JOC*Note*

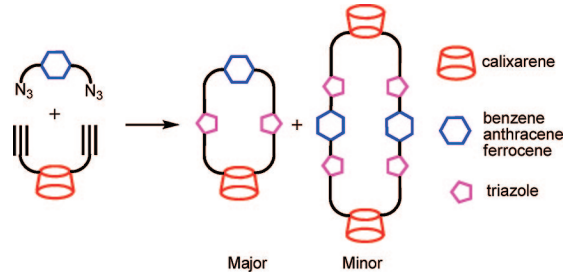
Synthesis of Calixarene-Based Cavitands and Nanotubes by Click Chemistry

Julia Morales-Sanfrutos, Mariano Ortega-Muñoz, Javier Lopez-Jaramillo, Fernando Hernandez-Mateo, and Francisco Santoyo-Gonzalez*

Instituto de Biotecnología, Departamento de Química Orgánica, Facultad de Ciencias, Campus Fuentenueva s/n, Universidad de Granada, Granada E-18071, Spain

fsantoyo@ugr.es

Received April 22, 2008



The synthesis of a variety of calixarene-based cavitands (capped and functional calixarenes) and calix nanotubes is easily performed in good to high yields using "click chemistry" methodology through the Cu(I)-catalyzed ligation of adequate bis-alkyne and bis-azide derivatives.

Supramolecular chemistry has developed into a major research field since the syntheses and complexation properties of the first crown ethers, cryptands, and spherands were published.[1] In particular, the design and synthesis of macrocyclic compounds having intramolecular cavities that can act as host systems for the accommodation of either a cationic, anionic, or neutral guest through noncovalent interactions have been extensively studied with the main purpose of understanding and mimicking the types of directed interactions prevalent in nature. For the preparation of these supramolecular systems, one common approach is the use of macrocycles possessing a special topology acting as scaffolds, which are further modeled by additional covalent synthesis giving rise to a variety of molecular architectures such as cyclophanes,[2] cavitands,[3] nanotubes,[4] or molecular cages.[5]

In this respect, structures such as calixarenes[6] are frequently used as platforms for accessing supramolecular systems. Different chemical modifications have been envisaged through manipulation on both the smaller (lower) and the larger (upper) rims of these cyclophanes. One approach has been the introduction of bulky functional groups either to the upper rim, by means of electrophilic substitution reactions, or to the lower rim, by means of Williamson-type OH modifications, which works well in the case of calix[4]arene[6a,b] but not in the case of calixarenes of higher order.[7] An alternative approach has been the construction of simple or multiple intramolecular bridges or the intermolecular attachment by bridging normally a pair of calixarenes or even three or more calixarenes. For the construction of these intra- or intermolecular bridges a wide variety of reagents of different size, shape, and functionalities have been used. In particular, the use of bis- and multifunctional aromatic molecules allowed the capping of the calixarene ring, giving rise to cavitands.[6b,c] Calixarene-based nanotubes[6b,c,8] have also been designed for the construction of molecular containers that have been applied for the entrapping of gaseous molecules or metal ions.

Continuing our interest in copper(I)-catalyzed azido-alkyne cycloaddition (CuAAC)[9] (the archetype of the click chemistry concept[10]) and its implementation in the construction of well-defined multivalent structures (neoglycoconjugates, glycoclusters, glycocyclodextrins, glycopolymers, and ferrocene-carbohydrate conjugates)[11,12] and materials (glyco-silicas),[13] we now focused our attention in the application of this synthetic methodology in the synthesis of calixarene-based supramolecular systems. The efficiency and user-friendliness of CuAAC has established this reaction as a universal synthetic tool that has been rapidly adopted by almost all areas of chemistry, enabling applications in drug discovery,[14] bioconjugation,[15] polymer and science materials[16] and related areas,[17] and also in supramolecular chemistry.[18] However,

(1) (a) *Comprehensive Supramolecular Chemistry*; Lehn, J. M., Atwood, J. L., Davies, J. E. D., McNicol, D. D., Vogtle, F., Eds.; Pergamon, Elsevier Science: Oxford, 1996.

(2) Thilgen, C.; Azov, V. A. Cyclophanes: Definition and Scope. In *Encyclopedia of Supramolecular Chemistry*; Atwood, J. L., Steed, J. W., Eds.; Marcel Dekker: New York, 2004; pp 414−423.

(3) Bruce, C. G. Cavitands. In *Encyclopedia of Supramolecular Chemistry*; Atwood, J. L., Steed, J. W., Eds.; Marcel Dekker: New York, 2004; pp 219−222.

