ACTA CHEMICA SCANDINAVICA 8 (1954) 427—435

S-Benzylthiuronium Derivatives

Determination by Titration with Perchloric Acid, and some Comments on the Melting Points

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Titration in non-aqueous solution can be widely used in the identification of organic compounds. We have shown, in a previous paper [1], that xanthogenates can be titrated with perchloric acid in glacial acetic acid solution, and it has now been proved that S-benzylthiuronium derivatives of carboxylic acids can be determined in the same way.

In the determination of the equivalent weight of an acid, which may be found in the form of ester, salt, amide, nitrile or other compound, the S-benzylthiuronium derivative is easily prepared, and the nitrogen content of the derivative is determined by the Kjeldahl method as proposed by Veibel [2]. This procedure is extensively used for carboxylic acids, which are easily soluble in water and therefore difficult to isolate in the pure state from aqueous medium.

In our method the S-benzylthiuronium salt is dissolved in glacial acetic acid and titrated directly with perchloric acid in the same solvent. The titration may be carried out in the course of a few minutes, and the end-point determined either visually or potentiometrically. The reaction is represented as follows:

$$HClO_4 + CH_3COOH \longrightarrow CH_3COOH_2^+ + ClO_4^-$$

$$C_6H_5CH_2-S-C(=NH_2^+)-NH_2 \, , \, {}^-OOCR + CH_3COOH_2^+ \longrightarrow C_6H_5CH_2-S-C(=NH_2^+)-NH_2 + RCOOH + CH_3COOH$$

The S-benzylthiuronium salts have also been used in isolating carboxylic acids from natural products and from reaction mixtures, since they are easily and quickly prepared.

Fig. 1. shows the potentiometric titration curves for two derivatives. In the visual titration crystal violet is used as indicator, and the colour changes of

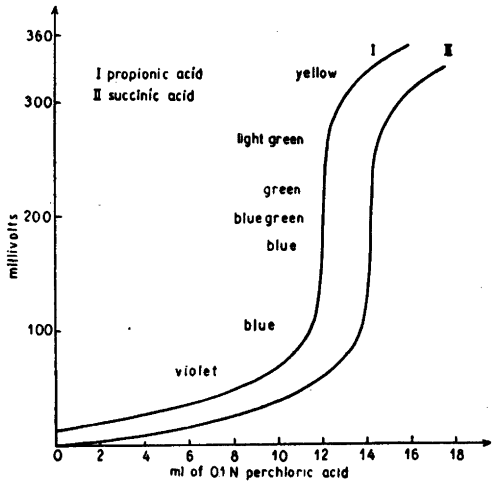


Fig. 1. Potentiometric titration curves of S-benzylthiuronium propionate and S-benzylthiuronium succinate, and colour changes of the indicator (crystal violet) during the titration.

crystal violet during the titration are given in the same figure. The greatest potential break appears at the colour change from blue to blue-green.

Some of the S-benzylthiuronium salts contain water of crystallization, which can interfere in the titration, since a water content in the medium gives fading end-points. However, it has been found that this slight increase of the water content in the solvent has no influence, and Fig. 1 shows that the titration curves for the propionic acid salt (anhydrous) and the succinic acid salt (2 molecules of water) are almost identical.

The water of crystallization in the S-benzylthiuronium salts may be determined by the Karl Fischer method. The modification proposed by Johansson [3] is used.

EXPERIMENTAL

Preparation of the S-benzylthiuronium salts. The derivatives are prepared according to Vogel [4] p. 359; this procedure is a modification of that given by Veibel and Lillelund [5], Veibel and Ottung [6] and by Donleavy [7].

Titration of the S-benzylthiuronium salts of carboxylic acids. Reagents used: Glacial acetic acid, not less than 99.7 % CH_3COOH. 0.1 *N* perchloric acid in glacial acetic acid. Crystal violet indicator, 0.5 g crystal violet dissolved in 100 ml glacial acetic acid. The 0.1 *N* perchloric acid is prepared and standardized according to Markunas and Riddick [8], except that we have adjusted the water content by the Karl Fischer method to between 0.02 and 0.05 %.

Procedure: 0.100—0.300 g of the derivative is dissolved in 15—20 ml glacial acetic acid. 2 drops of crystal violet indicator are added and the solution is titrated with 0.1 *N* perchloric acid to a blue-green colour. The subsequent colour of the solution will be green, and only about 0.02 ml 0.1 *N* perchloric acid is required to produce the colour change from blue-green to green. Sometimes the S-benzylthiuronium perchlorate is precipitated but this does not interfere with the titration. The results of the visual titration are given in Table 1 and indicate that the method is accurate.

