ORGANIC LETTERS

2005
Vol. 7, No. 26
5897−5900

The First Synthesis of a Methano[60]fullerene with an Electron-Donating Group at the Methano-Bridge Carbon: Synthesis and Reaction of Aminomethano[60]fullerene

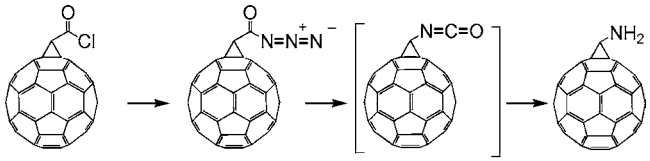
Tomoyuki Tada, Yasuhiro Ishida, and Kazuhiko Saigo*

Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

saigo@chiral.t.u-tokyo.ac.jp

Received October 17, 2005

ABSTRACT



The Curtius Rearrangement

Aminomethano[60]fullerene was synthesized for the first time as a trifluoromethanesulfonic acid salt by applying the Curtius rearrangement of azidocarbonylmethano[60]fullerene as the key reaction. Aminomethano[60]fullerene thus obtained was found to be able to react with various acyl chlorides to afford the corresponding amides.

Owing to easy accessibility by well-established synthetic methods and striking resemblance in physical properties to [60]fullerene (C_{60}), methano[60]fullerenes have been regarded as versatile building blocks for fullerene-containing functional materials.[1] In the synthesis and application of methano[60]fullerenes, substituents at the methano-bridge carbon of their cyclopropane rings have significant importance because they often bring a determinant influence on the properties of methano[60]fullerenes, and they can work as useful linkers to connect a C_{60} unit with other functional molecules.[1,2] Pioneering investigations have made various methano[60]fullerenes available. At the present time, however, synthetically available methano[60]fullerenes are restricted to those with at least one electron-withdrawing group, such as carboxyl (and its equivalents), keto, formyl, cyano, bromo, alkynyl, or aryl group.[2] Thus, the synthesis of simple methano[60]fullerenes with a complementary electron-donating functional group, such as aminomethano[60]fullerene and hydroxymethano[60]fullerene, still remains as a challenging target. The potent reactivity of such functional groups as amino and hydroxy groups would highly expand the utility of chemically functionalized fullerenes. Furthermore, methano[60]fullerenes with an electron-donating group are expected to be attractive motifs for the study on chemistry and physics related to fullerenes because the effects of such functionalities on the methano-bridge carbon have not been investigated yet. Here we report the first synthesis of aminomethano[60]-

(1) (a) Diederich, F.; Isaacs, L.; Philp, D. *Chem. Soc. Rev.* **1994**, *23*, 243. (b) Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157. (c) Keshavarz, K. M.; Knight, B.; Haddon, R. C.; Wudl, F. *Tetrahedron* **1996**, *52*, 5149. (d) Nierengarten, J.-F.; Habicher, T.; Kessinger, R.; Cardullo, F.; Diederich, F.; Gramlich, V.; Gisselbrecht, J.-P.; Boudon, C.; Gross, M. *Helv. Chim. Acta* **1997**, *80*, 2238.

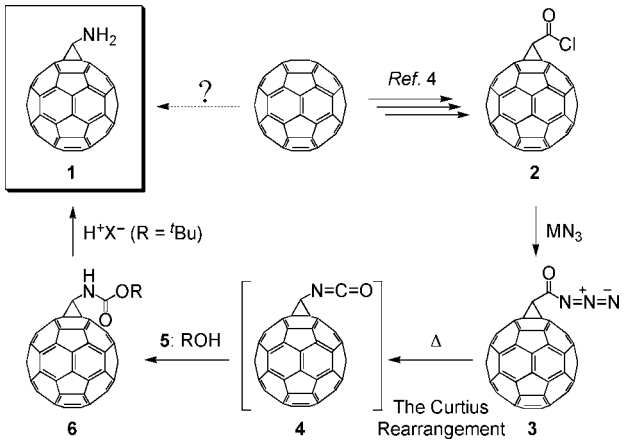
(2) For selected examples of functionalized methano[60]fullerenes, see: (a) Bingel, C. *Chem. Ber.* **1993**, *126*, 1957. (b) Bestmann, H. J.; Hadawi, D.; Röder, T.; Moll, C. *Tetrahedron Lett.* **1994**, *35*, 9017. (c) Benito, A. M.; Darwish, A. D.; Kroto, H. W.; Meidine, M. F.; Taylor, R.; Walton, D. R. M. *Tetrahedron Lett.* **1996**, *37*, 1085. (d) Hino, T.; Kinbara, K.; Saigo, K. *Tetrahedron Lett.* **2001**, *42*, 5065. (e) Hamada, M.; Hino, T.; Kinbara, K.; Saigo, K. *Tetrahedron Lett.* **2001**, *42*, 5069. (f) Burley, G. A.; Keller, P. A.; Pyne, S. G.; Ball, G. E. *J. Org. Chem.* **2002**, *67*, 8316.

