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Dibasic Acids Based on *p*-Chloromethylbenzoyl Chloride Containing Ether, Thioether or Sulfone Groups

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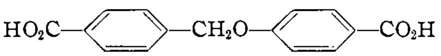
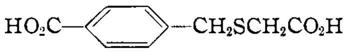
p-Chloromethylbenzoyl chloride is a particularly promising intermediate for the synthesis of dibasic acids. This paper describes the preparation of a number of such acids and methyl esters which are ethers, thioethers and sulfones prepared by appropriate displacement reactions in the chloromethyl group. The 2-ethylhexyl esters of five of these dibasic acids have been prepared by transesterification of the corresponding methyl esters.

Sodium *p*-chloromethylbenzoate, obtained by the alkaline hydrolysis of *p*-chloromethylbenzoyl chloride,[1] reacted with *p*-hydroxybenzoic acid, thioglycolic acid and *p*-mercaptobenzoic acid in aqueous alkali to give 73–93% yields of, respectively, *p*-carboxybenzyl *p*-carboxyphenyl ether (I), *p*-carboxybenzyl carboxymethyl sulfide (II) and *p*-carboxybenzyl *p*-carboxyphenyl sulfide.



I



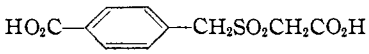
II

The reaction between *p*-chloromethylbenzoic acid and thioglycolic acid in *o*-dichlorobenzene in the presence of ferric chloride[2] yielded only 19% of *p*-carboxybenzyl carboxymethyl sulfide. Sodium *p*-chloromethylbenzoate reacted with aqueous sodium sulfide to give 94% of bis-(*p*-carboxybenzyl) sulfide.[3]

p-Carbomethoxybenzyl *p*-carbomethoxyphenyl sulfide was prepared in 49% yield from the acid and methanol in the presence of concentrated hydrochloric acid. In the other three cases sulfuric acid was used in place of hydrochloric acid and the yields of methyl esters were 71–82%.

All three of the sulfide methyl esters were oxidized to the corresponding sulfones by means of 30% hydrogen peroxide in glacial acetic acid. The yields were 61–91%.

2-Ethylhexyl esters of the following acids were prepared in 79–90% yields by the transesterification of the corresponding methyl esters in the presence of a *p*-toluenesulfonic acid catalyst: *p*-carboxybenzyl *p*-carboxyphenyl ether (I), *p*-carboxybenzyl *p*-carboxyphenyl sulfide, bis-(*p*-carboxybenzyl) sulfide and *p*-carboxybenzyl carboxymethyl sulfone (III).



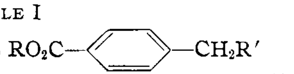
III

These esters were all undistillable oils. In the case of bis-(*p*-carbomethoxybenzyl) sulfone transesterification was not complete. Besides 52% of the waxy 2-ethylhexyl ester there was isolated 19% of *p*-carbomethoxybenzyl *p*-carbo-2-ethylhexoxybenzyl sulfone.

The properties of the various compounds prepared are summarized in Table I.

