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Transannular Interaction in Bifunctional Olefins and Ketones: A Semiempirical Electron Density Analysis[§]

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Abstract Electron densities on the olefinic carbons of some dimethylene compounds are calculated by semiempirical model PM3, and the values are compared with those of the corresponding monomethylene compounds. A relationship is observed between the change of electron density Δ(C) and the change of ^{13}C NMR chemical shift Δδ. A correlation is also found between Δ(C) and Δ(O), i.e. the carbon and oxygen atoms, of methylene-ketones. The electron density differences are induced by three types of transannular interactions: electrostatic force, orbital interactions through bond (TB) and orbital interactions through space (TS). Electrostatic force is the most prominent factor for ketones in which the high polarity of carbonyl group can apply a strong field effect onto nearby atoms. For nonpolar methylene groups, orbital interactions can be transmitted either TS or TB more effectively than electrostatic force. A conformational analysis, performed on a dimethylene compound **4c**, confirms the existence of TS interaction between the double bonds. © 1999 Elsevier Science Ltd. All rights reserved.

Introduction

^{13}C NMR chemical shift has been used as a sensitive probe for the measurement of transannular interaction between two π orbitals.[1] The theory is based on the change of electron density between orbitals which interact with each other. For example, the two methylene π orbitals of compound **1e** are located so close to each other that their p-lobes overlap through space.[2] Electron delocalization across the ring results to an increase in electron density on the quaternary carbons of the >C=C groups, yet a decrease on the terminal ones.[1,3] Compared with the corresponding carbons of monomethylene compound **1d**, the chemical shift of quaternary carbons of **1e** shows an upfield movement on NMR spectra (Δδ = -1.4 ppm), while that of the terminal ones showed a downfield movement (Δδ = 1.3 ppm).[3]

This concept has been applied successfully on several cases, and the results are generally consistent with other kinds of measurements.[1,4] There are two basic types of transannular interactions operating in these systems, i.e. orbital interactions and field effect.[5] The two π orbitals of **1e** may interact with each other either through space (TS) via direct overlapping of p-lobes or through bonds (TB) by mixing with σ orbitals.[6,7] It is gradually realized that σ bonds can perturb certain high lying π orbitals to a significant degree, and the effect is especially noteworthy in polycyclic systems. Non-conjugated π and/or n orbitals combine more extensively with σ bonds in such systems due to more complicated connectivity.

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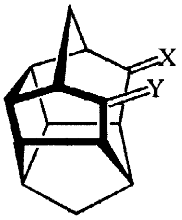
Field effect becomes significant in the presence of high polar substituents such as carbonyl groups. For example, the two C=O groups of diketone **2a** are located far away from each other, however, a significant change of ^{13}C NMR chemical shift of carbonyl carbons ($\Delta\delta$ = -3.8 ppm) was observed when compared with monoketone **2b**.[3] This phenomenon was believed to be electrostatic in nature according to an analysis on solvent effect.



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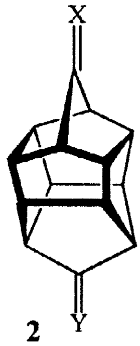
a $X=Y=O$
b $X=H_2$; $Y=O$
c $X=O$; $Y=CH_2$
d $X=H_2$; $Y=CH_2$
e $X=Y=CH_2$



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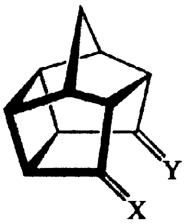

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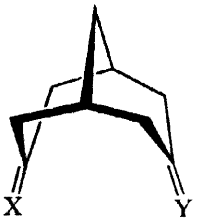

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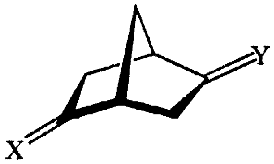

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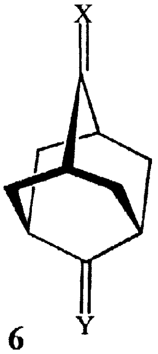

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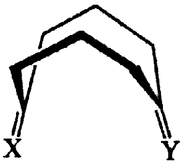

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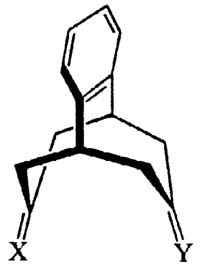

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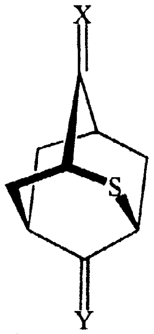

