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Studies of Thioacids and Their Derivatives

II. Carboxymethyl Dithioesters

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As intermediates for the preparation of thiohydrazides a number of new carboxymethyl dithioates have been synthesized. Three different routes to these compounds have been studied in detail: I. The reaction between chloroacetic acid and crude dithioacids, prepared by the Grignard reaction. II. The reaction between chloroacetic acid and crude dithioacids, prepared from aldehydes and ammonium polysulfide. III. Thiohydrolysis of *S*-carboxymethylthiopiperididium bromides, prepared from thiopiperidides and bromoacetic acid. Methods I and II are essential in special cases, but Method III is more generally applicable, and the yields obtained by this method are much higher than those obtained by Methods I and II (*cf.* Table 1).

In the synthesis of thiohydrazides carboxymethyl dithioates have proved to be very suitable starting materials. Apart from being good thioacylating agents these compounds have the advantage over ordinary dithioesters of being crystalline solids forming water-soluble sodium salts. Two of these compounds, *viz.* carboxymethyl dithiobenzoate and dithiophenylacetate, were prepared by Holmberg [1] and Kjær [2,3]. Both authors have shown that these compounds are powerful thioacylating agents [2–5].

For the preparation of the carboxymethyl dithioesters we used three methods of which a description is given in the following.

Method I. According to this method the magnesium halide salts of dithioacids were prepared by the well-known reaction of Grignard compounds with carbon disulfide [6–9] and were subsequently esterified with chloroacetic acid,

$$RMgX + CS_2 \longrightarrow RCSSMgX \xrightarrow{ClCH_2COONa} RCSSCH_2COONa$$

Using this procedure, Kjær [2,3] obtained good yields of carboxymethyl dithiobenzoate * and dithiophenylacetate. We have applied the method to the pre-

* The first of these compounds has been prepared almost a hundred times by different workers in this laboratory, but it has not been possible again to obtain the yield given by Kjær; generally 50–55 g instead of 77 g, *i.e.* 36–40 % instead of 56 % is obtained, and often the yield is much lower. Several experiments have been carried out to find the cause of this discrepancy, but without positive result. It can only be said that the lower the yields are, the more is formed of an insoluble by-product. The conditions given by Kjær are not very critical, and it seems to be unnecessary to use a nitrogen atmosphere and "reversed addition".

paration of several carboxymethyl dithioesters with varying yields (Table 1). In addition to the compounds listed in Table 1, we have without success tried to prepare carboxymethyl esters of the following dithioacids: dithiopropionic acid (even authentic dithiopropionic acid did not give the expected carboxymethyl ester on reaction with sodium chloroacetate), dithiopivalic acid, β-phenyldithiopropionic acid, 8-quinolinedithiocarboxylic acid, 3-pyridinedithiocarboxylic acid and α-thiophenedithiocarboxylic acid. The lack of success in the first three cases is in accord with the low yields generally obtained in the preparation of aliphatic dithioacids from Grignard compounds [9]. The lack of success in the last case is remarkable because α-thiophenedithiocarboxylic acid is obtained in good yield by method II.

Aromatic dithioacids may also be prepared from trichlorocompounds, *e.g.* Holmberg [1] prepared carboxymethyl dithiobenzoate from benzotrichloride. This method may also be used to prepare certain heterocyclic dithioacids, *e.g.* König *et al.*[10] prepared dithio*iso*nicotinic acid in this way. Furthermore potassium dithioformate has been prepared from chloroform [11], but we were unable to prepare dithioacetic acid from 1,1,1-trichloroethane. Potassium dithioformate reacts with sodium chloroacetate with formation of a compound having the composition of carboxymethyl dithioformate, but it is colourless and does not show any thioacylating properties. It is possibly a trimeric compound [12].

