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Open-Shell Phenalenyl in Transition Metal-Free Catalytic C−H Functionalization

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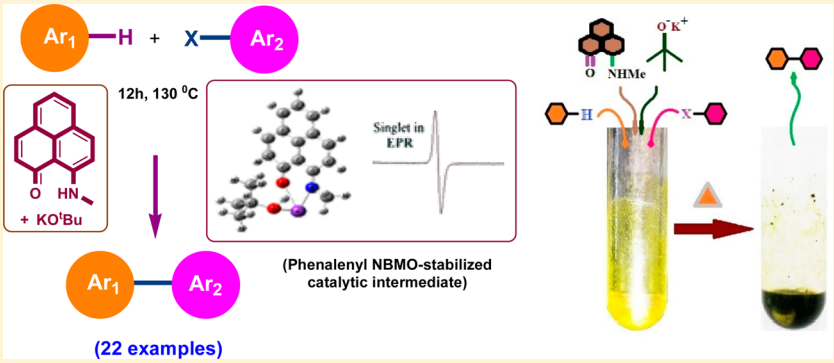
Supporting Information



ABSTRACT: Open-shell phenalenyl chemistry has widely been explored in the last five decades demonstrating its potential in various applications including molecular switch, spin memory device, molecular battery, cathode material, etc. In this article, we have explored another new direction of open-shell phenalenyl chemistry toward transition metal-free catalytic C−H functionalization process. A phenalenyl ligand, namely, 9-methylamino-phenalen-1-one (4a), promoted chelation-assisted single electron transfer (SET) process, which facilitates the C−H functionalization of unactivated arenes to form the biaryl products. The present methodology offers a diverse substrate scope, which can be operated without employing any dry or inert conditions and under truly transition metal based catalyst like loading yet avoiding any expensive or toxic transition metal. This not only is the first report on the application of phenalenyl chemistry in C−H functionalization process but also provides a low-catalyst loading organocatalytic system (up to 0.5 mol % catalyst loading) as compared to the existing ones (mostly 20−40 mol %), which has taken advantage of long known phenalenyl based radical stability through the presence of its low-lying nonbonding molecular orbital.

INTRODUCTION

The phenalenyl (PLY), a highly symmetric (D_{3h}) odd alternant tricyclic hydrocarbon, is a well-known molecular building block in various fields of research ranging from synthetic organic chemistry to materials chemistry to device physics, which is attributed to its distinguished electronic property due to the presence of a unique nonbonding molecular orbital (vide infra).[1−3]

Since the pioneering suggestion by Haddon that the neutral phenalenyl radical can be used as a building block to prepare molecular organic conductors and superconductors,[3] the last four decades witnessed several synthetic efforts to realize the phenalenyl based radicals in solid state.[4−18] Commencing with the first crystallographically characterized PLY based radical **I**[6] (Chart 1), various other multifunctional electronic and magnetic phenalenyl motifs (**II**−**VI**, Chart 1) were synthesized successively.[9,15−22]

Historically, the stabilization of this radical state of the phenalenyl system has been attributed to the presence of a nonbonding molecular orbital (NBMO) which houses the free electron and becomes a singly occupied molecular orbital (SOMO), without compromising the pi-electron delocalization energy (Chart 2).[2,3] In the past few years, we have taken an alternative approach where we have shown that the empty NBMO of phenalenyl, i.e., its cationic state, can be utilized for spin injection avoiding isolation of free radicals,[23−26] which led to the development of the first phenalenyl based spin filter (phenalenyl-zinc complex) with potential for future spin memory device,[25] cathode material (phenalenyl-iron complex) for H_2O_2 fuel cells having superior power density output.[26]

From the above discussion, it is evident that phenalenyl based radicals have a rich history with enormous potential in various research fields (reviewed recently by Morita, Takui,[16a] and Hicks[16b]). In addition, we recently observed that coordination of phenalenyl based ligands with metals creates an empty NBMO ready for electron injection.[25,26] All of these findings prompted us to explore the catalytic activity of phenalenyl based

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Chart 1. Examples of Well-Known Phenalenyl Radicals Characterized by Single Crystal X-ray Structure

