The Revival of Fullerenes?

by Nazario Martín

Fullerenes—and in particular the C_{60} molecule, the first and most abundant carbon molecular allotrope with a soccer-ball shape—were first reported in a seminal paper by H. W. Kroto, R. F. Curl, and the late R. E. Smalley in 1985,[1] thus differentiating its properties from the well-known reticular allotropes graphite and diamond. Soon afterwards, carbon nanotubes (CNTs), the hollow cylindrical multiple and single wall carbon nanotubes, were discovered (in 1991) by S. Iijima;[2] and most recently, A. Geim and K. Novoselov reported the isolation of the first graphene, the one atom-thick flat sheets of carbon.[3] Since then, a large number of studies have been dedicated to these new and intriguing nanoforms of carbon (Fig. 1).

The variety of carbon nanoforms is significantly larger than the aforementioned species and other carbon nanoforms such as nanohorns, nano-onions, peepods, nanotorus, nanobuds, nanocups, etc. are only some of the less-known possible presentations of carbon whose properties and chemical reactivity are nowadays scarcely known.[4]

The main interest in the new nanoforms of carbon stems from the excitement in realizing and testing their unique mechanical, optical, and electronic properties in a wide variety of applications. In particular, the most recent single wall carbon nanotubes (SWCNTs), as well as pristine graphene (G) or its oxidized form (GO), have received great attention in the scientific community due to the expectations of these materials for practical purposes.

The interest and excitement of 1D SWCNTs, and 2D G and GO for a variety of applications must not obscure the fact that there still is considerable interest on fullerenes from both fundamental and practical viewpoints. Actually, the chemical reactivity of fullerenes has been used as a benchmark for the study of the reactivity in CNTs, G, and GO.

Despite the large number of scientific papers devoted to fullerenes, there are many important chemical aspects that still have not properly been addressed by the scientific community. Furthermore, there are important new possibilities where fullerenes can play a fundamental role either for a better understanding of basic scientific aspects or/and in the search for practical purposes. In this article, some representative examples studied in our group at the Complutense University and IMDEA-Nanoscience Institute in Madrid will illustrate the current unabated interest of fullerenes to address important questions in different scientific areas, thus renewing the expectations for these hitherto not well-exploited carbon allotropes.

Our recent results in a variety of topics not previously addressed or scarcely studied will be shown, namely: the facile synthesis of chiral fullerenes through efficient asymmetric catalysis, the search for supramolecular highly efficient concave receptors for hosting convex fullerenes, the use of fullerenes as new alligators for the study of molecular wires at the nanoscale, and some recent advances in the use of fullerenes for biomedical applications. Whereas the first two aspects fall under basic covalent and supramolecular research, respectively, the remaining two topics refer to studies in materials science and bio-medical applications. Needless to say that the following results were carried out in an interdisciplinary way and, therefore, they have required the participation of different scientific groups with diverse expertise.

Chiral Fullerenes by Asymmetric Synthesis

The large number of papers, reviews, and books written in the last two decades on fullerenes as molecular carbon allotropes give an idea of the unabated interest on these spherical molecules. Although nowadays there is a deep understanding of the chemical reactivity of fullerenes, the fine control of some fundamental aspects such as stereoselectivity and chirality are issues of paramount importance which, however, still remain to be properly addressed.[5]

Chirality is a fundamental concept in chemistry and life which is among the most important scientific and technological
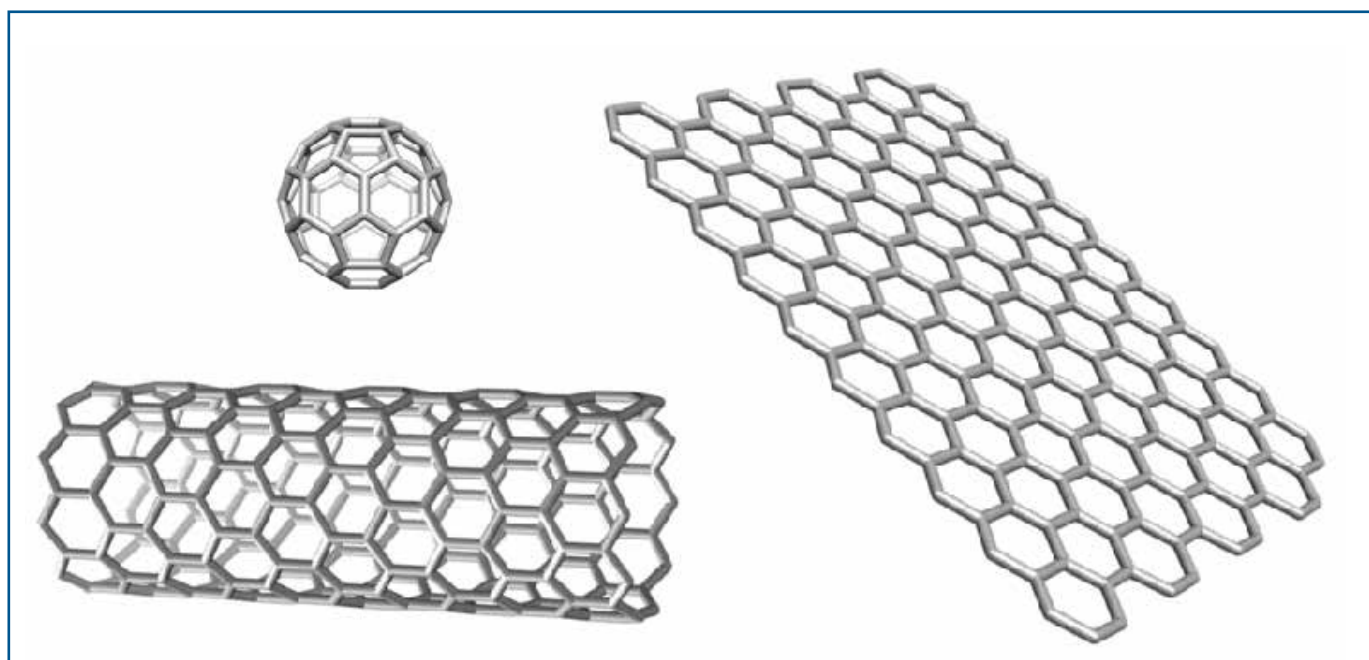
FIG. 1. *Chemical structures of [60]fullerene, single-wall carbon nanotubes (SWCNTs), and graphene.*

