

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

Colegio de Ciencias e Ingenierías

Programación, termodinámica y termodinámica estadística
en química computacional
.Proyecto de investigación

Carlos Patricio Espinosa Gavilanes

Química

**Trabajo de titulación presentado como requisito para la obtención del
título de Químico**

Quito, 17 de diciembre 2015

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ
COLEGIO DE CIENCIAS E INGENIERÍAS

**HOJA DE CALIFICACIÓN
DE TRABAJO DE TITULACIÓN**

**Programación, termodinámica y termodinámica estadística en química
computacional**

Carlos Patricio Espinosa Gavilanes

Calificación:

Nombre del profesor, Título académico

F. Javier Torres , Ph.D.

Firma del profesor

Quito,17 de diciembre de 2015

Derechos de Autor

Por medio del presente documento certifico que he leído todas las Políticas y Manuales de la Universidad San Francisco de Quito USFQ, incluyendo la Política de Propiedad Intelectual USFQ, y estoy de acuerdo con su contenido, por lo que los derechos de propiedad intelectual del presente trabajo quedan sujetos a lo dispuesto en esas Políticas.

Asimismo, autorizo a la USFQ para que realice la digitalización y publicación de este trabajo en el repositorio virtual, de conformidad a lo dispuesto en el Art. 144 de la Ley Orgánica de Educación Superior.

Firma del estudiante: _____

Nombres y apellidos: Carlos Patricio Espinosa Gavilanes

Código: 00107386

Cédula de Identidad: 1718382482

Lugar y fecha: Quito, 17 de diciembre 2015

RESUMEN

La asociación intermolecular de doce combinaciones entre seis ácidos de Lewis y bases de Lewis diferentes (es decir, $R_3A-BR'_3$ donde $A = B$ y Al; $B = N$ y P; $R = H, F,$ y C_6F_5 ; $R' = H, CH_3$ y $C(CH_3)_3$) fue descrito teóricamente por medio de cálculos DFT realizados en B97D / 6-311 ++ G (2d, 2p) como nivel de teoría incluyendo tolueno como solvente a través del esquema de solvente PCM-SMD. Todos los pares de Lewis estudiados parecen ser estable sobre la base de energías de interacción calculadas corregidos-BSSE; Sin embargo, las energías libres de formación calculadas en solución () indican que tres combinaciones de ácido-base de Lewis pueden ser considerados pares de Lewis frustrados (FLP). Además de los cuatro rasgos que caracterizan a los FLP; a saber: (i) las grandes distancias entre los centros de ácido y de base (es decir, A y B, respectivamente), (ii) cambios insignificantes en la geometría del ácido, (iii) energías de interacción débiles, y (iv) la dispersión no covalente de la energía que contribuye a casi toda la energía de interacción, se introduce en el siguiente trabajo dos índices actuales ad hoc destinadas a cuantificar los factores electrónicos y estéricos, que tienen un efecto directo en la asociación intermolecular de ácidos de Lewis y bases de Lewis y se puede utilizar para distinguir FLPs de aductos clásicos de Lewis. Sobre la base de los índices ad-hoc antes mencionados, se propone la existencia de un nuevo tipo de complejos que son "intermedio" entre los complejos clásicos y los complejos FLP.

Palabras clave: Aductos de Lewis clásicos, pares Lewis frustrados , efectos electrónicos , efectos estéricos .

Abstract.

The intermolecular association of twelve combinations of six different Lewis acids and Lewis bases (i.e., $\mathbf{R}_3\mathbf{A}-\mathbf{BR}'_3$ where $\mathbf{A} = \mathbf{B}$ and Al; $\mathbf{B} = \mathbf{N}$ and P; $\mathbf{R} = \mathbf{H}$, F, and C_6F_5 ; $\mathbf{R}' = \mathbf{H}$, CH_3 , and $\text{C}(\text{CH}_3)_3$) was theoretically described by means of DFT calculations conducted at the B97D/6-311++G(2d,2p) level of theory including toluene as solvent through the PCM-SMD implicit solvent scheme. All the studied Lewis pairs appeared to be stable on the basis of computed BSSE-corrected interaction energies; however, the free energies of formation computed in solution (ΔG^\ddagger) indicate that three Lewis acid-base combinations can be considered Frustrated Lewis Pairs (FLPs). Besides the four features that characterize FLPs; namely: (i) large distances between the acid and base centers (i.e., \mathbf{A} and \mathbf{B} , respectively), (ii) negligible changes in the geometry of the acid, (iii) weak interaction energies, and (iv) non-covalent dispersion energy contributing to almost the entire interaction energy, we introduce in the present work two *ad-hoc* indexes intended to quantify the electronic and steric factors, which have a direct effect in the intermolecular association of Lewis acids and Lewis bases and can be used to distinguished FLPs from classical Lewis adducts. Based on the aforementioned *ad-hoc* indexes, the existence of a new kind of complexes that are “intermediate” between classical complexes and FLPs are proposed.

Keywords: Classical Lewis Adducts, Frustrated Lewis Pairs, electronic effects, steric effects.

