

# Prevalence of the Alkyl/Phenyl-Folded Conformation in Benzylic Compounds $C_6H_5CH_2-X-R$ ( $X = O, CH_2, CO, S, SO, SO_2$ ): Significance of the $CH/\pi$ Interaction as Evidenced by High-Level Ab Initio MO Calculations\*\*

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**Abstract:** Ab initio MO calculations were carried out to examine the conformational energies of various benzylic compounds  $C_6H_5CH_2XR$  ( $X = O, CH_2, CO, S, SO, SO_2$ ;  $R = CH_3, C_2H_5, iC_3H_7, tC_4H_9$ ) at the MP2/6-311G(d,p)//MP2/6-31G(d) level. Rotamers with R/Ph in *gauche* relationship are generally more stable than the R/Ph *anti* rotamers. In these stable geometries, the interatomic distance in the interaction of  $\alpha$ - or  $\beta$ -CH

in the alkyl group and the *ipso*-carbon atom of the phenyl ring is short. The computational results are consistent with experimental data from supersonic molecular jet spectroscopy on 3-*n*-pro-

pyltoluene and NMR and crystallographic data on structurally related ketones, sulfoxides, and sulfones. In view of this, the alkyl/phenyl-congested conformation of these compounds has been suggested to be a general phenomenon, rather than an exception. The attractive  $CH/\pi$  interaction has been suggested to be a dominant factor in determining the conformation of simple aralkyl compounds.

**Keywords:** ab initio calculations · conformational analysis · hydrogen bonds · noncovalent interactions · pi interactions

## Introduction

The  $CH/\pi$  interaction<sup>[1]</sup> is the weakest nonconventional hydrogen bond.<sup>[2]</sup> This attractive molecular force has been recognized as the interaction of soft acids with soft bases,<sup>[3]</sup> in contrast to the conventional hydrogen bond, that is, the interaction between hard acids and hard bases. The electronic effect of the substituent on the stereoselectivity of complex formation,<sup>[4]</sup> conformational equilibrium,<sup>[5]</sup> crystal packing,<sup>[6]</sup> and enantioselectivity<sup>[7]</sup> has demonstrated that the  $CH/\pi$  interaction is by no means a mere dispersion force, but has a distinct hydrogen-bond character. Recently, a number of high-level ab initio<sup>[8]</sup> and DFT<sup>[9]</sup> calculations supporting the  $CH/\pi$  concept have appeared. Though weak, the  $CH/\pi$  interaction plays significant roles in various fields of chemistry, including the conformation of molecules,<sup>[10]</sup> self-assembly,<sup>[11]</sup> chiral recognition,<sup>[12]</sup> solid-state reactions,<sup>[13]</sup> and drug design.<sup>[14]</sup> Evidence has also been presented for the significance of

$CH/\pi$  interactions in the structure of proteins<sup>[15, 16, 17]</sup> and nucleic acids.<sup>[18]</sup>

In a previous paper, we studied, by ab initio MO calculations, the conformation of 2-phenylpropionaldehyde and alkyl 1-phenylethyl ketones  $PhCH(CH_3)COR$  ( $R = H, CH_3, C_2H_5, iC_3H_7, tC_4H_9$ ).<sup>[19]</sup> These molecules were shown to prefer the conformation in which the alkyl group R is *gauche* to Ph and *anti* to the benzylic methyl group. The result was interpreted on the basis of the  $CH/\pi$  interaction between CH groups in R and the  $\pi$ -electron system of Ph. The effects of the  $CH_3 \cdots C=O$  hydrogen bond and unfavorable electrostatic  $C=O/Ph$  interaction were also invoked. To explore the generality and to reveal the origin of the alkyl/aryl-congested structure, we studied, by high-level ab initio MO calculations, the conformation of a series of benzylic compounds  $C_6H_5CH_2XR$  ( $X = O, S, CH_2, CO, SO, SO_2$ ;  $R = CH_3, C_2H_5, iC_3H_7, tC_4H_9$ ; Figure 1). These molecules are structurally related to alkyl 1-phenylethyl compounds  $C_6H_5CHCH_3XR$ , but the benzylic methyl group is absent. We will show that the alkyl/aryl-folded geometry with a  $CH/\pi$  interaction is a general feature of these aralkyl compounds.

