MOLECULAR CONFORMATONS OF SOME TEN-MEMBERED RING SESQUITERPENES

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ABSTRACT

The conformations and geometries adopted by some ten-membered ring sesquiterpenes in the solid state has been examined. A preponderance of the Boat-Chair-Boat over all other forms is observed. The effect of substituents in determining the conformation has been elucidated. An inadequately assigned conformation in the literature has been revised, while conformations have been assigned to some of these rings for which no conformation had been earlier specified in the literature.

INTRODUCTION

The methods for calculation of conformations of normal and medium rings have the general limitation of increasing complexity as the ring size increases. Only for cyclopentane has mathematical expressions been developed for elucidating all the conformations in the pseudorotational circuit[1]. For medium size rings the greater flexibility affords a larger number of different shapes[2], and makes the development of mathematical expressions similar to those of cyclopentane rather difficult. This is partly because there are more rings representing energy minima of comparable magnitude and partly because these are of lower symmetry than rings like cyclohexane, in which all carbons are geometrically identical. Infact, for medium rings available evidence tends to implicate only symmetrical conformers as candidates of preferred energy minima, hence the confinement of analyses of medium rings to symmetrical forms[3].

In particular, no satisfactory systematic way for specifying the various conformations encountered for ten-membered rings in natural products has been worked out. According to Hendrickson[2], the basic symmetry elements through a ten-membered ring are either a plane or a two-fold axis of symmetry through the molecule, passing through either a pair of opposite atoms (type A) or midpoints of a pair of opposite bonds (type B). Some rings have only one of such symmetry elements, while some have more. Each definition of the symmetry element(s) in a ring produces a family of individual conformations, one of which will be the energetically preferred representative[3]. While the sign notation[2,4-5] or asymmetric parameters[5-8] may be used to describe the conformation of carboxylic rings, for some ten-membered rings this may not be an easy task. Infact, some ten-membered rings so described with three or more like signs in sequence are either not rings at all, or contain such severe interpenetrations of non-bonded atoms as not to be serious candidates for viable molecular conformations[3]. Consequently, several x-ray structure determinations of ten-membered rings have been reported in the literature[9-13] in which the authors were silent on the conformations of these rings.

We have shown elsewhere[5] that a combination of both the sign notation and other conformational parameters facilitates the unambiguous specification of ring conformations. This study was therefore, carried out to systematically parameterize the various conformations of cyclodecane ring derivatives in the solid state using the sign notation systrem proposed by Hendrickson[2], and the asymmetric parameters (ΔC_2 and ΔC_s) defined by Duax et al.[8]. Attempts have also been made to decipher factors which determine the various conformations adopted by these rings in various natural products with a view to facilitating the assignment of conformations following x-ray structure determinations.

EXPERIMENTAL

Calculation

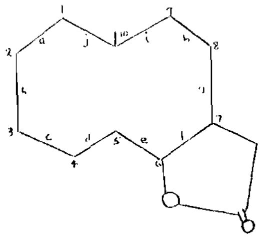
Structural data

Primary structural data for various compounds of sesquiterpenoid families were obtained from X-ray analyses in the literature with [illegible] generally less than 10%

Asymmetric and geometric parameters

Calculations of the conformational or asymmetric parameters (ΔC_s and ΔC_2) and (Σ/ϕ /) respectively, were made as described in previous papers[5-7]. The sequence of signs of the torsion angles was also used to further determine the conformation.

