

INFRARED STUDY OF CHAIR-BOAT EQUILIBRIA  
AND DEFORMATIONS IN DERIVATIVES  
OF *trans*-BICYCLO[4,3,0]NONANE:  
A COMPARISON WITH *trans*-DECALIN SYSTEM

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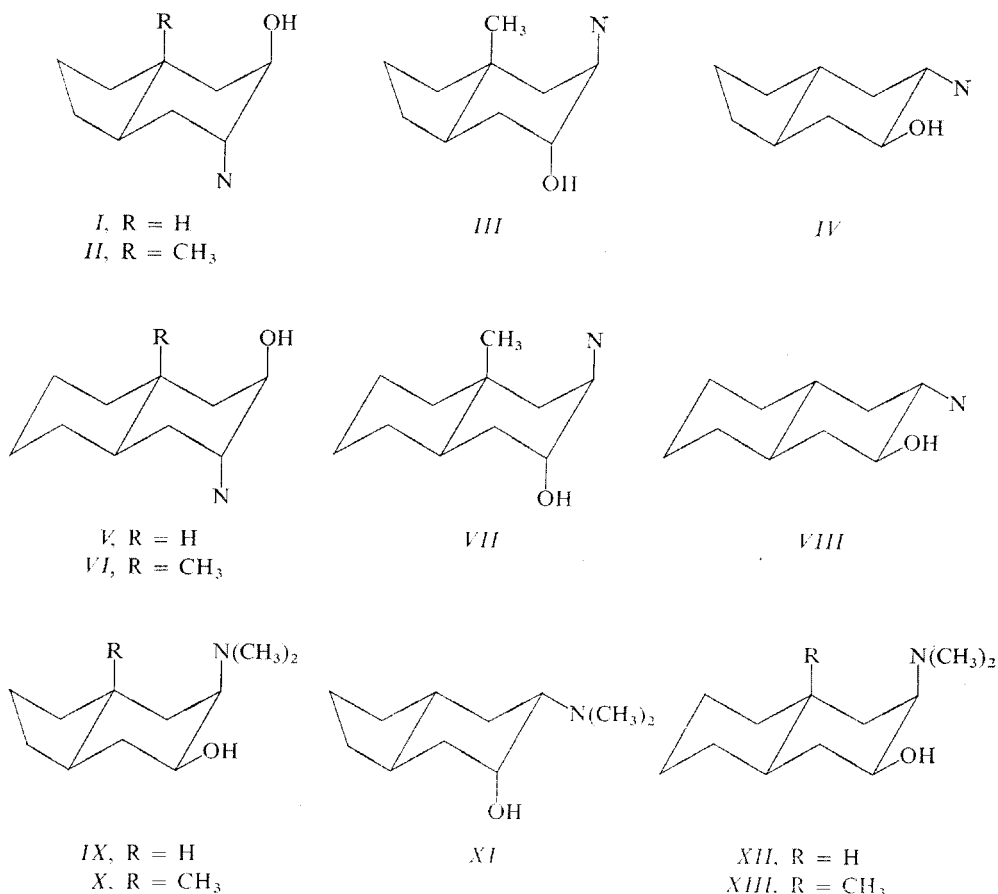
Chair-boat equilibria in some vicinal amino alcohols derived from *trans*-bicyclo[4,3,0]nonane (*trans*-perhydroindane) and 1-methylbicyclo[4,3,0]nonane were studied quantitatively by infrared spectroscopic detection of hydrogen bond in the boat conformer. Greater amount of boat form was invariably found in *trans*-perhydroindane derivatives relative to the analogous *trans*-decalin derivatives. Possible reasons for this behaviour are discussed in terms of flexibility and deformations of the six-membered ring.