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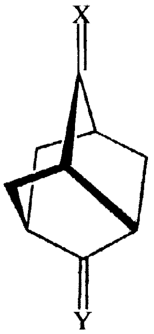

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The electron densities of several ketones and diketones, such as compounds **2-6**, have been analyzed by Paddon-Row.[8] It was concluded that the change of ^{13}C NMR chemical shift in all these compounds is caused mainly by electrostatic force. No clear comment has been given on the influence caused by a C=C group in similar systems. To clarify this point, it would be desired to exam the effect of methylene derivatives (**c-e**) in addition to ketones (**a-c**). Electron density data for selected methylene derivatives are calculated in this report, which are compared with ^{13}C chemical shifts, in order to get a better understanding on long-range nonconjugate orbital interactions.

Results and Discussion

Choice of theoretical models

There are various ways for defining the electron density, or charge, of an atom in a molecule,[9] and the choice of method generally relies on the suitability for the purpose of a specific analysis. The purpose of our study is to estimate the amount of electron density difference on carbon and oxygen atoms between bifunctional and monofunctional compounds, e.g. the difference on carbon atoms (Δ(C)) between bimethylenes **1e-10e** and methylenes **1d-10d** and the difference on oxygen atoms (Δ(O)) between methylene-ketones **1c-10c** and ketones **1b-10b**. The calculated values of Δ(C) will then be compared with the experimental chemical shift differences (Δδ) between each pair of compounds. In this study, the differences Δ(C) and Δ(O) between each pair of data is more meaningful than the absolute values of the data. A methodology of choice should be able to properly reflect the subtle change between each pair of monofunctional and bifunctional compounds.

On the selection of computational models, *ab initio* calculation with a large basis set will certainly produced a more accurate result than semiempirical calculations. In our study the semiempirical method PM3 is used in order to save computing time. The suitability of PM3 for such an analysis has to be examined before getting into more detailed discussion on the results. A comparison between the data obtained from PM3 and *ab initio* HF/6-31G*//3-21G[10] for five ketones (**2b-6b**) and diketones (**2a-6a**) is given in Table 1. The latter method has been claimed to yield reliable data for this series of compounds. In our calculations, the geometries are optimized first by molecular mechanics, followed by single point calculations by PM3 (MOPAC 5)[11] to obtain atomic charges. As listed in Table 1, the Δ(C) values calculated by both methods are reasonably consistent with the Δδ values, i.e. the electron densities on the carbonyl carbon of diketones **2a-6a** are increased (negative values) with respect to those of monoketones **2b-6b**, while their corresponding chemical shifts move toward upfield (negative values). Within the limit of uncertainty, it seems that the fitness of PM3 to Δδ is comparable to that of HF/6-31G*. The Δ(C) and Δ(O) values obtaind by PM3 agree nicely with those obtained by HF/6-31G*.

Further comparisons among bifunctional methylene-ketones **2c-6c**, monoketones **2b-6b**, and monomethylenes **2d-6d** are shown in Table 2. The quaternary carbons of the methylene groups of **2c-6c** show an increase in electron density (Δ(C) < 0) with respect to those of monomethylenes **2d-6d**, while the terminal carbons of the methylene groups of **2c-6c** show an opposite effect. Both PM3 and HF/6-31G* methods yielded results consistent with each other. Some of Δ(C) values in Table 2 do not comply with the signs (upfield or downfield) of Δδ, for eample, the Δ(>C=) value of **2c** and the Δ(C) of C=O groups of **3c** and **4c**. The irregularity may be ascribed to the strong field effect of C=O group, which overshadows the weak TB and TS orbital interactions. Calculated results for several other structures, i.e. **1c** and **7c-10c**, are listed in Table 3. In this Table it is clear that Δ(C) and Δδ values agree well with each other. All atoms with an upfield chemical shift show an increase in electron density, and vice versa. It is apparent that a relationship exists between Δ(C) and Δδ, which can be predicted properly by PM3.

