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Synthesis and Reactivity of 2*H*-Pyran Moiety in [60]Fullerene Cage Skeleton

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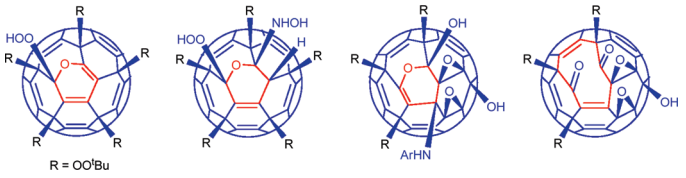

The cyclopentadienyl type hexa-adduct $C_{60}(OO{\it t}Bu)_6$ **1** is readily converted into 2*H*-pyran containing fullerene derivative $C_{60}(O)(OOH)(OO{\it t}Bu)_5$ **2** in the presence of $NaHCO_3$ and hydroquinone. In the process, O−O bond of the *tert*-butylperoxo group on the central pentagon is cleaved, and the fullerene-bound oxygen radical inserts into a 5,6-junction to form the 2*H*-pyran moiety. Further reactions of **2** led to open-cage fullerenes with a nine-membered orifice and also both 3,4-dihydro-2*H*-pyran and 3,6-dihydro-2*H*-pyran containing fullerene derivatives. Mechanisms are proposed involving intramolecular S_N2' and aza-Michael addition and ketal formation processes.

Introduction

Numerous fullerene derivatives have been reported in the literature over the past 20 years. Most of these fullerene derivatives are prepared through addition reactions on the fullerene double bonds, in which the fullerene cage skeleton remains unchanged.[1,2] Modification of the fullerene cage skeleton is one of the frontier areas in fullerene chemistry. Successful skeleton modification could make it possible to fine tune the electronic structure of the spherical pi system, thus leading to materials suitable for practical application such as in solar cell.[3] In addition novel fullerene derivatives such as heterofullerenes[4] and open-cage fullerenes[5] may be prepared through skeleton modification. Because of the unique cage structure, fullerenes usually exhibit reactivity different from that of classical organic compounds,[6] and well-established organic reactions may not work when

(1) (a) Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*, Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2005. (b) Thilgen, C.; Diederich, F. *Chem. Rev.* **2006**, *106*, 5049. (c) Martin, N. *Chem. Commun.* **2006**, 2093. (d) Matsuo, Y.; Nakamura, E. *Chem. Rev.* **2008**, *108*, 3016.

(2) For recent examples of fullerene functionalization, see: (a) Tzirakis, M. D.; Alberti, M. N.; Nye, L. C.; Drewello, T.; Orfanopoulos, M. *J. Org. Chem.* **2009**, *74*, 5746. (b) Li, F. F.; Yang, W. W.; He, G. B.; Gao, X. *J. Org. Chem.* **2009**, *74*, 8071. (c) Li, F. B.; Liu, T. X.; Huang, Y. S.; Wang, G.-W. *J. Org. Chem.* **2009**, *74*, 7743. (d) Filippone, S.; Maroto, E. E.; Martin-Domenech, A.; Suarez, M.; Martin, N. *Nat. Chem.* **2009**, *1*, 578. (e) Nambo, M.; Wakamiya, A.; Yamaguchi, S.; Itami, K. *J. Am. Chem. Soc.* **2009**, *131*, 15112. (f) Zhou, N. Z.; Zhao, Y. M. *J. Org. Chem.* **2010**, *75*, 1498. (g) Kooistra, F. B.; Leuning, T. M.; Martinez, E. M.; Hummelen, J. C. *Chem. Commun.* **2010**, *46*, 2097. (h) Megiatto, J. D., Jr.; Schuster, D. I.; Abwandner, S.; de Miguel, G.; Guldi, D. M. *J. Am. Chem. Soc.* **2010**, *132*, 3847.

(3) (a) Sariciftci, N. S.; Smilowitz, L.; Heeger, A. J.; Wudl, F. *Science* **1992**, *258*, 1474. (b) Yu, G.; Gao, J.; Hummelen, J. C.; Wudl, F.; Heeger, A. *Science* **1995**, *270*, 1789. (c) Thompson, B. C.; Frechet, J. M. J. *Angew. Chem., Int. Ed.* **2008**, *47*, 58. (d) He, Y. J.; Chen, H.-Y.; Hou, J. H.; Li, Y. F. *J. Am. Chem. Soc.* **2010**, *132*, 1377.

(4) (a) Hummelen, J. C.; Bellavia-Lund, C.; Wudl, F. *Top. Curr. Chem.* **1999**, *199*, 93. (b) Hirsch, A.; Nuber, B. *Acc. Chem. Res.* **1999**, *32*, 795. (c) Vostrowsky, O.; Hirsch, A. *Chem. Rev.* **2006**, *106*, 5191. (d) Zhang, G. H.; Huang, S. H.; Xiao, Z.; Chen, Q.; Gan, L. B.; Wang, Z. M. *J. Am. Chem. Soc.* **2008**, *130*, 12614. (e) Zuo, T. M.; Xu, L. S.; Beavers, C. M.; Olmstead, M. M.; Fu, W. J.; Crawford, T. D.; Balch, A. L.; Dorn, H. C. *J. Am. Chem. Soc.* **2008**, *130*, 12992.

(5) (a) Rubin, Y. *Top. Curr. Chem.* **1999**, *199*, 67. (b) Iwamatsu, S.-i; Murata, S. *Synlett* **2005**, *14*, 2117. (c) Murata, M.; Murata, Y.; Komatsu, K. *Chem. Commun.* **2008**, 6083. (d) Vougioukalakis, G. C.; Roubelakis, M. M.; Orfanopoulos, M. *Chem. Soc. Rev.* **2010**, *39*, 817. (e) Gan, L. B.; Yang, D. Z.; Zhang, Q. Y.; Huang, H. *Adv. Mater.* **2010**, *22*, 1498.

(6) (a) *Organic Peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1971. (b) Koenig, T. *Free Radicals I*; Kochi, J. K., Ed.; Wiley-Interscience: New York, 1973. (c) *The Chemistry of Organic Peroxides*; Patai, S., Ed.; Wiley-Interscience: New York, 1983. (d) Lane, B. S.; Burgess, K. *Chem. Rev.* **2003**, *103*, 2457.

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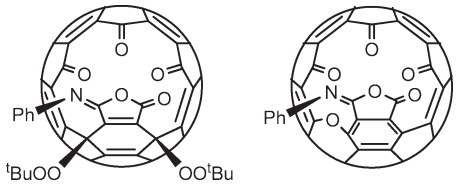
applied to fullerenes. The reactivity of functional groups directly bound on the fullerene cage and isolated functional moieties on the cage skeleton needs to be studied to provide enough information for rationally designing a cage-skeleton-modification pathway.