aspects in modern industry with important economic impact in, for example, pharmaceutical companies. In this regard, how chirality modifies the electronic properties of the carbon nanoforms is still an open question with important fundamental and technological interest. A chiral molecule has a non-superimposable mirror image. Therefore, a chiral molecule has two enantiomers or optical isomers that are mirror images. The interest of the enantiomers is based in the fact that they can exhibit different chemical reactivity and biological properties. However, despite this being a fundamental scientific issue, the preparation of chiral fullerenes has not been properly addressed so far.

A major breakthrough occurred, however, with the introduction of asymmetric metal catalysis to induce chirality onto the non-coordinating molecule of [60]fullerene. Thus, the first asymmetric catalysis on fullerenes was carried out on the 1,3-dipolar cycloaddition reaction of metal catalyzed azomethyne ylides to [60]fullerene in the presence of chiral ligands, giving rise to chiral pyrrolidino[3,4:1,2][60]fullerenes with complete control of the stereochemical outcome.[6]

The suitable combination of metal salts and chiral ligands has allowed the diastereoselective cycloaddition of N-metalated azomethine ylides (AMY) toward the *trans* or *cis* 2-alkoxycarbonyl 5-aryl pyrrolidino[3,4:1,2][60]fullerenes. Furthermore, the (R)-Fesulphos chiral ligand along with Cu(AcO)$_2$ directed the enantioselectivity to the (2S,5S)-cis adduct, whereas the (−) -1,2-bis((2R, 5R)-2,5-diphenylphospholano)ethane silver acetate complex (Ag(I)/(−)BPE) switched the cycloaddition toward the opposite (2R,5R)-cis enantiomer. More recently an enantiodivergent synthesis for the trans diastereoisomer with excellent ee values has also been achieved.[7] Moreover, due to the growing interest of higher fullerenes, this methodology has also been successfully extended to higher fullerenes, namely C$_{70}$,[8] as well as to metallofullerenes, namely La@C$_{72}$(C$_6$H$_3$Cl$_2$).[9] The high degree of stereocontrol achieved demonstrates that this methodology is able to face different levels of selectivity and stereocontrol, affording either the *cis* or *trans* adducts at will with excellent enantiomeric excesses (Fig. 2).

The aforementioned results pave the way to the synthesis of very useful fulleropyrrolidines, probably the most common and versatile fullerene derivatives, with complete control of their stereochemistry, thus broadening the scope of the use of chiral fullerenes for biomedical and materials science applications.

