STEREOCHEMISTRY OF NITROGEN HETEROCYCLES.

66.* SYNTHESIS AND X-RAY DIFFRACTION ANALYSIS OF $C_{(4)}$-EPIMERIC 1-METHYL-trans-DECAHYDRO-4-QUINOLINOLS

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$C_{(4)}$-Epimeric 1-methyl-trans-decahydro-4-quinolinols, which are of interest as model compounds for stereochemical investigations, were obtained. It was shown by means of x-ray diffraction analysis that the crystalline compound that we synthesized and not the liquid compound described in the literature is the actual 1-methyl-trans-decahydro-4-quinolinol with an axial hydroxy group. Different pathways of weakening of the OH/H 1,3-syn-peri-planar repulsive interactions were observed: torsional twisting of the cyclic system for the equatorial alcohol and an increase in the $O-C_{(4)}-C_{(10)}$ and $C_{(4)}-C_{(10)}-C_{(5)}$ bond angles. The previously unknown isomorphic forms of equatorial trans-decahydro-4-quinolinol and 1-methyl-trans-decahydro-4-quinolinol were obtained.

In connection with an investigation of the dependence of the local-anesthetic activity [2] and rates of hydrolysis [3, 4] of benzoates of substituted decahydro-4-quinolinols on their three-dimensional structures we needed the benzoates of $C_{(4)}$-epimeric 1-methyl-trans-decahydro-4-quinolinols as model compounds. These esters could be obtained most simply by benzoylation of the described isomers of 1-methyl-trans-decahydro-4-quinolinol. In connection with the contradictions between our data and the literature data relative to the conditions of formation, the physicochemical characteristics, and the structures of these amino alcohols and proceeding from their importance as model compounds in various investigations [5, 6] we devoted the present paper to the synthesis and proof of the configurations of isomers of 1-methyl-trans-decahydro-4-quinolinol.

1-Methyl-trans-decahydro-4-quinolinols I and II were synthesized almost simultaneously by Grob and Mistryukov. Grob [5] obtained them by reduction of 1-methyl-trans-decahydro-4-quinolinone (VII), while Mistryukov obtained them by reduction of trans-decahydro-4-quinolinone (VIII) [7] with subsequent methylation of the resulting trans-decahydro-4-quinolinols III and IV [8, 9] and dequaternization of the 1-methyl-trans-decahydro-4-quinolinol methiodides V and VI [8], which were obtained, in turn, by reduction of 1-methyl-trans-decahydro-4-quinolinone methiodide (IX) [8] and by reduction of 1-methyl-trans-decahydro-4-quinolinone [10] (see the scheme). However, it should be noted that Mistryukov did not isolate the isomers themselves of 1-methyl-trans-decahydro-4-quinolinol but characterized them exclusively in the form of the methiodides.

Since we have developed a simple variant of the synthesis of trans-decahydro-4-quinolinone (VIII) [11], it seemed natural to obtain the needed I and II by reduction of ketone VIII with subsequent methylation of the isomeric hydroxy amines III and IV.

Ketone VIII was reduced by hydrogenation on a platinum catalyst; the mixture of isomers of trans-decahydro-4-quinolinol was separated, and the individual isomeric amino alcohols III and IV were methylated by heating with formaldehyde and formic acid. Within the limits of the permissible deviations, the melting points of the isomeric methiodides V and VI that we obtained coincide with those presented by Mistryukov [8, 9] (Table 1). In contrast to

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*See [1] for Communication 65.

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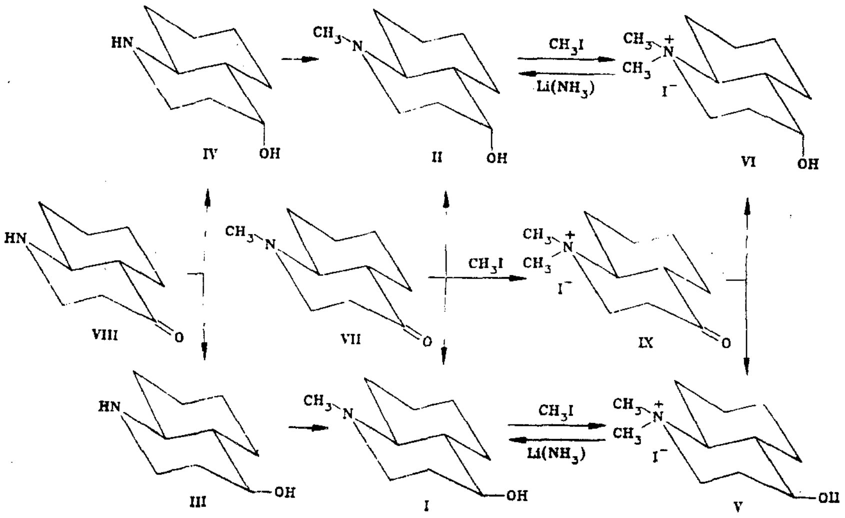
Mistryukov, we obtained the N-unsubstituted equatorial alcohol III in the form of two isomorphic modifications – one with mp 128-129°C (as compared with mp 126-130°C for the compound obtained by Mistryukov) and a previously undescribed form with mp 138-139°C; the high-melting form, to which the low-melting form is converted during storage, is stable. The two isomorphic forms give the same derivatives and have the same IR and PMR spectra (solutions).



