ORGANIC LETTERS

2007
Vol. 9, No. 11
2083−2086

Ring-Opening Reaction of Cyclopropanated [60]Fullerenes: Unexpected Transformation of Methano[60]fullerenes Having an Electron-Donating Group on the Methano-Bridge Carbon

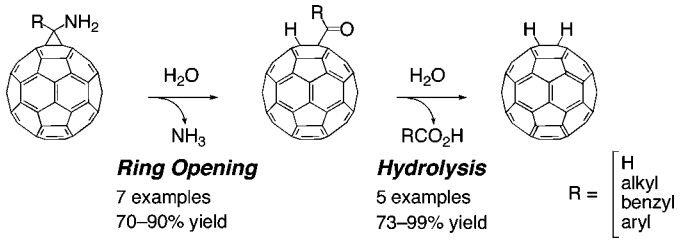
Tomoyuki Tada, Yasuhiro Ishida,* and Kazuhiko Saigo*

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 March 7, 2007

ABSTRACT



A series of novel transformations of [60]fullerene derivatives were found, starting from methano[60]fullerenes with an electron-donating group on the methano-bridge carbon. Aminomethano[60]fullerenes, in situ generated by the treatment of their trifluoromethanesulfonic acid salts with a base, were readily converted into 1-acyl-1,2-dihydro[60]fullerenes via the ring opening of the cyclopropane moiety. The aldehyde/ketones thus obtained were easily hydrolyzed to give 1,2-dihydro[60]fullerene in the presence of hydroxide anions.

Methano[60]fullerenes have been recognized as one of the most fascinating classes of chemically modified [60]fullerene derivatives.[1] Owing to their synthetic accessibility, stability, and ease in handling, as well as their remarkable resemblance to [60]fullerene in physical properties, the application of methano[60]fullerenes to materials science has been of particular interest. In addition, methano[60]fullerenes are potential precursors for the synthesis of novel [60]fullerene derivatives; within the framework of general organic chemistry, it is well-known that the constraint of cyclopropane rings facilitates their cleavage reaction and sometimes affords peculiar chemical species which cannot be accessed by other methods.[2] Thus, the ring-opening reaction of methano[60]-fullerenes should provide us a powerful and promising methodology in [60]fullerene chemistry. At the present time, however, studies on the ring-opening reactions of methano-[60]fullerenes have been surprisingly limited, contrary to the case of the usual cyclopropane compounds.[3] This is most likely because (i) methano[60]fullerenes themselves are attractive targets even at present as described above, and (ii) most of the precedented methano[60]fullerenes possess an

(1) (a) Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157. (b) Diederich, F.; Isaacs, L.; Philip, D. *Chem. Soc. Rev.* **1994**, *23*, 243. (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 reviews of the cyclopropane-opening reactions, see: (a) Kuwajima, I.; Nakamura, E. In *Comprehensive Organic Synthesis*; Trost, B. M., Flemming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 2, pp 441−454. (b) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151. (c) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321.

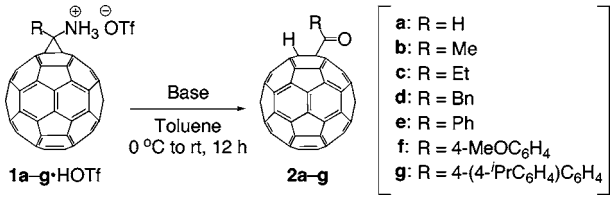
10.1021/ol0705705 CCC: $37.00
Published on Web 04/24/2007

electron-withdrawing group on their methano-bridge carbon, which efficiently stabilizes the cyclopropane moiety toward a ring-opening reaction.[4] Recently, we have reported the first synthesis of methano[60]fullerenes bearing an *electron-donating* group (amino group) on the methano-bridge carbon, in which the rearrangement of an electron-withdrawing group on the methano-bridge carbon was the key reaction.[5] Considering the electron-donating characteristic of the amino group, aminomethano[60]fullerenes would be suitable as the starting materials to realize our concept. Here we report unprecedented transformation of aminomethano[60]fullerenes via the ring-opening reaction of the cyclopropane rings and the easy hydrolysis of the resultant aldehyde/ketones.

