[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

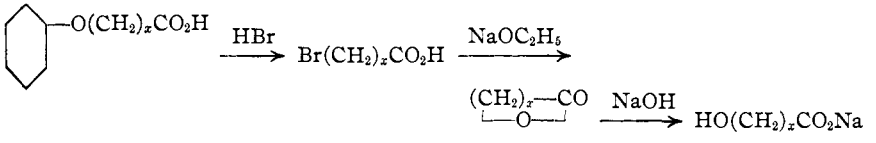
THE PREPARATION OF THE SODIUM SALTS OF OMEGA-HYDROXYBUTYRIC, -VALERIC AND -CAPROIC ACIDS

BY C. S. MARVEL AND E. R. BIRKHIMER

RECEIVED JULY 30, 1928 PUBLISHED JANUARY 8, 1929

Several studies have been made of the hydroxy and amino acids in an attempt to find whether or not they give the same end products in metabolism in the animal organism. In order to gain further information concerning this problem, the preparation of the salts of some ω-hydroxy acids was undertaken so that they might be compared with the ω-amino acids which have recently been studied by Corley.[1]

The general procedure which was used for the preparation of these compounds can be illustrated by the following reactions



Although these reactions are not essentially new, the methods have not been described in sufficient detail to make possible the easy production of any considerable amounts of these compounds.

γ-Phenoxybutyric acid was prepared by the method of Lohmann[2] except that the hydrolysis was carried out under a reflux condenser and not in closed tubes. γ-Bromobutyric acid was obtained from it by the method devised by Merchant, Wickert and Marvel[3] for converting phenoxy acids to the corresponding bromo acids. The bromo acid was converted to γ-butyrolactone by the method which Cloves[4] has described for the preparation of δ-valerolactone from δ-bromovaleric acid. The lactone was saponified in the usual way with dilute sodium hydroxide solution.

δ-Valerolactone was prepared by the same series of reactions, starting with δ-phenoxyvaleric acid, and then hydrolyzed to give sodium δ-hydroxyvalerate. However, when Cloves' method of preparing a lactone was applied to ε-bromocaproic acid, a very poor yield of ε-caprolactone was obtained. This material was apparently a compound of the type $[O(CH_2)_5COO(CH_2)_5CO]_x$, since on hydrolyzing with aqueous hydroxide solution it gave a salt which by analysis agreed with sodium hydroxycaproate.

[1] Corley, *J. Biol. Chem.*, **70**, 99 (1926).

[2] Lohmann, *Ber.*, **24**, 2640 (1891).

[3] Merchant, Wickert and Marvel, THIS JOURNAL, **49**, 1828 (1927).

[4] Cloves, *Ann.*, **319**, 367 (1901).

Experimental Part

γ-Phenoxybutyric Acid.—A mixture of 500 g. of phenoxypropyl cyanide and 2500 cc. of concentrated hydrochloric acid (sp. gr., 1.19) was boiled under a reflux condenser for about five hours. The phenoxybutyric acid was extracted with benzene, the benzene evaporated and the product distilled under reduced pressure. The yield was 340 g. (61% of the theoretical amount) boiling at 192–197° (18 mm.).

γ-Bromobutyric Acid.—A mixture of 340 g. of γ-phenoxybutyric acid and 550 cc. of 48% hydrobromic acid was placed in a 1-liter round-bottomed flask attached to a 1-meter fractionating column by means of a mercury seal. The reaction mixture was heated to such a point that the temperature of the vapors at the top of the column was about 120°. After about five hours no more phenol was distilling. The reaction mixture was diluted with water and the γ-bromobutyric acid was extracted with ether. The product was distilled under reduced pressure. The yield was 220 g. (70% of the theoretical amount) of γ-bromobutyric acid, b. p. 124–127° (7 mm.).

γ-Butyrolactone.—To a solution of 7.8 g. of sodium in 500 cc. of absolute alcohol was added 60.5 g. of γ-bromobutyric acid. The reaction mixture was boiled under a reflux condenser for about five hours. During this time sodium bromide separated. The alcohol was distilled from a steam-bath and the lactone was separated from the sodium bromide by extraction with ether. The ether was evaporated and the lactone distilled under ordinary pressure. The yield was 21.2 g. (67% of the theoretical amount) of a product boiling at 202–206°; sp. gr. $\frac{28}{28}$, 1.1054; $n_D^{26.5}$, 1.4343.

Sodium γ-Hydroxybutyrate.—A mixture of 16.3 g. of γ-butyrolactone and 7.4 g. of sodium hydroxide dissolved in 30 cc. of water was boiled under a reflux condenser for about three hours. At the end of this time more water was added to dissolve the salt and the solution was filtered and evaporated to dryness under reduced pressure. The salt was recrystallized from alcohol. The yield was 11.5 g. (40% of the theoretical amount).

