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Synthesis of C_{60}-Fused Tetrahydrocarbazole/Dibenzothiophene/Benzothiophene and Dibenzofuran Derivatives via Metal-Free Oxidative Dehydrogenative Carboannulation

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S *Supporting Information*

ABSTRACT: A transition-metal-free oxidative dehydrogenative coupling reaction has been developed for the direct construction of novel C_{60}-fused tetrahydrocarbazoles, dibenzothiophenes, benzothiophenes, and dibenzofurans. This new carboannulation reaction features high atom economy, operational simplicity, broad substrate scope, and excellent functional-group tolerance and provides a convenient access to a scarce class of fullerene derivatives.

Functionalized fullerenes are an important class of high-performance molecules with wide applications in material science, electronic devices, and biomedicine, among others.[1] Among the diverse range of fullerene derivatives prepared during the past three decades,[2] fullerene carbocyclic adducts with fused three-, five-, and six-membered ring systems have been studied extensively as electron acceptor materials for organic photovoltaic (OPV) solar cells and exhibited excellent conversion efficiency.[1e,f] Therefore, the development of new and efficient methods to construct C−C bonds that enable the formation of novel fullerene-fused carbocyclic compounds is highly desirable, which provides important opportunities to improve their overall functionality and expand their applications.

Compared with existing methods for the synthesis of methanofullerenes,[3] cyclopentane-, cyclopentene-, and cyclopentenone-fused fullerenes,[4] the methods available for the construction of fullerene fused six-membered carbocyclic derivatives are quite limited. The thermal Diels−Alder reaction is one of the most commonly used methods for the preparation of fullerene fused six-membered carbocyclic adducts,[5] but the substrates required for these reactions are not necessarily easily available and usually involve the preintroduction and re-elimination of functionalized groups. A handful of other synthetic methods have also been reported, which include the photochemical reaction,[6] the 1,4-dipolar reaction,[4k] transition-metal-promoted/catalyzed cyclization reaction,[7] radical reaction,[4e,g] and directed C−H activation.[8] Despite these advances, a direct, flexible, and practical method for the preparation of a diverse range of six-membered carbocyclic fused [60]fullerenes from easily available materials with a broad substrate scope is still rarely reported. On the other hand, the cross-dehydrogenative coupling (CDC) reactions represent one of the most efficient transformations for the atom-economical construction of C−C bonds without the need for a prefunctionalized site.[9] However, there have been very few reports pertaining to the application of this strategy to the functionalization of fullerenes. With an endeavor to develop new methods for the synthesis of various fullerene derivatives,[10] we report herein a direct metal-free oxidative dehydrogenative carboannulation reaction to provide access to a unique series of C_{60}-fused tetrahydrocarbazole, dibenzothiophene, benzothiophene, and dibenzofuran derivatives. Notably, this reaction proceeds under simple reaction conditions with a wide range of substrate scope and exceptional functional group compatibility.

The reaction of C_{60} with 3-benzyl-1,2-dimethyl-1*H*-indole (**1a**) was initially chosen as a model reaction to screen various oxidants. The peroxide agents $K_2S_2O_8$, Oxone, and TBHP, as well as the hypervalent iodine(III) compounds $PhI(OAc)_2$ and $PhI(OOCCF_3)_2$, were ineffective in promoting this reaction (see Supporting Information). We then turned our attention to quinone compounds, which are often used in dehydrogenative cross-coupling reactions.[9,11] *p*-Benzoquinone (BQ), DDQ, and *p*- and *o*-chloranil were all investigated, and the results revealed that DDQ gave the best results, with the formation of **2a** in 27% yield (Table 1, entries 1−4). It is noteworthy that C_{60}-fused tetrahydrocyclopentaindole **3a** was also obtained in 8% yield except for the desired product **2a**, when the reaction was carried out in the presence of *o*-chloranil (Table 1, entry 3). Further screening of reaction time, temperature, and amount of **1a** and DDQ revealed that the yield of **2a** could be enhanced to 42% when the reaction was conducted with 0.7 equiv of DDQ

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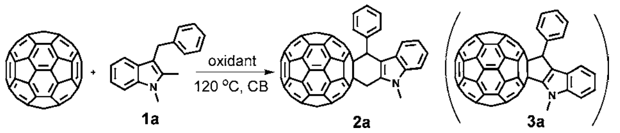
Table 1. Optimization of the Reaction Conditions[a]



