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-ethynyl-decahydro-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).

LITERATURE CITED

1. D. R. Brown, R. Lygo, J. McKenna, J. M. McKenna, and B. G. Butley, J. Chem. Soc., B, 1184 (1967).
2. A. A. Akhrem, L. I. Ukhova, N. F. Marchenko, G. P. Kukso, and V. M. Gorul'ko, Khim. Geterotsikl. Soedin., No. 2, 221 (1977).
3. A. A. Akhrem, L. I. Ukhova, and N. F. Uskova, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 304 (1962).
4. A. A. Akhrem. L. I. Ukhova, and N. F.Uskova, Izv. Akad. Nauk SSSR, Ser. Khim., 900 (1970).
5. A. F. Casy and K. M. J. McErlane, J. Chem. Soc., Perkin I, 726 (1972).

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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TABLE 1. Parameters of the PMR Spectra of 2,9-Dimethyl- and 1,2,9-Trimethyldecahydro-4-quinolones (solutions in CCL_4, 20°C)

Compound	δ, ppm						J, Hz				Width of the 2-H multiplet, Hz
	9-CH_3	N—H, N—CH_3	3-H_a	3-H_e	2-H	2-CH_3	2-H, 2-CH_3	2-H, 3-H_a	2-H, 3-H_e	3-H_a, 3-H_e	
I	1,27	2,10	1,92	2,23	3,31	1,14	6	11	3	14	32
II	0,95	2,12	1,94	2,24	3,34	1,16	6	11	4	14	34
IV	0,75	2,24	—	—	2,86	1,18	6	12	4	—	34

showed that it is a mixture of three isomers [34, 58, and 8% of each according to the results of gas–liquid chromatography (GLC)]. Fractional crystallization of the mixture of stereoisomeric picrates and the hydrochlorides yielded two individual picrates and hydrochlorides, decomposition of which on aluminum oxide gave two amino ketone bases I and II with mp 38-40° and 40-42°, respectively. An attempt to isolate isomer III by preparative TLC was unsuccessful because of its facile isomerization in solution to ketone I.

During TLC of 1,2,9-trimethyldecahydro-4-quinolone on Al_2O_3 it was found that it is also a mixture of three stereoisomers in a ratio of 6:67:27 according to GLC. Crystallization of the mixture of picrates or hydrochlorides yielded the individual picrate and hydrochloride, decomposition of which on Al_2O_3 gave liquid ketone IV. Attempts to isolate ketones V and VI through their crystalline derivatives by preparative TLC were unsuccessful because of their instability.

The PMR spectra of ketones I and II differ mainly only with respect to the chemical shift of the signal of the protons of the 9-CH_3 group (Table 1). The signal of the protons of the 9-CH_3 group of I is found in weaker field as compared with the analogous signal of II, and this indicates cis fusion of the rings of ketone I [4]. The 2-H proton of ketones I, II, and IV gives a 32-34-Hz-wide multiplet containing vicinal constants of coupling with the 3-H protons of 11-12 and 3-4 Hz; this constitutes evidence for axial orientation of this proton and equatorial orientation of the methyl group in ketones I, II, and IV. The presence of a methyl group attached to the nitrogen atom in ketone IV gives rise to shielding of the 9-CH_3 group and the 2-H proton as compared with ketone II. Since individual ketone IV is formed in the methylation of 2,9-dimethyldecahydro-4-quinolone (II) with a mixture of formaldehyde and formic acid, the former was assigned a structure similar to that of ketone II. Methylation of ketone I under the same conditions leads to a mixture of ketones IV-VI.

To confirm the three-dimensional structures of ketones I, II, and IV we studied the stereochemistry of these ketones under various conditions (Table 2). The reduction of trans-ketones II and IV with an axial 9-CH_3 group with hydrogen in the presence of Raney nickel or complex metal hydrides proceeds stereoselectively to give only one stereoisomer of 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols (VII, IX), which has an axial hydroxyl group, in 85-98% yields. Secondary alcohols VIII and X with an equatorial hydroxyl group

TABLE 2. 2,9-Dimethyl- and 1,2,9-Trimethyldecahydro-4-quinolols

Compound	mp, °C	Found, %*			Yield, †			
		C	H	N	H_2, Raney Ni†	$NaBH_4$	$LiAlH_4$	Na, ethanol
VII	132—133	72,3	11,6	7,6	98 (90)	91	88	0
VIII	161—161	72,1	11,5	7,7	0 (0)	0	0	50
IX	171—172	72,9	11,6	7,0	98 (85)	95	85	0
X	121—122	73,4	11,7	6,9	0 (0)	0	0	40
XI	149—150	72,3	11,7	7,6	97 (88)	60	70	0
XII	150—151	72,0	11,4	7,8	0 (0)	30	22	70
XIII‡	51—53	73,2	11,2	7,0				
XIV‡	71—72	72,9	11,5	7,1				

*Calculated from 2.9-dimethyldecahydro-4-quinolols: ($C_{11}H_{21}NO$): C 72.1; H 11.5; N 7.6%. Calculated from 1,2,9-trimethyldecahydro-4-quinolols ($C_{12}H_{23}NO$): C 73.1; H 11.7; N 7.1%.

