

## Conformational flexibility of longifolene\*

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**Abstract.** The flexibility of the bicyclo[2.2.1]heptane-based tricyclic bridged system in longifolene is analysed based on x-ray structural data. In this context, the molecular structure of three differently substituted longifolenes has been analysed. The highly substituent-dependent conformation provides scope for the synthesis of a variety of commercially oriented products.

**Keywords.** X-ray structure analysis; longifolene derivatives; norbornane conformation; cycloheptane conformation.

### 1. Introduction

Longifolene ( $C_{15}H_{24}$ ) has been a molecule of interest to structural chemists because of the flexibility of its bicyclo[2.2.1]heptane-based tricyclic bridged system, and to natural product chemists because of the variety of commercially-oriented products (for example, perfumes) that the molecule can generate owing to this flexibility. From the time this compound was isolated (Simonsen 1920) substantial chemical research has resulted, the highlights of which are reported in recent reviews (Jadhav and Nayak 1980; Sukh Dev 1981a, b). Longifolene has such built-in stereoelectronic features in its rather complex tricyclic moiety that more often than not chemical transformation reactions have led to unexpected results. These abnormal products, more appropriately, sterically-diverted products (Sukh Dev 1981b) lead to newer and exciting chemistry and because of the complexity, x-ray crystallography would be the most appropriate tool for establishing the structures for such compounds. One such example is the structure of alloisolongifolene (Shitole *et al* 1983). The bicyclic[2.2.1]heptane moiety is by far the most important of bridged systems because of its frequent occurrence in many mono-, di- and sesquiterpenes. Indeed, this moiety (also called norbornane) has been subject to extensive physical and chemical studies by itself. Detailed empirical force field calculations at various levels of sophistication (Allinger *et al* 1968; Altona and Sundaralingam 1970; Engler *et al* 1973) have been performed to obtain reliable information regarding the geometry of this moiety. Besides norbornane, the longifolene has another flexible moiety, the seven-membered cycloheptane ring. Several strain energy calculations (Hendrickson 1961; Bixon and Lifson 1967; McPhail

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Figure 1. Structural formulae for HACPLB, DIBRLB and AILFNB.

and Sim 1973) have been performed on this moiety and several energetically stable conformational states are realised.

We report here the structure determination of three derivatives of longifolene (figure 1) which demonstrate the nature of flexibility in the system:

(a) 4-hydroxy-12-acetoxy cyclopent-[3-1'-ene-2'-oxo]-longiborane, hereafter referred to as HACPLB.

(b) 8,11-dibromo longibornane, hereafter referred to as DIBRLB.

(c) Alloisolongifolol-*p*-nitrobenzoate, hereafter referred to as AILFNB.

We have also analysed the overall conformation of the longifolene molecule in terms of these crystal data along with the already available crystal structure data from literature. This analysis is done mainly in two steps (i) the norbornane moiety in terms of the twist induced due to substitution from the expected  $C_{2v}$  symmetry and (ii) the cycloheptane moiety in terms of the deviation from  $C_2$  or  $C_s$  symmetry.

## 2. Structure determination of HACPLB, DIBRLB and AILFNB

The data were collected on a diffractometer (Enraf-Nonius CAD4-11M) using the  $\omega/2\theta$  scan technique upto  $2\theta = 48^\circ$ . Three standard reflections were monitored after every 2000 seconds of exposure time to check for crystal decay, if any. The experimental details are listed in table 1. All the structures were refined using full matrix least squares technique (Gantzel *et al* 1961) with anisotropic temperature factors for non-hydrogen atoms. Hydrogen atoms were fixed based on stereochemical considerations and their positions verified by difference Fourier synthesis.

### 2.1 HACPLB

Attempts to solve the structure in the automatic mode of MULTAN-78 (Main *et al* 1978) failed. By a careful examination of the convergence map it was decided to change the origin fixing reflections. Four other reflections were chosen for multi solution to yield overall 64 sets. The set with the best combined figure of merit did not yield the structure. However, the set with the lowest psi zero gave a five-atom fragment which eventually led to the structure solution after a Karle recycling followed by a Fourier synthesis. The

Table 1. Crystallographic data.

