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SPATIAL STRUCTURES OF NATURAL SESQUITERPENES OF THE HUMULENE TYPE

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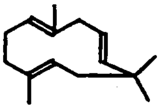
UDC 548.737

The spatial structures of the natural sesquiterpenes α-,β-, and γ-humulenes have been studied by the method of molecular mechanics (MM). The conformational states of the 11-membered macrocycle in the humulenes have been analyzed on the basis of calculated figures and x-ray structural results. It has been shown that four conformational states, differing by the mutual positions of the C14 and C15 methyl groups and the C7 and C8 atoms relative to the plane of the macrocycle are characteristic for all humulenes. These conformational states are denoted as $_{14}U^{8}{}_{7}$, $^{14}U^{8}{}_{7}$, $_{14}U^{7}{}_{8}$, and $^{14}U^{7}{}_{8}$. The conformational flexibility of the 11-membered ring in the humulenes has been evaluated.

Derivatives of humulenes — monocyclic sesquiterpenes — are precursors of bicyclic sesquiterpenes widely distributed in Nature [1]. The first representative of the humulene derivatives — α-humulene (1) — was isolated from a plant as long ago as 1895 [2]. The complete hydrogenation of (1) forms a compound identical with the 4,10,11,11-tetramethylcycloundecane (4) obtained synthetically [3]. In the 1960's, together with α-humulene, its isomer, β-humulene (2), was detected in plants [4], and, later, so was γ-humulene (3) [5]. Various derivatives of these isomers — esters, epoxides, ketones, alcohols, and other compounds — have also been detected in Nature.



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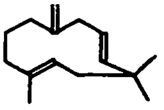

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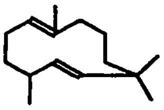

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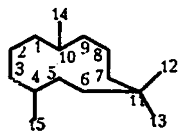

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In the humuladienes and humulatrienes, the double bonds exhibit different reactivities on hydrogenation and oxidation, which is due to their different configurations. Theoretically, in terms of differences in the orientations of the *cis*- and *trans*- configurations of the 1(10), 4(5), and 7(8) double bonds, the α-humulenes may form six subgroups. 1(10),4(5),7(8)-*trans*(E)-humulatrienes, 1(10),4(5)-*trans*(E)-humuladienes, and 1,(10)-*trans*(E),4(5)-*cis*(Z)-humuladiene, called α-apienes [6] (see below), have been found in Nature. Representatives of the β- and γ-humulenes isolated from plants have been little studied, and, therefore, there is as yet no such classification for them. It is assumed that the β- and γ-humulenes have, respectively, the 4(5),7(8)E- and 1(10),5(6)E- configurations of the double bonds [1].

The conformation of the labile 11-membered macrocycle in a humulene determines the chemical behavior of the molecule. In particular, on the transannular cyclization of the cyclopolyenes the yield of final product largely depends on the conformational state of the molecule [7, 8]. On the basis of results of the low-temperature PMR spectroscopy of the humulenes, Roberts et al. [9] have shown the existence of a barrier to conformational transitions, but they did not demonstrate precisely what stable conformations exist in solution, even though general approaches to a description of the 11-membered ring are given in the literature [10, 11]. Up to the present time, the stereochemical aspects of the 11-membered ring for natural humulenes have not been generalized, as has been done, for instance, for the germacrolides [12]. Individual

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TABLE 1. Calculated Torsion Angles (degrees) and Strain Energies (kcal/mole) of the Four Conformations of 1(10),4(5)E-Humuladiene and 1(10), 4(5), 7(8)E-Humulatriene [13] (in parentheses)

