Fullerenes

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Dancing on a Fullerene Surface: Isomerization of $Y_3N@$(*N*-Ethylpyrrolidino-C_{80}) from the 6,6 to the 5,6 Regioisomer**

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The prototype of the family of trimetallic nitride template (TNT) endohedral fullerenes $Sc_3N@C_{80}$ was first synthesized in 1999.[1] In these fullerenes the least stable icosahedral (I_h) isomer of C_{80} is stabilized by a formal six-electron transfer from the TNT moiety to the carbon cage.[2,3] Since the $M_3N@C_{80}$ species can be isolated in a quite remarkably high yield, the design of $M_3N@C_{80}$ derivatives has considerable potential in material science and biochemistry. Several reports of the functionalization of endohedral metallofullerenes with isolated and well-characterized adducts exist.[4–17] Among these, the pyrrolidinofullerene derivatives of $Sc_3N@C_{80}$ and $Y_3N@C_{80}$ show unexpected chemical and electrochemical properties.[18] Cycloaddition reactions on

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$Sc_3N@C_{80}$ usually take place regioselectively at a 5,6 ring junction (corannulene-type site) on the I_h C_{80} isomer. A Diels–Alder derivative and two 1,3-dipolar cycloadducts of *N*-ethyl- and *N*-methylazomethine ylide which give rise to the *N*-ethyl- and *N*-methylpyrrolidinofullerene, respectively, are examples of such a regioselectivity.[6,9,11,13] However, Dorn and co-workers have recently obtained a mixture of the 5,6 and 6,6 regioisomers in the synthesis of the *N*-tritylpyrrolidinofullerene adduct.[19] Interestingly, similar cycloaddition reactions on the I_h $Y_3N@C_{80}$ derivative occur exclusively at a 6,6 ring junction (pyrene-type site).[8] Isomerization of the 6,6 regioisomer of $Y_3N@$(*N*-ethylpyrrolidino-C_{80}) to produce exclusively the 5,6 regioisomer after thermalization has been reported by Echegoyen and co-workers.[18] Figure 1 illustrates the two possible sites of addition to the I_h C_{80} fullerene cage, the double bonds between a five- and a six-membered ring and between two six-membered rings. Hence, reactivity of TNT endohedral metallofullerenes toward exohedral chemical functionalizaton is affected and controlled by the nature of the endohedral metal cluster. In the case of the 1,3-dipolar *N*-ethylazomethine cycloaddition on $Y_3N@C_{80}$, the experimental results suggest that the reaction gives rise to the kinetic product. The 5,6 regioisomer would be the most stable minimum energy form because it is the unique isomer found after thermalization. Thus, the transition state (TS) to obtain the 6,6 isomer should be lower in energy than the TS that yields the 5,6 isomer. Herein, we report on the thermodynamic stability of reactants, intermediates, and products of the 1,3-dipolar *N*-ethylazomethine cycloaddition on $M_3N@C_{80}$ (M = Sc, Y), as well as on the different reactivity observed in experiments with the scandium- and yttrium-based compounds.

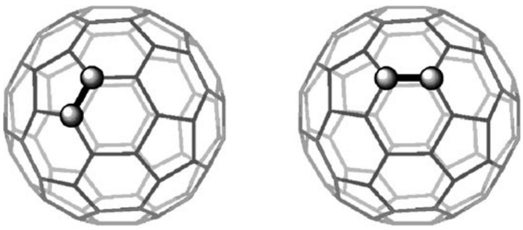

Figure 1. Two possible sites of addition to the I_h C_{80} cage: on the left, a 5,6 ring junction (a corannulene-type site), and on the right, a 6,6 ring junction (a pyrene-type site).