TABLA DE CONTENIDO

Introducción	8
Desarrollo del Tema	11
Conclusiones	21
Referencias bibliográficas	23

ON THE THERMODYNAMIC STABILITY OF THE INTERMOLECULAR ASSOCIATION BETWEEN LEWIS ACIDS AND LEWIS BASES: A DFT STUDY

Marcos Becerra^{a,b}, Misael Real^{a,b}, Carlos Espinosa-Gavilanes^{a,b}, Cesar H. Zambrano^{a,b},
Rafael Almeida^c, F. Javier Torres^{a,b,d} and Luis Rincón^{a,b,c}

^aUniversidad San Francisco de Quito, Instituto de Simulación Computacional (ISC-USFQ),
Diego de Robles y Vía Interoceánica, Quito, Ecuador 17-1200-841

^bUniversidad San Francisco de Quito, Grupo de Química Computacional y Teórica (QCT-USFQ),
Departamento de Ingeniería Química, Diego de Robles y Vía Interoceánica, Quito, Ecuador 17-1200-841

^cDepartamento de Química, Facultad de Ciencias, Universidad de Los Andes, La Hechicera,
Mérida-5101, Venezuela

^dUniversité de Bordeaux, ISM, UMR 5255, 351, Cours de la Libération, Talence F-33405, France

Introduction

In 1923, G.N. Lewis introduced his classical definition of acids and bases in order to rationalize the behavior of numerous chemical reactions [1]. According to Lewis' definition, an acid is a molecule able to accept a pair of electrons, whereas a base is a molecule able to donate a pair of electrons. Thus, it can be stated that, at least in principle, a stable complex or adduct is always formed when acids and bases are combined as a consequence of the electron-donor/electron-acceptor interaction between the two species. The previous canon is considered one of the cornerstones in the chemistry of acids and bases, and it is also recognized as one of the most fundamental principles in organic as well as inorganic chemistry.

Even if most of the combinations of Lewis acids and bases results in a dative adduct, occasionally some combinations of bulky acids and bases appears to deviate from the Lewis simple rule [2-5]. Historically, this anomaly has been attributed to steric effects existing between the Lewis acid and the Lewis base that preclude the encounter between the reactive centers. Therefore, the thermodynamic stability and other factors governing the formation of Lewis adducts have become an aspect of growing interest, specially since the existence of the so-called Frustrated Lewis Pairs (FLP) was confirmed in 2006 by D. W. Stephan [6-7]. Stephan and collaborators showed, in an unprecedented experiment, that the combination of boranes and phosphines possessing bulky substituent groups are able to cleave the H—H bond under very mild conditions, representing the first example of a reversible H₂ activation without the aid of a transition metal. This unusual reactivity is attributed to the use of a combination of a Lewis acid and a Lewis base in which the steric demand *frustrates* the formation of the classical dative adduct. As a result, the chemistry of FLPs has evolved in the last ten years as one of the most fructiferous

strategies for metal free activation of small molecules using both intermolecular and intramolecular combinations of Lewis acids and Lewis bases [8-11].

It must be emphasized that understanding the factors that affect the stability and reactivity of the association of Lewis acid and bases represents a great challenge for electronic structure calculations. Theoretical studies agree that the weak non-covalent interactions between Lewis acids and Lewis bases are the driving forces in the formation of FLPs [12-21]. This point has been addressed recently by Skara et al., who have investigated fourteen different Lewis pairs of various sizes using the Ziegler-Rauk energy decomposition in order to assess the relative contribution of: (i) the electrostatic and the orbital interactions, (ii) the steric effects, and (iii) the dispersion energy contribution to the total binding energy [20, 22]. In Skara's work, the orbital interactions were computed by employing a Natural Orbital Chemical Valence (NOCV) analysis [23], whereas the non-covalent interactions were described by using the Non-covalent Interaction (NCI) method [24]. Interestingly, the results of the study revealed that the weak forces present between a Lewis acid and a Lewis base are the main energetic effects leading the mechanism of FLPs formation. More recently, state-of-the-art electronic structure methods have been also applied to investigate FLPs built up from tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) and different phosphines (PR_3 ; with $R=2,4,6$ -MeC₆H₂ and t-Bu) [21]. In agreement with the results of Skara et al., the latter study showed that the weak non-covalent interactions, in particular the dispersion interactions, are the driving factors for the formation of FLPs.

In this work, a further investigation of twelve combination of different Lewis acids and Lewis bases (i.e., $R_3A—BR'_3$ where $A = B$ and Al; $B = N$ and P; $R = H, F$, and C_6F_5 ; $R' = H, CH_3$, and $C(CH_3)_3$) is presented in order to gain deeper insights on the stability of the intermolecular association between Lewis acids and Lewis bases. In particular, the

energetic factors that control the overall thermodynamic stability of Lewis pairs in liquid toluene (i.e., a representative non-polar solvent) is analyzed by means of DFT calculations performed at the B97D/6-311++G(2d,2p) level of theory. In contrast with previous theoretical studies that were focused on the analysis of FLPs, the combinations of Lewis acids and Lewis bases employed herein broaden the scenario from very strong classical Lewis adducts to FLPs possessing different degrees of electronic character (i.e., **R** groups with different electron-withdrawing and electron-donating character) as well as steric effects (i.e., **R** groups of various sizes). By employing the latter models, a general perspective of the intermolecular association between Lewis acids and Lewis bases is obtained, being this description not biased towards the idea of “frustration” of the Lewis adducts. In more detail, the geometric and energetic changes occurring on the Lewis acids and Lewis bases are analyzed, and special emphasis in the contribution of the non-covalent dispersion interactions to the total energy is made. Moreover, two *ad-hoc* indexes are introduced to account for the electronic and steric effects in the Lewis acids and the Lewis bases. Here, it is shown that these indexes can be easily calculated for the separated free gas-phase Lewis acids and Lewis bases, and they can be used to predict *a priori* whether a classical Lewis adduct or a FLPs is formed.

