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What Is the Preferred Structure of the Meisenheimer−Wheland Complex Between *sym*-Triaminobenzene and 4,6-Dinitrobenzofuroxan?

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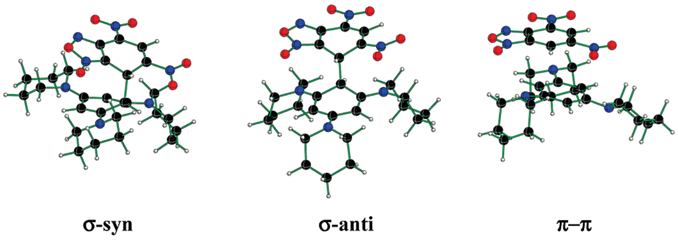

The geometries, energies, and electronic properties of possible configurations of Meisenheimer−Wheland (M−W) complexes of *sym*-triaminobenzenes and 4,6-dinitrobenzofuroxan (DNBF) were investigated theoretically by MP2 and a variety of DFT methods. The $\pi-\pi$ complex is preferred thermodynamically by more than 15 kcal/mol over the σ-complexes for the unsubstituted species. However, the N-substituents of the 1,3,5-triaminobenzenes influence the relative stabilities of the alternative configurations significantly. The σ-*syn* configuration of the M−W complex of 1,3,5-tris(*N*-piperidyl)benzene and DNBF has the lowest energy, followed closely by the σ-*anti* and $\pi-\pi$ forms. The small energy differences between different configurations are consistent with the dynamic interconversion of three homomeric structures observed experimentally by NMR. The ca. 1.63 Å C−C interring bond exchanges among three equivalent sites. Quantum theory of atoms in molecules (QTAIM) analysis provided insights into the nature of the intermonomer interactions. Charge transfer and σ bonding account for the stability and remarkably large binding energies of the M−W complexes.

1. Introduction

Meisenheimer (anionic) complexes[1] and Wheland (cationic) complexes[2] are believed to be the reactive intermediates in nucleophilic and electrophilic aromatic substitutions, respectively.[3] Amazingly, zwitterionic Meisenheimer−Wheland (M−W) complexes with C−C bonds were prepared in 2005 by mixing equimolar amounts of three different 1,3,5-tris(*N*,*N*-dialkylamino)benzene derivatives (supernucleophiles) and 4,6-dinitrobenzofuroxan (DNBF, a superelectrophile) in CD_2Cl_2 solution at low temperatures (Scheme 1).[4] As the zwitterionic products could not be isolated in crystalline form, no X-ray structures were determined. Two types of σ complexes, one with a *syn* and the other with an *anti* orientation of the two monomer units (Figure 1), were deduced from the NMR (nuclear magnetic resonance) evidence. The ^{13}C chemical shift of the connecting

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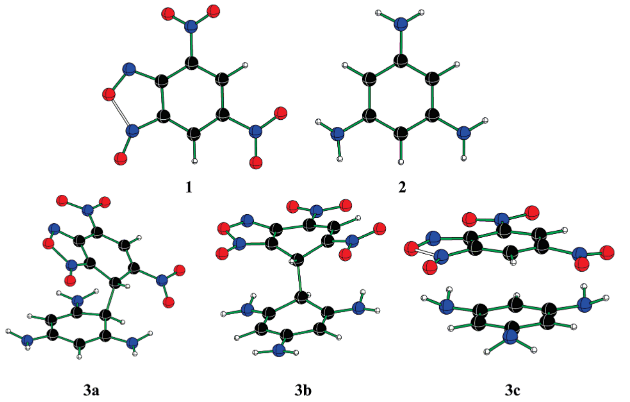
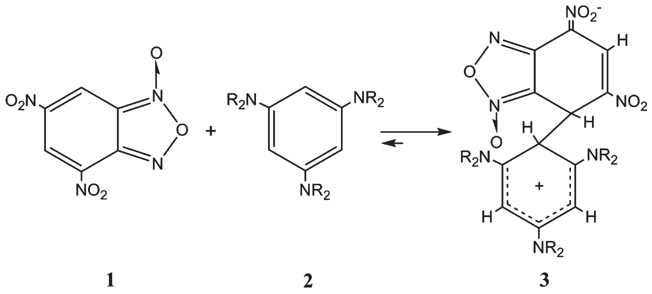


FIGURE 1. Monomers **1** and **2** and three possible Meisenheimer–Wheland complexes: σ structure in *syn* conformation, **3a**; σ structure in *anti* conformation, **3b**; π–π complex, **3c**. All geometries were optimized at the MP2/6-31+G* level of theory. Color scheme: C, black; N, blue; O, red; H, white.

