by drop during twenty-five minutes with mechanical stirring to a suspension of 0.2 g. of zinc dust in 15 ml. of acetic acid and 5 ml. of water held at 52–56°. To insure a suitable distribution of zinc in the mixture, the first portion having formed into clumps, 0.2 g. more was added slowly and stirring was continued for twenty minutes with the bath at 58–60°.[10] The mixture was filtered into 100 g. of ice, the zinc was washed with a small quantity of acetic acid, the precipitated solid was removed by filtration, washed thoroughly with water, and dried *in vacuo* over sulfuric acid; slightly yellow, m. p. 120–150°, 244 mg. The filtrate was diluted with 100 ml. of water and the cloudy solution was extracted with ether. Suitable purification of the ether solution gave an oil which was united with similar material from other mother liquors, but no crystalline material was obtained from this part. Three recrystallizations of the crude solid from ether gave 62 mg. of **10-methyl-D-homosteradiene-15,17a-dione**, m. p. 150–163.6°, large colorless rectangular crystals.

Anal. Calcd. for $C_{19}H_{24}O_2$: C, 80.2; H, 8.5. Found: C, 80.2; H, 8.55.

An additional 82 mg., m. p. 148–167.6°, was obtained from the ether mother liquors. This was treated with 2,4-dinitrophenylhydrazine. At room temperature, inseparable mixtures of mono- and bis-hydrazones were obtained. Boiling such a mixture with twice its weight of 2,4-dinitrophenylhydrazine in ethanol for a half hour, filtration, washing with 2 *N* hydrochloric acid and water, boiling with ethyl acetate, and recrystallizing, first from anisole and then from benzene, gave the **bis-2,4-dinitrophenylhydrazone**; 257–260° (dec.).

Anal. Calcd. for $C_{31}H_{32}N_8O_8$: N, 17.4. Found: N, 17.5.

Summary

1. A 1-ethynyl-10-methylnaphthiten-1-ol has been hydrogenated to a 10-methyl-1-vinylnaphthiten-1-ol which was dehydrated to a mixture of hydrocarbons.

2. Reaction with *p*-benzoquinone demonstrated the presence of the 1-vinyl-1-naphthitene group in one of the components of the mixture, since the product of the reaction was converted to chrysene.

3. This product was isomerized to an octahydrochrysene-*ar*-1,4-diol and reduced to a 10-methyl-D-homosteradiene-15,17a-dione in which one C=C bond is probably in ring A and the other in ring C.

BELTSVILLE, MARYLAND RECEIVED SEPTEMBER 13, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KANSAS CITY]

p-Alkoxybenzenesulfonic Acid Esters

BY MARIE H. CARR[1] AND HAROLD P. BROWN

Unsuccessful attempts[1a] to prepare the sulfur analog of the local anesthetic procaine, the diethylaminoethyl ester of *p*-aminobenzoic acid, have been reported in the literature. Because of the recognized chemotherapeutic value of many sulfur compounds the syntheses of the sulfur analogs of another group of efficient local anesthetics,[2,3,4,5] namely, the *p*-alkoxybenzoic acid esters, was undertaken. Using sodium *p*-hydroxybenzenesulfonate as a starting material, the methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, β-chloroethyl and β-bromoethyl esters of *p*-methoxy, *p*-ethoxy, *p*-*n*-propoxy and *p*-*n*-butoxybenzenesulfonic acids were prepared. Attempts to prepare the β-diethylaminoethyl esters were not successful. The syntheses were accomplished by (1) etherification of the *p*-hydroxy group, (2) conversion of the sodium salt to the sulfonyl chloride, and (3) esterification by the appropriate alcohol. Solubilities in water and organic solvents, melting points, boiling points, sulfur content, saponification equivalents, and preliminary indications of physiological activity were determined.

(1) Condensed from a thesis submitted to the Faculty of the Department of Chemistry of the University of Kansas City in partial fulfillment of the requirements for the degree of Master of Arts.