Compound name	4-hydroxy-12-acetoxy Cyclopent-[3-1'-ene- 2'-oxo]-longibornane: HACPLB	8,11-dibromo longibornane: DIBRLB	Alloisolongifolol- <i>p</i> -nitrobenzoate: AILFNB
Molecular formula	C <sub>20</sub> H <sub>28</sub> O <sub>4</sub>	C <sub>15</sub> H <sub>24</sub> Br <sub>2</sub>	C <sub>23</sub> H <sub>30</sub> NO <sub>4</sub>
Molecular weight	332.4	364.2	384.2
Crystal dimensions	0.1 × 0.1 × 0.6 mm	0.1 × 0.25 × 0.5 mm	0.25 × 0.18 × 0.6 mm
Solvent of crystallization	methanol	methanol	acetone
Crystal system	monoclinic	orthorhombic	monoclinic
Cell dimensions	<i>a</i> = 9.774 (1) Å <i>b</i> = 7.217 (1) <i>c</i> = 13.968 (2), <i>β</i> = 109.46 (1)° <i>V</i> = 928.9 Å <sup>3</sup>	<i>a</i> = 8.524 (3) Å <i>b</i> = 8.773 (2) <i>c</i> = 20.372 (4) <i>V</i> = 1523.3 Å <sup>3</sup>	<i>a</i> = 7.440 (5) Å <i>b</i> = 34.963 (6) <i>c</i> = 7.909 (2) <i>β</i> = 105.42 (3)° <i>V</i> = 1983.2 Å <sup>3</sup>
Space group	<i>P</i> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub>
<i>Z</i>	2	4	4
<i>D<sub>m</sub></i> (by floatation) (Mg m <sup>-3</sup> )	1.18	1.52	1.25
<i>D<sub>c</sub></i> (Mg m <sup>-3</sup> )	1.19	1.51	1.24
Radiation employed	MoK <sub>α</sub> (λ = 0.7107 Å)	MoK <sub>α</sub> (λ = 0.7107 Å)	MoK <sub>α</sub> (λ = 0.7107 Å)
<i>μ<sub>r</sub></i> (mm <sup>-1</sup> )	(graphite monochromator) 0.74	(graphite monochromator) 3.84	(graphite monochromator) 0.72
<i>F</i> (000)	360	736	828
No. of independent reflections	1579	1202	3382
No. of reflections with <i>F</i> > 3σ ( <i>F</i> )	568	442	795
<i>θ</i> <sub>max</sub>	24°	24°	24°
Method of structure determination	direct methods, MULTAN-78	direct methods, MULTAN-78	direct methods, MULTAN-78
Reliability index, <i>R</i>	0.057	0.057	0.095
<i>R<sub>w</sub></i>	0.059	0.060	0.099
Weighting scheme	<i>a</i> = 4, <i>b</i> = 1, <i>c</i> = 0.044	<i>a</i> = 3.5, <i>b</i> = 1, <i>c</i> = 0.025	<i>a</i> = 3.5, <i>b</i> = 1, <i>c</i> = 0.025
(Cruickshank's type)			

final positional and  $B_{eq}$  thermal parameters for non-hydrogen atoms are given in table 2a. Figure 2a shows the perspective view of the molecule.

## 2.2 DIBRLB

From a routine run of MULTAN-78, the highest two peaks were considered to be the bromine atoms and these were used in a subsequent Fourier synthesis to yield the entire structure. The final positional and  $B_{eq}$  thermal parameters for non-H atoms are listed in table 2b and a view of the molecule is shown in figure 2b.