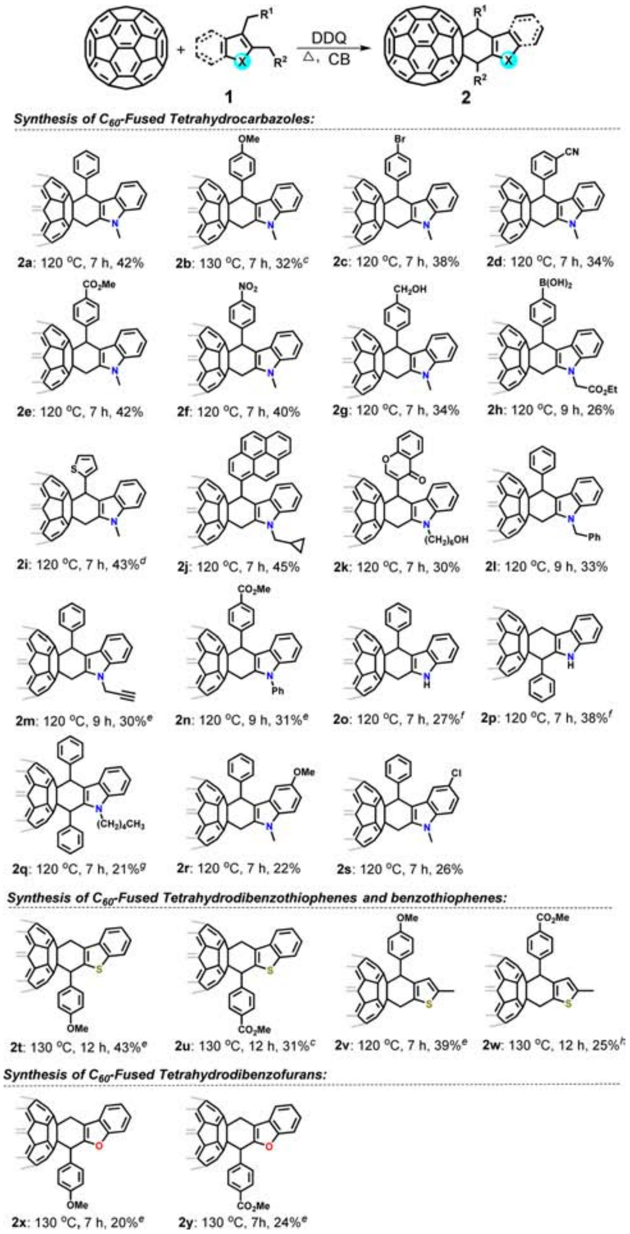
entry	oxidant	molar ratio[b]	time (h)	yield (%)[c]
1	BQ	1:2:2	5	<5
2	DDQ	1:2:2	5	27 (81)
3	*o*-Chloranil	1:2:2	5	10 (29)[d]
4	*p*-Chloranil	1:2:2	5	21 (60)
5	DDQ	1:2:2	7	34 (76)
6	DDQ	1:2:2	7	25 (56)[e]
7	DDQ	1:3:2	7	33 (79)
8	DDQ	1:2:3	7	30 (65)
9	DDQ	1:2:1	7	35 (83)
10	DDQ	1:2:0.7	7	42 (92)
11	DDQ	1:2:0.5	7	36 (89)
12	DDQ	1:2:0.7	7	35 (79)[f]

[a] All reactions were performed with the designated molar ratio of C_{60}/**1a**/oxidant in 5 mL of chlorobenzene (CB) at 120 °C under air unless specified otherwise. [b] Molar ratio refers to C_{60}/**1a**/oxidant. [c] Isolated yield; that in parentheses was based on consumed C_{60}. [d] The byproduct **3a** was obtained in 8% yield. [e] The reaction was operated at 130 °C. [f] The reaction was carried out under a nitrogen atmosphere.

for 7 h (Table 1, entries 5−11). By running this reaction under N_2, a slightly lower yield was obtained (Table 1, entry 12). In addition, solvent effects were also considered through the use of CH_3CN, DMSO, and DMF as the cosolvent, but no higher yield was achieved.

