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Co-Catalyzed Radical Cycloaddition of [60]Fullerene with Active Dibromides: Selective Synthesis of Carbocycle-Fused Fullerene Monoadducts

Shirong Lu,[†,§] Weili Si,[†] Ming Bao,[‡] Yoshinori Yamamoto,[†,‡] and Tienan Jin*[,†]

WPI-Advanced Institute for Materials Research (WPI-AIMR), Tohoku University, Sendai 980-8577, Japan, and State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, China

tjin@m.tohoku.ac.jp

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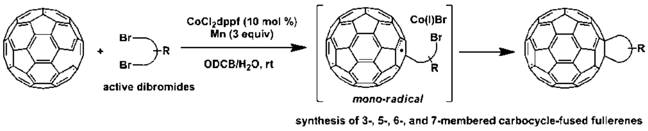
ABSTRACT



An efficient and highly selective Co-catalyzed radical cycloaddition of [60]fullerene with active dibromides for the synthesis of three-, five-, six-, and seven-membered carbocycle-fused fullerene monoadducts has been reported. The controlled experiments unambiguously disclosed that the reaction proceeds through the formation of a fullerene monoradical as a key intermediate.

Functionalization of fullerene offers much opportunity for creating diverse fullerene-based materials with potential applications in biological, materials science, and medicinal chemistry.[1] The fullerene cycloadducts fused by carbocycles, such as tetrahydronaphthalene or cyclopentane, exhibit high thermostability and have been demonstrated to serve as durable electron acceptors for high-performance polymer solar cells,[1f,2] as well as photosensitive biochemical probes.[1a,3] The thermal Diels–Alder reaction of C_{60} with *o*-quinodimethane is one of the most employed and straightforward methods for the construction of tetrahydronaphthalene-fused fullerenes,[4] but it usually requires a high reaction temperature and produces a mixture of multiadducts with low selectivity for a monoadduct. The syntheses of cyclopentane-, cyclopentene-, and cyclopentenone-fused fullerenes were also reported,[5] which include thermal [3 + 2] cycloaddition of methylenecyclopropanone and cyclopropenone ketals with C_{60};[5a,b] cyclization of a

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[†] Tohoku University.

[‡] Dalian University of Technology.

[§] Present address: Shirong Lu, Department of Materials Science and Engineering, University of California, Los Angeles, California, CA 90024, USA.

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$C_{60}{}^{2-}$ dianion with 1,3-dihalalkanes;[5c] phosphine- or DMAP-mediated or -catalyzed cycloaddition of C_{60} with electron-deficient alkynes, alkenes, and allenes;[5d−f] photocycloaddition of dienyl cyclopropanes with C_{60};[5g] and Mn-mediated radical cycloaddition of C_{60} with α-aryl active methylenes.[5h] However, a flexible and practical method that can construct carbocycle-fused fullerenes with various sizes is still rarely reported. It has been proven that functionalization of fullerenes catalyzed by transition-metal catalysts exhibits high efficiency and selectivity under mild reaction conditions as well as high compatibility with a wide range of functional groups.[6] However, to the best of our knowledge, the transition-metal-catalyzed cycloaddition of C_{60} for the preparation of those carbocycle-fused fullerenes has never been reported to date.

Recently, we have developed a novel cobalt-catalyzed radical hydroalkylation of C_{60} with various activated alkyl bromides, such as benzyl bromide and allyl bromide, producing the corresponding hydrofullerenes in good to high yields with high monoselectivity.[6j] Herein, we report a new and efficient Co-catalyzed radical carbocyclization of C_{60} with various active dibromides, which produced the [3 + 2], [4 + 2], [5 + 2], and [2 + 1] fullerene cycloadducts in good to high yields and high monoadduct selectivity at rt (eq 1).