(4) (a) Harada, A.; Li, J.; Kamachi, M. *Nature* **1993**, *364*, 516. (b) Ikeda, A.; Shinkai, S. *Chem. Commun.* **1994**, 2375. (d) Matthews, S. E.; Schmitt, P.; Felix, V.; Drew, M. G. B.; Beer, P. D. *J. Am. Chem. Soc.* **2002**, *124*, 1341. (e) Kim, S. K.; Sim, W.; Vicens, J.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44*, 805.

(5) (a) *Container Molecules and Their Guests*; Cram, D. J., Cram, J. M., Eds.; Royal Society of Chemistry: Cambridge, U.K., 1997. (c) Jeppesen, J. O.; Nielsen, M. B.; Becher, J. *Chem. Rev.* **2004**, *104*, 5115. (d) Jasat, A.; Sherman, J. C. *Chem. Rev.* **1999**, *99*, 931.

(6) (a) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: London, 1989. (b) Gutsche, C. D. *Calixarenes Revisited*; Royal Society of Chemistry: Cambridge, 1998. (c) *Calixarenes in Action*; Mandolini, L., Ungaro, R., Eds.; Imperial College Press: London, 2000. (d) Ikeda, A.; Shinkai, S. *Chem. Rev.* **1997**, *97*, 1713. (h) Gutsche, C. D. *Aldrichimica Acta* **1995**, *28*, 3. (e) Bohmer, V. *Angew. Chem., Int. Ed.* **1995**, *34*, 713.

(7) Otsuka, H.; Araki, K.; Matsumoto, H.; Harada, T.; Shinkai, S. *J. Org. Chem.* **1995**, *60*, 4862.

(8) (a) Zyryanov, G. V.; Rudkevich, D. M. *J. Am. Chem. Soc.* **2004**, *126*, 4264. (b) Kim, S.; Lee, J. K.; Lee, S. H.; Lim, M. S.; Lee, S. W.; Sim, W.; Kim, J. S. *J. Org. Chem.* **2004**, *69*, 2877. (c) Le Gac, S.; Zeng, S.; Reinaud, O.; Jabin, I. *J. Org. Chem.* **2005**, *70*, 1204. (d) Organo, V. G.; Leontiev, A. V.; Sgarlata, V.; Dias, H. V. R.; Rudkevich, D. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3043. (e) Organo, V. G.; Sgarlata, V.; Firouzbakht, F.; Rudkevich, D. M. *Chem. Eur. J.* **2007**, *13*, 4014.

(9) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596. (b) Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.

(10) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2005.

(11) Perez-Balderas, F.; Ortega-Muñoz, M.; Morales-Sanfrutos, J.; Hernandez-Mateo, F.; Calvo-Flores, F. G.; Calvo-Asin, J. A.; Isac-Garcia, J.; Santoyo-Gonzalez, F. *Org. Lett.* **2003**, *5*, 1951.

(12) (a) Calvo-Flores, F. G.; Isac-García, J.; Hernandez-Mateo, F.; Perez-Balderas, F.; Calvo-Asín, J. A.; Sanchez-Vaquero, E.; Santoyo-González, F. *Org. Lett.* **2000**, *2*, 2499. (b) Ortega-Muñoz, M.; Morales-Sanfrutos, J.; Perez-Balderas, F.; Hernandez-Mateo, F.; Giron-Gonzalez, M. D.; Sevillano-Tripero, N.; Salto-Gonzalez, R.; Santoyo-Gonzalez, F. *Org. Biomol. Chem.* **2007**, *5*, 2291.

(13) Ortega-Muñoz, M.; Lopez-Jaramillo, J.; Hernandez-Mateo, F.; Santoyo-Gonzalez, F. *Adv. Synth. Catal.* **2006**, *348*, 2410.

(14) (a) Kolb, H. C.; Sharpless, K. B. *Drug Discovery Today* **2003**, *8*, 1128. (b) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278.

