Synthesis of Open-cage Fullerenes with 4-Alkynylphenyl Groups on the Rim of the Orifice

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Alkynyl anilines react with a diketo open-cage fullerene derivative and expand the orifice size from 11- to 18-membered rings. Benzyl azide reacts with the terminal alkynyl group under Click conditions. Single crystal X-ray structure of the Cs symmetric bis-3-alkynylaniline derivative showed the formation of a head to tail dimer due to strong H-bonding and π-π interactions.

Keywords Fullerenes, open-cage, alkyne, Click reaction, dimer

Introduction

Several methods have been reported for the preparation of open-cage fullerene derivatives (1). These methods usually yield orifices with different sizes and different functional groups on the rim of the orifice, which may be used for further reactions to modify the orifice. The reaction between carbonyl groups on the rim of some open-cage C₆₀ derivatives with arylhydrazine has been proven an effective method to expand the size of the orifice (2). Coupling of carbonyl groups is a key step of reclosing the orifice in the preparation of H₂@C₆₀ and H₂O@C₆₀ (3). The addition of aryl diamine to open-cage derivative with two carbonyl groups results in a remarkable change of aromaticity and absorption in the Near IR region (4).

Fullerene derivatives containing terminal alkyne groups have been used to couple to various targets for material and biological studies. For example, up to 15 sugar moieties (5) and up to 12 porphyrins (6) have been readily introduced to [60]fullerene core through Click reactions using fullerene derivatives with terminal alkyynes. Porphyrin-fullerene dyads (7) and well-defined star shaped polymer-fullerene hybrids (8) have been prepared by similar Click chemistry using fullerene derivatives with terminal alkyynes. We have reported a peroxide-mediated method for preparation of open-cage fullerenes and prepared a number of open-cage fullerene derivatives (9). To explore the Click chemistry of open-cage fullerenes, here we report the synthesis of open-cage fullerenes with terminal alkyne group(s) and preliminary results of its Click reactions.

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**Results and Discussion**

The open-cage fullerene compound 1 can be prepared from C\text{60} in 6 steps. The addition of two different aniline groups in a stepwise fashion yields the unsymmetric open-cage product 3 as we have reported previously (10a). By following the same procedure, we prepared compounds 4 with one terminal alkyne group. For the preparation of the symmetric product 5 with two terminal alkyne groups, excess 3-ethynylaniline was added in one portion followed by reduction with CuBr (10b).

Spectroscopic data of compounds 4 and 5 are in agreement with the structures depicted in Scheme 1. The $^1$H NMR spectrum of 4 showed the alkyne proton at 3.06 ppm. On its $^{13}$C NMR spectrum there are four signals at 83.14, 77.87, 77.50, 77.38 ppm corresponding to the two alkyne and the two sp$^3$ fullerene carbons. Presence of four carbonyl groups at 183.94, 183.88, 182.28, 174.96 ppm is in agreement with its $C_1$ symmetry. The IR spectra of 4 and 5 showed strong CO stretching band at 1743 cm$^{-1}$. The UV-Vis spectrum of 5 exhibits absorption with onset at 600 nm but with no sharp absorption band. Both compounds showed satisfactory ESI-FT-ICR-HRMS.

The structure of compound 5 was further confirmed by single crystal X-ray analysis as shown in Figure 1. The two phenyl planes are twisted in respect to the 1,3-diiminopentenone plane on the fullerene cage with angles at 58.9° and 86.3°, respectively. Both alkyne groups point in the direction opposite from the center of the orifice. Besides
forming intra-molecular H-bonds with the adjacent imino nitrogen atoms, the hydroxyl groups also form inter-molecular H-bonds with the corresponding hydroxyl groups of another molecule, thus forming a head to tail dimer. The two molecules in the dimer show a slight slippage. So the dimer has a $C_1$ instead of $C_s$ symmetry. The mirror planes of the two molecules are parallel and separated from each other at a distance of 1.71 Å. The x-ray data also showed weak inter-dimer $\pi-\pi$ interactions. Each molecule in the dimer is in contact with one of the molecules of three adjacent dimers and a solvent toluene molecule with distances ranging from 3.05 to 3.39 Å.

