH_3S(\rightarrow O)OCH_3$, because of its analogous relationship to both dimethyl sulfoxide and to methyl acetate, would also react with strong bases to form methoxysulfinyl carbanion, $CH_3OS(\rightarrow O)CH_2^-$. Refluxing the ester in the presence of sodium methoxide and deuteriomethanol, CH_3OD, failed to bring about any deuterium exchange. Likewise, its reaction with sodium hydride in hexane, in tetrahydrofuran, and in the absence of any diluent failed to produce a carbanion which would enter into a Claisen-type reaction with benzophenone.



$$\mathrm{CH_3\overset{O}{\overset{\uparrow}{S}}CH_3 + B^- \longrightarrow CH_3\overset{O}{\overset{\uparrow}{S}}CH_2^- + BH}$$

Previous work in this laboratory[2] has demonstrated that methyl methanesulfinate is saponified at a rate too rapid to measure by ordinary means. The resulting solution, therefore, can serve as a ready source of the methanesulfinate anion or, if acidified, as a source of methanesulfinic acid. The reactions reported in this paper chiefly take advantage of this type of reactivity.

The saponified ester was caused to react with various compounds containing active halogen atoms and resulted in forming the corresponding sulfones in good yield. No product could be obtained, however, when the saponified ester was treated with *t*-butyl chloride. This result corresponds to the failure of Darwish and McLaren to obtain reactions between *t*-butyl chloride and sodium arenesulfinates.[5]

The saponified ester was also treated with methanesulfenyl chloride forming methyl methanethiolsulfonate, $CH_3SO_2SCH_3$.

There has been renewed interest recently in the Mannich-type reactions between sulfinic acids, formaldehyde, and compounds containing amine and amide groups.[6,7] It seemed of interest to attempt reactions of this type with saponified ester solutions which had been made acidic with formic acid. Reaction took place readily with urea, benzamide, acetamide, methanesulfonamide, and *p*-toluidine.

Experimental Section

Methyl methanesulfinate was prepared by the method previously described.[2] Elemental analyses were carried out by the Schwartzkopf Microanalytical Laboratories, Woodside, N. Y. We are indebted to Dr. Ralph Hill of this department for determining pmr and infrared spectra. The former were obtained by the use of a Varian Associates Model A-60 nmr spectrometer, the scale of which was calibrated frequently with a solution containing 1% chloroform and 1% tetramethylsilane in carbon tetrachloride. Chemical shifts for most of the compounds prepared are listed in Table I. All spectra, unless otherwise noted, were measured using approximately 10% solutions in trifluoroacetic acid. Infrared spectra were obtained by the use of a Baird Associates Model 4-55 infrared spectrometer and are reproduced in the thesis from which most of the data in this paper are taken.

Alcoholysis Reactions.—Methyl methanesulfinate (14.1 g, 0.15 mole), excess 1-butanol (16.6 g, 0.22 mole), and 0.25 ml of concentrated sulfuric acid were refluxed together for 45 min. At the end of this time the insertion of a Dean–Stark trap below the condenser allowed the collection of 5.6 ml of methanol. Distillation of the remaining liquid under the reduced pressure of an aspirator yielded 16.4 g of product boiling at 72–72.5° (10 mm) and having $n^{25}\mathrm{D}$ 1.4375. The infrared spectrum of the product was identical with that of an authentic sample of *n*-butyl methanesulfinate although the refractive index was somewhat lower than that of a pure sample.[2] The yield was 79%.

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[1] Taken in part from a thesis presented by F. J. Ward in partial fulfillment of the requirements for the M.S. degree, June 1966.

[2] I. B. Douglass, *J. Org. Chem.*, **30**, 633 (1965).

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

[4] For a recent review of base-catalyzed reactions of organosulfur compounds, see T. J. Wallace, *J. Chem. Educ.*, **41**, 542 (1964).

[5] D. Darwish and R. McLaren, *Tetrahedron Letters*, 1231 (1962).

[6] H. Bredereck and E. Bader, *Ber.*, **87**, 129 (1954).

[7] J. B. F. N. Engberts and J. Strating, *Rec. Trav. Chim.*, **83**, 733 (1964).

