Lanthanum Endohedral Metallofulleropyrrolidines: Synthesis, Isolation, and EPR Characterization

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Abstract: Lanthanum endohedral metallofulleropyrrolidines have been synthesized for the first time through addition of an azomethine ylide to La@C_{82}-A in toluene. It was found that the addition reaction is very efficient and, to some extent, regioselective. Two major endohedral metallofulleropyrrolidines, a monoadduct and a bisadduct of La@C_{82}-A with abundance ratio of ~1:0.4, have been isolated by HPLC chromatography and characterized by mass spectrometry, UV/Vis-NIR absorption, and EPR spectroscopy. The electronic structure of La@C_{82}-A has been modified slightly upon monoaddition and significantly upon bisaddition of the pyrrolidines.

Keywords: cycloaddition • endohedral metallofullerenes • fullerenes • fulleropyrrolidines

Introduction

Endohedral metallofullerenes—molecules with a positively charged metal core surrounded by a negatively charged carbon cage—present unique structures and novel properties together with considerable potential application perspectives which arise from the incarcerated metal and are not expected for empty fullerenes.[1] Driven by their novel structures and properties, organic functionalization of metallofullerenes, though only limited cases have been reported,[2–10] has generated some applicable materials such as new therapeutic radiopharmaceuticals,[9] and MRI contrasting and X-ray imaging agents.[10] Relative to metallofullerenes, organic derivatization of empty fullerenes has been extensively investigated.[11–12] Among the successful functionalization methodologies, the 1,3-dipolar cycloaddition of azomethine ylides to C_{60} via a decarboxylation route has been broadly accepted and referred to as the Prato reaction.[13,14] The fulleropyrrolidines thus formed present novel properties that are absent for the pristine C_{60}.[15,16] Addition of azomethine ylides to C_{60} and carbon nanotubes has generated some applicable materials such as C_{60}-modified HPLC stationary phases,[17] C_{60}-functionalized unnatural peptides with antimicrobial activity against two representative bacteria,[18] and soluble carbon nanotubes suitable for preparation of nanocomposites.[19,20] Yet to the best of our knowledge, the Prato reaction has never been exploited for functionalization of metallofullerenes; endohedral fulleropyrrolidines have not been reported yet. Whether the successful addition reaction of azomethine ylides to the neutral cages of C_{60} and carbon nanotubes could be working on the negatively charged carbon-cage of metallofullerene is still an unsolved problem. Here, we clear up this problem and present the first synthesis, isolation, and characterization of endohedral fulleropyrrolidines.

Results and Discussion

Illustrated in Figure 1 are the integrated tracing EPR spectra. As seen in Figure 1, after heating for one minute, the EPR intensity of the starting material La@C_{82}-A decreased and some new signals from products were detected, suggesting that La@C_{82}-A is very reactive toward the azomethine ylide for endohedral fulleropyrrolidines. As the reaction progressed and the starting materials were consumed, however, the new signals did not increase as expected; this indicates that the concentrations of adducts in solution were not raised. An HPLC analysis on the solution of reaction mixture showed the same results as well (Figure 2). In fact, some black precipitates were observed during the reaction, implying the lanthanum endohedral metallofulleropyrrolidines have low solubility in toluene. After reaction for 30 minutes, almost all of the La@C_{82}-A was consumed. The reaction was then terminated, and the precipitates were

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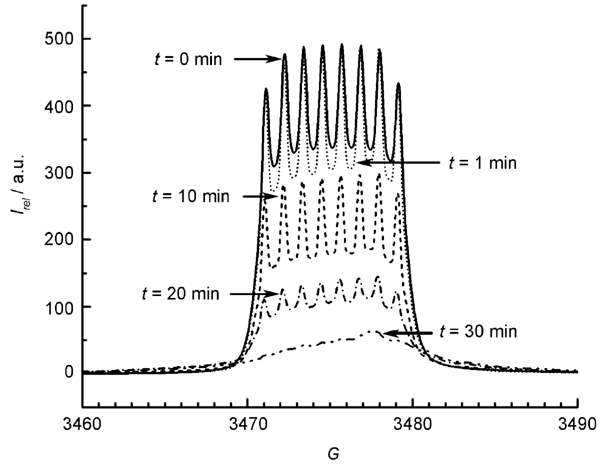


Figure 1. Integrated tracing EPR spectra of the reaction mixture in toluene recorded under the same conditions but different heating time. After heating for 1 min, the EPR intensity of La@C_{82}-A decreased and some new signals from products were detected; as the reaction was going, however, the new signals didn't increase as expected.

