

Lewis Acids

How to Deal with Charge in the Ranking of Lewis Acidity: Critical Evaluation of an Extensive Set of Cationic Lewis Acids

Philipp Erdmann, Manuel Schmitt, Lukas M. Sigmund, Felix Krämer, Frank Breher, and Lutz Greb*

Abstract: The quantification of Lewis acidity is of fundamental and applied importance in chemistry. However, if neutral and charged Lewis acids are compared, a coherent ranking has been elusive, and severe uncertainties were accepted. With this study, we present a systematic computational analysis of Lewis base affinities of 784 mono-, di- and tricationic Lewis acids and their comparison with 149 representative neutral Lewis acids. Evaluating vacuum fluoride ion affinities (FIA) reveals a charge-caused clustering that prohibits any meaningful ranking. Instead, solvation-corrected FIA_{solv} is identified as a metric that overcomes charge sensitivity in a balanced manner, allowing for a coherent evaluation of Lewis acidity across varying charge states. Analyzing the impact of molecular volume on solvation-induced FIA damping provides rationales for fundamental trends and guidelines for the choice or design of neutral and cationic Lewis acids in the condensed phase. Exploring alternative scales, explicit counteranion effects, and selected experimental case studies reaffirms the advantages of solvation-corrected FIA_{solv} as the most versatile and practical approach for the quantitative ranking of general (thermodynamic) Lewis acidity.

Introduction

Lewis acids are ubiquitous reagents in chemistry, materials, and life science.^[1] Combining suitable acceptor atoms with appropriate ligands enables the fine-tuning of Lewis acidity to the “amount” for the desired mode of action or optimized catalytic turnover. However, the quantification, the prediction, and the explanation of this “amount” are still poorly understood—despite the formulation of this model already 100 years ago.^[2] Numerous parameters related to the ranking of Lewis acids have been established, and a classification of scaling approaches into three groups was outlined recently by some of us.^[3] In short, thermodynamic parameters of Lewis pair formation (ΔH , ΔG) are termed *general/global Lewis acidity (gLA)*, Lewis acid binding-induced effects at a Lewis basic probe as *effective Lewis acidity (eLA)*, and Lewis acid-inherent properties (e.g., LUMO energy) as *intrinsic Lewis acidity (iLA)*. Connections between these perspectives were identified by a statistical

analysis of the Gutmann-Beckett method, which is the most common eLA scale.^[4] In the following work, we will narrow ourselves on the evaluation of the influence of charge on Lewis acidity by correlating large data sets.

The fluoride ion affinity (FIA) represents the most widely used *gLA* scale and defines Lewis superacids (LSA) as those exceeding the FIA of SbF_5 *in vacuo*.^[5] This metric has two advantages resulting from the strong donor ability and the small size of the fluoride ion (Figure 1a). The first advantage emerges from the broadly covered energy range of around 600 kJ mol^{-1} (Figure 1a, red box). This feature attributes high “resolution” that allows the identification of subtle differences and renders the method less sensible to errors inherent to the computational process. The second advantage is that fluoride ions bind exothermically to even the weakest acceptors that would not form adducts with

[*] P. Erdmann, Dr. M. Schmitt, L. M. Sigmund, Prof. Dr. L. Greb
 Anorganisch-Chemisches Institut, Ruprecht-Karls-Universität Heidelberg
 Im Neuenheimer Feld 270, 69120 Heidelberg (Germany)
 E-mail: greb@uni-heidelberg.de

Dr. F. Krämer, Prof. Dr. F. Breher
 Institute of Inorganic Chemistry, Karlsruhe Institute of Technology (KIT)
 Engesserstr. 15, 76131 Karlsruhe (Germany)

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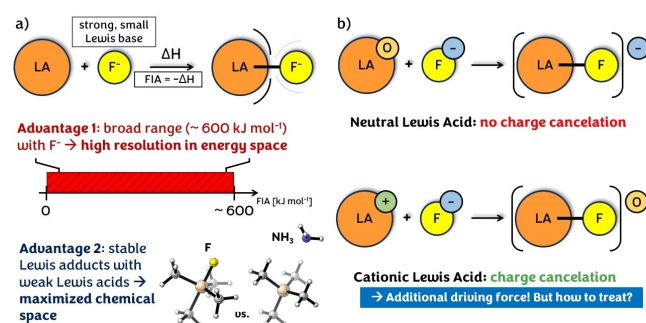


Figure 1. FIA scale properties. a) Strong donor that allows generally favorable adduct formation and evaluation from weak to strong Lewis acids with high resolution in enthalpy. b) Different scenarios for Lewis acids with different molecular charges if reacted with an anionic Lewis base.

weaker Lewis bases (e.g., SiMe₄ binds F⁻ but not NH₃, Figure 1a). This property allows the inclusion of extensive chemical space in the discussion of Lewis acidity and warrants maximized generality in the derived statements.