The characteristics of only one of the isomers that we obtained, viz., equatorial isomer I (1-methyl-trans-decahydro-4α-quinolinol),* coincided with the data of Grob [5]; like its isostructural nor analog III, it also has two isomorphic forms – forms with mp 95-96°C and 105-106°C (only one form with mp 108-109°C was described by Grob). The low-melting form, which is converted to the high-melting form during storage for several days, primarily crystallizes from acetone. The low-melting form is formed when the high-melting form is melted and the melt is crystallized rapidly. The two forms give the same derivatives (Table 1).

The second isomer that we obtained, viz., axial isomer II (1-methyl-trans-decahydro-4β-quinolinol) was completely different from the compound described by Grob: in the case of Grob the base is a liquid, and the picrate has mp 204°C and the methiodide has mp 257°C; in our case the base is crystalline with mp 123°C, and the picrate has mp 182°C and the methiodide has mp 282°C.

Since Grob obtained isomeric 1-methyl-trans-decahydro-4-quinolinols I and II by reduction of 1-methyl-trans-decahydro-4-quinolinone (VII), we decided to reproduce his synthesis, assuming that the reduction of this ketone may have some peculiarities. We obtained ketone VII by the Grob method [5] (as in the case of Grob, the picrate had mp 185-186°C; Mistryukov [12] presents a melting point of 193-194°C for it). By reduction of this ketone by both lithium aluminum hydride under the conditions described by Grob [5] and by means of catalytic hydrogenation on a platinum catalyst we obtained the same isomers of 1-methyl-trans-decahydro-4-quinolinol (I and II) as those synthesized previously by methylation of secondary hydroxy amines III and IV [it should be noted that in the reduction with lithium aluminum hydride Grob obtained primarily the axial alcohol (a:e = 70:30), whereas we, on the other hand, obtained primarily the equatorial alcohol (a:e = 15:85)].

Thus a situation in which two absolutely different compounds lay claim to the same structure has been created.

This contradiction arose during the synthesis of decahydro-4-quinolinols. In 1962 Mistryukov [8], having obtained the methiodide (V) of the equatorial alcohol, erroneously assigned an axial orientation of the hydroxy group to it. Grob in 1965 [5], in describing the epimeric 1-methyl-trans-decahydro-4-quinolinols obtained by him, cited the work of Mistryukov [8] in confirmation of the coincidence of his data for the axial amino alcohol (methiodide: mp 257°C) with the data of Mistryukov (methiodide: mp 260°C). But in the same year Mistryukov [13] corrected the configurations of trans-decahydro-4-quinolinols III and IV with respect to the $C_{(4)}$ atom – the methiodide with mp 260°C now began to have an equatorial orien-

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*The symbol α denotes a trans orientation of the substituent relative to 9-H, while β denotes a cis orientation.

TABLE 1. Physicochemical Characteristics of Isomers of 1-R-trans-Decahydro-4-quinolinols and Their Derivatives

Compound	R	Derivative	mp,* °C	mp, °C according to the data		IR spectrum (in CCl_4)		PMR spectrum, δ, ppm (J or half width W/2, Hz)				Orientation of OH
				[7—10]	[5]	νC—O	νOH	4-H	2-H_e	2-H_a	N—CH_3	
I	CH_3	Base	105—106 (95—96)	—	108—109	1035	3602 w, 3622 m	3,17 (10; 10; 5)	2,85 (11; 3,3; 3,3)	2,1 (11; 11; 2)	2,22	*e*
Ia		Hydrochloride	209—210	—	—	—	—					
Ib		Picrate	153—154	—	151—152	—	—					
V		Methiodide	256—257	260—260,5	—	—	—					
II	CH_3	Base	122—123	—	—**	1026	3626	3,73 (8)	2,3—2,7 m		2,25	*a*
IIa		Hydrochloride	215—216	—	—	—	—					
IIb		Picrate	181—182	—	—							
VI		Methiodide	281—282	281—282	256—257	—	—					
III	H	Base	138—139 (128—129)	126—130	—	—	—	3,19 (11; 9; 4,5)	3,05 (12; 4,5; 2,6)	2,65 (12; 12; 2,6)	—	*e*
IIIa		Hydrochloride	274—275	274—275	—	—	—					
IV	H	Base	169—170	169—170	—	—	—	3,80 (8)	2,80 (12,5; 3,6; 3,6)	2,9—3,2 m	—	*a*
IVa		Hydrochloride	225—226	229—230	—	—	—					

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*For I and III the labile isomorphic form is presented in parentheses.

**For IIa boiling point of 112°C (0.05 mm) is presented.

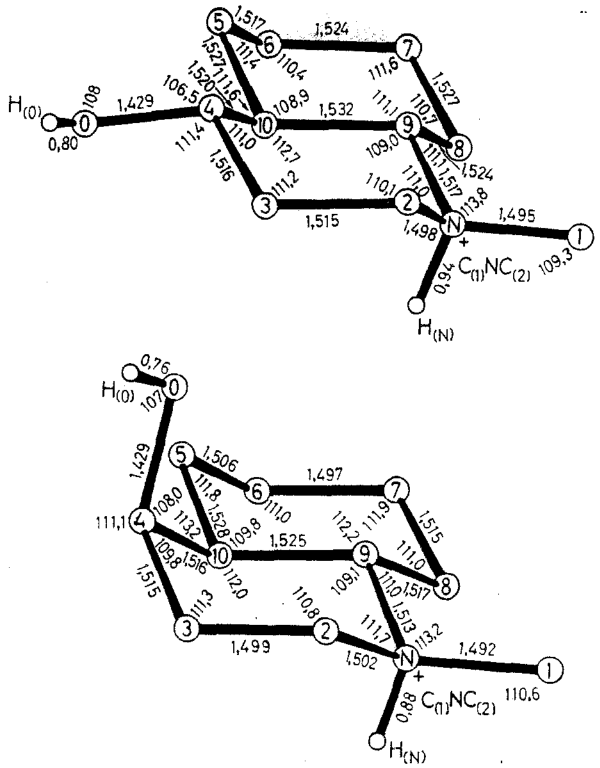

Fig. 1. General form, bond lengths, and bond angles of cations I^+ and II^+.

