Probing the Association of Frustrated Phosphine−Borane Lewis Pairs in Solution by NMR Spectroscopy

Luca Rocchigiani,*,[†] Gianluca Ciancaleoni,[‡] Cristiano Zuccaccia,[†] and Alceo Macchioni*,[†]

[†]Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, Via Elce di Sotto 8, I-06123 Perugia, Italy
[‡]Istituto del CNR di Science e Tecnologie Molecolari, c/o Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, I-06123 Perugia, Italy

S *Supporting Information*

ABSTRACT: $^{19}F,^1H$ HOESY, diffusion, and temperature-dependent ^{19}F and ^1H NMR studies allowed us to unequivocally probe the association between the frustrated $PR_3/B(C_6F_5)_3$ (**1**, R = CMe_3; **2**, R = 2,4,6-$Me_3C_6H_2$) Lewis pairs in aromatic solvents. No preferential orientation is favored, as deduced by combining $^{19}F,^1H$ HOESY and DFT results, suggesting association via weak dispersion rather than residual acid/base interactions. The association process is slightly endoergic [K = 0.5 M^{-1}, ΔG^0(298 K) = +0.4 kcal/mol for **2**], as derived from diffusion NMR measurements.

The past few years have witnessed an explosion of interest in the so-called frustrated Lewis pairs (FLPs), which are combinations of a Lewis acid (LA) and a Lewis base (LB) that cannot fulfill their natural propensity to form coordinative complexes.[1] FLPs exhibit a rich and rather important chemistry;[2] indeed, they are capable of activating small molecules such as hydrogen,[2,3] carbon dioxide,[2b,4] or alkenes[5] under rather mild conditions and can be exploited also as homogeneous catalysts, in particular in hydrogenation reactions.[6] In-depth theoretical calculations[7,8] suggest that the key feature of FLPs reactivity relies on synergistically using LA empty orbital and the lone pair of electrons of LB to activate polar molecules or polarize and subsequently activate apolar molecules (Scheme 1). This behavior resembles that of

Scheme 1. Small-Molecule Activation by FLPs

transition metal fragments having both σ-acidity and π-basicity.[9] In order to contemporarily exploit their potential as electron acceptor and donor toward a substrate, it is thought that LA and LB have to closely approach each other, forming an encounter complex in which the empty orbital of LA is directed toward the lone pair of electrons of LB (Scheme 1). Unfortunately, very little experimental evidence is available about the structure of the LA/LB encounter complex and, in general, about the tendency of LA and LB to associate.[10−16] Over the past two decades,[17] we have been developing NMR methodologies for investigating intermolecular structure in solution which have been successfully applied to study ion

pairing in organometallic complexes[18] and supramolecular adducts of important materials.[19] Such methodologies are mainly based on NOE and diffusion NMR techniques[20,21] and provide precious information about the association tendency of non-covalently bonded moieties (diffusion NMR) and their relative orientation within the intermolecular adducts (NOE). These seem to be just the pieces of information that are missing for FLPs.[22]

Here we report the results of an in-depth $^{19}F,^1H$ HOESY, diffusion, and temperature-dependent line broadening NMR study on $PR_3/B(C_6F_5)_3$ mixtures (**1**, R = CMe_3; **2**, R = 2,4,6-$Me_3C_6H_2$), which provide robust evidence of their association in benzene and toluene. In addition, we demonstrate that LA and LB unspecifically associate, likely through H/F dispersion forces.

Stoichiometric phosphine−borane (220−230 mM) mixtures were prepared by dissolving suitable amounts of PR_3 and $B(C_6F_5)_3$ in dry benzene or toluene in a J-Young NMR tube. In analogy with the literature,[11] no shift of the resonances was observed in the ^1H, ^{31}P, and ^{19}F NMR spectra of the mixtures with respect to those of the pure components. Nevertheless, clear indications of association came from the $^{19}F,^1H$ HOESY NMR spectra (Figures 1 and S1, Supporting Information), where H/F intermolecular NOEs were observed. In particular, unselective NOE contacts were detected between all protons of PR_3 and all fluorine nuclei of $B(C_6F_5)_3$ (Figures 1 and S1). The relative intensities of such H/F NOEs in the F2 dimension substantially reflect those of the resonances in 1D ^{19}F NMR spectra. The same pattern of intermolecular interactions was detected also using 60 mM solutions (Figure S5).