TABLE I

CHEMICAL SHIFTS OF SOME METHYLSULFONYL COMPOUNDS

(δ units in parts per million)

Compound	CH_3SO_2	$SO_2CH_2N<$	$>CNHCO$	SO_2CH_2CO	CH_3CO	SCH_3
$CH_3SO_2CH_2C_6H_5$	2.95					
$CH_3SO_2CH_2COCH_3$	2.52			4.56	3.30	
$CH_3SO_2CH_2COC_6H_5$	3.33 (lit.[a] 3.12)			5.04 (lit.[a] 4.62)		
$CH_3SO_2SCH_3$[b]	3.31 (lit.[c] 3.17)					2.69 (lit.[c] 2.60)
$(CH_3SO_2CH_2NH)_2CO$	3.20	5.95 (J = 6.0 cps)	7.06 (J = 6.0 cps)			
$CH_3SO_2CH_2NHCOC_6H_5$	3.27	5.18 (J = 6.5 cps)	8.45 (J = 6.5 cps)			
$CH_3SO_2CH_2NHCOCH_3$	3.20	4.95 (J = 7.0 cps)	8.06 (J = 7.0 cps)		2.34	
$\overset{a}{CH_3}SO_2CH_2NHSO_2\overset{b}{CH_3}$	3.24 (a) 3.33 (b)	4.83 (J = 7.0 cps)	6.82 (J = 7.0 cps)			
$(CH_3SO_2CH_2)_2NC_6H_4CH_3$-*p*	2.90					

[a] See Table II, footnote *d*. [b] The δ shift values reported for this compound were measured using a 10% carbon tetrachloride solution after calibration of the instrument with a solution of 1% chloroform and 1% tetramethylsilane in carbon tetrachloride and are believed to be more accurate than those reported.[c] [c] G. R. Pettit, I. B. Douglass, and R. A. Hill, *Can. J. Chem.*, **42**, 2357 (1964).

In another experiment 14.1 g (0.15 mole) of methyl methanesulfinate was refluxed with 16.6 g (0.22 mole) of 1-butanol for 15 min in the presence of 0.5 g of sodium methoxide. Insertion of a Dean-Stark trap permitted the removal of 5.75 ml of methanol and, after acidification of the mixture with sulfuric acid, distillation under reduced pressure gave 17.5 g (85% yield) of *n*-butyl methanesulfinate boiling at 74° (12 mm) and having $n^{25}D$ 1.4385. Although the refractive index was lower than that of a pure sample,[2] the infrared spectra were identical.

A solution of methyl methanesulfinate (9.42 g, 0.10 mole), sodium-dried *t*-butyl alcohol (11.1 g, 0.15 mole), and 1 drop of concentrated sulfuric acid was heated for 3 hr under a partial reflux condenser. During this period 5.3 ml of distillate was collected from 65–83° (theoretical yield of methanol was 4.02 ml). Attempted high-vacuum distillation of the crude reaction mixture at 0.5 mm resulted in a vigorous decomposition. Subsequent distillation of the pot residue yielded methyl methanethiolsulfonate (0.7 g, infrared and pmr spectra identical with those of an authentic sample).

The gaseous decomposition products, condensed in a Dry Ice trap, were treated with bromine and yielded 1,2-dibromo-2-methylpropane, identified by its boiling point (149°), refractive index ($n^{25}D$ 1.509), and pmr spectrum which consisted of a singlet at δ = 1.88 ppm for $(CH_3)_2CBr$ and a singlet at δ = 3.84 ppm for $BrCH_2$ having peak areas in the ratio of 3:1.

Attempts to use sodium methoxide and sodium *t*-butoxide to catalyze the reaction with *t*-butyl alcohol were also unsuccessful.

Attempts to Demonstrate Deuterium Exchange.—To a solution of 0.23 g of sodium (0.01 g-atom) in 6.93 g (0.21 mole) of deuteriomethanol (CH_3OD) was added 9.40 g (0.1 mole) of methyl methanesulfinate and the mixture was refluxed for 15 hr. At first the mixture was yellow in color but darkened to brown by the end of the reflux period. Distillation under reduced pressure gave 5.47 g of product (58% recovery). Proton magnetic resonance spectra were obtained for four different fractions of the recovered product and in each case the area under the curve for the CH_3S protons (δ = 2.54 ppm) was exactly equal to that under the curve for the $CH_3OS(\rightarrow O)$ protons (δ = 3.68 ppm), thus indicating that there had been no deuterium exchange.

