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Synthesis and Reactions of 4-*cis*- and 4-*trans*-Hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinolines

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Abstract—By treating 2e-methyl-4-oxo-*trans*-decahydroquinoline with lithium acetylide a mixture of stereoisomeric 4-*cis*-hydroxy-2e-methyl- and 4-*trans*-hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinolines was obtained in ~3 : 2 ratio. Their reaction with acetonitrile in the presence of sulfuric acid (Ritter's reaction) results in a mixture of stereoisomeric 4-*cis*-acetylamino-2e-methyl- and 4-*trans*-acetylamino-2e-methyl-4-ethynyl-*trans*-decahydroquinolines in the same ratio. The ethynyl group of alcohols synthesized is not hydrated under conditions of Kuchrerov's reaction. The boiling of the alcohols with formic acid furnished a mixture of 4-acetyl-2e-methyl and 2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinolines in 1 : 7 ratio. The former of these compounds under conditions of Ritter's reaction yielded a mixture (1 : 1.4) of stereoisomeric 4-acetyl-4-*trans*-acetylamino- and 4-acetyl-4-*cis*-acetylamino-2e-methyl-*trans*-decahydroquinolines. From 2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline under the same conditions were obtained both already mentioned stereoisomeric 4-acetylamino-2e-methyl-4-ethynyl-decahydroquinolines (53% of *cis*-isomer and 35% of *trans*-isomer in the mixture) and 4-acetyl-4-acetylamino-2e-methyldecahydroquinolines (7% of *cis*-isomer and 5% of *trans*-isomer).

Quinoline rings, also partially or completely hydrogenated, are constituents of a number of natural biologically active compounds, in particular, of alkaloids [1]. Chemical reactions furnishing versatile derivatives of this series with potential biological activity were investigated for a long time.

The preparation from alkyl-substituted decahydro-4-quinolinones of the corresponding ethynylcarbinols by treating with acetylene in liquid ammonia in the presence of sodium amide was described long ago [2].

In the course of this study by treating 2e-methyl-4-oxo-*trans*-decahydroquinoline (**I**) with lithium acetylide we performed a synthesis of stereoisomeric 4-*cis*-hydroxy-2e-methyl- and 4-*trans*-hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinolines (**II**) and (**III**), and their transformations involving ethynyl and hydroxy groups were investigated.

The separation of compounds **II** and **III** was difficult, and they were obtained in pure state only by means of chromatography (see EXPERIMENTAL). On the contrary, the hydrochlorides of the stereoisomeric 4-hydroxy-2e-methyl-4-ethynyldecahydroquinolines (**IV**) and (**V**) were easily separated by recrystallization from water.

The spatial structure of compounds **II**–**V** was established from the data of NMR spectroscopy. In the ^{1}H NMR spectra of ethynylcarbinols **II** and **III** and their hydrochlorides **IV** and **V** the chemical shifts of protons attached to carbon atoms C^2 and C^{10} are only slightly different. These signals in the spectra of isomers with the equatorial position of hydroxy group **II** and **IV** are observed downfield from the corresponding resonances of *trans*-isomers **III** and **V** where a 1,3-diaxial interaction arises between the proton of the hydroxy group and hydrogen atoms at C^2 and C^{10} (see Table 1). The *trans*-junction of the piperidine and cyclohexane rings in compounds **II**–**V** is evidenced by the multiplicity of signals from protons linked to C^{10} atoms. The observed two coupling constants of J ~11.2 Hz corresponding to axial-axial interaction indicate the axial orientation of H^{10} and H^5 protons corresponding to *trans*-configuration of the decahydroquinoline. The same coupling constant belonging to the second downfield proton signal (H^2) demonstrates its axial orientation and therefore equatorial orientation of the methyl group in all these compounds.

Thus the obtained stereoisomeric ethynylquinolols **II** and **III** (or their hydrochlorides **IV** and **V**) are dissimilar only in orientation of ethynyl and hydroxy substituents at C^4 atom. The structure with equatorial orientation of the hydroxy group, in *cis*-position with respect to methyl. was assigned to the isomer prevail-

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Table 1. ^{1}H NMR spectra of *cis*- and *trans*-4-hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinolines **II, III** of their hydrochlorides **IV, V**, of *cis*- and *trans*-4-acetylamino-2e-methyl-4-ethynyl-*trans*-decahydroquinolines (**VI, VII**), of 2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**IX**), 4-acethyl-2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**X**) and *cis*- and *trans*-4-acethyl-4-acethylamino-2e-methyl-*trans*-decahydroquinolines (**XII**) and (**XIII**), δ, ppm[a]

