Bis-1,3-dipolar Cycloadditions on Endohedral Fullerenes $M_3N@I_h-C_{80}$ ($M = \text{Sc, Lu}$): Remarkable Endohedral-Cluster Regiochemical Control

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* Supporting Information

ABSTRACT: In this work, we briefly report some attempts to control regioisomeric bisadditions on Sc$_3$N@$I_h$-C$_{80}$ and Lu$_3$N@$I_h$-C$_{80}$ using the tether-controlled multifunctionalization method. We then describe the use of independent (nontethered) bis-1,3-dipolar cycloaddition reactions and the characterization of 5 new bisadducts, 3 for Sc$_3$N@C$_{80}$ and 2 for Lu$_3$N@C$_{80}$ which have never been reported before. Unexpectedly and remarkably, 4 of these compounds exhibit relatively high symmetry and 2 of these bisadducts are the first examples of intrinsically chiral endohedral compounds, due to the addition pattern, not to the presence of chiral centers on the addends. Since an analysis of the statistically possible number of bisadduct isomers on an $I_h$-C$_{80}$ cage has not been reported, we present it here.

INTRODUCTION

In 1985, Kroto et al. discovered the fullerenes, which constituted new allotropic forms of carbon. Since the early days of fullerene research, it was shown that they were capable of encapsulating atoms in their interior, and these compounds were collectively denoted as endohedral fullerenes (EFs). Endohedral fullerenes can also encapsulate small molecules, one or more metals, and metallic-based clusters. Our recent work has been mainly focused on the trimetallic nitride cluster endohedral metallofullerenes (TNT-EMFs), initially discovered by Stevenson et al. in 1999 when they isolated Sc$_3$N@$I_h$-C$_{80}$. These compounds exhibit considerable charge transfer from the trapped cluster to the carbon cage, formally represented as a six electron transfer leading to [Sc$_3$N]$^{6+}$[C$_{80}$]$^{6-}$.

Since the first functionalization of EMFs in 1995 by Akasaka, many have explored their reactivities and other properties, allowing their characterization and enhancing their potential applications in biomedicine (as MRI contrast agents, in tumor diagnosis and radioimmunotherapy), in materials science and in photovoltaics solar cells, among others. However, the complete structural, chemical and electronic properties of EMFs are not totally understood at the present time. Specifically, the factors controlling the regiochemistry of multiple additions to EFs remain largely unexplored and poorly understood.

Multiple functionalizations of empty fullerenes have led to compounds that are very active as acceptors in organic photovoltaic (OPV) solar cells. Controlling and understanding the formation of specific regioisomers of fullerene derivatives is important, because it has been shown that some regioisomerically pure fullerene bisadducts perform better in OPV solar cell devices than their corresponding isomeric mixtures. There are very few methods available to regiochemically control bisadditions to fullerenes, and the most widely utilized one is the tether-controlled remote multifunctionalization. Since this method is extremely useful with [60]-fullerene and [70]-fullerene, we decided to use it to control regiochemical bisadditions to Sc$_3$N@$I_h$-C$_{80}$ and Lu$_3$N@$I_h$-C$_{80}$.

Independent (nontethered) bisadditions to endohedral fullerenes have been reported before, but very few details about their regiochemistry have been discussed. Yamakoshi et al. reported regioselective bis-1,3-dipolar cycloaddition reactions using M$_3$N@$I_h$-C$_{80}$ (M = Y and Gd) and described one predominant and unsymmetrical bipyrrolidine isomer, presumably controlled by the encapsulated cluster. However, structural details were somewhat limited.

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In this work, we briefly report some attempts to control regioisomeric bisadditions on Sc$_3$N@I$_x$C$_{80}$ and Lu$_3$N@I$_x$C$_{80}$ using the tether-controlled multifunctionalization method. We then describe the use of independent (nontethered) bis-1,3-dipolar cycloadditions and the characterization of 5 new bisadducts: 3 for Sc$_3$N@C$_{80}$ and 2 for Lu$_3$N@C$_{80}$.

