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THE PSEUDOROTATION OF CYCLOHEPTANE—I

W. M. J. Flapper and C. Romers*

Gorlaeus Laboratoria, X-ray and Electron Diffraction Section, Rijksuniversiteit, Leiden, The Netherlands

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Abstract—The pseudorotation of cycloheptane is described by means of the Fourier expansion of the endocyclic torsion angle $\omega_i = A \sin \phi_j + B \sin 3\phi_j + C \sin 5\phi_j + D \sin 7\phi_j$; $\phi_j = \Delta/2 + 2\pi j/7$; $j = 0, 1, \ldots, 6$; $i = 2j + 4$, mod 7 and Δ being a phase angle.

The topography of the pseudorotational itineries for the chair/twist-chair and the boat/twist-boat families is discussed. X-ray diffraction data concerning the geometry of 7-membered rings occurring in fused ring compounds are analysed by means of the proposed relationship. The least squares procedure for evaluation of the parameters A, B, C and D is given in an appendix.

The calcium salt of cycloheptane carboxylic acid, $(C_7H_{13}{\cdot}COO)_2Ca{\cdot}5H_2O$ in solid state, displays disorder closely related to pseudorotation. Preliminary X-ray diffraction data of this structure (to be published elsewhere) are given.

INTRODUCTION

The X-ray diffraction analysis[1,2] of the calcium salt of cycloheptane carboxylic acid, $(C_7H_{13}{\cdot}COO)_2Ca{\cdot}5H_2O$, was started a few years ago in order to inspect the conformation of its 7-membered ring (hereafter 7-ring) in view of the predictions given by Hendrickson.[3] Disorder, closely related to pseudorotation, hampered this analysis and induced us to investigate the phenomenon of pseudorotation in more detail.

The concept of pseudorotation was introduced by Pitzer[4,5] for the description of the non-planarity of cyclopentane. It implies that the instantaneous shape—a certain spatial arrangement of ring atoms—propagates as a wave through the molecular framework. The ventral segments and nodes of the "wave" are the symmetrical C_s and C_2 conformers designated as envelope and half-chair.

Instead of using Pitzer's formula

$$Z_j = \left(\frac{2}{5}\right)^{1/2} q \cdot \cos\left(\Delta' + \frac{4\pi}{5} j\right), \quad j = 0,1,2,3,4 \qquad (1)$$

where q is the amplitude of puckering, Δ' is the phase angle and Z_j the height of atom no j from the mean plane of the ring, Geise *et al.*[6] introduced the empirical relationship[†]

$$\omega_j = \omega_m \sin\left(\frac{\Delta}{2} + \frac{4\pi}{5} j\right), \quad j = 0,1,2,3,4 \qquad (2)$$

where ω_j is the endocyclic torsion angle about the bond between atoms no j and no j + 1, and ω_m is the maximum puckering angle. Using (2) one finds for $\Delta = 0,72,144,\ldots°$ the C_s conformers and for $\Delta = 36,108,180,\ldots°$ the C_2 forms.

An essentially similar formula was later proposed by Lifson and Warshel.[8] It was pointed out by Dunitz[9] that Eqn (2) can be derived from (1) and that both hold only for substantially puckered rings. However up to a puckering of 50°, Eqn (2) holds[10] with a precision of better than 0·1°.

A similar equation was proposed by Buys and Geise[11] for the pseudorotation of boat-shaped cyclohexane:

$$\omega_j = \omega_m \cos\left(\Delta + \frac{2\pi}{3} j\right), \quad j = 0,1,2,3,4,5. \qquad (3)$$

For phase angles $\Delta = 0,60,120\ldots°$ one finds in the itinerary the ideal boat conformers with C_{2v} symmetry and for $\Delta = 30,90\ldots°$ twist-boats with D_2 symmetry, the in-between-forms having the symmetry of subgroup C_2. In contrast with relation (2) Eqn (3) is rather inaccurate and only permits a precision of about 2°.

The main importance of empirical relations such as (2) and (3) lies in the easy method of reproducing the topology of pseudorotational conformers and of characterizing the conformation of 5- and 6-membered rings occurring in a variety of molecules, including biologically important molecules such as alkaloids, terpenoids, steroids and nucleic acids.[12,13] The aim of the present paper is to investigate the pseudorotational behaviour of cycloheptane and to propose a method for calculating internal as well as cartesian coordinates of conformers at any desired point in the two possible pseudorotational pathways.

Hendrickson[3] has inspected the geometry of cycloheptane and other medium-sized rings and calculated the total energy by means of minimization of strain energy. He predicted that cycloheptane occurs in two itineraries pseudorotating between symmetrical C_s and C_2 conformers. The first itinerary (Fig. 1a) is a pathway in the chair/twist-chair family, the second (Fig. 1b) in the boat/twist-boat family.

Hendrickson[3d] calculated the geometries and relative energies of the four principal symmetrical forms and concluded that the energy difference between these forms is rather small, the difference with respect to the most stable twist-chair (TC) being 1·4, 2·4 and 2·6 kcal/mol for the chair (C) twist-boat (TB) and boat (B), respectively. The energy barrier between the two families amounts, however, to about 8·5 kcal/mol.

In-between-forms were, however, not considered. Moreover, more sophisticated molecular mechanics calculations were recently introduced by Boyd,[14] Allinger,[15] Lifson and Warshel[16] and Altona and Faber.[17] Using the programs of Altona and Faber we recalculated the geometries and relative energies of the principal forms of

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[†] The precise formula was $\omega_j = \omega_m \sin(\Delta''' + 4\pi j/5)$, while one year later Altona, Geise and Romers[7] used the modified form $\omega_j = \omega_m \cos(\Delta''/2 + 4\pi j/5)$. Note that $\Delta' + \pi/2 = \Delta''' = \Delta/2$ and $\Delta'' = \Delta - \pi$.

cycloheptane. The resulting geometries (Table 1) predicted by the various fields do not differ very much. On the other hand the total energy contents are not comparable and depend to a large degree on the parameters introduced for the various interactions.[17] All calculations (Table 1) point to the twist-chair as the most stable form, its energy content being ~1·2 kcal lower than the energy of the chair form. In view of the relatively large energy differences calculated for the TB and B forms using the field of Boyd and Lifson it is plausible that the latter forms only can play an important role as conformers in strained molecules containing 7-rings. We return to this point in section 5.

