

Are Heavy Pnictogen- π Interactions Really “ π Interactions”?

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Abstract: The noncovalent interactions of heavy pnictogens with π -arenes play a fundamental role in fields like crystal engineering or catalysis. The strength of such bonds is based on an interplay between dispersion and donor/acceptor interactions, and is generally attributed to the presence of π -arenes. Computational studies of the interaction between the heavy pnictogens As, Sb and Bi and cyclohexane, in comparison with previous studies on the interaction between heavy pnictogens and benzene, show that this concept probably has to be revised. A thorough analysis of all the different energetic components that play a role in these

systems, carried out with state-of-the-art computational methods, sheds light on how they influence one another and the effect that their interplay has on the overall system. Furthermore, the analysis of such interactions leads us to the unexpected finding that the presence of the pnictogen compounds strongly affects the conformational equilibrium of cyclohexane, reversing the relative stability of the chair and boat-twist conformers, and thus suggesting a possible application of tuneable dispersion energy donors to stabilise the desired conformation.

Introduction

Pnictogen- π arene interactions have received considerable interest as structure-forming and structure determining components in novel compounds, molecular and supramolecular assemblies.^[1–5] For the lighter elements their potential for catalyst design was discussed more recently.^[6] What makes this type of interaction special is that in addition to a dispersion contribution due to the large and polarisable main group element, there is a donor-acceptor contribution that can be modified through substituents on either partner of an intra- or intermolecular interaction.^[7–10] In a series of recent studies, we have extensively investigated the main group element- π arene interactions in general and pnictogen- π arene interactions specifically.^[1,11–14]

For the classical “ π - π interactions” in organic compounds, pioneering work by Grimme et al.^[15] showed, that these are not truly dominated by the π -electrons, but that the sigma framework contributes as much to the interaction. By comparing saturated and unsaturated systems it was shown how the

stronger interactions between aromatic molecules are actually due to dispersion and not to any special interactions that necessarily include the π orbitals. In the following years, many structural motifs like π - π interaction and ion- π interactions have been revisited,^[16–19] and our view on π interactions is slowly changing towards a more refined description, unravelling the details of dispersion interactions. This inspired us to focus our attention on a prototype system that cannot exhibit “pnictogen- π ” interactions, as it does not contain a π system, in spite of its structural similarity to benzene: cyclohexane. The results are compared with those obtained for the corresponding aromatic system in a previous study^[10] to address the question whether pnictogen- π arene interactions actually require the π -system. In order to address this question, we compute interaction energy curves for MR_3 and cyclohexane (chair and boat-twist conformers) for three different group 15 elements (i.e., M=As, Sb and Bi) and for three different substituents with increasing potential for donor-acceptor interaction (i.e., R=CH₃, OCH₃ and Cl). We analyse the interactions between heavy pnictogen compounds and cyclohexane in the optimised structures and the conformational changes induced by the presence of MR_3 . In the following, an analysis of such effects is provided by dissecting the total interaction energy into different components to rationalise the trends and understand the interplay between the different forces that hold these MR_3 -cyclohexane systems together.

Computational Methods

A schematic representation of all the calculations carried out throughout the work can be found in Scheme 1.

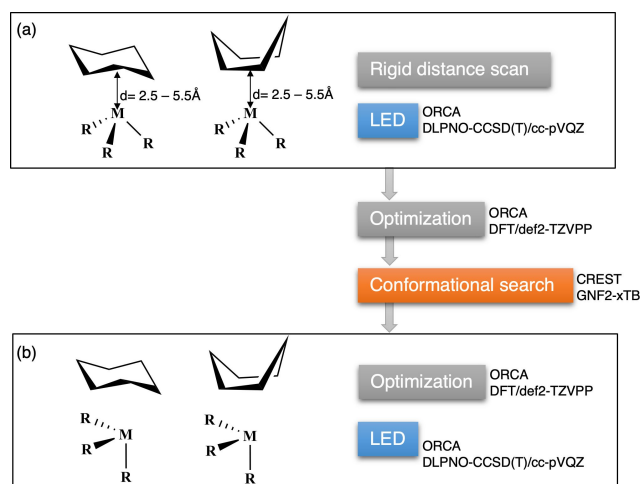
In agreement with previous studies on benzene, we choose rigid scans for idealised geometries with the MR_3 molecule perpendicular to the cyclohexane, with the central M atom pointing towards the