**RESULTS AND DISCUSSION**

**Tethered Bisadditions.** We initially tried the following tether-controlled bisaddition reactions on M$_3$N@I$_x$C$_{80}$ (M = Sc and Lu): (a) a bis-1,3-dipolar cycloaddition reaction using phthalaldene and N-ethyl glycine;\(^{27}\) (b) a bis-bicyclopropanation reaction using 1,3-dibenzoylpropane-bis-p-toluene-sulfonyl hydrazone;\(^{36}\) and (c) a bis-Bingel cyclopropanation reaction using 1,3-phenylenedimethyl-diethylmalonate (PDM).\(^{25}\) of all of which are known to work efficiently on C$_{60}$ and C$_{70}$.\(^{25,27,29}\)

Remarkably, all of these reactions failed completely when applied to M$_3$N@I$_x$C$_{80}$ (M = Sc and Lu). MALDI and NMR techniques showed that none of the tethered bisadduct led to detectable amounts of the expected bisderivatives. Instead, monoadductions were observed in all cases. The obvious implication derived from these results is that the clusters must exert a very strong directing effect that prevents the addition of the second adduct, which is primarily directed by the tether length. Since Yamakoshi et al. were also unsuccessful at preparing isolable amounts of nontethered bisadducts of M$_3$N@I$_x$C$_{80}$ (M = Sc and Lu), we wondered if these specific TNT-EMFs were intrinsically unreactive toward bisadditions in general. To investigate this behavior, we decided to attempt the independent (nontethered) bis-1,3-dipolar cycloadditions on M$_3$N@I$_x$C$_{80}$ (M = Sc and Lu).

**General Considerations.** I$_x$C$_{80}$ endohedral fullerenes possess two different types of double bond addition sites: [5,6]-junctions (bonds between two six-membered rings) and [5,6]-junctions (bonds between one five membered ring and one six membered ring). Mono-adductions of N-ethylazomethine ylides to I$_x$C$_{80}$ endohedral fullerenes have been shown to result in [5,6] or [6,6] fulleropyrrolidines.\(^{37-39}\) The addition position of the monopyrrolidine adducts is strongly influenced by the size of the encapsulated cluster.\(^{37-39}\) For example, in the case of yttrium or gadolinium nitride cluster fullerenes, the [6,6]-monoadduct is the thermodynamically preferred product, while in the case of the smaller scandum and lutetium nitride cluster EMFs, the [5,6]-monoadduct is the thermodynamically preferred product.\(^{37-40}\)

Since a detailed analysis of the statistically possible number of bisadduct isomers on an I$_x$C$_{80}$ cage has not been reported, we present it here, see Figure 1. Assuming that the two addends are identical, and assuming that both [5,6] or [6,6] additions can occur, the total number of statistically possible bisadduct isomers is 91. Of the 91 possible regioisomers, 30 correspond to additions at [5,6]-[5,6]-bonds, 31 to additions at [5,6]-[6,6]-bonds, and 30 to additions at [6,6]-[6,6]-bonds (Figure 1). Of the 30 [5,6]-[5,6]-bisregioisomers, 7 possess a plane of symmetry (C$_s$-symmetric) and 5 possess a C$_2$ rotation (C$_2$-symmetric). Similarly, of the 30 [6,6]-[6,6]-bisregioisomers, 7 are C$_s$-symmetric and 5 are C$_s$-symmetric. For the [5,6]-[6,6]-bisregioisomers, only 4 are C$_s$-symmetric. Of the 91 statistically possible regioisomers, a large majority, 63, possess no symmetry (C$_i$).

The C$_s$ symmetric bisadduct regioisomers, if obtained, would possess inherent chirality based on the addition pattern. There are very few examples of chiral endohedral fullerene derivatives, and all of them are chiral because of the presence of asymmetric centers.\(^{41,42}\)