In Appendix II is shown how the resulting internal coordinates d_j (bond length between atoms j and j + 1) and bond angles θ_j (angle between bonds d_{j-1} and d_j) can be converted into cartesian coordinates. Due to the restricted number of degrees of freedom (15)* the torsion angles ω_j (dihedral angle between the plane of atoms j − 1, j, j + 1 and the plane of atoms j, j + 1, j + 2) are related to the bond lengths and bond angles. The relations are also given in the Appendix.

Relationship between ω and Δ

A quantitative analysis of the torsion angles displayed by the principal forms induced us to test the following Fourier expansion† between the torsion angle ω_i and the

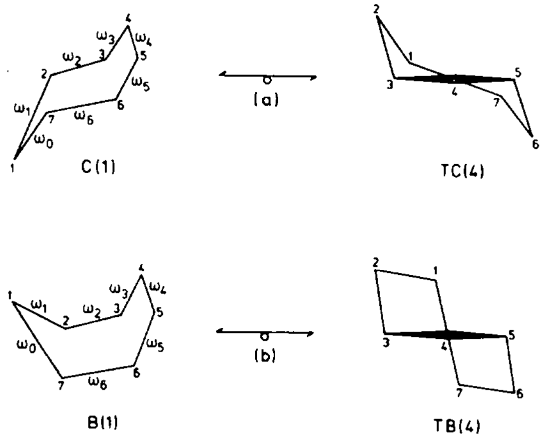

Fig. 1. C_s and C_2 forms in the chair, twist-chair family (a) and the boat, twist-boat family (b). C(1) and B(1) are a chair and a boat, respectively, with a mirror plane through atom 1 and bisecting bond 4–5. TC(4) and TB(4) designate a twist-chair and a twist-boat with a dyad running through atom No. 4 and the midpoint of bond 1–7. For the shown conformers the relations between the torsion angles are:

$$\omega_4 = 0 \text{ for } C_s \text{ form}, \ \omega_3 = \pm\omega_5, \ \omega_2 = \pm\omega_6 \text{ and } \omega_1 = \pm\omega_0,$$

the plus sign indicating the C_2 form, the minus sign referring to the C_s form.

Table 1. Calculated angular entities (°) and relative energy (kcal/mol) of cycloheptane conformers; column 1 refers to procedure specified below. Angles ε, φ and ψ are defined in Appendix

C	ε	φ	ψ	θ_1	θ_2	θ_3	θ_4	ω_1	ω_2	ω_3	ω_4	A	B	C	D	Energy
a	5·6	45·7	56·5	116·6	116·6	116·6	116·6	52·8	−81·4	68·2	0	82·7	34·5	−1·8	−1·1	
b	4·5	48·4	59·7	115·0	115·0	115·0	115·0	55·3	−86·0	71·7	0	87·0	36·5	−2·2	−1·3	
c	7·2	55·7	56·6	115·0	114·0	115·0	118·0	63·8	−83·5	66·1	0	89·2	29·0			1·42
d	7·2	54·2	55·8	115·7	115·2	115·1	118·5	62·6	−81·9	64·7	0	86·8	27·6			1·04
e	8·2	53·3	54·3	116·2	115·4	115·6	119·6	62·4	−79·8	63·0	0	86·0	27·0			0·63
f	6·9	58·7	59·8	112·5	112·7	113·1	116·6	67·1	−88·1	68·8	0	93·0	30·2			1·58
TC,a				116·6	116·6	116·6	116·6	37·2	−84·0	66·8	−47·4	82·7	34·5	−1·8	−1·1	
b				115·0	115·0	115·0	115·0	38·8	−88·9	70·3	−49·6	87·0	36·5	−2·2	−1·3	
c				116·0	115·0	113·0	115·0	39·1	−88·1	72·3	−54·3	89·1	34·6			0
d				117·2	115·9	116·4	116·4	38·1	−85·0	69·4	−51·7	85·6	33·7			0
e				119·1	117·3	116·5	116·5	36·3	−80·8	70·3	−56·2	85·7	29·5			0
f				115·1	114·0	113·5	113·5	39·7	−90·8	75·4	−56·9	92·5	35·0			0
B,a	5·6	−45·7	56·5	116·6	116·6	116·6	116·6	−52·8	−31·6	68·2	0	−1·6	69·4			
b	4·5	−48·4	64·5	115·0	115·0	115·0	115·0	−55·3	−33·4	71·7	0	−1·9	72·9			
c	5·5	−50·2	58·9	115·0	115·0	115·0	116·0	−57·5	−30·9	69·9	0	−0·9	73·3			2·64
d	6·1	−49·1	58·8	115·9	115·8	114·4	116·5	−56·6	−30·8	69·1	0	−0·6	71·4			2·60
e	6·3	−44·4	55·6	117·2	117·6	116·6	117·4	−51·7	−30·8	66·6	0	1·5	67·8			4·45
f	4·7	−48·4	60·4	115·2	115·1	114·2	115·1	−55·4	−33·5	71·9	0	1·9	73·1			5·66
TB,a				116·6	116·6	116·6	116·6	43·2	−61·4	−16·9	70·8	−1·6	69·4			
b				115·0	115·0	115·0	115·0	45·4	−64·4	−17·9	74·6	−1·8	72·9			
c				115·0	115·0	115·0	115·0	45·4	−64·4	−17·9	74·6	−1·8	72·9			2·40
d				114·9	115·0	116·3	115·7	44·7	−65·8	−14·9	68·9	−0·9	71·4			2·66
e				117·8	117·3	117·6	116·5	41·8	−58·9	−18·1	70·8	−3·2	67·7			4·40
f				115·4	115·3	115·2	114·0	44·8	−62·5	−20·5	77·6	−4·1	73·9			5·64

a,b All distances equal and θ = 116·6° and θ = 115·0° from references 3[d], using equations (7), (8), (9), (see Appendix).
c Hendrickson's values[3d], ε, φ and ψ according to (7), (8) and (9).
d Molecular mechanics program of Altona, using a modified Allinger field[17b].
e Ibid, using Lifson's field[16].
f Ibid, using Boyd's field[14].

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*One calculates 15 degrees of freedom from 3n − 6 = 15 for n = 7. This is strictly true for cartesian coordinates and the case discussed in Appendix II. However, 15 internal coordinates are not always sufficient to define unambiguously a 7-ring, because non-linear relations exist between internal coordinates (*cf*[18]).