†The yields in the reduction of the hydrochlorides are presented in parentheses.

‡Decahydroquinolols XIII and XIV were obtained by methylation of alcohols XI and XII, respectively.

TABLE 3. Parameters of the PMR Spectra of 2,9-Dimethyl- and 1,2,9-Trimethyldecahydro-4-quinolols and Their Esters (solution of $CDCl_3$, 20°C)

Compound	δ, ppm						J, Hz						Width of the 4-H multiplet, Hz
	9-CH$_3$	2-CH$_3$	2-H	4-H	4-CH$_3$	N-CH$_3$	2-CH$_3$, 2-H	2-H 3-H$_a$	2-H$_a$, 3-H$_e$	4-H, 3-H$_e$	4-H, 3-H$_a$	4-H, 10-H	
VII	1,28	1,04	3,34	3,87	—	—	6	12	3	—	—	—	8
VIII	1,04	1,07	3,08	3,49	—	—	6	12	3	5,2	10	10	25,5
IX	1,09	1,09	2,83	3,77	—	2,20	5,5	11	2,5	—	—	—	8
X	0,85	1,10	2,56	3,39	—	2,17	6	12	3	4,5	10,5	10,5	25,5
XI	1,13	1,05	3,32	4,06	—	—	6	12	3	3	3	3	9
XII	1,17	1,06	2,95	3,87	—	—	6	12	2,3	4,5	10	10	25
XIII	1,05	1,03	3,09	4,12	—	2,17	6	12	2	—	—	—	18
XIV	1,21	1,02	2,50	3,63	—	2,14	6	12	3	4	12	12	28
XV	0,96	0,98	2,61	4,78	1,91	2,08	5,5	11	2,3	—	—	—	8
XVI	0,88	1,12	2,56	4,55	1,94	2,09	6	12	3	5	11	11	26,5
XVII	1,07	1,04	3,04	5,19	1,94	2,14	6	12	2	4	7	7	18
XVIII	1,24	1,02	2,60	4,97	1,93	2,14	6	12	3	4,5	12	12	28

were obtained in 40 and 50% yields in the reduction of the same ketones with sodium in alcohol. The reduction of cis-ketone I with hydrogen in the presence of Raney nickel and with sodium in alcohol proceeds in the same way as the reduction of ketones II and IV to give, in the first case, the axial epimer of alcohol XI (in 98% yield) and, in the second case, the equatorial epimer of secondary alcohol XII (in 70% yield). In contrast to this, a mixture of two epimeric secondary alcohols with predominance of the axial epimer of XI (60% in the case of reduction with sodium borohydride and 70% in the case of reduction with lithium aluminum hydride) is formed in the reduction of ketone I with complex metal hydrides. Starting ketones I, II, and IV are detected (in 10-50% amounts) along with secondary alcohols VII-XII, in the reaction products in the case of reduction of ketones I, II, and IV with complex metal hydrides and with sodium in alcohol, as well as in the case of reduction of the hydrochlorides of ketones I, II, and IV in the presence of Raney nickel.

The signal of the 4-H proton in the PMR spectra of secondary alcohols VII, IX, and XI is found at weaker field as compared with the signal of the same proton in the spectra of epimeric alcohols VIII, X, and XII (Table 3). The width of the multiplet of the 4-H proton in the spectra of alcohols VII, IX, and XI is 8 Hz, as compared with ∿26 Hz in the spectra of VIII, X, and XII. These data constitute evidence for equatorial orientation of the proton and axial orientation of the hydroxyl group attached to C_4 in alcohols VII, IX, and XI and for axial orientation of the proton and equatorial orientation of the hydroxyl group in alcohols VIII, X, and XII. The axial 4-OH group deshields the axial methyl group attached to C_9 in secondary alcohols VII and IX; this also confirms the configuration of the alcohols obtained [5]. The vicinal spin-spin coupling constants (SSCC) of the 4-H proton with the 10-H methylidyne proton in the spectra of secondary alcohols VIII, X, and XII constitute evidence for axial orientation of the 10-H proton relative to the piperidine ring.

The signal of the 10-H proton in the spectrum of the benzamide obtained from ketone II is distinctly resolved in the form of a quartet centered at δ 2.96 ppm. The SSCC of this proton with the 5-H protons (10 and 3 Hz) indicate its axial orientation relative to the cyclohexane ring. The angular 10-H proton in ketone II is thus axially oriented relative to both rings, and this attests to their trans fusion.

It was shown by GLC that the mixture of stereoisomeric 2,9-dimethyldecahydro-4-quinolones contains more ketone I, which has cis-fused rings, than ketone II, which has trans-fused rings. The literature data [6] on 9-methyl- and 10-methyldecahydro-3-isoquinolones also provide evidence for predominance of the cis isomer as compared with the trans isomer in the mixture of stereoisomers. The incorporation of a methyl group at the nitrogen atom changes the ratio of the resulting stereoisomeric 1,2,9-trimethyldecahydro-4-quinolones in favor of stereoisomer IV with trans-fused rings.

