

## Interaction between stacked aryl groups in 1,8-diarylnaphthalenes: Dominance of polar/ $\pi$ over charge-transfer effects

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**Abstract:** Several 1,8-diarylnaphthalenes have been prepared, and the barrier to rotation around the aryl/naphthalene bond has been measured. In these molecules steric congestion forces the aryls in a parallel stacked geometry. The barriers to rotation were used to evaluate the strength and to investigate the nature of the interaction between the arenes. The variance of the  $\Delta G^\ddagger$  for the rotation upon arene substitution with electron donating or electron withdrawing groups indicates that polar/ $\pi$  electrostatic effects dominate over charge-transfer effects in determining the arene/arene interaction.

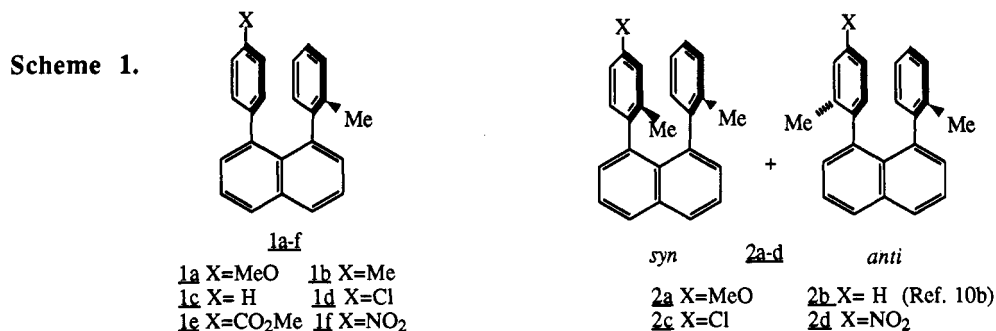
Non covalent interactions between aromatic units (1) play a major role in determining the properties and the behavior of molecules in a variety of processes, such as stereocontrol of organic reactions (2) and molecular recognition (3), and in affecting the structure of many biologically relevant molecules (4). In order to establish the influence exerted by arene/arene interactions on these phenomena and to learn how to use them in molecular design, we must understand the relative importance of the factors contributing to the interaction.

The energy of the interaction between two arene units divides roughly into a polar (electrostatic and induction) and a van der Waals term (dispersion) (1). The polar term depends on the relative charge distribution and on the interaction between the charge of one arene with the induced change in the charge of the other. The van der Waals term depends on the contact surface area. Since in the case of two interacting benzenes the surface area is relatively small, the polar term should dominate the interaction (1).

The charge distribution in benzene can be described as an electron rich central core surrounded by an electron poor periphery (5). This description is in agreement with the preference shown by crystalline (6), liquid (7), and gaseous benzene (8) for the edge-to-face, T-shaped geometry, and predicts an unfavorable repulsive interaction for the face-to-face stacked disposition, and a favorable attractive one for the offset stacked arrangement. On this basis, the interaction between two parallel stacked benzenes can be studied only in those systems in which this geometry is imposed by steric factors.

We reasoned that the steric congestion at the *peri* positions of naphthalene should indeed force two phenyl rings in the required orientation (9). This orientation is lost when a phenyl group rotates around the phenyl/naphthalene bond (10, 11). Thus, the barrier to rotation should depend on the strength of the parallel stacked interaction, and, in a homologous series of compounds, the variance of the barrier upon substitution of the aryls with electron donating (EDG) and electron withdrawing (EWG) groups should provide a new insight into the nature of the  $\pi/\pi$  interaction.