Compd. no.	H_2	2-CH_3	H^3	H^{10}	≡CH	OH, NH	$COCH_3$	Others
II	3.18 m, $^2J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.29 d, ^3J 7.0 Hz	1.70 d.d (H_a), $2J$ 13.2 Hz, $^3J_{a,a}$ 11.2 Hz, 2.10 d.d (H_e), $^3J_{a,e}$ 3.6 Hz	2.68 d.t, $23^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	3.09 s	–	–	2.08 d.q (H^6_e, ^2J 12.0, 3^3J 3.6 Hz), 1.96 m (3H), 1.40 m (5H)
III	3.27 m, $^2J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.22 d, ^3J 7.0 Hz	1.77d.d (H_a), ^2J13.2Hz, $^3J_{a,a}$ 11.2 Hz, 2.17 d.d (H_e), $^3J_{a,e}$ 3.6 Hz	2.79 d.t, $2^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	2.94 s	–	–	1.96 m (3H), 1.79 d.t (H^5, $2^3J^{a,a}$ 11.2, $^3J_{a,e}$ 3.6 Hz), 1.45 m (5H)
IV	3.22 m, $^2J_{Me}$ 6.8 Hz, $^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.32 d, ^3J 6.8 Hz	1.77 m (H_a), 2.07 m (H_e)	2.76 d.t, $2^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	3.41 s	5.75 (OH), 8.90, 9.50 (NH)	–	2.07 m (3H), 1.77 m (3H), 1.58 d.t (H5, $23^3J_{a,a}$ 11.2, $^3J_{a,e}$ 3.6 Hz), 1.48 k.t (H^8_a, $2J$ 12.4, $23^3J_{a,a}$ 11.2, $2^3J_{a,e}$ 3.6 Hz), 1.20 m (3H)
V	3.32 m, $^2J_{Me}$ 6.8 Hz, $^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.26 d, ^3J 6.8 Hz	1.65 d.d (H_a), $^3J_{a,a}$ 11.2 Hz, ^2J 13.6 Hz, 2.03 m (H_e)	2.93 d.t, $2^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	3.27 s	5.64 (OH), 8.90, 9.20 (NH)	–	2.03 m (3H), 1.92 d.q (H^6_e, $2J$ 12.0, $2^3J_{a,a}$ 11.2, $^3J_{a,e}$ 3.6 Hz), 1.75 d.q (H^9_e, ^2J 12.0, $2^3J_{a,a}$ 11.2, $^3J_{a,e}$ 3.6 Hz), 1.47 m (2H), 1.20 m (3H)
VI	3.20 m, $^2J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.31 d, ^3J 7.0 Hz	1.76 d.d (H_a), ^2J 13.2 Hz, $^3J_{a,a}$ 11.2 Hz, 2.19 d.d (H_e), $3J_{a,e}$ 3.6 Hz	2.70 d.t, $2^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	3.06 s	–	1.89 s (3H)	2.12 d.q (H^6_e, ^2J 12.2, $3^3J_{a,e}$ 3.6 Hz), 1.96 m (3H), 1.40 m (5H)
VII	3.30 m, $^2J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.23 d, ^3J 7.0 Hz	1.83 d.d (H_a), 2^3J 13.2 Hz, $^3J_{a,a}$ 11.2 Hz, 2.24 d.d (H_e), $^3J_{a,e}$ 3.6 Hz	2.81 d.t, $2^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz	2.91 s	–	1.92 s (3H)	1.97 m (3H), 1.76 d.t (H^5, $2^3J_{a,a}$ 11.2 Hz, $^3J_{a,e}$ 3.6 Hz), 1.45 m (5H)

Table 1. (Contd.)