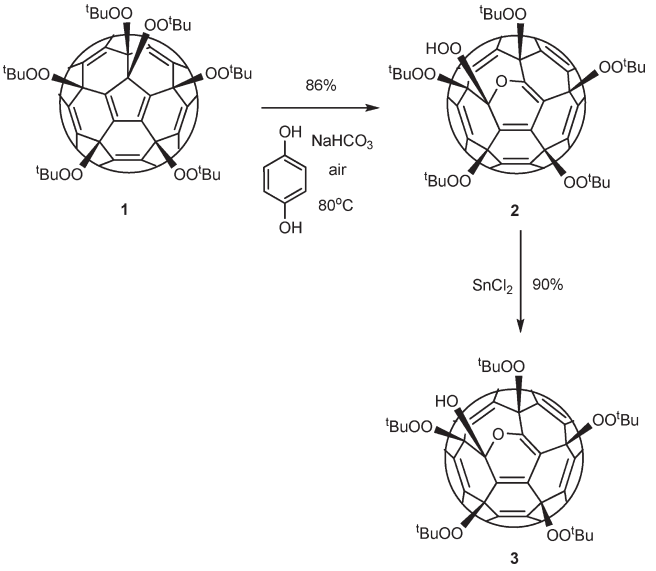
We have reported the preparation of fullerene-mixed peroxides with the general formula $C_{60}(O)_x(OOtBu)_y$ ($x = 0$ or 1 and $y = 2-6$).[7] Further study of these peroxides has revealed various unprecedented reaction patterns and led to the formation of some open-cage fullerenes such as those shown above.[8] Here we report the preparation of fullerene derivatives containing a pyran or dihydropyran moiety on the fullerene skeleton and its reactions leading to open-cage fullerenes.

Results and Discussion

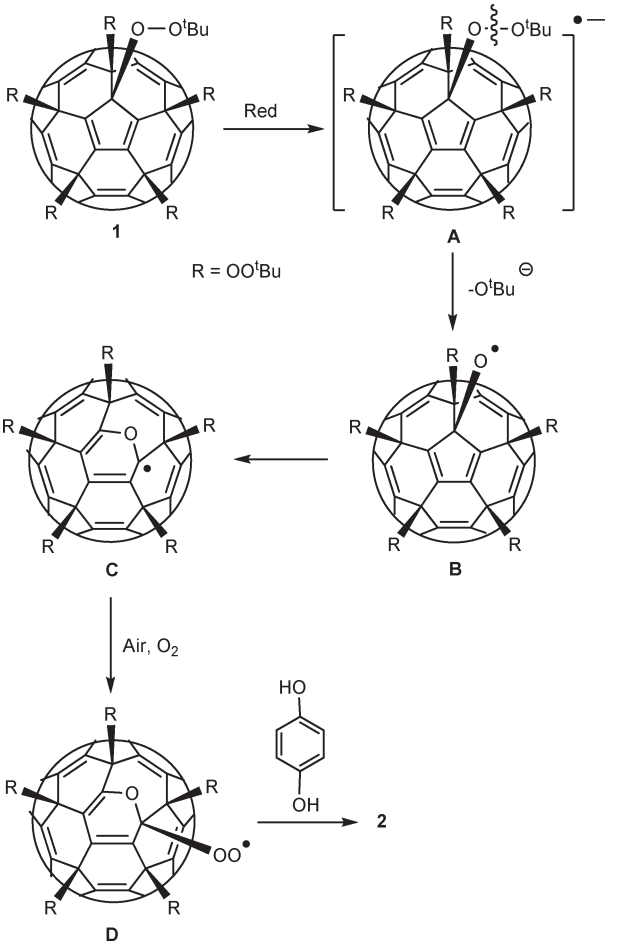
Preparation of 2*H*-Pyran Containing Fullerenes 2 and 3. The hexa-adduct fullerene peroxide **1** was prepared through addition of *tert*-butylperoxo radical to C_{60}.[7b,9] The peroxo group on the central pentagon was shown to be the most reactive among the six peroxo groups. Both photolysis under visible light[7a] and thermolysis[10] at 100 °C led to its fragmentation as we have reported previously. To test its redox behavior, we treated **1** with hydroquinone under basic condition in the presence of air. The flask was wrapped with aluminum foil to avoid light-induced cleavage pathways. The reaction gave compound **2** with a hydroperoxo-bound 2*H*-pyran moiety in good yield (Scheme 1). The hydroperoxo group was readily reduced into a hydroxyl group by stannous chloride. Under the same conditions, stannous chloride reacted with **1**, yielding a complicated mixture of products.

A possible mechanism for the formation of **2** is shown in Scheme 2. The first step is the reduction of **1** by hydroquinone to form the radical anion intermediate **A**. Addition of sodium hydrogen carbonate increases the reducing power of hydroquinone, but stronger bases led to other byproducts. The loss of *tert*-butoxide on the central peroxo group from **A** gives the oxygen-centered radical intermediate **B**. Rearrangement of **B** results in the carbon-centered radical **C** with a 2*H*-pyran moiety. Here insertion is favored at the 5,6-junction instead of the 6,6-junction, which would result in a formally cyclopentadienyl radical but not planar and thus not stable. Oxygen then adds to the carbon radical **C** to form the peroxo radical **D**. Hydroquinone reduces **D** into

SCHEME 1. Formation 2*H*-Pyran Moiety



SCHEME 2. Possible for Mechanism Formation 2*H*-Pyran Moiety



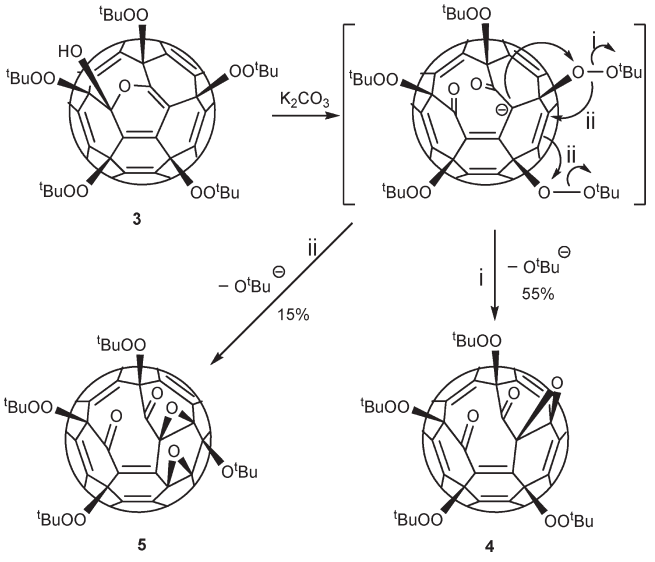
(7) (a) Gan, L. B.; Huang, S. H.; Zhang, X.; Zhang, A. X.; Cheng, B. C.; Cheng, H.; Li, X. L.; Shang, G. *J. Am. Chem. Soc.* **2002**, *124*, 13384. (b) Xiao, Z.; Wang, F. D.; Huang, S. H.; Gan, L. B.; Zhou, J.; Yuan, G.; Lu, M. J.; Pan, J. Q. *J. Org. Chem.* **2005**, *70*, 2060.

