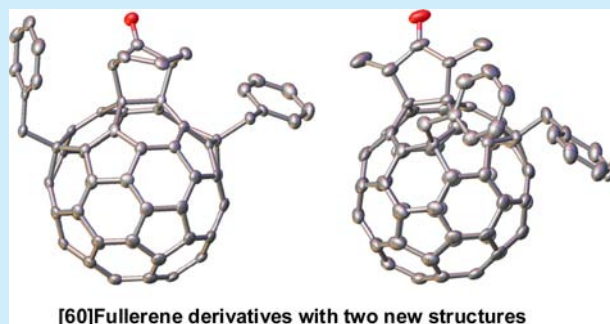


Base-Promoted Consecutive Enolate Addition Reaction of [60]Fullerene with Ketones

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Supporting Information

ABSTRACT: [60]Fullerene derivatives with novel 1,4,9,25- and 1,4,9,12-configurations were obtained by reactions of C₆₀ with aliphatic ketones and benzyl bromide under basic conditions. The structures of the products were determined by X-ray single-crystal diffraction and spectroscopic characterization. The reactions were rationalized by a monoenolate addition experiment and in situ vis-NIR spectroscopy.



As an important electro-organic material with promising applications in areas such as photovoltaic devices,¹ the physical and chemical properties of fullerene derivatives are intimately related to the specific configuration of the compounds.² Consequently, the exploration of [60]fullerene derivatives with novel structures is of great importance, but at the same time, the task is full of challenges due to complications posed by the three-dimensional structure of the carbon cages.³ Compared to the well-studied 1,2;1,2-addition (double 1,2-additions) [60]fullerene chemistry, where all eight possible regioisomers have been obtained,⁴ much less work has been carried out on the 1,4;1,4-addition (double 1,4-additions) [60]fullerene chemistry. In principle, there are more regioisomers for the 1,4;1,4-adducts with respect to the 1,2;1,2-adducts because a 1,4-addition involves only one hexagon for the reaction, while a 1,2-addition involves two neighboring hexagons for the reaction. Surprisingly, only two types of 1,4;1,4-adducts with the structures of 1,4,10,24- and 1,4,11,15-addition patterns have been reported so far.^{5,6}

Enolate addition to [60]fullerene involving bromomalonate with the formation of methanofullerenes is one of the most important and earliest studied reactions in fullerene chemistry.⁷ Direct reaction of C₆₀ with ketones under basic conditions results in acetals via the addition of an enolate followed by oxidative cycloaddition under the effect of O₂.⁸ However, to the best of our knowledge, no work on successive deprotonation of carbonyl compounds has been reported in fullerene chemistry, and consequently, no report on consecutive additions of the same enolate moiety to C₆₀ has appeared.

We have recently discovered a stable [60]fullerene-functionalized monoanionic intermediate with the 1,4,9-configuration (Figure 1a).⁹ Further examination of the intermediate indicates

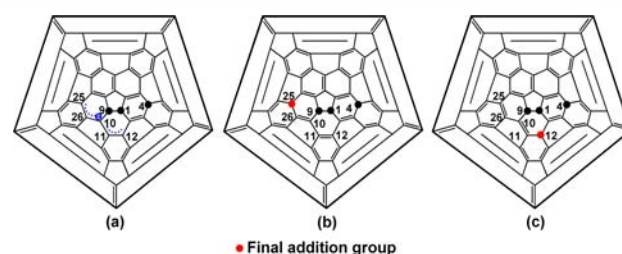


Figure 1. Schlegel diagrams of (a) 1,4,9-C₆₀ monoanionic intermediate and (b) 1,4,9,25- and (c) 1,4,9,12-C₆₀ adducts.

that it would produce 1,4,9,25- and 1,4,9,12-adducts, which are new structures for C₆₀ derivatives, if the final addition occurs at C25 or C12 with respect to C9 (Figure 1b,c) when there is enough steric hindrance.¹⁰ Herein, we report the synthesis of these 1,4,9,25- and 1,4,9,12-C₆₀ derivatives via reactions of C₆₀ with aliphatic ketones and BnBr (benzyl bromide) under basic conditions.

