[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Michael Type Condensations with Methyl Vinyl Sulfone[1]

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Methyl vinyl sulfone undergoes a Michael type condensation with a variety of compounds containing active methylene groups. Diethyl malonate, ethyl acetoacetate, ethyl cyanoacetate, benzyl cyanide, acetylacetone and bis-(methanesulfonyl)-methane are disulfonethylated. Diethyl phenylmalonate, phenylacetone, phenacyl *p*-tolyl sulfone, bis-(benzenesulfonyl)-methane and bromoform give monosulfonethylated products, while ethyl phenylacetate, acetophenone and benzyl *p*-tolyl sulfone do not react.

There are a few references in the literature to Michael type condensations with vinyl sulfones. β-Phenylvinyl *p*-tolyl sulfone[2] reacts like the corresponding unsaturated ketone with diethyl malonate in the presence of a basic catalyst. Similar results were obtained with benzothiophene 1-dioxide.[3] Nitromethane reacts with methyl vinyl sulfone to form tris-(2-methanesulfonylethyl)-nitromethane.[4]

This paper reports on the reaction of methyl vinyl sulfone with compounds containing active methylene groups to give products in which the active hydrogens are replaced by β-methanesulfonylethyl groups. This Michael type condensation is analogous to "Cyanoethylation"[5] and is referred to as "Sulfonethylation"

$$CH_3—SO_2—CH=CH_2 + R_1—CH_2—R_2 \xrightarrow[\text{catalyst}]{\text{basic}} (CH_3—SO_2—CH_2—CH_2)_2CR_1R_2$$

where R_1 and R_2 are activating groups. The hydrogen donors were of such a variety with respect to their activating groups[6] as to establish the general applicability of this reaction. The sulfonethylation reactions required the presence of a basic catalyst, a particularly effective one being benzyltrimethylammonium hydroxide, Triton B.[5] Most of these reactions were carried out in absolute ethanol which was found to be sufficiently inert to be used as a solvent. A total of fourteen compounds (Table I), containing active methylene groups, was treated with methyl vinyl sulfone. The products obtained are reported here for the first time.

The structures of several of the sulfonethylated compounds were established by independent syntheses which were carried out by alkylation of the appropriate hydrogen donor with β-chloroethyl methyl sulfide.[7] The resulting sulfides were not isolated but were oxidized[8] directly to the corresponding sulfones (Table II)

$$R_1—CH_2—R_2 + 2Cl—CH_2—CH_2—S—CH_3 \xrightarrow[\text{solvent}]{\text{basic catalyst}} (CH_3—S—CH_2—CH_2)_2CR_1R_2$$

$$(CH_3—S—CH_2—CH_2)_2CR_1R_2 \xrightarrow[\text{HOAc, reflux}]{30\%\ H_2O_2} (CH_3—SO_2—CH_2—CH_2)_2CR_1R_2$$

Sulfonethylation of acetylacetone yielded the disulfonethylated product, which simultaneously was partially cleaved (under the basic conditions) to 1,1-bis-(β-methanesulfonylethyl)-acetone. Such cleavage is commonly observed with β-diketones[9,10] and occurred during the alkylation of acetylacetone with β-chloroethyl methyl sulfide; the dialkylated product and its cleavage product could be obtained in small yields only. Similarly, sulfone cleavage by the basic catalyst was obtained in attempts to prove the structure of bis-(methanesulfonyl)-bis-(β-methanesulfonylethyl)-methane by dialkylation of bis-(methanesulfonyl)-methane[11]; however, the latter compound was sulfonethylated in excellent yield.

Bromoform gave only a small amount of 1,1,1-tribromo-3-(methanesulfonyl)-propane, most of the bromoform being recovered. This is similar to the cyanoethylation of this compound.[12] The proof of structure of the product was accomplished by reduction to methyl *n*-propyl sulfone, an authentic sample of which was prepared from sodium methanesulfinate and *n*-propyl iodide.

Yields in the sulfonethylation reactions were appreciably affected by experimental conditions such as temperature, type of catalyst and reaction time.[13] All of these factors will influence retrogression and possible side reactions such as cleavage reactions or rearrangements so common with Michael condensations.[14,15] No attempt was made at a quantitative study of these variables and their effects upon the reaction.

It should be pointed out that the negative results obtained with ethyl phenylacetate, acetophenone and benzyl *p*-tolyl sulfone are in contrast to the results obtained with vinyl ketones[13,16] and acrylonitrile[5] and indicate the relative activating effect of the sulfonyl, keto and nitrile groups.

