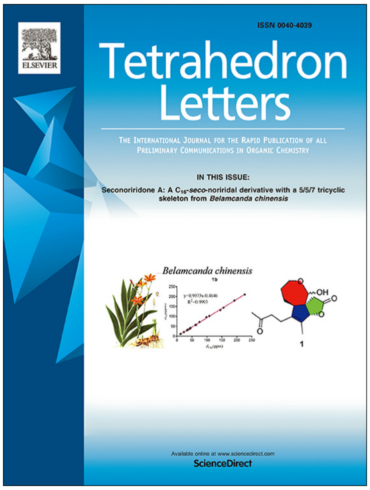

Reactions of the electrochemically generated dianion of [60]fullerene with bulky secondary alky bromides

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Graphical Abstract

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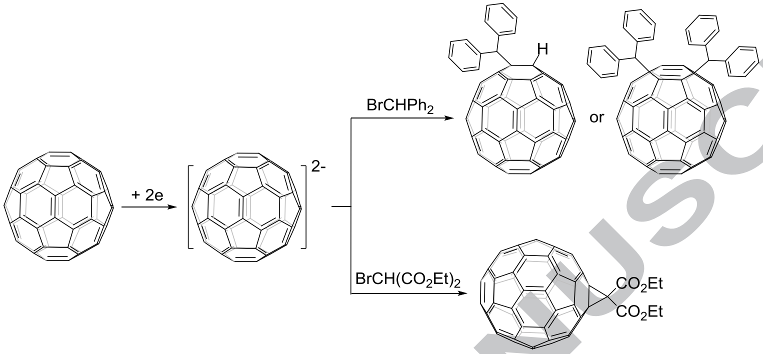

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Reactions of the electrochemically generated dianion of [60]fullerene with bulky secondary alky bromides

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ABSTRACT

Reactions of the electrochemically generated dianion of [60]fulllerene (C_{60}^{2-}) with bulky secondary alkyl bromides exhibits different reaction behaviors. Reaction of C_{60}^{2-} with diphenylbromomethane gives rise to $C_{60}HR$ or $C_{60}R_2$ (R = $CHPh_2$) adducts, while reaction of C_{60}^{2-} with diethyl 2-bromomalonate unexpectedly affords methanofullerene $C_{60}{>}CR_2$ (R = CO_2Et). Plausible reaction mechanisms have been proposed to explain the formation of the observed products.

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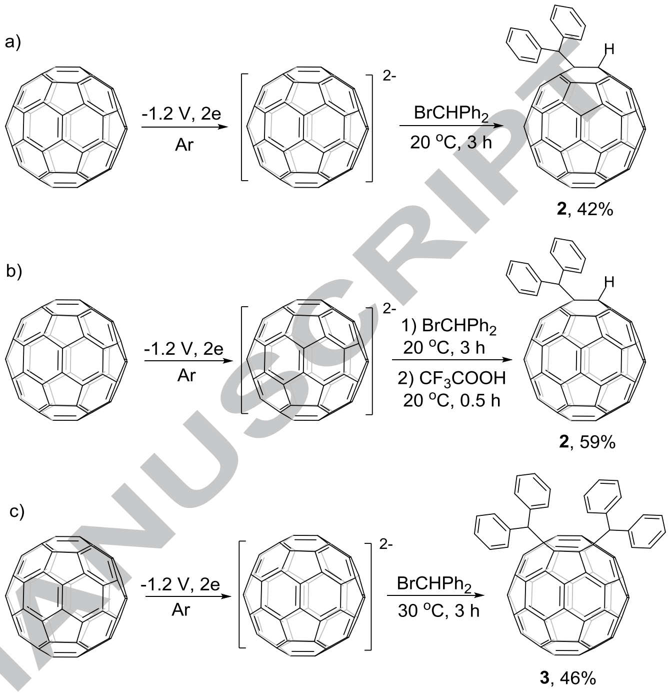
Introduction

[60]Fullerene (C_{60}) has attracted great attention since it was discovered in 1985.[1] For the wide applications in materials and biological science, great efforts have been made in the synthesis of fullerene derivatives.[2] Numerous methods have been established to synthesize functionalized fullerene derivatives.[3] Among these methods, fullerene dianion C_{60}^{2-}, which can be generated either chemically or electrochemically, is considered as an excellent building block in fullerene chemistry.[4] Electrochemical generation of C_{60}^{2-} is a preferable way to accurately realize and control its formation.[5]