(8) (a) Xiao, Z.; Yao, J. Y.; Yang, D. Z.; Wang, F. D.; Huang, S. H.; Gan, L. B.; Jia, Z. S.; Jiang, Z. P.; Yang, X. B.; Zheng, B.; Yuan, G.; Zhang, S. W.; Wang, Z. M. *J. Am. Chem. Soc.* **2007**, *129*, 16149. (b) Pankewitz, T.; Klopper, W. *Chem. Phys. Lett.* **2008**, *465*, 48.

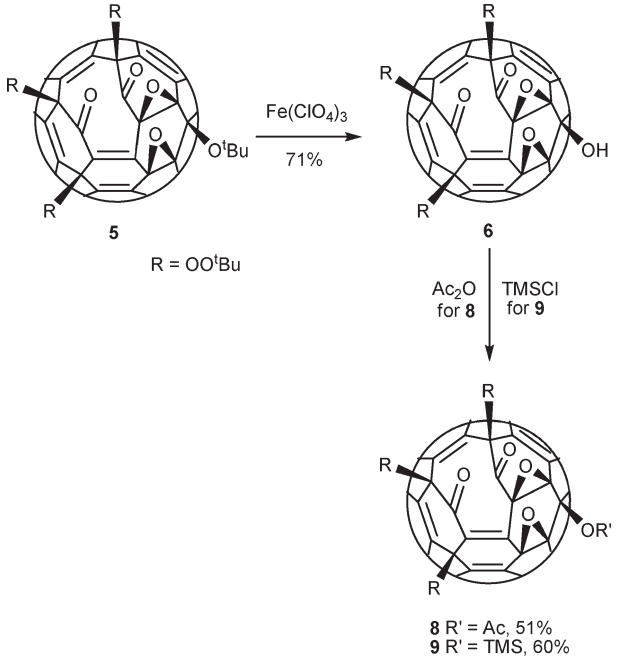
(9) Wang, F. D.; Xiao, Z.; Yao, Z. P.; Jia, Z. S.; Huang, S. H.; Gan, L. B.; Zhou, J.; Yuan, G.; Zhang, S. W. *J. Org. Chem.* **2006**, *71*, 4374.

(10) Yao, J. Y.; Yang, D. Z.; Xiao, Z.; Gan, L. B.; Wang, Z. M. *J. Org. Chem.* **2009**, *74*, 3528.

SCHEME 3. Formation Open-Cage Fullerenes



SCHEME 4. Conversion of *tert*-Butoxy Group



compound **2** in the final step. The yield and rate of the reaction were not much different under pure oxygen atmosphere. So the rate-limiting step should not be the reaction of oxygen with **C**. The presence of oxygen is essential for the formation of **2**; under nitrogen atmosphere, the reaction was very slow and hardly any **2** was detected. Hydroquinone is known to reduce oxygen to hydrogen peroxide, so coupling of hydroperoxo radical with radical **C** may have also contributed to the formation of **2**. Heating **1** with H_2O_2 at 80 °C in the presence of $NaHCO_3$ could give compound **2** but in low yields (less than 10%) at a much slower rate.

Open-Cage Fullerene Derivatives. Formation of the 2*H*-pyran moiety in compound **2** cleaved a fullerene C−C skeleton bond and inserted a oxygen atom at the 5,6-junction. To make fullerene derivatives with an orifice on the cage, we tried various conditions to hydrolyze the 2*H*-pyran moiety. Hydrolysis under acidic conditions gave a complicated mixture of products probably due to the cleavage of peroxo bonds. In the presence of potassium carbonate, compound **3** changed into compounds **4** and **5**, both of which have a nine-membered orifice (Scheme 3). The peroxo analogue **2** did not give any characterizable product under the same conditions.

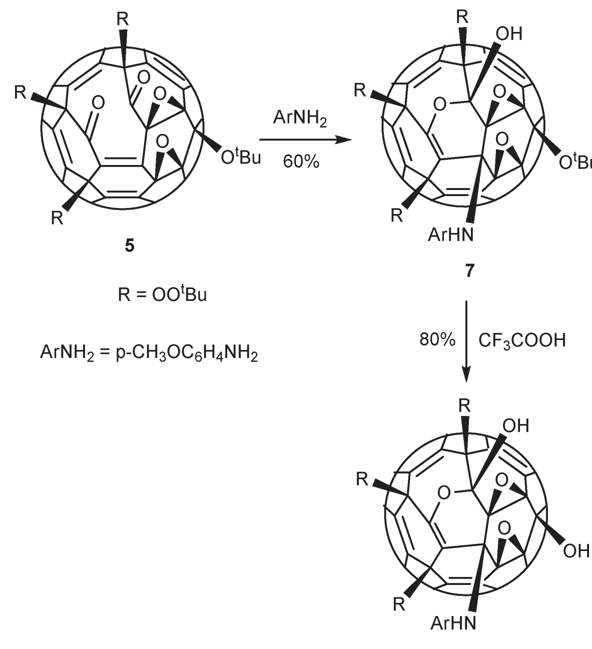
Compound **4** was prepared previously in one step from photolysis of **1** in 25% yield.[7a] Here three steps are involved from **1** to **4** with a total yield of 43%. Even though two more steps are needed, preparation of **4** is actually easier by the present procedure than that by the one-step photolysis method. Photolysis of **1** gave other byproducts difficult to be separated from **4** by column chromatography. The mechanism for the formation of **4** probably starts from deprotonation of the hydroxyl group of **3** by potassium carbonate, followed by ring-opening rearrangement of the 2*H*-pyran moiety to form the two carbonyl groups. Then heterolysis of the O−O bond in a neighboring *tert*-butylperoxo group results in the epoxy group (Scheme 3, Route i). Formation of compound **5** was not expected. Addition of *tert*-butanol or potassium *tert*-butoxide to the reaction solution did not increase the yield of **5**. Under the same conditions as the formation of **4** and **5** from **3**, isolated compound **4** could not be converted to **5**. So the *tert*-butoxyl group in **5** may come from heterolysis of the *tert*-butyl peroxo group, i.e., through a concerted intramolecular chain process (Scheme 3, Route ii).

The *tert*-butoxyl group appears to be the most reactive among all the functional groups in **5** under acidic conditions. We tried various Lewis acids to open the epoxy groups such as tris(pentafluorophenyl)boron, ferric chloride and perchlorate. All the reactions resulted in hydrolysis of the *tert*-butoxyl group into a hydroxyl group and formation of compound **6**. The hydroxyl group can be readily transformed into OAc and OTMS groups in **8** and **9** respectively under mild conditions (Scheme 4). Just like in the case of **5**, the OAc and OTMS groups hydrolyzed back to the hydroxyl derivative **6** when treated with Lewis acid such as ferric perchlorate. The hemiketal hydroxyl group of **3** could not be converted to OAc or OTMS under the present conditions probably as a result of steric hindrance.

