SATURATED NITROGEN-CONTAINING HETEROCYCLES.
14.* SYNTHESIS AND THREE-DIMENSIONAL STRUCTURES OF N-R-DICYCLOPENTA[b,e]PIPERIDINES

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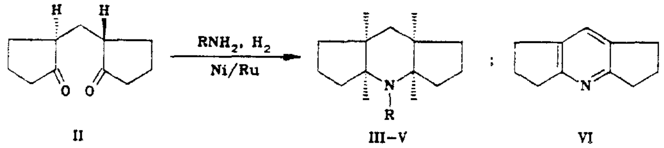
The catalytic hydroamination of threo-methylenedicyclopentanone using ammonia, methylamine, and monoethanolamine as the aminating agents proceeds stereospecifically with the formation of N-R-cis-syn-cis-dicyclopenta[b,e]piperidines (R = H, CH_3, CH_2CH_2OH). The structures of the latter were proved by ^{13}C NMR spectroscopy. The molecular structure of N-(β-hydroxyethyl)cis-syn-cis-dicyclopenta[b,e]piperidinium acid tartrate was investigated by x-ray diffraction analysis, and the absolute configuration of its chiral centers was determined.

N-R-Perhydroacridines with cis-anti-cis and cis-syn-cis configurations are formed in the catalytic hydroamination of 2,2'-methylenedicyclohexanone (I). N-Unsubstituted perhydroacridine is realized in the form of cis-syn-cis and trans-anti-cis isomers [1].

To ascertain the effect of the size of the alicyclic fragment in the substrate molecule on the direction of the reaction and the stereoisomeric composition of the resulting azaheterocycles we studied the transformations of 2,2'-methylenedicyclopentanone (II) under hydroamination conditions.

It was established that the catalytic reductive amination of the threo form of diketone II using methylamine or ethanolamine as the aminating agent proceeds in the same way as for threo-methylenedicyclohexanone with the formation of N-substituted dicyclopenta[b,e]piperidines III and IV in high yields (74-98%). The character of the transformations of diketones I and II under the influence of hydrogen and ammonia is similar. In the case of II this reaction leads to the development of a mixture of dicyclopenta[b,e]piperidine (V) and its isolog VI:



III R=CH_3; IV R=CH_2CH_2OH; V R=H

In the presence of a weak nucleophile – aniline – methylenedicyclopentanone II, in contrast to diketone I, does not undergo azacyclization but rather reduction of the carbonyl groups to give 2,2'-methylenedicyclopentanediol (VII). The results obtained are in agreement with the results of a study of the reaction of bicyclic diketones with aromatic amines [2].

Another peculiarity of the catalytic hydroamination of threo-methylenedicyclopentanone II is its stereoselectivity. Regardless of the presence or absence of a substituent attached to the heteroatom, azaheterocycles III-V with side cyclopentane rings were isolated in one isomeric form with a cis-syn-cis configuration.

The presence of six resonance signals corresponding to a dicyclopentapiperidine fragment in the ^{13}C NMR spectra (Table 1) of bases III-V constitutes evidence for the symmetrical

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*See [1] for Communication 13.

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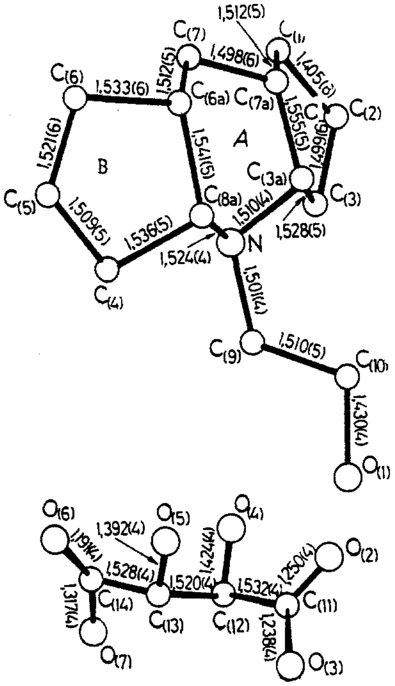

Fig. 1. Geometry and interatomic distances of the N-(β-hydroxyethyl)-cis-syn-cis-dicyclopenta[b,e]-piperidinium acid tartrate (VIII) molecule.