Angle	Conformation			
	${}_{14}U^{7}_{8}$	${}^{14}U^{8}_{7}$	${}_{14}U^{8}_{7}$	${}^{14}U^{7}_{8}$
1-2-3-4	46 (45)	47 (46)	34 (37)	54 (54)
2-3-4-5	−105 (−105)	−99 (−103)	−42 (−46)	−103(−105)
3-4-5-6	173 (173)	172 (172)	172 (174)	178 (174)
4-5-6-11	−126 (−127)	−141 (−131)	−147 (−141)	−120 (−120)
5-6-11-7	42 (39)	43 (36)	37 (31)	47 (47)
6-11-7-8	−102 (−107)	64 (72)	55 (54)	−96 (−101)
11-7-8-9	150 (148)	−147 (−168)	−153 (−168)	157 (154)
7-8-9-10	−83 (−89)	88 (97)	58 (84)	−66 (−68)
8-9-10-1	93 (84)	−91 (−77)	62 (66)	−62 (−64)
9-10-1-2	−172 (−168)	172 (168)	−167 (−166)	172 (174)
10-1-2-3	74 (81)	−111 (−120)	142 (175)	−113 (−115)
E stress	25.1 (23.7)	23.1 (24.8)	27.1 (27.4)	22.7 (24.0)

TABLE 2. Torsion Angles (from XSA) of the 1(10),4(5), 7(8)E- Humulatrienes and 1(10),4(5)E-Humuladienes

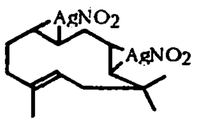
Angle	5	6	7	8*	9	10	11
	${}_{14}U^{7}_{8}$				${}^{14}U^{8}_{7}$	${}^{14}U^{7}_{8}$	
1-2-3-4	35	54	52	60	57	61	50
2-3-4-5	−109	−104	−109	−111	−88	−103	−95
3-4-5-6	172	157	157	158	167	175	161
4-5-6-11	−126	−138	−123	−127	−166	−132	−115
5-6-11-7	55	58	47	55	50	62	64
6-11-7-8	−102	−100	−106	−102	60	−96	−118
11-7-8-9	156	153	169	153	−132	147	151
7-8-9-10	−94	−94	−89	−91	84	−71	−59
8-9-10-1	95	81	73	87	−110	−64	−41
9-10-1-2	−162	−157	−153	−153	173	167	172
10-1-2-3	77	77	89	63	−102	−110	−130

results on the determination of crystal structure and calculations of the conformational states of α- and β-humulenes are given in [13]. The present paper is an attempt to analyze the conformation of the 11-membered carbon backbone of the α-, β-, and γ-humulenes (including the α- and γ-apienes) on the basis of x-ray structural results and calculations by the MM method.

α-Humulenes

Several conformational states are possible for the saturated 4, 10, 11, 11-tetramethylundecane (4) — humulane — but the endo-inclusion of double bonds (or the stereochemically equivalent epoxy groups) in the ring sharply decreases their number. In [10], four conformational forms have been determined by the MM method for α-humulene, with three *trans*-double bonds: chair-chair (CC), chair-twist (CT), twist-chair (TC), and twist-twist (TT).

According to calculations performed by the MM method [13], in the 1(10),4(5),7(8)E-humulatrienes the CC and CT conformations are energetically the most favorable. This has been confirmed experimentally by the results of x-ray structural analysis (XSA) of the adduct of a humulene with $AgNO_3$ (5) [14] and of the triepoxyhumulene (6) [15], in each of which the macrocycle assumes the CT conformation.



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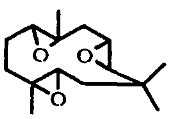

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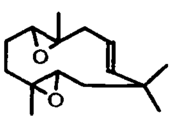

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Depending on the presence of various endo- and exocyclic substituents in the 11-membered macrocycle, the torsion angle between the plane moieties varies and the conformations proposed above are not retained. For example, in the presence of a sp^2 C9 atom the macrocycle is appreciably distorted, while in the absence of the C1=C10 double bond in the structures

