

The Preparation and Examination of

β -Ethylmercaptopropionic acid

and

β -Butylmercaptopropionic acid

Introduction

pg 1

Historical

pg 1

Discussion

pg 2

Experimental

pg 3

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β -Ethylmercaptopropionic acid

pg 3

β -Butylmercaptopropionic acid

pg 4

Presented in Partial Fulfillment of the Requirements
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Submitted

pg 7

by

pg 7

Washington and Lee University

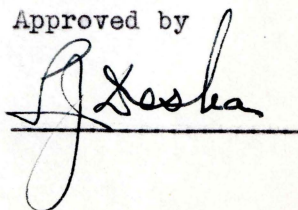
pg 8

George H. Denny, Jr.

Washington and Lee University

1950

Approved by



INTRODUCTION

work on the sulfide acids of the type $RSC(=S)CH_2COOH$ was initiated at the suggestion of Dr. E. Dwan Reid, Professor Emeritus of Chemistry, The Johns Hopkins University. The project has been carried out under the direction of Dr. Lucius J. Deane, Professor of Chemistry, Washington State University.

Table of Contents

Introduction	pg 1
Historical Background	pg 1
Discussion	pg 2
Experimental	pg 3
β-Ethylmercaptopropionic acid	pg 3
β-Butylmercaptopropionic acid	pg 5
Summary of Properties	pg 6
Derivatives	pg 7
Summary	pg 7
Bibliography	pg 8

HISTORICAL BACKGROUND

It was pointed out by Dr. Reid that the available information regarding the β-alkylmercapto acids is notably deficient. Langport, Smith, and Norman¹ have reported some properties of the octyl (mp 40-1), decyl (mp 53-3, bp_{3.5mm} 180-5), and dodecyl (mp 61-2) analogs. Grashar and Deane² have recently reported some data on the tert-butyl (mp_{1mm} 98-9) and heptyl (bp_{1mm} 110-14) compounds. The esterification and hydrolysis velocities of the methyl and ethyl analogs have been determined by Fehnel et al.³ The ester methyl β-ethylmercaptopropionate, $CH_3CO_2CH_2CH_2CH_2S$, has been isolated by Wagner-Smith, et al.,⁴ from the highly volatile material from pineapple fruit pulp. Methyl β-butylmercaptopropionate has been prepared by Fehnel and Gammart,⁵

INTRODUCTION

Work on the sulfide acids of the type $\text{RSCH}_2\text{CH}_2\text{COOH}$ was initiated at the suggestion of Dr. E. Emmet Reid, Professor Emeritus of Chemistry, The Johns Hopkins University. The project has been carried out under the direction of Dr. Lucius J. Desha, Professor of Chemistry, Washington and Lee University.

Acknowledgement is due also to Dr. Thomas L. Gresham, who has offered several suggestions which have been of great value in carrying out the syntheses. Research samples of β -chloropropionic acid and β -mercaptopropionic acid have been generously supplied by the B. F. Goodrich Company.

I wish to thank the entire staff of the Washington and Lee Chemistry Department for their interested coöperation during all phases of this work. The refractive index measurements were made with the assistance of Major Belvey W. Mundy, of the Virginia Military Institute.

HISTORICAL BACKGROUND

It was pointed out by Dr. Reid that the available information regarding the β -alkylmercapto acids is notably deficient. Rapoport, Smith, and Newman⁸ have reported some properties of the octyl [mp 40-1], nonyl [mp 52-3, bp_{3.5mm} 180-5], and dodecyl [mp 61-2] analogs. Gresham and Shaver³ have recently reported some data on the tert-butyl [bp_{1mm} 98-9] and hexyl [bp_{1mm} 110-14] compounds. The esterification and hydrolysis velocities of the methyl and ethyl analogs have been determined by Palomaa and Kaski⁷. The ester methyl β -methylmercaptopropionate, $\text{CH}_3\text{SCH}_2\text{CH}_2\text{COOCH}_3$, has been isolated by Haagen-Smit, et. al.,⁴ from the higher boiling volatile material from pineapple fruit pulp. Methyl β -butylmercaptopropionate has been prepared by Fehnel and Carmack²,

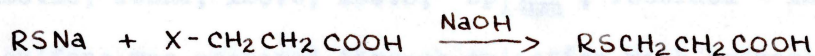
who also studied its ultraviolet absorption spectrum.