structure of this fragment. At the same time, one also cannot exclude the possibility of the conformational equilibrium that occurs in the case of isomers with cis fusion of the carbo- and heterocycles. In the case of hydrindans it has been shown [3] that annelation of the cyclohexane and cyclopentane rings leads, for both the cis and trans isomers, to a weak-field shift of the signals of the nodal carbon atoms as compared with the corresponding decalins. Taking these regularities and the known data for perhydroacridines [1] into account one may conclude that the rings in dicyclopenta[b,e]piperidines III-V have cis character (cis-anti-cis or cis-syn-cis). Since the cis-anti-cis isomer is optically active, in its reaction with (+)-tartaric acid one might expect the formation of two diastereomeric tartrates, which would be reflected in a change in the number of signals in the spectrum. Tartrate VIII, which was obtained from equimolar amounts of base III and (+)-tartaric acid, has a spectrum with 10 resonance signals, six of which belong to the dicyclopentapiperidine fragment. On the basis of this it may be concluded that isomer III has a cis-syn-cis configuration. The closeness of the chemical shifts of the $C_{(7)}$, $C_{(6a)}$, and $C_{(7a)}$ atoms in azaheterocycles III-V constitutes evidence that they have the same configuration. In contrast to cis-syn-cis-perhydroacridines [1], N-R-cis-syn-cis-dicyclopenta[b,e]piperidines III-V are not conformally labile, as indicated by the high values of the chemical shifts of the $C_{(2)}$ and $C_{(5)}$ atoms.

To ascertain the conformational peculiarities of the nitrogen bases obtained, one of them — N-(β-hydroxyethyl)cis-syn-cis-dicyclopenta[b,e]piperidine in the form of acid tartrate VIII — was subjected to x-ray diffraction analysis. The interatomic distances in its molecule are presented in Fig. 1. The coordinates of the nonhydrogen atoms are presented in Table 2, and the bond angles are presented in Table 3.

The absolute configurations of the asymmetric carbon atoms in the cation of the VIII molecule were determined unequivocally on the basis of the known absolute configuration of (+)-tartaric acid: S for the $C_{(3a)}$ and $C_{(7a)}$ atoms and R for the $C_{(6a)}$ and $C_{(8a)}$ atoms.

The central piperidinium A ring in the cation has a boat configuration; the deviations of the N and $C_{(7)}$ atoms from the mean square plane passing through the $C_{(3a)}$, $C_{(6a)}$, $C_{(7a)}$, and $C_{(8a)}$ atoms and realized with an accuracy of 0.028 (4) Å are −0.623(2) and −0.589(4) Å, respectively. The methylene groups of the five-membered rings bonded to the $C_{(8a)}$, $C_{(6a)}$, $C_{(7a)}$ and $C_{(3a)}$ atoms, like the β-hydroxyethyl substituent attached to the N atom, are equatorially oriented with respect to the heteroring, and, consequently, the five-membered carbocycles have cis-syn-cis fusion with it.

TABLE 1. ^{13}C NMR Chemical Shifts of Dicyclopentapiperidines III-V and VIII and Pyridine VI (δ, ppm, in $CdCl_3$)

Compound	$C_{(1)}$, $C_{(6)}$	$C_{(2)}$, $C_{(5)}$	$C_{(3)}$, $C_{(4)}$	$C_{(3a)}$, $C_{(8a)}$	$C_{(6a)}$, $C_{(7a)}$	$C_{(7)}$	R
III	34,21	25,12	34,08	66,92	39,63	32,17	41,17
IV	33,62	24,46	33,50	65,19	39,62	31,71	55,24; 59,19
IV*	33,52	24,25	33,37	63,56	39,56	31,68	54,51; 58,47
V	33,73	24,54	34,75	58,00	37,63	31,73	—
VI	30,51	23,64	33,90	169,36	134,17	128,38	—
VIII*	32,83	24,03	30,03	63,67	37,40	29,46	53,36; 55,10

*The spectrum was recorded with DMSO as the solvent; the signal of the solvent at 39.60 ppm was used as the standard.

TABLE 2. Coordinates of the Nonhydrogen Atoms ($\cdot 10^4$) in the VIII Structure*

