[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF CALIFORNIA]

Sulfones. I. Methods for the Preparation of Certain Alkanes, Alkenes, Acids and Lactones with Bis-(ethylsulfonyl)-methane[1]

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A study of the potential value for synthetic purposes of bis-(alkylsulfonyl)-methanes has been initiated. Satisfactory conditions for the mono- and dialkylations of bis-(ethylsulfonyl)-methane have been developed and several reactions of the dialkylated products are described. At 220° in cyclohexane over Raney nickel 5,5-bis-(ethylsulfonyl)-2,8-dimethylnonane gives 5-ethylsulfonyl-2,8-dimethylnonane (72%); while at 250°, 2,8-dimethylnonane (78%) is obtained. In aqueous alkali at 250° three hydrocarbons are produced: 2,8-dimethylnonane (14%), *trans*-2,8-dimethyl-4-nonene (55%), and 3-isoamyl-6-methyl-2-heptene (14%). This C_{11}-alkene is also obtained in 61% yield by the action of lithium aluminum hydride on the same disulfone. A mechanism is suggested for this reaction. With Raney nickel alloy in aqueous alkali 4,4-bis-(ethylsulfonyl)-5-phenylpentanoic acid gives 5-phenylpentanoic acid (74%); while at 220° in aqueous alkali over Raney nickel 4,4-bis-(ethylsulfonyl)-7-methyloctanoic acid gives 4-hydroxy-7-methyloctanoic acid isolated as the lactone (87%). The reactions are rationalized.

An investigation of the preparation and reactions of bis-(ethylsulfonyl)-alkanes and certain related structures was prompted by the possibility of using a disulfone such as bis-(ethylsulfonyl)-methane, $CH_2(SO_2C_2H_5)_2$, as the intermediate reagent for a sequence of reactions which would resemble in a general way the use of malonic esters but which could terminate in a desulfurization to give the substituted methane RCH_2R' instead of the substituted acetic acid RR'CHCOOH. There was the added possibility that if the sulfones could be reduced to the corresponding mercaptoles these might be converted into the ketones RCOR'.

Fromm[2] first demonstrated that β-disulfones could be alkylated; however, the application of this reaction

$$RX + NaCH(SO_2C_2H_5)_2 \longrightarrow RCH(SO_2C_2H_5)_2 + NaX$$

has been limited to the lower alkyl iodides and benzyl halides.[3a] Usually dialkylated products have been isolated and in general the yields have not been satisfactory. Only three monoalkylations of any type of β-disulfone have been reported.[4]

Several procedures for the preparation of the monoalkyl derivatives of bis-(ethylsulfonyl)-methane were studied. Heating the sodio salt with the alkyl halide in dimethylformamide was the most satisfactory method for the primary halides. Direct fusion of the sodio salt and the alkyl halide at 160–180° worked as well for the less volatile halides and with 2-octyl bromide this method gave a better yield. Butyl bromide in refluxing ethanol with the sodio salt gave a good yield of the monoalkylated product but required 24 to 36 hours for complete reaction as compared to 30 to 60 minutes in dimethylformamide at the same temperature. By reaction of the disulfone with sodium ethoxide in ethanol followed by the addition of ether a crystalline, non-hygroscopic form of the sodio salt was obtained which was stable when protected from carbon dioxide and moisture.

Other methods which gave monoalkylated derivatives, but in slightly less satisfactory yields, were the use of anhydrous potassium carbonate in absolute ethanol and potassium hydroxide in diethyl carbitol.[5]

Several of the products obtained by reaction of alkyl halides with sodio bis-(ethylsulfonyl)-methane are listed in Table I. Since the reagent is soluble in dilute sodium hydroxide, while the monoalkylated products are not soluble and are generally solids, this provides another useful derivative for the identification of the alkyl halides. The ready bromination of the monoalkylated sulfones could result in a series of second derivatives if desired.[2]

The most satisfactory method for the introduction of a second alkyl group involved the preparation of the sodio derivative of the monoalkylated sulfone using sodium hydride in dimethylformamide. The normal alkyl bromide was then added and the mixture was heated 18 hours at 90–100°.

$$RCH(SO_2C_2H_5)_2 + NaH \longrightarrow NaCR(SO_2C_2H_5)_2 \xrightarrow{RX} R_2C(SO_2C_2H_5)_2 + NaX$$

In early experiments the mixture was heated to hasten the rather slow reaction of the monoalkylated sulfones with the sodium hydride. Rather low yields were then obtained.[6] Either for the mono- or dialkylation it was found advantageous to keep the temperature of the reaction mixture below 30° until nearly all of the sodium hydride had reacted.

The alkylation reactions seemed to be influenced somewhat by steric factors as indicated by a comparison of the introduction of two isoamyl groups (55%) and two *n*-butyl groups (87%). The hindrance offered by the sulfone groups to intermolecular reactions on adjacent carbons[7] probably accounts also for the predominance of the intramolecular alkylation giving the cyclobutane derivative in the reaction between bis-(ethylsulfonyl)-methane and trimethylene dibromide (Table I).

It had been expected that although the sulfones were notoriously resistant to reduction or replace-

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[1] Presented in part before the Division of Organic Chemistry, American Chemical Society, Philadelphia, Pennsylvania, April, 1950.

[2] E. Fromm, *Ann.*, **253**, 141 (1889).

[3a] C. M. Suter, "Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, (a) p. 739; (b) pp. 682–683.

[4] R. Camps, *Ber.*, **25**, 248 (1892); E. Fromm, A. Forster and B. Scherschewitzke, *Ann.*, **394**, 346 (1912); R. L. Shriner, H. C. Struck and W. J. Jorison, THIS JOURNAL, **52**, 2060 (1930).

[5] C. Weizmann, E. Bergmann and M. Sulzbacher, *J. Org. Chem.*, **15**, 918 (1950).