It is interesting to note that in several experiments where disulfonethylated products were obtained, unreacted hydrogen donors and polymerized

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(2) E. P. Kohler and H. Potter, THIS JOURNAL, **57**, 1316 (1935).

(3) F. G. Bordwell and W. H. McKellin, *ibid.*, **72**, 1985 (1950).

(4) G. D. Buckley, *et al.*, *J. Chem. Soc.*, 1514 (1947).

(5) H. A. Bruson, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 79.

(6) H. Henecka, *Chem. Ber.*, **81**, 197 (1948).

(7) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 136, 345.

(8) H. Gilman and N. J. Beaber, THIS JOURNAL, **47**, 1449 (1925).

(9) A. Combes, *Ann. chim. phys.*, [6] **12**, 250 (1887).

(10) R. G. Pearson and E. A. Mayerle, THIS JOURNAL, **73**, 926 (1951).

(11) E. Fromm, *Ann.*, **253**, 135 (1889); D. T. Gibson, *J. Chem. Soc.*, 2637 (1931).

(12) H. A. Bruson, *et al.*, THIS JOURNAL, **67**, 601 (1945).

(13) R. Connor and W. R. McClellan, *J. Org. Chem.*, **3**, 570 (1939).

(14) R. Connor, *et al.*, *ibid.*, **6**, 690 (1941).

(15) C. K. Ingold and W. J. Powell, *J. Chem. Soc.*, **119**, 1976 (1921).

(16) R. Connor, *et al.*, THIS JOURNAL, **58**, 1386 (1936).

TABLE I: SULFONETHYLATION OF HYDROGEN DONORS WITH METHYL VINYL SULFONE

R is the β-methanesulfonylethyl group ($CH_3—SO_2—CH_2—CH_2—$)

Hydrogen donor, moles	Solvent and reflux time, hours	Product formula	Recryst. solvent	M.p., °C.	Yield, % (and % conversion)	Analyses, % Calculated C	H	S	N	Found C	H	S	N
Diethyl malonate 0.025	EtOH 7	$EtOOC—C(R)_2—COOEt$[a]	H_2O (EtOH)	84.5	64.5	41.90	6.45	17.20		41.93	6.42	17.17	
Diethylphenylmalonate 0.05	EtOH 12	$EtOOC—C(R)(C_6H_5)—COOEt$[b]	H_2O (EtOH)	74–75	58 (30)	56.20	6.44	9.36		56.08	6.48	9.47	
Ethyl acetoacetate 0.05	EtOH 4	$CH_3—C(=O)—C(R)—COOEt$	H_2O (EtOH)	122	70.2	42.11	6.44	18.71		42.17	6.40	18.66	
Ethyl cyanoacetate 0.05	EtOH 4	$N\equiv C—C(R)—COOEt$	EtOH Cellosolve	158–159	81.5	40.62	5.85	19.70	4.31	40.61	5.95	19.78	4.42
Benzyl cyanide 0.05	EtOH 24 *t*-BuOH	$C_6H_5—C(R)—CN$	EtOH	189	68 (36.2)	51.07	5.77	19.45	4.25	51.06	5.73	19.45	4.31
Acetylacetone 0.05	EtOH 10	$CH_3—C(=O)—C(R)—C(=O)—CH_3$	EtOH	159–160	36	42.30	6.41	20.51		42.23	6.41	20.47	
		$CH_3—C(=O)—CH(R)$	EtOH	111	24	40.00	6.67	23.70		40.08	6.70	23.66	
Phenylacetone 0.05	EtOH 9	$C_6H_5—CH(R)—C(=O)—CH_3$	H_2O Cellosolve	76	61 (30)	60.00	6.67	13.33		59.53	6.69	13.32	
Phenacyl *p*-tolyl sulfone 0.025	Cellosolve 3 EtOH 5	$C_6H_5—C(=O)—C(SO_2—C_6H_4—CH_3)—R$	EtOH Cellosolve	185–186	61.4	56.84	5.26	16.84		57.02	5.14	16.84	
Bis-(benzenesulfonyl)-methane 0.05	EtOH 20	$C_6H_5SO_2—C(R)—SO_2C_6H_5$	EtOH H_2O	152–153	81.6	47.72	4.48	23.80		47.91	4.50	23.78	
Bis-(methanesulfonyl)-methane 0.05	EtOH 5	$CH_3—SO_2—C(R)—SO_2—CH_3$	EtOH H_2O	189	84	28.12	5.21	33.33		28.25	5.23	33.36	
Bromoform 0.09	None 15	$Br_3C—CH_2—CH_2—SO_2—CH_3$	Pet. ether (60–70°)	124	74[8]	13.42	1.95	Br, 66.90		13.50	1.81	Br, 66.93	
Ethyl phenylacetate 0.1	EtOH 18	No reaction	Starting materials were recovered										
Acetophenone 0.05	EtOH 12	No reaction	Starting materials were recovered										
Benzyl *p*-tolyl sulfone 0.025	EtOH	No reaction	Starting materials were recovered										