**Independent Bisadditions.** The reported bis-1,3-dipolar cycloaddition reactions on M$_3$N@I$_x$C$_{80}$ (M = Y and Gd) yielded only one NMR-characterized regioisomer.\(^{16}\) On the basis of NMR spectroscopic experiments and DFT calculations, Yamakoshi et al. assigned the observed isomers to [6,6]-[6,6]-bisadducts, all of which were unsymmetric. Presumably, the [6,6]-[6,6]-bisadduct isomer of Y$_3$N@I$_x$C$_{80}$ was converted to an uncharacterized isomeric mixture after thermal treatment, but no details of the specific transformations or characterizations of the new products were provided. Surprisingly, when they used the same reaction conditions with Sc$_3$N@I$_x$C$_{80}$ and Lu$_3$N@I$_x$C$_{80}$ they were unable to detect significant amounts of any bisadducts, even when a large excess of N-ethylglycine was added.\(^{16}\) They attributed this behavior to the lower reactivity of the thermodynamically stable [5,6]-monoadduct of Sc$_3$N@I$_x$C$_{80}$ and Lu$_3$N@I$_x$C$_{80}$ which in principle are the precursors for the formation of the bisadducts.\(^{16}\)

In this work, we successfully synthesized and characterized bispypyrrrolidine adducts of both Sc$_3$N@I$_x$C$_{80}$ and Lu$_3$N@I$_x$C$_{80}$ for the first time, using similar reaction conditions. Interestingly, most of the bisadducts we purified and characterized exhibit much higher symmetry than the one reported.\(^{16}\)

**Synthesis and Characterization of Sc$_3$N@I$_x$C$_{80}$ Bisregioisomers.** Bisadducts 1–3 were synthesized via the 1,3-dipolar cycloaddition reaction of N-ethylglycine and formaldehyde with Sc$_3$N@I$_x$C$_{80}$ in ortho-dichlorobenzene (o-DCB).\(^{43}\) Bisadducts 1–3 were purified using silica gel column chromatography and preparative thin layer chromatography (TLC) in 6%, 13%, and 15% yield, respectively. The matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectra confirmed the presence of [M + H]$^+$ peak for the bisadduct products (m/z 1252 for all bisadducts 1–3).

The $^1$H NMR spectrum of bisadduct 1 exhibited 4 AB quartets corresponding to unequivocal methylene of the two pyrrolidines and two overlapping quartets corresponding to the methylenes of the N-ethyl groups (Figure 2a). Therefore, bisadduct 1 is an unsymmetric regioisomer, similar to the one reported for Y$_3$N@C$_{80}$\(^{16}\) Due to the lack of symmetry of bisadduct 1 and the large number of possible C$_s$-symmetric regioisomers (63), based solely on NMR we cannot assign it to a specific isomer.

![Figure 1. The 91 possible bisadduct regioisomers on an I$_x$C$_{80}$ cage. The first pyrroline is attached to the bond marked in black. Pink bonds denote C$_s$-symmetric regioisomers, cyan bonds denote C$_s$-symmetric regioisomers, and purple bonds denote C$_s$-symmetric regioisomers. (a) [5,6]-[5,6]-bisadducts; (b) [5,6]-[6,6]-bisadducts; (c) [6,6]-[6,6]-bisadducts.](image-url)
To determine the addition pattern of bisadduct 1, density functional theory (DFT) full optimizations at the BP86-D$_2$/TZP(COSMO:o-dCB) level were performed using ADF and the related QUILD computational packages. In principle, all 63 possible C$_1$-symmetric bisadduct regioisomers should be considered to elucidate the preferred unsymmetric bisadduct. However, the thermodynamic stability of the [5,6]-mono-1,3-dipolar cycloadduct of Sc$_3$N@I$_2^{-}$C$_{80}$ is higher than that of the [6,6]-monocycloadduct by ca. 8 kcal/mol difference. For these reasons, we only considered [5,6]-[5,6] additions in the case of Sc$_3$N@I$_2^{-}$C$_{80}$.[2,4,48,49] In contrast, for Lu$_3$N@I$_2^{-}$C$_{80}$, [5,6] and [6,6]-based bisadducts were considered, since the thermodynamic stability of both [5,6]- and [6,6]-adducts are similar.