DISCUSSION

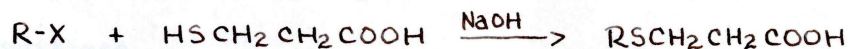
It is desired that, ultimately, a complete set of data may be collected for each of these acids, so that regularities [or irregularities] in densities, boiling points, melting points, and refractive indexes may be traced throughout the series. As a starting point, the two compounds containing the ethylmercapto and butylmercapto groups, respectively, substituted in the β -position, were chosen for study.

Various convenient methods have been proposed for synthesizing this type of compound in the laboratory. Among the possible routes are listed:

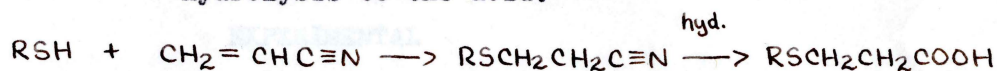
- [A] Condensation of the sodium mercaptide with a halo-acid.⁵



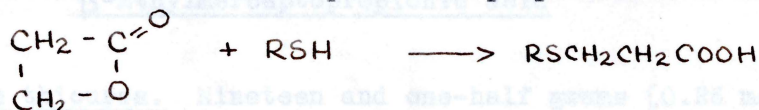
- [B] Addition of the alkyl halide to a mercapto acid.



- [C] Addition of the mercaptan to acrylonitrile followed by hydrolysis to the acid.⁸



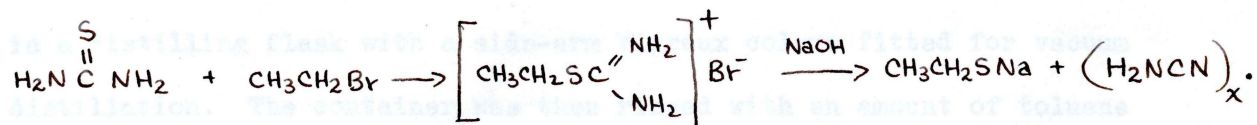
- [D] Reaction of the mercaptan with propionolactone.³



Whenever a study of the physical properties of a compound is to be made, it is always desirable to obtain the compound by at least two independent methods. This makes it possible to check the properties of the separate synthetic products against each other and provides an added criterion for the purity of the compound. Accordingly, type reactions [A] and [B] were chosen as feasible methods for making the acids.

In order to become familiar with the technique involved in running these reactions without the loss of valuable starting material, a trial

run was performed using sodium ethyl mercaptide and chloroacetic acid in reaction [A]. Ethyl thioglycolic acid is recorded in the literature⁶ and Claesson¹ reports to have obtained its amide [mp 44°]. The sodium ethyl mercaptide was conveniently synthesized in the laboratory by refluxing together thiourea and ethyl bromide in an aqueous medium, finally decomposing the resulting isothiuronium bromide by the addition of sodium hydroxide:



The properties of the final reaction product, which was purified by vacuum distillation, were found to be in reasonable agreement with the recorded values for ethyl thioglycolic acid: Neut. equiv. Calc. for $\text{C}_4\text{H}_8\text{O}_2\text{S} = 120.16$, found, 120.6, 120.3; $\text{bp}_{14\text{mm}}$, recorded = 124-5, observed, = 139. The sulfone was prepared through oxidation with hydrogen peroxide, it was seen to be a clear, oily liquid. Repeated attempts to obtain the amide were fruitless.

