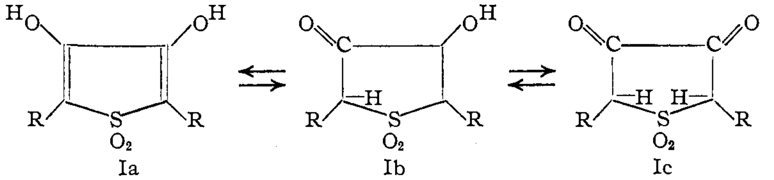
[CONTRIBUTION FROM THE INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Cyclic Sulfones. The Condensation of Ethyl Oxalate with Arylmethyl Sulfones

BY C. G. OVERBERGER, SALOMON P. LIGTHELM[1] AND EDWIN A. SWIRE[1]

We have undertaken the preparation of thiophene-1-dioxides in order to study the attack of free radicals on a vinyl sulfone group ($—CH=CH—SO_2—$) contained in a ring. We are also interested in the reactivity of these thiophene-1-dioxides as dienes in the Diels–Alder reaction. This paper will describe the condensation of ethyl oxalate with arylmethyl sulfones (R = β-naphthyl, phenyl, *p*-chlorophenyl) to give 2,5-diaryl-3,4-dihydroxythiophene-1-dioxides (I). The method is outlined below.

$$R—CH_2—SO_2—CH_2—R + (COOEt)_2 \overset{Na^+OET^\ominus}{\rightleftarrows} \text{sodium salt} \xrightarrow{H^+}$$



Ia Ib Ic

Claisen and Ewan[2] have shown that benzyl ketone and ethyl oxalate react in the presence of sodium ethoxide to give a keto–enol mixture of the carbonyl analog of I. Shriner, Struck and Jorison[3] have shown that benzyl sulfone forms a sodium salt with metallic sodium and with sodium ethoxide. There was, therefore, good reason to suspect that a condensation of this type would occur. 3,4-Diphenylthiophene-1-dioxide,[4a,b] the *p*-chloro analog[4c] and 2,3,4,5-tetraphenylthiophene-1-dioxide[4a] (all prepared by oxidation of the corresponding thiophene derivatives) have been characterized, but no other derivatives of thiophene dioxides have previously been described.

The aryl sulfides and sulfones were prepared by conventional procedures, although in individual cases, experimental modifications were important for high yields of product. The physical constants of *p*-chlorobenzyl sulfone previously reported in the literature were found to be in error and this compound has been correctly characterized.

The most satisfactory yields of condensates (I) were obtained with a large excess of diethyl oxalate and with sodium ethoxide as the base. The use of sodium hydride or powdered sodium gave lower yields. Keto–enol tautomerism of the 2,5-diphenyl-3,4-dihydroxythiophene-1-dioxide (I) was demonstrated by a positive ferric chloride test, the solubility in dilute sodium carbonate, the formation of a dibenzoate, the preparation of a quinoxaline, and the ultraviolet absorption spectrum (Fig. 1).

The absorption spectrum described in Fig. 1 can be largely attributed to a 1,4-diphenylbutadiene structure corresponding to the enol form of I.[5] In 95% ethanol solution (9.72×10^{-5} m./l.), this was $\lambda_{max.}$ 3200 Å., ε, 13,100; $\lambda_{min.}$ 2650 Å., ε, 2500.[6] This conclusion seems reasonable although it should be emphasized that this evidence is qualitative and only indicates the existence of the enol structure. Likewise, the formation of a quinoxaline requires the vicinal positions of the carbonyl groups and further demonstrates the structure of the condensate. The quinoxaline is somewhat unstable when recrystallized from polar solvents.

The sodium salts obtained from the condensates can be isolated in quantitative yield. Treatment of the salts with dimethyl sulfate resulted in the formation of the dimethylated thiophene-1-dioxides. Whereas the direct condensation products were somewhat unstable toward base due to the reversibility of the condensation reaction, the dimethylated derivatives

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[1] This paper comprises parts of theses presented by Salomon P. Ligthelm and Edwin A. Swire in partial fulfillment of the requirements for the Master of Science degree in the graduate school of the Polytechnic Institute of Brooklyn.

[2] Claisen and Ewan, *Ann.*, **284**, 245 (1895).

[3] Shriner, Struck and Jorison, THIS JOURNAL, **52**, 2060 (1930).