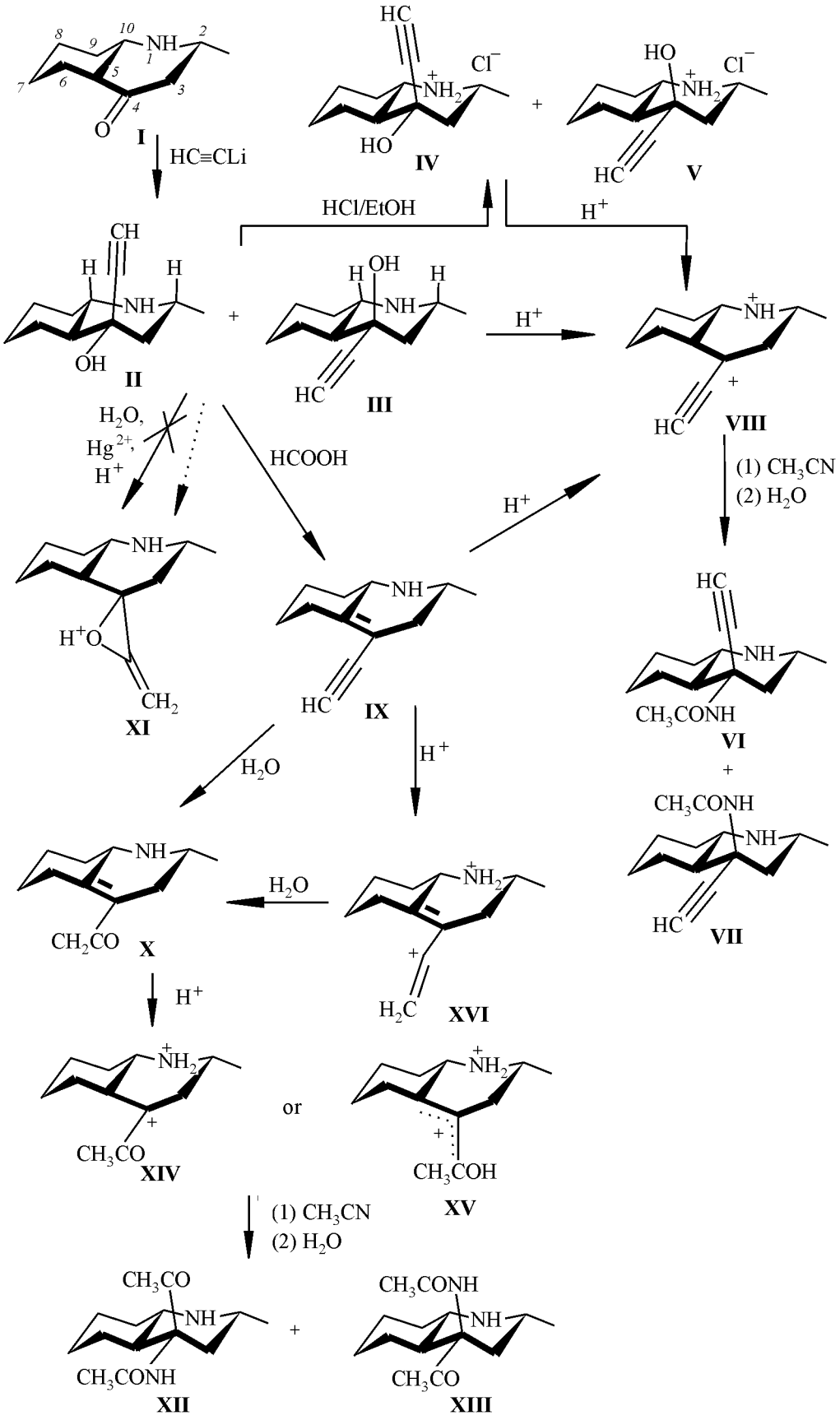
Compd.	H_2	2-CH_3	H^3	H^{10}	≡CH	OH, NH	$COCH_3$	Others
IX	3.02 m, $^3J_{Me}$ 6.5 Hz, $^3J_{a,a}$ 12.4 Hz, $^3J_{a,e}$ 2.8 Hz	1.10 d, ^3J 6.5 Hz	1.36 t (H_a), ^2J 12.8 Hz, $^3J_{a,a}$ 12.4 Hz, 2.01 d.d (H_e), $^3J_{a,e}$ 2.8 Hz	2.51 d.d, $^3J_{a,a}$ 12.4 Hz, $^3J_{a,e}$ 3.0 Hz	2.50 s	5.65	–	1.82 m (5H), 1.22 m (3H)
X	3.55 m, $^3J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 12.4 Hz, $^3J_{a,e}$ 3.0 Hz	1.48 d, ^3J 7.0 Hz	2.12 d.d (H_a), ^2J 13.2 Hz, $^3J_{a,a}$ 12.4 Hz, 2.45 d.d (H_e) $^3J_{a,e}$ 3.0 Hz	3.12 d.d, $^3J_{a,a}$ 12.4 Hz, $^3J_{a,e}$ 3.2 Hz	–	5.80	2.25 s (3H)	1.78 m (5H), 1.20 m (3H)
XII	3.26 m, $^3J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 12.0 Hz, $^3J_{a,e}$ 3.6 Hz	1.37 d, ^3J 7.0 Hz	1.96 d.d (H_a), ^2J 13.2 Hz, $^3J_{a,a}$ 12.0 Hz, 2.16 d.d (H_e) $^3J_{a,e}$ 3.6 Hz	2.73 d.t, $2^3J_{a,a}$ 11.9 Hz, $^3J_{a,e}$ 3.6 Hz	–	5.85 (2H)	2.00 s (3H, keton),1.92 s (3H, amide)	1.98 d.q (H^6_e, ^2J 12.4, 3^3J 3.6 Hz), 1.68 m (3H), 1.42 m (2H), 1.28 m (3H)
XIII	3.35 m, $^3J_{Me}$ 7.0 Hz, $^3J_{a,a}$ 12.2 Hz, $^3J_{a,e}$ 3.6 Hz	1.26 d, ^3J 7.0 Hz	2.02 d.d(H_a), ^2J 13.2 Hz, $^3J_{a,a}$ 12.2 Hz, 2.22 d.d (H_e), $^3J_{a,e}$ 3.6 Hz	2.85 d.t, $2^3J_{a,a}$ 11.8 Hz, $^3J_{a,e}$ 3.6 Hz	–	5.55, 5.68	2.00 s (3H, amide), 2.24 s (3H, keton)	1.90 d.q ((H^6_e,, $2^3J_{a,a}$ 11.8, 2^3J 12.4, $^3J_{a,e}$ 3.6 Hz), 1.66 m (3H), 1.45 m (2H), 1.30 m (3H)

[a] The NMR spectra were recorded in the following solvents: for compounds **II, III, VI, VII**, deuteromethanol; for compounds **IV, V**, DMSO-d_6, for compounds **IX, X, XII** and **XIII**, $CDCl_3$.

