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Intramolecular CH–π interaction. Substituent effect as a probe for hydrogen bond-like character

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ABSTRACT: The contribution of a charge-transfer term to the CH–π interaction is supported by *ab initio* calculations and experiments on the substituent effect. NOE is an effective tool to determine the CH–π interacted folded conformers separately from the stretched conformer. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: intramolecular CH–π interaction; substituent effect; charge transfer; hydrogen bond

INTRODUCTION

More than 20 years have passed since the unusual stability of the CH–π proximate conformation of 1-phenylethyl *tert*-butyl sulfoxide was found.[1] Since then, many examples of such CH–π proximate conformers and CH–π approached arrangements in molecular assemblies have been reported.[2] Through these studies, CH–π proximate conformations have been revealed to prevail generally in contrast to the bulk repulsive concept. Intermolecular CH–π approached arrangements have also been shown to appear frequently in organic, organometallic and biological systems.[2]

Before our early conformational studies, the presence of CH–π interactions had been recognized with typical CH acids, such as chloroform and acetylene.[3] The phenomenon has been understood as the formation of a weak hydrogen bond. The T-shaped geometry of benzene dimer has attracted interest in relation to the CH–π interaction. It was first explained by an electrostatic model.[4] Recently, Hozba and co-workers carried out more sophisticated calculations and the phenomenon was described as anti-hydrogen bond.[5]

For the case of intermolecular interaction, the stabilization energy is an important quantity to measure the strength of the interaction. We determined the stabilization energies of chloroform–arene complexes, and showed that the interaction becomes stronger when the arene becomes more electron-rich.[6] On the other hand, the stabilization energy of hydrogen bonds was shown to be attributable to the combined contributions of coulombic, delocalization, dispersion and exchange repulsion terms between hydrogen (XH) and other non-bonded electronegative atoms.[7,8ab] Quantum mechanical calculations indicated the contribution of similar energy terms to OH–π and CH–π interactions.[8] As the delocalization energy is perturbed apparently by the σ^*_{CH} and π energy levels, the major part of the electronic substituent effect on hydrogen bond-like interactions should originate from the delocalization term.

In this paper, we demonstrate that the CH–π interaction resembles other weak hydrogen bonds in many respects.

RESULTS AND DISCUSSION

MO calculations

Total stabilization energy and optimized geometry charge-transfer energy term from energy decomposition analysis,[8ab] overlap population between supposedly CH–π interacted H and C atoms, and exact electron charge distribution map from MO calculations provide criteria to judge the presence of CH–π interactions.

In cases of intramolecular CH–π interactions, the net interaction energy cannot be evaluated easily because it is obscured by other energy terms comprising the conformational energy. In such cases, the overlap population is an easily accessible quantity to establish the presence of bonding interactions between specified atoms.[9] We carried out MP2/6–31 + G* and B3LYP/6–31 + G* level calculations on some alkene molecules and evaluated the overlap populations between non-bonded hydrogen and sp^2 carbon atoms ($N_{CH/\pi}$). The results are given in Table 1. When the molecule takes a folded

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Table 1. Intramolecular CH–π interaction characterized by overlap population between non-bonded H and C(sp^2) atoms

Compound	Calculation	Abundance of CH–π conformer (%)	Proximate H/C(sp^2) and their distance	Atoms (Å)	Non-bonded H–C(π) overlap population ($\times 10^2$)
1-Butene	MP2/6–31G*	17.8	C(2)—H(4)	2.927	0.14
	MP2/6–31 + G*	12.5	C(2)—H(4)	2.938	−0.37
1-Pentene	MP2/6–31G*	44.7	C(2)—H(5)	2.771	1.25
	MP2/6–31 + G*	37.6	C(2)—H(5)	2.786	3.28
	B3LYP/6–31 + G*	23.8	C(2)—H(5)	2.873	6.66
5-Fluoro-1-pentene	MP2/6–31 + G*	Conf. 1	C(2)—H(5)	2.853	7.96
		Conf. 2	C(2)—H(5)	2.867	10.6
1,5-Hexadiene	MP2/6–31G*	45.6	C(2)—H(5)	2.834	1.14
	MP2/6–31 + G*	41.2	C(2)—H(5)	2.859	0.15
	B3LYP/6–31 + G*	26.6	C(2)—H(5)	2.919	2.76

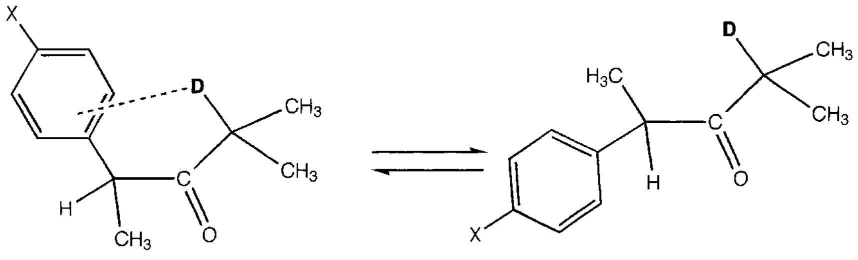
conformation, some of C—H hydrogen atoms approach the ethylenic π-orbital within van der Waals contact. In such a situation, $N_{\mathrm{CH}/\pi}$ usually takes a positive non-zero value and can be used to locate the CH–π interaction. In the case of 1-butene, hydrogen approaches from the direction of the nodal plane of its π-orbital and must be unfavorable for interaction.

