Alkaloid−Fullerene Systems through Photocycloaddition Reactions[1]

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Received February 4, 2000

The photocycloaddition of tertiary amines to [60]fullerene (C_{60}) is an interesting and useful reaction. We wished to extend the applications of this type of reaction through an investigation of the photoaddition of alkaloids to C_{60} for the purpose of synthesizing novel and complex photoadducts that are difficult to obtain by usual methods. Irradiation of tazettine (**2**) or gramine (**3**) with C_{60} in toluene leads to formation of one monoadduct (**6** or **7**), whereas scandine (**1a**) or 10-hydroxyscandine (**1b**) reacts with C_{60} photochemically to give two products, the expected [6,6] monoadduct (**5a**, **5b**) and a new type of monoadduct with a bis-[6, 6] closed structure (**4a**, **4b**). These new structures were characterized by UV−vis, FT-IR, ^{1}H NMR, ^{13}C NMR, ^{1}H−^{1}H COSY, ROESY, HMQC (heteronuclear multiple-quantum coherence), and HMBC (heteronuclear multiple-bond connectivity) spectroscopy. The techniques of time-of-flight secondary ion MS (TOF-SIMS) and field desorption MS (FD-MS) were used for the mass determination. ^{3}He NMR analysis of the product mixture from photoaddition of **1a** to C_{60} containing a ^{3}He atom (^{3}He@C_{60}) led to two peaks at −9.091 and −11.090 ppm relative to gaseous ^{3}He, consistent with formation of a [6,6]-closed monoadduct and a bis-[6,6] closed adduct. Presumably, the bis-[6, 6] closed adducts are formed by an intramolecular [2 + 2] cycloaddition of the vinyl group to the adjacent 6,6-ring junction of C_{60} after the initial photocycloaddition.

Introduction

One of the most important applications of fullerenes is their potential to act as therapeutic agents. To date, a variety of fullerene derivatives possessing interesting biological properties have been synthesized.[2] Fullerene derivatives as HIV protease inhibitors and DNA-cleavage reagents have been reported by Wudl, Schuster, and by Nakamura, respectively.[3,4] Bioactive lipophilic fullerene steroids that inhibit radiolabeled estradiol binding to the cytosolic estrogen receptor have also been prepared.[5] Amino acid fullerene derivatives and fullerene peptides have also attracted attention as biologically active compounds.[6,7] Despite these exciting findings, much work remains to be done in developing new methods to produce suitable fullerene derivatives for biological investigations.

Naturally occurring alkaloids have historically proven to be effective biological weapons. We sought to develop a novel class of fullerene derivatives in which complex natural alkaloids are attached directly to the cage, thereby introducing C_{60} into the alkaloid family. Derivatives of this kind should be interesting candidates for biological investigation; however, few examples were found in the literature. One example, fulleronicotine, was obtained through a 1,3-dipole thermal addition.[8] Unfortunately, this method could not be extended to introduce complex alkaloids to C_{60}. The photocycloaddition of tertiary amines to C_{60} has been previously studied.[9] However, little attention has been directed toward expanding this type of reaction toward more complex photoadducts. We have recently reported that scandine

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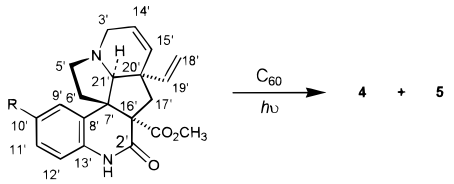
10.1021/jo000156h CCC: $19.00
Published on Web 05/20/2000

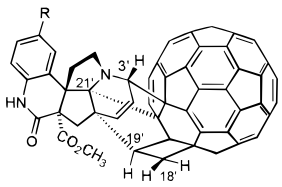
1a adds directly to C_{60} under irradiation to form a novel C_{60} adduct.[10] Herein, we report further investigations resulting in the synthesis of scandine-, 10-hydroxyscandine-, tazettine-, and gramine-containing [60]fullerenes. These fulleroalkaloids are structurally novel and difficult to obtain through conventional methods. ^{3}He NMR spectroscopy, developed by Saunders and co-workers,[11] was employed as a part of the characterization of the product of reaction of ^{3}He@C_{60} with **1a**.[12] As will be shown, ^{3}He NMR spectroscopy is a valuable tool for determining the number and type of isomers formed from additions of unsymmetrical reagents to fullerenes.

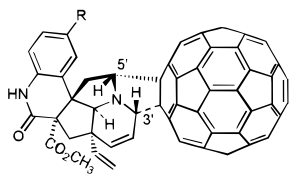
Results and Discussion

Synthesis of Scandine- and 10-Hydroxyscandine-[60]fullerene. Irradiation of a toluene solution containing C_{60} and scandine (**1a**) for 2 h resulted in products **4a** and **5a** at 41% and 37% yields, based on consumed C_{60}. These adducts were readily separable by flash chromatography on silica gel using methylene chloride as eluant. Adduct **4a** can be further purified by recrystallization from CH_2Cl_2/EtOAc. Adduct **5a** is more polar and much less soluble than **4a**. The reaction was proven to be photoinduced, as overnight heating of the reaction mixture at 60−70 °C in a covered flask led to no observable product. Under light, the reaction proceeded smoothly. Various household light bulbs can be used as the light source. In our experiments, a 60 W household tungsten bulb was effective.



1a R=H
1b R=OH





4a R=H
4b R=OH

5a R=H
5b R=OH

^{3}He encapsulated inside the C_{60} cage has proven useful in probing the magnetic field inside the fullerene.[12,13] All examples to date show that [6,6] closed monoadducts have ^{3}He resonances in a restricted range between −9.0 and −9.6 ppm relative to ^{3}He,[12b] with the exception of adducts attached via a three-membered ring.[12d] ^{3}He@C_{60} was subjected to the same irradiation conditions with **1a** and produced the same two products with about a 1:1 ratio. The ^{3}He NMR spectrum of the crude mixture in methylnaphthalene showed peaks at −9.091 and −11.090 ppm, apart from unreacted ^{3}He@C_{60} (−6.38 ppm). The ^{3}He@**5a** peak is at −9.091 ppm is in the range of [6,6] closed monoadducts, while the peak for ^{3}He@**4a** is at −11.090 ppm, well outside that range and the range for [6,5] open methylene-bridged adducts (−6.63 ppm)[12b] indicative of a novel structure. Interestingly, mass spectral analysis confirmed that both **4a** and **5a** are monoadducts.

