SATURATED NITROGEN-CONTAINING HETEROCYCLES.

11.* THE SYNTHESIS AND STRUCTURAL STUDIES OF OCTAHYDROINDOLYLALKANOLS

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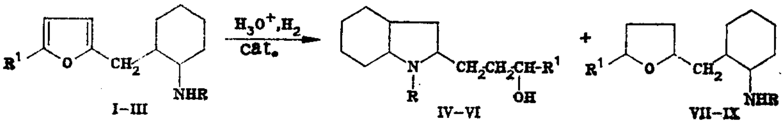
A catalytic synthesis was carried out for 3-(1-R-2-octahydroindolyl)alkanols using nickel promoted by ruthenium, Raney nickel, and Raney cobalt previously treated with acetic acid. An x-ray diffraction structural study of the acid tartrate of 3-(1-methyl-2-octahydroindolyl)-1-propanol gave the absolute configuration and conformational and structural features of the cation and tartrate anion.

We have reported the formation of octahydroindole alcohols upon the hydrogenation of furfurylcyclohexylamines in aqueous acid solutions in the presence of Raney nickel (Ni_{Ra}) or Raney cobalt (Co_{Ra}) catalysts [2, 3]. The hydrogenation of the furan ring is a concrete step in this reaction.

In light of the importance of octahydroindolylalkanols for the preparation of biologically active compounds [4], we continued our studies to find more selective catalysts for the synthesis of these compounds and to determine their three-dimensional structure.

The promotion of Raney nickel by ruthenium or its prior acid treatment by 2% acetic acid leads to a significant increase in yield from 18-24% to 41-55% and in the rate of formation of the octahydroindolyl alcohols:



I, IV, VII R=R'=H; II, V, VIII R=CH_3, R'=H, III, VI, IX R=R'=CH_3

The treatment of Raney cobalt by acid did not lead to an increase in its activity. Ni/Ru was found to be the most effective catalyst for this reaction and is recommended for its resistance to acid and for permitting us to carry out the reaction at 60°C, i.e., 40°C less than for the other catalysts (Table 1).

Gas-liquid chromatographic analysis of aminoalcohols IV-VI carried out on various phases independently of the type of catalyst used showed that the reaction occurs with steric specificity and the octahydroindolylalkanols are obtained in one of the possible geometrical isomers in 90-93% purity. PMR and ^{13}C NMR spectroscopy did not permit us to establish the fine structure of these products and we undertook an x-ray diffraction structural analysis of tartrate X obtained from the isomer obtained of 3-(1-methyl-2-octahydroindolyl)-1-propanol (V) and (+)-tartaric acid. Tartrate X was isolated as well-formed crystals. The geometry of the cation and acid tartrate anion (in its absolute configuration) is shown in Fig. 1 with the bond lengths. The atomic coordinates excluding the H(C) atoms and their isotropically equivalent temperature factors (isotropic temperature factors for the hydrogen atoms) are given in Table 2.

The conformation of the five-membered heterocycle is close to half-chair, which is seen from the torsion angles given in Table 3. The exocyclic bonds for the N, $C_{(2)}$, and $C_{(9)}$ atoms

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TABLE 1. Hydrogenation of 2-(5-R-2-Furfuryl)cyclohexylamines in Acidic Aqueous Solution at pH 4, 100 atm, and 100°C

Starting compound	Catalyst	Time, h	Yield, %	
			IV	VII
I	Ni$_{\text{ск}}$^{a} Ni$_{\text{ск}}$(2% CH_3COOH) Ni/Ru Ni/Ru^{c} Co$_{\text{ск}}$ Co$_{\text{ск}}$(2% CH_3COOH)	7^{b} 3 6 12 21^{b} 6	18 43 41 42 48 30	62 35 30 28 — —
			V	VIII
II	Ni$_{\text{ск}}$^{a} Ni$_{\text{ск}}$(2% CH_3COOH) Ni/Ru	7 3 6	24 42 55	42 46 30
			VI	IX
III	Ni/Ru^{c}	12	27	50

[a] Reaction temperature 110-120°C. [b] Described in our previous work [2, 3]. [c] Reaction temperature 60°C.