Table 1 lists the screening of reaction conditions and substrate scope. Cyclohexanone was used for the reaction screening. Product 1 with the 1,4-addition pattern was obtained when only 1 equiv of OH⁻ with respect to C₆₀ was employed. Compound 2a with a 1,4;1,4-addition pattern and 1,4-Bn₂C₆₀ (5) were obtained when 3 equiv of OH⁻ with respect to C₆₀ was used (see Figure S8 in Supporting Information (SI) for HPLC). Further increasing the amount of OH⁻ to 5 equiv also resulted in 2a, but with a slightly decreased yield, indicating that the use of 3 equiv of OH⁻ is appropriate for the reaction. A lower temperature of 30 °C

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Table 1. Screening of the Reaction Conditions and the Substrate Scope^a

| entry | ketone ^b | OH ⁻ (equiv) | temp (°C) | time ^c (h) | product and yield ^d (%) |
|-------|---------------------|-------------------------|-----------|-----------------------|--|
| 1 | Cyc-H | 1 | 30 | 0.5 | 1 (76) |
| 2 | Cyc-H | 3 | 30 | 0.5 | 2a (43), 5 (12) |
| 3 | Cyc-H | 5 | 30 | 0.5 | 2a (39), 5 (10) |
| 4 | Cyc-H | 3 | 30 | 1.5 | 2a (32), 5 (11) |
| 5 | Cyc-H | 3 | 50 | 1.5 | 2a (19), 5 (8) |
| 6 | Cyc-P | 3 | 30 | 0.5 | 3a (38), 5 (14) |
| 7 | Cyc-P | 3 | 30 | 1.5 | 3a (29), 5 (12) |
| 8 | 3-P | 3 | 30 | 0.5 | mixture |
| 9 | 3-P | 3 | 30 | 1.5 | mixture |
| 10 | 3-P | 3 | 50 | 0.5 | 4a (26), 4b (35), 5 (4) |
| 11 | 3-P | 3 | 70 | 0.5 | 4a (24), 4b (34), 5 (4) |
| 12 | 3-P | 3 | 100 | 0.5 | mixture |
| 13 | 3-P | 3 | 50 | 1.5 | 4a (19), 4b (29), 5 (5) |

^aReaction conditions: C₆₀ (36 mg) and 50 equiv of ketone were put into *o*-DCB (*o*-dichlorobenzene) (15 mL). The mixture was stirred for 15 min under argon at the preset temperature. Then OH⁻ (TBAOH, tetra-*n*-butylammonium hydroxide, 1.0 M in CH₃OH) was added into the solution, and the reaction was allowed to proceed for 0.5 or 1.5 h, followed by addition of 20 equiv of BnBr with a reaction time of 1 h under Ar. ^bCyc-H, cyclohexanone; Cyc-P, cyclopentanone; 3-P, 3-pentanone. ^cTime for the reaction of C₆₀ with ketone under basic conditions before BnBr was added. ^dIsolated yield.

seems to be appropriate for the reactions of cyclohexanone and cyclopentanone, while a higher temperature of 50 °C is required for the reaction of 3-pentanone. For all cases, a shorter reaction time of 0.5 h between C₆₀ and ketone under basic conditions is more preferential over a longer reaction time of 1.5 h, likely due to the effect of side reactions. 1,4-Bn₂C₆₀ (**5**) was obtained as a byproduct for all the entries except entry 1. In addition, only one type of 1,4;1,4-adduct (**2a** and **3a**) with 1,4,9,25-configuration was obtained when cyclohexanone or cyclopentanone was used, while two types of 1,4;1,4-adducts (**4a** with 1,4,9,25-configuration and **4b** with 1,4,9,12-configuration) were obtained when 3-pentanone was used, where **4a** is composed of both the *cis*- and *trans*-isomers.

The structure of **1** was resolved by single-crystal X-ray diffraction, which shows disorders in the positions of the fullerene cage, the carbonyl, and the toluene solvent due to the presence of two pairs of enantiomers. Figure 2 displays the X-ray

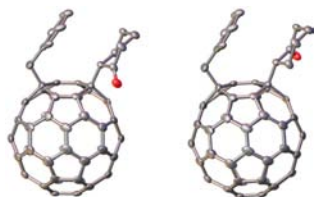


Figure 2. X-ray single-crystal diagrams of the two diastereomers of **1** with 50% thermal ellipsoids. Hydrogen atoms and solvent molecules were omitted for clarity.

single-crystal diagrams of the two diastereomers out of the two pairs of enantiomers of **1**, where a cyclohexanone and a benzyl were bound to C₆₀ in a 1,4-addition pattern, suggesting the existence of significant steric hindrance between the two addends.

