Fullerene Heterocycles Hot Paper

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Fullerene-Based Macro-Heterocycle Prepared through Selective Incorporation of Three N and Two O Atoms into C_{60}

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Abstract: *A 14-membered heterocycle is created on the C_{60} cage skeleton through a multistep procedure. Key steps involve repeated PCl_5-induced hydroxylamino N–O bond cleavage leading to insertion of nitrogen atoms, and also piperidine-induced peroxo O–O bond cleavage leading to insertion of oxygen atoms. The hetero atoms form one pyrrole, two pyran, and one diazepine rings in conjunction with the C_{60} skeleton carbon atoms. The fullerene-based macrocycle showed unique reactivities towards fluoride ion and copper salts.*

Macrocyclic compounds have been well studied because of their widespread applications, in particular as ligands for metal ions. Most of the classical macrocyclic compounds are planar molecules with either a flexible skeleton, such as crown ether, or rigid framework, such as phthalocyanine. Fullerenes are spherical molecules consisting only of carbon atoms. Numerous novel structures can be envisioned based on the selective replacement and/or removal of the carbon cage skeleton.[1] A number of "truncated fullerenes" including $C_{54}N_4$ with a porphyrin-like moiety[2] and the compound $C_{56}N_2O$ with a N,O-hetero-macrocycle moiety[3] were proposed and investigated by theoretical calculations (Figure 1). It is predicted that such fullerene-based macrocycles have similar properties to traditional macrocycles, such as phthalocyanine, but offer many unique features because of their spherical structure. Synthesis of these compounds is a challenging problem. None of the proposed fullerene macrocycles have been reported. A number of open-cage fullerenes have been reported.[4,5] Starting from these open-cage fullerenes, oxygen,[6] sulfur,[7] and selenium[8] atoms have been inserted onto the rim of the orifice. These open-cage fullerenes cannot be used as a heterocyclic ligand to form coordination complexes. Reactions of open-cage fullerenes with $Ru_3(CO)_{12}$ have been reported to form ruthenium complexes with modified orifice sizes.[9] We have reported the preparation of various fullerene-mixed peroxides. Further work showed that the peroxo groups can promote efficient fullerene skeleton bond cleavage and also partial removal of the skeleton carbon.[10] Herein we report the preparation of open heterofullerenes with a 14-membered N,O-heterocycle embedded on the fullerene cage. Preliminary results on their reactivity are also presented.

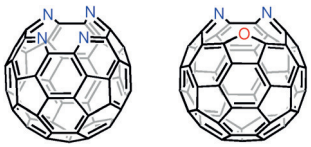

Figure 1. Structure of $C_{54}N_4$ and $C_{56}N_2O$.

Compound **1**[11] was previously prepared as a precursor to the diazafullerene $C_{58}N_2$,[12] which was detected in the gas phase by MALDI-TOF mass spectrometry. The key step for the introduction of the two nitrogen atoms on the cage skeleton to give **1** is the addition of hydroxylamine and subsequent PCl_5-induced rearrangement processes. To introduce another nitrogen atom, we replaced the chlorine atom with hydroxylamine to form compound **2** (Scheme 1). The 4-bromoaniline and naphthalene-2-amine both with a NH_2 group also reacted with **1** to form analogous compounds **2b** and **2c**, respectively. As expected, treatment of the hydroxylamino derivative **2a** with PCl_5 resulted in insertion of the nitrogen atom into a fullerene C–C bond to form the C_s symmetric compound **3**. Unlike the chlorine atom in compound **1,** the chlorine atom in **3** could not be replaced by hydroxylamine or other primary amines, such as aniline.

When we treated **3** with secondary amines such as the 4-methylpiperidine, compound **4** was obtained as the major product. Compounds **2a** and **3** could be isolated and purified for spectroscopic characterization, but they are relatively unstable and crude products were usually used directly in the synthesis of **4**. A large excess of 4-methylpiperidine could be used in the conversion of **3** into **4**, indicating that **4** is stable under moderate basic condition and is also quite inert towards further addition by weak nucleophiles. The two *t*-butylperoxo groups in **4** could be converted into two hydroxy groups to form **5** by reduction with excess sodium sulfide.