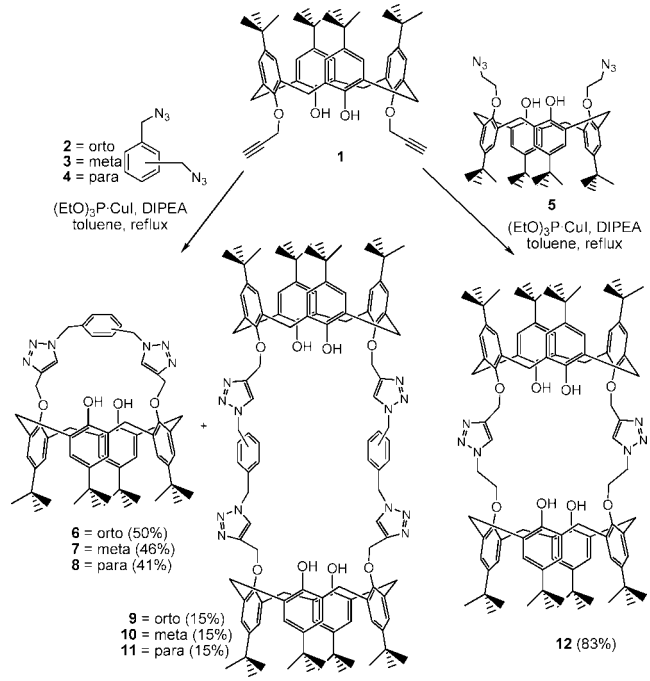
10.1021/jo801325c CCC: $40.75
Published on Web 08/22/2008

in the particular case of calixarenes click chemistry has been applied up to the present in limited cases to decorate both the upper and the lower rim of such macrocycles[19] but not for the assembly of these scaffolds in the construction of supramolecular motifs. This Note describes the validity of click chemistry for the synthesis of a variety of calixarene-based supramolecular structures.

Our strategy was based in the use of the dipropargylated calix[4]arene derivative **1**[20] as a clickable pivotal compound that should allow capping at its lower rim when reacted with diazide reagents, fixing the calix[4]arenes in a rigid cone conformation by means of 1,2,3-triazole rings acting as heterocyclic bridges. 1,2-, 1,3-, and 1,4-Bis-azidomethyl benzene (**2**, **3**, and **4**)[21] were reacted with **1** using $(EtO)_3P\cdot CuI$ as catalyst in refluxing toluene. The reactions were complete in short reaction times, and the capped calixarenes **6**−**8**, resulting from a 1:1 addition process (cyclomonomers), were isolated as the major products together with minor amounts of the tube-like doubly interbridged bis(calix[4]arenes) **9**−**11** that result in a 2:2 addition reaction (cyclodimers) (see Scheme 1). It was also proved that the tail-to-tail-linked doubled calix[4]arene **12** is easily formed by reacting **1** with the diazide calix[4]arene **5**.[12a] Compound **12** was obtained as the only detectable compound in 83% yield (see Scheme 1). This result is illustrative of the regioselectivity of the CuAAC as the free Cu(I) thermal ligation of such reagents, previously reported by us,[12a] gave a mixture of three regioisomers.

Considering the easy formation of discrete calixarene-based clicked structures, it was sought that calixarene-based functional cavitands with enhanced properties could be reached by reacting **1** with adequate diazide derivatives of fluorophores and electroactive compounds. In this respect, it should be mentioned that calixarene-derived fluorescent probes have been fashioned by appending fluorophores at both the upper and lower rim of these scaffolds.[22] In particular, Huang et al. reported a novel bridged fluorescent calix[4]arene bearing 1,8-diaminoantracene at the upper rim which exhibited selective anion recognition.[23] On the other hand, the grafting of one or more ferrocene moieties on both the lower and upper rims of calixarene frameworks has been reported, and their electrochemical properties and analytical

SCHEME 1. Synthesis of Capped and Bis-calixarenes



applications as ionophores have been described.[24] In addition, CuAAC has previously demonstrated its value for the preparation of a variety of ferrocene-containing molecules (chiral ferrocenes,[25] ferrocene-carbohydrate[26] and ferrocene-polysaccharide conjugates,[27] and ferrocene-containing polymers[28]) and some functional materials (ferrocene-modified silicon surfaces[29] and ferrocene-functionalized electrode surface[16]). To attain our goal, the azidomethyl anthracene and ferrocene derivatives **13**[30] and **14**[26] were selected to act as bridged reagents for the construction of sensing receptors with fluorescence and redox-active groups in their frameworks that can be potentially exploited for the detection of host−guest binding events. The CuAAC reaction of **1** with **13** and **14** under the same reaction conditions described above easily led to the diametrical 1,3-capped calix[4]arene cyclomonomers **15** and **16**, respectively (see Scheme 2). In the particular case of the ferrocenyl derivative **14**, the reaction also furnished the cyclodimer **17** as a nonstable minor product that was characterized through its ^{1}H NMR and MALDI-TOF mass spectra. The anthracenyl derivative **13** was also reacted with propargyl alcohol in order to get the bis-triazole derivative **18** (Scheme 3) to be used as a model compound in the fluorescence studies to be performed.