Whereas the conformation of monocyclic cyclohexane derivatives has been investigated extensively, quantitative conformational studies of systems where the cyclohexane ring is fused to another ring are not so numerous. Most of them concern systems in which another six-membered ring is anellated to the cyclohexane ring, *e.g.* steroid, terpene or decalin derivatives. The recent synthetic availability<sup>1,2</sup> of stereoisomeric 3-amino-4-hydroxy-*trans*-bicyclo[4,3,0]nonanes and their 1-methyl derivatives has made it possible to study some conformational aspects of *trans*-bicyclo[4,3,0]nonane (*trans*-perhydroindane) system and to compare the obtained results with *trans*-decalin system.

The conformational equilibria and deformations were followed by spectroscopic detection of intramolecular hydrogen bond between the functional groups; this approach has been shown previously to be a tool of great value<sup>3-6</sup>. The studied compounds are depicted in Scheme 1.

#### EXPERIMENTAL

Most of the compounds are already known<sup>1-3,7,8</sup>, the synthesis of the derivatives *II*, *III* and *X* will be described in our next paper<sup>9</sup>. The derivatives *VIb* and *VIIb* were prepared by Clarke-Eschweiler methylation of *VIa* and *VIIa*, respectively<sup>6</sup>: 3 $\alpha$ -Dimethylamino-2 $\beta$ -hydroxy-9 $\beta$ -methyl-



In the formulae: *a.* N = NH<sub>2</sub>, *b.* N = N(CH<sub>3</sub>)<sub>2</sub>

SCHEME 1

-*trans*-decalin (VIb), m.p. 112–113°C (pentane). For C<sub>13</sub>H<sub>25</sub>NO (211.3) calculated: 73.88% C, 11.92% H, 6.63% N; found: 73.85% C, 11.74% H, 6.73% N.

2β-Dimethylamino-3α-hydroxy-9β-methyl-*trans*-decalin (VIIb), b.p. 103°C/0.2 Torr. For C<sub>13</sub>H<sub>25</sub>NO (211.3) calculated: 73.88% C, 11.92% H, 6.63% N; found: 73.93% C, 11.64% H, 6.41% N.

The infrared measurements were carried out on a Perkin-Elmer 621 instrument in 2 cm Infracell cells; calibration with gaseous ammonia. The compounds (containing less than 2% impurities according to gas-liquid chromatography) were measured in 5 · 10<sup>-3</sup>M tetrachloroethylene solutions at 35°C. The bands were separated numerically under the assumption of Lorentzian (Cauchy) type of bands, using the already described programme<sup>10</sup>. At least two independent measurements were taken and the molar integrated intensity values were reproducible within 5%.

## RESULTS AND DISCUSSION

*trans-Derivatives*

The diaxial amino and dimethylamino alcohols *I–III* as well as the corresponding decalin derivatives *V–VII* (Scheme 1) are very suitable models for following the chair-boat equilibria in the given systems (Scheme 2). As evident from the geometry of the compounds, any intramolecular hydrogen bond found in the spectra of these compounds must be due to a non-chair form (see discussion in ref.<sup>4</sup>).



N = NH<sub>2</sub> or N(CH<sub>3</sub>)<sub>2</sub>; n = 1 or 2

SCHEME 2

In our previous papers we used two methods for the calculation of the conformational population from the obtained spectral data. The first approach is the comparison of the measured molar integrated intensity of the bonded or free hydroxyl band of the studied compound with the corresponding molar integrated intensity of a conformationally homogeneous compound chosen as a standard<sup>4,5</sup>. As standard for the boat conformation we can take the bonded hydroxyl band in the spectrum of *IV* or *VIII*, since the geometry of the hydrogen-bonded part of the molecule in the boat form is probably similar to that in the diequatorial chair (as indicated also by the  $\nu(\text{OH})$  values). For the chair conformation the choice of standards is more complicated since of the diaxial compounds only *Va* is conformationally homogeneous and could thus serve as a true standard.

The second approach was based on a hypothetical standard value of molar integrated intensity of the free or bonded hydroxyl band, calculated from the spectral data of the whole set of measured compounds, as described in detail in our earlier paper<sup>11</sup>. The advantage of this approach is that it does not need conformationally homogeneous standards.

