

scribed above was charged with ammonium chloride, *p*-hydrazotoluene and potassium amide. The same induction and discharge of color were observed as in the case above.

### Summary

1. Mercuric nitride and bismuth nitride have been shown to have the properties of nitridizing agents.

2. Hydrazobenzene and *p*-hydrazotoluene have been nitridized to the corresponding azo compounds in liquid ammonia solution using iodine, mercuric nitride and bismuth nitride.

3. Because of the formation of highly colored salts, both hydrazobenzene and hydrazotoluene may be used as sensitive acid-base indicators in liquid ammonia solutions.

COLUMBUS, OHIO

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

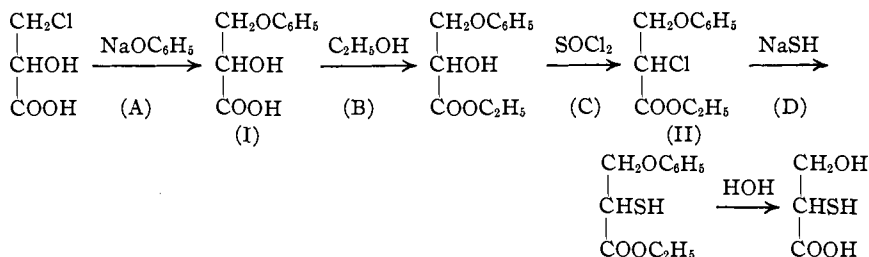
## THE MONOPHENYL ETHERS OF GLYCERIC ACID

By C. FREDERICK KOELSCH

RECEIVED JANUARY 11, 1930

PUBLISHED JUNE 8, 1930

Investigations on the oxidation of  $\beta$ -thioglyceric acid, whose preparation was described in a previous paper,<sup>1</sup> showed the desirability of extending the study there outlined to the still unknown  $\alpha$ -thioglyceric acid. It was considered feasible to attempt the preparation of this compound through the following reactions:



Reactions A, B and C were carried out successfully. Reaction D did not proceed as indicated; when ethyl  $\alpha$ -chloro- $\beta$ -phenoxypropionate (II) was treated with sodium hydrosulfide, a practically quantitative yield of phenol was obtained. The remainder of the reaction mixture was a black tar, the constituents of which are as yet unidentified. A study of this reaction is in progress.

This paper deals with the substances obtained in Reaction A. The reaction between  $\beta$ -chlorolactic acid and sodium phenoxide gave a satisfactory yield of  $\beta$ -phenoxy-lactic acid (I), but when the reaction mixture was worked over, it was found that this was not the sole product. Along

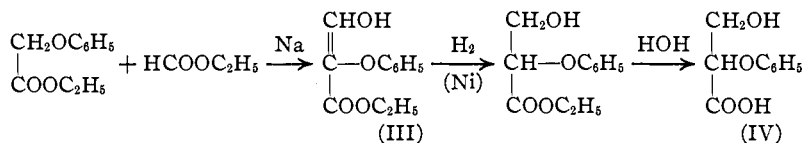
<sup>1</sup> Koelsch, THIS JOURNAL, 52, 1105 (1930).

with the  $\beta$ -phenoxyactic acid melting at 157.5–159°, there was obtained about 1% of a more soluble acid melting at 107–109°. The analysis and neutral equivalent of this compound indicated that it was isomeric with  $\beta$ -phenoxyactic acid.

On treatment with hydriodic acid, the low-melting acid gave phenol and  $\beta$ -iodopropionic acid, the same products which were obtained by a similar treatment of  $\beta$ -phenoxyactic acid. It seemed probable, therefore, that the low-melting compound was  $\alpha$ -phenoxyhydracrylic acid (IV).

That the acid melting at 157.5–159° was the expected  $\beta$ -phenoxyactic acid was proved by converting it into the chloro ester (II) which was dehalogenated to give ethyl  $\beta$ -phenoxypropionate. The acid resulting from the hydrolysis of this ester was identified as  $\beta$ -phenoxypropionic acid by comparison with a sample prepared from  $\beta$ -bromopropionic acid.

