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Oxazolination of 1,4-$(PhCH_2)_2C_{60}$: Toward a Better Understanding of Multiadditions of Heteroaddends

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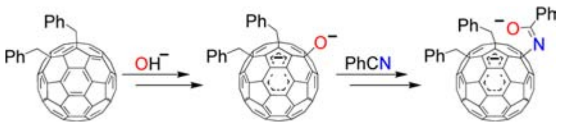
ABSTRACT



Multiadditions of heteroaddends to C_{60} are achieved via the oxazolination reaction of 1,4-$(PhCH_2)_2C_{60}$ with OH^- and PhCN, which exhibit a unique regioselectivity regarding the addition sites of the heteroatoms.

The exploration of multiaddition reactions involving fullerenes[1,2] has developed rapidly in recent years inspired by the promising potentials of functionalized fullerenes in the areas of biological[3] and materials science.[4,5] However, the chemistry of multiadditions is often complicated by the formation of many regioisomers, especially for cycloadditions,[1,6] which has stimulated broad interest in improving the regioselectivity.[7] Impressively, a high regioselectivity is shown for multiaddition reactions involving 1,4-additions, where tetraadducts with a 1,2,4,15-configuration[8] and hexaadducts with a 1,2,4,11,15,30-configuration are often obtained.[2,9−13] Such a selectivity is shown for organofullerenes with various addends including halogens (Cl, Br), alkyl, aryl, alkenyl, silyl, and amino groups,[2,9−13] indicating that the preference of such configurations is likely related to the intrinsic reactivity of C_{60}, which has been interpreted in terms of the special stability of the 10π $R_3C_{60}^-$ indenyl anion and $R_5C_{60}^-$ cyclopentadienide anion.[12b,c,13]

However, studies on the multiadditions of heteroaddends to C_{60} are rare.[12d] We have recently shown

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oxazolination of C_{60} by reacting with hydroxide and PhCN via an anion relay mechanism,[14] further benzylation of the oxazoline dianion results in a cis-1 1,4-benzylated oxazoline via a charge-directed mechanism.[14,15] It is of interest to apply this protocol to a less symmetrical C_{60} 1,4-adduct, since it may reveal new information regarding the regioselectivity for heteroaddend additions, which would be unlikely to be observed when C_{60} with high symmetry was used. Herein, we report the oxazolination of 1,4-$(PhCH_2)_2C_{60}$, which affords compounds **1** and **2** via a unique regioselectivity, whose structures are illustrated in Figure 1.

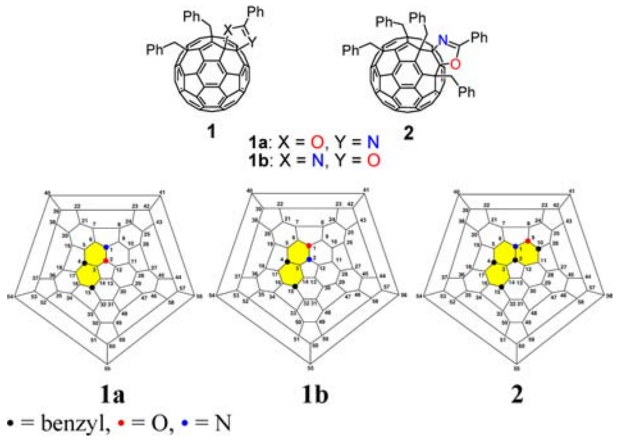

Figure 1. Illustrated structures and Schlegel diagrams of possible configurations for **1** and **2**.