Supramolecular Highly Efficient Concave Receptors for Hosting Convex Fullerenes

The construction of versatile carbon-based nanosized supramolecular electron donor–acceptor systems is among the major objectives in our research group, and to this aim we have studied the combination of TTFs and π-extended TTFs (exTTFs) with different carbon nanostructures, such as fullerenes, carbon nanotubes and graphene. Tetrathiafulvalene (TTF) is a well-known electron donor molecule that has been exploited to construct a variety of molecular devices, including photo and electroactive donor–acceptor dyads and triads, organic field-effect transistors, cation sensors, and bistable molecular shuttles and catenanes.[10] Its π-extended analogues—in which the 1,3-dithiole rings are covalently connected to a π-conjugated core—have mainly been exploited as electron donor fragments in covalently linked donor–
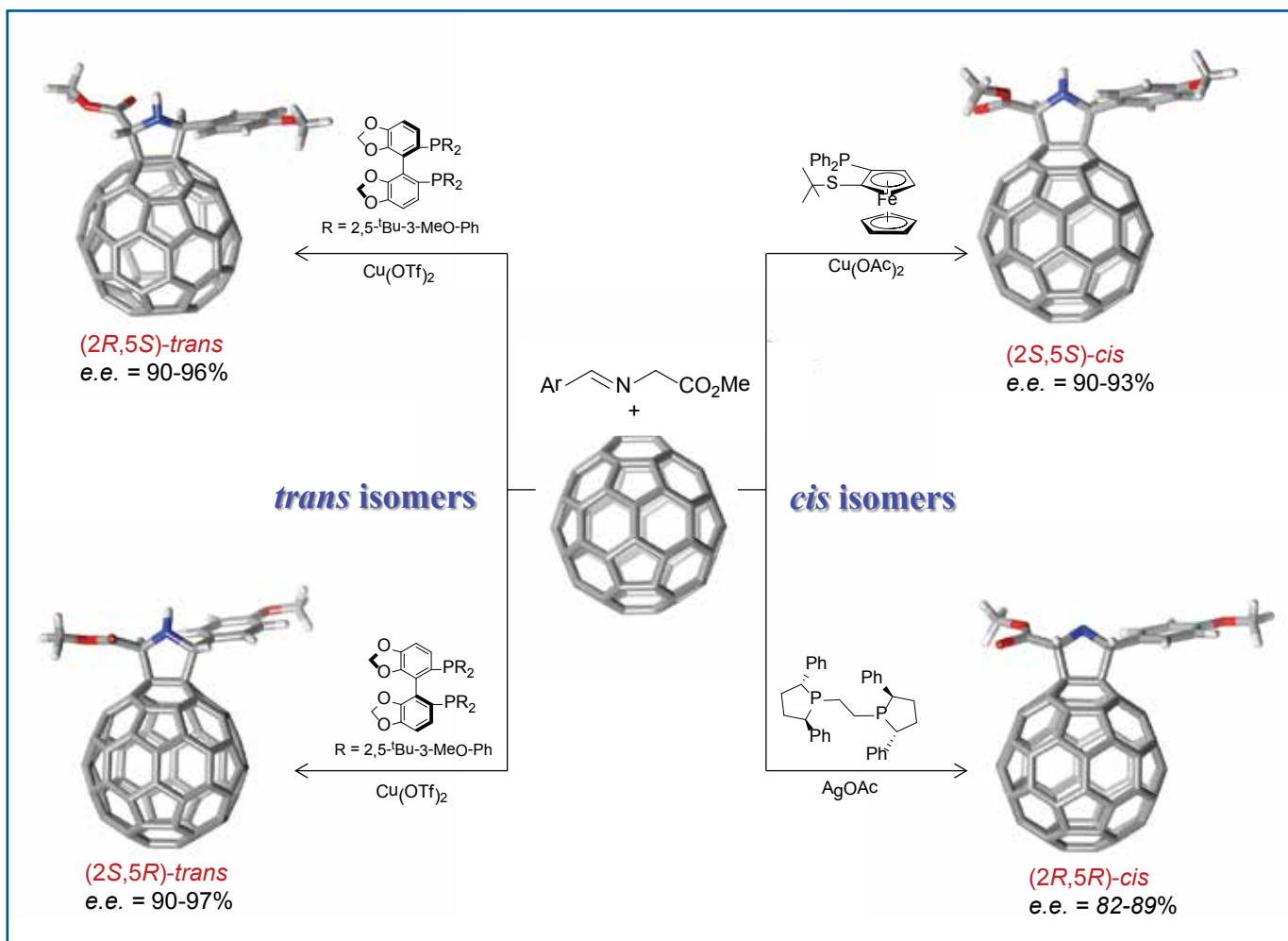

FIG. 2. *Asymmetric synthesis of fulleropyrrolidines with complete control of the stereoselectivity.*

acceptor conjugates.[11] In contrast, while the supramolecular chemistry of TTF is nowadays a well-trodden path, that of its π-extended analogues has remained virtually unexplored.

Some years ago, we reported that the shape complementarity between the concave aromatic face of 2-[9-(1,3-dithiol-2-ylidene)-anthracen-10(9H)-ylidene]-1,3-dithiole (exTTF) and the convex surface of fullerenes leads to large and positive non-covalent interactions. Indeed, DFT calculations predict positive binding energies of up to 7.0 kcal mol^{-1} between a single unit of exTTF and C_{60}. However, we have not observed conclusive experimental evidence of association in either UV-vis or NMR titrations. In the light of these results, we decided to follow different strategies to improve the complexing ability of our exTTF-based receptors, namely: (1) increasing the number of dithiole (*i.e.*, the electron rich character) and the number of benzene rings (*i.e.,* the surface available for van der Waals interactions) in the same molecule,[12] (2) increasing the number of exTTF units,[13] (3) use of the efficient macrocyclic effect[14] and (4) combination with other supramolecular interactions[15] (Fig. 3).

By using the aforementioned approaches, binding constants as high as 10^6-10^7 M^{-1} in aromatic solvents have been achieved, thus forming a new family of purely organic receptors for fullerenes with a relatively low degree of preorganization, ease synthetic preparation, and endowed with electroactive properties.[16] From a supramolecular chemistry point of view, very weak, non-directional dispersion interactions, namely van der Waals and π,π-interactions, account for the binding energy in these formed host-guest complexes. Since these forces depend directly on surface area, the shape complementarity between host and guest becomes critical. In this sense, distorted from planarity concave recognition motifs, as is the case of the exTTF molecules, seem ideally suited for the association of the convex fullerene surfaces.