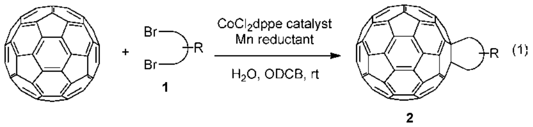
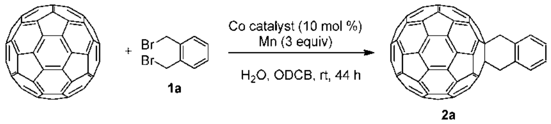


Table 1. Optimization of Reaction Conditions[a]

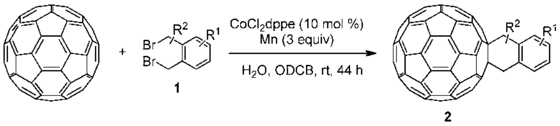


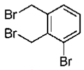
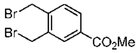
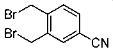
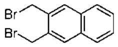
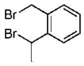
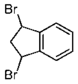
entry	catalyst (10 mol %)	yield of **2a** (%)[b]	recovered C_{60} (%)[b]
1	$CoCl_2$dppe	57	34
2	$CoCl_2$dppb	53	34
3	$CoCl_2$BINAP	25	68
4	$CoCl_2$dppf	70 (67)	5
5	none	0	91
6[c]	$CoCl_2$dppf	0	94
7[d]	$CoCl_2$dppf	0	95

[a] Reaction conditions: A 1,2-dichlorobenzene (ODCB, 4 mL) solution of catalyst (10 mol %), Mn (3 equiv), C_{60} (21.6 mg), H_2O (9 equiv), and **1a** (1.5 equiv, 0.045 mmol) under an Ar atmosphere was stirred at rt for 44 h. [b] HPLC yield using C_{70} as an internal standard. Isolated yield is shown in parentheses. [c] Without Mn additive. [d] Without water additive.

Initially, we tested the reaction of C_{60} with 1,2-bis(bromomethyl)benzene (**1a**) under the monoalkylation conditions by using $CoCl_2$(dppe) (10 mol %) as the catalyst, a Mn reductant (3 equiv), and a H_2O additive (9 equiv) at rt under an Ar atmosphere in 1,2-dichlorobenzene (ODCB),[6j] and the corresponding dihydronaphthyl fullerene **2a** was obtained in 57% yield (Table 1, entry 1). Among the other ligands, such as BINAP, dppb, and dppf that were tested, the use of dppf obviously increased the yield of **2a** up to a 67% isolated yield (entries 2−4). The reaction did not proceed without the cobalt catalyst or Mn reductant (entries 5−6). It is interesting to note that, although we assumed that the H_2O additive should be a proton source for the formation of the hydroalkylated fullerenes in the previous Co-catalyzed hydroalkylation of C_{60} (Scheme 1),[6j] the water additive is also indispensable for the success of the present cycloaddition (entry 7). We found that upon the addition of H_2O to the $CoCl_2$dppf complex in ODCB, the color of the mixture was changed to an orange solution, while $CoCl_2$dppf in ODCB showed a dark green suspension (Figure S1). Although the exact structure of the cobalt complex formed from the reaction of $CoCl_2$dppf with water is yet to be verified, we thought that the cobalt hydrate complex formed *in situ* should be the actually active catalytic species. As byproducts, a very small amount of biscycloadducts was produced together with the recovered C_{60}. The high selectivity of the monocycloadduct should be attributed to the mild reaction conditions.

Table 2. Co-Catalyzed [4 + 2] Cycloaddition for Synthesis of Fullerene-Fused Tetrahydronaphthalenes[a]