The kinetics of NOE build-up was determined by recording a series of $^{19}F,^1H$ HOESY NMR spectra with variable mixing time (100−2800 ms, Supporting Information) in order to ascertain the reliability of intermolecular NOEs and better evaluate the possible presence of preferential $PR_3/B(C_6F_5)_3$ orientations. Studies were mainly focused on **2** since it contains several reporter resonances that allow different relative LA/LB orientations to be probed.

Experimental NOE data (Table 1) were carefully contrasted to those expected if one of the two static orientations **2**/$B(C_6F_5)_3$**_a** and **2**/$B(C_6F_5)_3$**_b** optimized by DFT calculations (see below) were present (Supporting Information). The discrepancy is so marked that the selective presence of each of
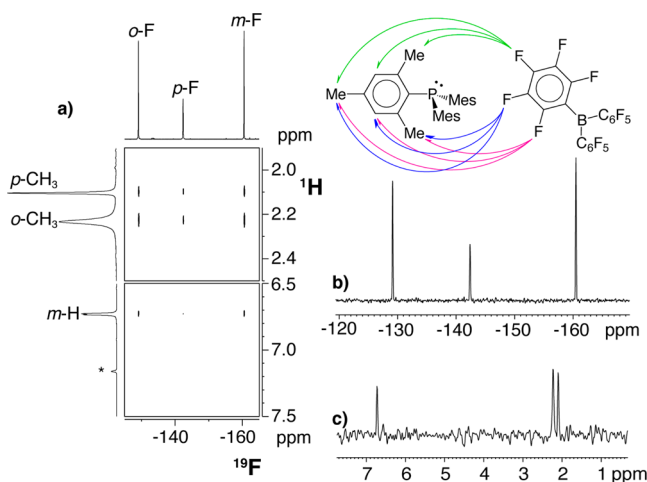
Figure 1. (a) $^{19}F,^1H$ HOESY NMR spectrum of $2/B(C_6F_5)_3$ (C = 228 mM, T = 298 K, solvent = benzene-d_6, relaxation delay = 7.5 s, mixing time = 200 ms). (b) F2 trace at δ_H = 2.1 ppm. (c) F1 trace at δ_F = −160.5 ppm. Asterisk denotes residual solvent.

Table 1. Relative Intensities Obtained from the Quantitative $^{19}F,^1H$ HOESY NMR Spectrum of $2/B(C_6F_5)_3$[a]

	ortho-Me	*meta*-H	*para*-Me
ortho-F	0.73	0.81	0.80
meta-F	1	0.93	0.85
para-F	0.72	0.39	0.58

[a]C = 228 mM, T = 298 K, solvent = benzene-d_6, relaxation delay = 7.5 s, mixing time = 200 ms. Integrated areas were corrected by a $(n_F + n_H)/(n_F n_H)$ factor, where n_F and n_H are the numbers of magnetically equivalent F and H spins.

the two orientations can be ruled out. Particularly, it is difficult to justify the relatively strong *para*-F/*para*-Me (0.58) and *ortho*-F/*meta*-H (0.81) NOEs (Supporting Information). Consequently, $^{19}F,^1H$ HOESY NMR experiments strongly point toward the formation of aggregates in which phosphine and borane have a random relative orientation, likely stabilized by peripheral (H/F) interactions. In order to validate this hypothesis, we considered it worthwhile to investigate a chemical system different from Lewis pairs, having components that may undergo similar peripheral interactions and thus, in principle, exhibit a similar pattern of intermolecular NOE interactions. The $2/C_6F_6$ system appeared to be a suitable candidate for our aims. Indeed, the $^{19}F,^1H$ HOESY NMR spectrum of a 1:1 mixture of 2 and C_6F_6 in benzene-d_6 (Figure S9) showed intermolecular NOEs between fluorine nuclei of C_6F_6 and all the protons of 2, exactly as observed with $B(C_6F_5)_3$. Also in this case, NOE interactions were not very selective, and almost the same intensities were measured, for example, for *ortho*-Me and *para*-Me moieties. This analogy in the behavior of C_6F_6 and $B(C_6F_5)_3$ supports the hypothesis that H/F interactions play a central role in driving the association of perfluoroaryl boranes and phosphines in intermolecular FLPs.