[a] Saponification number: calcd.: 188; found: 189. [b] Saponification number: calcd.: 171; found: 168

TABLE II

INDEPENDENT SYNTHESES OF SULFONETHYLATED PRODUCTS

Hydrogen donors mole	Alkylation procedure	Solvent and catalyst	Recryst. solvent	M.p., °C.	Mixed melting point, °C.	Yield, %
Diethyl malonate	A[17]	EtOH	EtOH–H_2O	84.5–85	84–85	8
0.05	One step	EtONa				
Diethyl phenylmalonate	B[18]	EtOH	H_2O–EtOH	74–75	74–75	3
0.1	One step	EtONa				
Ethyl acetoacetate	C[19]	*t*-BuOH	H_2O–EtOH	122.5	122	63
0.05	Two steps	*t*-BuOK				
Ethyl cyanoacetate	A	EtOH	EtOH–H_2O	159–159.5	159	76
0.075	One step	EtONa				
Benzyl cyanide	D[20,21]	Ether	EtOH–H_2O	188.5–189	189	34
0.1	Two steps	$NaNH_2$				
Acetylacetone	E[22,23]	EtOH	EtOH–H_2O	159	158–159	1.3
	One step	EtONa				
			EtOH	110–111	109–110	<1
Phenylacetone	C[24]	*t*-BuOH	H_2O–	76–77	77	46
0.05	One step	*t*-BuOK	Cellosolve			
Phenacyl *p*-tolyl sulfone	A	EtOH	EtOH	184–186	185–186	34
0.01	One step	EtONa				
Bis(benzenesulfonyl)methane	E[23]	EtOH	EtOH–H_2O	152–153	152	58
0.005	One step	EtONa				

methyl vinyl sulfone were recovered but monosulfonethylated products could not be isolated. These results are in agreement with the cyanoethylation reactions[6] in which all available reactive hydrogens are generally involved.

While condensations of a sulfone with a vinyl ketone[24] or with acrylonitrile[25] are known, such a condensation between a vinyl sulfone and a disulfone as the addendum molecule is being reported here for the first time.

Experimental

Methyl Vinyl Sulfone.—This compound was prepared from β-chloroethyl methyl sulfide[7] according to known procedures.[4] β-Chloroethyl methyl sulfide (134 g.) gave methyl vinyl sulfone (98 g.) in a 76.2% yield. The product had a boiling point of 95–97° (8 mm.).

Phenacyl *p*-Tolyl Sulfone.—This compound was prepared according to the method of Shriner[15] and Otto[26] from 20.0 g. (0.1 mole) of sodium *p*-toluenesulfinite and 15.5 g. (0.1 mole) of phenacyl chloride. Recrystallization from an ethanol–cellosolve solution gave 17.0 g. of product, m.p. 110°. The yield was 50%.

Bis-(benzenesulfonyl)-methane.—This was prepared according to known procedures[19,27] from thiophenol (33 g., 0.3 mole) and diiodomethane (40 g., 0.15 mole) followed by oxidation.[8] The product, m.p. 122° (literature 119°), was obtained in 70% yield.

Benzyl *p*-Tolyl Sulfone.—This compound was prepared from sodium *p*-toluenesulfinate and benzyl chloride according to known procedures[15,26] and was obtained in 65% yield, m.p. 144° (literature 141–142°).