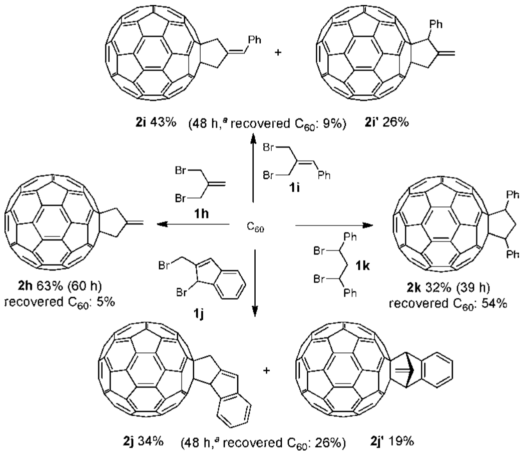


entry	dibromides	1	time (h)	2	yield (%)[b]	recovered C_{60} (%)[b]
1	 Br Br Br	**1b**	42	**2b**	58	15
2	 Br Br CO_2Me	**1c**	22	**2c**	64	6
3	 Br Br CN	**1d**	36	**2d**	64	17
4	 Br Br	**1e**	27	**2e**	56	24
5	 Br Br	**1f**	53	**2f**	60	21
6	 Br Br	**1g**	62	**2g**	44	37

[a] Reaction conditions: A 1,2-dichlorobenzene (ODCB, 4 mL) solution of $CoCl_2$dppf (10 mol %), Mn (3 equiv), C_{60} (21.6 mg), H_2O (9 equiv), and dibromide **1** (1.5 equiv) under an Ar atmosphere was stirred at rt. [b] Isolated yield.

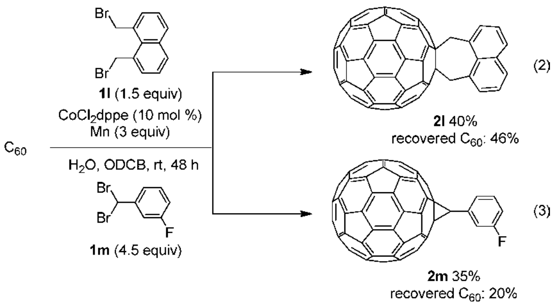
Under the optimized conditions, the scope of the Co-catalyzed cycloaddition of C_{60} with various active dibromides was examined. All the reactions were monitored by HPLC. The corresponding products **2** and the recovered C_{60} were isolated using HPLC. The results of a [4 + 2] cycloaddition of the substituted 1,2-bis(bromomethyl)benzenes with C_{60} are shown in Table 2. Dibromides **1** having a bromo- (**1b**), ester- (**1c**), and cyano-group (**1d**) on the benzene ring produced the corresponding C_{60}-fused tetrahydronaphthalenes **2b**–**d** in good yields with excellent monocycloaddition selectivity (entries 1–3 and HPLC spectra in the Supporting Information).[2a] 2,3-Bis(bromomethyl)naphthalene **1e** is also an active dibromide source, affording the corresponding monocycloadduct **2e** in 56% yield (entry 4). The cycloaddition also showed good compatibilities with dibromides **1f** and **1g** having a substituent at the β-position, furnishing the corresponding products **2f** and **2g** in 60% and 44% yields, respectively (entries 5 and 6). It was noted that the indene monoadduct **2g** has been demonstrated as an efficient electron acceptor for polymer solar cells.[2b]

Scheme 1. Co-Catalyzed [3 + 2] Cycloaddition for Synthesis of Cyclopenta-Fused Fullerenes under Standard Conditions



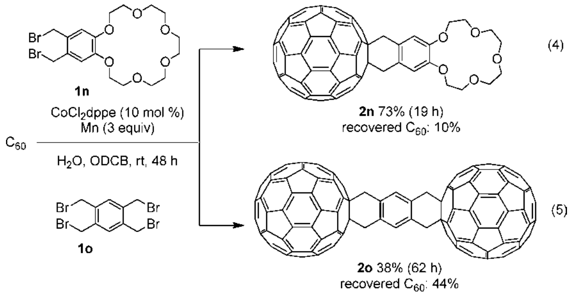
[a] A mixture of two products.