[4] (a) Hinsberg, *Ber.*, **48**, 1611 (1915); (b) Backer, Bolt and Stevens, *Rec. Trav. Chim.*, **56**, 1063 (1937); Backer and Stevens, *ibid.*, **59**, 423 (1940); (c) Overberger, Mallon and Fine, unpublished results.

(5) Compare $\lambda_{max.}$ 3280 Å., ε, 41,000 in alcohol (Braude, *Ann. Repts. on Progress Chem.* (*Chem. Soc. London*), **42**, 105 (1945); $\lambda_{max.}$ 3250 Å., ε, 51,200; $\lambda_{min.}$ 2600 Å., ε, 1200 (Radulescu and Barbulescu, *Ber.*, **64**, 2225 (1931); Radulescu and Alexa, *ibid.*, p. 2230) for 1,4-diphenylbutadiene. See also Hausser, Kuhn and Smakula, *Z. physik. Chem.*, **B29**, 384 (1935). The amount of enol present depends both on the solvent used and the concentration. The other groups in the molecule which could possibly contribute to the absorption are $C_6H_5—CH_2—SO_2—CH_2—C_6H_5$, —CO—CO—, and $—CH=CH—SO_2—$. Fehnel and Carmack [THIS JOURNAL **71**, 231 (1949)] have recently shown that there is no difference between the absorption spectrum of benzoyl sulfone and 1,3-diphenylpropane, hence this group should not contribute. 1,2-Dicarbonyl compounds which have little tendency to enolize have very small intensities in the range of the spectrum reported here: compare glyoxal, $\lambda_{max.}$ 280, ε, 2.5 and $\lambda_{max.}$ 463, ε, 3.5; also oxalic acid, $\lambda_{max.}$ 250, ε, 50. Other 1,2-dicarbonyl compounds which have greater intensities do so by virtue of enolization. In the aldehyde and acid, there is little tendency for enolization and the small extinction coefficients noted may be due to the —CO—CO— grouping. The α,β-unsaturated sulfone group ($—CH=CH—SO_2—$) may contribute to the portion of the curve (Fig. 1) below 2400 Å. (see Fehnel and Carmack). It should be pointed out that no direct comparison with the diphenylbutadiene can be made, especially in regard to the extinction coefficient recorded. Thus, the three stereoisomers of the diphenylbutadiene have different intensities. The $\lambda_{max.}$ varies from 2990 Å., *cis-cis* form, to 3280 Å., *trans-trans* form [Pinchard, Wille and Zechmeister, *ibid.*, **70**, 1938 (1948)].

(6) All melting points are corrected unless otherwise noted.

were relatively stable and easy to work with. The structure of these alkylated products is now under investigation.

The preparation of α-naphthylmethyl sulfide and sulfone and *p*-nitrobenzylbenzyl sulfone are described in the experimental section. In the latter case, the reaction of *p*-nitrobenzyl chloride with benzyl mercaptan in alcohol by introducing a slow stream of ammonia resulted in a 96% yield of product and represents an improved synthetic modification for this type of mixed sulfide.

Experimental[6]

2,5-Diphenyl-3,4-dihydroxythiophene-1-dioxide.—Benzyl sulfide was prepared according to the method of Shriner, Struck and Jorison[3] except for a minor detail in the isolation of the product. From 126.6 g. (1.0 mole) of freshly distilled benzyl chloride in 300 ml. of absolute alcohol and 120.2 g. (0.5 mole) of sodium sulfide nonahydrate in 60 ml. of water, there was obtained 99.5 g. (92.8%) of impure benzyl sulfide. When the reaction mixture was poured onto ice, a solid precipitate resulted in a short time. Crystallization from acetic acid gave a product m. p. 49–50° (49°, 83%).[3]

Benzyl sulfone was prepared according to the method of Rheinboldt and Giesbrecht.[7] From 10.7 g. (0.05 mole) of benzyl sulfide in 30 ml. of glacial acetic acid and 15 g. (0.13 mole) of 30% hydrogen peroxide at 95° a yield of 11.8 g. (95.8%) of impure benzyl sulfone was obtained. Crystallization from ethyl alcohol gave a product, m. p. 151–151.5°; (151.7°, no yield)[7]; (149.5–150°, 23.7%[3] prepared by chromic anhydride oxidation) (150°, no yield).[8]