Formation of Dihydro-2*H*-pyan Containing Fullerenes. The structure of compound **5** is quite unusual. Conclusive structural assignment is not possible without the help of X-ray diffraction analysis data. Efforts failed to obtain single crystals for compound **5** and its derivatives **6**, **8**, and **9**. To investigate its reactivity and also to obtain suitable single crystals related to **5**, we treated **5** with 4-methoxyaniline. The amino group added to the α,β-conjugated ketone moiety to form compound **7** with a 3,4-dihydro-2*H*-pyran moiety (Scheme 5). Mechanism of the reaction is reminiscent to the aza-Michael addition. Because of their close proximity, the two carbonyl groups coupled into a hemiketal group. None of the two epoxy groups opened into a hydroxyl group, which would be adjacent to the bulky *tert*-butoxy group. Under such a basic amination condition, the *tert*-butoxy group is stable. Addition of trifluoroacetic acid to **7** hydrolyzed the *tert*-butoxy to the hydroxyl group in compound **10**.

Single crystals of compound **7** were obtained from slow evaporation of its solution in a mixture of dichloromethane and 2-propanol. The structure as shown in Figure 1 revealed

SCHEME 5. Formation 3,4-Dihydro-2*H*-pyran Moiety



clearly a *tert*-butoxyl group attached to the cage. The 2*H*-pyran ring adopts a boat conformation with the oxygen atom above the plane by 0.505 Å and the nitrogen-bound fullerene carbon above the plane by 0.434 Å. The hexagon bearing the two epoxy groups is almost planar with the nitrogen-bound and *tert*-butoxy-bound fullerene carbons slightly above the plane at 0.130 and 0.175 Å respectively. Bond distances and angles are about the same between the two epoxy groups. The *tert*-butoxyl oxygen is bound to the cage more closely (1.418 Å) than those of peroxo *tert*-butyl groups (from 1.422 to 1.448 Å).

Amination could also take place at the 2*H*-pyran moiety of compounds **2** and **3**. Aryl and alkyl amines are too reactive and gave complicated mixtures of products. Hydroxylamine reacted selectively with **2** and **3** to form analogous compounds **11** and **13**, respectively (Scheme 6). Oxidation with (diacetoxyiodo)benzene converts the hydroxyamino group of **11** and **13** into the corresponding nitrosyl group in compounds **12** and **14**. Hydrogen iodide reduced the hydroperoxo group of **11** to form **13**. The same reduction reaction with **12** gave an uncharacterized product instead of compound **14**.

Spectroscopic Data and Structural Assignment. All of the compounds exhibit satisfactory spectroscopic data, but because all new compounds are C_1-symmetric, it is difficult to assign their structure conclusively just based on their spectroscopic data. The X-ray structure of **7** played a key role for the structural assignment of compounds **5** and **10** and other related compounds. Compound **2** and **3** exhibit similar NMR pattern. Their hemiketal carbon signals appear at 113.0 and 106.0 ppm respectively on the ^{13}C NMR spectra. The peroxo proton for **2** appears at 9.83 ppm and the hydroxyl proton for **3** appears at 5.78 ppm. ^{13}C NMR signal of the methyl carbon on the unique *tert*-butoxy group in compounds **5** and **7** appear at relatively lower field (31.3 and 31.2 ppm) than those of methyl groups on *tert*-butylperoxo groups (all at around 26 ppm). The open-cage

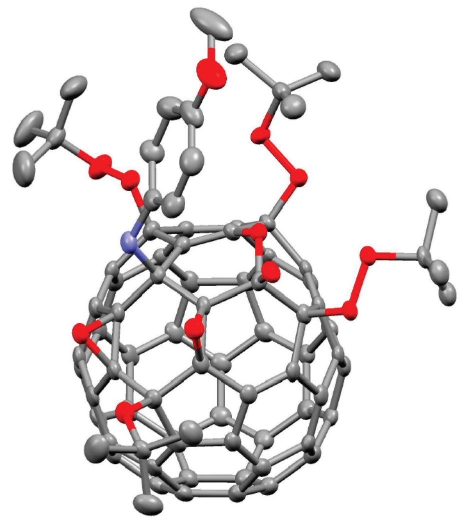
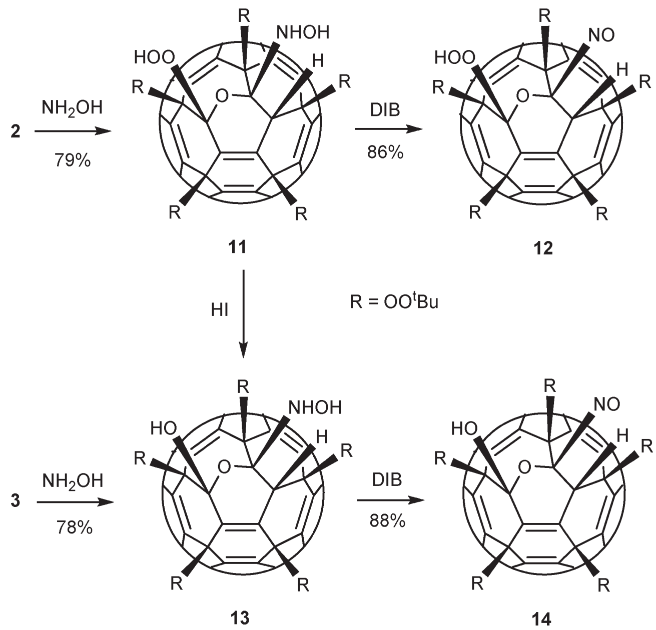
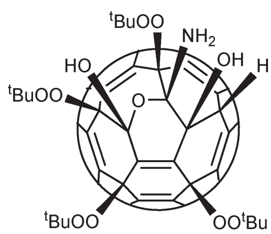


FIGURE 1. X-ray structure of compound **7**. Ellipsoids were drawn at 50% level, for clarity hydrogen atoms were not shown. Gray, carbon; red, oxygen; blue, nitrogen.

SCHEME 6. Formation 3,6-Dihydro-2*H*-pyran Moiety



compounds **5**, **6**, **8**, and **9** all show essentially the same carbonyl stretching frequency at either 1745 or 1756 cm^{-1}. Their carbonyl carbon also show the same chemical shifts at 190.5 (6) and 191.5 (6) ppm on the ^{13}C NMR spectrum.