Atom	x	y	z	Atom	x	y	z
$O_{(1)}$	1383(3)	6069(2)	141(2)	$C_{(5)}$	−3340(5)	8601(3)	2193(3)
$O_{(2)}$	−2745(3)	4939(2)	2967(1)	$C_{(6)}$	−2511(6)	8736(3)	3078(3)
$O_{(3)}$	−1540(3)	6163(1)	3546(1)	$C_{(6a)}$	−605(5)	8538(2)	2930(2)
$O_{(4)}$	−3180(3)	4140(2)	4426(1)	$C_{(7)}$	328(5)	8153(2)	3706(2)
$O_{(5)}$	443(3)	4386(2)	4424(1)	$C_{(7a)}$	2082(5)	7815(2)	3481(2)
$O_{(6)}$	−53(4)	3936(2)	6141(2)	$C_{(8a)}$	−547(4)	7921(2)	2126(2)
$O_{(7)}$	−1903(3)	5056(2)	6311(1)	$C_{(9)}$	338(5)	6421(2)	1550(2)
N	317(3)	7030(2)	2325(2)	$C_{(10)}$	1195(5)	6789(2)	745(2)
$C_{(1)}$	2980(9)	7312(4)	4203(3)	$C_{(11)}$	−2181(4)	5406(2)	3580(2)
$C_{(2)}$	3752(8)	6535(3)	3869(3)	$C_{(12)}$	−2363(4)	4989(2)	4486(2)
$C_{(3)}$	2782(5)	6267(2)	3069(2)	$C_{(13)}$	−627(4)	492(2)	493(2)
$C_{(3a)}$	2088(4)	7147(2)	2706(2)	$C_{(14)}$	−808(4)	4567(2)	5864(2)
$C_{(4)}$	−2419(5)	7789(3)	1846(2)				

*The coordinates of the hydrogen atoms and the temperature factors can be obtained from the authors.

The conformations of the five-membered rings differ somewhat. The B ring [$C_{(6a)}C_{(8a)}$-$C_{(4)}C_{(5)}C_{(6)}$] has an envelope conformation; the torsion angles in it (Table 4) virtually do not differ from the values calculated by molecular mechanics for an ideal cyclopentane envelope [4]. The $C_{(5)}$ atom deviates 0.606(4) Å from the $C_{(4)}C_{(6)}C_{(6a)}C_{(8a)}$ plane, which is realized with an accuracy of 0.003(4) Å. The conformation of the C ring [$C_{(1)}C_{(2)}C_{(3)}C_{(3a)}$-$C_{(7a)}$] is intermediate between an envelope and a half chair but closer to the former (Table 4). The $C_{(1)}$ and $C_{(2)}$ atoms experience significant thermal vibrations in a direction perpendicular to the rest of the ring, which reflects their random character with respect to two energically equivalent positions [the $C_{(2)}$ atom "below" the $C_{(3)}C_{(3a)}C_{(7a)}$ plane, and the $C_{(1)}$ atom "above" it, or vice versa] and is due to the ease of interconversion of the two indicated equivalent half-chair conformations. The effective shortening of the length of the $C_{(1)}$—$C_{(2)}$ single bond to 1.405(8) Å can be explained by this random character. The remaining C—C bond lengths in the VIII cation have the usual values [5, 6]. The length of the $C_{(10)}$—$O_{(1)}$ bond coincides with the standard value for the C_{sp^3}—OH bond, which is equal to 1.426 Å [5]. The lengths of the N—$C_{(1)}$, N—$C_{(3a)}$, and N—$C_{(8a)}$ bonds have the usual values for a quaternary nitrogen atom: for example, they are 1.48-1.51 Å in the piperidinium cation [7], 1.49-1.52 Å in the octahydroindolinium cation [8], and 1.48-1.53 Å in the cyclopentapyrrolidinium cation [9]. In the acid tartrate anion of salt VIII the lengths of the C—O bonds [1.250(4) and 1.238(4) Å] of the singly ionized carboxylate group $C_{(14)}O_{(2)}O_{(3)}$ are virtually equal and coincide with the analogous values in acid [8, 9] and doubly ionized tartrate anions [10]. As in the structures investigated in [8-10], the anion of salt VIII contains an $O_{(4)}$—$H_{(O4)}$-$O_{(2)}$ intra-anionic hydrogen bond (Table 5).

In addition, a branched system of interionic hydrogen bonds in which all of the active H atoms participate exists in the VIII crystal (Table 5). Through the $O_{(7)}$—$H_{(O7)}$-$O_{(2)}$ bond the anions form helixes around the 2_1 helical axis in the c direction. The $O_{(1)}$ atom of the cation and the $O_{(4)}$ atom of the anion each participate in the formation of two hydrogen bonds. Thus, in addition to the above-indicated intra-anionic hydrogen bond, in which the $O_{(4)}$ atom acts as a donor, it, as an acceptor, forms a hydrogen bond with the $O_{(1)}$ atom; in turn, the $O_{(1)}$ atom, as an acceptor, participates in a hydrogen bond with the $O_{(5)}$H group. Through the

