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Computational Chemistry

Maximum Aromaticity as a Guiding Principle for the Most Suitable Hosting Cages in Endohedral Metallofullerenes**

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Fullerenes are a recently discovered carbon allotrope in which carbon atoms are arranged into 12 pentagons and a variable number of hexagons in a more or less spherical shape.[1] The most stable empty neutral fullerenes strictly obey the isolated-pentagon rule (IPR) formulated by Kroto[2] in 1987. This rule states that all pentagons must be surrounded by hexagons to alleviate the strain produced by two fused pentagons (a pentalene unit). The pentagon adjacency penalty rule (PAPR) quantifies the destabilization produced by adjacent pentagon pairs (APPs) at about 19–24 kcal mol^{-1} per APP.[3]

For a C_{2n} cage, the number of possible IPR-violating isomers is much larger than those obeying the IPR.[4] Non-IPR fullerenes can be stabilized through exohedral functionalization or through inclusion of metal clusters inside the C_{2n} cage leading to the so-called endohedral metallofullerenes (EMFs).[5] Hitherto, metal clusters containing one to seven atoms have been incarcerated in a variety of C_{2n} cages ($2n = 66$–104).[6] As result of a formal charge transfer from the cluster to the fullerene,[7] fullerenes experience important changes in their reactivity trends,[6e,8] aromaticity,[8b,9] and relative stability.[10] In these charged fullerenes, the added electrons are mainly located in the five-membered rings (5-MRs),[11] which render them diatropic. This is not completely surprising, as both anionic cyclopentadiene and doubly anionic pentalene species are aromatic, unlike their neutral analogues.[12] Finally, the relative stability of the different C_{2n} isomers changes because of charge transfer. Interestingly, Popov and Dunsch[10] showed that the relative stabilities of different $M_3N^{6+}@C_{2n}^{6-}$ ($2n = 68$–98) isomers correlate well with those of the empty C_{2n}^{6-} cages.

Out of a myriad of possible isomers that can exist for a given C_{2n} fullerene,[4] usually one is overwhelmingly preferred for a particular incarcerated cluster. Often, the most suitable confinement is a non-IPR cage (Figure 1).[5,6b,c,13] In a study of the relative stabilities of isomers of charged C_{60} and C_{70} fullerenes, Alcamí et al.[14] established that non-IPR isomers having a uniform and well-separated distribution of APPs (negatively charged) and pyrene motifs (positively charged) are more stable than IPR ones. Later on, Poblet and co-workers[11] proposed the maximum pentagon separation rule that states that the most suitable carbon cages for negatively charged fullerenes are those with the largest separation among the 12 negatively charged pentagons. The authors defined the inverse pentagon separation index (IPSI) to measure the pentagon separation for a given carbon cage. They found that, in a series of IPR or non-IPR isomers with the same number of APPs, the most stable isomers are those with the lowest IPSI values. However, IPSI is unable to explain why, in some cases, a non-IPR EMF isomer is more stable than an IPR one, because comparisons can be performed only among isomers with the same number of APPs.

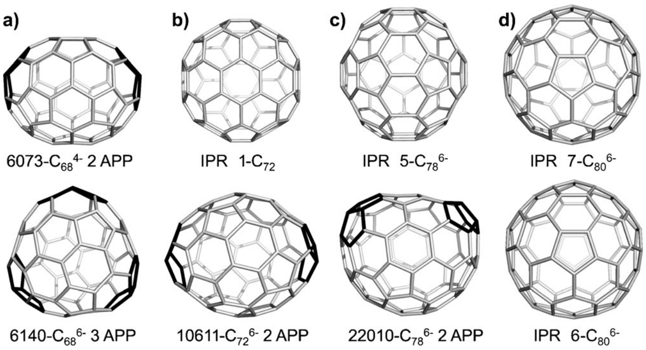

Figure 1. The most stable isomers of: a) C_{68}^{4-} and C_{68}^{6-}, b) C_{72} and C_{72}^{6-}, c) C_{78}^{6-}, and d) C_{80}^{6-}.

The driving force behind IPSI is that, in principle, by maximizing the separation among the negatively charged pentagons, their Coulomb repulsion would be minimized.[11] Surprisingly, we have found that this notion turns out to be incorrect: calculation of the Coulomb repulsion between the 12 pentagon rings (using Eq. S6 in the Supporting Information) indicates that the most stable cages are not those that minimize the electrostatic repulsion among the 5-MRs in the cage. As shown in Figure 2a, the IPR C_{72}^{6-} isomer is the one