## 2.3 AILFNB

With two molecules to be located in the asymmetric unit, this structure involved determination of 54 atoms. The first MULTAN-78 run gave one of the nitrobenzoate fragments and this followed by successive Fourier synthesis gave the entire structure. The positional coordinates and  $B_{eq}$  temperature factors for non-H atoms are listed in table 2c and a view of the two molecules in the asymmetric unit is shown in figure 2c. This structure establishes an altogether new facet of longifolene chemistry. The adopted reaction pathway obviously is not an energetically more favourable one which indicates a lack of understanding of all the factors which influence carbocation rearrangements (Shitole *et al* 1983). The bond lengths, bond angles, positional parameters for hydrogen atoms, final anisotropic thermal parameters for all the non-H atoms and the values of calculated and observed structure factors for all the above mentioned structures can be supplied by the authors on request.

## 3. Discussion

In order to make a comparative study of the effect of substitution on longifolene, a few other structures whose x-ray crystallographic study is already available are included along with the structures described above. Figure 3 depicts all the structures taken for comparison. However, structure AILFNB is not included in these discussions due to (i) not possessing cycloheptane ring and (ii) limited accuracy.

### 3.1 Bicyclo-[2.2.1]-heptane (norbornane)

Extensive experimental studies on the derivatives of norbornane have revealed that the system is moderately strained and its conformation changes slightly but significantly due to substitution. In an ideal situation when there are no substituents on the norbornane moiety, the system would have  $C_{2v}$  symmetry. The norbornane system can be regarded as a three-ring system: ring R, ring L and ring B (table 3). By using valence force field calculations (Altona and Sundaralingam 1970), the torsion angles in an ideal norbornane moiety have been calculated. The values obtained for rings R and L in all the crystallographic studies taken for comparison show significant deviations. The different modes of twisted norbornane are shown in figure 4. The presence of substituents on the edge atoms *i.e.* atoms 7, 8, 10 and 11 appear to induce larger twist. Altona and Sundaralingam (1970) predict that substitutions on these atoms cause a

**Table 2a.** Positional parameters and  $B_{eq}$  values for 4-hydroxy-12-acetoxy cyclopent-(3-1'-ene-2'-oxo)-longibornane: HACPLB.

Atom	x	y	z	$B_{eq}$
C (1)	0.320 (1)	0.142 (2)	0.3464 (8)	4.9 (6)
O (2)	-0.0596 (9)	0.045 (1)	-0.0931 (6)	4.6 (4)
C (2)	0.327 (1)	0.127 (2)	0.2348 (8)	4.0 (5)
C (1)	0.149 (1)	0.080 (2)	0.0539 (7)	4.1 (5)
C (2)	-0.007 (2)	0.069 (2)	0.002 (1)	4.9 (5)
C (3)	-0.089 (1)	0.083 (3)	0.0731 (9)	3.5 (5)
C (3)	-0.171 (1)	0.103 (2)	0.1562 (8)	2.6 (4)
O (4)	0.022 (1)	0.268 (1)	0.2270 (6)	4.8 (4)
C (4)	0.031 (1)	0.103 (2)	0.1796 (8)	3.1 (4)
C (5)	0.010 (1)	-0.071 (2)	0.2439 (9)	4.2 (5)
C (6)	0.108 (2)	-0.091 (2)	0.3528 (9)	4.3 (6)
C (7)	0.275 (1)	-0.056 (2)	0.3651 (8)	3.7 (4)
C (8)	0.336 (1)	-0.182 (2)	0.2961 (8)	4.2 (5)
C (9)	0.418 (1)	-0.051 (2)	0.2536 (7)	4.3 (6)
C (10)	0.556 (1)	0.014 (2)	0.3440 (8)	4.0 (6)
C (11)	0.494 (1)	0.154 (2)	0.4055 (9)	4.7 (6)
O (12)	0.557 (1)	-0.265 (1)	0.2012 (5)	4.3 (4)
C (12)	0.463 (1)	-0.113 (2)	0.1663 (8)	3.0 (5)
C (13)	0.615 (1)	-0.346 (2)	0.1302 (9)	6.2 (7)
O (13)	0.573 (2)	-0.293 (2)	0.041 (1)	7.3 (8)
C (14)	0.715 (2)	-0.508 (2)	0.179 (1)	4.5 (6)
C (15)	0.066 (2)	0.048 (3)	0.4248 (9)	6.3 (7)
C (16)	0.094 (2)	-0.289 (2)	0.382 (1)	5.9 (6)
C (17)	0.379 (1)	0.307 (2)	0.1977 (9)	4.3 (6)