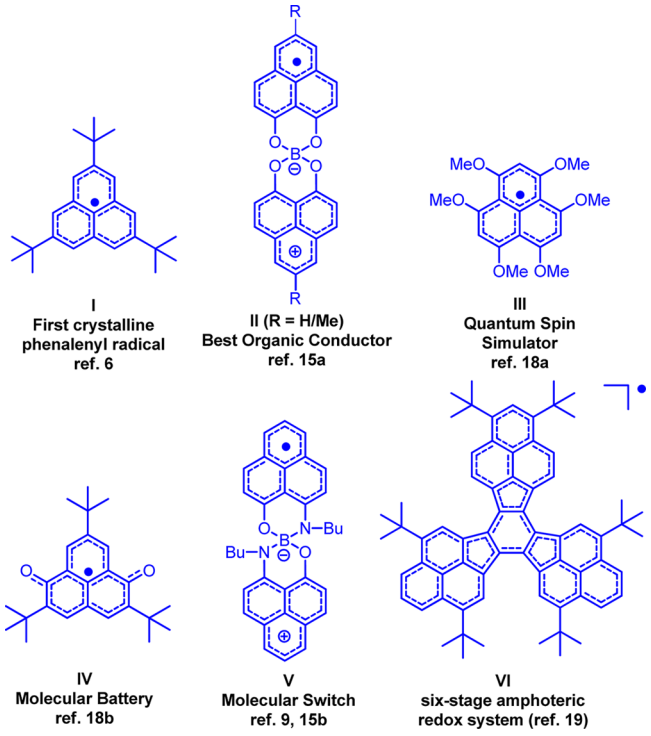
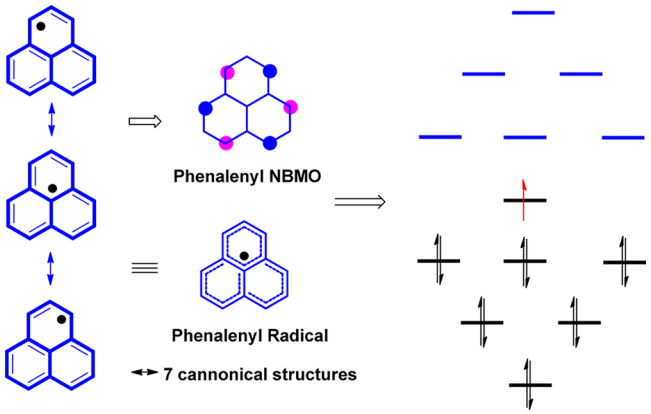


Chart 2. Stabilization of Phenalenyl Radical Revealing that the Free Electron is Accommodated in a Formally Nonbonding Molecular Orbital



radicals generated in situ in the C−H functionalization process avoiding any transition metal. We argue that through nontransition metal ion coordination, the cationic state of the phenalenyl ligand can be created, which will pose an empty NBMO. Subsequent electron injection into this empty NBMO will generate the phenalenyl based radical, and the SOMO will initiate the single electron transfer (SET) process activating the aryl halide substrate. It is worth mentioning that transition metal catalyzed arylation reactions through C−H functionalization techniques have long been a matter of interest to scientists, due to its atom and step-economical approach toward regioselective functionalization of aromatic compounds.[27−33] However, these transition metal catalyzed reactions suffer from a number of drawbacks: (i) high expense of catalysts; (ii) toxicity of transition metals; (iii) difficulties in the removal of trace amounts of transition-metal residues from the desired product; (iv) oxygen and moisture-sensitivity of transition-metal catalysts; and finally, (v) the large consumption of transition metals, which do not meet the requirement of sustainable development.[34−44] Therefore, there is a burgeoning interest in developing newer methods avoiding the use of transition metals as a catalytic source. Development of a transition metal-free single electron transfer approach, with the aid of an organic ligand, thus appeared to be the most logical choice to facilitate a smooth arylation protocol. The last few years therefore witnessed the investment of a great deal of time from various research groups to find a solution.[45−54] Commencing with an initial report by Itami,[45] the transition metal-free arylation protocol promoted the development of various ligands including DMEDA (*N*,*N*′-dimethylethane-1,2-diamine),[46] 1,10-phenanthroline,[47] and its derivatives,[48] cyclic and acyclic diols and diamines,[50] zwitterionic radicals,[51] *N*-heterocyclic carbenes,[52] amino acids,[53] macrocycles,[54] etc. as mediators in the coupling of haloarenes and arenes. Such transition metal-free arylation reactions proceed through homolytic aromatic substitution (HAS), where the organic catalyst is generally employed along with a base (mostly, sodium/potassium tertiary butoxide). The process involves the formation of an aryl radical from the corresponding aryl halide via a single electron transfer (SET) process from the catalyst.[55−59] It is now well documented that the electron itself can act like a catalyst.[60] Although, most of these simple small molecular catalysts can produce the corresponding biaryl products in satisfactory yields, they usually suffer from the drawbacks of high reaction time, limited substrate scope, and, most crucially, the use of very high catalyst loading (20−40 mol %).[45−53] Requirement of such a high loading of catalyst may be attributed to the extremely low-stability of the radical intermediate, which is formed by single electron transfer from the base to the antibonding orbital of the organic molecule that has been proposed during the reaction mechanism.[48] Thus, it is considered as a major challenge to carry out the C−H functionalization process with a catalyst loading on par with a typical transition metal based catalyst loading (1−5 mol % loading). Therefore, there is a need to develop an effective transition metal-free catalyst, which can produce the desired biaryl products in a cost-effective manner, with a wide substrate scope under truly transition metal like catalyst loading conditions.

