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Synthesis of 1-Methyl and 1-Benzyl 3,5-Bis(ω-Mercaptoalkyl) Isocyanurates

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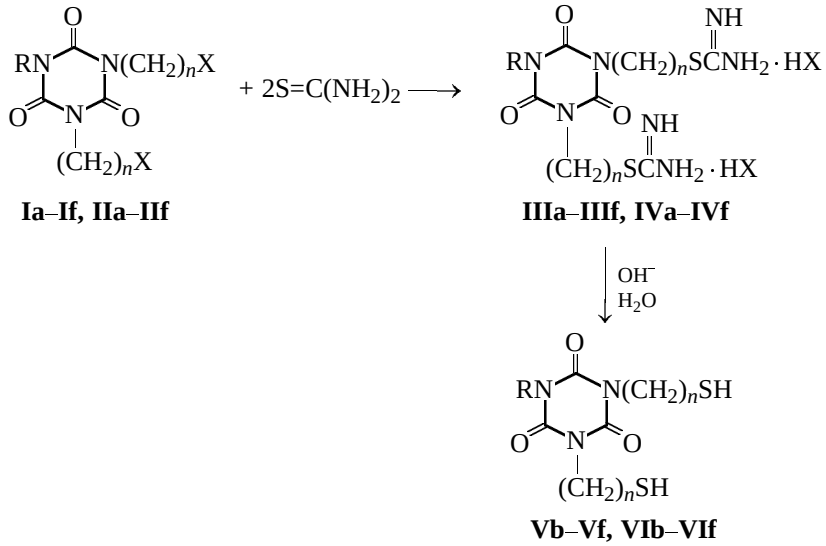
Abstract — 1-Methyl and 1-benzyl 3,5-bis(ω-haloalkyl) isocyanurates were reacted with thiourea to obtain 1-methyl and 1-benzyl 3,5-bis[ω-[amino(imino)methylmercapto]alkyl] isocyanurates, respectively. Hydrolysis of the latter gave the corresponding 3,5-bis(ω-mercaproalkyl) izocyanurates.

Mercaptoalkyl isocyanurates have scarcely been studied. The synthesis of 2-mercaptoethyl isocyanurate by acid hydrolysis of 2,3,6,7-tetrahydro-4*H*-thiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione has been described [1]. Patented has been the method for preparing tris(3-mercaptopropyl) isocyanurate by hydrolysis of the adduct of thioacetic acid with 1,3,5-triallyl isocyanurate [2]. Earlier we showed that 1,3-dimethyl and 1,3-diallyl 5-(ω-bromoalkyl) isocyanurates react with thiourea to give the corresponding isothiuronium salts whose hydrolysis yields 1,3-dimethyl and 1,3-diallyl 5-(ω-mercaptoalkyl) isocyanurates [3].

In the present work we report the synthesis of 1-methyl and 1-benzyl 3,5-bis(ω-mercaptoalkyl) isocyanurates which present interest as starting materials for synthesis of various compounds, including macroheterocycles.



Ia–**If, IIa**–**IIf** **IIIa**–**IIIf, IVa**–**IVf**

Vb–**Vf, VIb**–**VIf**

R = CH_3 (**I, III, V**), $C_6H_5CH_2$ (**II, IV, VI**), *n* = 1 (**a**), 2 (**b**), 3 (**c**), 4 (**d**), 5 (**e**), 6 (**f**); X = Cl (**Ia, IIa, IIIa, IVa**), Br (**Ib**–**Ie, IIb**–**IIe, IIIb**–**IIIe, IVb**–**IVe**).

Isothiuronium salts **IIIa**–**IIIf, IVa**–**IVf** are formed in high yields (Table 1) on boiling of equimolar amounts of 1-methyl or 1-benzyl 3,5-bis(ω-haloalkyl) isocyanurates **Ia**–**If**, **IIa**–**IIf** and thiourea in an alcohol (methanol or 2-propanol). They are white crystalline substances, hygroscopic, readily soluble in water and methanol. The IR spectra of isothiuronium salts **IIIa**–**IIIf, IVa**–**IVf** show a characteristic band of the iso-

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Table 1. Yields, melting points, and elemental analyses of isothiuronium salts **IIIa**–**IIIf, IVa**–**VIf**

