SYNTHESIS AND INVESTIGATION OF BACTERICIDAL ACTIVITY OF HEXAMETHYLENIMMONIUM DERIVATIVES OF 2,5-DIHALOTHIOPHENOLS

A. M. Kuliev, F. Yu. Rachinskii,
O. D. Shapilov, K. Z. Guseinov,
F. N. Mamedov, V. T. Osipyan,
and T. G. Potapenko

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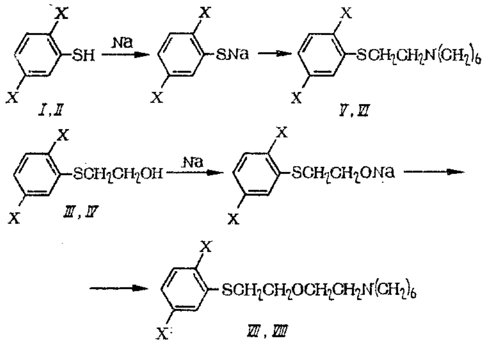
During the continued investigation in the field of synthesis of hexamethylenimine with a potential bactericide activity we have obtained a series of hexamethylenimmonium compounds.

The starting products were 2,5-dichloro- and 2,5-dibromothiophenols (I and II) and also β-hydroxyethylmercapto-2,5-dihalobenzenes obtained based on I and II. Thiophenols were obtained by the reduction of the corresponding sulfochlorides [1] with zinc dust in the presence of mineral acids [2]. The reaction of 2,5-dihalothiophenols with ethylenechlorohydrin in the presence of sodium hydroxide aqueous solution yielded the corresponding β-hydroxyethylmercapto-2,5-dichloro- and β-hydroxyethylmercapto-2,5-dibromobenzene (III and IV).

The reaction of thiophenolates or alcoholates of the compounds cited above with N-(β-chloroethyl)-hexamethylenimine yielded the corresponding compounds (V, VI, or VII, VIII):



I, III, V, VII : X=Cl
II, IV, VI, VIII : X=Br

These sulfur-containing tertiary amines represent viscous liquids readily decomposed when distilled in vacuo (1 mm). Subsequent alkylation of these amines with haloalkyls or with monochloroacetates yielded quarternary ammonium compound soluble in water and alcohol.

The data in Tables 1 and 2 show that the group of compounds under study revealed more defined bactericidal activity with respect to St. aur. than with respect to B. coli. The replacement of an alkyl residue with a monochloroacetate residue affected in a complex way the bactericidal activity of compounds. Dichloro- and dibromo- compounds of thiophenol revealed approximately equal bactericidal effect. An increase in the distance between the nitrogen atoms of hexamethylenimine and thiophenol sulfur increased in most cases the bactericidal activity of compounds (compounds IX and XIX, X and XX, XIV and XXIV, XV and XXV, XVI and XXVI). At the same time it was found that compound XII, in which the distance between

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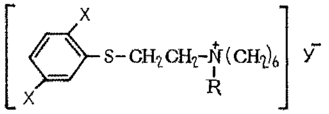
Institute of Chemistry of Additives, Academy of Sciences of the Azerbaidzhan SSR, Baku. S. M. Kirov Military-Medical Academy, Leningrad. Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 5, No. 9, pp. 11-14, September, 1971. Original article submitted December 22, 1969.

TABLE 1. Quaternary Ammonium Salts of Compounds V and VI



Com-pound	X	R	y	Melting point (degrees)	Solubility in water g/100 g	Found, %			Empirical formula	Calculated, %			The lowest concentration leading to the death of task-microbes under exposition for 30 mm	
						halo-gen*	N	S		halo-gen	N	S	B. coli	St. aur.
IX	Cl	$C_{10}H_{21}$	Br	170—2	0,5	15,63	2,42	6,25	$C_{24}H_{40}BrCl_2NS$	15,21	2,67	6,10	1:400	1:3 200
X	Cl	$C_{12}H_{25}$	Br		0,5	14,30	2,38	6,58	$C_{26}H_{44}BrCl_2NS$	14,44	2,53	5,79	1:1 600	1:3 200
XI	Cl	$C_{16}H_{33}$	Br		0,5	13,42	2,80	5,39	$C_{30}H_{52}BrCl_2NS$	13,11	2,31	5,26	1:400	1:3 200
XII	Cl	$CH_2COOC_{10}H_{21}$	Cl		0,5	6,28	2,82	5,62	$C_{26}H_{42}Cl_3NO_2S$	6,58	2,60	5,95	1:6 400	1:25 600
XIII	Cl	$CH_2COOC_{12}H_{25}$	Cl		0,5	6,10	2,50	5,50	$C_{28}H_{46}Cl_3NO_2S$	6,25	2,47	5,65	1:400	1:12 800
XIV	Br	$C_{10}H_{21}$	Br	250(decomp)	0,5	12,70	2,45	5,45	$C_{24}H_{40}Br_3NS$	13,01	2,28	5,22	1:200	1:1 600
XV	Br	$C_{12}H_{25}$	Br		1,0	12,20	2,30	5,30	$C_{26}H_{44}Br_3NS$	12,44	2,18	4,99	1:400	1:1 600
XVI	Br	$CH_2COOC_{10}H_{21}$	Cl		2,5	6,10	2,50	5,31	$C_{26}H_{42}Br_2ClNO_2S$	5,65	2,23	5,10	1:800	1:6 400
XVII	Br	$CH_2COOC_{12}H_{25}$	Cl		2,0	5,80	2,37	4,80	$C_{28}H_{46}Br_2ClNO_2S$	5,40	2,13	4,89	1:800	1:6 400

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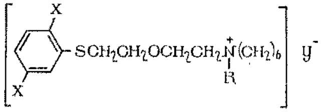
*In an ionic state.