Computational Details

All calculations of the present study were performed employing the Gaussian 09 suite of programs [25]. Equilibrium geometries were obtained using the dispersion corrected B97D exchange correlation functional [26] together with the large 6-311++G(2d,2p) basis set [27-29] as level of theory. An ultra-fine grid was adopted for all the calculations since Lewis adducts have many soft vibrational modes. The Berni algorithm in redundant internal coordinates [30] was adopted for the geometry optimizations, and the thresholds for convergence were set to 0.00045 a.u. and 0.0003 a.u. for maximum force and root-mean-square (rms) force, respectively. The errors due to the basis set superposition (BSSE) were estimated by employing the standard counterpoise method as proposed by Boys and Bernardi [31]. Upon obtaining the equilibrium geometries of the models, a vibrational analysis was performed at the same level of calculation in order to confirm that the computed structures correspond to true minima in the potential energy surface. Subsequently, the resulting vibrational frequencies were employed to compute the zero-point energy and thermal corrections (i.e., ZPE and ET, respectively) in the ideal gas approximation at 298.15 K and 1 atm. Although previous studies [12-19] have shown that the B97D functional provides correct qualitative trends regarding the intermolecular association of Lewis acids and Lewis bases, it must be indicated that free energy differences below 2 kcal/mol obtained with the present computational scheme are expected to be greatly affected by the non-negligible errors introduced in entropic contributions from the application of the rigid-rotor and the harmonic approximation for frequencies smaller than 100 cm^{-1} . In order to take into account the effect of the solvent, the polarizable continuum model (PCM) with the radii and non-electrostatic terms for Cramer and Truhlar solvation model was adopted. A dielectric constant value of 2.3741, corresponding to liquid toluene, was considered to perform single point calculations on

the equilibrium geometry of the systems as obtained at the gas-phase. A concentration correction of $1.89 \text{ kcal mol}^{-1}$ in the calculation of solvation free energies was used to account for the change in conditions when going from 1 atm to 1 M concentration (i.e., when going from gas phase to a solution regime) [32-34].

Results and Discussion

For a sake of clarity, the present Section has been divided into three parts: (a) the analysis of the factors that contribute to the thermodynamic stability of the intermolecular association of Lewis acids and Lewis bases, (b) the geometric and energetic changes upon the formation of the Lewis adducts, and (c) a digression on the interplay between electronic and steric factors in the intermolecular association of Lewis acids and Lewis basis.

(a) The thermodynamic stability of the intermolecular association of Lewis Acids and Lewis Bases.

The different Lewis acids and Lewis bases that form the twelve pairs (**1-12**) considered in the present work are reported in Table 1 together with their corresponding BSSE–uncorrected and BSSE–corrected interaction energy (and , respectively) obtained at the B97D/6-311++G(2d,2p) level of theory. Dimers **1** to **4** correspond to the cases where the substituent groups in the acids (i.e., boranes and alanes) and bases (i.e., amines and phosphines) are H, dimers **5** to **8** are the cases where the substituents in the acids are F and the substituents in the bases are CH_3 , and finally, dimers **9** to **12** are the systems where the substituents on the acid are C_6F_5 and the substituents on the base are $\text{C}(\text{CH}_3)_3$. Taking into consideration the latter descriptions, it can be stated that pairs **5-8** represent cases of increasing acidity/basicity character and modest or negligible changes

concerning the steric effects when compared with **1-4**, whereas the pairs **9-12** represent systems of increasing acidity/basicity character as well as increasing steric effects with respect to **1-4**. From the data reported in the column 5 of Table 1, it can be observed that all the considered combinations resulted in *stable* complexes (i.e.,). However, the degree of stability in each case is different, allowing the various complexes to be classified into four categories as follows: *very strong* if the interaction energy is lower than -30 kcal/mol (a category containing the two AlF₃ complexes **7-8**), *strong* if the interaction energy is between -30 and -20 kcal/mol (5 complexes), *weak* if the interaction energy is between -20 and -10 kcal/mol (4 complexes), and *very weak* if the interaction energy is below -10 kcal/mol (1 complex). Afterwards, it will be commented on how this preliminary classification provides relevant information for the discrimination of FLPs among the group of the Lewis acid-base pairs considered in the present study. Upon comparison of columns 4 and 5, it is observed that the BSSE values (i.e., the difference) depend on the size of the substituent groups of the Lewis pairs as follows: the larger the components of a pair the larger its BSSE. Thus, the BSSE values are within the 0.36-0.25 kcal/mol, 1.36-2.03 kcal/mol, and 2.80-3.11 kcal/mol ranges for the groups of dimers **1-4**, **5-8**, and **9-12**, respectively. In column 6 of Table 1, the values of the gas phase enthalpy computed at 298.15 K, are reported. When subtracting these values from the ones, the contribution of the zero-point energy and the thermal corrections to the enthalpy are obtained. In contrast to the BSSE values, a particular trend is not found regarding either the zero-point energy or the thermal corrections to the enthalpy. The sum of these corrections span the 1.21 to 3.64 kcal/mol range, being the two greatest values the quantities associated to **1** and **12** (i.e., H₃B—NH₃, (C₆F₅)₃Al—P(C(CH₃)₃)₃, respectively). Values reported in column 7 are the gas phase free energy of formation (ΔG°) computed at 298.15 K. The difference between these data and the gas phase enthalpy corresponds to the gas phase

entropic components (ΔS^\ddagger), which is a positive quantity for all cases and span the 8.83 to 16.87 kcal/mol range. Previous works have remarked that the gas phase entropy is the most destabilizing component in the intermolecular association of Lewis pairs [19-21], and it could lead to the formation of FLPs. In agreement with the latter statement, the largest value (16.28 kcal/mol) obtained in the present study corresponds to the $(\text{C}_6\text{F}_5)_3\text{Al}-\text{P}(\text{C}(\text{CH}_3)_3)_3$ pair (**12**), which possesses bulky R substituents. However, it must be indicated that relatively large ΔS^\ddagger values are also found in other pairs including some of those possessing less bulky R groups. The last thermodynamic quantities reported in Table 1 correspond to the PCM-SMD free energy values (ΔG^\ddagger). By analyzing the computed values, it can be pointed out that the formation of dimers **9**, **10**, and **11** is not favorable from the thermodynamic point of view, and they can be suggested as FLPs. The last Lewis pair (**12**) is particularly interesting because, notwithstanding it has the theoretic conditions to give rise to a FLP, its formation is slightly favorable according to its ΔG^\ddagger value of -4.46 kcal/mol. A plausible explanation for this is that **12** has some characteristics of a classic Lewis adduct as well as a FLP; thus, it represents an “intermediate” system.

