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Aromaticity as the driving force for the stability of non-IPR endohedral metallofullerene Bingel–Hirsch adducts†

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We have studied the relative stabilities of Bingel–Hirsch non-IPR endohedral metallofullerene monoadducts having one, two, or three adjacent pentagon pairs. The most stable addition always leads to an open adduct and never occurs on [5,5] bonds. Our results show that the thermodynamics of the addition is governed by the additive local aromaticity of the rings of the final adducts.

Right after the fullerene discovery, the first endohedral metallofullerene (EMF) La@C_{60} was detected.[1] The number of EMFs reported since then has increased over the years.[2] Given the low yields obtained in many cases, computations have been crucial for a correct elucidation of the structure and reactivity of EMFs and their derivatives.[3]

When a metal or metallic cluster is encapsulated inside a fullerene cage, a formal charge transfer from the inner moiety to the carbon structure takes place. Poblet and co-workers reported that this negative charge transferred from the metal clusters to the carbon cages in EMF systems is mainly localized on the five-membered rings (5-MRs) of the fullerene.[4] Apart from that, it was shown that charged cages are good models for describing relative stabilities of EMFs.[5] Neutral empty fullerenes strictly obey the so-called isolated pentagon rule (IPR), which states that the most stable cages are those that do not contain adjacent 5-MRs.[6] Nevertheless, many EMFs violate the IPR rule.[7] Some of us have recently shown that the most stable charged fullerene cages (*i.e.* the most suitable cages in EMFs)[5] are determined by the Maximum ARomaticity Criterion (MARC), where the aromaticity of the EMF is computed by the Additive Local Aromaticity (ALA) index (see ESI† for a description of ALA).[8]

Functionalization of EMFs is mainly achieved *via* cycloaddition reactions, principally through Diels–Alder (DA), 1,3-dipolar, and nucleophilic [2+1] Bingel–Hirsch (BH) additions. It has been shown

that the strain induced by the inner metal cluster on the carbon structure plays an important role in determining the regioselectivity of exohedral functionalizations of the EMFs.[9] Electronic effects are also essential due to the formal charge transfer from the metal cluster to the fullerene cage.[10] In most cases the best criterion for chemical-reactivity predictions of EMFs is provided by a combination of short bond lengths, high pyramidalization angles, and appropriate shape of some of the LUMOs.[9a] However, a single parameter for correctly describing and predicting EMF regioselectivity has not been described yet.

In light of the above-mentioned considerations, one might expect chemical functionalization of non-IPR EMFs to occur preferentially on the [5,5] bonds of the pentalene units (the different bond types are described in Scheme S1, ESI†). These 8π-electron systems have, according to the Hückel $(4n + 2)$ aromatic/$(4n)$ antiaromatic rule, a destabilizing effect over the π electronic structure[6,11] alleviated in part by the charge transferred from the inner metal cluster. In addition, [5,5] bonds usually have large pyramidalization angles and are located in highly strained fullerene regions. Indeed, the DA reaction on the non-IPR Y$_3$N@C_2-C_{78} system was computationally predicted to occur on a [5,5] type E bond.[9b] However, there are some recent experimental examples of BH cycloadditions on non-IPR EMFs where the addition does not occur on type E [5,5] bonds. For instance, the BH addition to Sc$_3$N@D$_3$(6140)C_{68},[12] takes place on a [6,6] bond, and that to Gd$_3$N@C_{2n} ($2n$ = 82 and 84) occurs on a [5,6] bond.[13] Interestingly, the most stable adducts were formed on long C–C bonds with high pyramidalization angles.[13,14] In fact, the least stable adducts were those on short C–C bonds. With a few exceptions,[15] BH addition to EMFs leads to open-cage adducts (termed fulleroids).