†A slightly different expression, containing the first two terms and only valid for ω_4 was first suggested by Altona and Geise (see footnote on p. 24 in ref. 7).

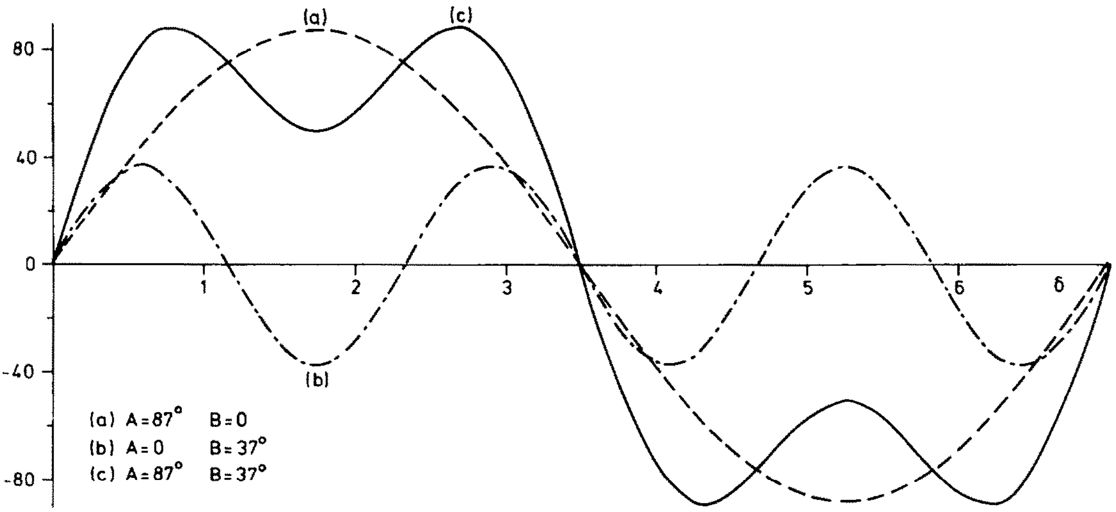


Fig. 2. Graphical representation of ω_4 as a function of phase angle Δ for the parts A sin ϕ(a), B sin 3ϕ(b) and the sum A sin ϕ + B sin 3ϕ(c).

phase of pseudorotation Δ:

$$\omega_i = A\sin\phi_j + B\sin 3\phi_j + C\sin 5\phi_j + D\sin 7\phi_j \quad (4)$$

$$\phi_j = \frac{\Delta}{2} + \frac{j}{2}\delta,\ j = 0,1\dots.6 \quad (5)$$

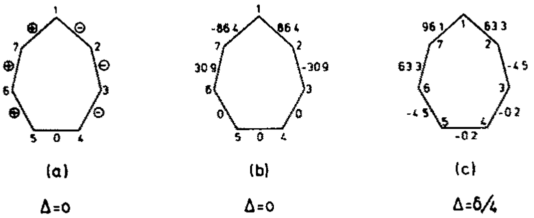
$$i = 2j + 4, \bmod 7;\ \delta = 4\pi/7. \quad (6)$$

The part A sin ϕ is a simple sine wave with a period 4π which is illustrated for ω_4 in Fig. 2 (curve a). Note that $\omega_4 = 0$ for phase $\Delta = 0$. It accounts for a 7-ring with C_s symmetry for $\Delta = n\delta$ (chair) and $\Delta = (n+\frac{1}{2})\delta$ (ring-inverted chair), n being an integer, and with C_2 symmetry for $\Delta = (n+\frac{1}{4})\delta$ and $\Delta = (n-\frac{1}{4})\delta$ (twist-chair and ring-inverted twist-chair, respectively). The chair and its inverted counterpart are indistinguishable for cycloheptane, but form a conformational pair for substituted cycloheptane. The same is valid for the boat and its inverted form.

The part B sin 3 ϕ(curve b, Fig. 2) has a period $4\pi/3$ and represents boat conformers with C_s symmetry for $n(\delta/3)$ and $(n+\frac{1}{2})(\delta/3)$ (boat and ring-inverted boat) and with C_2 symmetry for $\Delta = (n \pm \frac{1}{4})(\delta/3)$ (Twist-boat and ring-inverted counterpart).

A special case is the series with B = −0·61 A, C = D = 0. The resulting wave has the same period (4π) and the same symmetry as the wave corresponding to the C/TC family. The torsion angles of the 7-ring for Δ = 0 and Δ = $\delta/4$ are depicted in Figs. 3b and c. In conformer (b) the atoms 2,3, . . . , 7 are exactly coplanar and atom 1 is outside the plane. We designate this conformer with symmetry C_s as a sofa, S(1). Conformer (c) has atoms 1 and 7 below and above the nearly planar configuration of atoms 2,3, . . . , 6. We call this conformer with symmetry C_2 a twist-sofa, TS(4). The S/TS family does not occur in cycloheptane but can appear in polycyclic compounds containing 7-rings, see section on X-ray data.

The waves C sin 5ϕ and D sin 7ϕ have periods $4\pi/5$ and $4\pi/7$, but do not represent models with a physical meaning. This becomes clear if one substitutes zero for Δ. The former produces a C_s form with three successive torsion angles having the same sign (Fig. 3a). It is, however, impossible to close such a ring unless one resorts to unrealistic values for some bond distances and valency angles. The latter predicts that *all* torsion angles are equal in sign and magnitude for any phase angle and zero for Δ = 0 (planar form). The ventral and nodal parts of the curves C sin 5ϕ and D sin 7ϕ have the proper symmetry, however. The third and fourth term may, therefore, be included in expression (4) in order to obtain a better fit with the torsion angles resulting from experiments or from models obtained by strain-energy minimization. The constants A, B, C and D are obtained from a least-squares fit (Appendix II) using the torsion angles predicted by force-field calculations (Table 1). The resulting values with a standard deviation of 0·03 (degrees) indicate that the third and fourth terms of (4) are, indeed, small correction terms.



(a) Δ=0

(b) Δ=0

(c) Δ=δ/4

Fig. 3. Signs (a) and magnitudes (b and c) of dihedral angles. The case (a) refers to the part C sin 5ϕ. The cases (b) and (c) to A sin ϕ + B sin 3ϕ for B = −0·61 A and A = 87°.