A distinctive advantage of the simplicity of the tweezer-like design is that it can easily be adapted to construct more elaborate supramolecular assemblies at relatively low synthetic cost. For instance, in our group, based on the exTTF tweezers, linear[17] and hyperbranched[18] supramolecular polymers, covalent dendrimers capable of associating several units of C_{60}[19] and extended the design to associate and solubilize carbon nanotubes in aqueous solution[20] have been accomplished.

In this very brief account only a few general considerations regarding the design principles for the construction of this new family of hosts for fullerenes, has been provided.

Fullerenes for the Study of Molecular Nanowires

In the last decade, a wide variety of fullerenes covalently connected to an electron donor moiety through different bridges have been prepared in our group.[21]

Donor-Bridge-Acceptor (DBA) systems in which the bridge mediates the transport of charge between the donor and the acceptor, provide good models to study the electron transfer processes at the molecular level, thus mimicking the photosynthetic process. In these systems, the rate of charge transfer (CT) is a combination of a strongly distance-dependent tunneling mechanism (or superexchange) and a weakly distance-dependent incoherent transport (or hopping).[22]

A new and challenging procedure for determining the transport of charge through a bridge or molecule is connecting it to two metal electrodes and using the STM technique. The highly attractive concept of integrating individual molecules into electronic devices is drawn from ideas that molecules can behave as functional components in everyday devices. However, most of the methods that have been developed to measure single molecule conductance at room temperature cannot directly determine the number of molecules contained in individual molecular junctions. In this regard, it is accepted that these methods can result in an uncontrolled number of molecules bridging the two electrodes,[23] which is both inefficient and undesirable. The most effective solution is the *in situ* molecular break junction (BJ) technique, skillfully demonstrated by N. J. Tao and collaborators, in which the tip of a scanning tunneling microscope (STM) is driven in and out of contact with a substrate immersed in a solution of molecules.[24] As
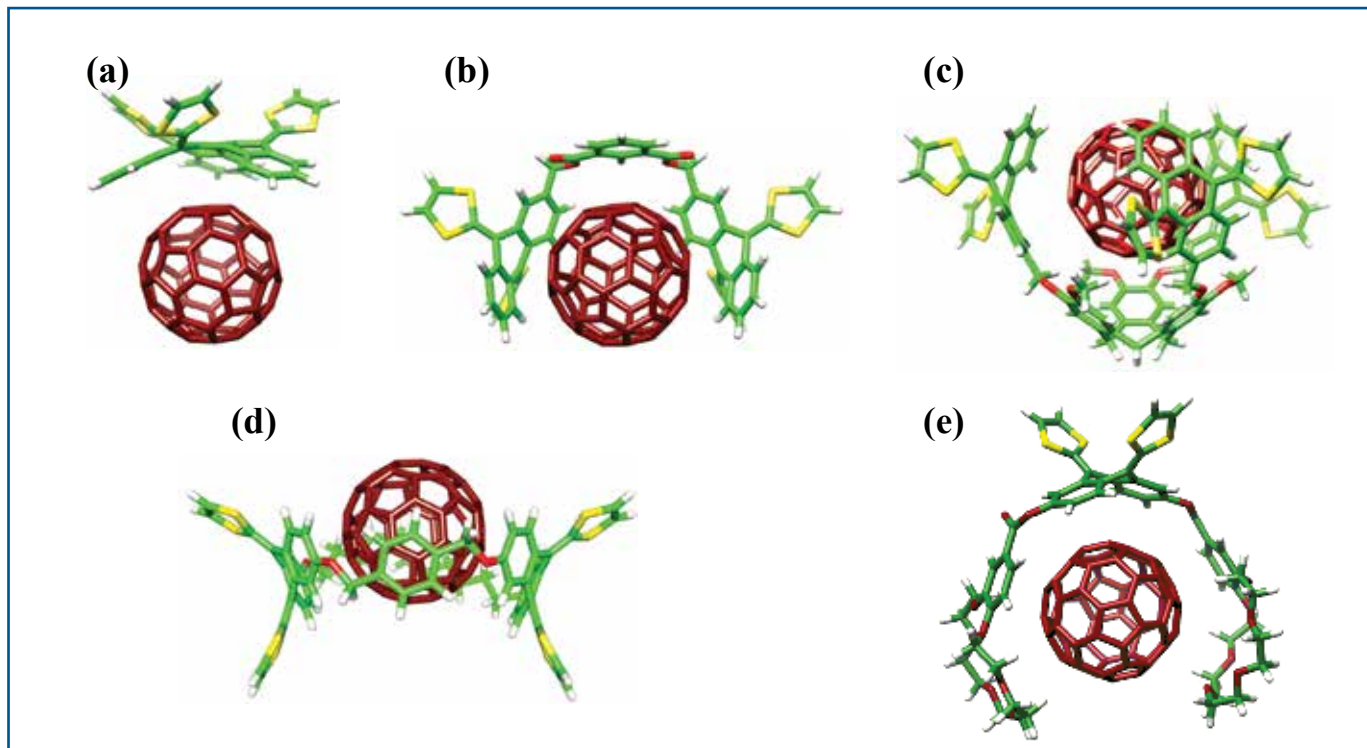
Fɪɢ. 3. *Representative examples of supramolecular exTTF/C_{60} complexes formed considering different strategies, namely: (a) increasing the number of aromatic and donor units; (b) using a two-exTTF molecular tweezers; (c) using three units of exTTF; (d) using the macrocyclic effect; and (e) using a combination of supramolecular interactions.*

a result of the variability in the number of molecules and their mode of anchoring, analyzing junction conductance alone cannot reveal the presence of just one molecule. This severely limits the potential for performing reliable direct electrical experiments on single molecule junctions.