For BH additions to EMFs (see Scheme S2 in the ESI†), none of the usually employed parameters for describing the preferred addition sites is able to reproduce the experimental observations. Moreover, we recently showed that regioselectivity changes of the DA cycloaddition to C_{60}^{n-} (n = 0–6) can be rationalized using measures of local aromaticity.[16] In the present work, we explore the role played by aromaticity in determining the relative BH adduct stabilities of three types of non-IPR EMF systems: Gd$_3$N@C$_s$(51365)-C$_{84}$ with 1 adjacent pentagon pair (APP),[17] Y$_3$N@C_2(22010)-C$_{78}$ with 2 APPs,[18]

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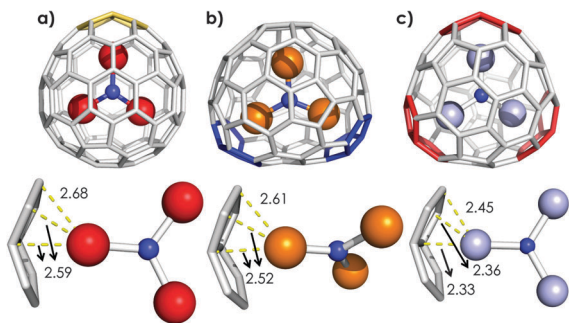
Fig. 1 Representation of: (a) $Gd_3N@C_s(51365)$-C_{84}; (b) $Y_3N@C_2(22010)$-C_{78}; and (c) $Sc_3N@D_3(6140)$-C_{68} EMF structures and metal–$C_{pentalene}$ distances (in Å). Adjacent pentagon pairs (APP) units are highlighted in color.

and $Sc_3N@D_3(6140)$-C_{68} with 3 APPs[19] (see Fig. 1). For $Gd_3N@C_s(51365)$-C_{84} and $Sc_3N@D_3(6140)$-C_{68} BH reactions have been experimentally reported.[12,13] $Y_3N@C_2(22010)$-C_{78} has an intermediate number of APP units and size, and its DA cycloaddition reaction was studied by our group previously.[9b] As presented in Fig. 1, in all the studied cases the orientation of the inner moiety is equivalent and the metal ions are always pointing to the APP junctions. Moreover, the TNT cluster rotation is hindered or partially hindered for the three studied systems.[9b,13,14] We investigate here whether MARC can explain or not the relative stabilities of a series of BH adducts in non-IPR EMFs.

In Fig. 2, the bonds considered in the present study are represented (the selection was based on the previous experimental and computational studies reported for these EMFs).[9b,13,14] We use the ALA index that is a sum of the local aromaticities of all rings in the BH adducts, except the three-membered ring of the closed-cage adducts (see Fig. S1 and computational details in the ESI†).

As noted above, it is usually considered that the cycloaddition to a given bond on a fullerene or EMF is favored when this bond has a short distance and a large pyramidalization angle. For the studied EMFs, although [5,5] bond types do not always have the

shortest bond distances (see Table S1, ESI†), they exhibit by far the largest pyramidalization angles for the empty cages. In addition, the presence of the metal clusters in EMFs increases the pyramidalization angles of the [5,5] bonds (see the metal–C distances and deformations in Fig. 1, Fig. S2 and S3, ESI†). The strain on the fullerene cage can be quantified as the energy difference between the optimized empty and EMF carbon cage structures. Our results indicate that the strain represents a destabilization of 9.3, 18.5, and 20.7 kcal mol^{-1} for the C_{68}, C_{78}, and C_{84} EMFs, respectively. One could expect that the exohedral functionalization of EMFs would be favored if the attack occurs on the [5,5] bonds to alleviate the strain in the carbon structure (see Fig. 1). Surprisingly, experiments and calculations confirmed that the preferred attack does not occur on type E [5,5] bonds.[13]

As can be seen in Table S2 (ESI†) and Fig. 2, in general, the thermodynamically most favorable products are those corresponding to the attack on [5,6] type D bonds. In most of the cases and always for the most stable adducts, an open-cage structure is obtained (see Fig. S1, ESI†).