It is remarkable that the zero-point energy, the gas phase thermal corrections to the enthalpy, and the entropic correction to the gas phase free energy are approximately similar in each of the complexes (i.e., deviations not larger than 3 kcal/mol) regardless of the fact that these systems are different regarding the electron-withdrawing/electron-donating character of the R substituent groups or the nature of the centers of the Lewis acid and Lewis base (with the notable exception of **12**). As a final remark of the present section, it can be denoted that the average increase in energy from $\text{R}_3\text{Al} + \text{R}_3\text{P}$ to $\text{R}_3\text{Al} \cdots \text{R}_3\text{P}$ is 11.76 kcal/mol and 15.04 kcal/mol from $\text{R}_3\text{Al} + \text{R}_3\text{P}$ to $\text{R}_3\text{Al} \cdots \text{R}_3\text{P}$ for the bulky substituents (**9-12**). These values are slightly lower than values previously reported, for instance, Skara et al. have obtained values for fourteen FLPs with an increment in energy between 16.4 and 21.5 kcal/mol (an average

of 18.29 kcal/mol) from to using \square B97x -D/6-311++G(d,p), and Bannwarth, Hansen and Grimme have reported a value of 13.3 kcal/mol for the pair $\text{B}(\text{C}_6\text{F}_5)_3\text{-P}(\text{t-Bu})_3$ from to and 12.4 kcal/mol from to by employ the COSMO-RS solvation model [21].

(b) Geometric and energetic changes upon the combination of the Lewis acids and Lewis bases

Conceptually, the formation of a Lewis pair can be ideally divided into two steps: (i) the distortion of the Lewis acid and the Lewis base to the geometry that these species adopt when compose the complex and (ii) the subsequent establishment of a binding interaction between the acid and the base reactive centers. Thus, it results reasonable to analyze the binding energies obtained for systems **1-12** as a sum of the above-mentioned contributions by considering the following expression:

$$(1)$$

where E_{AB} is the energy of X with the geometry in the dimer AB and E_{X} is the optimized energy for X. E_{AB} and E_{X} are always destabilizing terms, whereas the last term, E_{int} , corresponds to the stabilizing effects due to polarization, exchange, and charge transfer between the Lewis acid and the Lewis base at the fixed complex geometry. The terms of the energy decomposition in Ec. (1) are presented in Table 2 together with some relevant geometrical features of systems **1-12**. Table 2 also includes the change in the dispersion energy correction, E_{disp} , obtained at the B97D level for the different Lewis acid-base pairs upon comparison with their free components. Results reported in Table 2 are commented in a more detailed manner in the following paragraphs.

In general terms, the bond distance between the Lewis acid and the Lewis base can be ascertained from the covalent distances between the electron donor and electron acceptor atoms; therefore, the trend, $\text{B-N} < \text{B-P} \approx \text{Al-N} < \text{Al-P}$ is expected for the studied

molecules. From the data reported in Table 2, it is observed that the latter trend applies only in the case of the Lewis pairs **1-8**, whereas much larger values (almost twice as larger) were observed for the bulkier systems (**9-11**), excluding pair **12**, where some favorable interaction is evident from the calculated (2.71 Å) shorter distance.

From a structural consideration, it can be stated that the trigonal planar structure of free Lewis acids must be deformed to acquire a pseudo-tetrahedral configuration in order to interact with a Lewis base. In view of the latter rule, the angle **R-A-B** can be used as an indicator of the degree of change in the geometry of a Lewis acid when being part of a Lewis adduct. In principle, large deviations from 90° (i.e., characteristic of an undeformed acid) are associated with significant geometrical distortions and great distortion energies. In classic Lewis adducts this deformation tends to be large, being more significant for boranes than for alanes. On the other hand, for the case of FLPs, almost negligible changes in the **R-A-B** angle are determined.

As explained previously, the BSSE, the thermal correction to the enthalpy, the entropic factor, and the solvation energy, produce an increase in the binding energy on the order of 15-20 kcal/mol for bulky substituents like complexes **9-12** (Table 1), and on the order of 10-12 kcal/mol for the small substituents (**1-8**). This increment produces a positive Free energy of complexation for weak and very weak interactions, being this characteristic observed in FLPs.