NMR spectra of compounds **2a**, **2b**,and **2c** showed the expected C_1 symmetry. The unique fullerene carbon bound with three nitrogen atoms appear at $\delta = 90.8$, 87.7 and 87.3 ppm for **2a**, **2b**, and **2c**, respectively, based on their

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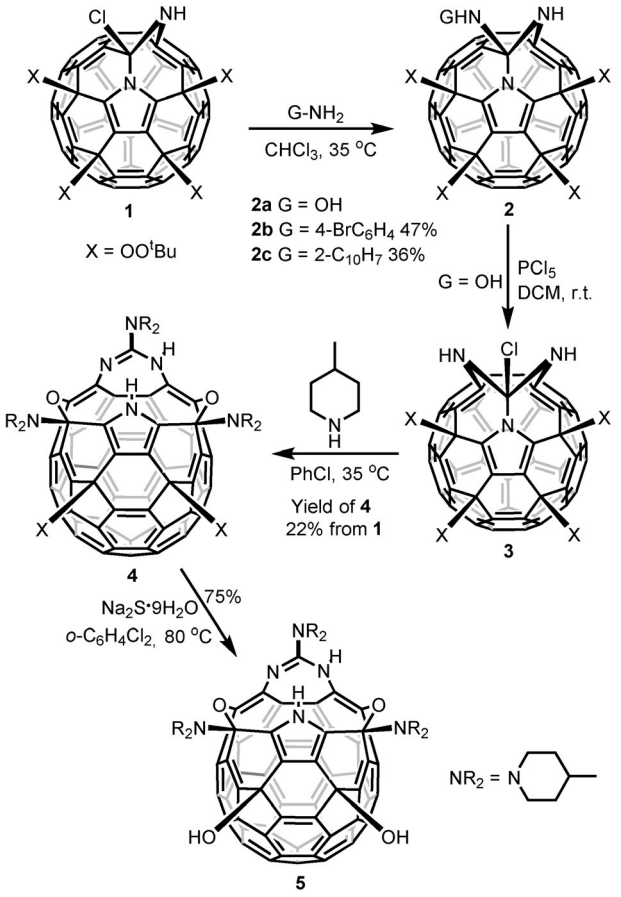


Scheme 1. Synthesis of fullerene based heterocycle.