Theoretical calculations indicated that the TNT unit may easily rotate inside the cage in underivatized $Sc_3N@C_{80}$, a finding that is in good agreement with ^{13}C NMR spectroscopic analysis.[2] We have observed that the TNT unit may also rotate inside the fullerene cage in $Y_3N@C_{80}$ because several orientational isomers show energy differences of less than 3 kcal mol^{-1}. For the two different pyrrolidinofullerene regioisomers, we performed a conformational search for the position of the TNT with respect to the C–C bond of the cage where the pyrrolidine was formed. A representation of the isomers considered in the search is found in Figure 2. Reaction energies are fairly exothermic for all the isomers (Table 1), regardless of the type of metal cluster, Y_3N or Sc_3N.

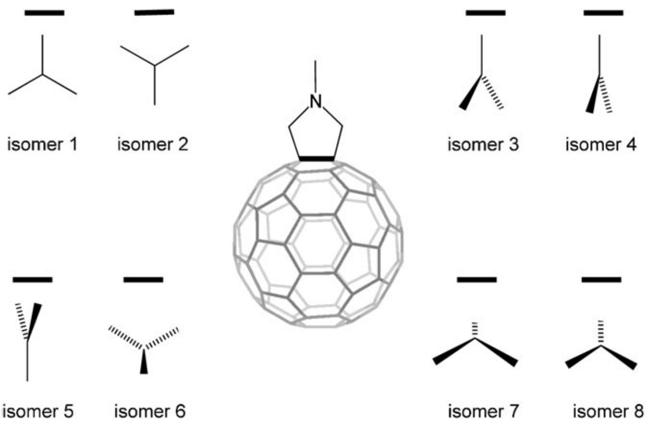

Figure 2. Representation of the relative position of the TNT unit with respect to the C–C bond of the fullerene where the adduct is formed for the different isomers that have been computed in this work.

Table 1: Reaction energies for the different product isomers of the 1,3-dipolar cycloaddition of *N*-ethylazomethine to $M_3N@C_{80}$ (M = Sc, Y).[a]

	$Y_3N@$pyrrolidino-C_{80}		$Sc_3N@$pyrrolidino-C_{80}	
Isomer	5,6 [kcal mol^{-1}]	6,6 [kcal mol^{-1}]	5,6 [kcal mol^{-1}]	6,6 [kcal mol^{-1}]
1	−33.6	−33.6	−26.5	−19.8
2	−33.2	−22.7	−36.1	−24.6
3	−35.6	−33.7	−26.3	−21.5
4	−34.0	−31.5	−24.2	−19.8
5	−20.8	−22.9	−24.7	−25.0
6	−35.2	−22.5	−37.0	−24.6
7	−23.7	−18.3	−25.5	−18.5
8	−22.3	−22.5	−24.6	−21.6

[a] The reaction energies for the cycloaddition to the bonds between a five- and a six-membered ring and between two six-membered rings of C_{80} are −50.2 and −35.5 kcal mol^{-1}, respectively.

From Table 1, it is evident that the rotation of the TNT unit inside the functionalized fullerene is more hindered than in the underivatized $M_3N@C_{80}$ counterparts. Moreover, the TNT unit rotates more easily in the 5,6 regioisomer than in the 6,6 one. Recently, Yamada et al. also suggested on the basis of computed electrostatic potential maps of $La_2@C_{80}$-$(CH_2)_2NH$ that the La_2 unit is fixed in the 6,6 isomer, but it can move randomly in the 5,6 isomer.[17]

The relative stability of the 5,6 regioisomer with respect to the 6,6 regioisomer in pyrrolidino-C_{80} (14.7 kcal mol^{-1}) is reduced when the fullerene cage encapsulates the TNT unit. For M = Sc, the stability of the two regioisomers is similar only for a few orientations of the TNT unit that lay at high energies (isomers **5** and **8**). For M = Y, however, there are several orientational isomers with low energy for which the energy difference between the two regioisomers is small. For the Y-based metallofullerene, the lowest energy 5,6 isomer **3** is only 1.9 kcal mol^{-1} more stable than the most stable 6,6 structure, whereas for the Sc-based metallofullerene the corresponding difference is 12 kcal mol^{-1}. Therefore, the relative stability of the 5,6 versus 6,6 coordination is decreased when Sc is changed for Y. A larger charge transfer to the cage and a larger size of the TNT derivative (Y > Sc) appear to stabilize the 6,6 regioisomer with respect to the 5,6 regioisomer.