TABLE I

DIBASIC ACIDS AND ESTERS



R	R′	Yield, %[a]	M.p., °C.[b]	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found[c]
CH_3	*p*-$OC_6H_4CO_2CH_3$	82	139.5–140.0	68.0	68.0	5.33	5.23
H	SCH_2CO_2H	75	184.0–184.5	53.1	53.5	4.42	4.59
CH_3	$SCH_2CO_2CH_3$	76	[d]	56.7	56.6	5.51	5.60
CH_3	*p*-$SC_6H_4CO_2CH_3$	49	131.0–131.5	64.6	64.6	5.06	5.00
CH_3	*p*-$SCH_2C_6H_4CO_2CH_3$	71	100.5–101.0	65.5	65.5	5.46	5.68
CH_3	$SO_2CH_2CO_2CH_3$	82	104.5–105.0	50.4	50.4	4.89	4.68
CH_3	*p*-$SO_2C_6H_4CO_2CH_3$	61	209–210	58.6	58.0	4.59	4.50
CH_3	*p*-$SO_2CH_2C_6H_4CO_2CH_3$	91	236–237	59.7	59.4	4.97	5.10
C_8H_{17}	*p*-$OC_6H_4CO_2C_8H_{17}$	79	....	75.0	74.0	8.87	8.42
C_8H_{17}	*p*-$SC_6H_4CO_2C_8H_{17}$	83	....	72.5	71.8	8.79	8.35
C_8H_{17}	*p*-$SCH_2C_6H_4CO_2C_8H_{17}$	82	....	73.0	72.2	8.73	8.54
C_8H_{17}	$SO_2CH_2CO_2C_8H_{17}$	90	....	64.7	64.7	8.71	8.74
C_8H_{17}	*p*-$SO_2CH_2C_6H_4CO_2C_8H_{17}$	52	Wax	68.8	69.0	8.24	8.11

[a] These are crude yields in the final step of the preparation, not for material of analytical purity. [b] All melting points are uncorrected. Those given in this table are for the analytical samples. [c] All of the analyses are microanalyses performed by Mr. P. J. Adams and Mr. Donald Stoltz of this laboratory and by the Micro-Tech Laboratories, 8000 Lincoln Ave., Skokie, Illinois. [d] B.p. 171.0–171.5° (0.35–0.40 mm.).

Experimental

Starting Materials.—Sodium *p*-chloromethylbenzoate was prepared as needed by the alkaline hydrolysis of *p*-chloromethylbenzoyl chloride. Methyl *p*-chloromethylbenzoate and *p*-chloromethylbenzoic acid were prepared as described previously.[1] *p*-Mercaptobenzoic acid was prepared by the procedure described for thiosalicylic acid[4] in 76% yield, m.p. 216–218° (219°).[5] The *p*-hydroxybenzoic acid was Eastman Pure and the thioglycolic acid was Eastman Practical, freshly distilled.

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[1] Emerson and Heimsch, THIS JOURNAL, **72**, 5152 (1950).

[2] Method of Eby, U. S. Patent 2,472,471.

[3] Moses, *Ber.*, **33**, 2623 (1900), prepared this acid by the hydrolysis of *p*-cyanobenzyl thiocyanate with hydrochloric acid at 180° in a sealed tube.

[4] Allen and MacKay, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p. 580.

[5] Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1936, Vol. II, p. 567.

p-Carboxybenzyl p-Carboxyphenyl Ether.—A mixture of 95 g. of p-chloromethylbenzoyl chloride, 20 g. of sodium hydroxide and 250 cc. of water was stirred under reflux for one-half hour. Then a solution of 69 g. of p-hydroxybenzoic acid and 60 g. of sodium hydroxide in 500 cc. of water was added and the entire mixture stirred under reflux for 19 hours. Upon cooling, the solution was filtered and acidified with 1:1 sulfuric acid. The precipitated p-carboxybenzyl p-carboxyphenyl ether was separated by filtration, washed with water and dried. It weighed 100 g. (73% yield).

The methyl ester was prepared by boiling a solution of 10 g. of p-carboxybenzyl p-carboxyphenyl ether in 150 cc. of methanol containing 5 g. of concentrated sulfuric acid for 90 hours. The product was collected in two crops, 7.5 g., m.p. 138.5–140.0°, and 1.5 g., m.p. 133–135°, to give a total yield of 9.0 g. The analytical sample was recrystallized from methanol.

p-Carboxybenzyl Carboxymethyl Sulfide. Method A.—A mixture of 284 g. of p-chloromethylbenzoyl chloride, 60 g. of sodium hydroxide and 1.5 l. of water was boiled under reflux for 15 minutes. After a solution of 147 g. of thioglycolic acid and 158 g. of sodium hydroxide in 750 cc. of water had been added to the mixture, the entire mass was stirred under reflux for 20 hours. Upon cooling, it was filtered and then acidified with 1:1 sulfuric acid. The precipitate of p-carboxybenzyl carboxymethyl sulfide was separated by filtration, washed with water and dried. It weighed 255 g., m.p. 180–184°.

