2-HALOGENOETHYL AND 2-HALOGENOETHYLTHIOL ESTERS OF FURAN SERIES CARBOXYLIC ACIDS

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The corresponding 2-chloroethyl (2-chloroethylthiol) esters are synthesized by the action of ethylene chlorohydrin (chloroethylmercaptan) on the acid chlorides of 5-nitrofuran carboxylic acid and 3-(5-nitrofuryl-2)acrylic acid. The acid chlorides of benzoic, furan carboxylic, and 3-(furyl-2)-acrylic acids react with ethylene sulfide, to give 2-chloroethyl esters of those acids. Ethylene oxide does not react with the acid chlorides of benzoic acid and furan series carboxylic acids either at room temperature or on heating at 50° for 1 hour.

Ethylene oxide reacts readily with acetyl iodide, giving 2-iodoethyl acetate, whereas acetyl chloride reacts extremely slowly [1]. Ethylene sulfide behaves similarly. The acid iodides and bromides of acetic and benzoic acids react readily with ethylene sulfide [2–5], but it requires a long time to prepare the 2-chloroethyl ester from acetyl chloride and ethylene sulfide [6]. The literature does not give any information regarding the reaction of acid chlorides of aromatic and heterocyclic carboxylic acids with ethylene sulfide.

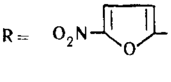
We investigated the reaction of acid chlorides with ethylene oxide and ethylene sulfide with a view to preparing the chloroethyl and chloroethylthiol esters of benzoic and furan series acids.

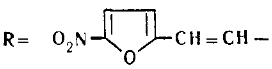
Even over a period of several months at room temperature the acid chlorides of furan carboxylic, furylacrylic, 5-nitrofuran carboxylic, 5-nitrofurylacrylic acids and benzoyl chloride do not react with ethylene oxide. Benzoyl chloride does not undergo reaction with ethylene oxide in 1 hr at 50°. The 2-chloroethyl esters of 5-nitrofuran carboxylic (I) and 5-nitrofurylacrylic (II) acids were prepared by treating the acid chlorides with ethylene chlorohydrin in toluene in the presence of triethylamine.

The 2-chloroethyl esters of furan carboxylic and furylacrylic acids, prepared similarly, are described in the literature [7].

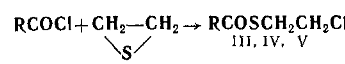
Ethylene sulfide reacts more readily with acid chlorides than does ethylene oxide. Thus by heating ethylene sulfide with benzoyl chloride and the acid

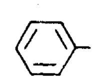
$$RCOCl + HOCH_2CH_2Cl \rightarrow \underset{I,\ II}{RCOOCH_2CH_2Cl}$$

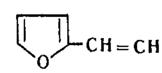
I R= 

II R= 

chloride of furan carboxylic and furylacrylic acids, in the absence of solvent, for 10 hours at 50–60°, the corresponding 2-ethylthiol esters are formed (III, IV, V).



III R=  IV R= 

V R= 

Reaction does not take place in dry ether.

It did not prove possible to isolate the desired reaction product when the acid chlorides of 5-nitrofuran carboxylic and 5-nitrofurylacrylic acids were treated with ethylene sulfide. The 2-chloroethylthiol esters of those acids are obtained by treating the corresponding acid chlorides with 2-chloroethyl mercaptan in the presence of pyridine.

$$RCOCl + HSCH_2CH_2Cl \xrightarrow{\text{pyridine}} \underset{VI,\ VII}{RCOSCH_2CH_2Cl}$$

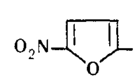
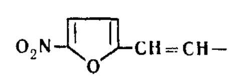
VI R=  VII R= 

Table 1

2-Chloroethyl and 2-Chloroethylthiol Esters Synthesized

Compound no.	Mp, °C	Bp, °C (pressure, mm)	Formula	Found, %					Calculated, %					Yield, %
				C	H	Cl	N	S	C	H	Cl	N	S	
I	59–60	—	$C_7H_6ClNO_5$	38.39	2.85	16.22	6.45	—	38.29	2.75	16.15	6.38	—	95
II	89–90	—	$C_9H_8ClNO_5$	44.16	3.33	14.35	5.76	—	44.01	3.28	14.44	5.70	—	95
III	—	141–145(5)	C_9H_9ClOS	53.80	4.35	—	—	—	53.86	4.52	—	—	—	76
IV	38–39	117–118(1–2)	$C_7H_7ClO_2S$	44.38	3.67	18.37	—	16.54	44.09	3.70	18.60	—	16.82	74
V	—	136–139(1–2)	$C_9H_9ClO_2S$	50.01	4.24	—	—	—	49.88	4.19	—	—	—	69
VI	51–52	—	$C_7H_6ClNO_4S$	35.80	2.60	15.69	5.95	13.57	35.68	2.57	15.05	5.94	13.61	77
VII	104–105	—	$C_9H_8ClNO_4S$	41.67	3.10	13.82	5.45	12.37	41.31	3.08	13.55	5.35	12.37	80

Table 2

2-Iodoethyl and 2-Iodoethylthio Esters Synthesized

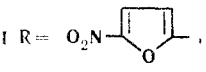
Compound no.	Reaction time, hr	Mp, °C	Recrystallization solvent	Formula	Found, %					Calculated, %					Yield, %
					C	H	I	N	S	C	H	I	N	S	
VIII	60	90—91	Heptane	C_7H_6INO	27.00	2.27	41.09	4.77	—	27.03	1.94	40.80	4.50	—	90
IX	90	89—90	Heptane	C_9H_8INO	32.46	2.69	37.13	3.93	—	32.07	2.39	37.69	4.16	—	74
X	50	63—64	Hexane or hexane-dry ether (1:3)*	$C_7H_7IO_2S$	29.77	2.54	45.81	—	11.44	29.80	2.50	44.99	—	11.37	71
XI	50	64—66	Hexane	$C_9H_9IO_2S$	35.35	3.02	40.98	—	10.48	35.08	2.94	41.19	—	10.41	32
XII	40	76—78	Hexane	$C_7H_5INO_4S$	25.91	1.79	38.65	4.50	9.72	25.70	1.85	38.80	4.28	9.80	92
XIII	50	125—127	Heptane	$C_9H_8INO_4S$	30.81	2.46	36.18	4.14	9.19	30.61	2.28	35.93	3.97	9.08	57

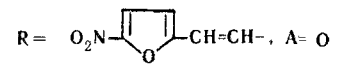
* Cooled to −40°, −50°.