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Structures of compounds **11** to **14** are assigned by comparison of their NMR spectra to those of compound **15**,[7a] which

was obtained from compound **4** and characterized by single crystal X-ray analysis as we reported before. They all have the 3,6-dihydro-2*H*-pyran moiety in the center of the molecule. Thus they exhibit the same ^{13}C NMR pattern in terms of the number of sp^2 and sp^3 fullerene carbons. The ^{13}C NMR chemical shifts of the fullerene C−H appear in the range from 39.9 to 42.2 ppm for compounds **11** to **14**. There are two signals with essentially the same chemical shifts (115.5 and 115.6 ppm) in the ^{13}C NMR spectrum of compounds **12** and **14**, which may be assigned to the chemical shifts of the nitrosyl-bound fullerene carbon. Both signals are relatively intense, indicating NOE enhancement from the adjacent fullerene-bound hydrogen. Thus the hydrogen atom connected to the fullerene cage should be adjacent to the nitrosyl group instead of the OH or OOH group, i.e., hydroxylamine addition to the 2*H*-pyran moiety of **2** and **3** is a 1,2-addition rather than a 1,4-addition.

Conclusion

Fullerene-mixed peroxides show various interesting reactions unprecedented in classical organic peroxides. Cleavage of the O−O bond can result in either insertion of the fullerene-bound oxygen into a 5,6-junction to form a 2*H*-pyran moiety or formation of an epoxy group at a 5,6- or 6,6-junction. The pyran moiety could be opened into open-cage fullerenes with a nine-membered orifice, which may be closed into a 3,4-dihydro-2*H*-pyran moiety by treating with arylamine. Fullerene derivatives containing a 3,6-dihydro-2*H*-pyran moiety have also been prepared by addition of hydroxylamine to the 2*H*-pyran moiety. Most of the present reactions show good to excellent regio- and chemoselectivity. Further work is in progress to explore fullerene skeleton modification methods to make open-cage fullerenes and heterofullerenes.

Experimental Section

All reagents were used as received. Dichloromethane was distilled over phosphorus pentaoxide. Toluene and benzene were distilled from sodium. Other solvents were used as received. The reactions were carried out in air. Compound **1** was prepared according to the improved procedure.[9] **Caution**: a large amount of peroxides is involved in some of the reactions, care must be taken to avoid possible explosion.

Compound 2. Hydroquinone (614 mg, 5.58 mmol) and $NaHCO_3$ (872 mg, 10.4 mmol) were added to a stirred dark solution of compound **1** (872 mg, 0.695 mmol) in freshly distilled toluene (109 mL) at 80 °C. After about 9.5 h, the solution was directly transferred onto a silica gel column (40 mm × 60 mm) and eluted with toluene/petroleum ether (1:2). The first band was a trace amount of unreacted **1** and uncharacterized compounds. The eluent was then changed to CH_2Cl_2. The second band was collected and evaporated to give compound **2** as a reddish solid (713 mg, 0.587 mmol, 84%). ^1H NMR (400 MHz, $CDCl_3$): δ 9.83(s, 1H), 1.42 (s, 27H), 1.38(s, 9H), 1.29(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 155.42, 149.73, 149.04, 148.81(2C), 148.58, 148.53, 148.46, 148.36 (2C), 148.34, 148.33, 148.31, 148.28, 147.92(2C), 147.85, 147.71, 147.61, 147.58, 147.53, 147.48, 147.13, 146.98, 146.73, 146.57, 146.54, 145.75, 145.67, 145.54, 145.46, 145.26, 144.67, 144.50, 144.47, 144.45, 144.43, 144.37, 143.84, 143.75, 143.71, 143.47, 143.36, 142.87, 142.17, 140.38, 140.17, 140.10, 139.05, 138.73, 137.62, 133.28, 126.96, 121.60, 113.02, 94.12, 93.00, 84.04, 83.07, 82.10, 81.89, 81.66, 81.58, 81.30, 81.22, 26.95 ($3CH_3$), 26.89 ($3CH_3$), 26.82 ($3CH_3$), 26.77 ($6CH_3$). FT-IR (microscope, cm^{-1}): 3435, 2979, 2931, 1388, 1364, 1192, 1087, 1011. ESI-HRMS ($CHCl_3$/MeOH) for $C_{80}H_{50}NO_{13}$ ($M + NH_4^+$): calcd 1232.3282, found 1232.3248.

Compound 3. $SnCl_2$ (52 mg, 0.274 mmol) was added to a stirred solution of compound **2** (55 mg, 0.045 mmol) in $CHCl_3$ (109 mL). After 5 min, the solution was directly transferred to a silica gel column (20 mm ×20 mm) and eluted with CH_2Cl_2. The first band was a trace amount of unknown compounds. The second band was collected and evaporated to give compound **3** as a reddish solid (49 mg, 0.041 mmol, 90%). ^1H NMR (400 MHz, $CDCl_3$): δ 5.78(s, 1H), 1.51 (s, 9H), 1.43(s, 9H), 1.38(s, 9H), 1.35(s, 9H), 1.33(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 155.24, 149.57, 149.02, 148.93, 148.75, 148.58(2C), 148.42, 148.33(2C), 148.28(2C), 148.22, 148.17, 147.83, 147.78, 147.69(3C), 147.58, 147.55, 147.50, 147.14, 147.10, 146.81, 146.67, 146.52, 146.10, 145.64, 145.36, 145.28, 144.82, 144.65, 144.48(2C), 144.42(2C), 144.16, 143.94, 143.67(3C), 142.91, 142.85, 142.41, 140.98, 140.44, 140.36, 139.77, 136.89, 135.72, 133.77, 128.76, 121.79, 106.01, 94.35, 92.48, 84.46, 82.69, 82.00(2C), 81.53, 81.38, 81.32, 81.08, 26.81 ($3CH_3$), 26.74 ($3CH_3$), 26.66 ($6CH_3$), 26.62. FT-IR (microscope, cm^{-1}): 3512, 2978, 2931, 1387, 1364, 1192, 996. ESI-HRMS ($CHCl_3$/MEOH) for $C_{80}H_{50}NO_{12}$ ($M + NH_4^+$): calcd 1216.3333, found 1216.3328.

Compounds 4 and 5. K_2CO_3 (1.528 g, 11.07 mmol) was added to a stirred solution of compound **3** (2.654 g, 2.215 mmol) in CH_2Cl_2 (660 mL) and DMSO (66 mL). After about 9 h, the solution was directly transferred to a silica gel column (40 mm ×20 mm) and eluted with CH_2Cl_2. The eluted solution was washed with water four times. Then the organic layer was dried and evaporated to give crude product. The crude product was transferred to a silica gel column (40 mm ×60 mm) and eluted with toluene. The first band was collected and evaporated to give compound **4** as a reddish solid (1.37 g, 1.219 mmol, 55%). Then the eluent was changed to CH_2Cl_2/AcOEt (50:1). The second band was collected and evaporated to give compound **5** as a brown solid (362 mg, 0.322 mmol, 15%). ^1H NMR (400 MHz, $CDCl_3$): δ 1.59(s, 9H), 1.34(s, 9H), 1.32(s, 9H), 1.27(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 191.54, 190.58, 153.06, 152.41, 150.93, 150.70, 150.42, 150.32, 149.74, 149.39, 149.15, 149.13, 148.84, 148.74(2C), 148.59, 148.53, 148.47, 148.42, 148.06, 148.02, 148.01, 147.93, 147.82, 147.70, 147.57, 146.96, 146.63, 146.27, 145.26, 145.23, 145.21, 144.95, 143.96, 143.43, 143.37, 142.95, 142.71, 142.49, 141.95, 141.79, 141.25, 140.68, 140.62, 140.40, 140.33, 139.33, 138.46, 138.26, 137.47, 135.78, 124.41, 91.86, 90.83, 85.68, 82.32, 82.19, 82.15, 79.27, 76.02, 74.91, 74.07, 69.47, 66.12, 31.25 ($3CH_3$), 26.64 ($3CH_3$), 26.57($6CH_3$). FT-IR (microscope, cm^{-1}): 2979, 2929, 1745, 1389, 1365, 1191, 1021. ESI-HRMS ($CHCl_3$/MEOH) for $C_{76}H_{36}O_{11}K$ ($M + K^+$): calcd 1163.1895, found 1163.1895.

