2-CHLOROETHYLTHIOL ESTERS OF DICARBOXYLIC ACIDS

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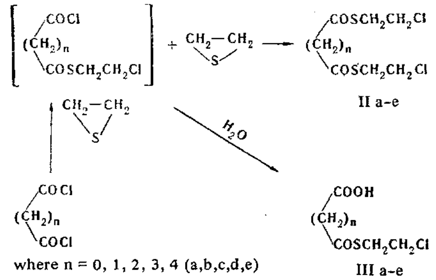
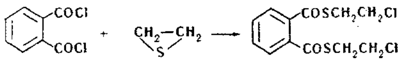
Mono- and bis(2-chloroethyl)thiol esters of aliphatic, aromatic, and heterocyclic dicarboxylic acids have been obtained by the reaction of the dicarboxylic acid chlorides with ethylene sulfide or 2-chloroethanethiol. The compounds were characterized by their electronic spectra.

The present work was devoted to the preparation of bis(2-chloroethyl)thiol esters of dicarboxylic acids. They were prepared by the method used in an earlier paper [1] for the preparation of 2-chloroethylthiol esters of aromatic and heterocyclic carboxylic acids. The dicarboxylic acid chlorides, however, reacted more vigorously with ethylene sulfide than did the monocarboxylic acid chlorides. This is apparently due to the –I effect of the second carbonyl group activating the chlorine of the first group in a similar way to that occurring in halo-substituted acid chlorides [2].



where n = 0, 1, 2, 3, 4 (a,b,c,d,e)

Use of only one mole of ethylene sulfide per mole of dicarboxylic acid chloride gave the dicarboxylic acid monoester, thus confirming the suggested reaction scheme (Tables 1 and 2). Phathaloyl chloride reacts with ethylene sulfide in a similar way to aliphatic dicarboxylic acid dichlorides:

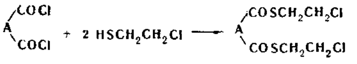


IV

The liquid bisthiol esters (IIb, IId, and IIe decompose on distillation in vacuo, despite their close similarity in structure to the diethyl bisthiol carboxylates which distill smoothly under reduced pressure [3], while diethyl dithiol oxalate distills even at atmospheric pressure [4]. In order to purify the bis(2-chloroethyl)thiol esters, we recrystallized them from boiling light petroleum, isolating the crystalline or oily product which separated on cooling to –60°. Repetition of this procedure enabled analytically pure compounds to be obtained.

Fumaroyl chloride behaved differently in its reaction with ethylene sulfide. Mixing of the reactants led to a violent reaction, and the reaction mixture solidified. The product, in contrast to the other thiol esters, was a light-colored amorphous powder, sparingly soluble in ether. Its structure was not established.

Bis(2-chloroethyl)thiol fumarate was obtained by heating a mixture of the acid chloride with 2-chloroethanethiol. It resembled the other thiol esters in being readily soluble in ether. By the same method there was obtained bis(2-chloroethyl)furan-2, 5-dithiol carboxylate. Reaction of ethylene sulfide with furan-2, 5-dicarbonyl chloride afforded, as in the case of fumaric acid, a product of variable composition containing sulfur and chlorine.



Va,b

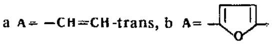


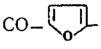
Table 1

$ClCH_2CH_2S—A—SCH_2CH_2Cl$

Compound	A	Mp, °C	n_D^{20}	d_4^{20}	Molecular formula	Found, %				Calculated, %				Yield, %
						C	H	Cl	S	C	H	Cl	S	
IIa	COCO	34—35	—	—	$C_6H_8Cl_2O_2S_2$	29.02	2.97	29.16	26.38	29.14	3.26	28.68	25.93	44
IIb	$COCH_2CO$	Oil	1.5777	1.387	$C_7H_{10}Cl_2O_2S_2$	32.15	3.85	27.55	24.15	32.19	3.86	27.14	24.55	87
IIc	$CO(CH_2)_2CO$	48—50	—	—	$C_8H_{12}Cl_2O_2S_2$	34.70	4.38	25.65	23.02	34.91	4.39	25.72	23.30	81
IId	$CO(CH_2)_3CO$	Oil	1.5548	1.3092	$C_9H_{14}Cl_2O_2S_2$	37.50	5.02	24.98	21.70	37.37	4.82	24.51	22.17	57
IIe	$CO(CH_2)_4CO$	Oil	1.5446	1.2719	$C_{10}H_{16}Cl_2O_2S_2$	39.51	5.51	23.00	21.33	39.60	5.31	23.38	21.14	88
IV	o-$C_6H_4(CO)_2$	Oil	1.6145	—	$C_{12}H_{12}Cl_2O_2S_2$	44.49	3.97	21.80	19.70	44.58	3.74	21.93	19.84	87
Va	COCH=CHCO	127—129	—	—	$C_8H_{10}Cl_2O_2S_2$	35.03	3.80	26.27	23.18	35.17	3.62	25.95	23.44	44
Vb	2,5-$C_4H_2O(CO)_2$	98—99	—	—	$C_{10}H_{10}Cl_2O_3S_2$	38.66	3.51	22.61	20.61	38.34	3.22	22.64	20.47	68