TABLE 3. Torsion Angles (from XSA) of the 1(10)E,4(5)Z-Humuladienes

Angle	14[28]*		15[29]*		16[30]*		17[32]	18[33]	19[34]
	$_{14}U^7_8$		$_{14}U^7_8$	$^{14}U^7_8$	$_{14}U^7_8$		$^{14}U^7_8$	$_{14}U^7_8$	$^{14}U^7_8$
1–2–3–4	65	64	63	74	67	64	80	63	70
2–3–4–5	–113	–108	–108	–107	–119	–118	–110	–117	–97
3–4–5–6	5	–12	–4	–1	1	–2	–3	1	–3
4–5–6–11	134	137	136	141	124	128	134	128	153
5–6–11–7	–73	–65	–72	–64	–71	–71	–74	–79	–68
6–11–7–8	–74	–79	–79	–70	–70	–70	–54	–69	–66
11–7–8–9	131	145	140	145	152	156	154	149	130
7–8–9–10	–73	–84	–78	–66	–91	–93	–71	–89	–60
8–9–10–1	103	94	96	–58	82	78	–56	91	–69
9–10–1–2	–172	–164	–168	168	–147	–151	153	–151	175
10–1–2–3	70	82	80	–101	79	86	–97	79	–102

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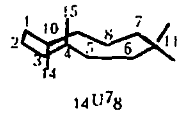
*In the crystal there are two molecules of the substance in the independent part of the unit cell.

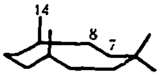
TABLE 4. Torsion Angles of the Four Conformers of β-Humulene (from MM results) and of Natural 4(5),7(8)E-Humuladienes (from XSA results)

Angle	2 (β-Humulene)				20		21	22
	$^{14}U^8_7$	$_{14}U^7_8$	$_{14}U^8_7$	$^{14}U^7_8$	$_{14}U^8_7$	$^{14}U^7_8$	$^{14}U^7_8$	$^{14}U^7_8$
1–2–3–4	57	52	46	64	63	78	80	82
2–3–4–5	–115	–119	–118	–122	67	–95	–97	–98
3–4–5–6	175	172	172	178	–164	166	167	166
4–5–6–11	–121	–122	–136	–109	110	–104	–104	–101
5–6–11–7	39	41	32	49	–53	45	45	45
6–11–7–8	52	–92	52	–84	112	–120	–119	–128
11–7–8–9	–175	173	–171	176	–177	168	167	167
7–8–9–10	113	–106	89	–94	115	–119	–120	–123
8–9–10–1	–76	84	71	–66	–56	47	45	48
9–10–1–2	137	–145	–146	135	99	80	79	75
10–1–2–3	–101	63	55	–88	–160	–154	–152	–154

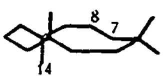
of humulene dihydronitroside [18] and other nitro derivatives of humulene [19] (see below) it assumes new "nonstandard" forms. Consequently, it is just the conformation of the macrocycle that determines the positions of the C14 methyl group and of the C7 and C8 atoms relative to the mean square plane of the 11-membered ring. The conventional conformations CC, CT, TC, and TT may be denoted as $_{14}U^8{}_7$, $^{14}U^8{}_7$, $_{14}U^7{}_8$, and $^{14}U^7{}_8$, respectively. The indices show the positions of the atoms relative to the plane of the humulane ring. Perspective views of these conformational states are given below.