Accordingly, if performed at a sufficient computational level and anchored to a reference system by quasi-isodesmic schemes, computed FIAs enable a robust and meaningful ranking among known and hypothetical Lewis acidic compounds.^[6]

However, do these favorable features remain for Lewis acids of different charge states? Numerous cationic Lewis acids have been developed and applied in spectacular transformations.^[7] To permit a discussion of Lewis acids regardless of their charge, including the stringent definition of LSA (FIA > SbF₅), it is necessary to rank cationic and neutral acceptors on a unified metric. However, cationic Lewis acids experience charge cancellation during adduct formation with anionic reference Lewis bases, whereas for neutral Lewis acids, the overall charge is conserved (Figure 1b).^[8] The attractive Coulomb force between two opposite point charges within 2.8 Å distance (cf. Na–Cl in its solid-state structure) amounts to 496 kJ mol⁻¹. Such massive neutralization energy turns cations inherently more attractive toward anionic donors. Accordingly, cationic Lewis acids do easily exceed the criterion of Lewis superacidity on the conventional vacuum FIA scale. Although this classification is *a priori* no violation of the original definition (FIA > SbF₅ in vacuum!) and reasonable in several cases, it introduces an uncertainty that prohibits a coherent Lewis acidity ranking.

The discrepancies between vacuum computations and condensed phase reactivity originate from the systematically affected stability of neutral vs. charged species in vacuum vs. solution.^[9] Anions (e.g., the fluoride ion or the F-adducts of neutral Lewis acids) respond differently to solvation than cations or neutral species (e.g., the states involved in the FIA reaction of cationic Lewis acids).^[10] Due to their weakly bound valence electrons, the valence orbitals of anions are more affected by solvation than those of neutral or cationic compounds.^[11] This difference leads to different outcomes when reactions that involve a change in the charge sum (neutralization) are compared in vacuum vs. environment-corrected computations—even on a qualitative scale. It should be noted that the environmental polarity has an effect on the stability of Lewis pairs already on its own,^[12] overall complicating a comparison of neutral and charged Lewis acids that would enable any rational selection of suitable reagents or catalysts for synthetic applications. Unfortunately, a collection of affinity values for cationic Lewis acids that would allow a systematic evaluation of charge effects, or an attempt to merge global Lewis acidity scales across different charge states, has not been pursued.

In the present work, we follow our data-driven approach to address shortcomings in the theory of Lewis acidity. The FIA of 784 cationic literature-known or hypothetical Lewis acids are calculated. The comparison with 149 representative values of neutral Lewis acids scrutinizes the effect of molecular charge, charge density, and the influence of solvation correction, counter anions and alternative scales.

A statistical evaluation of all considered strategies allows a conclusive statement on the most plausible treatise of charge in Lewis acid ranking and gives a guideline for the future development of this sparkling field.

Results and Discussion

Vacuum vs. Solvation Corrected Fluoride Ion Affinities

The structures of 754 monocationic, 27 dicationic, 3 tricationic, and 149 neutral Lewis acids were optimized at PBEh-3c or carried over from previous work,^[6] overall covering 520 group 13, 214 group 14, 132 group 15, 61 group 16, 3 group 17 and 3 group 12 compounds including boron to thallium, carbon to tin, phosphorus to bismuth, sulfur to tellurium, iodine and zinc (Figure S3a). Main attention was given to literature-known Lewis acids obtained from a survey with considerable variability on ligands and molecular volume, while also including hypothetical Lewis acids constructed by systematic ligand variations. The Lewis acids cover varying ligand denticity, with 556 monodentate ligands, 236 bidentate ligands, 74 tridentate ligands and 22 tetradentate ligands. Five Lewis acids are atomic (B⁺, Al⁺, Ga⁺, In⁺, Tl⁺), and 40 Lewis acids either as π -complexes or higher denticity (Figure S2). The average bond length deviation from optimized Lewis acids ($\Delta r_{\text{avg}}=0.001$ Å, maximum $\Delta r=0.06$ Å) and fluoride adducts ($\Delta r_{\text{avg,F}}=0.002$ Å, maximum $\Delta r=0.11$ Å) with and without the Solvation Model based on Density (SMD)^[13] revealed negligible influence of solvation effects on the obtained structures (RMSD_{avg}=0.03 Å, RMSD_{avg,F}=0.08 Å). Hence, the optimized vacuum structures were used throughout (Figure S1).

All final FIAs were calculated on RI-DSD-BLYP-(D3BJ)/def2-QZVPP^[14] density functional theory and anchored quasi-isodesmically with the TMS system.^[5d,6] The first series of computations was performed without explicit counter anions and solvation correction, yielding the bare FIA in vacuum, in the following denoted as FIA (without subscript). Subsequently, solvation correction was performed with the Conductor-like Screening Model for Realistic Solvents (COSMO-RS)^[15] for CH₂Cl₂, cyclohexane, toluene, acetonitrile, and water as the solvent, denoted as FIA_{solv} (=FIA_{CH₂Cl₂}, FIA_{C₆H₁₂}, FIA_{Ph-Me}, FIA_{MeCN} and FIA_{H₂O}, Table S1). COSMO-RS was chosen as it performs exceptionally well for ions and neutrals, but also other solvation methods (CPCM^[16] and SMD) were screened and compared (Table S3).^[11] We are aware that the consideration of explicit solvation effects would be mandatory for ultimate accuracy, though such an approach is not practicable for the number of compounds considered in this study.