In this regard, it is interesting to recall the fact that phenalenyl motifs can effectively accommodate the incoming electrons in its NBMO to stabilize the radical state and that it can release electrons from its SOMO without any significant destabilization (as evident from its reversible redox activity, reported earlier[9,15b,26]). This property of phenalenyl based molecules prompted us to investigate their activity as a mediator of SET during the arylation process under low-catalyst loading conditions. During this study, we have used the 9-methylamino-phenalen-1-one (**4a**) ligand. We presumed that the N and O centers present in such a phenalenyl motif will be appropriate to chelate with potassium *tert*-butoxide, thereby facilitating the SET process from the butoxide moiety to the NBMO of phenalenyl. Subsequent interaction of the SOMO of the phenalenyl radical with aryl halide was then expected to facilitate the HAS, thereby producing the biaryl product. Herein we report our methodology on transition metal-free C−H functionalization using a phenalenyl based molecule as catalyst under low catalyst loading conditions (down to 0.5 mol % catalyst loading). To the best of our knowledge, this is the first report of organocatalytic C−H functionalization, where the

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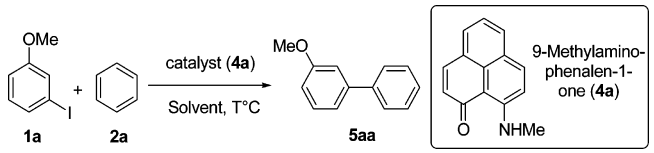
Table 1. Optimization of Reaction Conditions Using 1a and 2a as Substrates[a]



entry	base	solvent	catalyst (mol %)	temp. (°C)	time (h)	yield (%)
1	KO^{t}Bu	THF	1	130	8	<1
2	KO^{t}Bu	MeCN	1	130	8	<1
3	KO^{t}Bu	DCM	1	130	8	<1
4	KO^{t}Bu	benzene	1	130	8	36
5	KO^{t}Bu	benzene	1	130	12	43
6	KO^{t}Bu	benzene	1	130	24	44
7	KO^{t}Bu	benzene	1	120	12	32
8	KO^{t}Bu	benzene	1	140	12	42
9	KO^{t}Bu	benzene	0.5	130	12	36
10	KO^{t}Bu	benzene	2	130	12	74
11	KO^{t}Bu	benzene	5	130	12	94[b]
12	LiO^{t}Bu	benzene	5	130	12	<1
13	NaO^{t}Bu	benzene	5	130	12	<1
14	KOAc	benzene	5	130	12	<1
15	KHMDS	benzene	5	130	12	85
16	KO^{t}Bu	benzene	5	130	12	94[c]
17	KO^{t}Bu	benzene	5	130	12	82[d]
18	KO^{t}Bu	benzene	0	130	12	<1[e]
19	none	benzene	5	130	12	<1

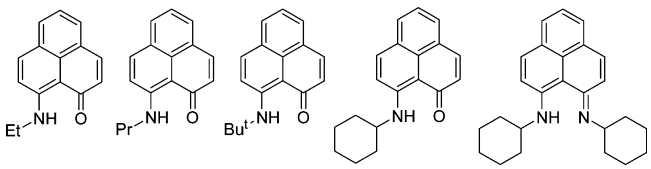
[a]The reactions were performed in sealed tubes in the presence of 2.5 equiv of base, without inert or dry conditions, and the indicated yields are based on ^{1}H NMR spectroscopy. [b]Isolated yield. [c]Using 3 equiv of KO^{t}Bu; [d]Using 2 equiv of KO^{t}Bu. [e]Using 2.5, 3, and 5 equiv of KO^{t}Bu in three different sets of reactions.

phenalenyl NBMO is utilized as an efficient mediator for single electron transfer.

RESULTS AND DISCUSSION

Our initial studies involved the development of optimized reaction conditions to carry out the arylation chemistry, where 3-iodo anisole (**1a**) and benzene (**2a**) were chosen as the model coupling partners. Preliminary attempts to arylate **2a** were mainly based on solvent screening. The reaction partners (**1a** and **2a**) along with potassium *tert*-butoxide (**3a**) and 9-methylamino-phenalen-1-one (**4a**), under 1 mol % catalyst loading conditions, were heated in a sealed tube at 130 °C in a variety of solvents to facilitate the arylation reaction. Interestingly, when benzene (**2a**) was used as the solvent as well as reactant, the desired biaryl product **5aa** was produced with 43% yield (Table 1, entry 5) after 12 h. However, THF, acetonitrile, and DCM failed to initiate the desired reaction (Table 1, entries 1−3). It was observed from the solvent-screening study that the yield does not improve with increasing temperature but drops with lowering of temperature (Table 1, entries 6−7), and 130 °C was found to be the optimal thermal condition to carry out the reaction. Aiming at quantitative productivity, catalyst loading was further tuned. To our delight, it showed that catalyst loading as low as 0.5 mol % is able to offer catalytic activity; however, the yield was only 36% (Table 1, entry 9). This was improved to 74% on increasing the catalyst loading to 2 mol % (Table 1, entry 10). On increasing the catalyst loading further to 5 mol %, the desired biaryl product was isolated with 94% yield (Table 1, entry 11). The reaction was performed without applying inert or dry conditions. In order to investigate whether other bases can also facilitate this reaction, the optimized reaction conditions were repeated with different bases, and it was found that, apart from KHMDS (potassium bis(trimethylsilyl)amide) (Table 1, entry 15, 85% yield), all other bases were ineffective and unable to even initiate the reaction (Table 1, entries 12−14). It is interesting to note that the presence of 2.5 equiv of potassium *tert*-butoxide seems to be necessary to carry out the arylation effectively, as lowering its amount was found to diminish the product yield (Table 1, entries 16 and 17). We have also performed some control experiments, which unambiguously proves the necessity of both the phenalenyl catalyst as well as the KO^{t}Bu base to perform the arylation effectively (Table 1, entries 18 and 19). Finally, we evaluated the catalytic efficacy of a series of phenalenyl ligands (**4b−f**), and interestingly, **4b−d** were found to catalyze the arylation reaction with almost equal efficiency, whereas **4e** and **4f** remained ineffective under the optimized reaction conditions (Table 2).