In these studies, the fluorescence spectra of compounds **15** and **18** in various solvents were registered. The individual spectrum is

(15) (a) Pieters, R. J.; Rijkers, D. T. S.; Liskamp, R. M. J. *QSAR Comb. Sci.* **2007**, *26*, 1181. (b) Dirks, A. J.; Cornelissen, J.; van Delft, F. L.; van Hest, J. C. M.; Nolte, R. J. M.; Rowan, A. E.; Rutjes, F. *QSAR Comb. Sci.* **2007**, *26*, 1200. (c) Salisbury, C. M.; Cravatt, B. F. *QSAR Comb. Sci.* **2007**, *26*, 1229. (d) Angell, Y. L.; Burgess, K. *Chem. Soc. Rev.* **2007**, *36*, 1674. (e) Baskin, J. M.; Bertozzi, C. R. *QSAR Comb. Sci.* **2007**, *26*, 1211. (f) Lutz, J. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 2182.

(16) (a) Binder, W. H.; Kluger, C. *Curr. Org. Chem.* **2006**, *10*, 1791. (b) Nandivada, H.; Jiang, X. W.; Lahann, J. *Adv. Mater.* **2007**, *19*, 2197. (c) Lutz, J. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1018. (d) Fournier, D.; Hoogenboom, R.; Schubert, U. S. *Chem. Soc. Rev.* **2007**, *36*, 1369. (e) Golas, P. L.; Matyjaszewski, K. *QSAR Comb. Sci.* **2007**, *26*, 1116. (f) Devaraj, N. K.; Collman, J. P. *QSAR Comb. Sci.* **2007**, *26*, 1253.

(17) (a) Wu, P.; Fokin, V. V. *Aldrichimica Acta* **2007**, *40*, 7. (b) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249. (c) Kalesh, K. A.; Yang, P. Y.; Srinivasan, R.; Yao, S. Q. *QSAR Comb. Sci.* **2007**, *26*, 1135. (d) Santoyo-Gonzalez, F.; Hernandez-Mateo, F. *Top. Heterocycl. Chem.* **2007**, *7*, 133. (e) Lutz, J.-F.; Schlaad, H. *Polymer* **2008**, *49*, 817.

(18) (a) Miljanic, O. S.; Dichtel, W. R.; Aprahamian, I.; Rohde, R. D.; Agnew, H. D.; Heath, J. R.; Stoddart, J. F. *QSAR Comb. Sci.* **2007**, *26*, 1165. (b) Aprahamian, I.; Miljanic, O. S.; Dichtel, W. R.; Isoda, K.; Yasuda, T.; Kato, T.; Stoddart, J. F. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 1856. (c) Braunschweig, A. B.; Dichtel, W. R.; Miljanic, O. S.; Olson, M. A.; Spruell, J. M.; Khan, S. I.; Heath, J. R.; Stoddart, J. F. *Chem. Asian J.* **2007**, *2*, 634.

(19) (a) Ryu, E.-H.; Zhao, Y. *Org. Lett.* **2005**, *7*, 1035. (b) Dondoni, A.; Marra, A. *J. Org. Chem.* **2006**, *71*, 7546. (c) Bew, S. P.; Brimage, R. A.; L'Hermite, N.; Sharma, S. V. *Org. Lett.* **2007**, *9*, 3713.

(20) Collins, E. M.; McKervey, M. A.; Madigan, E.; Moran, M. B.; Owens, M.; Ferguson, G.; Harris, S. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3137.

(21) Abu-Orabi, S. T.; Harmon, R. E. *J. Chem. Eng. Data* **1986**, *31*, 379.

(22) Kim, J. S.; Quang, D. T. *Chem. Rev.* **2007**, *107*, 3780–3799.

(23) Miao, R.; Zheng, Q.-Y.; Chen, C.-F.; Huang, Z.-T. *Tetrahedron Lett.* **2005**, 2155.

(24) (a) Bodine, K. D.; Gin, D. Y.; Gin, M. S. *Org. Lett.* **2005**, *7*, 4479. (b) Evans, A. J.; Matthews, S. E.; Cowley, A. R.; Beer, P. D. *Dalton Trans.* **2003**, 4644. (c) Tomapatanaget, B.; Tuntulani, T. *Tetrahedron Lett.* **2001**, *42*, 8105. (d) Tomapatanaget, B.; Tuntulani, T.; Chailapakul, O. *Org. Lett.* **2003**, *5*, 1539. (e) Gale, P. A.; Chen, Z.; Drew, M. G. B.; Heath, J. A.; Beer, P. D. *Polyhedron* **1998**, *17*, 405.