Attempted Carbanion Formation.—A well-stirred solution of methyl methanesulfinate (9.4 g, 0.1 mole) in 50 ml of hexane was treated under nitrogen with sodium hydride (2.4 g, 0.1 mole, 62.4% in mineral oil) in 80 ml of hexane. The mixture was stirred for 20 min and then 27.6 g of benzophenone (0.1 mole) in 100 ml of hexane was added, the temperature was raised to 60°, and stirring was continued for 15 min. At the end of this period, the reaction mixture had turned green. Addition of concentrated hydrochloric acid caused a vigorous reaction, the liberation of hydrogen gas, decolorization of the mixture, and the formation of a white precipitate. Upon filtration of the mixture and evaporation of the hexane, a nearly quantitative yield of benzophenone was recovered. No other products could be isolated.

In another experiment 15.0 g of methyl methanesulfinate (0.16 mole) in a large test tube was cooled to −70° and treated with a small amount of sodium hydride (62.4% in mineral oil). The temperature was raised, until at 20° a reaction began; then it was lowered to −30° and held below 0° during the addition of the remaining sodium hydride (total 0.60 g, 0.025 mole).

The reaction produced hydrogen gas, a white precipitate, and a red color in the solution. When evolution of gas had stopped, benzophenone (4.56 g, 0.25 mole) was added and the mixture was well stirred. After acidification with hydrochloric acid and standing, sodium chloride separated. No material other than unreacted benzophenone could be isolated, however, from the reaction mixture.

Sulfones from Sulfinate Esters.—In preparing the sulfones listed in Table II, the following procedure was employed. Sodium hydroxide (4.0 g, 0.1 mole) dissolved in 25 ml of water was added to a solution of 9.4 g (0.1 mole) of methyl methanesulfinate in about 25 ml of methanol. Although saponification was probably complete immediately, the solution was usually stirred for about 10 min before adding the halogen compound dissolved in a convenient quantity of methanol. After refluxing for 2–3 hr, the methanol was evaporated and the resulting sulfone was recrystallized from an appropriate solvent.

TABLE II

SULFONES

Sulfone	Mp, °C	Yield, %
$CH_3SO_2CH_2C_6H_5$	126–127 (lit.[a] 127)	50
$CH_3SO_2CH_2CH_2CH_2CH_3$	28–30 (lit.[b] 30)	
$CH_3SO_2CH_2COCH_3$	54.5–55.5 (lit.[c] 54)	23
$CH_3SO_2CH_2COC_6H_5$	108–109 (lit.[d] 91–92)	77
$CH_3SO_2C_6H_3(NO_2)_2$-2,4	184–185 (lit.[e] 185, 189.5)	64

[a] E. B. Ruiz, *Acta Salmenticensia, Ser. Cienc.*, **2**, 64 (1958); *Chem. Abstr.*, **54**, 7624*b* (1960). [b] Y. Yamamoto, *J. Pharm. Soc. Japan*, **72**, 1124 (1952); *Chem. Abstr.*, **47**, 6407*b* (1953). [c] D. W. Cowie and D. T. Gibson, *J. Chem. Soc.*, 46 (1934). [d] K. Griesbaum, A. A. Oswald, and B. E. Hudson, Jr., *J. Am. Chem. Soc.*, **85**, 1969 (1963). [e] R. W. Bost, P. K. Starnes, and E. L. Woods, *ibid.*, **73**, 1968 (1951).

Thiolsulfonates from Sulfinate Esters.—A sample of methyl methanesulfinate (0.1 mole) was hydrolyzed without the use of solvent methanol. The resulting solution was then cooled below 0° and treated with methanesulfenyl chloride. The product boiled at 118.5° (11 mm) and had $n^{25}D$ 1.5107 [lit.[8] 114° (13 mm) and $n^{25}D$ 1.5112]. Its infrared spectrum was identical with that of an authentic specimen of methyl methanethiolsulfonate.