(1a) G. E. Crossen, G. L. Jenkins and C. E. Rogers, *Pharm. Arch.*, **12**, 21 (1941).

(2) C. Rohmann and B. Scheurle, *Arch. Pharm.*, **274**, 110 (1936).

(3) C. Rohmann and K. Friedrick, *Ber.*, **728**, 1333 (1939).

(4) C. Rohmann and A. Koch, *Arch. Pharm.*, **276**, 154 (1938).

(5) W. A. Lott, S. E. Harris and W. G. Christiansen, *J. Am. Pharm. Assoc.*, **27**, 661 (1938).

Experimental

A. *p*-Alkoxybenzenesulfonic Acids.—The method recommended by Fieser[6] for the preparation of aryl-alkyl ethers was found satisfactory and produced good yields. The following modified procedures were adopted:

Sodium *p*-Methoxybenzenesulfonate.—To 120 g. of sodium *p*-hydroxybenzenesulfonate dissolved in 200 ml. of 15% sodium hydroxide, were added 100 ml. of methanol and 80 ml. of methyl sulfate. With the mouth of the flask partially closed by a funnel, the mixture was heated on a water-bath for one hour, chilled thoroughly, and the resulting fine white crystals filtered off. The sodium *p*-methoxybenzenesulfonate was washed with small quantities of ice water, then dried. An average yield of 75% was obtained.

Sodium *p*-Ethoxybenzenesulfonate.—This compound was prepared in essentially the same manner, using 90 ml. of ethyl sulfate. As ethanol did not increase the yield of ethoxysulfonate, it was omitted and replaced by 100 ml. of water. The average yield was 73%.

Sodium *p*-*n*-Propoxybenzenesulfonate.—*n*-Propyl bromide and ethanol were used in this synthesis. The reaction mixture was refluxed fifteen to eighteen hours according to the procedure of Hartley.[7] A yield of 68% was obtained.

Sodium *p*-*n*-Butoxybenzenesulfonate.—This compound was prepared in the same manner as the propoxy, using 70 ml. of *n*-butyl bromide. The yield was 65%.

The sodium *p*-alkoxybenzenesulfonates were all white crystalline compounds, very soluble in water and hot alcohol, insoluble in acetone, ether, chloroform, benzene, and ligroin. On heating, they charred without melting.

B. *p*-Alkoxybenzenesulfonyl Chlorides.—The sodium *p*-alkoxybenzenesulfonates were readily converted to the sulfonyl chlorides by heating equal quantities of the well

(6) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Company, New York, N. Y., 1941, p. 374.

(7) G. Spencer Hartley, *J. Chem. Soc.*, 1828 (1939).

TABLE I

MELTING POINTS, °C.

	Obs.[a]	Richter	Beilstein	Huntress and Carten[b]
p-$MeOC_6H_4SO_2Cl$	41.0	40.5	40.5	
p-$EtOC_6H_4SO_2Cl$	37.0	36.5–39	36.5–39	
p-$PrOC_6H_4SO_2Cl$	23.0			
p-$BuOC_6H_4SO_2Cl$	19.0			
p-$MeOC_6H_4SO_2NH_2$	110.0	108–116	113–116	110–111
p-$EtOC_6H_4SO_2NH_2$	151.5	149–150	149–150	149–150
p-$PrOC_6H_4SO_2NH_2$	119.5			116–117
p-$BuOC_6H_4SO_2NH_2$	106.0			103–104

[a] Melting points below 30° were determined by plateau, those above 30° by capillary tube; all temperatures are corrected. [b] These temperatures are uncorrected.

chloroform and acetone, sparingly soluble in ligroin and insoluble in water. They were readily crystallized from ether or ligroin. At room temperature, they were slowly hydrolyzed by water, but remained unchanged for months if well dried and kept in glass-stoppered bottles in a refrigerator.