At IMDEA-Nanoscience, we have addressed the issue of wiring just one molecule under ambient conditions by designing an experiment which allows visualization of discrete molecules using a room temperature STM operated in air. Visualization allows us to target precisely one molecule before wiring the molecule and measuring electron transport. The images we take directly before measurements give us the explicit information necessary to prove that only one molecule can be wired in the junction.[25] To achieve this level of control we have utilized a C_{60} capped bifluorene molecular wire (described as a fullerene-dumbbell). The C_{60} groups provide the clear visual signature for the molecule while also serving as effective anchoring groups (Fig. 4). We incorporated a fluorene spacer due to their excellent wire properties, while the central C-9 carbon atom possesses the potential to have functional groups added at a later date. We draw attention to the fact that, other than fluorene, many chemical groups can be incorporated between the C_{60} termini giving a wide scope for this method. Employing C_{60} as an anchoring group for molecular wires has recently been suggested with preliminary studies carried out using the standard break junction technique.[26]

The ease in substituting the chemical group at the center of the dumbbell is also highly advantageous. Combined with the experimental single molecule precision, the versatility of the C_{60}-dumbbell system will provide a straightforward approach to explore the role of chemical structure in relation to electron transport in one-molecule electrical junctions. Furthermore, we describe a new and straightforward protocol for unambiguously isolating a single organic molecule on a metal surface and wiring it inside a nanojunction under ambient conditions.

Our strategy employs C_{60} terminal groups that act as molecular beacons allowing molecules to be visualized and individually targeted on a gold surface using an STM. After isolating one molecule, we then use the C_{60} groups as alligator clips to wire it between the tip and surface. Once wired, we can monitor how the conductance of a purely one molecule junction evolves with time, stretch the molecule in the junction, observing characteristic current plateaus upon elongation, and also perform direct I-V spectroscopy. By characterizing and controlling the junction, we can draw stronger conclusions about the observed variation in molecular conductance than was previously possible.

Fullerenes for Biomedical Applications

Soon after the discovery of fullerenes, biochemical and biomedical applications of these carbon allotropes and, particularly C_{60}, attracted a lot of attention in the scientific community. Biological properties of fullerenes have been tested in different areas such as DNA photocleavage, neuroprotection, antibacterial and antiviral activity, antioxidation, and drug delivery, to name a few examples.[27]

Focusing on a particular case, carbohydrate derivatives of fullerenes, the so-called glycofullerenes, had been previously studied due to the combination of interesting biological properties.[28] However, most of these derivatives showed an amphiphilic character with the fullerene being the lipophilic part of the structures. Recently, in a collaborative work, we have shown that this amphiphilic character of sugar-fullerene conjugates can be avoided by synthesizing hexakis-adducts of [60]fullerene in which the C_{60} sphere is completely surrounded by sugar moieties in a *T*-symmetrical octahedral addition pattern.[29] In fact, some of the advantages of fullerenes in comparison to other carbon nanostructures are related to its 3D structure and the possibility to functionalize different positions of the C_{60} cage in a controlled fashion.[30] In this sense, fullerenes can

be considered very attractive spherical scaffolds for a multivalent presentation of ligands in a globular shape. In this regard, it is well-known that carbohydrate–protein interactions govern many biological processes including inflammation, embryogenesis, tumor progression and metastasis, pathogen infection, and so on.[31] These interactions are characterized by a high selectivity, metal ion dependence, and a low affinity compensated in nature by multivalency.

We have recently obtained glycofullerenes with 12 to 36 sugar moieties on the periphery of C_{60} by using a Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) methodology to click sugar residues to alkyne substituted Bingel-Hirsch hexakis-adducts.[32] These compounds are water soluble and interact with Concanavalin A in a multivalent manner, thus demonstrating the accessibility of these sugars on the fullerene surface to be recognized by a lectin. Moreover, these compounds show a good stability and low toxicity, which confirm the appropriate features to be used in cellular assays.

In a very recent study, we have proved that dendritic molecules decorated with carbohydrates (mannoses or fucoses) can be considered as good ligands to interact with and block the receptor DCSIGN which is a C-type lectin able to interact with glycoconjugates present on the surface of several pathogens, including viruses like HIV or Ebola (Fig. 5).[33] Due to the importance of this lectin in infection processes, the discovery of new compounds with an appropriate affinity for this receptor is of great interest.