[6] In experiments conducted by Mr. Ted Flanagan it was found that the sodium hydride reacted with the dimethylformamide very slowly at 50° and more rapidly at higher temperatures and that the reaction product consumed the alkyl halide. If sodium hydride, an alkyl bromide and dimethylformamide were heated the dialkyl ether was obtained unless water was completely excluded; in which case only water-soluble material resulted.

[7] F. G. Bordwell and G. D. Cooper, THIS JOURNAL, **73**, 5184 (1951).

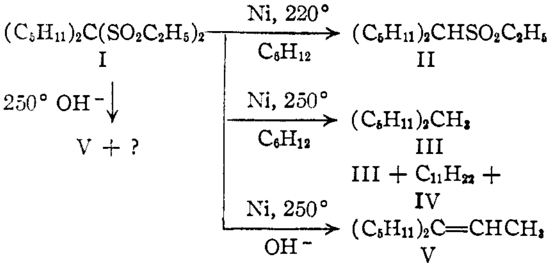
TABLE I

Alkyl halide	M.p., °C., of $RCH(SO_2C_2H_5)_2$	Method used	Yield, %	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Sulfur Calcd.	Sulfur Found
Methyl iodide	74–75[a,b]	A								
Ethyl iodide	77–78[b,c]	A								
n-Propyl bromide	71–73[d]	A		$C_8H_{18}S_2O_4$	39.67	39.55	7.49	7.53	26.42	26.33
Isopropyl bromide	94–95[d]	A		$C_8H_{18}S_2O_4$	39.67	40.01	7.49	7.56	26.42	26.34
Allyl chloride	62–63.5	A		$C_8H_{16}S_2O_4$	40.00	40.31	6.72	6.74	26.64	26.82
n-Butyl bromide	59.5–61[e]	A	90							
		B	66	$C_9H_{20}S_2O_4$	42.17	42.22	7.86	7.93	24.97	24.84
		D	86[f]							
Isobutyl bromide	93–94	A		$C_9H_{20}S_2O_4$	42.17	42.26	7.86	7.92	24.97	24.62
n-Amyl bromide	35–36	A		$C_{10}H_{22}S_2O_4$	44.44	44.30	8.21	8.17	23.68	23.63
Isoamyl bromide	51.5–53	A	85							
		B	76	$C_{10}H_{22}S_2O_4$	44.44	44.44	8.21	8.23	23.68	23.07
		C	73							
n-Octyl bromide	46–47	B	95	$C_{13}H_{28}S_2O_4$	49.99	49.37	9.04	8.78	20.49	20.09
2-Octyl bromide	58–60	A	10							
		B	25	$C_{13}H_{28}S_2O_4$	49.99	48.45	9.04	8.49	20.49	20.49
Octadecyl	85–87	B	83	$C_{23}H_{48}S_2O_4$	61.03	61.15	10.69	10.54	14.14	13.74
Benzyl chloride	133–135	B	71							
		D	73	$C_{12}H_{18}S_2O_4$	49.65	49.50	6.25	6.19	22.05	21.84
Phenylethyl bromide	73–74	A		$C_{13}H_{20}S_2O_4$	51.31	50.99	6.62	6.49	21.03	20.71
Phenylpropyl bromide	85–87	B	88							
chloride		B	83	$C_{14}H_{22}S_2O_4$	52.82	53.38	6.97	6.98	20.11	19.29
Cyclohexyl bromide	121–123	B	3.5	$C_{11}H_{22}S_2O_4$	46.80	46.46	7.86	7.79	22.67	22.85
Ethylene dibromide	(1) 206–207[g]	B (1)	60	$C_{12}H_{26}S_4O_8$	33.80	33.83	6.15	5.82	30.02	29.95
	(2) 131–132[h]	(2)	26							
Trimethylene dibromide	109–111	B	83	$C_8H_{16}S_2O_4$	40.00	40.08	6.72	6.73	26.64	26.78
Tetramethylene dibromide	130–132	B	80	$C_9H_{18}S_2O_4$	42.52	42.59	7.53	7.39	25.17	24.95
Pentamethylene dibromide	118–120[f]	A	85[i]	$C_{10}H_{20}S_2O_4$	44.75	44.28	7.46	7.32	23.85	23.55

[a] Reference 2, m.p. 75°. [b] These derivatives prepared by Naji Omar Fansah. [c] Reference 2, m.p. 77°. [d] These derivatives prepared by Willie Newton Smith. [e] Melts 56.5, resolidifies, melts 59.5–61°. [f] These derivatives prepared by Eugene Zavarin. [g] Disubstituted product. [h] Rothstein, *J. Chem. Soc.*, 1560 (1940), reports 131–132° for the melting point of $\underbrace{CH_2CH_2C}(SO_2C_2H_5)_2$. [i] Crude yield, 98%, about 15% of another product was separated by virtue of its insolubility in CCl_4.

ment by hydrogen[3b,8] they might be subject to desulfurization with Raney nickel since a reaction of this type has been reported.[9] However, all efforts to bring about desulfurization of disulfones of the type $R_2C(SO_2C_2H_5)_2$ with Raney nickel under the usual conditions or by Schwenk's[10] procedure were unsuccessful. Some desulfurization generally occurred but not enough to be significant. Finally 5,5-bis-(ethylsulfonyl)-2,8-dimethylnonane (I) was heated to 220° with three times its weight of Raney nickel in cyclohexane under 2500 pounds of hydrogen and there was obtained about 8% of the desulfurized hydrocarbon. The majority of the product, obtained in 72% yield, was 5-ethylsulfonyl-2,8-dimethylnonane (II). Both sulfone groups were removed only after heating the disulfone (I) to 250° for 36 hours giving 78% of 2,8-dimethylnonane (III).