With the optimized reaction conditions in hand, we next explored the scope and generality of this transformation, as shown in Scheme 1. The results revealed that this new carboannulation progress was compatible with a variety of indole derivatives bearing different aryl groups (R^1). For example, substrates bearing methoxy (**1b**), halogen (**1c**), nitrile (**1d**), ester (**1e**), and nitro (**1f**) groups on their phenyl ring at different positions were all well tolerated under the optimized conditions, affording the desired products **2b**−**f** in 32−42% yields. Pleasingly, substrates bearing active functional groups, such as benzyl hydroxy (**1g**) and boronic acid (**1h**) groups, also reacted smoothly under the current reaction system to give the corresponding products **2g** and **2h** in moderate yields, providing an additional handle for further elaboration of products. Thienyl- (**1i**) and pyrenyl- (**1j**) substituted indole derivatives also reacted as expected to yield the corresponding adducts **2i** and **2j** in 43% and 45% yields, respectively. Interestingly, the chromonyl-substituted indole derivative (**1k**) was also found to be a suitable substrate and afforded thetetrahydrocarbazole derivative **2k** in 30% yield. Besides *N*-methyl substituted indole derivatives, several *N*-substituted substrates, including *N*-ethyl acetate (**1h**), *N*-(cyclopropyl-methyl) (**1j**), *N*-(6-hexanyl-1-ol) (**1k**), *N*-benzyl (**1l**), *N*-propargyl (**1m**), and *N*-phenyl (**1n**) all underwent an efficient annulation reaction to furnish the desired products **2h** and **2j**−**n** in moderate to good yields. Notably, the two free (N−H) indole compounds 2-methyl-3-benzyl- (**1o**) and 2-benzyl-3-methyl-1*H*-indole (**1p**) both performed well to give expected products **2o** and **2p** in 27% and 38% yields, respectively. Furthermore, this newly developed method was also found to be applicable to the 2,3-dibenzyl substituted indole derivative (**1q**), albeit the corresponding product **2q** was obtained in a slightly lower yield (21%) presumably due to the steric hindrance. It was noteworthy that the electronic nature of the substituents on the benzene ring of indole has an obvious influence on the reaction. For example, substrates **1r** and **1s** bearing an electron-donating or -withdrawing group at the 5-position of their indole moiety decreased the reaction conversion and produced 22% and 26% yields of **2r** and **2s**, respectively. Unfortunately, only trace product was detected when 1,2,3-trimethyl-1*H*-indole was employed under the same reaction conditions.

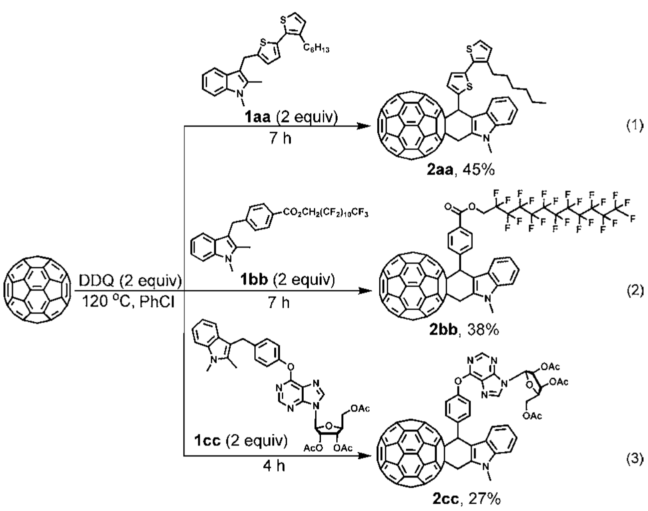
Scheme 1. Scope of Carboannulation Reaction[a,b]



[a] All the reactions were carried out with a molar ratio of C_{60}/**1**/DDQ = 1:2:0.7 in 5 mL of CB unless specified otherwise. [b] Isolated yields. [c] C_{60}/**1b** (**1u**)/DDQ = 1:3:1. [d] 1 equiv of DDQ was used. [e] 3 equiv of **1** were used. [f] 2 equiv of DDQ were used. [g] C_{60}/**1q**/DDQ = 1:4:2. [h] 4 equiv of **1w** were used.