Compound 1,4-$(PhCH_2)_2C_{60}$ was obtained following previous procedures.[16] Compound **1** (25% isolation yield) was obtained via the reaction of 1,4-$(PhCH_2)_2C_{60}$ (30 mg, 33.3 μmol) with HO^- (1.0 M TBAOH/CH_3OH, 73.3 μL, 2.2 equiv) and PhCN (solvent), followed by quenching with I_2 (21.1 mg, 83.3 μmol, 2.5 equiv), by procedures similar to those described previously.[14] Compound **2** (40% isolation yield) was obtained following similar procedures for producing **1**, except the reaction mixture was quenched with $PhCH_2Br$ (30 equiv) instead of I_2. The HPLC trace for each reaction (Figures S1 and S2) shows only one major fraction for the product.

The positive accurate MS of compound **1** (Figure S3) shows a protonated molecular ion at 1022.15273, indicating the formation of a dibenzylated C_{60} phenyl oxazoline ($C_{81}H_{19}NO$, calcd 1022.15394 for $[M + H]^+$). The ^1H NMR spectrum of the compound (Figure S4) shows two AB quartets centered at δ 3.52 ($\Delta\nu$ = 120.6 Hz, J_{AB} = 13.2 Hz) and 2.50 ppm ($\Delta\nu$ = 217.2 Hz, J_{AB} = 13.2 Hz), arising from the methylene protons of two benzyls. Resonances corresponding to the phenyl protons from the benzyls and the oxazolino phenyl are shown in the aromatic region; the number of protons is consistent with the structural assignment.

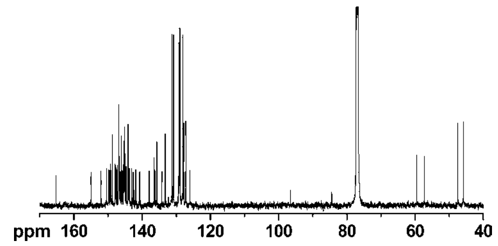

Figure 2. ^{13}C NMR spectrum of **1** recorded in $CDCl_3$.

Figure 2 displays the ^{13}C NMR spectrum of **1**, where 47 resonances for the sp^2 C_{60} carbons are shown from 154.98 to 136.23 ppm, indicating a C_1 symmetry for the molecule. The most downfield resonance at 165.31 ppm is due to the imine carbon of the oxazolino group as indicated by the HMBC NMR (Figure S6); while 12 resonances from 135.64 to 126.02 ppm are from the phenyls of the oxazolino and benzyl groups. Resonances for the sp^3 methylene carbons are shown at 47.48 and 45.85 ppm, while the sp^3 C_{60} carbons bonded to the two benzyls appear at 59.54 and 57.23 ppm, and those due to the sp^3 C_{60} carbons bonded to the O- and N-atoms are shown at 96.55 and 84.49 ppm respectively, consistent with the reported data for C_{60} oxazolines.[14,15,17,18]

The HMBC NMR spectrum of **1** shows no correlations between the methylene protons and the sp^3 C_{60} carbons bonded to O- and N-atoms, indicating that the methylene protons are at least four bonds away from the oxazolino functionality,[19] implying that the oxazolino group is not positioned within the same hexagon of 1,4-dibenzyls.

Apparently, compound **1** is different from the cis-1 1,4-dibenzylated C_{60} oxazoline obtained by benzylation of a C_{60} oxazoline dianion.[14,15] Previous work on C_{60} reactions involving tandem 1,4- and 1,2-additions has shown that the reactions usually result in products with a 1,2,4,15-configuration;[10,11,12b,12c,13,14] it is therefore likely that **1** is also a 1,2,4,15-adduct. Such an assignment is supported by the UV/vis absorptions (Figure S7) of the compound in light of the result of 1,2,4,15-$(PhCH_2)_4C_{60}$,[10] since the UV/vis is sensitive to the configurations of organofullerenes rather than the nature of the addends[20] and has been widely used for structural elucidation of complicated fullerene derivatives.[6]

