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Can Hydrogen Atoms in Alkyl Group Interact with π-Electrons of Double Bonds ? Theoretical Study for the CH--π Interaction on Organic Molecules

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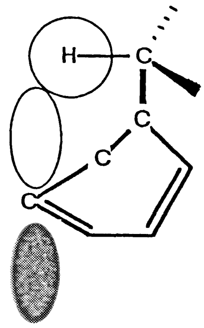
Theoretical study for the CH--π interaction, which is considered to be exerted between π-electrons of olefinic carbons and proximate hydrogen atoms in alkyl group, has been made by molecular mechanics and molecular orbital (ab initio and AM1) calculations for the model molecule 5-isopropyl(R)-2-methyl-1,3-cyclohexadiene.

Hydrogen atom attached to the electronegative atom such as oxygen and nitrogen (hard acid) can interact with hard bases to form a hydrogen bond. A hydrogen bond can be classified by the ionic nature of the bond and the strength of the hydrogen bond. It is an intriguing aspect whether hydrogen atoms in alkyl group (weak acid) can interact with π-electrons of unsaturated bonds (weak base). We have been investigating this weak attractive interaction, for which we termed CH--π interaction, by the experimental method (IR, NMR) and showed the evidence for the existence of CH--π interaction.$^{1)}$



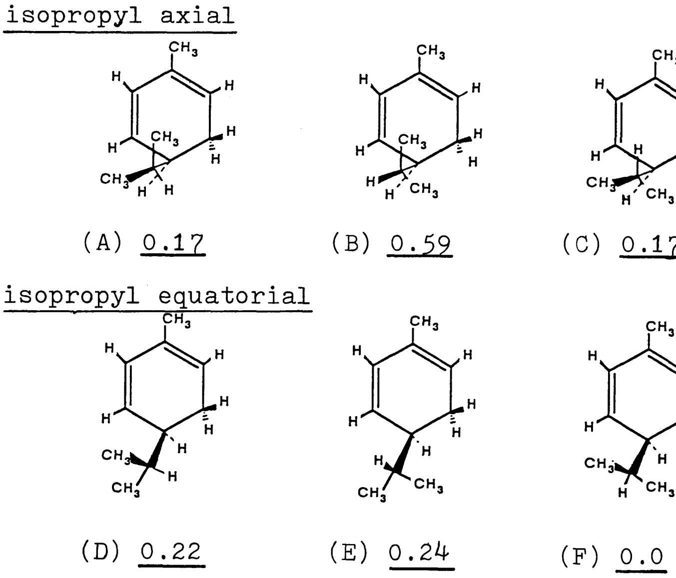
In this communication, the nature of the CH--π interaction and the conditions required to maintain attractive interaction are discussed from the viewpoint of electronic interaction. First of all, alkyl group must be located the proximity to π-system so as to form the CH--π interaction. The CH--π proximate structure are often found in naturally occurring di- and triterpenoids as revealed by the X-ray crystallographic and CD spectral measurements.$^{2)}$

α-Phellandrene, (R)-5-isopropyl-2-methyl-1,3-cyclohexadiene, is a typical example of the CH--π interaction system. It has an enough simple structure to exercise a sophisticated ab initio calculations and, therefore, is chosen as a model compound for a theoretical study on the CH--π interaction. At first, structures of stable conformers were studied by using MMP2(82)$^{3)}$ molecular mechanics program. Next, ab initio full geometry optimization was carried out on the STO-3G basis sets by the special version of IMSPAK program$^{4)}$ for the stable conformers estimated by MMP2(82). At STO-3G geometries, the energies and electron distributions were recalculated with the 4-31G basis set. In addition, semi-empirical molecular orbital calculation (AM1)$^{5)}$ was carried out in order to compare the calculated results with those of ab initio.