We also examined the [3 + 2] cycloaddition of C_{60} with allylic dibromides for the construction of the fullerene-fused five-membered carbocycles. As shown in Scheme 1, the reaction of 3-bromo-2-(bromomethyl)prop-1-ene **1h** with C_{60} gave the corresponding cyclopenta-fused fullerene monoadduct **2h** in 63% yield, while the reaction of (3-bromo-2-(bromomethyl)prop-1-en-1-yl)benzene **1i** with C_{60} produced the corresponding cycloadducts as a mixture of two regioisomers **2i** and **2i′** in 69% total yield due to the allylic migration. Similarly, 1-bromo-2-(bromomethyl)-1*H*-indene **1j** also exhibited high activity, which afforded a mixture of two indene derivatives **2j** and **2j′** in 53% yield. Although 1,3-dibromo-1,3-diphenylpropane **1k** showed relatively low activity, we were able to obtain the corresponding diphenyl-substituted cyclopenta-fused fullerene monoadduct **2k** in moderate yield with a mixture of *cis* and *trans* isomers.



The reaction was further extended to the construction of the seven- and three-membered carbocycles. For example, 1,8-bis(bromomethyl)naphthalene (**1l**) underwent the [5 + 2] cycloaddtion with C_{60} to afford the seven-membered carbocycle-fused fullerene cycloadduct **2l** in 40% yield (eq 2). Moreover, the [2 + 1] cycloaddition of 1-(dibromomethyl)-3-fluorobenzene (**1m**) with C_{60} under the standard conditions gave the corresponding phenylmethanofullerene **2m** in moderate yield (eq 3). Unfortunately, the [2 + 2] cycloaddition of C_{60} with active dibromides such as ethyl 2,3-dibromo-3-phenylpropionate or *meso*-1,2-dibromo-1,2-diphenylethane did not proceed at all under the standard conditions. It should be noted that the unactive aliphatic dibromides such as 1,4-dibromobutane and 1,3-dibromopropane were totally inactive for the present cycloaddition.

The present cobalt catalysis was successfully applied to the construction of a crown ether appended fullerene, which has potential application in supramolecular assemblies, ion sensors, and fluorescence devices.[7] For example, under the standard conditions, the [4 + 2] cycloaddition of C_{60} with 1,2-bis(bromomethyl)benzene derivative **1n** bearing a crown ether moiety afforded the fullerene-bound crown ether **2n** in 73% yield (eq 4). This reaction also provided an interesting opportunity for the synthesis of the potentially useful fullerene dimer containing two fullerene units bridged through an electroactive spacer.[8] The reaction of C_{60} with 1,2,3,4-tetrakis(bromomethyl)benzene **1o** (0.8 equiv) produced fullerene dimer **2o** in 38% yield (eq 5).



To gain further insight into the reaction details, we carried out the following control reactions as shown in Scheme 2. Although our previous Co-catalyzed monofunctionalization of C_{60} showed that the water additive was a hydrogen source for the formation of the monosubstituted hydrofullerenes,[6j]

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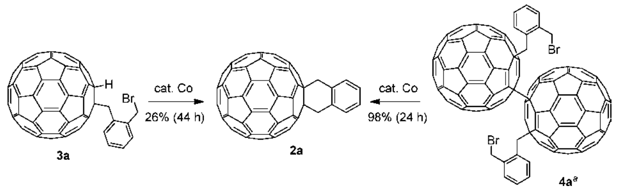
(6) For selected transition-metal-catalyzed functionalization of fullerenes, see: (a) Becker, L.; Evans, T. P.; Bada, J. L. *J. Org. Chem.* **1993**, *58*, 7630. (b) Martín, N.; Altable, M.; Filippone, S.; Martín-Domenech, A.; Echegoyen, L.; Cardona, C. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 110. (c) Nambo, M.; Noyori, R.; Itami, K. *J. Am. Chem. Soc.* **2007**, *129*, 8080. (d) Nambo, M.; Wakamiya, A.; Yamaguchi, S.; Itami, K. *J. Am. Chem. Soc.* **2009**, *131*, 15112. (e) Zhu, B.; Wang, G.-W. *J. Org. Chem.* **2009**, *74*, 4426. (f) Zhu, B.; Wang, G.-W. *Org. Lett.* **2009**, *11*, 4334. (g) Filippone, S.; Maroto, E. E.; Martín-Domenech, A.; Suarez, M.; Martín, N. *Nat. Chem.* **2009**, *1*, 578. (h) Xiao, Z.; Matsuo, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2010**, *132*, 12234. (i) Maroto, E. E.; De Cózar, A.; Filippone, S.; Martín-Domenech, A.; Suarez, M.; Cossío, F. P.; Martín, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 6060. (j) Lu, S.; Jin, T.; Bao, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **2011**, *133*, 12842. (k) Lu, S.; Jin, T.; Kwon, E.; Bao, M.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 802.