Comp. no.	Yield, %	mp, °C	Found, %					Formula	Calculated, %				
			C	H	Br(Cl)	N	S		C	H	Br(Cl)	N	S
IIIa	93	160–163	24.33	3.38	17.89	24.79	16.18	$C_8H_{15}Cl_2N_7O_3S_2$	24.49	3.85	18.07	25.00	16.35
IIIb	85	125–128	23.63	3.80	31.34	18.91	12.33	$C_{10}H_{19}Br_2N_7O_3S_2$	23.58	3.76	31.38	19.25	12.59
IIIc	94	94–95	26.74	4.26	29.80	17.87	11.82	$C_{12}H_{23}Br_2N_7O_3S_2$	26.93	3.95	29.86	18.32	11.98
IIId	74	76–78	30.10	5.02	28.56	16.92	11.60	$C_{14}H_{27}Br_2N_7O_3S_2$	29.74	4.81	28.27	17.34	11.34
IIIe	81	70–72	32.17	5.15	26.40	16.32	10.61	$C_{16}H_{31}Br_2N_7O_3S_2$	32.28	5.25	26.93	16.52	10.91
IIIf	100	–	34.82	5.34	25.38	15.76	10.26	$C_{18}H_{35}Br_2N_7O_3S_2$	34.91	5.68	25.18	15.78	10.32
IVa	97	172	36.20	3.92	15.10	20.25	13.24	$C_{14}H_{19}Cl_2N_7O_3S_2$	35.90	4.09	15.14	20.93	13.69
IVb	48	164	32.70	3.89	27.00	16.15	10.44	$C_{16}H_{23}Br_2N_7O_3S_2$	32.83	3.96	27.30	16.75	10.96
IVc	68	104–106	35.02	4.40	25.84	15.87	10.46	$C_{18}H_{27}Br_2N_7O_3S_2$	35.24	4.44	26.06	15.98	10.45
IVd	95	89–90	37.21	5.20	25.10	15.01	10.24	$C_{20}H_{31}Br_2N_7O_3S_2$	37.45	4.87	24.92	15.29	10.00
IVe	96	75–78	39.81	5.27	23.43	14.25	9.34	$C_{22}H_{35}Br_2N_7O_3S_2$	39.48	5.27	23.88	14.65	9.58
IVf	65	52–55	41.00	5.60	22.70	13.72	9.44	$C_{24}H_{39}Br_2N_7O_3S_2$	41.32	5.64	22.91	14.06	9.19

Table 2. IR and ^{1}H NMR spectra of isothiuronium salts **IIIa**–**IIIf, IVa**–**IVf**

Comp. no.	IR spectrum (mineral oil)[a], cm^{-1}				^{1}H NMR spectrum (DMSO-d_6), δ, ppm						
	isocyanurate ring	C=O	$\delta(NH_2)$	ν(NH)[b]	C_6H_5	C_6H_5–CH_2	CH_3	NCH_2	CH_2S	–CH_2–	NH_2
IIIa	766 s	1686 v.s	1640 v.s	3200 s	–	–	3.20 s	5.40 s		–	10.2 s
IIIb	755 s	1680 v.s	1640 v.s	3200 s	–	–	3.15 s	4.00 t	3.50 t	–	8.95 s
IIIc	750 s	1680 v.s	1630 v.s	3200 s	–	–	3.17 m	4.00 t	3.17 m	2.09 m	8.90 s
IIId	750 s	1680 v.s	1620 v.s	3200 s	–	–	3.15 m	3.63 t	3.15 m	1.67 m	8.60 s
IIIe	755 s	1680 v.s	1620 v.s	3200 s	–	–	3.16 m	3.63 t	3.16 m	1.52 m	8.98 s
IIIf	760 s	1680 v.s	1625 v.s	3200 s	–	–	3.17 m	3.73t	3.17 m	1.42 m	8.90 s
IVa	764 s	1686 v.s	1640 v.s	3230 s	7.27 s	4.93 s	–	5.43 s		–	9.43 s
IVb	760 s	1686 v.s	1640 v.s	3200 s	7.27 s	4.97 s	–	4.08 t	3.42 m	–	9.06 s
IVc	750 s	1670 v.s	1626 v.s	3200 s	7.27 s	4.95 s	–	3.88 m	3.23 m	1.95 m	9.00 s
IVd	755 s	1680 v.s	1630 v.s	3200 s	7.21 s	4.90 s	–	3.77 m	3.15 t	1.68 m	8.87 s
IVe	756 s	1670 v.s	1620 v.s	3200 s	7.23 s	4.93 s	–	3.80 m	3.12 m	1.55 m	8.94 s
IVf	756 s	1680 v.s	1630 v.s	3200 s	7.25 s	4.94 s	–	3.75 m	3.15 m	1.40 m	8.95 s

[a] The IR spectrum of compound **IIIf** was measured in thin film. [b] Broad band.

cyanurate ring near 760 cm^{-1} [4], strong bands near 1680 [ν(C=O)] and 1620–1630 cm^{-1} [$\delta(NH_2)$], as well as a very strong and broad band in the range 2800–3300 cm^{-1} due to NH stretching absorption [5]. The ^{1}H NMR spectrum contains a broad $\delta(NH_2)$ singlet in the range 8.9–10.3 ppm (Table 2).