Plotting FIA against FIA_{solv} for all Lewis acids yields an insightful and elusive correlation (Figure 2). Upon solvation correction, the FIA_{solv} values get drastically reduced. It reveals a separation into clusters of neutral, mono-, di-, and tricationic species, showcasing the systematic effect of the Lewis acids' charge state.

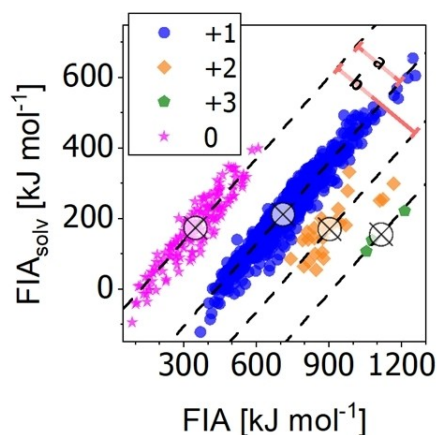


Figure 2. FIA_{solv} vs. FIA for neutral, mono-, di- and tricationic Lewis acids with molecular charge as label and the result of a global linear fit ($FIA_{\text{solv}}^{\text{chrg}} = m \cdot FIA^{\text{chrg}} + y_0^{\text{chrg}}$) with $m=0.773$ and $y_0^0 = -94$, $y_0^{+1} = -336$, $y_0^{+2} = -526$, $y_0^{+3} = -706$ kJ mol^{-1} , respectively (black dotted lines). The offset of clusters is analyzed by the perpendicular distance of fitted lines (red distances, $d = \frac{|y_0^{\text{chrg}} - y_0^{\text{ref}}|}{\sqrt{m^2 + 1}}$); FIA_{avg} are highlighted with cross-marks.

The FIA values experience a discontinuous increase, stepwise with increasing positive charge, while the FIA_{solv} values span the affinity space without discontinuity.

The underlying increments can be attributed to charge cancellation (cf. Figure 1b). From the perpendicular distance of the lines from a linear fit for each charge state with the slope as a global parameter, charge neutralization contribution to the FIA can be estimated as $+191$ kJ mol^{-1} for monocationic (distance a in Figure 2) and $+342$ kJ mol^{-1} for dicationic Lewis acids (distance b in Figure 2). Due to the low number of tricationic species, no estimate was attempted for this group. The average vacuum phase FIA_{avg} (cross-marks in Figure 2) for monocationic Lewis acids is $709(146)$ kJ mol^{-1} , for dicationic $901(101)$ kJ mol^{-1} , and $1115(70)$ kJ mol^{-1} for tricationic, while neutral compounds exhibit a much lower average affinity ($FIA_{\text{avg}} = 347(115)$ kJ mol^{-1} , all values given in parentheses refer to standard deviations).

The systematic offsets and the formation of distinct clusters for neutral and charged Lewis acids render a unified ranking with varying charge state by non-solvation-corrected FIA meaningless. A hand-waving solution would be the formulation of separate vacuum scales for each charge state. These scales could stand independently and use cationic reference Lewis acids as new thresholds for LSA. As an example of monocations, the prominent $FP(C_6F_5)_3^+$ ($FIA = 767$ kJ mol^{-1}) could be used in a sense: “*Monocationic molecular Lewis acids that exceed the FIA of $FP(C_6F_5)_3^+$ in the gas phase are monocationic Lewis superacids*”. However, this ranking would prevent to merge the discussion of different charge Lewis acids quantitatively. Furthermore, as we will see in the next section, solvation and its dependence on the molecular volume is neglected. It would promote a perspective that deviates from the relevant behavior in the condensed phase and thus from every real-life application.

For these reasons, separate charge-selected scales cannot be recommended and other solutions are needed.

Interestingly, the average solvation-corrected $FIA_{\text{solv,avg}}$ compared for the different charge states are relatively constant at $174(99)$ kJ mol^{-1} for neutral, $212(117)$ kJ mol^{-1} for monocationic, $171(70)$ kJ mol^{-1} for dicationic and $156(49)$ kJ mol^{-1} for tricationic Lewis acids (crossmarks in Figure 2). Similar results were obtained with other solvation correction methods, such as CPCM and SMD ($r(\text{COSMO-RS}; \text{CPCM}) = 0.993$, $r(\text{COSMO-RS}; \text{SMD}) = 0.985$, $r(\text{CPCM}; \text{SMD}) = 0.992$), see section S3 in the ESI, Figure S6) and other solvents (see Figure S4, Table S2). These findings allow deriving two pivotal conclusions:

- 1) FIA_{solv} can be considered charge insensitive across varying molecular charges and solvents. Thus, we propose FIA_{solv} as a more general feature for Lewis acidity than FIA , as will be further validated and stressed below.
- 2) The specific choice of the solvation-correction model is of minor importance in the present context. The aspect is valuable for the applied computational chemist.