Compound 6. $Fe(ClO_4)_3 \cdot 6H_2O$ (145 mg, 0.314 mmol) was added to a stirred solution of compound **5** (256 mg, 0.228 mmol) in CH_2Cl_2 (64 mL). After 1 h, the solution was directly transferred to a silica gel column (20 mm ×40 mm) and eluted with CH_2Cl_2. The first band was a trace amount of unreacted **5**. Then the eluent was changed to CH_2Cl_2/AcOEt (50:1). The second band was collected and evaporated to give compound **6** as a brown solid (173 mg, 0.162 mmol, 71%). ^1H NMR (400 MHz, $CDCl_3$): δ 4.00 (s, 1H), 1.34(s, 9H), 1.32(s, 9H), 1.26(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 191.62, 190.47, 154.23, 152.63, 150.94, 150.76, 150.48, 150.32, 149.67, 149.41, 149.22, 149.16(2C), 148.84, 148.76, 148.47, 148.33, 148.12, 148.10, 147.99, 147.87, 147.86, 147.83, 147.82, 147.69, 147.50, 147.17, 146.73, 146.71, 145.99, 145.35, 145.15, 144.99, 143.85(2C), 143.32, 143.12, 142.63, 142.18, 141.72, 141.60, 140.71, 140.63, 140.49, 140.35, 138.43, 138.35, 137.96, 137.01, 136.15, 135.98, 123.27, 91.92, 91.02, 85.88, 82.44,

82.31, 82.27, 75.16, 74.56, 70.24, 69.43, 66.41, 26.64((3CH_3)), 26.54(6CH_3). FT-IR (microscope, cm^{-1}): 3532, 2980, 2931, 1746, 1388, 1364, 1191, 1020. ESI-HRMS ($CHCl_3$/MEOH) for $C_{72}H_{32}NO_{11}$ ($M + NH_4^+$): calcd 1086.1975, found 1086.1963 ($M + NH_4^+$).

Compound 7. 4-Methoxyaniline (168 mg, 1.37 mmol) was added to a stirred solution of compound **5** (155 mg, 0.138 mmol) in freshly distilled CH_2Cl_2 (155 mL) at 35 °C . After about 13 h, the solution was directly transferred to a silica gel column (20 mm × 40 mm) and eluted with CH_2Cl_2/AcOEt (100:1). The first band was unreacted **5** (40 mg, 0.036 mmol). The eluent was then changed to CH_2Cl_2/AcOEt (50:1). The second band was collected and evaporated to give compound **7** as a reddish solid (103 mg, 0.083 mmol, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01(s, 1H), 7.12(d, 2H, J = 8.0 Hz), 6.96(d, 2H, J = 8.0 Hz), 5.23(s, 1H), 3.89(s, 3H), 1.59(s, 9H), 1.41(s, 9H), 1.36(s, 9H), 1.22(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 162.39, 157.54, 156.22, 150.82, 150.46, 150.25, 149.85, 149.53, 149.37(Ar), 149.04, 148.76, 148.44, 148.41, 148.32(2C), 148.11, 148.06, 147.97, 147.92, 147.77, 147.75, 146.92, 146.60, 146.55, 146.35, 145.78, 145.40, 145.35, 145.04, 144.70, 144.10, 143.89(2C), 143.30(2C), 142.65, 142.22, 141.64, 141.52, 141.45, 141.39, 141.07, 140.57, 139.87, 139.62, 138.63, 138.47, 137.13, 135.95, 135.93, 127.87(Ar), 120.58, 113.82(Ar),100.78, 94.26, 87.48, 82.67, 81.55, 81.53, 80.65, 78.47, 76.48, 74.31, 73.24, 72.82, 71.22, 59.28, 55.36, 31.20 (3CH_3), 26.75 (3CH_3), 26.60 (3CH_3), 26.51 (3CH_3). FT-IR (microscope, cm^{-1}): 3514, 3339, 2978, 2930, 1510, 1389, 1364, 1192, 1181, 1078, 993. ESI-HRMS ($CHCl_3$/MEOH) for $C_{83}H_{46}NO_{12}$ ($M + H^+$): calcd 1248.3020, found 1248.3015.

Single crystals were obtained from slow evaporation of **7** in CH_2Cl_2/iPrOH. Crystal data for **7**: $C_{83}H_{45}NO_{12}$, M_w = 1248.24 g mol^{-1}, T = 113(2) K, monoclinic, space group $P2_1/c$. Unit cell dimensions: a = 18.907(7) Å, b = 13.564(5) Å, c = 27.919(10) Å, β = 103.790 (4)°, V = 6954(4) $Å^3$. Z = 4, ρ_{calcd} = 1.193 Mg m^3, μ = 0.080 mm^{-1}. Reflections collected/unique 39963/12238 [R(int) = 0.0673]. Final R indices [$I > 2\sigma(I)$], R_1 = 0.0795, wR_2 = 0.2032. CCDC-773905.

