

C-alkylation, to form the intracyclic γ -lactone of the bi-annular, 3-hydroxy-1-carboxycyclobutane carboxylic ester. The four-membered hydrocarbon ring in this compound is very stable to heat and alkali, but is ruptured by boiling hydrochloric acid with saponification, to yield the dilactone of γ,δ -dihydroxypropylmalonic acid.

4. The relative stabilities of the rings in the lactone of 3-hydroxy-1-carboxycyclobutane carboxylic acid and the dilactone of γ,δ -dihydroxypropylmalonic acid toward heat, dilute and strong alkali, and mineral acid are opposed to the rela-

tions postulated from Baeyer's "Strain Theory."

5. It was not found possible to prepare an enolate of a δ -lactonic ester; the compounds examined polymerized spontaneously.

6. Malonic esters with different ester radicals have been prepared by effecting an interchange between one of the ester radicals and a chlorohydrin in the presence of hydrogen chloride. Experiments to prepare γ - and δ -lactonic esters from these compounds were successful only in the case of a γ -derivative.

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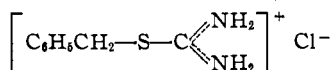
The Utilization of S-Benzyl Thiuronium Chloride for the Isolation and Identification of Organic Acids

BY JOHN J. DONLEAVY

The reaction of benzyl chloride upon thiocarbamide was first investigated by Bernthsen and Klinger¹ in 1879. Some years later Werner² again studied this reaction and obtained the reaction product in a state of purity for the first time. Werner established its composition and recorded a melting point of 172–174° for the pure salt. He observed, however, upon three occasions the formation of a low melting product (m. p. 146–148°) and as a result suggested it to be a possible case of dimorphism.

Taylor³ attempted to account for the existence of the two forms upon a structural basis but the original suggestion of Werner was shown to be the correct explanation by Lecher⁴ and his co-workers as the result of an extensive investigation.

Lecher named the product S-benzyl thiuronium chloride and assigned to it the structure



Following the work of Taylor and prior to the publications of Lecher, the writer was engaged in a study of the salts of benzyl pseudothiocarbamide with various carboxylic and sulfonic acids. The marked ease of formation and the well-defined crystalline nature of these salts suggested immediately their possible use in the isolation and

identification of the acids. An investigation was undertaken and a preliminary report made.⁵

While the work was still in progress Chambers and Scherer⁶ published a paper describing the benzyl pseudothiurea salts of some naphthalene sulfonic acids. In this paper, conspicuous for its lack of analytical data and reference to earlier workers in the field, they erroneously described the reaction of benzyl chloride upon thiourea with the evolution of hydrochloric acid. In order to correct this error and because of the current interest now manifested in this field the results of our investigation are here recorded.

S-benzyl thiuronium chloride is obtained in practically quantitative yields when benzyl chloride reacts upon thiourea. The following procedure is the best to employ.

Preparation of S-Benzyl Thiuronium Chloride.

—A mixture of 126 g. of benzyl chloride, 76 g. of thiourea and 200 cc. of alcohol is gently heated upon a reflux condenser for one-half hour. A vigorous reaction ensues and a homogeneous solution soon results. Upon cooling the product solidifies to a crystalline magma. The crude salt may be purified by recrystallization from alcohol or a mixture of one part of concentrated hydrochloric acid and one part of water. The pure salt melts at 172–174°. At times the lower melting form (146–148°) is obtained. This form may be

(1) A. Bernthsen and H. Klinger, *Ber.*, **12**, 574 (1879).

(2) E. A. Werner, *J. Chem. Soc.*, **57**, 285 (1890).

(3) J. Taylor, *ibid.*, **111**, 650 (1917).

(4) H. Lecher and C. Heuck, *Ann.*, **438**, 169 (1924); H. Lecher, *et al.*, *ibid.*, **445**, 35 (1925).

(5) Meeting of A. C. S., New Haven, April, 1923.

(6) R. F. Chambers and P. C. Scherer, *Ind. Eng. Chem.*, **16**, 1272 (1924).

converted readily into the higher melting form by dissolving it in alcohol and seeding with several crystals of the higher melting variety. This is not essential, however, since either form may be employed and will yield the identical thiuronium salt of any organic acid.

Anal. Calcd. for $C_8H_{11}N_2SCl$: N, 13.82; S, 15.80; halogen, 17.53. Found: N, 13.70–13.64; S, 15.80–15.86; halogen, 17.60–17.57.

