Cage Compounds

DOI: 10.1002/ange.201107490

Chemistry at the Nanoscale: Synthesis of an $N@C_{60}$–$N@C_{60}$ Endohedral Fullerene Dimer**

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Endohedral fullerenes—carbon cages with one or more heteroatoms incarcerated within them—are one of the most exotic classes of molecules. They possess a wealth of fascinating functional properties, including magnetism and photoactivity. While the properties of individual endohedral fullerene molecules are remarkable,[1] the full functional potential of many of these species will likely be realized in systems where two or more of these molecules are connected. One prominent example is the endohedral fullerene radical species $N@C_{60}$. The highly symmetric central location of the nitrogen atom within the C_{60} cage,[2] with minimal mixing between the nitrogen atom and fullerene electron wavefunctions, imparts a degree of isolation to the nitrogen radical that is usually only attainable using an ion trap or in an atomic gas. This isolation allows the nitrogen center to retain a $^4S_{3/2}$ electron spin ground state[3] and to have an extraordinarily long electron spin coherence time (T_{2e} of 250 μs).[4] This remarkable spin coherence time has lead many research groups to study the potential and feasibility of an $N@C_{60}$-based quantum computer over the past decade.[5] Owing to a number of synthetic challenges associated with $N@C_{60}$, experimental electron spin resonance studies have so far been restricted to probing the interaction of ensembles of molecules each containing a single $N@C_{60}$ spin center. These challenges center on the low-yielding production methods available to synthesize $N@C_{60}$, thus producing at best a 500 ppm $N@C_{60}/C_{60}$ mixture,[2,6] and the time consuming processing techniques currently required to enrich the ratio of $N@C_{60}$ to C_{60}.[7] In addition, compared to C_{60}, chemically functionalized $N@C_{60}$ derivatives have significantly lower thermal and photo stability.[8,9] To further explore the potential of $N@C_{60}$ as a quantum computing element, including the creation of controlled entanglement between electron spins, an array of at least two $N@C_{60}$ centers with fixed separation is required to understand the interaction of neighboring spin centers with one another and investigate methods of selective manipulation of one of the spin centers.

Herein we describe a one-pot method, using a double 1,3-dipolar cycloaddition, for the synthesis of a two-center $N@C_{60}$ molecule with fixed spatial separation (Scheme 1), thus providing a platform for future experiments to probe the nature of the electron interaction between two $N@C_{60}$ molecules to assess the potential capabilities of a 2 qubit $N@C_{60}$ quantum computer. To the best of our knowledge, this is the first endohedral fullerene dimer comprising two chemically linked $N@C_{60}$ spin centers.

A Prato 1,3-dipolar cycloaddition reaction was chosen to link the two $N@C_{60}$ molecules owing to its proven compatibility with the stability[10] of $N@C_{60}$ and the wide range of amino acid and aldehyde derivatives that it has been reported to be compatible with. A dibenzaldehyde-terminated oligo(*p*-phenylene polyethylene) (OPE) molecule (Ald-3Bz) was synthesized and used as the spacing unit because of its rigidity and modular construction. The incorporation of long alkyl chains on the central phenyl group enhances the inherent poor solubility of the rigid, linear molecule, thus allowing the reaction to be performed at high concentration and making the product fullerene dimer (dimer-3Bz) soluble in common solvents such as chloroform. Previous work has shown that the structure of the amino acid derivative used makes a significant difference to the rate and yield of the 1,3-dipolar cycloaddition reaction.[11] Work within our group has found that the *N*-(4-(hexyloxy)benzyl)glycine amino acid derivative greatly enhances the dimer formation reaction rate compared to more commonly used amino acid derivatives such as *N*-(ethyl)glycine (see the Supporting Information). In addition, the amino group produces a fullerene dimer that can be purified using standard single-pass HPLC methods.

We synthesized three grams of a $N@C_{60}/C_{60}$ mixture using an ion implantation method,[12] thus yielding an average purity of 50 ppm of $N@C_{60}$ in C_{60}. Extensive purification of this sample followed. After 19 recycling HPLC runs,[13] a high purity $N@C_{60}/C_{60}$ peak was isolated. The integrated area of the $N@C_{60}/C_{60}$ peak indicated the total mass of $N@C_{60}/C_{60}$ to be 10 μg. This sample then underwent quantitative ESR analysis of the total number of $N@C_{60}$ spin centers present, thereby giving a lower bound for the mass of $N@C_{60}$ to be 4.6 μg.

