crystals that deposited on the addition of ether were filtered off, washed with ether, and dried. This gave 0.38 g (95%) of oxybis(butylviridiflorine) dichloride with mp 162-163°C. Compound (IVb) was obtained similarly.

SUMMARY

The reaction of α,ω-dibromoalkanes with trachelanthimidine and its derivatives and of bis(4-chlorobutyl) ether with the alkaloids lindelofine and viridiflorine have yielded bisquaternary salts of the pyrrolizidine series.

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SYNTHESIS OF SOME BISQUATERNARY SALTS OF THE ALKALOIDS LOLINE AND LOLININE

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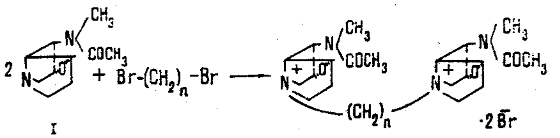
Continuing investigations of the synthesis of bisquaternary salts of the pyrrolizidine bases [1], in order to obtain potential curaremimetic compounds we have studied the reaction of 1,10-dibromoedecane, 1,9-dibromononane, and 1,8-dibromooctane with the alkaloid lolinine (I). Bisquaternary compounds of the latter (IIa-c) were obtained by the reaction of the α,ω-dibromoalkanes with lolinine at room temperature in a ratio of one equivalent of dihalogenoalkane to two equivalents of alkaloid in ethanolic solution with high yields (78-96%).

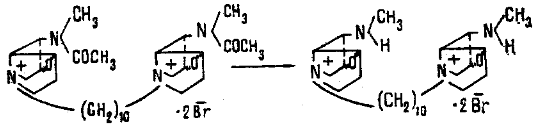
A bisquaternary salt of the alkaloid loline (IIIa) was obtained by hydrolyzing (IIc) with concentrated hydrochloric acid at room temperature.



I

a. n = 8
b. n = 9
c. n = 10

IIa-c



IIc

IIIa

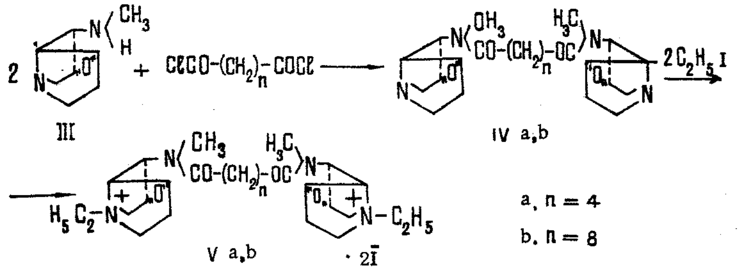
Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 371-374, May-June, 1977. Original article submitted December 31, 1976.

TABLE 1

Compound	*n*	Initial compound	Yield, %	mp, °C*	Empirical formula
II^{a}	8	I a	78	244–245(decomp)	$C_{28}H_{48}O_4N_4Br_2$
II^{b}	9	I a	88	220–222(decomp)	$C_{29}H_{50}O_4N_4Br_2$
II^{c}	10	I a	96	159–160	$C_{30}H_{52}O_4N_4Br_2$
III^{a}	10	IIc	91	220–222	$C_{26}H_{48}O_2N_4Br_2$
IV^{a}	4	IIa	81	122–123	$C_{22}H_{34}O_4N_4$
IV^{b}	8	IIb	71	131–133	$C_{26}H_{42}O_4N_4$
V^{a}	4	IV^{a}	89	141–142	$C_{26}H_{44}O_4N_4I_2$
V^{b}	8	IV^{b}	94	193–194	$C_{30}H_{52}O_4N_4I_2$
VI^{a}	4	V^{a}	93	171–173	$C_{26}H_{44}O_4N_4Cl_2$
IV^{b}	8	V^{b}	91	165–167	$C_{30}H_{52}O_4N_4Cl_2$
VII	—	III	78	159–160	$C_{15}H_{17}O_4N_3$
VIII	—	VII	96	96–97	$C_{17}H_{22}O_4N_3I$

*Compounds (IIa–c) and (IIIa) were purified by reprecipitation of ethanolic solutions with ether. Compound (IVa) was recrystallized from carbon tetrachloride (IVb) and (VIb) from petroleum ether, (Va, b) and (VIII) from acetone, and (VIa) and (VII) from hexane.