Interaction among dimethylene derivatives

A comparison of Δ(C) values between 10 dimethylene compounds and mono-methylene compounds are performed using PM3, and the results are listed in Table 4. Among the 10 compounds, five (**2e**, **5e**, **6e**, **9e** and **10e**) can be regarded as possessing TB type of interactions only, while others (**1e**, **3e**, **4e**, **7e** and **8e**) may have both TB and TS types of interactions. The observed chemical shift differences Δδ for **2e-6e** are comparatively smaller (ca. 1-5 ppm, Table 4) than those of the corresponding diketones **2a-6a** (ca. 4-10 ppm, Table 1). This is due to the lack of strong polar effect in the former as mentioned earlier. Despite of smaller magnitudes, the sign of Δδ agrees with the sign of Δ(>C=) and Δ(=CH_2). The quaternary carbons, which generally move toward upfield, showed an increase in electron density, while the terminal ones with downfield shifts showed a

Table 1. A comparison of HF/6-31G* and PM3 results on the calculations of Δ(C) and Δ(O). Chemical shift differences Δδ are obtained between diketones **2a**-**6a** and monoketones **2b**-**6b**.

diketone - ketone	Δδ[a]	Δ(C)[b]		Δ(O)[b]	
		6-31G*[c]	PM3	6-31G*[c]	PM3
2a - **2b**	-3.8[d]	-0.6	-0.4	7.2	7.0
3a - **3b**	-9.5[e]	-15.0	-20.1	26.8	24.2
4a - **4b**	-3.9[e]	-17.3	-11.1	32.5	20.6
5a - **5b**	-5.8[e]	-7.5	-8.0	15.5	14.7
6a - **6b**	-4.9[e]	-4.5	-2.8	9.9	10.4

[a] Negative sign indicates upfield shift, unit in ppm. [b] Atomic charge differences in m*e*. [c] Data from ref. 8. [d] Data from ref. 3. [e] Data from ref. 1c.

Table 2. A comparison of HF/6-31G* and PM3 results on the calculations of Δ(C) and Δ(O). Chemical shift differences Δδ are obtained among methylene-ketones **2c**-**6c**, ketones **2b**-**6b** and methylenes **2b**-**6b**.

methylene-ketone		*methylene* (**2d**-**6d**) → *methylene-ketone*			*ketone* (**2b**-**6b**) → *methylene-ketone*				
		Δδ[a]	Δ(C)[b]		Δδ[a]	Δ(C)[b]		Δ(O)[b]	
			6-31G*[c]	PM3		6-31G*[c]	PM3	6-31G*[c]	PM3[d]
2c	C=O	---	---	---	-1.1[e]	-0.6	-0.1	2.0	1
	>C=	0.7[e]	-0.2	-4.9	---	---	---	---	---
	=CH$_2$	1.7[e]	5.9	8.2	---	---	---	---	---
3c	C=O	---	---	---	-4.1[f]	2.9	0.9	8.3	3
	>C=	-5.1[f]	-29.7	-37.5	---	---	---	---	---
	=CH$_2$	2.4[f]	34.2	29.2	---	---	---	---	---
4c	C=O	---	---	---	-3.2[f]	6.2	0.5	2.5	6
	>C=	-8.4[f]	-40.6	-28.2	---	---	---	---	---
	=CH$_2$	6.9[f]	48.8	32.7	---	---	---	---	---
5c	C=O	---	---	---	-1.5[f]	-2.1	-0.3	3.9	2
	>C=	-6.3[f]	-15.6	-18.4	---	---	---	---	---
	=CH$_2$	3.5[f]	16.4	19.6	---	---	---	---	---
6c	C=O	---	---	---	-1.4[f]	-0.9	-1.4	2.2	2
	>C=	-4.8[f]	-9.9	-9.9	---	---	---	---	---
	=CH$_2$	2.9[f]	10.6	13.2	---	---	---	---	---

[a] Negative sign indicates upfield shift, unit in ppm. [b] Atomic charge differences in m*e*. [c] Data from ref. 8. [d] Only one digit is taken for the data. [e] Data from ref. 3. [f] Data from ref. 1c.

Table 3. Comparison of Δδ, Δ(C) and Δ(O) among methylene-ketones (c), ketones (b) and methylenes (d).

methylene-ketone (c)		*methylene* (d) → *methylene-ketone* (c)		*ketone* (b) → *methylene-ketone* (c)		
		Δδ[a]	Δ(C)[b]	Δδ[a]	Δ(C)[b]	Δ(O)[c]
1c	C=O	---	---	-2.5[d]	-0.1	4
	>C=	-4.0[d]	-27.8	---	---	---
	=CH$_2$	5.2[d]	30.0	---	---	---
7c	C=O	---	---	-1.9[e]	-1.1	2
	>C=	-5.3[e]	-23.0	---	---	---
	=CH$_2$	5.6[e]	22.5	---	---	---
8c	C=O	---	---	-2.7[e]	-0.8	8
	>C=	-4.5[e]	-42.7	---	---	---
	=CH$_2$	5.5[e]	47.3	---	---	---
9c	C=O	---	---	-1.0[e]	-1.3	1
	>C=	-4.1[e]	-9.3	---	---	---
	=CH$_2$	2.9[e]	12.5	---	---	---
10c	C=O	---	---	-1.3[e]	-1.4	2
	>C=	-5.0[e]	-10.6	---	---	---
	=CH$_2$	3.7[e]	14.8	---	---	---

[a] Negative sign indicates upfield shift, unit in ppm. [b] Atomic charge differences in *me*. [c] Only one digit is taken for the data. [d] Data from ref. 3. [e] Data from ref. 1c.