The structure of α-phellandrene is flexible. Its diene moiety is not planar and has a twisted structure. From MM2 calculations, this molecule has six similarly populated stable conformations defined by the direction of isopropyl group (axial or equatorial) and the rotation about the bond connecting the isopropyl group to the ring (Fig. 1). The relative steric energy (ΔE) derived from MMP2 calculations indicates that conformer **(F)**, where isopropyl group takes equatorial position, is the most stable. However, axial confomers **(A)**, **(B)**, **(C)** are almost as stable as **(F)**.⁶⁾ For the most stable conformer **(F)** and other 2 next stable conformers **(A)**, **(C)**, full geometry optimization was carried out by ab initio and AM1.⁷⁾ The calculated results are shown in Table 1. As well as the MMP2 calculations, both MO calculations predicted that axial conformers **(A)** and **(C)** were not so unstabilized comparing with the most stable equatorial conformer **(F)**. This tendency that axial conformers are stabilized allows us to anticipate that hydrogen atoms in isopropyl group can interact with π-electrons of olefinic carbons to result in CH--π interaction.

In order to look into the nature of CH--π interaction further, the overlap population and frontier orbitals were studied on the 4-31G//STO-3G calculations (Table 1). In the case that sp^2 carbon is located proximate to hydrogen in isopropyl group within the sum of van der Waals radii, attractive interaction is expected to occur between both atoms judging from the positive overalp population between the relevant atoms. The strength of the CH--π interaction estimated in the scale of overalp population is about 10^{-2} which is almost the same for the case of CH_3--Ph carbon in 1-pheny-2-propanol⁸⁾ by 4-31G//STO-3G ab initio calculations. It is exceptional that negative overlap population is observed between C(4) and H(20) of conformer **(F)** though sp^2 carbon is located proximate to hydrogen atom. In this case, however, H(20) in **(F)** is placed around the nodal plane of the π-orbital. For the attractive CH--π interaction, the orbitals of hydrogen in isopropyl group and sp^2 carbon must be in-phase interacted as well as both groups are located proximately.

The characteristic and the shape of frontier orbitals for CH--π interacted system is another interesting points. Frontier orbitals (HOMO and LUMO) are comprised mostly of π-orbitals of diene moiety and a little orbital component can be found at isopropyl group. In HOMO and LUMO of the CH--π interacted conformers **(A)** and **(C)**, relevant hydrogen and olefinic carbon pair is in-phase interacted. Furthermore, mixing of the atomic orbitals of isopropyl hydrogens with the diene π-orbitals in HOMO and LUMO is increased. This can be ascribed to the increasing orbital interaction between hydrogen in alkyl group



isopropyl axial

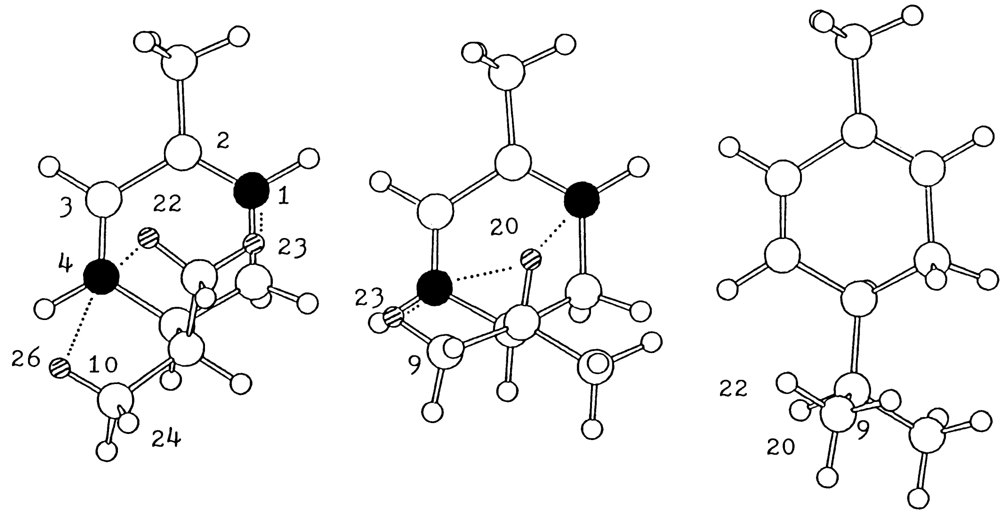
(A) 0.17 (B) 0.59 (C) 0.17

isopropyl equatorial

(D) 0.22 (E) 0.24 (F) 0.0

Fig. 1. Relative steric energy of stable 6 conformers : ΔE / kcal mol^{-1} (MMP2)