In aqueous alkali at 250° over Raney nickel three hydrocarbons were obtained. The saturated and unsaturated C_{11}-hydrocarbons (III) and (IV) had rather close boiling points but since the mixture consisted of about 80% IV and 20% III it was possible to isolate a relatively pure sample of the



alkene (IV) as shown by analysis and quantitative hydrogenation. The infrared spectrum of IV corresponded to that of a *trans*-1,2-dialkylated ethylene.[11] The boiling points, refractive indices and infrared spectra of III and hydrogenated IV were identical; thus IV is tentatively designated as *trans*-2,8-dimethyl-4-nonene. Presumably IV was formed from the monosulfone (II) by an elimination reaction initiated by base attack on the β-carbon in the C_{11}-chain. In support of this a sample of the same material, contaminated with a little III, was obtained in low yield by heating the monosulfone (II) in alkali under a hydrogen atmosphere at 250°.[12] The third product from

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[8] At the time this work was undertaken the reduction of sulfones to sulfides with lithium aluminum hydride had not been reported by F. G. Bordwell and W. H. McKellin, THIS JOURNAL, **73**, 2251 (1951); Abstracts of the Division of Organic Chemistry, Chicago meeting of the American Chemical Society, September, 1950, p. 77N.

[9] R. Mozingo, U. S. Patent 2,371,642; *C. A.*, **39**, 4618 (1945).

[10] E. Schwenk, D. Papa, B. Whitman and H. Ginsberg, *J. Org. Chem.*, **9**, 1 (1944).

[11] We are indebted to Dr. N. K. Freeman, Department of Medical Physics, University of California, Berkeley, for all of the infrared spectra referred to in this paper and for their interpretation.

[12] According to Fenton and Ingold, *J. Chem. Soc.*, 3127 (1928); 2338 (1929); 705 (1930), it might be expected that in the normal alkaline sulfone cleavage of both I and II the predominant reaction would give ethylene and the salt of the C_{11} sulfinic acid. This is

the reaction over nickel, V, was a $C_{13}H_{26}$ unsaturated hydrocarbon as indicated by its boiling point, analysis and hydrogenation data. Ozonolysis of V in ethyl acetate and decomposition of the ozonide over Raney nickel gave acetaldehyde and a ketone whose dinitrophenylhydrazone analyzed correctly as a derivative of diisoamyl ketone. Both crude derivatives were purified by passing over silicic acid[13] and there was no evidence of appreciable amounts of any other carbonyl components. Thus V must be 3-isoamyl-6-methyl-2-heptene.

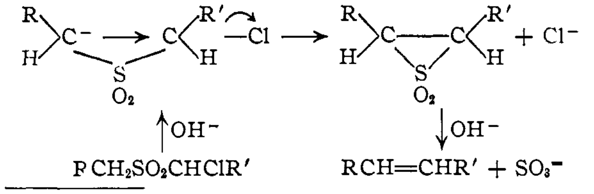
That the alkene (V) resulted from the direct action of alkali on the disulfone was indicated by heating I in 10% sodium hydroxide at 250° for 24 hours. There was obtained a 33% conversion to V; however, another reaction must also be involved since there was no recovered starting material and the other reaction products were alkali soluble.[12]

Early in our investigation of the possible methods of reduction for the sulfone group we had attempted an unsuccessful reduction of a disulfone of the type $RCH(SO_2C_2H_5)_2$ with lithium aluminum hydride. Bordwell and McKellin's reduction[8] of sulfones of the type RSO_2R to the sulfides RSR prompted a reinvestigation of the reaction with the dialkylated sulfones since these could not give a salt which might resist further reaction. The reduction did not proceed as expected, for in place of a mercaptole there was obtained from 5,5-bis-(ethylsulfonyl)-2,8-dimethylnonane an unsaturated hydrocarbon $C_{13}H_{26}$ whose 2,4-dinitrobenzenesulfenyl chloride adduct and infrared spectrum established its identity with V.[14]

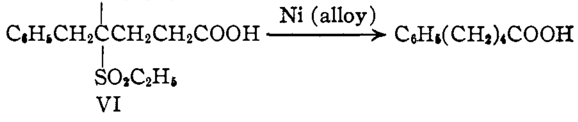
$$\underset{\text{I}}{R_2C(SO_2C_2H_5)_2} + LiAlH_4 \longrightarrow \underset{\text{V}}{R_2C{=}CHCH_3}$$

Similarly the action of lithium aluminum hydride on 5,5-bis-(ethylsulfonyl)-nonane gave a $C_{11}H_{22}$-alkene, which on ozonolysis gave acetaldehyde and a ketone whose semicarbazone identified it as di-*n*-butyl ketone.

A mechanism for these reactions was suggested by a comparison with a similar reaction of α-halosulfones[15] whose mechanism has recently been elucidated by Bordwell and Cooper[16,17] who have proposed an intramolecular displacement to give an intermediate three membered sulfone which subsequently loses SO_2 to give the alkene. By analogy the attack of a nucleophilic reagent on the α-hydrogen of a β-disulfone could initiate a similar 1,3-nucleophilic displacement of sulfinate in place of halide.[18] That lithium aluminum hydride does not behave in the same manner toward all of the disulfones is indicated by the results obtained with 1,1-bis-(ethylsulfonyl)-cyclobutane which has given at least one sulfur-containing product, and 5,5-bis-(ethylsulfonyl)-nonane which gave 13% of 5-ethylthiononane.