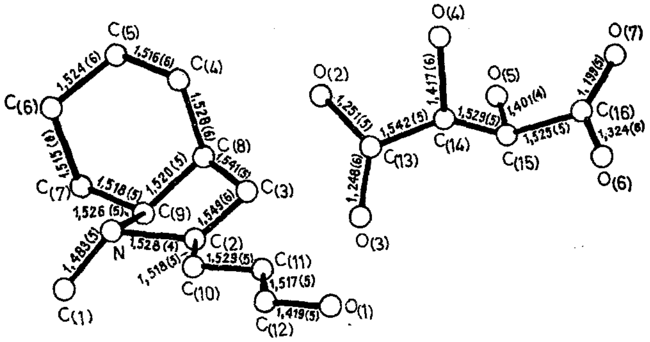

Fig. 1. Geometry of a fragment of the structure of acid tartrate X and bond lengths.

of this heterocycle have pseudoequatorial orientation, while $C_{(8)}$ has pseudoaxial orientation. $C_{(4)}$, $C_{(7)}$, and $C_{(10)}$ are on one side of the mean plane of the heterocycle and $C_{(1)}$ is on the other side.

The conformation of the cyclohexane ring is an asymmetrical chair (Table 3). The nitrogen atom occupies an axial position, while $C_{(3)}$ is equatorial. These atoms have cis orientation relative to each other. Thus, the 2-azabicyclo[4.3.0]nonane fragment has cis-fusion of the six- and five-membered rings, which is most advantageous for such systems and involves some deformation of the six-membered ring (analogously to hydrindanes [5]). The C–C bond lengths in the cation have ordinary values [6, 7]. The $C_{(12)}-O_{(1)}$ bond length (1.419(5) Å) is virtually the same as the standard value for the $C_{(sp^3)}-OH$ bond (1.426(5) Å) [6, 7]. The slight extension of the $\overset{+}{N}-C$ bonds [1.483(5), 1.526(5), and 1.528(4) Å] relative to the standard value, 1.47 Å [7] for the $N_{(sp^3)}-C_{(sp^3)}$ bond is common for the quaternary nitrogen atom (for example, this value is 1.48-1.51 Å in piperidinium cations [8] and 1.49-1.52 Å for pyrrolidinium cations [9]).

As we should have expected, the lengths of the C–O bonds of the deprotonated carboxylate group $C_{(13)}O_{(2)}O_{(3)}$ in the acid tartrate anion (1.248(6) and 1.251(5) Å) are identical to each other and correspond with the analogous values (1.244-1.255 Å) in the tartrate anion [10]. The $O_{(2)}C_{(13)}O_{(3)}$ bond angle (127.1(4)°, Table 4) is somewhat greater than the analogous values [123.8 and 123.9(2)°] given by Fair and Schlemper [10], which may be the result of the formation of intraanionic hydrogen bond $O_{(4)}-H_{(04)}\cdots O_{(2)}$ [$O_{(2)}\cdots O_{(4)}$, 2.618(4) Å; $O_{(4)}-H_{(04)}$,

TABLE 2. Atomic Coordinates ($\cdot 10^4$, $\cdot 10^3$ for the hydrogen atoms) and Their Isotropically Equivalent (for nonhydrogen atoms)^a and Isotropic (for hydrogen atoms) Temperature Factors