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Supporting information for this article is available on the WWW under <https://doi.org/10.1002/chem.202102418>

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Scheme 1. Schematic representation of the computational study to rationalise the interaction between pnictogen compounds and cyclohexane in comparison to π -systems like benzene.

centre of the ring (Scheme 1a, Figure 1a and Figure S3 in the Supporting Information) at the DLPNO-CCSD(T)/cc-pVQZ (cc-pwCVQZ-pp for M) level of theory with the SK-MCDHF-RSC effective core potential.^[20–26] Interaction energies are defined with respect to the isolated monomers: $\Delta E = E_{\text{cyclohex}+\text{BiR}_3} - (E_{\text{cyclohex}} + E_{\text{BiR}_3})$. Such scans of the potential energy surface have also been carried out at the DFT level, with a few different functionals (i.e., PBE,^[27] PBE0,^[28] B3LYP^[29] and M062x^[30]) and the def2-QZVPP basis set.^[31] The DFT scans can be found in the Supporting Information. The natural bond orbital (NBO) charges (Figure 1e) are computed at the PBE-D3/def2-QZVPP level,^[32,33] through the NBO6.0 program,^[34] interfaced with ORCA. The charge transfer is obtained from the sum of the NBO charges on the MR₃ molecule in the adducts. The analysis of the contributions to the interaction energies is carried out using the local energy decomposition (LED) analysis^[35,36] as implemented in the ORCA program package.^[37] With this approach, we achieve the “gold standard” accuracy of CCSD(T) while being able to analyse different contributions to the interaction. In the analysis of the equilibrium structures, several conformers have been generated with the CREST program,^[38,39] by the GNF2-xTB semiempirical method,^[40] and have subsequently been optimised at the PBE-D3/def2-SVP level of theory. The ten lowest energy conformers have then been optimised again at the PBE-D3/def2-TZVPP level to determine the most stable one. Lastly, a DLPNO-CCSD(T) single point with the LED is performed on the most stable conformers obtained in this way (Scheme 1b, bottom of Figure 4).

Results and Discussion

Figure 1 depicts the results in comparison to our previous data for benzene.^[10]

The curves in the top graphs (Figure 1b) represent the total interaction energy between MR₃ and cyclohexane at any given distance between the two molecules in the idealised perpendicular structures (Figure 1a). Figure 1c–e depicts the interaction without dispersion contribution, dispersion interactions only, and charge transfer between the molecules, respectively. Indeed, all general trends are the same for benzene: for all the pnictogen compounds, the interaction exhibits a strong dis-

persion contribution and increases with stronger donor-acceptor (D/A) character from methyl via methoxide to chloride along with decreasing intermolecular distances.

While the donor-acceptor contribution is less pronounced for cyclohexane, it is still noticeable and reaches the same magnitude (Figure 1b and Table S1) as expected for aromatic hydrocarbons with small D/A contributions like with electron withdrawing substituents as nitrobenzene.^[9] The natural bond orbital partial charges (Figure 1e) confirm that the charge transfer is negligible for CH₃ and OCH₃ and becomes significant in the case of Cl. This implies that the presence of a π system is not necessary for noncovalent binding to hydrocarbons and that the interaction with cyclohexane exhibits all features of a so called “pnictogen- π arene interaction”.

In Figure 2, the total interaction energies at the equilibrium distances and their dispersion contributions are depicted for the different cyclohexane conformers and benzene. For the interaction energy contributions in the minima of the scans, the dispersion contribution is the largest component for all compounds. Here, it does appear like the dispersion contribution to the interaction energy is larger for benzene than for cyclohexane. However, a glance at the different contributions and their distance dependence (Figure 1) shows that the dispersion contributions (Figure 1d) are indeed almost identical for the π systems and the corresponding saturated ones. Inspection of the non-dispersion contributions (Figure 1c) yields an explanation for the difference that is observed in the minima of the scans: for benzene, the donor/acceptor contribution is slightly repulsive for the methyl system, then it progressively increases moving to OMe and to Cl. This leads to shorter interaction distances, for which the dispersion contribution is higher. In this way, the D/A contribution to the total energy, though remaining not very large, induces an increase in dispersion by pulling the molecules closer together. This synergic effect explains why the differences and trends are appear to be more prominent for the benzene systems.