Optimized reaction conditions and an efficient purification method for the one-pot dimer synthesis were identified and scaled down to work using only 20 μg of the C_{60} starting

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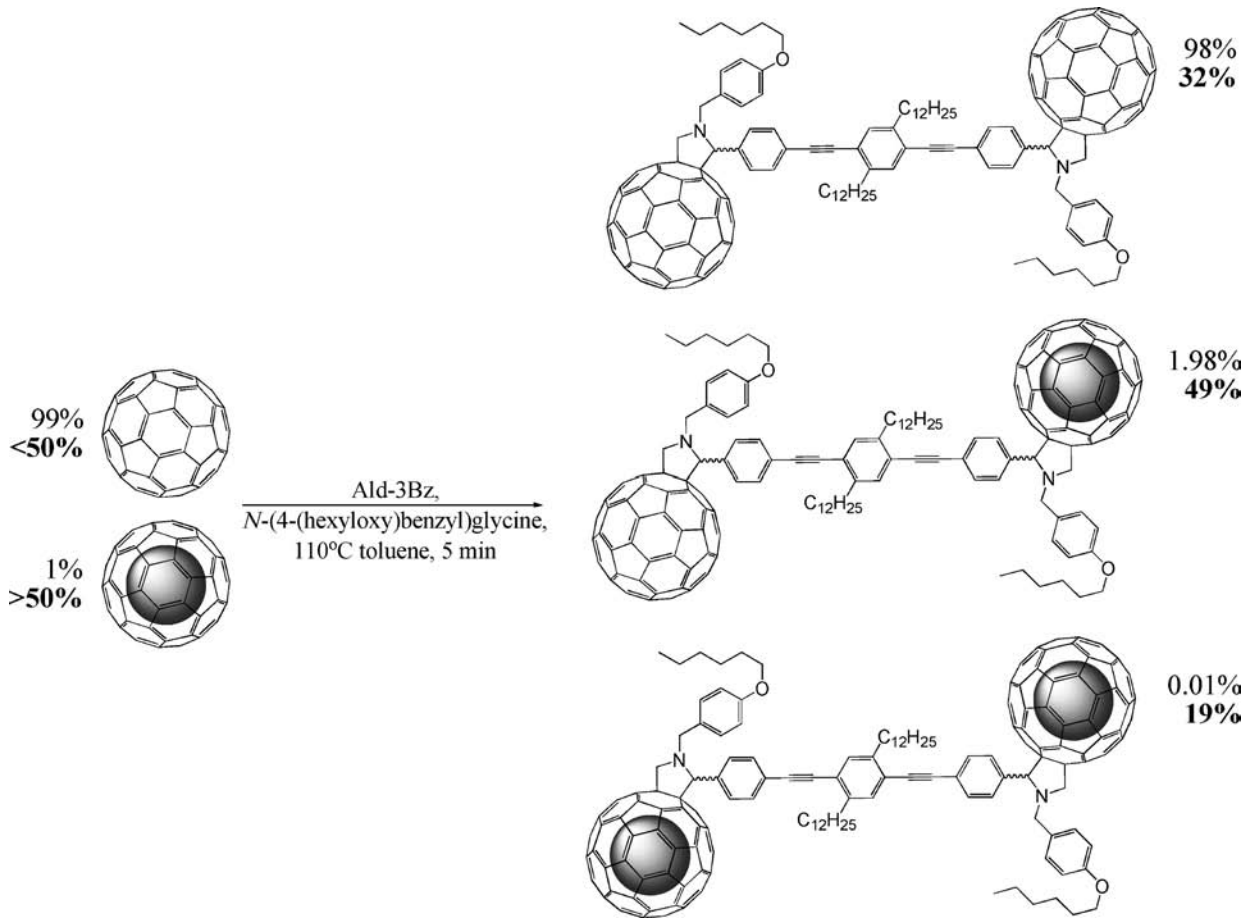
[**] We acknowledge the EPSRC and NSF for funding (EP/F028806/01). B.J.F. is supported by the EPSRC through a DTA studentship. A.A. and A.N.K. are supported by the Royal Society. We thank Dr. Simon Plant for valuable suggestions and discussions during the course of this work.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201107490.