DFT calculations indicate that the preferred unsymmetrical bisaddition site for Sc$_3$N@I$_2^{-}$C$_{80}$ corresponds to the bond denoted as 54$^{-}$72 (Figure 3. The first adduct is always attached to bond 1$^{-}$5). Many examples reported in the literature show that monopyrrolidines on scandium nitride have the metals far from the addition site.$^{46-48}$ Indeed, as observed for the most stable scandium-based [5,6]-monooadduct,$^{45}$ the most favorable unsymmetric bisadduct (bond 54$^{-}$72) has the metal atoms far from the functionalized C-C bonds. The other C$_1$-symmetric isomers calculated are >1.5 kcal/mol higher in energy than the 54$^{-}$72 based bisadduct.

The $^1$H NMR spectrum of bisadduct 2 shows a more symmetric resonance pattern, with two AB quartets corresponding to the methylenes of the pyrrolidines and one quartet...
fullerene are 30.9 kcal/mol for bisadduct 11–29, whereas it is ca. 37 kcal/mol for the second and third most stable additions. Thus, bisadduct formation at position 11–29 is dramatically favored in the EMF, as the fullerene cage is less distorted. This C₃-symmetric bisadduct has one of the metal atoms of the Sc₃Nₐ cluster directly adjacent to the functionalized [5,6]-bond. This was totally unexpected, since this is usually observed for EMFs containing larger TNT clusters. We performed Energy Decomposition Analysis (EDA) calculations to better rationalize the TNT orientation preference. With the use of the EDA scheme, the total energy of the system is partitioned into a deformation term (the energy required to distort the fragments into the geometry they adopt in the final structure), and an interaction portion, which includes the electrostatic interaction, Pauli repulsion and orbital interaction terms. Empty fullerene structures are taken as the references. Calculations indicate that there exists a correlation between the relative stabilities and both the deformation of the carbon bisadduct cage and the TNT–fullerene interaction energies for bisadduct 11–29. The preferred orientation of the cluster inside the cage actually corresponds to the one possessing the lowest deformation and the largest interaction energy (which mainly results from the orbital interaction term).

The redox potentials of Sc₃N@I₆-C₈₀ bisadducts 1–3 were measured by cyclic voltammetry (CV) in o-DCB solutions (Table 1). The CV of bisadducts 1–3 exhibited irreversible reduction processes similar to those observed for Sc₃N@I₆-C₈₀. Unlike the pristine fullerene Sc₃N@I₆-C₈₀ bisadducts 1–3 showed irreversible oxidation potentials cathodically shifted by approximately 450 mV. Consequently, bisadducts 1–3 should exhibit better donor properties and smaller band gap (see Supporting Information).

### Table 1. Redox Potentials (V) of Sc₃N@I₆-C₈₀ Bisadducts 1–3

<table>
<thead>
<tr>
<th>Compound</th>
<th>E⁺(+2)/E⁺(+1)</th>
<th>E⁺(+1)/E⁺(+0)</th>
<th>E⁺(+0)/E⁺(+1)</th>
<th>E⁺(+1)/E⁺(+0)</th>
</tr>
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<tr>
<td>Sc₃N@I₆-C₈₀</td>
<td>1.09</td>
<td>0.39</td>
<td>1.26</td>
<td>1.62</td>
</tr>
<tr>
<td>C₃[5,6]:[5,6]</td>
<td>0.66</td>
<td>0.02</td>
<td>1.34</td>
<td>1.62</td>
</tr>
<tr>
<td>C₃[5,6]:[5,6]</td>
<td>0.36</td>
<td>0.15</td>
<td>1.29</td>
<td>1.68</td>
</tr>
<tr>
<td>C₃[5,6]:[5,6]</td>
<td>0.66</td>
<td>0.05</td>
<td>1.27</td>
<td>1.60</td>
</tr>
</tbody>
</table>

Synthesis and Characterization of Lu₃N@I₆-C₈₀ Bisregioisomers. Unexpectedly, when the 1,3-dipolar cycloaddition reaction was done with Lu₃N@I₆-C₈₀ instead of Sc₃N@I₆-C₈₀, only two main bisadduct isomers were obtained, bisadducts 4 and 5, in 7% and 22% yields, respectively. The mass spectra confirmed the presence of [M + H]+ peak for the bisadduct products (m/z 1642 for both bisadducts 4 and 5).