Thus it can be concluded that for all compounds, the dispersion contribution dominates the interaction and that the potential due to dispersion is practically the same for the aromatic and the non-aromatic systems. For the π systems, which are much more susceptible to changes in the D/A character, this can be described as a synergic effect of the two components of the interactions. (See Figure S4 for further comparison between benzene and cyclohexane.)

For the influence of the pnictogen, a very clear trend of increasing interaction going down the pnictogen group is observed: As < Sb < Bi. This is obvious for benzene, while the differences in the saturated cases are not so evident. These differences can once again be attributed mainly to the D/A part of the interaction. As discussed above, the aromatic system is much more sensitive to a change in this part of the interaction. It should be noted that cyclohexane, in the presence of electronegative ligands, does experience an increased charge transfer going from As to Bi (Figure 1e, right). The more polarisable the central atom, the more efficient the electron-withdrawing effect of the ligand, making it ready to accept charge from the other molecule. Figure 1e also shows how the

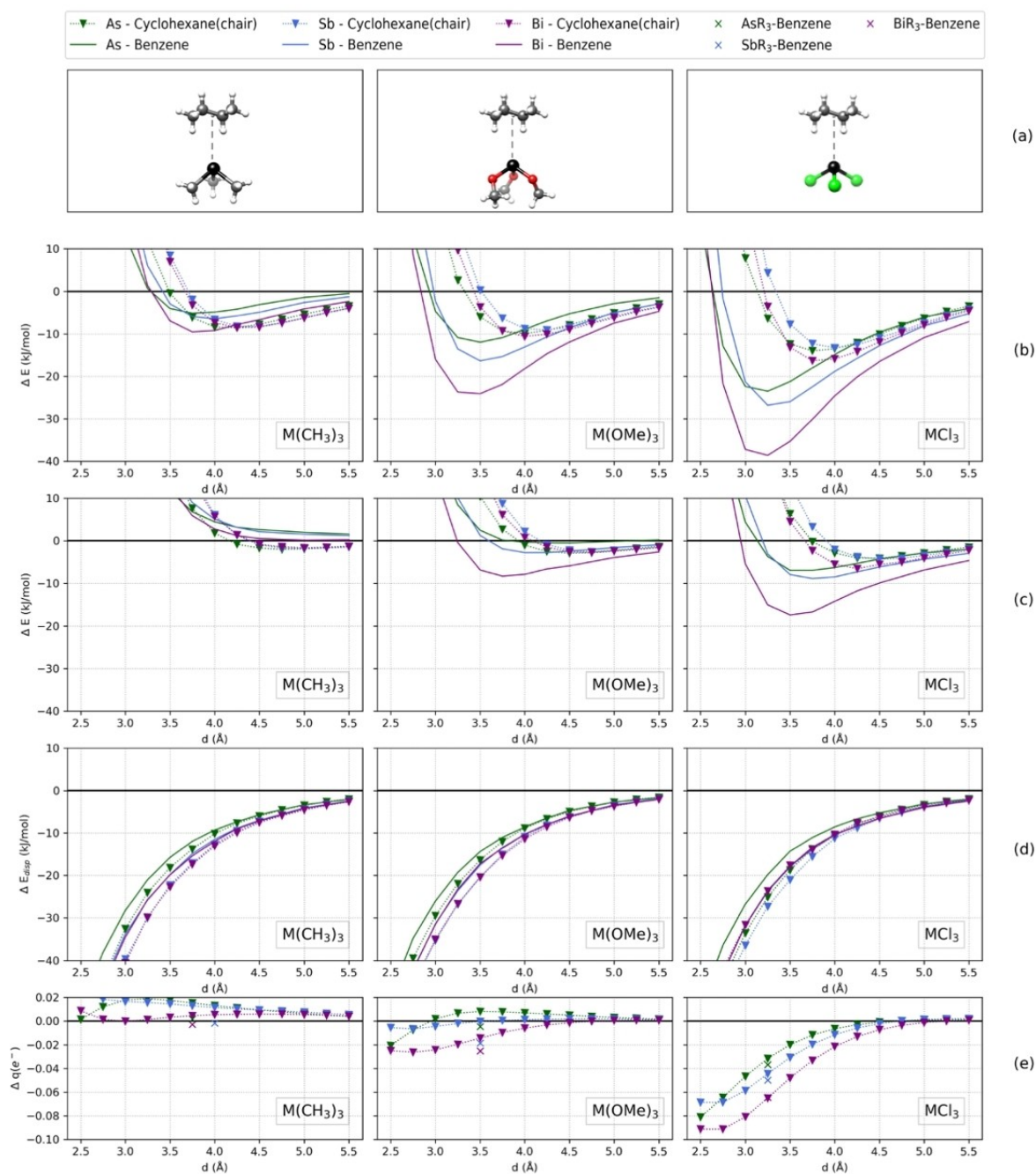