The positive ion TOF-SIMS spectrum of **4a** displayed a moderately strong molecular ion peak at *m/z* 1069 (relative intensity 34%, $[M + H]^+$ for $C_{81}H_{21}N_2O_3$) along with a base peak at *m/z* 720 corresponding to C_{60}, indicating that one molecule of **1a** was attached to C_{60} with loss of two hydrogens. As expected, a very obvious $[M + Ag]^+$ ion peak appeared at *m/z* 1177,[14] further confirming the identity of the molecular ion peak. In our previous paper,[10] the proposed structure of **4a** was confirmed by UV−vis, FT-IR, TOF-SIMS, ^{1}H NMR, and ^{13}C NMR and further substantiated by HMQC, HMBC, and ROESY spectra. Interestingly, the path to **4a** involves a [2 + 2] cycloaddition between the vinyl group and the C_{60} double bond adjacent to the previously formed ring connection. The tertiary amino group and the vinyl group on the scandine moiety are fused to two 6,6-ring junctions of the same six-membered ring on the C_{60} moiety, thereby forming a bis-[6,6] closed structure analogous to 1,2,3,4-$C_{60}H_4$. The ^{3}He@**4a** peak at −11.090 ppm is in the range of the corresponding peak for ^{3}He@1,2,3,4-$C_{60}H_4$. The exact shift of ^{3}He@1,2,3,4-$C_{60}H_4$ is unknown but lies between −10.30 and −12.79 ppm.[12c] This range can therefore be used for compounds with this addition pattern. Finally, the UV spectrum of **4a** in methylene chloride also exhibits a shoulder around 430 nm, which is characteristic of [6,6] closed structures.[6d] However, in light of this result and other reports, compounds that are not [6,6] closed adducts may also show a shoulder at 430 nm.[13b,15]

The structure of **5a** was determined on the basis of the MS and NMR spectrum. TOF-SIMS failed to give the molecular ion. However, FDMS generated the molecular ion signal at *m/z* 1067 $[M^+ - H]$ as the base peak and the expected fragment for C_{60} at *m/z* 720, confirming a monoadduct of **1a** to C_{60}. The ^{1}H NMR spectrum exhibits the expected features similar to the spectrum of **1a** except for the disappearance of the signal for the two protons on the $C_{3'}$ and $C_{5'}$, indicating that they are the connecting sites. In the ^{1}H NMR spectrum of **5a**, the remaining $H_{3'}$ signal appeared at δ 5.35 ppm (dd, 1H, J 4.2, 1.8 Hz), whose vicinal coupling constant with $H_{14'}$ and allylic coupling constant with $H_{15'}$ are 4.2 and 1.8 Hz, respectively. The remaining $H_{5'}$ signal at 5.06 ppm (dd, 1H, J 8.4, 3.6 Hz) had vicinal coupling constants of 8.4 and 3.6

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(14) For TOF-SIMS spectroscopy, samples were prepared by dissolving each of the respective adducts in carbon disulfide and allowing a drop of the solution to dry on a silver plate and allowing the CS_2 to evaporate prior to analysis. As a result, a M^+ peak is always accompanied by a $[M + Ag]^+$ peak.

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Hz with the two nonequivalent $H_{6'}$ atoms. All the other proton signals were clearly identified by their chemical shifts and coupling patterns (see experimental). The ^{13}C NMR spectrum of **5a** is complicated; however, on the basis of HMQC and HMBC experiments, all the carbon signals pertaining to the **1a** moiety were identified. The two characteristic quaternary sp^3 carbon signals of the C_{60} cage appeared at 78.5 and 82.6 ppm, respectively. In light of the ^{3}He@**5a** NMR data and the two fullerene sp^3 carbons, it is safe to assume a [6,6] closed structure for **5a**. In the HMBC spectrum, the $H_{6'}$ at 4.04 ppm is two bonds away to $C_{5'}$ (75.4 ppm), $C_{7'}$ (62.5 ppm) and the three bonds away to $C_{16'}$ (65.8 ppm) and the sp^3 carbon of C_{60} at 82.6 ppm. This provides further evidence for the proposed structure of the adduct.

The stereochemistry of **5a** was confirmed by the presence of an NOE effect between protons $H_{3'}$ and $H_{5'}$. In the ROESY spectrum, an obvious correlation peak was observed between $H_{3'}$ and $H_{5'}$. Examination of molecular models indicates that the proposed stereochemistry for $C_{3'}$ and $C_{5'}$ is the only one in agreement with the NOE data.

Compound **1b** is analogous to **1a** in structure. Under similar reaction conditions, **1b** reacts with C_{60} to yield products **4b** (17%) and **5b** (20%). Due to the presence of the hydroxyl group, a longer reaction time is required and the products are much less soluble in common organic solvents such as carbon disulfide, toluene, methylene chloride, and chloroform. Separation of the products **4b** and **5b** was accomplished by flash chromatography on silica gel. The polarities are similar to that of **4a** and **5a** with **4b** being less polar than **5b**. In the case of **5b**, all attempts at further purification were unsuccessful due to it's poor solubility.

