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CONFORMATION OF HEDYCARYOL ISOMERS

Eiji Ōsawa[a], Kazuaki Shimada[b], Mitsuaki Kodama[b] and Shô Itô[b]*
a) Department of Chemistry, Hokkaido University, Sapporo 060, Japan
b) Department of Chemistry, Tohoku University, Sendai 980, Japan

Ground state conformation for all possible geometrical isomers of hedycaryol was estimated by the molecular mechanics calculations. All isomers are indicated to exist in more than two conformations and the parallel conformation (TC or TT) is most stable for all isomers.

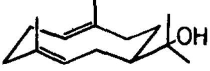
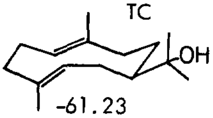
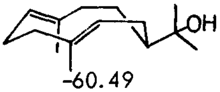
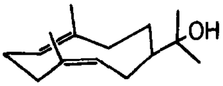
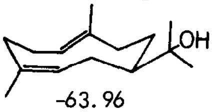
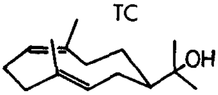
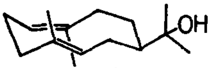
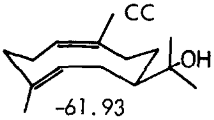
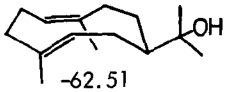
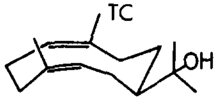
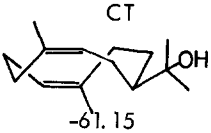
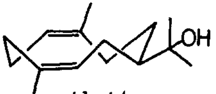
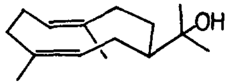
Conformation of germacrenes has attracted considerable interest in connection with their geometry in transannular reactions[1]. Although X-ray analysis and nuclear Overhauser effect in PMR spectrum have been successfully employed in some cases, they need either a crystal (e.g. $AgNO_3$ complex[2]) or distinct proton signals[3] and therefore can not be applied to establish the geometry of simple germacradienes. In his variable-temperature PMR study[4], Wharton has concluded for hedycaryol **1** that (1) **1** consists mainly of one crossed and two parallel conformations, (2) conformational change is rapid at 90° and slow at -30°, (3) the parallel conformations predominate to the extent of 75% at -30°, and (4) they are favored to the crossed forms at higher temperatures. In connection with our studies on transannular reactions of hedycaryol isomers[5], we have investigated some physical properties of all four geometrical isomers. Although all of them showed the presence of some transannular interaction (UV spectra) and dynamic processes (variable-temperature PMR spectra), the complexity of the PMR change precluded complete analysis of the processes to allow reasonable estimation on the stability of conformers. We have therefore applied molecular mechanics calculations which have been proved useful in many cases[6].

Empirical force field calculations on all four isomers were performed using Program "MMI" (QCPE 318)[7] to deduce principal conformations with energy minima for each isomers. The approximate shape of four principal conformers and their heats of formation (ΔH_f) are listed in Table[8]. Population of each conformer was further derived assuming that all of them are in equilibrium at 25° and also listed in Table.

The result on E,E-isomer **1** shows that TC form is most stable and parallel conformations (both TC) amounts to 62% in conformational composition, being in agreement with Wharton's result[4]. However, the calculations revealed one parallel and two crossed forms as important contributors in equilibrium. The calculations for the other isomers show the presence of two predominant contributors (TT and TC) for Z,E-isomer, all four for E,Z-isomer, and three (CT, CC, TT) for Z,Z-isomer.

Although small differences in calculated heat of formation among the conformers preclude precise assesment of stabilities, the most important conclusion here is that the most stable conformer in each isomer has parallel orientation of two double bonds (TC or TT conformation) without exception. Thus, the preferred

Table: Heat of Formation (Cal/mol. 25°C) and Population (%) of Conformers for Hedycaryol Isomers

	CC	TC	TC	CT
2E,6E-				
ΔH_f	-60.72	-59.40	-61.23	-60.49
populations	21.84	2.61	59.46	16.20
	CT	TT	TC	CC
2Z,6E-				
ΔH_f	-61.23	-63.96	-63.96	-61.80
populations	0.53	45.72	52.69	1.03
	TC	CT	CC	TT
2E,6Z-				
ΔH_f	-63.13	-63.05	-61.93	-62.51
populations	49.42	34.16	5.20	11.23
	TC	CT	CC	TT
2Z,6Z-				
ΔH_f	-59.19	-61.15	-61.64	-61.87
populations	0.53	13.13	20.81	65.45

ground state conformations are quite different from those in the transition state of transannular reactions for three (E,E-, Z,E- and E,Z-) isomers and are the same for Z,Z-isomer$^{5)}$.

References and Notes

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8) ΔH_f values in the Table refer to those of the most stable side chain rotamers, while populations shown are the sum of these rotamer populations.

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