Both the approaches used in the calculation of boat content in dimethylamino alcohols (N = N(CH<sub>3</sub>)<sub>2</sub>) gave very similar results. Since the compounds where N = NH<sub>2</sub> exhibit a considerable proportion of free hydroxyl even in the diequatorial compounds which should serve as boat standards and considerable error would be introduced in the calculation of the content of the chair forms from the free hydroxyl

TABLE I

Wavenumbers,  $\nu(\text{OH})$  ( $\text{cm}^{-1}$ ), and Apparent Molar Integrated Intensities,  $B$  ( $\text{l cm}^{-2} \text{ mol}^{-1}$ ) (in parentheses), of the Free and Bonded Hydroxyl Bands in the Spectra of Compounds *I–VIII* and the Found Energy Differences,  $\Delta G$  ( $\text{kcal mol}^{-1}$ ), between Chair and Boat Conformations (Scheme 2) (measured in  $5 \cdot 10^{-3} \text{M}$  tetrachloroethylene solutions at  $35^\circ\text{C}$ )

Compound	$\nu(\text{OH})_{\text{free}} (B)$	$\nu(\text{OH})_{\text{bonded}} (B)$	$\Delta G, (\% \text{ boat})$	
			from $B_{\text{bonded}}$	from $B_{\text{free}}$
Amino alcohols ( $\text{N} = \text{NH}_2$ )				
<i>Ia</i>	3 623 (1 730)	3 486 (300)	1.3 (10) <sup>a</sup>	--
<i>IIa</i>	3 615 (420)	3 493 (550)	0.87 (19) <sup>a</sup>	--
	3 627 (1 060)			
<i>IIIa</i>	3 623 (1 340)	3 503 (800)	0.60 (27) <sup>a</sup>	--
<i>IVa</i>	3 607 (180)	3 527 (2 900)	--	--
	3 632 (480)			
<i>Va</i>	3 621 (300)	--	--	--
	3 630 (1 450)			
<i>VIa</i>	3 620 (460)	3 497 (450)	1.1 (14) <sup>b</sup>	--
	3 633 (1 300)			
<i>VIIa</i>	3 629 (1 470)	3 513 (600)	0.87 (19) <sup>b</sup>	--
<i>VIIIa</i>	3 604 (150)	3 532 (3 100)	--	--
	3 631 (570)			
N,N-Dimethylamino alcohols ( $\text{N} = \text{N}(\text{CH}_3)_2$ )				
<i>Ib</i>	3 620 (270)	3 444 (1 600)	0.63 (26) <sup>c,g</sup>	0.63 (26) <sup>c,g</sup>
	3 630 (1 320)			
<i>IIb</i>	3 619 (110)	3 457 (5 250)	— 1.03 (85) <sup>c</sup>	— 0.73 (77) <sup>e</sup>
	3 633 (390)			
<i>IIIb</i>	3 622 (230)	3 458 (5 150)	— 0.95 (83) <sup>c</sup>	— 1.3 (89) <sup>e</sup>
<i>IVb</i>	--	3 467 (6 150)	--	--
<i>Vb</i>	3 619 (270)	3 458 (500)	1.56 (7) <sup>d</sup>	1.2 (12) <sup>f</sup>
	3 630 (1 440)			
<i>VIb</i>	3 618 (330)	3 467 (3 200)	0.05 (48) <sup>d</sup>	0.19 (42) <sup>f</sup>
	3 633 (810)			
<i>VIIb</i>	3 622 (160)	3 464 (4 500)	— 0.45 (68) <sup>d,h</sup>	— 0.35 (64) <sup>f,h</sup>
	3 630 (550)			
<i>VIIIb</i>	--	3 477 (6 200)	--	--