Table 2. Screening of Phenalenyl Based Molecules as Catalysts[a]



4b	4c	4d	4e	4f
	4b	4c	4d	4e	4f
yield	96%	97%	94%	<1%	<1%

[a]The reactions were performed in sealed tubes in the presence of 2.5 equiv of base and 5 mol % catalysts, without applying inert or dry conditions, and the indicated yields are based on ^{1}H NMR spectroscopy.

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Further, to investigate the lifetime of the catalytic intermediate, we performed a longevity test. In this experiment, we loaded the catalyst only once and performed the catalytic reaction for several cycles by adding fresh substrates after each catalytic cycle but without incorporating any additional catalyst. In this study, we employed **1a** and **2a** as coupling partners where **2a** (benzene) was taken in excess and **4a** as catalyst under optimized reaction conditions. After the completion of each catalytic cycle, we added fresh **1a** (1 equiv) as well as 1 equiv of KO^{t}Bu in the reaction mixture and allowed the next catalytic cycle in the presence of excess **2a** already present in the reaction medium. However, we did not add anymore catalyst (**4a**) to the reaction medium. As depicted in Figure 1,

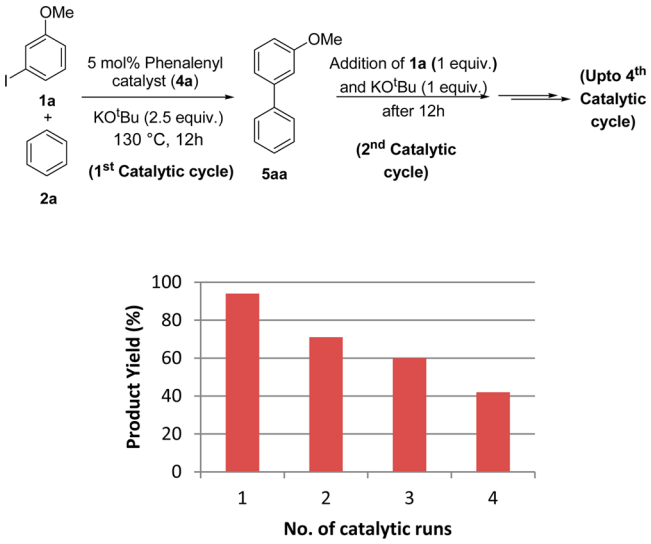
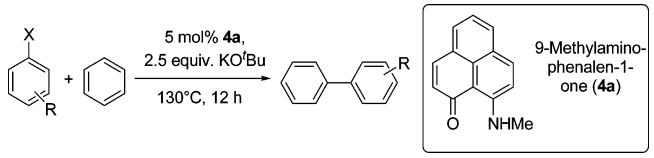


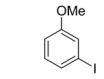
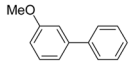
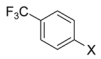
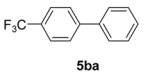
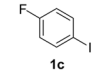
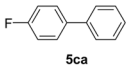
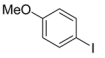
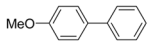
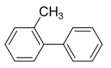
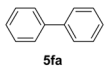
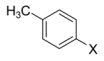
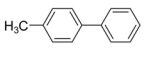
Figure 1. Longevity test of the catalytic intermediate, employing **1a** and **2a**, under optimized reaction conditions.

the catalytic effect of **4a** can be observed up to the fourth cycle though with gradual decrease in catalytic efficiency from one cycle to the next. Nevertheless, such sustained catalytic activity over several catalytic cycles suggests that the catalytically active intermediate is sufficiently stable to show its activity over successive catalytic cycles (vide infra).

Further, to expand the substrate scope under these optimized reaction conditions, we performed the coupling reaction for a range of substrates. More specifically, we aimed at justifying its feasibility by employing different haloarenes as well as benzene and substituted benzenes. To our delight, iodoarene **1b**, containing the electron-deficient trifluoromethyl moiety efficiently participated in the reaction, and 4-trifluoromethyl biphenyl **5ba** was produced in 87% yield (Table 3, entry 2). Another electron-deficient iodoarene **1c**, in a similar fashion, also reacted under the optimized conditions to produce 4-fluoro biphenyl **5ca** with 95% yield (Table 3, entry 4). With its demonstrated applicability in both electron-donating and electron-withdrawing arylating precursors, the methodology was further expanded with various other iodoarene substrates. As represented in Table 3, substituted iodophenyls **1d**–**h**, competently produced the corresponding biphenyls with 81%–97% yield (Table 3, entries 5–11). Besides, when iodophenyls were replaced with 1-iodonaphthalene **1i**, 1-phenyl naphthalene **5ia** was produced in 76% yield (Table 3, entry 12). On further extension, the methodology yielded the *p*-terphenyl **5ja** in 92% yield, when 4-iodobiphenyl was employed for arylation of **2a**