Compounds **4b** and **5b** were also characterized spectroscopically. The FDMS spectra gave the base molecular ion peak at *m*/*z* 1083 for **4b** [$M^+ - H$] and *m*/*z* 1085 for **5b** [$M^+ + H$] along with the fragmentation product C_{60}. In the case of **5b**, its UV−vis spectrum is very similar to that of 1,2-$C_{60}H_2$,[16] showing three strong absorptions at 222, 250, and 310 nm and a weak absorption at 430 nm. The UV−vis spectrum of **4b** is quite different from that of 1,2-$C_{60}H_2$, with only two strong absorptions (222 and 250 nm) in the ultraviolet region. In the low-absorbing visible region a weak absorption at 430 nm was observed. In agreement with the proposed structure of **4b**, the ^1H NMR spectrum reveals a doublet at 5.08 ppm (1H, d, *J* 5.4 Hz) for H_3. The vicinal coupling constant of H_3 with H_{14} (6.71 ppm, dd, *J* 9.6, 5.4 Hz) is 5.4 Hz. The allylic coupling constant of H_3 with H_{15} (6.86 ppm, d, *J* 9.6 Hz) was not observed. The signal for H_{21} was not observed indicating that C_{21} is attached to the fullerene. The H_{19} proton resonated at 4.26 ppm (1H, dd, *J* 3.60, 10.20 Hz) and the two H_{18} protons resonated at 3.77 (1H, dd, *J* 3.60, 13.80 Hz) and 3.64 ppm (1H, *J* 10.20, 13.80 Hz), respectively. Their chemical shifts and coupling constants reveal that they are no longer vinyl protons. The HMQC spectrum shows signals for C_{18} and C_{19} at 32.6 and 53.4 ppm, indicating they are sp^3-hybridized carbons. The ^{13}C NMR spectrum of **4b** also reveals four fullerene sp^3 carbon signals at 78.5, 76.8, 68.4, and 61.3 ppm, indicative of a bis-[6,6]-closed addition pattern on the fullerene cage. The ^1H NMR signal assignment was confirmed by the $^1H-^1H$ COSY spectrum, and the ^{13}C signal assignment was supported by the HMQC and HMBC spectra.

The ^1H NMR spectrum of **5b** is also in agreement with the proposed structure. As expected, the H_3 signal appears at 5.40 ppm as a doublet of doublets (1H, dd, *J* 4.2, 1.8 Hz), whose vicinal coupling constant with H_{14} and allylic coupling constant with H_{15} is 4.2 and 1.8 Hz, respectively. The H_5 resonates at 5.13 ppm also as a doublet of doublets (1H, dd, *J* 3.0, 8.4 Hz), whose coupling constants with the two nonequivalent C_6 protons (4.08 and 3.18 ppm, respectively) are 8.4 and 3.0 Hz. In light of their chemical shifts and coupling patterns, all the other proton signals can be clearly identified. Due to the poor solubility of **5b**, it was not possible to obtain its ^{13}C NMR spectrum.

For the mechanism of formation of **4a**, **4b**, **5a,** and **5b** (outlined in Scheme 1), evidence provided by previous investigators[9a,b,e] suggests that a photoinduced electron transfer from the tertiary amino group to C_{60} yields a radical ion pair in the first step. Deprotonation of the amine cation by the C_{60} anion to give **I** and $C_{60}H$ as a radical pair follows. Subsequent combination of the radical pair leads to intermediate **II** which can undergo further electron transfer, proton transfer, and radical pair combination processes to form **5a**, **5b** and intermediate **III**. In this process, the electron transfer could be intermolecular or intramolecular, since the monofunctionalized C_{60} can continue to serve as an electron acceptor.[9e] However, there is no readily available explanation for how the two protons are eliminated from intermediate **II** to form **5a**, **5b** and intermediate **III**. We suspect that it is due to an oxidation process since C_{60} is a good sensitizer for generation of singlet O_2,[4,17] which may abstract protons. However, even when photoirradiation was carried out under an inert atmosphere, the oxidation process was not prevented.

In the case of **III**, following the initial intermolecular reaction, an intramolecular [2+2] cycloaddition between the C_{60}−alkaloid system and the vinyl group occurs to produce **4a** and **4b**. This arrangement is the result of the vinyl group reacting with the closest double bond relative to the already existing connection to the alkaloid. The [2 + 2] cycloadditions to C_{60} are not easy and less common; only a few examples of simple olefins undergoing photoadditions to C_{60} have been reported.[18] In this case, however, the reaction proceeds easily, most likely promoted by increased localization of the electrons in C_{60} following the first addition. The unique [2 + 2] photocycloaddition of simple olefins to C_{60} following [3 + 2] cycloadditions of tertiary amines suggests that a "tether" (alkaloid in this case) can cause the reaction of olefins in close proximity with double bonds on the fullerene sphere.

Synthesis of Tazettine- and Gramine[60]fullerene. To explore the photoreaction further, two other types of alkaloids, namely, tazettine (**2**) and gramine (**3**), were investigated. Under photoirradiation, **2** reacts with C_{60} in toluene at room temperature to give **6** in 43% yield