Several of the monoalkylated disulfones were condensed with acrylonitrile and the corresponding acids, obtained by hydrolysis in hydrochloric acid–acetic acid, were then treated with Raney nickel alloy in alkaline solution.[10] From 4,4-bis-(ethylsulfonyl)-5-phenylpentanoic acid (VI) there was obtained 75% of 5-phenylpentanoic acid.



$$\underset{\text{VI}}{C_6H_5CH_2\overset{SO_2C_2H_5}{\underset{SO_2C_2H_5}{C}}CH_2CH_2COOH} \xrightarrow{\text{Ni (alloy)}} C_6H_5(CH_2)_4COOH$$

When the alkyl group was isoamyl, however, the sulfones were again refractory and were removed only after heating to 220° with Raney nickel under hydrogen in dilute sodium hydroxide solution. After the removal of the nickel, acidification of the alkaline solution gave an oil which contained traces of the expected 7-methyloctanoic acid, but the majority of the product (87%) was a neutral compound whose saponification equivalent and

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borne out by the low yield of C_{11}-alkene obtained from the monosulfone (II) with alkali in the absence of nickel; however, in the presence of nickel the large proportion of the C_{11}-alkene (IV) obtained from I, presumably by way of the monosulfone (II), indicates the possibility of a different mechanism operating over the catalyst. The nature of this reaction and the effect of other types of basic reagents on the disulfones are being investigated at present.

(13) J. O. Roberts and C. Green, *Anal. Chem.*, **18**, 335 (1946).

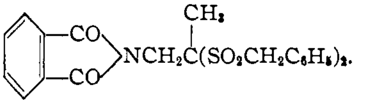
(14) There was a slight carbonyl band in the spectrum of the C_{13}-alkene from the nickel reaction which was not present in the lithium aluminum hydride material, otherwise the spectra were identical.

(15) Ramberg and Bäckland, *Arkiv Kemi Mineral. Geol.*, **13A**, No. 27 (1940); *C. A.*, **34**, 4725 (1940).

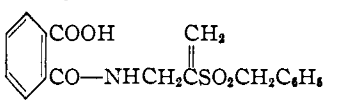
(16) F. G. Bordwell and G. D. Cooper, This Journal, **73**, 5187 (1951).

(17) We are indebted to Prof. C. C. Price for informing us of Bordwell's work and to Prof. Bordwell for a communication of his results.

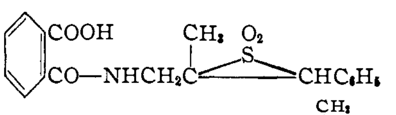
(18) This reaction seems to offer an explanation for the observations (Ref. 19) on the alkaline decomposition of the disulfone.



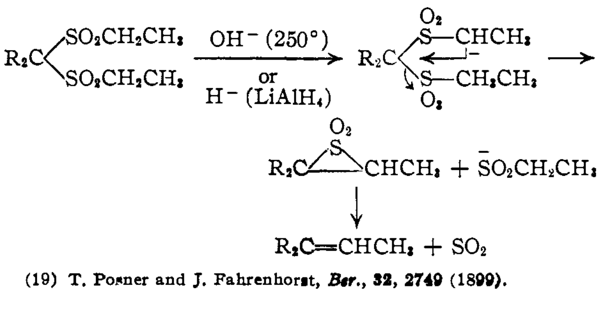
They obtained an acid postulated as



which was hydrolyzed in acid to give an amine which was assigned the structure $H_2NCH_2\overset{CH_2}{\overset{\|}{C}}CH_2C_6H_5$. If theirs was a 1,3-displacement the acid would be the missing intermediate



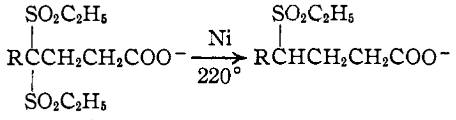
and the amine would have the structure $H_2NCH_2\overset{CH_3}{\overset{|}{C}}{=}CHC_6H_5$.



(19) T. Posner and J. Fahrenhorst, *Ber.*, **32**, 2749 (1899).

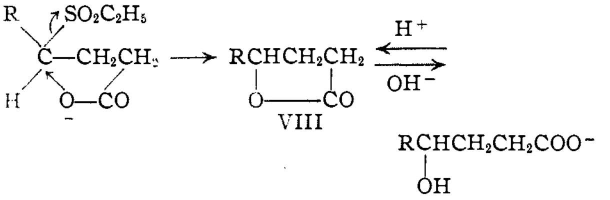
analysis indicated a C_9-lactone. Permanganate oxidation gave a keto acid identical with 4-keto-7-methyloctanoic acid.[20,21] The S-benzylthiouronium salt of the hydroxy acid was also compared with the derivative of the hydroxy acid obtained by catalytic reduction of the known keto acid.

Since the temperature necessary for the conversion of the disulfone acid to the hydroxy acid is about the same as that required for the hydrogenolysis of one sulfone group from the simple dialkylated disulfone, and since the sulfone group is subject to intramolecular nucleophilic displacement as indicated by the 1,3-displacement, it seems likely that the hydroxy acid originates by way of an intramolecular nucleophilic displacement of the sulfone by carboxylate ion.



$$R\overset{SO_2C_2H_5}{\underset{SO_2C_2H_5}{C}}CH_2CH_2COO^- \xrightarrow[220°]{Ni} R\overset{SO_2C_2H_5}{C}HCH_2CH_2COO^-$$

VII, R = isoamyl



VIII

The fact that the benzyl substituted acid VI was desulfurized with Raney nickel at a much lower temperature without substitution by hydroxyl may be rationalized on the basis of an elimination reaction[22,12] initiated by the attack of base on the methylene activated by the phenyl group. The unsaturated sulfone so produced might be desulfurized directly or it could be hydrogenated and a repetition of this process would give the sulfur-free acid.

The role of the nickel in the high temperature desulfurizations was rather interesting since it was apparently able to function at least partially as a hydrogenation catalyst in the presence of the rather large amount of sulfur. The pressure drop for the reactions carried out in cyclohexane and for the lactone reaction indicated an absorption of over two mole equivalents of hydrogen. On the other hand the nickel was sufficiently deadened so that the alkenes (IV) and (V) were isolated as the major products. There was no indication of any appreciable amount of hydrocarbon corresponding to saturated V. In the desulfurization of the acid (VII) the amount of nickel necessary to give the maximum yield corresponded to an atomic Ni:S ratio of 4:1 while a ratio of only 1.5:1 was nearly as effective (Table II).