The most intriguing observation concerning FLPs is the fact that the contribution of the non-covalent dispersion interactions is larger than . Previous works have revealed that, although several kinds of weak interactions such as dispersion, π - π stacking, C-H \cdots π interactions, weak hydrogen bonding and halogen bonding are present in FLPs [20], the dispersion forces are dominant since they counteract the destabilizing factors caused by the steric factors of the bulky substituents [12-21]. From data in Table 2, it is observed

that the complex between $\text{Al}(\text{C}_6\text{F}_5)_3$ and $\text{P}(\text{t-Bu})_3$ (**12**) is unique in the sense that the dispersion energy accounts for almost the whole binding energy value; however, this pair cannot be considered a FLP because it represents a thermodynamic stable system as determined on the basis of its free energy computed in solvent (Table 1). From the data of Table 2, it is also observed that the three pairs identified as FLPs (**9-11**), on the basis of their positive ΔE_{int} values (Table 1), are characterized by the following four properties: (i) very large distances between the acid and base center (i.e., $\text{A}-\text{B} > 4 \text{ \AA}$), (ii) almost negligible changes in the geometry of the Lewis acid (i.e., $\text{R}-\text{A}-\text{B}$ bond angle close to 90° and 180°), (iii) weak BSSE-corrected interactions energies (see Table 1) and ΔE_{int} (i.e., $\Delta E_{\text{int}} < 0$ and $\Delta E_{\text{int}} < -10 \text{ kcal/mol}$), and (iv) very large values of the change of the dispersion energy, ΔE_{disp} , which is the primary stabilizing factor.

(c) The interplay between electronic and steric effects in the intermolecular association of FLPs

In this section, a rationalization of the changes in interaction energy associated to the stabilization of Lewis adducts is addressed. As previously indicated, systems **1-8** have been identified as classic Lewis complexes, whose stability can be rationalized, almost entirely, on the basis of electronic factors. The most popular and simplest electronic descriptor for Lewis pairs is the energy difference between the LUMO of the Lewis acid and the HOMO of the Lewis base, $\Delta E_{\text{LUMO-HOMO}}$. However, other global reactivity descriptors within the framework of the hard-soft acid-base principle have been proposed [35] as quantities that relate the charge transfer with the binding energy in a simple way. For compounds **1-4**, the interaction energy (ΔE_{int}) reported in Table 1 decreases in the following order $\mathbf{1} > \mathbf{3} > \mathbf{2} > \mathbf{4}$ in agreement with the values of $\Delta E_{\text{LUMO-HOMO}}$ that are found to be 3.36 eV for B-N, 3.84 eV for Al-N, 3.87 eV for B-P, and 4.36 eV for Al-P. The same behavior applies for the case of

5-8 for which the computed are 2.37 eV for Al-N, 2.77 eV for Al-P, 4.20 eV for B-N and 4.60 eV for B-P. Interestingly the order of the frontier orbital gap is reverse in the case of systems possessing bulkier substituents. The stronger complex **12** has the largest value, 1.50 eV, whereas the weaker system **9** has the smallest, 0.30 eV. Clearly, for the last four complexes, steric factors play a relevant role in determining the interaction. Unfortunately, even if the concept of steric effects are commonly invoked to explain phenomena occurring at the molecular level, finding an unique definition of steric descriptors has been referred to as one of the most elusive problems in chemistry [35]. One reason for this is the fact that steric effects are not linked to any direct physical observable, and they are, therefore, subject to interpretation. In the case of a Lewis pair, the steric effects come from two main sources: (i) on one hand, it is evident that steric effects increase with the volume of the substituents attached to the acid and base center and (ii) on the other hand (although this is not completely evident), the steric effects depends on the size of the reactivity center. Therefore, centers belonging to the second row of the periodic table (Al or P) present lower steric effects than first period centers for a given R substituent group. It must be indicated that the second assumption is related to the simple observation that the energy necessary to deform a Lewis acid or a Lewis base is lower for second period atoms. Based on these assumptions, an *ad-hoc* steric index can be introduced by dividing the “volume” of the substituent by the “radii” of the Lewis acid or Lewis base center. It must be noted that the previous principle is independent of the precise definition of “volume” or “radii”.

In order to obtain an estimation of the volume of the substituents, the Weizsaker kinetic energy functional can be used,

(2)

The Weizsacker energy was used because it has proven to be an indication of the changes in the volume of a given system [37-39], and it can be easily calculated by employing the wavefunction file (i.e., WFN output), obtained with the program Gaussian, through our in-home implementation of the Becke integration methodology based on the atomic fuzzy Voronoi polyhedral [40]. For each atomic basin, the radial integration has been performed using 40 points in the Chebyshev's quadrature, while for the angular part, the Lebedev's quadrature method with 194 points has been employed. Changes in E_{Weiz} are related to the changes in the volume of the system; therefore, a simpler estimation of the steric contribution of the substituents in the Lewis acid and the Lewis base can easily be associated to the change in the Weizsacker energy when they are compared with a reference substituent (i.e., $\mathbf{R}=\mathbf{R}'=\text{H}$). In view of this, the steric volumen for a substituent \mathbf{R} in the Lewis acid is defined as $V_{\text{steric}}^{\text{LA}} = \frac{E_{\text{Weiz}}(\mathbf{R}) - E_{\text{Weiz}}(\text{H})}{E_{\text{Weiz}}(\text{H}) - E_{\text{Weiz}}(\text{H})}$, where $\mathbf{A} = \text{B}$ or Al . In a similar fashion, the steric volume for a substituent in the Lewis base is defined as $V_{\text{steric}}^{\text{LB}} = \frac{E_{\text{Weiz}}(\mathbf{R}) - E_{\text{Weiz}}(\text{H})}{E_{\text{Weiz}}(\text{H}) - E_{\text{Weiz}}(\text{H})}$, where $\mathbf{B} = \text{N}$ or P . In order to consider the effect of the different centers, the contributions of the Lewis acid and the Lewis base is divided by the Bragg-Slater radii of the reactive center (in atomic units) [41]. On this manner, the steric indexes $\sigma_{\text{steric}}^{\text{LA}}$ and $\sigma_{\text{steric}}^{\text{LB}}$ are introduced for Lewis acids and Lewis bases, respectively. For a Lewis pair, the steric index is defined as the mean of the steric indexes of the individual Lewis acid and Lewis base, $\sigma_{\text{steric}} = \frac{\sigma_{\text{steric}}^{\text{LA}} + \sigma_{\text{steric}}^{\text{LB}}}{2}$. This *ad-hoc* steric effect definition is more illustrative for the present case than the changes in the Weizsacker energy associated with the dimer formation that tends to be negative due to a diminishing effect in the molecular volume of the complex when compared to the free Lewis acid and Lewis base [36-39]. Figure 1 shows a plot of the electronic index, defined as $\sigma_{\text{electronic}}$ in units of eV^{-1} , versus the steric index σ_{steric} in units of Hartree/Bohr for the twelve complexes studied in the work. Three zones can be identified in this plot: (i) the lower-left corner characterized by the presence of all the eight classical adducts for which the electronic index is lower than 1 eV^{-1} and the