Alcohols IX and X were obtained in good yields by methylation of alcohols VII and VIII with a mixture of formaldehyde and formic acid, and 1,2,9-trimethyl-substituted secondary alcohols of the cis series XIII and XIV were isolated in the methylation of alcohols XI and XII under the same conditions. The signal of the 4-H proton in the PMR spectrum of decahydroquinolol XIII is shifted to weaker field as compared with the signal of the same proton, epimeric with respect to C_4, of decahydroquinolol XIV (Table 3). On the basis of this, an equatorial orientation was assigned to this 4-H proton in the spectrum of alcohol XIII,

TABLE 4. 1,2,9-Trimethyl-4-acetoxy- and 1,2,9-Trimethyl-4-ethynyl-4-acetoxydecahydroquinolines

Compound	mp, °C		Reaction temp., °C	Found, %*				Yield, %
	base	hydrochloride		C	H	Cl	N	
XV	—	163—165	60	60,7	9,4	12,9	5,3	78
XVI	45—47	218—219	20	60,9	9,3	12,8	4,9	84
XVII	—	239—240	60	60,8	9,2	12,9	5,3	72
XVIII	48—50	256—257	20	61,2	9,4	13,1	5,0	76
XXXII	110—111	248—250	100	72,9	9,6	—	5,4	85
XXXIII	71—72	220—222	95	73,1	9,7	—	5,3	82

*Calculated for the hydrochlorides of bases XV-XVIII ($C_{14}H_{25}NO_2 \cdot HCl$): C 61.0; H 9.4; Cl 12.9; N 5.4%. Calculated from free bases XXXII and XXXIII ($C_{16}H_{25}NO_2$): C 73.0; H 9.5; N 5.3%.

whereas an axial orientation was assigned to the analogous proton in epimeric alcohol XIV. The sum of the vicinal SSCC of the 4-H proton (28 Hz) in the spectrum of alcohol XIV is in agreement with the relative value of its chemical shift, whereas it is 18 Hz instead of the usual 8-9 Hz in the spectrum of alcohol XIII. The observed anomaly can evidently be explained by partial deformation of the molecule of axial secondary alcohol XIII when a methyl substituent is incorporated at the nitrogen atom.

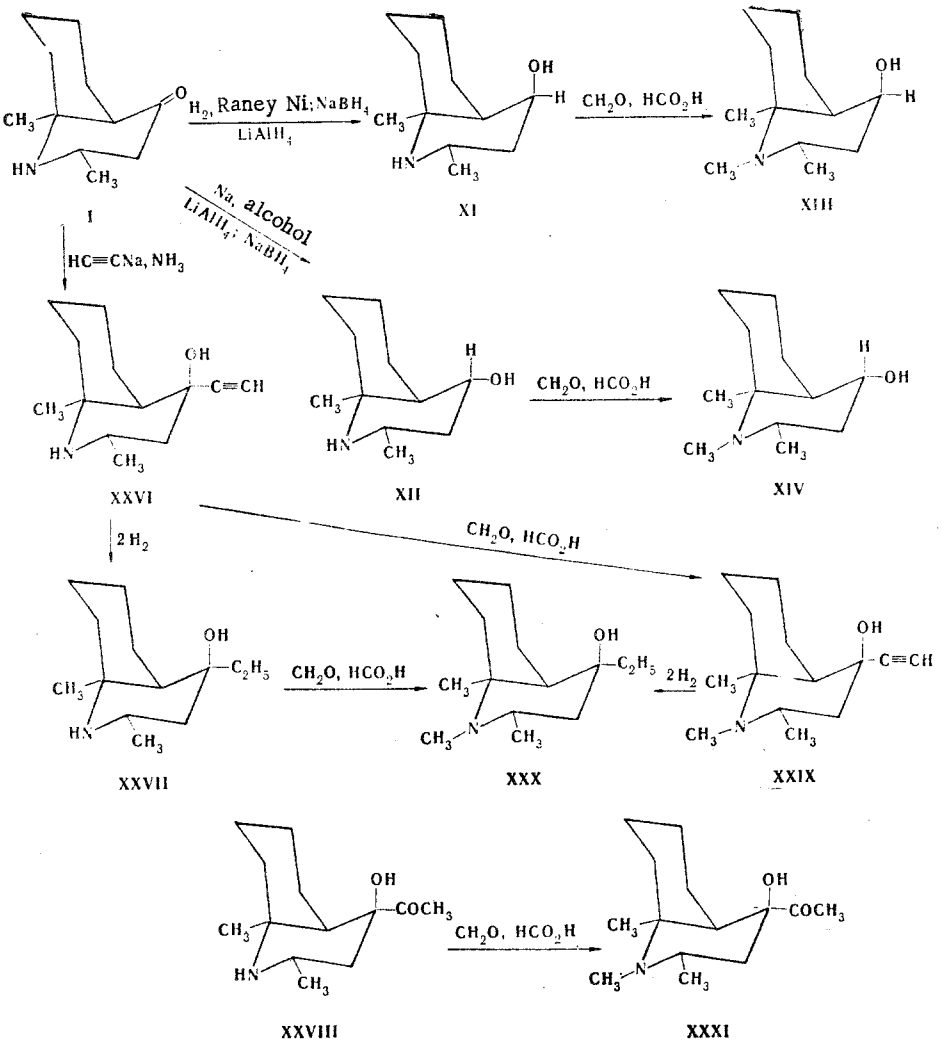
Esters XV-XVIII (Table 4) were obtained by acetylation of alcohols XI-XIV with a mixture of acetic anhydride and acetyl chloride in benzene. The esterification of alcohols XII and XIV with an equatorial hydroxyl group proceeds under milder conditions (at room temperature) than the esterification of the axial epimers of secondary alcohols XI and XIII (at 60°); this is in agreement with the data in the alicyclic series [7]. In the PMR spectra of esters XV-XVIII the signals of the 4-H protons, which are deshielded by the adjacent acetoxy group, are shifted to weaker field as compared with the analogous signals of the corresponding alcohols XI-XIV. The SSCC of the protons of the piperidine ring in esters XV-XVIII and the observed regularities in the chemical shifts are the same as in the spectra of the corresponding starting secondary alcohols XI-XIV (Table 3).