In this work, we have shown for the first time the potential application of glycodendrofullerenes as antiviral agents. The antiviral activity of these compounds in an Ebola pseudotyped infection model were in the low micromolar range for fullerenes with 12 mannoses. Interestingly, the increase of valency in glycofullerenes induced a loss of antiviral effect. This could be probably related to steric congestion of sugars at the surface of the fullerene. One important factor to achieve high affinity in binding processes is not only the spatial

(a) **(b)** **(c)** **(d)**

Before   After
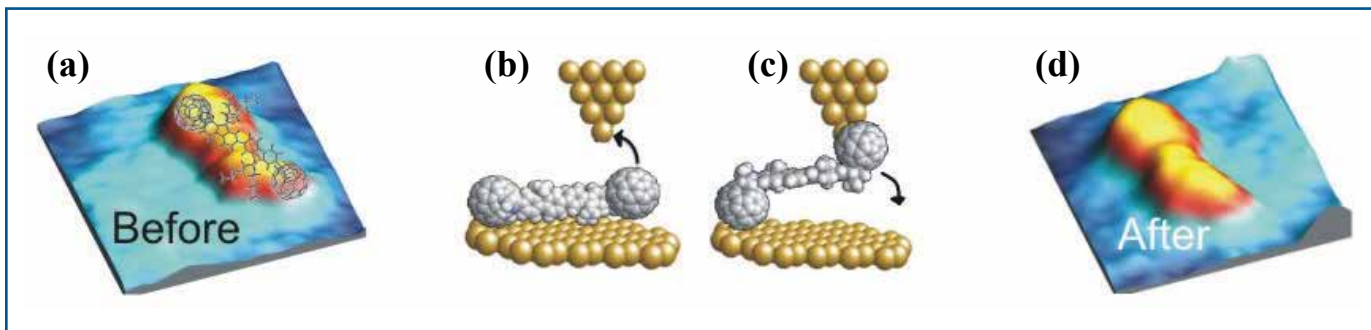
Fig. 4. *(a) 4 x 4 nm STM image of a single molecule of C_{60}-Fl$_2$-C_{60} taken at Ubias = 1.0 V and Iset = 0.5 nA before disabling the feedback loop and recording the conductance. A sketch of the molecule has been overlaid. (b) Schematic view of the molecule attaching to the tip and the surface. (c) STM image recorded after 60 seconds of recording the conductance with the tip above the molecule with identical conditions as in (a) and from the same starting coordinates.*
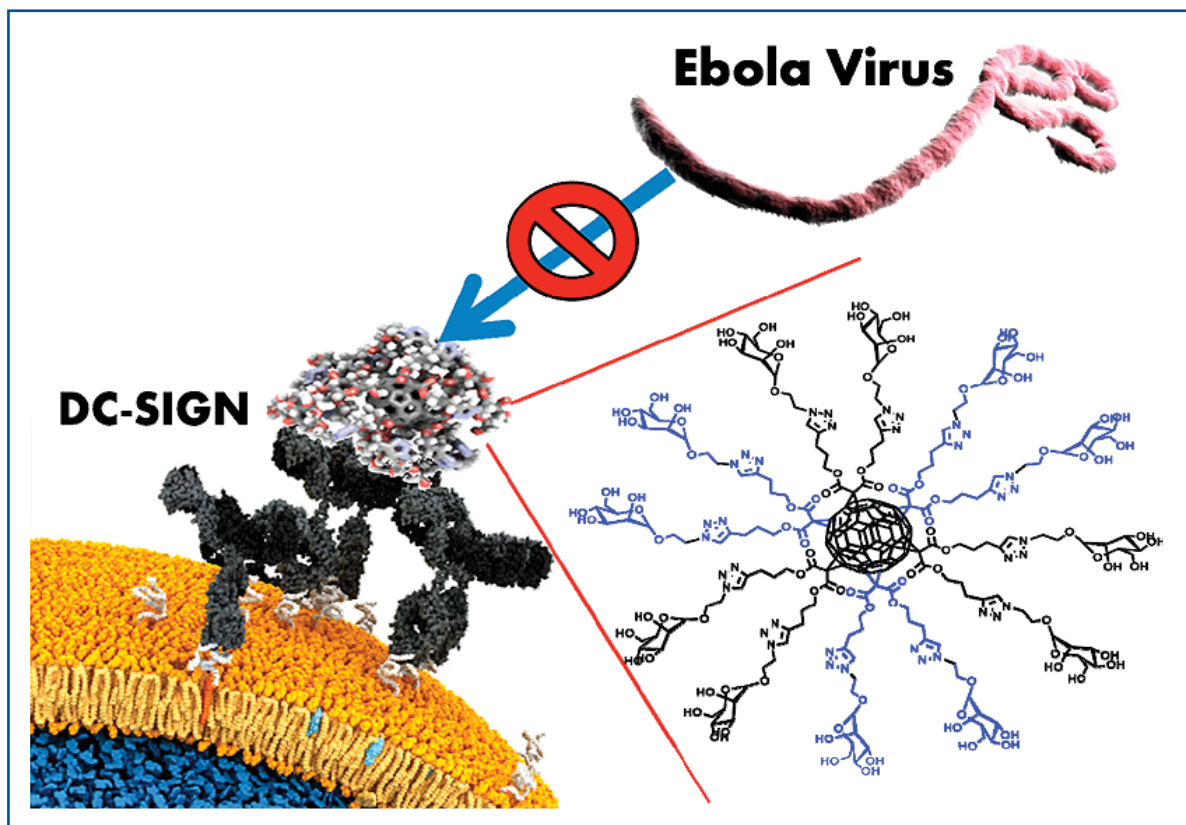
Fig. 5. *Glycofullerenes interact efficiently and block the receptor DCSIGN on the surface of the cell.*

presentation of the ligand but also the adequate accessibility of these ligands to interact with the corresponding receptor. Using a glycodendrofullerene showing the same valency but including a longer spacer, we have increased remarkably the inhibitory activity of these compounds with IC50 in the nanomolar range, probably due to a more efficient interaction with DC-SIGN. This result highlights the importance of combining an adequate scaffold to achieve the multivalency (the spherical fullerene) with the right ligand accessibility and flexibility. Based on these results, we can consider fullerenes as very attractive scaffold for a globular multivalent presentation of sugars. These promising results pave the way to new glycodendrofullerenes endowed with other biologically active molecules in the search for new applications.