(25) Fukuzawa, S.; Oki, H.; Hosaka, M.; Sugasawa, J.; Kikuchi, S. *Org. Lett.* **2007**, *9*, 5557.

(26) Casas-Solvas, J. M.; Vargas-Berenguel, A.; Capitan-Vallvey, L. F.; Santoyo-Gonzalez, F. *Org. Lett.* **2004**, *6*, 3687.

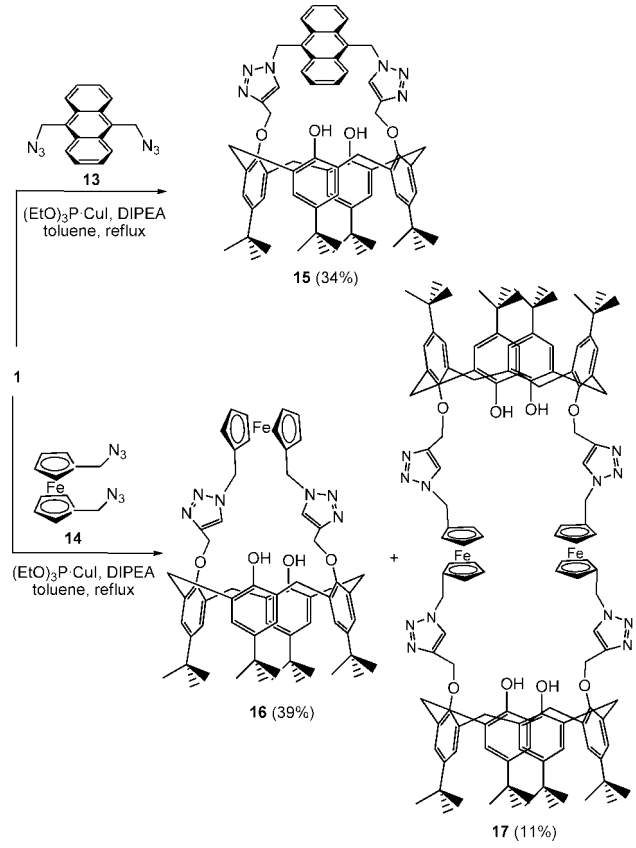
(27) Hasegawa, T.; Umeda, M.; Numata, M.; Li, C.; Bae, A.-H.; Fujisawa, T.; Haraguchi, S.; Sakurai, K.; Shinkai, S. *Carbohydr. Res.* **2005**, *341*, 35.

(28) Jim, C. K. W.; Qin, A.; Lam, J. W. Y.; Haeussler, M.; Tang, B. Z. *J. Inorg. Organomet. Polym. Mat.* **2007**, *17*, 289.

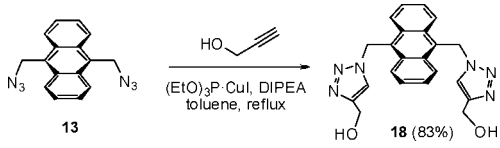
(29) Marrani, A. G.; Dalchiele, E. A.; Zanoni, R.; Decker, F.; Cattaruzza, F.; Bonifazi, D.; Prato, M. *Electrochim. Acta* **2008**, *53*, 3903.

(30) Grundberg, H. E.; Wendt, O. F.; Nilsson, U. J. *Tetrahedron Lett.* **2004**, *45*, 6083.

SCHEME 2. Synthesis of Anthracenyl and Ferrocenyl-calix[4]arenes



SCHEME 3



composed of a triple emission with peaks at around 407, 426, and 452 nm independently of the nature of solvent. However, in the case of **15** the fluorescence intensity is dependent on the nature of the solvent increasing in the order MeOH < CH_3CN < THF ≅ $CHCl_3$, whereas in the case of **18** only minor changes are detected. The emission maximum appears at 426 nm except in the case of CH_3CN in which this maximum corresponds to 452 nm. From this result, it can be concluded that the calixarene framework influences the fluorescence properties of compound **15**. To elucidate its host properties and prove its sensing capabilities, a comparative study in the emission spectral changes produced by the addition of a series of salts (TBABr, TBAI, LiBr, LiI and TBAHS) were next performed. These experiments indicate that the anionic part of the salt is the guest complexed by the calixarene-based host and also that the binding capability is dependent on the nature of that anion as the emission intensity at 452 nm is gradually increased when the TBABr, TBAI, LiBr and LiI concentration raise (being more pronounced in the case of iodine salts, Figure 1) but slightly decreased in the case of TBAHS. These results are in contrast with those observed by Huang et al. in the related anthracenyl calix[4]arene mentioned above[23] that showed a quenching in the anthracene fluorescence in the selective interaction with CH_3COO^- in CH_3CN. In addition, a quenching in the fluorescence of compound **18** was observed upon the addition of TBAI. This result suggests that the 1,2,3-triazole ring can play a role as an anion