Table 3. Substrate Scope of Aryl Halides and Arenes[a]



entry	aryl halide	product	yield(%)
1	 1a	 5aa	94
2	 1b (X=I)	 5ba	87
3	1b' (X=Br)	5ba	49
4	 1c	 5ca	95
5	 1d	 5da	95
6	 1e	 5ea	85
7	 1f (X=I)	 5fa	97
8	1f' (X=Br)	5fa	81
9	 1g (X=I)	 5ga	92
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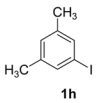
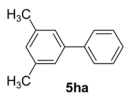
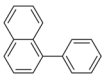
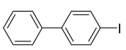
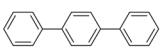
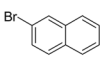
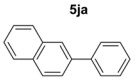
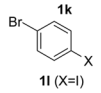
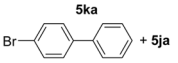
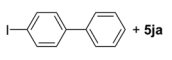
11	 1h	 5ha	94
12	 1i (X=I)	 5ia	76
13	1i' (X=Br)	5ia	43
14	 1j	 5ja	92
15	 1k	 5ka	77
16	 1l (X=I)	 + 5ja 5la	78[b](10[c])
17	1l' (X=Br)	5la + 5ja	45[b](8[c])
18	 1m	 + 5ja 5ma	55[b](26[c])

[a]The reactions were performed in sealed tubes in the presence of 2.5 equiv of base and 5 mol % **4a** as a catalyst, without applying inert or dry conditions, and the indicated yields are isolated yields. [b]Yield of the biaryl product. [c]Yield of terphenyl product.

(Table 3, entry 14). Meanwhile, the C–H arylation protocol was also tested with a series of bromoaryl substrates. Direct arylation of **2a** with bromobenzene **1f′**, as well as with its substituted analogues **1b′** and **1g′**, smoothly took place and produced the corresponding biaryls with moderate to high yields (Table 3, entries 3, 8, and 10). Both 1-bromo and

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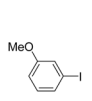
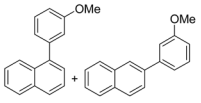
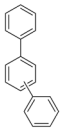
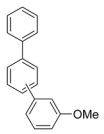
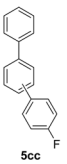
2-bromo naphthalenes (**1i′** and **1k**) also participated in the reaction (Table 3, entries 13 and 15); however, a significant difference between the corresponding product yields was observed (**5ia**, 43%; **5ka**, 77%). Such findings can be explained by considering the higher steric repulsion introduced in **5ia** than in **5ka**. Some interesting observations were also noted, when dihalophenyl substrates were employed in the reaction medium. They tend to participate in two consecutive C−H functionalization cycles, thereby producing biaryl as well as triaryl products (Table 3, entries 16−18). 1-Bromo-4-iodobenzene **1l**, for example, produced the usual biaryl product (Table 3, entry 16), 4-bromobiphenyl **5la** (78%), along with 10% *p*-terphenyl (**5ja**). 1−4-Dibromobenzene **1l′**, however, produced **5la** and **5ja** with 45% and 8% yields, respectively (Table 3, entry 17). However, in a similar attempt employing 1,4-diiodobenzene **1m**, biaryl product **5ma** was isolated with 55% yield along with *p*-terphenyl **5ja** with 26% yield (Table 3, entry 18). To sum up, both in terms of substrate scope and product yields, the present method is as efficient as earlier reports, but the catalytic reaction can be carried out at a much lower catalyst loading (down to 0.5 mol % loading) of 5 mol % unlike the earlier reports.[45−53] Further, the present catalyst loading is comparable to that of a typical transition metal based catalyst loading. Subsequent application of this arylation chemistry on other unactivated arenes was also studied under the standardized reaction conditions, where naphthalene **2b** reacted with 3-iodoanisole **1a**, under neat conditions, producing a 1:0.3 regioisomeric mixture of 1-(3-methoxyphenyl)-naphthalene (**5ab**) and 2-(3-methoxyphenyl)-naphthalene (**5ab′**), with an overall yield of 87% (Table 4, entry 1). On further extension, biphenyl **2c**, exhibited its participation in the reaction in a very interesting fashion. Thus, **2c**, on reaction with simple unactivated iodobenze **1f**, produced the corresponding terphenyl products with 86% overall yield, where *o*-, *m*-, and *p*-terphenyls (**5fc**) were produced with almost equal preference in 0.9:0.8:1 ratio (Table 4, entry 2). The reaction also proceeds efficiently, when either an electron-rich or electron-deficient arylating agent was employed. When **2c** reacted with 3-iodoanisole **1a**, 3-methoxy-terphenyls (**5ac**) were formed with 92% overall yield (Table 4, entry 3; *o*/*m*/*p* = 3:2.3:2.1). In a similar fashion, 4-fluoro-terphenyls (**5cc**) were generated with a regioisomeric ratio of *o*/*m*/*p* = 1:0.8:0.4, having 88% overall yield, when 4-fluoro- iodobenzene **1c** was employed in the reaction medium (Table 4, entry 4). It is worth mentioning that this is the first report on organocatalyzed C−H functionalization of biphenyl under such conditions avoiding transition metals to give triaryl products. All of the products were characterized by ^{1}H NMR and ^{13}C NMR spectroscopy and were compared with the literature reports.[61−73]