Table 2. ^{13}C NMR spectra of 2e-methyl-*trans*-decahydroquinoline (*I*), *cis*- and *trans*-4-hydroxy-2*e*-methyl-4-ethynyl-*trans*-decahydrohydroquinolines **II, III**), and of their and their Hydrochlorides **IV** and **V**, δ_C, ppm[a]

Compd. no.	C^2	C^3	C^4	C^5	C^6	C^7	C^8	C^9	C^{10}	C^{11}	-C=	=CH
I	53.6 d	51.1 t	210.1 s	56.1 d	25.7 t	24.2 t	25.4 t	34.7 t	61.9 d	23.3 q	–	–
II	47.4 d	49.5 t	68.9 s	52.0 d	26.7 t	27.6 t	26.4 t	34.6 t	55.8 d	22.2 q	72.3 s	80.9 d
III	48.2 d	50.3 t	71.6 s	53.2 d	26.6 t	27.1 t	26.3 t	34.2 t	58.4 d	22.2 q	75.9 s	81.2 d
IV	48.3 d	44.5 t	69.0 s	50.9 d	24.5 t	24.9 t	24.2 t	29.9 t	57.3 d	18.3 q	77.6 s	81.9 d
V	47.2 d	44.7 t	71.9 s	48.0 d	25.4 t	25.6 t	25.0 t	30.1 t	55.2 d	18.4 q	74.2 s	82.3 d

[a] The spectra were recorded in the following solvents: for compound **I**, in $CDCl_3$, for compounds **II**, **III**, in CD_3OD, for compounds **IV** and **V**, in D_2O.


I
HC≡CLi
IV
V
HCl/EtOH
H+
II
III
VIII
H2O,
Hg2+,
H+
HCOOH
(1) CH3CN
(2) H2O
XI
IX
VI
VII
H2O
XVI
X
XIV
or
XV
XII
XIII

ing in the product basing on the ^{13}C NMR data (Table 2). The chemical shift of carbinol carbon is known [3] to have larger value by the isomer with the axial hydroxy group, and with the tertiary alcohols this difference amounts to 2–3 ppm [4]. In our case the chemical shift of the C^4 atom in the prevailing isomer equals to 68.9, and 71.6 ppm in the second isomer (69.0 and 71.9 ppm in the spectra of the respective hydrochlorides); therefore we assigned to the former isomer *cis*-4e-OH, and to the latter *trans*-4a-OH structure. Our conclusions on the spatial geometry of stereoisomers **II** and **III** based on NMR spectra are in agreement with the data of [2] where the axial position of ethynyl substituent was derived from the difference in the IR and UV spectra of the stereoisomeric ethynylcarbinols.

We showed time and again that stereochemistry of organolithium compounds addition, in particular, in the case of lithium acetylide [5], was controlled not by thermodynamical but by sterical factors. Therefore the observed isomer ratio (3 : 2) is caused not by relative thermodynamic feasibility of isomer formation with a hydroxy group in the equatorial position, but by relative spatial accessibility of the α- and β-sides of the molecule.

Tertiary alcohols **II** and **III** (in a mixture) and also their hydrochlorides **IV** and **V** (as individual compounds) were brought into Ritter's reaction. We showed formerly [5, 6] that in reaction proceeding through a "classical" carbocation the ethynyl substituent virtually was not affected in the course of reaction, and the process gave rise to the corresponding ethynylamines. If the "nonclassical" charge delocalization is possible, then the ethynyl group would suffer hydration and transform into acetyl group; then in the reaction form the corresponding amidoketones. Since the formation of nonclassical carbocations is not characteristic of decahydroquinoline compounds, substances **II**–**V** eliminate the hydroxy group and are converted into the stereoisomeric 4-*cis*-acetylamino-2e-methyl- and 4-*trans*-acetylamino-2e-methyl-4-ethynyl-*trans*-decahydroquinolines (**VI**) and (**VII**). The isomer ratio (3 : 2) is independent of the stereochemistry of the initial alcohol thus confirming that the reaction proceeds through a "classical" propargyl cation **VIII**.

The proper nucleophilic center (a nitrogen atom) in the initial compounds **II**–**V** may attack cation **VIII** at the C^4 atom resulting in formation of a significant amount of polymerization (polycondensation) products. The latter fraction was partially reduced by carrying out the process in 3-fold excess of acetonitrile as compared with the common procedure. The quantity of sulfuric acid was also somewhat increased for, firstly, the initial substrates were bases and partially bound the acid, and, secondly, the reaction was performed in excess acetonitrile, and thus at the usual amount of acid (4-fold with respect to substrate) the rate of the corresponding amide formation became too slow. The amount of polymerization products formed from hydrochlorides **IV, V** is somewhat smaller. It is apparently due to the reduced nucleophilicity of the nitrogen in both these compounds because it is already protonated before acid addition.