**Table 2b.** Positional parameters and  $B_{eq}$  values for 8,11-dibromo longibornane: DIBRLB.

Atom	x	y	z	$B_{eq}$
Br (1)	1.0430 (6)	0.9512 (7)	0.0712 (2)	5.6 (5)
Br (2)	0.8896 (8)	0.6209 (7)	0.2329 (3)	4.4 (5)
C (1)	1.177 (3)	0.651 (4)	0.070 (1)	2.3 (4)
C (2)	1.114 (4)	0.499 (6)	0.064 (2)	2.4 (4)
C (3)	1.222 (4)	0.336 (5)	0.088 (2)	2.8 (4)
C (4)	1.380 (6)	0.368 (6)	0.114 (2)	6.3 (5)
C (5)	1.392 (5)	0.458 (6)	0.175 (2)	5.8 (4)
C (6)	1.331 (4)	0.617 (5)	0.183 (1)	3.4 (5)
C (7)	1.174 (4)	0.658 (5)	0.152 (2)	2.6 (3)
C (8)	1.056 (6)	0.523 (5)	0.169 (2)	2.6 (4)
C (9)	0.955 (5)	0.499 (3)	0.100 (1)	2.8 (4)
C (10)	0.878 (5)	0.649 (5)	0.072 (2)	2.9 (4)
C (11)	1.032 (5)	0.752 (6)	0.047 (2)	3.7 (4)
C (12)	1.308 (3)	0.632 (5)	0.260 (1)	5.6 (5)
C (13)	1.443 (6)	0.759 (5)	0.166 (2)	5.0 (5)
C (14)	1.082 (6)	0.443 (5)	-0.015 (1)	4.7 (4)
C (15)	0.843 (4)	0.370 (4)	0.103 (2)	3.1 (4)