## Computational Methods

The Gaussian 98 program<sup>[20]</sup> was used. The basis sets implemented in the program were employed without modification. Electron correlation energies were calculated by applying second-order Møller–Plesset (MP2) perturbation theory. Geometries of the molecules were optimized at the MP2/6-31G(d) level of theory. Single-point calculations were

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[\*\*] A comprehensive literature list for the  $CH/\pi$  interaction is available at <http://www.tim.hi-ho.ne.jp/dionisio>

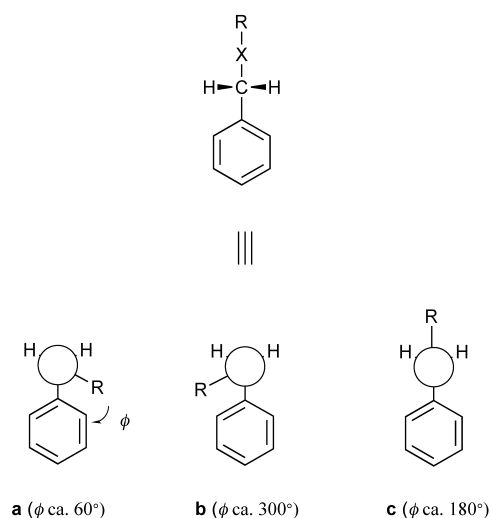


Figure 1. Possible rotamers of benzylic compounds  $C_6H_5CH_2XR$ .

performed on these geometries at the MP2/6-311G(d,p) level to estimate the exact energies of conformers. Vibrational frequencies were calculated by using the analytical second derivatives at the same level of geometry optimization for each conformer. These results were used to add thermal energy corrections to the total energy at 298.15 K and 1 atm, by using the principal isotope for each element. Furthermore, for benzylic compounds  $C_6H_5CH_2XR$  **3** ( $X = CH_2$ ) and **1** ( $X = O$ ,  $R = CH_3$ ), **2** (S), **5** (SO), and **6** ( $SO_2$ ), geometry optimizations were performed at the MP2/6-31G(d,p), MP2/6-31 + G(d), and MP2/6-311G(d) levels to examine the basis set dependency for relative steric energies.

## Results and Discussion

Table 1 lists the relative Gibbs energy at 298.15 K and 1 atm of the stable conformations of various benzylic compounds  $C_6H_5CH_2XR$ : **1** ( $X = O$ ), **2** (S), **3** ( $CH_2$ ), **4** (CO), **5** (SO), and **6** ( $SO_2$ ). The optimized torsion angles R-X-C-Ph are also given.

To determine the effect of diffuse functions, we calculated the conformational energies of alkylbenzenes **3** ( $X = CH_2$ ) at different levels of theory (Table 2). (Note that values reported in this table are the relative steric energies and not the Gibbs energies.) The steric energy indeed depended on the basis sets used for geometry optimization. However, the variation in  $\Delta_{ac}$  is insignificant, and the order of rotamers does not vary from method to method. Further, in other benzylic compounds **1** ( $X = O$ ,  $R = CH_3$ ), **2** (S), **5** (SO), and **6** ( $SO_2$ ),  $\Delta_{ab}$  and  $\Delta_{ac}$  did not significantly vary on adding diffuse functions (data not shown).

Table 3 lists interatomic  $CH \cdots \pi$  ( $\alpha$ - or  $\beta$ -CH in R and  $C_{ipso}$  in Ph;  $C_{ortho}$ -H and C in  $C=O$  for **4**) and  $CH \cdots O$  ( $C_{ortho}$ -H in Ph and O for **4–6**) distances in the respective geometries. Figure 2 shows stereo views of the most stable rotamers of **1–6** ( $R = CH_3$ ).

**General aspects:** In almost all cases, rotamer **a** (**a** and **b** for **5**) is more stable than rotamer **c**. Exceptions are noted for *tert*-butyl-substituted **2**, **3**, **5**, and **6**. In the most stable rotamers of **1–6** ( $R = CH_3$ ; see Figure 2) a C–H bond is directed toward the phenyl ring. Short  $CH \cdots \pi$  distances are noted in every case between an  $\alpha$ - or a  $\beta$ -CH in R and the *ipso*-carbon atom (2.57–2.78 for **1**, 2.61–2.76 for **2**, 2.56–2.76 for **3**, 2.84–3.10

