the presence of cyclic anhydride V in the reaction mixture was observed by IR spectroscopy. The low intensity of the absorption bands corresponds to the low percentage of anhydride V in the reaction products. The changes in the intensities of the bands of anhydride V are insignificant in samples selected at reaction mixture temperatures from 120 to 135°. This makes it possible to assume that cyclic anhydride V is formed at approximately the same temperatures as quinolone VI and that the rate of formation of anhydride V evidently differs little from the rate of its conversion to quinolone VI.

EXPERIMENTAL

The IR spectra were measured with a UR-20 spectrometer. The cyclization reaction was carried out by the method described in [1-3]. The samples for the spectral studies were selected from the reaction mixture at temperatures from 80 to 145°; prior to the start of carbon dioxide evolution (<100°) and at 110-145°, initially every 10 min and then every 5 min. The 120-130° temperature range, over which the measurements showed that the intensity of the bands of the cyclic anhydride was at a maximum, was particularly thoroughly investigated. At these temperatures samples were selected from the reaction mixture every 2 min.

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STEREOCHEMISTRY OF THE QUATERNIZATION OF 2- AND 4-EPIMERIC trans-1-ALKYL-2-METHYL-4-ETHYNYLDECAHYDRO-4-QUINOLOLS WITH ALKYL HALIDES

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The quaternization of trans-1-alkyl-2-methyl-4-ethynyldecahydro-4-quinolols containing an equatorial 2-CH_3 group by means of methyl iodide proceeds with predominant axial incorporation of the methyl group, whereas quaternization of the corresponding trans-1,2-dimethyl-4-ethynyldecahydro-4-quinolols by means of ethyl and n-propyl iodide takes place with predominant equatorial incorporation of the alkyl group; the ratios of the stereoisomers in the products of forward and reverse quaternization are approximately identical. Methylation of amino alcohols with an axial 2-CH_3 group also leads to the predominant formation of epimers of the quaternary salts with an axial methyl group attached to the nitrogen atom, whereas the reverse quaternization of these amino alcohols proceeds nonstereoselectively to give an approximately equimolar mixture of the epimers of the quaternary salts.

In the case of quaternization of trans-1-alkyldecahydroquinolines [1] and trans-1-alkyl-4-ethynyldecahydro-4-quinolols [2] with alkyl halides it was found that the addition

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TABLE 1. Chemical Shifts and Ratios of the Products of the Forward and Reverse Quaternization of trans-1-Alkyl-2-methyl-4-ethynyldecahydro-4-quinolols

Starting compound	Reagent	Quaternization products					
		compound	mp of the crude mixture, °C	δ_{N-CH_3}, ppm	N-CH_3 orientation	yield, %	
						in allylation	in methylation
I	C_2H_5I	X	220—222	3,17	I*e*	3	0
IV	CH_3I	XI		3,01	I*a*	97	100
II	C_2H_5I	XII	239—241	3,18	I*e*	6	4,5
V	CH_3I	XIII		3,00	I*a*	94	95,5
III	C_2H_5I	XIV	240—242	3,20	I*a*	50	80
VI	CH_3I	XV		3,12	I*e*	50	20
I	n-C_3H_7I	XVI	207—209	3,04	I*a*	100	100
VII	CH_3I						
II	n-C_3H_7I	XVII	222—224	3,00	I*a*	100	100
VIII	CH_3I						
III	n-C_3H_7I	XVIII	224—227	3,14	I*a*	50	79
IX	CH_3I	XIX		3,07	I*e*	50	21
I	HCl	XX	233—235	2,88	I*e*	81	—
		XXI		2,70	I*a*	19	—
II	HCl	XXII	247—249	2,86	I*e*	79	—
		XXIII		2,68	I*a*	21	—
III	HCl	XXIV	242—250	2,93	I*a*	18	—
		XXV		2,82	I*e*	82	—

of a methyl group occurs primarily from the axial region, whereas the addition of substituents with a large number of carbon atoms takes place primarily from the equatorial region with less selectivity than in the case of methylation.

In order to ascertain the effect of the orientation of the methyl substituent in the position relative to the nitrogen atom on the stereochemistry of quaternization, in the present research we studied the quaternization of three stereoisomeric trans-1,2-dimethyl-4-ethynyldecahydro-4-quinolols [3, 4] (with 2e4a, 2e4e, and 2a4e orientations of the methyl and ethynyl substituents for I-III, respectively) and their 1-ethyl (IV-VI) and 1-propyl (VII-IX) analogs. The starting tertiary bases (IV-IX) were obtained either by reaction of 1-alkyl-2-methyldecahydro-4-quinolones with acetylene or by alkylation of the stereoisomeric 2-methyl-4-ethynyldecahydro-4-quinolols. The reaction products were analyzed by PMR spectroscopy from the chemical shifts and the intensities of the signals of the protons of the n-methyl groups (Table 1).