Solvation Effects and Molecular Volume

A closer consideration of solvation effects shall be discussed based on the FIA -damping parameter defined as $\Delta = FIA - FIA_{\text{solv}}$. The calculated average Δ_{avg} is significantly larger for cationic compounds (+1: $497(44)$ kJ mol^{-1} , +2: $731(63)$ kJ mol^{-1} , +3: $959(23)$ kJ mol^{-1}) than for neutral Lewis acids ($173(43)$ kJ mol^{-1}). What is the origin of these qualitative differences? The parameter Δ is composed of three contributions 1–3 (Figure 3a):

- 1) *The solvation enthalpy of the fluoride ion in dichloromethane*, $\Delta H_{\text{solv},F^-} = -340$ kJ mol^{-1} . It is the largest of all contributions to Δ , generally stabilizes the educts, and disfavors F-adduct formation in solution (Figure 3a, green frame). The stabilization of the fluoride ion gets larger in water ($\Delta H_{\text{H}_2\text{O},F^-} = -822$ kJ mol^{-1}) but reduced for less polar cyclohexane ($\Delta H_{\text{C}_6\text{H}_{12},F^-} = -277$ kJ mol^{-1}), toluene ($\Delta H_{\text{C}_6\text{H}_5, F^-} = -304$ kJ mol^{-1}), or acetonitrile ($\Delta H_{\text{MeCN},F^-} = -333$ kJ mol^{-1}). However, as it is a constant independent of the Lewis acid and their charge, it is not responsible for the clustering described above.
- 2) *The solvation enthalpy of the free Lewis acids*, $\Delta H_{\text{solv},LA^{(+)}}$. Charged compounds generally experience a more negative solvation enthalpy than neutral species. This trend is confirmed by the mean solvation enthalpies of monocationic Lewis acids ($\Delta H_{\text{solv},LA^+_{\text{avg}}} = -228(23)$ kJ mol^{-1}) compared to the neutral F-adducts ($\Delta H_{\text{solv},LA-F_{\text{avg}}} = -70(31)$ kJ mol^{-1}). Hence, in the case of cationic Lewis acids, Δ is dominated by the solvation energy of the free Lewis acid (Figure 3a, red frame).
- 3) *The solvation enthalpy of the fluoride adducts*, $\Delta H_{\text{solv},LA-F^{(-)}}$. In the case of neutral Lewis acids, the fluoride adducts are anionic and dominate Δ (Figure 3a, blue frame). This assumption aligns with the on average larger ΔH_{solv} of the anionic F-adduct products ($\Delta H_{\text{solv},LA-F^-_{\text{avg}}} = -209(35)$ kJ mol^{-1}) vs. the neutral Lewis

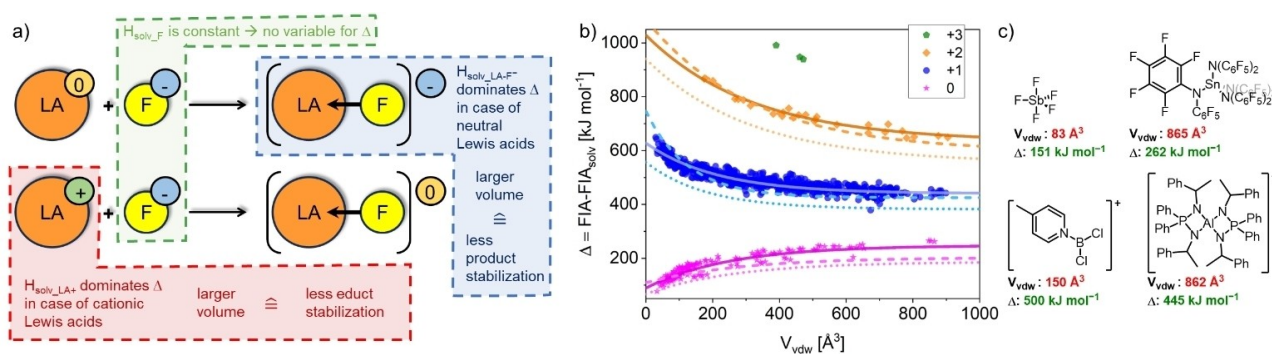


Figure 3. a) Representation of different contributions and their size dependence on Δ for neutral and cationic Lewis acids. b) Evolution of $\Delta = FIA - FIA_{solv}$ with the increase of the van der Waals volume (V_{vdw}) with exponential curve fitting for dichloromethane (solid line), acetonitrile (dashed line), and cyclohexane (dotted line, scatter plot not shown for clarity, see Figure S8). c) Examples showcasing the effect of molecular volume for neutral and cationic Lewis acids.

acid ($\Delta H_{solv,LA,avg} = -42(20) \text{ kJ mol}^{-1}$). Identical trends occur in cyclohexane, toluene, acetonitrile, and water (section S5, Figure S8 in the ESI).