TABLE 3. Bond Angles (ω) in the VIII Molecule

Angle	ω°	Angle	ω°
$C_{(3a)}NC_{(8a)}$	112,1(2)	$C_{(3a)}C_{(7a)}C_{(7)}$	113,4(3)
$C_{(8a)}NC_{(9)}$	111,6(2)	$NC_{(8a)}C_{(4)}$	111,4(3)
$C_{(3a)}NC_{(9)}$	112,1(2)	$NC_{(8a)}C_{(6a)}$	112,1(3)
$C_{(2)}C_{(1)}C_{(7a)}$	110,0(5)	$C_{(4)}C_{(8a)}C_{(6a)}$	106,0(3)
$C_{(1)}C_{(2)}C_{(3)}$	107,7(4)	$NC_{(9)}C_{(7a)}$	115,8(3)
$C_{(2)}C_{(3)}C_{(5a)}$	104,4(3)	$O_{(1)}C_{(10)}C_{(9)}$	107,7(3)
$NC_{(3a)}C_{(3)}$	111,4(3)	$O_{(2)}C_{(11)}O_{(3)}$	128,2(3)
$NC_{(3a)}C_{(7a)}$	111,6(3)	$O_{(2)}C_{(11)}C_{(12)}$	115,2(3)
$C_{(3)}C_{(3a)}C_{(7a)}$	105,9(3)	$O_{(3)}C_{(11)}C_{(12)}$	116,5(3)
$C_{(5)}C_{(4)}C_{(8a)}$	104,4(3)	$C_{(11)}C_{(12)}C_{(13)}$	111,1(2)
$C_{(4)}C_{(5)}C_{(6)}$	102,8(3)	$O_{(4)}C_{(12)}C_{(11)}$	110,2(2)
$C_{(5)}C_{(6)}C_{(6a)}$	104,7(3)	$O_{(4)}C_{(12)}C_{(13)}$	111,1(2)
$C_{(5)}C_{(6a)}C_{(7)}$	115,0(3)	$C_{(12)}C_{(13)}C_{(14)}$	111,7(2)
$C_{(7)}C_{(6a)}C_{(8a)}$	112,9(3)	$O_{(5)}C_{(13)}C_{(12)}$	108,8(2)
$C_{(6)}C_{(6a)}C_{(8)}$	105,3(3)	$O_{(5)}C_{(13)}C_{(14)}$	112,9(2)
$C_{(6a)}C_{(7)}C_{(7a)}$	112,7(3)	$O_{(6)}C_{(14)}C_{(13)}$	123,9(3)
$C_{(1)}C_{(7a)}C_{(3a)}$	104,0(3)	$O_{(7)}C_{(14)}C_{(13)}$	111,0(2)
$C_{(1)}C_{(7a)}C_{(7)}$	114,9(4)	$O_{(6)}C_{(14)}O_{(7)}$	125,0(3)

TABLE 4. Endocyclic Torsion Angles (τ) in the VIII Structure

A ring		B ring		C ring	
angle	τ, °	angle	τ, °	angle	τ, °
$NC_{(3a)}C_{(7a)}C_{(7)}$	2,9(3)	$C_{(1)}C_{(2)}C_{(3)}C_{(3a)}$	29,5(5)	$C_{(6)}C_{(5)}C_{(4)}C_{(8a)}$	−39,5(4)
$C_{(3a)}C_{(7a)}C_{(7)}C_{(7a)}$	−52,7(4)	$C_{(2)}C_{(3)}C_{(3a)}C_{(7a)}$	−24,4(5)	$C_{(5)}C_{(4)}C_{(8a)}C_{(6a)}$	24,4(4)
$C_{(7a)}C_{(7)}C_{(6a)}C_{(8a)}$	48,4(4)	$C_{(2)}C_{(3a)}C_{(7a)}C_{(1)}$	7,0(5)	$C_{(4)}C_{(8a)}C_{(6a)}C_{(6)}$	0,7(4)
$C_{(7)}C_{(6a)}C_{(8a)}N$	4,6(3)	$C_{(3a)}C_{(7a)}C_{(1)}C_{(3)}$	11,2(5)	$C_{(8a)}C_{(6a)}C_{(6)}C_{(5)}$	−24,4(4)
$C_{(7a)}C_{(8a)}NC_{(3a)}$	−54,7(4)	$C_{(7a)}C_{(1)}C_{(2)}C_{(3)}$	−25,6(4)	$C_{(6a)}C_{(6)}C_{(5)}C_{(4)}$	39,7(4)
$C_{(8a)}NC_{(3a)}C_{(7a)}$	50,3(4)				

hydrogen bonds of the $O_{(1)}$ atom the cations and anions form chains along the a axis. The cations are also joined to the anions by the $N-H_{(N)}-O_{(3)}$ bond.