Since only the *p*-methoxy and *p*-ethoxybenzenesulfonyl chlorides have been previously reported in the literature, specimens of each of the four were converted to the respective amides and their melting points determined. The method of Huntress and Carten[9] was used and the yield was nearly quantitative. Ethanol (20%) and acetone (60%) were found to be equally satisfactory for recrystallization. Melting points of the *p*-alkoxybenzenesulfonyl chlorides and their corresponding amides are given in Table I.

C. *p*-Alkoxybenzenesulfonic Acid Esters.—All the *p*-alkoxybenzenesulfonic acid esters except the butyl esters were prepared by the general method described by Földi[10]

TABLE II

R′	R″	Mol. wt.	Sapon. equiv.	Melting[a] point, °C.	Boiling point (1 mm.)	Empirical formula	Sulfur, % Found	Sulfur, % Calcd.
CH_3	CH_3[b]	202.22	203	32.0	168–172	$C_8H_{10}O_4S$	15.1	15.8
CH_3	C_2H_5	216.24	214	5.0	169–172	$C_9H_{12}O_4S$	14.8	14.8
CH_3	$C_3H_7(n)$	230.26	227	Oil	180	$C_{10}H_{14}O_4S$	14.3	13.9
CH_3	$C_3H_7(i)$	230.26	129[c]	35.0	dec.			
CH_3	$C_4H_9(n)$	244.28	245	Oil	198	$C_{11}H_{16}O_4S$	13.1	13.1
CH_3	$(CH_2)_2Cl$	250.70	172	28.5	192	$C_9H_{11}O_4SCl$	13.1	12.8
CH_3	$(CH_2)_2Br$	295.16	147	35.0	206	$C_9H_{11}O_4SBr$	10.4	10.9
C_2H_5	CH_3	216.24	213	47.5	172–173	$C_9H_{12}O_4S$	14.5	14.8
C_2H_5	C_2H_5	230.26	217	18.0	180	$C_{10}H_{14}O_4S$	14.1	13.9
C_2H_5	$C_3H_7(n)$	244.28	237	Oil	187	$C_{11}H_{16}O_4S$	12.6	13.1
C_2H_5	$C_3H_7(i)$	244.28	129[c]	26.0	dec.			
C_2H_5	$C_4H_9(n)$	258.30	257	9.5	184	$C_{12}H_{18}O_4S$	12.8	12.4
C_2H_5	$(CH_2)_2Cl$	264.72	187	47.5	202	$C_{10}H_{13}O_4SCl$	12.4	12.1
C_2H_5	$(CH_2)_2Br$	309.18	167	33.5		$C_{10}H_{13}O_4SBr$	11.1	10.4
C_3H_7	CH_3	230.26	236	11.0	180–182	$C_{10}H_{14}O_4S$	13.4	13.9
C_3H_7	C_2H_5	244.28	244	33.5	186	$C_{11}H_{16}O_4S$	13.1	13.1
C_3H_7	$C_3H_7(n)$	258.30	253	Oil	174–176	$C_{12}H_{18}O_4S$	12.6	12.4
C_3H_7	$C_3H_7(i)$	258.30	113	Oil	167	$C_{12}H_{18}O_4S$	12.5	12.4
C_3H_7	$C_4H_9(n)$	272.32	265	Oil	187–188	$C_{13}H_{20}O_4S$	11.5	11.8
C_3H_7	$(CH_2)_2Cl$	278.74	147	15.0	179	$C_{11}H_{15}O_4SCl$	11.8	11.5
C_3H_7	$(CH_2)_2Br$	323.20	175	35.0	195	$C_{11}H_{15}O_4SBr$	10.1	9.9
C_4H_9	CH_3	244.28	245	11.0	181	$C_{11}H_{16}O_4S$	12.5	13.1
C_4H_9	C_2H_5	258.30	260	23.0	177	$C_{12}H_{18}O_4S$	12.5	12.4
C_4H_9	$C_3H_7(n)$	272.32	259	Oil	185	$C_{13}H_{20}O_4S$	11.7	11.8
C_4H_9	$C_3H_7(i)$	272.32	145[c]	Oil	dec.			
C_4H_9	$C_4H_9(n)$	280.34	282	12.5	178	$C_{14}H_{22}O_4S$	11.3	11.2
C_4H_9	$(CH_2)_2Cl$	292.76	237	20.0	182	$C_{12}H_{17}O_4SCl$	11.4	10.9
C_4H_9	$(CH_2)_2Br$	337.22	189	35.0	177	$C_{12}H_{17}O_4SBr$	9.8	9.5