Atomic numbering scheme for 10-membered ring of sesquiterpenes



RESULTS AND DISCUSSION

Ring symmetries for the cyclodecane ring derivatives under study together with the ring conformations (obtained by the sign sequence of the torsion angles) are shown in Table 1. The basic symmetry element is either a two fold rotational axis or a mirror plane through the ring, the most prevalent element being the C_2 rotational axis. The C_s plane is observed clearly only in structures T3 and T13. In some cases (T10, T11, T22, T23), the mirror plane is destroyed probably because of severe distortions resulting from steric crowding of substituents on the cyclodecane ring. Conformation (ΔC_s and ΔC_2) and geometric (Σ/ϕ /) parameters are given in Table 2. The corresponding torsion angles are listed in Table 3. Figure 1 shows the shapes of some viable ten- membered rings encountered in this study while Figure 2 shows a plot of the asymmetric parameters ΔC_2(2-3) versus ΔC_s(3) or ΔC_s(5) of some of the cyclodecane ring derivatives. Chart 1 shows the molecular environments of the various rings examined.

Table 1: Geometric and conformational parameters for some cyclodecane ring derivatives.

Compound Code	Σ/ϕ /	ΔC_s	ΔC_2	Approx. symm. of torsion angle	Ref.
T1	739	38.3	30.1	C_2(1-2)	10
T2	941	25.4	7.2	C_2(1-2)	14
T3	942.1	33.03	55.4	C_s(2-3)	11
T4	951.9	32.5	51.3	C_2(2-3)	11
T5	843	56.1	44.1	C_2(4-5)	15
T6	660	85.5	36.1	C_2(4-5)	15
T7	904	43.8	22.01	C_2(2-3)	16
T8	872	56.1	47.8	C_2(2-3)	12
T9	898	42.3	42.2	C_2(2-4)	17
T10	884.8	-	41.8	C_2(3-4)	13
T11	914.1	-	39.5	C_2(3-4)	13
T12	778	57.9	48.2	C_2(2-3)	18
T13	957.3	43.9		C_s(4)	9
T14	1041	32.5	16.3	C_2(2-3)	19
T15	1062	30.15	21.65	C_2(2-3)	18
T16	1038.8	30.3	17.6	C_2(2-3)	20
T17	1056.3	32.2	19.4	C_2(2-3)	21
T18	1054	32.18	19.4	C_2(2-3)	21
T19	1049.1	36.4	12.18	C_2(2-3)	22
T20	1042	33.9	24.17	C_2(2-3)	23
T21	1038	33.2	30.7	C_2(2-3)	24
T22	853.3	-	67.2	C_2(2-3)	23
T23	889	-	70.1	C_2(4-5)	15

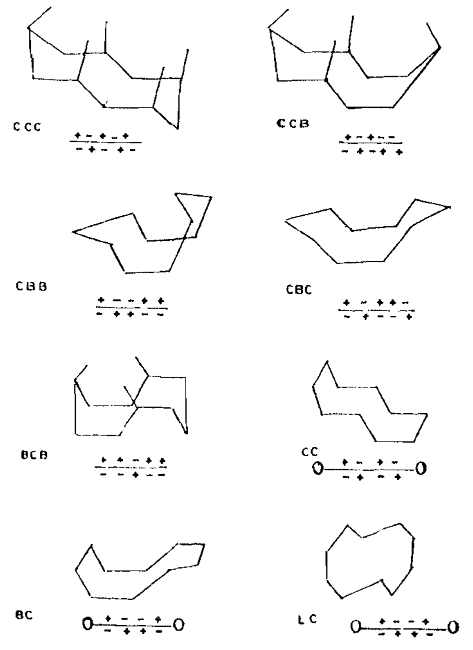
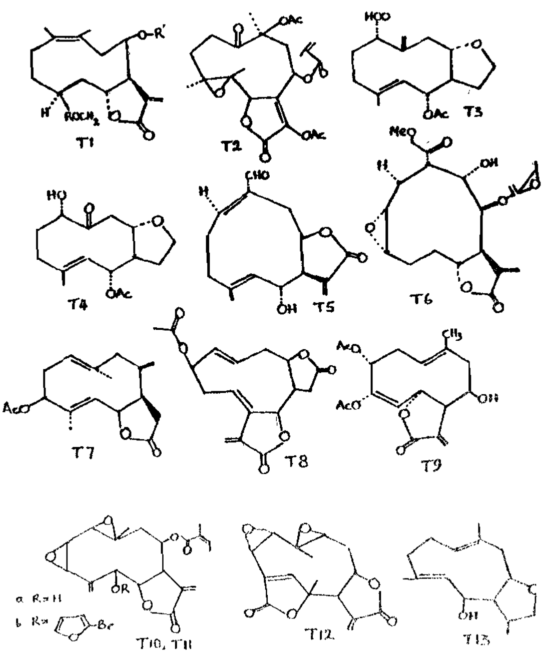