The potentiometric titration is carried out using a calomel electrode, fibre type, as reference and a glass electrode connected to a potentiometer (Radiometer, pH-meter 3).

When calculating the equivalent weight by means of the S-benzylthiuronium salt, it should be remembered that some salts contain water of crystallization.

Table 1. Analysis of S-benzylthiuronium derivatives of carboxylic acids by titration with perchloric acid.

Acid	Amount g	ml $HClO_4$ 0.1000 *N*	Equivalent weight		Deviation %
			calc.	found	
Formic	0.2647	12.37	212.3	214.0	0.8
Acetic	0.2286	9.30	244.3 [a]	245.8	0.6
Propionic	0.2039	8.50	240.3	239.9	0.2
n-Butyric	0.0924	3.62	254.3	255.2	0.4
*Iso*butyric	0.2397	9.43	254.3	254.2	—
n-Valeric	0.3466	12.90	268.4	268.7	0.1
*Iso*valeric	0.2537	9.48	268.4	267.6	0.3
n-Caproic	0.3131	11.07	282.4	282.8	0.1
n-Caprylic	0.4537	14.60	310.5	310.8	0.1
Monochloroacetic	0.2225	8.57	260.7	259.6	0.4
Trichloroacetic	0.3907	11.80	329.6	331.1	0.5
Oxalic	0.2422	11.40	211.3	212.5	0.6
Succinic	0.2825	11.56	243.3 [b]	244.4	0.5
Adipic monosalt	0.4230	13.44	312.4	314.7	0.7
Adipic disalt	0.2856	11.91	239.3	239.8	0.2
Sebacic	0.5075	18.91	267.4	268.4	0.4

[a] The derivative contains one molecule of water of crystallization.
[b] The derivative contains two molecules of water of crystallization.

S-*p*-chloro-[9], S-*p*-bromo[10]- and S-*p*-nitrobenzylthiuronium salts may also be used in the identification of carboxylic acids, and we have found that these derivatives also can be titrated by the method described.

S-benzylthiuronium salts of sulfonic acids. The sulfonic acids are also characterized through their S-benzylthiuronium salts [5,7,11], and we have prepared the derivative of benzene-, *p*-toluene- and β-naphthalenesulfonic acid, but none of these can be titrated with perchloric acid. This must be due to the fact that the sulfonic acids are highly ionized in glacial acetic acid, as pointed out by Hantzsch and Langbein [12]. Trichloroacetic acid, which has approximately the same acid strength in aqueous solution as benzenesulfonic acid, gives a salt which is readily titrated.

Titration of other types of thiuronium compounds. In the identification of alkylhalides the S-alkylthiuronium picrates are used and it has been found, that they may be accurately titrated in glacial acetic acid solution, and in this way the equivalent weight of unknown halides can be determined indirectly. The titration is carried out as described for the S-benzylthiuronium salts of carboxylic acids. As proposed by Veibel [12], the picrate itself can be used as an indicator when titrating visually, due to the colour change of the solution from yellow to colourless, when all the picrate ions are converted to picric acid.

COMMENTS ON THE PREPARATION OF THE DERIVATIVES

It is well known that it is important not to allow the reaction mixture to become appreciably alkaline, since the free S-benzylthiuronium base then decomposes rapidly yielding benzyl mercaptan. In order to prevent this decomposition the carboxylic acid should only be partially neutralized [5,6]. This is accomplished by adding alkali to the colour change of *methyl red*. Donleavy [7], however, states that the neutral sodium or potassium salt of the organic acid should be used, *e. g.* neutralization using *phenolphthalein* and then addition of hydrochloric acid until the colour of the indicator disappears.

We have tried both procedures, and our experiments show that these methods are equally well applicable, except in the preparation of the adipic acid derivative.

Adipic acid can give derivatives with either one mole or two moles of S-benzylthiuronium chloride. On using methyl red in the neutralization a derivative consisting of a mixture of the monosalt and the disalt was precipitated. A pure disalt was produced when using phenolphthalein as the indicator, while the pure monosalt could be prepared by addition of S-benzylthiuronium chloride to an exactly half-neutralized adipic acid.

COMMENTS ON THE MELTING POINTS OF THE DERIVATIVES

The derivatives of carboxylic acids. The melting points of the S-benzylthiuronium salts recorded in the literature show large deviations. In order to explain these discrepancies we have carried out experiments on some of the factors which can influence the determination. Melting points from our experiments and from the literature are listed in Table 2. It is seen that there are great differences between the melting points found by Veibel *et al.*[5,6] and by Donleavy [7]. Melting points for the S-*p*-chloro- and the S-*p*-bromobenzylthiuronium salts are also given in the table in order to demonstrate the small dispersion in the melting points for all types of S-benzylthiuronium salts.