Method II. According to this method the dithioacids were prepared from aldehydes by reaction with ammonium polysulfide, the esterification being performed as above:

$$RCHO \xrightarrow{(NH_4)_2S_x} RCSSH \xrightarrow{ClCH_2COONa} RCSSCH_2COOH$$

For the preparation of the dithioacids we followed the directions given by Bost and Shealey [13], but since we did not extract the dithioacids from the resinous material produced in the course of the reaction, we generally got lower yields than these authors. This method has the advantage of being fast and convenient, but the yields are rather low and they are very dependent on the structure of the aldehyde used. The best results are obtained with aromatic hydroxyaldehydes and non-nitrogenous heterocyclic aldehydes. The method is especially valuable for the preparation of dithioesters derived from thiophene carboxaldehyde, furfural, salicylaldehyde, and *p*-hydroxybenzaldehyde. *o*-Methoxybenzaldehyde gave nothing, and anisaldehyde only 3—4 % of a product which was difficult to purify. *o*-Chlorobenzaldehyde gave only a trace of the dithioester, the *m*- and *p*-compound 3—4 %. The last two compounds could, however, be obtained in excellent yields by method III, but this method also failed with the *o*-compound. Bruni and Levi [14] report on the preparation of dithiocinnamic acid from cinnamic aldehyde and ammonium polysulfide, but we were unable to duplicate this result. Nor could we obtain dithioacids from 3- and 4-pyridinealdehydes or from pivalaldehyde.

Method III. Since Sakurada [15] prepared a large number of dithioesters by treating thioimidoesters in ether solution with hydrogen sulfide, this method was tried for the preparation of the carboxymethyl esters of dithioacetic and dithiobenzoic acids according to the following scheme:

Table 1. Carboxymethyl dithioates, $RCSSCH_2COOH$.

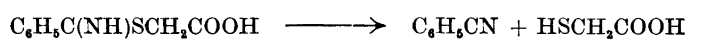
R	Yield, %, by method of preparation			M.p., °C	Colour	Formula	Analyses							
							Carbon		Hydrogen		Sulfur		Nitrogen	
	I	II	III				Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.
Phenyl [a]	40		82	126–127	red	$C_9H_8O_2S_2$								
Benzyl [b]			50	77– 78	yellow	$C_{10}H_{10}O_2S_2$								
β-Phenylethyl [b]			55	92– 93	yellow	$C_{11}H_{12}O_2S_2$	55.20	54.97	5.17	5.03	26.71	26.68		
o-Tolyl [a]	46			122–124	orange	$C_{10}H_{10}O_2S_2$	53.05	53.07	4.66	4.45	28.14	28.33		
p-Tolyl [a]	34			118–119	red	$C_{10}H_{10}O_2S_2$	53.35	53.07	4.59	4.45	28.46	28.33		
o-Hydroxyphenyl [a]		16		124–125	yellow	$C_9H_8O_3S_2$	47.10	47.35	3.49	3.54	28.50	28.09		
p-Hydroxyphenyl [c]		32		194–197	orange	$C_9H_8O_3S_2$	47.50	47.35	3.58	3.54	27.80	28.09		
o-Methoxyphenyl [d]		0	38	96– 98	red	$C_{10}H_{10}O_3S_2$	49.70	49.57	4.20	4.16	26.48	26.46		
p-Methoxyphenyl [a]		4	67	124–125	or.-yel.	$C_{10}H_{10}O_3S_2$	49.75	49.57	4.18	4.16	26.59	26.46		
o-Propoxyphenyl [d]			46*	93– 94	orange	$C_{12}H_{14}O_3S_2$	53.25	53.30	5.24	5.22				
o-*Iso*propoxyphenyl [e]			40	145–146	orange	$C_{12}H_{14}O_3S_2$	53.50	53.30	5.40	5.22	23.58	23.73		
o-Butoxyphenyl [d]			58*	108–109	orange	$C_{13}H_{16}O_3S_2$	54.85	54.90	5.86	5.67				
p-Butoxyphenyl [d]			96*	113–115	salmon	$C_{13}H_{16}O_3S_2$	55.00	54.90	5.60	5.67				
o-*Iso*butoxyphenyl [f]			20**	104–105	orange	$C_{13}H_{16}O_3S_2$	54.60	54.90	5.32	5.67	22.96	22.55		
o-*sec*-Butoxyphenyl [f]			16**	94– 95	orange	$C_{13}H_{16}O_3S_2$	55.05	54.90	5.71	5.67	22.32	22.55		
m-Chlorophenyl [a]		3	85	124–126	or.-red	$C_9H_7ClO_2S_2$	44.00	43.81	2.98	2.86	26.25	26.02		
p-Chlorophenyl [b]	4		82	115–117	or.-red	$C_9H_7ClO_2S_2$	44.10	43.81	2.95	2.86	26.20	26.02		
m-Nitrophenyl [a]			71	145–147	red	$C_9H_7NO_4S_2$	42.60	42.01	2.97	2.74			5.15	5.45
p-Acetamidophenyl [g]		8	94*	206–208	red	$C_{11}H_{11}NO_3S_2$	49.25	49.05	4.27	4.12			5.35	5.20
α-Naphthyl [a]	54			142–144	or.-yel.	$C_{13}H_{10}O_2S_2$	59.60	59.50	3.89	3.84	24.36	24.44		
β-Naphthyl [a]	15			147–148	pink	$C_{13}H_{10}O_2S_2$	59.53	59.50	3.74	3.84	24.50	24.44		
2-Furyl [a]		21		132–133	or.-red	$C_7H_6O_3S_2$	41.80	41.57	3.17	2.99	31.65	31.70		
2-Thienyl [a]	0.7	26		123–124	red	$C_7H_6O_2S_3$	38.45	38.48	2.94	2.77	44.16	44.10		
2-Pyrryl [a]	21			140–141	yellow	$C_7H_7NO_2S_2$	41.85	41.77	3.64	3.51			6.76	6.96
3-Indolyl [h]	22			163–166	yellow	$C_{11}H_9NO_2S_2$	52.60	52.57	3.57	3.61			5.44	5.57
Methyl [i]	0		60	80– 81	yellow	$C_4H_6O_2S_2$	32.15	31.98	4.24	4.03	42.80	42.67		
Ethyl [i]	0		60	51– 52	yellow	$C_5H_8O_2S_2$	36.65	36.56	5.03	4.91	39.20	39.04		
*Iso*propyl [i]	70***			48– 49	yellow	$C_6H_9O_2S_2$	40.30	40.45	5.80	5.66	36.29	35.95		

