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Dominance of Polar/π over Charge-Transfer Effects in Stacked Phenyl Interactions

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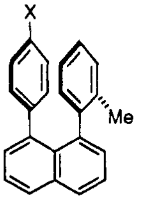
Molecular recognition, the keystone of supramolecular chemistry,[2] depends on a variety of noncovalent interactions. Among these, arene–arene interactions play a fundamental role in the selective complexation of π-neutral guests inside cyclophane cavities and molecular clefts.[3] The interactions between simple arenes comprise π-acid/base (charge-transfer), van der Waals (dispersive), and polar electrostatic (Coulombic) components.[4] Rational design of molecular receptors requires a substantial understanding of the component basis for these arene-arene interactions.[5]

The inherent polarity of benzene stems from its electron-rich core being surrounded by an electron-poor torus of hydrogens. This electrostatic description accounts for the energetic preference of the T-shaped over the π-stacked dimer of benzene. Still, interactions between phenyls with strong electron-donating groups and those with strong electron-withdrawing groups (EWG) often manifest conspicuous charge-transfer (CT) spectra.[6] This raises the question of the relative contributions of polar/π vs CT interactions to the stability of a stacked conformation of two substituted phenyls. This question is addressed through the study of a series of doubly substituted 1,8-diarylnaphthalenes. In these compounds the aryl groups "face-off" in a stacked geometry due to steric crowding.[7]

The view that the repulsive interaction between two benzenes reduces as the electron density of either reduces accounts for the known trend in the stereodynamics of **1a–f** and **2a–d**.[8] If an EWG does not remove enough electron density to reverse the polarity of the core, then a residual partial negative charge must remain. Therefore, the Coulombic repulsion should be minimized for the interaction between two electron-poor rings, maximized for two electron-rich rings, and intermediate for one electron-rich and one electron-poor ring. Viewed from another perspective, the case with one electron-rich ring and one electron-poor ring offers the possibility of a CT interaction. If this effect were overall dominant, then the acceptor/donor interaction would be the least repulsive, followed by acceptor/acceptor, and then donor/donor.



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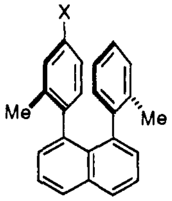

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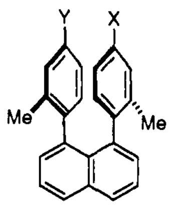

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1a, **2a** X= OMe
1b X = Me
1c, **2b** X = H
1d, **2c** X = Cl
1e X = CO$_2$Me
1f, **2d** X = NO$_2$

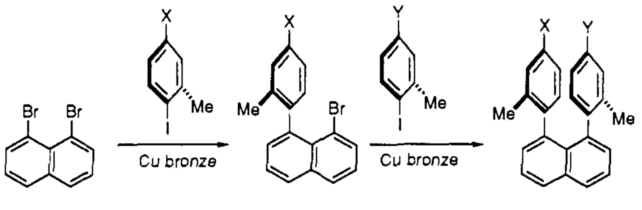
3a X=Y=OMe
3b X=OMe; Y=COOMe
3c X=Y=COOMe
3d X=OMe; Y=NO$_2$
3e X=COOMe; Y=NO$_2$

Table I. Barriers to Syn/Anti Epimerization in **3a–e** and **2c**[a]

compd	substituents	$\Sigma\sigma^{b}$	$\Delta G^{\ddagger}_{\text{syn-anti}}$	$\Delta G^{\ddagger}_{\text{anti-syn}}$
3a	OMe/OMe	–0.54	24.0	24.8
3b	OMe/COOMe	0.25	24.4	25.3
3c	COOMe/COOMe	1.04	24.8	25.5
3d	OMe/NO$_2$	0.51	24.7	25.6
3e	NO$_2$/COOMe	1.30	25.4	26.2
2c	H/NO$_2$	0.78	24.9	25.8

[a] All barriers were determined at 145 °C except **3e** (160 °C) in DMSO; values are in kcal/mol. [b] Sum of σ_{para} for X and Y.

