Click Dendrimers and Triazole-Related Aspects: Catalysts, Mechanism, Synthesis, and Functions. A Bridge between Dendritic Architectures and Nanomaterials

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CONSPECTUS

One of the primary recent improvements in molecular chemistry is the now decade-old concept of click chemistry. Typically performed as copper-catalyzed azide−alkyne (CuAAC) Huisgen-type 1,3-cycloadditions, this reaction has many applications in biomedicine and materials science. The application of this chemistry in dendrimer synthesis beyond the zeroth generation and in nanoparticle functionalization requires stoichiometric use of the most common click catalyst, $CuSO_4 \cdot 5H_2O$ with sodium ascorbate.

Efforts to develop milder reaction conditions for these substrates have led to the design of polydentate nitrogen ligands. Along these lines, we have described a new, efficient, practical, and easy-to-synthesize catalytic complex, [Cu^I(hexabenzyltren)]Br, 1 [tren = tris(2-aminoethyl)amine], for the synthesis of relatively large dendrimers and functional gold nanoparticles (AuNPs). This efficient catalyst can be used alone in 0.1% mol amounts for nondendritic click reactions or with the sodium-ascorbate additive, which inhibits aerobic catalyst oxidation. Alternatively, catalytic quantities of the air-stable compounds hexabenzyltren and CuBr added to the click reaction medium can provide analogously satisfactory results. Based on this catalyst as a core, we have also designed and synthesized analogous Cu^I-centered dendritic catalysts that are much less air-sensitive than 1 and are soluble in organic solvents or in water (depending on the nature of the terminal groups). These multivalent catalysts facilitate efficient click chemistry and exert positive dendritic effects that mimic enzyme activity. We propose a monometallic CuAAC click mechanism for this process.

Although the primary use of click chemistry with dendrimers has been to decorate dendrimers with a large number of molecules for medicinal or materials purposes, we are specifically interested in the formation of intradendritic [1,2,3]-triazole heterocycles that coordinate to transition-metal ions via their nitrogen atoms. We describe applications including molecular recognition of anions and cations and the stabilization of transition metal nanoparticles according to a principle pioneered by Crooks with poly(amido amine) (PAMAM) dendrimers, and in particular, the control of structural and reactivity parameters in which the intradendritic [1,2,3]-triazoles and peripheral tripodal tri(ethylene glycol) termini play key roles in the click-dendrimer mediated synthesis and stabilization of gold nanoparticles (AuNPs). By varying these parameters, we have stabilized water-soluble, weakly liganded AuNPs between 1.8 and 50 nm in size and have shown large differences in behavior between AuNPs and PdNPs. Overall, the new catalyst design and the possibilities of click dendrimer chemistry introduce a bridge between dendritic architectures and the world of nanomaterials for multiple applications.
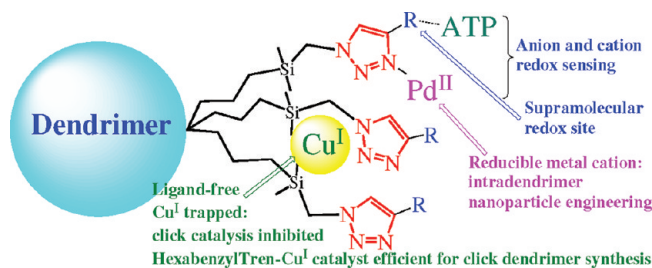
Introduction

The study of dendrimers[1−21] is now a broad and crucial supramolecular research field[8−11] that has applications *inter alia* in catalysis,[11−14] materials science,[11,15,16] and nanomedicine.[17−21] Click dendrimers have evolved in 2004[22] subsequently to Sharpless' concept of easy and practical

SCHEME 1. Comparison of Noncatalyzed and Cu^I-Catalyzed Alkyne–Azide Cycloadditions^a


Huigen's 1-3-dipolar cycloaddition:

CuAAC reaction:

the 1,5-isomer is not formed

1,4-isomer only
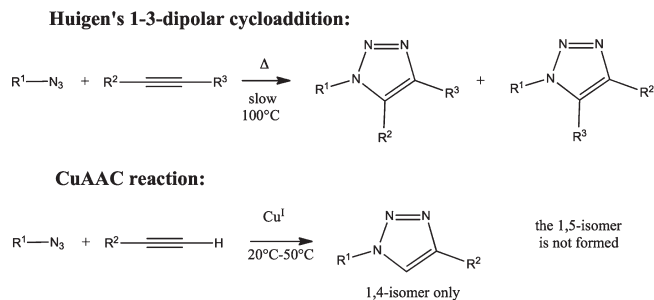
^{a}The noncatalyzed Huisgen reaction is faster with electron-withdrawing alkyne substituent(s) than with electron-rich alkynes.

SCHEME 2. Synthesis of the Dendrimer **5** Catalyzed by [Cu^I(hexabenzyltren)]Br, **1**, Compared with the Use of CuSO$_4$ + Sodium Ascorbate and the Catalyst Cu^I[tren(C$_{18}$H$_{37}$)$_6$]Br, **2**

assembly of molecular fragments.[23] Among the various click reactions,[23] the copper-catalyzed azide–alkyne cycloaddition (CuAAC)[24–28] rapidly appeared as the most useful one and will be examined here (Scheme 1). There are indeed myriad ways to synthesize dendrimers,[1–11] but the CuAAC click reaction has recently appeared as one of the most efficient and productive.[29–32]