Figure 1. PES scans for cyclohexane- MR_3 and benzene- MR_3 ^[10] $\text{M} = \text{As}$ (green), Sb (blue) and Bi (purple) $\text{R} = \text{CH}_3$, OMe , Cl , from left to right. Energies computed at the DLPNO-CCSD(T)/cc-pVQZ (cc-pwCVQZ-pp for M) level of theory. Cyclohexane is in its chair conformation. From top to bottom: a) geometries used for the rigid scans, b) total interaction energy, c) interaction energy without dispersion contribution, d) dispersion interaction energy, e) charge transfer. Colour code: M (black), C (gray), H (white), O (red), Cl (light green).

charge transfer (CT) component is systematically larger for benzene.

A more detailed examination of the charge transfer in these systems, including the second order perturbation theory analysis, can be found in Tables S2–S7).

This small change in CT for the saturated systems contributes very little to the total interaction, which remains dominated by dispersion forces (Figure 2). As mentioned above,

these forces are not really sensitive to any of the chemical modifications that were made in the systems (i.e., central atom, substituents). Even though we can see a slight increase from As to Bi and Sb, due to the fact that bigger, more polarisable atoms are better dispersion energy donors, this is very small and pretty much negligible with respect to the changes induced by the D/A character.

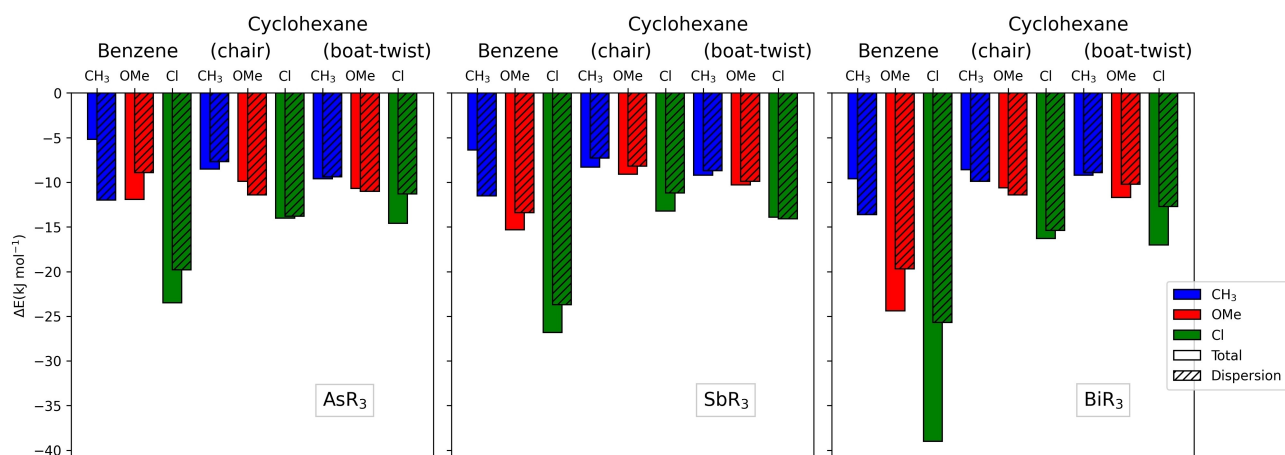


Figure 2. Comparison of the interaction energies at the equilibrium distance between benzene and cyclohexane from the rigid scans (Figure 1). Data for benzene are taken from ref. [10].