SCHEME 1. Reaction of DNBF (1) with 1,3,5-Triaminobenzene (2) To Give a Meisenheimer–Wheland Complex (3) with a C–C Bond[a]



[a] NR_2 = *N*-piperidyl, *N*-morpholinyl, or *N*-pyrrolidinyl.

carbon atoms indicated their sp^3 hybridization; this excluded an alternative π–π complex structure with parallel planar rings. However, such π–π species might be involved in the degenerate equilibria responsible for the variable-temperature NMR behavior. These observations show that the M–W complexes interconvert among three homomeric structures by exchanging the C–C attachment sites.[4] Following these first examples, Forlani's group[5,6] reported that M–W complexes formed in the S$_E$Ar reactions of aminothiazoles with DNBF, as well as by reaction of 1,3,5-tris(*N*,*N*-dialkylamino)benzenes and 4,6-dinitrotetrazolo [1,5-*a*]pyridine. Unfortunately, these experiments provided no structural details.

As no related computational study has been reported to our knowledge, we have undertaken a systematic theoretical investigation of the structures of such M–W complexes. We hope that our *ab initio* and density functional theory (DFT) studies on the geometries, energies, electronic properties, and nature of the bonding of possible isomeric prototype *sym*-triaminobenzene and DNBF M–W complexes will stimulate and facilitate further experimental characterization of these systems.

TABLE 1. Relative Energies (kcal/mol) of the Three Unsubstituted M–W Complex Structures at Various Computational Levels

	method	*σ-syn* **3a**	*σ-anti* **3b**	*π–π* **3c**
MP2 reference	MP2[a]	15.1	20.3	0.0
	MP2[b]	15.6	22.2	0.0
set 1	B3LYP	0.6	8.5	0.0
	DFT-D	0.1	7.7	0.0
	M06	1.8	8.6	0.0
	M06-L	7.3	14.5	0.0
	M06-2X	1.9	9.3	0.0
set 2	M05-2X	0.0	7.4	1.6
	M06HF	0.0	7.2	2.4
	MPW1PW91	0.0	7.8	4.6
	MPWB1K	0.0	8.7	4.2
set 3	BH&H	0.0	9.8	10.2

[a] MP2/6-31+G*//MP2/6-31+G*. [b] MP2/cc-pVTZ//MP2/6-31+G*.

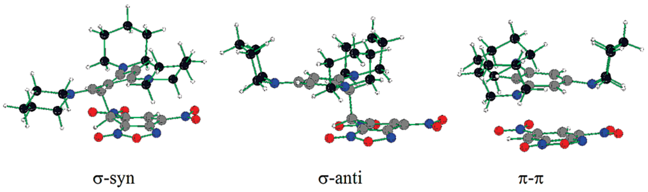


FIGURE 2. Three possible Meisenheimer–Wheland configurations optimized at the M06-2X/6-311+G* level. Color scheme: C atoms in the two benzene rings, gray; other C, black; N, blue; O, red; H, white.

2. Computational Methods

Instead of the three bulky *N*-alkyl 1,3,5-triaminobenzene derivatives studied experimentally, we first employed the unsubstituted monomer **2** (Figure 1) for simplification. Three different configurations of the complexes, *σ-syn* **3a**, *σ-anti* **3b** and π–π **3c**, were considered. The results helped us calibrate the performance of different theoretical methods.

The geometries of the three configurations of these simplified models were fully optimized and characterized to be local minima by harmonic vibrational frequency analysis using a variety of density functionals including B3LYP,[7] BH&H,[8] MPW1PW91,[9] MPWB1K,[10] M05-2X,[11] M06, M06-2X,[12] M06-L,[13] and M06HF[14] with the standard 6-311+G* basis set[15] implemented in Gaussian 09.[16]

The geometries also were optimized at the MP2/6-31+G* level[17,18] with the Molpro code.[19] The relative energies were further refined by single point MP2 computation with Dunning's

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TABLE 2. Computed Relative Energies (kcal/mol) and HOMO-LUMO Gap Energies (eV, in parentheses) of the Three Piperidyl-Substituted M−W Complexes with Selected Functionals[a]