Scheme 1. Reaction scheme for the synthesis of the dimer-3Bz using 1% N@C_{60} in C_{60} and >50% N@C_{60} in C_{60} (bold typeface). The scheme indicates the predicted statistical distribution of the N@C_{60} in the dimers collected together as the product fraction. For the reaction using 1% N@C_{60} in C_{60}, the distribution was calculated using the number of N@C_{60} centers per fullerene cage in the starting material (0.01); C_{60}–$C_{60}=0.99^2$, N@C_{60}–$C_{60}=0.01\times0.99$, N@C_{60}–N@$C_{60}=0.01^2$. For the reaction using >50% N@C_{60} in C_{60}, the distribution was calculated from the number of N@C_{60} centers per fullerene cage in the product dimer fraction, measured using HPLC peak and ESR signal integration to be 0.43(5); C_{60}–$C_{60}=0.565^2$, N@C_{60}–$C_{60}=0.435\times0.565$, N@C_{60}–N@$C_{60}=0.435^2$.

material. To minimize thermal degradation of the spin-active endohedral fullerene dimer the reaction was additionally optimized to produce a 45% yield of the dimer product using only a five-minute reaction time (Figure 1). Using the final reaction conditions with a partially enriched N@C_{60}/C_{60} sample produced a 79% retention of spin centers in the dimer product compared to the N@C_{60} starting material. After demonstrating that the reaction conditions were compatible with N@C_{60}, a higher purity N@C_{60}–C_{60} dimer sample was synthesized using 150 μg of approximately 1% N@C_{60} in C_{60} (Scheme 1). A frozen solution CW ESR spectrum of the dimer product is shown in Figure 2. This spectrum was simulated using the Easyspin software package[14] to characterize the environment of the three unpaired electrons present in the N@C_{60}–C_{60} dimer. The fitted simulated model used the following parameters: hyperfine splitting term ($A_{iso}=15.736$ MHz), axial zero-field term ($D=14.19$, $E=0.74$), line-width 0.121 G, and $g_{iso}=2.0027$ with a RMS residual fit of 0.014. The principal fitting error is assigned to a minor component of the ^{15}N@C_{60}–C_{60} dimer present in the sample. These fitted parameters were consis-

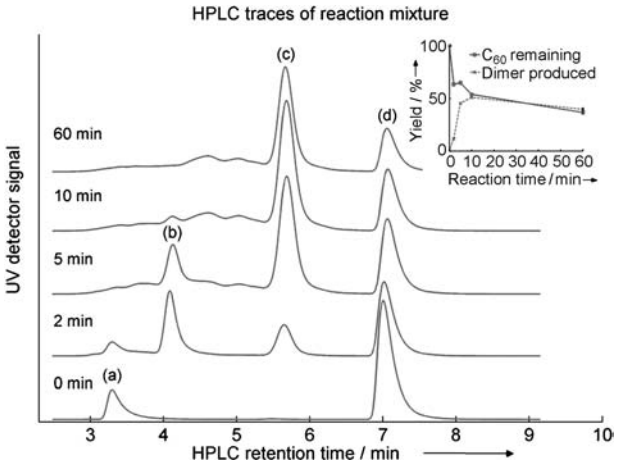


Figure 1. Reaction progress for the formation of C_{60}–C_{60} dimer (dimer-3Bz) after 0, 2, 5, 10, and 60 min reaction times, followed by HLPC. a) Unreacted bis(aldehyde), b) mono-3Bz, c) dimer-3Bz, d) unreacted C_{60}. Insert: quantification of dimer-3Bz yield and unreacted C_{60}, based on integrated area of HPLC peaks.

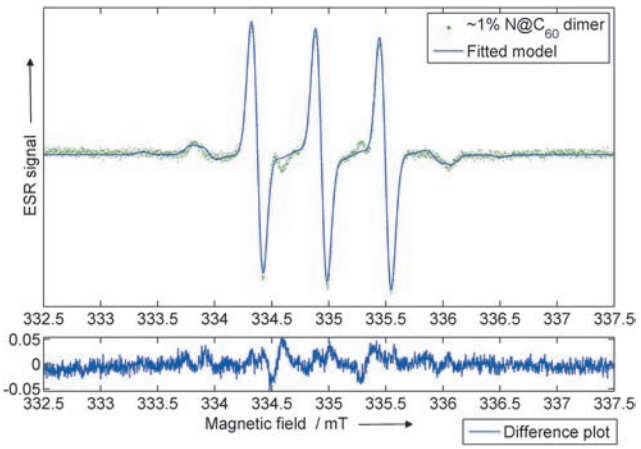


Figure 2. Frozen-solution CW ESR spectra taken at 90 K of N@C_{60}–C_{60} dimer (dimer-3Bz) from 1% N@C_{60}/C_{60} dimer reaction (green dots) fitted to a model spectrum (blue line) using the following parameters: hyperfine splitting term (A_{iso} = 15.736 MHz), axial zero-field term (D = 14.19, E = 0.74), line-width 0.121 G, and g_{iso} = 2.0027 with a RMS residual fit of 0.014.