The structure of stereoisomeric ethynylamides **VI** and **VII** was established from IR, ^1H NMR, and mass spectra (Table 3). The IR spectra of the compounds contain absorption bands corresponding to vibrations of amide carbonyl at 1650 cm^{-1}, of amide NH group at 1550 and 3420 cm^{-1}, of the NH group in the ring at 3080 cm^{-1}, and also the bands from vibrations of acetylene bond ≡C–H (3310 cm^{-1} in the *cis*-isomer of amide **VI** and 3250 cm^{-1} in the *trans*-isomer **VII**). In the mass spectra of compounds **VI** and **VII** appear the peaks of molecular ions M^+ 236 with relative intensity 17 and 14% to the maximal peak respectively.

In the ^1H NMR spectra of stereoisomeric amides **VI** and **VII** are observed the singlets from amide acetyl groups at ~1.9 ppm, and the rest of the spectra are similar to those of the corresponding alcohols (see Table 1). The *cis*-structure was assigned to the prevailing isomer because the proton signals at C^2 and C^{10} in the spectrum of this isomer are located upfield as compared to the corresponding signals of the minor product. It corresponds (see above) to the equatorial orientation of the acetylamino group attached to C^4. This stereochemical result is well consistent with the more favorable addition of the nucleophile to cation **VIII** from the more spatially accessible side. The fact that the *cis/trans* ratio was the same in the reaction products at ethynylation of ketone **I** and nucleophilic substitution in alcohols **II, III** is due to the similarity of the size of the entering ethynyl and nitrile groups.

We failed to hydrate the ethynyl group in compounds **II** and **III** by Kucherov's reaction. According to published data [7] the presence of an amino group in the molecule prevents the Kucherov's reaction, and no proposals have been advanced how to overcome this obstacle. We tried an alternative procedure for conversion of ethynyl group into acetyl one: The initial ethynylcarbinol was heated with concn. formic acid (Rupe rearrangement). It is believed that

Table 3. IR and mass spectra and melting points of 4-*cis*- and 4-*trans*-4-hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinolines (**II**), (**III**) of their hydrochlorides **IV, V**, of *cis*- and *trans*-4-acetylamino-2e-methyl-4-ethynyl-*trans*-decahydroquinolines (**VI**), (**VII**), 2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**IX**), 4-acetyl-2e-methyl-1,2,3,6,7,8,9,10-octahydroquinoline (**X**), and *cis*- and *trans*-4-acetyl-4-acetylamino-2e-methyl-*trans*-decahydroquinolines (**XII**) and (**XIII**)

Compd. no.	mp, °C	IR spectrum, ν, cm^{-1}	Mass spectrum, *m/z*
II	206–207	3420 (OH), 3320 (≡C–H), 3130 (NH), 2980, 2950, 2930, 2890, 2860 (C–H), 2100 (C≡C)	193 (M^+, 23%), 178 (M^+–CH_3, 100%), 160 (M^+–CH_3–H_2O), 150, 136, 124, 110, 91, 82, 68, 53, 44
III	127–129	3450 (OH), 3250 (≡C–H), 3130 (NH), 2980, 2940, 2925, 2890, 2860 (C–H), 2100 (C≡C)	193 (M^+, 21%), 178 (M^+–CH_3, 100%), 160 (M^+–CH_3–H_2O), 150, 136, 124, 110, 91, 82, 68, 53, 44
IV	>300	3440 (OH), 3320 (≡C–H), 3200 (NH), 2980, 2950, 2930, 2890, 2860 (C–H), 2750, 2720, 2660, 2520, 2470, 2400 (NH^+), 2100 (C≡C)	194 (M^+, 30%), 179 (M^+–CH_3), 160 (M^+–CH_3–H_3O^+), 151 (100%), 136, 124, 110, 108, 91, 82, 67, 53, 44
V	>300	3450 (OH), 3250 (≡C–H), 3200 (NH), 2980, 2940, 2930, 2890, 2860 (C–H), 2750, 2720, 2660, 2520, 2470, 2400 (NH^+), 2100 (C≡C)	194 (M^+, 26%), 179 (M^+–CH_3), 160 (M^+–CH_3–H_3O^+), 151 (100%), 136, 124, 110, 108, 91, 82, 67, 53, 44
VI	235–236	3420 (NH), 3310 (≡C–H), 3080 (NH), 2980, 2950, 2930, 2890, 2860 (C–H), 2100 (C≡C), 1660 (C=O, amide), 1550 (NH)	236 (M^+, 17%), 221 (M^+–CH_3), 206 (M^+–$2CH_3$), 178 (M^+–CH_3–$COCH_3$), 152 (M^+–CH_3–NH_2COCH_3, 100%), 136, 124, 110, 91, 82, 68, 58, 53, 44
VII	195–196	3420 (NH), 3250 (≡C–H), 3080 (NH), 2980, 2950, 2930, 2890, 2860 (C–H), 2100 (C≡C), 1660 (C=O, amide), 1550 (NH)	236 (M^+, 14%), 221 (M^+–CH_3), 206 (M^+–$2CH_3$), 178 (M^+–CH_3–$COCH_3$), 152 (M^+–CH_3–NH_2COCH_3, 100%), 136, 124, 110, 91, 82, 68, 58, 53, 44
IX	186–188	3190 (≡C–H), 3130 (NH), 2970, 2930, 2860, 2830 (CH), 2100 (C≡C), 1620 (C=C conjugated)	175 (M^+, 18%), 160 (M^+–CH_3), 150 (100%), 136, 124, 110, 91, 82, 68, 53, 44
X	182–183	3120 (NH), 2970, 2930, 2850, 2820 (CH), 1700 (C=O conjugated), 1620 (C=C conjugated)	193 (M^+, 15%), 178 (M^+–CH_3), 150 (M^+–$COCH_3$, 100%), 136, 124, 110, 108, 91, 82, 68, 53, 44, 43
XII	212–214	3360, 3120 (NH), 2980, 2950, 2930, 2890, 2860 (C–H), 1720 (C=O, ketone), 1660 (C=O, amide), 1550 (NH)	252 (M^+, 11%), 237 (M^+–CH_3), 222 (M^+–$2CH_3$), 196 (M^+–CH_3–$COCH_3$), 180 (M^+–CH_3–NH_2COCH_3, 100%), 158 (M^+–$2COCH_3$), 152, 136, 124, 110, 91, 82, 68, 58, 53, 44
XIII	168–169	3350, 3110 (NH), 2980, 2960, 2920, 2880, 2840 (C–H), 1720 (C=O, ketone), 1660 (C=O, amide), 1550 (NH)	252 (M^+, 9%), 237 (M^+–CH_3), 222 (M^+–$2CH_3$), 196 (M^+–CH_3–$COCH_3$), 180 (M^+–CH_3–NH_2COCH_3), 158 (M^+–$2COCH_3$), 152 (100%), 136, 124, 110, 91, 82, 68, 58, 53, 44