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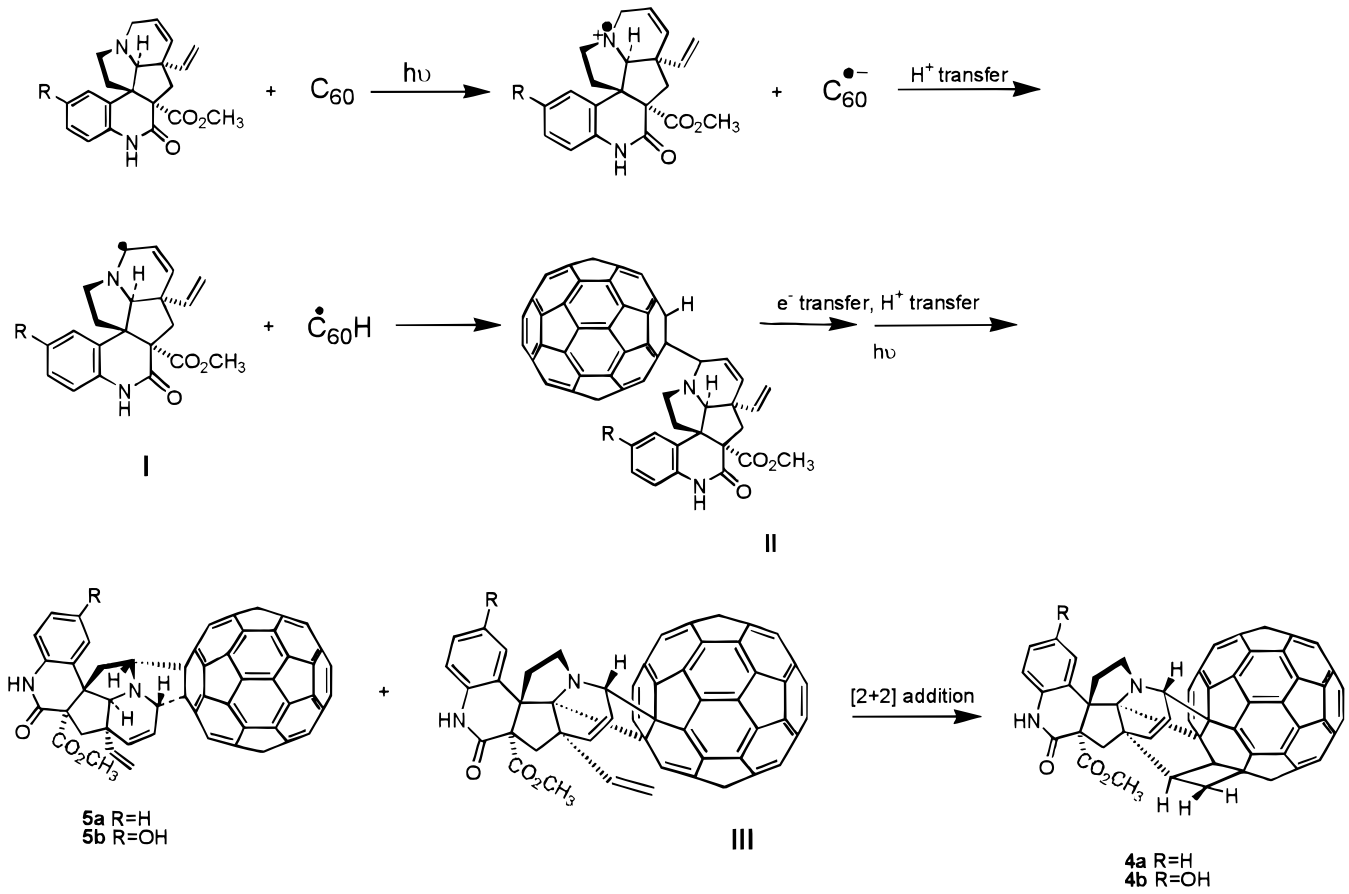
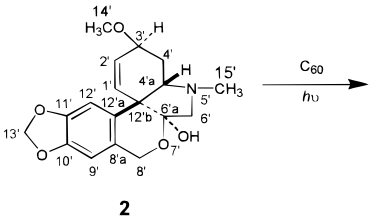
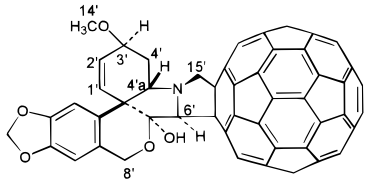
Scheme 1



based on the C_{60} consumed. The structure of **6** was determined on the basis of the MS, NMR, and IR spectral data. TOF-SIMS analysis of **6** shows the [MH^+] ion peak at *m*/*z* 1050. The presence of the hydroxyl group is indicated by an absorbance at 3427 cm^{-1} in the IR spectra.



2



6

The ^1H NMR spectrum of compound **6** (600 MHz, $CDCl_3$) shows separate signals for each proton, with each being identified on the basis of the $^1H-^1H$ COSY spectrum and the ^1H NMR data of **2** from the literature.[19] In accordance with the proposed structure of **6**, the ^1H NMR spectrum exhibits the aromatic 9′- and 12′-hydrogens at 6.56 and 6.88 ppm as singlets. The olefinic 1′- and 2′-hydrogens appear at 5.77 and 6.42 ppm as broad doublets whose small coupling with the 3′-hydrogen results in the peak broadening. The 3′-proton is a broad multiplet centered at 4.58 ppm. The 4′a-proton resonates at 3.78 ppm as a broad singlet. The two 4′-protons are nonequivalent, appearing at 2.71 and 1.86 ppm as multiplets due to the geminal coupling and the coupling to the adjacent 3′- and 4′a-protons. This coupling relationship among 3′-, 4′- and 4′a-protons was confirmed by $^1H-^1H$ COSY NMR. The two 8′-protons are also nonequivalent and show only geminal coupling, appearing as doublets at 5.19 and 5.01 ppm. Interestingly, the two 13′-protons are also nonequivalent but show no observable geminal coupling, appearing as singlets at 5.95 and 5.94 ppm. The disappearance of the geminal coupling is most likely due to two adjacent oxygen atoms with strong electronegativity. Importantly, the ^1H NMR spectrum displays only one CH_3 signal at 3.58 ppm (s, 3H, OCH_3). The signal for NCH_3 has disappeared, and instead, a CH_2 singlet appears at 5.07 ppm (s, 2H) which is assigned to NCH_2-. The 6′-proton signal appears as a singlet at 5.34 ppm (s, 1H). Thus, the ^1H NMR data are in excellent agreement with the proposed structure of the tazettine−C_{60} moiety. In the ^{13}C NMR spectrum, there are a total of 10 sp^3 signals in the range 30−81 ppm, corresponding to the eight sp^3 carbons except for the 6′a- and 13′-carbons of the tazettine moiety, and the two fullerene bridgehead sp^3 carbons at 71.2 and 68.8 ppm, indicative of a 6, 6-closed addition pattern on the fullerene cage. The 6′a- and 13′-carbons are expected to shift significantly downfield, and indeed appear at 102.8 and 100.9 ppm. The

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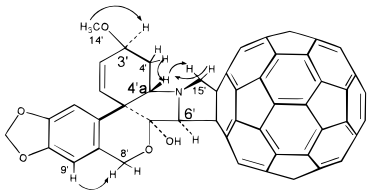
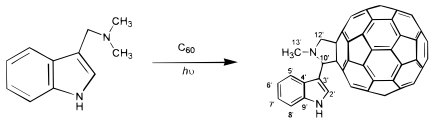