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The two global minima **3** and **6** for the 5,6 adduct of Y_3N@pyrrolidino-C_{80} are almost degenerate, with an energy difference of only 0.4 kcal mol^{-1}. The X-ray structure,[10] which shows some disorder in the position of the Y atoms inside the cage, is almost identical to the structure computed for isomer **6** (see the Supporting Information). The most stable isomers for the 6,6 adduct, have one Y atom oriented toward the substituted C–C bond.

We have also looked for the transition states so as to unravel the mechanism of the 1,3-dipolar cycloaddition to TNT endohedral fullerenes and to shed light on the different behavior of Sc- and Y-based compounds. Figure 3 displays the energy profiles for the stepwise addition of *N*-methylazomethine (our computational model) to $M_3N@C_{80}$. When M = Y, the electronic barrier for the addition to a bond between two six-membered rings ($TS_{1,66}$) is 0.4 kcal mol^{-1}, a value that is much smaller than the barrier of 3.9 kcal mol^{-1} found for the addition to a bond between a five and a six-membered ring ($TS_{1,56}$). The intermediate that gives rise to the 6,6 adduct (I_{66}) is around 5 kcal mol^{-1} more stable than the intermediate that originates the 5,6 adduct (I_{56}). We have also located the TS that connects I_{66} with the 6,6 adduct ($TS_{2,66}$). It lies 0.8 kcal mol^{-1} higher in energy than I_{66}, so it is also an almost barrierless step. Although transition states that connect I_{56} to the 5,6 adduct have not been located ($TS_{2,56}$), we assume that these processes are almost barrierless as well. Therefore, present DFT calculations confirm that the formation of the 6,6 adduct from the reaction between $Y_3N@C_{80}$ and *N*-ethylazomethine is under kinetic control.[20] For M = Sc (Figure 3 b), transition states for 5,6 and 6,6 additions show similar energies, with $TS_{1,56}$ being slightly favored. As the experiment shows only the presence of the 5,6 adduct, we infer from our energy profile that the process is thermodynamically controlled.