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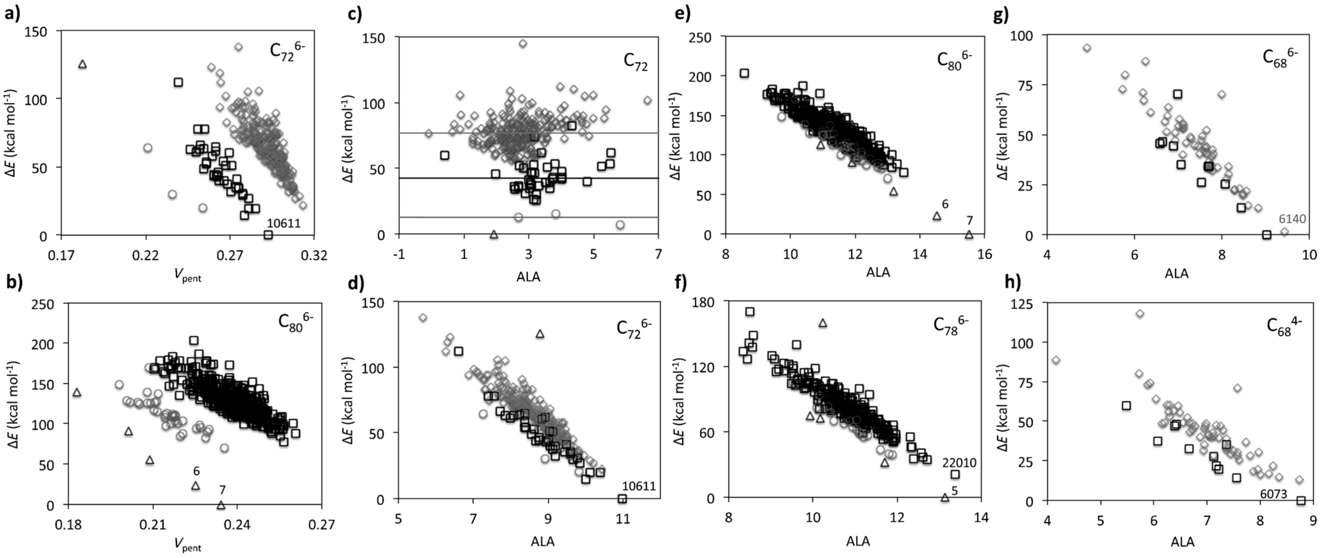

Figure 2. Relative stability of IPR and non-IPR a) C_{72}^{6-} and b) C_{80}^{6-} isomers with 1–3 APPs versus the total coulombic repulsion between the 12 pentagons (calculated using Eq. S6). Relative stability of IPR and non-IPR with 1–3 APPs isomers of c) C_{72}; d) C_{72}^{6-}; e) C_{80}^{6-}, f) C_{78}^{6-}, g) C_{68}^{6-} and h) C_{68}^{4-} with respect to the ALA index. IPR (△), non-IPR 1 APP (○), non-IPR 2 APPs (□), non-IPR 3 APPs (◇). The lines in (c) indicate the relative average energies with respect to the IPR case for each isomeric type. Isomers experimentally observed in EMFs are indicated with their corresponding number (Figure 3 and Table S1).

that has the lowest Coulombic repulsion energy among their pentagon rings. However, the C_{72}^{6-} IPR isomer is not the most stable. The energetically most favored hexaanionic C_{72} cage is isomer 10611, a non-IPR isomer with two APPs (Figure 1 b). Moreover, 10611-C_{72}^{6-} is not the one with the lowest 5-MRs Coulomb repulsion among all of the isomers, but just the opposite (Figure 2 a). The same situation is found for the C_{80} hexaanion (Figure 2 b).

Consequently, the choice of the most suitable EMF cage is not governed by a minimal Coulomb repulsion among 5-MRs. Given the relevance of aromaticity in charged cages,[8b] we decided to investigate the possible role played by aromaticity in determining the most suitable cages for EMFs. To this end, we defined the additive local aromaticity (ALA) index as the sum of the local aromaticities of all rings in the cage:

$$\mathrm{ALA} = \sum_{i=1}^{n} A_i \tag{1}$$

where A_i is the local aromaticity of ring i, and n is the number of rings in the fullerene, including both 5- and 6-MRs (see the Supporting Information).

We have chosen here C_{72} as example because it has only one IPR isomer and a reasonable number of non-IPR APP1, APP2, and APP3 (APP$n = n$ adjacent pentagon pairs). Figure 2 c,d show a plot of the relative stabilities of neutral and hexaanionic C_{72} isomers, respectively. The graph for the neutral C_{72} isomer (Figure 2 c) is simply a confirmation of the IPR and PAPR rules.[2,3] The lines in Figure 2 c indicate the relative average energies with respect to the IPR case for each isomeric type. As expected from the IPR and PAPR rules, the stability of the different isomer types for neutral fullerene cages decreases as the number of APPs increases. The IPR rule is thus perfectly fulfilled. Moreover, the local aromaticity of the rings plays no role in the final stability of the fullerene isomers. Hence, aromaticity in these neutral species is not relevant, as far as their stabilization is concerned.