The method of most general application for the preparation of S-benzyl thiuronium salts of organic acids from S-benzyl thiuronium chloride is briefly as follows.

A concentrated solution of the neutral sodium or potassium salt of the organic acid is prepared in aqueous alcohol or water. This solution is added rapidly with stirring to a slight excess of a 15% solution of S-benzyl thiuronium chloride in hot alcohol solution. Upon cooling the S-benzyl thiuronium salt of the organic acid usually crystallizes in a high state of purity. If necessary the salts may be recrystallized from ethyl alcohol. In a few cases it was necessary to evaporate the solvent in order to obtain the crystalline product. This was the case with the salts of the aliphatic hydroxy acids.

It is, of course, necessary to bear in mind that since many organic acids are very weak, hydrolysis of the salts readily occurs. This can be avoided, however, by employing to a large extent non-aqueous media. When dealing with strong acids such as the sulfonic acids, aqueous media can be used and are to be preferred.

The method has been very successfully and extensively employed in this Laboratory and has been utilized by Anderson⁷ in the biochemical field.

The advantages of the method are: (1) the ease of preparation of the reagent; (2) the rapidity of the operation; (3) the ease of recovery of the acids; (4) the well-defined physical properties of the salts which make identification, isolation, analysis, etc., most convenient.

The disadvantages are: (1) the melting points of the fatty acid salts do not exhibit as wide a range as desired. The use of mixed melting points, however, readily obviates this difficulty as shown by actual experiment. (2) Careless manipulation leads to hydrolysis of the salts. The free base then decomposes rapidly, yielding benzyl

mercaptan which possesses disagreeable properties. This disadvantage, however, is entirely obviated by proper use of solvents, etc.

Acid used	M. p., corr. °C.	Nitrogen Calcd.	(Kjeldahl) Found
1 Formic	146	13.20	13.10
2 Acetic	134	12.96	12.63
3 Propionic	148	11.66	11.48
4 <i>n</i> -Butyric	146	11.02	10.96
5 Isobutyric	143	11.02	11.12
6 Isovaleric	153	10.44	10.38
7 Lauric	141	7.65	7.73
8 Myristic	139	7.10	6.98
9 Palmitic	141	6.63	6.75
10 Stearic	143	6.22	6.15
11 Oxalic	193	13.27	12.95
12 Succinic	149	11.56	11.60
(2H ₂ O)			
13 Maleic (acid salt)	163	9.92	10.18
14 Fumaric	178	12.50	12.32
15 Crotonic	162	11.11	11.18
16 Glycolic	141	11.57	11.50
17 Lactic	153	10.93	10.98
18 Diglycolic	154	12.01	12.10
19 Benzoic	166	9.72	9.80
20 <i>o</i> -Nitrobenzoic	159	12.61	12.48
21 <i>m</i> -Nitrobenzoic	163	12.61	12.70
22 <i>p</i> -Nitrobenzoic	182	12.61	12.57
23 <i>o</i> -Aminobenzoic	142	13.86	13.70
24 <i>m</i> -Aminobenzoic	149	13.86	13.78
25 <i>p</i> -Aminobenzoic	166	13.86	13.73
26 <i>o</i> -Toluic	140	9.27	9.20
27 <i>m</i> -Toluic	164	9.27	9.33
28 <i>p</i> -Toluic	190	9.27	9.26
29 <i>o</i> -Hydroxybenzoic	146	9.21	9.40
30 <i>m</i> -Chlorobenzoic	155	8.68	8.72
31 <i>m</i> -Bromobenzoic	168	7.62	7.73
32 <i>p</i> -Methoxybenzoic	177	8.80	8.86
33 Phthalic	151	11.21	11.24
34 Cinnamic	175	8.91	9.00
35 Mandelic	166	8.80	8.86
36 Diphenylacetic	145	7.40	7.46
37 Benzene sulfonic	144	8.64	8.50
38 <i>m</i> -Nitrobenzene sulfonic	140	11.40	11.35
39 <i>p</i> -Toluene sulfonic	178	8.28	8.40

Summary

1. A method has been described for the preparation of the S-benzyl thiuronium salts of organic acids.

2. The use of these salts for the isolation and identification of organic acids has been outlined.

3. A series of salts have been prepared and their melting points recorded.

The writer is still engaged in the study of similar salts for the identification of acids of all types.

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(7) R. J. Anderson, *J. Biol. Chem.*, **74**, 548 (1927).