Since our initial interest in iterative reactions[33] on the way to dendrimers, we have developed dendrimer synthetic pathways that involve the Williamson reaction,[34,35] cross olefin metathesis,[36] and finally the CuAAC click reaction. The latter was used by either introducing the azido groups at the periphery and the ethynyl group at the focal point of incoming dendrons[37] or the converse.[38] We will first delineate here the specific problems encountered for the click synthesis of nanosystems that led us to disclose new efficient catalysts including dendritic ones. Then, whereas in the rich click literature the purpose was to assemble useful functional groups, our goal has also been to utilize the inorganic properties of the coordination and supramolecular interactions of the intradendritic [1,2,3]-triazole link. Designed applications are toward control of transition-metal nanoparticle growth and molecular recognition and will also be the subject of this Account.
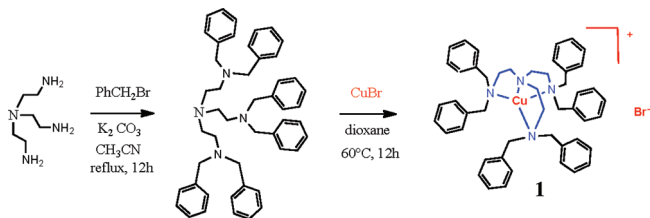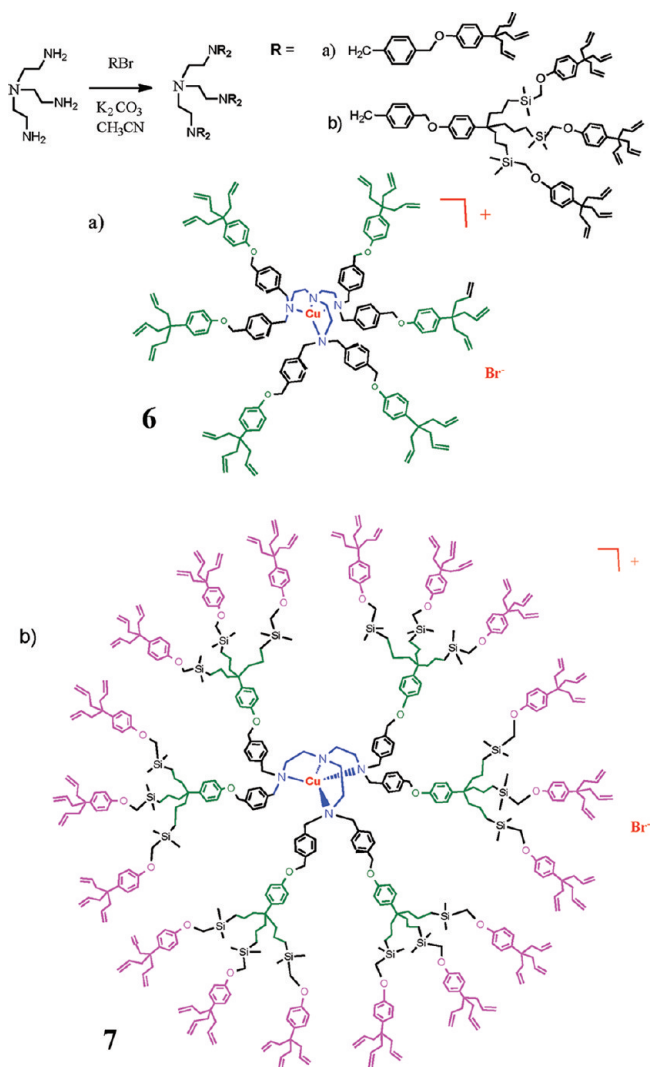
CuAAC Click Synthesis in Nanoscience: A New, Efficient, and Easily Available Catalyst

The CuAAC click reaction is catalyzed by a large variety of Cu^I species that can be either generated *in situ* or directly introduced into the reaction medium.[23–32] One of the most important properties of the Sharpless catalyst, CuSO$_4$ + sodium ascorbate, is its simplicity and easy use including in aqueous solvents. Another key property, shared by all the Cu^I catalysts, is that it yields a single triazole isomer, the 1,4-substituted one, whereas the noncatalyzed Huisgen
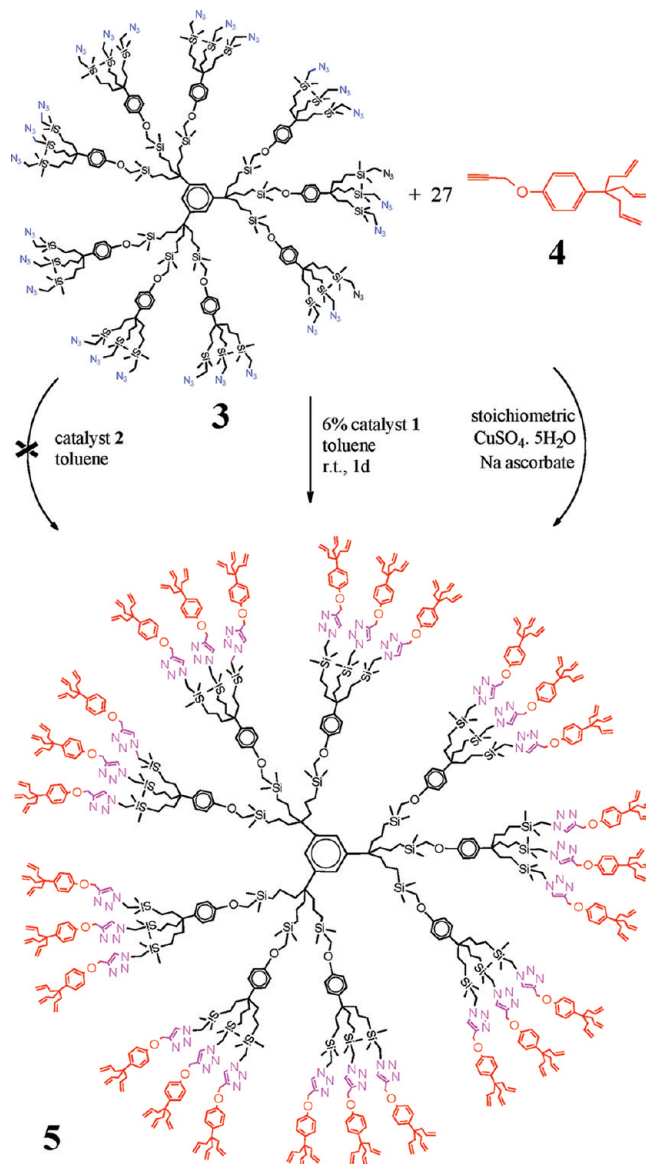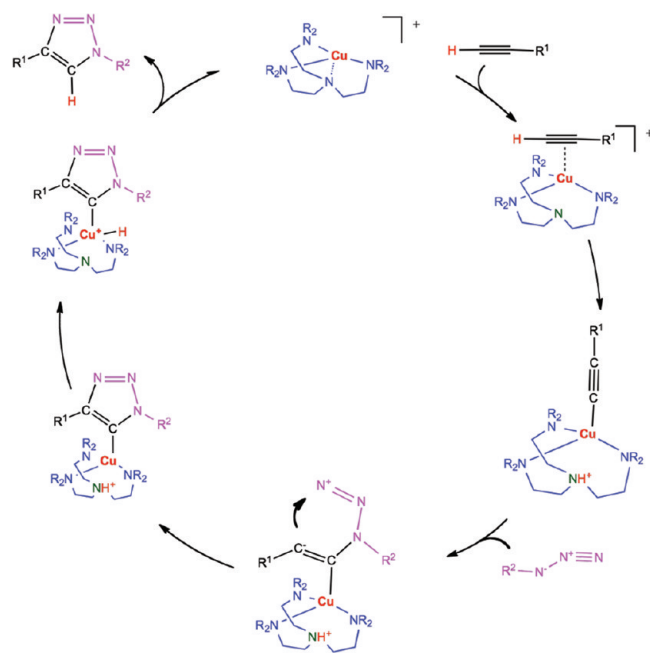
cycloaddition produces a mixture of 1,4- and 1,5-disubstituted triazoles (Scheme 1).