Hydrolysis of isothiuronium salts **IIIb**–**IIIf, IVb**–**IVf** in aqueous solutions with solutions of K_2CO_3 or NaOH leads respectively to 1-methyl and 1-benzyl 3,5-bis(ω-mercaptoalkyl) isocyanurates **Vb**–**Ve, VIb**–**VIe** (Table 3). Compounds **Va, VIa** were not isolated under these conditions.

The thiols obtained are transparent oils (**Vc**–**Vf**, **VIb**, **VId**–**VIf**) or white crystals (**Vb, VIc**). They are readily soluble in benzene, carbon tetrachloride, and acetone. The IR spectra of thiols **Vb**–**VIe, VIb**–**VIe** lack, compared with those of the starting isothiuronium salts, ν(NH) and $\delta(NH_2)$ bands and show a new weak band at 2560 cm^{-1} due to ν(SH) (Table 4).

EXPERIMENTAL

The IR spectra were obtained on a Specord IR-75 instrument for thin films or suspensions in Vaseline oil. The ^{1}H NMR spectra were recorded on a Varian T-60 spectrometer at 60 MHz, internal reference TMS.

Table 3. Yields, R_f, melting points, and elemental analyses of 1-methyl and 1-benzyl 3,5-bis(ω-mercaptoalkyl) isocyanurates **Vb**–**Vf**, **VIb**–**VIf**

Comp. no.	Yield, %	R_f (diethyl ether–hexane, 1 : 1)	Found, %				Formula	Calculated, %			
			C	H	N	S		C	H	N	S
Vb[a]	65	0.40	36.12	4.47	15.90	24.14	$C_8H_{13}N_3O_3S_2$	36.49	4.98	15.96	24.35
Vc	38	0.29	41.07	5.98	14.07	21.83	$C_{10}H_{17}N_3O_3S_2$	41.22	5.88	14.42	22.01
Vd	56	0.32	44.96	6.40	12.75	20.41	$C_{12}H_{21}N_3O_3S_2$	45.12	6.63	13.15	20.08
Ve	61	0.45	47.98	7.74	12.24	18.46	$C_{14}H_{25}N_3O_3S_2$	48.39	7.25	12.09	18.39
Vf	29	0.45	51.47	7.85	10.91	17.39	$C_{16}H_{29}N_3O_3S_2$	51.17	7.78	11.19	17.08
VIb	25	0.45	49.40	5.04	12.88	18.94	$C_{14}H_{17}N_3O_3S_2$	49.54	5.05	12.38	18.89
VIc[b]	50	0.40	52.21	6.05	11.40	17.62	$C_{16}H_{21}N_3O_3S_2$	52.30	5.76	11.44	17.45
VId	54	0.50	54.16	6.74	10.68	16.28	$C_{18}H_{25}N_3O_3S_2$	54.66	6.37	10.69	16.21
VIe	21	0.54	65.25	6.82	9.70	15.02	$C_{20}H_{29}N_3O_3S_2$	56.71	6.90	9.70	15.14
VIf	36	0.60	58.18	7.12	9.48	14.25	$C_{22}H_{33}N_3O_3S_2$	58.50	7.36	9.48	14.20

[a] mp 125°C. [b] mp 65–66°C.