10.1021/ol052509a CCC: $30.25
Published on Web 12/01/2005

fullerene, which is also the first example of the rearrangement of a functional group at the methano-bridge carbon of methano[60]fullerene. Aminomethano[60]fullerene thus obtained was proved to be a versatile precursor for the synthesis of various methano[60]fullerene derivatives.

For the preparation of aminomethano[60]fullerene (**1**), one of the most straightforward strategies is to treat C_{60} with a cyclopropanating reagent bearing an amino group or its equivalent. Despite its simplicity, this method seems to be hardly possible because the electron-donating functional group, attached to the methylene/methyne carbon in the cyclopropanating reagent, is unsuitable for the preservation of the reactivity of the carbon and/or for the stabilization of the reactive intermediate generated.[1,2] Therefore, as a conceptually novel method for the preparation of functionalized methano[60]fullerenes, we focused on the rearrangement reaction of a functional group adjacent to the methano-bridge carbon of a cyclopropane ring. Among general functional groups, a carbonyl group is a suitable functional group for our strategy because of the ease of its introduction to a methano[60]fullerene structure and because of its possible transformation to an amino group via well-known rearrangement reactions, such as the Curtius, Hofmann, Schmidt, and Lossen reactions.[3] Taking into account the intolerance of fullerene derivatives to strong acids and bases, we targeted on a synthetic route using the Curtius rearrangement as the key reaction, as shown in Scheme 1.

Scheme 1. Synthetic Scheme for Aminomethano[60]fullerene (**1**)



As the starting material for the preparation of the acyl azide **3**, we used the acyl chloride **2**, of which the synthetic method was recently established by our group.[4] For the successful synthesis of **3**, the selection of azidating reagent and/or reaction conditions is crucial because the particular properties of C_{60}, such as bulkiness, electron-withdrawing characteristic, and poor solubility, often bring an unpredictable effect on the reactivity of functional groups attached to C_{60}. In fact, the efficiency of the conversion from **2** to **3** significantly depended on azidating reagents (Table 1). For example,

Table 1. Transformation of the Acyl Chloride **2** to the Acyl Azide **3**[a]

entry	MN_3 (equiv)	additive (equiv)	time (h)	yield (%)
1	$(CH_3)_3SiN_3$ (5.0)	none	18	trace
2	$(CH_3)_3SiN_3$ (5.0)	ZnI_2 (1.2)	18	trace
3	$(CH_3)_3SiN_3$ (5.0)/NaN_3 (1.0)	18-Crown-6 (1.0)	18	34
4	n-Bu_3SnN_3 (3.0)	none	0.5	84

[a] The reactions were conducted in PhBr at room temperature.

treatment of **2** with trimethylsilyl azide in bromobenzene gave only a trace amount of **3**, and even in the presence of an activator, the yield was only slightly improved (entries 1−3). Finally, we found that tributyltin(IV) azide readily reacted with **2** at room temperature to afford **3** in good yield (entry 4).[5] The acyl azide **3** thus obtained was found to be so stable that it could be isolated by preparative TLC.[6]

We next tried the Curtius rearrangement of the acyl azide **3** to the isocyanate **4**. Upon heating an *o*-xylene or toluene solution, **3** was quantitatively converted to a material with high polarity, suggesting that the Curtius rearrangement proceeded successfully to afford the isocyanate **4**. However, to avoid the possible 1,3-dipolar cycloaddition of the isocyanate to a C_{60} core, **4** was not isolated but directly converted to the carbamates **6** by conducting the rearrangement in the presence of alcohols.[7] For the transformation of **4** to **6**, the alcohols **5a**−**d** were selected because the resultant **6a**−**d** were expected to be cleaved by well-established reactions to afford aminomethano[60]fullerene (**1**). The addition of **5** to **4** was significantly influenced by the reaction temperature (Table 2). In refluxing toluene, a large excess amount of **5a** was required in order to achieve the addition in acceptable yield (entry 1 vs entry 2). In contrast, at a higher temperature (in refluxing *o*-xylene), a relatively small amount of **5a** was adequate to afford **6a** in good yield (entries 3 and 4).

