SYNTHESIS OF BIQUATERNARY AMMONIUM DERIVATIVES OF DECAMETHYLENEDIAMINE

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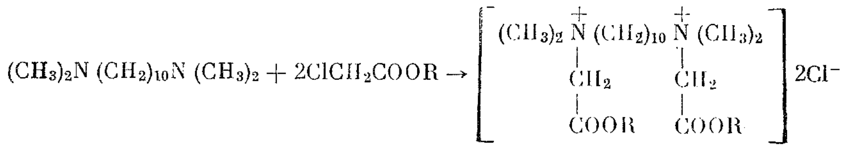
It was shown in [1, 2] that the replacement of the two symmetrical methyl groups in the hexonium cation by alkyl acetate radicals substantially changes the biological properties of the substance. In this case the cholinolytic properties of the compound are substantially weakened, and a broad spectrum of antibacterial action, intensified with increasing size of the radicals, is detected in substances containing comparatively heavy alkyl radicals (beginning with $C_{17}H_{15}$ and above).

For comparison, we synthesized a number of analogous biquaternary ammonium derivatives of decamethylenediamine, the structure and properties of which are reflected in the table. The starting materials were N,N'-tetramethyldecamethylenediamine, which was produced by the previously described method [3], and complex alkyl esters of monochloroacetic acid [1]. The bitertiary diamine reacted almost quantitatively with two nitrogen atoms, forming biquaternary ammonium salts, in benzene medium and in the presence of a small excess of the alkyl ester of chloroacetic acid



$$(CH_3)_2N(CH_2)_{10}N(CH_3)_2 + 2ClCH_2COOR \rightarrow \left[\begin{array}{ccccc}(CH_3)_2 & \overset{+}{N} & (CH_2)_{10} & \overset{+}{N} & (CH_3)_2\\ & | & & | & \\ & CH_2 & & CH_2 & \\ & | & & | & \\ & COOR & & COOR & \end{array}\right]2Cl^-$$

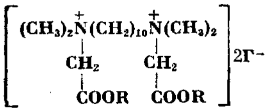
The dichlorides of this structure (I-VIII and XI) represent white crystalline substances, highly hygroscopic, soluble in alcohol and insoluble in ether and benzene. The salts of compounds (IX, X, XI and XII) with chlorine anions were produced in the form of a white gel-like mass, which is not separated from the solvent in which the reaction occurred. As a result of the highly hygroscopic character, their purification by recrystallization was difficult. Hence, except for (I), they were all converted to the diiodides, which dissolve with comparative difficultly in the cold and more readily in hot water, by an exchange reaction with potassium iodide. These salts represent light yellow crystalline substances, with the exception of compounds (X, XI) and (XII), which were obtained in the form of reddish brown, greasy, viscous, noncrystallizing products. They are readily soluble in alcohol, somewhat more difficultly in benzene, acetone, and chloroform, and practically insoluble in ether.

In contrast to the decamethonium $[(CH_3)_3\overset{+}{N}(CH_2)_{10}\overset{+}{N}(CH_3)_3]2I^-$, which, as is well known, manifests a strong curariform action, the salts described practically do not possess this property. As the size of the alkyl radical R is increased (beginning with C_5H_{11} and higher), an antibacterial action is noted, which is intensified as R becomes heavier. In comparison with the analogs containing a hexamethylene or ethylene chain instead of the decamethylene [1], the antibacterial activity of this series of compounds is considerably weaker.