As compared with esterification, a reverse relationship in the reaction rates is observed in the oxidation of secondary alcohols VII-XIV with chromic anhydride in acetic acid [8]: axial epimers VII, IX, XI, and XIII are oxidized twice as fast as equatorial epimers VIII, X, XII, and XIV. The corresponding individual starting ketones I, II, and IV are formed as a result of oxidation of secondary alcohols VII-XII, while oxidation of secondary alcohols XIII and XIV, obtained by methylation of cis-2,9-disubstituted alcohols XI and XII, proceeds with isomerization and, instead of the corresponding cis-ketone, gives a mixture of trans-ketone IV (89 and 82%) and ketone V (11 and 18%), respectively.

The ethynylation of trans-ketone IV with sodium acetylide in liquid ammonia and ethynylmagnesium bromide and under the conditions of the Favorskii reaction takes place with the formation, in all cases, of the same 1,2,9-trimethyl-4-ethynyldecahydro-4-quinolol (XXII) in 91, 32, and 21% yields, respectively [9]. The reaction of ketone IV with ethyl- and vinylmagnesium bromides gives, respectively, 4-ethyl- and 4-vinyl-substituted alcohols XXIII and XXIV in 76 and 88% yields, respectively; these alcohols are identical to the alcohols obtained by exhaustive and selective hydrogenation of acetylenic alcohol XXII.

The addition of sodium acetylide in liquid ammonia to trans-ketone II gives the corresponding 2,9-dimethyl-4-ethynyldecahydro-4-quinolol (XIX) in 95% yield, while the Grignard reaction gives 2,9-dimethyl-4-ethyldecahydro-4-quinolol (XX) in 72% yield; the latter is identical to the product of exhaustive hydrogenation of acetylenic alcohol XIX. The corresponding 4-acetyldecahydro-4-quinolols (XXI and XXV) were obtained from acetylenic alcohols XIX and XXII by hydration in the presence of mercurous sulfate. Methylation in 2,9-dimethyl-substituted alcohols XIX-XXI leads to the corresponding 1,2,9-trimethyldecahydro-4-quinolols (XXII, XXIII, and XXV).

cis-Ketone I reacts slowly with sodium acetylide in liquid ammonia to give 2,9-dimethyl-4-ethynyldecahydro-4-quinolol (XXVI) in low yield (42%); a portion of ketone I is recovered from the reaction mixture. 2,9-Dimethyl-4-ethyldecahydro-4-quinolol (XXVII) was obtained by exhaustive hydrogenation of acetylenic alcohol XXVI, whereas 2,9-dimethyl-4-acetyldecahydro-4-quinolol (XXVIII) was obtained by hydration in the presence of mercurous sulfate.



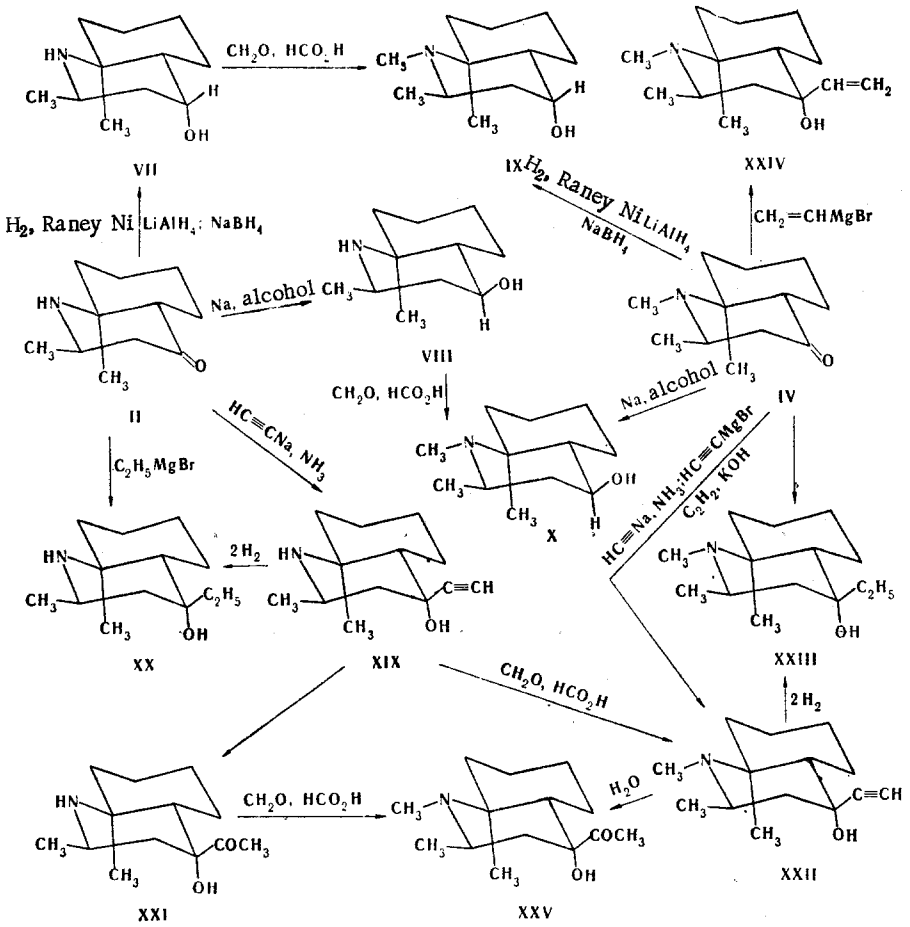
The expected 4-ethyl-substituted alcohol is not formed as a result of the reaction of cis-ketone I with ethylmagnesium bromide, and a considerable amount of the starting ketone undergoes resinification. The corresponding 1,2,9-trimethyl-substituted XXIX-XXXI were synthesized by methylation of cis-2,9-dimethyl-4-ethynyl (ethyl and acetyl) decahydro-4-quinolols XXVI-XXVIII.