We began to study the barrier to rotation in the series of compounds **1a-f** and **2a-d**. These were prepared (12) starting from 1,8-dibromonaphthalene by sequential Ullmann couplings with the corresponding iodobenzenes and iodotoluenes (Scheme 1). The phenyl rings in these series of compounds are perpendicular to the naphthalene plane, as shown by the X-ray structure of 1-(2-methylphenyl) naphthalene (13) and of other 1,8-diarylnaphthalenes (9), and as predicted by AM1 (14) semiempirical calculations (12). Therefore, the methyl of the *o*-tolyl group in **1a-f** and **2a-d** makes diastereotopic the two regions of space above and below the naphthalene plane. Restricted rotation around the aryl/naphthalene bond results in the observation of different signals for the *o/o'* and *m/m'* protons in compounds **1a-f**, and allows the use of variable temperature  $^1\text{H-NMR}$  spectroscopy to evaluate the barrier to rotation.



Coalescence of the *o/o'* and *m/m'* protons was observed upon warming samples of **1a-f** in DMSO-*d*<sub>6</sub>. From line shape analysis the barriers reported in Table 1 were determined. The barrier was lowest for compound **1a** (X = OMe),  $\Delta G^\ddagger = 13.9$  kcal/mol, and increased along the series to **1f** (X = NO<sub>2</sub>),  $\Delta G^\ddagger = 17.3$  kcal/mol.

**TABLE 1.** Barriers to rotation for compounds **1a-f**.

Compound	Substituent	$\Delta G^\ddagger$ (kcal/mol)	Coalescence temp. °C
<b>1a</b>	OMe	13.9	65
<b>1b</b>	Me	14.4	65
<b>1c</b>	H	14.7	70
<b>1d</b>	Cl	15.5	75
<b>1e</b>	CO <sub>2</sub> Me	16.9	75
<b>1f</b>	NO <sub>2</sub>	17.3	85

**TABLE 2.** Barriers to rotation for compounds **2a-d**.

Compound	Substituent	$\Delta G^\ddagger$ (kcal/mol)	
		(kin. ep. at 40°C)	(2D-NMR at 145°C)
<b>2a</b>	OMe	23.8	24.8
<b>2b</b>	H	24.1 (Ref. 10b) -	
<b>2c</b>	Cl	24.2	25.7
<b>2d</b>	NO <sub>2</sub>	24.8	26.1

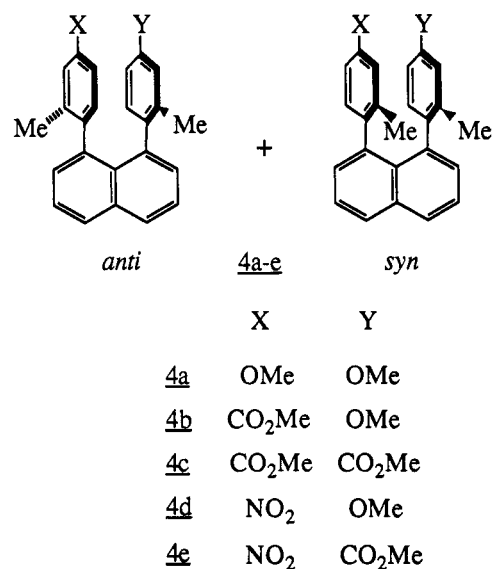
The perpendicular disposition of the aryl groups in compounds **2a-d** led to the formation of *anti/syn* diastereoisomers. In all cases they were obtained in a roughly 3.5 : 1 ratio, as determined by  $^1\text{H-NMR}$  (15). Barrier evaluation was achieved by two methods. Compounds **2a**, **2c**, and **2d** were enriched in their *anti* isomer by iterative column chromatography, and the kinetic epimerization to reach the equilibrium mixture was followed by  $^1\text{H-NMR}$  at 40°C in CDCl<sub>3</sub>. In these conditions Roberts (10b) established the barrier value reported for **2b** in Table 2. Much more conveniently, the barriers were also obtained by 2D-NMR using an EXSY pulse sequence experiment (16) carried out at 145°C on DMSO-*d*<sub>6</sub> solutions of the isomeric mixtures. The barrier values for compounds **2a-d** are reported in Table 2 (17).

Independent of the method used, the trend was constant: lowest barrier for **2a** (X = OMe) and highest for **2d** (X = NO<sub>2</sub>). The plots of  $\Delta G^\ddagger$  for the barrier to rotation vs the  $\sigma_{para}$  values of the substituents showed a good linear correlation in both cases (12).