According to the procedure we have recently reported, seven kinds of aminomethano[60]fullerenes were prepared as trifluoromethanesulfonic acid (HOTf) salts (**1a**−**g**·HOTf).[5] As an initial study to investigate the properties/reactivities of these unprecedented species, we attempted to generate free aminomethano[60]fullerenes **1a**−**g** by the dissociation of the ion pairs. For example, when **1c**·HOTf was treated with triethylamine, to our surprise the starting material **1c**·HOTf was immediately converted into the ketone **2c** (60% isolated yield) instead of the expected free amine **1c** (Table 1, entry 2). The ketone **2c** was unambiguously identified by $^{1}H/^{13}C$ NMR and MS spectra, which are in good agreement with the reported ones.[6] Worth noting is the fact that such a dramatic change in the structure, involving a C−C bond cleavage, took place readily and cleanly under mild conditions.

A further detailed study revealed that the choice of the base was one of determinant factors to control this reaction. The use of 1,8-diaza[5,4,0]bicycloundec-7-ene (DBU) in the place of triethylamine caused complicated side reactions (Table 1, entry 1). Contrary to this, relatively weak bases could efficiently promote this reaction to give the ketone **2c** in moderate to good yields (entries 3 and 4). Interestingly, the addition of a catalytic amount of 4-(dimethylamino)-pyridine (DMAP) to pyridine led to the notable improvement of the yield, which was superior to those achieved by using either of the two bases alone (entry 6 vs entries 3 and 4). Although the role of DMAP is unclear at present, such a special effect was undoubtedly attributable to some characteristic of DMAP, because the use of triethyamine in the place of DMAP merely resulted in the moderate yield of **2c** (entry 5).

Table 1. The Ring-Opening Reaction of Aminomethano[60]fullerenes **1**



entry	base (equiv)	product (R)	yield (%)[a]
1	DBU (2.1)	**2c** (Et)	—[b]
2	Et_3N (2.1)	**2c** (Et)	60
3	DMAP (2.1)	**2c** (Et)	64
4	pyridine (2.1)	**2c** (Et)	77
5	pyridine (2.1)/Et_3N (cat.)	**2c** (Et)	64
6	pyridine (2.1)/DMAP (cat.)	**2c** (Et)	87
7	pyridine (2.1)/DMAP (cat.)	**2b** (Me)	86
8	pyridine(2.1)/DMAP (cat.)	**2d** (Bn)	90
9	pyridine (2.1)/DMAP (cat.)	**2e** (Ph)	90
10	pyridine (2.1)/DMAP (cat.)	**2f** (4-$MeOC_6H_4$)	88
11	pyridine (2.1)/DMAP (cat.)	**2g** (4-(4-$^{i}PrC_6H_4$)C_6H_4)	76
12	pyridine (2.1)/DMAP (cat.)	**2a** (H)	70[c]

[a] Isolated yield. [b] A complex mixture. [c] A mixture of the target compound **2a** and 1,2-dihydro[60]fullerene **3** was obtained (**2a**:**3** = 77:23), which could not be separated because of the poor solubility of **2a** to common organic solvents.

With the optimized conditions in hand, we then applied the ring-opening reaction to the transformation of various aminomethano[60]fullerenes into the corresponding carbonyl compounds. As a result, it was clearly proved that a wide range of substituents on the methano-bridge carbon were tolerant in our method, including alkyl, benzyl, and aryl groups, as well as proton (Table 1, entries 6−12). Worth noting is the unique structure of the resultant aldehyde/ketones **2a**−**g**, in which a carbonyl group is directly connected to a [60]fullerene core and is expected to bring a significant effect on the chemical/physical properties of the [60]fullerene moiety.[7] To the best of our knowledge, most of the carbonyl compounds **2a**−**g** have not been synthesized elsewhere, except for **2c**, which has been synthesized by a photochemical reaction in unsatisfactory yield.[6,8] Among

(3) (a) Win, W. W.; Kao, M.; Eiermann, M.; McNamara, J. J.; Wudl, F. *J. Org. Chem.* **1994**, *59*, 5871. (b) Knight, B.; Martin, N.; Ohno, T.; Orti, E.; Rovira, C.; Veciana, J.; Vidal-Gancedo, J.; Viruela, P.; Viruela, R.; Wudl, F. *J. Am. Chem. Soc.* **1997**, *119*, 9871. (c) Yanilkin, V. V.; Toropchina, A. V.; Morozov, V. I.; Nastapova, N. V.; Gubskaya, V. P.; Sibgatullina, F. G.; Azancheev, N. M.; Efremov, Y. Y.; Nuretdinov, I. A. *Electrochim. Acta* **2004**, *50*, 1005.

(4) For selected examples of methano[60]fullerenes functionalized with electron-withdrawing group(s), 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.