Finally, catalysis allows one to conduct the reactions under much milder conditions (20–60 °C) than the uncatalyzed reactions, which require temperatures above 100 °C, especially if the alkyne substituent is electron-rich. Indeed this catalyst presently is by far the most used CuAAC catalyst.[24] Several research groups have synthesized click dendrimers using this catalyst.[29,30] We have found, however, that catalytic amounts of this Sharpless catalyst probed in several solvents and under various temperatures could not lead to completion of the click reaction in the dendrimers
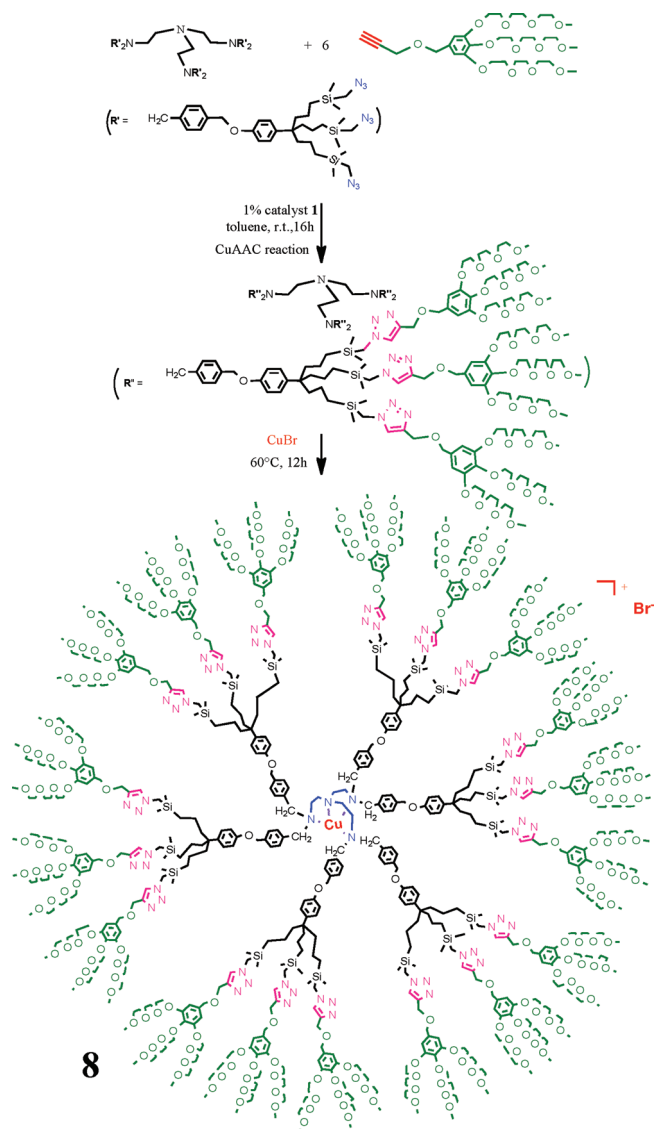
SCHEME 3. Synthesis of the Catalyst Cu^I(hexabenzyltren), **1**, of the CuAAC Reaction

SCHEME 4. Synthesis of the Dendritic Cu^I Catalysts **6** and **7** of the CuAAC Reaction