Experimental[23]

Bis-(ethylsulfonyl)-methane.—A mixture of 445 cc. (6 moles) of ethyl mercaptan and 255 cc. (3 moles) of 37% formaldehyde was stirred at room temperature under a carbon dioxide–acetone cooled condenser and 1 cc. of concentrated hydrochloric acid was added. After the initial reaction had subsided 10 cc. of acid was added and the stirring was continued for two hours. If the reaction became too vigorous it was moderated by stopping the stirrer. To this solution was added 1500 cc. of acetic acid and the mixture was cooled in an ice-bath and 1300 cc. (16 moles) of 35% hydrogen peroxide[24,25] was added with stirring at such a rate that the temperature was not allowed to go above 15–20°, nor was the solution kept cooler than this. After about $^1/_3$ of the peroxide had been added over a four-hour period the remainder could be added quite rapidly. Stirring was continued and the ice-bath was then replaced with a running water-bath which was regulated so that the temperature of the reaction mixture did not rise above 27–30° during the next 48 hours.[26] The water-bath was removed and the mixture was allowed to stand until the temperature of the solution, which remained from 1–5° higher, had dropped to room temperature. This generally required two to three days at 25°. If there was any tendency for the temperature to rise above 30° the mixture was returned to the water-bath. A large mass of crystalline material separated during this time. The solution was diluted with two liters of water, cooled in ice and filtered; evaporation of the filtrate on the steam-bath in a large evaporating dish and trituration of the residue with water followed by filtration and crystallization of the combined solids from alcohol gave 503 g. (84%) (including a second crop from the alcohol) of bis-(ethylsulfonyl)-methane with a melting range of 98–104°, lit. 104°.[27] This material was of sufficient purity for the following reactions.

Sodio **Bis-(ethylsulfonyl)-methane.**—To a solution of 14.4 g. (0.625 mole) of sodium in 200 cc. of warm absolute ethanol was added 125 g. (0.625 mole) of bis-(ethylsulfonyl)-methane. The mixture was swirled and warmed for a few minutes to give a clear solution and it was then cooled rapidly to room temperature and dry ether (200–250 cc.) was added in portions with swirling until a faint cloudiness appeared. The ether should not be used to force the product from solution or it will be amorphous and hygroscopic. If the salt did not immediately crystallize the mixture was warmed momentarily. After cooling in ice, filtration and washing with 1:1 alcohol–ether there was obtained 132 g. (90%) of sodio bis-(ethylsulfonyl)-methane; m.p. 155–160°. The salt was stable as long as it was protected from carbon dioxide and moisture. Since the material did not change its appearance noticeably when exposed to air, older samples were tested for purity by checking their water solubility.

Monoalkylation of Bis-(ethylsulfonyl)-methane. Method A.—(1) Molecular equivalents of the sodio salt of the disulfone and the alkyl halide were thoroughly mixed in a volume of dimethylformamide which was generally 1.5 to 2 times the weight of the sodio salt. The time required to reach a nearly neutral solution was about 30 minutes at 80–90° for a normal bromide and an hour at 115–120° for a normal alkyl chloride; however, when the reaction was used for preparative purposes these times were doubled and the solution was stirred. After dilution of the reaction mixture with water it was steam distilled to remove any unreacted halide. Usually the product crystallized upon cooling and it was collected after the addition of alkali to dissolve any unreacted bis-(ethylsulfonyl)-methane. If the product remained an oil it was extracted with ether, dried, concentrated, and crystallization was induced with petroleum ether.

(2) With β-disulfones other than the bis-(ethylsulfonyl)-methane the sodio salt was made in the dimethylformamide by adding the bis-(alkylsulfonyl)-methane to a stirred suspension of sodium hydride in dimethylformamide cooled in an ice-bath. After the initial vigorous reaction had sub-

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[20] J. Cason, This Journal, **64**, 1106 (1942).

[21] We are indebted to Prof. Cason for an authentic sample of this acid.

[22] Analogous to the elimination of a sulfone β to a carboxyl, W. Autenrieth, *Ann.*, **259**, 336 (1890).

[23] Analyses by the Microanalytical Laboratory of the Department of Chemistry, University of California. All melting points are corrected. It was found that several of the $R_2C(SO_2Et)_2$ types seemed to give consistently low values for C, H while giving satisfactory values for sulfur.

[24] The oxidation is a modification of the method used on a small scale by H. Boehme, *Ber.*, **69B**, 1610 (1936).

[25] The hydrogen peroxide was Albone "35" obtained from the Electrochemicals Department of E. I. du Pont de Nemours and Co., Inc.

[26] If the oxidation is not carried out as described it is potentially rather vigorous. If, as long as 12 hours after the addition of the peroxide, the solution is removed from the water-bath the temperature may rise slowly over a period of six to eight hours until it becomes violent above 60–70°.

[27] E. Baumann, *Ber.*, **19**, 2811 (1884).

sided the mixture was stirred at room temperature until nearly all of the sodium hydride had reacted before the addition of the alkyl halide.

Method B.—Equivalent amounts of the sodio salt and the normal alkyl bromide were heated and stirred in an oil-bath at 155–165° for 15 to 30 minutes. The product was worked up as in Method A. Normal chlorides and secondary bromides required higher temperatures and longer heating.

Method C.[5]—Potassium hydroxide was melted in ten times its weight of diethyl carbitol and the solution was stirred during cooling. The disulfone was added and the mixture was stirred and heated in an oil-bath. When the internal temperature had risen to 130°, and most of the water had been removed by distillation, the alkyl bromide was added and the stirring and heating was continued in an oil-bath maintained at 150–160° for an hour or until the solution was neutral.