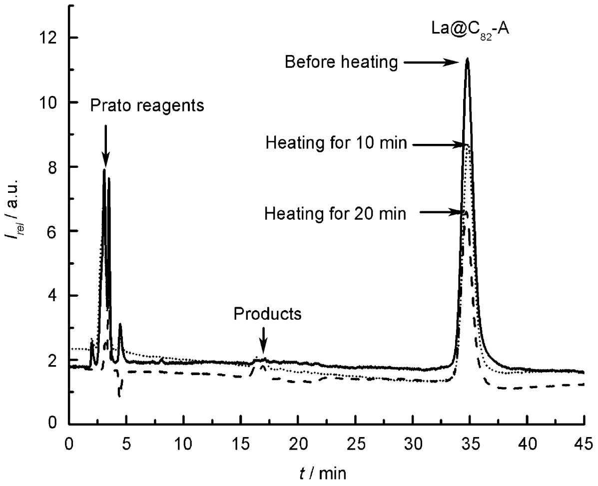


Figure 2. HPLC chromatograms of the reaction mixture in toluene recorded under the same conditions but different heating time (Buckyprep column). The concentrations of products did not increase with the consumption of La@C_{82}-A.

taken out and washed completely with toluene and hexane to remove the unreacted reagents. It was found that the precipitates are soluble in CS_2, chlorobenzene, *o*-dichlorobenzene, and 1,2,4-trichlorobenzene and the solutions are brown.

The precipitates were dissolved in chlorobenzene for multi-step HPLC separation. As shown in Figure 3, five components were resolved by HPLC. Mass spectroscopic analyses demonstrated the first three fractions consist of bisadducts and the last two monoadducts. Because of overlapping with each other, the two major fractions, bisadduct (III) and monoadduct (I), were collected, respectively, in the first stage and re-injected into HPLC for complete isolation in the second stage. By two HPLC processes, they were isolated in isomer-free form that was further confirmed by HPLC (Figure 3, insets a) and b)) and EPR (Figure 6) analyses and present a brown color in chlorobenzene or CS_2. As expected, their HPLC behaviors toward the Buckyprep column are different from each other and from that of their pristine La@C_{82}-A. With respect to the Buckyprep column under the same conditions, for example, the retention times of La@C_{82}-A, monoadduct (I), and bisadduct (III) decrease as the number of cycloaddition of pyrrolidine increases. Since HPLC retention time depends strongly on the geometric and electronic structures of the eluted molecule, the phenomena mentioned above suggest that the molecular geometry and electronic structure of La@C_{82}-A have been modified by addition of the pyrrolidine group, which is further substantiated by EPR and UV/Vis-NIR absorption spectroscopic analyses.

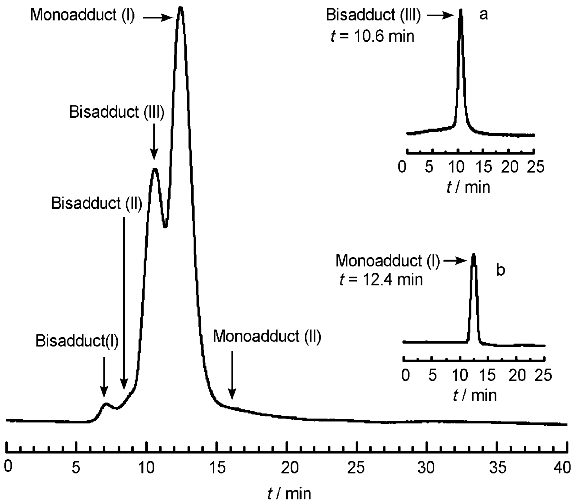


Figure 3. HPLC chromatograms for separation and purity measurement of lanthanum metallofulleropyrrolidines with a Buckyprep column. Insets a) and b) are the isolated bisadduct (III) and monoadduct (I), respectively. The HPLC retention times for bisadduct (III) and monoadduct (I) are 10.6 and 12.4 min, respectively.