SCHEME 5. Monometallic Mechanism for the Click Reaction, Based on the Fokin–Finn Mechanism and Extended to Cu^{I}tren^a
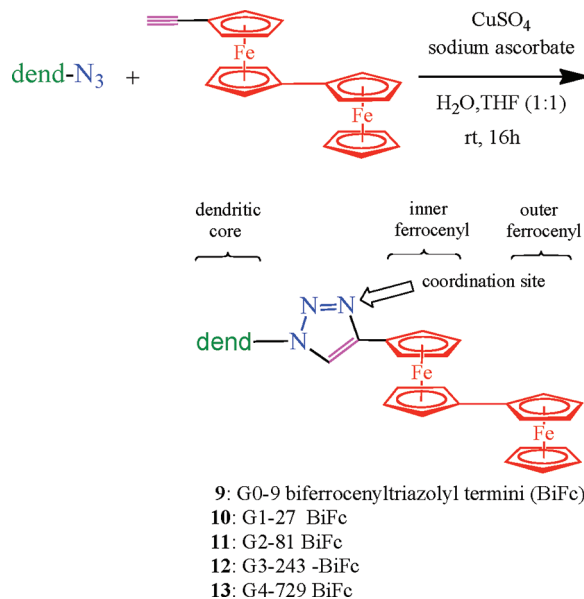

^{a}Th Fokin–Finn mechanism involves azide attack on the metal before migration to the alkynyl ligand and a σ,π-bimetallic Cu^I intermediate that does not appear to be possible with the Cu^I-centered dendritic catalysts **6**, **7**, and **8**.

from the coordination of the Cu^I species to two or several intradendritic triazoles formed in the reactions, blocking further catalysis. The dendrimer topology facilitates this entropy-favored interbranch chelation of Cu^I in dendrimers, a problem that is not encountered in nondendritic click syntheses. We also noticed that the click CuAAC functionalization of gold nanoparticles (AuNPs) that were reported in the literature had involved very low reaction yields.[39] We could improve the click CuAAC functionalization of AuNPs with a variety of alkynes by carrying out the reaction under inert atmosphere, but again a stoichiometric amount of Sharpless catalyst[40] or even more[41] was required. Matyjaszewski's group showed that the Me$_6$tren [tren = tris(2-aminoethyl)-amine] ligand accelerates the Cu^I click catalysis by a factor of 50 compared with CuBr.[42] Subsequently, the pentane-soluble complex Cu[tren($C_{18}H_{37}$)$_6$]Br, **2**, was shown to catalyze the click functionalization of a zeroth-generation dendrimer bearing nine azido termini,[43] but this catalyst was inefficient for the click synthesis of the corresponding first-generation dendrimer because of its bulk.[44] On the other hand, the new toluene-soluble complex Cu[tren(CH$_2$Ph)$_6$]Br, **1**, was an efficient catalyst for the CuAAC click reaction of the first-generation (G1) dendrimer **3** containing 27 azido termini with a dendron **4** functionalized at the focal point with a propargyl group, cleanly yielding dendrimer **5** with 81 allyl termini (Scheme 2).[44]

and that a stoichiometric amount of catalyst was required to obtain a satisfactory result beyond the zeroth dendritic generation.[37,38] The use of large quantities of toxic copper reagent is not compatible with green conditions required for biomedical use; thus improvements are needed. This problem in dendrimers and other branched nanosystems results

SCHEME 6. Synthesis of the Water-Soluble Catalyst **8** Including Click Ligand Synthesis Catalyzed by **1**

8

SCHEME 7. Click Synthesis of the Triazolylbiferrocenyl Dendrimers **9**−**13** from Five Generations of Azido-Terminated Dendrimers and Ethynylbiferrocene

9: G0-9 biferrocenyltriazolyl termini (BiFc)
10: G1-27 BiFc
11: G2-81 BiFc
12: G3-243 -BiFc
13: G4-729 BiFc

This complex was also an efficient catalyst in 10 mol % for the click functionalization of AuNPs. The complex **1** was synthesized by reaction of commercial tren with benzylbromide followed by heating hexabenzyltren with CuBr in dioxane (Scheme 3).

Although the medium is air-sensitive, the click reactions using this catalyst work well under air in the additional presence of sodium ascorbate. Alternatively, catalysis can be carried out as well if equal molar amounts of the air stable compound hexabenzyltren and CuBr are added together to the reaction medium in catalytic quantities. The catalytic use of **1** in click dendrimer synthesis and AuNP functionalization shows that the hexabenzyltren ligand of **1** resists full decoordination that would trap Cu[I] stoichiometrically as in the case of the Sharpless Cu[I] catalyst. This is also in favor of the monometallic mechanism shown in Scheme 2 for the series of Cu[I] tren catalysts.

Reactions using the catalyst **1** or its above components are best conducted in toluene in which **1** is soluble, because the triazole reaction products are insoluble in this solvent and thus easily separated.[44]

Positive Dendritic Effects in CuAAC Click Catalysis and Catalysis "on" Water

Cu[tren(CH$_2$Ph)$_6$]Br-centered dendritic catalysts of zeroth and first generations, **6** and **7**, have been synthesized by covalently attaching dendrons in the para position of the phenyl groups of **1**,[44] according to a 1 → 3 connectivity (Scheme 4).[45−47] Aerobic Cu[I] oxidation to μ-oxo-bridged dicopper species is sterically prevented in these Cu[I]-centered dendrimers. These dendritic catalysts are consequently much less air-sensitive than the parent complex **1**, due to the absence of possible inner-sphere oxidation pathways. Catalytic click reactions in toluene were also shown to proceed faster with **6** and **7** than with the parent catalyst **1**. Some click reactions such as that of phenyl acetylene with benzylazide are even faster with the G1 catalyst **7** than with the G0 catalyst **6**, indicating that intradendritic Cu[I]−substrate supramolecular interactions are reminiscent of enzymatic catalysis. Thus for small substrates, the dendritic effect[48] is positive. This also shows that a monometallic mechanism is efficient for the click reaction (Scheme 5), because the