Sulfonethylation Reactions.—All hydrogen donors listed in Table I were sulfonethylated in a similar manner. The hydrogen donor (0.05 mole) was dissolved in 10–25 g. of absolute ethanol contained in a three-neck, round-bottom flask, fitted with a stirrer, reflux condenser and a dropping funnel. "Triton B" (3–4 g.) was added with stirring to obtain a homogeneous solution, heating, if necessary. To this well-stirred solution was added an amount of methyl vinyl sulfone equivalent to the number of active hydrogens of the hydrogen donor. The reaction was usually exothermic and therefore the vinyl sulfone was added slowly. More Triton B (1–2 g.) was then added and the reaction mixture was continuously stirred and kept at reflux temperature for 4 to 24 hours. After cooling and careful neutralization with dilute hydrochloric acid, the reaction mixture was poured onto 100 ml. of ice-water. A solid was found to precipitate out of solution and was allowed to settle out by standing in the cold for 24 hours. The solid was then filtered off and recrystallized from various solvents, as indicated in Table I. White crystalline products were obtained. Where the conversions were below 50%, the filtrates were distilled under vacuum. Unreacted hydrogen donors could be recovered in small amounts as indicated by both the per cent. yield and the per cent. conversion given for these experiments. In all instances only a few drops of methyl vinyl sulfone could be recovered, b.p. 95–102° (7 mm.), while a highly viscous residue was left which could not be distilled and was not investigated further. It was believed that this residue consisted chiefly of polymerized methyl vinyl sulfone. The individual reactions are summarized in Table I.

Independent Syntheses of Sulfonethylated Products.—All reactions were carried out in a round-bottom, three-neck flask fitted with stirrer, reflux condenser and dropping funnel; usually they were carried out under a dry nitrogen atmosphere. Table II presents the results.

General Procedure.—The individual alkylation procedures A through E (Table II) differ only in the method of addition of the reactants, time and temperature of reaction, and catalyst and solvent used.

In method A the solvent–catalyst solution was slowly added to a mixture of the hydrogen donor and β-chloroethyl methyl sulfide while in methods B through E the hydrogen donor was added first to the solvent–catalyst solution followed by the addition of the alkylating agent. In all cases the solution was then heated for one to three hours with stirring. After removing the solvent under a vacuum, the reaction product was extracted with ether which was then stripped off. For dialkylation the indicated procedure was repeated. The reaction product was then oxidized with hydrogen peroxide in glacial acetic acid. After refluxing for one to two hours the final product was poured onto ice-water. Recrystallization of the resulting precipitate from an appropriate solvent gave a pure product which was used for the determination of a mixed melting point with the corresponding sulfonethylated product.

The essential feature of method E is the use of large amounts of solvent, which apparently decreases the rate of cleavage and makes alkylation possible.

(17) M. A. Phillips, *Ind. Chemist*, **21**, 678 (1945).
(18) W. L. Nelson and L. H. Cretcher, THIS JOURNAL, **50**, 2758 (1928).
(19) W. B. Renfrow, Jr., *ibid.*, **66**, 144 (1944).
(20) P. Jullien, *Bull. soc. chim.*, (6) 1252 (1939).
(21) R. Levine and C. R. Hauser, THIS JOURNAL, **68**, 760 (1946).
(22) J. Salkind, *Chem. Centr.*, **76**, II, 753 (1905).
(23) R. L. Shriner, *et al.*, THIS JOURNAL, **52**, 2060 (1930).
(24) C. M. Suter and A. W. Weston, *ibid.*, **64**, 533 (1942).
(25) H. A. Bruson and T. W. Riener, THIS JOURNAL, **70**, 214 (1948).
(26) R. Otto and W. Otto, *Ber.*, **21**, 1691 (1888).
(27) E. P. Kohler and M. Tishler, THIS JOURNAL, **57**, 217 (1935).

Reduction of 1,1,1-Tribromo-3-methanesulfonylpropane.—This compound (1 g.) was added to 15 ml. of ethanol (95%) followed by the addition of zinc dust (1–2 g.). To catalyze the reduction, 1 ml. of a 5% solution of copper sulfate was added and the mixture was refluxed gently with shaking for 30 minutes. The alcohol solution was filtered while hot, and evaporated under vacuum. About 0.5 ml. of a yellow liquid remained. This was purified by micro-distillation. It was found to have a boiling point of 129–130° (19 mm.) and a refractive index, $n^{20}D$ 1.4493. This was identical with the physical constants of methyl *n*-propyl sulfone prepared independently by the following process: Iodopropane (10 g.) and 5.1 g. of sodium methanesulfinate[28] were dissolved in 50 ml. of absolute ethanol. The solution was refluxed with stirring for 6 hours. The salt (NaI) formed was filtered off and the solution was distilled under vacuum. After removal of ethanol, a high boiling colorless liquid was obtained, b.p. 128–129° (19 mm.), $n^{20}D$ 1.4503. The yield was 53.4%.