EXPERIMENTAL

β-Ethylmercaptopropionic acid

[a] From thiourea. Nineteen and one-half grams [0.26 mole] of thiourea, 27.2 grams [0.25 mole] of ethyl bromide and 23 ml. of water were placed in a 200 ml. 3-necked flask equipped with a dropping funnel, stirring motor, and condenser. These were refluxed together for two hours and fifteen minutes at a temperature of 37-9°. A solution of 12 grams of sodium hydroxide in water was added to the hot reaction mixture. The flask was allowed to come to room temperature, then cooled in crushed ice. When cold, 11 grams of sodium hydroxide in water and 25 grams of crushed ice were added. To this was added a solution made by carefully neutralizing

27.1 grams [0.25 mole] of β -chloropropionic acid with 35.5 grams of sodium carbonate decahydrate. This mixture was kept cold for an hour, then at room temperature for several hours and finally warmed for a few minutes on the water bath. The solution was filtered through a folded filter, cooled, and acidified with 60 ml. of concentrated hydrochloric acid. The product was finally extracted with ether.

The crude acid thus obtained was weighed [yield, 25.4%] and put in a distilling flask with a side-arm Vigreux column fitted for vacuum distillation. The container was then rinsed with an amount of toluene about equal in volume to the acid and this was added to the distilling flask. The toluene-water mixture was distilled off without reducing the pressure. The pressure was then lowered to 8 mm and the acid started coming over at about 131°, accompanied by a fine, white solid. This material, presumably polymerized cyanamide, could not be removed by redistillation. In view of the presence of this impurity it would be preferred to use RSNa obtained by neutralizing the pure thiol from the stock room with sodium hydroxide. This procedure was accordingly followed in subsequent syntheses.

[b] From sodium ethyl mercaptide. Twenty grams [0.5 mole] of sodium hydroxide were dissolved in 100 ml. of water and placed in a 500 ml. 3-necked flask equipped with a stirrer, condenser, and dropping funnel. Twenty-five grams [0.5 mole] of ethyl mercaptan were added dropwise, with stirring and cooling. Another solution was made similarly from 20 grams of NaOH, 100 ml. of water, and 56.5 grams [0.52 mole] of β -chloropropionic acid. These two solutions were refluxed together, with stirring, for 1 hour and 20 minutes at the reflux temperature of 105°. At the end of this time the mixture was acidified with 115 ml. of concentrated hydrochloric acid. This was allowed to cool slowly and the product was extracted with ether and purified as in the previous procedure. Center cut distilled at 133-4₈mm; Neut. equiv. Calc. for $C_5H_{10}O_2S$ = 134.19; found, 134.5, 134.8.

[c] From ethyl bromide. A solution of 40 grams [1 mole] of sodium hydroxide in 200 ml. of water was placed in a 500 ml. 3-necked flask equipped with a stirrer, condenser, and dropping funnel. This was cooled and 53 grams [0.5 mole] of β -mercaptopropionic acid were added dropwise over a period of 1.5 hours, with stirring and cooling. Next, 36.3 grams [0.5 mole] of ethyl bromide were added dropwise over a period of 15 minutes. The solution was then refluxed for two hours, allowed to stand overnight, and acidified with 58.5 ml. of concentrated HCl. After ether extraction, the acid was distilled as previously. Center cut taken at 131-5_{11mm}. This fraction was redistilled: 125-8_{12mm}. Neut. equiv. Calc. for $C_5H_{10}O_2S$ = 134.19; found, 129.5, 129.3. YIELD, 75 %.

β -Butylmercaptopropionic acid

[a] From sodium butyl mercaptide. Procedure followed was similar to that used in the preparation of the ethyl analog. Used 45.5 grams [0.5 mole] of butyl mercaptan. Reflux time: 1.5 hours, temperature: 99°. Acid layer separated immediately upon acidification. Center cut came over at 150-152.5_{8mm}. The crude acid represented a 94.5 % yield. Neut. equiv. Calc. for $C_7H_{14}O_2S$ = 162.24; found, 164.2, 164.5.