Table 4. Changes of chemical shift Δδ and electron density between the carbon atoms of dimethylenes (**1e**-**10e**) and methylenes (**1d**-**10d**).

dimethylene	Δδ[a]	Δ(>C=)[b]	Δδ[a]	Δ(=CH$_2$)[b]	interaction type
1e	-1.4[c]	-3.4	1.3[c]	7.5	TB + TS
2e	0.3[c]	-1.0	0.4[c]	1.4	TB
3e	-1.0[d]	-2.7	-0.3[d]	6.3	TB + TS
4e	-5.0[d]	-4.4	3.1[d]	10.0	TB + TS
5e	-1.9[d]	-2.1	1.3[d]	2.8	TB
6e	-1.3[d]	-2.6	0.8[d]	2.3	TB
7e	-1.9[d]	-3.5	1.1[d]	4.2	TB + TS
8e	-1.6[d]	-8.2	0.7[d]	14.5	TB + TS
9e	-1.2[d]	-0.2	0.6[d]	1.5	TB
10e	-1.8[d]	-2.9	1.2[d]	2.9	TB

[a] Negative sign indicates upfield shift, unit in ppm. [b] Atomic charge differences in *me*. [c] Data from ref. 3. [d] Data from ref. 1c.

decrease in electron density. Although the values of Δδ and Δ(C) are not directly proportional to each other, the observed trend is still meaningful in a quantitative sense. For the data in Table 4, only two minor mismatches are observed, i.e. the values of Δδ vs. Δ(C) of **2e** (0.3 vs. -1.0) and **3e** (-0.3 vs. 6.3). It could be ascribed to solvent effect or due to uncertainties in our modeling. Such irregular data appeared occationally for methylene-ketones, too, as shown in Table 2.

In our earlier analysis on several derivatives of **1** and **2**, it was suggested that orbital interactions exists in **1a**, **1c** and **1e**, but not in **2a**, **2c** and **2e**.[3] The chemical shift differences in the latter are thought to have been induced mainly by field effect, i.e. electrostatic interaction. However, the calculated results for 10 structures in Table 4 indicates that the change of electron densities can also be induced by long range TB interactions. For the 10 compounds, however, there seems to have no clear distinction between TB and TS interactions regarding the magnitude of Δδ values. The admantandiene derivatives **6e**, **9e**, and **10e** are regarded as possessing only TB interactions, so that their Δδ and Δ(C) values are comparable to each other. The slight variations in Δδ and Δ(C) among them are caused mainly by the differences on their geometries. For cyclooctandiene derivatives **4e**, **7e** and **8e**, both TB and TS interactions are operating together. In Table 4 the estimated Δ(C) values of **4e** (-4.4 and 10.0) and **8e** (-8.2 and 14.5) are slightly larger than those of **7e** (-3.5 and 4.2), where the former are considered having a higher degree of TB interactions than the latter. Although the Δδ values observed in these three compounds do not show clear differences.

Conformation analysis on TS interactions

Since TS interactions are caused by the overlap of orbitals, it should be sensitive to distance between the atoms. In compound **4e**, for example, the overlap of p-lobes of double bonds should appear when the distance between quaternary carbons becomes shorter then 3.4 Å. The conformation of **4e** is adjustable so that the two fused cyclohexane moieties may be either in boat or in chair form. Force field calculations indicates that a double-chair form is more stable than a boat-chair form. Even in a double-chair conformation, the distance between double bonds is still flexible. A plot of the heat of formation (HF) of **4e** versus the distance between the double bonds is shown in Figure 1. In a range of 2.8-3.3 Å, the HF values change about 1 kcal/mol. Yet in the same range, a substantial difference may occur on the extent of orbital overlapping.

Electron densities calculated for the quaternary carbons and terminal ones of **4e** are plotted in Figure 2.