Condensation with Sodium Ethoxide as Base.—A 300-ml. three-necked, round-bottomed flask was fitted with a sealed stirrer, nitrogen inlet and reflux condenser to which was attached a calcium chloride tube. Under nitrogen, 35 ml. of absolute alcohol was placed in the flask and 2.3 g. (0.1 g. atom) of freshly cut sodium was slowly added in small pieces through the condenser. The mixture was gently heated to get complete reaction of the sodium and then cooled. Forty milliliters of absolute alcohol was added, followed by the addition of 12.3 g. (0.05 mole) of benzyl sulfone in the solid state and finally 9.8 g. (0.067 mole) of ethyl oxalate. The mixture was refluxed for two hours with thorough stirring; on refluxing the color slowly changed from colorless to a light yellow and then to a light brown. The mixture was cooled to room temperature and poured into a mixture of approximately 50 g. of ice and 200 ml. of distilled water. The unreacted benzyl sulfone was then removed by filtration (2.04 g.) and the yellow colored filtrate acidified with 10% hydrochloric acid solution until acid to litmus paper. The precipitate was collected and washed twice with distilled water and dried. The crude material, 11.2 g. (74.6% yield) was crystallized from 75% alcohol with the use of "Norite" and was then recrystallized four times from a 50–50 equal volume mixture of toluene and alcohol, white crystals, m. p. 238–239°, uncor. $\lambda_{max.}$, 3200 Å., ϵ, 13,100 in 95% ethanol (9.72×10^{-5} m./l.). *Anal.* Calcd. for $C_{16}H_{12}O_4S$: C, 63.99; H, 4.03. Found: C, 63.72; H, 4.02.

The dioxide was soluble in acetone, alcohol and chloroform, slightly soluble in benzene and toluene, and practically insoluble in water. It was soluble in 10% solutions of ammonia, sodium carbonate and sodium hydroxide, and gave a reddish-brown color with 5% ferric chloride solution.

A modification of the above procedure was used to isolate the solid sodium salt. A large excess of diethyl oxalate was used. Sodium ethoxide was prepared from 5 g. (0.219 g. atom) of sodium metal and 65 ml. of absolute ethanol. Benzyl sulfone (24.6 g., 0.1 mole) and 100 ml. of ethyl oxalate were added and the reaction mixture was refluxed for three hours. After the reaction mixture had stood for an additional nine hours the yellow sodium salt had completely separated; the mother liquor was decanted and the crystals washed three times with small volumes of petroleum ether (b. p. 60–68°) to remove the excess ethyl oxalate. The crystals were then collected and dried in an oven. A quantitative yield of the sodium salt thus could be obtained. This sodium salt dissolved completely in water, with no immediate separation of benzyl sulfone.

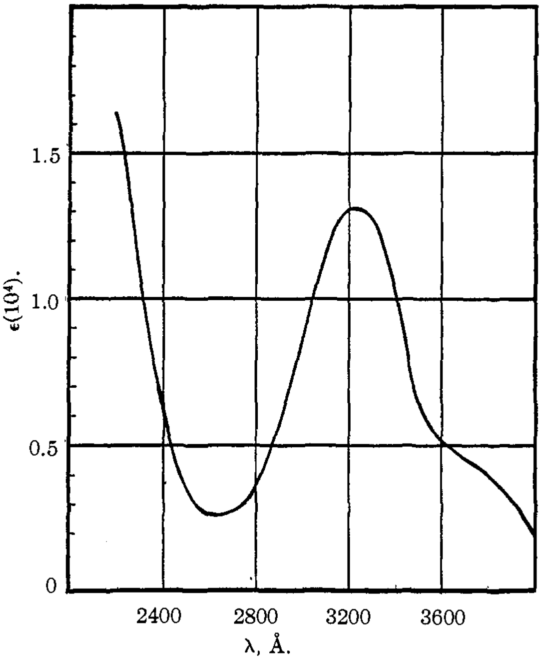

Fig. 1.—Ultraviolet absorption spectrum of 2,5-diphenyl-3,4-dioxythiophene-1-dioxide in 95% ethanol, concn. 9.72×10^{-5} m./l.

Derivatives of 2,5-Diphenyl-3,4-dihydroxythiophene-1-dioxide. A. Dibenzoate.—The dibenzoate was prepared according to the method described by Hickenbottom.[9] From 0.75 g. (0.0025 mole) of 2,5-diphenyl-3,4-dihydroxythiophene-1-dioxide and 0.9 g. (0.0064 mole) of benzoyl chloride in 5 g. of dry pyridine there was obtained 1.2 g. (95.2%) of product. Recrystallization from a mixture of ethyl acetate and ethyl alcohol gave white crystals, m. p. 192.5–193.8 (uncor.). *Anal.* Calcd. for $C_{30}H_{20}O_6S$: C, 70.86; H, 3.96. Found: C, 71.16; H, 3.91.