α-hydroxyacetylenes isomerize under these conditions to yield α,β-unsaturated ketones. It turned out however that the main transformation which underwent ethynylcarbinols **II** and **III** was merely a dehydration into 4-ethynyl-2e-methyl-1,2,3,6,7,8,9,10-octahydroquinoline (**IX**). The isomerization product, 4-acetyl-2e-methyl-1,2,3,6,7,8,9,10-octahydroquinoline (**X**), formed as a minor component (~12%). The low yield of ketone **X** apparently originated from the structure of the intermediate preceding its formation: The latter should be a protonated form of oxirane ring with a semicyclic methylene group [8] possessing large skeleton strains. Since in the initial compounds **II** and **III** the hydroxy group is in the ring, in the intermediate **XI** should occur a spiro-joint of the oxirane and decalin rings. Obviously compound **X** arises in this case as a result of the secondary hydration of the preliminary formed enyne **IX**; this assumption is supported by results of its conversion in Ritter's reaction that are discussed further.

Compounds **IX** and **X** were isolated from the reaction mixture in the individual state by crystallization from acetone. Their structure was deduced from IR, ^{1}H NMR, and mass spectra, In the IR spectrum of enyne **IX** in contrast to the initial carbinols lacked the band of he hydroxy group but appeared a band at 1620 cm^{-1} characteristic of a conjugated double bond. In the mass spectrum of the compound is present a molecular ion peak M^+ 75 with integral intensity 18% relative to the maximal one. The double bond at dehydration arose in keeping with Zaitsev rule, between C^4 and C^5 atoms as show the data of ^{1}H NMR spectroscopy: Firstly, in the spectrum of compound **IX** are no signals characteristic of olefin protons; secondly, the signal of H^{10} proton (δ 2.51 ppm) has a single coupling constant characteristic of an axial-axial coupling (12.4 Hz). In the IR spectrum of α,β-unsaturated ketone **X** appear absorption bands at 1700 and 1620 cm^{-1} characteristic of enone fragment. The peak of molecular ion in the mass spectrum M^+ 193 (15%) corresponds to the isomerization product. In the ^{1}H NMR spectrum of compound **X** appears a singlet from the acetyl group at 2.25 ppm with integral intensity corresponding to three protons. The position of the double bond in the ring was established basing on the same reasoning as was used for enyne **IX**.