Figure S3 depicts the same analysis for the boat-twist conformer of cyclohexane. We don't observe any major difference in the trends upon changing conformation and all the arguments discussed so far remain valid for the boat-twist conformer.

Closer inspection of the relative energies of the two conformers reveals a striking feature: while it is well-established

that, for isolated cyclohexane, the chair conformer is far more stable than the boat-twist conformer,^[41] the presence of MR_3 seems to invert the relative stability of the two conformers in most cases (Figure 3). In order to investigate this remarkable finding in more detail, we focus on the fully optimised (PBE-D3/def2-TZVP) adducts of MR_3 and the two conformers of cyclohexane (Figure 3). Given the many conformational degrees

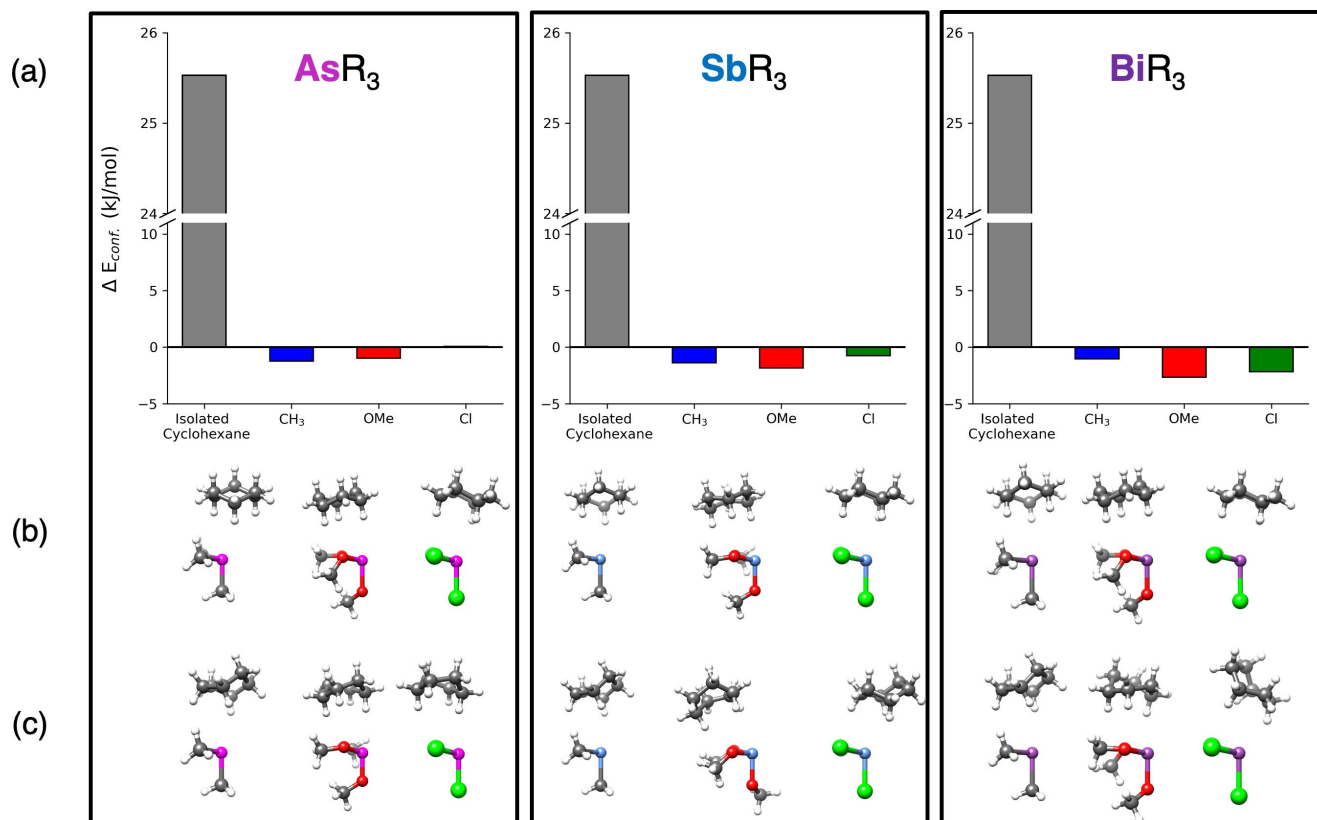


Figure 3. Energy difference between the boat-twist and the chair (top) conformers of cyclohexane at the DLPNO-CCSD(T)/cc-pVQZ level of theory. Equilibrium geometries of the cyclohexane- MR_3 structures for the chair (middle) and boat-twist (bottom) conformers obtained from PBE-D3/def2-TZVP optimisations. Colour code: As (magenta), Sb (blue), Bi (purple), C (grey), H (white), O (red), Cl (light green).

of freedom present in such systems, a conformational search has been performed by generating hundreds of different conformers from the optimised DFT structure. These conformers have been optimised again at the PBE-D3 level in two steps with increasingly large basis sets (def-SVP, then def2-TZVP). This ensures that the presented geometries are the actual low-energy conformations.

A previous study on benzene, investigating the angle dependence of the interaction energy, reported a preference for tilted structures. In agreement with these data, the equilibrium geometries depicted in Figure 3 (middle and bottom) appear tilted. For the benzene systems, the LED analysis on the DLPNO-CCSD(T) energies showed a large dispersion contribution, due to the increased contact area.^[10] Among the established concepts on noncovalent intermolecular interactions, the σ -hole model and its implications have been controversially discussed in recent years, especially in the context of halogen bonding.^[42–44] While all studies agree on the fact that a depletion of electron density opposite of a sigma bond leads to a fairly strong interaction that is strongly directional,^[45,46] different analysis tools indicate that it could either be regarded as electrostatic or as charge-transfer including orbital interactions.