SCHEME 8. Selective Oxidation of the Outer Ferrocenyl Groups of the Triazolylbiferrocenyl Dendrimer **10** Using Ferrocenium Hexafluorophosphate Producing the Mixed-Valence Dendrimer **14**
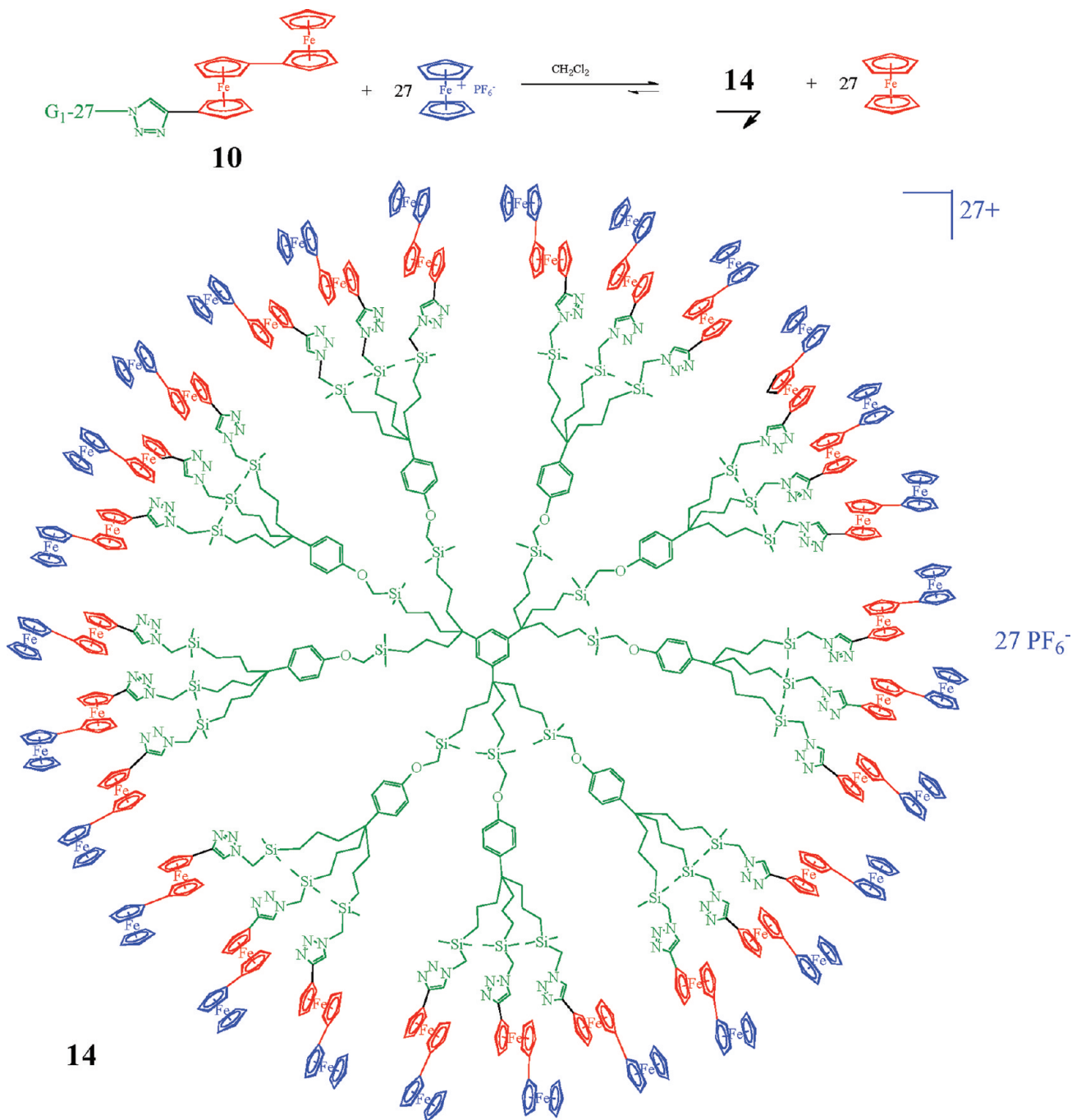
dendritic frame inhibits the approach of a second Cu^I-centered dendrimer.

Following detailed kinetic studies, Fokin and Finn pointed out the possibility of a σ,π-bimetallic Cu^I intermediate.[28,49−51] Indeed, in the absence of bulky (dendritic) polydentate accelerating ligands, a bimetallic mechanism is favored, because the $\pi−Cu^I$ coordination of the σ-alkynyl ligand decreases the electronic density on this ligand, which facilitates the azide attack.

If the tridentate ligand is not bulky, partial decoordination (even in the case of **1**) can eventually also give rise to this bimetallic mechanism. This was shown by the Scripps group using very efficient click catalysts of the type $Cu^I\{tris-(triazolylmethyl)amine\}$ and related catalysts.[28,51]

Finally, a water-soluble $Cu[tren(CH_2Ph)_6]^+$-centered click catalyst **8** was synthesized by CuAAC click reaction between the $Cu[tren(CH_2Ar)_6]Br$ core functionalized in the *para* aryl
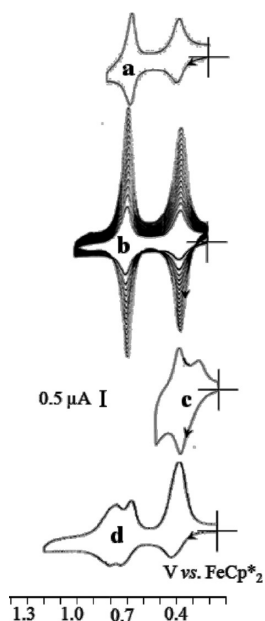
FIGURE 1. Selective roles of the inner and outer ferrocenyl groups of the 81-biferrocenyl dendrimer in the redox recognition of ATP^{2-} and Pd^{2+}. Cyclic voltammograms of the G2-81-biferrocenyl dendrimer **11** (a) in CH_2Cl_2, [n-Bu$_4$N][PF$_6$] 0.1 M, (b) progressive adsorption upon scanning around the potential of the biferrocenyl potential area, (c) splitting of the outer-ferrocenyl CV wave upon addition of ATP, and (d) addition of Pd(OAc)$_2$ provoking the splitting of the inner ferrocenyl CV wave at 0.7 V.