Hints about the association between LA and LB were also obtained by investigating non-stoichiometric mixtures comprising a large excess of PR_3 or $B(C_6F_5)_3$. When solid $B(C_6F_5)_3$ was added[23] to a 387 mM solution of 2, leading to a phosphine/borane molar ratio of 57, marginal shifts of the ^{19}F resonances of $B(C_6F_5)_3$ occurred, whereas a substantial line broadening (>500 Hz for *para*-F) was observed. In contrast, no changes in the ^1H and ^{31}P NMR spectra were evidenced (up to B/P =

150) when a 463 mM solution of $B(C_6F_5)_3$ was titrated with sub-stoichiometric amounts of 2. The large broadening of the ^{19}F NMR spectrum in non-stoichiometric $2/B(C_6F_5)_3$ mixtures encouraged us to explore the temperature effect on the signal width on both phosphine and borane. For pure 2, the signal due to *ortho*-Me had a temperature-dependent line broadening that is likely due to the hindered rotation of the mesityl ring on the P−C bond (Figure 2a).[24]
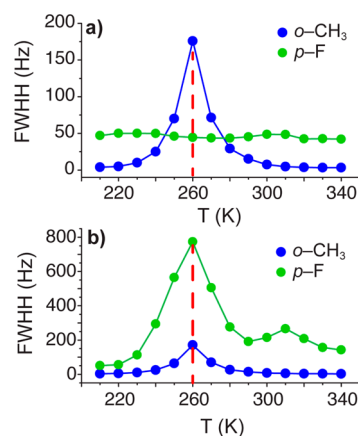

Figure 2. Evolution of the Full Width at Half-Height (FWHH) as a function of temperature (T) of the signals due to the *ortho*-Me of 2 (240 mM) and *para*-F of $B(C_6F_5)_3$ (15 mM) in pure species (a) and in mixture (b).

On the other hand, the width of the ^{19}F NMR resonances of pure $B(C_6F_5)_3$ remains almost the same in the 210−340 K temperature range. The effect of changing the temperature on the NMR spectra of a mixture of 2 (240 mM) and $B(C_6F_5)_3$ (15 mM) was remarkable. As a matter of fact, broadening was observed not only for 2 but also for borane resonances. For example, the width of *para*-F was found to be strongly dependent on temperature, passing from 51 Hz at 210 K up to 773 Hz at 260 K (Figure 2b),[25] and strictly matched the temperature trend of the *ortho*-Me of 2 (this was true also for *ortho*-F and *meta*-F, Supporting Information). A reasonable explanation for this observation is that $B(C_6F_5)_3$ is affected by the restricted mesityl rotation of 2, and this appears to be possible only if 2 and $B(C_6F_5)_3$ are associated in solution, supporting the NOE results.

The tendency of phosphine and borane to associate was quantified by means of diffusion ^1H and ^{19}F NMR spectroscopy, which allowed the hydrodynamic volume (V_H) of the dissolved species to be determined. It is reasonable to assume that, under the present experimental conditions, the measured V_H values of phosphine and borane (V_H^{obs}) are equal to the average of those of free (V_H^{free}) and associated (V_H^{assoc}) species weighted by the relative molar fractions (eq 1). In eq 1, x and

$$V_H^{obs} = x V_H^{assoc} + (1 - x) V_H^{free} \qquad (1)$$

V_H^{assoc} are the unknowns. As a first approximation, the latter can be fixed as the addition of the hydrodynamic volumes of free phosphine and borane (490 + 384 = 874 Å^3). Consequently, the molar fraction x was determined by diffusion NMR experiments for non-stoichiometric mixtures (Supporting Information and Table 2).

Table 2. Hydrodynamic Volumes (V_H), Molar Fraction of Associates (x), and Equilibrium Constant Values (K) Obtained by Means of Diffusion NMR Experiments on Solutions Containing Different Concentrations (C) of 2 and $B(C_6F_5)_3$[a]

C, mM		V_H, Å^3		x^b	K, M^{-1}
2	$B(C_6F_5)_3$	**2**	$B(C_6F_5)_3$		
3.1	463.0	536	387	0.12	0.3
4.5	357.5	569	405	0.20	0.7
5.8	251.6	550	384	0.15	0.7
38.7	463.0	552	426	0.16	0.4
345.7	40.7	670	430	0.10	0.3
47.0	–	490	–	–	–
–	38.0	–	384	–	–

[a]Solvent = benzene-d_6, T = 298 K. [b]Relative to the less concentrated species of the solution.