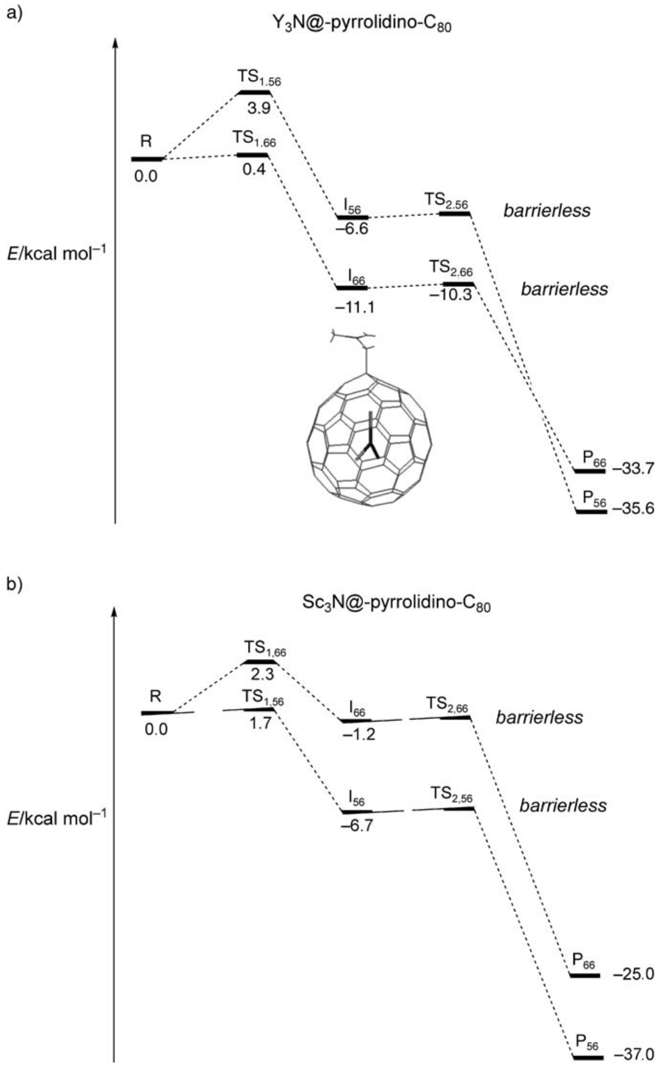

Figure 3. Energy profile of the most relevant stationary points for the *N*-methylazomethine addition to the endohedral metallofullerene a) $Y_3N@C_{80}$ and b) $Sc_3N@C_{80}$.

We finally addressed the 6,6-to-5,6 isomerization observed in experiments after thermalization of the kinetically favored product. A pirouette-kind of mechanism has been proposed by the research groups of both Echegoyen and Dorn.[18,19] Furthermore, Echegoyen and co-workers have shown this transformation directly by NMR spectroscopy, starting with the pure 6,6 regioisomer, which transformed quantitatively to the 5,6 isomeric form. Based on this experimental evidence and on the computed energy profile for the stepwise cycloaddition (Figure 3 a), we put forward the mechanism depicted in Figure 4. The 6,6 adduct (P_{66}) is converted into a 5,6 intermediate (I'_{56}) through a TS (TS_{66to56}) with an energy similar to I'_{56}. The formation of I_{66} through TS_{66} is energetically favored, but no isomerization process is then possible. Rotation around the remaining C1–C3 bond is needed to obtain a 5,6 adduct. Either clockwise or anticlockwise rotations will involve situations in which the C2-C1-C3-N dihedral angle is zero or near to zero (namely, eclipsed bonds). Our estimation for the energy of such an "eclipsed TS" is 1.8 kcal mol^{-1}.[21] This value is smaller than the energy of $TS_{1,56}$, so the isomerization mechanism is more favored than the mechanism involving retrocycloaddition–cycloaddition to the bond between a five-and a six-membered ring (3.9 kcal mol^{-1}). Therefore, during thermalization, pyrrolidine "dances" on the fullerene surface when the "couple" inside is Y_3N, but no isomerization is observed once the most stable regioisomer is formed, as occurs for $Sc_3N@C_{80}$.

The somewhat different exohedral reactivity and stability of the resulting adducts of $M_3N@C_{80}$ fullerenes (M = Sc, Y) seems to be related to the size of the TNT unit and the amount of charge transfer to the cage. The larger the size of TNT and the charge transfer (Y > Sc) the more stable are the 6,6 regioisomers with respect to 5,6 regioisomers. Preliminary results for M = La that show orientational isomers for which the 6,6 adduct is more stable than the 5,6 adduct also point to this direction.

Methods Section

The calculations were carried out by using DFT methodology with the ADF 2004 program.[22,23] The exchange-correlation funtionals of Becke[24] and Perdew[25] were used. Relativistic corrections were included by means of the ZORA formalism. Triple-ζ polarization basis sets were employed to describe the valence electrons of the C, N,