tation of the hydroxy group — and a contradiction between the data of Mistryukov and Grob thus arose. Nevertheless, in 1968 in describing the preparation of the methiodide (VI) of axial 1-methyl-trans-decahydro-4β-quinolinol with mp 281°C Mistryukov [9] makes reference to the synthesis and assignment of Grob [4] but does not note that the melting points of the methiodides (VI) of the axial amino alcohol now differ markedly.

1-Methyl-trans-decahydro-4-quinolinol was also used as a model compound for investigation of heterolytic fragmentation by Marshall and Bobler [6], who obtained it by the method of Grob [5]; however, the melting points of the 1-methyldecahydro-4-quinolinols and their derivatives are not presented.

In this connection let us dwell on the proof of the configurations of the epimeric 1-methyl-trans-decahydro-4-quinolinols (I and II) presented by Mistryukov and Grob.

Mistryukov [7] obtained both isomers of decahydro-4-quinolinone in the form of 1-benzoyl derivatives. On reduction each of them gave its pair of $C_{(4)}$-epimeric decahydro-4-quinolinols (base VIII and hydrochloride VIIIa on reduction also give the same pair of epimeric alcohols). Only one of the isomers of decahydro-4-quinolinol formed an oxazine derivative with p-nitrobenzaldehyde [12], and, consequently, the pair of epimers to which it is related has cis fusion of the rings, while the other pair has trans fusion of the rings [8, 12]. The orientation of the hydroxy group in the epimeric pairs was proved on the basis of the stereopreferableness of the reduction methods and the frequencies of the C—O vibrations [13]. Since a change in the configurations does not occur on methylation, methiodides V and VI of tertiary hydroxy amines I and II should have the same configurations as the corresponding secondary hydroxy amines III and IV.

According to Grob [5], starting 1-methyldecahydro-4-quinolinone has trans fusion of the rings (VII), since it does not undergo a change under the influence of sodium methoxide. Consequently, the amino alcohols I and II obtained from it should also have trans fusion of the rings. This is confirmed by reduction of the tosylate of liquid axial alcohol II to 1-methyl-trans-decahydroquinoline, which was identified by comparison (with respect to the IR spectra and a mixed-melting-point determination of the picrates) with the known 1-methyl-trans-decahydroquinoline [14]. The trans fusion of the rings and the equatorial character of the hydroxy group of the amino alcohol with mp 109°C (I) are proved by its formation as the only product in the reduction of ketone VII with sodium in alcohol and also by the

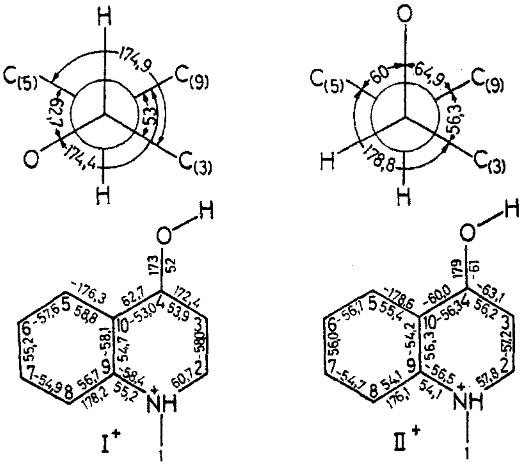

Fig. 2. Torsion angles and Newman projections along the $C_{(4)}$–$C_{(10)}$ bond of cations I^+ and II^+:

	cation I^+	cation II^+
$C_{(3)}—C_{(4)}—C_{(10)}—C_{(5)}$	−174,9	178,8
$C_{(4)}—C_{(10)}—C_{(9)}—C_{(8)}$	177,4	179,1
$C_{(8)}—C_{(9)}—N—C_{(2)}$	178,9	179,7
$N—C_{(9)}—C_{(10)}—C_{(5)}$	179,1	−177,0
$C_{(10)}—C_{(9)}—N—C_{(1)}$	177,9	178,0
$O—C_{(4)}—C_{(10)}—C_{(9)}$	−174,4	−64,9

fact that liquid axial amino alcohol II is converted to it by isomerization in the presence of aluminum isopropoxide. The configuration of liquid isomer II (trans fusion of the rings, axial hydroxy group) is proved by reduction of its tosylate to 1-methyl-trans-decahydroquinoline and its conversion by the action of potassium acetate to the O-acetate of the equatorial alcohol (inversion of the configuration at the $C_{(4)}$ atom). The orientation of the substituent was also proved from the width of the 4-H signals in the PMR spectra of the tosylates of the amino alcohols: the broad signal (half width 21 Hz) in the spectrum of the tosylate of crystalline alcohol I is due to the $4\text{-}H_a$ proton, while the narrow signal (half width 8 Hz) in the spectrum of the tosylate of liquid alcohol II is due to the $4\text{-}H_e$ proton.