EXPERIMENTAL SECTION

Decamethylene-1,10-bis(dimethylcarbmethoxymethylammonium) Dichloride. N,N'-Tetramethyldecamethylenediamine (2 g) was mixed with 10 ml of benzene, and 2.4 g of the methyl ester of monochloroacetic acid was added. Turbidity was thereupon observed, which, however, grew no stronger even after half an hour of heating on a water bath

Properties of Diquaternary Derivatives of Decamethylenediamine with the Structure



$$\left[\begin{array}{c}(CH_3)_2\overset{+}{N}(CH_2)_{10}\overset{+}{N}(CH_3)_2 \\ \quad | \qquad\qquad\quad | \\ CH_2 \qquad CH_2 \\ \quad | \qquad\qquad\quad | \\ COOR \qquad COOR\end{array}\right] 2\Gamma^-$$

No. of substance	R	Yield, %	M.p., °C	Found, %		Formula	Mol. wt.	Calculated	
				N	Hal			N	Hal
I	CH_3	Quantitative	140—142	6,10 6,40	15,43 15,46	$C_{20}H_{42}O_4N_2Cl_2$	445,5	6,29	15,92
II	C_2H_5	»	73—75	4,02 4,26	38,55 38,98	$C_{22}H_{46}O_4N_2I_2$	656,4	4,27	38,67
III	n-C_3H_7	»	65—67	3,92 3,87	36,75 37,57	$C_{24}H_{50}O_4N_2I_2$	684,5	4,09	37,08
IV	i-C_3H_7	»	128—130	3,98 4,04	36,70 37,00	$C_{24}H_{50}O_4N_2I_2$	684,5	4,09	37,08
V	n-C_4H_9	»	60—65		35,43 34,90	$C_{26}H_{54}O_4N_2I_2$	712,6		35,62
VI	i-C_4H_9	»	70—72	3,94 3,75	35,64 35,75	$C_{26}H_{54}O_4N_2I_2$	712,6	3,93	35,62
VII	n-C_5H_{11}	»	78—80	3,60 3,83	34,64 33,95	$C_{28}H_{58}O_4N_2I_2$	740,6	3,78	34,27
VIII	i-C_5H_{11}	»	88—90	3,59 3,72	34,04 34,75	$C_{28}H_{58}O_4N_2I_2$	740,6	3,78	34,27
IX	n-C_7H_{15}	»	88—90	3,51 3,82	32,28 31,53	$C_{32}H_{66}O_4N_2I_2$	796,7	3,52	31,86
X	n-C_8H_{17}	»			30,00	$C_{34}H_{70}O_4N_2I_2$	824,8		30,77
XI	n-C_9H_{19}	»	—		29,10 29,61	$C_{36}H_{74}O_4N_2I_2$	852,8		29,76
XII	n-$C_{10}H_{21}$	»	—			$C_{38}H_{78}O_4N_2I_2$	880,9		28,81
XIII	$C_6H_5CH_2$	»	98—100	3,53 3,51	32,87 32,53	$C_{32}H_{50}O_4N_2I_2$	780,6	3,59	32,52

under a reflux condenser. The cooled and hermetically covered reaction mixture was allowed to stand at room temperature for 7 days. During the first 24 hours the reaction mixture was converted to a gel-like mass, which gradually crystallized during the subsequent days. The white hygroscopic crystals were filtered off and washed with absolute ether. For recrystallization, the substance obtained was dissolved in absolute alcohol, from which it was precipitated by the addition of absolute ether. The filtered crystals were dried in a vacuum desiccator. Yield quantitative. The dichlorides of compounds (II-XIII) were synthesized by an analogous method. For conversion to the diiodides, concentrated aqueous solutions were prepared from them, to which dry potassium iodide was added until saturation. A yellow oily mass floated up to the surface, which crystallized in a period of 3 to 7 days. The crystals were removed from the surface of the solution, washed with cold water, and recrystallized by the method described above.

The data on the biological properties of the compounds were kindly provided us by N. N. Sudnik, for which the authors would like to express their profound gratitude.

CONCLUSIONS

1. We synthesized 13 derivatives of decamethonium, containing alkyl acetate radicals in place of the two symmetrical methyl groups. Twelve of them were produced in the form of dichlorides and diiodides.

2. Some data are cited on the biological properties of these compounds.

LITERATURE CITED

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