The measured hydrodynamic volumes (V_H^{obs}, Table 2) are only slightly larger than those of pure species. For example, when **2** is in large defect with respect to the borane (B/P between 150 and 12), an average $V_H \approx 550$ Å^3 is measured. This value is only 60 Å^3 larger than that of pure **2** in benzene-d_6, confirming that the fraction of the associated phosphine is low and giving an average association constant $K = 0.5 \pm 0.2$ M^{-1} (Table 2). This means that the formation of $2/B(C_6F_5)_3$ aggregate is a slightly endoergonic process [$\Delta G^0(298\ K) = +0.4 \pm 0.2$ kcal/mol], in agreement with previously reported computational data.[26]

Preliminary DFT calculations were performed in order to shed some light on the structure of associates in solution and on the nature of LA/LB interactions. The BP86 functional with D3 correction for dispersion was used (Supporting Information)[27] to take into account weak interactions, paying particular attention to **2**. Two limit structures were optimized, having the phosphorus atom directly in front of the boron atom (2/$B(C_6F_5)_3$_**a**) and pointing toward the opposite direction (2/$B(C_6F_5)_3$_**b**) (Figure 3). 2/$B(C_6F_5)_3$_**a** was found to be more

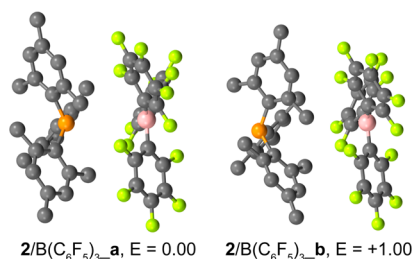2/$B(C_6F_5)_3$_**a**, E = 0.00   2/$B(C_6F_5)_3$_**b**, E = +1.00

Figure 3. Optimized geometries and relative energies of 2/$B(C_6F_5)_3$_**a** and 2/$B(C_6F_5)_3$_**b** FLPs. Hydrogen atoms have been removed for clarity. Energies are in kcal/mol.

stable than 2/$B(C_6F_5)_3$_**b** by 1.8 kcal/mol in the gas phase and only 1 kcal/mol in solution (COSMO model, solvent = benzene), making also 2/$B(C_6F_5)_3$_**b** easily accessible.

The energy decomposition analysis[28] on 2/$B(C_6F_5)_3$_**a** and 2/$B(C_6F_5)_3$_**b** shows that all the attractive contributions (orbital interaction, electrostatic, and dispersion energies) are more negative in the former than in the latter. On the other hand, in 2/$B(C_6F_5)_3$_**a** the steric repulsion and the preparation energy (the amount of energy required to deform the separate fragments from their equilibrium structure to the geometry that they acquire in the aggregate) are more positive than in 2/

$B(C_6F_5)_3$_**b**. The two factors compensate each other leading to very similar energies for the two configurations. Finally, the nature of the P−B interaction in 2/$B(C_6F_5)_3$_**a** was investigated by charge displacement analysis[29] (Supporting Information). According to such analysis, there is a net flow of electron density (Δq) from the phosphine to the borane, which amounts to −0.084 e at the boundary between the two moieties (Figure S25).[30] Interestingly, some hydrogen atoms pointing toward the borane show an accumulation of negative charge, as they accept electron density from the closest fluorine atoms of the borane underlying the presence of H/F interaction (Figure S37), as already noted elsewhere.[7a]

In conclusion, we have provided unprecedented experimental evidence for the association and structure of $PR_3/B(C_6F_5)_3$ frustrated Lewis pairs in solution. Importantly, we found that there is not any preferred approaching orientation between LA and LB. This has been mainly deduced from $^{19}F,^1H$ HOESY NMR studies and confirmed by DFT calculations, which estimated a difference of only 1 kcal/mol between two extreme orientations having P and B atoms facing each other or pointing in opposite directions. Consequently, the general picture that emerges from our findings is that a number of roughly equiprobable LA/LB orientations are present in solution, likely including the kinetically relevant one shown in Scheme 1, having the empty orbital of LA in front of the lone pair of LB.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details of NMR measurements and DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors
luca.rocchigiani@progetti.unipg.it
alceo.macchioni@unipg.it
Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) (a) Brown, H. C.; Schlesinger, H. I.; Cardon, S. Z. *J. Am. Chem. Soc.* **1942**, *64*, 325. (b) *Topics in Current Chemistry: Frustrated Lewis Pairs I (Uncovering and Understanding)*; Erker, G., Stephan, D. W., Eds.; Springer-Verlag: Berlin/Heidelberg, 2013.

