Notes

UDC 547.2'789.5

Hisashi Tanaka, Minoru Yano, and Katsunosuke Machida : Studies on the Syntheses of Polymethylene-bisthioureas and their Derivatives. II.[1] Syntheses of Polymethylenediamino-2,2'-bis(4-methylthiazolium) and S,S'-Dialkyl-polymethylene-bisthiuronium Salts.

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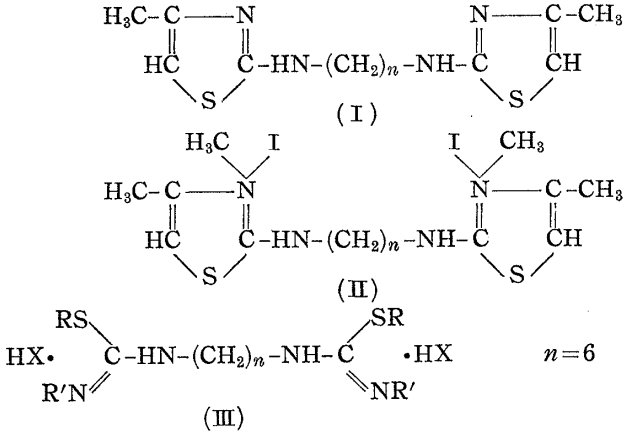
In the previous report, syntheses of polymethylene-bisthioureas were described. This report deals with the syntheses of polymethylenediamino-2,2'-bis(4-methylthiazoles) (I), polymethylenediamino-2,2'-bis(4-methylthiazolium) salts (II) and S,S'-dialkyl-polymethylene-bisthiuronium salts (III). They were submitted to pharmacological tests as a ganglion blocker.



Polymethylene-bisthioureas were reacted with monochloroacetone in ethanol and crystallized polymethylene-bisthiazole hydrochlorides were treated with sodium carbonate. The free polymethylene-bisthiazoles obtained were converted into methiodides by the action of methyl iodide in a sealed tube. This reaction mixture was a viscous jelly and recrystallization was difficult. It was better not to prolong the reaction time to prevent jelly-formation which decreases the yield.

Table I. Polymethylenediamino-2,2'-bis(4-methylthiazoles)

n	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Found C	Found H	Yield (%)
2	214	$C_{10}H_{14}N_4S_2$	47.21	5.55	47.61	5.79	73
4	183	$C_{12}H_{18}N_4S_2$	51.03	6.42	51.29	6.61	68
6	148	$C_{14}H_{22}N_4S_2$	54.15	7.14	54.27	7.45	64

Table II. Polymethylenediamino-2,2'-bis(4-methylthiazolium) Methiodides

n	m.p. (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Found C	Found H	Yield (%)
2	265	$C_{12}H_{20}N_4I_2S_2$	26.77	3.75	27.17	3.98	52
4	236	$C_{14}H_{24}N_4I_2S_2$	29.69	4.27	29.83	4.29	56
6	202	$C_{16}H_{28}N_4I_2S_2$	32.33	4.75	32.62	4.99	48

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1) Part I: This Bulletin, **7**, 206(1959).

When the reaction time was increased from 1 hour to 5 hours, the yield decreased from 50% to 10%. Tables I and II show the m.p. and the analytical data of the polymethylene-bisthiazoles and -bisthiazolium salts obtained.

On the other hand, previously reported hexamethylene-bisthioureas were reacted directly with several alkyl halides and bisthiuronium salts shown in Table III were obtained. Generally, these hexamethylene-bisthiuronium salts were soluble in ethanol and recrystallized from ether-ethanol.