Through all of the indicated hydrogen bonds the cations and anions in the VIII structure are united in layers parallel to the ac plane; the contacts between the layers are realized at the van der Waals distances.

EXPERIMENTAL

The VIII crystals were rhombic and had the following parameters: a = 7.7994(7), b = 14.950(1), c = 15.3772(7) Å, V = 1793.0(2) Å^3, d_{calc} = 1.25 g/cm^3, Z = 4, space group $P2_12_12_1$. The cell parameters and the intensities of 1854 independent reflections with $F^2 \geq 2\sigma$ were measured with a Hilger–Watts Y/290 four-circle automatic diffractometer (λ Mo K_α, graphite monochromator, θ/2θ scanning, $\theta \leq 30°$). The structure was decoded by the direct method by means of the MULTAN program and was refined by the total-matrix method of least squares, initially within the isotropic approximation and then within the anisotropic approximation. All of the H atoms [except for the H atoms attached to the $C_{(1)}$ and $C_{(2)}$ atoms] were ascertained objectively in differential synthesis and were included in the refinement within the isotropic approximation. The final R factor was 0.0417 (R_W = 0.0413). The calculations were made with an Eclipse S/200 computer by means of INEXTL programs [11].

The ^{13}C NMR spectra were recorded with a Varian FT-80A spectrometer (20 MHz) at room temperature with tetramethylsilane as the internal standard.

The catalytic hydroamination of diketone II using ammonia, methylamine, monoethanolamine, and aniline as the aminating agents was carried out by the methods in [12, 13] in the presence of Raney nickel modified with ruthenium. Compounds IV and VII were characterized in [13] and [12], respectively.

N-Methyl-cis-syn-cis-dicyclopenta[b,e]piperidine (III). This compound was isolated in 98% yield and had bp 146°C (4 mm) and n_D^{20} 1.4951. Found: C 80.2; H 11.8; N 7.6%. $C_{12}H_{21}N$. Calculated: C 80.4; H 11.7; N 7.8%.

Bases V and VI were separated as follows. Evaporation of the hydrogenation product at room temperature (to ~3/4 of the original volume) gave a crystalline precipitate of dicyclo-

TABLE 5. Hydrogen Bonds in the VIII Structure

D—H...A bond (x, y, z)	D···A, Å	H···A, Å	D-H, Å	Angle D—H...A, deg
N—H(11)···O(3) (x, y, z)	2,702(3)	1,714(3)	0,989(4)	177,4(3)
O(1)—H(O1)···O(4) (−1/2−x, 1−y, −1/2+z)	2,747(3)	2,106(4)	0,642(4)	175,3(3)
O(4)—H(O4)···O(2) (x, y, z)	2,566(3)	2,081(3)	0,788(3)	119,8(3)
O(5)—H(O5)···O(1) (1/2−x, 1−y, 1/2+z)	2,794(3)	2,034(3)	0,765(3)	172,5(3)
O(7)—H(O7)···O(2) (−1/2−x, 1−y, 1/2+z)	2,562(3)	1,768(5)	0,896(4)	146,3(3)

penta[b,e]piperidine (VI), with mp 79-81°C [14], in 70% yield. The residue after separation of VIwas evaporated and distilled in vacuo to give cis-syn-cis-dicyclopenta[b,e]piperidine (V), with bp 92-95°C (4 mm) and n_D^{20} 1.5069, in 30% yield. Found: C 79.6; H 11.2; N 8.8%. $C_{11}H_{19}N$. Calculated: C 79.9; H 11.5; N 8.5%.

N-(β-Hydroxyethyl)-cis-syn-cis-dicyclopenta[b,e]piperidinium Acid Tartrate (VIII). A solution of 2.38 g (0.016 mole) of (+)-tartaric acid in 30 ml of absolute ethanol was added to a solution of 3.3 g (0.016 mole) of base III in 15 ml of absolute ethanol, and the mixture was heated for 5 min on a boiling-water bath. It was then cooled, and the crystalline precipitate of tartrate VIII was separated and recrystallized from absolute ethanol to give a product with mp 176-177°C in 80% yield. Found: C 56.9; H 8.1; N 4.1%. $C_{17}H_{29}NO_7$. Calculated: C 56.8; H 8.1; N 3.9%.

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