That the acid melting at 107–109° was  $\alpha$ -phenoxyhydracrylic acid was shown by its synthesis according to the following series of reactions



The reduction of formylphenoxyacetic ester (III) with zinc dust and acetic acid, with amalgamated zinc and acetic acid, or with amalgamated aluminum in neutral solution caused phenol to be eliminated from the molecule. The *o*-benzoate of the enol was unaffected by amalgamated aluminum. The reduction of the free enol was finally accomplished by using molecular hydrogen in the presence of catalytic nickel.

The first explanation for the formation of  $\alpha$ -phenoxyhydracrylic acid which suggested itself was that the  $\beta$ -chlorolactic acid used was contaminated with  $\alpha$ -chlorohydracrylic acid, and that the sodium phenoxide reacted with this to replace the halogen atom directly with the phenoxy radical. Certain facts militating against this explanation may be brought forward. The  $\beta$ -chlorolactic acid<sup>1,2</sup> used was prepared from  $\alpha$ -monochlorohydrin obtained by the action of hydrogen chloride on glycerol.<sup>3</sup> This monochlorohydrin subjected to the further action of hydrogen chloride gives a dichlorohydrin which has been shown to be nearly free of the  $\alpha, \beta$ -compound.<sup>4</sup> Hence the monochlorohydrin used contained very little of the  $\beta$ -isomer, which would be the precursor of  $\alpha$ -chlorohydracrylic acid. Although the above evidence does not preclude the possibility that only 1%

<sup>2</sup> The acid melting at 45–72° obtained from the oxidation was used without recrystallization. The unsharp melting point is considered to be caused by the presence of oxalic acid and, mainly, water.

<sup>3</sup> Conant and Quayle, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1923, Vol. II, p. 33.

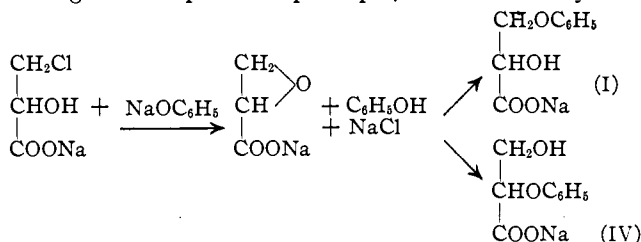
<sup>4</sup> Conant and Quayle, THIS JOURNAL, 45, 2771 (1923).

of  $\alpha$ -chlorohydracrylic acid may be present, Melikoff's experiments indicate that this acid would yield  $\beta$ -phenoxyacetic acid rather than  $\alpha$ -phenoxyhydracrylic acid.

Melikoff<sup>5</sup> treated  $\alpha$ -chlorohydracrylic acid with ammonia and was able to isolate only *iso*-serine,  $\text{CH}_2\text{NH}_2\text{—CHOH—COOH}$ , from the reaction mixture. He postulated that the  $\alpha$ -chlorohydracrylic acid first lost hydrogen chloride, forming glycidic acid, which compound then added ammonia to form *iso*-serine.<sup>6</sup> Melikoff showed that glycidic acid added ammonia thus and considered this as evidence for the correctness of his assumed reaction mechanism.

According to the partition principle of Michael,<sup>7</sup> the addition of an unsymmetrical reagent to an unsymmetrical unsaturated compound (or ethylene oxide) gives rise to two isomers, the amount of each isomer thus produced being in proportion to the amount of chemical energy set free in its formation.

If a reaction mechanism analogous to that postulated by Melikoff is considered in the light of the partition principle, Reaction A may be formulated



This formulation appears to account most satisfactorily for the formation of both  $\beta$ -phenoxyacetic acid and  $\alpha$ -phenoxyhydracrylic acid in the reaction which is reported here.

### Experimental

**$\beta$ -Phenoxyacetic and  $\alpha$ -Phenoxyhydracrylic Acids from  $\beta$ -Chlorolactic Acid.**—A mixture of 600 g. of phenol, 400 g. of  $\beta$ -chlorolactic acid and a solution of 360 g. of sodium hydroxide in two liters of water was refluxed for two hours, acidified and the excess phenol removed by steam distillation. Cooling the solution gave crude  $\beta$ -phenoxyacetic acid. The mother liquor contained  $\beta$ -phenoxyacetic acid,  $\alpha$ -phenoxyhydracrylic acid and sodium chloride, which were separated by evaporation and fractional crystallization. The  $\alpha$ -phenoxyhydracrylic acid crystallized out only after the volume of the solution had been reduced to some 150 ml.