Alkylation reactions of C_{60}^{2-} had been studied extensively in the literature. Previous studies showed that C_{60}^{2-} could react with alkyl bromides or iodides to generate bisadducts 1,2- and/or 1,4-$C_{60}R_2$.[4] When C_{60}^{2-} reacted with methyl iodide, the least steric hindered electrophile, the 1,2-bisadduct (1,2-$C_{60}Me_2$) was the main product along with the 1,4-bisadduct (1,4-$C_{60}Me_2$) as the minor product.[4a] However, when C_{60}^{2-} reacted with other steric bulkier primary halides, the regioselectivity was reversed. That is to say, 1,4-bisadducts were obtained predominantly or exclusively.[4b-h] Interestingly, it was reported that C_{60}^{2-} could react with the sterically hindered diethyl 2-bromo-2-methylmalonate, a tertiary alkyl halide, to provide 1,4- and 1,16-bisadducts $C_{60}[\text{-CMe}(CO_2Et)_2]_2$ in 35% and 7% yields, respectively.[6] We were wondering what would happen if a bulky secondary alkyl halide was utilized to react with C_{60}^{2-}. With this question in mind and our continuous interest in fullerene chemistry using fullerene anions as the reactants,[7] herein we report the reactions of C_{60}^{2-} with diphenylbromomethane ($BrCHPh_2$) and diethyl 2-bromomalonate ($BrCH(CO_2Et)_2$) as the representative bulky secondary alkyl halides.

Results and discussion

We first examined the reaction of C_{60}^{2-} with $BrCHPh_2$. A solution of 14.5 mg (0.02 mmol) of C_{60} in 15.8 mL of *ortho*-dichlorobenzene (ODCB) containing 0.1 M tetra-*n*-butylammonium perchlorate (TBAP) was electroreduced by controlled potential electrolysis (CPE) at −1.20 V vs SCE under argon atmosphere at 20 °C. The potentiostat was turned off when the theoretical number of coulombs required for full conversion of C_{60} into C_{60}^{2-} was reached. Then, 24.6 mg (0.10 mmol) of $BrCHPh_2$ was added to the solution of C_{60}^{2-}. The reaction mixture was allowed to stir for 3 h, and filtered through a silica gel plug to remove TBAP. Column separation over silica gel afforded 1,2-dihydrofullerene **2** in a yield of 42% along with 25% of recovered C_{60} (Scheme 1a). The yield of **2** could not be further increased by extending the reaction time to 5 h, and no other products could be isolated in an amount enough for spectral characterization. We noted that the color of the reaction mixture before the filtration through silica gel to remove TBAP was greenish, indicating that the fullerenyl monoanion $C_{60}(CHPh_2)^-$ should exist in the solution and captured a proton during the filtration through silica gel to provide **2**.[7e] Therefore, an acid was added to completely protonate the fullerenyl anion before workup. To our satisfaction, the yield of **2** was increased to 59% when 1 equiv. of trifluoroacetic acid (TFA) was added to quench the reaction (Scheme 1b). Compound **2** was previously synthesized from the monoalkylation of $C_{60}H_2$ with 109 equiv of $BrCHPh_2$ in the presence of excess tetrabutylammonium hydroxide (TBAOH) at room temperature.[8] In this case, the formation of bisalkylated product **3** was not observed, consistent with the fact that we could not isolate compound **3** at ambient temperature even after prolonged reaction time. To our delight, the desired product **3** could be selectively obtained in 46 % yield when the reaction temperature was elevated to 30 °C and allowed to react for 3 h (Scheme 1c). The details for monitoring the reaction mixture at 30 °C by high-performance liquid chromatography can be found in Figure S1. It should be noted that no appreciable amount of 1,2- and 1,16-bisadducts could be identified.



Scheme 1. Reaction of C_{60}^{2-} with $BrCHPh_2$ under different conditions.