We rationalize (12) these results by a through space polar/ $\pi$  interaction between the two arenes. As mentioned above, the parallel stacked disposition of the 1,8-aryls in **1a-f** and **2a-d** is strongly repulsive. Therefore, substitution of a hydrogen by an EDG group such as methoxy increases the repulsion and, by destabilizing the parallel stacked ground state conformation, lowers the barrier. On the other hand, substitution by an EWG group such as nitro reduces the repulsion and, by lowering the energy of the parallel stacked ground state conformation, increases the barrier. In other words: the "unnatural" (1) parallel stacked arrangement of the two arenes is made more unfavorable by EDG group substitution, and less unfavorable by EWG group substitution. Other possible explanations of the barrier trend based on conjugation of the rotating aryl with the naphthalene spacer, or on a charge-transfer interaction between the aryls, are in disagreement with the observed barrier trend, and could be ruled out on the basis of literature results and experimental findings (18, 19).

To address further the question of the relative importance of the contribution of polar/ $\pi$  vs charge-transfer interaction, we prepared the doubly substituted compounds **4a-e** reported in Scheme 2 by the same synthetic approach employed above (20). As before these compounds were obtained as roughly 3.5 : 1 mixtures of *anti* /*syn* isomers. The  $\Delta G^\ddagger$  for the epimerization was determined by 2D-NMR (145°C, DMSO- $d_6$  solution) for both the *syn* to *anti* and the *anti* to *syn* processes. The barrier values are reported in Table 3, where the  $\Delta G^\ddagger$  for the isomerization of compound **2d** was also included for sake of comparison.

Scheme 2.

TABLE 3. Barriers to rotation for compounds **4a-e** and **2d** determined at 145°C.

Compound	Substituents X	Y	$\Delta G^\ddagger_{s \rightarrow a}$ (kcal/mol)	$\Delta G^\ddagger_{a \rightarrow s}$ (kcal/mol)
<b>4a</b>	OMe	OMe	24.0	24.8
<b>4b</b>	CO <sub>2</sub> Me	OMe	24.4	25.3
<b>4c</b>	CO <sub>2</sub> Me	CO <sub>2</sub> Me	24.8	25.5
<b>4d</b>	NO <sub>2</sub>	OMe	24.7	25.6
<b>2d</b>	H	NO <sub>2</sub>	24.9	25.8
<b>4e</b>	NO <sub>2</sub>	CO <sub>2</sub> Me	25.4	26.2

As can be seen from the reported data (20), and as expected on the basis of the polar/ $\pi$  interaction hypothesis (12), the bismethoxy compound **4a** showed the lowest and the nitro/carbomethoxy derivative **4e** the highest barrier. The nitro/methoxy compound **4d**, the best candidate in the series to feature charge-transfer effects (21), had an intermediate barrier, the value of which does not deviate appreciably from the linear correlation observed for the plot of  $\Delta G^\ddagger$  vs the sum of  $\sigma_{para}$  for the two substituents (20). Obviously, if charge-transfer were dominating the interaction, then **4d** would have the highest barrier, followed by **4e** and then by **4a**.

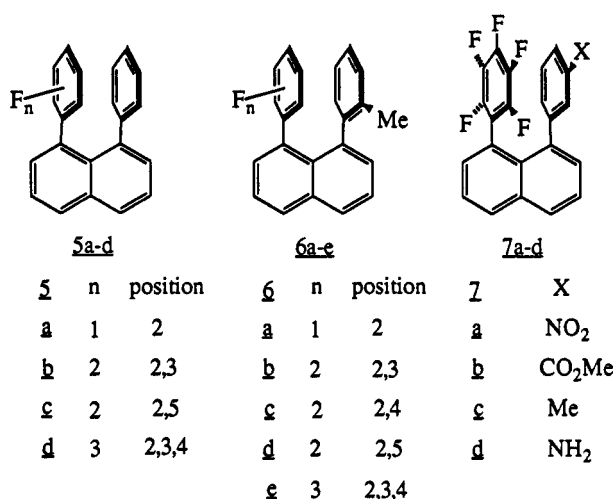
The strong support to the polar/ $\pi$  hypothesis provided by these results led us to investigate further the dependence of the arene/arene interaction on the polarity of the interacting units. To this end, we studied other 1,8-diarylnaphthalenes in which the charge distribution of one of the rings is perturbed by insertion of