Table 1. Relative Gibbs energies [kcal mol<sup>-1</sup>] at 298 K and 1 atm of the stable conformations of benzylic compounds,  $C_6H_5CH_2XR$  **1** ( $X = O$ ), **2** (S), **3** ( $CH_2$ ), **4** (CO), **5** (SO), and **6** ( $SO_2$ ), calculated by the ab initio method. Optimized R-X- $CH_2$ -Ph torsion angles  $\phi$  [°] are given in parentheses. Numbers in square brackets for rotamer **a** (rotamers **a** and **b** for **5**) of the ethyl and isopropyl compounds indicate the number of atoms forming the intramolecular CH/ $\pi$  hydrogen bond.

	rotamer <b>a</b>	rotamer <b>b</b>	rotamer <b>c</b>
$C_6H_5CH_2OR$ <b>1</b>			
CH <sub>3</sub>	0.00 (68) [5]		0.79 (177)
C <sub>2</sub> H <sub>5</sub>	0.00 (70) [5]		0.87 (177)
	1.09 (69) [5]		2.11 (167)
	2.18 (89) [6]		
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.00 (71) [5]		1.06 (165)
	1.14 (93) [6]		3.34 (167)
	3.41 (92) [6]		
<i>t</i> C <sub>4</sub> H <sub>9</sub>	0.00 (92) [6]		0.05 (166)
$C_6H_5CH_2SR$ <b>2</b>			
CH <sub>3</sub>	0.00 (58) [5]		0.97 (180)
C <sub>2</sub> H <sub>5</sub>	0.00 (54) [5]		1.16 (176)
	0.33 (60) [5]		1.29 (180)
	0.86 (57) [6]		
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.00 (54) [5]		1.19 (174)
	0.95 (59) [6]		1.60 (180)
	2.22 (64) [6]		
<i>t</i> C <sub>4</sub> H <sub>9</sub>	0.81 (72) [6]		0.00 (180)
$C_6H_5CH_2CH_2R$ <b>3</b>			
CH <sub>3</sub>	0.00 (62) [5]		0.04 (180)
C <sub>2</sub> H <sub>5</sub>	0.00 (62) [5]		0.13 (180)
	0.39 (59) [5]		0.66 (177)
	1.53 (60) [6]		
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.00 (59) [5]		0.39 (176)
	1.37 (61) [6]		1.05 (180)
	2.51 (64) [6]		
<i>t</i> C <sub>4</sub> H <sub>9</sub>	1.56 (65) [6]		0.00 (180)
$C_6H_5CH_2COR$ <b>4</b>			
CH <sub>3</sub>	0.00 (80) [5]		
C <sub>2</sub> H <sub>5</sub>	0.00 (83) [5]		
	1.29 (81) [5]		
	2.10 (95) [6]		
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.00 (78) [5]		
	1.41 (99) [6]		
	2.22 (95) [6]		
<i>t</i> C <sub>4</sub> H <sub>9</sub>	0.00 (95) [6]		
$C_6H_5CH_2SOR$ <b>5</b>			
CH <sub>3</sub>	0.84 (65) [5]	0.00 (306) [5]	1.66 (179)
C <sub>2</sub> H <sub>5</sub>	0.30 (64) [5]	0.00 (305) [5]	1.26 (177)
	0.70 (59) [5]	0.47 (307) [5]	1.44 (177)
	2.13 (60) [6]	0.62 (305) [6]	2.15 (178)
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.54 (63) [5]	0.00 (310) [5]	1.62 (173)
	1.55 (61) [6]	0.77 (304) [6]	1.65 (175)
	2.90 (66) [6]	2.37 (302) [6]	1.84 (177)
<i>t</i> C <sub>4</sub> H <sub>9</sub>	1.12 (68) [6]	0.78 (302) [6]	0.00 (174)
$C_6H_5CH_2SO_2R$ <b>6</b>			
CH <sub>3</sub>	0.00 (54) [5]		1.38 (180)
C <sub>2</sub> H <sub>5</sub>	0.00 (51) [5]		1.43 (180)
	0.29 (54) [5]		1.60 (180)
	0.63 (54) [6]		
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.00 (56) [5]		1.39 (177)
	0.85 (64) [6]		1.41 (180)
	1.45 (57) [6]		
<i>t</i> C <sub>4</sub> H <sub>9</sub>	0.26 (59) [6]		0.00 (180)

for **4**, 2.58–2.75 for **5**, and 2.60–2.82 Å for **6**). The results compare well with the data of our crystallographic database survey for intramolecular CH/ $\pi$  bonding (2.63 and 2.70 Å, respectively, for five- and six-membered interactions).<sup>[21]</sup> The

Table 2. Basis set dependencies of relative steric energies [kcal mol<sup>-1</sup>] of the stable conformations of alkylbenzene compounds C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>R **3**, calculated by the ab initio method.