Computational studies at the B3LYP/6-31G(d) level were also performed to give a better understanding of the regioselectivity for the bisalkylation process.[9] Figure 1 shows the partial natural bond orbital (NBO) charge distribution of the optimized intermediate $C_{60}(CHPh_2)^-$. According to the calculated charge distribution, C2 (−0.105) of $C_{60}(CHPh_2)^-$ is the most negatively charged carbon atom among the nonfunctionalized C_{60} carbon atoms, and should be more prone to react with a less steric hindered electrophile. The less negatively charged carbon atoms are C4 (−0.080) and C11 (−0.077) followed by C16 (−0.048). Thus, the most electronegative C2 is preferable for protonation due to the small size of the proton. The introduction of the second $CHPh_2$ group at the C2 atom would lead to bisalkylated 1,2-$C_{60}(CHPh_2)_2$, while reaction at both C4 and C11 results in 1,4-$C_{60}(CHPh_2)_2$. In parallel, the reaction of $BrCHPh_2$ with $C_{60}(CHPh_2)^-$ at the C16 atom would provide 1,4-$C_{60}(CHPh_2)_2$. The relative energies of the optimized 1,2-, 1,4- and 1,16-adducts with two $CHPh_2$ groups were performed and the results are shown in Figure 1. The calculated energy of 1,4-$C_{60}(CHPh_2)_2$ is lower those of 1,2-$C_{60}(CHPh_2)_2$ and 1,16-$C_{60}(CHPh_2)_2$ by 11.8 and 10.6 kcal/mol, respectively. These computation results are consistent with the selective formation of 1,4-$C_{60}(CHPh_2)_2$, and can explain the observed regioselectivity of C_{60}^{2-} with $BrCHPh_2$, which is dominantly governed by the steric hindrance rather than charge density distribution due to the two bulky $CHPh_2$ addends.

According to the experimental and computation results, a plausible mechanism is outlined in Scheme 2. First, C_{60} is

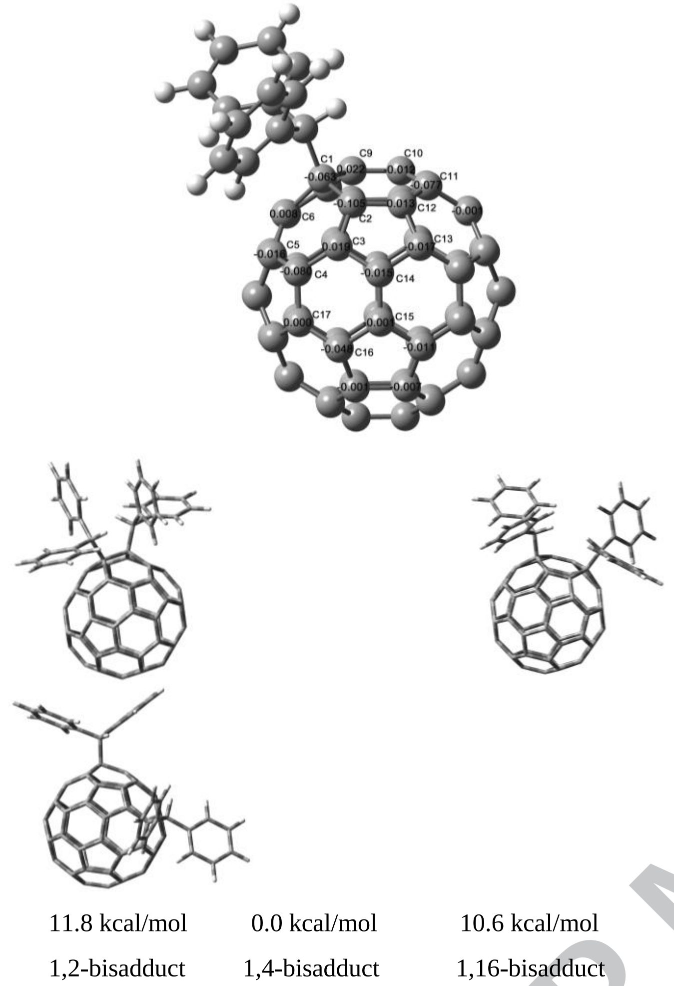
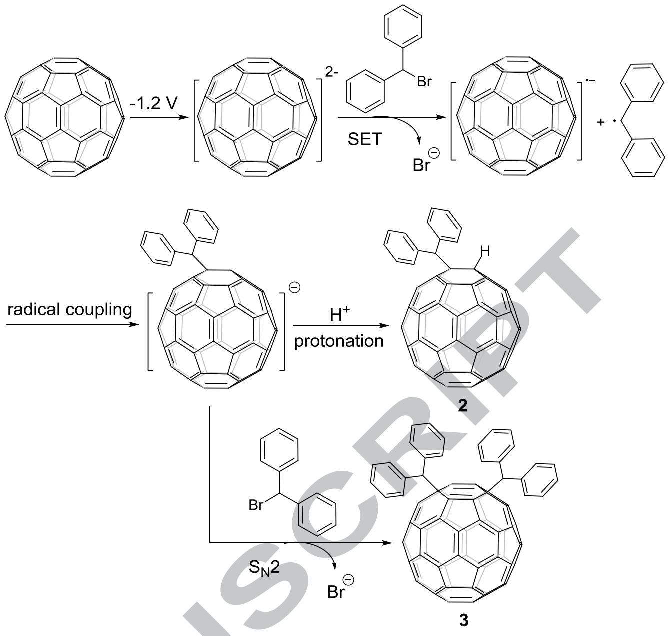