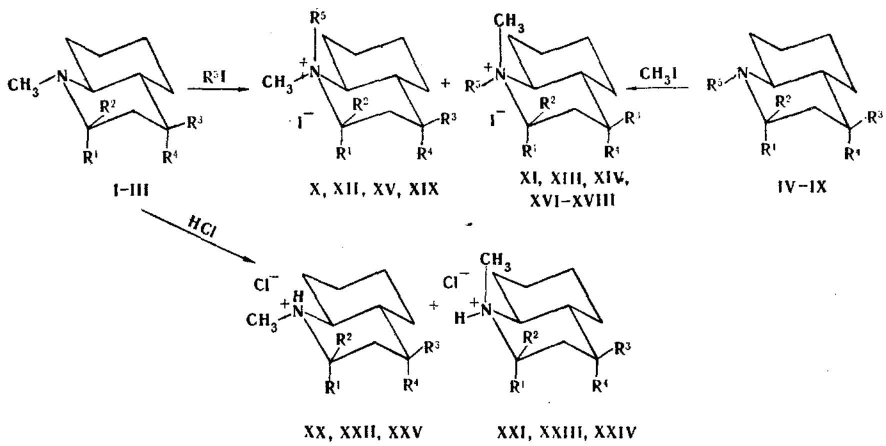
In the reaction of amino 4-epimeric amino alcohols I and II with ethyl iodide in each case we obtained a mixture of two quarternization products in which the epimer with an equatorial ethyl group attached to the nitrogen atom predominated (as evidenced by the intense $N{-}CH_3$ signal at stronger field) (Table 1). The PMR spectra of the products of the reaction of amino alcohols I and II with propyl iodide were detected from the singlet of the N-methyl groups, and it was assumed that the epimers of quaternary salts with an equatorial propyl group attached to the nitrogen atom are formed stereoselectively in this case.

Reverse quaternization — methylation of bases IV, V, VII, and VIII — led to the formation of an epimeric mixture with a composition close to that of the mixture obtained by alkylation of the corresponding 1-methyl-substituted base I and II.

The data in Table 1 constitutes evidence that the orientation of the substituents in the 4 position does not have an appreciable effect on the epimeric composition of the products of forward and reverse quaternization.

The products of quaternization of decahydro-4-quinolol III, which has an axial 2-CH_3 group, with ethyl and n-propyl iodide have two signals of N-CH_3 groups of approximately equal intensity in their PMR spectra; this indicates the absence of stereoselectivity in these reactions.

Methylation of 1-ethyl- and 1-propyl-substituted bases VI and IX, which are analogs of amino alcohol III, gives a mixture of isomeric quaternary salts, in the PMR spectra of which more intense N-CH_2 signals are found at weaker field. With allowance for the data in [5] obtained for methiodides of 1,2-dimethyl-4-phenylpiperidines, the more intense signal at weaker field should be assigned to the axial N-methyl group, and, on the basis of this, it should be concluded that axial incorporation of the methyl group is preferred.



I, II, IV, V, VII, VIII, X—XIII, XVI, XVII, XX—XXIII $R^1=H$, $R^2=CH_3$; I, IV, VII, X, XI, XVI, XX, XXI $R^3=OH$, $R^4=C\equiv CH$; I—VI, X—XV $R^5=C_2H_5$; VII—IX, XVI—XIX $R^5=n\text{-}C_3H_7$; III, VI, IX, XIV, XV, XVIII, XIX, XXIV, XXV $R^1=CH_3$, $R^2=H$; II, III, V, VI, VIII, IX, XVII—XIX, XXII—XXV $R^3=C\equiv CH$, $R^4=OH$

Thus, quaternization of trans-1-alkyl-2-methyl-4-ethynyldecahydro-4-quinolols containing an equatorial 2-CH_3 group by means of methyl iodide proceeds with predominant axial incorporation of the methyl group, whereas quaternization of the corresponding trans-1,2-dimethyl-4-ethynyldecahydro-4-quinolols with ethyl and n-propyl iodide takes place with predominant equatorial incorporation of the alkyl group; the products of forward and reverse quaternization have similar epimeric compositions.

Methylation of amino alcohols with an axial 2-CH_3 group also leads to the predominant formation of epimers of the quaternary salts with an axial methyl group attached to the nitrogen atom, whereas reverse quaternization of these amino alcohols proceeds nonstereoselectively. The data in Table 1 confirm that methylation of amino alcohols with an equatorial 2-CH_3 group takes place with a higher stereoselectivity than with the epimeric bases containing an axial 2-CH_3 group.

The PMR spectra of the products of quaternization of stereoisomeric amino alcohols I-III with hydrogen chloride each contained two signals of an N-methyl group. Moreover, the presence of a more intense N-CH_3 signal at weaker field is characteristic for the isomeric mixtures of hydrochlorides obtained from amino alcohols I and II. In contrast to this, the mixture of hydrochlorides obtained from amino alcohol III displayed a more intense signal of an N-methyl group at stronger field. On the basis of these data, it was concluded that protonation of amino alcohols I-III takes place primarily axially.