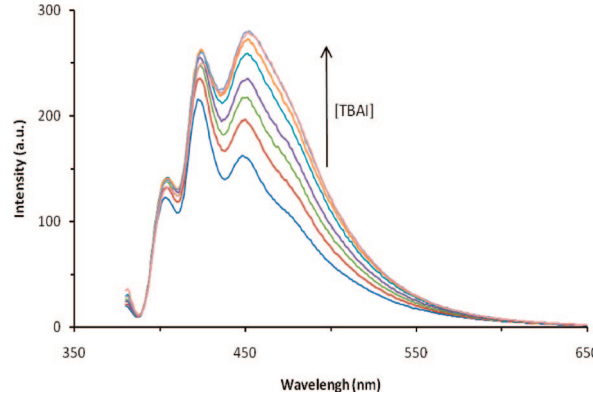


FIGURE 1. Fluorescence spectral changes of **15** upon the addition of TBAI; [**15**] = 100 μm, MeOH, temp = 20 °C, λ = 378 nm.

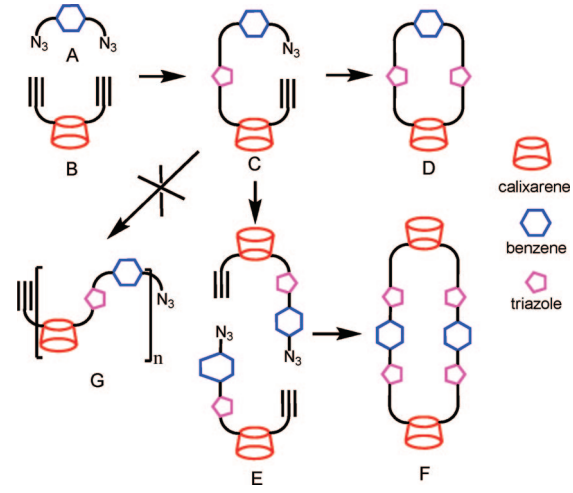


FIGURE 2. Different possible pathways in the CuACC of diazides with dialkynes.

binding motif in accordance with a recent report.[31] Nevertheless, the opposite behaviors observed for **15** and **18** also point to the idea that the calixarene framework should influence the anion binding. The assembly of our observations supports the capability of compound **15** to act as a fluoroionophore for halide recognition.

The electrochemical properties of the calixarene **16** were studied by cyclic voltammetry. The cyclic voltammogram showed reversible redox couples of ferrocene/ferricinium being also observed that the half-wave potential value ($E_{1/2}$) of the ferrocene core increases in compound **16** respecting to the ferrocene/methanol (0.539 versus 0.346). An increase of the $E_{1/2}$ value is generally associated with an electron-acceptor property of the substitutent.[32]

The results described above show that, in the studied cases, the CuAAC reactions of the dialkyne and diazide calixarene derivatives have a propensity for the formation of cyclic compounds through molecular connections formed by an interintramolecular tandem process leading to discrete molecular receptors with only minor formation of the corresponding dimerization compounds (Figure 2). This fact should be highlighted as the azide-alkyne cycloaddition of bifunctional alkyne and azide monomers has proved to be a useful methodology for the formation of ill-defined polymeric structures with 1,2,3-triazoles in the main chain through a step-growth polymerization process. In fact, nowadays click-chemistry is a well-established complementary tool for most of the major

(31) Kumar, A.; Pandey, P. S. *Org. Lett.* **2008**, *10*, 165, and references cited therein.

(32) (a) Mason, J. G.; Rosenblum, M. *J. Am. Chem. Soc.* **1960**, *82*, 4206. (b) Hall, D. W.; Russell, C. D. *J. Am. Chem. Soc.* **1967**, *89*, 2316.