Our melting points were determined by the capillary tube method. An electrically-heated paraffin bath with mechanical stirrer [22] was used, so that the rate of heating could be accurately regulated. Only the temperature at which the compound melts completely is registered.

First we investigated the position of the melting point when the temperature of the heating-bath was previously raised to within 15° C of the melting point, before introducing the substance, and secondly the melting point was determined when the capillary tube was inserted in the heating-bath at room temperature. In both cases the same melting point was registered, when the rate of heating was constant.

Table 2. Melting points of some S-benzylthiuronium derivatives.

Acid	S-benzylthiuronium salt				S-*p*-chloro-benzyl-[9]	S-*p*-bromo-benzyl-[10]
	Own results [a]	Veibel *et al.* [5,6]	Donleavy [7]	Other authors		
Formic	152° C	150—151°C	146° C	150—151 °C[14]	148°C	148°C
Acetic	136	135—136	134	143—144[14],136—138[15] 135—136[16,17],146—147[18]	140	149
Propionic	153	151—152	148	—	143	146
n-Butyric	150	—	146	—	139	142
*Iso*butyric	150	—	143	—	—	—
n-Valeric	156	—	—	—	142	146
*Iso*valeric	159	—	153	—	148	138
n-Caproic	157	—	—	154—155[18]	143	146
n-Caprylic	157	—	—	—	—	147
Monochloro-acetic	160	159—160	—	156[16]	158	154
Trichloro-acetic	149	148—149	—	150[16]	148	146
Oxalic	198	195—196; 203	193	199—200[14],191—192[16]	194	194
Succinic	154	154—155	149	153[19],145—146[20]	167	167
Adipic monosalt	164	—	—	—	—	—
Adipic disalt	163	—	—	159 [b]	—	—
Sebacic	155	—	—	—	—	—

a) All our m.p. are corrected and determined by the capillary tube method; rate of heating: 4° C per minute.

b) The melting point of the adipic acid derivative is given by Smith and Jones [21] and as it is prepared according to Donleavy [7] one must expect it to be the disalt.

Next we altered the rate of heating for the last 15° C below the melting point, and this proved to be of great significance. Rates of heating of 1° C per minute and 4° C per minute were used. We observed that there was a difference of up to 9° C between the melting points found for the same sample, when heating at 1° C/min and at 4° C/min. The results are shown in Table 3. For all the examples given there was a deviation of several degrees when the rate of heating was varied.

The discordant values for the melting points given by Veibel *et al.*[5,6] and Donleavy [7] can be explained from what has been mentioned above. On com-

Table 3. Melting points of some S-benzylthiuronium derivatives. Dependence on the rate of heating.

Acid	Rate of heating *		Deviation
	1° C/min	4° C/min.	
Formic	147° C	152° C	5° C
Acetic	131	136	5
Propionic	146	153	7
n-Butyric	144	150	6
*Iso*butyric	143	150	7
n-Valeric	149	156	7
*Iso*valeric	151	159	8
n-Caproic	150	157	7
n-Caprylic	150	157	7
Monochloroacetic	151	160	9
Trichloroacetic	142	149	7
Oxalic	193	199	6
Succinic	147	154	7
Adipic monosalt	157	164	7
Adipic disalt	154	163	9
Sebacic	148	155	7
Benzenesulfonic	149	149	0
p-Toluenesulfonic	183	183	0
β-Naphthalene-sulfonic	192	192	0

* In determining the melting points given in the table, the temperature of the paraffin bath was raised to within 15° C of the melting point before introducing the capillary tube.

paring the results in Table 2 and our results in Table 3 it appears that Donleavy probably used a slower rate of heating than Veibel *et al.* The melting points found by us (rate of heating: 4° C per minute) are in excellent accordance with those given by Veibel *et al.*

The explanation of the fact that the melting points are highly dependent on the rate of heating must be that these salts undergo destruction around the melting point. This is accompanied by an evolution of gas by most of the salts. Probably this destruction commences below the true melting point, when the temperature of the bath is raised too slowly. Thus the derivative

becomes contaminated with its own destruction products and the melting point will naturally be depressed.