Atom	x	y	z	B^{eq}_{iso} and B_{iso}, Å^2
$O_{(1)}$	−66 (4)	−5928 (3)	−9115 (5)	4,59 (10)
$O_{(2)}$	−3090 (3)	−7966 (2)	−2180 (3)	3,36 (7)
$O_{(3)}$	−1997 (3)	−9393 (3)	−2321 (4)	3,33 (7)
$O_{(4)}$	−241 (4)	−7137 (3)	−2765 (4)	3,33 (7)
$O_{(5)}$	684 (3)	−7803 (3)	790 (4)	3,26 (7)
$O_{(6)}$	3772 (3)	−8443 (3)	−1855 (4)	3,51 (7)
$O_{(7)}$	3735 (3)	−7206 (3)	−118 (3)	3,42 (7)
N	−6119 (4)	−5694	−4780 (4)	2,33 (7)
$C_{(1)}$	−7122 (6)	−6564 (4)	−5242 (7)	3,47 (12)
$C_{(2)}$	−4187 (4)	−5761 (3)	−4960 (5)	2,52 (8)
$C_{(3)}$	−3280 (5)	−4972 (3)	−3789 (5)	3,51 (10)
$C_{(4)}$	−5461 (5)	−3697 (3)	−3444 (5)	3,35 (10)
$C_{(5)}$	−7112 (5)	−3454 (3)	−2755 (6)	4,13 (12)
$C_{(6)}$	−8470 (5)	−4230 (3)	−3148 (6)	3,80 (11)
$C_{(7)}$	−7726 (5)	−5140 (3)	−2361 (5)	3,44 (11)
$C_{(8)}$	−4638 (4)	−4616 (3)	−2729 (5)	2,77 (9)
$C_{(9)}$	−5986 (5)	−5393 (3)	−2874 (5)	2,61 (9)
$C_{(10)}$	−3987 (4)	−5742 (3)	−6867 (5)	2,75 (9)
$C_{(11)}$	−2039 (5)	−5793 (3)	−7000 (5)	2,94 (9)
$C_{(12)}$	−1848 (5)	−5928 (3)	−8892 (5)	3,29 (10)
$C_{(13)}$	−1881 (4)	−8530 (3)	−2266 (4)	2,52 (9)
$C_{(14)}$	−77 (4)	−8093 (3)	−2351 (4)	2,42 (8)
$C_{(15)}$	1239 (4)	−8234 (3)	−637 (5)	2,38 (9)
$C_{(16)}$	3059 (4)	−7890 (3)	−823 (5)	2,43 (2)
$H_{(01)}$	29 (7)	−548 (4)	−883 (6)	5 (1)
$H_{(04)}$	−115 (5)	−702 (3)	−247 (5)	3,3 (9)
$H_{(05)}$	75 (6)	−727 (3)	74 (6)	5 (1)
$H_{(06)}$	492 (7)	−839 (4)	−179 (7)	7 (1)
$H_{(N)}$	−663 (4)	−523 (3)	−560 (5)	3,0 (8)

$^a B^{eq}_{iso} = \frac{1}{3} \sum_i \sum_j B_{i,j} a^*_i \cdot a^*_j (\vec{a}_i \cdot \vec{a}_j)$.

TABLE 3. Some Experimental Torsion Angles in Cation X and Calculated Torsion Angles [14] in Two Ideal Conformations of the Five-Membered Saturated Carbocycle

Bond angle	τ, deg		
	cation X	ideal envelope	ideal half-chair
$C_{(8)}C_{(9)}NC_{(2)}$	46,6 (4)	40	42
$C_{(9)}NC_{(2)}C_{(3)}$	−35,2 (4)	−25	−34
$NC_{(2)}C_{(3)}C_{(8)}$	10,6 (3)	0	13
$C_{(2)}C_{(3)}C_{(8)}C_{(9)}$	18,0 (4)	+25	13
$C_{(3)}C_{(8)}C_{(9)}N$	−39,5 (4)	−40	−34
$C_{(4)}C_{(5)}C_{(6)}C_{(7)}$	57,6 (4)		
$C_{(5)}C_{(6)}C_{(7)}C_{(9)}$	−52,5 (4)		
$C_{(6)}C_{(7)}C_{(9)}C_{(8)}$	45,9 (4)		
$C_{(7)}C_{(9)}C_{(8)}C_{(4)}$	−43,3 (4)		
$C_{(9)}C_{(8)}C_{(4)}C_{(5)}$	48,4 (4)		
$C_{(8)}C_{(4)}C_{(5)}C_{(6)}$	−56,0 (4)		