Since the reactions of ketones II and IV with sodium acetylide and the Grignard reagent proceed with the same stereospecificity, an equatorial orientation should be assigned to the ethynyl group in alcohols XIX and XXII obtained from these ketones. Acetylenic alcohol XXVI and, consequently, acetylenic alcohol XXIX, which correspond to cis-ketone I, cannot be compared with the product of the Grignard reaction in view of the absence of the latter. Ketone I, because of the axial orientation of the C_9-C_8 bond is, like ketones II and IV, evidently hindered, as a consequence of which acetylenic alcohol XXVI is formed from it as a result of equatorial approach of the reagent.

To establish the spatial orientation of the ethynyl group in acetylenic alcohols XIX, XXII, XXVI, and XXIX, we studied the IR absorption spectra of ketols XXI, XXV, XXVIII, and XXXI and acetoxy derivatives XXXII and XXXIII obtained from them.

The spectrum of 4-ethynyl-4-acetoxydecahydroquinoline XXXII in the region of stretching vibrations of the C-O bond contains a doublet absorption band with maxima at 1234 and 1212 cm^{-1}, as compared with the unresolved doublet (1232 and 1220 cm^{-1}) in the spectrum of acetoxy derivative XXXIII. The spectra of ketols XXI, XXV, XXVIII, and XXXI are characterized by the presence of an unsplit carbonyl band at 1703-1709 cm^{-1} and a single band in the region of the stretching vibrations of associated hydroxyl groups (ν_{O-H}3464 cm^{-1}).

The results are in agreement with the literature data on 1,2-dimethyl-4-quinolols [10, 11] and attest to equatorial orientation of the ethynyl groups in acetylenic alcohols XIX, XXII, XXVI, and XXIX.



EXPERIMENTAL

Analysis of the ketones by GLC was accomplished with a Khrom-31 chromatograph in glass capillary columns (102 m by 0.5 mm) on an Apiezon K stationary phase at 160° and a helium pressure of 1.1 atom at the inlet. The PMR spectra were recorded with a JEOL PS-100 spectrometer; the chemical shifts were obtained with a UR-20 spectrometer at room temperature. The reaction was monitored by TLD on Al_2O_3; 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolones I-VI and 1,2,9-trimethyl-4-acetoxydecahydroquinolines XV-XVIII were eluted with hexane–ether (1:1), while 2,9-dimethyl- and 1,2,9-trimethyldecahydro-4-quinolols VII-XIV and the corresponding 4-substituted XIX-XXXI were eluted with hexane–ether–ethanol (9:10:1).

Ketones I, II, and IV were isolated from the mixtures by fractional crystallization of the picrates and hydrochlorides from alcohol.

Chemically-pure-grade lithium aluminum hydride and sodium borohydride were used for the reduction of ketones I, II, and IV. Raney nickel was prepared by the method in [12]. Methylation of the secondary bases to tertiary bases was carried out with a mixture of 40% formalin and 85% formic acid (1-2 and 2-5 moles, respectively, per mole of ketone). The esterification of the secondary alcohols was accomplished with a twofold excess of acetyl chloride and acetic anhydride. The secondary alcohols were oxidized with chromic anhydride in acetic acid at room temperature [7]. The oxidation products were investigated by TLC and GLC and were identified in the form of the picrates.

2,9-Dimethyldecahydro-4-quinolones (I and II). Fractional crystallization of the mixture of picrates obtained from 10 g (55 mmole) of the mixture of ketones and 12.6 g (55 mmole) of picric acid gave 9.1 g (40%) of a ketone I-enriched fraction with mp 200-204° (from acetone) and 4.6 g (20%) of ketone II-enriched fraction with mp 179-190° (from acetone). Further purification of the fractions yielded, respectively, 3.8 g of picrate Ia, with mp 207-208° (from acetone) and R_f 0.50, and 2.1 g of picrate IIa with mp 196-197° (from acetone) and R_f 0.41. Another 1.2 g (5%) of picrate IIa, with mp 196-197° (from acetone) and R_f 0.41, was isolated from the mother liquor after prolonged standing.