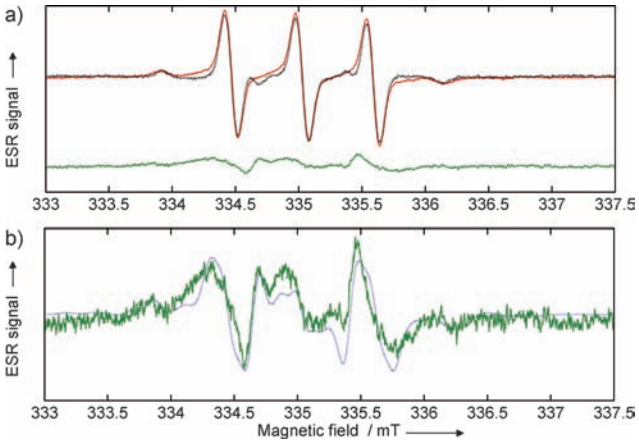


Figure 3. a) Frozen-solution CW ESR spectra taken at 90 K of, the N@C_{60}–C_{60} dimer (dimer-3Bz) from the 1% N@C_{60}/C_{60} dimer-3Bz reaction (dotted black line); a mixture of N@C_{60}–N@C_{60} and N@C_{60}–C_{60} dimers (dimer-3Bz) from the >50% N@C_{60}/C_{60} dimer-3Bz reaction (solid red line); and a difference plot of the two spectra (green) below. b) Difference spectrum (solid green line) fitted to simulated spectra of an N@C_{60}–N@C_{60} model with a maximum dipolar coupling strength between the two spin centers of 2.67 MHz (dotted blue line). The model is corrected for a 5.(6)% ^{15}N@C_{60} impurity present in the N@C_{60}–C_{60} spectra.

tent with those found for previously reported pyrrolidine-functionalized N@C_{60} adducts.[10,15]

Finally the reaction was repeated using the high purity N@C_{60} sample shown in Scheme 1 and the dimer component isolated by HPLC (see the Supporting Information). The presence of a doubly filled dimer was probed using room temperature (RT) and frozen-solution CW ESR spectroscopy. By quantifying the number of moles of dimer produced using the reaction HPLC trace (500 ng) and the total number of N@C_{60} spin centers present, calculated from the integral of the RT CW ESR spectra, the average number of spin centers per cage was calculated to be 0.43(5). By assuming similar chemical reactivity of N@C_{60} and C_{60}, the fraction of N@C_{60}–N@C_{60} dimer and N@C_{60}–C_{60} dimer can be calculated to be 19 and 49%, respectively (Scheme 1). A low temperature frozen-solution ESR spectrum of the dimer fraction was recorded and compared to a sample that only contained N@C_{60}–C_{60} dimer molecules (Figure 3).

The principal features of the two spectra are similar, with inhomogeneous line broadening and the addition of zero-field splitting peaks resulting from the reduction in the symmetry of the fullerene cage after exohedral functionalization. By subtracting the contribution of the N@C_{60}–C_{60} dimer in the mixed dimer sample the resulting ESR difference spectra can be fitted to the simulated spectrum of a N@C_{60}–N@C_{60} dimer using the parameters fitted to the N@C_{60}–C_{60} spectra shown in Figure 2, with the addition of a dipolar coupling parameter resulting from the interaction of the two spin centers. The best simulation was obtained using an isotropic distribution of molecular orientations with a maximum dipolar coupling magnitude of 2.67 MHz, which corresponds to a separation of the two N@C_{60} centers of 2.7 nm. This value is in excellent agreement with the expected average distance between the two N@C_{60} moieties in the fullerene dimer, which is estimated by molecular modeling to be between 2.63 nm to 2.75 nm (see the Supporting Information for details). This is the first evidence of dipolar coupling between two covalently bonded N@C_{60} molecules.

Herein we demonstrate the enhanced 1,3-dipolar cycloaddition reaction rate that can be achieved using the amino acid derivative *N*-(4-(hexyloxy)benzyl)glycine to form a fullerene dimer in one pot. A 45% yield of fullerene dimer product could be recovered after a mere five-minute reaction time. We also show that this reaction can be scaled down to work using a 0.014 μmol scale, thus providing a route to chemically functionalized, high purity, rare endohedral fullerenes, such as N@C_{60}.