Both of these proofs would be convincing and sufficient if the difference in the melting points of the compounds that lay claim to the axial 1-methyl-trans-decahydro-4-quinolinol structure were not substantial.

In connection with this contradiction we attempted to determine the structures of the I and II isomers that we obtained by means of their IR and PMR spectra.

It is apparent from the spectral data (Table 1) that the IR spectra attest to an equatorial orientation of the hydroxy group of alcohol I and an axial orientation of the hydroxy group of alcohol II: ν_{C-O} of alcohol I is greater and ν_{O-H} is smaller than in the case of alcohol II, and the ν_{O-H} band is symmetrical for alcohol II and asymmetrical for alcohol I. The PMR spectra confirm an equatorial orientation of the hydroxy group of alcohols I and III (the $4\text{-}H_a$ signals – δ 3.17 and 3.19 ppm – are triplets of doublets with two J_{aa}) and an axial orientation of alcohols II and IV [the $4\text{-}H_e$ signals – δ 3.73 and 3.80 ppm – are narrow (8 Hz) weakly resolved quartets]. However, because of the complexity of the PMR spectra, we were unable to reliably identify the 9-H signals; this made it impossible to determine the character of the ring fusion.

In this connection, considering the importance of the isomers of 1-methyl-trans-decahydro-4-quinolinol (I and II) as model compounds in stereochemical investigations, we resorted to x-ray diffraction analysis of their hydrochlorides (Ia and IIa).

It was established by x-ray diffraction investigation that the cations of amino alcohols I and II (they will subsequently be designated as cation I^+ and cation II^+) have trans fusion of the rings in the chair conformation with an equatorial orientation of the methyl group attached to the nitrogen atom and differ only with respect to the orientation of the hydroxy group: it is equatorial in cation I^+, whereas it is axial in cation II^+. There are two forms of cations – I^+A and I^+B – in crystalline amino alcohol hydrochloride Ia. Since the parameters of the cations are close (they differ most significantly for the atoms that participate in the formation of hydrogen bonds), their averaged values are generally presented. The angle of ring fusion [the angle between the central $C_{(2)}C_{(3)}C_{(10)}C_{(9)}$ (plane Π_1) and $C_{(6)}C_{(7)}C_{(9)}C_{(10)}$ (plane Π_2) planes, satisfied with an accuracy of no less than 0.01 Å] is 178.5° for cation I^+ and 178° for cation II^+, i.e., it virtually does not differ from the ideal value of 180° [15]. The N, $C_{(4)}$, $C_{(5)}$, and $C_{(8)}$ atoms in cation I^+ deviate from planes Π_1 and Π_2 by, respectively, −0.69, 0.63, 0.68, and −0.67 Å (the dihedral angles between the peri and central planes are 54.3°, 48.2°, 53.2°, and 50.4°), as compared with −0.67, 0.67, 0.66, and −0.64 Å in cation II^+ (with dihedral angles 52.1°, 50.6°, 50.9°, and 48.4°). The bond lengths and bond and torsion angles in cations I^+ and II^+ are, with certain exceptions, which will be discussed below, close and have the usual values (Figs. 1 and 2).

In analyzing the fine differences in the geometries of cations I^+ and II^+ it may be noted that they are associated with different orientations of the hydroxy groups and interactions of them with the 1,3-syn-peri-planar hydrogen atoms of the cyclic system: in the case of cation I^+ with an equatorial hydroxy group there is one such interaction with the 5-H_e atom, while in the case of cation II^+ with an axial hydroxy group there are three – with the 2-H_a, 5-H_a, and 9-H_a atoms. The geometry of the cations changes in such a way as to weaken these interactions; the character of the changes depends on the orientation of the hydroxy group and the direction of the repulsive interactions.

It is apparent from the Newman projection along the $C_{(4)}-C_{(10)}$ bond (Fig. 2) that in cation I^+, as a consequence of repulsion between the OH and 5-H_e groups, the carbonyl fragment with center $C_{(4)}$ rotates about the $C_{(4)}-C_{(10)}$ bond, during which the hydroxy group is shifted toward the "small" H atom attached to the $C_{(10)}$ atom: torsion angle $O-C_{(4)}-C_{(10)}-C_{(5)}$ increases to 62.7°, while torsion angles $O-C_{(4)}-C_{(10)}-C_{(9)}$, $C_{(3)}-C_{(4)}-C_{(10)}-C_{(9)}$ and $C_{(3)}-C_{(4)}-C_{(10)}-C_{(5)}$ decrease to, respectively, −174.4°, −53.0°, and −174.9°. As a consequence of the "rigidity" of the bond between the O atom and the peri-$C_{(4)}$ atom and the bond between the 5-H_e atom and the peri-$C_{(5)}$ atom there is a decrease in the degree of folding of the first ring and an increase in the degree of folding of the second: the angle of deflection of the $C_{(3)}C_{(4)}C_{(10)}$ plane from plane Π_1 decreases to 48.2°, and the angle of deflection of the $C_{(5)}C_{(6)}C_{(10)}$ plane Π_2 increases to 53.2° (in the case of cation II^+ they are, respectively, 50.6° and 50.9°). Twisting, as it were, of the cyclic system occurs.