position with azido groups and a tri(ethylene glycol)-terminated dendron bearing a propargyl group at the focal point. The click synthesis of the dendritic tren ligand of **8** was also catalyzed by the parent click catalyst **1** (Scheme 6). This complex catalyzed the CuAAC click reactions of water-insoluble substrates "on" water under air at ambient temperature and was recyclable several times without loss of activity. Catalysis of reactions "on" water is a broad research field that has recently been reviewed.[52]

Recognition of Transition-Metal Cations and Oxo-Anions Using the Coordination of Intradendritic [1,2,3]-Triazolyl Groups

Click dendrimer syntheses were designed not only as a very practical way to decorate dendrimers with useful organometallic groups,[53,54] water-solubilizing sugars,[55] and thermally robust carboranes (which advantageously bring a large number of such groups within a single molecular assembly)[56] but also specifically in order to benefit from the intradendritic generation of [1,2,3]-triazolyl ligands for coordination to transition-metal ions.[37,38] For instance, with PdCl$_2$(PhCN)$_2$, an X-ray crystal structure determination allowed the location of the [1,2,3]-triazole coordination site of PdCl$_2$ on the terminal N atom next to the substituent of the alkyne precursor of the

triazole.[57] Such a coordination allowed the recognition of Cu^I, Cu^{II}, Pd^{II}, and Pt^{II}.[37] In the case of Pd^{II}, titration could indicate a 1:1 triazole/Pd^{II} stoichiometry and predict the number of Pd^0 atoms, confirmed by transmission electron microscopy, in intradendritic PdNPs formed by reduction of these Pd^{II} ions in large dendrimers. This strategy generated with precise PdNP catalytic studies[58−60] was inspired by Crooks' pioneering studies of the poly(amido amine) (PAMAM)-dendrimer encapsulated PdNP catalysts.[61,62] Extremely efficient ("homeopathic") PdNP catalysts were disclosed in this way,[58] including some that were very efficient in aqueous media.[60] Along this line, note Yamamoto's approach who also conducted dendrimer encapsulation of transition-metal species using intradendritic phenylazomethine ligands for catalysis and materials science purposes.[63,64]

A recent remarkable use of triazole-containing dendrimers was achieved with biferrocenyl triazole dendrimers **9**−**13**, which were synthesized by click reactions between five generations of azido-terminated dendrimers, constructed with 1 → 3 connectivity, and ethynylbiferrocene (Scheme 7).[65]

Biferrocenyl-containing nanomaterials have been extensively studied by Nishihara's group and present unique mixed-valence properties.[66] Mixed-valence biferrocenium triazole dendrimers such as **14** were synthesized by oxidation of the neutral metallodendrimers with ferricinium hexafluorophosphate (Scheme 8).

