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MOLECULAR MECHANICS STUDIES ON HUMULENE CONFORMATIONS AND ITS RELATIONS TO BIOSYNTHETIC ROUTE TO ILLUDOIDS

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In a transannular cyclization of medium sized cyclopolyene, the product is often determined by the stable conformation of starting material.[1] Our recent study of the complex transannular cyclizations of humulene[2] prompts us to investigate its conformational behavior, which may dictate the course of reaction. Inspection of molecular models shows that each plane of three trans double bonds are placed approximately perpendicular to the average molecular plane so that four stable conformations could soon be envisaged (CT, CC, TT, TC shown in Fig. 1).[3] In its crystalline complex with $AgNO_3$, humulene is known to assume the CT form by X-ray analysis.[4] Roberts and his co-workers[5] examined the pmr spectra of humulene at low temperatures, however, he could only estimate the flipping barrier of humulene ring and gave no information about the most stable conformation in solution state.

In the absence of any experimental clue to the predominant conformation of humulene in solution, we resorted to molecular mechanics calculations[6] to assess relative stabilities of its conformers. Energy minimization of the four principal conformers could be successfully achieved indicating that they certainly represent four local minima in humulene energy super-

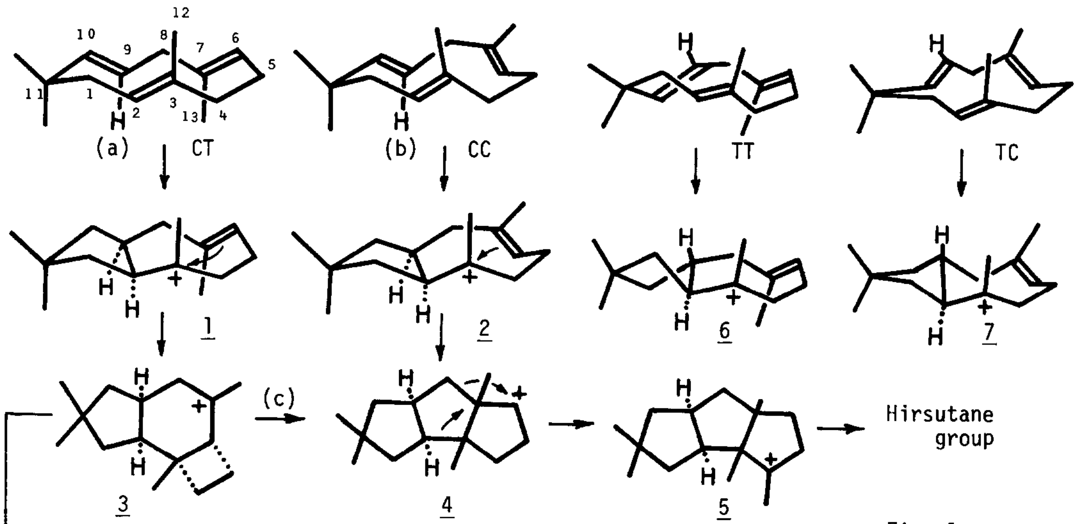

Fig. 1

surface. Table 1 summarizes heats of formation and dihedral angles of fully reluxed basic conformers and their perspective stereodrawings are depicted in Fig. 2. As shown in the table, conformations CT and CC are significantly more stable than others.

These results coincide with the facts observed in the biosynthesis of illudoids[7)] and in the humulene chemistry.[1c,2)] In the illudoids biosynthesis[7)] and also in the transannular cyclization of humulene with Hg^{++},[2)] C_2-C_9 bond is formed exclusively so as to give cis-bicyclo-[6.3.0]undecane system (3,6-secoprotoilludene; 1 and 2 shown as cations). The conformers TT and TC would have led to a trans bicyclic compound (pseudo-3,6-secoprotoilludene; 6 and 7 shown as cations) which has been found neither in natural products nor in the products of trans-annular reactions of humulene, so far. If the conformations CT and CC would be kept almost unchanged through the reactions to illudoids, the existence of two biosynthetic paths[8)] (CT→protoilludane (a) and CC→hirsutane (b)) can be implied instead of assuming a single route (CT→protoilludane→hirsutane (c)).[9)] These suppositions reminds us of a fact[10)] that co-occurrence of hirsutanoids and other illudoids has not been recognized.

References and Notes

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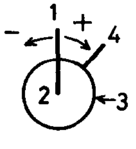
Table 1

		$AgNO_3$ complex*	CT	CC	TT	TC	
Heats of Formation		19.54	4.24	4.47	7.86	5.30	Kcal/mol (25°, gas)
Dihedral Angles	1--2==3--4#	-172.2	-173.2	-174.2	-173.6	-172.3	
	2==3--4--5	108.6	105.3	105.0	105.7	103.0	
	3--4--5--6	-35.1	-44.8	-45.1	-37.2	-46.4	
	4--5--6==7	-77.0	-80.9	124.7	-75.3	120.5	
	5--6==7--8	161.8	167.6	-173.9	166.4	-168.4	
	6==7--8--9	-95.0	-84.2	44.7	-66.3	77.1	
	7--8--9==10	94.0	88.7	58.2	-83.8	-97.2	
	8--9==10--11	-156.5	-167.9	-174.5	167.6	168.3	
	9==10--11--1	102.2	107.4	121.0	-54.9	-71.9	
	10--11--1--2	-55.0	-39.7	-44.4	-31.2	-35.7	
	11--1--2==3	126.2	127.4	110.4	140.6	130.7	

* Co-ordinates of carbons are taken from ref. 4 and those of hydrogens are placed so that the conformation has least strain.