For $Gd_3N@C_s(51365)$-C_{84}, the most stable monoadducts are those derived from the functionalization of D2 and D1 [5,6] bonds. The latter is only 1.9 kcal mol^{-1} less stable than D2 (see Table S2, ESI†). These [5,6] bonds are situated on the perimeter of the APP unit. It should be noted that additions on B1 and B2 [6,6] bonds, which are only 2.8 and 4.3 kcal mol^{-1} destabilized as compared to D2, respectively, are placed far from the pentalene unit. Thus, no relationship between the position of the attacked bond and the corresponding product stabilities was found. Interestingly, the BH addition on the [5,5] bond is highly disfavored (the [5,5]-adduct is *ca.* 12 kcal mol^{-1} less stable than the [5,6] one). The addition to type F [5,6] bonds situated next to the [5,5] junction is also extremely disfavored (*ca.* 24 kcal mol^{-1} less stable than the preferred type D [5,6] adduct). Except for the products D2 and D1, the relative energy ordering obtained in our work agrees with the results reported in ref. 13.

In the case of $Y_3N@C_2(22010)$-C_{78}, the most stable product corresponds to the addition to the [5,6] Dl bond. This bond is
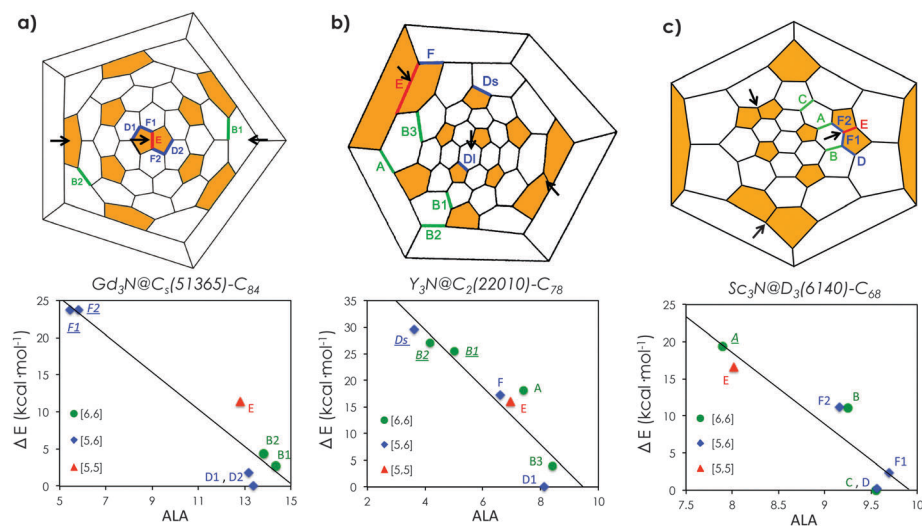
Fig. 2 Schlegel diagram representation with the considered bonds and the relative stability of BH monoadducts (at BP86-D_2/TZP//BP86-D_2/DZP level) with respect to the ALA index of: (a) $Gd_3N@C_s(51365)$-C_{84}; (b) $Y_3N@C_2(22010)$-C_{78}; and (c) $Sc_3N@D_3(6140)$-C_{68} EMFs. Green circles, blue diamonds, and red triangles represent [6,6], [5,6], and [5,5] bonds, respectively. Closed-cage products are in italics and underlined. The positions of metallic atoms are symbolized by black arrows and 5-MRs are highlighted in orange.

positioned close to one of the metallic atoms of the cluster (see Fig. 2). This is basically translated into a high pyramidalization angle of the bond. Again, the highly pyramidalized type E [5,5] and type F [5,6] bonds are very unreactive with relative stabilities of *ca.* 15 kcal mol^{-1} with respect to the Dl-product.