^[47] For the interaction of heavy pnictogen atoms and the π -system, as discussed in ref. [10], a thorough analysis of the angle-dependence of the interaction energies, however, showed that the potential energy surfaces appear very flat. Local minima in arrangements where the σ -hole interaction would be present are only a few kJ mol^{-1} more stable. Furthermore, the LED analysis reported in ref. [10] shows electrostatic and D/A contributions are attractive only for two of the compounds under examination ($\text{Bi}(\text{OMe})_3$ and BiCl_3). This is true also for cyclohexane: despite the fact that some tilted minima would agree with a σ -hole involvement, the interaction here is mostly dispersion (Figure 4). As discussed above, the D/A contribution to the binding energy is either repulsive, or very small. Hence, we would rather argue against a possible presence of a σ -hole interaction, and ascribe the tilt in the geometries to a simple increase in contact area, generating a larger dispersion contribution.

The energy difference between the boat-twist and chair conformers reported in Figure 3 (top) is defined as $\Delta E_{\text{conf}} = E_{\text{boat}} - E_{\text{chair}}$. Along with the reversed conformational equilibrium in the presence of the MR_3 moieties, we can also observe some trends with respect to the central atom and the substituent.

While it appears that, for the methyl group, no major changes in the stabilisation of the boat-twist are recorded upon change in the central atom, this is not the case for methoxide and chloride, where a clear trend can be observed, with increasing stabilisation moving from As, to Sb, to Bi.

Also the structural change in the presence of these more electronegative substituents seems to be more pronounced, with the C_6H_{12} moiety interacting more strongly with different parts of the MR_3 molecule (Figure 3 top, middle).

An explanation for such differences in trends and geometries can be found by splitting the DLPNO-CCSD(T) energies in their different components through a LED analysis of the interaction energies (Figure 4). By observing the different

energetic contributions for the chair and the boat-twist we can assess which components dominate the overall energy difference. For $\text{M}(\text{CH}_3)_3$ we can observe that the largest difference between the boat-twist and the chair lies in the dispersion contribution. Whereas the difference in the non-dispersion part of the interaction is very small and slightly more unfavourable for the boat-twist. It should also be noted that the geometric preparation term is almost zero, thereby indicating that no major geometrical changes occur to the $\text{M}(\text{CH}_3)_3$ and cyclohexane moieties in creating the adduct.