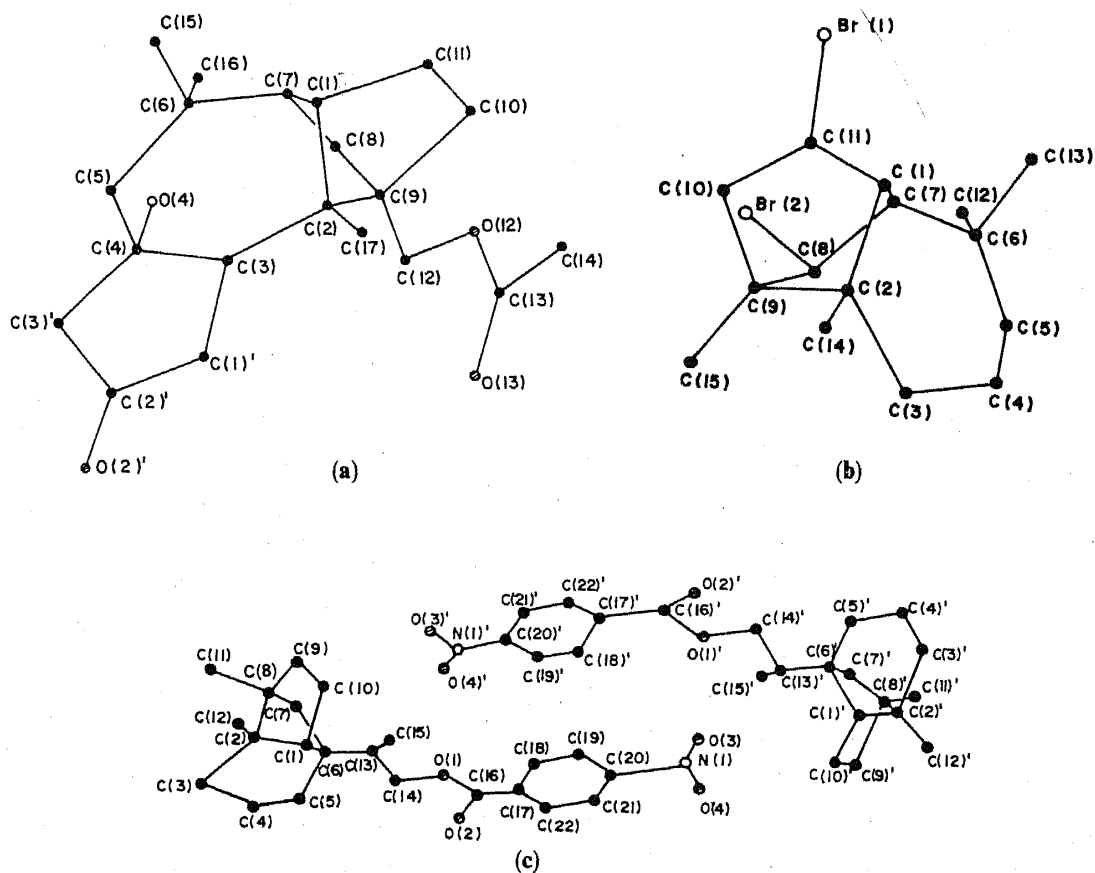


Figure 2. (a) A view of the molecule HACPLB.  
 (b) A view of the molecule DIBRLB.  
 (c) A view of the molecule AILFNB.

synchro twist  $S(+, +)$  or  $S(-, -)$  and substituents on atoms 1 and 9 cause contra twist namely  $C(+, -)$  and  $C(-, +)$  respectively. However, from the examination of figure 5, in the case of longifolenes atleast, no such generalisation can be arrived at. Indeed, structures 1 and 3 have substitution at atom 9 and are generally structurally similar but yet show different kinds of twist. However, in longifolenes a synchro twist appears to be energetically favourable.

### 3.2 The cycloheptane moiety

Another feature of longifolene is the presence of a cycloheptane ring which is flexible and undergoes pseudo rotation. Strain-energy minimization calculations (Hendrickson 1961) have shown that the twist-chair ( $\tau C$ ) is energetically most stable than the chair ( $C$ ), boat ( $B$ ) and twist-boat ( $\tau B$ ) forms. Another set of strain energy calculations (Bixon and Lifson 1967) has skew-chair, chair, boat and skew-boat with energies 5.55, 6.22, 7.95 and 8.19 kcal/mol respectively. McPhail and Sim (1973) have developed relations to check the deviation of the ring from  $C_2$  or  $C_s$  symmetry (figure 6) as