Method D.—Equivalent amounts of the sodio salt of the disulfone and the *n*-alkyl bromide were allowed to reflux in absolute ethanol for 36 to 48 hours, the alcohol was removed, and the product was obtained as in Method A.

5,5-Bis-(ethylsulfonyl)-2,8-dimethylnonane (I).—To a well-stirred, ice-cooled suspension of 2.4 g. (0.10 mole) of sodium hydride in 25 cc. of dimethylformamide was added 27 g. (0.10 mole) of 1,1-bis-(ethylsulfonyl)-4-methylpentane. After five minutes the ice-bath was removed and the mixture was stirred for two to three hours during which time nearly all of the sodium hydride reacted. To this solution was added 16.0 g. (0.105 mole) of isoamyl bromide. After 18 hours of stirring in an oil-bath maintained at 90–95° the mixture was diluted with several hundred cc. of water and steam distilled to remove any unreacted bromide or ether. The solid product obtained upon cooling was filtered and allowed to crystallize from alcohol giving 24.5 g. (72%) of 5,5-bis-(ethylsulfonyl)-2,8-dimethylnonane; m.p. 117–119.5. Recrystallization from alcohol produced fine needles, m.p. 118–119.5°.

Anal. Calcd. for $C_{15}H_{32}S_2O_4$: C, 52.92; H, 9.48; S, 18.80. Found: C, 52.25; H, 9.17; S, 18.59.

It was also found convenient to prepare the dialkylated derivatives in the dimethylformamide without isolation of the monoalkyl. The over-all yield for the two steps by this method was 55%.

5,5-Bis-(ethylsulfonyl)-nonane.—To a solution of 22.2 g. (0.1 mole) of sodio bis-(ethylsulfonyl)-methane in 20 cc. of dimethylformamide was added 14.0 g. (0.102 mole) of *n*-butyl bromide and the mixture was stirred for an hour at 80–85°. After it had been cooled in an ice-bath 2.4 g. (0.105 mole) of sodium hydride was added and the solution was stirred for three hours at room temperature until nearly all of the sodium hydride had reacted. Fourteen grams of butyl bromide was added and the solution was stirred and heated for 16 hours at 85–90°. The product was isolated as described above and there was obtained by crystallization from alcohol 27.2 g. (87%) of 5,5-bis-(ethylsulfonyl)-nonane melting at 129–132°. Recrystallization from ethanol gave platelets, m.p. 132–134°.

Anal. Calcd. for $C_{13}H_{28}S_2O_4$: C, 49.99; H, 9.03; S, 20.49. Found: C, 49.21; H, 8.52; S, 20.69.

Desulfurization of 5,5-Bis-(ethylsulfonyl)-2,8-dimethylnonane (I). 220°.—Eighteen grams (0.053 mole) of the disulfone (I) and 50 g. of Raney nickel[28] made up to a total volume of 90 cc. with cyclohexane were heated and shaken at 220° for eight hours under 2500 pounds of hydrogen. Approximately 0.12 mole of hydrogen was absorbed. Removal of the nickel and fractionation[29] of the product gave 0.8 g. (8%) of 2,8-dimethylnonane (III), b.p. 77° (20 mm.), $n^{25}D$ 1.4105 and 9.5 g. (72%) of 5-ethylsulfonyl-2,8-dimethylnonane (II), b.p. 143° (2 mm.), $n^{25}D$ 1.4562.

Anal. Calcd. for $C_{13}H_{28}SO_2$: C, 62.87; H, 11.36; S, 12.89. Found: C, 62.70; H, 11.33; S, 12.88.

A 75% conversion of I to II was obtained in a similar experiment in which ethanol was used as the solvent; however, the pressure increased during the hydrogenation due to the decomposition of the alcohol.

250°. Cyclohexane.—5,5-Bis-(ethylsulfonyl)-2,8-dimethylnonane (I) (40.8 g., 0.12 mole) and 110 g. of Raney nickel were heated in 150 cc. of cyclohexane under 2500 pounds of hydrogen at 250° for 36 hours. Fractionation of the product gave 14.6 g. (78%) of 2,8-dimethylnonane (III), b.p. 77° (20 mm.), $n^{25}D$ 1.4109.

Anal. Calcd. for $C_{11}H_{24}$: C, 84.52; H, 15.48. Found: C, 84.76; H, 15.39.

250°. Aqueous.—A suspension of 51 g. (0.15 mole) of I and 140 g. of Raney nickel in 200 cc. of 10% sodium hydroxide was shaken under 2500 pounds of hydrogen for 36 hours at 250°. Fractionation of the product gave 16.2 g. with a boiling range of 73–76° (21 mm.), $n^{25}D$ 1.4178 and 3.8 g. with a b.p. of 96–98° (21 mm.), $n^{25}D$ 1.4344. The 73–76° fraction was refractionated and four fractions were collected at 21 mm. (1) 2 g., 73°, $n^{25}D$ 1.4198; (2) 6 g., 73–74°, $n^{25}D$ 1.4190; (3), 6 g., 74–75°, $n^{25}D$ 1.4171; (4) 2 g., 75–76°, $n^{25}D$ 1.4155. Since fraction 1 apparently contained a small amount (2–5%) of an impurity, fraction 2 was analyzed.

Anal. Calcd. for $C_{11}H_{22}$: C, 85.63; H, 14.37. Found: C, 85.61; H, 14.47.

Quantitative hydrogenation indicated about 90% of one unsaturation, and the infrared spectrum of the hydrogenated product was identical with the spectrum of III.

From the indices of refraction it can be seen that the 73–76° fraction contained about 80% *trans*-2,8-dimethyl-4-nonene (IV) and 20% of the 2,8-dimethylnonane (III). Quantitative hydrogenation of the 96–98° fraction (V) indicated exactly one double bond.