* Yield based on the thiopiperidide. ** Plus 50–60 % of oily ester; the *o*-ethoxy-, *o*-pentyloxy- and *o*-hexyloxydithiobenzoates were only obtained as red oils. *** From pure dithio*iso*butyric acid. Solvents used for recrystallisation: a) benzene; b) light petroleum (b.p. 100–140°C); c) water; d) benzene-light petroleum (b.p. 60–100°C); e) methylcellosolve-water; f) *n*-heptane; g) ethanol; h) benzene-ethanol; i) light petroleum (b.p. 60–100°C).

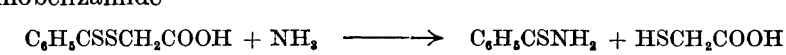
However, the reaction produced none of the desired products.

While this work was in progress a paper by Marvel *et al.*[16] appeared describing a modification of Sakurada's method in which the thioimidoester salt was treated with hydrogen sulfide in dry pyridine. We also tried this method and obtained a low yield (24 %) of impure carboxymethyl dithioacetate, whereas the attempted preparation of carboxymethyl dithiobenzoate was unsuccessful, yielding thiobenzamide (20 %) as the only product. Similarly, attempts to prepare methyl trichlorodithioacetate or pyridine dithiocarboxylates from the corresponding nitriles *via* the thioimidic esters gave negative results.

The poor results of these experiments may be partly ascribed to decomposition of the thioimidoester upon liberation from its salt by dissolution in pyridine, since Holmberg [17] has shown that the reaction



takes place when the thioimidoester is liberated from its salt in aqueous solution. Furthermore, any dithioester formed may react with ammonia and give the thiobenzamide



The formation of thiobenzamide from benzonitrile and hydrogen sulfide is unlikely as it has been shown [18] that this reaction does not take place in pyridine solution unless a strong base is present. Finally, the thioimidoester may undergo ring closure with formation of thiazolones (*cf.* number VII in this series).

Since Marvel *et al.*[16] described only the preparation of aliphatic dithioesters we tried to prepare methyl and ethyl dithiobenzoate by their method. Ethyl dithiobenzoate was obtained from *S*-ethylthiobenzamidium bromide in 75 % yield. It was contaminated with thiobenzamide, from which it could be separated by extraction with light petroleum. However, when *S*-methylthiobenzamidium iodide was treated with hydrogen sulfide in pyridine, only traces of methyl dithiobenzoate was produced, the main product being thiobenzamide. *O*-Methyl thiobenzoate was prepared in 90 % yield from *O*-methylbenzamidium chloride (methyl benzimidate hydrochloride).