$$\Sigma_2 = [ |W_1 - W_6| + |W_2 - W_5| + |W_3 - W_4| ], \quad (1)$$

$$\Sigma_s = [ |W_1 + W_7| + |W_2 + W_6| + |W_3 + W_5| + |W_4| ]. \quad (2)$$

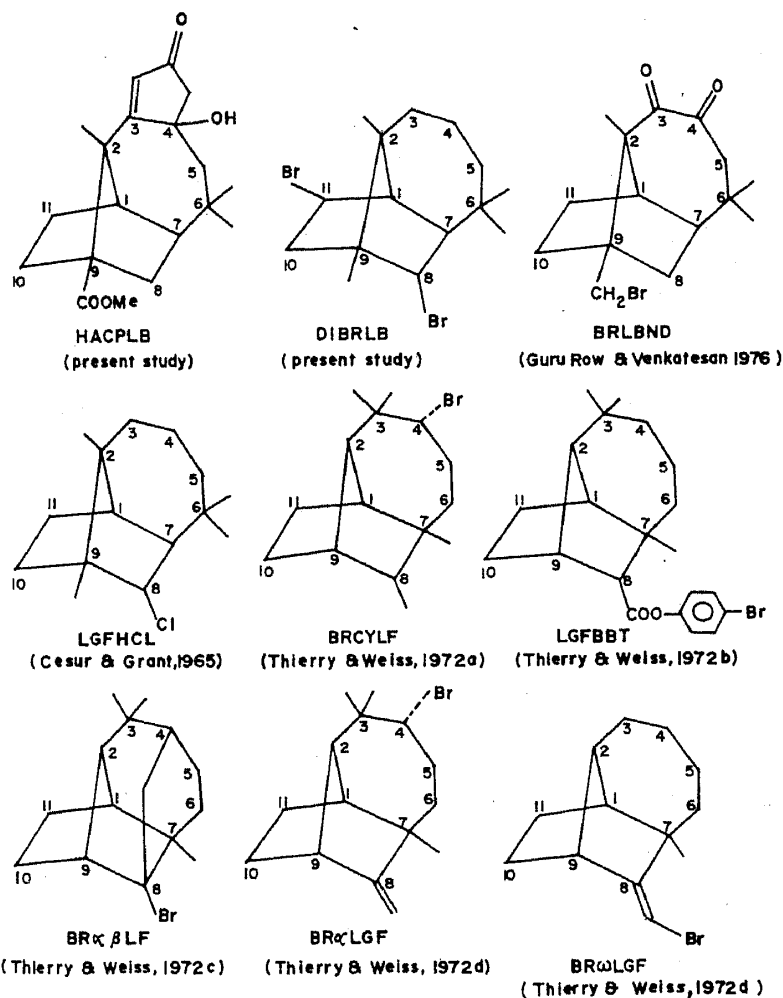


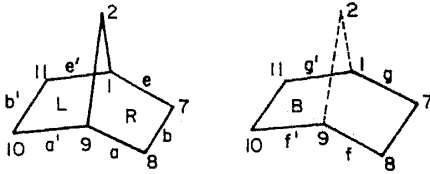
Figure 3. Structural formulae for all structures taken for comparison.

Table 4 lists a comparison of torsion angles in all the above structures and the theoretically predicted values. It is generally seen that the presence of exocyclic carbonyls and endocyclic double bonds result in large deviations from the  $C_2$  and  $C_s$  conformations. Indeed, the ratio  $\Sigma_2 / (\Sigma_2 + \Sigma_s)$  is a clear measure of the probability of having either  $C_2$  or  $C_s$  symmetry. The ratio obtained in all the structures (table 4) is around 0.5 which indicates that the seven-membered ring in longifolene is neither near  $C_2$  symmetry nor near  $C_s$  symmetry. However in HACPLB, DIBRLB, BRLBND and LGFHCL, this ratio is closer to the chair conformation as predicted by Lifson and Bixon. In the remaining structures the presence of a methyl substituent in 7 position seems to considerably distort the molecule.

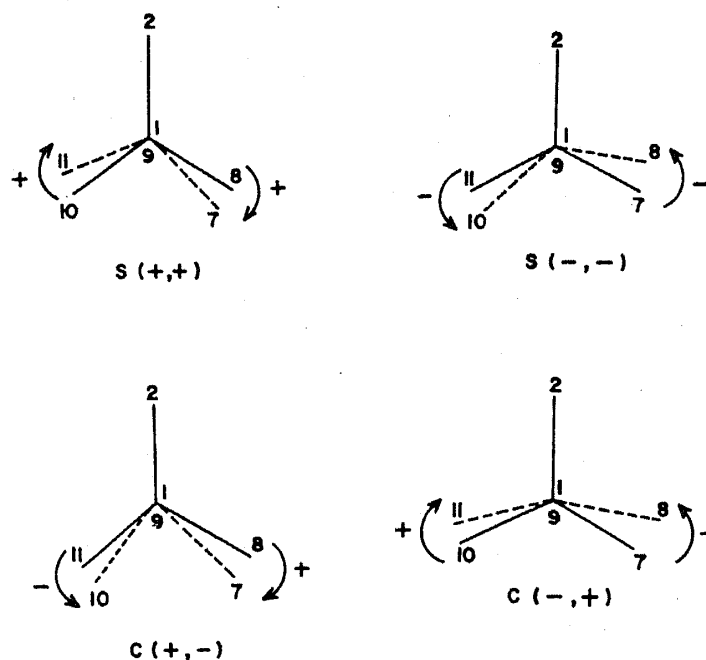
#### 4. Conclusion

It is obvious that longifolene, even after twenty five years from its structure elucidation, continues to generate unusual products. The endowed flexibility as seen from the previous sections complicates the problem further but leads to very exciting chemistry.