Table 2

$ClCH_2CH_2S—A—COOH$

Compound	A	Mp, °C	Molecular formula	Found, %				Calculated, %				Yield, %
				C	H	Cl	S	C	H	Cl	S	
IIIa	CO	Oil	$C_4H_5ClO_3S$	28.60	3.12	20.90	18.75	28.49	2.98	21.02	19.02	40
IIIb	$COCH_2$	Oil	$C_5H_7ClO_3S$	33.16	4.08	19.32	17.35	32.88	3.86	19.41	17.55	88
IIIc	$CO(CH_2)_2$	69—71	$C_6H_9ClO_3S$	36.33	4.48	18.31	16.70	36.64	4.61	18.03	16.30	15
IIId	$CO(CH_2)_3$	40—42	$C_7H_{11}ClO_3S$	39.92	5.22	16.50	15.58	39.90	5.27	16.82	15.22	25
IIIe	$CO(CH_2)_4$	45—47	$C_8H_{13}ClO_3S$	42.55	5.84	15.89	14.35	42.76	5.78	15.75	14.27	41
	CO– 	153—155	$C_8H_7ClO_4S$	41.19	2.77	14.93	13.30	40.95	3.01	15.10	13.66	10*

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*By-product from the synthesis of Vb.

Table 3. The Spectral Characteristics of Mono- and Bisthiolo Esters of Dicarboxylic Acids

Compound	Solvent	λ_{max}, nm (ε)
IIa	Alcohol	277 (5040)
	Hexane	277 (4480)
IIIa	Alcohol	257 (2180)
	Hexane	268 (750*)
IIb	Alcohol	233 (6780), 309 (5860)
	Hexane	233 (6630)
IIIb	Alcohol	232 (4440), 277 (880)
IIc	Alcohol	230 (8660)
IIIc	Alcohol	229 (4060)
IId	Alcohol	231 (7760)
IIId	Alcohol	230 (3940)
IIe	Alcohol	229 (7940)
IIIe	Alcohol	229 (5620)
Va	Alcohol	229 (13640), 292 (9040)
IV	Alcohol	258 (3660), 263 (3640)
Vb	Alcohol	220 (11360), 268 (12380), 305 (18400)

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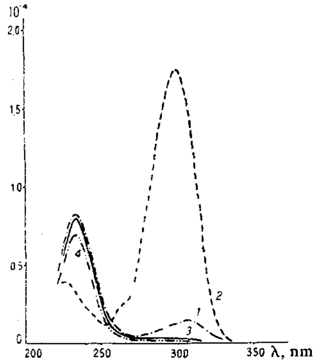
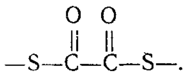
*The low solubility of the compound in hexane made it necessary to make a qualitative measurement.



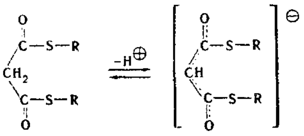
The UV spectra of bis(2-chloroethyl)thiol ester of malonic acid: 1) in 96% ethanol; 2) in ethanol in the presence of NaOH (0.001 N solution); 3) in ethanol in the presence of HCl (0.001 N solution); 4) in hexane.

The electronic spectra (Table 3) of the bisthiol esters of succinic, glutaric, and adipic acids were similar to those of other aliphatic thiol esters [5], having maxima in the region of 230 nm. The monothiol esters have absorption maxima at the same wavelength but of about half the intensity. It is known that the absorption maximum is shifted toward longer wavelengths if the two chromophores are not separated by methylene groups [6, 7]. This effect occurs in the case of bis(2-chloroethyl)thiol oxalate (λ_{max} 277 nm). This compound has a greenish color. The coloration of thiol oxalate esters has already been pointed out in the literature [4, 8]. The common chromophore appears to be the grouping



$$-S-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-S-.$$

Bis(2-chloroethyl)thiol ester of malonic acid has two absorption maxima, at 233 and 309 nm. The first of these may be assigned to the electron transfer of the thiol ester grouping. The appearance of a second maximum is attributed to the presence of the anion of the diketone in alcoholic solution:



The addition of sodium hydroxide facilitates ionization, and the intensity of the long wavelength band is greatly increased, whilst in the presence of traces of hydrochloric acid ionization is suppressed and the maximum at 300 nm disappears. It is also absent in the inert solvent hexane (see figure). This is in agreement with several workers [9–12] who found that the acidic properties of the methylene hydrogens in diethyl thiomalonates influence the course of the reaction. The presence of unsaturated groups between the thiol ester chromophores renders more difficult the interpretation of the separate maxima.