TABLE 4. Bond Angles ω in the Structure of X

Bond angle	ω, deg	Bond angle	ω, deg	Bond angle	ω, deg
$C_{(1)}NC_{(2)}$	113,4 (3)	$C_{(3)}C_{(8)}C_{(4)}$	112,0 (3)	$O_{(3)}C_{(13)}C_{(14)}$	117,8 (3)
$C_{(1)}NC_{(9)}$	114,2 (3)	$C_{(3)}C_{(8)}C_{(9)}$	103,9 (3)	$O_{(4)}C_{(14)}C_{(13)}$	111,5 (3)
$C_{(2)}NC_{(9)}$	102,9 (2)	$C_{(4)}C_{(8)}C_{(9)}$	112,6 (3)	$O_{(4)}C_{(14)}C_{(15)}$	110,0 (3)
$NC_{(2)}C_{(3)}$	103,9 (3)	$NC_{(9)}C_{(7)}$	115,2 (3)	$C_{(13)}C_{(14)}C_{(15)}$	111,2 (3)
$NC_{(2)}C_{(10)}$	111,9 (3)	$NC_{(9)}C_{(8)}$	101,4 (3)	$O_{(5)}C_{(15)}C_{(14)}$	112,1 (3)
$C_{(3)}C_{(2)}C_{(10)}$	116,2 (3)	$C_{(7)}C_{(9)}C_{(8)}$	115,5 (3)	$O_{(5)}C_{(15)}C_{(16)}$	111,2 (3)
$C_{(2)}C_{(3)}C_{(8)}$	106,5 (3)	$C_{(2)}C_{(10)}C_{(11)}$	110,6 (3)	$C_{(14)}C_{(15)}C_{(16)}$	109,8 (3)
$C_{(5)}C_{(4)}C_{(8)}$	113,1 (3)	$C_{(10)}C_{(11)}C_{(12)}$	110,7 (3)	$O_{(6)}C_{(16)}O_{(7)}$	125,3 (4)
$C_{(4)}C_{(5)}C_{(6)}$	110,6 (4)	$O_{(1)}C_{(12)}C_{(11)}$	113,3 (3)	$O_{(6)}C_{(16)}C_{(15)}$	111,3 (3)
$C_{(5)}C_{(6)}C_{(7)}$	111,4 (4)	$O_{(2)}C_{(13)}O_{(3)}$	127,1 (4)	$O_{(7)}C_{(16)}C_{(15)}$	123,4 (3)
$C_{(6)}C_{(7)}C_{(9)}$	112,9 (3)	$O_{(2)}C_{(13)}C_{(14)}$	115,1 (3)		

0.80(4) Å, $O_{(2)}\cdots H_{(04)}$, 2.07 Å, $O_{(2)}H_{(04)}O_{(4)}$, 126.3°]. The existence of such a bond is also indicated by the decrease in the $O_{(2)}C_{(13)}C_{(14)}$ bond angle [117.8(3)°]. An analogous hydrogen bond was found by Fair and Schlemper [10]. In addition, of the other potential partners for the formation of a hydrogen bond with the $O_{(4)}H$ hydroxyl group, only $O_{(5)}$ of the other hydroxy group has a close contact [$O_{(4)}\cdots O_{(5)}$, 2.878(4) Å], although the corresponding distances $O_{(4)}\cdots H_{(05)}$ (2.69(5) Å) and $O_{(5)}\cdots H_{(04)}$ (2.88(4) Å) are too great for the formation of a hydrogen bond. The distance of $O_{(4)}$ from the other closest possible hydrogen acceptors is greater than 3.2 Å.

The C–O bond lengths [$C_{(16)}$–$O_{(7)}$, 1.199(5) Å; $C_{(16)}$–$O_{(6)}$, 1.324(6) Å] in the $C_{(16)}O_{(6)}O_{(7)}$ carboxyl group corresponds to that found in the structure of (+)-tartaric acid [1.109 and 1.315(2) Å] given by Hope and de la Camp [11]. The bond angles at $C_{(16)}$ are almost indistinguishable from those given by Hope and de la Camp [11]. The remaining bond angles in the anion of X correspond to those found by other workers [10, 11] and standard values [6, 7].

In addition to the abovementioned intraanionic $O_{(4)}$–$H_{(04)}\cdots O_{(2)}$ hydrogen bond in the crystal of X, there are an additional four hydrogen bonds, i.e., all the active hydrogen atoms, specifically three H(O) and the H(N) atoms form hydrogen bonds, whose indices are given in Table 5. $O_{(2)}$ and $O_{(6)}$ form a strong hydrogen bond between the anions [2.578(3) Å] which accounts for the formation of infinite chains of anions in the direction of the *a*-axis. On the whole, the hydrogen bond parameters are similar to standard values [12]. The remaining hydrogen bonds given in Table 5 bind the cations and anions to form the three-dimensional framework.

The absolute configuration of the carbon atoms of the octahydroindole ring was determined unequivocally on the basis of the known absolute configuration of (+)-tartaric acid which is a component of salt X. The asymmetrical carbon atoms have the following configuration: $C_{(2)}$ has R configuration, $C_{(8)}$ has S configuration, and $C_{(9)}$ has S configuration.