(2) (a) Stephan, D. W. *Org. Biomol. Chem.* **2008**, *6*, 1535. (b) Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 46. (c) Stephan, D. W. *Dalton Trans.* **2009**, 3129.

(3) Welch, G. C.; Juan, R. R. S.; Masuda, J. D.; Stephan, D. W. *Science* **2006**, *314*, 1124.

(4) (a) Momming, C. M.; Otten, E.; Kehr, G.; Frohlich, R.; Grimme, S.; Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2009**, *48*, 6643. (b) Berkefeld, A.; Piers, W. E.; Parvez, M. *J. Am. Chem. Soc.* **2010**, *132*, 10660. (c) Ashley, A. E.; Thompson, A. L.; O'Hare, D. *Angew. Chem., Int. Ed.* **2009**, *48*, 9839.

(5) McCahill, J. S. J.; Welch, G. C.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 4968.

(6) (a) Chen, D.; Wang, Y.; Klankermayer, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 9475. (b) Axenov, K. V.; Kehr, G.; Frohlich, R.; Erker, G. *J.*

Am. Chem. Soc. **2009**, *131*, 3454. (c) Spies, P.; Schwendemann, S.; Lange, S.; Kehr, G.; Frohlich, R.; Erker, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 7543. (d) Chase, P. A.; Welch, G. C.; Jurca, T.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 8050. (e) Chernichenko, K.; Madarasz, A.; Papai, I.; Nieger, M.; Leskelä, M.; Repo, T. *Nat. Chem.* **2013**, *5*, 718.

(7) (a) Rokob, T. A.; Hamza, A.; Stirling, A.; Soos, T.; Pàpai, I. *Angew. Chem., Int. Ed.* **2008**, *47*, 2435. (b) Rokob, T. A.; Bakò, I.; Stirling, A.; Hamza, A.; Pàpai, I. *J. Am. Chem. Soc.* **2013**, *135*, 4425.

(8) Guo, Y.; Li, S. *Inorg. Chem.* **2008**, *47*, 6212.

(9) Eisenstein, O.; Crabtree, R. H. *New J. Chem.* **2013**, *37*, 21.

(10) For 2,2,6,6-tetramethylpiperidine/$B(C_6F_5)_3$ pairs, NMR experiments suggested an LA/LB association through hydrogen-bonding: Sumerin, V.; Schulz, F.; Nieger, M.; Leskela, M.; Repo, T.; Rieger, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 6001.

(11) Welch, G. C.; Stephan, D. W. *J. Am. Chem. Soc.* **2007**, *129*, 1880.

(12) Marwitz, A. J. V.; Dutton, J. L.; Mercier, L. G.; Piers, W. E. *J. Am. Chem. Soc.* **2011**, *133*, 10026.

(13) Greb, L.; Tussing, S.; Schirmer, B.; Ona-Burgos, P.; Kaupmees, K.; Lokov, M.; Leito, I.; Grimme, S.; Paradies, J. *Chem. Sci.* **2013**, *4*, 2788.

(14) Schulz, F.; Sumerin, V.; Heikkinen, S.; Pedersen, B.; Wang, C.; Atsumi, M.; Leskelä, M.; Repo, T.; Pyykkö, P.; Petry, W.; Rieger, B. *J. Am. Chem. Soc.* **2011**, *133*, 20245.

(15) For an accurate NMR investigation in the solid state related to a series of intramolecular FLPs, see: Wiegand, T.; Eckert, H.; Ekkert, O.; Fröhlich, R.; Kehr, G.; Erker, G.; Grimme, S. *J. Am. Chem. Soc.* **2012**, *134*, 4236.

(16) Dang, X. L.; Schenter, G. K.; Chang, T. -M.; Kathmann, S. M.; Autrey, T. *J. Chem. Phys. Lett.* **2012**, *3*, 3312.