	MP2/6-31G(d)		MP2/6-31G(d,p)		MP2/6-31 + G(d)		MP2/6-311G(d)	
	rotamer <b>a</b>	rotamer <b>c</b>	rotamer <b>a</b>	rotamer <b>c</b>	rotamer <b>a</b>	rotamer <b>c</b>	rotamer <b>a</b>	rotamer <b>c</b>
CH <sub>3</sub>	0.00	0.26	0.00	0.28	0.00	0.10	0.00	0.52
C <sub>2</sub> H <sub>5</sub>	0.00	0.35	0.00	0.36	0.00	0.30	0.00	0.61
	0.38	0.93	0.31	0.90	0.49	0.93	0.23	1.07
	1.81		1.70		1.66		1.43	
<i>i</i> C <sub>3</sub> H <sub>7</sub>	0.00	0.62	0.00	0.64	0.00	0.72	0.00	0.93
	1.61	1.30	1.55	1.29	1.34	1.61	1.35	1.55
	2.01		1.88		2.18		1.85	
<i>t</i> C <sub>4</sub> H <sub>9</sub>	0.82	0.00	0.72	0.00	0.58	0.00	0.34	0.00

somewhat larger values calculated for **4** may reflect the difference in the R-C<sub>sp<sup>2</sup></sub>-C bond angle (ca. 120°) versus sp<sup>3</sup>-hybridized C, O, or S (ca. 105°). Short CH...O distances were also found between one of the two *ortho*-CH moieties of the phenyl group and the oxygen atom in **1**, **2**, **5**, and **6**. The data are comparable with the accepted values of van der Waals distances (2.9 Å and 2.7 Å, respectively, for CH/C<sub>sp<sup>2</sup></sub> and CH/O).<sup>[22]</sup> Figure 3 shows the results schematically and the possible interactions involved. With respect to rotation around the X-C<sub>α</sub> (alkyl) bond, three stable geometries were found for rotamer **a** (**a** and **b** for **5**) of the ethyl and isopropyl compounds. In the most stable geometry, an α-CH group points toward Ph, and a five-membered CH/π interaction is formed with the *ipso*-carbon atom of the phenyl group (Figure 4). A five-membered CH/π interaction, therefore, is more effective than a six-membered interaction (with β-CH) in stabilizing the R/Ph-congested conformation. The result is reasonable in view of the notion that an intramolecular hydrogen bond is more feasible for a five-membered than for a six-membered ring.<sup>[15, 23]</sup> Another significant point is that the CH...π distance in the geometry of the stable rotamers is shorter than the sum of the van der Waals radii of the relevant atoms.<sup>[24]</sup>

**Benzyl alkyl ethers C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>OR:** In benzyl alkyl ethers **1** (X = O), rotamer **a** (= **b**) is calculated to be more stable than rotamer **c**; the difference in Gibbs energy Δ<sub>ac</sub> is 0.79–1.06 kcal mol<sup>-1</sup> for the lower alkyl homologues. In rotamer **a**, the distance between the relevant hydrogen atom (α- or β-CH in R) and the *ipso*-carbon atom in Ph (CH...π distance) is short. The above facts suggest that CH/π interactions operate in stabilizing the R/Ph-congested geometry (Figure 3a). It is noted that Δ<sub>ac</sub> is the smallest (0.05 kcal mol<sup>-1</sup>, i.e., insignificant in view of the accuracy of the present method) for R = *t*Bu, and the CH...π distance is longer than in the lower homologues. The torsion angle φ is larger in the *tert*-butyl ether (92°) than in the lower ones (68–71°). Larger values of φ are also noted for the ethyl (89°) and isopropyl compounds (93, 92°) in geometries in which a CH<sub>3</sub> group points toward the phenyl group. In these geometries, formation of a six-membered CH/π interaction is only feasible by using one of the three CH groups of CH<sub>3</sub>.

Table 3. Interatomic CH...π(Ph), CH...π(C=O), and CH(*ortho*)...O distances [Å] of the stable conformations of benzylic compounds C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>XR **1** (X = O), **2** (S), **3** (CH<sub>2</sub>), **4** (CO), **5** (SO), and **6** (SO<sub>2</sub>), calculated by the ab initio method. Numbers in the square brackets for the ethyl and isopropyl analogues indicate the number of atoms forming the intramolecular CH/π hydrogen bond.