The structures of **2a** and **4b** were also determined by single-crystal X-ray diffraction, which shows unambiguously that they

possess the 1,4,9,25- and 1,4,9,12-configurations. The structure of **4b** contains a disordered interstitial CS₂ solvent molecule, and the utility SQUEEZE was applied to remove its contribution from the structure.¹¹ Figure 3 displays the X-ray single-crystal

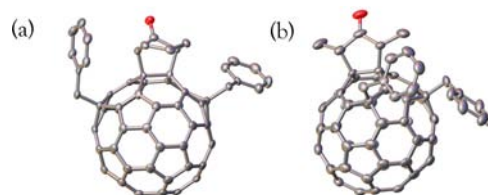


Figure 3. X-ray single-crystal diagrams of (a) **2a** and (b) **4b** with 50% thermal ellipsoids. Hydrogen atoms and solvent molecules were omitted for clarity.

diagrams of **2a** and **4b**, where the two molecules have a common 1,4,9-subunit, with one benzyl at C4 and a 3'-cyclopentanone unit at C1 and C9 across five- and six-membered rings of C₆₀. The configuration difference between the two structures lies in the position of only one benzyl, which is positioned at C25 in **2a** and C12 in **4b**. Notably, the C25 and C12 are both the para positions with respect to C9, indicating that **2a** and **4b** are likely formed via the intermediate with the same 1,4,9-configuration.

Further examination of **2a** reveals that there also exists a bridged cyclohexanone unit arising from the starting material. Interestingly, this cyclohexanone ring is preferentially positioned over a hexagon rather than a pentagon of the C₆₀ cage, which blocks the C12 for further benzylation in the 1,4,9-intermediate and rationalizes the exclusive formation of **2a** as C25 is the only site available for the para addition. On the contrary, both C12 and C25 are available in the 1,4,9-intermediate formed from 3-pentanone, which affords both the 1,4,9,25-adduct (**4a**) and 1,4,9,12-adduct (**4b**). Notably, the single-crystal structure of **4b** exhibits a *cis*-configuration for the C₆₀-fused 3'-cyclopentanone ring, with the hydrogen atoms positioned toward the benzyl group at C12, likely due to the evasion of the steric hindrance caused by the C12-benzyl and the methyls.

The structural assignments of **1**, **2a**, and **4b** were further supported by the HRMS, UV-vis, and ¹H and ¹³C NMR characterizations. The ¹H and ¹³C NMR spectra of **1** (Figures S6 and S7) exhibit much more peaks than expected for one single isomer (a total of 83 peaks due to the sp² carbon atoms of C₆₀). The HPLC analysis confirmed the purity of the compound (Figures S2 and S3), consistent with the existence of two pairs of enantiomers in **1**, as revealed by the single-crystal X-ray diffraction. The ¹³C NMR spectrum of **2a** (Figure S12) shows 27 peaks for the sp² carbon atoms of C₆₀, in agreement with the C_s symmetry of the molecule. The HSQC and HMBC NMR spectra of **2a** (Figures S13–S15) reveal that one of the 4'-protons in the bridged cyclohexanone ring is significantly deshielded (2.71 ppm) compared with the counterpart proton in cyclohexanone (1.67 ppm, Figure S16), suggesting the formation of C–H⋯π bonding for this proton. Further examination of the single crystal of **2a** shows a distance of 2.487 Å and an angle of 145.31° for the C–H⋯π bond (Figures S17 and S18), which falls well into the range of C–H⋯π bonding,¹² rationalizing the preferential position of the cyclohexanone over the hexagon of C₆₀. As for **4b**, the ¹³C NMR spectrum (Figure S37) shows 51 peaks due to the sp² carbon atoms of C₆₀, consistent with the C₁ symmetry of the molecule.