Fractional crystallization of the mixture of hydrochlorides obtained from 20 g of the mixture of ketones and dry hydrogen chloride in anhydrous ether yielded 8.6 g (36%) of hydrochloride IIb, with mp 237-238° (from alcohol), and 4.6 g (20%) of hydrochloride Ib with mp 199-200° (from alcohol). Decomposition in a column filled with Al_2O_3 (activity II, 1:30, $CHCl_3$) of picrate Ia and hydrochloride Ib yielded ketone I with mp 38-40° (from pentane) and R_f 0.50. Found: C 72.7; H 10.3; H 7.6%. $C_{11}H_{19}NO$. Calculated: C 72.9; H 10.5; H 7.7%. Decomposition of picrate IIa and hydrochloride IIb gave ketone II with mp 40-42° (from pentane) and R_f 0.41. Found: C 72.8; H 10.5; N 7.6% $C_{11}H_{19}ON$. Calculated: C 72.9; H 10.5; N 7.7%.

1,2,9-Trimethyldecahydro-4-quinolone (IV). Repeated reprecipitation of the mixture of hydrochlorides obtained from 10 g of the mixture of ketones from ethanol solution by the addition of ether yielded 7.4 g (63%) of hydrochloride IVb with mp 189° (from alcohol) and R_f 0.62.

Fractional crystallization of 14.7 g of the mixture of picrates from ethanol yielded 9.3 g (63%) of picrate IVa with mp 187° (from methanol) and R_f 0.62. Decomposition of hydrochloride IVb and picrate IVa in a column filled with Al_2O_3 gave ketone IV with bp 98° (1 mm) and n_D^{20} 1.5020. Found: C 62.4; H 9.6; N 5.9%. $C_{12}H_{21}NO \cdot HCl$. Calculated: C 62.2; H 9.5; N 6.0%.

trans-1,2,9-Trimethyl-4-ethynyldecahydro-4-quinolol (XXII). A) A solution of 7 g (36 mmole) of decahydroquinolone IV in 100 ml of anhydrous ether was added dropwise with stirring at −76° to sodium acetylide, prepared from 3 g (130 mg-at) of sodium in 150 ml of liquid ammonia and acetylene, after which the mixture was stirred for another 2 h. The reaction product was treated at −15° with 50 ml of water, and the aqueous mixture was extracted with ether. The ether extract was neutralized with carbon dioxide gas, dried with $MgSO_4$, and worked up to give 7.2 g (91%) of decahydroquinolone XXII with mp 147-148° (from acetone). Found: C 76.1; H 10.5; N 6.1% $C_{14}H_{23}NO$. Calculated: C 76.0; H 10.5; N 6.3%.

B) A solution of 3.5 g (18 mmole) of decahydroquinolone IV in 10 ml of anhydrous ether was added dropwise at −10° to a suspension of 3 g (50 mmole) of powdered KOH in 160 ml of anhydrous ether saturated with acetylene, after which the mixture was stirred for another 4 h at 0°. The reaction product was treated with 75 ml of water, and the aqueous mixture was extracted with ether. The ether extract was neutralized with carbon dioxide gas, dried with $MgSO_4$ and worked up to give 3.2 g of a resinified product, crystallization of which from acetone yielded 0.82 g (21%) of alcohol with mp 147-148°. No melting-point depression was observed for a mixture of this product with acetylenic alcohol XXII. Vacuum fractionation of the mother liquor gave 1.8 g (45%) of starting ketone with bp 124-128° (1 mm) and n_D^{20} 1.5060.

C) A solution of ethylmagnesium bromide, prepared from 0.7 g (30 mg-at) of magnesium and 3.2 g (30 mmole) of ethyl bromide in 50 ml of anhydrous tetrahydrofuran (THF), was added in small portions in the nitrogen atmosphere to a solution of acetylene in THF. A solution of 2.8 g (14 mmole) of ketone IV in 50 ml of THF was added at −6° to the resulting ethynylmagnesium bromide, after which the reaction was carried out and the mixture was worked up as in [13]. Crystallization of 2.5 g of the solid resinified product from acetone gave 1.06 g (34%) of acetylenic alcohol XXII with mp 147-148°.

trans-2,9-Dimethyl-4-ethynyldecahydro-4-quinolol (XIX). A solution of 1.2 g (6.6 mmole) of ketone II in 50 ml of anhydrous ether was added dropwise at −76° to sodium acetylide, prepared from 0.7 g (25 mg-at) of sodium in 80 ml of liquid ammonia and acetylene. The reaction was carried out and the mixture was worked up as described above to give 1.3 g (95%) of acetylenic alcohol XIX with mp 143-144° (from acetone). Found: C 75.5; H 10.4; N 6.7%. $C_{13}H_{21}NO$. Calculated: C 75.3; H 10.2; N 6.8%.