We have recently reported a similar head to tail dimer for the open-cage compound 6 $C_{59}$(O)$_4$(NAr)$_2$ (Ar = $p$-$t$BuC$_6$H$_4$) (11). The main difference is the lack of the two OH groups in this $C_{59}$ derivative, thus lack of H-bonding within the dimer. The two molecules in this $C_{59}$ dimer are better aligned. The distance between the two mirror planes of each molecule is 0.86 Å compared with the 1.71 Å in the present case. The x-ray structure of open-cage compound 7 $C_{60}$(O)$_4$(NPh)$_2$ has also been reported (10b), which does not exhibit dimeric interaction. Apparently, the two alkyne groups in the present compound 5 are essential for the formation of a dimeric structure.

Figure 1. X-ray structure of 5. For clarity hydrogen atoms were not shown for the ellipsoid model. H-Bond distances are in Å.
To test the reactivity of the terminal alkyne group in the open-cage compound, we treated 5 with benzyl azide under standard Click conditions (Scheme 2). The reaction was much slower compared to other classical organic compounds (Scheme 2). Yield of the reaction was also low at 15%. One possible reason is that the open-cage compound 5 could react with OH\(^-\) at the active carbonyl groups on the rim of the orifice under the slightly basic condition. It was difficult to remove minor solvent impurities from the compounds completely because compound 8 slowly decomposed on silica gel. But its NMR spectra and HRMS can still suggest the formation of Click product. The HRMS of 8 indicates that just one of the two alkyne groups reacted with benzyl azide. The \(^{13}\)C NMR spectrum of 8 showed four signals at 83.10, 83.04, 77.91, 77.84 ppm for the two alkyne carbons and the two sp\(^3\) fullerene carbon, in agreement with mono Click reaction for compound 5. It was not possible to form the double Clicked product by using excess azide and extending reaction time.

In summary, alkynyl anilines are attached on to the rim of open-cage derivative with an 18-membered orifice. Presence of the alkynyl groups induces strong intra-molecular H-bonding and formation of head to tail dimers. The terminal alkyne group can react with benzyl azide under Click conditions. The present open-cage compounds with terminal alkyne group(s) can act as suitable synthons in Click reactions to form more complex compounds for functional property investigations.

**Experimental Section**

All reagents were used as received. Toluene used for the reactions was distilled from potassium under nitrogen. Dichloromethane (DCM) was distilled from phosphorus pentoxide. Other solvents were used as received. All the reactions were carried out in air except the
preparation of 6 which was under nitrogen atmosphere. The NMR spectra were obtained at 25°C unless noted.

Caution: A large amount of peroxides is involved in some of the reactions. Care must be taken to avoid possible explosion.

Preparation of Compound 4

Compound 1 was prepared by oxidation of its dihydroxyl precursor (10a) (87 mg, 0.079 mmol) with iodobenzene diacetate (DIB) (47 mg, 0.15 mmol) in benzene (30 mL) at 30°C. Aniline (7.3 mg, 0.16 mmol) dissolved in benzene was slowly added into the reaction mixture of compound 1. After compound 2 reached its maximum yield as indicated by TLC, 3-Aminophenylacetylene (25 mg, 0.21 mmol) was added. Stirring was continued for another 10 minutes. Then the solution was transferred onto a silica gel column and eluted with toluene. The first brown band was collected and evaporated to give the precursor of 4. CuBr (56 mg, 0.4 mmol), 30 μL water was added to the solution of the precursor of 4 in CH2Cl2 (10 mL), and the resulting solution was stirred in dark at room temperature for 3 hours. The solution was then transferred onto a silica gel column and eluted with toluene. The first red band was collected and evaporated to give 4 (19 mg, 0.018 mmol, yield from 1 to 4 23%). 1H NMR (CDCl3, CS2, 400 MHz): δ 7.51 (s, 2 H), 7.49-7.48 (1H), 7.46 (1H), 7.42-7.38 (3H), 7.36-7.32 (2H), 7.27 (2H), 3.06 (1H). 13C NMR (CDCl3, CS2, 100 MHz): All signals represent 1C except noted. δ 183.94, 183.88, 182.28, 174.96, 155.80, 155.07, 149.40, 149.26, 149.16, 149.14, 149.05(2C), 148.99(2C), 148.97(2C), 147.91(3C), 147.86, 147.74(2C), 147.56(2C), 146.77(2C), 146.53, 146.25(2C), 145.37, 145.24, 145.07(2C), 144.96, 144.54(2C), 144.52, 144.45, 144.19(4C), 143.10(2C), 142.61, 142.55, 142.34(2C), 140.32(2C), 136.53(2C), 135.45, 135.40, 130.35, 128.16(2C), 128.11, 128.06, 128.02, 127.27, 126.41, 126.39, 125.33, 122.53(2C), 122.39, 122.21, 83.14, 77.87, 77.50, 77.38. FT-IR (microscope): 3516, 3295, 2923, 2852, 1743, 1570, 1494, 1474, 1412, 1109, 1037, 793, 737, 692. HRMS (ESI) for C74H12N2NaO6 [M+Na]: calculated 1047.0588, found 1047.0582.