B. Quinoxaline.—The quinoxaline was prepared according to the method described in Hickenbottom.[10] From 1.1 g. (0.01 mole) of recrystallized *o*-phenylenediamine and 2.98 g. (0.01 mole) of 2,5-diphenyl-3,4-dihydroxythiophene-1-dioxide dissolved in equal parts of acetone and alcohol, there was obtained after three hours of reflux, a yellow voluminous precipitate. This was removed by filtration, washed with alcohol and dried, 3.5 g. (94.1%). The quinoxaline was slightly soluble in hot alcohol, acetone and benzene and soluble in hot ethyl acetate, nitromethane and nitrobenzene. It gave a purple quinoxaline test[10] with concentrated sulfuric acid. The quinoxaline was recrystallized from nitromethane for analysis. In a melting point tube, it started to sinter at 175°, the color had turned slightly gray at 210°, and became dark gray at 230°, with melting at 243°, dec. *Anal.* Calcd. for $C_{22}H_{16}N_2O_2S$: N, 7.52. Found: N, 7.22.

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[7] Rheinboldt and Giesbrecht, THIS JOURNAL, **68**, 973 (1946).

[8] Vogt and Henniger, *Ann.*, **165**, 362 (1873). Prepared by the action of benzyl chloride on potassium sulfite.

[9] Hickenbottom, "Reaction of Organic Chemistry," 1st ed., Longmans, Green & Co., London, 1948, p. 79.

[10] Ref. 9, p. 294.

β-Naphthylmethyl Sulfide.—β-Chloromethylnaphthalene was prepared according to the method of Tarbell, Fukushima and Dam,[11] by the chlorination of β-methylnaphthalene at 240–250° in the presence of phosphorus trichloride as catalyst. From 142 g. (1 mole) of redistilled β-methylnaphthalene and 5 g. of phosphorus trichloride there was obtained, on chlorination in the presence of a 200 watt lamp, 71 g. (40.2%) of β-chloromethylnaphthalene. The compound was crystallized once from alcohol, m. p. 47–49°, b. p. 164–170° (22 mm.) [(m. p. 48–49°, b. p. 163–170°) (22 mm.), 53%].[11]

The β-naphthylmethyl sulfide was prepared by a procedure similar to that previously described for the preparation of benzyl sulfide except a much shorter reaction time was employed. To 36 g. (0.203 mole) of β-chloromethylnaphthalene, was added a solution of 25 g. (0.104 mole) of sodium sulfide nonahydrate in 15 ml. of water and 230 ml. of absolute alcohol. After refluxing for six hours, the flask was cooled and the contents, which consisted of a white precipitate and clear liquid, was poured into water. The resulting precipitate was collected on a filter, washed with water, dried and crystallized from alcohol, 26.5 g. (84.4%), m. p. 125.5–127°, large crystals: 123–124°, small crystals. *Anal.* Calcd. for $C_{22}H_{18}S$: C, 84.03; H, 5.77. Found: C, 83.71; H, 5.71.

β-Naphthylmethyl Sulfone.—Twenty-five grams (0.08 mole) of β-naphthylmethyl sulfide was dissolved in 400 ml. acetic acid and treated with a solution of 26 g. (0.26 mole) of chromic anhydride in 15 ml. water and 50 ml. acetic acid at 60° and then refluxed for three hours, 5 g., m. p. 231–232° and 3.5 g. (total yield, 30.7%) m. p. 236–237°. The latter fraction was crystallized from acetic acid. *Anal.* Calcd. for $C_{22}H_{18}O_2S$: C, 76.26; H, 5.23. Found: C, 76.26; H, 5.41.

2,5-Di-(β-naphthyl)-3,4-dihydroxythiophene-1-dioxide.—This was prepared by a procedure similar to that used in the condensation of the benzyl sulfone with the exception that after the reaction had taken place, the excess alcohol and ethyl oxalate were removed under reduced pressure, the flask was cooled and 25 ml. of absolute ethanol were added. The product was then isolated as described previously. From 1.73 g. (0.005 mole) of β-naphthylmethyl sulfone, 15 ml. of dry ethyl oxalate and 0.68 g. (0.01 mole) of sodium ethoxide there was obtained 2.00 g. (100%) of crude product. Recrystallization from a mixture of alcohol and toluene gave a product, m. p. 299.5° (dec.). *Anal.* Calcd. for $C_{24}H_{16}O_4S$: C, 71.99; H, 4.03. Found: C, 71.98; H, 4.25.