Anal. Calcd. for $C_{13}H_{26}$: C, 85.63; H, 14.37. Found: C, 85.70; H, 14.30.

The alkene readily gave an adduct with 2,4-dinitrobenzenesulfenyl chloride[30] which melts at 121–123° with previous shrinking, after several recrystallizations from ethanol.

Anal. Calcd. for $C_{18}H_{29}N_2SClO_4$: C, 54.71; H, 7.01. Found: C, 55.01; H, 7.13.

The alkene V was treated with excess O_3 in ethyl acetate at −60° and the ozonide was immediately decomposed by the addition of Raney nickel[31] which had been deadened by refluxing in acetone.[32] Upon distillation of about 1/4 of the ethyl acetate into 0.005 *N* dinitrophenylhydrazine in 1.5 *N* hydrochloric acid[33] there was obtained the D.N.P. of acetaldehyde with a m.p. of 147.5–149° after purification over silicic acid[13]; the mixed m.p. with the D.N.P. of acetaldehyde was undepressed. After removal of the nickel the remaining ethyl acetate was distilled and to the residue in alcohol the D.N.P. reagent was added slowly. The derivative remained oily and after extraction with ether it was chromatographed on the silicic acid column and the product crystallized from ethanol, m.p. 44–45°.

Anal. Calcd. for $C_{17}H_{26}N_4O_4$: C, 58.27; H, 7.48; N, 15.99. Found: C, 58.35; H, 7.32; N, 16.05.

Reaction of II with Alkali at 250°.—A suspension of 6.12 g. of the sulfone II in 35 cc. of 10% sodium hydroxide was heated and shaken in a hydrogen atmosphere for 48 hours at 250°. There was obtained 0.8 g. of a product whose b.p., 76° (20 mm.), and refractive index, $n^{25}D$ 1.4170, indicated about the same composition of III and IV as was obtained in the presence of the catalyst. The remainder of the product was water soluble.

Reaction of I with Alkali at 250°.—After 24 hours of shaking 10.2 g. (0.03 mole) I with 50 cc. of 10% sodium hydroxide in a hydrogen atmosphere at 250° there was obtained 1.8 g. (33%) of V with a boiling point of 96–98° (20 mm.), $n^{25}D$ 1.4364. The 2,4-dinitrobenzenesulfenyl adduct had a melting point of 121–123° and was undepressed when mixed with the derivative from the nickel reaction.

Reaction of Lithium Aluminum Hydride with 5,5-Bis-(ethylsulfonyl)-2,8-dimethylnonane (I).—To a suspension of 4.0 g. (0.10 mole) of lithium aluminum hydride in 200 cc. of ether was added 10.2 g. (0.03 mole) of I and the mixture was stirred for 24 hours. After the cautious addition of 100 cc. of 1:1 hydrochloric acid the ether extract was washed

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[28] The catalyst used was the commercially prepared material obtained from the Raney Catalyst Co., Chattanooga, Tenn.

[29] All fractionations were carried out in a 60 × 0.6 cm. column packed with wire gauze according to J. R. Bower and L. M. Cooke, *Anal. Chem.*, **15**, 290 (1943).

[30] N. Kharasch and C. M. Buess, THIS JOURNAL, **71**, 2724 (1949).

[31] N. C. Cook and F. C. Whitmore, *ibid.*, **63**, 3540 (1941).

[32] G. B. Spero, A. V. McIntosh and R. H. Levin, *ibid.*, **70**, 1907 (1948).

[33] O. L. Brady and G. V. Elsmie, *Analyst*, **51**, 77 (1926).

with water, sodium bicarbonate, dried and fractionated to give 3.3 g. of V, b.p. 98–99° (20 mm.), n^{25}D 1.4335. The 2,4-dinitrobenzenesulfenyl chloride adduct was the same as the product obtained from the nickel reaction. One gram of unreacted sulfone I was obtained by crystallization of the distillation residue from alcohol.

Reaction of Lithium Aluminum Hydride with 5,5-Bis-(ethylsulfonyl)-nonane.—When 5,5-bis-(ethylsulfonyl)-nonane in tetrahydrofuran was treated with the same ratio of lithium aluminum hydride as described above there was obtained 63% of 3-butyl-2-heptene, b.p. 80–81° (20 mm.), n^{25}D 1.4310.[34]

Anal. Calcd. for $C_{11}H_{22}$: C, 85.63; H, 14.37. Found: C, 85.56; H, 14.53.

In another run in ether in which the mole ratio of lithium aluminum hydride to sulfone was 4:1 there was obtained 50% of 3-butyl-2-heptene and 13% of 5-ethylthiononane, b.p. 116–118° at 20 mm., n^{25}D 1.4595.

Anal. Calcd. for $C_{11}H_{24}S$: C, 70.16; H, 12.85; S, 16.99. Found: C, 70.75; H, 12.64; S, 16.38.

Ozonization of 3-butyl-2-heptene as described previously gave acetaldehyde and a ketone whose semicarbazone melted at 90–91° and was undepressed on admixture with the semicarbazone of di-*n*-butyl ketone.

4,4-Bis-(ethylsulfonyl)-5-phenylpentanonitrile.—Acrylonitrile, 3.0 g. (0.05 mole), was added to a suspension of 14.5 g. (0.05 mole) 1,1-bis-(ethylsulfonyl)-2-phenylethane in a solution of 0.25 g. of potassium hydroxide in 50 cc. of *t*-butyl alcohol. The solution was stirred for two hours, during which time the sulfone dissolved and product began to crystallize. After 24 hours the nitrile was filtered and washed with alcohol; yield 15.0 g., 87.7%, m.p. 128–132°. Recrystallization from alcohol and acetonitrile gave fine needles with a m.p. of 132–134°.