Figure 1.

olefinic 1′- and 2′-carbons appear at 128.1 and 133.8 ppm. The aromatic 8′a-, 9′-, 12′-, and 12′a-carbons appear at 125.5, 103.9, 108.8 and 123.7 ppm. In the 135−160 ppm range, 52 signals are observed, some of which overlap, corresponding to the aromatic 10′- and 11′-carbons and the 58 fullerene sp^2 carbons. The ^{13}C signals were assigned on the basis of the HMQC spectrum and the ^{13}C NMR data of **2** from the literature.[20]

Both ^{13}C and ^1H NMR spectra indicate compound **6** is stereoisomerically pure. The stereochemistry of tazettine is known.[21] To determine the configurations of the nitrogen and 6′-carbon atoms of **6**, a ROESY spectrum of compound **6** was measured. The observable NOE effects are shown in Figure 1, where it was found that both of the two 15′-protons spatially interact with the 4′a-proton, thus confirming a cis relationship. However, no hydrogen atoms show NOE effects with the 6′-hydrogen. Upon examination of molecular models considering the tension of the C_{60}-fused pyrrolidine ring, it can be concluded that the 6′-carbon has the *S*-configuration as shown in Figure 1. Recently, Wilson et al reported that a cotton effect near 430 nm in the circular dichroism (CD) spectrum can provide additional information for the determination of the absolute configuration of C_{60} derivatives with the [6, 6] closed structure.[22] According to the proposed sector rule, compound **6** with the stereochemistry shown in Figure 1 should yield a negative cotton effect centered at 430 nm. Indeed, the CD spectrum of **6** displays a negative cotton effect near 430 nm, confirming the *S*-configuration of the 6′-carbon.

Treatment of gramine (**3**) with C_{60} under photoirradiation in toluene at ambient temperature gave a major product **7** in 24% yield based on reacted C_{60}. The structure of **7**, which is relatively simple, contains an interesting indole core in addition to the C_{60}-fused pyrrolidine ring. The FD-MS spectrum shows clearly the molecular ion at *m*/*z* 892, confirming a monoadduct of **3** to C_{60}. In the ^1H NMR spectrum, the NH signal appears at 9.93 ppm as a singlet. Four characteristic aromatic proton signals appear at 8.07 (1H, broad singlet), 7.20 (1H, d, *J* 8.25 Hz), 6.98 (1H, dd, *J* 6.76, 7.27 Hz), and 6.94 (1H, dd, *J* 8.25, 6.76 Hz) ppm, assigned to H_5, H_8, H_6 and H_7. It was found that the H_5 signal shifted downfield and showed broadening. The downfield shift and broadening can be explained by the close proximity of this proton to the tertiary N atom resulting in a hydrogen bond. The olefinic 2′-proton resonates at 7.45 ppm as a singlet. The methine 10′-proton appears at 5.27 ppm also as a singlet. The methylene 12′-protons are nonequivalent, show geminal coupling, and appear at 4.98 and 4.23 ppm as doublets. Finally, a methyl singlet appears at 2.81 ppm and is assigned to the NCH_3. Thus, all the proton signals in the ^1H NMR spectrum are identified and are in excellent agreement with the proposed structure. In the ^{13}C NMR spectrum, there are a total of five sp^3 signals in the range 30−80 ppm, corresponding to the three protonated sp^3 carbons of the gramine moiety: C10′ (70.6 ppm), C12′ (40.5 ppm) and C13′ (30.2 ppm), and the two fullerene quaternary sp^3 carbons at 79.1 and 78.2 ppm, indicative of a 6,6-closed addition pattern on the fullerene cage. For the fullerene sp^2 carbons, 43 signals are observed in the 135−158 ppm range, some of which overlap, consistent with the asymmetric structure of **7**. In compound **7**, there is only one chiral center; the 10′-carbon. Since compound **3** is achiral, the product is necessarily an enantiomeric 1:1 mixture.



3 **7**

Pathways similar to Scheme 1 involving photoinduced sequential electron transfer, proton transfer and radical recombination can also explain the formation of compounds **6** and **7**.

In summary, the photoinduced reaction of tertiary amines with C_{60} has been shown to be an effective method for the synthesis of fullerene-alkaloid derivatives. All products obtained are cycloadducts: two single bonds are formed at the carbons adjacent to a tertiary nitrogen atom to connect the C_{60} cage with the skeleton of the alkaloid remaining intact. In the case of **1a** and **1b**, an unusual [2 + 2] cycloaddition of a free vinyl group with a C_{60} double bond in close proximity took place following the initial [3 + 2] cycloaddition of the tertiary amino group. This suggests that an alkaloid "tether" can force simple olefins to react with nearby double bonds on the fullerene. These novel derivatives are interesting structurally, and for their potential biological applications.

Experimental Section

General Methods. The samples of scandine, 10-hydroxyscandine, and tazettine were provided by Professor Y.-L. Zhou, Shanghai Institute of *Materia Medica*, Chinese Academy of Sciences, whose group isolated and purified these natural alkaloids from plants.[23,24] The sample of gramine was purchased from Roth Incorporation. All solvents were distilled prior to use. All reactions were carried out under atmosphere without any special caution to exclude air. All photochemical reactions were carried out similarly. Various household light bulbs can be used as the light source. In this experiment, a 60 W household tungsten bulb was used for all reactions. No cooling was applied, and the reaction solutions were allowed to warm from the heat of the light bulb. ^3He NMR spectra were taken at Yale University on a Brucker AM-500 spectrometer. The yields of products **4a**, **4b**, **5a**, **5b**, **6**, and **7** are based on consumed C_{60}. The recovered C_{60} and all of the isolated products were washed with ether and methanol, respectively, to correctly calculate the yields of the products.