EXPERIMENTAL

The UV spectra were recorded on an SF-4a spectrometer, in 96% ethanol or hexane (c 10^{-4} M, l = 0.5 and 0.45 cm).

2-Chloroethylthiol was obtained by known methods [13]. Dry hydrogen chloride was passed into a solution of 12 g (0.2 mole) of ethylene sulfide in 200 ml of dry ether for 10 hr, the temperature being kept at 10–15° C. The ether was distilled off, and the residue distilled through a short fractionating column. The fraction bp 113–116° C was collected (bp 113–118.5° C [13]). Yield 11.2 g (58%), n_D^{20} 1.4920.

Bis(2-chloroethyl)thiol esters of dicarboxylic acids. A) Bis(2-chloroethyl)thiol oxalate. To 5.1 g (0.04 mole) of oxalyl chloride was added, with cooling at 0–5° C, 5.3 ml (0.088 mole) of ethylene sulfide. The reaction mixture was heated in a bath at 60° C for 10 hr, cooled, 200 ml of ether added and washed with saturated sodium bicarbonate until evolution of carbon dioxide ceased, then with water until neutral to litmus. The ether layer was dried over anhydrous sodium sulfate, and the ether removed in vacuo to give 4.35 g (40%) of light green oil, which was purified by solution in boiling light petroleum with the addition of activated charcoal. The solution was filtered hot and placed in a freezing mixture of carbon dioxide and acetone. The solvent was decanted from the light-colored oil which separated, and the whole operation was repeated twice more. On the last occasion, the reaction product separated as light green crystals which were filtered off on a cooled funnel and dried in vacuo, mp 34–35° C.

Bis(2-chloroethyl)thiol esters of malonic, succinic, glutaric, adipic, and phthalic acids. These were prepared and purified in a similar way. The oils which separated were recrystallized, and dried in vacuo for 4 hr.

B) **Bis(2-chloroethyl)thiol ester of fumaric acid.** A mixture of 3.82 g (0.025 mole) of fumaryl chloride and 4.82 g 0.05 mole) of 2-chloroethanethiol were heated on the water bath for 2 hr. The crystalline reaction mixture was cooled and triturated several times with saturated sodium bicarbonate solution, the aqueous layer being removed by decantation. The oily mass was washed with water and recrystallized from ethanol to give 3.01 g (44%) of the ester, mp 127–120° C.

C) **Bis(2-chloroethyl)thiol ester of furan-2, 5-dicarboxylic acid.** To a solution of 3.82 g (0.02 mole) of furan-2, 5-dicarbonyl chloride in 20 ml of dry benzene was added dropwise with stirring 3.16 g (0.04 mole) of pyridine, followed by a solution of 3.86 g (0.04 mole) of 2-chloroethanethiol in 15 ml of dry benzene. The temperature of the mixture rose from 20 to 30° C. After stirring for 1 hr, the pyridine hydrochloride was filtered off and the benzene solution washed with water, 2 N HCl, saturated sodium bicarbonate, then several times with water. The solution was dried over anhydrous sodium sulfate, and the benzene distilled off to give 4.2 g of product. Recrystallization from a large volume of hexane (about 800 ml) gave 3.6 g (58%) of slightly yellowish material. An analytically pure sample (colorless needles) had mp 98–99° C (from hexane).

The hexane insoluble fraction of the reaction product (about 0.5 g) was recrystallized from benzene, mp 153–155°. Found, %: C 41.19; H 2.77; Cl 14.93; S 13.30. Calculated for $C_8H_7ClO_4$, %: C 40.95; H 3.01; Cl 15.10; S 13.66. The analytical results agree with the mono(2-chloroethyl)thiol ester of furan-2, 5-dicarboxylic acid.

Mono(2-chloroethyl)thiol ester of malonic acid. Seven grams (0.05 mole) of malonyl chloride was cooled in ice water and mixed with 3 ml (0.05 mole) of ethylene sulfide. The reaction mixture was heated at 60° C for 10 hr, dissolved in 200 ml of ether, and washed with saturated sodium bicarbonate until evolution of carbon dioxide ceased. The ether layer was separated, dired over anhydrous sodium sulfate, and evaporated to give bis(2-chloroethyl)thiol ester of malonic acid. The aqueous solution was acidified with HCl and extracted with ether (3 times in 100 ml). The ether extracts were dried over sodium sulfate and evaporated to afford 7.95 g (88%) of mono(2-chloroethyl)thiol ester of malonic acid as a viscous yellow oil which was purified from a mixture of light petroleum and ether (with cooling to −60° C). The compound crystallized on keeping in the refrigerator.

Mono(2-chloroethyl)thiol esters of oxalic, succinic, glutaric and adipic acids were obtained similarly.

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