cis-2,9-Dimethyl-4-ethynyldecahydro-4-quinolol (XXVI). Reaction of 3.3 g (18 mmole) of ketone I and sodium acetylide, prepared from 1.8 g (75 mg-at) of sodium, under similar conditions gave 3.25 g of a mixture, from which 1.32 g (40%) of starting ketone I and 1.64 g (42%) of acetylenic alcohol XXVI, with mp 101-102° (from hexane), were obtained by chromatography with a column filled with Al_2O_3 [activity II, 1:60, petroleum ether–ether (3:1)]. Found C 75.5; H 10.1; N 6.8%. $C_{13}H_{21}NO$. Calculated: C 75.3; H 10.2; N 6.8%.

cis-1,2,9-Trimethyl-4-ethynyldecahydro-4-quinolol (XXIX). Methylation of 1 g (4.8 mmole) of acetylenic alcohol XXVI with a mixture of 0.6 g (8 mmole) of 40% formalin and 1 g (18 mmole) of 85% formic acid on a boiling-water bath for 3 h gave 1.0 g of acetylenic alco-

hol XXIX with mp 143° (from acetone). Found: C 76.2; H 10.2; N 6.1%. $C_{14}H_{23}NO$. Calculated: C 76.0; H 10.5; N 6.3%.

trans-1,2,9-Trimethyl-4-ethyldecahodro-4-quinolol (XXIII). A solution of 2.5 g (13 mmole) of ketone IV in 30 ml of ether was added to ethylmagnesium bromide, obtained from 1.5 g (60 mg-at) of magnesium and 7.3 g (60 mmole) of ethyl bromide in 50 ml of anhydrous ether, and the mixture was stirred with cooling for 2 h and at room temperature for 2 h. The ether was removed, and the residue was diluted with anhydrous toluene. The mixture was then heated at 100° for 2 h. The usual workup and removal of the solvent gave 2.2 g (76%) of decahydroquinolol XXIII with mp 127-128° (from hexane). Found: C 74.5; H 11.9; N 6.3%. $C_{14}H_{27}NO$. Calculated: C 74.7; H 12.0; N 6.2%.

trans-2,9-Dimethyl-4-ethyldecahydro-4-quinolol (XX). The reaction of ethylmagnesium bromide [1.8 g (75 mg-at) of magnesium and 8.6 g (75 mmole) of ethyl bromide in 50 ml of anhydrous ether] and 3 g (16 mmole) of ketone II gave 2.5 g (72%) of alcohol XX with mp 91-93° (from hexane). Found: C 73.9; H 12.0; N 6.5%. $C_{13}H_{25}NO$. Calculated: C 73.9; H 11.8; N 6.6%.

1,2,9-Trimethyl-4-vinyldecahydro-4-quinolol (XXIV). A solution of 3 g (16 mmole) of ketone IV in 50 ml of THF was added dropwise with cooling (to −25°) and stirring to vinylmagnesium bromide [1.5 g (60 mg-at) of magnesium and 7.5 g (70 mmole) of vinyl bromide] in 50 ml of anhydrous THF, and the subsequent reaction was carried out as a Grignard reaction. The usual workup gave 3 g (88%) of decahydroquinolol XXIV with mp 112-113° (from hexane). Found: C 75.5; H 11.5; N 6.2%. $C_{14}H_{25}NO$. Calculated: C 75.3; H 11.3; N 6.3%.

Hydrogenation of 4-Ethynyldecahydroquinolols XIX, XXII, and XXVI. A) Selective hydrogenation of 2 g of acetylenic alcohol XXII [227 ml of H_2, 742 mm, 20°] in 30 ml of ethanol in the presence of Pb-Pb/$CaCO_3$ gave 2 g of a reaction product with mp 111-112° (from hexane). No melting-point depression was observed for a mixture of a sample of this product with vinyl alcohol XXIV.

B) Exhaustive hydrogenation of 1.4 g of acetylenic alcohol XXII in 30 ml of ethanol in the presence of Pd/$CaCO_3$ until hydrogen absorption ceased gave 1.4 g of a saturated alcohol with mp 126-127° (from hexane). No melting-point depression was observed for a mixture of this product with amino alcohol XXIII.

C) Exhaustive hydrogenation of 1 g of acetylenic alcohol XXIX in 30 ml of ethanol in the presence of Pd/$CaCO_3$ until hydrogen absorption ceased gave 1 g of saturated alcohol XXX with mp 83° (from petroleum ether). Found: C 74.8; H 12.1; N 6.1%. $C_{14}H_{27}NO$. Calculated: C 74.7; H 12.0; N 6.2%.

D) The addition of 2 moles of hydrogen (121 ml of H_2, 754 mm, 21°) to 0.5 g of acetylenic alcohol XIX gave 0.5 g of hydrogenation product with mp 92-93° (from hexane). No melting-point depression was observed for a mixture of this product with saturated alcohol XX.

E) A solution of 1 g of acetylenic alcohol XXVI in 30 ml of ethanol was hydrogenated exhaustively in the presence of Pd/$CaCO_3$ until hydrogen absorption ceased. Removal of the catalyst and the solvent gave 1 g of alcohol XXVII with mp 78-79° (from petroleum ether). Found: C 73.8; H 12.1; N 6.5%. $C_{14}H_{25}NO$. Calculated: C 73.9; H 11.8; N 6.6%.

