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The Identification of Organic Compounds

IV. S-Benzylthiuronium Derivatives of Some Dicarboxylic Acids

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Eleven mono- and two di-S-benzylthiuronium salts of dicarboxylic acids are described. The monosalts of oxalic acid and of succinic acid previously described by Chabrier [2] are shown to be disalts. S-Benzylthiuronium derivatives of several dicarboxylic acids are found to crystallise with variable amounts of water of crystallisation and it is not always possible to obtain a derivative with a well-defined composition.

Mixed melting point test has been shown to be of no value in identifying S-benzylthiuronium derivatives.

In a previous paper [1] it was reported that maleic acid forms both a mono- and a di-S-benzylthiuronium salt. It has now been found that some other dicarboxylic acids also form mono- and disalts. The data are given in Table 1.

Charbrier [2] stated that oxalic acid and succinic acid give monosalts upon addition of S-benzylthiuronium chloride to a half-neutralised solution of the acid. We now find this to be incorrect. The precipitates give analytical values corresponding to nearly pure (*ca.* 98 %) di-S-benzylthiuronium oxalate and di-S-benzylthiuronium succinate dihydrate, respectively, identical with those previously described by Berger.[3] Pure monosalts could not be prepared. No analytical data are given by Chabier.[2] The melting points found are about twenty degrees lower than the values given by Chabrier. We are, however, able to reproduce the higher melting points reported by Chabrier for the "monosalts" by using another technique ("Kofler Heizbank").

The disalt of ethylmalonic acid is described as a dihydrate, m.p. 120—121°.[4] It has not been possible, however, to obtain a disalt with a well-defined amount of water of crystallisation even after recrystallisation. The salt cannot be dried without decomposition. The melting point found is in accordance with the literature value. The water content varied from *ca.* 1.7 % to *ca.* 4 % in several preparations (corresponding to 0.5—1.05 molecules of water of crystallisation). The same difficulties arose in the preparation of the monosalt of ethylmalonic acid, not previously described. We found two melting points

Table 1. Melting points and analyses of some new S-benzylthiuronium derivatives.

Acid	Salt	m.p. °C	Formula	% C		% H		Ethanol added to reaction mixture, ml	Equiv. wt. (0.1 N $HClO_4$)		Recrystallisation solvent
				calc.	found	calc.	found		calc.	found	
Benzylidene malonic	mono-	134 decomp.	$C_{18}H_{18}N_2O_4S$	60.33	60.06	5.06	5.03	5	358.4	359.3	decomp.
Benzylidene malonic	di-	148 decomp.	$C_{26}H_{28}N_4O_4S_2$	59.53	59.75	5.38	5.49	0	262.3	261.0	ethanol
Benzylmalonic	mono-	145 decomp.	$C_{18}H_{20}N_2O_4S$	59.99	59.91	5.59	5.61	5	360.4	359.7	ethanol
(+)-Camphoric	mono-	158 decomp.	$C_{18}H_{26}N_2O_4S$	58.99	59.07	7.15	7.23	5	366.5	368.7	ethanol (20 %)
Cinnamylidene malonic	mono-	163 decomp.[a]	$C_{20}H_{20}N_2O_4S$	62.48	62.66	5.24	5.34	30	384.4	382.4	ethanol (20 %)
Cinnamylidene malonic	di- (dihydrate)	125 and 135 decomp.[b]	$C_{28}H_{30}N_4O_4S_2$, $2H_2O$	57.32	57.37	5.84	5.94	10	293.4	291.4[c]	decomp.
Citraconic	mono-	158	$C_{13}H_{16}N_2O_4S$	52.69	52.95	5.44	5.50	0	296.3	296.9	ethanol
Ethylmalonic	mono-	99 (cf. text)	$C_{13}H_{18}N_2O_4S$	52.34	52.49	6.08	6.18	0	298.4	298.5	water
Itaconic	mono-	131	$C_{13}H_{16}N_2O_4S$	52.69	52.71	5.44	5.35	0	296.3	297.6	decomp.
5-Nitroisophthalic	mono- (monohydrate)	205 decomp.[d]	$C_{16}H_{15}N_3O_6S$, $1H_2O$	48.60	48.48	4.33	4.24	5	395.4	393.8[e]	ethanol (50 %)
Phthalic	mono-	157 [f]	$C_{16}H_{16}N_2O_4S$	57.81	57.82	4.85	4.94	0	332.4	331.9	ethanol (30 %)
Pimelic	mono-	151	$C_{15}H_{22}N_2O_4S$	55.20	55.37	6.79	6.94	0	326.4	324.7	decomp.
Suberic	mono-	170	$C_{16}H_{24}N_2O_4S$	56.44	56.66	7.11	7.05	5	340.4	340.1	ethanol

a) M.p. (lit.[2]) 153°. *b*) Depending on the temperature at which the capillary tube is introduced into the bath. *c*) % water calc. 6.14, found 6.13 (Karl Fischer-titration). *d*) Capillary tube introduced at 90°. *e*) % water calc. 4.56, found 4.62 (Karl Fischer-titration). *f*) M.p. (lit.[2]) 152°.

for the monosalt. After melting at 79° it resolidifies and melts again at 91°. This is probably not due to polymorphism but more likely to a small amount of water of crystallisation. After drying for one hour at 75° an anhydrous salt is obtained and the m.p. is now 99°.