Preparation of Compound 5

Compound 1 was prepared by oxidation of its dihydroxy precursor (220 mg, 0.20 mmol) (10a)10a with DIB (117 mg, 0.36 mmol) in benzene (60 mL) at 30 °C, progress of the reaction was monitored by TLC. When the reaction was finished, the temperature was lowered to 15°C, 3-Aminophenylacetylene (117 mg, 1.0 mmol) was slowly added. After the resulting solution was stirred for 10 minutes it was transferred onto a silica gel column and eluted with toluene to give the precursor of compound 5. CuBr (50.0 mg, 0.35 mmol) and 100 μL water was added to the solution of the precursor of 5 in CH2Cl2 (30 mL) at r.t. The resulting solution was stirred for 3 hours and transferred onto a silica gel column and eluted with toluene. The first red band was collected and evaporated to give 5 (64 mg, 0.061 mmol, yield from 1 to 5 30%). 1H NMR (400 MHz, CDCl3): δ: 7.62 (d, 2H), 7.54 (s, 2H), 7.47 – 7.38 (m, 6H), 3.11 (s, 2H). FT-IR (microscope): 3518, 3295, 2923, 2852, 1743, 1570, 1494, 1474, 1411, 1218, 1109, 1036, 1015, 934, 791, 738, 690. ESI-HRMS: C76H13N2O6 (M + H+ ) calcd 1049.0768, found 1049.0758.

Suitable crystals were obtained from slow evaporation of 5 in CH2Cl2/Toluene at r.t. Crystal data for compound 5: C84H22Cl2N2O6, T = 173(2) K, Triclinic, space group P-1, Unit cell dimensions: a = 12.041(2) Å, b = 14.314(3) Å, c = 16.834(4) Å, α = 108.046(3), β = 108.592(2), γ = 92.088(2)°. V = 2585.1(9) Å3. Z = 2, ρcalcd = 1.575 Mg/m3.
Reflections collected / unique 34750/11819 [R(int) = 0.0405]. Final R indices [I>2σ(I)]
R1 = 0.0736, wR2 = 0.1599. CCDC 924880.

Preparation of Compound 8

CuSO4·5 H2O (25 mg, 0.10 mmol), sodium ascorbate (50 mg, 0.25 mmol), benzyl azide
(5 mg, 0.038 mmol) and 5 (32 mg, 0.031 mmol) were dissolved in 25 mL CHCl3 and 25 mL
water and the resulting solution was stirred at 60°C for 24 hours. The reaction solution
was extracted with DCM (3 × 30 mL). The combined organic extracts were dried over
anhydrous Na2SO4, filtered and concentrated in vacuo. The residue was chromatographed
on a silica gel column eluting with toluene. The first red band was collected and evaporated
to give 8 (5.6 mg, 0.0047 mmol, yield 15%). 1H NMR (400 MHz, CDCl3): δ7.60-7.05 (m,
16H), 5.56 (d, 1H,), 4.73 (d, 1H), 3.10 (1H). FT-IR (microscope): 3528, 3296, 2920, 2850,
2106, 1750, 1725, 1591, 1568, 1486, 1462, 1359, 1261, 1200, 1108, 1073, 1039,
1015, 912, 790, 739, 699. HRMS (ESI) for C83H20N5O6 [M + H+]: calculated 1182.1408,
found 1182.1425.

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