2,9-Dimethyl- and 1,2,9-Trimethyl-4-acetyldecahydro-4-quinolols (XXI, XXVIII, XXV, and XXXI). Hydration of 0.5 g of acetylenic alcohol XIX with a mixture of 0.5 g mercurous sulfate, 10 ml of water, and 0.5 ml of concentrated H_2SO_4 for 20 min at room temperature and subsequent treatment with zinc dust and 25% ammonium hydroxide gave 0.51 g (94%) of ketol XXI with mp 86-87° (from petroleum ether). Found: C 69.2; H 10.2; N 5.9%. $C_{13}H_{23}NO_2$. Calculated: C 69.3; H 10.3; N 6.3%.

From 0.64 g of acetylenic alcohol XXVI under the same conditions we synthesized 0.66 g (93%) of ketol XXVIII with mp 55-56° (from petroleum ether). Found: C 69.4; H 10.4; N 6.3%. $C_{13}H_{23}NO_2$. Calculated: C 69.3; H 10.3; N 6.3%.

Hydration of 0.5 g of acetylenic alcohol XXII gave 0.53 g (98%) of ketol XXV with mp 116-117° (from hexane). Found: C 70.4; H 10.7; N 6.0%. $C_{14}H_{25}NO_2$. Calculated: C 70.2; H 10.5; N 5.8%. Similarly, reaction of 0.82 g of alcohol gave 0.85 g (96%) of ketol XXXI with mp 65-66° (from petroleum ether). Found: C 70.5; H 10.7; N 6.1%. $C_{14}H_{25}NO_2$. Calculated: C 70.2; H 10.5; N 5.8%.

LITERATURE CITED

1. A. A. Akhrem, B. B. Kuz'mitskii, L.I. Ukhova, and N. F. Uskova, Dokl. Akad. Nauk SSSR, 169, 724 (1966).
2. B. B. Kuz'mitskii, A. A. Akhrem, L. I. Ukhova, and N. F. Uskova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2775 (1970).
3. I. N. Nazarov, L. I. Ukhova, and V. A.Rudenko, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, No. 3, 498 (1953).
4. N. Bhacca and D. Williams, Applications of NMR Spectroscopy in Organic Chemistry, Holden-Day (1964).
5. V. S. Bogdanov, L. I. Ukhova, N. F. Uskova, A. N. Sergeeva, A. P. Marochkin, A. M. Moseenkov, and A. A. Akhrem, Khim. Geterotsikl. Soedin., No. 8, 1078 (1973).
6. K. Blaga, O. Chervinka, and Ya. Kovar, Fundamentals of Stereochemistry and Conformational Analysis [Russian translation], Khimiya, Leningrad (1974), p. 89.
7. D. H. R.Burton, J. Chem. Soc., No. 5, 1027 (1953).
8. C. Djerassi and E. Lippman, J. Amer. Chem. Soc., 80, 1236 (1958).
9. A. A. Akhrem, L. I. Ukhova, N. F. Uskova, and B. B.Kuz'mitskii, USSR Author's Certificate No. 221,706; Byull. Izobr., No. 22, 33 (1968).
10. B. V. Unkovskii, Yu. F. Malina, I. P. Bioko, T. D. Sokolova, and M. G. Zaitsev, Zh. Org. Khim., 3, 757 (1967).
11. V. I. Mamonov, G. G. Dvoryantseva, N. P. Shulaev, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 4, 664 (1969).
12. A. A. Pavlic and H. Adkins, J. Amer. Chem. Soc., 68, 1471 (1946).
13. A. A. Akhrem, L. I. Ukhova, and N. F. Uskova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 10, 2305 (1970).

STRUCTURE AND ABSORPTION SEPCTRA OF 3-PHENYL-4-HYDROXYISOQUINOLINE

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It was shown by IR spectroscopy that 3-phenyl-4-hydroxyisoquinoline exists in the hydroxy form in solution in organic nonpolar solvents. The splitting of the ν_{OH} band in the IR absorption spectra was assigned to the S-cis and S-trans orientations of the OH group relative to the phenyl ring. An intramolecular hydrogen bond is formed in the cis form of 3-phenyl-4-hydroxyisoquinoline due to interaction of the hydroxyl hydrogen atom with the π-electron system of the phenyl ring. An interpretation of the first two absorption maxima in the electronic spectra of the neutral and ionic forms of the 4-hydroxyisoquinoline and 3-phenyl-4-hydroxyisoquinoline molecules is given within the framework of the MO method and the Pariser–Parr–Pople approximation. It is shown that the introduction of a phenyl group in the 3 position of 4-hydroxyisoquinoline, protonation of the ring nitrogen atom, the ionization of the exocyclic β-hydroxyl group affect the energy of the upper occupied molecular orbital, leaving the lower vacant molecular orbital of 4-hydroxyisoquinoline almost unchanged.

In our previous paper [1] we demonstrated by UV spectroscopy that the 3-phenyl-4-hydroxyisoquinoline (II) molecule, like the 4-hydroxyisoquinoline (I) molecule, exists, depending on the polarity of the solvent, in neutral (N) and dipolar (D) forms in neutral media and in cationic (C) and anionic (A) forms in acid and alkaline media, respectively.

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