(28) Supplied by J. P. Milionis, this Laboratory.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM VENEREAL DISEASE EXPERIMENTAL LABORATORY, U. S. PUBLIC HEALTH SERVICE, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA]

A New Synthesis of Unsymmetrical Phosphinic Acids

BY LEON D. FREEDMAN AND G. O. DOAK

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A number of diaryl- and arylalkylphosphinic acids have been prepared by the reaction between diazonium fluoborates and dichlorophosphines in ethyl acetate in the presence of cuprous bromide. Evidence is presented which indicates that unsymmetrical phosphorus compounds disproportionate to symmetrical compounds under the conditions of this reaction. Several aminophosphinic acids have been obtained by reduction of the corresponding nitro compounds.

The synthesis of arylphosphonic and diarylphosphinic acids by the reaction between diazonium fluoborates and phosphorus trichloride has been described in recent papers[1] from this Laboratory. The major reaction product was invariably the phosphonic acid; however, by proper choice of solvent and catalyst, a fair yield of the symmetrical phosphinic acid could be obtained. We have now found that the phosphinic acid can be obtained as the main product of the reaction between diazonium fluoborates and aromatic or aliphatic dichlorophosphines. By means of this reaction, symmetrical diaryl-, unsymmetrical diaryl- and arylalkylphosphinic acids can be readily prepared. No phosphine oxide was isolated in any reaction so far investigated.

The unsymmetrical phosphinic acids were isolated in somewhat smaller yields than the total yields of organophosphorus compounds obtained in the reaction described earlier.[1a] This decrease is due not only to a lower yield of crude product, but also to greater difficulties experienced in the purification of the unsymmetrical compounds. These difficulties are associated with the presence of symmetrical phosphinic acids in reaction products in which only unsymmetrical acids should be expected. Thus, from the reaction between *p*-nitrobenzenediazonium fluoborate and ethyldichlorophosphine, we have isolated not only (*p*-nitrophenyl)-ethylphosphinic acid but also a small amount of bis-(*p*-nitrophenyl)-phosphinic acid. From the reaction between *m*-nitrobenzenediazonium fluoborate and ethyldichlorophosphine, we obtained a 4% yield of bis-(*m*-nitrophenyl)-phosphinic acid and none of the expected (*m*-nitrophenyl)-ethylphosphinic acid.

The symmetrical compounds are probably formed by a reaction of the type

$$2RR'PX_3 \rightleftharpoons R_2PX_3 + R'_2PX_3$$

Similar redistribution reactions of lead and mercury compounds have been extensively studied by Calingaert.[2] The disproportionation of aromatic dichlorophines has been postulated by Kosolapoff and Huber.[3]

The unsymmetrical nitro substituted phosphinic acids were reduced to amino derivatives by the method previously used.[1b] Since (*p*-aminophenyl)-ethylphosphinic acid was rather soluble in water, it was found convenient to reduce the corresponding nitro compound in methanol. After removal of the catalyst by filtration, the amino acid was obtained by vacuum concentration of the filtrate. The crude product was recrystallized from methanol.

The compounds prepared, together with their analyses, yields, and m.p.'s, are listed in Table I. With the exception of diphenylphosphinic acid, none of these compounds have previously been described.

Materials.—All of the phosphinic acids described in the present paper, with the exception of the amino compounds, were prepared by the reaction between phenyl- or ethyldichlorophosphine and the appropriate diazonium fluoborate. The phenyldichlorophosphine was kindly furnished us by the Victor Chemical Works. The ethyldichlorophosphine was prepared by the method of Kharasch, Jensen and Weinhouse.[4] The tetraethyllead needed for this preparation was obtained through the courtesy of the Ethyl Corporation. The diazonium fluoborates were prepared and analyzed as described in an earlier paper[5] from this Laboratory. The solvents and other chemicals used were reagent grade and were not further purified.

Experimental

The apparatus and procedure employed were similar to those developed in this Laboratory for the preparation of arylphosphonic and symmetrical diarylphosphinic acids.[1a] A short lag period (30 minutes or less) after mixing the solvent, diazonium fluoborate, dichlorophosphine and catalyst, was followed by a violent reaction. The residual liquid, after the steam distillation, was evaporated to approximately

(1) (a) G. O. Doak and L. D. Freedman, THIS JOURNAL, **73**, 5658 (1951); (b) G. O. Doak and L. D. Freedman, *ibid.*, **74**, 753 (1952).

(2) G. Calingaert and H. A. Beatty, in Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1806.

(3) G. M. Kosolapoff and F. W. Huber, THIS JOURNAL, **69**, 2020 (1947).

(4) M. S. Kharasch, E. V. Jensen and S. Weinhouse, *J. Org. Chem.*, **14**, 429 (1949).

(5) G. O. Doak and L. D. Freedman, THIS JOURNAL, **73**, 5656 (1951).