<sup>a</sup> Calculated using *IVa* as standard ( $B = 2 900$ ); <sup>b</sup> *VIIIa* used as standard ( $B = 3 100$ ); <sup>c</sup> calculated using hypothetical standard,  $B = 6 200$ ; <sup>d</sup> calculated using hypothetical standard,  $B = 6 600$ ; <sup>e</sup> calculated using hypothetical standard,  $B = 2 140$ ; <sup>f</sup> calculated using hypothetical standard,  $B = 1 950$ ; <sup>g</sup> previously found<sup>16</sup>: 18–40% boat; <sup>h</sup> previously found boat content: 55% (ref.<sup>4</sup>), 42–55% (ref.<sup>17</sup>).

bands, the equilibria in *Ia–IIIa*, *VIa* and *VIIa* were determined only from the bonded hydroxyl bands, using the integrated intensities of the bonded hydroxyl bands in *IVa* and *VIIIa* as standards for *trans*-perhydroindane and *trans*-decalin series, respectively.

The molar integrated intensities of the *trans*-amino alcohols, together with the chair-boat equilibrium data, are given in Table I. From the spectral data we can calculate that the amount of the boat form in the amino alcohols *Ia*, *IIa* and *IIIa* is 10%, 19% and 27%, respectively. On the other hand, in the decalin derivatives *Va*, *VIa*, and *VIIa* there is considerably less of the boat conformation, the respective amount being ~0%, 14% and 19%. We see that whereas the decalin system in *Va* can hold the hydroxy and amino groups in the axial positions, the corresponding perhydroindane derivative *Ia* already exists to the extent of about 10% in the boat form.

As expected, the amount of the boat in the dimethylamino derivatives *Ib*, *IIb* and *IIIb* is much higher than in the amino derivatives (~26%, ~80% and ~85%, respectively) since the dimethylamino group is bulkier and the energy gain of the hydrogen bond in the boat form is greater than in the amino compounds. Again the equilibria in the decalin compounds *Vb*, *VIb* and *VIIb* are shifted more toward the side of the chair conformation (boat content: ~10%, ~45% and ~66%, respectively).

Thus, in all cases there is a much higher proportion of the boat form in the studied perhydroindane derivatives than in the analogous *trans*-decalin compounds, the energy difference amounting about 0.8 kcal mol<sup>-1</sup> for the dimethylamino alcohols.

This relative preference of the chair form in decalin derivatives may be caused by two probable reasons. One is the fact that the chair form in the perhydroindane system is more flattened<sup>12,13</sup> than in the decalin derivatives which means a certain destabilisation of the chair conformation in the former system. The second, and probably decisive, factor may be the geometry of the boat form. Models show that in the perhydroindane system the non-chair conformation with the least angle strain is the twisted boat form which as such is regarded as the energetically most advantageous non-chair form (see *e.g.* ref.<sup>14</sup>). On the other hand, in the decalin system there are two possible classical boats without angle strain whereas the intermediate twisted boat is strained. Thus, in *trans*-decalin skeleton the angle strain (preferring the classical boat) works against the otherwise energetically most advantageous twisted boat<sup>15</sup> whereas, contrariwise, in the perhydroindane system the angle strain leads to this twisted conformation.

A comparison of the wavenumbers of the bonded hydroxyl bands may be instructive in this respect. If the boat form in perhydroindane compounds of the type *I–III* is twisted, the distance between the hydrogen bonded functional groups should be shorter (torsion angle about 50°) and therefore the bonded hydroxyl band in these compounds should be situated at lower wavenumbers than that in the corresponding decalin derivatives where a more "classical-like" boat (torsion angle about 65°)

is anticipated on the basis of calculations<sup>15</sup>. In actual fact, the bonded hydroxyl band in the derivatives *Ib*, *IIa*, *IIb*, *IIIa* and *IIIb* is indeed shifted for about  $10\text{ cm}^{-1}$  toward lower wavenumbers as compared with the bands in the spectra of the decalin derivatives *Vb*, *VIa*, *VIb*, *VIIa* and *VIIb*. This shift was observed for all studied *trans*-diaxial pairs of compounds and it lends thus further support to the above conclusions concerning the detailed geometry of the boat forms. However, there is at least one case, where X-ray analysis found a twisted boat form of ring A in a steroid amino alcohol (pancuronium bromide<sup>16</sup>).