fluorine atoms. It is well known that hexafluorobenzene has an inverted charge distribution with respect to benzene, featuring a positively charged central core surrounded by an electron rich periphery (5, 22). By the usual synthetic approach we prepared compounds 5a-d, 6a-e, and 7a-d reported in Scheme 3 (23, 24).

The barriers to rotation, as determined by  $^1\text{H}$ - and  $^{19}\text{F}$ - 2D-NMR are reported in Tables 4-6. In the case of compounds 6a-e it is worth mentioning the good agreement between the barrier values determined by  $^1\text{H}$ - and  $^{19}\text{F}$ - NMR spectroscopy.

As can be seen from the data obtained for compounds 5a-d and 6a-e, the insertion of each fluorine atom leads to an increase in the barrier of *ca.* 0.5 kcal/mol. This trend seems independent of the fluorine atom position, and was expected on the basis of our polar/ $\pi$  hypothesis, since the fluorinated rings becomes more and more electron poor upon addition of new fluorine atoms. Only pentafluoro substitution as in compounds 7a-d achieves the above mentioned inversion of polarity with respect to benzene. For this series of compounds the polar/ $\pi$  rationale predicts a favorable interaction between the two arenes, when X is an EDG group as in 7c and 7d, since the negatively charged core of the X substituted ring interacts with the positively charged core of the pentafluorophenyl ring, and the positively charged periphery of the X substituted ring interacts with the negatively charged periphery of the pentafluorophenyl ring. On the other hand, the situation should be less favorable when the meta substituent is EWG as in 7a and 7b.

Scheme 3.

TABLE 4. Barriers to rotation for compounds 5a-d determined at 24°C.

Compound	No. of F	position	$\Delta G^\ddagger$ (kcal/mol)
<u>5a</u>	1	2	17.1
<u>5b</u>	2	2,3	17.6
<u>5c</u>	2	2,5	17.7
<u>5d</u>	3	2,3,4	18.1

TABLE 5. Barriers to rotation for compounds 6a-e determined at 120°C.

Compound	No. of F	position	$\Delta G^\ddagger$ ( $^1\text{H}$ -NMR)		$\Delta G^\ddagger$ ( $^{19}\text{F}$ -NMR)	
			(kcal/mol)	(kcal/mol)	(kcal/mol)	(kcal/mol)
<u>6a</u>	1	2	<i>s-a</i> 21.4	<i>a-s</i> 21.9	<i>s-a</i> 21.3	<i>a-s</i> 21.8
<u>6b</u>	2	2,3	21.8	22.3	22.0	22.5
<u>6c</u>	2	2,4	21.9	22.4	-	-
<u>6d</u>	2	2,5	21.6	22.0	21.8	22.2
<u>6e</u>	3	2,3,4	22.2	22.6	22.3	22.6

TABLE 6. Barriers to rotation for compounds 7a-c determined at 80°C.

Compound	Substituent	$\Delta G^\ddagger$ (kcal/mol)
<u>7a</u>	NO <sub>2</sub>	19.5
<u>7b</u>	CO <sub>2</sub> Me	19.8
<u>7c</u>	Me	20.2

Unfortunately, compound **7d** turned out to be unstable to prolonged stay in solution even at room temperature, and the barriers could be measured only for compounds **7a-c**. However, even if the variation of  $\Delta G^\ddagger$  was rather limited, we were pleased to find that the barrier increased along the series **7a** (X = NO<sub>2</sub>) to **7b** (X = COOMe) to **7c** (X = Me), a trend in full agreement with our interpretation (25).