In the case of cation II^+ the torsional mobility of the axial hydroxy group is decreased, since the O atom in the Newman projection is "squeezed" between the $C_{(5)}$ and $C_{(9)}$ atoms. The steric repulsion experienced by the hydroxy group on the part of the 2-H_a, 5-H_a, and 9-H_a atoms therefore decreases in this structure primarily due to an increase in the $C_{(4)}-C_{(10)}-C_{(5)}$ bond angle to 113.2° and in the $O-C_{(4)}-C_{(10)}$ bond angle to 108.0° (the analogous angles in cation I^+ are, respectively, 111.6° and 106.5°, angle $C_{(4)}-C_{(10)}-C_{(5)}$ in the 1,8e-dimethyl-trans-decahydroquinolinium ion is 111.7°, and the values for the 8a- and 8e-tert-butyl-trans-decahydroquinolinium ions are 111.1° and 111.0° [16]).

Although the differences in the angles in the cations are relatively small, they exceed the errors in the measurements and evidently reflect the pathways via which the molecules strive to decrease the repulsive interactions of the valently nonbonded atoms that develop in them.

In correspondence with the number of active hydrogen atoms, there are four independent hydrogen bonds of the $OH\cdots Cl^-$ and $N^+H\cdots Cl^-$ type between the cations and anions in amino alcohol hydrochloride Ia and four such bonds in amino alcohol hydrochloride IIa (the parameters of the H bonds are presented in Table 3); this is reflected in the IR spectra of crystals of the hydrochlorides: the spectrum of equatorial alcohol Ia contains two ν_{OH} bands and two ν_{N^+H} bands, while the spectrum of axial alcohol IIa contains one band of each vibration.

In the Ia crystal each cation of one sort (A and B) is bonded by H bonds with two anions also of only one sort (A or B, respectively), so that symmetrically independent zigzag-shaped chains along the *a* axis in which the anions and cations alternate are formed. In the IIa crystal the cations and anions form zigzag-shaped chains along the b axis. In the chains of hydrogen bonds the antipodes form individual ···–ℓ–ℓ–··· and ···–d–d–··· chains in the Ia crystals and mixed ···–ℓ–d–ℓ–d–··· chains in the IIa crystals.

EXPERIMENTAL

The IR spectra of KBr (for the bases) and KCl (for the hydrochlorides) pellets and of

TABLE 2. Coordinates of the Atoms ($\cdot 10^4$; $\cdot 10^5$ for the Cl Atoms and $\cdot 10^3$ for the H Atoms) in the Ia and IIa Structures

Atom	IaA			IaB			IIa		
	x	y	z	x	y	z	x	y	z
Cl	18849(6)	15145(3)	92749(2)	5272(6)	87399(3)	81524(2)	12425(7)	26232(4)	56517(5)
O	264(2)	2225(1)	3978(1)	2363(2)	7628(1)	3525(1)	−721(2)	3837(1)	1288(2)
N	4635(2)	3225(1)	3040(1)	−2065(2)	6391(1)	4358(1)	−1214(2)	6466(1)	1681(2)
$C_{(1)}$	5905(3)	3587(1)	2606(1)	−3304(3)	5923(1)	4763(1)	−1459(4)	7341(2)	750(3)
$C_{(2)}$	2851(3)	3823(1)	3008(1)	−314(2)	5787(1)	4303(1)	−2607(3)	5724(2)	1308(3)
$C_{(3)}$	1658(3)	3551(1)	3494(1)	829(2)	6101(1)	3838(1)	−2438(3)	4888(2)	2301(3)
$C_{(4)}$	1122(2)	2507(1)	3469(1)	1460(2)	7199(1)	3990(1)	−824(3)	4333(2)	2470(2)
$C_{(5)}$	2369(2)	842(1)	3385(1)	352(2)	8818(1)	4282(1)	2256(3)	4588(2)	3051(3)
$C_{(6)}$	4148(3)	218(1)	3407(1)	−1399(3)	9446(1)	4334(1)	3617(3)	5355(2)	3441(3)
$C_{(7)}$	5399(3)	518(1)	2934(1)	−2659(3)	9022(1)	4767(1)	3451(3)	6185(2)	2443(3)
$C_{(8)}$	5932(2)	1567(1)	2964(1)	−3259(2)	8003(1)	4601(1)	1804(2)	6710(2)	2199(2)
$C_{(9)}$	4120(2)	2179(1)	2969(1)	−1483(2)	7393(1)	4539(1)	421(2)	5943(1)	1831(2)
$C_{(10)}$	2908(2)	1890(1)	3455(1)	−266(2)	7816(1)	4087(1)	576(2)	5088(1)	2833(2)
$H_{(O)}$	−64(3)	256(2)	402(1)	316(3)	726(1)	343(1)	−142(3)	345(2)	113(3)
$H_{(N)}$	529(5)	331(1)	342(1)	−276(3)	643(1)	399(1)	−125(2)	670(2)	246(2)