The dioxide was soluble in 10% solutions of ammonia, sodium carbonate and sodium hydroxide with formation of the characteristic yellow color, similar to the phenyl analog. It gave a positive quinoxaline test[10] with *o*-phenylenediamine and subsequent treatment with sulfuric acid. The compound was soluble in alcohol and toluene, and insoluble in ether and petroleum ether.

***p,p'*-Dichlorobenzyl Sulfide.**—The procedure was similar to that described by reference 3, except that a shorter reaction time was employed and the product crystallized on pouring onto ice. From 120.2 g. (0.5 mole) of sodium sulfide nonahydrate dissolved in 100 ml. of water, and 161 g. (1.0 mole) of *p*-chlorobenzyl chloride in 300 ml. of ethanol, there was obtained, on refluxing for three and one-half hours, 140.9 g. of crude product, m. p. 35–37.5°. This reaction was more exothermic initially than similar reactions previously described and no outside heating was necessary for reflux for the first 15 minutes. Recrystallization from absolute ethanol with rapid cooling gave 121.4 g. (85.7%), m. p. 40.5–41.0°. Jackson and White[12] reported a melting point of 42° for the sulfide prepared in a similar way, no yield reported.

***p,p'*-Dichlorobenzyl Sulfoxide.**—Twenty-eight grams (0.247 mole) of 30% hydrogen peroxide was added slowly with stirring to a solution of 28.3 g. (0.1 mole) of *p,p'*-dichlorobenzyl sulfide dissolved in 200 ml. of glacial acetic acid. The solution was stirred for one hour at room temperature and the mixture was poured into an excess of water. The resulting precipitate was removed by filtration and washed thoroughly with water, 28 g., m. p. 161–163°. Recrystallization from absolute ethanol gave 24.7 g. (82.6%), m. p. 164.8–165.1°. Jackson and White[12] had previously reported a compound with a similar melting point (165°) as the sulfone described below, no yield reported. Reference 8 had also reported a m. p. of 167° for the sulfone described below, prepared from *p*-chlorobenzyl chloride and potassium sulfite with no yield stated. *Anal.* Calcd. for $C_{14}H_{12}Cl_2OS$: C, 56.19; H, 4.04. Found: C, 55.97; H, 4.03.

***p,p'*-Dichlorobenzyl Sulfone.**—The sulfone was prepared from the sulfide using the procedure of Rheinboldt and Giesbrecht[7] with the following modifications. Since ref. 12 and possibly ref. 8 may have erroneously reported this compound, some detail in its preparation seems advisable. To a solution of 28.3 g. (0.1 mole) of *p,p'*-dichlorobenzyl sulfide in 150 ml. of glacial acetic acid at 70° was added slowly with stirring 56.6 g. (0.5 mole) of 30% hydrogen peroxide and the solution was stirred at 70° for three hours. The reaction mixture was allowed to cool to room temperature and the resulting precipitate removed by filtration, 31.2 g., m. p. 244–245.5°. After washing with water, ethanol and acetone, recrystallization from dioxane gave 29.8 g. (94.6%); m. p. 246–247°. *Anal.* Calcd. for $C_{14}H_{12}Cl_2O_2S$: C, 53.34; H, 3.80. Found: C, 53.38; H, 3.89. This sulfone was insoluble in hot and cold water, acetone, ethanol, benzene, toluene, ether, ethylene dichloride and was slightly soluble in tetrahydrofuran.

2,5-(*p,p'*-Dichlorophenyl)-3,4-dihydroxythiophene-1-dioxide.—The procedure was similar to that described for the preparation of the phenyl analog except for the following modifications. From 31.5 g. (0.1 mole) of *p,p'*-dichlorobenzyl sulfone, 100 ml. of diethyl oxalate, and sodium ethoxide prepared from 5 g. (0.219 g. atoms) of sodium in 65 ml. of absolute ethanol, there was obtained, after washing with petroleum ether (b. p. 60–68°) and drying, a quantitative yield of a light orange sodium salt. This was dissolved in a minimum of water, the solution was filtered to remove any insoluble material (4.2 g.), cooled to 0° and carefully acidified with 1:1 water–acetic acid solution. The resulting precipitate was removed by filtration, washed with water until neutral to litmus and dried, 36.2 g., m. p. 231–234°. Recrystallization from ethanol gave 33.6 g. (91.1%), m. p. 239–241.5°. *Anal.* Calcd. for $C_{16}H_{10}Cl_2O_4S$: C, 52.05; H, 2.73. Found: C, 52.42; H, 2.89.