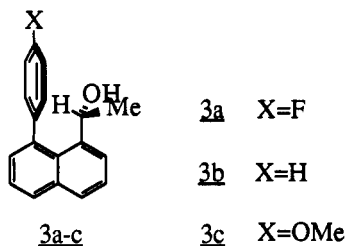
Despite extensive work on  $\pi/\pi$  interactions reported in the literature, we think that this is the first experimental study of a simple aromatic system that clarifies the relative importance of the various factors affecting this kind of interactions. A number of experimental observations for different systems involving  $\pi/\pi$  or ion/ $\pi$  interactions are in full agreement with and can be rationalized by our polar/ $\pi$  interaction hypothesis. These range from stereocontrol in Diels-Alder cycloadditions (**2b**, **2e**) to stereodynamics of sterically congested molecules (**26**), from molecular recognition of neutral aromatic (**3b**, **3d**, **3f**, **3j**) and positively charged (**27**) guests by neutral aromatic hosts to self assembly of aromatic molecules (**3h**). Very recently, through space polar/ $\pi$  effects were also shown to influence the acidity and the hydrogen bonding capacity of carboxylic acids (**28**). We feel therefore that the polar/ $\pi$  rationale can represent a useful tool to understand a variety of phenomena, and can provide new ideas for use in molecular design.

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17. Because of the logarithmic relationship between  $k$  and  $\Delta G^\ddagger$ , the major contribution to the error in determining  $\Delta G^\ddagger$  is the error in the temperature. On the basis of this assumption we estimate the errors to be at most 0.3 kcal/mol. The difference in the barriers for compounds **2a**, **2c**, and **2d** obtained by the two methods results from the difference in the temperature at which the evaluation was made. A  $\Delta S^\ddagger$  term of - 5 eu brings the values in accordance with one another.
18. If conjugation were dominating the interaction (transition state stabilization) both the methoxy- and the nitrosubstituted compounds should conjugate with naphthalene better than the unsubstituted one, that would feature a higher barrier. Furthermore, conjugation was found to have a small effect on the barrier to rotation in 4,4'-disubstituted biphenyls: (a) M. Oki, H. Iwamura, G. Yamamoto *Bull. Chem. Soc. Jpn.* **44**, 262 (1971). (b) M. Oki and G. Yamamoto *Bull. Chem. Soc. Jpn.* **44**, 266 (1971). Finally, the racemic naphthalene derivatives **3a-c** here reported had virtually identical barriers to rotation.



19. If charge-transfer were dominating the interaction (ground state stabilization) both the methoxy- and the nitrosubstituted compounds should interact with the neutral arene, and therefore have a higher barrier. In addition, no absorptions were observed in the UV-spectra of our compounds above 350 nm. The spectra can be considered simple composite of the naphthalene and of the phenyl chromophores.
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21. As in the case of compounds 1a-f and 2a-d we did not observe any long wavelength absorption in the UV spectra of compounds 4a-e.
22. Thus, the parallel stacked dimer of hexafluorobenzene still experiences strong Coulombic repulsion, while the parallel stacked heterodimer of benzene and hexafluorobenzene has an attractive Coulombic interaction.
23. For full  $^1\text{H}$ -,  $^{13}\text{C}$ -, and  $^{19}\text{F}$ -NMR characterization of these compounds, and for the determination of their barriers by different NMR techniques and computational methods, see: R. Annunziata, F. Ponzini, L. Raimondi *Magn. Res. Chem.*, in press. Compounds 6a-e were obtained as roughly 2 : 1 mixtures of *anti* and *syn* isomers. Compound 7d was obtained by reduction of 7a.
24. In the case of compounds 7a-d the desymmetrizing X group was introduced in the *meta* position to minimize the steric influence of the different size of the substituents.
25. Although of limited significance, since it features only three points, the plot of  $\Delta G^\ddagger$  vs  $\sigma_{para}$  for compounds 7a-c shows a good linear fit.
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