	CH...π(Ph)	CH...O	CH...π(C=O)	φ [°]
<b>C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>OR <b>1</b></b>				
CH <sub>3</sub>	2.665 [5]	2.622		68
C <sub>2</sub> H <sub>5</sub>	2.639 [5]	2.599		70
	2.581 [5]	2.605		69
<i>i</i> C <sub>3</sub> H <sub>7</sub>	2.686 [6]	2.576		89
	2.567 [5]	2.594		71
	2.656 [6]	2.546		93
<i>t</i> C <sub>4</sub> H <sub>9</sub>	2.805 [6]	2.532		92
	2.783 [6]	2.524		92
<b>C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>SR <b>2</b></b>				
CH <sub>3</sub>	2.764 [5]			58
C <sub>2</sub> H <sub>5</sub>	2.679 [5]			54
	2.734 [5]			60
	2.705 [6]			57
<i>i</i> C <sub>3</sub> H <sub>7</sub>	2.647 [5]			54
	2.673 [6]			59
	2.654 [6]			64
<i>t</i> C <sub>4</sub> H <sub>9</sub>	2.605 [6]			65
<b>C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>R <b>3</b></b>				
CH <sub>3</sub>	2.761 [5]			62
C <sub>2</sub> H <sub>5</sub>	2.728 [5]			62
	2.717 [5]			59
	2.619 [6]			59
<i>i</i> C <sub>3</sub> H <sub>7</sub>	2.686 [5]			60
	2.576 [6]			61
	2.620 [6]			64
<i>t</i> C <sub>4</sub> H <sub>9</sub>	2.564 [6]			65
<b>C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>COR <b>4</b></b>				
CH <sub>3</sub>	2.925 [5]	2.796	2.929	80
C <sub>2</sub> H <sub>5</sub>	2.901 [5]	2.766	2.908	83
	2.901 [5]	2.818	2.905	81
	2.908 [6]	2.512	2.808	95
<i>i</i> C <sub>3</sub> H <sub>7</sub>	2.840 [5]	2.807	2.826	78
	2.845 [6]	2.492	2.818	99
	3.031 [6]	2.521	2.797	95
<i>t</i> C <sub>4</sub> H <sub>9</sub>	3.101 [6]	2.498	2.795	95
<b>C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>SOR <b>5</b></b>				
CH <sub>3</sub>	2.751 [5]			65
	2.638 [5]	2.565		306
C <sub>2</sub> H <sub>5</sub>	2.693 [5]			64
	2.693 [5]			59
	2.751 [6]			60
<i>i</i> C <sub>3</sub> H <sub>7</sub>	2.651 [5]	2.589		305
	2.595 [5]	2.465		307
	2.573 [6]	2.562		305
	2.676 [5]			63
	2.657 [6]			61
<i>t</i> C <sub>4</sub> H <sub>9</sub>	2.640 [6]			66
	2.531 [5]	2.477		310
	2.632 [6]	2.595		304
	2.628 [6]	2.444		302
	2.576 [6]			68
<i>t</i> C <sub>4</sub> H <sub>9</sub>	2.572 [6]	2.445		302
<b>C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>-SO<sub>2</sub>-R <b>6</b></b>				
CH <sub>3</sub>	2.823 [5]	2.627		54
C <sub>2</sub> H <sub>5</sub>	2.769 [5]	2.557		51
	2.692 [5]	2.655		54
	2.779 [6]	2.627		54
<i>i</i> C <sub>3</sub> H <sub>7</sub>	2.735 [5]	2.536		56
	2.612 [6]	2.663		64
	2.688 [6]	2.521		57
<i>t</i> C <sub>4</sub> H <sub>9</sub>	2.603 [6]	2.516		59

