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CONFORMATIONAL ASPECTS OF CARYOPHYLLENE.
POPULATION OF STABLE CONFORMERS AND RING INVERSION BARRIER OF TRANS CYCLONONENE RING PORTION

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Summary Cmr measurements of caryophyllene revealed two major conformers equilibrating in a ratio 76:24 at room temperature. The energy ordering of four possible conformers of caryophyllene predicted by molecular mechanics calculations agrees well with the experimental observation. The barrier of interconversion between the two conformers was determined as 16.25 kcal/mol.

Recently we have analysed¹⁾ conformational behavior of humulene and based on these analyses developed hitherto unknown "conformational selective transannular reactions".²⁾ We wish to report here population of stable conformers and ring inversion barrier of caryophyllene. Warnhoff et al³⁾ recognized the existence of two stable conformers of caryophyllene through an elabolate series of chemical reactions on a mixture of two stereoisomeric epoxides of caryophyllene which were thought to be derived from caryophyllene itself. They further attempted to show the existence of an equilibrium of two stable conformers, βα and ββ,⁴⁾ by means of variable temperature pmr spectrum but could not get conclusive results.

Molecular models indicate four strain minimum conformers (βα,ββ,αα,αβ)(Fig 1) which can be distinguished by the directions of exomethylene and olefinic methyl groups. The precise geometries and relative stabilities of the four principal conformers were obtained by application of molecular mechanics method.⁵⁾ Table 1 summarizes heats of formation and population at room temperature of the fully relaxed conformers.

Some of the cmr signals of caryophyllene are accompanied by a small peak at room temperature (Table 2). These pairs of peaks collapse at 120°. The temperature change in the spectra was reversible and thus should be attributed to conformational alternation. Analysis of the cmr spectra under gated decoupling without NOE mode revealed that population of the major conformers⁶⁾ was 76:24, which are in excellent conformity with the calculated one(Table 1). Moreover, the conformer ratio estimated by reactions with the 6,7-double

Table 1 Heats of formation (ΔH, kcal/mol) and populations(%) of four basic conformers

	βα	αα	ββ	αβ
ΔH	12.94	14.78	13.69	16.94
a	75.33	3.37	21.22	0.09
b	76		24	
c	78∼85		15∼22	
d	75		25	

a) Calculated populations
b) Values observed by cmr
c,d) The values estimated from the ratio of stereoisomeric products in the epoxidations(c)³⁾ and hydroboration(d).¹⁰⁾

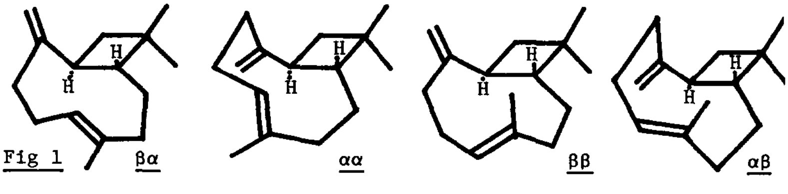

Fig 1 βα αα ββ αβ

bond coincides with this value as well.7) Signal assignments were made by comparison with the spectra of 6,7-epoxy- and 13-hydroxy-caryophyllene (Table 2). Dynamic cmr spectra were measured in nitrobenzene. The line shapes of three signals due to C-12, C-10 and C-2 (Table 1, denoted as A,B,C) were simulated8) to give an activation free energy of 16.25 kcal/mol (standard deviation: 0.11) at 35° for the conformational interconversion of caryophyllene (Fig 2). The observed value is unexpectedly small since values no less than 19.1 kcal/mol, the barrier of flipping in trans-cyclononene9), had been anticipated. The trans-fused cyclobutane ring and its attached exocyclic methylene group must have removed some of the freedom of inversion of the 9 membered ring in caryophyllene, but it appears that the balance of angle and torsional strain and non-bonded interactions in the pseudorotational transition state became less serious than in trans-cyclononene itself.

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References and Footnotes

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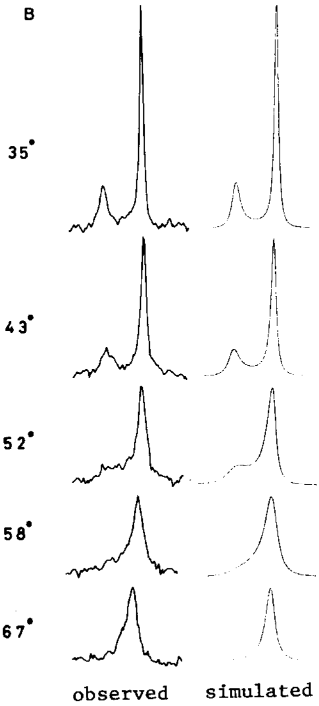

Fig 2

Temperature change of peak B (See Text and Table 2)

Table 2 Cmr spectra of caryophyllene(I) and its derivatives(II: 13-hydroxy-, III: 6,7-epoxy-caryophyllene) (δ $CDCl_3$)

		I	II	III
C-3		154.3s	155.3s	151.6s
C-7		134.9s	139.6s	59.5s
C-6		124.4d	126.4d	63.5d
C-12		117.7t	110.5t	112.7t
	A	(110.9)		
C-2 or	B	(55.9)d		
C-10		53.7d	52.0d	50.8d
C-2 or	C	(49.3)d		
C-10		48.5d	40.5d	48.7d
		(42.6)		
		40.5t	40.1t	39.8t
		40.0t	35.1t	39.1t
		34.8t	27.2t	30.2t
C-11		32.9s	33.2s	34.1s
		(31.4)		
C-14 or C-15		30.0q	30.0q	29.9q
		29.4t	26.6t	29.9t
		28.4t	25.1t	27.6t
C-14 or C-15		22.7q	22.9q	21.6q
		(22.0)q		
C-13		16.2q	66.9t	17.0q

Signals of the second conformer in parentheses.

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