[a] Melting points below 30° were determined by plateau, those above 30° by capillary tube. All temperatures are corrected. [b] Melting point was reported as 30°, boiling point as 160°, by Frérejacque.[12] [c] These saponification equivalents were determined before distillation, all others after distillation.

dried salt and phosphorus pentachloride on a water-bath for sixty to ninety minutes according to the method of Quilico.[8] The resultant pale yellow oily mass was poured slowly into a large beaker of crushed ice and the sulfonyl chloride washed by decantation with large quantities of ice water until essentially neutral to litmus. During this process, solidification usually occurred. Because of their low melting points (19 to 41°), these materials were collected on chilled filters. The yield was nearly the theoretical.

All the *p*-alkoxybenzenesulfonyl chlorides were white crystalline compounds, very soluble in benzene, ether, and by Izmail'skii and Razorenov,[11] modified as indicated in the following procedure:

To *p*-alkoxybenzenesulfonyl chloride dissolved in an excess of the requisite alcohol, a saturated solution of sodium hydroxide was added dropwise with constant agitation till slightly alkaline. The reaction mixture was kept cold in an ice-bath during this operation to minimize

(8) A. Quilico, *Atti Accad. Lincei*, [6] **6**, 512 (1927).

(9) E. H. Huntress and F. H. Carten, THIS JOURNAL, **62**, 603 (1940).

(10) Zoltan Földi, *Ber.*, **53B**, 1836 (1924).

(11) V. A. Izmail'skii and B. A. Razorenov, *J. Russ. Phys.-Chem. Soc.*, **52**, 359 (1920).

(12) M. Frérejacque, *Ann. Chim.*, **14**, 147 (1930).

hydrolysis. The ester and alcoholic solution were then slowly poured into a large beaker of crushed ice and, after washing repeatedly with cold water until neutral to litmus and free from alcohol, the esters were dried over calcium chloride. The yields varied from 45% for the isopropyl esters to 95% for the chloroethyl and bromoethyl esters.

Because of the immiscibility of *n*-butyl alcohol and water, the theoretical amount of sodium was dissolved in an excess of *n*-butyl alcohol and this solution used instead of aqueous sodium hydroxide in the preparation of the butyl esters.

Attempts were made to prepare β-diethylaminoethyl *p*-alkoxybenzenesulfonates by (1) esterification of the sulfonyl chlorides by β-diethylaminoethanol, (2) coupling of chloroethyl and bromoethyl esters with diethylamine, and (3) reaction between sodium *p*-alkoxybenzenesulfonates and β-diethylaminoethyl chloride. None of these attempts produced the desired results.

All the *p*-alkoxybenzenesulfonic acid esters were found to be very soluble in benzene, ether, chloroform, acetone and dioxane, sparingly soluble in ligroin and insoluble in water. Most of them were difficult to obtain in crystalline form because of their tendency to supercool, and some were never solidified, even though cooled to −75° by Dry Ice and acetone. The melting points ranged from 5.0 to 47.5° and the boiling points from 165 to 204° at 1 mm. pressure. Sulfur determinations were made by the Parr bomb method. The results are given in Table II. Saponification equivalents were determined by the method of Shriner and Fuson[13] using *N* potassium hydroxide in diethylene glycol as a hydrolyzing agent. The saponification values, shown in Table II, were approximately the same before and after distillation and agreed fairly well with the theoretical molecular weights for the methyl, ethyl, *n*-propyl and *n*-butyl esters; those for the *i*-propyl esters were little more than half the theoretical value. The explanation for this latter irregularity has not been established. Low values for the chloroethyl and bromoethyl esters were due to hydrolysis of the chloro and bromo groups (compare Földi[10]).