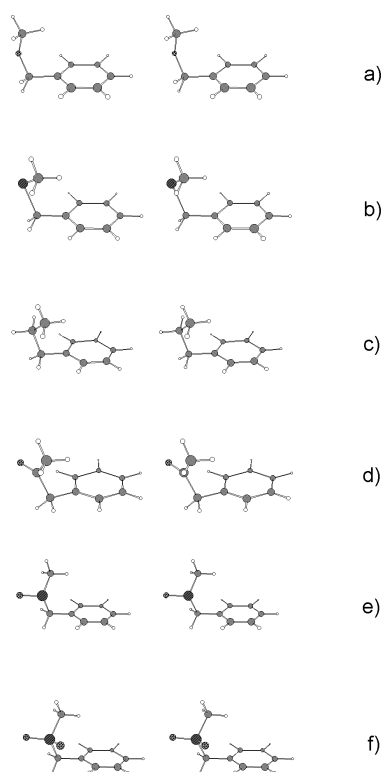


Figure 2. Stereo views of the most stable rotamers of benzylic compounds. a)  $C_6H_5CH_2OCH_3$ , b)  $C_6H_5CH_2SCH_3$ , c)  $C_6H_5CH_2CH_2CH_3$ , d)  $C_6H_5CH_2COCH_3$ , e)  $C_6H_5CH_2SOCH_3$ , f)  $C_6H_5CH_2SO_2CH_3$ .

**Benzylic alkyl sulfides  $C_6H_5CH_2SR$ :** Compounds **2** ( $X=S$ ) differ from **1** in that the oxygen atom is replaced by a sulfur atom. In these sulfides rotamer **a** ( $=b$ ) is also found to be more stable than **c** for the lower homologues (Figure 3a). The difference in Gibbs energy  $\Delta_{ac}$  is 0.97–1.19 kcal mol $^{-1}$ . For the *tert*-butyl sulfide, rotamer **c** is more stable than **a** ( $\Delta_{ac} = -0.81$  kcal mol $^{-1}$ ). The torsion angle  $\phi$  of rotamer **a** of the lower homologues is much smaller in **2** (54–58°) than in **1** (68–71°). This presumably reflects the difference in the C–X bond length of **1** (C–O) and **2** (C–S).

**Alkylbenzenes  $C_6H_5CH_2CH_2R$ :** For alkylbenzenes **3** ( $X=CH_2$ ), the difference in Gibbs energy  $\Delta_{ac}$  was calculated to be 0.04, 0.13, and 0.39 kcal mol $^{-1}$  for *n*-propylbenzene ( $R=CH_3$ ), *n*-butylbenzene ( $C_2H_5$ ), and isopentylbenzene ( $iC_3H_7$ ), respectively. These values are too small to be significant in view of the approximation used here. The results, however, suggest that the CH/ $\pi$  interaction is also operative in stabilizing the R/Ph-congested geometry in these hydrocarbons. Seeman et al. in fact showed, by supersonic molecular jet spectroscopy, that 3-*n*-propyltoluene exists in *gauche* conformations, as well as in an *anti* conformation.<sup>[25]</sup> In this regard, the number of vicinal H/H interactions is three in rotamer **a**, but only two in rotamer **c** (Figure 3b). According to Wertz and Allinger, this type of interaction is strongly destabilizing.<sup>[26]</sup> In contrast to ethers **1**, sulfides **2**, and ketones **4** (vide infra), the torsion angle  $\phi$  of rotamer **a** of **3** is very close to 60° (59–62° for lower alkyl, 65° for *t*Bu). This shows the importance of the unfavorable H/H interaction; departure from 60° may make the H/H repulsion more severe.