It has not been emphasized previously that the melting points are *highly* dependent on the rate of heating. Vogel [4 p. 360] has pointed out that there is several degrees difference in the melting point of a S-benzylthiuronium salt determined on the hot stage and in a paraffin bath, and Kass *et al.*[23] have mentioned that the S-benzylthiuronium derivatives of octadecenoic acids cannot be used due to similarity of melting points and dependence of the melting point on rate of heating.

An attempt was made to use the Kofler "Heizbank" but this apparatus cannot be employed for these derivatives.

The conclusion must be that it is essential to use an apparatus which affords an accurate regulation of the rate of heating, and for the reasons stated above we prefer a rate of heating of 4° C per minute. Furthermore, we wish to stress that it is important to analyse the derivatives, since the melting points cannot always be used in the identification due to similarity.

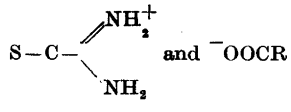
The derivatives of sulfonic acids. The melting points of three sulfonic acids salts are recorded in Table 3, and it is seen that the melting points for this type of S-benzylthiuronium salts do not show any dependence on the rate of heating. The melting point is sharp and these derivatives are valuable for the characterization of sulfonic acids. It has also been found that the Kofler "Heizbank" may be used in the determination.

However, if the sulfonic acid contains other functional groups, *e. g.* sulfanilic acid, it has been found that there is a dependence on the rate of heating.

The derivatives of adipic acid. There is only a very small difference in the melting points of the disalt and the monosalt prepared from adipic acid (Table 2) and furthermore, it has been found that a mixture of the two salts showed no depression of the melting point. According to this it is impossible to deduce the composition of a adipic acid derivative on the basis of the melting point.

In order to confirm that the mixed derivative which was prepared from adipic acid using methyl red as indicator in the neutralization really was a mixture of the monosalt and the disalt, such as the titration with perchloric acid had shown, an X-ray analysis was carried out. This confirmed that it was a mechanical mixture of the two salts.

The similarity of the melting points of the two salts of adipic acid and of their mixture must be explained on the basis of the fact that the melting points of the substituted and the unsubstituted S-benzylthiuronium salts of the carboxylic acids given in Table 2 cover only a small range of temperature. This suggests, as pointed out by Walker [24] that "the forces which bind crystals of this type together are comparable in strength throughout the series of carboxylic acids and that the radicals attached to the two groups



respectively make little or no contribution to the stability of the crystal."

On basis on this explanation one would expect that other derivatives of this type will show melting points which are not well dispersed. We have prepared the S-*p*-nitrobenzylthiuronium derivatives of propionic, *n*-butyric, *iso*butyric, *n*-valeric and *iso*valeric acid and the melting points were 139° C, 137° C, 137° C, 144° C and 137° C respectively (rate of heating: 4° C/min.).

The S-*p*-nitrobenzylthiuronium chloride and the derivatives were prepared according to Rupe and Zweidler [25]. Our derivatives were analyzed by titration with perchloric acid and the observed results agreed with the theoretical values within 0.5 %. These derivatives have no advantage over the other S-benzylthiuronium salts, and furthermore we have observed that they are sensitive to light.

Although the melting points of S-benzylthiuronium salts show a poor dispersion and are strongly dependent on the rate of heating, they have the advantage that they are very easily prepared and, furthermore, it has now been shown that the equivalent weight is readily determined by titration. Therefore, one must expect that they still will be used in the identification of carboxylic acids.

SUMMARY

It is shown that the S-benzylthiuronium salts of carboxylic acids can be accurately titrated with perchloric acid in glacial acetic acid solution. The titration can be carried out either potentiometrically or visually using crystal violet as an indicator.

The method described is recommended for the determination of the equivalent weight of carboxylic acids which are difficult to isolate as pure compounds.

Some of the derivatives contain water of crystallization which is determined according to Karl Fischer.

The derivatives of sulfonic acids are practically neutral in acetic acid solution and cannot be titrated by the method described.

S-alkylthiuronium picrates prepared from aliphatic halides are also titrated with perchloric acid. The equivalent weight of the halide can thus be determined indirectly.

Melting points of nineteen S-benzylthiuronium derivatives, some of which have not previously been recorded in the literature, are given.

A survey of the literature shows that there are disagreements concerning the melting points given for the S-benzylthiuronium salts of carboxylic acids. It is shown that the reason for this is that the melting points are extremely dependent on the rate of heating.

The S-*p*-nitrobenzylthiuronium salts of some aliphatic carboxylic acids have been prepared, but these derivatives appear to have no advantage over other S-benzylthiuronium salts.

The author is greatly indebted to the head of the department, Professor, dr. H. Baggesgaard Rasmussen, for valuable advice and criticism during the work.

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Received December 18, 1953.