The mass spectra of isolated endohedral metallofulleropyrrolidines are depicted in Figure 4. The parent peaks at *m*/*z* 1180 in Figure 4a and 1237 in Figure 4b unambiguously demonstrated that they are from the monoadduct and bisadduct of La@C_{82}-A, respectively. As seen in Figure 4a, the monoadduct (I) was clearly free of bisadduct (III). In addition, several fragments, where the mass peaks correspond to La@$C_{82}(CH_2)_2N$, La@$C_{82}(CH_2)_2$, La@$C_{82}CH_2$, and La@C_{82}, were formed by loss of CH_3, NCH_3, CH_2NCH_3, and $(CH_2)_2NCH_3$, respectively, from the metallofulleropyrrolidine La@$C_{82}(CH_2)_2NCH_3$ during the laser desorption process for mass spectrum. This clearly demonstrates that the azomethine ylide has been added by cycloaddition to La@C_{82}-A affording the metallofulleropyrrolidine by the Prato reaction (Scheme 1). In the mass spectrum of bisadduct (III) (Figure 4b), some fragments were observed as well. Since EPR and HPLC analyses had verified that the metallofulleropyrrolidine was in a pure and isomer-free form, the peaks at *m*/*z* 1194 and 1180 are unambiguously the fragments of bisadduct (III) by loss of CH_2NCH_3 and $(CH_2)_2NCH_3$, respectively.

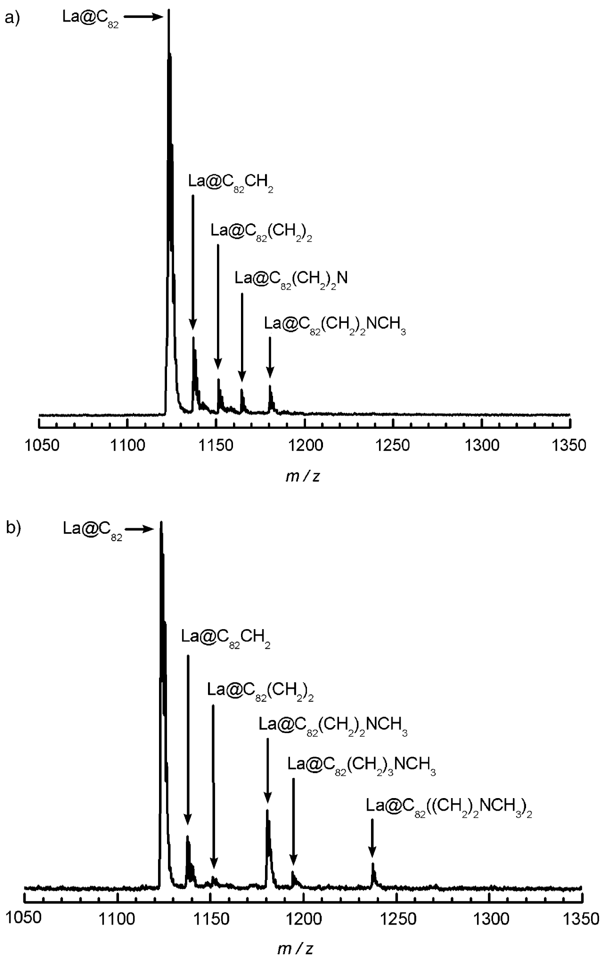


Figure 4. LD TOF mass spectra of isolated lanthanum metallofulleropyrrolidines: a) Monoadduct (I); b) bisadduct (III).