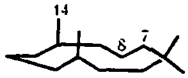
$_{14}U^7{}_8$



$_{14}U^8{}_7$



$_{14}U^8{}_7$



$_{14}U^7{}_8$

In our opinion, these conventional conformational states can be considered as applicable to the 1(10),4(5)E-humuladienes, as well. In actual fact, on comparing the experimental torsion angles of humulane triepoxide [15] and humulane diepoxide (7) [20] no appreciable differences are found; i.e., in the crystal, humulane diepoxide has the same $_{14}U^7{}_8$ conformation as is realized in humulane triepoxide. Calculations of the model α-humuladiene that we have performed by the MM method confirm the above conclusion. The calculated torsion angles of the four conformational states of α-humuladiene and of the model 1(10),4(5)E-humuladiene are given in Table 1. Differences are observed in the torsion angles 11–7–8–9 (a systematic decrease averaging 18° because of the absence of a double bond) and 7–8–9–10 (26°) in the $_{14}U^8{}_7$ conformation, while in the others the difference does not exceed 10-12°. In the model humuladiene, the $^{14}U^7{}_8$ and $^{14}U^8{}_7$ conformations proved to be energetically favorable, and not $_{14}U^7{}_8$ and $^{14}U^8{}_7$, as in humulatriene [13]. In both cases, the $_{14}U^8{}_7$ conformation was unfavorable. It was 3-4 kcal/mole less favorable than the other three, although the latter differed by not more than 1.1 kcal/mole.

TABLE 5. Torsion Angles of the Four Conformational States of Model γ-Apiene (from MM results)

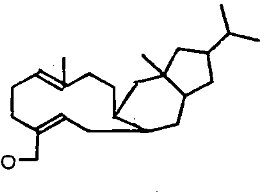
Angle	Conformation			
	${}_{14}U^7{}_8$	${}^{14}U^8{}_7$	${}_{14}U^8{}_7$	${}^{14}U^7{}_8$
1–2–3–4	57	73	55	70
2–3–4–5	–86	–83	–87	–85
3–4–5–6	–3	–1	–2	–2
4–5–6–11	175	176	175	175
5–6–11–7	–102	–135	–130	–96
6–11–7–8	–64	68	57	–54
11–7–8–9	99	–93	–115	112
7–8–9–10	–79	74	67	65
8–9–10–1	107	–115	64	–67
9–10–1–2	–177	177	–177	177
10–1–2–3	82	–96	84	–96

TABLE 6. Strain Energies of the Four Conformational States in the Sesquiterpene α-, β-, and γ-Humulenes

Compound	E_{strain}, kcal/mole			
	${}_{14}U^7{}_8$	${}^{14}U^8{}_7$	${}_{14}U^8{}_7$	${}^{14}U^7{}_8$
1. 1(10)E,4(5)E,7(8)E-Humulatriene [7]	23.7	24.8	27.4	24.0
1(10)E,4(5)E-Humulatriene	25.1	23.1	27.1	22.7
12. 1(10)E,4(5)Z,7(8)E-Humulatriene	23.8	23.8	23.9	23.7
13. 1(10)E,4(5)Z-Humuladiene (α-apiene)	22.1	24.4	24.6	20.9
14. Juniferol	25.3*	28.1	28.3	23.9*
15. Juniferdin	44.1*	47.3	47.3	43.2
16. Fexerol	25.6*	–	28.3	–
17. Caucalol	27.8*	–	29.8	–
2. β-Humulene	20.1	20.5	21.2	20.7
20. Humulene nitrosite [16]	67.3*	81.0	84.3	65.9*
3. γ-Humulene	25.1	23.9	24.9	24.4
4(15),5(6)Z-γ-Humulene	26.6	31.6	27.5	28.5
23. Fecerol	28.9	24.8	25.6	27.8
24. Farvalol	26.9	26.0	26.6	26.9

*Conformation experimentally observed in crystals.

Attention is attracted by the fact that the bulk of the humuladienes with known structures consists of bicyclic diterpene humulanes — the dollabellanes (**8**–**15**), isolated from plants of the Barbiophozia family and containing in the 7(11) position a *trans*-linked substituted five-membered ring. In spite of the condensation of the humulane skeleton with a fairly rigid six- or five-membered ring, in *p*-bromophenacyl stellatate (**8**) [21] the ${}^{14}U^8{}_7$ conformation is realized, while in 6β,12β-dihydroxydolabella-3E,7E-diene 6-*p*-bromobenzoate (**9**) [22] and 6β-acetoxy-3S,4S-epoxy-12β-hydroxydolabella-3E,7E-diene (**10**) [22] the macrocycle has a ${}^{14}U^7{}_8$ conformation, close to one of the four mentioned above.