When a metallic cluster is encapsulated inside a fullerene, the IPR rule is no longer fulfilled. For example, in 2003, Shinohara and co-workers determined that $La_2^{6+}@C_{72}^{6-}$ possesses the 10611-C_{72} isomeric cage, which has two APPs (see Figure 1 b).[15] The main question that arises is: Why is the non-IPR 10611-C_{72}^{6-} isomer the preferred cage to host La_2? The answer is given in Figure 2 d, where we show the correlation between relative energies and the ALA index obtained for the IPR and non-IPR APP1, APP2, and APP3 isomers of C_{72}^{6-}. Our calculations indicate that the 10611-C_{72} cage is the most stable, and moreover, it is the most aromatic among all of the IPR and non-IPR isomers with one, two, or three APPs (out of 269 isomers in total).

Thus, we have shown that the maximum aromaticity criterion (MARC) is the key concept for understanding why the IPR rule can be violated in the particular case of $La_2@C_{72}$, and to rationalize where the extra stability of these non-IPR structures comes from. Furthermore, we have shown that, by using the ALA index, one can directly compare the stability of all isomers for a given fullerene C_{2n}, independently of the isomer type (IPR, non-IPR) or the number of APPs. This is in contrast to what can be done with the IPSI index, which requires separately treating IPR and non-IPR isomers. However, does the ALA vs. ΔE correlation hold for all EMFs synthesized to date?

We find many instances in the literature where the most suitable fullerene cage to host a metallic cluster is an IPR isomer. For example, this is the case for C_{80}^{6-}, which includes the $Sc_3N@I_h$-C_{80} EMF, the third most abundant fullerene after C_{60} and C_{70}.[16] C_{80}-based EMFs synthesized to date are either the 7-I_h or the 6-D_{5h} IPR isomers (Figure 1 d). As shown in

Figure 2e, the selected 7-I_h and 6-D_{5h} cages are the two most stable hexaanions, and also the two most aromatic isomers. Thus, MARC holds not only when the most favored isomers are non-IPR, but also for an IPR-based EMF.

Examples also exist where both IPR and non-IPR isomers are found experimentally for a given cage. One of the most studied examples is the X@C_{78} EMF.[8a,17] As can be seen in Figure 2f, the most aromatic C_{78}^{6-} isomers are the IPR isomer 5 and the non-IPR APP2 22010, which are also those that experimentally encapsulate the metallic cluster inside. The final preference for one of the two isomers (Figure 1c) depends on the fullerene strain energy caused by the encapsulated metallic cluster.[17b] This is why the 22010-C_{78}^{6-} isomer is preferred for larger metallic clusters such as Y_3N and Gd_3N. The IPR isomer 5 is instead preferred for the smaller clusters (Sc_3N).

Depending on the nature of the metallic cluster, the formal charge transfer to the fullerene can be different and may lead to dissimilar isomers for EMF formation. For example, it is known that $Sc_2C_2^{4+}$@C_{68}^{4-} corresponds to the non-IPR 6073 isomer with two APPs,[18] whereas the Sc_3N^{6+}@C_{68}^{6-} structure is assigned to the 6140 non-IPR isomer with three APPs (Figure 1a).[19] The different hosting cages can be explained again by the MARC, as shown in Figure 2g and 2h. The ALA index indicates that isomers 6073 and 6140 are the most aromatic tetra- and hexaanionic isomers, respectively, among all possible C_{68} isomers. Thus, MARC can also predict the different hosting cages with metallic clusters that formally transfer a different number of electrons.

To fully validate our ALA criterion, we have carried out a systematic study including all of the most common C_{2n} ($2n=66$–104) EMFs reported to date (Figure 3; see also Table S1, and ΔE vs. ALA in Figure S4). We have explored both IPR and non-IPR cages in their anionic form, depending on the formal electron transfer from the metallic cluster to the fullerene. The local aromaticity is not only a very good indicator for the relative stability of isomers in small C_{2n} ($2n=66$–78) EMFs, but also for heavier ones (C_{100} or C_{104}).

It should be emphasized that ALA predictions are excellent, even in those cases where different EMF isomers are experimentally synthetized for one metallic cluster. This is the case for Er_2^{6+}@C_{82}^{6-}, which has been characterized to be the 6, 8, or 9 IPR C_{82} isomer.[20] As shown in Figure 3 (see also Table S1), the 6, 8, and 9 isomers of C_{82}^{6-} are among the most aromatic, with isomer 8 being the most aromatic of all.