**Table 3.** Comparison of torsion angles ( $^{\circ}$ ) for the norbornane moiety. 1-records the values obtained by Altona and Sundaralingam (1970).


	1	HACPLB	DIBRLB	BRLBND	LGfHCL	BRCYLf	LGfBBT	BR $\alpha$ $\beta$ LF	BR $\alpha$ LGF	BR $\omega$ LGF
<b>Ring L</b>										
<i>a'</i>	36	34.0	-23.1	32.2	29.8	-28.8	-38.5	-36.1	-32.3	-34.3
<i>b'</i>	0	4.1	-4.1	4.5	5.0	-9.7	2.1	-2.9	-5.6	-4.3
<i>c'</i>	36	-38.5	31.9	-39.3	-38.3	44.5	35.3	40.7	41.4	41.2
<i>d'</i>	56	-58.2	47.5	-56.4	-52.2	54.8	60.7	59.8	56.9	58.6
<i>e'</i>	56	59.3	-50.5	58.9	52.8	-60.9	-57.5	-61.2	-60.2	-61.7
<b>Ring R</b>										
<i>a</i>	36	-37.3	47.8	37.2	-44.8	48.9	26.4	36.9	36.0	37.4
<i>b</i>	0	4.6	-20.6	4.9	11.2	-15.3	7.7	-1.6	-2.3	-4.2
<i>c</i>	36	27.3	-17.9	29.1	27.7	-23.2	-39.9	-33.9	-32.1	-30.0
<i>d</i>	56	-48.3	-67.0	53.2	59.9	-60.3	-48.9	-55.2	-52.9	-52.7
<i>e</i>	56	53.0	56.6	-50.4	-54.9	52.1	54.6	53.7	51.8	50.6
<b>Ring B</b>										
<i>f'</i>	71	-75.0	68.5	-74.1	-72.8	75.8	69.1	74.3	74.2	74.6
<i>g'</i>	71	66.2	-68.1	68.0	67.9	-65.2	-71.9	-68.9	-66.3	-69.8
<i>f</i>	71	68.9	-52.5	68.8	63.5	-58.0	-78.1	-70.5	-69.3	-69.4
<i>g</i>	71	-72.9	85.7	-75.2	-76.7	82.2	63.4	71.8	72.2	76.6

**Figure 4.** Theoretically predicted modes of twist in norbornane.

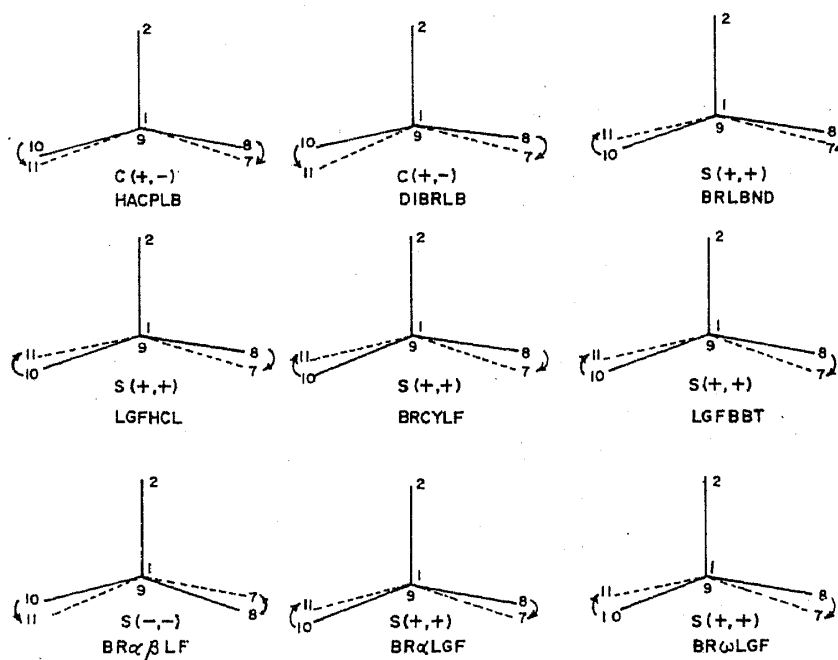


Figure 5. Twist modes for norbornane for all structures under comparison.