steric index never reaches 500 Hartree/Bohr. (ii) the top-right corner characterized by the presence of FLPs for which the electronic factors exceed 1 eV^{-1} and the steric index is above 1000 Hartree/Bohr, and (iii) a zone between i and ii, where the system, identified as “intermediate” (**12**), resides having an electronic factor between $0.5\text{-}1.5 \text{ eV}^{-1}$ and a steric index between 600-1000 Hartree/Bohr. Before concluding, some comments on the limitations of our approach must be conveyed. The numerical values of the electronic index described above () can change slightly when different methodologies and basis sets are adopted; however, previous works [35] shows that the relative trends might be maintained regardless the computational method employed. In contrast, the steric index introduced is approximately independent of the level of calculation because it is based in the electron density and a standard definition of atomic radii. Therefore, it is expected that similar conclusions could be obtained when adopting other levels of theory.

Conclusions

We thoroughly investigate the interactions between twelve Lewis pairs, that span from classical adducts to FLPs, with the purpose of gaining deeper insights in the factors associated with their thermodynamic stability. On the basis of their binding energies all complexes are stable at different degrees; however, due to thermal corrections to the enthalpy, entropic factors and solvation effects, a positive value was computed for three complexes, which were identified as FLPs. When compared with classical complexes, the three identified FLPs show the following unique characteristics: (i) the bond distance between the acid and base center are larger than 4.0 Å, a distance in which negligible interactions between the centers is expected, (ii) the geometry of the Lewis acid is almost undeformed, (iii) the interaction energy is negative but larger than -15 kcal/mol (weak interaction), and (iv) the contribution from non-covalent dispersion term represents the largest contribution to the total interaction energy.

In order to rationalized these results we introduce a classical electronic index based on the difference in energy between the LUMO of the acids and the HOMO of the base, and an *ad-hoc* steric index that takes into account two considerations: (i) the larger the volume of the substituents attached to the acid or the base center the more important the steric effect and (ii) the larger the center radii the less significant the steric effect. In our definition, we take as a reference for the steric index the Lewis acids and Lewis bases with H as substituents where the volume of the substituents were estimated using the Waizsacker kinetic energy functional. On this way, we could discriminate classical adducts and FLPs using a plot of the electronic versus the steric indexes. Moreover, a third kind of intermolecular complexes was identified. We described this system as an “intermediate” complex, whose free energy in solution is slightly negative (i.e.,

characteristic of a classical complexes), but its non-covalent dispersion energy contributes to most of the total interaction energy (i.e., characteristic of a FLP).

In the present work our *ad-hoc* indexes were employed for discriminating FLPs from classical adducts. However, it must be pointed out that these indexes can also be employed for the classification of the different reactivity character (in terms of reversible uptake of H₂, irreversible uptake of H₂ or no reactivity with H₂) of the members of a particular FLP family. This particular idea is a matter of future investigations in this field. As a final remark, it can be indicated that this work employs a restricted sampling of twelve combinations of acids and bases, in which only three of them can be considered as FLPs; therefore, the generalizations presented could be considered at a first instance quite speculative. Certainly, a more extended scrutiny of Lewis acid-base systems is mandatory to confirm the potential of the present approach to classify intermolecular complexes between Lewis pairs. However, we anticipate few changes in the overall distribution of the plot shown in Figure 1 when considering a more extended group of cases since the studied complexes span a broad spectrum in terms of centers and substituents.

Acknowledgements

This work has been performed by employing the resources of the USFQ's High Performance Computing system (HPC-USFQ). The authors would like to thank USFQ's chancellor and collaboration grants program for financial support.

References

1. Lewis GN (1923) Valence and the Structure of Atoms and Molecules. Chemical Catalogue Company, New York.
2. Brown HC, Schlesinger HI, Cardon SZ (1942) Studies in Stereochemistry. I. Steric Strains as a Factor in the Relative Stability of Some Coördination Compounds of Boron. *J Am Chem Soc* 64:325-329.
3. Brown HC, Kanner B (1966) Preparation and Reactions of 2,6-Di-*t*-butylpyridine and Related Hindered Bases. A Case of Steric Hindrance toward the Proton. *J Am Chem Soc* 88:986-992.
4. Wittig G, Benz E (1959) Über das Verhalten von Dehydrobenzol gegenüber nucleophilen und elektrophilen Reagenzien. *Chem. Ber.* 92:1999-2013.
5. Tochtermann W (1966) Structures and Reactions of Organic ate-Complexes. *Angew. Chem. Int. Ed. Engl.* 5:351-371.
6. Welch GC, San Juan RR, Masuda JD, Stephan DW (2006) Reversible, Metal-Free Hydrogen Activation. *Science* 314:1124-1126.
7. Welch GC, Stephan DW (2007) Facile Heterolytic Cleavage of Dihydrogen by Phosphines and Boranes. *J Am Chem Soc* 129:1880-1881.
8. Stephan DW, Erker G (2010) Frustrated Lewis Pairs: Metal-free Hydrogen Activation and More. *Angew Chem Int Ed* 49:46-76.