TABLE 3. Parameters of the Hydrogen Bonds in Ia and IIa Crystals

A···H—D	D···A, Å	H···A, Å	D—H, Å	Angle D—H...A, deg.
$Cl^- \cdots H—O$(IaA) ($1/2+x, 1/2-y, 1/2+z$)	3,085(1)	2,29(2)	0,80(2)	172(1)
$Cl^- \cdots H—O$(IaB) ($-1/2+x, 1/2-y, 1/2+z$)	3,119(1)	2,32(2)	0,80(2)	177(1)
$Cl^- \cdots H—O$(IIa) ($1/2+x, 1/2-y, 1/2+z$)	3,136(2)	2,38(3)	0,76(3)	175(3)
$Cl^- \cdots H—N^+$(IaA) ($-1/2+x, 1/2-y, 1/2+z$)	3,090(1)	2,14(2)	0,95(2)	177(1)
$Cl^- \cdots H—N^+$(IaB) ($1/2+x, 1/2-y, 1/2+z$)	3,063(1)	2,15(2)	0,92(2)	170(1)
$Cl^- \cdots H—N^+$(IIa) ($-x, 1-y, 1-z$)	3,064(2)	2,19(2)	0,88(2)	175(2)

solutions in CCl_4 were recorded with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ (for the bases) and CD_3OD (for the hydrochlorides) were recorded with a BS-487C spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. Analysis of GLC was carried out with a Khrom-41 chromatograph with a flame-ionization detector with columns with an internal diameter of 3 mm and a length of 2.4 m filled with Chromosorb W (60-80 mesh) with 10% PEG-6000 and 3% KOH applied to it; the thermostat temperature was 170°C, and the carrier-gas (nitrogen) flow rate was 22 ml/min. The retention times were as follows: 7.1 min for ketone VII, 9.6 min for alcohol II, 11.0 min for alcohol I, 10.0 min for ketone VIII, 12.2 min for alcohol IV, and 13.8 min for alcohol III. Thin-layer chromatography (TLC) was carried out on activity ~III alkaline aluminum oxide by elution with dioxane or dioxane—water (20:1) with development by iodine vapors. The R_f values in dioxane—water (the values in dioxane are given in parentheses) were as follows: 0.67 (0.55) for ketone VIII, 0.86 (0.83) for ketone VII, 0.19 (0.05) for alcohol III, 0.09 (0.03) for alcohol IV, 0.56 (0.42) for alcohol I, and 0.53 (0.39) for alcohol II.

trans-Decahydro-4-quinolinone (VIII). This compound was obtained by the method in [10]. The base had mp 46-47°C, and the hydrochloride had mp 221-222°C. 1-Methyl-trans-decahydro-4-quinolinone (VII) was obtained by the method in [5]. The IR spectrum showed that the product had absorption bands at 1610 and 1670 cm^{-1}, and it was therefore additionally purified through the picrate in the form of yellow crystals with mp 185-186°C (from methanol). For isolation of base VII the picrate was shaken with dilute hydrochloric acid, the picric acid was extracted with ether, the hydrochloric acid solution was treated with potassium carbonate, and the base was extracted with ether, dried, and distilled in vacuo to give a colorless liquid with bp 97-99°C (2 mm) and n_D^{20} 1.4950. IR spectrum (thin layer): 1375 (CH_3), 1721 (C=O), 2790 cm^{-1} ($N—CH_3$). Literature data: bp 67-68°C (0.1 mm) and n_D^{20} 1.4958; picrate, mp 193°-194°C [17]; bp 95°C (0.05 mm), n_D^{17} 1.4944, IR spectrum (CH_2Cl_2): 730, 5.82, 3.60 μ; picrate, mp 185-186°C [5].

trans-Decahydro-4-quinolinols. A 7.0 g sample of trans-decahydro-4-quinolinone in 200 ml of aqueous KOH solution (0.1 M) was hydrogenated on a platinum Adams catalyst (0.8 g of PtO_2). After the calculated amount of hydrogen had been adsorbed, the catalyzate (which contained 51% equatorial alcohol III and 49% axial alcohol IV (GLC)) was acidified with hydrochloric acid and evaporated, and the residue was decomposed by the gradual addition of potassium carbonate. The resulting precipitate was removed by filtration, washed with a small amount of water, dried, and recrystallized from acetone to give 1.63 g of trans-decahydro-4β-quinolinol (IV) with mp 169-170°C. IR spectrum (KBr): 1038 (C—O), 1582 (N—H), 3080 (OH), 3360, 3466 cm^{-1} (NH). Hydrochloride IVa was obtained by neutralization of the base with a solution of dry HCl in anhydrous ethanol. The colorless crystals had mp 225-226°C (from aqueous ethanol).

The aqueous solution after separation of decahydroquinolinol IV was saturated with potassium carbonate, and the base was extracted with ether. The extract was dried with potassium carbonate, the ether was removed, and the base was converted to the hydrochloride by the addition of a solution of dry HCl in anhydrous ethanol. Fractional crystallization from anhydrous ethanol gave 2.71 g of trans-decahydro-4α-quinolinol hydrochloride (IIIa) with mp 274-275°C. Alternation of fractional crystallization of the base from acetone and of the hydrochloride from anhydrous ethanol as described above gave a total of 2.91 g (41%) of axial trans-decahydro-4β-quinolinol (IV) with mp 169-170°C and 3.86 g (47%) of equatorial trans-decahydro-4α-quinolinol hydrochloride (IIIa) with mp 274-275°C. Hydrochloride IIIa (3.0 g) in aqueous solution was decomposed with potassium carbonate, and the base was extracted with chloroform. After drying of the extract with sodium sulfate and removal of the solvent, 2.4 g of a crystalline substance with mp 128-129°C remained. In the case of crystallization from acetone the first portion of crystals of trans-decahydro-4α-quinolinol (III) melted at 128-129°C, while the subsequent portions melted at 138-139°C, and the melting point did not change on recrystallization from acetone. After storage for 3 days, the first portion also melted at 138-139°C. (In the case of crystallization from acetone of the mixture of isomeric alcohols III and IV obtained by hydrogenation of ketone VIII on platinum in ethanol and containing 86% alcohol III and 14% alcohol IV equatorial alcohol III crystallized with extended mp 126-129°C, but it was also converted to a high-melting form with mp 138-139°C during storage). IR spectrum (KBr): high-melting form: 988, 1038, 1059, 1080 (C—O region), 3092 (OH), 3275 (NH); low-melting form: 1038, 1058, 1078 (C—O region), 1590, 1690 (NH), 3055 (OH), 3258, 3396 cm^{-1} (NH).