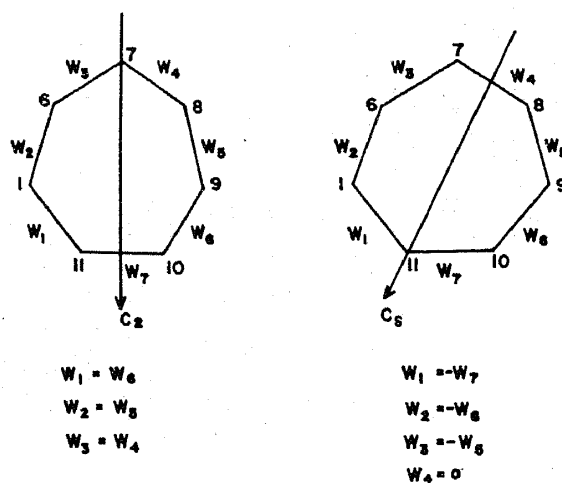


Figure 6. The  $C_2$  and  $C_s$  conformations of cycloheptane ring (the numbering of atoms is arbitrary).

This analysis however provides an insight into the effects of substitution which might enable the chemist to engineer to obtain desired products.

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Table 4. Comparison of torsion angles ( $^{\circ}$ ) in different structures with Hendrickson's (H) and Lifson and Bixon's (LB).

	$W_1$	$W_2$	$W_3$	$W_4$	$W_5$	$W_6$	$W_7$	$\Sigma_2$	$\Sigma_s$	$\frac{\Sigma_2}{\Sigma_2 + \Sigma_s}$
Boat (H)	57	34	-74	0	74	-34	-57	205	0	1
Boat (LB)	58	34	-73	-1	74	-33	-58	203	3	1
Twist boat (H)	19	68	-48	-48	68	19	-79	0	215	0
Twist boat (LB)	19	67	-46	-47	65	21	-79	5	214	0
Chair (H)	-70	92	-71	0	71	-92	70	114	0	1
Chair (LB)	-56	81	-82	20	55	-90	67	162	67	0.71
Twist chair (H)	-76	97	-41	-41	97	-76	53	0	141	0
Twist chair (LB)	-74	94	-40	-40	90	-70	51	8	137	0.05
HACPLB	67.4	-100.9	69.3	3.0	-68.1	67.3	-45.6	99.2	59.6	0.63
DIBRLB	-65.4	96.6	-69.2	-0.4	63.8	-60.2	39.8	106.8	67.8	0.60
BRLBND	66.2	-100.2	65.9	7.2	-80.0	72.5	-42.6	85.2	71.6	0.54
LGFHCL	62.5	-96.7	67.6	5.2	-74.1	69.6	-41.2	92.0	60.2	0.60
BRCYLF	-55.0	94.9	-70.3	54.6	-76.7	90.9	-29.7	223.2	331.5	0.40
LGFBBI	-30.5	84.8	-81.5	49.9	-49.7	78.2	-51.0	274.7	425.7	0.39
BR $\alpha$ $\beta$ LF	-34.6	86.1	-78.8	52.9	-59.5	82.5	-44.9	394.4	439.3	0.47
BR $\alpha$ LGf	-39.9	88.7	-78.1	54.2	-64.7	88.6	-43.2	414.2	457.4	0.48
BR $\omega$ LGf	-36.6	86.8	-75.6	46.4	-52.6	80.3	-45.9	378.3	424.2	0.47

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