(5) (a) Tada, T.; Ishida, Y.; Saigo, K. *Org. Lett.* **2005**, *7*, 5897. (b) Tada, T.; Ishida, Y.; Saigo, K. *Synlett* **2007**, 235.

(6) Siedschlag, C.; Luftmann, H.; Wolff, C.; Mattay, J. *Tetrahedron* **1997**, *53*, 3587.

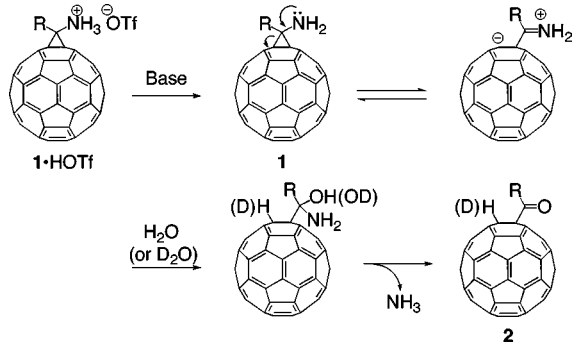
(7) For theoretical studies on the properties of 1-substituted 1,2-dihydro-[60]fullerenes, see: (a) Van Lier, G.; Safi, B.; Geerlings, P. *J. Chem. Soc., Perkin Trans. 2* **1998**, *349*. (b) Amat, M. C.; Van Lier, G.; Sola, M.; Duran, M.; Geerling, P. *J. Org. Chem.* **2004**, *69*, 2374.

(8) For selected examples of 1-substituted 1,2-dihydro[60]fullerenes, see: (a) Hirsch, A.; Soi, A.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 766. (b) Fagan, P. J.; Krusic, P. J.; Evans, D. H.; Lerke, S. A.; Johnston, E. *J. Am. Chem. Soc.* **1992**, *114*, 9697. (c) Komatsu, K.; Murata, Y.; Takimoto, N.; Mori, S.; Sugita, N.; Wan, T. S. M. *J. Org. Chem.* **1994**, *59*, 6101. (d) Anderson, H. L.; Faust, R.; Rubin, Y.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1366. (e) Timmerman, P.; Anderson, H. L.; Faust, R.; Nierengarten, J.-F.; Habicher, T.; Seiler, P.; Diederich, F. *Tetrahedron* **1996**, *52*, 4925. (f) Murata, Y.; Motoyama, K.; Komatsu, K.; Wan, T. S. M. *Tetrahedron* **1996**, *52*, 5077. (g) Tanaka, T.; Komatsu, K. *Synth. Commun.* **1999**, *29*, 4397. (h) Chronakis, N.; Vougioukalakis, G. C.; Orfanopoulos, M. *Org. Lett.* **2002**, *4*, 945. (i) Chen, Z.-X.; Wang, G.-W. *J. Org. Chem.* **2005**, *70*, 2380.

these carbonyl compounds, **2a** was expected to be further derivatized into other [60]fullerene-containing molecules, considering the potential reactivity of its formyl group.

The most plausible reaction mechanism for this transformation is depicted in Scheme 1. The treatment of the salt

Scheme 1. A Plausible Reaction Mechanism for the Ring-Opening Reaction of the Aminomethano[60]fullerenes **1**.

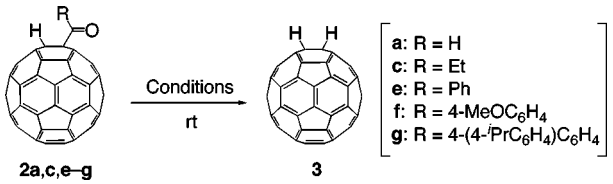


with a base generates the free amine **1**, of which the cyclopropane ring spontaneously opens owing to the cooperative effect of the electron-donating amino group and the electron-accepting [60]fullerene core. The resultant iminium moiety is hydrolyzed to give a carbonyl group, and the carbanion in the [60]fullerene core is protonated. The participation of external water to the reaction was confirmed by a control experiment conducted in the presence of a small amount of D_2O; the reaction resulted in the formation of deuterated **2**.[9] Although analogous ring-opening reactions have already been reported several decades ago for cyclopropane compounds bearing a hydroxy or amino group,[10] the most prominent characteristic of the present reaction is its remarkable efficiency. In the traditional examples, strongly basic conditions were required, because the deprotonation of the hydroxy or amino group was indispensable for the ring cleavages. Contrary to this, aminomethano[60]fullerenes **1** would be directly converted into the iminium intermediates without the formation of amide anions, considering the fact that even weak bases, such as pyridine, could induce the transformation. Such propensity of the cyclopropane ring in the methano[60]fullerenes for the ring cleavage might be attributable to the strong electron-withdrawing ability of the [60]fullerene moiety and/or the highly constrained structure of the three-membered ring embedded in the [60]fullerene core.