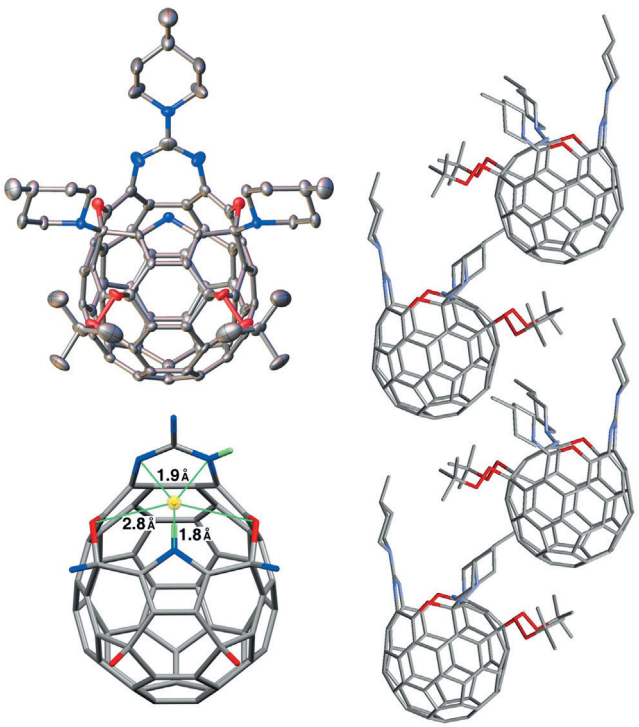


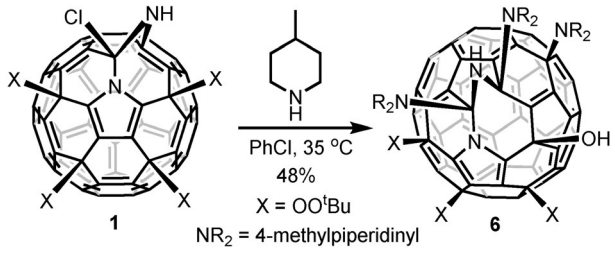
Figure 2. Single-crystal X-ray structure of compound **4**. left: Thermal ellipsoids are set at 50% probability; Hydrogen atoms in the ellipsoid model and all the non-directly attached groups in the stick model are omitted for clarity. C gray, N blue, O red, H green, calculated centroid for the five heteroatoms (3 N and 2 O) on the macrocycle is shown as a yellow ball in the stick model. Right: packing into chains in the solid state.

relatively higher intensity caused by the NOE effect of the NH groups. The C_s symmetric **3** showed the expected number of carbon signals and the unique fullerene carbon bound with three nitrogen atoms and one chlorine atom appear at $\delta =$ 105.3 ppm. The ^{13}C NMR spectra of **4** and **5** showed C_1 symmetry with a few overlapped signals.

Single crystal X-ray diffraction data of **4** provided conclusive structural assignment (Figure 2). Suitable crystals for X-ray diffraction were obtained from slow evaporation of its solution in a mixture of benzene and methanol. Unlike the C_1 symmetric structure shown in Scheme 1, compound **4** appears as C_s symmetric in the X-ray structure because of disorder of the hydrogen atom of the NH group in the guanidine moiety (two enantiomeric molecules occupy equivalent locations in 50% ratio). Facile 1,3-H shift from NH to the imino N in the guanidine moiety may be responsible for the disorder. The four atoms in the guanidine moiety (3 N and 1 C) and the two fullerene carbon atoms bound to the guanidine moiety are coplanar, and the dihedral angle between this plane and the other plane consisting four fullerene carbon atoms in the diazepine ring is 41.6°. The centroid in Figure 2 was calculated for the three N and two O atoms on the N,O-heterocycle. The distances from the centroid to the heteroatoms range from 1.8 to 2.8 Å. In the crystal packing the two *t*-butylperoxo groups and the two 4-methylpiperidine groups surrounding the pyrrole ring form a pocket hosting the fullerene cage of an adjacent molecule, thus forming a linear chain structure.

The formation of **4** involves a quite complex process, which includes cleavage of C–Cl, C–N, C–C, and O–O bonds. The cleavage of the pyrrole N–C bond is due to a formal 1,3-hydrogen shift. The peroxo O–O bond is cleaved by heterolysis giving off *t*-butoxide, and the resulting oxonium then inserts into the fullerene C–C bond, followed by addition of 4-methylpiperidine to form the hemiaminal moiety. It is difficult to determine which step initiated the multiple bond cleavage and formation process (see Supporting Information for a proposed mechanism).

To get more information about the mechanism leading to the formation of **4**, we treated compound **1** with 4-methylpiperidine under the same conditions (Scheme 2). Compound **6** with three 4-methylpiperidinyl groups was obtained as the major product. The enamine double bond in **1** is an active *anti*-Bret double bond, which is prone to further addition either in the 1,2-addition pattern for sterically less hindered addends such as methanol[11] or the 1,4-addition pattern for bulky addends as in the present case. Stoichiometrically two hydrogen atoms from the two 4-methylpiperidine converted a *t*-butylperoxo group into *t*-butanol and the hydroxy group in **6**. There is no hemiaminal moiety in **6**. So the local ring strain in **3** is a key driving force for the opening of the cage to form the hetero-macrocycle. The structure of **6** was confirmed by



Scheme 2. Reaction of 4-methylpiperidine with **1**.