9. Stephan DW (2015) Frustrated Lewis Pairs: From Concept to Catalysis. *Acc Chem Res* 48:306-316.
10. Stephan DW, Erker G (2014) Frustrated Lewis pair chemistry of carbon, nitrogen and sulfur oxides. *Chem Sci* 5:2625-2641.
11. Stephan DW, Erker G (2015) Frustrated Lewis Pair Chemistry: Development and Perspectives. *Angew Chem Int Ed* 54:6400-6441.
12. Rokob TA, Hamza A, Stirling A, Soos T, Papai I (2008) Turning Frustration into Bond Activation: A Theoretical Mechanistic Study on Heterolytic Hydrogen Splitting by Frustrated Lewis Pairs. *Angew Chem Int Ed* 47:2435-2438.
13. Rokob TA, Hamza A, Papai I (2009) Rationalizing the Reactivity of Frustrated Lewis Pairs: Thermodynamics of H₂ Activation and the Role of Acid–Base Properties. *J Am Chem Soc* 131:10701-1710.
14. Hanza A, Stirling A, Rokob TA, Papai I (2009) Mechanism of hydrogen activation by frustrated Lewis pairs: A molecular orbital approach. *Int J Quantum Chem* 109:2416-2425.
15. Momming CM, Fromel S, Kehr G, Frohlich R, Grimme S, Erker G (2009) Reactions of an Intramolecular Frustrated Lewis Pair with Unsaturated Substrates: Evidence for a Concerted Olefin Addition Reaction. *J Am Chem Soc* 131:12280-12289.
16. Grimme S, Kruse H, Goerigk L, Erker G (2010) The Mechanism of Dihydrogen Activation by Frustrated Lewis Pairs Revisited. *Ang Chem Int Ed* 49:1402-1405.
17. Schimmer B, Grimme S (2010) Electric field induced activation of H₂-Can DFT do the job? *Chem Commun* 46:7942-7944.
18. Rokob TA, Bako I, Stirling A, Hamza A, Papai I (2013) Reactivity Models of Hydrogen Activation by Frustrated Lewis Pairs: Synergistic Electron Transfers or Polarization by Electric Field? *J Am Chem Soc* 135:4425-4437.

19. Zeonjuk LL, Vankova N, Mavrandonakis A, Heine T, Roschenthaler GV, Eicher J (2013) On the Mechanism of Hydrogen Activation by Frustrated Lewis Pairs. *Chem Eur J* 19:17413-17424.
20. Skara G, Pinter B, Top J, Geerlings P, De Proft F, De Vleeschouwer F (2015) Conceptual Quantum Chemical Analysis of Bonding and Noncovalent Interactions in the Formation of Frustrated Lewis Pairs. *Chem Eur J* 21:1-11.
21. Bannwarth C, Hansen A, Grimme S (2015) The Association of Two “Frustrated” Lewis Pairs by State-of-the-Art Quantum Chemical Methods. *Isr J Chem* 55: 235–242.
22. Ziegler T, Rauk A On the calculation of bonding energies by the Hartree Fock Slater method. I. The transition state method. (1977) *Theor Chim Acta* 46:1-10.
23. Mitoraj MP, Michalak A, Ziegler T (2009) A Combined Charge and Energy Decomposition Scheme for Bond Analysis. *J Chem Theor Comp* 5:962-975.
24. Johnson ER, Keinan S, Mori-Sánchez P, Contreras-García J, Cohen AJ, Yang W (2010) Revealing Noncovalent Interactions. *J Am Chem Soc* 132:6498-6506.
25. Gaussian 09, Revision C.01. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JA, Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin, KN, Staroverov VN, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam JM, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas Ö, Foresman JB, Ortiz JV, Cioslowski J, Fox DJ (2009) Gaussian, Inc., Wallingford CT.

26. Grimme S (2006) Semiempirical GGA-type density functional constructed with a long-range dispersion correction. *J Comp Chem* 27:1787-1799.
27. Raghavachari K, Binkley JS, Seeger R, Pople JA (1980) Self-Consistent Molecular Orbital Methods. 20. Basis set for correlated wave-functions. *J Chem Phys* 72:650-654.
28. McLean AD, Chandler GS (1980) Contracted Gaussian-basis sets for molecular calculations. 1. 2nd row atoms, Z=11-18. *J Chem Phys* 72:5639-48.
29. Frisch MJ, Pople JA, Binkley JS (1984) Self-Consistent Molecular Orbital Methods. 25. Supplementary Functions for Gaussian Basis Sets. *J Chem Phys* 80:3265-3269.
30. Schelegel HB (1987) Optimization of equilibrium geometries and transition structures. *Adv Chem Phys* 67:249-286.
31. Boys SF, Bernardi F (1970) Calculation of Small Molecular Interactions by Differences of Separate Total Energies - Some Procedures with Reduced Errors. *Mol Phys* 19:553-566.
32. Tomasi J, Mennucci B, Cammi R (2005) Quantum mechanical continuum solvation models. *Chem Rev* 105:2999-3093.
33. Scalmani G, Frisch MJ (2010) Continuous surface charge polarizable continuum models of solvation. I. General formalism. *J Chem Phys* 132:114110
34. Marenich AV, Cramer CJ, Truhlar DG (2009) Universal solvation model based on solute electron density and a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions. *J Phys Chem B* 113:6378-6396.
35. Changrakumar KRS, Pal S (2002) A systematic study on the reactivity of Lewis Acid-Base complexes through the Local Hard-Soft Acid-Base principle. *J Phys Chem A* 106:11775-11781.