Thus, a ring-opening reaction of aminomethano [60]fullerenes was established, of which the scope and reaction pathway were clearly proved. The current reaction is a rare example of the ring-opening reaction of cyclopropanated [60]fullerenes and has potential utility in the synthesis of new [60]fullerene derivatives; as far as we know, there have been reported three examples of similar reactions,[3] but only one of them realized a ring-opening reaction without resorting to an electrochemical method.[3a,11]

In the next stage, we investigated the reactivities of the aldehyde/ketones **2a**−**g** thus obtained, which were expected to be different from those of the conventional analogues, such as 1-alkyl/alkenyl/alkynyl/aryl-1,2-dihydro[60]fullerenes, owing to the characteristic arrangement of a carbonyl group.[7,8] Among the carbonyl compounds **2a**−**g**, we chose the aromatic ketone **2e** as a model compound and treated it under various conditions (Table 2, entries 1−4). Surprisingly,

Table 2. The Hydrolysis of the Aldehyde/Ketones **2**



entry	conditions	substrate (R)	yield (%)[a]
1[b]	SiO_2/CS_2	**2e** (Ph)	90
2[c]	Al_2O_3/toluene	**2e** (Ph)	95
3[d]	$NaOH/H_2O$/toluene	**2e** (Ph)	99
4[e]	$TsOH/H_2O$/toleuene	**2e** (Ph)	no reaction
5[b]	SiO_2/CS_2	**2f** (4-$MeOC_6H_4$)	84
6[b]	SiO_2/CS_2	**2g** (4-(4-^{i}PrC_6H_4)C_6H_4)	94
7[b]	SiO_2/CS_2	**2c** (Et)	trace
8[c]	Al_2O_3/toluene	**2c** (Et)	93
9[b,f]	SiO_2/CS_2	**2a** (H)	74
10[c,f]	Al_2O_3/PhBr	**2a** (H)	73

[a] Isolated yield. [b] The ketone/aldehyde **2** was subjected to silica gel thin layer chromatography developed with CS_2. [c] The ketone/aldehyde **2** was subjected to alumina gel (basic) column chromatography eluted with toluene. In the case of **2a**, bromobenzene was used in the place of toluene because of the poor solubility of **2a** to toluene. [d] Aqueous NaOH (1.0 N)/toluene = 1:1 (v/v), 1 h. [e] Water/toluene = 1:10 (v/v) containing *p*-toluenesulfonic acid monohydrate (10 equiv), 18 h. [f] A mixture of **2a** and **3** (**2a**:**3** = 77:23) was used as the starting material. The yield was estimated on the basis of the ratio of the amount of **3** increased through the reaction to the initial amount of **2a**.

the ketone **2e** was quantitatively converted into 1,2-dihydro-[60]fullerene (**3**)[12] under very mild conditions, such as simple treatment with silica or alumina gel (entries 1 and 2). Further studies revealed that the presence of hydroxide anions was essential for this reaction; alkaline conditions efficiently promoted the reaction (entry 3), whereas no reaction took place even in the presence of a strong acid (entry 4). Thus,

(9) Considering the relatively high acidity of [60]fullerenyl proton in **2**, the H/D exchange after the formation of **2** was considered to be another pathway to generate deuterated **2**. However, we confirmed that the H/D exchange of **2** hardly took place under the reaction conditions used here.

(10) (a) Magrane, J. K., Jr.; Cottle, D. L. *J. Am. Chem. Soc.* **1942**, *64*, 484. (b) DePuy, C. H.; Breitbeil, F. W.; DeBruin, K. R. *J. Am. Chem. Soc.* **1966**, *88*, 3347. (c) Nickon, A.; Lambert, J. L.; Williams, R. O.; Werstiuk, N. H. *J. Am. Chem. Soc.* **1966**, *88*, 3354. (d) Walborsky, H. M.; Ronman, P. E. *J. Org. Chem.* **1973**, *38*, 4213.