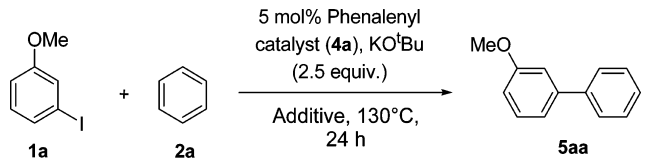
With such a diversified substrate scope in hand, we tried to investigate the underlying mechanism of this arylation chemistry. As discussed in the introductory section, development of the present scheme was hypothesized on the basis of a single electron transfer approach. Therefore, studies on the effect of radical terminators seem to be the next rational step. TEMPO, a well-known radical scavenger, was thus introduced in the reaction medium under the optimized reaction conditions. Such an attempt efficiently paralyzes the catalysis, and no biaryl product was found to form even after 24 h (Table 5, entry 2), which unambiguously supports involvement of a radical intermediate in the reaction, and a similar observation was also noted in literature reports.[45−47]

Table 4. Substrate Scope of Arenes[a]

entry	aryl halide	arene[b]	product[c]	yield(%)
1	 **1a**	 **2b**	 **5ab** **5ab′** (α : β = 1 : 0.3)	87
2	 **1f**	 **2c**	 **5fc** (*o* : *m* : *p* = 0.9 : 0.8 : 1)	86
3	 **1a**	 **2c**	 **5ac** (*o* : *m* : *p* = 3 : 2.3 : 2.1)	92
4	 **1c**	 **2c**	 **5cc** (*o* : *m* : *p* = 1 : 0.8 : 0.4)	88

[a]The reactions were performed under neat conditions in sealed tubes in the presence of 2.5 equiv of base and 5 mol % **4a**, without inert or dry conditions, and the indicated yields are isolated yields. [b]Arylation of toluene, however, proceeded with low product yield (34%), which was increased to 78% (overall yield of regioisomeric mixture) when **4a** was replaced with **4d**. [c]The ratio of the regioisomers was determined by ^{1}H NMR spectroscopy.

Table 5. Effect of Radical Scavenger on the Reaction Between 1a and 2a[a]



entry	base	additive	temp. (°C)	time (h)	yield (%)
1	KO^{t}Bu	TEMPO (5 mol %)	130	2	50
2	KO^{t}Bu	TEMPO(1 equiv)	130	24	<1

[a]The reactions were performed in sealed tubes in the presence of 2.5 equiv of base and 5 mol % **4a**, without inert or dry conditions, and the indicated yields are based on ^{1}H NMR spectroscopy.

To gain further insight into the radical initiation step, we performed a competition reaction between electron-rich (**1d**) and electron deficient arylating agent (**1c**, Scheme 1). As represented in Scheme 1, such catalysis should not have any preference for either substrate, if the involvement of an aryl radical is considered in the mechanistic pathway. Since the relative yields of the corresponding products are not affected by the reactivity of different aryl halides, the aryl radical formation (vide infra) step is not expected to be the rate-determining step. It was observed that in this competition reaction, the products **5ca** (44%) and **5da** (48%) were formed without being biased by electronic effect, which indicates the involvement of a radical intermediate during the catalytic cycle. It is interesting

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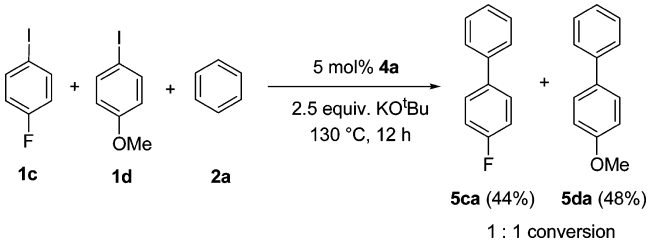
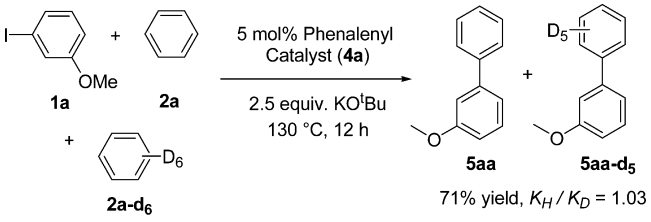
Scheme 1. Competition Reaction between Different Aryl Iodides Revealing Nearly Equal Population of Both Products



to note that similar competitive arylations reported by others[48] also led to a similar conclusion regarding the involvement of a radical intermediate.