The crude  $\beta$ -phenoxyacetic acid after treatment with charcoal, crystallized from water in colorless plates melting at 157.5–159° (uncorr.); yield, 400–425 g.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{10}\text{O}_4$ : C, 59.33; H, 5.49. Found: C, 59.35; H, 5.90. *Mol. wt.* (by titration). Calcd.: 182. Found: 185.5.

<sup>5</sup> Melikoff, *Ber.*, **13**, 1265 (1880).

<sup>6</sup> The same result has been obtained more recently with  $\alpha$ -bromohydracrylic acid and ammonia [Neuberg and Mayer, *Biochem. Z.*, **3**, 119 (1907)].

<sup>7</sup> Michael, *J. prakt. Chem.*, [2] **60**, 290 (1899).

A solution of the compound in concentrated sulfuric acid was colorless until warmed, when it became deep, violet-red.

The crude  $\alpha$ -phenoxyhydracrylic acid was separated from tarry impurities by extraction with hot toluene. It was finally crystallized from chloroform, from which solvent it was deposited in fine needles melting at 107–109°; yield, 3.8–6.0 g.

*Anal.* Calcd. for  $C_9H_9O_4$ : C, 59.33; H, 5.49. Found: C, 59.00; H, 5.61. *Mol. wt.* (by titration). Calcd.: 182. Found: 183, 183.5.

TABLE I

DERIVATIVES OF $\alpha$ -PHENOXYHYDRACRYLIC AND $\beta$ -PHENOXYLACTIC ACIDS							
No.	Compound		Remarks		Yield, %		
1	Methyl $\alpha$ -phenoxyhydracrylate <sup>a</sup>		Oil		69		
2	Ethyl $\alpha$ -phenoxyhydracrylate <sup>a</sup>		Oil		71		
3	$\alpha$ -Phenoxyhydracrylamide <sup>b</sup>		Needles fr. water		54		
4	$\alpha$ -Phenoxyhydracrylanilide <sup>c</sup>		Needles fr. water		82		
5	Silver $\alpha$ -phenoxyhydracrylate		Flat needles		..		
6	Methyl $\beta$ -phenoxy lactate <sup>a</sup>		Oil		82		
7	Ethyl $\beta$ -phenoxy lactate <sup>a</sup>		Fine needles fr. dil. alc.		74		
8	$\beta$ -Phenoxy lactamide <sup>b</sup>		Plates fr. water		65		
9	$\beta$ -Phenoxy lactanilide <sup>c, e</sup>		Plates fr. dil. alc.		85		
10	Silver $\beta$ -phenoxy lactate		Fluffy plates		..		

No.	B. p. or m. p. °C. (mm.) (uncorr.)	$d_{25}^{25}$	$n_D^{25}$	Calcd. $M_D$	Obs.
1	B. 168–169 (14)	1.1966	1.5213	49.92	49.90
2	B. 174–175 (16)	1.1545	1.5117	54.52	54.55
3	M. 137–139	....	....	...	...
4	M. 129–131 <sup>d</sup>	....	....	...	...
6	B. 168–170 (17)	1.1934	1.5190	49.92	49.96
7	M. 71–72; (b. 173–175) (17)	....	....	...	...
8	M. 149–150	....	....	...	...
9	M. 122–123	....	....	...	...