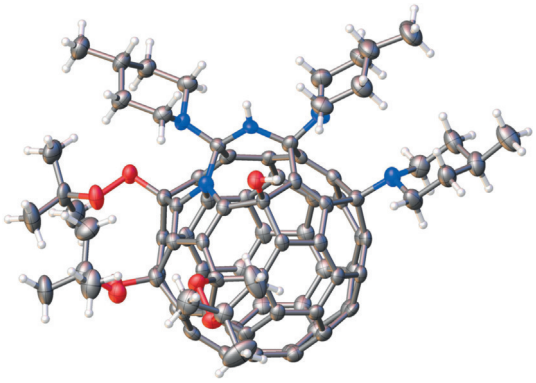
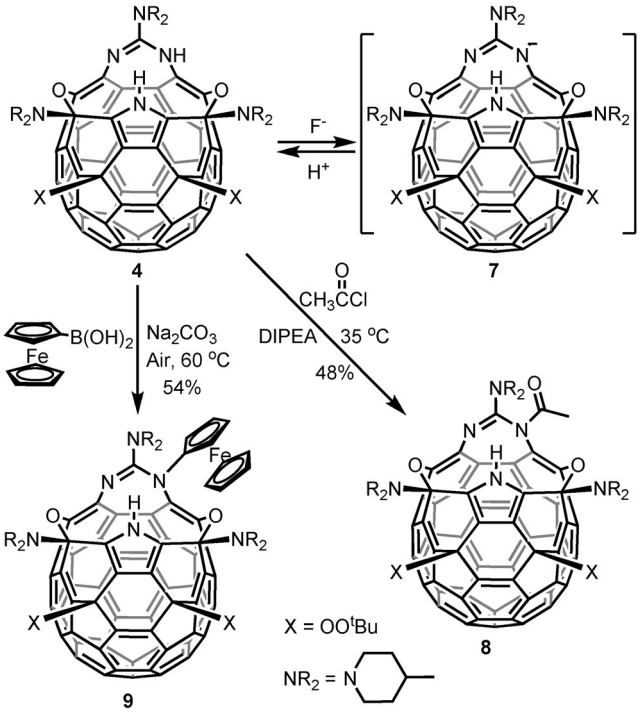


Figure 3. Single-crystal X-ray structure of compound *rac*-**6**. Ellipsoids are set at 50% probability; One enantiomer is shown. C gray, N blue, O red, H white.



Scheme 3. Reactions of the amino group on the guanidine moiety.

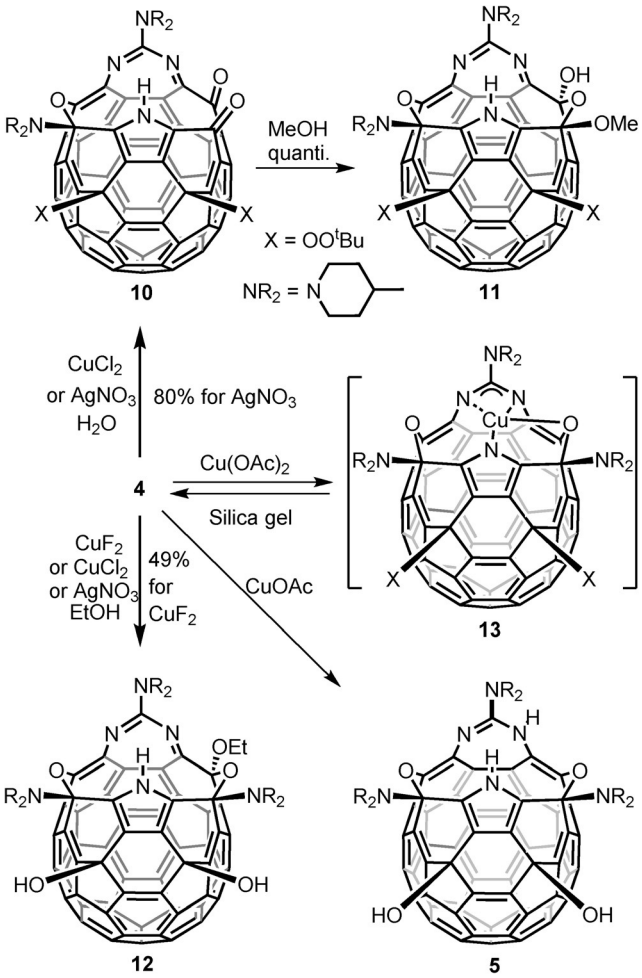
spectroscopic data and single-crystal X-ray analysis (Figure 3).