In fact, also other isomers, including the diequatorial isomers *IVa* and *IVb* exhibit a similar shift of the bonded hydroxyl band. Since no similar shift in the position of the free hydroxyl bands was observed we think that the shift of the bonded hydroxyl bands is not due to an inherent spectral property of the perhydroindane system as such but that it really indicates a somewhat stronger hydrogen bond in these derivatives. This might be a result of a generally greater flexibility of the perhydroindane system which allows the two hydrogen-bonded functional groups to get closer together. Whatever the explanation is it does not of course affect the above argumentation concerning the boat forms.

#### *cis*-Derivatives

Only N,N-dimethylamino alcohols were investigated. Spectral data for the *cis*-derivatives *IX*–*XIII* are listed in Table II. Considerable flattening of the chair form was observed previously<sup>6</sup> in N-axial O-equatorial N,N-dimethylamino alcohols of the type *XII*. In compound *XII* the strong bonded hydroxyl band at  $3382\text{ cm}^{-1}$  was assigned to flattened chair species whereas the very weak band at  $3500\text{ cm}^{-1}$  was ascribed to a boat conformer. In the methyl derivative *XIII* the band at  $3500\text{ cm}^{-1}$

TABLE II

Wavenumbers,  $\nu(\text{OH})$  ( $\text{cm}^{-1}$ ) and Integrated Intensities,  $B$  ( $1\text{ cm}^{-2}\text{ mol}^{-1}$ ) (in parentheses), of Hydroxyl Bands in the Spectra of Dimethylamino Alcohols *IX*–*XIII* ( $5 \cdot 10^{-3}\text{ M}$ ) Solutions in tetrachloroethylene,  $35^\circ\text{C}$

Compound	$\nu(\text{OH})_{\text{free}} (B)$	$\nu(\text{OH})_{\text{bonded}} (B)$	
<i>IX</i>	3 623 (200)	3 530 (200)	3 359 (5 000)
<i>X</i>	3 632 (300)	3 501 (5 250)	3 325 (2 650)
<i>XI</i>	--	3 473 (6 500)	
<i>XII</i>	3 622 (550)	3 540 (100)	3 381 (5 700)
<i>XIII</i>	3 621 (200)	3 503 (3 800)	3 402 (1 800)

is very intense, indicating that this compound exists mainly in a boat conformation. The spectra of the perhydroindane derivatives *IX* and *X* are completely analogous to those of *XII* and *XIII*. The bands here are assigned analogously as in the decalin derivatives *XII* and *XIII*. Since the bands in the  $3350\text{ cm}^{-1}$  region are very broad, considerable error is involved in the calculation of their integrated intensities. No quantitative treatment was therefore attempted. The similar ratio of integrated intensity of the band at  $3380\text{ cm}^{-1}$  to that of the band at  $3500\text{ cm}^{-1}$  for the pairs *IX*–*X* and *XII*–*XIII* indicates that there are no great energy differences between chair forms in the N-axial O-equatorial isomers in the two series. Nevertheless, the geometry of the flattened chair differs probably slightly as indicated by the position of the bonded hydroxyl bands in the region  $3300\text{--}3400\text{ cm}^{-1}$ . The bonded hydroxyl bands due to the flattened chair in the spectra of perhydroindane derivatives *IX* and *X* ( $3359\text{ cm}^{-1}$  and  $3325\text{ cm}^{-1}$ , respectively) are situated at lower wavenumbers than the bands in the spectra of the corresponding decalin derivatives *XII* and *XIII* ( $3382\text{ cm}^{-1}$  and  $3380\text{ cm}^{-1}$ , respectively). This indicates a shorter distance between the two functional groups and is in accord with the assumption that the chair in the perhydroindane system is already slightly flattened.

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