Furthermore, to gather information on the rate-determining step, **1a** was employed in the reaction medium with an equimolar mixture of C_6H_6 (50 equiv) and C_6D_6 (50 equiv), where **5aa** and its deuterated analogue **5aa-d$_5$** were produced with almost equal preference (Scheme 2), and the K_H/K_D value

Scheme 2. KIE Experiment Employing Benzene and Benzene-d_6 Revealing a Low K_H/K_D Value



was found to be 1.03. Interestingly, such low K_H/K_D values were also reported for phenanthroline ligand-based catalysis (K_H/K_D = 1.07)[48] as well as *N*,*N*′-dimethylethylenediamine promoted catalysis (K_H/K_D = 1.29),[46] indicating that C−H bond cleavage is not involved in the rate-limiting step.

To further understand the mechanistic cycle, we performed a stoichiometric reaction to isolate the catalytically active intermediate. The stoichiometric reaction between the ligand **4a** and KO^{t}Bu in C_6D_6 was performed and followed by a ^{1}H NMR spectrum of the reaction mixture. It revealed that the N−H proton of the free ligand **4a** (at δ 12.01 ppm) disappeared completely on reaction with 1 equiv of KO^{t}Bu suggesting deprotonation of **4a** and complexation with the potassium ion and formation of ^{t}BuOH (see SI, Figure S3). Our all attempts to crystallize this complex were failed using different solvents and reaction condition. However, a preliminary DFT calculation has been very useful, which suggests the formation of an in situ generated ^{t}BuOH coordinated potassium complex of ligand **4a** (intermediate **II**; see Figure 2). The DFT calculations were performed at the M06-2*X*/6-311+g(d,p) level of theory. The DFT optimized geometry of the ligand calculates that the N−H bond distance is 1.02 Å in free **4a**, which significantly elongates on interaction with KO^{t}Bu to 1.86 Å. This elongation is suggestive of the deprotonation process, and it was observed that this proton was finally engaged with the oxygen of the KO^{t}Bu having the bonding interaction with a bond distance of 0.98 Å. Finally, the DFT optimized structure revealed a ^{t}BuOH coordinated potassium complex (**II**, in Figure 2) as a plausible intermediate. It is worth mentioning that, there is also a possibility of involving a benzyne intermediate in the mechanistic cycle since under some specific conditions, KO^{t}Bu is found to react with aryl iodides to form benzynes.[74] However, such a possibility was ruled out from the outcome of control experiments (Table 1, entries 18 and 19), where in the absence of the phenalenyl catalyst or KO^{t}Bu base, the desired arylation reaction fails to proceed.

On the basis of all these findings, and considering the existing literature data on the mechanistic course of such organocatalytic arylation protocols,[45−53,74,75] we propose a plausible mechanistic cycle as depicted in Scheme 3. The formation of complex **II** can be rationalized by considering the potassium coordinated complex **I** and ^{t}BuOH on interaction with **4a** and KO^{t}Bu as shown in Scheme 3. The coordination of ligand **4a** with potassium ion creates the cataionic state of the phenalenyl ligand as can be understood by considering the following resonating structures as presented in Figure 2c. The canonical forms presented in Figure 2c suggest that on coordination with potassium ion, the phenalenyl unit creates a positive charge as also previously observed by Haddon and co-workers on B(III) coordination.[10b] Also, this type of metal ion coordination assisted cationic state generation of phenalenyl ligand is well-documented from our previous studies.[23b,24a,25,26] This cationic state generation of the phenalenyl ligand on potassium ion coordination in complex **II** explains the calculated LUMO by DFT calculation (Figure 2d). The DFT calculation also suggests that in intermediate **II**, the LUMO predominantly resides over the phenalenyl part of the molecule (Figure 2d). This indicates that any electron transfer will be controlled by the phenalenyl ligand as previously noted.[23b,24a,25,26] Thus, complex **II** with an empty NBMO now can readily interact with the in situ generated *tert*-butanol when the SET can take place into the empty NBMO of the phenalenyl ligand via the formation of a radical transition state **III**. Subsequently, the SOMO of the phenalenyl based radical **III** can transfer the electron to the aryl halide, forming an aryl-halide radical anion intermediate (Scheme 3). Such a proposition is further reinforced by Shirakawa and Hayashi's[48] mechanistic outline, where SET is originated from a formal NaO^{t}Bu-phenanthrolene complex to the corresponding aryl iodide, generating an aryl radical through a radical anion. It is worth mentioning that while performing a blank reaction without **1a**, we observed a sharp color change from yellow to dark green, which was presumed to be the indication of a radical intermediate formation. On EPR analysis, it was found to be EPR active, producing a sharp singlet (see SI, Figure S2), which indicates the formation of a phenalenyl-based radical intermediate. On transfer of the electron to the aryl halide (after the first SET process), the phenalenyl based radical complex **III** further transforms into a radical cation transient species, **IV**, along with the formation of aryl radical. The aryl radical was then trapped by benzene to form **V**, and a concomitant SET process from **V** to **IV** regenerates the active catalyst **II** and aryl substituted cation **VI**. The cation **VI** then undergoes a base assisted (by reacting with KO^{t}Bu) deprotonation followed by aromatization, thereby generating the biphenyl product. This mechanism explains the requirement of at least 2 equiv of KO^{t}Bu in this catalytic protocol as noted during our optimization study (see Table 1). This mechanism is supported by low K_H/K_D values indicating that the C−H bond cleavage is not the rate-limiting step,[48] which explains the fact that electronic effects do not have any effect on the reaction rate.