[b] From butyl bromide. Procedure similar to that used for the ethyl analog. Sixty-eight and one-half grams [0.5 mole] of butyl bromide were used. Reflux time: 1 hour, 40 minutes, temperature: 105°. Due to an error in stoichiometry, 116 ml. of concentrated HCl, twice the required amount, was used to acidify the reaction mixture. Center cut distilled at 150-9_{6mm}. Yield obtained: 99% [crude acid]. Neut. equiv. Calc. for $C_7H_{14}O_2S$ = 162.24; found, 159.8, 164.2, 165.0, 165.6.

SUMMARY OF PROPERTIES

The following table is a summary of the physical constants for the samples of β -ethylmercaptopropionic acid and β -butylmercaptopropionic acid which were obtained by this experimenter. The specific gravity measurements were made with a Sprengel type pycnometer. The values for the boiling point at 20 mm were obtained by graphical interpolation of a straight line graph representing the plot of $\log p$ versus $1/T$. The same thermometer was used throughout, no correction being applied. The observed boiling point of pure chlorobenzene as taken in the modified Cottrell apparatus was 130.3°C , as compared with the correct boiling point of 130.9°C . A Bausch and Lomb refractometer was used in making the refractive index measurements.

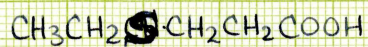
TABLE OF PHYSICAL MEASUREMENTS

OF THE SULFIDE ACIDS:

- I] β -Ethylmercaptopropionic acid
 II] β -Butylmercaptopropionic acid

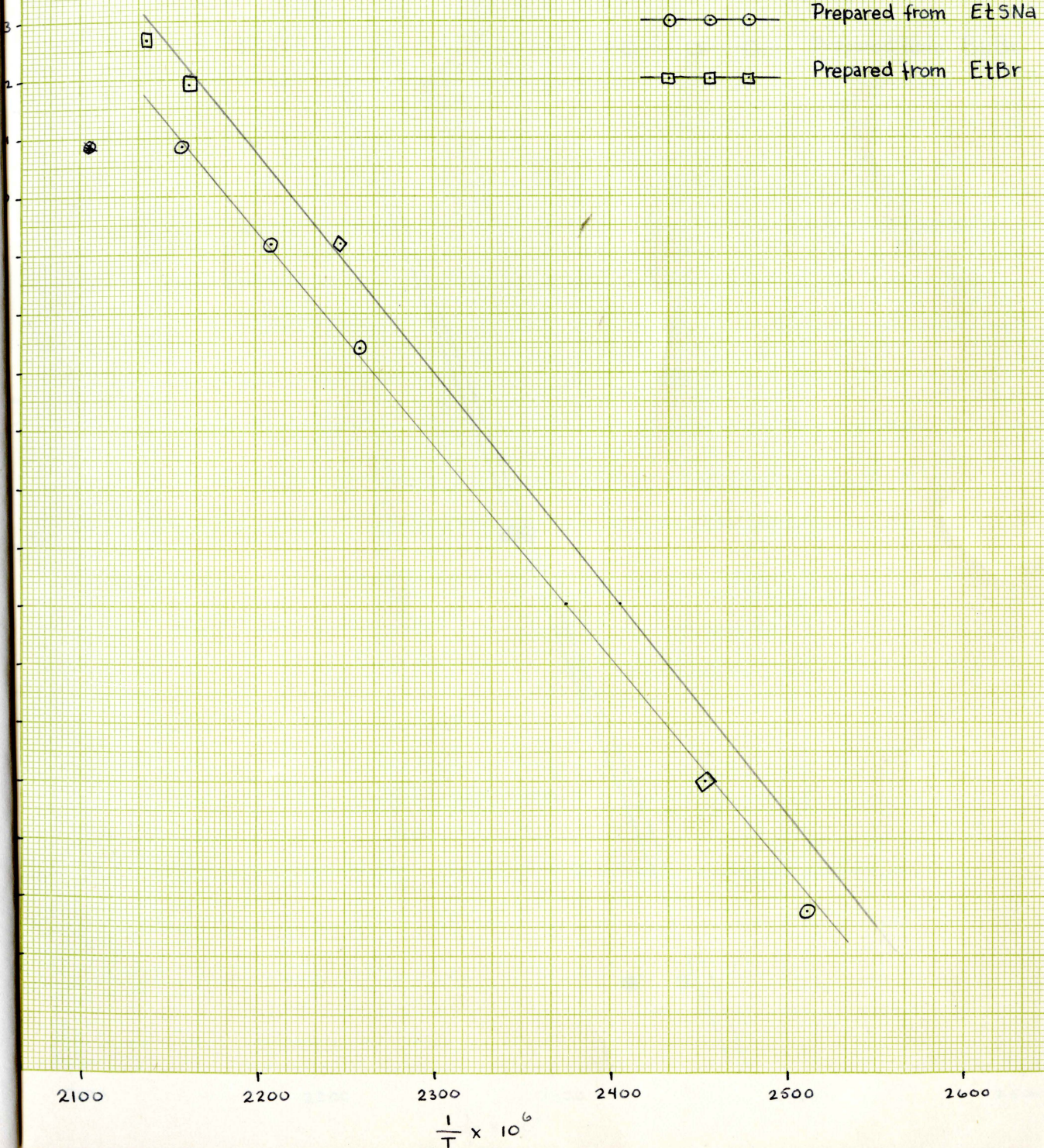
	β -[EtS]CH ₂ CH ₂ CO ₂ H		β -[BuS]CH ₂ CH ₂ CO ₂ H	
	IA <u>from EtSNa</u>	IB <u>from EtBr</u> [redistilled]	IIA <u>from BuSNa</u>	IIB <u>from BuBr</u>
sp. gr. 25/4	1.103 1.103 1.103	1.122 1.122 1.122	1.043 1.043 1.043	1.043 1.042 1.042
b.p. $^{\circ}\text{C}_{\text{mm}}$	149 ₂₀	143 ₂₀	169 ₂₀	168 ₂₀
n_{D}^{25}	1.4756 1.4757	1.4768 1.4766	1.4704 1.4707	1.4706 1.4709