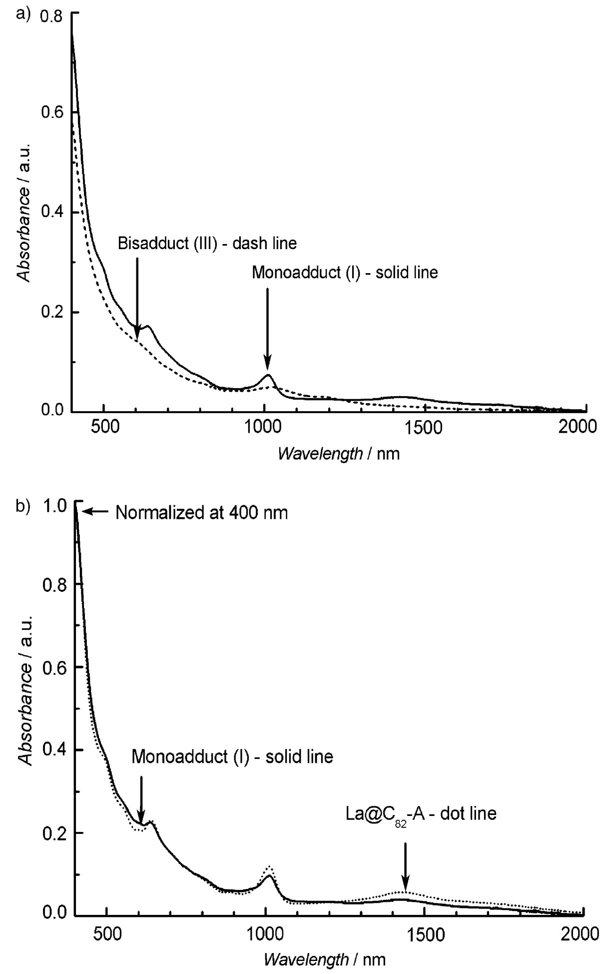
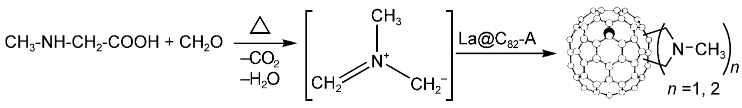


Figure 5. UV/Vis-NIR absorption spectra: a) Isolated monoadduct (I) and bisadduct (III); b) La@C_{82}-A and monoadduct (I) (normalized to have the absorbance at 400 nm at unit intensity for comparison).



Scheme 1. Prato reaction of La@C_{82}-A.

Figure 5a and b show the UV/Vis-NIR absorption spectra of the lanthanum endohedral metallofulleropyrrolidines together with that of La@C_{82}-A for comparison. It is found that the absorption features of monoadduct (I) are very similar to, but not the same with, those of its pristine La@C_{82}-A. For comparison, the absorption spectra of monoadduct (I) and La@C_{82}-A were normalized to have the absorbance at 400 nm at unit intensity (Figure 5b). With respect to La@C_{82}-A, the typical absorption peaks of monoadduct (I) are flattened, and the corresponding absorption centers are blue-shifted by ~3 nm for the absorption around 637 nm and by 7 nm for that around 1430 nm while that around 1010 nm remains unmoved. Substantial changes relative to their pristine La@C_{82}-A were observed in the absorption of bisadducts. Featureless absorption, for example, was seen for bisadducts (I) and (II). Relative to La@C_{82}-A, the only typical absorption peak of bisadduct (III) (around 1021 nm) is flattened and its center is red-shifted by 11 nm (Figure 5a). The phenomena mentioned above suggest that the electronic structure of La@C_{82}-A has been modified slightly upon monoaddition and significantly upon bisaddition of the pyrrolidines.

The EPR spectra of monoadduct (I) and bisadduct (III) of La@C_{82}-A are shown in Figure 6a and b, respectively. An EPR spectrum with an equally spaced octet hyperfine structure was observed for all the two endohedral metallofulleropyrrolidines, indicating isolation of the species is complete. The endohedral and octet EPR characters of the encased metal survived the reaction. The hyperfine coupling constants (HFCC), g values, and peak-to-peak linewidths (ΔH_{pp}) of the EPR spectra for the metallofulleropyrrolidines are listed in Figure 6. In terms of the three parameters and compared with that of bisadduct (III), the EPR spectrum of monoadduct (I) is closer to that of the pristine La@C_{82}-A (HFCC = 1.15207 G, g value = 2.00110, ΔH_{pp} = 0.36046 G), suggesting that modification on the electronic structure of La@C_{82}-A upon monocycloaddition of the pyrrolidine is less than that upon biscycloaddition. This is in good agreement