Reactivity of the N,O-heterocycle was investigated under various conditions. The dark green solution of **4** in $CHCl_3$ changed into light yellow after addition of CF_3COOH, which could be changed back into the dark green color of **4** with triethylamine. Addition of Bu_4NF into the dark green solution of **4** led to an intense red solution as a result of deprotonation of the NH group in the guanidine moiety (Scheme 3). Addition of excess CF_3COOH into the red solution resulted in a light yellow solution. As above, addition of excess triethylamine into the light yellow solution gave back the original dark green solution of **4**. UV/Vis spectra for these processes are available in the Supporting Information. The deprotonation of **4** by fluoride ion appears to be selective. Other common halides, such as Bu_4NCl, Bu_4NBr, and Bu_4NI did not cause any change. There was no reaction between **4** and relatively weak bases including NaOAc, DBU, and Et_3N. An open-cage fullerene with an enamine moiety on the orifice was reported to act as a selective sensor for fluoride ion.[13]

To verify the deprotonation at the guanidine moiety rather than the pyrrole moiety, we treated **4** with acetyl chloride to obtain compound **8**. Compound **4** could also react with ferrocenyl boronic acid under basic condition to form the ferrocenyl derivative **9**. Similar reactions between aryl boronic acid and amino compounds have been well documented under both metal-catalyzed and metal-free conditions.[14] Just like many other classical amides, there are two rotamers for **8**, a result of the hindered rotation of the amide bond. The ratio of the two rotamers is around 2:1 as determined from the ^{1}H NMR integrals. The signals for the pyrrole protons in **8** and **9** appeared at $\delta = 9.35$ and 7.28 ppm, respectively, in their ^{1}H NMR spectra. By comparison to the ^{1}H NMR spectra of **8** and **9**, the guanidine NH and the pyrrole NH protons for compounds **4** and **5** can be assigned as $\delta =$ 6.54, 8.71 ppm for **4** and $\delta = 6.54$, 8.86 ppm for **5** respectively. Even though the structures of **8** and **9** were based only on spectroscopic data, steric effect can rule out the possibility that the acetyl and ferrocenyl groups are attached to the pyrrole moiety instead of the guanidine moiety.

Preliminary results on the coordination chemistry of **4** showed unique behavior towards copper salts (Scheme 4). There was no change when **4** was treated with $CuSO_4 \cdot 5H_2O$, whereas complicated products were produced with $Cu(NO_3)_2 \cdot 3H_2O$. The reaction with $CuCl_2 \cdot x H_2O$ resulted in the formation of compound **10** with an expanded orifice. The reaction of **4** with various silver salts such as $AgNO_3$ and AgOAc also yielded compound **10** as the major product. Methanol readily adds to **10** to form **11** with a hemiketal/ketal moiety. Analogous carbonyl reactions have been reported for open-cage fullerene with two adjacent carbonyl groups.[15] In the presence of ethanol, the same reaction with cupric and silver salts yielded **12**, in which the two *t*-butylperoxo groups were reduced into two hydroxy groups besides the formation of the aminalketal moiety. Reaction with cuprous acetate was similar to the Na_2S reaction in Scheme 1, in which the *t*-butylperoxo groups were reduced to hydroxy groups to form **5**. Mechanisms for the formation of **10** and **12** are not clear. The copper and silver metal salts probably acted as both Lewis acid and oxidant.

The two carbonyl groups appear at $\delta = 180.4$ and 186.3 ppm on the ^{13}C NMR spectrum of **10**. The hemiaminal carbon atoms appear in the range from $\delta = 98$ to 103 ppm for



Scheme 4. Reactions of **4** with metal salts.

compounds **4**, **5**, **8**, **9**, **11** and **12**. In the ^{13}C NMR spectrum of **11**, there are three signals at $\delta = 101.7$, 97.7 and 93.3 ppm which can be assigned to the hemiaminal, ketal, and hemiketal carbons, respectively. The hemiketal signal at $\delta =$ 93.3 ppm is relatively intense owing to the NOE effect of the OH group. The HMBC spectrum of **11** also agrees with these assignments, which showed correlation between the methyl proton and the signal at $\delta = 97.7$ ppm. The analogous compound **12** showed three signals at $\delta = 101.2$, 98.3, and 92.8 ppm, which can be assigned to the two hemiaminal, and the ketal carbons, respectively.