EXPERIMENTAL

The crystals of X are monoclinic with a = 7.719(1), b = 14.440(2), c = 7.761(1) Å, β = 101.15(1)°, V = 838.7(4) Å^3, d_{calc} = 1.36 g/cm^3, Z = 2, space group $P2_1$. The unit cell parameters and intensities of 1478 independent reflections with $F^2 \geq 3.5\sigma$ were measured at room temperature on a Hilger-Watts Y/290 four-circle automatic diffractometer using λMoK_α radiation, graphite monochromator, θ/2θ scan, θ ≤ 30°. The structure was solved by the direct method using the MULTAN program and refined by the method of least squares in the full-matrix anisotropic approximation (isotropic approximation for the hydrogen atoms) to give R = 0.0353 (R_w = 0.0339). All the calculations were carried out on an Eclipse S/200 minicomputer using the INEXTL programs [13].

The gas-liquid chromatographic analysis was carried out on an LKhM-8MD chromatograph using a flame ionization detector. The columns were packed with TND-TS-M Inza brick modified with 3% KOH and impregnated with 5% Apiezon L and cellite containing 10% SE-30 siloxane elastomer. The column lengths were 1-2 m, column temperature 170-190°C, argon gas carrier flow rate 1.2 liters/h. The retention time for aminoalcohol IV was 6.0 and 9.4 sec; the corresponding values were 6.7 and 10.0 sec for aminoalcohol V on these supports.

Aminoalcohols IV-VI and tetrahydrofuran amines VII-IX were prepared according to our previous procedures [2, 3]. The Ni/Ru, Raney nickel, and Raney cobalt catalysts were initially treated with 2% acetic acid down to pH 4.

TABLE 5. Hydrogen Bonds in the Structure of X

Bond $D–H\cdots A_{x,y,z}$	D–H, Å	D···A, Å	H···A, Å	D–H...A bond angle, deg
$O_{(1)}$—$H_{(01)}\ldots O_{(3)\ -x,\ y+1/2,\ -z-1}$	0,72 (5)	2,830 (5)	2,13 (5)	163 (5)
$O_{(4)}$—$H_{(04)}\ldots O_{(2)\ x,\ y,\ z}$	0,80 (4)	2,618 (4)	2,07 (4)	126 (3)
$O_{(5)}$—$H_{(05)}\ldots O_{(1)\ x,\ y,\ z+1}$	0,78 (5)	2,772 (6)	2,04 (5)	156 (5)
$O_{(6)}$—$H_{(06)}\ldots O_{(2)\ x+1,\ y,\ z}$	0,88 (5)	2,578 (3)	1,74 (5)	159 (5)
N—H(N) $\ldots O_{(3)\ x-1,\ y+1/2,\ -z-1}$	0,96 (4)	3,073 (4)	2,13 (4)	170 (3)

Acid Tartrate of 3-(1-Methyl-2-octahydroindolyl)-1-propanol (X). A hot solution of 0.77 g (5 mmoles) (+)-tartaric acid in 8 ml abs. ethanol was added to a solution of 1 g (5 mmoles) aminoalcohol V in 8 ml absolute ethanol. Cooling and partial evaporation gave tartrate X as a crystalline precipitate with mp 132-133°C (from abs. ethanol) in 64% yield. Found: C, 55.3; H 8.6; N, 4.0%. Calculated for $C_{16}H_{29}NO_7$: C, 55.3; H, 8.3; N, 4.0%.

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SATURATED NITROGEN-CONTAINING HETEROCYCLES.

12.* STRUCTURAL STUDIES OF CYCLOPENTA(b)PYRROLIDINYLALKANOLS

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^{13}C NMR spectroscopy and x-ray diffraction structural analysis were used to establish the stereochemistry of 3-[N-methyl-2-cyclopenta(b)pyrrolinyl]-1-propanol and its acetyl derivative. The absolute configuration was determined for 3-[N-methyl-2-cyclopenta(b)pyrrolidinyl]-1-propanol acid tartrate dihydrate and the conformational aspects of its cation and tartrate anion were studied.

The present communication is devoted to a study of the stereochemistry of the isomers of cyclopenta(b)pyrrolidinylalkanols obtained in the hydrogenation of furfurylcyclopentylamines in aqueous acid solutions [2] and in the catalytic hydroamination of furfurylidenecyclopentanone in acidic water—ethanol [3].

Gas-liquid chromatographic analysis indicated that both these reactions proceed with steric specificity and the cyclopentapyrrolidine alcohols I-III are formed, independently of their method of preparation and nature of the catalyst used, as one of the possible geometric isomers with 97% chromatographic purity. ^{13}C NMR spectroscopy, x-ray diffraction structural analysis

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*For Communication 11, see [1].

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