Anal. Subs., 0.2106: Na_2SO_4, 0.1171. Calcd. for $C_4H_7O_3Na$: Na, 18.25. Found: Na, 18.02.

δ-Valerolactone.—δ-Valerolactone was obtained in 58% yield from δ-bromovaleric acid by the method of Cloves.[4] It boiled at 215–220° at atmospheric pressure; sp. gr. $\frac{20}{20}$, 1.1130; n_D^{20}, 1.4600.

Sodium δ-Hydroxyvalerate.—This material was prepared by the method used for the corresponding butyric acid derivative. From 11 g. of lactone and 4 g. of sodium hydroxide in 20 cc. of water there was obtained 6.6 g. (47% of the theoretical amount) of product.

Anal. Subs., 0.2140: Na_2SO_4, 0.1085. Calcd. for $C_5H_9O_3Na$: Na, 16.43. Found: Na, 16.42.

Sodium ε-Hydroxycaproate.—To a solution of 9 g. of sodium in 500 cc. of absolute alcohol was added 77 g. of ε-bromocaproic acid. The solution was boiled under reflux for about five hours and then the alcohol was distilled and the residue in the flask extracted with ether. The ether was evaporated and an attempt was made to distil the residue. About 10 g. of material which seemed to be slightly impure ε-caprolactone was obtained, boiling at 135–140° (35 mm.). It gave a slight test for bromine; sp. gr. $\frac{24}{24}$, 1.0306; n_D^{24}, 1.4481.

There was considerable residue (25–30 g.) left in the distilling flask which did not distil when heated to about 200° under 35 mm. pressure. This residue was hydrolyzed by boiling with an aqueous solution of about 6 g. of sodium hydroxide. This solution was decolorized with decolorizing carbon (Norite), filtered and evaporated to dryness. The residue was recrystallized from alcohol. In this manner 14.5 g. of the sodium salt was obtained.

Anal. Subs., 0.2012: Na_2SO_4, 0.0943. Subs., 0.1987: CO_2, 0.3126; H_2O, 0.1277. Calcd. for $C_6H_{11}O_3Na$: Na, 14.93; C, 46.75; H, 7.14. Found: Na, 15.05; C, 46.81; H, 7.14.

Summary

Convenient procedures for the preparation of the sodium salts of the ω-hydroxy derivatives of butyric, valeric and caproic acids have been described.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

SALTS OF AROMATIC NITRILES. II. POTASSIUM PHENYLACETONITRILE

BY MARY M. RISING, IRVING E. MUSKAT AND EDMUND W. LOWE

RECEIVED AUGUST 3, 1928 PUBLISHED JANUARY 8, 1929

There appeared recently a paper[1] by one of the present authors and Dr. Tsoh-Wu Zee in which were discussed the method of preparation and the behavior of sodium phenylacetonitrile, $[(C_6H_5)HC{=}C{=}N]Na$ and $[(C_6H_5)(CN)HC]Na$, and of sodium α-phenylbutyronitrile,[2] $[(C_6H_5)(C_2H_5)C{=}C{=}N]Na$ and $[(C_6H_5)(C_2H_5)(CN)C]Na$. The paper was accompanied by a statement to the effect that the purity and identity of these salts, which were obtained a number of times by Rising and Zee, were established conclusively from the analytical data and the reactions of the compounds, but that since the departure of Dr. Zee for China it had proved so far impossible to repeat his work and obtain the salts again in pure form.

In view of the experimental difficulties encountered in obtaining the sodium salts by the workers who followed Zee, a study of the potassium salts of phenylacetonitrile and α-phenylbutyronitrile was undertaken, and the present paper describes the preparation of potassium phenylacetonitrile, $[(C_6H_5)HC{=}C{=}N]K$, and $[(C_6H_5)(CN)HC]K$, and its conversion into α-phenylbutyronitrile in fairly good yield by treatment with ethyl iodide. The method used by Zee to obtain the sodium salts has been modified slightly and a method of purification of the potassium salt has been developed which will undoubtedly prove useful for other salts of this variety.

A few weeks after the publication of our last report on the sodium salts, the attention of one of the present authors was called by F. W. Upson and T. J. Thompson to a paper of theirs[3] which appeared in 1922 upon

[1] Rising and Zee, THIS JOURNAL, **50**, 1699 (1928).

[2] This salt was described in an earlier paper by Rising and Zee, *ibid.*, **49**, 541 (1927).

[3] Upson and Thompson, *ibid.*, **44**, 181 (1922).