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Even though compound **1** is assigned as the 1,2,4,15-adduct, there are still two possible regioisomers (**1a** and **1b**), in which the addition sites for the heteroatoms are switched. Since there is only one set of ^{13}C NMR resonances and one major HPLC fraction for the reaction product, it indicates that only one regioisomer is obtained from the reaction. However, the exact structure of **1** cannot be resolved just based on the spectral characterizations. Even the X-ray single crystal diffraction may not be able to discern the two structures unambiguously due to similar electron densities between the N- and O-atoms.[18]

Previous work has shown that GIAO calculations on the ^{13}C NMR resonances are quite reliable for elucidating the structures of complicated C_{60} derivatives.[21] The calculations were therefore performed for **1a** and **1b** with the Gaussian03 program using the B3LYP/6-31G(d) method based on the structures optimized at the same level. The results predict that the sp^3 C_{60} carbons bonded to the O- and N-atoms are resonating at 98.34 and 89.55 ppm for **1a** and 93.73 and 93.91 ppm for **1b**, implying that the obtained compound is likely to have the structure of **1a**, since the calculated values are better matched with the experimental results (96.55 and 84.49 ppm).

The structure of **1** is finally resolved on the basis of **2**, which is obtained by quenching the reaction mixture of 1,4-$(PhCH_2)_2C_{60}/OH^-/PhCN$ with $PhCH_2Br$. In light of previous results,[14,15] compound **2** (dibenzylated **1**) is expected to have a structure in which the oxazolino group and the newly added benzyls are positioned with a cis-1 configuration. The positive accurate MS of **2** (Figure S8) shows the monoisotopic $[M + H]^+$ at m/z = 1204.26360, confirming the formation of **2** ($C_{95}H_{33}NO$, $[M + H]^+$ calcd: 1204.26349). The ^{1}H NMR (Figure S9) shows four sets of AB quartets due to methylene protons from four different benzyls, which can be grouped with an HMBC NMR spectrum (Figure 3 below) and are labeled as Ia/Ib, IIa/IIb, IIIa/IIIb, and IVa/IVb, with resonances at δ 3.86 ($\Delta\nu$ = 197.4 Hz, J_{AB} = 13.2 Hz), 3.59 ($\Delta\nu$ = 220.2 Hz, J_{AB} = 13.2 Hz), 3.18 ($\Delta\nu$ = 529.8 Hz, J_{AB} = 13.2 Hz), and 2.87 ppm ($\Delta\nu$ = 123.6 Hz, J_{AB} = 13.2 Hz). Resonances arising from the phenyl protons of the oxazolino functionality and benzyls are shown in the aromatic region, in agreement with the formation of a tetrabenzylated C_{60} phenyl oxazoline.

The ^{13}C NMR spectrum of **2** (Figure S10) shows 46 resonances for the sp^2 carbons of C_{60} and 19 resonances for the phenyl carbons. The presence of four benzyls are distinctly shown by the appearance of four methylene carbons resonating at 46.76, 46.38, 45.36, and 43.54 ppm and four resonances at 61.59, 60.05, 58.19, and 56.22 ppm, arising from the sp^3 C_{60} carbons bonded to the benzyls. Resonances due to the two sp^3 C_{60} carbons bonded to oxygen and nitrogen atoms are shown at 97.65 and 87.13 ppm,[14,15,17,18] while a resonance from the imine carbon of the oxazolino heterocycle is positioned at 161.11 ppm, as evidenced by the cross peak with the proton doublet at 7.95 ppm (Figure S11) via $^3J_{CH}$ couplings.

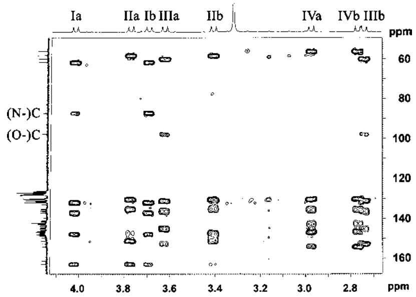

Figure 3. Expanded HMBC NMR spectrum of **2** recorded in CS_2 with DMSO-d_6 as the external lock.