Figure 4 shows the UV-vis spectra of **1**, **2a**, and **4b** from 350 to 750 nm. Product **1** exhibits a broad band at 445 nm, which is

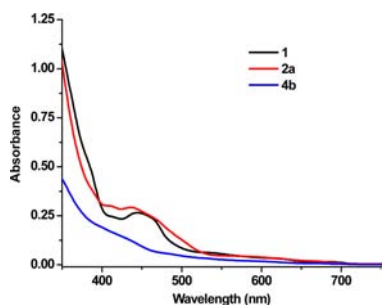


Figure 4. UV-vis spectra of **1**, **2a**, and **4b** (5.0×10^{-5} M) measured in toluene using a 1 cm cuvette at rt.

typical for 1,4- C_{60} adducts.¹³ Compound **2a** exhibits a broader and stronger visible absorption band compared to that of **1** with λ_{max} at 438 nm, indicating that the two 1,4-additions with the 1,4,9,25-configuration interact synergistically to enhance the light-harvesting ability of the compound. However, the visible absorption of compound **4b** is rather weak, suggesting that the light absorption ability of 1,4-addition is likely canceled via the interactions of the two 1,4-additions positioned with the 1,4,9,12-configuration.

For compounds **3a** and **4a**, the UV-vis spectra of the compounds (Figures S20 and S30) exhibit absorptions similar to those of **2a**, indicating explicitly that these two compounds are 1,4,9,25-adducts, as the UV-vis spectra of C_{60} derivatives are characteristic of the addition patterns.¹⁴ The HRMS of the two compounds (Figures S21 and S31) show protonated molecular ions at 985.15674 (calcd 985.15869) and 987.17404 (calcd 987.17434), respectively, consistent with the assigned structures. The ^{13}C NMR spectrum of **3a** reveals that there are 27 peaks for the sp^2 C_{60} carbon atoms in the molecule, in agreement with the C_s symmetry of the molecule. Surprisingly, the ^{13}C NMR spectrum of **4a** shows a total of 52 peaks corresponding to the sp^2 carbon atoms of C_{60} (Figure S33), which seems to be too many for a 1,4,9,15-adduct with C_s symmetry, indicating that this product is likely composed of two components.

In fact, only one fraction was shown for **4a** when the compound was purified over an HPLC silica column (Figure S26), which was used for purifying all compounds in this work. However, the obtained **4a** exhibited three fractions when it was eluted over a Buckyprep-M column (Figure S27), suggesting the presence of multiple components in **4a**. Interestingly, the major fraction (**4a-I**) collected from the Buckyprep-M column afforded the same three fractions when it was injected back into the same column immediately (Figure S28), implying that the three components constituting **4a** exist in a fast equilibrium. The result is consistent with the computational calculations (Gaussian 09, B3LYP/6-311G(d)//B3LYP/6-31G) that show the three regioisomers for **4a** (2 *cis* and 1 *trans* isomers, Figure S29) are all stable, with relative energies at 0.0, 1.0, and 1.1 kcal/mol, respectively. The result indicates that the C- C_{60} bond over the [5,6]-bond of C_{60} in **4a** is rather weak, which can be cleaved and reconnected easily with the conversion between the two *cis*- and one *trans*-configurations. To the best of our knowledge, this is the first time that a weak C- C_{60} bond has been demonstrated, which is different from the typically strong C- C_{60} bond reported in literature. Notably, no such isomerization is observed for **2a**, **3a**, and **4b**. For **2a** and **3a**, there are bridged ring structures in the molecules that prohibit the transformation of the C_{60} fused ring. For **4b**, it has a structure different from that of **4a**. Even though one of the *trans*-isomers with the C9-methyl pointing to C12-

benzyl (Figure S38) is predicted to be stable by calculations (1.7 kcal/mol higher than **4b**), the existence of only one isomer for **4b** indicates that the weak [5,6] C- C_{60} bond is likely related to the specific 1,4,9,25-structure of **4a**.

Figure 5 shows the in situ vis-NIR spectra for the reaction of C_{60} with cyclohexanone and OH^- . Absorption bands character-