(17) Bellachioma, G.; Cardaci, G.; Macchioni, A.; Reichenbach, G.; Terenzi, S. *Organometallics* **1996**, *15*, 4349.

(18) (a) Zuccaccia, D.; Belpassi, L.; Tarantelli, F.; Macchioni, A. *J. Am. Chem. Soc.* **2009**, *131*, 3170. (b) Zuccaccia, C.; Bellachioma, G.; Cardaci, G.; Macchioni, A. *J. Am. Chem. Soc.* **2001**, *123*, 11020.

(19) (a) Kang, H.; Facchetti, A.; Jiang, H.; Cariati, E.; Righetto, S.; Ugo, R.; Zuccaccia, C.; Macchioni, A.; Stern, C. L.; Liu, Z.; Ho, S. -T.; Brown, E. C.; Ratner, M. A.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 3267. (b) Burini, A.; Fackler, J. P., Jr.; Galassi, R.; Macchioni, A.; Omary, M. A.; Rawashdeh-Omary, M. A.; Pietroni, B. R.; Sabatini, S.; Zuccaccia, C. *J. Am. Chem. Soc.* **2002**, *124*, 4570. (c) Zuccaccia, D.; Pirondini, L.; Pinalli, R.; Dalcanale, E.; Macchioni, A. *J. Am. Chem. Soc.* **2005**, *127*, 7025.

(20) (a) Macchioni, A.; Ciancaleoni, G.; Zuccaccia, C.; Zuccaccia, D. *Chem. Soc. Rev.* **2008**, *37*, 479. (b) Rocchigiani, L.; Zuccaccia, C.; Zuccaccia, D.; Macchioni, A. *Chem.—Eur. J.* **2008**, *14*, 6589. (c) Rocchigiani, L.; Bellachioma, G.; Ciancaleoni, G.; Crocchianti, S.; Laganà, A.; Zuccaccia, C.; Zuccaccia, D.; Macchioni, A. *ChemPhysChem* **2010**, *11*, 3243.

(21) Pregosin, P. S.; Kumar, P. G. A.; Fernàndez, I. *Chem. Rev.* **2005**, *105*, 2977.

(22) (a) The relative anion/cation orientation in solution of phosphonium borate ion pairs, obtained by H_2 activation, was recently elucidated by $^{19}F,^1H$ NOE studies: Greb, L.; Daniluc, C.; Bergander, K.; Paradies, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 5876. (b) $^{19}F,^1H$ NOE has been used also to probe the tendency of olefins to interact with boranes and form van der Waals complexes: Zhao, X.; Stephan, D. W. *J. Am. Chem. Soc.* **2011**, *133*, 12448.

(23) In the first additions, the formation of borate byproducts was observed. At this stage we are not able to understand if this reactivity is intrinsic of the system or is due to impurities of solvents or reagents.

(24) McFarlane, W.; Regius, C. T. *Polyhedron* **1997**, *16*, 1855.

(25) The additional smaller broadening at 310 K seems to be peculiar to $B(C_6F_5)_3$ (see Figure S11) and not dependent on the interaction with the phosphine.

(26) Bakò, I.; Stirling, A.; Balint, S.; Papài, I. *Dalton Trans.* **2012**, *41*, 9023.

(27) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. *J. Chem. Phys.* **2010**, *132*, 154104.

(28) Ziegler, T.; Rauk, A. *Inorg. Chem.* **1979**, *18*, 1558.

(29) (a) Cappelletti, D.; Ronca, E.; Belpassi, L.; Tarantelli, F.; Pirani, F. *Acc. Chem. Res.* **2012**, *45*, 1571. (b) Belpassi, L.; Reca, M. L.; Tarantelli, F.; Roncaratti, L. F.; Pirani, F.; Cappelletti, D.; Faure, A.; Scribano, Y. *J. Am. Chem. Soc.* **2010**, *132*, 13046.

(30) For **2**/$B(C_6F_5)_3$**_b**, $\Delta q = -0.036$ e; for **1**/$B(C_6F_5)_3$, $\Delta q = -0.069$ e (Supporting Information).

115

dx.doi.org/10.1021/ja41191691 | *J. Am. Chem. Soc.* 2014, 136, 112−115