Moving to $\text{M}(\text{OMe})_3$, the difference in dispersion contribution is still observable. However, we can see a difference in the nondispersion contribution that becomes increasingly less unfavourable for the boat-twist moving down the pnictogen group. As the difference in dispersion contribution is constant with respect to M, it is this nondispersion term that gives rise to the trend observed in Figure 3, top. This is also consistent with what has been described in the previous sections, showing that the D/A interactions are more evident in the presence of Bi, which can more easily be polarised by the electronegative substituents.

We can also observe a higher geometric preparation contribution for both conformers, with respect to $\text{M}(\text{CH}_3)_3$. This contribution is also slightly increasing going down the group, following the same trend as the nondispersion contribution. This can be considered as a geometrical reorganisation that accompanies the electron density polarisation due to the stronger D/A component. With the most electronegative substituent (i.e., Cl) an even stronger effect of the non-dispersion contribution is observed. In the case of AsCl_3 , the difference between the dispersion and nondispersion contributions are very small and of opposite sign so they cancel out, giving rise to the only case where the interaction energy and relative stability of the two cyclohexane conformers are basically the same. Moving down the group, dispersion changes very slightly, remaining largely the same for both conformers. However, the nondispersion term becomes steadily less unfavourable for the boat-twist, giving rise to the observed trend in stability.

What has been observed for the optimised minimum structures is very much in line with the observations made on the rigid scans on the idealised geometries. Dispersion does play a very important role in holding these systems together. However, it does not account for the changes observed with respect to the substituents and it is marginally relevant for the change with respect to the central atom. Being mainly a function of contact area and proximity of the atoms, it is only indirectly affected by the chemical nature of the systems. All the changes can instead be ascribed to changes in the D/A character of the system, that sometimes causes a change in dispersion by altering the geometry. Such changes in the D/A part of the interaction are enhanced with larger and more polarisable central atoms, giving rise to the trends observed going down the pnictogen group.