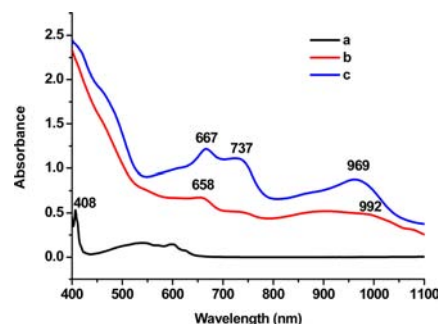
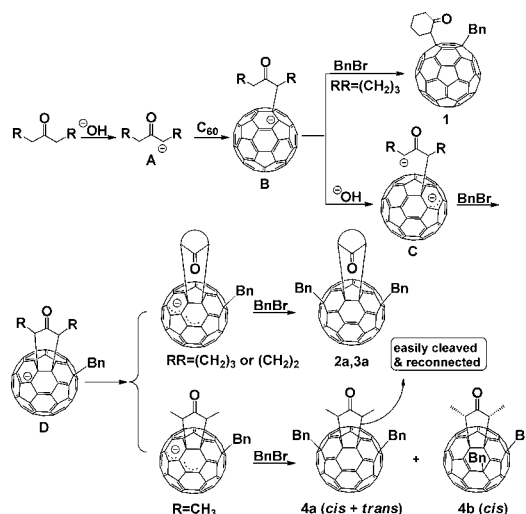


Figure 5. In situ vis-NIR spectra of (a) solution of C_{60} (36 mg) and cyclohexanone (50 equiv) in *o*-DCB (30 mL); (b) after adding OH^- (3 equiv) for 2 min; (c) after adding OH^- for 10 min. The measurement was carried out with 1 mm cuvette under argon at 30 °C.

istic of the monoanionic singly bonded C_{60} species (RC_{60}^-) appeared at 658 and 992 nm immediately after OH^- was added into the solution of C_{60} and cyclohexanone,¹⁵ suggesting the formation of RC_{60}^- (see intermediate **B** in Scheme 1) by addition

Scheme 1. Proposed Mechanism for the Formation of **1**, **2a**, **3a**, **4a**, and **4b**



of a cyclohexanone enolate anion to C_{60} . Interestingly, new absorption bands appear at 667, 737, and 969 nm as the reaction proceeded, which are characteristic for the type of RC_{60}^- intermediate,^{13c,15c,16} suggesting that intermediate **B** (RC_{60}^-) is further deprotonated by OH^- , with the formation of a dianionic singly bonded C_{60} intermediate (intermediate **C** in Scheme 1), in which both the addend and the C_{60} cage bear one negative charge.^{16,17} The spectrum of RC_{60}^- remains unchanged before being quenched with BnBr, indicating explicitly that novel [60]fullerene derivatives are formed from this intermediate.

A reaction mechanism for the formation of **1**, **2a**, **3a**, **4a**, and **4b** is proposed in Scheme 1. The reaction is initiated by abstracting

the α -proton of ketones to generate enolate anion **A**, which would attack C_{60} and afford intermediate **B** (RC_{60}^-). The reaction may result in **1** by quenching intermediate **B** with $BnBr$ when less OH^- is used (entry 1 in Table 1), or it may result in a unique dianionic singly bonded C_{60} intermediate **C** ($R^-C_{60}^-$) via a subsequent abstraction of the α' -proton from the ketone moiety in **B** when extra OH^- is present. Benzoylation of **C** would result in the 1,4,9-functionalized monoanionic intermediate **D** by adding the benzyl at the *para*-carbon with respect to the existing $R-C_{60}$ bond, accompanied by the closure of the 3'-cyclopentanone ring at the [5,6]-bond of C_{60} along with an electron transfer from the enolate to the carbon cage. The preferential formation of intermediate **D** by *para* addition is likely due to the steric effect between the benzyl and the ketone moiety, as exhibited in **1**, because benzoylation of $R^-C_{60}^-$ may also result in intermediates with 1,2,3-configuration by *ortho* addition when there is less hindrance.¹⁷

In conclusion, [60]fullerene derivatives with 1,4,9,25- and 1,4,9,12-configurations containing double 1,4-additions are synthesized via the reaction of C_{60} with ketones followed by benzoylation reaction under basic conditions, where the consecutive deprotonation of the ketones with the formation of the $R^-C_{60}^-$ intermediate and steric effect are crucial. Interestingly, the $C-C_{60}$ bond over the [5,6]-bond of a 1,4,9,25- C_{60} adduct is shown to be rather weak, different from the typically strong $C-C_{60}$ bond. The work provides new perspectives on the enolate reaction in fullerene chemistry and may shed light on the preparation of fullerene derivatives with new structures.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02528.

Experimental data, HPLC traces, spectra of the new compounds, and computational details (PDF)

Crystallographic data for **1** (CIF)

Crystallographic data for **4b** (CIF)

Crystallographic data for **2a** (CIF)

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Notes

The authors declare no competing financial interest.

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