Table III. S,S'-Dialkyl-hexamethylene-bisthiuronium Halides

R	R'	X	m.p. (°C)	Formula	Analysis (%) Calcd. N	Analysis (%) Found N	React. time (hr.)	Yield (%)
C_6H_5-CH_2-	H	Cl	145	$C_{22}H_{32}N_4Cl_2S_2$	11.47	11.27	1.5	81.2
〃	C_6H_5-	〃	179	$C_{34}H_{40}N_4Cl_2S_2$	8.76	8.58	3.0	23.2
〃	C_6H_5NH-	〃	167	$C_{34}H_{42}N_6Cl_2S_2$	12.56	12.80	3.0	41.5
〃	NH_2-	〃	125～126	$C_{20}H_{34}N_6Cl_2S_2$	16.24	16.40	3.0	40.3
〃	CH_3-	〃	60～62	$C_{24}H_{36}N_4Cl_2S_2$	10.87	10.90	3.0	23.2
α-$C_{10}H_7$-CH_2-	H	〃	208	$C_{30}H_{36}N_4Cl_2S_2$	9.54	9.53	1.5	75.8
〃	C_6H_5-	〃	177	$C_{42}H_{44}N_4Cl_2S_2$	7.58	7.47	4.0	33.9
〃	CH_3-	〃	82～83	$C_{32}H_{40}N_4Cl_2S_2$	9.10	9.17	4.0	71.3
β-$C_{10}H_{11}$-CH_2-	C_6H_5-	〃	158～159	$C_{42}H_{44}N_4Cl_2S_2$	7.51	7.47	4.0	65.2
〃	CH_3-	〃	61～62	$C_{32}H_{48}N_4Cl_2S_2$	8.98	8.98	3.0	68.7
CH_2=CH-CH_2-	H	Br	129	$C_{14}H_{28}N_4Br_2S_2$	11.72	11.44	8.0	73.3
〃	C_6H_5-	〃	145	$C_{26}H_{36}N_4Br_2S_2$	8.93	8.65	8.0	48.9
CN-CH_2-CH_2-	〃	Cl	135～136	$C_{26}H_{34}N_6Cl_2S_2$	14.56	15.10	8.0	35.2
H_2NCO-CH_2-	〃	〃	124～125	$C_{24}H_{34}O_2N_6Cl_2S_2$	14.66	14.50	7.0	38.8

The authors extend their deep gratitude to Dr. Seishi Takagi for his encouragement and guidance. They are also indebted to the members of the microanalysis laboratory of the University of Kyoto for the analytical data.

Experimental

(1) **Polymethylenediamino-2,2'-bis(4-methylthiazoles)(I)**—A suspension of polymethylene-bisthioureas (0.01 mole) in 200 cc. of EtOH was warmed at 70° on a water bath. Under stirring, 0.03 mole of monochloroacetone was added dropwise, thereby the reaction mixture became clear soon, and stirring was continued for 3 hr. at 70°. The solution was concentrated to 5 cc. *in vacuo*. After cool, precipitated crystals were dissolved in 15 cc. of water, treated with activated carbon, filtered, and the filtrate was neutralized with saturated aq. Na_2CO_3 solution (ca. 5 cc.). After standing overnight, precipitated white crystals were collected and recrystallized from EtOH.

(2) **Polymethylenediamino-2,2'-bis(4-methylthiazolium) Methiodides (II)**—A solution of polymethylene-bisthiazole (0.01 mole) and MeI (0.02 mole) in 15 cc. of EtOH was heated in a sealed tube on a water bath for 1 hr. After cool, the solvent was distilled off, the viscous residue was dissolved in as small an amount of EtOH as possible. Dehyd. Et_2O was carefully added and precipitated crystals were recrystallized from EtOH-Et_2O.

(3) **S,S'-Dialkylhexamethylene-bisthiuronium Halides(III)**—A solution of hexamethylene-bisthiourea (0.01 mole) in 100 cc. of EtOH, added with 0.2 mole of alkyl halide, was heated on a water bath. The solvent was distilled off *in vacuo* and the residue was recrystallized from a mixture of EtOH and Et_2O.

(Received September 3, 1958)