FIG. 1: SOME VIABLE 10-MEMBERED RINGS WITH PLANES OF SYMMETRY (PLANE / ATOM)



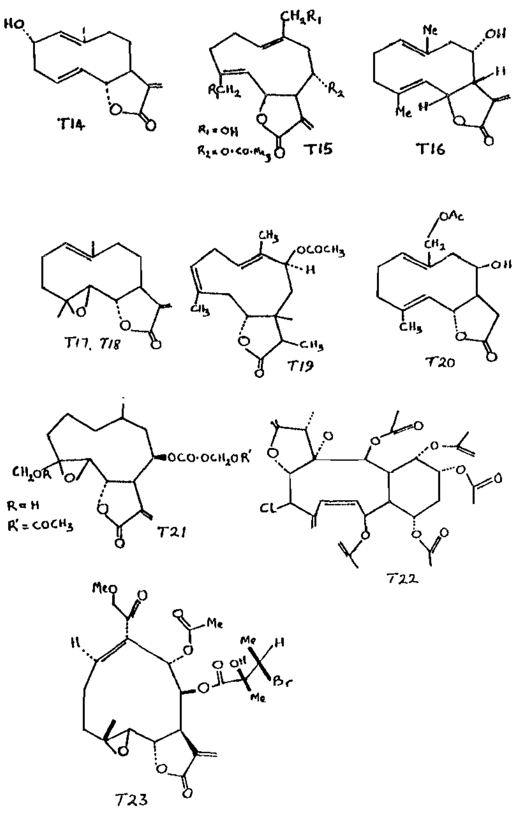


Chart 1: Structural formulas of compounds discussed showing the molecular environments of the cyclodecane derivatives.

The conformations of the rings with the chair central sub-unit i.e. Boat-Chair-Boat, BCB (T1-T11) appear to be the most viable owing to the peculiarly favourable torsion energy which outweighs the non-bonded strain situation, that is the 1,2-, 1,3- and 1,4-nonbonded interactions[2]. This form also has an axis perpendicular to its plane of symmetry; two parallel planes of three severely interacting substituents each found above and below the molecular plane (Fig. 3) and, as can be seen from Figure 2, does not undergo pseudo-rotation. The boat forms or boat regions in the conformations are identified by a pair of like signs occurring together as can be seen in Figure 1. It is observed that the cyclodecane ring derivatives adopting the BCB conformation generally have bulky substituents at either the C(8) and/or C(10) positions or may have a γ-lactone ring attached to the C(7) and C(8) positions (Chart 1). Relatively bulky substituents at the C(1), C(2) or C(3) position may also impose the BCB conformation on the ring, (T9). A keto substituent at C(10) as in T3 and T4 also tends to confer a BCB conformation on the ring.