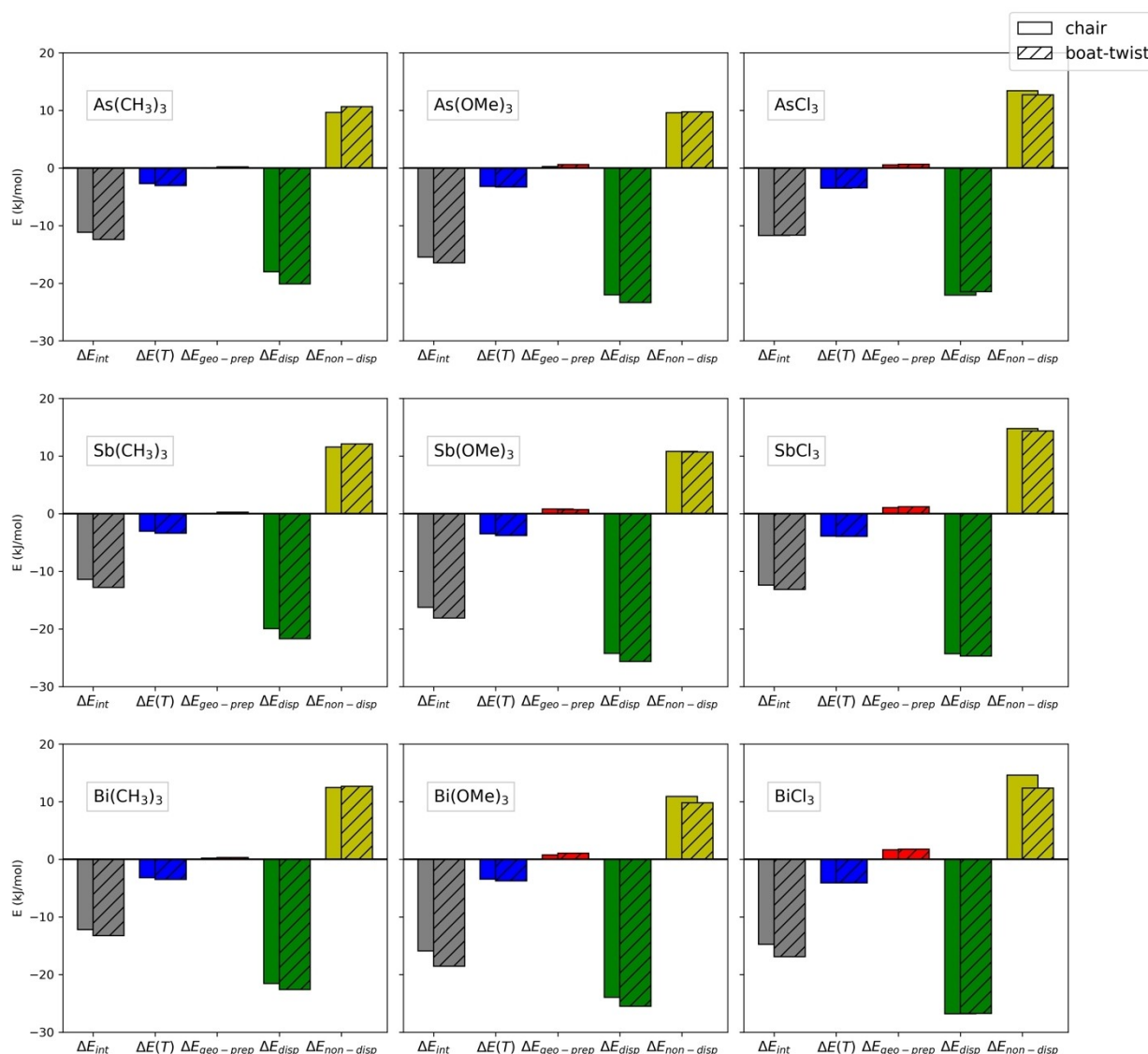


Figure 4. LED analysis of the DLPNO-CCSD(T)/cc-pVQZ energies of the lowest-energy conformers of the cyclohexane- MR_3 adducts. Solid filled bars represent the chair conformer of cyclohexane, and hatched bars the boat-twist. ΔE_{int} is the total DLPNO-CCSD(T) interaction energy, $\Delta E(T)$ represents the contribution of the perturbative triples to the interaction energy, $\Delta E_{geo-prep}$ is the term due to the geometrical rearrangement of the molecules upon formation of the adduct, ΔE_{disp} is the dispersion contribution to the interaction energy; the nondispersion term $\Delta E_{non-disp}$ sums up all the remaining contributions that are not dispersion related, i.e., exchange, electrostatic, nondispersion correlation and electronic preparation.

Conclusion

On the basis of the presented data, the answer to the title question: “Are heavy pnictogen- π interactions really π interactions?” should simply be “no”, as the pnictogen- π interactions do not necessarily rely on “ π -systems”. However, we suggest identifying the “pnictogen π -arene interaction motif” as rather only one manifestation of pnictogen dispersion interactions that has the same features for saturated bulky compounds. The unique feature of pnictogen compounds is that, besides being excellent dispersion energy donors, their interactions can be tuned by adding donor/acceptor character to their interaction by substitution. When aromatic systems are involved, an increase in the strength of these interactions is observed.

However, this should not be attributed to any special π interactions, rather to a stronger D/A component and to the synergic effect of this component and dispersion.

Embracing this idea and studying the interactions of pnictogen compounds of As, Sb and Bi with nonaromatic dispersion energy donors instead led us to unexpected findings in the adducts of MR_3 with cyclohexane. For these, the dispersion-dominated interaction with a heavy main group element significantly alters the stability of different conformers. The preferred interaction of such compounds with a boat-twist conformer generates an inversion of the conformational equilibrium of cyclohexane. This implies applications in fields such as catalytic transformations of unsaturated hydrocarbons

or the stabilisation of unusual compounds using saturated counterparts of terphenyl ligands^[5] and inspires further studies.

Acknowledgements

This work was funded by the SPP 1807 “Control of London dispersion interactions in molecular chemistry” by the Deutsche Forschungsgemeinschaft. A.A.A. would like to acknowledge support from the MPI für Kohlenforschung and the Max Planck Society. K.B. acknowledges the Alexander von Humboldt Foundation for postdoctoral fellowship. Open Access funding enabled and organized by Projekt DEAL.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: ab initio calculations · coordination chemistry · dispersion interactions · main-group element chemistry · noncovalent interactions · organometallic chemistry

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Manuscript received: July 5, 2021

Accepted manuscript online: August 3, 2021

Version of record online: September 13, 2021