Under optimized conditions, we carried out the reaction of **4** to **6**. The addition of the primary alcohols **5a**−**c** gave the corresponding carbamates **6a**−**c** in moderate to good yields (Table 2, entries 4−6).[7] Only in the case of the tertiary alcohol **5d** did the carbamate formation proceed sluggishly to afford **6d** in poor yield, which is most likely due to the

(3) For a selected review, see: Maruoka, K.; Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B., Flemming, I., Eds.; Pergamon: Oxford, 1991; Vol. 6, pp 763−793.

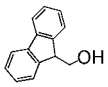
(4) Ito, H.; Tada, T.; Sudo, M.; Ishida, Y.; Hino, T.; Saigo, K. *Org. Lett.* **2002**, *5*, 2643.

(5) Saito, S.; Yamashita, S.; Nishikawa, T.; Yokoyama, Y.; Inaba, M.; Moriwake, T. *Tetrahedron Lett.* **1989**, *30*, 4153.

(6) All of the new compounds except for **1**·HOTf and **4** were purified by preparative TLC and identified by ^{1}H NMR, FT-IR, and MALDI-TOF-MS spectroscopies. In the cases of the amides **8a** and **8e**, their ^{1}H NMR spectra could not be obtained because of their poor solubility in most solvents (see Supporting Information).

(7) (a) Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F. *J. Am. Chem. Soc.* **1992**, *114*, 7301. (b) Grser, T.; Prato, M.; Lucchini, V.; Hirsch, A.; Wudl, F. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1343. (c) Irngartigner, H.; Weber, A. *Liebigs Ann.* **1996**, 1845.

Table 2. Transformation of the Acyl Azide **3** to the Carbamates **6**[a]

entry	ROH	(equiv)	solvent	time / h	yield / %
1	**5a**: $(CH_3)_3Si$–OH	(30)	Toluene	3	80
2		(10)	Toluene	3	33
3		(5.0)	*o*-Xylene	3	65
4		(5.0)	*o*-Xylene	6	88
5	**5b**: 	(5.0)	*o*-Xylene	6	64
6	**5c**: 	(5.0)	*o*-Xylene	6	57
7	**5d**: 	(5.0)	*o*-Xylene	6	11 (79[a])

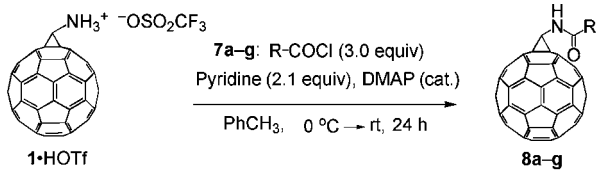
[a] The alcohol **5d** was used as a cosolvent (*o*-xylene/**5d** = 2/1, v/v).

steric hindrance of the *tert*-butyl group. In contrast, by using **5d** as a cosolvent (*o*-xylene/**5d** = 2/1, v/v), the desired **6d** was obtained in good yield (entry 7).[6] Taking into account the sufficient volatility of **5d**, the utilization of **5d** as a cosolvent is not a serious drawback of this reaction.