For the smaller Sc$_3$N@D$_3$(6140)-C$_{68}$ cage, C [6,6] and D and F1 [5,6] adducts are most favored from a thermodynamic point of view. D and F1 have relative energies with respect to C of only 0.2 and 2.4 kcal mol^{-1}, respectively (see Table S2, ESI†). In contrast to the other two EMFs, the reaction on the F1 bond is relatively favored. This bond is next to the type E [5,5] junction. The BH cycloadduct corresponding to the attack on the F2 bond is highly unfavorable (*ca.* 11 kcal mol^{-1} less stable than the C adduct). However, it should be emphasized here that bonds F1 and F2 have almost the same C–C bond distances and pyramidalization angles (see Table S1, ESI†). Another striking result is the high reactivity of the pyrene-type bond called C. This bond is surrounded by hexagonal rings and is located in a flat area of the fullerene structure (it has the lowest pyramidalization angle, see Table S1, ESI†). In addition, it is situated far from the influence of the metal atoms. Thus, bond distances and pyramidalization angles are totally unable to justify the final stabilities found (see Tables S1 and S2, ESI†). It is worth mentioning that relative stabilities found here agree quite well with those reported in ref. 12 and 14. Moreover, the experimental reaction, which takes place under *kinetic* control, yields product B according to ^{13}C NMR data[12] and theoretical studies.[14]

The results shown above clearly indicate that based on the most commonly used criteria (bond distances and pyramidalization angles), it is not possible to rationalize the calculated relative stability of the BH cycloadducts. In contrast, the BH relative stabilities are well-understood if the total aromaticity of the products (in terms of the ALA index) is analyzed. In Fig. 2, we show the correlations between the relative stabilities of the corresponding BH monoadducts and the ALA index. The lowest energy products are those that are more aromatic. Interestingly, the closed-cage adducts are the least stable and the least aromatic (see Fig. S1, ESI†). In the case of open-cage, all fullerene carbons keep their sp^2 hybridization (large π electron delocalization) resulting in the so-called homofullerenes.[20] This is in contrast to the hybridization change of the attacked C atoms in closed-cage adducts (from sp^2 to sp^3, without allowing π delocalization). Those products that show similar ALA indices have similar stabilities. Thus, for instance, one can justify: (1) why product C in Sc$_3$N@D$_3$(6140)-C$_{68}$ is practically as stable as product D, the relative energies are 0.0 and 0.2 kcal mol^{-1} and their ALA values are 9.56 and 9.57, respectively; (2) why products F1 and F2 have largely different stabilities although their bond distances and pyramidalization angles are equivalent. The MARC[8] (*i.e.* "most aromatic adduct = the most stable") applies to all bonds of the fullerene systems regardless of their type, pyramidalization, or position of the metal cluster.

In summary, we have shown that there exists a direct relationship between the relative stabilities of BH adducts of non-IPR EMFs and their aromaticity as measured with the ALA index. The good correspondence found for all cases, irrespective of the number of APP units present on the structure and the position

of the bond with respect to pentalene units, confirms that MARC is a very powerful tool for analyzing and rationalizing the final stability of BH products. This observation is of great relevance, as there are no previous studies where a single parameter, either geometric or electronic (such as fullerene strain, bond length, pyramidalization angles, *etc.*), was able to unequivocally describe and rationalize the preferred addition sites. Our results demonstrate that aromaticity is the driving force for the thermodynamic stability of BH adducts. More research is underway to determine whether the kinetic behavior can also be explained through the aromaticity of intermediates and transition states.