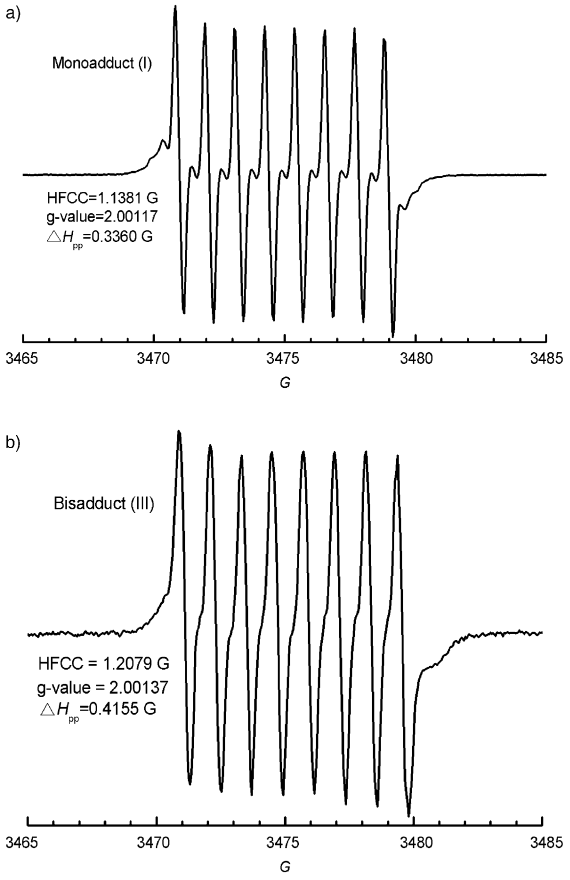


Figure 6. EPR spectra of isolated lanthanum metallofulleropyrrolidines: a) Monoadduct (I); b) bisadduct (III).

with the conclusion reached on the basis of absorption spectroscopic analysis. In addition, with respect to La@C_{82}-A, the octet EPR peaks of monoadduct (I) are a bit narrower in linewidth with a slightly smaller HFCC while those of bisadduct (III) behave oppositely. This also suggests impacts on the magnetic and electronic properties of La@C_{82}-A upon monoaddition of the pyrrolidine are different from those upon bisaddition.

Based on HPLC and EPR analyses, the total conversion yield of La@C_{82}-A to its metallofulleropyrrolidines in the reaction is up to 99%; the relative content of two major adducts—monoadduct (I) together with bisadduct (III)—is more than 95% in product. These clearly suggest that the Prato reaction of La@C_{82}-A is very efficient and, to some extent, regioselective; the addition reaction of azomethine ylide to the negatively charged carbon-cage of metallofullerene is successful. Furthermore, by use of different aldehydes (R^2CHO) and various N-functionalized glycines (R^1-NH-CH_2-COOH), and by replacement of La with other atoms or clusters, varied endohedral 2-R^2-N-R^1-3,4-metallofulleropyrrolidines with diversity of functions could be generated. Consequently, the scope of the Prato reaction of endohedral metallofullerenes could be very broad. The successful synthesis and isolation of lanthanum endohedral metallofulleropyrrolidines might open the way to new functionalized metallofullerenes with diversity of functions.

Conclusion

Two lanthanum endohedral fulleropyrrolidines have been produced, isolated, and spectroscopically characterized. Addition of the azomethine ylides to La@C_{82}-A is very efficient and, to some extent, regioselective. Introduction of pyrrolidines to the endohedral metallofullerene La@C_{82}-A cannot alter the octet EPR and endohedral characters of the encased metal atom but varies the electronic structure of the metallofullerene. The Prato reaction is also a valuable and versatile functionalization methodology for endohedral metallofullerenes, which could afford various endohedral metallofulleropyrrolidines with diversity of functions.

Experimental Section

La@C_{82}-A was prepared by arc discharge method and isolated by HPLC chromatography as reported previously.[21] On the basis of mass spectroscopic, HPLC, and EPR analyses, the purity of La@C_{82}-A was more than 99.9%. A toluene solution containing La@C_{82}-A (~1 mg) was sealed in an EPR quartz tube with excess N-methylglycine (extra pure, Wako, used as received) and paraformaldehyde (extra pure, Merck, Germany, used as received) and heated at 100°C (a Prato reaction of La@C_{82}-A, Scheme 1). The reaction process was traced with EPR and HPLC analyses, respectively. EPR spectra were recorded on a Bruker EMX-T EPR spectrometer (toluene or CS_2 solution, room temperature). Multi-step HPLC separation processes with a Buckyprep column were employed to isolate the lanthanum endohedral metallofulleropyrrolidines (Nacalai Tesque, i.d. 4.6×250 mm; eluant: chlorobenzene; flow rate: 1 mL min^{-1}; room temperature). Mass spectroscopic measurements were carried out on a MALDI Biflex III spectrometer, BRUKER (LD TOF MS, negative ion mode, with 9-nitroanthracene as matrix). UV/Vis-NIR absorption spectra were measured on a UV-3150 spectrometer (SHIMADZU) in CS_2 solution at room temperature.

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