1-Methyl-trans-decahydro-4-quinolinols. A. A mixture of 4.50 g (0.029 mole) of trans-decahydro-4α-quinolinol (III), 4.4 g (0.035 mole) of a 24% aqueous solution of formaldehyde, and 1.9 g (0.036 mole) of 87% formic acid was heated with a reflux condenser on a boiling-water bath for 2 h (with monitoring by TLC). A 30 ml sample sample of 5% hydrochloric acid was added to the cooled reaction mixture, the aqueous solution was washed with ether and treated with potassium carbonate, and the base was extracted with ether. The extract was dried with potassium carbonate, and the ether was removed by distillation. Crystallization of the residue from acetone gave 3.9 g (79%) of 1-methyl-trans-decahydro-4α-quinolinol (I), which crystallized in two isomorphic forms with mp 95-96°C and 105-106°C (primarily the former). During storage for several days the low-melting form underwent conversion to the high-melting form. The low-melting form was formed when the melt of the high-melting form crystallized. IR spectrum (KBr): the form with mp 96°C: 1047, 1056, 1084 (C—O region), 1365 (CH_3), 2790 (N—CH_3), 3150 (OH); the form with mp 106°C: 1048, 1064, 1088 (C—O region), 1367 (CH_3), 2772 (N—CH_3), 3153 cm^{-1} (OH). Found: C 70.5; H 11.5; N 8.3%. $C_{10}H_{19}NO$. Calculated: C 71.0; H 11.3; N 8.3%. Hydrochloride Ia was obtained in quantitative yield by neutralization of the base with a solution of dry HCl in anhydrous ethanol. The colorless crystals had mp 209-210°C (from anhydrous ethanol). IR spectrum (KCl): 988, 1028, 1055, 1076 (C—O region), 1323 (CH_3), 2506, 2590 (N^+—H), 3290, 3320 cm^{-1} (OH) (x-ray diffraction analysis demonstrated that there are two types of N^+—H···Cl^- and OH···Cl^- hydrogen bonds in the crystal). Found: C 58.8; H 9.6; Cl 16.9; N 6.6%. $C_{10}H_{19}NO \cdot HCl$. Calculated: C 58.4; H 9.8; Cl 17.2; N 6.8%. Picrate Ib was obtained in 85% yield by mixing equimolar amounts of the base and picric acid in methanol. The yellow crystals had mp 153-154°C (from isopropyl alcohol). Found: 48.6; H 5.5; N 14.3%. $C_{10}H_{19}NO \cdot C_6H_3N_3O_7$. Calculated: 48.2; H 5.6; N 14.1%. Methiodide V was obtained in 95% yield by reaction of the base with excess methyl iodide in acetone. The precipitate that formed almost immediately was recrystallized from ethanol. The colorless needles had mp 256-257°C. Found: C 42.8; H 7.2; I 41.3%. $C_{11}H_{22}INO$. Calculated: C 42.5; H 7.1; I 40.8%.

B. A 4.40 g sample of trans-decahydro-4β-quinolinol (IV) was methylated as described above. Crystallization of the product from acetone gave 3.94 g (82%) of 1-methyl-trans-decahydro-4β-quinolinol (II) in the form of colorless crystals with mp 122-123°C. IR spectrum (KBr): 990, 1005, 1023, 1065 (C—O region), 1320 (CH_3), 2802 (N—CH_3), 3127 cm^{-1} (OH). Found: C 71.5; H 11.4; N 8.2%. $C_{10}H_{19}NO$. Calculated: C 71.0; H 11.3; N 8.3%. Hydrochloride IIa was obtained in quantitative yield as described above. The colorless crystals had mp 214-215°C (from anhydrous ethanol). IR spectrum (KCl): 978, 1039, 1053, 1064, 1085 (C—O region), 1331 (CH_3), 2505, 2578 (N^+—H), 3287 cm^{-1} (OH). Found: C 58.5; H 9.8; Cl 16.9; N 6.6%. $C_{10}H_{19}NO \cdot HCl$. Calculated: C 58.4; H 9.8; Cl 17.2; N 6.8%. The picrate was obtained as described above in 84% yield. The yellow crystals had mp 181-182°C (from isopropyl alcohol). Found: C 48.6; H 5.5; N 14.5%. $C_{10}H_{19}NO \cdot C_6H_3N_3O_7$. Calculated: C 48.2; H 5.6; N 14.1%. Methiodide VI was obtained in quantitative yield by the method described above (the solution was refluxed for 5 min to complete the reaction). The colorless crystals had mp 281-282°C. Found C 42.7; H 7.0; I 41.2; N 4.3%. $C_{11}H_{22}INO$. Calculated: C 42.5; H 7.1; I 40.8; N 4.5%.