The ¹H NMR spectrum of bisadduct 4 of Lu₃N@I₆-C₈₀ exhibited a very similar resonance pattern to that of bisadduct 3 of Sc₃N@I₆-C₈₀ with two AB quartets corresponding to the methylenes of the pyrroldines and an ABX pattern corresponding to the methylenes of the N-ethyl groups (Figure 2c). As already discussed, there are only 5 [5,6]:[5,6]-regioisomers out of the 30 possible isomers that can show this chiral (C₃) resonance pattern. Even if hybrid [5,6]:[5,6]-bisadducts were considered, no chiral addition patterns would be possible. [6,6]:[6,6]-Bisadditions could give rise to intrinsically chiral compounds, but these possess much higher energies (see Figure S35E), and thus were not considered based on DFT calculations.
The 5 possible bis-[5,6]-[5,6]-chiral isomers of Lu₃N@I₅-C₈₀ were optimized using DFT calculations considering 8 different orientations of the TNT cluster. Not surprisingly, the lowest energy [5,6]-[5,6] C₂-symmetric regioisomer of Lu₃N@I₅-C₈₀ is the same as for Sc₃N@I₅-C₈₀ (addition to bond 11−29). This bisadduct is >7 kcal/mol more stable than the other 4 possible C₂-symmetric bisadducts (Figure 5a, 5c).

The ¹H NMR spectrum of bisadduct 5 also shows a high degree of symmetry. Since two resonances are uncorrelated singlets at 4.74 and 4.46 ppm (from COSY and NOESY spectra), they cannot correspond to a [5,6]-pyrrolidine addition and must correspond to a [6,6]-pyrrolidine. Furthermore, these two singlets indicate that the second pyrrolidine must be in a position that does not perturb the symmetry of the [6,6]-adduct, and this can only occur by positioning the second pyrrolidine in a relative perpendicular orientation. Similarly, since only one AB quartet is observed, corresponding to the methylenes of the other pyrrolidine, the [6,6]-adduct is not altering the symmetry of the [5,6]-one. Two separate quartets for the methylenes of the N-ethyl groups are also observed, confirming that the two pyrrolidines are not symmetrically equivalent (Figure 4b).

Exclusively on the basis of the NMR observations, it is possible to assign the structure of this bisadduct to one of only 4 possibilities, all of which exhibit a [5,6]-[6,6]-bisaddition pattern, with mutually perpendicular pyrrolidines. To the best of our knowledge, this is the first mixed (hybrid) bisaddition compound observed for an endohedral system, a rather unanticipated and very interesting result. While the ¹H NMR spectrum suggests a very high symmetry, it is also a C₂-symmetric compound.

This unique perpendicular arrangement of the pyrrolidines was confirmed by DFT calculations. DFT calculations indicate that the most favorable C₂-symmetric bisaddition corresponds to bond 65−78 (Figure 5b,d), leading to a mutually perpendicular bisadduct arrangement. The computed thermodynamic stabilities show that the [5,6]-[5,6] bisadduct 4 (11−29) is 6.7 kcal/mol more stable than the [5,6]-[6,6] 5 (65−78). Linear transit (LT) calculations, i.e., restrained optimization along the reaction coordinate, indicate that the 1,3-dipolar cycloaddition reaction on [6,6]-bonds is kinetically more favored than for [5,6]-additions. This was also observed experimentally by high performance liquid chromatography (HPLC) analysis. Indeed, a thorough investigation of the lowest energy unoccupied molecular orbitals (LUMOs) of Lu₃N@I₅-C₈₀ demonstrates that bond 65−78 (leading to bisadduct 5) exhibits LUMO orbital lobes that can effectively interact with the HOMO of the dipole, whereas bond 11−29 (bisadduct 4) is better aligned to interact via its LUMO + 1 (−3.93 eV), which is 9 kcal/mol higher in energy (Figure 6a). Thus, using Frontier Molecular Orbital (FMO) theory to predict the kinetics of the 1,3-dipolar cycloaddition, we observed that the interaction of the HOMO of the dipole with the LUMO of the monoaadduct is ca. 5 kcal/mol more favorable than with the LUMO + 1 (Figure 6a). The fact that bond 65−78 has a properly aligned LUMO orbital to react with the dipole while bond 11−29 has an optimally
synthesized and characterized the first bisadducts of Sc₃N@Ih-C₈₀ and Lu₃N@Ih-C₈₀ using independent, nontethered bis-1,3-dipolar cycloaddition reactions. A very limited number of bisadducts were observed, 3 for Sc₃N@Ih-C₈₀ and 2 for Lu₃N@Ih-C₈₀. Surprisingly, only one of the 5 observed compounds lacks symmetry (C₁), while 2 exhibit C₂ symmetry and 2 others have C₃ symmetry, based on ¹H NMR analyses. In concert with DFT calculations, it was possible to unambiguously assign the structures of all of the 5 new compounds isolated. The 2 C₂ symmetric compounds are the first intrinsically chiral endohedral fullerenes ever reported, whose chirality arises as a consequence of the intrinsic bisaddition pattern. One of the C₃ symmetric compounds, corresponding to a bisadduct of Lu₃N@C₈₀, is the first hybrid compound, exhibiting addition of one pyrrolidine on a [5,6]-bond and the other on a [6,6]-bond. DFT calculations were used to rationalize the origins of the differences in regioselectivity observed for scandium and lutetium based bisadducts. This study demonstrates the feasibility of bisadditions to Sc₃N@C₈₀ and Lu₃N@C₈₀ and establishes that the regiochemistry is more strongly determined by the endohedral clusters than by the use of exohedrally tethered-controlled bisadducts.