** A positive dihedral angle in an assembly 1--2--3--4 denotes a clockwise rotation of plane 2,3,4 with respect to the reference plane 1,2,3 when viewing the assembly from 2 to 3.



\# The symbol == denotes a double bond.

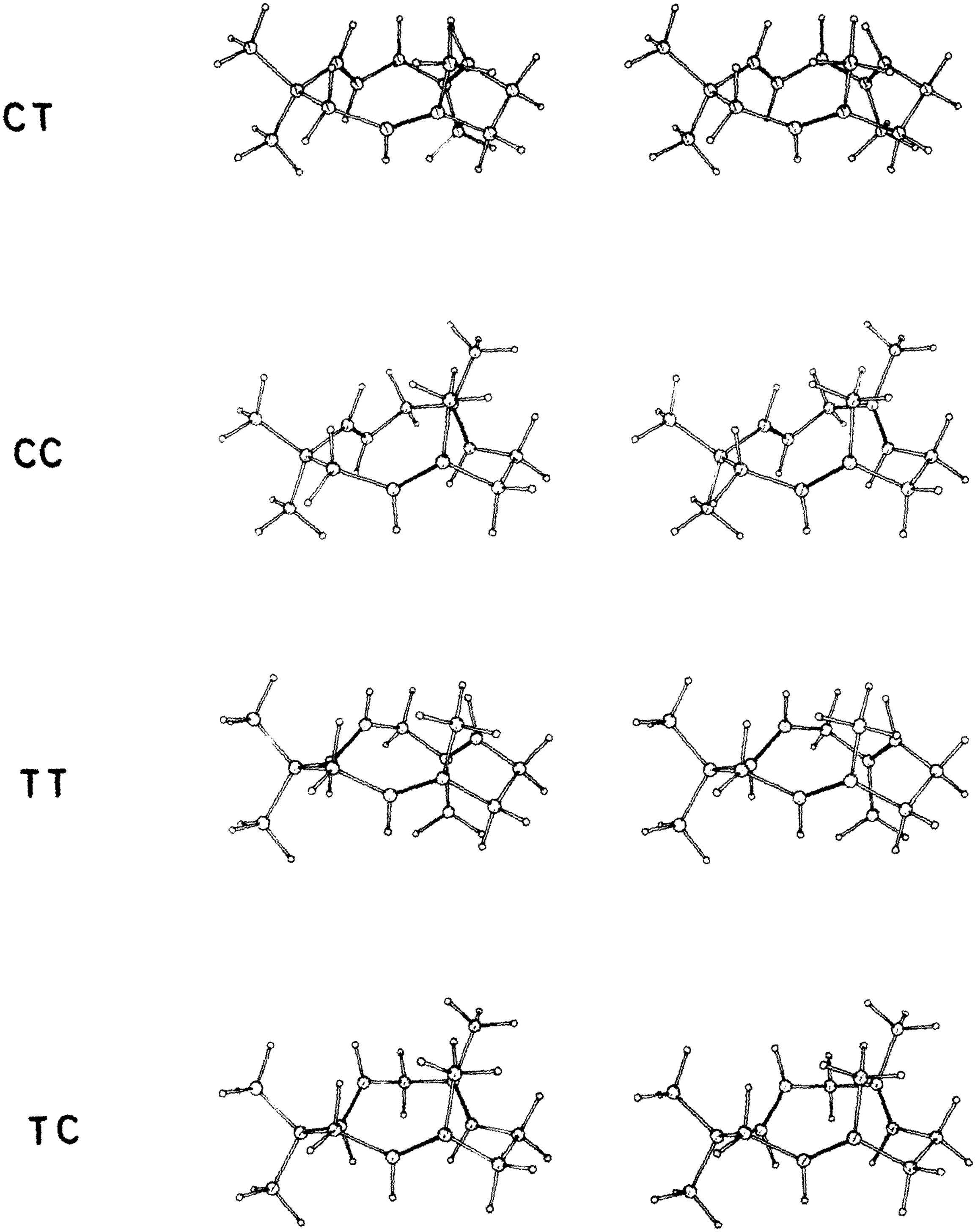


Fig. 2 ORTEP stereodrawing of minimum energy structures of four basic humulene conformers

3) To change cis and trans relationship concerning three groups, 12Me, 13Me, and 9H in turn, leads easily to these four conformers. C and T denote crossed and parallel arrangement of two double bonds respectively. Notation: See ref. 1a.

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