Peak and Stansfield [19] obtained good yields of dithiocarboxylic esters by thiohydrolysis of *S*-methylthiomorpholidium iodides in absolute ethanol. In the same way Doyle *et al.*[20] prepared methyl indole-3-dithiocarboxylate by thiohydrolysis of the corresponding *S*-methylthiomorpholidium iodide. We investigated the analogous thiohydrolysis of several *S*-carboxymethylthiopiperididium bromides in absolute ethanol

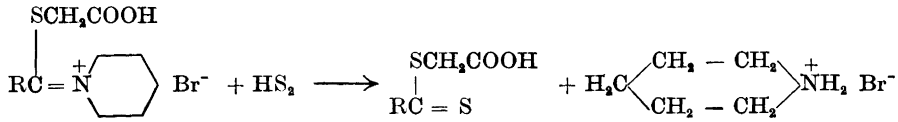
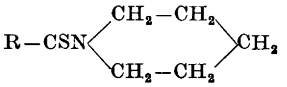


Table 2. Thiopiperidides. 

R	Yield %	M.p., °C	Formula	Analyses					
				Carbon		Hydrogen		Nitrogen	
				Found	Calc.	Found	Calc.	Found	Calc.
β-Phenylethyl [a]	37	67 – 68	$C_{14}H_{19}NS$	72.15	72.05	8.11	8.21	6.01	6.00
o-Methoxyphenyl [b]	70	92 – 93	$C_{13}H_{17}NOS$	66.15	66.34	7.06	7.28	5.87	5.95
p-Methoxyphenyl [a]	90	107 – 108	$C_{13}H_{17}NOS$	66.50	66.34	7.27	7.28	5.89	5.95
o-Ethoxyphenyl [c]	84	102 – 103	$C_{14}H_{19}NOS$	67.40	67.44	7.25	7.68	5.47	5.62
o-Propoxyphenyl [c]	73	60 – 61	$C_{15}H_{21}NOS$	68.45	68.41	7.82	8.04	5.20	5.32
p-Butoxyphenyl [c]	88	59 – 60	$C_{16}H_{23}NOS$	69.03	69.27	8.27	8.36	5.21	5.05
m-Chlorophenyl [b,c]	72	63 – 64	$C_{12}H_{14}ClNS$	60.35	60.11	5.83	5.89	5.93	5.84
p-Chlorophenyl [b,c]	84	108 – 109	$C_{12}H_{14}ClNS$	60.30	60.11	6.19	5.89	5.68	5.84
m-Nitrophenyl [b]	51	91 – 92	$C_{12}H_{14}N_2O_2S$	57.80	57.58	5.60	5.64	11.20	11.19
p-Nitrophenyl [d]	50	176 – 178	$C_{12}H_{14}N_2O_2S$	57.50	57.58	5.62	5.64	11.20	11.19
p-Acetamidophenyl [b]	82	201 – 202	$C_{14}H_{18}N_2OS$	64.00	64.09	7.03	6.91	10.53	10.68
Ethyl	57	b.p.111/1 mm	$C_8H_{15}NS$	61.30	61.09	9.47	9.61	8.86	8.91
*Iso*propyl [e]	71	b.p.130/3 mm	$C_9H_{17}NS$	62.40	63.11	9.86	10.01		
tert-Butyl [e]	97	81 – 82	$C_{10}H_{19}NS$	64.90	64.81	10.45	10.34	7.40	7.56

Solvents used for recrystallisation: a) light petroleum (b.p. 100 – 140°C); b) ethanol; c) light petroleum (b.p. 60 – 100°C); d) benzene; e) ethanol-water.

Thiopiperidides with R = *o-Iso*propoxyphenyl, *o*-butoxyphenyl, *o-iso*butoxyphenyl, *o-sec*-butoxyphenyl, *o*-pentyloxyphenyl and *o*-hexyloxyphenyl were isolated as oils and were not purified, the crude products being used directly for the preparation of the dithioesters.