(13) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 118.

Limited attempts were made to ascertain whether or not the *p*-alkoxybenzenesulfonic acid esters had any physiological action. A 2% suspension of methyl *p*-methoxybenzenesulfonate in mineral oil was placed on the lower lid of a rabbit's eye, a drop of plain mineral oil being used in the other eye as a control. The animal showed some evidence of pain for about ten minutes, but no dilatation or anesthesia was apparent up to thirty minutes. A 2% suspension of the same ester in physiological saline (0.85% sodium chloride) was next used in a similar manner with the same results. A 2% suspension of *n*-butyl *p*-*n*-butoxybenzenesulfonate in physiological saline seemed to cause no discomfort to a rabbit, neither did it produce dilatation or anesthesia. Results using a 5% suspension of the same ester were the same. The animals when examined twenty-four and forty-eight hours after the experiments showed no damage to their eyes. It appears that the *p*-alkoxybenzenesulfonic acid esters have little or no anesthetic activity.

Acknowledgment.—The authors wish to express their appreciation to Dr. J. F. Lewis for valuable assistance rendered.

Summary

1. Using sodium *p*-hydroxybenzenesulfonate as a starting material, four series of *p*-alkoxybenzenesulfonic acid esters were prepared.

2. Methods of syntheses of these esters and the necessary intermediate compounds are outlined.

3. Physical and chemical characteristics of these compounds are described.

4. Experiments to give preliminary indications of the possible anesthetic activity of *p*-alkoxybenzenesulfonic acid esters on the eyes of rabbits were performed and no evidence of activity was obtained.

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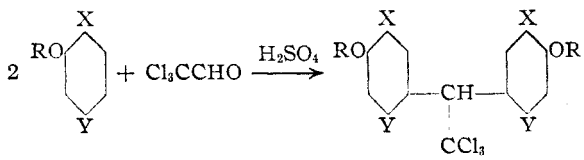
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Some Phenol–Chloral Condensations

BY JOSEPH B. NIEDERL AND AKSEL A. BOTHNER-BY[1]

The condensation of chloral with phenols may lead to oxygen heterocycles,[2] substituted phenyltrichloromethylcarbinols,[3] or diaryltrichloroethanes.[4] The latter reaction usually occurs in the presence of concentrated sulfuric acid, the products being phenol analogs of DDT. The value of these compounds and their ethers and esters as insecticides has been investigated by Stephenson and Waters,[5] who found that the free phenols and most of the esters have no activity, but that the lower ethers in some cases approach DDT in effectiveness.

In the present work it was decided to synthesize the chloral condensation products with thymol,[6] carvacrol, and a few of their alkyl ethers, according to the following scheme



Thymol: X = *i*-propyl, Y = methyl
Carvacrol: X = methyl, Y = *i*-propyl
R = H or alkyl

The ethers can be converted conveniently into diaryldichloroethenes by refluxing with alcoholic potassium hydroxide.[5,7] Both the ethers and the dehydrochlorinated compounds are easily obtained as pure crystalline substances with sharp melting points. It is suggested that they may be useful as

(1) Abstracted from the thesis of Aksel A. Bothner-By presented to the Graduate School of New York University, in partial fulfillment of the requirements for the degree of Master of Science, 1946.

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(2) Chattaway and Prats, *Anal. fis. quim.*, **26**, 75 (1928).

(3) Pauly and Schanz, *Ber.*, **56B**, 979 (1923).

(4) Zeidler and co-workers, *ibid.*, **7**, 1180 (1874).

(5) Stephenson and Waters, *J. Chem. Soc.*, 339 (1946).

(6) Jaeger, *Ber.*, **7**, 1197 (1874).

(7) Cristol and co-workers, THIS JOURNAL, **67**, 1495, 2222 (1945); **68**, 913 (1946).