**METHODS**

**Synthesis of Sc₃N@Ih-C₈₀ Bisregioisomers.** To a solution of Sc₃N@Ih-C₈₀ (6.14 mg, 5.54 × 10⁻³ mmol, 1 equiv) in 6 mL of o-DCB were added N-ethylglycine (8.57 mg, 8.31 × 10⁻² mmol, 15 equiv) and formaldehyde (8.31 mg, 0.28 mmol, 50 equiv). The reaction mixture was stirred and heated during 15 min at 120 °C under a N₂ atmosphere. The solvent from the reaction mixture was removed under nitrogen, and the crude product was purified by silica gel chromatography using initially CS₂ to elute the unreacted endohedral pristine fullerene, followed by CS₂/CHCl₃ 3:2 to elute the monoadduct of Sc₃N@Ih-C₈₀ (45%) and finally CHCl₃/EtOAc 9:1 to elute the bisadducts fraction (38%). Bisadducts 1, 2, and 3 were further purified by preparative TLC using CHCl₃/EtOAc 9:1 in 6%, 13%, and 15% yield, respectively.

**Synthesis of Lu₃N@Ih-C₈₀ Bisregioisomers.** To a solution of Lu₃N@Ih-C₈₀ (3.52 mg, 2.35 × 10⁻³ mmol, 1 equiv) in 4 mL of o-DCB were added N-ethylglycine (3.63 mg, 3.52 × 10⁻³ mmol, 15 equiv) and formamide (3.52 mg, 0.12 mmol, 50 equiv). The reaction mixture was stirred during 15 min and heated at 120 °C under a N₂ atmosphere. The solvent from the reaction mixture was removed under nitrogen, and the crude product was purified by silica gel chromatography using initially CS₂ to elute the unreacted endohedral pristine fullerene, followed by CS₂/CHCl₃ 3:2 to elute the monoadduct of Lu₃N@Ih-C₈₀ (41%), and finally CHCl₃/EtOAc 9:1 to elute the bisadduct 4 (7%) and bisadduct 5 (22%).

**Computational Details.** Density functional theory (DFT) full optimizations at the ZORA-BP86-D₂/TZP(COSMO:o-DCB) level were performed using ADF and the related QUILD computational packages. N-Ethyl substituents on the pyrrolidine ring were replaced by methyl groups to reduce the computational complexity of the calculations. Different orientations of the TNT unit were considered in all cases to properly model the TNT unit rotation inside the cage as performed in previous studies. All possible 30 [5,6]-[5,6] bisadducts were optimized for Sc₃N@Ih-C₈₀ considering 8 different orientations of the TNT cluster for the most stable bisadducts, whereas all possible 91 regioisomers with 8 different cluster orientations were optimized for Lu₃N@Ih-C₈₀ (ca. 800 full BP86-D₂/TZP optimizations). Energy Decomposition Analyses (EDA) were performed as implemented in the ADF computational package. In this EDA scheme, the total energy of the system is divided into