Method B.—To a mixture of 12 g. of p-chloromethylbenzoic acid, 2.0 g. of ferric chloride and 100 g. of o-dichlorobenzene there was added over a 30-minute period 10 g. of thioglycolic acid. The mixture was stirred at 100–125° for 1.5 hours longer, cooled and filtered. The filtrate was extracted with 5% sodium hydroxide. Acidification of this extract with concentrated hydrochloric acid precipitated 3.0 g. (19%) of crude p-carboxybenzyl carboxymethyl sulfide. Before analysis it was crystallized twice from methanol and benzene, m.p. 184.0–184.5°. When mixed with the product prepared by the other method, the melting point was 182–183°. By slurrying the initial precipitate with water to remove ferric chloride, 7.0 g. (69%) of p-chloromethylbenzoic acid was recovered.

p-Carboxybenzyl p-carboxyphenyl sulfide was prepared in the same way as p-carboxybenzyl carboxymethyl sulfide using Method A. The scale was 0.85-molar in 1 l. of water and the yield 93%.

p-Carbomethoxybenzyl carbomethoxymethyl sulfide was prepared by boiling 245 g. of p-carboxybenzyl carboxymethyl sulfide for 18 hours with 2.5 l. of methanol containing 50 cc. of concentrated sulfuric acid. The product was isolated by distilling most of the methanol, diluting with water and extracting with benzene. Distillation yielded 209.5 g. of p-carbomethoxybenzyl carbomethoxymethyl sulfide, b.p. (in two batches) 171.0–171.5° (0.30–0.55 mm.) and 184–187° (1.3–1.5 mm.), $n^{25}\text{D}$ 1.5472–1.5499. The analytical sample was a middle cut, b.p. 171.0–171.5° (0.35–0.40 mm.), $n^{25}\text{D}$ 1.5493, d^{25}_{25} 1.214.

p-Carbomethoxybenzyl p-carbomethoxyphenyl sulfide was prepared in the same way from 227 g. of p-carboxybenzyl p-carboxyphenyl sulfide, 2.3 l. of methanol and 115 cc. of concentrated hydrochloric acid. The crude product was isolated by crystallization and then by concentration of the mother liquor. It was recrystallized from methanol to give 122 g., m.p. 126.0–129.5°. The analytical sample was recrystallized twice from methanol. Both times the solution was treated with Norit before crystallization.

Bis-(p-carboxybenzyl) Sulfide.—A mixture of 662 g. of p-chloromethylbenzoyl chloride, 140 g. of sodium hydroxide and 1 l. of water was boiled under reflux for 1 hour. A solution of 420 g. of sodium sulfide nonahydrate and 150 g. of sodium hydroxide in 1 l. of water was added and the entire mass was stirred under reflux for 20 hours. After the addition of 750 cc. of water the solution was filtered and then acidified with 1:1 sulfuric acid to precipitate 495 g. (94%) of bis-(p-carboxybenzyl) sulfide.

The methyl ester was prepared by boiling the acid with 10 parts of methanol containing 5% of concentrated hydrochloric acid for 17 hours. Since esterification was not complete, the unreacted material was boiled for another 24 hours with additional methanol containing 10 cc. of concentrated sulfuric acid. The product was isolated in three crops: 58 g., m.p. 99.5–100.5°; 99 g., m.p. 96–98°; and 126 g., m.p. 90–94°. The total yield was 383 g. The analytical sample was recrystallized twice from methanol. Norit was used to decolorize the solution the second time.

When 57 g. of methyl p-chloromethylbenzoate was boiled with 12 g. of sodium sulfide nonahydrate in 100 cc. of dioxane for 5.5 hours, 51 g. (90%) of the methyl p-chloromethylbenzoate was recovered unchanged.