Table 3. S-Carboxymethyl-thiopiperidium bromides,

R	Yield %	M.p., °C	Formula	Analyses					
				Carbon		Hydrogen		Nitrogen	
				Found	Calc.	Found	Calc.	Found	Calc.
Benzyl	95	137–138	$C_{15}H_{20}BrNO_2S$	50.30	50.28	5.53	5.63	3.83	3.91
β-Phenylethyl	81	131–132	$C_{16}H_{22}BrNO_2S$	51.90	51.61	6.07	5.96	3.69	3.76
o-Methoxyphenyl	98	167–169	$C_{15}H_{20}BrNO_3S$	48.20	48.13	5.56	5.39	3.60	3.74
p-Methoxyphenyl	84	156–159	$C_{15}H_{20}BrNO_3S$	48.10	48.13	5.51	5.39	3.65	3.74
*o-Iso*propoxyphenyl	95	165 (d.)	$C_{17}H_{24}BrNO_3S$	50.60	50.75	5.96	6.02	3.59	3.48
*o-Iso*butoxyphenyl	90	146–148(d.)	$C_{18}H_{26}BrNO_3S$	51.68	51.92	6.14	6.30	3.37	3.36
o-sec-Butoxyphenyl	90	160 (d.)	$C_{18}H_{26}BrNO_3S$	51.70	51.92	6.17	6.30	3.40	3.36
m-Chlorophenyl	70	170–173	$C_{14}H_{17}BrClNO_2S$	44.40	44.40	4.63	4.53	3.61	3.70
p-Chlorophenyl	80	161–164	$C_{14}H_{17}BrClNO_2S$	44.55	44.40	4.57	4.53	3.54	3.70
m-Nitrophenyl	78	157–159	$C_{14}H_{17}BrN_2O_4S.\frac{1}{2}H_2O$	42.25	42.21	4.66	4.55	6.78	7.03
Methyl	95	168–169	$C_9H_{16}BrNO_2S$	38.30	38.30	5.47	5.72	4.84	4.96
Ethyl	86	121–122	$C_{10}H_{18}BrNO_2S$	40.45	40.54	6.15	6.12	4.65	4.73
*Iso*propyl	60	83– 84	$C_{11}H_{20}BrNO_2S$	41.70	42.57	7.05	6.50	4.42	4.51

and obtained excellent yields in all the cases tried (Table 1). The thiopiperidides, in our experience, showed definite advantages over the thiomorpholides.

The thiopiperidides (Table 2) were prepared by the Willgerodt-Kindler method or from piperidides and phosphorus pentasulfide.

The *S*-carboxymethyl-thiopiperididium bromides were prepared from the thiopiperidides and bromoacetic acid with benzene as solvent (Table 3). This is the method which Holmberg [21] used for the preparation of *S*-carboxymethyl-thiobenzpiperididium bromide.

p-Nitrothiobenzpiperidide and thiopivaloylpiperidine reacted very incompletely with bromoacetic acid, and we were therefore unable to prepare the corresponding carboxymethyl dithioesters. Thiopivaloylpiperidine, however, reacted well with methyl iodide in boiling acetone, and the resulting *S*-methyl-thiopivaloylpiperidinium iodide, on thiohydrolysis, afforded methyl dithiopivaloate. In principle there seems to be no difficulty in obtaining the higher homologues of the aliphatic carboxymethyl dithioesters, but they are waxy substances which are difficult to purify. Carboxymethyl hexanedithioate was prepared, but it was not obtained in a completely pure state.

EXPERIMENTAL *

Method I

Carboxymethyl α-dithionaphthoate. To a solution of α-naphthylmagnesium bromide, prepared from α-bromonaphthalene (53.4 g) and magnesium (6.5 g) in 300 ml of ether, was added, with ice-cooling and stirring, 23.8 ml of carbon disulfide. The mixture was kept overnight, thus acquiring room temperature. Ice was added and the ether layer separated. To the aqueous layer was added a solution of chloroacetic acid (24.4 g) neutralised with sodium carbonate. After standing for 24 h at room temperature the mixture was acidified with conc. hydrochloric acid. The carboxymethyl ester separated as brownish crystals, which were washed with water and dried. The product (57 g) on recrystallisation from benzene gave 35 g (54 %) of yellow crystals with m.p. 136—138°C. After two additional recrystallisations from benzene the substance was pure.