The combination of low thermal stability of chemically functionalized N@C_{60} and the requirement (assuming the absence of a catalyst) for elevated temperature to activate the 1,3 dipolar cycloaddition reaction made optimizing the rate of the dimer formation reaction key to the successful synthesis of an N@C_{60}–N@C_{60} dimer. A comparison of the product mixture at a number of reaction time intervals using the chosen amino acid *N*-(4-(hexyloxy)benzyl)glycine or the more commonly used *N*-(ethyl)glycine in the dimer-forming reaction (see the Supporting Information) shows that our chosen amino acid provides a substantial enhancement of the reaction rate. The addition of an aromatic substituent to the amino group can greatly enhance the rate of 1,3-dipolar cycloaddition to nanotubes;[16] rationalized by a preorganization of the ylide with the sp^2 nanotube surface through π–π stacking. The same preorganization is likely to be present between the fullerene cage and *N*-(4-(hexyloxy)benzyl)glycine. This could then produce a double rate enhancement: firstly, the probability of the three reagents meeting to react is enhanced, and secondly, the electrophilic fullerene could stabilize the formation of the ylide intermediate. It is also possible that the presence of the *o*-hexyl substituent enhances

the reaction rate, firstly by increasing the solubility of the amino acid in the reaction solvent, thus permitting a greater stoichiometric ratio to be used, and secondly by enhancing the π–π interaction between the fullerene and the amino acid benzene ring through mesomeric donation of the oxygen atom into the benzene ring.

The ESR spectrum arising from a two-spin-center N@C_{60}–N@C_{60} molecule suggests that the presence of two N@C_{60} functionalized molecules in close proximity to one another does not significantly affect the stability of the endohedral nitrogen species. This stability is a fundamental requirement for the successful implementation of N@C_{60} as a quantum logic element.

Since our reaction can be made to work with microgram quantities, the way is open for further chemical functionalization of high purity N@C_{60}. This method can be used to create two-spin-center N@C_{60} molecules with the required narrow coupling strength distribution that will allow N@C_{60} to be exploited for quantum information processing applications. The next step is the ability to orient the molecules with respect to a magnetic field. We are currently pursuing experimental methods to accomplish this.

Experimental Section

All ESR spectra where recorded in toluene, using a Bruker EMX spectrometer fitted with a liquid helium cooled cryoprobe.

Synthesis of C_{60}–C_{60} dimer (dimer-3Bz). Ald-3Bz (10 mg; 1.5×10–2 mmol), C_{60} (32 mg; 4.4×10–2 mmol), and *N*-(4-(hexyloxy)benzyl)glycine (32 mg; 1.4×10–1 mmol) were added to a two-neck 50 mL round bottom flask. The mixture was then sealed and degassed with a flow of argon. Dry toluene (20 mL) was added to a 50 mL schlenk tube, degassed using three freeze/pump/thaw cycles, and then transferred by cannula to the flask containing the solid reagents. The reaction mixture was soncicated for 30 min then attached a reflux condenser and heated to 110 °C for 1 hour in a preheated oil bath. The product mixture was passed through a short silica plug then concentrated and purified using HPLC (buckyprepM column ($20\times$ 250 mm); eluent: toluene; flow rate: 18 mL min^{-1}; retention time: 5.7 min). The product yield was 40 %.

Synthesis of double-spin-labeled N@C_{60}–N@C_{60} dimer (dimer-3Bz). *N*-(4-(hexyloxy)benzyl)glycine (20 μg; 7.5×10^{-2} μmol), ca. 50 % pure N@C_{60} (10 μg; 1.37×10^{-2} μmol) in C_{60} dissolved in toluene (100 μL), and of Ald-3Bz (50 μL; 0.137 mmol L^{-1}) in toluene were added to a new, 7 inch 5 mm NMR tube. The reaction mixture was concentrated to a final volume of 25 μL using a flow of argon gas and a 2×5 mm magnetic stirrer bar was added. The reaction mixture was heated to 110 °C for 5 min in a preheated oil bath then removed and quenched in an ice bath. The product mixture was passed through a short silica plug to remove amino acid residues and then purified using HPLC (4.6 mm × 250 mm BuckyprepM, eluent: 35 % *n*-hexane, 65 % toluene). A 3 % yield (500 ng) of the product was recovered.

Received: October 24, 2011
Published online: March 1, 2012

Keywords: cage compounds · cycloaddition · dimerization · fullerenes · synthesis design

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