synthetic polymerization techniques that allow control for the preparation of either linear polymer chains of diverse architectures or three-dimensional polymer networks.[16] Some relevant examples on the use of diazido aryl derivatives structurally related to compounds **2**−**4** have been reported by Reek et al.[33a] and Katrizzsky et al.[33b] In both cases, the exclusive high-yielding formation of linear polymers is efficiently achieved in polymerization reactions in which calixarenes are not involved. The absence of a polymerization process (structure G, Figure 2) in the reported cases herein can be tentatively ascribed to the conformational flexibility of the calixarene framework that after the first "click" (structure C, Figure 2) facilitates the approximation of the remaining clickable functions for the formation of cyclic monomer (1 + 1 addition, structure D in Figure 2) and cyclic dimer (2 + 2 addition, structure F in Figure 2) products through copper(I) organometallic intermediates. The formation of such intermediates has been postulated as a general mechanistic pathway in CuAAC by Finn et al.,[34] who studied the reaction of monoazides and monoalkynes with complementary conformationally constrained dialkynes and diazides in which the diazide **3** has been one of the substrates of choice. The results reported by these authors with those diazides suggest that the formation of the first triazole catalyzes the subsequent cycloaddition to yield the corresponding ditriazole derivatives.

The formation of those copper complexes can also be argued to explain the observed prevalence of cyclomonomers (compounds **6**−**8** and **15**−**16**, structure D in Figure 2) with respect to cyclodimers (compounds **9**−**11** and **17**, structure F in Figure 2) in the macrocyclization reactions of **1** with the diazides **2**−**4** and **14** that are formed in an almost constant 3:1 proportion in the reaction conditions used. This tendency is the opposite to that observed in numerous reported cases where the CuAAC of α,ω-functionalized substrates of diverse nature (carbohydrates, peptides, and others) led exclusively to cyclodimers.[35] This so-called "dimerization effect" has been explained by the formation of a dicopper intermediate in which two alkynes are involved in such a way that the azide units interact with the Cu atom that is not attached to the alkyne of the same substrate (structure E, Figure 2), opening a pathway that allows the larger entropy barriers needed to attain cyclic monomers to be overcome. Although this dimerization effect is not always applicable, in the particular case of polymers the synthesis of cyclic polymers has been achieved only when starting from clickable α,ω-hetero-heterodifunctional telechelic polymers by using high-dilution techniques, which avoid the intermolecular reactions, allowing the efficient head-to-tail ligation of such compounds and access to the corresponding monocyclic structures in high yields, which were previously unachievable by other coupling methods.[36] In our case, the favorable competition of the cyclomonomerization process is indicative of the preferred formation of intramolecular copper complexes after the first click ligation that can tentatively be explained by a proximity effect imposed by the grafting of the clickable functions onto the calixarene skeleton. In addition, the cumbersomeness of the calixarene framework should also preclude the formation of the corresponding intermolecular copper complexes that leads to cyclodimers (Figure 2). This hypothesis is clearly supported by the exclusive and high-yield formation of cyclomonomer **12** when two calixarenes are clicked such as in the case of the reaction of **1** and **5** regardless of the use of catalytic conditions, as described in the present study, or the use of thermal conditions, as previously reported by us.[12a] In fact, in this later case the formation of copper complexes cannot be argued in the formation of the triazole linkages as the corresponding polymers are not formed.

In summary, the modular preparation of calixarene-based supramolecular entities of diverse architectures (capped calixarenes, calix[4]arene tubes, and functional calixarenes) has been efficiently achieved by the click ligation of adequate bis-azides and bis-alkyne derivatives.

Experimental Section

Synthesis of Anthracenyl-calix[4]arenes 15. A solution of dialkyne **1** (220 mg, 0.30 mmol), diazide **13** (87 mg, 0.30 mmol), DIPEA (320 μL, 1.80 mmol), and the copper catalyst [$(EtO)_3P$·CuI] (33 mg, 0.09 mmol) in toluene (75 mL) was refluxed for 1 h. Evaporation of the solvent yields a crude that was purified by column chromatography (AcOEt−hexane 1:1) giving **15** (105 mg, 0.104 mmol 34%) as a solid: mp >250 °C (dec); IR (KBr) 3429, 1481, 1360, 1297, 1189, 1119, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.27 (m, 4 H, Ar antracene), 7.31 (m, 4 H, Ar antracene), 7.17 (s, 2 H, H-5 triazole), 6.99 (4 OH, Ar), 6.64 (s, 4 H, CH_2N), 6.53 (s, 4 H, Ar), 5.62 (s, 2 H, OH), 5.01 (s, 4 H, CH_2O), 3.75 (d, 4 H, J = 13.8 Hz, $ArCH_2Ar$), 3.11 (d, 4 H, J = 13.4 Hz, $ArCH_2Ar$), 1.31, 0.80 (2 s, 36 H, Me_3C); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 150.1, 147.1, 145.6, 141.8, 137.7, 130.5, 128.0, 127.9, 126.7, 125.5, 125.0, 123.5, 122.5, 70.8 (CH_2O), 46.3 (CH_2N), 33.9 (CMe_3), 31.8 (CMe_3), 31.5 ($ArCH_2Ar$), 30.9 (CMe_3); HRMS (FAB+) m/z calcd for $C_{66}H_{72}N_6O_4Na$ $[M + Na]^+$ 1035.5, found 1035.4.