	B3LYP	DFT-D	M06	M06-L	M06-2X	M05-2X	M06HF	*M06-2X (PCM)*
σ-syn	0.0 (3.09)	0.0 (1.73)[b]	0.0 (3.44)	0.2 (2.02)	0.0 (4.95)	0.0 (5.17)	0.0 (7.68)	*0.0 (4.99)*
σ-anti	6.2 (3.00)	6.9 (1.68)[b]	7.4 (3.44)	8.5 (2.04)	8.2 (5.02)	7.7 (5.20)	9.4 (7.71)	*3.4 (5.18)*
π−π	0.9 (1.39)	1.4 (0.67)[b]	3.0 (2.11)	0.0 (0.75)	4.5 (3.67)	7.5 (3.79)	11.2 (6.52)	*12.3 (3.63)*

[a]The relevant data including the solvent effect are given in italics. [b]These HOMO−LUMO gaps are given for the DFT/TPSS/6-311++G(3df,3pd) method; the addition of the empirical dispersion term has no effect on these values.

correlation-consistent polarized valence triple-ζ basis set (cc-pVTZ).[20] In addition, we evaluated the performance of the DFT-D/TPSS/6-311++G(3df,3pd) method. The DFT-D technique incorporates an empirical London dispersion energy term, which describes dispersion using the well-known C_6/R^6 term.[21] The polarizable continuum model (PCM)[22] was employed to investigate the effect of solvent (dichloromethane) on the relative energies of the configurations.

Based on their performance compared with MP2, several density functionals were selected to investigate the actual *N*-piperidyl substituted M−W complexes studied experimentally (see Section 3.1 for details).

To analyze the substituted M−W complexes further, we chose the M06-2X density functional because of its satisfactory performance in earlier studies,[12] as well as in our benchmark test (see below). The binding energies (E_b), defined as the energy difference of M−W complexes from those of the two separated monomers, were computed at M06-2X/6-311+G*, both without and with basis set superposition error (BSSE) corrections (using the Boys−Bernardi counterpoise correction scheme).[23] Atomic charges were based on Weinhold et al.'s[24] Natural Population Analysis (NPA). A quantum theory of atoms in molecules (QTAIM) study using the M06-2X/6-311+G* geometries and wave function was carried out using AIM2000 software.[25] The 3D molecular orbitals (MO) visualizations employed the gOpenmol program.[26]

3. Results and Discussion

3.1. Geometries and Stabilities. Unsubstituted M−W Complexes. The computed relative energies of the three simplified *σ-syn* **3a**, *σ-anti* **3b**, and *π−π* **3c** M−W configurations are compared in Table 1 at MP2 and at all density functional levels employed.

At the MP2 level, the *π−π* form of the simplified complex **3c** is thermodynamically most favorable; its energy is over 15 kcal/mol lower than that of the *σ*-complex alternatives, **3a** and **3b**. We assume that this behavior reflects the inherent preference of the *π−π* over the *σ*-complex structures, in the absence of steric effects. In contrast, the interpretation of the NMR spectra of the experimental derivatives with alkylated NR_2 substituents on **2** favored *σ* carbon-bound M−W complexes; *π*-stacked structures (related to **3c**) were totally excluded.[4] Obviously, the steric effects of the rather bulky substituents are important, and the simplified models cannot be expected to reflect the relative stabilities of the isomers of the actual systems. Consequently, we employed the MP2 relative energy data of the simplified system as a "benchmark" to evaluate the performance of the density functionals. Those functionals that passed this test were then used to study the much larger real systems.

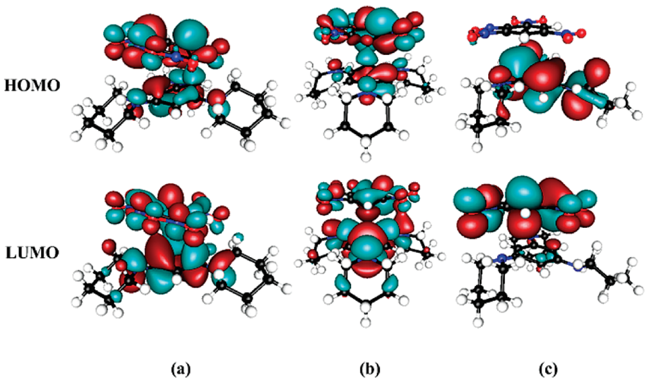

FIGURE 3. Frontier orbitals of the (a) *σ-syn*, (b) *σ-anti*, and (c) *π−π* complexes.