The other compounds shown in Table 1 (Method I) were prepared in the same way. 2-Pyrryl- and 3-indolylmagnesium bromides were made from pyrrole and indole with ethylmagnesium bromide [22,23]. It was found convenient to purify 3-indole-dithiocarboxylic acid *via* its sodium salt, which is only slightly soluble.

Method II

Carboxymethyl 2-furandithioate. A solution of furfural (25 ml) in ethanol (90 ml) was heated to 65°C, and 135 ml of an ammonium polysulfide solution (prepared according to Bost and Shealy [13]) was added in 10 ml portions during 10 min, the temperature being kept at 65°C by heating now and then. The resulting mixture was boiled for 10 min, immediately cooled in ice, and acidified with conc. hydrochloric acid. The dithioacid, which separated as a red oil, was extracted with ether (3 × 150 ml). The ether solution was extracted with 1 N NaOH (3 × 100), and to this solution was added a solution of chloroacetic acid (28 g) neutralised with sodium carbonate. The pH of the resulting mixture was adjusted to 7. After standing overnight at room temperature the dark solution was acidified with conc. hydrochloric acid. The carboxymethyl ester separated

* Some preliminary experiments were carried out in this laboratory in 1951—53 by P. Nedenskov and I. Crossland. The *o*-alkoxydithiobenzoates were prepared by H. R. Baccaro and O. Buchardt.

as an oil, which crystallised on cooling. It was filtered off and recrystallised from water. Orange-red crystals, yield 12.6 g (21 %), m.p. 130–132°C. After two recrystallisations from benzene the substance was pure.

The substances shown in Table 1 (Method II) were prepared in the same way.

Method III

p-*Methoxythiobenzpiperidide.* Anisaldehyde (24 ml, 0.2 mole), piperidine (30 ml, 0.3 mole), and sulfur (9.6 g, 0.3 mole) were refluxed for one hour. After cooling, water was added and the mixture acidified with conc. hydrochloric acid. The brown oil rapidly solidified to a hard cake, which was crushed, filtered off, and washed with water. Recrystallisation from ethanol (200 ml) gave 43 g (90 %) of yellow crystals with m.p. 104–106°C. After two recrystallisations from light petroleum (b.p. 100–140°C) the substance was pure, forming pale yellow crystals.

The other aromatic thiobenzpiperidides shown in Table 2 were prepared in the same way. They all formed yellow to pale yellow crystals.

β-Phenylthiopropionylpiperidine. Propiophenone (22 ml), piperidine (25 ml, 1.5 equiv.) and sulfur (8 g, 1.5 equiv.) were refluxed for 7 h. Excess piperidine was removed *in vacuo*, and the oily residue was extracted with ether; the ether solution was washed with dilute hydrochloric acid and water and dried (Na_2SO_4). After evaporation of the ether a brown, crystalline solid remained. It was recrystallised from light petroleum (b.p. 100–140°C). Yield 14 g (37 %), m.p. 66–68°C. After two additional recrystallisations from light petroleum the substance was pure, forming pale yellow crystals.

Thiopropionylpiperidine. Propionylpiperidine (40 g), dry pyridine (75 ml), and phosphorus pentasulfide (31 g) were refluxed for 2 h. After removal of the pyridine *in vacuo*, water and HCl were added, and the dark, oily layer was extracted with ether. The ether solution was dried (Na_2SO_4) and the ether removed. The residue was distilled, the fraction boiling at 110–115°C (2–3 mm) being collected. Yield 25 g (56 %). Before analysis the substance was redistilled, and the fraction boiling at 111–112°C (2–3 mm) collected. The pure product was a yellow oil.

Thiopivaloylpiperidine and thio*iso*butyrylpiperidine were prepared in the same way (Table 2). Thioacetylpiperidine was obtained in 65 % yield, m.p. 55–56°C (Russel [24] reports m.p. 60–61°C).