\[
\Delta E = \Delta E_{\text{def}} + \Delta E_{\text{int}}
\]

\[
\Delta E_{\text{int}} = \Delta V_{\text{int}} + \Delta E_{\text{Pauli}} + \Delta E_{\text{Pauli}}^\text{inter} = \Delta E_{\text{Pauli}}^\text{intra} + \Delta E_{\text{Pauli}}^\text{inter}
\]

**CONCLUSIONS**

We analyzed and described the 91 possible bisaddition regioisomers for an I₆-C₈₀ cage based on symmetry (C₁, C₂, or C₃-symmetric), assuming identical adducts. We successfully

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**Figure 5.** Representation of the most stable Lu-based bisadducts: (a) [5,6]-[5,6] C₃-symmetric regioisomer on bond 11–29, and (b) [5,6]-[6,6] C₃-symmetric on bond 65–78. (c) Schlegel representation of all possible [5,6]-[5,6] and [5,6]-[6,6]-bisadducts and their DFT relative stabilities (in kcal/mol). All possible addition sites are colored according to their symmetry: pink, cyan, and purple for C₃-symmetric additions, respectively.
where a deformation term ($E_{\text{def}}$) is the energy required to distort the fragments into the geometry they adopt in the final structure, and an interaction part ($E_{\text{int}}$). The latter includes the electrostatic interaction ($V_{\text{elst}}$), which corresponds to the classical electrostatic interaction between the unperturbed charge distributions of the fragments as they are brought together at the final geometry, Pauli repulsion ($E_{\text{Pauli}}$) comprising the destabilizing interactions between occupied orbitals, and is responsible for any steric repulsion; and orbital interaction ($E_{\text{oi}}$) term that accounts for electron pair bonding, charge transfer, and polarization. Pyramidalization (POAV) angles were computed using POAV3 program (see Supporting Information for complete computational reference list).

**Abbreviations.** LUMO, low unoccupied molecular orbital; HPLC, high performance liquid chromatography; o-DCB, ortho-dichlorobenzene; TLC, thin layer chromatography; NMR, nuclear magnetic resonance; COSY, correlation spectroscopy; HMQC, heteronuclear multiple-quantum correlation spectroscopy.

**ASSOCIATED CONTENT**

* Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b07207.

Detailed synthesis and characterization of compounds 1–5, DFT calculations results, and complete computational reference list (PDF)

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**Table 2. Redox Potentials (V) of Lu$_3$N@I$_h$-C$_{80}$ Bisadducts 4 and 5**

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<th>compound</th>
<th>$E_{pa}^{0+1}$</th>
<th>$E_{pc}^{0+/+1}$</th>
<th>$E_{pa}^{1/-2}$</th>
<th>$E_{pc}^{+/-2}$</th>
<th>$E_{pa}^{2/-3}$</th>
<th>$E_{pc}^{+/-3}$</th>
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<tr>
<td>Lu$_3$N@I$<em>h$-C$</em>{80}$</td>
<td>5.1</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>C$_2$-[5,6]-[5,6] Bisadduct 4</td>
<td>0.37</td>
<td>0.03</td>
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<td>-1.74</td>
<td>-2.22</td>
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<tr>
<td>C$_2$-[5,6]-[6,6] Bisadduct 5</td>
<td>0.34</td>
<td>0.24</td>
<td>-1.45</td>
<td>-1.81</td>
<td>-</td>
<td>-</td>
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*Figure 6. (a) Representation of the LUMO for Sc$_3$N@I$_h$-C$_{80}$ and Lu$_3$N@I$_h$-C$_{80}$ and their interaction with the HOMO of the dipole (isosurface value 0.02 au, energies in eV). (b) Representation of the POAV (Pi-Orbital Axis Vector) pyramidalization angle for Lu$_3$N@I$_h$-C$_{80}$ [5,6]-monoadduct.*