Scheme I



3a-e

Experimentally, the competition between polar/π and CT effects was probed by studying the variations in the barrier to epimerization of a series of substituted *syn* and *anti* 1,8-di-*o*-tolylnaphthalenes. Each tolyl ring bore a para substituent that varied among methoxy, hydrogen, carbomethoxy, and nitro, to make six compounds in all (**2c**, **3a–e**). 1,8-Diarylnaphthalenes **3a–e** were synthesized by methods analogous to those used previously to prepare **2a–d** (Scheme I),[8] and isolated by iterative gravity column chromatography on 230–400 mesh silica gel as equilibrated mixtures of *syn* and *anti* diastereomers.[9] The epimerization process was followed by two-dimensional NMR using an EXSY pulse sequence experiment.[10] From this the rates of epimerization at 145 °C were measured and Eyring free energies of activation ($\Delta G^{\ddagger}$) were calculated (Table 1). A plot of $\Delta G^{\ddagger}$ vs the sum of σ_{para} for the two substituents ($\Sigma\sigma_{\text{para}}$) showed a linear correlation. The bis-methoxy and nitro/carbomethoxy compounds manifested the lowest and highest barriers respectively; the nitro/methoxy derivative displayed an intermediate barrier, the value of which did not deviate significantly from the linear fit (Figure 1).

As discussed previously for **1a–e** and **2a–d**,[8] the observed trend in barriers cannot be explained by conjugation of the rotating aryl group with the naphthalene holder (transition-state stabilization). Conjugation manifests a very small effect on the barrier to rotation in mono-para-substituted biaryls.[11] At present, the most consistent reason for this trend is that the EWGs decrease

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[9] All compounds were fully characterized as mixtures of diastereomers (mp, ^{1}H and ^{13}C NMR, elemental analysis, UV [no long wavelength absorption]).

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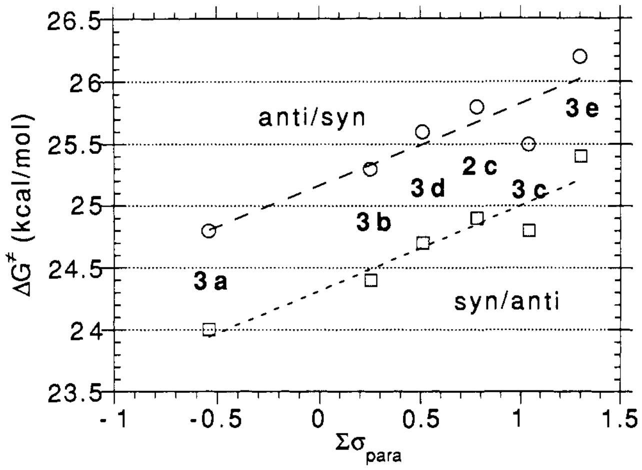
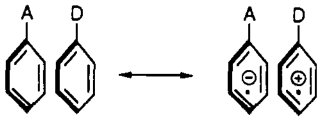


Figure 1. Plot of ΔG^{*} vs the sum of σ_{para} for the two substituents on compounds **2** and **3**. The relationship is shown to be linear.

the repulsive interactions between the two aryls that are forced, due to steric congestion, into the "unnatural" stacked conformation. Thus, EWGs cause a higher barrier to rotation as a result of "less unfavorable" electrostatic interactions in the ground state. Regarding this as a general phenomenon leads one to predict that the face-to-face complexation of a neutral aromatic guest with a neutral aromatic host should show increased stability when both partners are electron-poor.

The strong correlation between ΔG^{*} and $\Sigma\sigma_{para}$ clearly demonstrates the dominance of polar/π over CT effects in the interactions of stacked phenyl rings. This further documents the inconsistency of claims regarding simple phenyl π-stacking interactions as decisive elements of stereocontrol.[12] In hindsight, the lack of CT participation in arene-arene interactions heightens awareness of the overemphasis organic chemists place on orbital vis-à-vis electrostatic effects.[13]

In order for CT effects to participate in the ground-state interaction effectively, there must exist a resonance form (**II**) that contributes significantly to the description of the "bond" between the two rings. Resonance forms of this type create strong violations of the electroneutrality principle and therefore contribute only in cases where there exist strong compensating gains as a result of the electron density redistribution.[14] Thus, contrary to popular notion and consistent with experimental findings, one should expect small interaction terms originating from CT effects in these situations.[15]



I II

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[15] The interactions between strongly perturbed aromatics may show CT effects, but the possibility exists that the strong polarization creates an electrostatic distribution that accounts for the observed behavior.