Even terms, e.g. E sin 2ϕ, F sin 4ϕ, and so forth, were not added to the Fourier series (4), since they display the wrong symmetry at the required points and would destroy the symmetry of the resulting curve C (Fig. 2). Higher odd terms containing sin 9ϕ, sin 11ϕ, etc. have the correct symmetry, but were, nevertheless, not incorporated in (4), since they hardly contribute. Moreover at points where the total curve has C_2 or C_s symmetry these additional waves can be expressed in the lower terms. For this reason they cannot be obtained from the applied least-squares procedure.

Topography of the pseudorotational itinerary

The use of equation (4) permits a more detailed description of interconversions in the C/TC and B/TB families than was given by Hendrickson. We offer for inspection (Table 2) a topography of the two pseudorota-

Table 2. Pseudorotation itineraries of cycloheptane

Δ	0			$\frac{\delta}{4}$			$\frac{2\delta}{4}$	$\frac{\pi}{3}$		$\frac{3\delta}{4}$			δ		$\frac{2\pi}{3}$	$\frac{5\delta}{4}$			$\frac{6\delta}{4}$			π
	C(1)			TC(4)			C′(7)			TC′(3)			C(6)			TB(2)			C′(5)			TC′(1)
	a			a			a			a			a			a			a			i
ω_4	0			43			74			88			84			70			56			50
	B(1)	TB(2)	B′(3)	TB′(4)	B(5)	TB(6)	B′(7)	TB′(1)	B(2)	TB(3)	B′(4)	TB′(5)	B(6)	TB(7)	B′(1)	TB′(2)	B(3)	TB(4)	B′(5)	TB′(6)	B(7)	TB(1)
	e	e	e	e	e	e	e	i	a	a	a	a	a	a	a	a	a	a	a	a	a	i
ω_4	0	16	30	43	54	63	68	70	68	63	54	43	30	16	0	−16	−30	−43	−54	−63	−68	−70
Δ	π			$\frac{8\delta}{4}$			$\frac{9\delta}{4}$	$\frac{4\pi}{3}$		$\frac{10\delta}{4}$			$\frac{11\delta}{4}$		$\frac{5\pi}{3}$	$\frac{12\delta}{4}$			$\frac{13\delta}{4}$			2π
	TC′(1)			C(4)			TC(7)			C′(3)			TC′(6)			C(2)			TC(5)			C′(1)
	i			e			e			e			e			e			e			e
ω_4	50			56			70			84			88			74			43			0
	TB(1)	B′(2)	TB′(3)	B(4)	TB(5)	B′(6)	TB(7)	B(1)	TB(2)	B′(3)	TB′(4)	B(5)	TB(6)	B′(7)	TB′(1)	B(2)	TB(3)	B′(4)	TB′(5)	B(6)	TB(7)	B′(1)
	i	e	e	e	e	e	e	e	e	e	e	e	e	e	i	a	a	a	a	a	a	a
ω_4	−70	−68	−63	−54	−43	−30	−16	0	16	30	43	54	63	68	70	68	63	54	43	30	16	0
Δ	2π			$\frac{15\delta}{4}$			$\frac{16\delta}{4}$	$\frac{7\pi}{3}$		$\frac{17\delta}{4}$			$\frac{18\delta}{4}$		$\frac{8\pi}{3}$	$\frac{19\delta}{4}$			$\frac{20\delta}{4}$			3π
	C′(1)			TC′(4)			C(7)			TC(3)			C′(6)			TC′(2)			C(5)			TC(1)
	e			e			e			e			e			e			e			i
ω_4	0			−43			−74			−88			−84			−70			−56			−50
	B′(1)	TB′(2)	B(3)	TB(4)	B′(5)	TB′(6)	B(7)	TB(1)	B′(2)	TB′(3)	B(4)	TB(5)	B′(6)	TB′(7)	B(1)	TB(2)	B′(3)	TB′(4)	B(5)	TB(6)	B′(7)	TB′(1)
	a	a	a	a	a	a	a	i	e	e	e	e	e	e	e	e	e	e	e	e	e	i
ω_4	0	−16	−30	−43	−54	−63	−68	−70	−68	−63	−54	−43	−30	−16	0	16	30	43	54	63	68	70
Δ	3π			$\frac{22\delta}{4}$			$\frac{23\delta}{4}$	$\frac{10\pi}{3}$		$\frac{24\delta}{4}$			$\frac{25\delta}{4}$		$\frac{11\pi}{3}$	$\frac{26\delta}{4}$			$\frac{27\delta}{4}$			4π
	TC(1)			C′(4)			TC′(7)			C(3)			TC(6)			C′(2)			TC′(5)			C(1)
	i			a			a			a			a			a			a			a
	−50			−56			−70			−84			−88			−74			−43			0
	TB′(1)	B(2)	TB(3)	B′(4)	TB′(5)	B(6)	TB(7)	B′(1)	TB′(2)	B(3)	TB(4)	B′(5)	TB′(6)	B(7)	TB(1)	B′(2)	TB′(3)	B(4)	TB(5)	B′(6)	TB′(7)	B(1)
	i	a	a	a	a	a	a	a	a	a	a	a	a	a	i	e	e	e	e	e	e	e
	70	68	63	54	43	30	16	0	−16	−30	−43	−54	−63	−68	−70	−68	−63	−54	−43	−30	−16	0

C/TC itinerary: A = 87°, B = 37°.
B/TB itinerary: B = 70°.

tional itineraries and their interconversion pathways.*

The following features are obvious:

(1) The principal forms pseudorotate through the framework of carbon atoms.

(2) Change from C_s to C_2 forms takes place after a phase shift of $\delta/4$ in the C/TC and after a phase shift of $\delta/12$ in the B/TB family.

(3) The original conformer returns after a phase shift of 4π radians in the C/TC itinerary and after a shift of $4\pi/3$ radians† in the B/TB family.‡

(4) Interconversion (flipping) occurs at the points $n\delta/4, n = 0,1 \ldots 28$.

(5) During interconversion a substituent X changes the orientation of its bond C–X from a(axial) to e(equatorial) if it is bonded to a carbon atom directly involved in "flipping". The flipping from C to B is defined by a change of angle ϕ (Fig. 4) from a positive to a negative value. The flipping from TC to TB involves a twist of ~90° of bond 1–7 in TC(4) to its position in TB(4) (see Fig. 1).