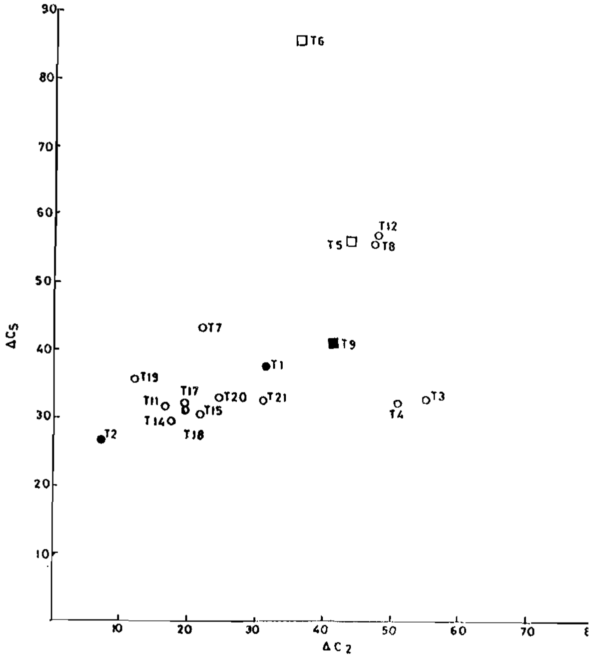


FIG. 2: CORRELATED VARIATION IN PRINCIPAL ASYMMETRY PARAMETERS $\Delta C_2(2-3)$, ○, $\Delta C_2(1\ 2)$, ●, $\Delta C_2(4-5)$, □, $\Delta C_2(3-4)$, ■, OF SOME CYCLODECANE DERIVATIVES

Table 2: Ring symmetries and conformations of some cyclodecane derivatives.

Compound code	Ring symmetry	Conformation
T1	C_2	BCB
T2	C_2	BCB
T3	C_s	BCB
T4	C_2	BCB
T5	C_2	BCB
T6	C_2	BCB
T7	C_2	BCB
T8	C_2	BCB
T9	C_2	BCB
T10	C_2	BCB
T11	C_2	BCB
T12	C_2	CCB
T13	C_s	CBC
T14	C_2	CCC
T15	C_2	CCC
T16	C_2	CCC
T17	C_2	CCC
T18	C_2	CCC
T19	C_2	CCC
T20	C_2	CCC
T21	C_2	CCC
T22	C_2	TCCC
T23	C_2	TCCC

T12 and T13 have the CCB and CBC conformations respectively (Table 2). The CCB which belongs to the same group as BCB (by having a chair central sub-unit) is intermediate in form between the more symmetrical CCC and the BCB conformers. With two lactone rings at the C(4)-C(6) and C(7)- C(8) bonds and two epoxide groups at C(1)-C(10) and C(2)-C(3); T12 adopts the CCB conformation. The CBC conformation belongs to another group of the boat family, that is the group that has a boat central sub-unit (BBB, CBB, CBC)[2]. All three forms suffer from non-bonded interactions, with the CBC having a 1,3-nonbonded interaction (Fig. 1). This is as a result of the strain imposed by the central boat unit and all three have two eclipsed bonds. T13 was reported to have the BB (type B) conformation[9] but is shown to have the CBC conformation (type A) in this study. The sign sequence of the torsion angles (Table 3) shows that T13 has a CBC conformation, with approximate Cs(4) symmetry for the torsion angles. Furthermore, the BB conformation is not a viable form of the type B cyclodecanes, having energetically unfavourable eclipsed butane units and severe H-H interpenetrations[4]. The position of the lactol ring (i.e. C(7)-C(8) in T13 and the absence of axial substituent may be responsible for the adoption of the transient (i.e. CBC) conformation of the cyclodecane derivative.

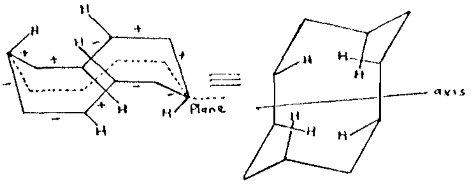


Fig.J BCB form of cyclodecane showing substituent positions and ring symmetry.

Table 3. Endocyclic torsion angles of some cyclodecane derivatives.