HEAT OF VAPORIZATION CURVES
FOR
 β -[ETHYLMERCAPTO]-PROPIONIC ACID

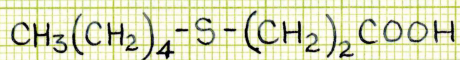


G. H. DENNY
May 6, 1950

○ ○ ○ Prepared from EtSNa
□ □ □ Prepared from EtBr



Heat of Vaporization Curves
for
 β -[Butylmercapto]-propionic acid



G.H. Denny
May 6, 1950

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□ — □ — □ — Prepared from BuBr

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DERIVATIVES

The usual method of amide preparation through the acid chloride failed with these two acids due to decomposition by thionyl chloride to a black, carbonaceous residue. The p-toluides and anilides were obtained in the form of unmanageable oils, except in the case of the p-toluide of the β -ethylmercaptopropionic acid from the ethyl bromide, which crystallized from the mother liquor in a crude form [mp 64-6°]. Attempts were made to prepare the p-bromophenacyl ester of the ethyl compound by refluxing the sodium salt with an alcoholic solution of p-bromophenacyl bromide [mp 109-10]. The reaction product, obtained as a fluffy yellow precipitate, was decolorized when crystallized from twice the required amount of hot methanol. A small sample of the white solid derivative was placed in an oven at 60° while still wet with methanol; it was absorbed by the plate. The main portion was dried over phosphoric anhydride. Melting points: 75-7; recrystallized from methanol, 77-9. These values were seen to be dangerously close to the corresponding values for the p-bromophenacyl ester of the butyl compound, which are: 77-8; recrystallized, 76.5-77.5. A mixed melting point gave the value, 74-5. Small portions of the alleged derivatives were boiled with 5 ml. of 2 N NaOH and lead acetate was added. Lead sulfide was not apparent in the precipitate. The results of the sodium fusion tests in both cases were: sulfur, positive; halogen, negative.

SUMMARY

β -Ethylmercaptopropionic acid and β -butylmercaptopropionic acid have each been prepared by two independent methods and their specific gravities, boiling points, and refractive indexes determined.

Lexington, Virginia

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