No.	Formula	C	Calcd. H	N	C	Found H	N
1	$C_{10}H_{12}O_4$	61.2	6.12	..	60.9	6.19	..
2	$C_{11}H_{14}O_4$	62.8	6.67	..	62.7	6.44	..
3	$C_9H_{11}O_3N$	..	..	7.74	..	..	7.46
4	$C_{13}H_{15}O_3N$	..	..	5.46	..	..	5.56
5	$C_9H_9O_4Ag$	..	(Ag)	37.4	..	(Ag)	36.9
6	$C_{10}H_{12}O_4$	61.2	6.12	..	60.9	6.20	..
7	$C_{11}H_{14}O_4$	62.8	6.67	..	62.6	6.78	..
8	$C_9H_{11}O_3N$	..	..	7.74	..	..	7.54
9	$C_{13}H_{15}O_3N$	..	..	5.46	..	..	5.14
10	$C_9H_9O_4Ag$	..	(Ag)	37.4	..	(Ag)	37.4

<sup>a</sup> From the acid by the method of E. Fischer and Speier, *Ber.*, **28**, 3252 (1895), using hydrogen chloride. <sup>b</sup> From the methyl ester and concd. aqueous ammonia. <sup>c</sup> From the acid by heating for four hours at 190° with a slight excess of aniline. <sup>d</sup> Sintered at 122°. A mixture with an equal amount of  $\beta$ -phenoxy lactanilide melted at 107–111°. <sup>e</sup> This compound could be obtained colorless for analysis only by crystallization from water, in which the colored impurities were insoluble. Four hundred ml. of boiling water was necessary to dissolve 0.4 g. of the substance; it was noted that all of the derivatives of  $\beta$ -phenoxy lactic acid were much less soluble than the corresponding derivatives of  $\alpha$ -phenoxyhydracrylic acid.

A solution of the compound in concd. sulfuric acid was colorless until warmed, when it became rose-red.

**Reaction of  $\beta$ -Phenoxylic and  $\alpha$ -Phenoxyhydracrylic Acids with Hydriodic Acid.**—Although heating  $\beta$ -phenoxylic acid with hydrochloric acid or with hydrobromic acid gave only black resins, similar treatment with hydriodic acid gave substances which were characterized successfully. The solution resulting from heating 5 g. of  $\beta$ -phenoxylic acid with 20 ml. of hydriodic acid ( $d$  1.96) in a sealed tube at 120–125° for four hours was diluted with water, decolorized with sulfur dioxide, and extracted with ether. By washing this extract with sodium carbonate and sodium hydroxide, there were obtained 4.0 g. of a mixture of unchanged  $\beta$ -phenoxylic acid and  $\beta$ -iodopropionic acid, and 1.4 g. of phenol (identified as phenyl benzoate). Since the mixture of acids could not be separated into its constituents by fractional crystallization, a portion (2.7 g.) was heated for three hours at 180° with aniline (4.0 g.), giving a mixture of neutral  $\beta$ -phenoxylicanilide with basic  $\beta$ -anilinopropionanilide<sup>8</sup> which were easily separated. The latter compound was identified by analysis of its hydrochloride (calcd.: Cl, 12.84; found: Cl, 12.84) and by mixed melting points with the same compound prepared from  $\beta$ -bromopropionic acid and aniline.

The treatment of  $\alpha$ -phenoxyhydracrylic acid (4.7 g.) with hydriodic acid was similar to that described immediately above. There were obtained 1.5 g. of phenol, and 3.4 g. of mixed acids. A hot benzene solution of a portion of the latter deposited a small amount of  $\alpha$ -phenoxyhydracrylic acid (m. p. 95–100°; mixed m. p. 100–104°); the  $\beta$ -iodopropionic acid remaining in the benzene melted, after crystallization from warm water, at 80–81°. The remainder of the mixed acids was treated with aniline, the resulting anilides being separated and identified as before.

**Esters of  $\alpha$ -Chloro- $\beta$ -phenoxypropionic Acid.**—The general method of Darzens<sup>9</sup> for the replacement of the hydroxyl group with chlorine by the use of thionyl chloride and pyridine was applied successfully to the methyl and ethyl esters of  $\beta$ -phenoxylic acid. The properties and analyses of the twice distilled esters are given in the accompanying table.