Figure 3 shows the expanded HMBC NMR spectrum of **2**. The spectrum shows, first, each AB quartet correlates with only one sp^3 C_{60} carbon bonded to the benzyl group, indicating that no benzyls are positioned with a 1,2-configuration in the molecule; second, AB_q I and II are correlated with the most downfield sp^2 C_{60} carbon at 166.39 ppm via the $^3J_{CH}$ couplings, indicating that the two benzyls are both located next to this carbon, which is consistent with the conclusion drawn by Meier et al. that the most downfield resonances for C_{60} are immediately adjacent to the sp^3 carbons of C_{60};[21b] and last, the spectrum shows that AB_q I are coupled with the C_{60}−N carbon (δ = 87.13 ppm), while AB_q III are coupled with the C_{60}−O carbon (δ = 97.65 ppm), indicating that these two benzyls and the oxazolino heterocycle are positioned with a cis-1 configuration, and the C_{60}−N bond is positioned next to the benzyl responsible for AB_q I, while the C_{60}−O bond is positioned next to the benzyl responsible for AB_q III. On the basis of the above discussions, the only possible structure for **2** is 1-N,9-O phenyl oxazolino-2,4,10,15-$(PhCH_2)_4C_{60}$ as shown in Figure 1, where the benzyls responsible for AB_q I, II, and III are located at C2, C10, and C4 respectively. The benzyl corresponding to AB_q IV should be located at C15 (Figure 1), considering the fact that 1,4-$(PhCH_2)_2C_{60}$ was used as the starting material, and no additional correlation with sp^3 C_{60} carbon is shown except the one with the carbon bonded to the benzyl group at 43.54 ppm.

Previous work has shown that the benzylation of the C_{60} oxazoline dianion affords a 1,4-benzylated C_{60} oxazoline with a cis-1 configuration, where the O-atom relocates from a [6,6]-bond to a [5,6]-bond.[15b] The presence of a cis-1 1,4-benzylated oxazolino unit in the molecule explicitly indicates that compound **2** is formed via the same benzylation mechanism from 1^{2-}. Consequently, from the structure of compound **2**, it can be deduced unequivocally that compound **1** has the structure of **1a** (1-N,2-O oxazolino-4,5-$(PhCH_2)_2C_{60}$, Figure 1), since only with this configuration the O-atom can migrate from a [6,6]-bond (C2) to a [5,6]-bond (C9), while the N-atom remains bonding to C_{60} during the benzylation reaction of 1^{2-}.[15b] The structural assignment for compound **1** is in good agreement with the GIAO calculations.

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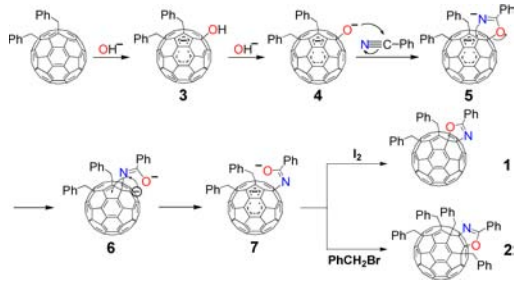
The exhibited regioselectivity for the N and O locations of **1** somehow seems contradictory to the $R_3C_{60}^-$ indenide monoanion principle,[12b,c,13] which has been quite successful in predicting the reaction sites for 1,4-multiadditions.[12−14] Previous work on multiple nucleophilic 1,4-additions to C_{60} has shown that the nucleophiles prefer to take the *para*-position relative to the existing addends probably due to the stability brought by the 10π indenyl resonance of this configuration.[12c,13,14] It is therefore rational that the OH^- would also follow the same regiochemistry when reacting with 1,4-$(PhCH_2)_2C_{60}$, by first taking the C1 position (Figure 1) to form an indenide monoanion intermediate (the addition at C30 is also possible, which would result in the enantiomer of the intermediate). The preference of the *para*-position over the *meta*-site for nucleophilic addition of OH^- to 1,4-$(PhCH_2)_2C_{60}$ is further supported by B3LYP/6-31+G(d) calculations (Figure S12), which predict that the *para*-carbons with respect to the existing benzyls have a much greater positive charge than the *meta*-carbons and should be more affinitive toward nucleophiles. However, the reaction would likely result in **1b** rather than **1a** if the heteroatoms remained with such regioselectivity. Apparently, the nucleophilic addition of OH^- to 1,4-$(PhCH_2)_2C_{60}$ followed by PhCN addition is more complicated, and a reaction mechanism is proposed as shown in Scheme 1.