To prepare VI the reaction was run in dry ether, while a better yield of VII is obtained in dry toluene. The action of sodium iodide on the chloroethylthiol and chloroethyl esters in acetone solution gives the corresponding iodoethyl derivatives (VIII-XIII).

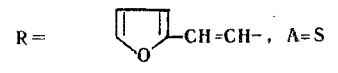
Tables 1 and 2 give chemical constants, yields and analytical data of the compounds prepared.

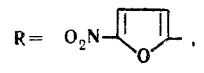
$$RCOACH_2CH_2Cl + NaI \rightarrow \underset{VIII - XIII}{RCOACH_2CH_2I} + NaCl$$

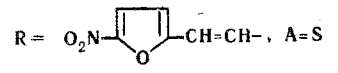
VIII R =  , A = O

IX R =  , A = O

X R =  , A = S

XI R =  , A = S

XII R =  , A = S

XIII R =  , A = S

EXPERIMENTAL

2-Chloroethyl ester of 5-nitrofuran-2-carboxylic acid (I). 5.05 g [0.05 mole) triethylamine and 4.03 g (0.05 mole) ethylene chlorohydrin were added to 8.78 g (0.05 mole) 5-nitrofuryl chloride dissolved in 100 ml toluene. The mixture was stirred and refluxed for 4 hr, cooled, and after separating off the triethylamine salt, the solvent was vacuum-distilled off. Yield of crude product 10.5 g (95%). After two recrystallizations from a large volume of low boiling petrol ether it had mp 59–60°.

2-Chloroethyl ester of 3-(5-nitrofuryl-2)acrylic acid (II). Prepared as above, using 6.04 g (0.03 mole) 3-(5-nitrofuryl-2)acrylyl chloride, 3.03 g (0.03 mole) triethylamine, and 2.41 g (0.03 mole) ethylene chlorohydrin in 150 ml toluene. Yield of crude product 7 g (95%). After recrystallizing from toluene-petrol ether it had mp 89–90°.

2-Chloroethylthiol ester of benzoic acid (III). 3.0 g (0.05 mole) ethylene sulfide and 7.0 g (0.05 mole) benzoyl chloride were heated together for 10 hr at 50–60° in a flask fitted with a reflux condenser. The reaction products were vacuum-distilled, and a cut bp 141–145° (5 mm) taken, yield 7.65 g (76%).

2-Chloroethylthiol ester of furan-2-carboxylic acid (IV). Prepared similarly to III, in the distillation a cut bp 117–118° (1–2 mm) was taken. The product in the receiver crystallized, mp 38–39°, yield 74%.

2-Chloroethylthiol ester of 3-(furyl-2)acrylic acid (V). Prepared similarly to III, the cut taken having bp 136–139° (1–2 mm), yield 69%.

2-Chloroethylthiol ester of 5-nitrofuran-2-carboxylic acid (VI). 3.5 g (0.02 mole) 5-nitrofuran-2-carbonyl chloride was dissolved in 20 ml dry ether, and 1.68 g (0.02 mole, 1.6 ml) pyridine added dropwise at 0°. Then 1.93 g (0.02 mole) 2-chloroethyl mercaptan in 10 ml dry ether was added dropwise at 0–2°, and the reaction mixture stirred for a further 1 hr at that temperature. The pyridine salt was filtered off, the yellow ether layer washed with water, then with dilute hydrochloric acid, saturated with sodium bicarbonate solution, and finally water, and dried over Na_2SO_4. Removal of the solvent by distillation gave 3.6 g (77%) of the reaction product, which after three recrystallizations from hexane had mp 51–52°.

2-Chloroethylthiol ester of 3-(5-nitrofuryl-2)acrylic acid (VII). 4.03 g (0.02 mole) 3-(5-nitrofuryl-2)acrylyl chloride was dissolved in 100 ml toluene, and a solution of 2.02 g (0.02 mole) triethylamine in 20 ml toluene added, followed by 1.93 g (0.02 mole) 2-chloroethylmercaptan added dropwise, and the mixture refluxed and stirred for 5 hr. After cooling the amine salt was filtered off, and the solvent vacuum-distilled off. The dark residue was boiled with heptane (about 600 ml), and filtered off. On cooling the solution deposited 4.2 g (80%) of a white crystalline material; after a few recrystallizations it had mp 104–105°.

Preparing the 2-iodoethyl and 2-iodoethylthiol esters of furan series carboxylic acids (VIII–XIII). 0.01 mole of 2-chloroethyl or 2-chloroethylthiol ester of the acid was dissolved in 100 ml acetone, 5 g NaI · $2H_2O$ added, and the mixture stirred and refluxed for 40–90 hr. The precipitate of NaCl was filtered off, the acetone vacuum-distilled off or allowed to evaporate off in air, and the residue treated with sodium thiosulfate solution to decolorize it. The product was filtered off, washed with water on the filter, and air-dried.

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