Code	a	b	c	d	e	f	g	h	i	j
T1	-119	48	79	-70	-65	143	-61	-45	105	-4
T2	-143	55	55	-149	102	-57	103	-148	61	68
T3	53.7	30.4	-1062	164.8	-108 1	65.4	-116.1	74.9	71.8	-150 7
T4	54.9	31.6	-106.9	163.5	-110 9	70.8	-116.2	70.4	73	-153.7
T5	-90	73	-87	165	-121	65	-38	-65	136	-3
T6	-56	14	-54	155	-101	36	-71	-44	125	4
T7	-91	53	-80.3	-163.2	122.5	14.4	-78.7	43.3	91.3	-166.2
T8	51	-115	109	1	-115	94	-54	113	-169	51
T9	-80	-58	92	4	-124	135	-80	61	-96	168
T10	-110.7	-0.9	92 4	-70.4	-64.8	158.6	-91.7	56.5	-87.6	151.2
T11	-114.6	-3.6	99.1	-69.2	-71.6	157.4	-93.7	66 4	-89.9	148.6
T12	66	-3	55	163	116	-2	-90	73	57	-153
T13	-71.3	-37	94	-158.8	90	56	-116.2	78 7	-92.4	162.7
T14	-101	54	-89	156	-132	87	-79	67	-111	165
T15	-107	50	-83	154	-137	93	97	76	-108	165
T16	97.5	50,4	-85.7	155	-136	89.9	-75.7	66.6	-115.4	166.6
T17	-109.7	52.5	-89.5	145.8	-121.3	95.8	-91.6	76.4	-105.8	167.9
T18	-105.1	93.3	-85.7	147.8	-126.8	95.7	-87.5	74.2	-111.2	168.7
T19	-100.3	50.5	-87.5	157.2	-130.0	86	-82.2	75.2	-114.8	164.8
T20	-100.1	50.1	-87.7	152.1	-133 6	98.6	-50.7	62.4	-108.7	168
T21	-101	55	-82	146	-131	101	-50	55	-111	176
T22	62	43.6	115.6	-5.4	129.3	-80	56.3	-99.5	132.9	-127.5
T23	-97	75	-92	147	-119	95	-83	56	132	13

The all-chair, (CCC) form, T14-T21 contain lactone rings fused at positions C(6)-C(7) and, in most cases, contain double bonds at C(1) and C(10) and C(4)-C(5). T17, T18 and T21 all have C(4)-C(5) epoxide instead of the double bond. Fusion of the five-membered ring (whether cis- or trans-) seems not to affect the conformation of the ten-membered ring. While this is also true for rings adopting the BCB conformation, the position of the five-membered ring appears to be one of the criteria for adopting the CCC conformation. All the rings that adopt the CCC conformation do not have β-oriented (axial) substituents at the C(8) position. T15 and T16 have β-oriented substituents at C(8), but this seems to be of no consequence to the conformation adopted by the rings.

T22 and T23 adopt conformations close to the twist-chair-chair-chair (TCCC). Both have three like signs in sequence (Table 3) and are either not rings at all or they contain severe interpenetrations of non-bonded substituent groups. Both have bulky and/or sterically demanding substituents at C(6) to C(10). This unusual conformation is probably adopted to minimize the enhanced unfavourable steric strain introduced into the CCC form by these substituents. A BCB conformation is not adopted in the two cases as this form is known to be sterically more strained than the all-chair form.

CONCLUSIONS

Although the preferred form of cyclodecane is thought to be the BCB form owing to its peculiarly favourable torsional energy compared to the all-chair form, a preponderance ratio 11 (BCB) rings to 8 (CCC) rings is observed in this study. The stereochemistry of fusion of the five-membered rings to the cyclodecane derivatives seem not to affect the conformation of the ten-membered rings. However, the position of the five-membered ring is important. The CBC conformation appears to require fusion of a five-membered γ-lactone ring at the C(6)-C(7) bond. An axial substituent on C(8) or at the C(2) and C(3) atoms of cyclodecane ring derivatives tend to prefer the BCB conformation. The conformation of T13 has been revised from the BB earlier assigned to it to the CBC conformation based on this study.

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