(6) A substituent X present in the moiety not involved in flipping maintains its orientation during interconversion.

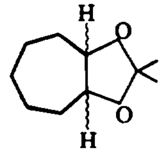
(7) The orientation of the bond C–X is i(isoclinal) if X is attached to a carbon atom through which runs a dyad.

As has been pointed out by Hendrickson[3a] a substituted cycloheptane compound never covers the total pseudorotation circuit, because for several points of the trajectory an axial substituent interferes with axial hydrogen atoms. Nevertheless the pathway is sufficiently long to permit a change of orientation of a C–X group, see next section.

Experimental evidence of pseudorotation

Hendrickson[19] demonstrated the use of his concepts in the conformational analysis of perhydroazulenic sesquiterpenes in connection with epimerization and Cotton effects of various isomers. However, very old experiments of the Delft school of Böeseken have been overlooked as a direct argument in favour of pseudorotation of cycloheptane. Böeseken and Derx[20,21] discovered that both 1,2-dihydroxy stereoisomers of cycloheptane form boric acid complexes as well as cyclic ketals with acetone. On the other hand[22] *cis*- and *trans*-1,2-cyclohexanediol neither form boric acid complexes nor cyclic ketals with acetone.

Inspection of pseudorotating Dreiding models of 1,2-substituted cycloheptane reveals the striking difference from cyclohexane. Irrespective of configuration two vicinal C–X bonds can, by pseudorotation along a part of the itinerary, be twisted towards favourable coplanar orientations which permit a easy approach by H_3BO_3 or acetone molecules. Depending on the configuration of 1,2-dihydroxycycloheptane the resulting bicyclic compound, e.g. I,



is *trans*- or *cis*-fused.

Structural information from X-ray diffraction data

So far no diffraction data on the evidence of pseudorotation and the geometry of non-fused 7-rings are available, while published data of fused systems (Table 3) are confined to spiro compound **1** and steroid **5**. Additional data are available for steroid **4**, triterpene **6** and the adduct of cycloheptatriene and 2-chlorotropone **11**, which however, contain double bonds in the 7-ring. Also available are sugar compounds **8**, **9** and **10** containing an oxygen atom in the 7-ring and compounds **2** and **3** containing a nitrogen atom in the "cycloheptane" fragment. Finally we discovered in the literature the very important (bis-(1,4)diazacycloheptane)-Cu^{II} compound **7** in which the two 7-ring ligands have distinct boat conformations. The following rules (in sequence of priority) were adopted for the numbering of atoms in the 7-ring:

1e. The atoms are numbered clockwise
2e. A double bond is located between atoms 4 and 5
3e. The 2-atom joint with other ring is between 4 and 5
4e. A 1,4 bridge will connect atoms Nos. 3 and 6
5e. A hetero atom is No. 1
6e. In monosubstituted or geminal-disubstituted 7-rings the substituent(s) is located at C_1.

The agreement is, as it should be, very good for No. 1, the sole compound with exclusively $C(sp^3)$–$C(sp^3)$ bonds in the 7-ring. Surprisingly the agreement is also good for compound **5** with an oxogroup in the 7-ring fragment and for compounds **6** and **4**, the latter being crystallized as dihydroiodide (**4a**) with one and as dihydrobromide (**4b** and **4c**) with two independent molecules per unit cell. Note, however, that **4** and **6** are double-bonded between atoms 4 and 5. In contrast with cyclohexene whose half-chair conformation totally differs from the chair form of cyclohexane, the cycloheptene conformation nicely fits with the C(1) chair of cycloheptane [25]($\omega_4 = 0$). This is the case, indeed, with compound **6**. The conformations of **4a**

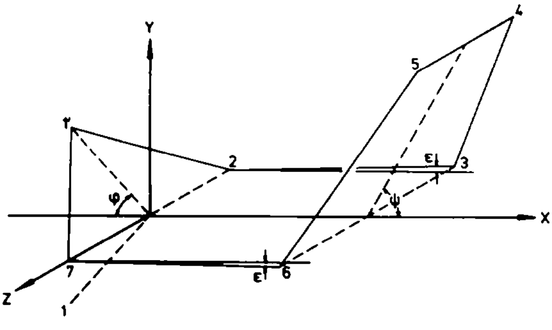


Fig. 4. The set up of cartesian axes. The atoms 2,3,6 and 7 are positioned in the XZ-plane, the X-axis bisects bond 2–7 and the Z-axis is colinear with the points 2 and 7. Position 1 indicates the chair (positive ϕ), position 1′ indicates the boat (negative ϕ).

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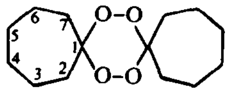
*In an earlier chart given by Hendrickson[3f] a different numbering was used in which atom No. 1 always coincides with the mirror plane or the dyad. Furthermore he solely uses the numbers 1,2,3 and 4, since symmetry implies relations between geometrical entities with numbers 5,6 and 7 and corresponding entities with the lower numbers. Such notation[3a,f] is unwieldy and we prefer a numbering in which the numbers 1, . . . , 7 are fixed to the same atoms, i.e. the geometrical forms pseudorotate through the framework.

†Using the mathematical model of Eqn (4) one only finds a period of $4\pi/3$ for the B/TB family if $A = C = D = 0$.