Mannich-Type Reactions.—After saponifying the methyl methanesulfinate in the manner already described, the alkaline solution was made acidic with formic acid until the pH was brought lower than 3. Equivalent amounts of 37% formaldehyde and the nitrogen compound (amide or amine) dissolved in methanol or ethyl acetate were added and the mixture, after stirring, was allowed to stand for 1–2 weeks. Precipitation of reaction product was facilitated by evaporation of solvent and the resulting solid was purified by recrystallization.

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(8) I. B. Douglass and B. S. Farah, *J. Org. Chem.*, **24**, 973 (1959).

The following compounds were prepared. Their chemical shifts are shown in Table I.

N,N′-Bis(methylsulfonylmethyl)urea, $(CH_3SO_2CH_2NH)_2CO$, was prepared in 38% yield, mp 178–179°, from water. *Anal.* Calcd for $C_5H_{12}N_2O_5S$: C, 24.58; H, 4.95; N, 11.47; S, 26.25. Found: C, 24.39; H, 5.51; N, 11.22; S, 26.22.

N-(Methylsulfonylmethyl)benzamide, $CH_3SO_2CH_2NHCOC_6H_5$, was prepared in 42% yield, mp 181–182°. *Anal.* Calcd for $C_9H_{11}NO_3S$: C, 50.69; H, 5.20; N, 6.57; S, 15.04. Found: C, 50.96; H, 5.21; N, 6.85; S, 14.90.

N-(Methylsulfonylmethyl)acetamide, $CH_3SO_2CH_2NHCOCH_3$, was prepared in 21% yield, mp 110–111°, from chloroform–carbon tetrachloride. *Anal.* Calcd for $C_4H_9NO_3S$: C, 31.78; H, 6.00; N, 9.27; S, 2 1.21. Found: C, 32.02; H, 6.13; N, 9.30; S, 20.96.

N-(Methylsulfonylmethyl)methanesulfonamide, $CH_3SO_2CH_2NHSO_4CH_3$, was prepared in 37% yield, mp 106–107°, from ethyl acetate. *Anal.* Calcd for $C_3H_9NO_4S_2$: C, 19.24; H, 4.85; N, 7.48; S, 34.25. Found: C, 18.75; H, 4.92; N, 7.71; S, 34.56.

N,N-Bis(methylsulfonylmethyl)-*p*-toluidine, $(CH_3SO_2CH_2)_2NC_6H_4CH_3$-*p*, was prepared on a 0.1-mole scale from *p*-toluidine, mp 141–144° dec. The pmr spectrum of a 10% solution in trifluoroacetic acid showed four singlets at 2.37 (CH_3C_6), 2.90 (CH_3SO_2), 5.48 (NCH_2SO_2), and 7.32 ppm (C_6H_4). The areas of the four peaks were in the ratio of 3:6:4:4. *Anal.* Calcd for $C_{11}H_{17}NO_4S_2$: C, 45.34; H, 5.88; N, 4.81; S, 22.01. Found: C, 45.31; H, 5.98; N, 4.96; S, 21.84.

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The Photolysis of Diazomethane and Ethyl Diazoacetate in the Presence of 4-Octyne[1]

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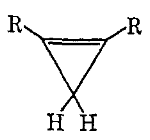
The addition of methylene and carboethoxycarbene, generated photochemically from diazomethane and ethyl diazoacetate, to 4-octyne yielded 1,2-di-*n*-propylcyclopropene and ethyl 1,2-di-*n*-propylcyclopropene-3-carboxylate, respectively. It is shown that a close to statistical reaction of methylene and a more discriminate reaction of carboethoxycarbene with the carbon–hydrogen bonds occur together with addition to the acetylenic bond. Diels–Alder reaction of 1,2-di-*n*-propylcyclopropene and 1,2-di-*n*-propylcyclopropene 3-carboxylate with cyclopentadiene afforded the *endo* adducts in both cases.