α-Naphthylmethyl Sulfide.—α-Chloromethylnaphthalene was prepared according to the method of Cambron.[13] From 192 g. (1.5 mole) of naphthalene, 60 g. (2 moles) of paraformaldehyde, 167 g. of glacial acetic acid, 186 ml. of concentrated hydrochloric acid and 90 ml. of sirupy phosphoric acid, there was obtained 143 g. (47%) of α-chloromethylnaphthalene; b. p. 113–115° (1 mm.), (b. p. 145–160° (6–8 mm.), 56.5%.[13]

The α-naphthylmethyl sulfide was prepared according to a modification of the procedure referred to for the preparation of benzyl sulfide. To 100 g. (0.565 mole) of α-chloromethylnaphthalene a solution of 67.6 g. (0.282 mole) of sodium sulfide nonahydrate in 30 ml. of water was added slowly with good stirring, and the reaction mixture was refluxed for three days. An oily layer separated out which solidified when the mixture was cooled to room temperature. This solid was crystallized from a 1:1 solution of ethyl alcohol and toluene, yield 80 g. (90.3%), m. p. 118.5–119°. *Anal.* Calcd. for $C_{22}H_{18}S$: C, 84.03; H, 5.77. Found: C, 83.98; H, 6.05.

α-Naphthylmethyl Sulfone.—In a three-necked flask fitted with a stirrer, dropping funnel and reflux condenser were placed 47.16 g. (0.15 mole) of α-naphthylmethyl sulfide and 150 ml. of glacial acetic acid. Seventeen grams (0.15 mole) of 30% hydrogen peroxide was added slowly with good stirring; the mixture was heated to 95° and another 17 g. of 30% hydrogen peroxide added. After two

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(11) Tarbell, Fukushima and Dam, THIS JOURNAL, **67**, 197 (1945).

(12) Jackson and White, *Am. Chem. J.*, **2**, 158 (1880-1881).

(13) Cambron, *Can. J. Research*, **17B**, 10 (1939).

hours of heating a sample from the flask was poured into water and the resulting precipitate gave a melting point of 120°. Another 34 g. of 30% hydrogen peroxide was added and the flask left standing for seven days. The mixture was then poured into water and the precipitate was removed by filtration, washed with water, dried and crystallized from alcohol, yield 50 g. (96.3%), m. p. 218.5–219°. *Anal.* Calcd. for $C_{22}H_{18}O_2S$: C, 76.26; H, 5.23. Found: C, 76.53; H, 5.45.

The sulfone was slightly soluble in cold alcohol and benzene; and soluble in chloroform, acetone, hot alcohol, hot toluene, hot benzene and hot acetic acid.

***p*-Nitrobenzylbenzyl Sulfide.**—In a 250-ml. Erlenmeyer flask was placed 34.3 g. (0.2 mole) of *p*-nitrobenzyl chloride, 24.82 g. (0.2 mole) of benzylmercaptan and 75 ml. of absolute alcohol. The flask was heated to about 50° and a slow stream of ammonia gas from a cylinder was introduced with intermittent cooling. The solution turned green, followed by the immediate precipitation of white crystals. The ammonia was introduced for thirty minutes, the precipitate collected; the filtrate on standing gave additional crystals, yield 49.2 g. (95%), m. p. 56–57°. *Anal.* Calcd. for $C_{14}H_{13}NO_2S$: N, 5.40. Found: N, 5.20.

Ultraviolet Absorption Spectrum.—The ultraviolet absorption spectrum of I was determined with a Beckmann quartz ultraviolet spectrophotometer with 95% ethanol as the solvent. The spectrum is shown in Fig. 1 in which the molar extinction coefficients are plotted against the wave lengths in ångström units.

Summary

1. *p,p'*-Dichlorobenzyl sulfoxide and sulfone, β-naphthylmethyl sulfide and sulfone, α-naphthylmethyl sulfide and sulfone, and *p*-nitrobenzylbenzyl sulfide have been prepared and characterized.