Compound 8. Ac_2O (1 mL, 11 mmol) and pyridine (0.7 mL, 6 mmol) were added to a stirred solution of compound **6** (173 mg, 0.162 mmol) in CH_2Cl_2 (35 mL) at 35 °C. After about 12 h, the solution was washed with water for 4 times, and the organic layer was dried with anhydrous Na_2SO_4 and evaporated to give crude product. Then the crude product was transferred to a silica gel column (20 mm × 40 mm) and eluted with toluene/petroleum ether (2:1). The first band was a trace amount of impurity. The eluent was then changed to toluene. The second band was collected and evaporated to give compound **8** (92 mg, 0.082 mmol, 51%). Then the eluent was changed to CH_2Cl_2/AcOEt (50:1). The third band was collected and evaporated to give unreacted **6** as a reddish solid (20 mg, 0.019 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33(s, 3H), 1.35(s, 9H), 1.32(s, 9H), 1.27(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 191.65, 190.25, 169.53, 153.37, 152.93, 151.00, 150.62, 150.53, 150.26, 149.60, 149.37, 149.14, 149.06, 148.85, 148.68, 148.47, 148.44, 148.41, 148.09, 148.05, 148.03, 147.97, 147.89, 147.81(2C), 147.68, 147.44, 147.02, 146.77, 145.94, 145.72, 145.25, 145.13, 144.97, 143.94, 143.75, 143.27, 142.63, 142.41, 142.21, 141.57, 141.55, 140.58, 140.53, 140.33-(2C), 138.49(2C), 137.97, 137.82, 136.87, 135.72, 123.23, 91.94, 90.74, 85.82, 82.41, 82.27, 82.26, 75.16, 73.92, 72.17, 71.74, 68.29, 29.66 (3CH_3), 26.62 (3CH_3), 26.54 (3CH_3), 26.51 (3CH_3). FT-IR (microscope, cm^{-1}): 2979, 2926, 2852, 1747, 1388, 1365, 1224, 1192, 1016. ESI-HRMS ($CHCl_3$/MEOH) for $C_{74}H_{34}NO_{12}$ ($M + NH_4^+$): calcd 1128.2081, found 1128.2040.

Compound 9. TMSCl (2.5 mL, 32 mmol) and pyridine (1.5 mL, 13 mmol) were added to a stirred solution of compound **6** (30 mg, 0.028 mmol) in CH_2Cl_2 (30 mL) at room temperature. After about 12 h, the solution was directly transferred to a silica gel column (20 mm ×40 mm) and eluted with CH_2Cl_2. The first band was collected and evaporated to give compound **9** as a reddish solid (19 mg, 0.017 mmol, 60%). Then the eluent was changed to CH_2Cl_2/AcOEt (50:1). The second band was collected and evaporated to give unreacted **6** (4 mg, 0.004 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34(s, 9H), 1.32(s, 9H), 1.26(s, 9H), 0.34(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 191.59, 190.56, 153.47, 152.24, 150.99, 150.73, 150.43, 150.32, 149.68, 149.43, 149.17(2C), 148.92, 148.77, 148.75, 148.63, 148.41(2C), 148.21, 147.99, 147.92, 147.89, 147.86(2C), 147.63, 147.60, 146.88, 146.78, 146.77, 145.19(2C), 145.03, 144.83, 143.90, 143.57, 143.40, 143.04, 142.86, 142.48, 141.87, 141.75, 141.19, 140.67, 140.57, 140.40, 140.31, 138.85, 138.56, 137.46, 137.20, 134.89, 124.23, 91.95, 90.89, 85.82, 82.37, 82.24, 82.18, 75.50, 74.20, 72.2, 71.78, 69.40, 26.65 (3CH_3), 26.55 (6CH_3), 2.24 (Si($\underline{C}H_3$)$_3$). FT-IR (microscope, cm^{-1}):2978, 2927, 1746, 1388, 1365, 1191, 1097. ESI-HRMS ($CHCl_3$/MEOH) for $C_{75}H_{40}SiNO_{11}$ ($M + NH_4^+$): calcd 1158.2371, found 1158.2377.

Compound 10. CF_3COOH (1.0 mL, 13 mmol) was added to a stirred solution of compound **7** (263 mg, 0.211 mmol) in CH_2Cl_2 (52 mL) at room temperature. After about 3 min, the solution was directly transferred to a silica gel column (20 mm × 50 mm) and eluted with CH_2Cl_2/AcOEt (60:1). The first band was a trace amount of unreacted **7**. Then the eluent was changed to CH_2Cl_2/AcOEt (20:1). The second band was collected and evaporated to give compound **10** as a reddish solid (200 mg, 0.168 mmol, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72(d, 2H, J = 8.6 Hz), 6.97(d, 2H, J = 8.0 Hz), 4.29(br, 1H), 3.89(s, 3H), 1.41(s, 9H), 1.37(s, 9H), 1.23(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 157.72, 156.52, 150.91, 150.75, 150.51, 149.75, 149.63, 149.59, 149.55, 149.44, 149.10, 148.85, 148.55, 148.37, 148.28(Ar), 148.21, 148.18, 147.95, 147.94, 147.63, 147.55, 147.13, 146.72, 146.50, 146.34, 145.82, 145.40, 145.31, 145.29, 145.12, 144.77, 143.91, 143.84(2C), 142.96, 142.82, 142.56, 142.11, 141.52, 141.38, 141.31, 140.71, 140.23, 139.63, 137.86, 137.15, 136.43, 136.19, 136.03, 135.90, 128.11(Ar), 120.35, 113.93 (Ar), 100.61, 94.28, 87.41, 82.95, 81.66 (3$(CH_3)_3$-$\underline{C}$OO), 80.65, 73.73, 73.37, 71.70, 69.40, 59.04, 55.40, 26.80 ($\overline{3}$$CH_3$), 26.60 (3$CH_3$), 26.53 (3$CH_3$). FT-IR (microscope, cm^{-1}): 3511, 3341, 2979, 2931, 1510, 1388, 1364, 1191, 1041. ESI-HRMS ($CHCl_3$/MEOH) for $C_{79}H_{38}NO_{12}$ ($M + H^+$): calcd 1192.2394, found 1192.2400.

Compound 11. $NaHCO_3$ (291 mg, 3.46 mmol), $NH_2OH \cdot HCl$ (209 mg, 3.01 mmol), and H_2O (2.5 mL, 140 mmol) were added to a stirred solution of compound **2** (250 mg, 0.206 mmol) in freshly distilled CH_2Cl_2 (100 mL). After about 10 min, the solution was directly transferred to a silica gel column (20 mm × 30 mm) and eluted with CH_2Cl_2. The first band was a trace amount of unreacted **2**. The eluent was then changed to CH_2Cl_2/AcOEt (20:1). The second band was collected and evaporated to give compound **11** as a reddish solid (202 mg, 0.162 mmol, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61(s, 1H), 5.58(s, 1H), 5.43(s, 1H), 1.45(s, 9H), 1.42(s, 9H), 1.35(s, 9H), 1.28(s, 9H), 1.25(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 149.42, 149.07, 148.93, 148.84(2C), 148.77(2C), 148.69(2C), 148.60, 148.48, 148.38, 148.36, 148.29(2C), 148.25, 148.22(3C), 147.87, 147.69(3C), 146.93, 146.70, 146.32, 145.71, 145.34, 144.97, 144.84, 144.79, 144.64(2C), 144.52, 144.41, 144.38, 144.18, 144.03, 143.73, 143.16(2C), 142.26, 141.93, 140.97, 140.94, 140.70, 140.48, 140.33, 139.53, 138.83, 138.15, 136.51, 128.53, 104.44, 93.87, 92.21, 90.68, 85.54, 83.19, 82.84, 82.10, 81.67, 81.61, 81.55, 80.96, 40.62, 27.03 (3CH_3), 26.85 (3CH_3), 26.80 (3CH_3), 26.77 (6CH_3). FT-IR (microscope, cm^{-1}): 3438, 3327, 2978, 2931, 1388, 1364, 1191, 1002. ESI-HRMS ($CHCl_3$/MEOH) for $C_{80}H_{50}NO_{14}$ ($M + H^+$): calcd 1248.3231, found 1248.3245.