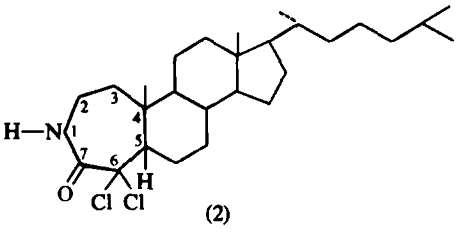
‡Although Hendrickson gives in his chart[3f] the same number of forms for the two families, he points out that there are three times as many B/TB forms as C/TC forms and he accounts for these extra B/TB forms in an earlier publication.[3a]

Table 3. List of compounds referred to in the Discussion. The indication (2×) means two independent molecules per unit cell. The rules of numbering are explained in the text

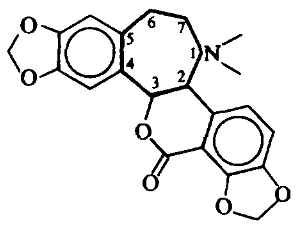


(1)

3,6-spiro-dicycloheptylidene-1,2,4,5-oxacyclohexane.[23]

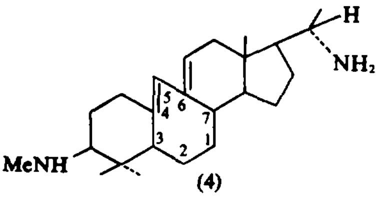


4,4-dichloro-2a-aza-A-homo-5β-cholestan-3-on.[24]



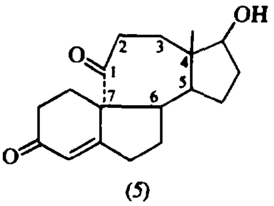
(3)

N-methylrhoeagenine iodide.[25]



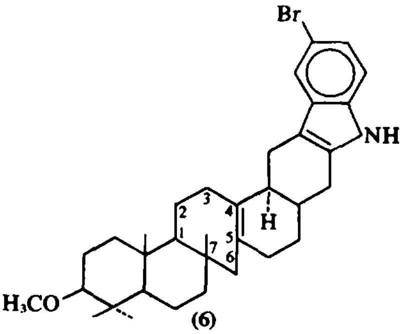
(4)

Buxenine-G dihydrobromide(2×) and dihydroiodide.[26]



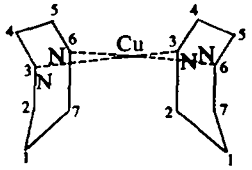
(5)

17β-hydroxy-8(9 → 10β)abeo-estr-4-en-3,10-dion.[27]



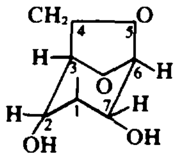
(6)

Bromoindol derivative of 3β-methoxy-21-keto-Δ^{13}-serratene.[28]



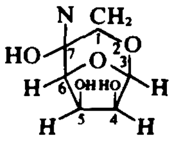
(7)

Numbering clockwise, looking from Cu to DACH.
$Cu'(DACH)_2NO_3'\cdot'Cu(DACH)_2H_2O'(NO_3)_2$
Bis-(1,4-diazacycloheptane)-copper(II)nitrate hemihydrate.[29]



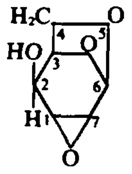
(8)

1,6-Anhydro-β-D-glucopyranose.[30]



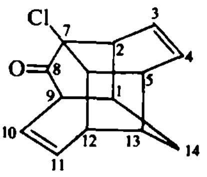
(9)

1,6-Anhydro-β-D-mannofuranose.[31]



(10)

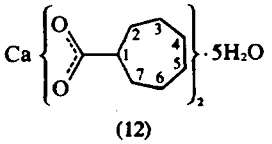
1,6:2,3-Dianhydro-β-D-gulopyranose.[32]



(11)

2-Chlorotropone-cycloheptatriene-adduct.[33]
Numbering of Fukazawa.

		1	2	3	4	5	6	7
Used in calculation	I	14	1	2	3	4	5	13
	II	14	1	9	10	11	12	13



(12)

Calcium cycloheptanecarboxylate pentahydrate.[2]

Table 4. Conformation, experimental and calculated torsion angles (°) of some 7-membered rings (see Table 3)

a: first row: experimental data
second row: calculated with A,B and Δ according to formula (4)

b. formula (4)

c: $\Sigma = [\frac{1}{6}\Sigma(\omega_j(\mathrm{exp}) - \omega_j(\mathrm{calc}))^2]^{1/2}$

d: According to the convention adopted in Ref. 12 and 13. C(5) means a chair with a mirror plane through atom No. 5; S(2) means a sofa with a mirror plane through atom No. 2; B(1) means a boat with a mirror plane through atom No. 1; TC(4) means a twist-chair with a dyad running through atom No. 4; TB(7) means a twist-boat with a dyad running through atom No. 7; TS(5) means a twist-sofa with a dyad running through atom No. 5.

Sofa: atoms 2-3-4-5-6-7 are coplanar.

Twist-sofa: atoms 3-4-5-6-7 are coplanar, atoms No. 1 and 2 above and below that plane, and a dyad through atom No. 5.

BS: boat-sofa: atoms 1-2-3-6-7 are coplanar
atoms 3-4-5-6 are coplanar
a mirror plane through atom No. 1.

Compound[a]	ω_0	ω_1	ω_2	ω_3	ω_4	ω_5	ω_6	A[b]	B[b]	Δ[b]	Σ[c]	Designation[d]
1	50	25	−80	75	−56	70	−89					
	51	27	−81	76	−57	68	−85	88	32	531	2·4	TC(1)–C(5)
2a	−2	39	−86	45	39	−75	30					
	−1	36	−79	43	45	−79	35	53	52	26	4·7	TC(4)
2b	−5	42	−86	46	37	−73	30					
	−4	37	−78	43	43	−78	37	54	50	26	6·0	TC(4)
3	50	−61	85	−59	−6	61	−66					
	53	−57	76	−58	−8	66	−73	79	29	365	5·6	C(1)
4a	−88	85	−34	−3	5	−2	36					
	−86	85	−35	−2	0	1	38	64	−30	1	2·7	S(1)
4b	−75	103	−61	19	−7	9	23					
	−76	100	−66	15	2	1	23	72	−28	−21	5·4	TS(5)
4c	−84	89	−37	2	1	−5	35					
	−84	86	−40	1	0	−1	37	65	−28	−1	2·8	S(1)
5	−72	88	−64	64	−83	60	6					
	−72	83	−64	67	−84	64	7	91	29	622	3·2	C(3)
6	66	−69	82	−66	6	62	−81					
	68	−67	81	−67	5	61	−82	90	26	357	1·4	C(1)
7a	53	−54	−39	78	2	−82	43					
	53	−53	−41	80	0	−80	41	9	79	0	2·1	B(1)
7b	44	−46	−45	83	−3	−82	49					
	44	−46	−45	84	−3	−82	49	16	78	−1	0·4	B(1)
7c	−49	48	46	−83	0	81	−44					
	−49	48	45	−82	−1	83	−44	13	79	360	0·8	B(1)
7d	35	−35	−56	89	3	−94	59					
	36	−35	−58	91	1	−92	57	29	81	0·4	2·1	B(1)
8	−46	47	46	−82	−1	83	−47					
	−46	46	46	−83	0	83	−46	15	78	360	0·8	B(1)
9	41	−42	−55	90	0	−87	56					
	40	−41	−53	90	−1	−89	54	23	81	0	1·5	B(1)
10a	2	−11	−63	98	−9	−84	83					
	0	−12	−64	97	−13	−88	79	52	72	−5	2·8	BS(1)
10b	0	−9	−64	97	−8	−85	84					
	−1	−9	−65	96	−12	−88	79	53	72	−5	2·9	BS(1)
11a	53	−50	−36	75	−1	−65	27					
	54	−50	−37	73	−3	−65	28	−5	70	241	1·2	B(1)
11b	−46	69	3	−55	8	66	−40					
	−44	67	5	−55	5	66	−44	11	66	591	2·5	TB(7)
12a	65	−75	31	36	−80	69	−50					
	67	−76	34	38	−77	66	−52	81	29	439	2·6	TB(3)
12b	76	−64	1	62	−79	57	−54					
	76	−65	2	63	−77	56	−55	81	30	461	1·4	C(6)
12c	79	−44	−28	77	−70	50	−60					
	79	−45	−29	76	−69	50	−62	80	31	482	1·3	C(6)–TC(2)
12d	33	−54	84	−43	−36	85	−60					
	33	−55	83	−46	−37	83	−60	74	41	383	1·8	TC(4)
12e	38	−52	67	−23	−50	87	−62					
	39	−63	75	−27	−47	76	−54	73	34	393	8·1	C(7)–TC(4)