The Sulfones.—To a solution of the sulfide in 3–10 parts of glacial acetic acid held at 40–50° was added a 50–60% excess of 30% hydrogen peroxide at a rate adequate to maintain this temperature (for a 0.57-molar run this required 50 minutes). The mixture was stirred for another half hour at this temperature, boiled for 1 hour, cooled and diluted with an equal volume of water. The crude product was separated by filtration and crystallized from an appropriate solvent before weighing. One recrystallization was adequate before analysis. The p-carbomethoxybenzyl carbomethoxymethyl sulfone was crystallized from aqueous methanol, m.p. 103–105°; the p-carbomethoxybenzyl p-carbomethoxyphenyl sulfone from 70 dioxane–30 methanol, m.p. 205–210°; and the bis-(p-carbomethoxybenzyl) sulfone from dioxane, m.p. 234–237°.

2-Ethylhexyl Esters.—These were prepared by dissolving 0.125 mole of the corresponding methyl ester in 0.5 mole of 2-ethylhexanol, adding 2.5–5.0% of p-toluenesulfonic acid and then heating under a 24-inch Vigreux column. The pot temperatures varied between 110 and 150° and sufficient vacuum was applied to maintain the temperatures in this range. The methanol distilled as formed. From 3 to 10.5 hours was necessary to complete the reaction. Upon cooling, the mixtures were diluted with benzene and ether, washed twice with aqueous sodium bicarbonate and then with water (2 to 3 washes) until neutral. After the solvents and excess 2-ethylhexanol had been distilled from the residues, they were heated for 45 to 90 minutes at temperatures and pressures ranging from 150° (0.25 mm.) to 200° (0.9 mm.). In two cases Norit was added before the solvents were distilled. The other two esters were stirred with Norit at 150° for one-half hour. Final purification of all the 2-ethylhexyl esters was effected by filtering free of Norit through a sintered glass filter. The properties of these esters are summarized in Table II. The sulfide esters were tan in color and the ether and the sulfone were light straw-colored.

TABLE II

2-ETHYLHEXYL ESTERS

$C_8H_{17}O_2C—C_6H_4—CH_2R$

R	$n^{25}\text{D}$	d^{25}_{25}
p-$OC_6H_4CO_2C_8H_{17}$	1.5248	1.043
p-$SC_6H_4CO_2C_8H_{17}$	1.5451	1.050
p-$SCH_2C_6H_4CO_2C_8H_{17}$	1.5329	1.043
$SO_2CH_2CO_2C_8H_{17}$	1.4992	1.069

Bis-(p-carbo-2-ethylhexoxybenzyl) sulfone was prepared in the same way as the other 2-ethylhexyl esters except that 100 cc. of xylene was added to the charge of 41.5 g. of bis-(p-carbomethoxybenzyl) sulfone, 58.5 g. of 2-ethylhexanol and 1.0 g. of p-toluenesulfonic acid. Twelve hours were required to complete the transesterification. After cooling, the semi-solid mass was slurried with 100 cc. of 10% sodium bicarbonate and filtered. This precipitate was crystallized twice from benzene–hexane to give 9.5 g. (19%) of p-carbomethoxybenzyl p-carbo-2-ethylhexoxybenzyl sulfone, m.p. 147–152°. An analytical sample was crystallized from benzene, m.p. 151–152°.

Anal. Calcd. for $C_{25}H_{32}O_6S$: C, 65.2; H, 6.96. Found: C, 64.9; H, 6.75.

The layers in the original filtrate were separated and the organic portion washed with water until neutral. After the xylene and excess octanol had been distilled, the residue solidified to a wax on cooling. Pure bis-(p-carbo-2-ethylhexoxybenzyl) sulfone (17 g.) was obtained on crystallization from hexane. The product had to be filtered under pressure rather than in a Buchner funnel to remove the solvent. Additional, less pure product (15 g.) was obtained by evaporating the filtrate.

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