C. A solution of 3.14 g (0.0188 mole) of 1-methyl-trans-decahydro-4-quinolinone (VII) in 30 ml of dry ether was added dropwise with stirring to a suspension of 0.84 g (0.022 mole) of lithium aluminum hydride (with an activity of 82%) in 30 ml of dry ether. After stirring for 12 h, the reaction mixture was treated carefully with hydrochloric acid until it was acidic (pH ~ 2), the aqueous solution was washed with ether and treated with potassium carbonate, and the base was extracted with methylene chloride. After drying of the extract with potassium carbonate and removal of the solvent, 3.05 g of a crystallized oil consisting of 85% alcohol I and 15% alcohol II (GLC), which corresponded to 82% and 14% yields (theoretical) of I and II, respectively, remained. The mixture was crystallized from heptane by slow evaporation of the solvent. The resulting crystals were separated mechanically into transparent and opaque crystals. The former contained ~90% alcohol I, while the latter contained ~90% alcohol II (GLC). Crystallization from heptane of the mixtures enriched with, respectively, alcohols I and II gave 1.2 g of 1-methyl-trans-decahydro-4α-quinolinol (I) with mp 95-96°C and 105-106°C and 0.24 g of 1-methyl-trans-decahydro-4β-quinolinol (II) with mp 122-123°C, which did not depress the melting points of samples of 1-methyl-trans-decahydro-4-quinolinols I and II obtained by methylation of the corresponding hydroxy amines III and IV, and their IR spectra were identical.

D. A 1.8 g sample of 1-methyl-trans-decahydro-4-quinolinone hydrochloride was hydrogenated on a Raney nickel catalyst (from 3 g of alloy) in 50 ml of water. After hydrogen absorption ceased, the catalyst contained 63% alcohol I and 32% alcohol II, which were described above, and 5% unidentified products (GLC).

X-Ray Diffraction Analysis. The crystals of 1-methyl-trans-decahydro-4α-quinolinol hydrochloride (Ia) had mp 209-210°C and were monoclinic. At −120°C they had the following parameters: a = 6.954(1), b = 14.087(3), c = 22.916(6) Å, β = 96.75(2)°, Z = 8, d_{calc} = 1.23 g/cm^3, space group $P2_1/n$, and two formula units (A and B) in an independent part of the cell. The cell parameters and the intensities of 2895 independent reflections with $F^2 \geq 3\sigma$ were measured with a Syntex $P2_1$ automatic four-circle diffractometer at −120°C (λ_{MoK_α}, graphite monochromator, θ/2θ scanning, $\theta \leq 26°$).

The crystals of 1-methyl-trans-decahydro-4β-quinolinol hydrochloride (IIa) had mp 215-216°C and were monoclinic. At 20°C they had the following parameters: a = 8.434(1), b = 13.106(1), c = 10.557(2) Å, β = 104.10(1)°, Z = 4, d_{calc} = 1.20 g/cm^3, and space group $P2_1/n$. The cell parameters and the intensities of 1731 independent reflections with $F^2 \geq 4\sigma$ were measured with a Hilger—Watts automatic four-circle diffractometer at 20°C (λ_{MoK_α}, graphite monochromator, θ/2θ scanning, $\theta \leq 30°$).

Both structures were decoded by the direct method by means of the MULTAN program and were refined by the total-matrix method of least squares, initially within the isotropic approximation and then within the anisotropic approximation. All of the hydrogen atoms revealed objectively in differential synthesis were included in the refinement within the isotropic approximation. The final R factors were 0.0285 (R_w = 0.0353) for Ia and 0.0353 (R_w = 0.0356) for IIa. The calculations were made with an Eclipse S/200 computer by means of INEXTL programs [18]. The coordinates of the nonhydrogen atoms, as well as the coordinates of the H(O) and H(N) atoms, are presented in Table 2, and the parameters of the hydrogen bonds are presented in Table 3. The geometries of the I^+ (A and B) and II^+ (bond lengths and bond and torsion angles) cations are shown in Figs. 1 and 2 (the average values are presented for the two independent A and B molecules of cation I^+). The errors were as follows: 0.002-0.003 Å for the interatomic distances, 0.2° for the bond angles, and 0.2-0.3° for the torsion angles.

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SYNTHESIS AND REACTIONS OF 3-(N-ARYLCARBAMOYL)-2-METHYLCINCHONINIC ACID

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The Pfitzinger reaction between acetoacetic acid arylamides and the potassium salt of isatinic acid leads in good yield to 3-(N-arylcarbamoyl)-2-methylcinchoninic acids. Refluxing the latter in 2-propanol produced N-substituted imides of 2-methylquinoline-3,4-dicarboxylic acids and, with benzaldehyde in p-xylene in the presence of piperidine, to N-phenylimides of 2-styrylquinoline-3,4-dicarboxylic acids.

The Pfitzinger reaction finds widespread usage in the synthesis of quinoline-4-carboxylic acids [1] but there has only been one application of this method to quinoline-3,4-dicarboxylic acids [1, 2].

Experiments have shown that 3-(N-arylcarbamoyl)-2-methylcinchoninic acids (Ia-g, Table 1) are formed in good yields by treating the potassium salt of isatinic acids with acetoacetic acid arylamides.

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