One of the many outgrowths of the chemistry of divalent carbon[2] has been the synthesis of cyclopropenes, especially the reactions of metal-catalyzed decomposition of diazoacetic esters[3] with acetylenes. Photolytic decomposition of diazomethane and methyl diazoacetate in the presence of 2-butyne has been reported[4] to yield 1,2-dimethylcyclopropene and methyl 1,2-dimethylcyclopropene-3-carboxylate, respectively. Because there was an interest in a one-step synthesis of ^{14}C-3 labeled cyclopropenes in this laboratory, the photoinduced reaction of diazomethane and ethyl diazoacetate with 4-octyne was investigated.

The photodecomposition of diazomethane was carried out at −78° with a high-pressure mercury lamp giving light only above 300 mμ by use of a filter. No solvent was used in order to keep the number of reaction products as low as possible. 1,2-Di-*n*-propylcyclopropene (**1**) was isolated in yields up to 25% based on N-nitrosomethylurea. Its half-life at room temperature is about 4 weeks, and it can be stored in the refrigerator without polymerization.[5]

Structural proof of **1** is based on elemental analysis, and infrared and nmr spectra. The empirical formula C_9H_{16} could imply three structural isomers, **1–1b**. The nmr spectrum shows two equivalent *n*-propyl groups and two allylic protons but no vinyl proton, thus supporting structure **1**. The infrared spectrum contains absorption at 1865[6] and 1007 cm^{-1} [7] with no absorption around 910 cm^{-1} [8] eliminating vinylcyclopropanes of the type **1a**. There is no ultraviolet absorption above 200 mμ. In accordance with structure **1**, a positive Halphen test[9] is observed.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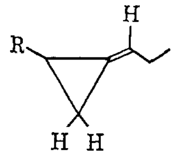
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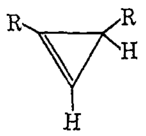
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R = *n*-C_3H_7

The adduction of **1** with excess cyclopentadiene[10] was carried out directly in the photolysis mixture to give the adduct **5a** in 75% yield. Elemental analysis and infrared and nmr spectra are in accord with the tricyclic structure. A choice between the *endo* or *exo* configuration for the tricyclooctene **5a** was accomplished by nmr spectroscopy. The cyclopropyl proton of *endo* form **5a** should be shielded by the double bond and therefore shifted to a higher field compared to that

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[1] This work was supported by Public Health Research Grant EF00499-03 from the Division of Environmental Engineering and Food Protection.

[2] P. Miginiac, *Bull. Soc. Chim. France*, 2000 (1962); E. Chinoporos, *Chem. Rev.*, **63**, 235 (1963); W. Kirmse, Organic Chemistry, Vol. I, Academic Press Inc., New York, N. Y., 1964.

[3] (a) I. A. D'yakonov and M. I. Komendatov, *Zh. Obshch. Khim.*, **29**, 1749 (1959); (b) R. Breslow, R. Winter, and M. Battiste, *J. Org. Chem.*, **24**, 415 (1959); (c) see F. L. Carter and V. L. Frampton, *Chem. Rev.*, **64**, 497 (1964), for further reference.

[4] W. von E. Doering and T. Mole, *Tetrahedron*, **10**, 65 (1960).

[5] Cyclopropene itself cannot be stored at −75°: M. J. Schlatter, *J. Am. Chem. Soc.*, **63**, 1733 (1941).

[6] Faure and Smith[7] found a weak absorption in sterculic acid at 1865 cm^{-1} and anticipate that the carbon–carbon double-bond stretching frequency in cyclopropenes should lie between those of simple olefins and acetylenes; for further references, see ref 3c.

[7] P. K. Faure and J. C. Smith, *J. Chem. Soc.*, 1818 (1956).

[8] This absorption is due to vinylic carbon–hydrogen out-of-plane vibrations: *cf.* L. F. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 51.

[9] F. C. Magne, *J. Am. Oil Chemists' Soc.*, **42**, 332 (1965).

[10] Cyclopropenes readily undergo Diels–Alder additions: (a) K. W. Wiberg and W. J. Bartley, *J. Am. Chem. Soc.*, **82**, 6375 (1960); (b) M. A. Battiste, *Chem. Ind.* (London), 550 (1961); *J. Am. Chem. Soc.*, **85**, 2175 (1963); (c) M. A. Battiste, *Tetrahedron Letters*, No. 50, 3795 (1964).