Scheme 2. Control Experiments under Standard Conditions for Formation of Cycloadduct **2a**

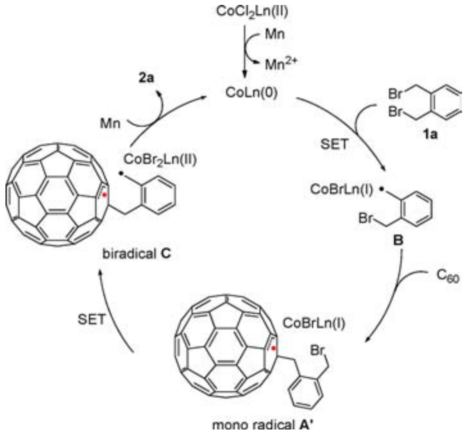


[a] A mixture of *meso* and *racemic* isomers.

we noticed that water was also indispensable for the present cycloaddition. This result led us to examine the reaction pathway from the hydrofullerene to cycloadduct. However, when hydrofullerene **3a** was treated with the standard conditions, the corresponding cycloadduct **2a** was obtained only in 26% yield and most of **3a** was decomposed, which is inconsistent with the result obtained from Table 1, entry 4. We further tested the cycloaddition using the single-bonded fullerene dimer **4a** as a substrate to investigate the involvement of the fullerene monoradical intermediate **A** (Scheme 3), because it was well demonstrated that the single-bonded fullerene dimers dissociate to the stable monoradicals in solution.[6k,9] Treatment of **4a** with the standard Co-catalyzed cycloaddition conditions produced the corresponding cycloadduct **2a** in 98% yield. These experimental results clearly indicate that the reaction might proceed predominantly through the formation of a fullerene radical intermediate followed by the intramolecular cycloaddtion without formation of the hydrofullerene.

On the basis of these experimental observations, the reaction mechanism is proposed as shown in Scheme 3. Initially, the Co(II) complex activated by water is reduced to the electron-rich Co(0) species by a Mn reductant.[6j] A single electron transfer (SET) from the Co(0) complex to an alkyl bromide in dibromide **1a** forms benzyl radical **B** along with a Co(I) complex.[6j,10] Addition of radical **B** to C_{60} generates the delocalized fullerene monoradical **A**, in which a SET from Co(I) to the remaining alkyl bromide affords biradical **C**[5g] together with a Co(II) complex. Intramolecular radical coupling in biradical **C** produces the corresponding cycloadduct **2a** along with the Co(0) catalyst upon treatment with the Mn reductant. The reactivity differences among the tested cobalt catalysts having varied ligands and the significant effect of the water additive in Table 1 indicate the interaction between the formed radical intermediates and cobalt complexes,[10] which may influence the reaction efficiency and selectivity.

Scheme 3. Proposed Reaction Mechanism



In summary, we have developed a new, efficient, and general method for the construction of carbocyle-fused fullerenes with various sizes via Co-catalyzed carbocycloaddition of C_{60} with active dibromides. Various carbocycle-fused fullerenes possessing 3-, 5-, 6-, and 7-membered rings were obtained in good to high yields with high monoadduct selectivity under very mild conditions. The use of a cobalt catalyst combined with a Mn reductant and water additive in argon is crucial for the selective implementation of the present cycloaddition efficiently. The results clearly indicate that the corresponding products were formed through the radical intermediates rather than the two-step process through the formation of hydrofullerene products. Investigation on further catalytic and selective synthesis of the fullerene biscycloadducts or multicycloadducts, and application to the electronic devices are in progress.

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

The authors declare no competing financial interest.

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