We used compounds **IX** and **X** as substrates for Ritter's reaction. It was established that enone **X** under conditions of this reaction furnished a mixture of stereoisomeric 4-acetyl-4-*cis*-acetylamino- and 4-acetyl-4-*trans*-acetylamino-2e-methyl-*trans*-decahydroquinolines (**XII**) and (**XIII**) in 9:7 ratio. The structure of compounds **XII** and **XIII** was established from the data of IR, ^{1}H NMR, and mass spectra. In the IR spectra of both compounds are present the absorption bands characteristic of ketone and amide carbonyls (1720 and 1660 cm^{-1} respectively), and also of amide (1550, 3350 cm^{-1}) and amine (3120 cm^{-1}) NH groups. In the mass spectra are observed molecular ion peaks M^+ 252 of integral intensity 11 and 9% relative to the maximal peak respectively. The prevailing component was assigned the *cis*-isomer structure basing on the ^{1}H NMR spectrum (see Table 1). As in the case of the above described amides **VI** and **VII** in the *trans*-isomer a 1,3-nonbonded interaction was observed between axial amide group and protons attached to C^2 and C^{10} atoms. Therefore the signals of protons H^2 and H^{10} shift downfield.

Note that formation of amidoketones of the mentioned structure corresponds formally to nucleophile (nitrile) addition to cation **XIV**. We previously [9] observed quite different behavior of α,β-unsaturated ketones in this reaction. The molecule was exclusively protonated at the carbonyl group affording oxyallyl cation, and then nucleophile added to the carbon the most removed from the hydroxy group; the subsequent transformations resulted in β-diamide. Presumably an analogous cation may form also from compound **X**, but the nucleophile addition to the β-atom of allyl-cation **XV** would be thermodynamically unfavored for it consists in introducing a bulky amide substituent into a nodal position of the decahydroquinoline ring.

It was presumable that under conditions of Ritter's reaction enyne **IX** and alcohols **II** and **III** (or their hydrochlorides **IV** and **V**) would furnish the same products for the reaction should proceed via the common carbocation **VIII**. It turned out however that amides **VI** and **VII** were although the principal but not the only reaction products. Alongside these amides in the reaction mixture were found two more compounds identified as amidoketones **XII** and **XIII**. Obviously the triple bond of enyne **IX** underwent partial hydration forming intermediately mesomerically stabilized ion **XVI**. The overall content of amides **XII** and **XIII** in the reaction mixture amounts to 12%, corresponding to the quantity of enone **X** in the products obtained by treating ethynylcarbinols **II** and **III** with formic acid. This fact suggests an assumption, that formation of 4-acetyl-substituted derivatives **X, XII**, and **XIII** occurs along similar mechanisms and is limited by the same factors: protonation rate and "life time" of cation **XVI**.

It should be noted that transformations of octahydroquinolines **IX** and **X** give rise to compounds with *trans*-junetion of the cyclohexane and the piperidine rings (derivatives of *trans*-decahydroquinoline) as show the ^{1}H NMR data. This stereochemical outcome of the reaction is consistent with the thermodynamically preferable *trans*-configuration of the decahydroquinoline ring; it is also in agreement with the published data [10] on exclusive formation of *trans*-decahydroquinolines at hydride reduction of N-substituted 4-oxo-1,2,3,4,6,7,8,9-octahydroquinolines.

EXPERIMENTAL

^{1}H NMR spectra were registered on spectrometers Bruker AC-200 (200 MHz) and Bruker DRX-500 (500 MHz). ^{13}C NMR spectra were taken on spectrometer Bruker AC-200. IR spectra were measured on Fourier spectrophotometer Protege-460

(Nicolet Co), mass spectra were recorded on an instrument Chromass GC/MS Hewlett Packard 5890/5972, column HP-5MS, ionizing electrons energy 70 eV. The reactions progress was monitored and the purity of products obtained was checked by GLC on chromatograph Chrom-5 equipped with glass column (200 × 2 mm) packed with Cromaton-N-AW-DMCS (0.16–0.20), stationary phase Apiezon L.

4-*cis*-Hydroxy- and 4-*trans*-hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinolines (II) and (III) were prepared by reaction of lithium acetylide (~50% excess) with 16.7 g (100 mmol) of 2e-methyl-4-oxo-decahydroquinoline (**I**) in tetrahydrofuran solution along procedure we had described before [5]. The most of products precipitate from the THF solution at quenching lithium alcoholate with water. The rest of acetylene alcohols mixture was isolated after solvent evaporation. After crystallization from ethanol we obtained 17.3 g (90%) of a mixture of ethynylcarbinols **II** and **III**. The separation of the isomers involved some difficulty since the compounds are sparingly soluble in most common solvents save lower alcohols. The crystallization from ethanol and methanol provided mixture with nearly the same composition as the initial one. Since compounds **II** and **III** as relatively strong bases actively take up the carbon dioxide from air, their separation by repeated crystallization also was unsuccessful. Small amounts of individual compounds **II** and **III** required for measuring ^{1}H nd ^{13}C NMR spectra were isolated by preparative TLC on silica gel (5/40), eluent THF–ethanol mixture, 4 : 1. The minor component of the reaction mixture, *trans*-isomer **III**, was more mobile (R_f 0.59), mp 127–129°C. Publ. data [2]: mp 127–128°C. The *cis*-isomer **II** has lower chromatographic mobility (R_f 0.38), mp 206–207°C. Publ. data [2]: 205–206°C.