Conclusions and Perspectives

The aforementioned results obtained in fundamental and basic research involving 3D fullerenes as well as applications in materials science and biomedical applications reveal the unabated interest that fullerenes exhibit for the scientific community. In this regard, the expectations raised by fullerenes since they were first prepared in multigram amounts in 1991 have not been satisfied so far. Although other more recent carbon nanoforms have been discovered, such as carbon nanotubes (single and multi-wall) and graphene, the spherical geometry of fullerenes as well as the fact they are discrete molecules formed by a precise number of carbon atoms gives a singularity to this allotrope of carbon showing singular properties. It is a better control on the chemistry of fullerenes that will lead to new properties and unprecedented applications.

Another important matter not discussed in this paper is related to those fullerenes that do not obey the "isolated pentagon rule" (IPR). It was Kroto who posited that the local strain in empty fullerenes increases with the number of bonds shared by two pentagons (pentalene unit), thus affording less-stable molecules (non-IPR fullerenes). Therefore, in fullerenes all pentagons must be surrounded by hexagons, thus forming the corannulene moiety. The resonance destabilization that results from the adjacent pentagons (8π electrons which do not satisfy the Hückel rule) and reduction of the π-orbital overlapping because of cage curvature, explains the lower stability of non-IPR fullerenes. In order to achieve non-IPR fullerenes, two different strategies have currently been developed to increase their stability, namely endohedral and exohedral derivatization.[34] In both approaches, the key issue to stabilize non-IPR fullerenes focus on how to release or decrease the strains of fused pentagons.

To sum up, there is currently a great interest in the search for the huge number of expected non-IPR fullerenes whose chemical reactivity and properties should be different from those known for IPR fullerenes and which represent a synthetic challenge for all those chemists involved in fullerene science. ■

About the Author

Nazario Martín is a professor at the University Complutense of Madrid and Vice-Director of the Institute for Advanced Studies in Nanoscience of Madrid (IMDEA-Nanoscience). He has published over 430 papers and co-edited six books and special journal issues related to carbon nanostructures. He has served as a member of the editorial boards of several well-known international journals. He is a fellow of The Royal Society of Chemistry. In 2006-2012 he was President of the Spanish Royal Society of Chemistry. He received the Dupont Prize of Science in 2007, and the Gold Medal and Research Award in 2012, the highest distinction given by the Spanish Royal Society of Chemistry. He received the Spanish national Jaime I Award for Basic Research 2012, and is the recipient of the Alexander von Humboldt Award and ECS Richard E. Smalley Research Award in 2013. He is the last chemist distinguished with the EuCheMS Lecture Award in 2012. He may be reached at nazmar@quim.ucm.es.