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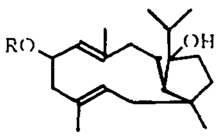


9 R=COC$_6$H$_5$. **10** R=COCH$_3$. **11** R=H

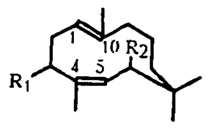
However, some of the dolabellanes also containing a condensed five-membered ring in the macrocycle depart from this relationship [24, 25]. Table 2 gives the torsion angles of the known humuladienes and humulatrienes obtained from XSA results. It follows from this table that in the crystals of 1(10),4(5),7(8)E-humulatrienes and 1(10),4(5)E-humuladienes it is mainly the ${}_{14}U^7{}_8$, ${}^{14}U^8{}_7$, and ${}^{14}U^7{}_8$ conformations that are realized. The ${}_{14}U^8{}_7$ conformation is the energetically most unfavorable and has not been detected experimentally in the known humulanes.

1(10),4(5)Z-Humuladienes — α-Apienes

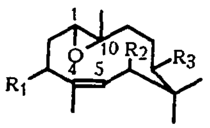
Humulenoids with 4(5)-*cis*- double bonds have been isolated only from plants of the Apiaceae family and have therefore acquired the name of apienes [6, 26]. To analyze the conformation of the 11-membered macrocycle we have used the results of x-ray structural investigations [25, 28-34].

The apienes are natural derivatives of cycloundecadiene and differ from the α-humulanes considered above by the *cis*-configuration of the 4(5) double bond. Compounds have been found in which there is an epoxy group in place of the double bond in the 1(10) position.

In an x-ray structural investigation of the spatial structure of juniferol (**14**) [29], it was found that two conformations of the 11-membered macrocycle are realized in the crystal. Analysis of the literature on the spatial structure of the α-apienes has shown that, as in other known compounds (**17**, **18**), again, both these stable conformations, which differ by the orientation of the C14 methyl group relative to the plane of the humulane ring, are realized.

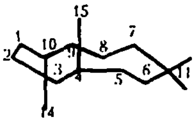


13 $R_1=R_2=H$
14 $R_1=R_2=\alpha OH$
15 $R_1=OCOC_5H_4OH, R_2=OH$

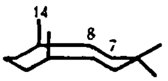


16 $R_1=R_2=\alpha OH, R_3=H$
17 $R_1=R_3=H, R_2=\beta OH$
18 $R_1=H, R_2=\beta OH, R_3=\alpha OH$

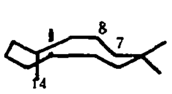
The conformations calculated by the MM method of 1(10)E,4(5)Z,7(8)E-humulatriene — α-humulene (**12**) — and of the unsubstituted model 1(10)E,4(5)Z-humuladiene — α-apiene (**13**) —, differing from (**12**) by the absence of the 7(8)- double bond, permit the conclusion that in these compounds, as well, four conformations are realized:



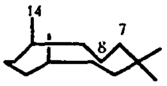
$_{14}U^{7}{}_{8}$



$^{14}U^{8}{}_{7}$



$_{14}U^{8}{}_{7}$



$^{14}U^{7}{}_{8}$

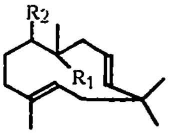
The four conformers possible for α-apiene are shown in the figure. It must be mentioned that in compounds (**14-18**), in spite of the absence of a C7–C8 double bond, the torsion angle 11-7-8-9 has a value close to that characteristic for the case where the double bond is present. The calculated torsion angles of the macrocycles in the natural α-apienes are comparable with the experimental values (Table 3) [27].