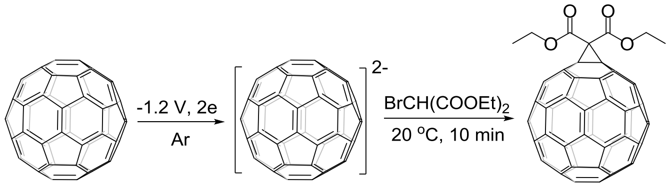
Figure 1. NBO charge distribution of the intermediate $C_{60}(CHPh_2)^-$, and relative energies of 1,2-, 1,4- and 1,16-bisadducts at B3LYP/6-31G(d) level.

electroreduced to its dianion C_{60}^{2-}. Then a single electron-transfer (SET) process takes place between C_{60}^{2-} and Ph_2CHBr and leads to C_{60} anion radical ($C_{60}^{-\cdot}$) and diphenylbromomethanyl radical $^{\cdot}CHPh_2$.[4b] Then, the coupling of these two radicals generates the intermediate $C_{60}(CHPh_2)^-$. The $C_{60}(CHPh_2)^-$ intermediate can undergo either protonation process to provide hydrofullerene **2** or an S_N2 reaction process with $BrCHPh_2$ at slightly elevated temperature to afford 1,4-bisadduct **3**.



Scheme 2. Proposed reaction mechanism of C_{60}^{2-} with diphenylbromomethane.

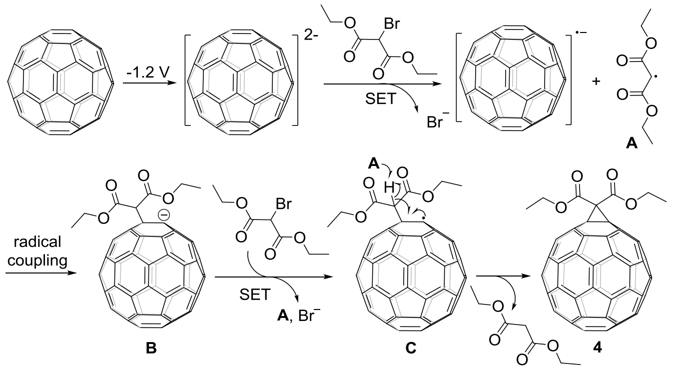
We then explored the reaction of C_{60}^{2-} with 2 equiv of $BrCH(CO_2Et)_2$, a bulky secondary alkyl bromide with two strong electron-withdrawing substituents. To our surprise, no expected 1,2- 1,4- or 1,16-bisadduct $C_{60}[CH(CO_2Et)_2]_2$ was obtained. Instead, the methanofullerene product **4** was unexpectedly isolated in 53% yield after reaction for only 10 min (Scheme 3). The same compound **4** was obtained in 45% yield from the Bingel reaction of C_{60} with 1.5 equiv of $BrCH(CO_2Et)_2$ in the presence of 10 equiv of NaH for 6.5 h.[10] Intriguingly, the same product **4** was also synthesized from the reaction of C_{60}^{2-} with excess amount of dibromomalonate ester $Br_2C(CO_2Et)_2$, yet in only 20% yield.[11,12] Therefore, our protocol for the synthesis of methanofullerene **4** has advantages over the previously reported procedures in term of higher product yield and shorter reaction time.