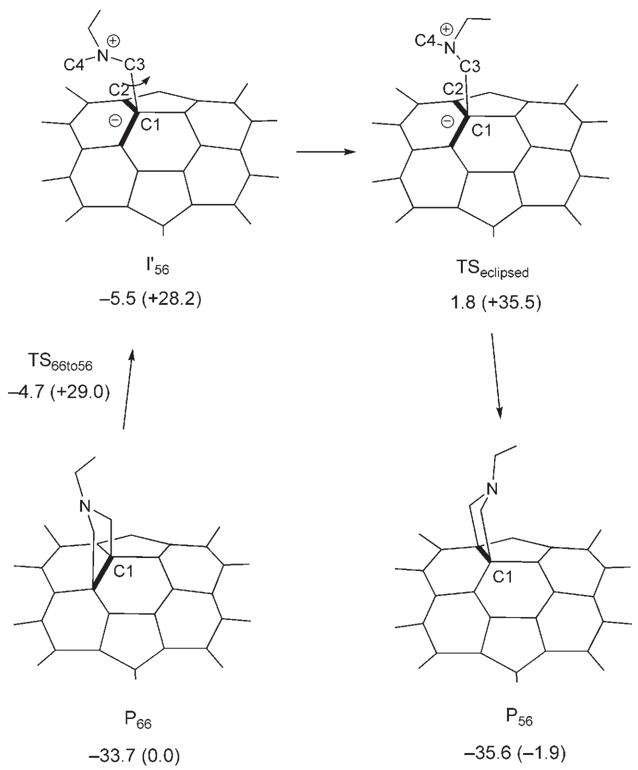

Figure 4. Proposed mechanism for the isomerization of the 6,6 regioisomer of Y_3N@pyrrolidino-C_{80} to the 5,6 regioisomer. Relative energies with respect to reactants in kcal mol^{-1} are displayed (relative to that of P_{66} in parenthesis). In the $TS_{eclipsed}$, the C–C bond between the five- and the six-membered ring and the C–N bond of the pyrrolidine are in an eclipsed conformation. The negative charge in I'_{56} and $TS_{eclipsed}$ is mainly delocalized over the three C atoms bonded to C1. Pyrrolidine "dances" on the fullerene surface when the "couple" inside is Y_3N.

Sc, and Y atoms. All the computed stationary points have closed-shell electronic structure. To locate the transition states, we made use of the metadynamics method associated with Car–Parrinello molecular dynamics,[26] as implemented in the CPMD program.[27] From the snapshots in the transition regions of the metadynamics trajectory we performed a conventional TS search with pseudo Newton–Raphson methods computing numerically the initial Hessian matrix and updating it progressively with the Broyden–Fletcher–Goldfarb–Shanno (BFGS) algorithm. The approximate final Hessian matrix, with a unique negative eigenvalue, is employed as the initial Hessian matrix in the TS search made with the ADF 2004 code. The stationary points with an approximate Hessian matrix with a unique negative eigenvalue are what we call TS thorough this study. The structures of the most representative stationary points are found in the Supporting Information.

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Keywords: density functional calculations · fullerenes · host–guest systems · isomerization · surface chemistry

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[20] We located a concerted TS that connects reactants and products directly. The concerted reaction is found to be very asynchronous: the two C···C distances in the TS are very different. The barriers are also very small: that for the 6:5 adduct is even slightly smaller than $TS_{1,56}$ (3.1 versus 3.9 kcal mol^{-1}). We have also computed the triplet state of I_{66} and have found it to be much destabilized (22 kcal mol^{-1} higher than the closed-shell singlet). Hence, we infer that a radical mechanism is not likely.

[21] To estimate the energy of $TS_{eclipsed}$, we have constructed a reaction path in which the C4···C2 distance was changed from 3.95 (the value for I'_{56}) to 2.05 Å. The highest energy of that path (+1.8 kcal mol^{-1}) is our best estimation of $E(TS_{eclipsed})$ (see the Supporting Information). The energy of TS_{66to56} (−4.7 kcal mol^{-1}) has been roughly estimated by adding 0.8 kcal mol^{-1},

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our estimation for the barrier of the second step of the reaction I_{66} to P_{66}, to $E(I'_{56})$.

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