Synthesis of Compounds 4a and 5a. A mixture of 37.2 mg of C_{60} (0.052 mmol) and 53.4 mg of **1a** (0.152 mmol, 2.9

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(22) Wilson, S. R.; Lu, Q.; Cao, J.; Wu, Y.; Welch, C. J.; Schuster, D. I. *Tetrahedron* **1996**, *52*, 5131.
(23) For scandine and 10-hydroxyscandine, see: (a) Zhou, Y.-L.; Ye, J.-H.; Li, Z.-M.; Huang, Z.-H. *Planta Med*. **1988**, *4*, 315. (b) Guo, L.-W.; Zhou, Y.-L. *Phytochem*. **1993**, *34*, 563.
(24) For tazettine, see: (a) Hong, S.-H.; Zhou, Y.-L. *Acta Pharm. Sinica* **1964**, *11*, 1. (b) Hong, S.-H.; Zhou, Y.-L. *Acta Pharm. Sinica* **1966**, *13*, 499.

equiv) was dissolved in 25 mL of toluene. The solution was stirred at ambient temperature and was irradiated with a 60 W bulb for 2 h. The color of the solution changed from purple to dark brown. The reaction mixture was separated on a silica gel column with toluene (to give unreacted C_{60} 13.5 mg) then methylene chloride/ethyl acetate (25:1) to afford compound **4a** (14.5 mg, yield 41%), and finally with methylene chloride−ethyl acetate (15:1) to afford compound **5a** (13.0 mg, 37%).

Compound 4a. Its UV−vis, FT-IR, TOF-SIMS, ^{1}H NMR, and ^{13}C NMR spectral data have been described elsewhere.[10]

Compound 5a. ^{1}H NMR (600 MHz, CS_2−CD_3COCD_3, 5:1): δ 7.37 (d, 1H, J = 7.8 Hz, $H_{9'}$), 7.07 (dd, 1H, J = 7.8, 7.2 Hz, $H_{11'}$), 6.89 (d, 1H, J = 7.8 Hz, $H_{12'}$), 6.82 (dd, 1H, J = 7.8, 7.2 Hz, $H_{10'}$), 6.62 (dd, 1H, J = 4.2, 9.6 Hz, $H_{14'}$), 6.08 (dd, 1H, J = 9.6, 1.8 Hz, $H_{15'}$), 5.43 (dd, 1H, J = 17.4, 11.4 Hz, $H_{19'}$), 5.35 (dd, 1H, J = 4.2, 1.8 Hz, $H_{3'}$), 5.06 (dd, 1H, J = 8.1, 3.3 Hz, $H_{5'}$), 4.98 (d, 1H, J = 17.4 Hz, $H_{18'}$), 4.85 (s, 1H, $H_{21'}$), 4.73 (d, 1H, J = 11.4 Hz, $H_{18'}$), 4.04 (dd, 1H, J = 8.1, 14.7 Hz, $H_{6'}$), 3.82 (s, 3H, OCH_3), 3.74 (d, 1H, J = 14.4 Hz, $H_{17'}$), 3.06 (dd, 1H, J = 14.7, 3.3 Hz, $H_{6'}$), 2.40 (d, 1H, J = 14.4 Hz, $H_{17'}$). ^{13}C NMR (150.9 MHz, CS_2−CD_3COCD_3, 5:1): δ 170.1 (ester C═O), 168.2 (amide C═O), 156.4, 155.4, 154.8, 154.5, 148.5, 147.5, 147.4, 147.3, 147.2, 146.7 (2), 146.6 (2), 146.5 (2), 146.4 (2), 146.3 (2), 146.1, 145.8 (2), 145.7 (2), 145.6 (2), 145.5 (2), 144.9 (2), 144.8, 144.7, 143.9, 143.7, 143.6, 143.3 (2), 143.2 (2), 143.1 (2), 143.0 ($C_{19'}$), 142.7 (2), 142.6 (2), 142.5, 142.4, 142.34, 141.8, 141.4, 141.3, 140.9, 140.8, 140.7, 136.5 ($C_{13'}$), 136.0 ($C_{15'}$), 135.5, 135.1, 134.4, 134.3, 128.2 ($C_{11'}$), 127.5 ($C_{9'}$), 123.3 ($C_{8'}$), 123.1 ($C_{14'}$), 123.0 ($C_{10'}$), 115.8 ($C_{12'}$), 114.1 ($C_{18'}$), 82.6 (sp^3 C of C_{60}), 78.5 (sp^3 C of C_{60}), 76.3 ($C_{21'}$), 75.4 ($C_{5'}$), 70.9 ($C_{3'}$), 65.3 ($C_{16'}$), 62.3 ($C_{7'}$), 52.1 (OCH_3), 48.3 ($C_{20'}$), 46.8 ($C_{17'}$), 43.8 ($C_{6'}$). The HMQC and HMBC spectra confirm the assignment of the carbon signals. UV−vis (CH_2Cl_2) λ_{max}: 224, 254, 310, 430 nm. FT-IR (KBr) ν: 3400, 1751, 1670, 523 cm^{-1}. FD-MS m/z (relative intensity): 1067 (M^+ − 1, 100), 720 (C_{60}, 37).

Synthesis of ^{3}He@4a and ^{3}He@5a. A mixture of 10.1 mg of ^{3}He@C_{60} (0.014 mmol) and 11.9 mg of **1a** (0.034 mmol, 2.4 equiv) was dissolved in 12 mL of toluene. The solution was stirred at ambient temperature and was irradiated with a 60 W bulb for 2 h. The color of the solution changed from purple to dark brown. The solvent was removed in vacuo. The residue was then submitted for ^{3}He NMR spectrometric analysis. The spectrum showed two new peaks at −9.091 and −11.090 ppm in addition to the C_{60} peak at −6.38 ppm (relative to gaseous ^{3}He at 0.00 ppm) in a ratio of ca. 1:1.

Synthesis of Compounds 4b and 5b. A 43.0 mg portion of C_{60} (0.057 mmol) and 115.2 mg of **1b** (0.315 mmol, 5.3 equiv) were dissolved in 40 mL of toluene; a little chloroform was added in order to completely dissolve **1b**. The resulting solution was stirred at ambient temperature and was irradiated with a 60 W bulb for 24 h. The color of the solution changed from purple to red. The reaction mixture was separated on a silica gel column with toluene (to remove unreacted C_{60} 25.0 mg), then methylene chloride/ethyl acetate (4:1) to afford compounds **4b** (4.6 mg, 17%) and **5b** (5.5 mg, 20%).