The reaction of **4** with $Cu(OAc)_2{\cdot}H_2O$ was quite different, which yielded a more polar product. Attempts of isolating this new compound **13** by silica gel column chromatography resulted decomposition and reformation of compound **4** together with other unidentified products. To get more information about the new compound, we carried out the reaction in $CDCl_3$ and monitored the process by ^1H NMR spectroscopy. After stirring a mixture of **4** and $Cu(OAc)_2{\cdot}H_2O$ in $CDCl_3$ for 1 h at 35 °C, the ^1H NMR spectrum showed complete disappearance of the two signals corresponding to the two NH protons on the pyrrole and guanidine moieties (see Figure 4). The originally overlapped singlet signal at $\delta =$ 1.40 ppm for the two *t*-butyl groups in **4** was split into two

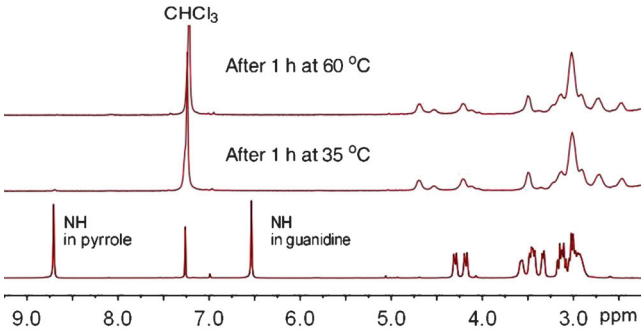


Figure 4. Section of the ^1H NMR spectra of compound **4** (bottom) and its reaction with $Cu(OAc)_2{\cdot}H_2O$ in $CDCl_3$ at different temperatures (middle and top).

singlets at $\delta = 1.37$ and 1.29 ppm. Further heating the solution of **4** and $Cu(OAc)_2{\cdot}H_2O$ in $CDCl_3$ for 1 h at 60 °C did not give any change as indicated by ^1H NMR spectroscopy. The ESI mass spectrum of the reaction mixture in $CDCl_3$ showed $[\mathbf{4}\text{-}2H]^+$ (*m*/*z* 1255.4) as the most intensive signal, and also a weak signal at *m*/*z* 1317.3, corresponding to $\mathbf{13}^+$. The reaction between **4** and $Cu(OAc)_2{\cdot}H_2O$ was also carried out in chlorobenzene, which gave similar results. The signal of $\mathbf{13}^+$ at *m*/*z* 1317.3 was more intense (13 % intensity relative to the base signal) in chlorobenzene than the signal in $CDCl_3$ (5 % intensity relative to the base signal). There were also signals which may be due to addition of two copper atoms in the ESI-MS spectra of the reaction in chlorobenzene. Under the same conditions compound **11** did not form detectable coordination complex formation with $Cu(OAc)_2{\cdot}H_2O$, indicating the importance of the NH group in the guanidine moiety for effective complexation with copper. The unique reactivity of $Cu(OAc)_2{\cdot}H_2O$ is probably due to the basicity of the acetate ion. To confirm the structure of **13**, a single-crystal X-ray structure is still needed.

In conclusion, hydroxylamino and *t*-butylperoxo addends have been shown to be effective groups for the introduction of nitrogen and oxygen atoms, respectively, into the fullerene skeleton. The mechanism may involve formation of nitrogen/oxygen cation or oxygen radical through the heterolysis of N–O/O–O bond or homolysis of O–O bond, and subsequent insertion of the intermediate into the fullerene skeleton C–C bond. Preliminary studies of the reactivity of the fullerene-based heterocycle showed promising coordination chemistry. Further work is under way to prepare more fullerene based heterocycles.

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