TABLE II  
PROPERTIES AND ANALYSES OF ESTERS

No.	Ester	B. p., °C. (18 mm.) (uncorr.)	Yield, %	$d_{25}^{25}$	$n_D^{25}$
1	Methyl	153–154	77	1.2177	1.5166
2	Ethyl	165–167	55	1.1812	1.5091

No.	Calcd. $M_D$	Obs.	Formula	Calcd.	Cl (Carius), % Found
1	53.34	53.25	$C_{10}H_{11}O_3Cl$	16.53	16.41
2	57.94	57.77	$C_{11}H_{13}O_3Cl$	15.53	16.36, 16.65, 16.54 <sup>a</sup>

<sup>a</sup> The third analysis of the compound was made on a sample purified by an additional distillation; the constants of this sample were identical with those measured for the twice distilled ester. The low yield and high chlorine content were probably caused by not cooling the mixture sufficiently during the addition of the thionyl chloride.

**Dehalogenation of Ethyl  $\alpha$ -Chloro- $\beta$ -phenoxypropionate.**—A mixture of 10 g. of ethyl  $\alpha$ -chloro- $\beta$ -phenoxypropionate, 20 g. of dry alcohol, 10 g. of acetic acid, 10 g. of zinc dust and a little copper carbonate was refluxed for eight hours. The mixture was then filtered and concentrated on a steam-bath. The addition of water precipitated an oil which distilled at 120–145° (15 mm.). A second distillation gave 3.4 g.

<sup>8</sup> Cf. Autenrieth and Pretzell, *Ber.*, **36**, 1262 (1903).

<sup>9</sup> Darzens, *Compt. rend.*, **152**, 1601 (1911).

of a halogen-free fraction boiling at 175–177° (50 mm.);  $d_{25}^{25}$  1.0821;  $n_D^{25}$  1.5055;  $M_D$ , calcd., 53.00; obs., 53.22. The boiling point of ethyl  $\beta$ -phenoxypropionate is reported to be 170° (40 mm.).<sup>10</sup>

The acid obtained by the hydrolysis of the ester with a mixture of equal weights of acetic acid, water and sulfuric acid melted alone or mixed with a sample of  $\beta$ -phenoxypropionic acid prepared from  $\beta$ -bromopropionic acid at 96–97° (uncorr.). The melting point of this acid is reported to be 98°.<sup>10</sup>

**Ethyl  $\alpha$ -Phenoxy- $\beta$ -hydroxyacrylate** ("Formylphenoxyacetic Ester," III).—This compound was prepared by the method of Johnson and Guest<sup>11</sup> by the action of sodium on a mixture of ethyl formate and ethyl phenoxyacetate in ether. Contrary to the statement<sup>12</sup> that the compound could not be distilled under reduced pressure without decomposition, it was found that no decomposition took place when the distillation was carried out with the aid of an efficient water pump. This was shown by distilling the compound repeatedly, under which treatment the boiling point was not changed; the thrice distilled compound gave a benzoate identical with that obtained from the crude undistilled product. The following constants were observed: b. p., 148–150° (11 mm.);  $d_{25}^{25}$  1.1637;  $n_D^{25}$  1.5210;  $M_D$  calcd. (keto), 53.18; (enol), 54.13; obs., 54.43.

*Anal.* Calcd. for  $C_{11}H_{12}O_4$ : C, 63.46; H, 5.77. Found: C, 63.45; H, 5.83.

**Benzoate.**—This compound was prepared from the ester by the Schotten-Baumann reaction. It crystallized from dilute alcohol in fine needles which melted at 76–77°.

*Anal.* Calcd. for  $C_{18}H_{16}O_5$ : C, 69.24; H, 5.13. Found: C, 68.93; H, 5.11.

**Ethyl  $\alpha$ -Phenoxyhydracrylate from Ethyl Formylphenoxyacetate.**—The oxymethylene compound was reduced in alcohol solution with hydrogen in the presence of catalytic nickel at a pressure of 150 atmospheres and at a temperature of 100°.<sup>13</sup> On distillation, the product boiled at 168–170° (10 mm.);  $d_{25}^{25}$  1.1558;  $n_D^{25}$  1.5125;  $M_D$ , calcd., 54.52; obs., 54.56; found: C, 62.50; H, 6.67. These constants agree well with those obtained for ethyl  $\alpha$ -phenoxyhydracrylate prepared from  $\beta$ -chlorolactic acid (*cf.* Table I, No. 2).