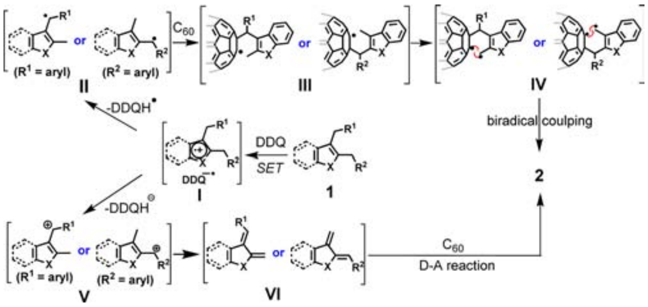
We also investigated the application of the current reaction to a substituted benzothiophene and thiophene derivatives with the aim of synthesizing C_{60}-fused tetrahydrodibenzothiophenes and benzothiophenes. To our satisfaction, benzothiophene derivatives **1t** and **1u**, as well as thiophene derivatives **1v** and **1w**, all reacted successfully under the current reaction conditions to give the desired annulation products **2t−w** in satisfactory yields. Further expanding the substrate scope to benzofuran derivatives **1x** and **1y** turned out to be viable, and the corresponding C_{60}-fused tetrahydrodibenzofurans **2x** and **2y** were obtained in relatively low yields. Additionally, an attempt to synthesize C_{60}-fused tetrahydronaphthalene adducts by employing 1-benzyl-2-methylbenzene compounds failed. This carboannulation reaction showed high chemical selectivity in the formation of **2**, no other byproducts were detected, and most of C_{60} was recovered.

Carbazole derivatives have been studied extensively as electron-donating optoelectronic materials and biologically active molecules,[12] whereas fullerenes are an important class of carbon materials with unique structures and properties. The combination of these functionalities in this study therefore provides access to a novel series of architecturally and electronically interesting hybrids, especially the potential for fullerene-bound macromolecules formed by the introduction of organic structural units, which could create new opportunities for various applications. For example, the adduct **2aa** bearing a 2,2′-bithiophene moiety, which is potentially useful for photovoltaic energy conversion,[13] was obtained in 45% yield through the reaction of C_{60} with the corresponding substrate **1aa** (eq 1). Similarly, the reaction of C_{60} with indole derivative **1bb** containing a long perfluorocarbon chain efficiently afforded fluorinated liquid crystal **2bb** in 38% yield (eq 2).[14] This method was also compatible with a nucleoside unit, successfully providing efficient access to the potentially bioactive macromolecule **2cc** in a satisfactory yield (eq 3).[15]



To shed light on the mechanism of the reaction, additional experiments were designed and carried out (see Supporting Information). The addition of a free radical scavenger, such as 2,2,6,6-tetramethylpiperidine-1-oxy (TEMPO), *N-tert*-butyl-α-phenylnitrone (PBN), or 1,1-diphenylethylene (DPE), could retard the carboannulation progress. However, they could not completely suppress the reaction even if using an excess of the radical scavengers, which indicated a free radical process and another reaction pathway might coexist in this transformation. Based on the above experimental results and review of literature, a possible mechanism to rationalize the formation of adduct **2** is depicted in Scheme 2. A single electron transfer (SET) from the substrate employed **1** to DDQ would generate radical **II** via ion pair **I**,[16a−f] which could be captured by C_{60} to produce the fullerenyl radical **III**. Subsequently, the species **III** was further oxidized to generate biradical intermediate **IV**, followed by a rapid intramolecular C-centered biradical coupling cyclization would give the final product **2**.[4g,10a] Alternatively, the carbocation **V** could also be produced under the present system,[16d−f] which further converted into heterocyclic *ortho*-quinodimethane intermediate **VI** via the basic deprotonation of the DDQH anion generated in situ,[16g−k] and then intermediate **VI** with C_{60} underwent Diels−Alder reaction to give the desired **2**.[5] The product **3a** might be formed via a similar intramolecular cyclization of another biradical species generated from oxidative demethylation of **III** in the presence of *o*-chloranil.

Scheme 2. Proposed Mechanism



In summary, we have developed a new synthetic method for the efficient construction of a series of novel C_{60}-fused tetrahydro-carbazole, dibenzothiophene, benzothiophene, and dibenzofuran derivatives from easily available materials via a direct oxidative dehydrogenative carboannulation reaction under transition-metal-free conditions. The features presented in this method, including a wide range of substrate scope, excellent functional group compatibility, and simple operation of the process, are notable and therefore provide an important tool for the generation of as-yet-unexplored nanocarbon materials with a wide range of potential applications.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01902.

Experimental procedures, spectral data, and NMR spectra of products **2a−y**, **2aa−cc**, and **3a** (PDF)

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Notes

The authors declare no competing financial interest.

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