According to Born's equation of solvation, it can be assumed that the Coulombic part of Δ depends on the charge density of the involved species, which is a function of the molecular charge and the molecular volume of the free Lewis acid.^[17] A larger molecular volume would correspond to less exothermic solvation. Indeed, plotting Δ against the molecular van-der-Waals volume V_{vdw} revealed trends, which differed depending on the Lewis acid charge (Figure 3b, V_{vdw} obtained from the MoloVol program package^{[18],[19]}

For neutral Lewis acids, an increasing V_{vdw} leads to an increase in Δ (Figure 3, violet curve). As explained above, for neutral Lewis acids, Δ is dominated by the anionic F-adducts. A larger V_{vdw} leads to decreasing charge density of the anionic F-adducts, decreasing product stabilization, and thus increasing Δ (Figure 3a). This knowledge is essential for designing neutral Lewis acids—the smaller, the more beneficial for anionic base binding (see Figure 3c for an example of a representative damping of a “small” and a “large” Lewis acid).

An inverse trend is identified for cationic Lewis acids (Figure 3a, blue and orange curve). Δ decreases with increasing V_{vdw} . This behavior can be explained by the dominating influence of ΔH_{solv} for the cationic Lewis acids, which decreases with increasing V_{vdw} (Figure 3b). In other words, the free Lewis acids become less stabilized with increasing size, and cationic Lewis acids tend to gain FIA_{solv} with V_{vdw} . This aspect is vital for the design of cationic Lewis acids and complementary to the neutral case—the larger, the more beneficial for anionic base binding (see Figure 3c for an example of a representative damping of a “small” and a “large” Lewis acid).

The volume-dependent FIA damping can be predicted by curve fitting of exponential functions (lines in Figure 3b):

$$FIA - FIA_{solv} = \Delta = \Delta_{large} - (\Delta_{large} - \Delta_{small}) \cdot e^{-k \cdot V_{vdw}} \quad (1)$$

with Δ_{large} , Δ_{small} and k solvent- and charge-dependent constants ($\Delta_{large} = \Delta$ at a large molecular volume of the Lewis acids where damping is negligibly altered, $\Delta_{small} = \Delta$ for smallest Lewis acids, $k = \text{charge dependent factor}$ for inherent decay of the influence of charge density, all parameters given in the ESI, Table S6). All these correlations also hold for different solvents, but with varying magnitudes (see dotted lines in Figure 3b as example for CH_3CN and cyclohexane and section S5 in the ESI).

Equation 1 enables the calculation of approximate solvation-corrected $FIA_{solv,approx}$ that do not require solvation correction, but only V_{vdw} as an input (FIA_{solv} vs. $FIA_{solv,approx}$ $r = 0.993$, $\text{MAE} = 12 \text{ kJ mol}^{-1}$). Similar results can be achieved even with only the number of atoms for the Lewis acid as an approximation of molecular volume (see section S5). A corresponding Excel sheet is provided as Supporting Information, or the software package to obtain V_{vdw} can be obtained free of charge [https://molovol.com/]. Finally, it was attempted if FIA damping correlates with the percent buried volume around the fluoride accepting atom, which was recently applied in the context of Lewis acidity ($\%V_{bur}$, see section S5, Figure S14).^[20] Larger Lewis acids tend to create a larger $\%V_{bur}$. However, with a certain molecular volume, the steric contribution from the local environment is constant and hence becomes an independent feature to FIA damping.

This first section offers a rationale for solvation effects in FIA and back-of-the-envelope design strategies. In the following, we probe if alternative scales based on other Lewis bases could be more suitable.

Alternative Affinity Scales

As an alternative to the perspectives spanned in the previous section, rankings based on other affinity scales were considered. It was perceived that, in contrast to the fluoride anion, a neutral reference Lewis base would not alter the overall charge state before and after adduct formation and, thus, would not experience charge cancellation effects.

Ammonia (NH_3) is an obvious choice for a neutral reference Lewis base (section S3 in the ESI).^[21] Indeed, no clustering was observed upon plotting the ammonia affinity (AA) vs. AA_{solv} (Figure 4a), indicating a general advantage of a non-charge-sensitive neutral Lewis base. However, the AA scale suffers from other problems that emerge from the weaker Lewis basicity of ammonia compared to the fluoride ion (cf. the introduction and Figure 1a). The generally lower binding affinity ($\text{AA}_{\text{avg}} = 117(74) \text{ kJ mol}^{-1}$ in the chosen dataset) prohibits the classification of many weak Lewis acids since the corresponding adducts are unstable and dissociate. Indeed, only 30% of the neutral Lewis acids did form stable ammonia adducts, leading to a severe restriction of the chemical space under consideration.^[22] Moreover, the lower range spanned by the affinity values (cf. $\sim 1200 \text{ kJ mol}^{-1}$ for FIA vs. $\sim 300 \text{ kJ mol}^{-1}$ for AA) leads to a diminished “resolution” of the information by a factor of four. It makes the scale more sensible to inherent errors from the computational method and less sensitive to detect subtle changes. Overall, this combination of drawbacks would limit the amount of debatable Lewis acids, lower the accuracy, and stray from the generally favorable FIA-based perspective on Lewis acidity. It should be noted that the AA and the FIA_{solv} are sufficiently linearly correlated ($r = 0.922$) (Figure 4b), indicating that FIA_{solv} combines the charge independence of neutral Lewis base scales with the beneficial FIA properties described in the introduction.