EXPERIMENTAL

The PMR spectra of CD_3OD solutions of the N,N-dialkyl-substituted quaternary salts (Table 1) were recorded with a JEOL PS-100 spectrometer at room temperature with tetramethylsilane as the internal standard.

TABLE 2. Quaternary Salts of trans-1-Alkyl-2-methyl-4-ethynyldecahydro-4-quinolols

Compound	mp, °C	Found, %				Empirical formula	Calc., %			
		C	H	N	halogen		C	H	N	halogen
XI	224—226	49,5	7.2	3,9	34,7	$C_{15}H_{26}INO$	49,7	7,2	3,9	34,8
XIII	240—242	49,8	7,1	3,8	34,7	$C_{15}H_{26}INO$	49,7	7,2	3,9	34,8
XIV	255—257	49,7	7,1	3,9	35,0	$C_{15}H_{26}INO$	49,7	7,2	3,9	34,8
XVI	219—220	51,1	7,4	3,5	33,4	$C_{16}H_{28}INO$	51,1	7,4	3,7	33,5
XVII	228—229	51,4	7,5	3,5	33,6	$C_{16}H_{28}INO$	51,1	7,4	3,7	33,5
XVIII	254—255	51,3	7,6	3,6	33,7	$C_{16}H_{28}INO$	51,1	7,4	3,7	33,5
XIX	221—222	51,2	7,4	3,7	33,6	$C_{16}H_{28}INO$	51,1	7,4	3,7	33,5
XX	240—241	63,9	9,3	5,8	14,5	$C_{13}H_{21}NO \cdot HCl$	64,0	9,1	6,0	14,5
XXII	251—253	64,1	9.2	5,9	14,4	$C_{13}H_{21}NO \cdot HCl$	64,0	9,1	6,0	14,5
XXV	267—269	63,9	9,0	6,1	14,7	$C_{13}H_{21}NO \cdot HCl$	64,0	9,1	6,0	14,5
XXVI	228—229	48,4	7,0	3,8	36,2	$C_{14}H_{24}INO$	48,2	6,9	4,0	36,4
XXVII	258—260	48,2	6,8	3,8	36,4	$C_{14}H_{24}INO$	48,2	6,9	4,0	36,4
XXVIII	276—278	48,5	7,1	3,8	36,7	$C_{14}H_{24}INO$	48,2	6,9	4,0	36,4

The quaternization of the 1,2-dimethyl-4-ethynyldecahydro-4-quinolols was carried out with alkyl iodides in benzene at 80°, and the methylation of 1-alkyl-2-methyl-4-ethynyldecahydro-4-quinolols was carried out with methyl iodide in diethyl ether at 5°. The end of the reaction was monitored by thin-layer chromatography (TLC) on Woelm aluminum oxide [ethanol—chloroform (3:1)]. The quaternization reaction went practically to completion. The individual quaternization products (Table 2) were isolated by fractional crystallization from ethanol.

1,2-Dimethyl-4-ethynyldecahydro-4-quinolol Propiodides (XVIII, XIX). A mixture of 1 g of alcohol III, 10 ml of n-C_3H_7I, and 30 ml of benzene was heated at 80° for 72 h, after which workup gave 1.8 g of a mixture of propiodides XVIII and XIX with mp 224-227°. PMR spectrum of the crude mixture: N-CH_3, δ 3.07 (~50%) and 3.14 ppm (~50%). Fractional crystallization of 0.4 g of the mixture yielded 0.1 g of propiodide XVIII, with mp 254-255° (δ 3.14 ppm), and 0.05 g of propiodide XIX with mp 221-222° (δ 3.07 ppm).

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STEREOCHEMISTRY OF THE SYNTHESIS OF 2,9-DIMETHYL- AND 1,2,9-TRIMETHYLDECAHYDRO-4-QUINOLONES AND SOME OF THEIR HYDROXY DERIVATIVES

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Individual 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolones were isolated by separation of mixtures of the stereoisomers. The stereochemistry of reactions involving the addition of hydrogen, acetylene, and organomagnesium compounds to the carbonyl group was studied. The structure of the 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolones and the corresponding amino alcohols were established on the basis of their IR and PMR spectra.

We have previously demonstrated the presence of n-cholinolytic activity in a number of derivatives of decahydroquinoline [1] and have made a detailed investigation of the relationship between the three-dimensional structure and the n-cholinolytic activity of the stereoisomers of 1,2,4-trisubstituted decahydro-4-quinolols [2]. In order to synthesize new decahydroquinoline derivatives and make a further study of the relationship between their structures and their biological activity, in the present research we studied the stereochemistry of 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolones and their derivatives.

Thin-layer chromatography (TLC) of 2,9-dimethyldecahydro-4-quinolone, obtained by cyclization of β-methoxypropyl-2-methyl-Δ'-cyclohexenyl ketone with ammonia [3] on aluminum oxide

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