We also obtained dilolides of dibasic acids (IVa, b) by the reaction of one equivalent of adipoyl or sebacoyl chloride with two equivalents of loline in the presence of triethylamine in absolute benzene. Then compounds (IVa, b) were converted into the bisquaternary compounds (Va, b) by the action of ethyl iodide.



By the action of silver chloride in methanolic solution, the diethiodides (Va, b) were converted into the diethochlorides (VIa, b). In addition, from loline and p-nitrobenzoyl chloride in the presence of diethylamine we synthesized N-p-nitrobenzoylloline (VII), which was also converted into the ethiodide (VIII). The structures of the compounds obtained were confirmed by elementary analyses and IR spectroscopy (Table 1).

The results of pharmacological trials have shown that compounds (IIa–c) have the same muscle-relaxing effect. The absence of an acetyl group from compound (IIIa) leads to a 2.5-fold increase in its activity as compared with (IIa–c) but it is inferior to the known bisquaternary salts diplacine [2] and dioksonii [3].

The quaternary and bisquaternary compounds (Va, b, VIII) possess a brief hypotensive action, which is due to their ganglion-blocking properties.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrophotometer. The loline and lolinine were isolated from the seeds of Lolium cuneatum [4]. The α,ω-dibromoalkanes and the adipoyl and sebacoyl chlorides were obtained by standard methods [5]. The homogeneity of the substances was checked by chromatography in a thin layer of silica gel in the ethanol–benzene–chloroform (3 : 1 : 6) system.

Decamethylenebislolinine Dibromide (IIc). A solution of 0.3 g (0.001 mole) of 1,10-dibromodecane and 0.4 g (0.002 mole) of lolinine in 5 ml of absolute ethanol was left at room temperature for a day, and the reaction product was precipitated with absolute ether. This gave 0.67 g (96%) of decamethylenebislolinine dibromide with mp 159–160°C.

The bisquaternary salts (IIa, b) were synthesized similarly.

Decamethylenebisloline Dibromide (IIIa). A mixture of 0.2 g (0.0003 mole) of decamethylenebislolinine dibromide and 1 ml of concentrated hydrochloric acid was kept at room temperature for 24 h. Then ethanol was added to the reaction mixture and it was evaporated to dryness. The residue was recrystallized from a mixture of absolute ethanol and absolute ether, giving 0.17 g (91%) of decamethylenebisloline dibromide with mp 220-222°C.

Sebasic Acid Dilolide (IVb). With stirring and ice cooling, 0.56 g (0.0023 mole) of sebacoyl chloride was added to a solution of 0.7 g (0.0045 mole) of loline and 0.5 g of triethylamine in 20 ml of absolute benzene. After 15 min, the reaction mixture was heated in the water bath for 2 h. A precipitate of triethylamine hydrochloride that had deposited was filtered off, and the filtrate was distilled. The residue was chromatographed on a column of alumina. Elution with ether–chloroform (2 : 3) yielded 0.73 g of the bislolide with mp 131-133°C (petroleum ether), R_f 0.36.

Diethiodide of Sebasic Acid Dilolide (Vb). To a solution of 0.7 g (0.0015 mole) of (IVb) in 10 ml of methanol was added 0.6 g of ethyl iodide. The mixture was heated in the water bath for 1 h. The solvent was distilled off to give 1.09 g of sebasic acid dilolide diethiodide with mp 193-194°C (acetone).

Diethochloride of Sebasic Acid Dilolide (VIb). By shaking 1.03 g of (Vb) and silver chloride in methanol we obtained 0.73 g of diethochloride with mp 165-167°C (petroleum ether).

Compounds (IVa), (Va), and (VIa) were synthesized similarly.

N-p-Nitrobenzoylloline (VII). In the presence of triethylamine in absolute benzene, 0.5 g (0.0032 mole) of loline and 0.62 g of p-nitrobenzoyl chloride yielded 0.77 g of N-p-nitrobenzoylloline with mp 159-160°C (hexane), R_f 0.52.

N-p-Nitrobenzoylloline Ethiodide (VIII). Compound (VIII) was obtained from (VII) and ethyl iodide in the same way as (Vb), mp 96-97°C (acetone).

SUMMARY

1. By the reaction of α,ω-dibromoalkanes with the alkaloid lolinine, bisquaternary salts have been synthesized the hydrolysis of the acetyl group of which has led to bisquaternary salts of loline.

2. Dilolamides have been obtained from loline and sebacoyl and acetoyl chlorides, and there have been converted into diethiodides by the action of ethyl iodide.

In this way, 12 new compounds not previously described in the literature have been synthesized.

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