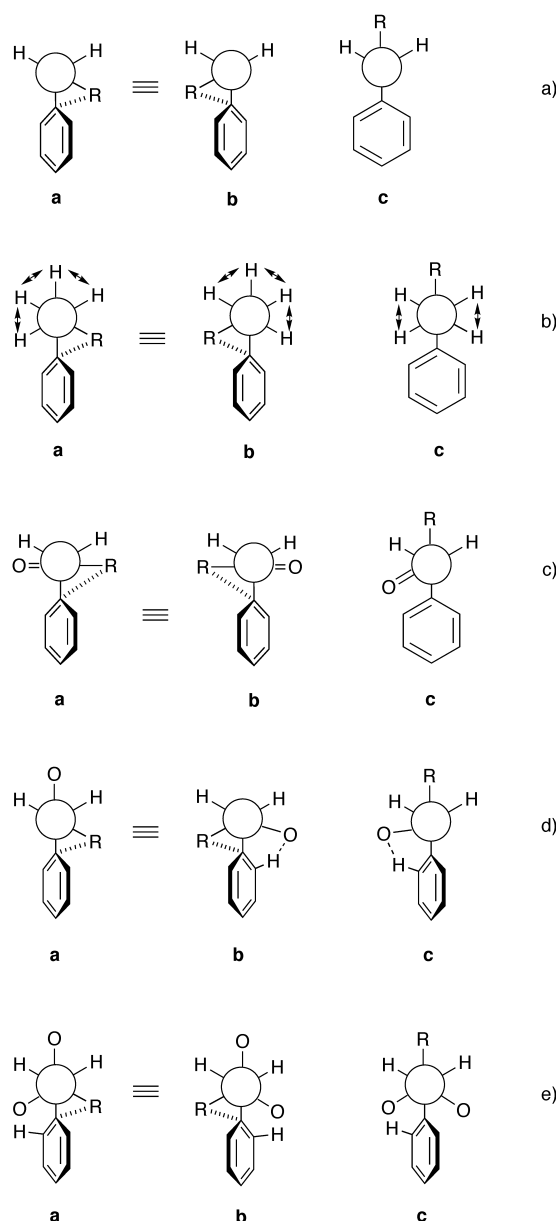


Figure 3. Rotamers of benzylic compounds  $C_6H_5CH_2XR$ . a)  $C_6H_5CH_2OR$  and  $C_6H_5CH_2SR$ , b)  $C_6H_5CH_2CH_2R$ , c)  $C_6H_5CH_2COR$ , d)  $C_6H_5CH_2SOR$ , e)  $C_6H_5CH_2SO_2R$ . CH/ $\pi$  interactions are indicated by dotted lines. Arrows in b) indicate unfavorable vicinal H/H interactions.

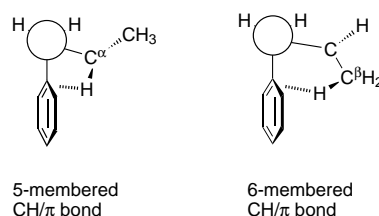


Figure 4. Five- and six-membered CH/ $\pi$  interactions (dotted lines).

An exception was noted for the *t*Bu compound: the *t*Bu/Ph *gauche* rotamer **a** is less stable than the *anti* rotamer **c** ( $\Delta_{ac} = -1.56$  kcal mol $^{-1}$ ). Here, formation of a five-membered CH/ $\pi$  interaction is unrealizable due to the absence of  $\alpha$ -CH groups in the *tert*-butyl compound. Accordingly, rotamer **a** may

become unstable relative to rotamer **c**. Table 1 shows that  $\Delta_{ac}$  is smaller in the *tert*-butyl derivative than in the lower homologues and also in other series of compounds: **1** (0.05 vs 0.79–1.06), **2** (–0.81 vs 0.97–1.19), **5** (–1.12 vs 0.82–1.08) and **6** (–0.26 vs 1.38–1.43 kcal mol<sup>–1</sup>).

**Benzyl alkyl ketones C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>COR:** In benzyl alkyl ketones **4** (R = CO), only rotamer **a** (= **b**) is possible energetically. In other words, a rotamer corresponding to geometry **c** cannot exist. This is consistent with earlier experimental and computational results that the R/Ph *gauche* geometry (corresponding to rotamer **a**) is the most stable in alkyl 1-phenylethyl ketones. A contribution from the attractive CH/π interaction is evident. Also likely is the importance of the destabilizing electrostatic interaction between the carbonyl dipole and the phenyl quadrupole (Figure 3c).

The torsion angle  $\phi$  in the lower alkyl analogues (80° for R = Me, 83, 81° for Et, 78° for *i*Pr) is much smaller than that found in the *t*Bu analogue (95°). A larger  $\phi$  is also noted for the ethyl (95°) and isopropyl (95, 99°) compounds when a  $\beta$ -CH<sub>3</sub> group in R is directed toward the phenyl group. In such a geometry only formation of a six-membered CH/π bond is feasible. In rotamers in which  $\alpha$ -CH interacts, on the other hand, formation of a more effective five-membered CH/π bond is likely (Figure 4). We also suggest that a factor in stabilizing rotamer **a** in **4** is another kind of CH/π interaction, which can occur between one of the *ortho*-CH groups of Ph and the carbonyl π orbital (Figure 5). Short distances between the relevant atoms are in fact observed (Table 2).

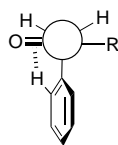


Figure 5. CH/π interaction between an *ortho* CH group and the carbonyl double bond.