The strain energies of the (**12-17**) molecules are given in Table 6, from which it can be seen that for the model 1(10)E,4(5)Z,7(8)E- compound — α-humulene —, all four conformations are energetically close and can therefore be realized with equal probabilities. However, in the unsubstituted model α-apiene (**13**) and its natural derivatives — juniferol (**14**) and juniferdin (**15**) — the $_{14}U^{7}{}_{8}$ and $^{14}U^{7}{}_{8}$ conformations must be realized with the greatest probability, even though only the $_{14}U^{7}{}_{8}$ conformation is observed in the juniferdin crystal. In fexerol and neocaucalol the $^{14}U^{8}{}_{7}$ and $^{14}U^{7}{}_{8}$ conformations are sterically impossible because of the strain due to the epoxy group in the C1–C10 position. However, the $^{14}U^{7}{}_{8}$ conformation is realized in caucalol, which differs from neocaucalol by the configuration of the epoxy attachment at C1–C10. In caucalol the $_{14}U^{7}{}_{8}$ and $_{14}U^{8}{}_{7}$ conformations are sterically impracticable.

The conformational transitions modeled in MM by the changes in the torsion angles at the C8–C9 and C9–C10 bonds in unsubstituted α-apiene and its natural derivatives amount to 7-9 kcal/mole [29], which shows the ease of a change in conformations at room temperature [35]. Calculations of the amounts of each of the isomers on the basis of the energy characteristics of the natural α-apienes show that in solution at room temperature the $_{14}U^{7}{}_{8}$ and $^{14}U^{7}{}_{8}$ conformations amount to 99.9%.

β-Humulenes

The existence of α-humulene and its isomer β-humulene (**2**), differing by the positions of the double bonds, was reported by Benešová et al. [4] in 1961. However, the conformation of the 11-membered macrocycle has been investigated mainly for the natural 10,14-dihydro derivatives of β-humulene (**20-22**) (they can also be regarded as 1,10-dihydro derivatives of α-humulene) by the XSA method, and calculations have been made by the MM method [18, 19]. The x-ray structural analysis showed that humulane nitrosite (**20**) crystallizes in two forms (acicular and tabular), and that these crystals contain different conformers of the same molecule [18]. The authors concerned [18] proposed four possible conformations of the macrocycle of the humulane nitrosite molecule. These conformations are also characterized by the mutual positions of the C14 and C15 methyl groups and the C7=C8 double bonds relative to the plane of the 11-membered macrocycle. In crystals of (**20**), the energetically close $_{14}U^{8}_{7}$ and $^{14}U^{7}_{8}$ conformers (the difference amounts to 1.4 kcal/mole) are realized, while $_{14}U^{7}_{8}$ and $^{14}U^{8}_{7}$ are appreciably inferior to them in energy. The strain energy in the latter two is 20 kcal/mole higher than in the other two. At room temperature (295 K) the amounts of the first two isomers in solution are 64 and 36%, respectively [18].



20 R_1=NO,R_2=NO_2
21 R_1=R_2=NO_2
22 R_1=ONO_2,R_2=NO_2

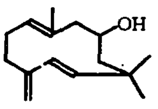
Calculations that we have performed by the MM method for the unsubstituted model β-humulene (**2**) likewise confirmed the presence of four conformations of the 11-membered macrocycle. The spatial structures of these conformers are shown above. For compound (**2**) the probability of the existence of the four conformations is high, as is shown by their energy characteristics (see Table 6). The difference in E_{strain} for these conformational states is not more than 1.1 kcal/mole.

Thus, depending on the presence of substituents in the 11-membered macrocycle and the influence of the medium (solvent or crystal field), the β-humulenes may assume any of the four conformations under consideration. It must be mentioned that in the model β-humulene and others of its nitro derivatives the $_{14}U^{8}_{7}$ conformation is energetically less favorable, similarly to what is observed in the α-humulenes.