36. Pinter B, Fievez T, Bickelhaupt FM, Geerlings P, De Proft F (2012) On the origin of the Steric Effect. *Phys Chem Chem Phys* 14:9846-9854.
37. Liu S (2007) Steric Effects: A quantitative description from density functional theory. *J Chem Phys* 126:244103
38. Rong C, Lu T, Liu S (2014) Dissecting molecular descriptors into atomic contributions in density functional reactivity theory. *J Chem Phys* 140:024109
39. Fang D, Piquelmann JP, Liu S, Cisneros GA (2014) DFT-steric-based energy decomposition analysis of intermolecular interactions. *Theor Chem Acc* 133:1484.
40. Rincon L, Almeida R (2012) Is the Hammett's constant free of steric effects? *J Phys Chem A* 116:7323-7530.
41. Slater JC (1965) *Quantum Theory of Molecules and Solids*. McGraw-Hill, New York.
42. Chermette H (1999) Chemical reactivity indexes in density functional theory. *J Comp Chem* 20:159-154.

TABLE 1

Interaction energies (E_{int}), basis set superposition error corrected interaction energies (E_{int}^{BSSE}), gas phase enthalpy (H_{gas}), gas phase free energies (G_{gas}) and PCM/SMD solution free energies (G_{sol}) of Lewis acid-base pairs calculated at the B97D/6-311++G(2d,2p) level. All energies are in kcal/mol.

#	Acid	Base	E_{int}	E_{int}^{BSSE}	H_{gas}	G_{gas}	G_{sol}
1	BH ₃	NH ₃	-28.41	-28.09	-24.45	-14.57	-18.14
2	BH ₃	PH ₃	-22.28	-22.03	-19.58	-9.76	-10.68
3	AlH ₃	NH ₃	-26.47	-26.11	-23.56	-14.49	-16.99
4	AlH ₃	PH ₃	-13.08	-12.80	-11.00	-2.49	-2.65
5	BF ₃	NMe ₃	-28.12	-26.10	-23.58	-11.1	-12.97
6	BF ₃	PMe ₃	-15.11	-13.70	-12.49	-2.51	-5.38
7	AlF ₃	NMe ₃	-46.43	-44.40	-41.94	-30.58	-31.19
8	AlF ₃	PMe ₃	-35.47	-34.11	-32.34	-23.35	-25.44
9	B(C ₆ F ₅) ₃	N(t-Bu) ₃	-12.49	-9.69	-7.95	4.34	7.69
10	B(C ₆ F ₅) ₃	P(t-Bu) ₃	-14.17	-11.16	-9.70	2.14	6.07
11	Al(C ₆ F ₅) ₃	N(t-Bu) ₃	-14.04	-10.99	-8.98	4.96	8.64
12	Al(C ₆ F ₅) ₃	P(t-Bu) ₃	-28.92	-25.81	-22.86	-6.58	-4.46

Table 2:

Acid-Base center bond distance and bond angles (A-B, B-A-R, R'-B-A), interaction energies (ΔE), distortion energies ($\Delta E(A)$, $\Delta E(B)$), binding energy ($\Delta E(AB)$) and dispersion energies (ΔE_{DISP}) of Lewis acid-base pairs. All energies are in kcal/mol and distances in Angstroms.

#	Acid	Base	A-B	B-A-R	R'-B-A	ΔE	$\Delta E(A)$	$\Delta E(B)$	$\Delta E(AB)$	ΔE_{DISP}
1	BH ₃	NH ₃	1.69	104.4	111.1	-28.41	11.91	0.06	-40.38	-2.38
2	BH ₃	PH ₃	1.95	103.7	118.2	-22.28	10.85	1.80	-34.93	-1.99
3	AlH ₃	NH ₃	2.12	98.7	111.6	-26.47	3.32	0.02	-28.81	-2.76
4	AlH ₃	PH ₃	2.57	96.5	119.4	-13.08	1.85	1.09	-16.02	-1.68
5	BF ₃	NMe ₃	1.71	105.1	109.4	-28.12	25.18	1.66	-54.96	-9.99
6	BF ₃	PMe ₃	2.09	104.6	112.6	-15.11	25.27	5.13	-45.51	-4.74
7	AlF ₃	NMe ₃	2.01	101.4	109.1	-46.43	7.50	1.46	-55.39	-9.79
8	AlF ₃	PMe ₃	2.43	101.6	113.2	-35.47	8.09	4.14	-47.70	-4.86
9	B(C ₆ F ₅) ₃	N(t-Bu) ₃	4.86	89.3	99.6	-12.49	0.42	0.10	-13.01	-46.27
10	B(C ₆ F ₅) ₃	P(t-Bu) ₃	4.20	90.4	112.3	-14.17	0.66	0.24	-15.07	-22.95
11	Al(C ₆ F ₅) ₃	N(t-Bu) ₃	4.54	90.3	100.2	-14.04	0.97	0.54	-15.55	-23.26
12	Al(C ₆ F ₅) ₃	P(t-Bu) ₃	2.71	107.9	110.5	-28.92	21.05	4.72	-54.69	-33.25

Figure 1.

Plots of the **Electronic Index** defined as the inverse of the difference between the LUMO of the Acid and the HOMO of the Base versus the **Steric Index** defined as the volume of the substituents relative to H divided by the radii of the reactivity center (see the text for details and units).