TABLE 2. Quaternary Ammonium Salts of Compounds VII and VIII



Compound	X	R	y	Solubility, in water g/100 g	Found, %			Empirical formula	Calculated, %			The lowest concentration leading to the death of task-microbes under exposition for 30 mm	
					halo-gen*	N	S		halo-gen	N	S	B. coli	St. aur.
XVIII	Cl	C_8H_{17}	Br	1,0	14,58	2,72	5,60	$C_{24}H_{40}BrCl_2NOS$	14,76	2,59	5,92	1:3 200	1:6 400
XIX	Cl	$C_{10}H_{21}$	Br	0,7	13,81	2,26	5,40	$C_{26}H_{44}BrCl_2NOS$	14,03	2,46	5,63	1:6 400	1:12 800
XX	Cl	$C_{12}H_{25}$	Br	0,5	13,18	2,63	5,68	$C_{28}H_{48}BrCl_2NOS$	13,37	2,34	5,36	1:3 200	1:12 800
XXI	Cl	$CH_2COOC_{10}H_{21}$	Cl	1,0	6,40	2,72	5,37	$C_{28}H_{46}Cl_3NO_3S$	6,08	2,40	5,50	1:1 600	1:6 400
XXII	Cl	$CH_2COOC_{12}H_{25}$	Cl	0,4	5,70	2,68	5,41	$C_{30}H_{50}Cl_3NO_3S$	5,80	2,29	5,25	1:800	1:12 800
XXIII	Br	C_8H_{17}	Br	3,0	12,45	2,39	5,32	$C_{24}H_{40}Br_3NOS$	12,68	2,22	5,09	1:3 200	1:3 200
XXIV	Br	$C_{10}H_{21}$	Br	0,1	11,90	2,25	5,10	$C_{26}H_{44}Br_3NOS$	12,14	2,13	4,87	1:3 200	1:6 400
XXV	Br	$C_{12}H_{25}$	Br	0,1	11,32	2,18	4,28	$C_{28}H_{48}Br_3NOS$	11,64	2,04	4,67	1:3 200	1:12 800
XXVI	Br	$CH_2COOC_{10}H_{10}H_{21}$	Cl	1,0	5,10	2,30	4,30	$C_{28}H_{46}Br_2ClNO_3S$	5,28	2,08	4,77	1:1 600	1:12 800
XXVII	Br	$CH_2COOC_{12}H_{25}$	Cl	2,0	5,35	2,28	4,45	$C_{30}H_{50}Br_2ClNO_3S$	5,07	2,00	4,58	1:1 600	1:12 800

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* Calculation of percentage content based on halogen in the ionic state.

the nitrogen and sulfur atoms is the smallest, revealed a fairly high bactericidal effect with respect to both B. coli and St. aur.

EXPERIMENTAL

N-(β-2,5-Dichlorophenylmercaptoethyl)-hexamethylenimine (V). Metallic sodium, 0.1 g atom, was added, gradually with stirring, to 0.1 mole of I in 30 ml of dry benzene. Upon dissolving the sodium, a solution of 0.1 mole of N-(β-chloroethyl)-hexamethylenimine in benzene was added to the reaction mixture at room temperature with stirring. The reaction mass was then heated on a boiling water bath for 8 h; after cooling, the resulting sodium chloride was filtered off. The resulting tertiary amine, a yellow-brown viscous liquid, failed to distill in vacuo at 1 mm. Yield, 50%. Found %: N 4.80; S 9.80; Cl 23.80. $C_{14}H_{19}Cl_2NS$. Calculated %: N 4.60; S 10.54; Cl 23.30.

Similarly, N-(β-2,5-dibromophenylmercaptoethyl)-hexamethylenimine (VI) was obtained.

β-(2,5-Dichlorophenylmercapto)-β'-(hexamethylenimino)diethyl ester (VII). To 0.1 mole of III (bp 120-121° (0.35 mm), n_D^{20} 1.6205, d_4^{20} 1.4148) in 80 ml of dry benzene, 0.1 g-atom of metallic sodium was added, gradually with stirring. Upon dissolving the sodium, 0.1 mole of N-(β-chloroethyl)-hexamethylenimine in benzene was added to the reaction mixture at room temperature with stirring. The reaction mass was heated on a boiling water bath for 12 h, cooled, and filtered off the sodium chloride. The resulting tertiary amine, a dark brown liquid, failed to distill in vacuo at 1 mm. Yield 48%. Found %: N 4.10; S 8.80; Cl 19.62. $C_{16}H_{23}Cl_2NOS$. Calculated %: N 4.02; S 9.20; Cl 20.36.

Similarly from IV [bp 141-142° (0.32 mm), mp 57-58°], β-(2,5-dibromophenylmercapto)-β'-(hexamethylenimine)-diethyl ester (VIII).

(N-Decyl-N-β-2,5-dichlorophenylmercaptoethyl)-hexamethylenimmonium bromide (IX). A mixture of 0.01 mole of V and 0.01 mole of decyl bromide in 25 ml of isopropyl alcohol was refluxed for 20 h, the solvent was removed in vacuo, and the residue treated with dry ether and held in a vacuum desiccator for 5-6 h. Yield 80%.

Other quaternary derivatives of hexamethylenimine were obtained in a similar way.

LITERATURE CITED

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2. A. M. Kuliev and K. Z. Guseinov, Zh. Organ. Kim., 3, 105 (1967).