Experimental evidence from substituent effect

As the CH–π interaction is extremely weak, it is difficult to observe the perturbation of physical properties caused by this interaction. Therefore, IR, NMR and other spectroscopic methods and x-ray crystallography could not be applied in the same manner as in cases of typical hydrogen bonds. For example, the IR hydrogen bond shift of the CH stretching absorption is very small even in the interaction of chloroform and π-bases.[10] A reverse high-frequency shift is often observed in intramolecular cases.[11,12]

In these circumstances, substituent effects on both the CH and π counterparts should give crucial evidence for the weak bonding interaction from the charge-transfer between them. Electron-withdrawing substituents on the CH carbon should lower the energy level of antibonding CH orbitals and electron-donating substituents on the π system should raise the level of the highest occupied π orbital; both substituent effects should favor a charge-transfer type interaction between interacting CH and π groups by narrowing the energy gap of the interacting orbitals. Hence the substituent on the π part should result in a negative ρ in the Hammett plot.[13] This can be a criterion for judging the contribution of the charge-transfer interaction.

The substituent effect on the C–D stretching bands of isopropyl-1-*d* 1-(4-substituted phenyl)ethyl ketones were examined in an early stage of our research.[11] It showed that the electron-donating substituent on a π-acceptor favors the CH–π proximate conformer, giving a negative ρ-value ($\rho = -0.189$) in the Hammett ($\varepsilon_{\mathrm{int}}/\varepsilon_{\mathrm{free}}$ vs σ) plot, where $\varepsilon_{\mathrm{int}}$ and $\varepsilon_{\mathrm{free}}$ are the absorption intensities of CH–π interacted and free species, respectively. In this experiment, the higher frequency C–D band is assigned to the CD–π proximate conformer by comparison with the C–D stretching bands of similar compounds. In order to gain support for the above assignment and to ensure the contribution of the delocalization term to the CH–π interaction, MP2 and density functional calculations were carried out on some simple model compounds capable of intramolecular CH–π interactions. The CH stretching frequencies of the supposedly CH–π interacted C—H bond in the CH–π proximate conformers were calculated to be higher than those of the free C—H



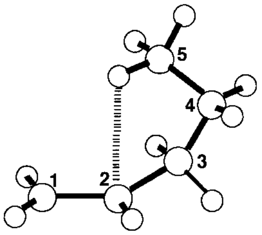
$\nu_{\mathrm{CD}} = 2177\ \mathrm{cm}^{-1}$ (X = H)

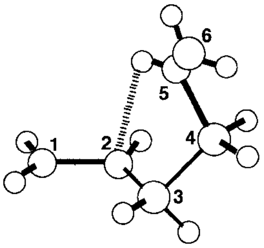
(A)

$\nu_{\mathrm{CD}} = 2136\ \mathrm{cm}^{-1}$ (X = H)

(B)

Table 2. Calculated high-frequency shifts (cm^{-1}) of CH–π interacted CH bonds in folded conformers[a]





	1-Pentene		1,5-Hexadiene	
	CH–π interacted	Free CH_3	CH–π interacted	Free CH_3
ν(CH) (cm^{-1})				
MP2/6–31 + G*	3043	3030	3057	3034
B3LYP/6–31 + G*	2957	2947	2994	2973

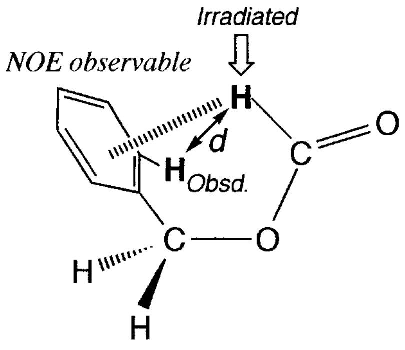
[a] Free ν(CH) is calculated as the mean of three CH in the corresponding stretched conformer.

bonds of the stretched conformers (Table 2). The high-frequency shift of ν_{CH} accompanies shortening (ca 0.001 Å) of the C—H bond involved in CH–π interaction, which might be an intramolecular example of an anti-hydrogen bond.[5] Simultaneously, the non-bonded overlap populations involving these CH become considerably positive.