Next, another affinity scale that would maintain the large mean-affinities (high binding tendency) and energy range

(high resolution) advantages of the FIA, while not requiring solvation correction, was conceived. We first investigated the affinity of Lewis acids toward molecular lithium fluoride (LiFA). The corresponding adduct structure optimizations were initialized with LiF coordinating linearly to the Lewis acid central atom. Indeed, plotting of LiFA vs. $\text{LiFA}_{\text{solv}}$ did not show the systematic clustering of differently charged Lewis acids (Figure 4c), while exhibiting a sufficiently large mean-affinity $\text{LiFA}_{\text{avg}} = 200(83) \text{ kJ mol}^{-1}$, and a reasonably large energy range ($\sim 600 \text{ kJ mol}^{-1}$). To check how much of the “original” FIA information, that only encodes the LA–F interaction, remains expressed in the LiFA values, FIA and FIA_{solv} were correlated with LiFA. A poor correlation ($r = 0.671$) is found between LiFA and vacuum FIA (Figure S5a). This discrepancy is expected and arises from the charge sensitivity, like for the FIA– FIA_{solv} comparison discussed above. The charge sensitivity gets resolved in the comparison of LiFA with FIA_{solv} (Figure 4d, $r = 0.872$). However, another discrepancy arises from Li^+ binding to potential donor sites in the Lewis acids, as exemplified in Figure 4g for $[\text{SbF}_6]^-$ that leads to an additional energy release. This extra interaction distorts the pristine LA–(central atom)–F interaction of interest, adds “noise” to the “Lewis acidity”, and disqualifies the LiFA scale as a suitable option.

Thus, a scale with the fluoride salt of more innocent NMe_4^+ was probed (NMe_4FA). Another motivation for this scale was the commercial availability and good solubility of NMe_4F , which would allow comparing and benchmarking of the computational affinity with experimental data by calorimetric studies. Equilibrium structures were found with CREST^[23] sampling before DFT optimization, and the NMe_4FA was obtained for all Lewis acids. As for the LiFA scale, prevention of the Lewis acid charge clustering was achieved (Figure 4e). More importantly, the correlation with the original FIA_{solv} increased substantially ($r = 0.926$ (FIA_{solv}), Figure 4f), given the weaker interaction of the less coordinating cation NMe_4^+ with the fluoride adducts. This is exemplified for NMe_4^+ with $[\text{SbF}_6]^-$, exhibiting weak hydrogen-bond type interaction and Coulomb interaction that is less strong than the interaction with Li^+ (Figure 4h). Further, NMe_4FA spans a sufficiently large range ($\sim 900 \text{ kJ mol}^{-1}$) and strongly binds to the weaker Lewis acids. Hence, one might think having found a good compromise between the advantages and information content of the FIA while creating charge independence, that would allow the discussion of general Lewis acidity irrespective of the molecular charge state and without requiring solvation correction. However, we consider this option tedious and error-prone (slow convergence due to flat potential energy surface), disqualifying NMe_4FA as a suitable alternative. Interestingly, FIA_{solv} and $\text{NMe}_4\text{FA}_{\text{solv}}$ correlate almost ideally ($r = 0.979$, Figure S5d), indicating that solvation correction of a counter anion-free scale successfully captures the presence of a counterion—a point that will be considered more in detail in the next section.

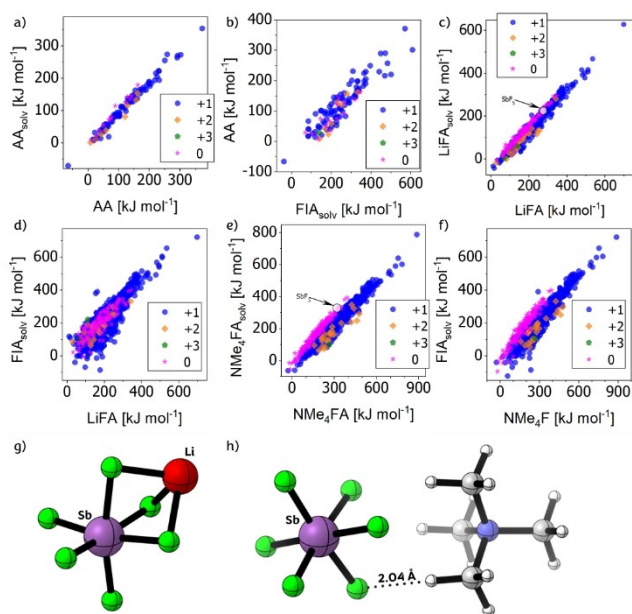


Figure 4. Correlation plot of: a) ammonia affinity AA and AA_{solv} , b) AA and FIA_{solv} , c) LiFA and $\text{LiFA}_{\text{solv}}$, d) LiFA and FIA_{solv} , e) NMe_4FA and $\text{NMe}_4\text{FA}_{\text{solv}}$, f) NMe_4FA and FIA_{solv} . All correlations are performed for a representative set of neutral, mono-, di- and tricationic Lewis acids. SbF_5 as marker compound for Lewis superacidity is highlighted with an encircled dot. g) Calculated adduct of SbF_5 with LiF with considerable secondary interaction with the lithium cation. h) Calculated adduct of SbF_5 with NMe_4F with the shortest found cation-anion distance.