These polycationic dendrimers result from selective oxidation of the outer ferrocenyl groups (*vide infra*), because the inner ferrocenyl groups are more difficult to oxidize due to the presence of the nearby electron-withdrawing triazolyl group. The Mössbauer spectrum at zero field of the mixed-valence dendrimer **14** with 27 biferrocenium termini showed a doublet for the ferrocenium groups and another one for the ferrocenyl groups indicating the localization of the mixed valence.[67] The cyclic voltammograms (CVs) of these dendrimers showed two chemically and electrochemically reversible waves at 0.4 and 0.7 V vs the internal reference decamethylferrocene,[68] although adsorption characterized by the decrease of the difference of potential between the anodic and cathodic waves decreased as the dendrimer generation increased (Figure 1). Addition of [Pd(MeCN)$_4$][PF$_6$]$_2$ to a CH_2Cl_2 solution of the dendrimer **11** containing 81 biferrocenyl triazole termini led to selective recognition by the second oxidation wave at 0.7 V, whereas addition of the oxo anion [n-Bu$_4$N]$_2$[ATP] to the same solution of **11** led to selective recognition by the first oxidation wave at 0.4 V. This confirms that the inner ferrocenyl groups that are located near the triazole rings are more difficult to oxidize than the
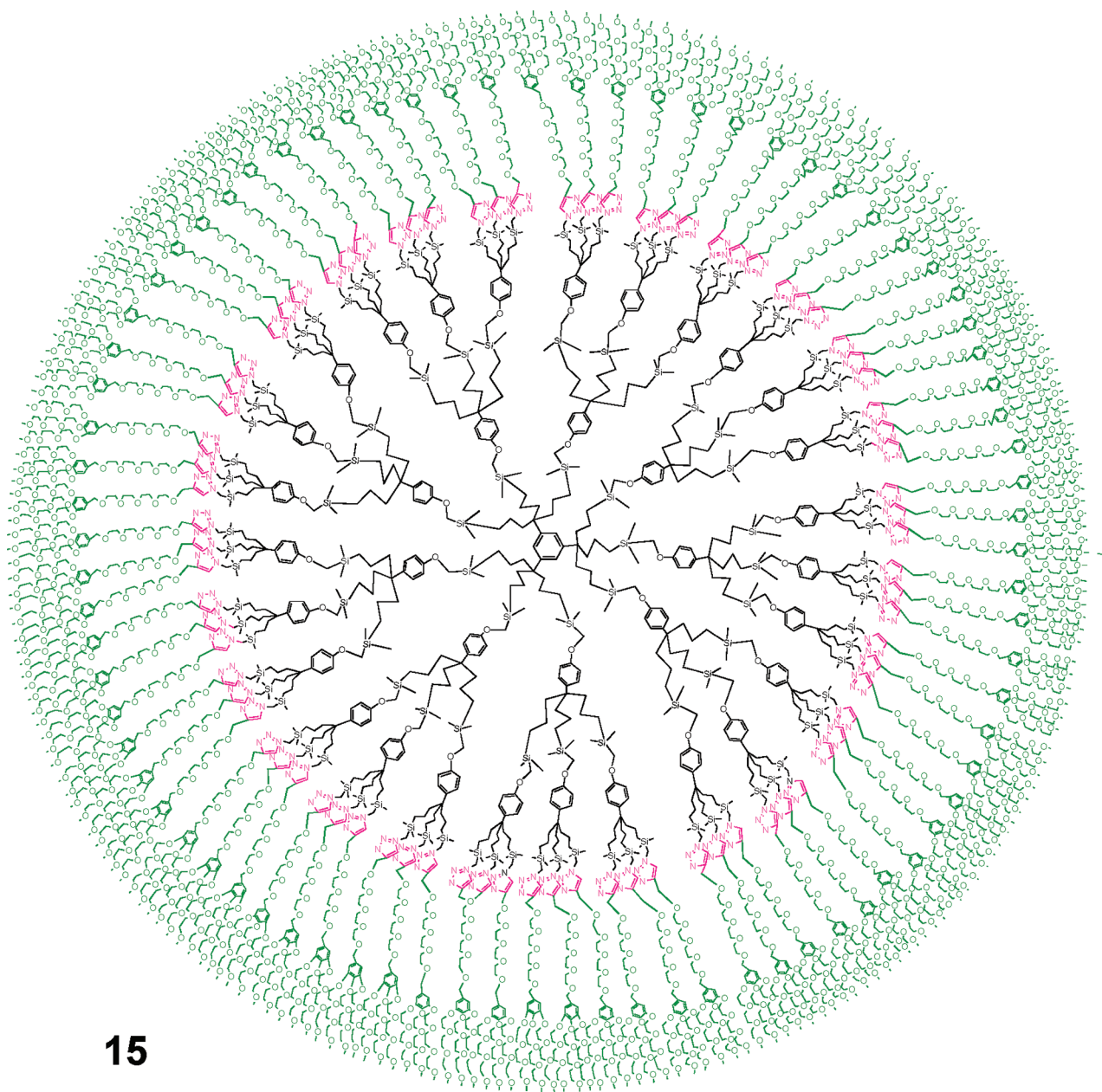
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FIGURE 2. Generation-2 click dendrimer **15** terminated by 243 tri(ethylene glycol) groups (81 Percec-type dendrons) and constructed with 1 → 3 connectivity.

outer ones. The easier oxidation of the outer ferrocenes to ferricinium selectively creates positive charges at the dendrimer periphery that form ion pairing with the [ATP] anions just by setting the potential between 0.4 and 0.7 V (Figure 1).

Use and Role of the Intradendritic [1,2,3]-Triazolyl Groups in the Formation of Water-Soluble Dendrimer-Stabilized Gold Nanoparticles (AuNPs)

Initial work on click dendrimer-mediated stabilization of nanoparticles involved catalytically active PdNPs as mentioned

above. We have recently been interested in click-dendrimer stabilization of water-soluble AuNPs because of the roles of AuNPs in catalysis (small AuNPs, in the range 1−3 nm)[69−73] and nanomedicine (large AuNPs, in the range 3−50 nm giving rise to plasmonic absorptions that are useful for both diagnostics and therapy).[41,74−77] Seminal work on PAMAM-dendrimer stabilization of AuNPs and other transition-metal NPs was carried out in the late 1990s,[78,79] in particular by the Crooks group, and has been reviewed including catalytic properties.[61,62,80,81]

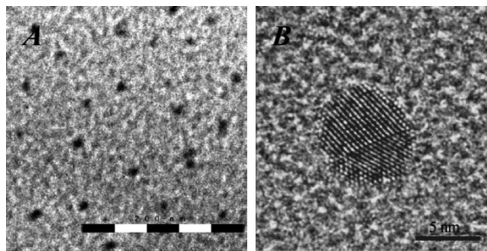In order to stabilize AuNPs in water, a variety of new dendrimers were synthesized from poly-azido-terminated

FIGURE 3. (a) TEM of the dendrimer **15** + 1 equiv of $HAuCl_4$ reduced by $[Fe^ICp(\eta^6-C_6Me_6)]$ and (b) HRTEM of the dendrimer **15** + 1 equiv of $HAuCl_4$ reduced by $[Fe^ICp(\eta^6-C_6Me_6)]$.

TABLE 1. Size Variation of AuNPs Stabilized by the Generation-2 Click Dendrimer **15** Terminated by 243 Tri(ethylene glycol) Groups (see Figure 3) in Methanol upon Reduction Using $NaBH_4$ in Methanol as a Function of the Addition of $HAuCl_4$

equiv. number of $HAu^{III}Cl_4$ per triazole	AuNP diameter (nm)
1	1.9 ± 0.2
3	3.8 ± 0.4
5	5.3 ± 0.5
7	6.8 ± 0.7
10	11.0 ± 1
20	11.3 ± 1

dendritic precursors (with 9, 27, and 81 azido groups) by CuAAC click reactions using $1 \rightarrow 3$ connectivity[44−46] with a Percec-type dendron[10] containing three tri(ethylene glycol) (TEG) termini and a tetra(ethylene glycol) functionalized with a propargyl group at the focal point (See the example of dendrimer **15** shown in Figure 2)