4, 53%

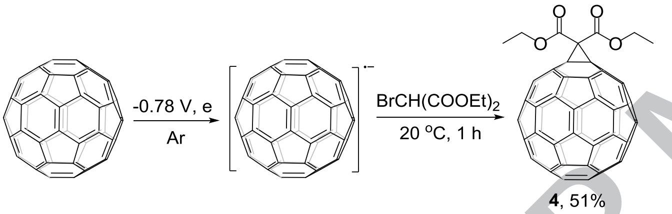
Scheme 3. Reaction of C_{60}^{2-} with diethyl 2-bromomalonate.

It is of interest to understand the reaction pathway for the formation of **4**. Although the exact reaction mechanism is not clear now, we believe that the first step should be an electron-transfer from C_{60}^{2-} to $BrCH(CO_2Et)_2$ to give $C_{60}^{-\cdot}$ and $^{\cdot}CH(CO_2Et)_2$ (**A**) with the removal of Br^-, followed by the radical coupling to afford fullerenyl anion $^-C_{60}[CH(CO_2Et)_2]$ (**B**).[4b] Owing to the attachment of two strong electron-withdrawing CO_2Et groups to the CHBr moiety, $BrCH(CO_2Et)_2$ is a better electron acceptor than other alkyl bromides such as $BrCHPh_2$ and may be able to accept an electron from anionic **B** to generate radical $^{\cdot}C_{60}[CH(CO_2Et)_2]$ (**C**). The trace amount of O_2 existed in the reaction system may also help to oxidize the anionic **B** to the radical **C**. Radical **C** prefers to undergo cyclization with the assistance of hydrogen abstraction by the generated **A** to provide the observed methanofullerene **4** (Scheme 4).



Scheme 4. Plausible reaction mechanism of C_{60}^{2-} with diethyl 2-bromomalonate.

In order to provide more evidence for the proposed electron-transfer process from the anionic **B** to BrCH(CO_2Et)$_2$, we performed the reaction of radical anion $C_{60}^{-\cdot}$ with BrCH(CO_2Et)$_2$. It turned out that the reaction indeed proceeded and afforded the same methanofullerene **4** in 51% yield (Scheme 5). It is believed that $C_{60}^{-\cdot}$ can transfer an electron to BrCH(CO_2Et)$_2$ to provide C_{60} and malonate radical **A**, which combine to form radical **C** and subsequent cyclization to provide **4**. A long reaction time of 1 h was required for $C_{60}^{-\cdot}$ than for with C_{60}^{2-}, probably due to the stronger electron-donating capability of the latter to BrCH(CO_2Et)$_2$.



Scheme 5. Reaction of $C_{60}^{-\cdot}$ with diethyl 2-bromomalonate.

Conclusion

In summary, the reactions of the electrochemically generated C_{60}^{2-} with diphenylbromomethane and diethyl 2-bromomalonate as representative bulky second alkyl bromides have been investigated. This study shows that different second alkyl bromides with different electronic properties exhibit different reaction behaviors towards C_{60}^{2-}. Plausible reaction mechanisms have been proposed to explain the observed formation of monoalkylation, bisalkylation and cyclopropylation products.

Acknowledgements

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12. The methanofullerene **4** was obtained in 53% yield when the reaction of C_{60}^{2-} with $Br_2C(CO_2Et)_2$ was performed under our conditions.

Supplementary Material

Supplementary data related to this article can be found at https://doi.org/10.1016/j.tetlet.

Highlights

- Reaction of the electrogenerated C_{60}^{2-} with bulky second alkyl bromides
- Different alkyl bromides exhibiting different reaction behaviors toward C_{60}^{2-}
- Reaction of C_{60}^{2-} with $BrCHPh_2$ affording 1,2-$C_{60}HR$ or 1,4-$C_{60}R_2$ (R = $CHPh_2$)
- Reaction of C_{60}^{2-} with $BrCH(CO_2Et)_2$ giving methanofullerene $C_{60}{>}CR_2$ (R = CO_2Et)