2. The condensation of ethyl oxalate and three arylmethyl sulfones has been described. Evidence has been presented to show that the product from benzyl sulfone and ethyl oxalate is a 2,5-diaryl-3,4-dihydroxythiophene-1-dioxide which exhibits keto–enol tautomerism.

BROOKLYN, N. Y. RECEIVED DECEMBER 2, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Acetylative Desulfation of Carbohydrate Acid Sulfates[1]

BY M. L. WOLFROM AND REX MONTGOMERY[2]

Progress in the determination of the structure of heparin and related sulfated polysaccharides has been impeded by the lack of a suitable desulfation procedure. We report herein a method whereby the sulfated polysaccharide is dissolved at low temperatures in essentially absolute sulfuric acid. When the resultant solution is treated with a large excess of acetic anhydride, the acetylated and desulfated product is obtained and can readily be isolated by convenient methods. It is desirable to answer two questions regarding this procedure. First, is Walden inversion involved and, second, is the reaction accompanied by significant glycosidic hydrolysis? The former question can be answered in the negative since the desulfation of D-glucose 3-sulfate and D-glucose 6-sulfate led to the isolation of α-D-glucopyranose pentaacetate. The extent of glycosidic hydrolysis is, however, dependent upon the nature of the glycosidic linkage, being negligible in the case of cellobiose and natural trehalose, but predominant in gentiobiose and melezitose (Table I). Sugars containing a fructofuranose residue were hydrolyzed with apparent destruction of the fructose portion and the acetylation of the remainder of the molecule. Thus sucrose gave α-D-glucopyranose pentaacetate. It is also of interest to note that when levoglucosan (1,6-anhydro-β-D-glucopyranose) was subjected to this acetylation procedure, α-D-glucopyranose pentaacetate was

TABLE I

ACETYLATION[a] OF SUGARS AND SUGAR DERIVATIVES WITH ACETIC ANHYDRIDE IN HYDROGEN SULFATE

Substance	Product[b]	Yield, %
1,2:5,6-Diisopropylidene-D-glucose	α-D-Glucopyranose pentaacetate	19
Sucrose	α-D-Glucopyranose pentaacetate	44–65
Melezitose	α-D-Glucopyranose pentaacetate	30
Gentiobiose	α-D-Glucopyranose pentaacetate[f]	37
Levoglucosan (1,6-anhydro-β-D-glucopyranose)	α-D-Glucopyranose pentaacetate	28
α-D-Glucose	α-D-Glucopyranose pentaacetate	53
D-Glucosamine hydrochloride[c]	Pentaacetyl-α-D-glucosamine[d]	51
	Pentaacetyl-β-D-glucosamine[d]	2
β-Cellobiose	α-Cellobiose octaacetate	41–45
Stachyose	α-D-Glucopyranose pentaacetate[f]	40
Raffinose	α-D-Glucopyranose pentaacetate[f]	24
α-D-Galactose	α-D-Galactopyranose pentaacetate[g]	20
Trehalose (natural)	Trehalose octaacetate	86
D-Mannitol	D-Mannitol hexaacetate[e]	84

[a] All substances were finely powdered and were dried under reduced pressure at 75–80° over phosphorus pentoxide. The acetylation procedure was that described for the simultaneous desulfation and acetylation of D-glucose 6-sulfate and the products were isolated in the same manner. The solutions of the sugars in hydrogen sulfate were nearly colorless save for those containing D-fructose which were initially brown and developed a green fluorescence in the acetylation mixture. Like results were also obtained on adding the solids to a similarly cooled mixture of hydrogen sulfate and acetic anhydride (1:10 by vol.). [b] Identification by melting point, mixed melting point and chloroform rotation. [c] Dissolved readily in the reaction mixture. [d] From ethanol–ether. [e] The product was crystalline and pure without recrystallization. [f] The compound was isolated from the sirupy reaction product by chromatographic analysis, as per W. H. McNeely, W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, 67, 527(1945). [g] The product did not crystallize for many months.

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[1] The data herein recorded supersede those reported by M. L. Wolfrom and F. A. H. Rice, *Abstracts Papers Am. Chem. Soc.*, **113**, 1Q (1948).

[2] Supported by fellowship funds granted by The Ohio State University Research Foundation to the University for aid in fundamental research (Projects 7670-148 and 1670-165).