**Benzyl alkyl sulfoxides C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>SOR:** In the sulfoxides **5** (X = SO) rotamer **b** (R/Ph *gauche*, S=O/Ph *gauche*) was found to be the most stable. Rotamer **a** (S=O/Ph *anti*) is less stable than **b**, and rotamer **c** (R/Ph *anti*) is the least stable (Figure 2d), except for R = *t*Bu.<sup>[27]</sup>

The **a**-type rotamer was suggested to be the most stable for a pair diastereoisomers of alkyl 1-phenylethyl sulfoxides **7** (Figure 6) by NMR experiments. In these conformations,

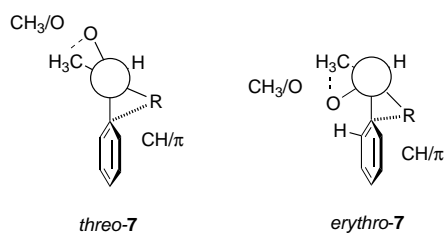


Figure 6. Stable conformations of the two diastereoisomers of alkyl 1-phenylethyl sulfoxides **7**. CH/π interactions are indicated by dotted lines. Formation of a five-membered CH/O hydrogen bond is feasible between CH<sub>3</sub> and S=O.

formation of a 1,5-intramolecular CH⋯O hydrogen bond<sup>[28]</sup> between the benzylic methyl and S=O groups is possible for both diastereoisomers. In the case of benzylic sulfoxides **5**, this kind of stabilization is not expected due to the absence of the CH<sub>3</sub> group. However, a CH⋯O hydrogen bond between the *ortho*-CH of Ph and the S=O oxygen atom may stabilize rotamer **b** (Figure 3d). In rotamer **a**, this type of CH⋯O bond cannot occur. It may therefore be that this type of hydrogen bond overcomes the effect of the unfavorable O⋯Ph electrostatic interaction. The CH⋯O distance in rotamer **b** of **5** is indeed very short.

**Benzyl alkyl sulfones C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>SO<sub>2</sub>R:** In sulfones **6** (X = SO<sub>2</sub>) rotamer **a** (= **b**) was found to be more stable than **c** (Figure 3e), except for R = *t*Bu. The result is reasonable in view of the CH/π interaction and the destabilizing electrostatic interaction; the latter can occur between the SO<sub>2</sub> group and Ph in rotamer **c**. The result is consistent with our earlier findings on the conformation of *tert*-butyl 1-phenylethyl sulfone C<sub>6</sub>H<sub>5</sub>CHCH<sub>3</sub>SO<sub>2</sub>C<sub>4</sub>H<sub>9</sub>, for which the *gauche* *t*Bu/Ph geometry was found by X-ray crystallography.<sup>[29]</sup>

## Conclusion

To summarize, rotamers with R/Ph in a *gauche* relationship are more stable than the *anti* conformations in a series of benzylic compounds C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>XR, irrespective of the nature of X and R, except for *tert*-butyl-substituted **2**, **3**, **5**, and **6**.

The significance of the present paper is threefold. First, high-level ab initio calculations gave results consistent with experimental data. Thus, the result agrees with the finding, by supersonic jet spectroscopy, that 3-*n*-propyltoluene exists in *gauche* conformations, as well as in an *anti*-R/Ph conformation. The present calculations are also consistent with experimental data on alkyl 1-phenylethyl compounds C<sub>6</sub>H<sub>5</sub>CHCH<sub>3</sub>XR: in ketones (X = CO; NMR<sup>[30]</sup>) and sulfoxides (X = SO; X ray,<sup>[31]</sup> ORD/CD,<sup>[32]</sup> NMR,<sup>[33]</sup> dipole moment<sup>[34]</sup>) *gauche* conformations were found to be more stable than *anti* conformations. In view of the above facts, we conclude that ab initio calculations can be used with confidence to predict the conformation of aralkyl compounds. These include ethers and hydrocarbons, for which experimental data are not easily obtainable.

Second, the relevance of the CH/π interaction to the conformation of organic molecules has been established. A number of papers demonstrate that the CH/π interaction plays a substantial role in determining the conformation of organic compounds,<sup>[21, 35]</sup> peptides,<sup>[36, 37]</sup> and transition metal complexes.<sup>[38, 39]</sup> The present study provides a firm theoretical ground for these observations.

Finally, the prevalence of the alkyl/phenyl-congested conformation has been demonstrated. Organic chemists customarily assume that “bulkier” groups are arranged remote from each other. However, the “bulky group” is often a phenyl or other aromatic group. Clearly, the above conjecture is invalid for compounds bearing an aromatic moiety at a terminus of the molecule. The bulk-repulsive approach ignores, or at least underestimates, attractive forces that may control the con-

formational equilibrium of aralkyl compounds. A number of stereochemical problems, still unsettled to date, will become clearer in the light of this new paradigm.

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