Table 4 gives the calculated (MM) torsion angles of the unsubstituted compound (**2**) and the experimental (XSA) values for its nitro derivatives. A comparison of the values of the torsion angles for the four conformations of (**2**) with those observed in (**20**), (**21**), and (**22**) shows the absence of symbaticity of their magnitudes. This permits the assumption that when the C_{sp^2}-hybridized C1 atom is replaced by C_{sp^3}, the possibility of the realization of new conformations of the 11-membered macrocycle increases, and it assumes a "nontraditional" form.

γ-Humulenes

Natural γ-humulenes (or γ-apienes) have been isolated only from plants of the *Ferula* genus belonging to the Apiaceae family. Fecerol (**23**) and its various esters [36, 37] were isolated from *F. cerotophylla* and *F. junipera*, and derivatives of fervanol (**24**) [6, 38] from *F. haussknechtii* and *F. juniperina*.



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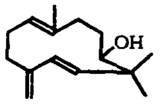

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Structurally, they differ from other humulenes by the positions of the double bonds. In the γ-apienes the double bonds are present in the C4=C15, C5=C6, and, traditionally, C1=C10 positions. The spatial structure of the γ-apienes has not so far been studied by the x-ray structural method.

We have calculated the conformational states of the 11-membered macrocycle in the γ-apienes. In them, the mobility of the 11-membered macrocycle is highly restricted because of the two fairly planar fragments (the C3–C6, C11 and the C1, C2, C9, C10 moieties) and their mutual repulsion. It must be mentioned that in the first planar section two mutual positions of the *exo*-4(15) and *endo*-5(6) double bonds (*trans*- and *cis*-) relative to the C4–C5 bond are possible.

As calculations by the MM method show, in the *trans*- variant for the γ-humulanes (like the α-apienes) there are four conformers with close energy states (see Tables 5 and 6). These conformational states of the 11-membered macrocycle can be characterized as ${}_{14}U^{7}_{8}$, ${}^{14}U^{8}_{7}$, ${}_{14}U^{8}_{7}$, and ${}^{14}U^{7}_{8}$. It can be seen from Table 6 that the difference in E_{strain} between the energetically favorable ${}^{14}U^{8}_{7}$ and most unfavorable ${}_{14}U^{8}_{7}$ conformations in the model γ-apiene is only 1.2 kcal/mole. Again, no clearly favorable conformation is observed in natural γ-apiene derivatives.

In the *cis*- variant, (the C15=C4 and C5=C6 double bonds in the *cis*- position) all four conformations of the 11-membered macrocycle are energetically less favorable than those considered above. According to Table 6, for the 4(15),5(6)-*cis*-γ-apienes the strain energy is higher by an average of 4 kcal/mole than for their *trans*- analogs, which show the realization of the *trans*- positions of the C4=C15 and C5=C6 double bonds. This fact has been confirmed by NMR investigations of fervanol esters [6].

Calculations performed for natural α-apienes show that in fervanol more than half (57%) of the molecules are in the ${}^{14}U^{8}_{7}$ conformation, least of all in the ${}^{14}U^{8}_{7}$ and ${}_{14}U^{7}_{8}$ (13% each), and 16% of the molecules in the ${}_{14}U^{8}_{7}$ conformation. In fecerol, the 11-membered macrocycle assumes mainly the ${}^{14}U^{8}_{7}$ (79%) and ${}_{14}U^{8}_{7}$ (20%) conformations.

Thus, analysis of the literature and calculations by the MM method show that the 11-membered macrocycle in the α-humuladienes, α-apienes, β-humulenes, and γ-apienes assumes four most probable conformations. In the α, β-, and γ-humulenes and their derivatives, the conformation of the 11-membered macrocycle may be denoted as ${}_{14}U^{7}_{8}$, ${}^{14}U^{8}_{7}$, ${}_{14}U^{8}_{7}$, and ${}^{14}U^{7}_{8}$.

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