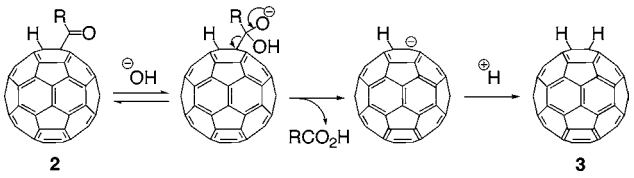
(11) Although the cyclopropane ring opening of methano[60]fullerenyl imino esters induced by a hydride reduction has been reported by Keller et al. (Burley, G. A.; Keller, P. A.; Pyne, S. G.; Ball. G. E. *J. Org. Chem.* **2002**, *67*, 8316), the authors later on found that the assignment of the starting materials was erroneous and reassigned them to [60]fullerenodihydropyrroles (Ball, G. E.; Burley, G. A.; Chaker, L.; Hawkins, B. C.; Williams, J. R.; Keller, P. A.; Pyne, S. G. *J. Org. Chem.* **2005**, *70*, 8572).

(12) Henderson, C. C.; Cahill, P. A. *Science* **1993**, *259*, 1885.

water molecules, likely activated on the surface of silica or alumina particles, were converted into hydroxide anions or similar species to promote the reaction (entries 1 and 2).

The other aldehyde/ketones **2** underwent the same reaction to give the identical product **3** (Table 2, entries 5−10), although the reactivity depended on the structure of substrates. Only in the cases of the reactions of aldehyde **2a**, yields were exceptionally low compared with those of the other substrates, most likely due to the poor solubility of **2a** to the solvents. To determine the structure of the fragment released from the [60]fullerene core, we thoroughly checked the products obtained from **2g**, of which the biphenyl moiety was expected to be a good probe for the detection and identification of the fragment. As a result, **3** and 4-(4-isopropylphenyl)benzoic acid were obtained in 87% and 60% yields, respectively, strongly suggesting that the transformation observed here is the hydroxide anion-promoted hydrolysis of the aldehyde/ketones (Scheme 2).[13] The difference in

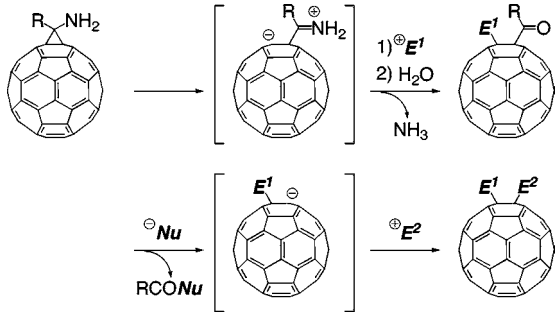
Scheme 2. A Plausible Reaction Mechanism for the Hydrolysis of the Aldehyde/Ketones **2**



reactivity between the substrates (aldehyde **2a** ≥ aromatic ketone **2e**−**g** > aliphatic ketone **2c**) could be elucidated by the lability of their carbonyl groups toward a nucleophilic attack by a hydroxide anion. Worth noting is the fact that the C−C bond in the ketones was easily and cleanly cleaved under relatively mild conditions. Such ease in the C−C bond cleavage would be again attributable to the strong electron-withdrawing ability of the [60]fullerene moiety, which is reminiscent of the role of a trihalomethyl group in the haloform reaction (Scheme 2). In other words, a [60]fullerenyl group should be recognized as a "good leaving group", of which the leaving ability was roughly estimated to be similar or superior to those of trihalomethyl groups.

In conclusion, we found a novel and uncommon series of reactions involving the ring cleavage of the cyclopropanated [60]fullerenes and the hydrolysis of the resultant [60]-fullerenyl aldehyde/ketones (Schemes 1 and 2) starting from methano[60]fullerenes having an amino group on the methano-bridge carbon. These reactions might play a complementary role to conventional methods in the chemical modification of fullerenes; by applying the present reaction, two kinds of [60]fullerenyl anions can be generated in a stepwise manner, and therefore, 1,2-disubstituted 1,2-dihydro[60]fullerenes with a wide structural diversity will become available by the reaction with electrophiles (Scheme 3), although only

Scheme 3. A Possible Application of the Ring-Opening Reaction of **1** and the Cleavage Reaction of **2** to the Synthesis of 1,2-Disubsituted 1,2-Dihydro[60]fullerene Derivatives



protons have been currently proved to be applicable as the electrophile in these reactions. Further investigation concerning the scope of electrophiles will be reported in the near future.

Acknowledgment. We acknowledge Prof. Eiji Yashima, Dr. Yoshio Furusho, and Dr. Hidetoshi Goto (ERATO, JST) for the use of the CSI-MS spectorometer.

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

OL0705705

(13) The substitution of an acyl group on the [60]fullerene core with a proton has been reported by Diederich et al. (ref 8e) and Komatsu et al. (ref 8f). However, both groups did not clearified the details of the reaction mechanism.