Compound 4b. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.59 (s, 1H, NH), 7.09 (br. s, 1H, $H_{9'}$), 6.86 (d, 1H, J = 9.6 Hz, $H_{15'}$), 6.71 (dd, 1H, J = 9.6, 5.7 Hz, $H_{14'}$), 6.36 (dd, 1H, J = 2.1, 8.4 Hz, $H_{11'}$), 6.07 (d, 1H, J = 8.4 Hz, $H_{12'}$), 5.08 (d, 1H, J = 5.7 Hz, $H_{3'}$), 4.27 (dd, 1H, J = 3.6, 10.2 Hz, $H_{19'}$), 3.77 (dd, 1H, J = 3.6, 13.8 Hz, $H_{18'}$), 3.64 (dd, 1H, J = 13.8, 10.2 Hz, $H_{18'}$), 3.63 (s, 3H, OCH_3), 3.47 (m, 1H, $H_{5'}$), 3.45 (d, 1H, J = 13.8 Hz, $H_{17'}$), 3.33 (m, 1H, $H_{5'}$), 3.26 (m, 1H, $H_{6'}$), 2.68 (d, 1H, J = 13.8 Hz, $H_{17'}$), 2.33 (m, 1H, $H_{6'}$). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 169.7 (ester C═O), 167.7 (amide C═O), 153.5, 152.5, 151.8 ($C_{10'}$), 150.2, 149.4, 149.0, 148.6, 148.5, 148.1, 147.9, 147.8, 147.7, 147.0, 146.6, 146.4, 146.3 (2), 146.2, 146.0 (2), 145.6, 145.5 (2), 145.3, 145.2, 144.9, 144.8, 144.7, 144.5 (2), 144.4 (2), 144.2 (2), 144.1, 143.9, 143.5, 143.0, 142.9 (2), 142.7, 142.5 (2), 142.4, 142.3, 142.2, 142.1, 142.0, 141.7, 141.6, 141.4, 140.6, 140.1, 138.3 ($C_{13'}$), 137.7, 137.3, 136.6, 135.5, 133.2 ($C_{15'}$), 126.7 ($C_{14'}$), 124.7 ($C_{8'}$), 117.9 ($C_{9'}$), 117.5 ($C_{12'}$), 115.8 ($C_{11'}$), 100.0 ($C_{21'}$), 78.5 (sp^3 C of C_{60}), 76.8 (sp^3 C of C_{60}), 68.5 (sp^3 C of C_{60}), 64.8 ($C_{16'}$), 61.3 (sp^3 C of C_{60}), 61.0 ($C_{3'}$), 58.8 ($C_{7'}$), 55.4 ($C_{20'}$), 53.4 ($C_{19'}$), 53.2 (OCH_3), 42.9 ($C_{5'}$), 42.3 ($C_{17'}$), 41.7 ($C_{6'}$), 32.6 ($C_{18'}$). The HMQC and HMBC spectra confirm the assignment of the carbon signals. UV−vis (CH_2Cl_2) λ_{max}: 222, 250, 430 nm. FT-IR (KBr) ν: 3409, 1724, 1660, 528 cm^{-1}. FD-MS m/z (relative intensity): 1083 (M^+ − 1, 100), 720 (C_{60}, 38).

Compound 5b. ^{1}H NMR (600 MHz, CS_2−$CDCl_3$, 1:1): δ 7.6 (s, 1H, NH), 7.04 (d, 1H, J = 2.4 Hz, $H_{9'}$), 6.69 (dd, 1H, J = 2.4, 8.4 Hz, $H_{11'}$), 6.64 (dd, 1H, J = 9.6, 4.2 Hz, $H_{14'}$), 6.58 (d, 1H, J = 8.4 Hz, $H_{12'}$), 6.11 (dd, 1H, J = 9.6, 1.8 Hz, $H_{15'}$), 5.55 (dd, 1H, J = 16.8, 10.8 Hz, $H_{19'}$), 5.40 (dd, 1H, J = 1.8, 4.2 Hz, $H_{3'}$), 5.12 (dd, 1H, J = 3.0, 8.4 Hz, $H_{5'}$), 5.08 (d, 1H, J = 16.8 Hz, $H_{18'}$), 4.97 (s, 1H, $H_{21'}$), 4.87 (d, 1H, J = 10.8 Hz, $H_{18'}$), 4.08 (dd, 1H, J = 15.0, 8.4 Hz, $H_{6'}$), 3.99 (s, 3H, OCH_3), 3.92 (d, 1H, J = 14.4 Hz, $H_{17'}$), 3.19 (dd, 1H, J = 15.0, 3.0 Hz, $H_{6'}$), 2.65 (d, 1H, J = 14.4 Hz, $H_{17'}$). UV−vis (CH_2Cl_2) λ_{max}: 222, 250, 310, 430 nm. FT-IR (KBr) ν: 3375, 1757, 1655, 526 cm^{-1}. FD-MS m/z (relative intensity): 1085 (M^+ + 1, 100), 720 (C_{60}, 66).

Synthesis of Compound 6. A mixture of 33.6 mg of C_{60} (0.047 mmol) and 55.4 mg of **2** (0.167 mmol, 3.6 equiv) was dissolved in 30 mL of toluene and was irradiated with a 60 W bulb for 19 h while stirring. The color of the solution changed from purple to red. The reaction mixture was separated on a silica gel column with toluene (to remove unreacted C_{60} (26.4 mg)) and then methylene chloride/ethyl acetate (40:1) to afford compound **6** (4.5 mg, 43%).