The worst correlations between the stabilities and ALA are those cases where the formal charge transfer to the fullerene is low, for example, for the C_{94}^{2-} case. When the formal charge transfer increases, local aromaticity gains more importance for determining the total energy of the systems, and then the correlations are strongly improved (see Figure S2 for C_{72}^{m-}, where $m=0, 2, 4, 6$).

In conclusion, the high success of the ALA predictions points out that cage aromaticity is the most important stabilizing factor in the process of EMF formation. Basically, there is an interplay between strain energy and aromaticity. In neutral empty fullerenes, reducing strain energy is the main factor for determining the stability of the isomeric carbon cages. This is reflected in the IPR rule. On the contrary, in highly charged fullerenes or EMFs, maximizing the total aromaticity is the main stabilizing force, and this is translated into the maximum aromaticity rule. Our ALA predictions offer a rational explanation for the breakdown of the IPR rule in EMFs: the most stable anionic fullerene isomer is the one whose total aromaticity is maximized. This simple criterion

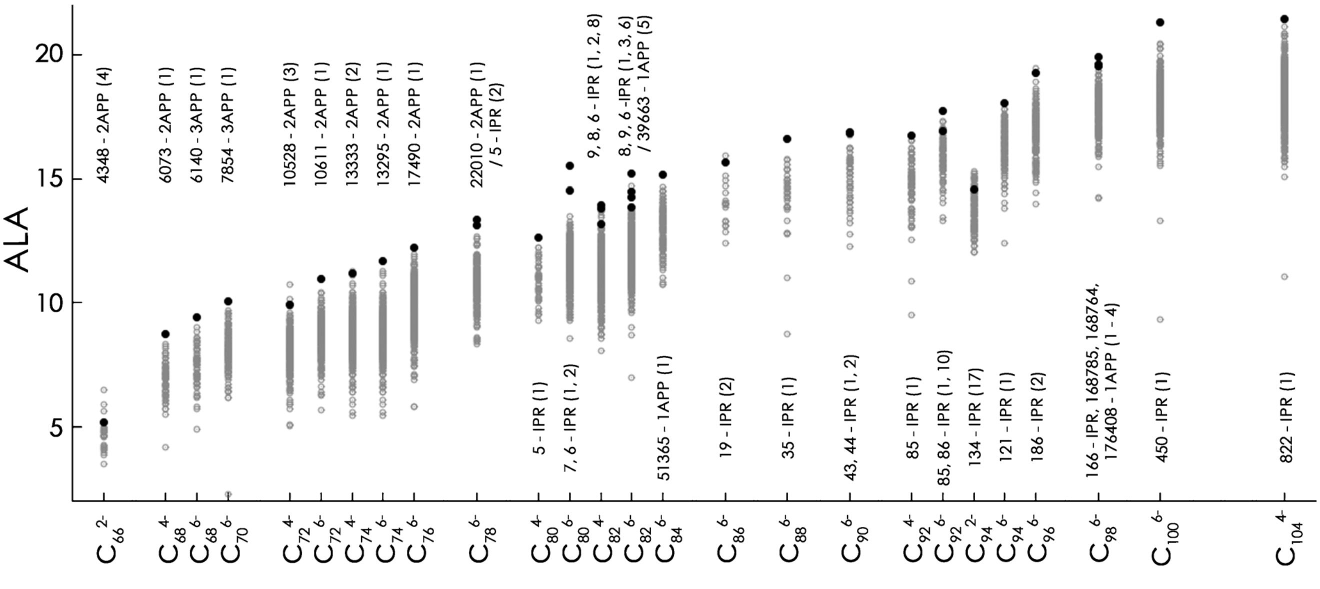

Figure 3. Classification in terms of the ALA index of the anionic IPR and non-IPR fullerene isomers with 1—3 APPs for the most common C_{2n} ($2n=66$–104) EMFs reported to date (Table S1). Isomers experimentally observed are marked using black dots, and their corresponding isomer numbers are indicated. The ALA prediction ordering for the experimentally observed isomers are given in parentheses. Figure S4 contains the ΔE vs. ALA data for all systems.

allows us to directly compare IPR and non-IPR anionic isomers regardless of the number of APPs they have. Hence, we are now able to justify the experimental formation of non-IPR or IPR EMFs, always using the same criteria: the most aromatic anionic isomer leads to the most stable EMF.

Experimental Section

Methods: The local aromaticity of each ring (A_i) can be computed using different aromaticity indices.[21] Herein, owing to the large number of isomers to compute (ca. 10300), we have chosen the low-computational-cost HOMA index,[22] which is calculated from the optimized geometries obtained with the Austin model 1 (AM1)[23] method (see the Methods section in the Supporting Information). To check our results, DFT optimizations (BP86/DZP)[24] and electronic multicenter index[25] calculations have also been performed for comparison, and confirmed the observed trends (see the Supporting Information).

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