Table 1. Conformational Energies and CH--π Interaction on Stable 3 conformers



	(A)	(C)	(F)
Conformational energy(ΔE/kcal mol^{-1})			
MMP2	+0.17	+0.17	0.0
AM1	+0.93	+0.55	0.0
STO-3G	+0.03	+0.43	0.0
4-31G//STO-3G	+0.49	+0.26	0.0
Overlap population (4-31G//STO-3G) and interatomic distance	C(1)--H(23) 8.80 X 10^{-4} 2.80 Å	C(1)--H(20) 1.18 X 10^{-2} 2.86 Å	C(4)--H(22) 7.58 X 10^{-3} 2.75 Å
	C(4)--H(22) 1.13 X 10^{-2} 2.86 Å	C(4)--H(20) 7.11 X 10^{-3} 2.79 Å	C(4)--H(20) -4.63 X 10^{-3} 2.72 Å
	C(4)--H(26) 5.51 X 10^{-3} 2.86 Å	C(4)--H(23) 1.18 X 10^{-2} 2.61 Å	

Frontier orbitals[a]		HOMO	LUMO		HOMO	LUMO		HOMO	LUMO
	C(1)	0.3013	-0.4680	C(1)	0.3021	-0.4795	C(1)	0.3046	0.4735
	C(2)	0.2482	0.3583	C(2)	0.2451	0.3692	C(2)	0.2443	-0.3556
	C(3)	-0.2177	0.3930	C(3)	-0.2159	0.3909	C(3)	-0.2199	-0.3978
	C(4)	-0.2573	-0.4826	C(4)	-0.2482	-0.4634	C(4)	-0.2585	0.4808
	H(22)	-0.0255	0.0058	H(20)	0.0020	-0.0438	H(20)	0.0237	-0.0409
	H(23)	0.0029	-0.1560	H(23)	-0.0189	-0.1038	H(22)	-0.0180	0.1587
	H(26)	-0.0163	-0.1664						

a) Coefficients of an outer-part $2P_y$ orbital component (π-orbital) are shown to image the shape of frontier orbitals.

and olefinic π-orbitals. Interaction can be exerted when the π-orbitals are perturbed owing to the approach of isopropyl group. In the conformer (**A**), the overlap population of the CH--π interacted C(10)-H(26) bond (0.7698) is lower than that of the uninteracted C(10)-H(24) bond (0.7772) on the same carbon atom. This indicates that electron-delocalization occurs due to the CH--π interaction.

In conclusion, a CH--π interaction can be classified as the attractive interaction between hydrogen in alkyl group (soft acid) and π-electrons (soft base) and the strength is estimated to be about 10^{-2} as measured by overlap population. When the both orbitals of relevant atoms are located proximately to interact, CH--π interaction can occur due to the electron-delocalization.9) Though the extent of the electron-delocalization is not so large as that found in the case of conventional hydrogen bond systems, the calculated results manifest the contribution of the electron-delocalizative force quite analogous to the case of hydrogen bonding. In short, the CH--π interaction can be assumed to be a weak hydrogen bonding from the viewpoint of weak electronic interaction.

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2) See Ref. 1 and references cited wherein.
3) N. L. Allinger and H. L. Flanagan, J. Comput. Chem.,4, 399 (1983).
4) There are restrictions in full geometry optimization by Gaussian 82 program. The maximum number of variables (N) that can be specified in an optimization must not exceed 50. As the N for the model compound in this paper is 72, a full geometry optimization cannot be carried out on Gaussian 82 program.
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7) The optimized geometries calculated by MMP2, ab initio, or AM1 are almost the same and remarkable change in geometries can not be found.
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9) The dispersion force also contributes largely to the CH--π interaction. However, the dispersion force cannot be evaluated at Hartree-Fock level ab intio calculation. Therefore only electron-delocalizative contribution to the CH--π interaction was studied in this report.

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