Effect of Counter Anions

Of course, every cationic Lewis acid brings an anion. The critical effect of anions has been emphasized by the work on weakly coordinating anions (WCA), allowing for the stabilization of unique cationic species and as game changers to increase the activity of cationic catalysts.^[7d,24] Up to this point of the study, and in essentially every other research concerned with the computational evaluation of the Lewis acidity of cationic species, a harsh approximation has been taken: *the omission of the counter anion of the Lewis acid*. Remarkably, the validity of this approximation has never been scrutinized. To address the explicit influence of the anion, a selected set of monocationic Lewis acids was investigated in the presence of $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^+$, $[\text{BAR}^F_{24}]^+$, $[\text{BAR}^F_{20}]^+$, $[\text{SbF}_6]^-$, $[\text{NTf}_2]^-$, OTf^- , and $[\text{ClO}_4]^-$ (Table 1). We will base the following discussion on damping the FIA values through the presence of a respective anion (anion damping), averaged over the 8 cationic Lewis acids in this test set (first of the bottom lines of Table 1). The notable average anion damping of 202 kJ mol^{-1} even for $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^+$ reflects the proximity (Figure 5a for an example structure), but which undoubtedly represents a maximum, as this salt would form solvent-separated ion pairs in solution.^[25]

With increasing coordination ability of the counter anion, e.g., with $[\text{SbF}_6]^-$, the anion FIA damping reaches 311 kJ mol^{-1} on average. The substantial interaction turns respective salts into quasi-neutral Lewis acids (Figure 5b for example), even more pronounced for OTf^- (372 kJ mol^{-1}). What happens upon solvation correction concerning the simulation of the counter anion effects?

While the coordination of the counteranion drastically affects the vacuum FIA, the FIA_{solv} data set is only modestly altered (bottom line of table 1), with almost no effect for the least coordinating WCA (-4 kJ mol^{-1}) to a maximum averaged anion damping in solution of only 73 kJ mol^{-1} for triflates in CH_2Cl_2 . This trend persists for solvation-corrected values from other solvents, reaching a maximum damping of 101 kJ mol^{-1} for OTf^- in cyclohexane (Table S7). Accordingly, the FIA_{solv} values for the salt pairs with WCAs are only moderately influenced compared to the FIA_{solv} values for the free cations. This latter finding reveals that the computation of FIA_{solv} under the approximation of the omitted counter anion is legitimate since the anion damping gets effectively absorbed upon solvation correction. Hence, further reliability is attributed to FIA_{solv} as a consistent metric for evaluating differently charged Lewis acids, even under the omission of counter anions.

Finally, a set of isolated cationic Lewis acids was investigated to showcase FIA_{solv} as a descriptor that correctly recovers experimental results (Figure 6).^[26] Standard vacuum calculation without explicit counter anion indicated substantial FIA values (red numbers) surpassing the threshold for Lewis superacidity ($\text{FIA} > 500 \text{ kJ mol}^{-1}$). However, all these compounds were isolated as $[\text{PF}_6]^-$ or $[\text{BF}_4]^-$ salts ($\text{FIA}(\text{BF}_3) = 346 \text{ kJ mol}^{-1}$, $\text{FIA}(\text{PF}_5) = 384 \text{ kJ mol}^{-1}$). Comparing the FIA_{solv} values instead (green

Table 1: FIA and FIA_{solv} for a set of cationic Lewis acids without anions (w/o) and in combination with different counter anions, and the anion damping ($\text{FIA} - \text{FIA}_{\text{solv}}^{\text{incl.WCA}}$) averaged over all Lewis acids in the bottom row. Values given in parentheses refer to standard deviations.

compound	w/o	$[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^+$	$[\text{BAR}^F_{24}]^+$	$[\text{BAR}^F_{20}]^+$	$[\text{SbF}_6]^-$	$[\text{NTf}_2]^-$	$[\text{ClO}_4]^-$	OTf^-
$[\text{CeEt}_3]^+$	836	294	559	276	279	406	342	340
$[\text{Si}(\text{Mes})_3]^+$	816	344	631	341	344	596	393	388
$[\text{Sn}(\text{PF}_5)]^+$	783	263	528	254	245	335	343	343
	733	279	578	280	530	538	520	393
	730	237	536	255	409	395	348	358
$[\text{FP}(\text{C}_6\text{F}_5)_3]^+$	767	262	524	208	249	455	381	376
$[\text{Sb}(\text{C}_6\text{F}_5)_4]^+$	696	202	517	208	435	418	384	420
$[\text{Cp}^*_2\text{Al}]^+$	669	181	488	177	405	400	422	438
average anion damping								
= $\text{average}(\text{FIA} - \text{FIA}_{\text{solv}}^{\text{incl.WCA}})$		202	209	8	311	311	362	372
= $\text{average}(\text{FIA}_{\text{solv}} - \text{FIA}_{\text{solv}}^{\text{incl.WCA}})$		(28)	(41)	(20)	(62)	(85)	(91)	(82)
		-4	(10)	(8)	7	17	55	73
					(8)	(34)	(49)	(56)