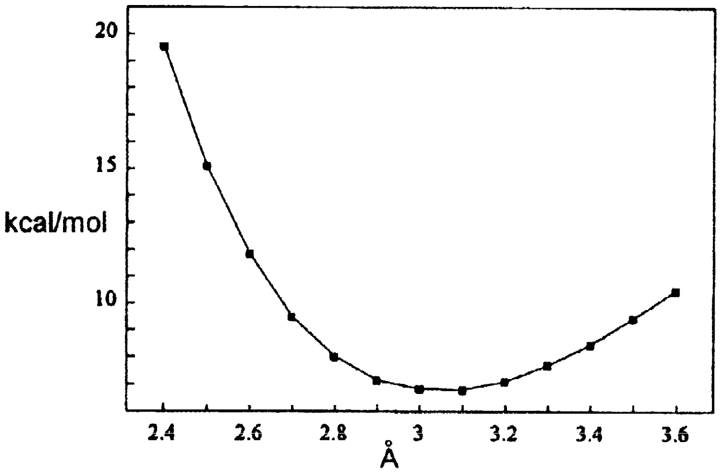

Figure 1: Heats of formation of **4e** at different distances between double bonds (quaternary carbons).

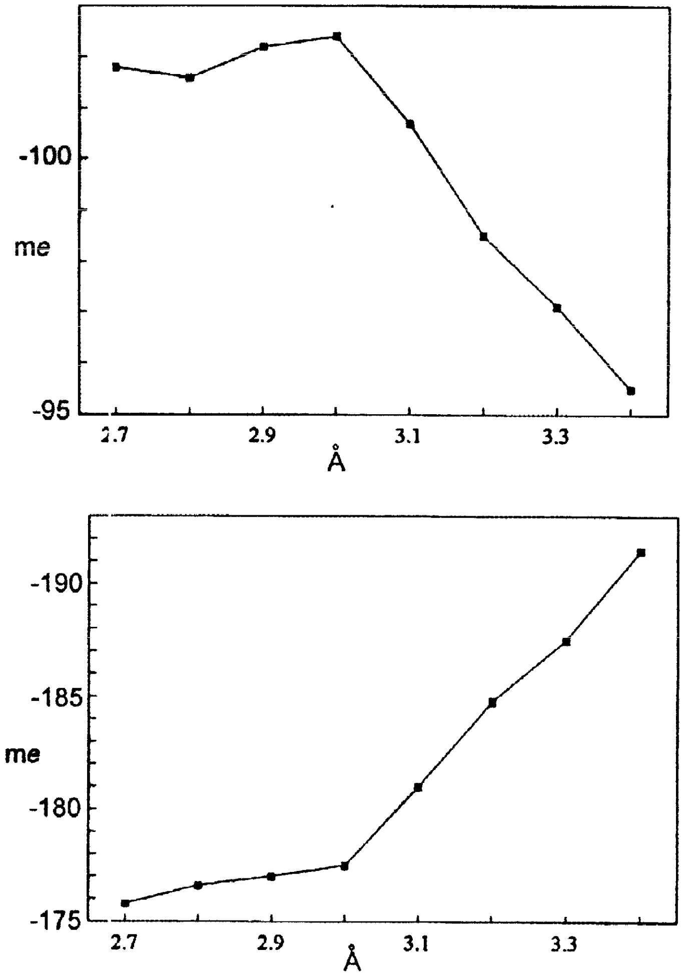

Figure 2: Charges on the quaternary (top) and terminal carbons (bottom) of **4e** at different distances between double bonds (quaternary carbons).

Just as predicted, a steady increase of electron density for the quaternary carbon appears in the range of 3.4-3.0 Å, while a steady decrease appears for the terminal ones. The changes level off at distance 3.0 Å, about where the minimun values of HF is estimated. At distances shorter than 3.0 Å, electrostatic repulsion among the occupied orbitals begins to increase. In the range of 2.7-3.0 Å, the two opposite forces are balanced so that no apparent change of electron density appear.

In this analysis, it is clearly shown that orbital overlap of TS type is related to electron density change, as originally proposed by Senda and Bishop.[1] The $\Delta\delta$ value is also influenced by TB interaction, in cases where both TS and TB interactions are operating on a single molecule.

Conclusion

The change on ^{13}C NMR chemical shift on bifunctional compounds **1-10** may be cuased either by transannular orbital interactions or by the polarity of carbonyl groups. In cases of ketones, the effect of polarity dominates. In cases of methylene derivatives, however, the effects of both TS and TB interactions become more pronounced than polarity. For more reliable and complete analyses on the origins of $\Delta\delta$ values, NMR chemical shift calculations by *ab initio* method are required.[12]

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