Notes and references

1 J. R. Heath, S. C. O'Brien, Q. Zhang, Y. Liu, R. F. Curl, F. K. Tittel and R. E. Smalley, *J. Am. Chem. Soc.*, 1985, **107**, 7779.
2 X. Lu, L. Feng, T. Akasaka and S. Nagase, *Chem. Soc. Rev.*, 2012, **41**, 7723.
3 (*a*) A. Rodriguez-Fortea, A. L. Balch and J. M. Poblet, *Chem. Soc. Rev.*, 2011, **40**, 3551; (*b*) S. Osuna, M. Swart and M. Sola, *Phys. Chem. Chem. Phys.*, 2011, **13**, 3585.
4 A. Rodríguez-Fortea, N. Alegret, A. L. Balch and J. M. Poblet, *Nat. Chem.*, 2010, **2**, 955.
5 A. A. Popov and L. Dunsch, *J. Am. Chem. Soc.*, 2007, **129**, 11835.
6 H. W. Kroto, *Nature*, 1987, **329**, 529.
7 M. N. Chaur, F. Melin, A. L. Ortiz and L. Echegoyen, *Angew. Chem., Int. Ed.*, 2009, **48**, 7514.
8 M. Garcia-Borràs, S. Osuna, M. Swart, J. M. Luis and M. Solà, *Angew. Chem., Int. Ed*, 2013, DOI: 10.1002/anie.201303636, early view.
9 (*a*) S. Osuna, M. Swart, J. M. Campanera, J. M. Poblet and M. Solà, *J. Am. Chem. Soc.*, 2008, **130**, 6206; (*b*) S. Osuna, M. Swart and M. Solà, *J. Am. Chem. Soc.*, 2009, **131**, 129; (*c*) M. Garcia-Borràs, S. Osuna, J. M. Luis, M. Swart and M. Solà, *Chem.–Eur. J.*, 2012, **18**, 7141.
10 M. Garcia-Borràs, A. Romero-Rivera, S. Osuna, J. M. Luis, M. Swart and M. Solà, *J. Chem. Theory Comput.*, 2012, **8**, 1671.
11 T. G. Schmalz, W. A. Seitz, D. J. Klein and G. E. Hite, *J. Am. Chem. Soc.*, 1988, **110**, 1113.
12 T. Cai, L. Xu, C. Shu, J. E. Reid, H. W. Gibson and H. C. Dorn, *J. Phys. Chem. C*, 2008, **112**, 19203.
13 N. Alegret, M. N. Chaur, E. Santos, A. Rodríguez-Fortea, L. Echegoyen and J. M. Poblet, *J. Org. Chem.*, 2010, **75**, 8299.
14 N. Alegret, A. Rodríguez-Fortea and J. M. Poblet, *Chem.–Eur. J.*, 2013, **19**, 5061.
15 T. Cai, L. Xu, C. Shu, H. A. Champion, J. E. Reid, C. Anklin, M. R. Anderson, H. W. Gibson and H. C. Dorn, *J. Am. Chem. Soc.*, 2008, **130**, 2136.
16 M. Garcia-Borras, S. Osuna, M. Swart, J. M. Luis and M. Solà, *Chem. Commun.*, 2013, **49**, 1220.
17 T. Zuo, K. Walker, M. M. Olmstead, F. Melin, B. C. Holloway, L. Echegoyen, H. C. Dorn, M. N. Chaur, C. J. Chancellor and C. M. Beavers, *Chem. Commun.*, 2008, 1067.
18 A. A. Popov, M. Krause, S. Yang, J. Wong and L. Dunsch, *J. Phys. Chem. B*, 2007, **111**, 3363.
19 (*a*) S. Stevenson, P. Fowler, T. Heine, J. Duchamp, G. Rice, T. Glass, K. Harich, E. Hajdu, R. Bible and H. Dorn, *Nature*, 2000, **408**, 427; (*b*) M. M. Olmstead, H. M. Lee, J. C. Duchamp, S. Stevenson, D. Marciu, H. C. Dorn and A. L. Balch, *Angew. Chem., Int. Ed.*, 2003, **42**, 900.
20 A. F. Kiely, R. C. Haddon, M. S. Meier, J. P. Selegue, C. P. Brock, B. O. Patrick, G.-W. Wang and Y. Chen, *J. Am. Chem. Soc.*, 1999, **121**, 7971.