TABLE 3. Computed NBO Charges of the Three Piperidyl Substituted M−W Complex Moieties at M06-2X/6-311+G*

moiety	*σ-syn*	*σ-anti*	*π−π*
1,3,5-tris(*N*-piperidinyl)benzene	0.89	0.86	0.06
DNBF	−0.89	−0.86	−0.06

The results of the diverse DFT methods employed for the simplified M−W models were grouped into three sets. Set 1, which agrees best with the MP2 stability order (**3c** > **3a** > **3b**), includes the B3LYP, DFT-D, M06, M06-L, and M06-2X DFT methods. Set 2, comprising the M05-2X, M06HF, MPW1PW91, and MPWB1K functionals, indicate that *σ-syn* **3a** has the lowest energy, and the *π−π* complex **3c** is preferred to *σ-anti* **3b**. Set 3 has only one member, BH&H, which computes *σ-syn* **3a** as the lowest energy configuration and the *π−π* complex **3c** to be least favorable. Evidently, both sets 2 and 3 underestimate the stability of **3c**, likely because they underestimate the strength of the *π−π* binding interaction between the aromatic rings.

Actual *N*-Piperidyl Substituted M−W Complexes. Since MP2 geometry optimizations of the larger systems were not practicable, the M−W complexes involving 1,3,5-tris(*N*-piperidyl)benzene were computed using the five MP2-consistent functionals of set 1. For further comparison, we also selected the M05-2X and M06HF functionals from set 2, since their results for **3a** and **3c** deviated least from set 1.

The optimized geometries for each configuration at the M06-2X/6-311+G* level are shown in Figure 2 (see Supporting Information for the Cartesian coordinates). The distances between the two sp^3 carbon atoms, around 1.63 Å in

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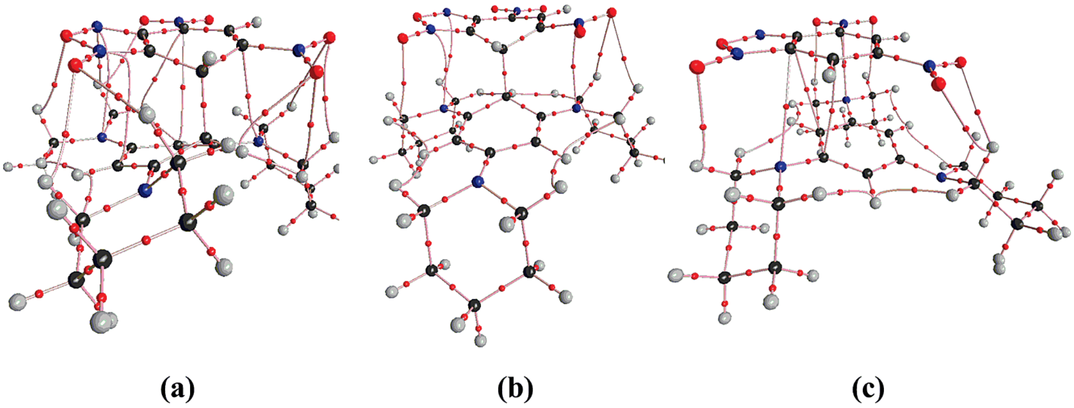

FIGURE 4. Molecular graphs of the (a) σ-*syn*, (b) σ-*anti*, and (c) $\pi-\pi$ configurations. Ring and cage BCPs are omitted for clarity.

both the σ-*syn* and σ-*anti* structures, imply C−C single bond formation. The substantial separations of the two benzene ring centers coupled with their longitudinal displacements, about 2.95 and 0.62, 3.79 and 3.35 Å, as well as 3.25 and 0.89 Å for the σ-*syn*, σ-*anti*, and $\pi-\pi$ configuration, respectively (see Supporting Information), decrease the π-electron repulsion and result in considerable binding energies between the two moieties in all the three configurations. These are computed to be 33.6 (26.3), 25.4 (19.1) and 29.1 (22.8) kcal/mol for σ-*syn* (a), σ-*anti* (b), and $\pi-\pi$ (c), respectively, at the M06-2X/6-311+G* (BSSE corrected) level.

Table 2 summarizes the relative energies of the three configurations of this complex. In the absence of solvent simulation, the functionals from set 1 or 2 compute the σ-*syn* > $\pi-\pi$ > σ-*anti* stability order with two exceptions. M06-L prefers $\pi-\pi$ over σ-*syn* by only 0.2 kcal/mol, while M06HF predicts a σ-*syn* > σ-*anti* > $\pi-\pi$ stability order. These data show that all three of the M−W complex structures are close in energy in the gas phase, and the σ-complexes are slightly more stable than the $\pi-\pi$ complex. When solvent simulation (dichloromethane) is taken into account (Table 2), the σ-*syn* configuration has the lowest energy followed by σ-*anti* (3.4 kcal/mol higher); the $\pi-\pi$ complex is the least favorable (by 12.3 kcal/mol).