S-*Carboxymethyl*-p-*methoxythiobenzpiperididium bromide.* *p*-Methoxythiobenzpiperidide (10 g) was dissolved in dry benzene (50 ml), and bromoacetic acid (6.5 g, 1.1 equiv.) was added. After a few minutes at room temperature a colourless oil began to separate. After 24 h at room temperature dry ether (150 ml) was added to precipitate the product completely. A little of the oily product was induced to crystallise by scratching and washing with dry ether, and the main portion was seeded with the crystals. The mixture was cooled to 0°C and the product filtered off and washed carefully with dry ether. Colourless crystals, yield 13.4 g (84 %), m.p. 150–152°C (decomp.). A sample was purified by dissolving it in absolute ethanol followed by precipitation with dry ether.

The other *S*-carboxymethyl-thiopiperididium bromides shown in Table 3 were prepared in the same way. They were all recrystallised from ethanol-ether and formed colourless crystals melting with decomposition. The *p*-acetamido compound was very hygroscopic, and purification was therefore not attempted. The *o*-propoxy and *o*- and *p*-butoxythiobenzpiperididium bromides were not isolated, but were transformed directly into the corresponding dithioesters.

Carboxymethyl p-*methoxydithiobenzoate.* *S*-carboxymethyl-*p*-methoxythiobenzpiperididium bromide (13.4 g) was dissolved in absolute ethanol (40 ml), and the solution was cooled in ice while hydrogen sulfide was passed through it for 3–4 h (2–3 bubbles per second). The red solution was kept overnight at 0°C and the ethanol then removed *in vacuo*. The residue was repeatedly extracted with ether until it became colourless (piperidinium bromide). The red ether solution was evaporated to dryness *in vacuo* and the residue recrystallised from benzene. Orange-yellow crystals, yield 5.9 g (67 %), m.p. 120–122°C.

The same procedure was used for the preparation of the other carboxymethyl dithioesters except in two cases, *viz.* the *p*-chloro- and the *p*-acetamidodithiobenzoates, which were too insoluble in ether to be easily extracted with this solvent. Instead they were

isolated by adding water to the residue which was obtained after evaporation of the ethanol. The product was then filtered off, washed with water, and dried. This procedure is easier and could possibly be used generally, but if any unreacted thioimidic ester is present it will be hydrolysed to an *S*-thioester ($RCOSCH_2COOH$), which will be very difficult to separate from the dithioester.

Ethyl dithiobenzoate. *S*-Ethylthiobenzamidium chloride [25] (30 g) was dissolved in pyridine (120 ml); the solution was cooled in ice, and hydrogen sulfide was passed through it for 3 h. After standing overnight at 0°C, the mixture was diluted with water and acidified with conc. hydrochloric acid. The red oil that separated was extracted with ether, the ether solution was dried (Na_2SO_4) and the ether removed *in vacuo*. The residue was distilled, the fraction boiling at 153–158°C (14 mm) being collected. During the distillation crystals of thiobenzamide began to separate in the distillate, wherefore this was mixed with 500 ml of light petroleum (b.p. 40–60°C), in which thiobenzamide is insoluble. After cooling, the thiobenzamide was filtered off and the light petroleum evaporated. Distillation of the residue gave 20.3 g (75 %) of material boiling at 153–154°C (13 mm). Gilman *et al.*[26] report the boiling point 155–160°C (15 mm).

S-Methylthiobenzamidium iodide (78.7 g) (prepared from thiobenzamide and methyl iodide) was treated with hydrogen sulfide in pyridine. The product that separated when water and hydrochloric acid was added to the pyridine solution was a solid contaminated with drops of a red oil (methyl dithiobenzoate); the mixture smelled strongly of methanethiol. The solid, when filtered off, dried, and washed with light petroleum, gave 16.4 g (47 %) of thiobenzamide. From *S*-methylthiobenzpiperididium iodide methyl dithiobenzoate was obtained in 99 % yield.

S-*Methylthiopivaloylpiperidinium iodide.* Thiopivaloylpiperidine (40 g) and methyl iodide (65 g) were dissolved in dry acetone (250 ml), and the solution was refluxed for one hour. Acetone and excess methyl iodide were removed *in vacuo*, and ether (400 ml) was added to the residual oil, causing it to crystallise. Yield 63 g (90 %), of m.p. 112–120°C. The product was purified by recrystallisation from absolute ethanol-ether. The pure compound formed colourless crystals of m.p. 129–130°C. (Found: C 40.40; H 6.78; N 4.19. Calc. for $C_{11}H_{22}INS$: C 40.37; H 6.76; N 4.27.)