and **4c** are, however, sofa's, S(1), with atom 1 outside the plane of atoms 2,3,4,5,6 and 7, while the conformation of **4b** is a twist-sofa, TS(5), with a dyad running through 5 and the midpoint of the bond 1–2 (see concluding remark in section 2).

There is also a good agreement for the aza compounds **2**, **3** and **7** and sugars **8**, **9** and **10**. It is a well-known fact that inclusion of hetero atoms X(N or O) in six-membered rings hardly effects[12] the preferred conformation since the C–X distance is only slightly smaller (at most 0·14 Å) than 1·54 Å and, moreover, the endocyclic valency angle C–X–C can easily adopt the required values in the range of 109–116°. For the same reason nitrogen and oxygen can be incorporated in a 7-ring and this explains why Eqn (4) still holds. The observed boat conformations of **8** and **9** are *hardly* surprising in view of the chemical constitution of these sugars: the axial orientations of $CH_2(4)$ and O(5) with respect of the 6-membered chair in **8** and the symmetrical orientations of C(7) and O(2) with respect to the furan ring with envelope form in compound **9**. In compound **10** atom C(1) is slightly above the planar part of atoms C(2), C(3), C(6) and C(7), while $CH_2(4)$ and O(5) are at large distances (1·1 Å) from this plane. We calll this conformation the boat-sofa BS form.

Special attention deserves the coordination compound **7**, in which both 1,4-diazacycloheptane rings occur as true boats. The planar square coordination of Cu^{II} by ligands is impossible if one or both 1,4-diazacycloheptane molecules should adopt a conformation in the C/TC family. It is, however, amazing that the observed conformation fits excellently with our empirical description.

Apart from the two 7-rings listed in Table 4 compound **11** contains another highly distorted 7-ring which does not obey our Eqn (4). For reasons of comparison the models **12a**, . . . , **12e** have been added to the list.

Disorder in solid $Ca(C_7H_{13}{\cdot}COO)_2{\cdot}5H_2O$

Possible evidence of pseudorotation is encountered in the crystal structure of the calcium salt of cycloheptane carboxylic acid crystallizing with five water molecules in an orthorhombic unit cell with dimension $a = 33{\cdot}122$, $b = 20{\cdot}094$ and $c = 6{\cdot}649$ Å. The space group is Abam or Aba2 and the cell contains eight formula units $Ca(C_7H_{13}{\cdot}COO)_2{\cdot}5H_2O$.

The X-ray diffraction analysis results in an ordered hydrophilic structure of water molecules, calcium ions and carboxylic anion groups in which Ca^{2+} is surrounded by eight O atoms. Instead of finding seven positive electron density areas for the C atoms of each ring the Fourier as well as difference maps only shows a ring-shaped diffuse area of positive electron density in which the positions of seven atoms more or less can be located. Apparently the hydrophobic part consists of a disordered frozen-in structure of cycloheptane rings in which various conformers of the C/TC family contribute to the scattering of X-rays. Calculation of structure factors without contribution of the ring carbon atom results in an agreement index of 25 per cent (based upon 803 reflexions measured with a diffractometer). Inclusion of ring carbon atoms distributed over five different conformers (model **12a**, . . . , **12e**, see Table 4) lowers the agreement index to a value of 16 per cent. Full details of the structure determination and discussion of the structure will be given elsewhere.

Acknowledgement—The authors are indebted to Dr. C. Altona for his criticism and suggestions during the preparation of the manuscript.

All calculations were executed in I.B.M. 360/65 and 370/158 computers of the Central Computing Laboratory of the University of Leiden. The programs used will be discussed elsewhere[2] and are available upon request.