Synthesis of Ferrocenyl-calix[4]arenes 16 and 17. A solution of dialkyne **1** (127 mg, 0.175 mmol), diazide **14** (52 mg, 0.175 mmol), DIPEA (187 μL, 1.05 mmol), and the copper catalyst [$(EtO)_3P$·CuI] (20 mg, 0.05 mmol) in toluene (75 mL) was refluxed for 1 h. Evaporation of the solvent yields a crude that was purified by column chromatography (AcOEt−hexane 2:1) giving **16** (70 mg, 0.069 mmol, 39%) as a solid: mp 198−200 °C; IR (KBr) 3430, 1484, 1363, 1300, 1207, 1046 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 2 H), 7.09 (s, 4 H), 7.01 (s, 2 H), 6.77 (s, 4 H), 5.22, 5.14 (2 s, 8 H), 4.33 (d, 4 H, J = 13.1 Hz), 4.12, 4.05 (2 s, 8 H), 3.37 (d, 4 H, J = 13.2 Hz,), 1.30, 091 (2 s, 36 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 149.8, 147.5, 145.0, 141.9, 132.3, 127.8, 125.7, 125.2, 123.2, 84.3, 70,7, 61.1, 49.2, 34.0, 33.9, 31.8, 31.5, 31.0; MS (MALDI-TOF) m/z calcd for $C_{62}Fe\ H_{72}N_6O_4Na$ 1043.485, found 1043.487. Eluted second was **17** (19 mg, 11%) as a nonstable amorphous solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.90(br s, 4 H), 7.54 (br s, 4 H), 7.02 (s, 8 H), 6.85 (s, 8 H), 5.57 (s, 4 H), 5.13 (2 s, 4 H), 4.51 (s, 8 H), 4.28 (s, 8 H), 4.15 (d, 8 H, J = 12.6 Hz), 1.25 (s, 36 H), 1.01 (s, 36 H); MS (MALDI-TOF) m/z calcd for $C_{124}Fe_2H_{144}N_{12}O_8Na$ 2063.982, found 2063.940.

Acknowledgment. We thank Dirección General de Investigación Científica ćnica for financial support (Project number CTQ2005-02219).

Supporting Information Available: General experimental methods, experimental procedures for preparation, and compound characterization data of **6**−**12**; copies of ^1H NMR, ^{13}C NMR, and MS spectra for compounds **6**−**12** and **15**−**18**; fluorescence spectra in different solvents and fluorescence titration of **15** and **18** upon the addition of LiBr, LiI, and TBAHS; and cyclic voltammogram of **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801325C

(33) (a) van Steenis, D. J. V. C.; David, O. R. P.; van Strijdonck, G. P. F.; van Maarseveen, J. H.; Reek, J. N. H. *Chem. Commun.* **2005**, 4333. (b) Katritzky, A. R.; Meher, N. K.; Hanci, S.; Gyanda, R.; Tala, S. R.; Mathai, S.; Duran, R. S.; Bernard, S.; Sabri, F.; Singh, S. K.; Doskocz, J.; Ciaramitaro, D. A. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *46*, 238.

(34) Rodionov, V. O.; Fokin, V. V.; Finn, M. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 2210.

(35) (a) Bodine, K. D.; Gin, D. Y.; Gin, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 1638. (b) Punna, S.; Kuzelka, J.; Wang, Q.; Finn, M. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 2. (c) Van Maarseveen, J. H.; Horne, W. S.; Ghadiri, M. R. *Org. Lett.* **2005**, *7*, 4503. (d) Turner, R. A.; Oliver, A. G.; Lokey, R. S. *Org. Lett.* **2007**, *9*, 5011. (e) Angell, Y. L.; Burgess, K. *Chem. Soc. Rev.* **2007**, *36*, 1674.

(36) (a) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238. (b) Qiu, X. P.; Tanaka, F.; Winnik, F. M. *Macromol.* **2007**, *40*, 7069. (c) Goldmann, A. S.; Quemener, D.; Millard, P.-E.; Davis, T. P.; Stenzel, M. H.; Barner-Kowollik, C.; Muller, A. H. E. *Polymer* **2008**, *49*, 2274.