These computational results agree well with the experiments. As found experimentally,[4] the DNBF moiety shifts rather freely among the three equivalent unsubstituted carbon binding sites offered by the tris(*N*,*N*-dialkylamino) benzene aromatic ring. Note that Boga et al.[4] observed the formation of a coral red precipitate when the reactants were mixed in acetonitrile at low temperature. This solid product is most likely a $\pi-\pi$ complex, since the color is typical for a charge transfer band, as is typically observed in the UV−vis spectra for aromatic $\pi-\pi$ complexes.[27] The measured UV−vis spectra depend on the choice of the solvent and the conditions. However, in dichloromethane solution, the σ-complexes are slightly favored over the $\pi-\pi$ complex, and thus the overwhelming concentration of the σ-complexes may account for the failure to observe the $\pi-\pi$ complex in the NMR experiments and the fact that the M−W complex is colorless[4] in CD_2Cl_2 solution. The formation of a small amount of the $\pi-\pi$ complex in the solid state may only reflect the drastic change of conditions.

3.2. Electronic Properties and Nature of the Bonding. The HOMO−LUMO gaps of the M−W complexes computed by all of the density functionals are significantly large (Table 2, Figure 3). All of the density functionals, except B3LYP and DFT-D, give the $\pi-\pi$ < σ-*syn* ≤ σ-*anti* order. In the two σ complexes, the HOMO and LUMO coefficients are well distributed on both moieties. In contrast, in the $\pi-\pi$ complex, the 1,3,5-triaminobenzene monomer dominates the HOMO, and the DNBF moiety dictates the LUMO.

The computed NBO charges (at M06-2X/6-311+G* in Table 3) reveal considerable charge transfer (ca. 0.90 e) between the two moieties of both C−C σ bond complexes. Hence, these electronic interactions as well as σ bonding contribute to their stability. In sharp contrast, the charge transfer (0.06 e) from the 1,3,5-tris(*N*-piperidyl)benzene to the DNBF moiety in the $\pi-\pi$ configuration is insignificant. Consistent with the relatively large distance between the two π stacked moieties, their $\pi-\pi$ interaction is not governed by charge transfer.

QTAIM topological analysis of the electronic density[25] gave further details of the bonding in the three isomers. Figure 4 depicts the molecular graphs (at M06-2X/6-311+G*) representing intramolecular interactions between the 1,3,5-tris(*N*-piperidyl)benzene and the DNBF moieties. The identical 0.19 au ρ_{bcp} electron densities at the sp^3-sp^3 carbon bond critical points (BCPs) for both the σ-*syn* and σ-*anti* complexes suggest almost identical bond strengths. In addition, the BCPs between each monomer pair for all of the configurations lead to a total of 15, 7, and 10 intermonomer bond paths for the σ-*syn*, σ-*anti*, and $\pi-\pi$ complexes, respectively. However, the small electron densities ρ_{bcp} (< 0.02 au) as well as negative Laplacian $\nabla^2\rho_{bcp}$ located at these BCPs indicate weak covalent interactions and limited contributions to the total stability.

4. Conclusions

Our DFT computational survey compared three possible configurations of the *sym*-triaminobenzene and DNBF Meisenheimer−Wheland complexes. The $\pi-\pi$ complex form of the parent unsubstituted systems is preferred thermodynamically over the σ-complexes by more than 15 kcal/mol. However, the steric effects of the N-substituents alter

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this order, and the three σ-*syn*, σ-*anti*, and π−π configurations of the experimentally investigated piperidyl substituted M−W complexes have rather small energy differences. Their ready interconversion is consistent with the reported NMR investigations. We hope that single crystal X-ray diffraction will verify our computational conclusions. Intermonomer charge transfer, while considerable (0.9 e) in the σ complexes, is negligible in the π−π complex. The last is characterized by weak covalent intermonomer interactions according to QTAIM analysis. Destabilizing π-electron repulsions between stacked aromatic rings are avoided in suitable orientations and lead to favorable binding energies. Similarly bonded molecular complexes may occur in enzyme−substrate complexes in biochemistry.

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Supporting Information Available: The optimized coordinates of the M−W complexes as well as the full citation of ref 16. This material is available free of charge via the Internet at http://pubs.acs.org.