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References

1. H. W. Kroto, J. R. Heath, S. C. O'Brien, R. F. Curl, and R. E. Smalley, *Nature*, **318**, 162 (1985).
2. S. Iijima, *Nature*, **354**, 56 (1991).
3. K. S. Novoselov, A. K. Geim, S. V. Morozov, D. Jiang, Y. Zhang, S. V. Dubonos, I. V. Grigorieva, and A. A. Firsov, *Science*, **306**, 666 (2004).
4. J. L. Delgado, M. A. Herranz, and N. Martín, *J. Mater. Chem.*, **18**, 1417 (2008).
5. N. Martín, *Chem. Commun.* 2093 (2006); C. Thilgen and F. Diederich, *Chem. Rev.*, **106**, 5049 (2006).
6. S. Filippone, E. E. Maroto, A. Martín-Domenech, M. Suarez, and N. Martín, *Nat. Chem.*, **1**, 578 (2009).
7. E. E. Maroto, S. Filippone, A. Martín-Domenech, M. Suarez, and N. Martín, *J. Am. Chem. Soc.*, **134**, 12936 (2012).
8. E. E. Maroto, A. de Cózar, S. Filippone, Martín-Domenech, M. Suárez, F. P. Cossío, and N. Martín, *Angew. Chem. Int. Ed.*, **50**, 6060 (2011).
9. K. Sawai, Y. Takano, M. Izquierdo, S. Filippone, N. Martín, Z. Slanina, N. Mizorogi, M. Waelchli, T. Tsuchiya, T. Akasaka, and S. Nagase, *J. Am. Chem. Soc.*, **133**, 17746 (2011).
10. J. L. Segura and N. Martin, *Angew. Chem. Int. Ed.*, **40**, 1372 (2001).
11. F. G. Brunetti, J. L. López, C. Atienza, and N. Martín, *J. Mater. Chem.*, **22**, 4188 (2012).
12. E. M. Pérez, M. Sierra, L. Sánchez, M. R. Torres, R. Viruela, P. M. Viruela, E. Ortí, and N. Martín, *Angew. Chem., Int. Ed.*, **46**, 1847(2007).
13. E. M. Pérez, L. Sánchez, G. Fernández, and N. Martín, *J. Am. Chem. Soc.*, **128**, 7172 (2006); E. Huerta, H. Isla, E. M. Pérez, C. Bo, N. Martín, and J. de Mendoza, *J. Am. Chem. Soc.*, **132**, 5351 (2010).
14. H. Isla, M. Gallego, E. M. Pérez, R. Viruela, E. Ortí, and N. Martín, *J. Am. Chem. Soc.*, **132**, 1772 (2010); D. Canevet, M. Gallego, H. Isla, A. de Juan, E. M. Pérez, and N. Martín, *J. Am. Chem. Soc.*, **133**, 3184 (2011).
15. B. Grimm, J. Santos, B. M. Illescas, A. Muñoz, D. M. Guldi, and N. Martín, *J. Am. Chem. Soc.*, **132**, 17387 (2010).
16. For a review, see: D. Canevet, E. M. Pérez, N. Martín, *Angew. Chem. Int. Ed.*, **50**, 9248 (2011).
17. G. Fernández, E. M. Pérez, L. Sánchez, and N. Martín, *Angew. Chem. Int. Ed.*, **47**, 1094 (2008).
18. G. Fernández, E. M. Pérez, L. Sánchez, and N. Martín, *J. Am. Chem. Soc.*, **130**, 2410 (2008).
19. G. Fernández, L. Sánchez, E. M. Pérez, N. Martín, *J. Am. Chem. Soc.*, **130**, 10674 (2008).
20. C. Romero-Nieto, R. García, M. A. Herranz, C. Ehli, M. Ruppert, A. Hirsch, D. M. Guldi, and N. Martín, *J. Am. Chem. Soc.*, **134**, 9183 (2012).
21. N. Martín, L. Sánchez, M. A. Herranz, B. Illescas, and D. M. Guldi, *Acc. Chem. Res.*, **40**, 1015 (2007).
22. D. M. Guldi, B. M. Illescas, C. Atienza, M. Wielopolski, and N. Martín, *Chem. Soc. Rev.*, **38**, 1587 (2009).
23. C. Li, I. Pobelov, T. Wandlowski, A. Bagrets, A. Arnold, and F. J. Evers, *J. Am. Chem. Soc.*, **130**, 318 (2008).
24. B. Q. Xu and N. J. J. Tao, *Science*, **301**, 1221 (2003).
25. E. Leary, M. T. González, C. van der Pol, M. R. Bryce, S. Filippone, N. Martín, G. Rubio-Bollinger, and N. Agraït, *Nano Lett.*, **11**, 2236 (2011).
26. C. A. Martin, D. Ding, J. K. Sorensen, T. Bjornholm, J. M. van Ruitenbeek, and H. S. J. van der Zant, *J. Am. Chem. Soc.*, **130**, 13198 (2008).
27. D. Pantarotto, N. Tagmatarchis, A. Bianco, and M. Prato, *Mini-Rev. Med. Chem.*, **1**, 339 (2001); A. Bianco and T. Da Ros, in *Fullerenes: Principles and Applications*, 2nd ed.; F. L. De La Puente and J.-F. Nierengarten, Eds., Royal Society of Chemistry (London), pp 507−545 (2011).
28. H. Kato, A. Yashiro, A. Mizuno, Y. Nishida, K. Kobayashi, and K. Shinohara, *Bioorg. Med. Chem. Lett.*, **11**, 2935 (2001).
29. J. F. Nierengarten, J. Iehl, V. Oerthel, M. Holler, B. M. Illescas, A. Muñoz, N. Martín, J. Rojo, M. Sanchez-Navarro, S. Cecioni, S. Vidal, K. Buffet, M. Durka, and S. P. Vincent, *Chem. Commun.*, **46**, 3860 (2010).
30. A. Hirsch and O. Vostrowsky, *Eur. J. Org. Chem.*, 829 (2011).
31. A. Varki, *Glycobiology*, **3**, 97 (1993).
32. M. Sánchez-Navarro, A. Munoz, B. M. Illescas, J. Rojo, and N. Martín, *Chem. Eur. J.*, **17**, 766 (2011).
33. J. Luczkowiak, A. Muñoz, M. Sánchez-Navarro, R. Ribeiro-Viana, A. Ginieis, B. M. Illescas, N. Martín, R. Delgado, and J. Rojo, *Biomacromolecules*, **14**, 431 (2013).
34. T.-Z. Tan, J. Li, F. Zhu, X. Han, W.-S. Jiang, R.-B. Huang, Z. Zheng, Z.-Z. Qian, R.-T. Chen, Z.-J. Liao, S.-Y. Xie, X. Lu, and L.-S. Zheng, *Nat. Chem.*, **2**, 269 (2010), and references therein; N. Martín, *Angew. Chem. Int. Ed.*, **50**, 5431 (2011).