4-*cis*-Hydroxy- and 4-*trans*-hydroxy-2e-methyl-4-ethynyl-*trans*-decahydroquinoline hydrochlorides (IV) and (V) we succeeded in preparation in small amount by passing gaseous HCl through a solution of acetylene alcohols **II** and **III** in THF. Compounds **II** and **III** precipitated. However this method is not fit for preparation of large quantities of hydrochlorides, for alcohols **II** and **III** are poorly soluble in THF. Therefore hydrochlorides **IV** and **V** were obtained by passing excess HCl through a solution of decahydroquinolines **II** and **III** in alcohol. On evaporation of solvent the mixture of hydrochlorides was obtained in quantitative yield. The mixture was separated by crystallization from water. From the solution first precipitated the hydrochloride of *cis*-isomer **IV** of the purity tolerable in the spectral measurements (no less than 98%). In the mother liquor remained a mixture of hydrochlorides **IV** and **V** containing ~12% of *cis*-isomer and 88% of *trans*-isomer. Hydrochloride **V** in virtually pure state was obtained from the alcoholic solution by careful precipitation with THF (on addition of excess THF both isomers precipitate). Both hydrochlorides **IV** and **V** melt over 300°C and are hygroscopic.

Ritter's reaction. To 10 ml (~200 mmol) of acetonitrile was added 10 mmol of substrate, and at vigorous stirring and cooling with cold water (15°C) was slowly added 5ml (~70 mmol) of sulfuric acid. Therewith the substrate suspension gradually dissolved. The reaction mixture was stirred at room temperature till completion of the process (GLC monitoring), then it was cautiously poured into an excess of diluted water solution of NaOH or KOH. The precipitated reaction product was filtered off, dried on the filter, and dissolved in ethanol or methanol. Insoluble residue (polymeric products) was separated by filtration. On distilling off the alcohol the mixture of stereoisomeric amides was separated by crystallization.

(a) By Ritter's reaction from a mixture of acetylene alcohols **II** and **III** were obtained 4-*cis*-acetylamino-2e-methyl-4-ethynyl-*trans*-decahydroquinoline (**VI**) and 4-*trans*-acetylamino-2e-methyl-4-ethynyl-*trans*-decahydroquinoline (**VII**) in 3 : 2 ratio. Yield 1.4 g (60%). Amides **VI** and **VII** were separated by repeated crystallization from ethanol. Therewith the crystal phase enriched with the *cis*-isomer of amide, and the mother liquor with the *trans*-isomer. The samples fit for spectral studies were obtained after 4–5 crystallizations.

(b) From individual hydrochlorides **IV** or **V** we obtained a mixture of stereoisomeric amides **VI** and **VII** in the same ratio but in somewhat higher yield (1.6 g, 68%).

(c) From 4-acetyl-2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**X**) was obtained a mixture of 4-acetyl-4-*cis*-acetylamino- and 4-acetyl-4-*trans*-acetylamino-2e-methyl-*trans*-decahydroquinolines **XII** and **XIII** in 9 : 7 ratio and in amount 1.56 g (yield 62%). The individual stereoisomers were isolated by the same procedure as used with amides **VI** and **VII**. Amidoketones **XII**, **XIII** are a little better soluble in acetone and chloroform than compounds **VI, VII**.

(d) From 2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**IX**) was obtained a mixture of compounds **VI, VII, XII, XIII** in 53 : 35 : 7 : 5 ratio

(GLC data). For separation of the minor components was used their better solubility in acetone than that of ethynylamides **VI** and **VII**. Each two-component mixture thus obtained was separated into isomers by repeated crystallization from alcohol (see above).

Kucherov's reaction was carried out by procedure developed for hydration of an ethynyl group in 2-hydroxy-2-ethynyladamantane [11]. Ethynyl derivatives **II** and **III** were not hydrated under these conditions. At more stringent conditions only increased the formation of polymer.

Rupe rearrangement was performed by boiling 5.9 g (30 mmol) of a mixture of compounds **II** and **III** with 24 ml of 87% HCOOH. The reaction was carried out till GLC analysis showed complete consumption of the initial compounds. The reaction mixture was diluted with water (~1 : 10), carefully neutralized with excess of diluted aqueous alkali, the separated precipitate was filtered off and dried on the filter, then dissolved in ethanol. Insoluble part (polymerization products) was separated, the alcoholic solution was evaporated to furnish a mixture of 2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**IX**) and 4-acetyl-2e-methyl-4-ethynyl-1,2,3,6,7,8,9,10-octahydroquinoline (**X**) (88 : 12), yield 3.9 g (72% calculated to 1 mol of products). Compounds **IX** and **X** were separated by crystallization from acetone. First precipitated the dehydration product **IX** as yellowish fine-crystalline powder. The mother liquor contained prevailingly acetyl derivative **X** with some impurity of compound **IX**. To purify compound **X** the mother liquor was evaporated, and the residue was recrystallized from ethanol. Compound **X** was obtained as lemon-yellow crystals.

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