S-*Methylthio*iso*butyrylpiperidinium iodide* was prepared analogously. M.p. 106–107°C. (Found: I 40.4. Calc. for $C_{10}H_{20}INS$: I 40.6.)

Methyl dithiopivaloate. *S*-Methylthiopivaloylpiperidinium iodide (45.6 g) in absolute ethanol (250 ml) was cooled in ice and treated with hydrogen sulfide for three hours. The mixture was kept overnight at 0°C, and a large volume of ether was added. The precipitated piperidinium iodide was filtered off, and the yellow ethanol-ether solution was distilled through a column packed with glass helices. The fraction boiling at 65–65.5°C (12 mm) was collected. Yellow oil, yield 13.9 g (68 %). (Found: C 48.62; H 8.38; S 43.12. Calc. for $C_6H_{12}S_2$: C 48.65; H 8.16; S 43.24.)

*Methyl dithio*iso*butyrate* was prepared by the same procedure. Yield 66 %. B.p. 86/50 mm. (Found: C 44.95; H 7.66. Calc. for $C_5H_{10}S_2$: C 44.74; H 7.50.)

In a similar way methyl *p*-butoxydithiobenzoate was prepared from *p*-butoxythiobenzpiperidide (2.77 g). The ethereal solution left on evaporation a red crystalline residue, which was recrystallised from methanol. Yield 1.5 g (63 %); m.p. 38–38.5°C. (Found: C 59.99; H 6.71. Calc. for $C_{12}H_{16}OS_2$: C 60.05; H 6.87.)

REFERENCES

1. Holmberg, B. *Arkiv Kemi, Mineral. Geol.* **17 A** (1943) No. 23.
2. Kjær, A. *Acta Chem. Scand.* **4** (1950) 1347.
3. Kjær, A. *Acta Chem. Scand.* **6** (1952) 327.
4. Holmberg, B. *Arkiv Kemi, Mineral. Geol.* **25 A** (1947) No. 18.
5. Holmberg, B. *The Svedberg Memor. Vol.* (1944) 299.
6. Houben, J. and Kesselkaul, L. *Ber.* **35** (1902) 3695.
7. Houben, J. *Ber.* **39** (1906) 3219.
8. Houben, J. and Pohl, H. *Ber.* **40** (1907) 1303.
9. Houben, J. and Pohl, H. *Ber.* **40** (1907) 1725.
10. König, H. B., Siefken, W. and Offe, H. A. *Chem. Ber.* **87** (1954) 825.

11. Levi, T. G. *Atti accad. nazl. Lincei* (5) **32 I** (1923) 569.
12. Levi, T. G. *Atti accad. nazl. Lincei* (6) **9** (1929) 170.
13. Bost, R. W. and Shealy, O. L *J. Am. Chem. Soc.* **73** (1951) 25.
14. Bruni, G. and Levi, T. G. *Gazz. chim. ital.* **54** (1924) 389.
15. Sakurada, Y. *Mem. Coll. Sci. Kyoto Imp. Univ.* **10** (1926–27) 79.
16. Marvel, C. S., Radzitzky, P. de and Brader, J. J. *J. Am. Chem. Soc.* **77** (1955) 5997.
17. Holmberg, B. *Arkiv Kemi, Mineral. Geol.* **20 A** (1945) No. 1.
18. Fairfull, A. F. S., Lowe, J. L. and Peak, D. A. *J. Chem. Soc.* **1952** 743.
19. Peak, D. A. and Stansfield, F. *J. Chem. Soc.* **1952** 4067.
20. Doyle, F. P. *et al. J. Chem. Soc.* **1956** 2853.
21. Holmberg, B. *Arkiv Kemi, Mineral. Geol.* **24 A** (1947) No. 3.
22. Oddo, B. and Mingoia, Q. *Gazetta chim. ital.* **56** (1926) 782.
23. McCay, C. M. and Schmidt, C. L. A. *J. Am. Chem. Soc.* **48** (1926) 1933.
24. Russel, W. F. *J. Chem. Soc.* **97** (1910) 953.
25. Bernthsen, A. *Ann.* **197** (1879) 341.
26. Gilman, H., Robinson, J. and Beaber, N. J. *J. Am. Chem. Soc.* **48** (1926) 2715.

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