Table 4. IR and ^{1}H NMR spectra of 1-methyl and 1-benzyl 3,5-bis(ω-mercaptoalkyl) isocyanurates **Va**–**Vf**, **VIb**–**VIf**

Comp. no.	IR spectrum (thin layer)[a], ν, cm^{-1}			^{1}H NMR spectrum (CCl_4), δ, ppm						
	isocyanurate ring	C=O	SH	C_6H_5	C_6H_5–C*H*$_2$	CH_3	NCH_2	CH_2S	–CH_2–	SH
Vb	760 m	1670 s	2550 m	–	–	3.30 s	4.00 t	2.73 m	–	1.30 t
Vc	760 m, 1450 s	1670 s	2560 m	–	–	3.27 s	3.92 t	2.45 m	1.92 m	1.39 t
Vd	760 m, 1440 s	1670 s	2560 w	–	–	3.27 s	3.80 t	2.50 m	1.68 m	1.17 t
Ve	760 m, 1460 s	1670 s	2560 w	–	–	3.28 s	3.79 t	2.55 m	1.57 m	1.14 t
Vf	760 m, 1450 s	1660 s	2560 w	–	–	3.27 s	3.80 t	2.55 m	1.55 m	1.17 t
VIb	760 m, 1450 s	1680 s	2555 w	7.15 s	4.90 s	–	3.93 t	2.70 m	–	1.23 t
VIc	760 m	1680 s	2560 w	7.23 s	4.95 s	–	3.95 t	2.51 q	1.92 m	1.42 t
VId	760 m, 1450 s	1670 s	2555 w	7.10 s	4.87 s	–	3.74 t	2.47 q	1.65 m	1.19 t
VIe	760 m, 1450 s	1670 s	2560 w	7.12 s	4.86 s	–	3.77 t	2.40 q	1.52 m	1.12 t
VIf	760 m, 1430 s	1670 s	2560 w	7.20 s	4.94 s	–	3.80 t	2.45 q	1.48 m	1.15 t

[a] The IR spectra of compounds **Vb** and **VIc** were mesured in mineral oil.

1-methyl and 1-benzyl 3,5-bis[ω-[amino(imino)-methylthio]alkyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-triones IIId–IIIf, IVb–IVf. Equimolar amounts of 1-methyl- or 1-benzyl-3,5-bis(ω-bromoalkyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione (**Id**–**If**, **IIb**–**IIf**) and thiourea were refluxed in anhydrous methanol for 2 h. After cooling, the thiourea precipitate was filtered off, the filtrate was evaporated in a vacuum, and the residue (isothiuronium salts **IIId**–**IIIf, IVb**–**IVf**) was washed with acetone and dried in a water-jet-pump vacuum on a water bath.

1-Methyl-3,5-bis[2-[amino(imino)methylmercapro]ethyl]-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione hydrobromide (IIIb). Equimolar amounts of 1-methyl-3,5-bis(2-bromoethyl)-1,3,5-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione (**Ia**) and thiourea were refluxed in anhydrous dioxane for 5 h. The dioxane was removed in a vacuum, the residue was treated with methanol, and the thiourea precipitate was filtered off. The filtrate was evaporated in a vacuum, salt **IIIb** was washed with acetone, and dried in a water-jet-pump vacuum on a water bath.

1-Methyl and 1-benzyl-3,5-bis[amino(imino)-methylmercapromethyl]-1,3,5-triazine-2,4,6-(1*H*,3*H*,5*H*)-trione hydrochlorides (IIIa, IVa). Equimolar amounts of 1-methyl- or 1-benzyl-3,5-bis-(chloromethyl)-1,3,5-triazin-2,4,6(1*H*,3*H*,5*H*)-trione (**Ia, IIa**) and thiourea were refluxed in anhydrous iso-

propanol for 1 h. After cooling, compounds **IIIa, IVa** precipitated. The residue was filtered off, washed with diethyl ether, and dried in water-jet-pump vacuum on a water bath.

1-Methyl and 1-benzyl-3,5-bis(ω-mercaptoalkyl)-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-triones (Va–Vf, VIa–VIf). To a solution of 0.005 mol of isothiuronium salt **IIIc–IIIf, IVa–IVf** in 20 ml water, 0.01 mol of aqueous K_2CO_3 (with compound **IIIb, IVb**, 0.01 mol of aqueous NaOH) was added with stirring. The mixture was heated on a water bath (90–95°C) for 1–2 h and then extracted with hot benzene. The benzene extracts were dried with $MgSO_4$, the solvent was removed in a vacuum, and the residue was subjected to chromatography on a column of silica gel, eluent benzene–ethyl acetate, 10 : 1 (**Vb–Vd, Vf, VIe**), benzene–ethyl acetate, 20 : 1 (**Ve**), benzene–ethyl acetate, 100 : 1 (**VIc**), benzene–dioxane, 50 : 1 (**VId**), or ether–hexane, 1 : 1 (**VIb, VIf**). Thiols **Vb, VIc** were recrystallized from diethyl ether–hexane.

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