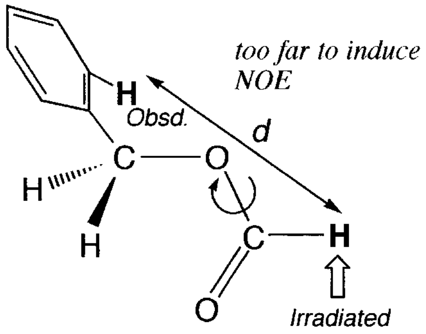
In order to survey the electronic substituent effect on a wider range of CH–π interacted systems, a more generally applicable method to observe the effect is necessary. NOE is an effective tool to detect the proximity of the two nuclei in a molecule. In our experiments, the enhancements [$f_{HAr}(H_{donor})$] of the aromatic signals were measured with irradiation of the CH signal of the donor. As NOE is a very short-range effect, the irradiation of the CH donor hydrogen in the stretched conformer (B′) cannot induce the enhancement of the aromatic proton signals to a measurable extent. Thus, the amount of CH–π proximate conformer (A′) should be proportional to the enhancement [$f_{HAr}(H_{donor})$] and could be determined without the interference of the co-existing stretched conformer (B′) by NOE.[14]

NOE enhancements $f_{HAr}(H_{donor})$ of several series of ar-substituted XC_6H_4—CHR—Y—CHR_2 compounds were measured and plotted against σ constants of the substituents X. The results of the Hammett plots are summarized in Table 3. f_0 is calculated as the intercept of the plot and corresponds to the statistically calculated NOE enhancement for the unsubstituted derivative. Without exception, ρ is negative and the charge transfer from π to CH in the CH–π interacted system is strongly supported.

As is easily understood from the above discussion, the absolute value of ρ is expected to serve as a relative scale to measure the contribution of delocalization terms to CH–π interactions, and hence can be a measure of the strength of the interaction. This trend is confirmed by examining a wide range of intramolecular hydrogen-bond-like interactions given in Table 4. $|\rho|$ is shown to increase as the hydrogen bond strengthens. Hence relatively small $|\rho|$ values for the CH–π interacted systems suggest that the charge-transfer interaction is considerably weaker than in hydrogen-bonded and OH–π interacted systems.



(A′)



(B′)

Table 3. Hammett (log K_{rel} vs σ) plots on the NOE enhancements of intramolecularly CH–π interacted systems in dimethyl-d_6 sulfoxide[a]

Compound	Ring size	Linear correlation parameters		
		ρ	(Log f)$_0$	r
$XC_6H_4CH_2OC\mathbf{H}{=}O$	5	−0.353	0.580	0.930
$XC_6H_4CH(CH_3)OC\mathbf{H}{=}O$	5	−0.439	0.675	0.988
$XC_6H_4CH_2OC\mathbf{H}(CH_3)_2$	5	−0.500	0.695	0.965
$XC_6H_4C({=}O)N(CH_3)C\mathbf{H}(CH_3)_2$	5	−0.152	1.119	(0.996)
$XC_6H_4CH_2C({=}O)N(CH_3)C\mathbf{H}(CH_3)_2$	6	−0.407	0.695	0.946
$XC_6H_4C(CH_3)_2C({=}O)N(CH_3)C\mathbf{H}(CH_3)_2$	6	−0.312	0.959	—
$XC_6H_4CH_2NHC({=}O)C\mathbf{H}(CH_3)_2$	6	−0.132	0.517	0.911
$XC_6H_4CH_2N(CH_3)C({=}O)C\mathbf{H}(CH_3)_2$	6	−0.286	0.569	0.980
$XC_6H_4OCH_2C({=}O)N(CH_3)C\mathbf{H}(CH_3)_2$	7	−0.524	0.237	0.950

[a] As $f_{HAr}(H_{donor})$ is proportional to the amount of CH–π interacted folded conformer, log[$f_{HAr}(H_{donor})$] was used as a substitute for log K_{rel}.

Table 4. The ρ values for the Hammett (log K_{rel} vs σ) plots of various intramolecularly hydrogen bonded and XH–π interacted molecules forming a five-membered chelate ring

Compound	Solvent	Interaction	ρ
XC_6H_4—O—CH_2—CO**OH**	CCl_4	OH–O	−0.939
XC_6H_4—O—CMe_2—CO**OH**	CCl_4	OH–O	−1.01
XC_6H_4—CH_2**OH**	CCl_4	OH–π	−0.43
XC_6H_4—CH_2**NH**C_6H_5	CCl_4	NH–π	−0.39
XC_6H_4—CHMeCO**CD**Me_2	CCl_4	CD–π	−0.189
XC_6H_4—CH_2—**N**MeC**H**Me_2	$CDCl_3$	CH–π	−0.345
XC_6H_4—CH_2—O—C**H**=O	$CDCl_3$	CH–π	−0.237

CONCLUSION

The CH–π interaction is similar to hydrogen bonding in many respects, except for the anomalous (presumably anti-hydrogen bond) behavior of the C—H bond involved. It is clearly different from simple dispersion and hydrophobic interactions. A single CH–π interaction is fairly weak, but many CH groups can undergo CH–π interaction in a simultaneous and cooperative manner, which intensifies the interaction. Many phenomena can be rationalized by attractive CH–π interactions, and the idea of CH–π interactions seems to be becoming accepted gradually by many chemists.

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