The monosalt of cinnamylidene malonic acid has been described by Chabrier [2] but no analytical data are given. These are included in Table 1. The precipitate always contained water of crystallisation (from *ca.* 0.6 % to *ca.* 2.5 %). An anhydrous salt was obtained by recrystallisation from ethanol (20 %).

The disalt of cinnamylidene malonic acid is very difficult to prepare in a pure state, partly because it crystallises with a varying amount of water of crystallisation (from 0 % to *ca.* 9 %). It must be emphasised that although we have obtained both an anhydrous salt and a pure dihydrate in our experiments we cannot give a procedure which always leads to a salt with a well-defined composition. The disalt hence cannot be recommended as a suitable derivative.

The disalt of citraconic acid also crystallised with varying amounts of water (*ca.* 1.9 % to *ca.* 4.0 %). No procedure can be given for preparation of an anhydrous disalt. The same applies to the disalts of itaconic acid and of 5-nitroisophthalic acid.

The monosalt of phthalic acid has been prepared by Chabrier [2] but no analytical data are given. Our values are included in Table 1.

Attempts to prepare monosalts from acetylenedicarboxylic acid, azelaic acid, sebasic acid and tetrachlorophthalic acid failed. A mixture containing mono- and disalt was obtained. No precipitate was formed in an attempt to prepare the monosalts from glutaric acid, (±)-tartaric acid and (±)-malic acid by the standard procedure.

Details about the solvents of recrystallisation are given in Table 1. Some of the derivatives could not be recrystallised to give a pure salt. This is indicated in Table 1 as "decomp". The data are therefore obtained on the crude product.

Disalts of some of the acids in Table 1 have already been described in the literature and are not included in this investigation.

MIXED MELTING POINT AS IDENTITY TEST

The identity of an S-benzylthiuronium salt is often confirmed by a mixed melting point test with an authentic sample. The following experiments have shown that one cannot rely on this test.

The S-benzylthiuronium derivatives of the following fatty acids all exhibit a melting point within the range 150—160°: *1.* Propionic acid (melting range of derivative 152—153°), *2.* butyric acid (151—152°), *3.* isobutyric acid (150—151°), *4.* valeric acid (154—155°) and *5.* isovaleric acid (158—160°). Approximately equal amounts of two derivatives were intimately mixed and the melting range of the mixture was determined in a silicone bath. The capillary tube was introduced at 135° and the rate of heating was 4°/min.

The results of the test are shown in Table 2. Only a very small depression is observed. Furthermore, it has previously been shown [1,3] that the melting

Table 2. Mixed melting point test for some S-benzylthiuronium derivatives. The first value of the melting range is the temperature at which liquid appears and the second indicates complete melting.

Derivatives mixed (Nos. 1, 2, 3, 4, 5. *cf.* above)	Melting range of the mixture °C	Melting range of the lowest melting compound °C
1 + 2	147.5 – 149.5	151 – 152
1 + 3	145.5 – 147.5	150 – 151
1 + 4	145.5 – 147.5	152 – 153
1 + 5	147 – 149	152 – 153
2 + 3	148 – 150	150 – 151
2 + 4	150.5 – 152.5	151 – 152
2 + 5	149 – 152.5	151 – 152
3 + 4	145 – 147.5	150 – 151
3 + 5	149.5 – 152	150 – 151
4 + 5	152 – 154.5	154 – 155

point of an S-benzylthiuronium salt is highly dependent on the rate of heating and also dependent on the temperature at which the capillary tube is introduced into the bath.

It must be concluded that such a test does not provide good evidence for the identity of two S-benzylthiuronium derivatives.

EXPERIMENTAL

The melting points (corrected) were determined in an electrically heated silicone bath.[3] Rate of heating: 4°/min. The capillary tube was introduced when the temperature of the bath was about 15 degrees lower than the expected melting point of the derivative. This is of outmost importance for reproducibility.[1]

The *monosalts* were prepared as previously described for S-benzylthiuronium hydrogen maleate. [1,p.1812]. The disalts are prepared as described for di-S-benzylthiuronium maleate. [1,p.1812] 0.005 mole and 0.025 mole of the acid have been used in the preparation of monosalts and disalts, respectively. As indicated in Table 1 ethanol has often been added to the reaction mixture. This is done in order to obtain a clear solution before the reagent is added.

The equivalent weight was determined by titration with perchloric acid in glacial acetic acid.[3]

The microanalyses have been performed by Mr. A. Bernhardt, Max-Planck-Institut, Mülheim, Germany.

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