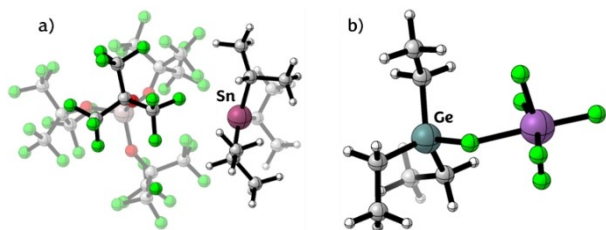


Figure 5. a) Exemplary equilibrium structures found after CREST conformer analysis with subsequent structure optimization on the PBEh-3c level of theory for a) $[\text{Sn}(\text{iPr})_3][\text{Al}(\text{OC}(\text{CF}_3)_3)_4]$ and b) $[\text{GeEt}_3][\text{SbF}_6]$.

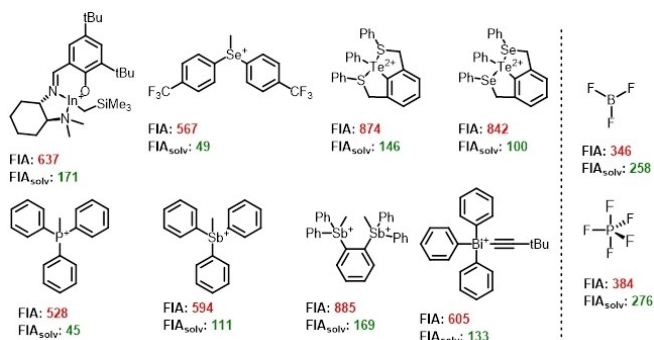


Figure 6. FIA and FIA_{solv} [kJ mol^{-1}] for cationic Lewis acids reported as isolated $[\text{PF}_6]^-$ or $[\text{BF}_4]^-$ salts, and the corresponding FIA and FIA_{solv} for BF_3 and PF_5 .

numbers) with $\text{FIA}_{\text{solv}}(\text{BF}_3) = 258 \text{ kJ mol}^{-1}$, $\text{FIA}_{\text{solv}}(\text{PF}_5) = 276 \text{ kJ mol}^{-1}$, the experimental results are well reflected.

Conclusion

The present study comprises the largest hitherto reported collection of Lewis base affinities for cationic compounds (784 Lewis acids; for a complete list, see ESI). A systematic charge-clustering of vacuum FIA values originating from charge cancellation in vacuum computations is showcased. This offset prohibits the meaningful comparison of FIA for Lewis acids with varying charges and represents a significant shortcoming of the original FIA scaling method. Three possibilities were assessed as solutions for the “charge” problem:

- 1) A separate scale and a marker Lewis acid for Lewis superacidity could be defined for each charge state (neutral, monocationic, dicationic). However, as this approach does not allow interscale comparisons and neglects critical solvation effects. It is not recommended.
- 2) Rankings with neutral reference Lewis bases, e.g., ammonia affinity, might be preferable, as they are charge-insensitive. However, simultaneously, the FIA scale’s main advantages—including weaker Lewis acids and high resolution—are lost. Attempts by “neutral” FIA complements, such as the lithium fluoride affinity or the NMe_4FA , point in the right direction but are

dismissed due to secondary interactions and practicability reasons.

- 3) Solvation-corrected FIA_{solv} data displays the energetic space of general Lewis acidity in its most coherent form. The “charge” issue is leveled and critical effects of molecular volume are disclosed. Notably, the specific choice of the solvation correction (COSMO-RS, CPCM, SMD) is found of minor importance. A closer analysis of the solvation-corrected data allows some further statements:
 - 3.1) The molecular volume of the Lewis acid is a critical parameter that influences the amount of solvation-induced FIA damping. The effects are inverse for neutral or cationic Lewis acids. The FIA_{solv} of neutral Lewis acids gets lower with increasing molecular volume, whereas the FIA_{solv} of cationic Lewis acids grows with increasing molecular volume.
 - 3.2) The solvation-induced FIA damping can be approximated with the molecular volume or the atom number as the only input. A corresponding Excel sheet is provided in the ESI.
 - 3.3) The explicit computation of the counter anion of a cationic Lewis acid is not required for a first approximation, as most of the effects from the counter anion are absorbed by solvation correction anyway.

The assessment of the considered approaches reveals that the treatise of general/global Lewis acidity should be based on the solvation-corrected FIA_{solv}. By doing so, we set the ground for the discussion of Lewis acid strength irrespective of the Lewis acid’s charge, and we confirm that the omission of the counteranion is legitimate. Although we have to accept potential shortcomings inherent to implicit solvation models, it represents the state-of-the-art for providing a coherent Lewis acidity metric with the maximum possible relevance to “condensed phase” reality, offering a valuable parameter that may confront applications of Lewis acids in synthesis, catalysis, and materials science.

Supporting Information

The authors have cited additional references within the Supporting Information.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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