These dendrimers were compared with other structurally related dendrimers built using Williamson coupling[34,35] instead of CuAAC click coupling, in order to investigate the influence of the intradendritic triazolyl motifs. The TEG termini provided ideal conditions for AuNP formation from $HAuCl_4$ either using $NaBH_4$ as the reductant or without external reductant.[82] With $NaBH_4$, however, it was also indispensable to use click dendrimers terminated by Percec-type TEG dendrons in order to introduce Au^{III} inside the dendrimer by coordination to the triazole rings, which adequately modulated the nucleation. With the smallest dendrimer of the series that was terminated by only 27 TEGs, the AuNPs formed were larger (4.1 ± 0.5 nm) than the dendrimers and thus were stabilized by several dendrimers and showed a plasmon band at 540 nm. The larger dendrimers containing 81 (Figure 2) and 243 terminal TEGs (Figure 3) encapsulated AuNPs that were too small (1.9 ± 0.4 nm) to present a plasmon band. For comparison, when the dendrimer structure contained only TEG termini but no [1,2,3]-triazole or [1,2,3]-triazoles but no TEG-terminated dendrons, $NaBH_4$ reduction led to unstable AuNPs that precipitated after a

few minutes. This was in contrast with PdNPs that were fully stabilized by such dendrimers and catalytically active in olefin hydrogenation and Suzuki−Miyaura reactions under ambient conditions.[58] On the other hand, in the absence of external reductant, Au^{III}−triazole coordination slowed Au^{III} reduction in dendrimers terminated by TEG dendrons, because the distal Percec-type dendron itself was the reductant. The semicavitand effect of the three TEGs of the dendron was then crucial, as shown by the failure of Au^{III} reduction using a click dendrimer terminated by a linear tetra(ethylene glycol) instead of a Percec-type TEG dendron. Dendrimer-stabilized AuNPs were formed with the click as well as nonclick dendrimers from $HAuCl_4$ in this way in the absence of additional reductant. Then AuNPs had a 23−42 nm size depending on the generation.[83] Choosing the $AuCl_4$/dendrimer stoichiometry also oriented the size of the AuNPs formed (Table 1).

Monoelectronic reductants such as ferrocene, ethynylferrocene, decamethylferrocene, and the electron-reservoir sandwich complex $[Fe^I(\eta^5-C_5H_5)(\eta^6-C_6Me_6)]$, which has 19 valence electrons on the iron valence shell,[33,84] have also been used for the first time for the reduction of $HAuCl_4$ to AuNPs (Figure 3). Their outer-sphere reduction mechanism[67] implied a much slower reduction than that involving the inner-sphere reductant $NaBH_4$, and the size of the dendrimer-stabilized AuNPs formed (between 7 and 38 nm) was directly related to the standard oxidation potentials of the Fe^I and Fe^{II} reductants. This provided the possibility to finely tune the size of the AuNPs.[83]

All these water-soluble dendrimer-stabilized PEGylated AuNPs were only weakly stabilized and are thus potentially useful for catalytic (small size) and biomedical applications (large size).

Conclusion and Prospects

The CuAAC click synthesis is a superb synthetic tool that has been usefully and successfully applied by the pioneers of this chemistry to the biological and biomedical field.[22−28] Concerning the synthesis of relatively large dendrimers and click functionalized transition-metal nanoparticles the design of new liganded catalysts was required as illustrated here by the efficient, practical, and easily made complex Cu[tren-$(CH_2Ph)_6$]Br. Very efficient dendritic analogue catalysts showed that a mononuclear Cu^I catalysis is involved, and the positive dendritic effect recalls enzymatic catalysis.[85] Even if the copper catalyst is not desired in green processes, it can be removed from the click reaction medium when these catalysts are used.

Alternatively, copper-free solutions are known either with electron-deficient alkyne substrates (the Huisgen cycloadditions are then possible in water under mild conditions)[86] or using strain-promoted alkyne−azide cycloaddition.[87] The synthesis of click dendrimers not only allows decoration of dendrimers with a large number of substrates of interest but also the introduction of the intradendritic [1,2,3]-triazoles to allow their use to coordinate transition-metal ions. Applications have been illustrated here in molecular recognition and for the fine-tuning of the formation of small catalytically active PdNPs as well as AuNPs of various sizes ranging from 1.8 to 42 nm. The difference of influence of the multiple structural and reactivity parameters on the stabilization and size of the NPs of these two metals is thus impressive. The intradendritic [1,2,3]-triazole ligands are also a key to redox recognition that is helpful for the control of the size of potentially useful, weakly liganded transition-metal nanoparticles.

In summary, CuAAC click chemistry plays a pivotal role in the interplay between dendritic architectures and nanoparticles, that is, between molecular nanoscience and nanomaterials, and this concept is clearly called for many further developments and applications.

BIOGRAPHICAL INFORMATION

Didier Astruc is Professor at the Université Bordeaux 1 and Member of the Institut Universitaire de France. He did his doctorates in Rennes, and a postdoctoral term with Richard R. Schrock at MIT. His interests are in inorganic chemistry and applications of nanosystems to catalysis, sensors, energy-related problems, and nanomedicine.

Liyuan Liang presented her Ph.D. thesis with Didier Astruc on dendritic nanoreactors and molecular recognition in 2011. She is now pursuing postdoctoral studies in Toronto with Doug Stephan. Her interests are in nanosciences.

Following undergraduate studies in Athens, **Amalia Rapakousiou**, is a graduate student in Didier Astruc's group. Her present research project is related to giant biferrocenyl dendrimers and nanosystems.

After undergraduate studies in Santiago de Chile, **Jaime Ruiz** passed his Ph.D. and Habilitation in Bordeaux on the reactivity 19-electron Fe(I) complexes. He has been a CNRS Engineer in Didier Astruc's group in Bordeaux for more than a decade, and his interests are in organometallic synthesis, electrochemistry, dendrimers, and nanoparticles.

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