Anal. Calcd. for $C_{15}H_{21}S_2NO_4$: C, 52.47; H, 6.17; N, 4.08; S, 18.64. Found: C, 52.48; H, 6.09; N, 4.36; S, 18.65.

4,4-Bis-(ethylsulfonyl)-5-phenylpentanoic Acid.—The nitrile, 10.3 g. (0.03 mole), was added to a mixture of 50 cc. of acetic acid and 50 cc. of concentrated hydrochloric acid and the mixture was allowed to reflux for 48 hours before dilution with water. An ether extract was washed with water and then with sodium bicarbonate. Acidification of the bicarbonate extract gave 9.3 g. (86%) of product with a m.p. of 120–124°. After recrystallization from acetone-water clear rhombs with a m.p. of 124–125.5° were obtained.

Anal. Calcd. for $C_{15}H_{22}S_2O_6$: C, 49.72; H, 6.12; S, 17.66. Found: C, 50.02; H, 6.06; S, 17.78.

5-Phenylpentanoic Acid.—Raney nickel alloy (30 g.) was added in portions to a stirred solution of 7.4 g. (0.02 mole) of the acid VI in 300 cc. of 10% sodium hydroxide maintained at 50–60°. After the addition was complete the solution was heated at 90–100° for six hours, filtered, poured into 125 cc. of concentrated hydrochloric acid, and cooled to give 2.7 g. (74%) of 5-phenylpentanoic acid, m.p. 58–62° and 61–62° after crystallization from pentane; lit. m.p. 58–59°.[35]

4,4-Bis-(ethylsulfonyl)-7-methyloctanonitrile.—1,1-Bis-(ethylsulfonyl)-4-methylpentane, 26.8 g. (0.10 mole), was added to 50 cc. of *t*-butyl alcohol containing 0.25 g. of potassium hydroxide and 5.5 g. (0.104 mole) of acrylonitrile. After a few minutes the temperature of the mixture rose to 40–45° and product started to separate. After standing six hours at 40°, 30.4 g. (95%) of nitrile, m.p. 111–114° was collected and washed with alcohol. Recrystallization from alcohol gave microcrystalline material with a m.p. of 113–115°.

Anal. Calcd. for $C_{13}H_{25}S_2NO_4$: C, 48.29; H, 7.79; N, 4.33; S, 19.79. Found: C, 48.09; H, 7.49; N, 4.34; S, 19.53.

4,4-Bis-(ethylsulfonyl)-7-methyloctanoic Acid (VII).—The nitrile (25 g., 0.077 mole) in 100 cc. of acetic acid and 75 cc. of hydrochloric acid was allowed to reflux for 24 hours. The acid crystallized upon cooling the reaction mixture which was then diluted with water and the filtered product was redissolved in bicarbonate and filtered through Super-Cel. Upon acidification of the filtrate and after drying the solid *in vacuo* at 100° there was obtained 25.4 g. (96%) of VII, m.p. 186–189°. Crystallization from acetone–pentane gave fine prisms, m.p. 187–189°.

Anal. Calcd. for $C_{13}H_{26}S_2O_6$: C, 45.61; H, 7.66; S, 18.70. Found: C, 45.05; H, 7.44; S, 18.70.

4-Hydroxy-7-methyloctanoic Acid Lactone (VIII).—When VII was treated with Raney nickel alloy as described for VI, 75% of the acid was recovered unchanged.

A summary of conditions necessary for the desulfurization of VII to give VIII is given in Table II, 3.4 g. (0.01 mole) of the acid VII was used in each trial.

TABLE II

Ni, g.	Temp., °C.	Hr.	Yield, %
8	180	8	10
8	200	8	44
8	220	8	85
4	220	8	85
1.5	220	8	75
2.5	220	2	55

On a larger scale 15.3 g. (0.045 mole) of VII in 70 cc. of 4% sodium hydroxide was shaken and heated at 220° with 20 g. of Raney nickel for eight hours under 2500 pounds of hydrogen. After removal of the nickel the acidified solution was extracted with ether, the ether was dried and evaporated and the residue was heated on the steam-bath for an hour to complete the lactonization. The lactone was then redissolved in ether and washed with a small amount of 2% sodium bicarbonate to remove any 7-methyloctanoic acid. There was obtained 6.1 g. (87%) of the lactone VIII, b.p. 117–118° (6 mm.), n^{25}D 1.4415.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.20; H, 10.32.

The S-benzylthiouronium salt of the hydroxy acid after preparation in, and recrystallization from, alcohol-water was obtained as fine needles, m.p. 125–126°. On admixture with the same derivative prepared from a sample of the hydroxy acid obtained by catalytic reduction of 4-keto-7-methyloctanoic acid there was no depression of melting point.

Anal. Calcd. for $C_{17}H_{28}N_2SO_3$: C, 59.98; H, 8.29. Found: C, 60.30; H, 8.14.

Oxidation of a sample of VII with alkaline permanganate at room temperature gave 4-keto-7-methyloctanoic acid, m.p. 47–49.5°, undepressed when mixed with an authentic sample.[20,21]

The bicarbonate extract from the lactone preparation was acidified and 0.2 g. of 7-methyloctanoic acid contaminated with the hydroxy acid was obtained. The S-benzylthiouronium salt was readily purified as it was much less soluble in alcohol than the corresponding salt of the hydroxy acid. Fine needles melting at 148–149° were obtained from ethanol. The melting point was undepressed when a sample was mixed with the salt of a known sample of the acid.[20,21]

Anal. Calcd. for $C_{17}H_{28}N_2SO_2$: C, 63.16; H, 8.73. Found: C, 63.28; H, 8.71.

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(34) The preparation of this compound was carried out by Mr. Ted Flanagan.

(35) A. Baeyer and O. R. Jackson, *Ber.*, 13, 122 (1880).