REFERENCES

[1] W. M. J. Flapper and C. Romers, *Acta Cryst.* to be published.
[2] W. M. J. Flapper, forthcoming thesis.
[3] J. B. Hendrickson, [a] *J. Am. Chem. Soc.* **83**, 4537 (1961); [b] *Ibid.* **84**, 3355 (1962); [c] *Ibid.* **86**, 4854 (1964); [d] *Ibid.* **89**, 7036 (1967); [e] *Ibid.* **89**, 7043 (1967); [f] *Ibid.* **89**, 7047 (1967).
[4] J. E. Kilpatrick, K. S. Pitzer and R. Spitzer, *Ibid.* **69**, 2483 (1947).
[5] K. S. Pitzer and W. E. Donath, *Ibid.* **81**, 3213 (1959).
[6] H. J. Geise, C. Altona and C. Romers, *Tetrahedron Letters* 1383 (1967).
[7] C. Altona, H. J. Geise and C. Romers, *Tetrahedron* **24**, 13 (1968).
[8] S. Lifson and A. Warshel, *J. Chem. Phys.* **49**, 5116 (1968).
[9] J. D. Dunitz, *Tetrahedron* **28**, 5459 (1972).
[10] C. Altona, personal communication.
[11] H. R. Buys and H. J. Geise, *Tetrahedron Letters* 5619 (1968).
[12] C. Romers, C. Altona, H. R. Buys and E. Havinga, *Topics in Stereochemistry* (Edited by E. L. ELiel and N. L. Allinger), Vol. 4, p. 39 (1969).
[13a] C. Romers, C. Altona, H. J. C. Jacobs and R. A. G. de Graaff, *Steroids and Terpenoids*, Vol. 4, p. 531 (1974); [b] C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.* **94**, 8205 (1972).
[14] S. Chang, D. McNally, S. S. Tehrany, M. J. Hickey and R. H. Boyd, *Ibid.* **92**, 3109 (1970).
[15] N. L. Allinger and F. Wu, *Tetrahedron* **27**, 5093 (1971).
[16] A. Warshel and S. Lifson, *J. Chem. Phys.* **53**, 582 (1970).
[17a] C. Altona and D. H. Faber, *Fortschr. Chem. Forschung* **45**, 1 (1974); [b] C. Altona and M. Sundaralingem, *J. Am. Chem. Soc.* **92**, 1995 (1970).
[18] J. D. Dunitz and J. Waser, *Ibid.* **94**, 5645 (1972).
[19] J. B. Hendrickson, *Tetrahedron* **19**, 1387 (1963).
[20] J. Böeseken and H. G. Derx, *Rec. Trav. Chim.* **40**, 529 (1921).
[21] H. G. Derx, *Ibid.* 41, 312 (1922).
[22] J. Böeseken and J. van Giffen, *Ibid.* **39**, 183 (1920).
[23] P. Groth, *Acta Chem. Scand.* **21**, 2631 (1967).
[24] H. Altenburg, D. Mootz and B. Berking, *Acta Cryst.* **B28**, 567 (1972).
[25] C. S. Huber, *Ibid.* **B26**, 373 (1970).
[26] R. T. Puckett, G. A. Sim and M. G. Waite, *J. Chem. Soc.* (B) 935 (1971).
[27] M. O. Chaney and N. D. Jones, *Cryst. Struct. Comm.* **1**, 197 (1972).
[28] F. H. Allen and J. Trotter, *J. Chem. Soc.* (B) 721 (1970).
[29] M. Sakhawat Hussain and Håkon Hope, *Acta Cryst.* **B25**, 1866 (1969).
[30] Y. J. Park, H. S. Kim and G. A. Jeffrey, *Ibid.* **B27**, 220 (1971).
[31] J. Lechat and G. A. Jeffrey, *Ibid.* **B28**, 3410 (1972).
[32] B. Berking and N. C. Seeman, *Ibid.* **B27**, 1752 (1971).
[33] Y. Fukazawa and S. Ito, *Ibid.* **B25**, 665 (1969).

APPENDIX

I. *Calculation of angles ε, φ and ψ.*

Angle ε: It follows from Fig. 4 that

$$z_3 = -\tfrac{1}{2}d_4 + d_3\cos\theta_4 = -d_1\sin\tfrac{1}{2}\theta_1 - d_2\sin\epsilon,$$

or

$$\sin\epsilon = (\tfrac{1}{2}d_4 - d_3\cos\theta_4 - d_1\sin\tfrac{1}{2}\theta_1)/d_2. \tag{7}$$

Angle φ: The scalar product of vectors 2–3 and 2–1 implies

$$(x_1 - x_2)(x_3 - x_2) + (y_1 - y_2)(y_3 - y_2) + (z_1 - z_2)(z_3 - z_2) = d_1d_2\cos\theta_2,$$

which can be written as:

$$\cos\phi = -(\cos\theta_2 + \sin\epsilon\,.\cos\tfrac{1}{2}\theta_1)/\cos\epsilon\sin\tfrac{1}{2}\theta_1. \tag{8}$$

Angle ψ: From the scalar product of vectors 3–2 and 3–4 follows

$$\cos\psi = -(\cos\theta_3 + \sin\epsilon \, . \, \cos\theta_4)/\cos\epsilon \, . \, \sin\theta_4 \tag{9}$$

The chair/boat definitions are:

$$\text{sign}\,(\phi) \times \text{sign}\,(\psi) = \pm \tag{10}$$

the plus and minus sign holding for chair and boat respectively.

II. *Coordinates of an arbitrary 7-ring.* Analytical and numerical methods are discussed elsewhere.[2] Although these methods are accurate, the former only give multisolutions (in general four boat- and two chair-like forms) and the latter is applicable provided that the form in question does not deviate widely from C_s conformers. For this reason we present here a method based upon application of Eqn (4).

Let us call S the sum of least squares:

$$\sum_j [A \sin\phi_j + B \sin 3\phi_j + C \sin 5\phi_j + D \sin 7\phi_j - \omega_j]^2 = S \qquad j = 0, \ldots, 6. \tag{11}$$

This sum has a minimum value under conditions

$$\frac{\partial S}{\partial A} = \frac{\partial S}{\partial B} = \frac{\partial S}{\partial C} = \frac{\partial S}{\partial D} = 0 \tag{12}$$

provided that Eqns (4)–(6) hold.

One obtains four linear equations from which A, B, C and D are solved. Substituting arbitrary values for Δ and applying again Eqn (4) one generates arbitrary 7-rings, with known internal coordinates.

Having used six bond distances $d_1, \ldots, d_6$, five bond angles $\theta_2, \ldots, \theta_6$ and four torsion angles $\omega_2, \ldots, \omega_5$, in total 15 internal coordinates, the model is determined uniquely.* The calculated value of d_7 deviates at most 0·2% (say 0·003 Å for a C–C bond) from its value in the original model, the valency angles θ_1 and θ_7 deviate at most 0·06°, while the maximum deviation for torsion angles ω_1, ω_6 and ω_7 is 0·1°.

---

*The fragments 1-2-3-4, 2-3-4-5, 3-4-5-6 and 4-5-6-7 are uniquely defined by 3 distances, 2 valency angles and 1 torsion angle, i.e. the required number of freedom 6 for an assembly of four points. Consequently the position of atom 7 is unambiguously defined and therefore also the 7-ring.