Compound 12. DIB (25 mg, 0.078 mmol) was added to a stirred solution of compound **11** (38 mg, 0.03 mmol) in freshly

distilled benzene (13 mL). After about 7 min, the solution was directly transferred to a silica gel column (20 mm × 30 mm) and eluted with CH_2Cl_2. The first band was collected and evaporated to give compound **12** as a reddish solid (32 mg, 0.026 mmol, 86%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54(s, 1H), 3.32(s, 1H), 1.38(s, 9H), 1.34(s, 9H), 1.27(s, 9H), 1.25(s, 9H), 1.05(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted):149.47, 149.06, 148.96(2C), 148.86(2C), 148.77(2C), 148.70, 148.67, 148.52(2C), 148.40(3C), 148.30, 148.24(2C), 148.02, 147.95, 147.85, 147.68, 146.50, 146.27, 146.02, 145.57, 145.35, 145.07, 144.77, 144.71, 144.68, 144.55, 144.48, 144.46-(2C), 144.31, 144.18, 143.77, 143.12, 142.99, 142.49, 141.85, 141.59, 141.05, 140.68, 140.11, 139.96, 139.85, 138.24, 136.85, 135.91, 130.17, 115.54, 105.09, 91.77, 89.47, 85.75, 83.08, 82.87, 81.72, 81.66, 81.62, 81.47, 80.91, 42.20, 26.96 ($3CH_3$), 26.76 ($3CH_3$), 26.72 ($3CH_3$), 26.64 ($3CH_3$), 26.37 ($3CH_3$). FT-IR (microscope, cm^{-1}): 3434, 2978, 2930, 1595, 1388, 1364, 1191, 1002. ESI-HRMS ($CHCl_3$/MEOH) for $C_{80}H_{51}N_2O_{14}$ (M + NH_4^+): calcd 1263.3340, found 1263.3321.

Compound 13. Method A: $NaHCO_3$ (85 mg, 1.01 mmol), $NH_2OH \cdot HCl$ (70 mg, 1.0 mmol), and H_2O (1.0 mL, 56 mmol) were added to a stirred solution of compound **3** (242 mg, 0.202 mmol) in freshly distilled CH_2Cl_2 (50 mL). After about 1 h, the solution was directly transferred to a silica gel column (20 mm × 30 mm) and eluted with CH_2Cl_2. The first band was a trace amount of unreacted **3**. The eluent was then changed to CH_2Cl_2/AcOEt (20:1). The second band was collected and evaporated to give compound **13** as a reddish solid (195 mg, 0.158 mmol, 78%). **Method B**: HI (10 drop, 0.149 mmol) was added to a stirred solution of compound **11** (36 mg, 0.029 mmol) in freshly distilled CH_2Cl_2 (12 mL). After about 10 min, the solution was directly transferred to a silica gel column (20 mm × 30 mm) and eluted with CH_2Cl_2/AcOE (40:1). The first band was a trace amount of unreacted **11**. Then the eluent was changed to CH_2Cl_2/AcOE-(20:1), and the second band was collected and evaporated to give compound **13** as a reddish solid (22 mg, 0.018 mmol, 62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.07(s, 1H), 5.50(s, 1H), 5.02(s, 1H), 1.52(s, 9H), 1.36(s, 9H), 1.34(s, 9H), 1.32(s, 9H), 1.25(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 149.31, 149.16, 148.88, 148.83, 148.78, 148.73, 148.70, 148.66(2C), 148.60, 148.48, 148.41, 148.36, 148.31, 148.26, 148.20, 148.17, 148.01, 147.82(2C), 147.78, 147.63, 147.30, 146.92, 146.71, 146.11, 144.84, 144.78, 144.69(3C), 144.49(3C), 144.21, 144.08, 143.55(2C), 143.35, 143.09, 142.00, 141.91, 141.44, 140.91, 140.85, 140.68, 140.17, 138.76, 135.51, 133.90-(2C), 131.68, 97.40, 93.42, 93.39, 89.85, 85.60, 83.78, 82.87, 81.92, 81.70, 81.63, 81.26, 81.00, 39.94, 27.11 ($3CH_3$), 26.92 ($3CH_3$), 26.80 ($3CH_3$), 26.77 ($6CH_3$). FT-IR (microscope, cm^{-1}): 3516, 3447, 3331, 2978, 2930, 1387, 1364, 1192, 1045, 997. ESI-HRMS for $C_{80}H_{50}NO_{13}$ (M + H^+): calcd 1232.3282, found 1232.3239.

Compound 14. DIB (48 mg, 0.15 mmol) was added to a stirred solution of compound **13** (74 mg, 0.060 mmol) in freshly distilled benzene (25 mL). After about 5 min, the solution was directly transferred to a silica gel column (20 mm × 30 mm) and eluted with CH_2Cl_2. The first band was collected and evaporated to give compound **14** as a reddish solid (65 mg, 0.053 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.16(s, 1H), 3.39(s, 1H), 1.35(s, 9H), 1.31(s, 9H), 1.30(s, 9H), 1.27(s, 9H), 1.04(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, all signals represent 1C except as noted): 149.37, 149.14, 148.87, 148.81(2C), 148.78(2C), 148.74, 148.70, 148.63, 148.49(3C), 148.47, 148.41, 148.37(2C), 148.19, 147.96, 147.92, 147.84, 147.71, 147.61, 147.02, 146.76, 145.80, 145.43, 144.94, 144.79, 144.76, 144.72, 144.70, 144.60, 144.52, 144.49, 144.48, 144.40, 144.06, 143.49, 143.45, 143.37, 142.52, 142.46, 141.71, 141.49, 140.94(2C), 140.53, 138.66, 135.78, 132.67, 131.85, 115.61, 98.44, 92.92, 88.69, 85.55, 83.62, 83.07, 81.66, 81.54, 81.33, 81.25, 81.00 42.37, 26.97 ($3CH_3$), 26.74 ($3CH_3$), 26.69 ($3CH_3$), 26.59 ($3CH_3$), 26.35 ($3CH_3$). FT-IR (microscope, cm^{-1}): 3519, 2979, 2931, 1739, 1594, 1388, 1364, 1193, 1016, 997. ESI-HRMS ($CHCl_3$/MEOH) for $C_{80}H_{51}N_2O_{13}$ (M + NH_4^+): calcd 1247.3391, found 1247.3374.

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Supporting Information Available: Selected spectroscopic data for all new compounds and crystallographic data for **7** including CIF file. This material is available free of charge via the Internet at http://pubs.acs.org.