The reagents usually employed for the reduction of oxymethylene compounds gave unsatisfactory results in the present instance. An ether solution of formylphenoxyacetic ester (10 g.) was treated with amalgamated aluminum according to the procedure described by W. Wislicenus.<sup>14</sup> From the ether solution there was obtained only phenol, which gave, on benzylation, 8.0 g. of pure phenyl benzoate. The reduction of the oxymethylene compound in glacial acetic acid with zinc dust or amalgamated zinc led to a like result.

Phenoxyhydracrylamide (found: N, 7.49) prepared by ammonolysis of the ester was identical (mixed m. p.) with that obtained from  $\beta$ -chlorolactic acid (*cf.* Table I No. 3). Saponification of the ester gave the free acid (found: C, 59.01; H, 5.54) which melted at 109–110°; a mixture with an equal amount of the acid obtained from  $\beta$ -chlorolactic acid melted at 108–110°. The acid obtained by reduction gave a colorless solution in concd. sulfuric acid, which became yellow on warming. The color reaction and slightly low melting point of the acid prepared from  $\beta$ -chlorolactic acid are probably

<sup>10</sup> Powell, *THIS JOURNAL*, **45**, 2708 (1923).

<sup>11</sup> Johnson and Guest, *Am. Chem. J.*, **42**, 285 (1909).

<sup>12</sup> Johnson and Heyl, *ibid.*, **37**, 636 (1907).

<sup>13</sup> This reduction was carried out by Professor Homer Adkins. The procedure will be described in detail in a forthcoming paper. The author wishes to express his sincere appreciation to Professor Adkins.

<sup>14</sup> W. Wislicenus, Böklen and Reuthe, *Ann.*, **363**, 359 (1908).

caused by the presence of a small amount of  $\beta$ -phenoxy-lactic acid which could not be removed by fractional crystallization.

The assistance given by Professor S. M. McElvain during the course of this work is gratefully acknowledged.

### Summary

The monophenyl ethers of glyceric acid,  $\beta$ -phenoxy-lactic acid and  $\alpha$ -phenoxyhydracrylic acid, and a number of their derivatives have been prepared and characterized.

The possibility that both of these isomers may be formed simultaneously in the reaction between  $\beta$ -chlorolactic acid and sodium phenoxide has been pointed out.

MADISON, WISCONSIN

---

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY,  
No. 626]

## THE INFLUENCE OF CERTAIN NEUTRAL SALTS UPON THE ACTIVITY OF MALT AMYLASE

BY H. C. SHERMAN, M. L. CALDWELL AND M. CLEAVELAND

RECEIVED JANUARY 30, 1930

PUBLISHED JUNE 6, 1930

Recent work<sup>1</sup> has shown that pancreatic amylase not only is dependent for its activity upon the presence of electrolytes but that it differs markedly in its response in activity to the presence of different salts. In view of this fact and of the recent findings of several investigators<sup>2</sup> that the influence of electrolytes upon enzymic activity is dependent on several interrelated factors, it seemed of special interest to continue our studies of typical starch-splitting enzymes of plant and animal origin by ascertaining whether quantitative differences might also be obtained in the action of malt amylase by the presence or absence of certain salts when the other factors were very fully controlled in the light of all present knowledge. One phase of this work, that dealing with the influence of acetate and phosphate upon the activity of malt amylase, has already been described.<sup>2</sup> The results of the quantitative study of the influence of other salts upon the activity of malt amylase are reported briefly here.

### Experimental

The general procedure employed in this investigation consisted in allowing the enzyme to act at 40° ( $\pm 0.01^\circ$ ) for thirty minutes upon 2% starch solutions which differed among themselves with respect to either the salt content or the hydrogen-ion activity or both as explained below. At the

<sup>1</sup> (a) Sherman, Caldwell and Dale, *THIS JOURNAL*, **49**, 2596 (1927); (b) Sherman, Caldwell and Adams, *ibid.*, **50**, 2529, 2535, 2538 (1928).

<sup>2</sup> Sherman, Caldwell and Boynton, *ibid.*, **52**, 1669 (1930), and references therein contained.