Scheme 1. Proposed Mechanism for the Reaction of 1,4-$(PhCH_2)_2C_{60}$ with OH^- and PhCN Quenched with I_2 or $PhCH_2Br$



As is shown in Scheme 1, the reaction is likely initiated by a nucleophilic addition of OH^- to 1,4-$(PhCH_2)_2C_{60}$,[14] with the OH^- at the *para*-position relative to the existing benzyl to form a stable indenyl monoanion **3** with a 10π-electron resonance. The intermediate is then deprotonated by excessive OH^- to form the reactive $(PhCH_2)_2C_{60}^-{-}O^-$ dianion (**4**),[14] which would probably attack PhCN to form dianionic imine species (**5**), followed by an intramolecular nucleophilic addition of the imine anion back to C_{60} at C2 (Figure 1, the adjacent [6,6]-carbon relative to the C_{60}−O bond), accompanied by simultaneous heterolytic cleavage of the C_{60}−O bond to form intermediate **6**.[14,15b,c] Due to the heterolytic cleavage of the C_{60}−O bond, the C_{60} sphere may carry only one negative charge even though intermediate **6** is a dianion. However, the 10π indenide resonance is ruptured in **6** because of the occupation of the N-atom at C2 (Figure 1). In such a configuration, the negative charge is more likely localized at the *ortho*-carbon (C1) with respect to the existing single addend at C2,[22] as supported by the facile formation of 1,2-HRC_{60} when protonating singly bonded RC_{60}^- intermediates.[23] The adjacent negative charge may induce the N-atom to rearrange for a more stable 10π indenyl intermediate **7**, which would result in compounds **1** and **2** via subsequent reactions.

It is noteworthy that a $(PhCH_2)_3C_{60}^-$ intermediate with the configuration of **6** was proposed previously.[10] However, such a regioselectivity of the *meta*-carbon with respect to the existing 1,4-dibenzyls was achieved via the electrophilic reaction of $(PhCH_2)_2C_{60}^{2-}$ with $PhCH_2Br$; in addition, the reported $(PhCH_2)_3C_{60}^-$ intermediate with the configuration of **6** did not undergo rearrangement as observed for intermediate **6**, probably due to the lower electronegativity of the C-atom compared with the N-atom, which results in the lack of driving forces for the negative charge-induced rearrangement.

The preference of **7** over **6** is in agreement with the computational calculations with Gaussian03 at the HF/6-31G level, which predict a 4.9 kcal/mol difference between the two intermediates. The calculated HOMO distributions (Figure S13) are consistent with the localization of the negative charge on the *ortho*-carbon with respect to the existing single addend for intermediate **6** and also in agreement with the presence of the 10π indenyl resonance in intermediate **7**.

In conclusion, reactions involving 1,4-multiadditions of heteroaddends to C_{60} are reported. The work shows the production of a C_{60} multiadduct with a novel structure, and a unique regioselectivity regarding the positions of heteroatoms, which can be rationalized by the charge-induced rearrangement of the N-atom in order to adopt the more stable 10π indenyl anion configuration. The results have provided further insights into the regioselectivity for multiadditions of heteroaddends to fullerenes, which may be helpful in obtaining a better understanding of fullerene chemistry.

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Supporting Information Available. Experimental and calculation details, and spectral data for **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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