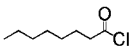
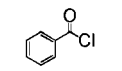
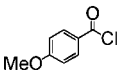
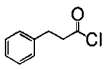
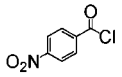
In the next stage, we attempted to transform the carbamates **6a**−**d** to aminomethano[60]fullerene (**1**). Although all of the four carbamates **6a**−**d** can potentially be converted to **1**, conventional methods for the cleavage of carbamates would not necessarily be applicable to **6a**−**d** because of the typical properties of a C_{60} core itself and the "special" cyclopropane ring embedded in the C_{60} core. Considering the intolerance of the [6,6]-double bonds of a C_{60} core to hydrogenation, we did not tried to convert **6b** to **1**. Then, we focused on the transformation of **6a**, **6c**, and **6d**, of which the alkyl moieties are likely to be cleaved by treatment with fluoride anion, a base, and an acid, respectively. Unexpectedly, treatment of **6a** with tetrabutylammonium fluoride and treatment of **6c** with piperidine caused an undesired retro-cyclopropanation reaction to give C_{60} in considerable yields.[8] In both cases, the most plausible reaction course is as follows: a β-elimination, triggered by fluoride for **6a** or by the base for **6c** initially took place, and the resultant carbamate or amide anion decomposed to C_{60} due to the characteristic of the cyclopropane ring. Although these observations showed the instability of the cyclopropane ring, they also gave us very valuable information that **1** would be unstable under basic conditions. With these results in mind, we then tried the acid-induced conversion of **6d** to **1**·HX, by using several Brønsted acids. Methanesulfonic acid and *p*-toluenesulfonic acid, however, could not promote this reaction at room temperature, and upon heating in *o*-xylene, two kinds of undesired products, C_{60} and an unidentified derivative, were generated. Contrary to these relatively weak acids, trifluoromethanesulfonic acid (TfOH) promoted the reaction, and the carbamate **6d** was consumed completely at room temperature without generating any undesired byproducts (TLC monitoring) to give **1**·HOTf in 88% yield (crude).[9] As far as we know, this is the first example of the synthesis of aminomethano[60]fullerene (**1**) and the first demonstration of the rearrangement of a functional group on the methano-bridge carbon of methano[60]fullerene.

To evaluate the utility of aminomethano[60]fullerene (**1**) as a precursor of various methano[60]fullerene derivatives, the condensation reaction with acyl chlorides was investigated. To our delight, the free amine **1**, gradually generated in situ by treatment of **1**·HOTf with a base, reacted with various acyl chlorides to afford the corresponding amides. When **1**·HOTf was mixed with the acyl chlorides **7**, pyridine, and 4-(dimethylamino)pyridine in toluene, the amides **8** were obtained in 20−84% yields; the yields were considerably influenced by the reactivity and/or bulkiness of **7** (Table 3).[6]

Table 3. Formation of the Amide **8** by the Condensation of the Ammonium Salt **1**·HOTf and Acyl Chlorides **7**



1·HOTf **8a–g**

entry		R-COCl	yield / %	entry		R-COCl	yield / %
1	**7a**:		64	5	**7e**:		42
2	**7b**:		83	6	**7f**:		20
3	**7c**:		70	7	**7g**:		46
4	**7d**:		84				

The formation of an unidentified byproduct was commonly observed for all entries, which would arise from the instability of the free-base **1**. Despite such low stability of **1**, the resultant amides **8** were found to be stable at least under neutral conditions, presumably owing to the electron-withdrawing effect of the acyl groups.[8]

(8) For examples of retro-cyclopropanation reactions of methanofullerenes, see: Herranz, M. Á.; Diederich, F.; Echegoyen, L. *Eur. J. Org. Chem.* **2004**, 2299 and references therein.

(9) The ammonium salt **1**·HOTf was obtained by collecting the insoluble precipitate, generated by the acid-promoted cleavage of the carbamate **6d**. Due to the poor solubility of **1**·HOTf in most solvents, it was impossible to purify **1**·HOTf. Therefore, the identification was carried out only by FT-IR and MALDI-TOF-MS spectroscopies (see Supporting Information). Although these analyses did not verify the purity of the sample, **1**·HOTf thus obtained was considered to be sufficiently pure for the use in usual organic synthesis because the condensation of **1**·HOTf with some acyl chlorides gave the corresponding amides in moderate to good yields (up to 84%, see Table 3).

In conclusion, we succeeded in the synthesis of aminomethano[60]fullerene (**1**) as a trifluoromethanesulfonic acid salt by applying the Curtius rearrangement of the acyl azide **3** as the key reaction. The amine, generated in situ from **1**·HOTf, was readily condensed with acyl chlorides **7** to give the corresponding amides **8**. The reactions showed that **1**·HOTf is a very useful precursor for the synthesis of various novel [60]fullerene derivatives. As far as we know, this is the first example of the rearrangement reaction of a functional group directly attached to the cyclopropane ring of methano[60]fullerene. Considering the analogy of C_{60} with other carbon clusters, such as C_{70}, other higher fullerenes, and single walled nanotubes, this conceptually novel method involving a rearrangement reaction would give us a clue to develop related materials possessing a wide variety of functional groups.

Supporting Information Available: Experimental procedures and characterization data for new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

OL052509A