Compound 6. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.88 (s, 1H, $H_{12'}$), 6.56 (s, 1H, $H_{9'}$), 6.42 (br. d, 1H, J = 10.52 Hz, $H_{2'}$), 5.95 (s, 1H, $H_{13'}$), 5.94 (s, 1H, $H_{13'}$), 5.77 (br. d, 1H, J = 10.52 Hz, $H_{1'}$), 5.34 (s, 1H, $H_{6'}$), 5.19 (d, 1H, J = 14.6 Hz, $H_{8'}$), 5.07 (s, 2H, $H_{15'}$), 5.01 (d, 1H, J = 14.6 Hz, $H_{8'}$), 4.58 (m, 1H, $H_{3'}$), 3.78 (br. s, 1H, $H_{4'a}$), 3.58 (s, 3H, OCH_3), 2.71 (m, 1H, $H_{4'}$), 1.86 (m, 1H, $H_{4'}$). The ^{1}H−^{1}H COSY spectrum confirms the assignment of the H signals. ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 156.3, 155.8, 154.3, 150.7, 147.2, 147.1, 146.8, 146.6, 146.2, 146.1, 146.0, 145.9, 145.9, 145.9 (2), 145.7 (2), 145.6, 145.4, 145.3, 145.2, 145.2, 145.2 (2), 145.1, 145.0 (2), 145.0 (2), 144.6, 144.5, 144.5, 144.5, 144.1, 143.1, 143.0, 142.5, 142.4, 142.4, 142.3, 142.1, 141.9, 141.8, 141.8 (2), 141.7, 141.78 (2), 141.7, 141.6, 141.5, 141.4, 140.1, 140.0, 139.9, 139.6, 139.4, 136.0, 135.2, 135.1, 133.8 ($C_{2'}$), 128.1 ($C_{1'}$), 125.4 ($C_{8'a}$), 123.7 ($C_{12'a}$), 108.8 ($C_{12'}$), 103.9 ($C_{9'}$), 102.8 ($C_{6'a}$), 100.9 ($C_{13'}$), 80.9 ($C_{6'}$), 72.2 ($C_{3'}$), 71.2 (sp^3 C of C_{60}), 69.9 (2C, $C_{4'a}$ + $C_{15'}$), 68.8 (sp^3 C of C_{60}), 61.5 ($C_{8'}$), 56.0 (OCH_3), 51.5 ($C_{12'b}$), 30.0 ($C_{4'}$). The HMQC spectrum confirms the assignment of the carbon signals. UV−vis (CH_2Cl_2) λ_{max}: 226, 255, 310, 365, 430 nm. FT-IR (KBr) ν: 3427, 1481, 1246, 1187, 1090, 1040, 750, 528 cm^{-1}. TOF-SIMS m/z (relative intensity): 720 (C_{60}, 100), 1050 (M^+ + 1, 76), 1157 (M^++Ag, 6).

Synthesis of Compound 7. A mixture of 34.5 mg of C_{60} (0.048 mmol) and 34.1 mg of **3** (0.196 mmol, 4.1 equiv.) was dissolved in 30 mL of toluene. The solution was stirred at ambient temperature and was irradiated with a 60 W bulb for 5 h. The color of the solution changed from purple to brown. Then the solvent was removed in vacuo. The residue was dissolved in CS_2 and separated on a silica gel with toluene: hexane (1:1) to remove unreacted C_{60} (9.5 mg), then pure toluene to afford compound **7** (7.4 mg, 24%).

Compound 7. ^{1}H NMR (600 MHz, CS_2−CD_3COCD_3, 5:1): δ 9.93 (s, 1H, NH), 8.07 (br. s, 1H, $H_{5'}$), 7.45 (s, 1H, $H_{2'}$), 7.20 (d, 1H, J = 8.25 Hz, $H_{8'}$), 6.98 (dd, 1H, J = 6.76, 7.27 Hz, $H_{6'}$), 6.94 (dd, 1H, J = 8.25, 6.76 Hz, $H_{7'}$), 5.27 (s, 1H, $H_{10'}$), 4.98 (d, 1H, J = 9.21 Hz, $H_{12'}$), 4.23 (d, 1H, J = 9.21 Hz, $H_{12'}$), 2.81 (s, 3H, N−CH_3). ^{13}C NMR (150.9 MHz, CS_2−CD_3COCD_3, 5:1): δ 157.3, 155.4, 154.8, 147.7, 147.6, 147.3, 147.1, 146.7, 146.6, 146.6, 146.5, 146.3, 146.2, 146.0 (2), 145.9, 145.8, 145.68 (2), 145.5, 145.1, 144.8, 143.5, 143.4, 143.1, 143.0 (2), 142.8 (2), 142.6 (2), 142.6 (2), 142.5, 142.4, 142.4, 142.3, 142.1, 142.0, 140.6, 140.5, 140.2, 140.1 (2), 140.0, 137.3 (2), 137.2, 137.1, 137.0 (2), 136.9, 136.3 (2), 136.1 (2), 135.5, 135.4, 135.1, 128.8, 125.6, 125.4, 122.7, 121.6, 120.3, 112.1, 79.1 (sp^3 C of C_{60}), 78.2 (sp^3 C of C_{60}), 70.6 ($C_{10'}$), 40.4 ($C_{12'}$), 30.2 (NCH_3). UV−vis (CH_2Cl_2) λ_{max}: 221, 248, 310, 430 nm. FT-IR (KBr) ν: 3409, 1452, 1179, 737, 527 cm^{-1}. FD-MS m/z (relative intensity): 892 (M^+, 28), 720 (C_{60}, 100).

Acknowledgment. We thank the National Science Foundation of China (29772005) and the Foundation of State Key Laboratory of Bioorganic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, for financial support.

Supporting Information Available: The ^{1}H NMR spectra for all the obtained C_{60} derivatives. The ^{13}C NMR spectra for all the obtained C_{60} derivatives except **5b**. The TOF-SIMS spectrum for **4a**. The COSY spectra for **4a**, **4b**, and **6**. The ROESY spectra for **4a**, **5a**, and **6**. The HMQC spectra for **4a**, **4b**, **5a**, and **6**. The HMBC spectra for **4a** and **5a**. The CD spectrum for **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO000156H