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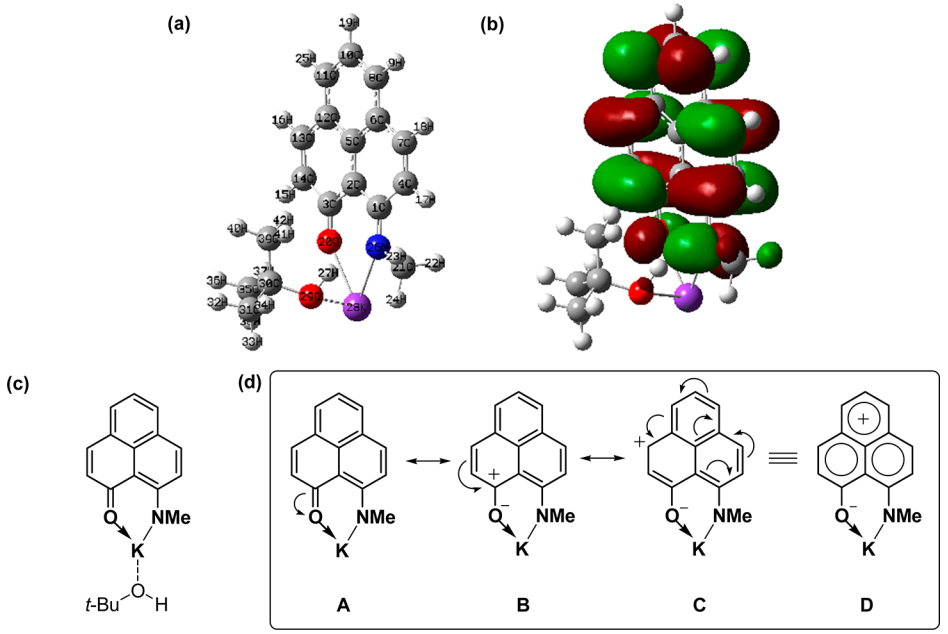
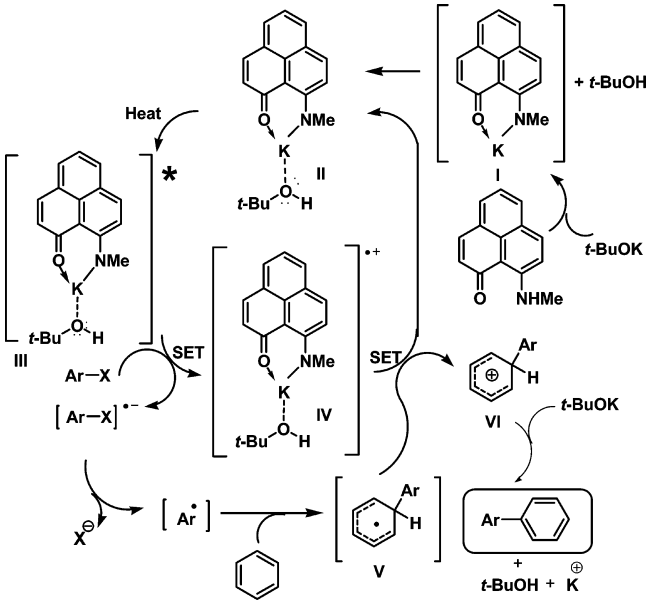


Figure 2. (a) Optimized structure of the catalytic intermediate **II** showing the interaction of in situ generated ^{t}BuOH with the potassium ion. Selected bond lengths (Å) and bond angles (deg): O(20)−K(28), 2.407; N(26)−K(28), 2.707; K(28)−O(29), 2.628; O(29)−C(30), 1.434; O(29)−H(27), 0.983; O(20)−K(28)−N(26), 65.45; O(29)−K(28)−N(26), 62.85; O(29)−K(28)−O(20), 80.85; C(30)−O(29)−K(28), 130.63; C(30)−O(29)−H(27), 109.38. (b) Computed LUMO of **II** revealing that it resides over the phenalenyl part of the molecule. (c) A structural drawing of energy optimized complex **II**. (d) Different canonical forms of complex **II** showing that the potassium ion coordination creates a phenalenyl centered cation where ^{t}BuOH is not shown for the sake of clarity.

Scheme 3. Plausible Reaction Pathway



CONCLUSIONS

The phenalenyl based radical chemistry has been practiced over several decades in multidisciplinary areas, and this article documents the first use of the phenalenyl based radical in the transition metal-free catalytic C−H functionalization process. The catalyst loading was found to be as low as a typical transition metal based catalyst (0.5−5 mol %) as opposed to the generally observed catalyst loading (20−40 mol %) in the case of other reported transition metal-free catalytic C−H functionalization processes. We propose that the NBMO assisted radical stabilization in phenalenyl based molecules plays a key role in improving the radical lifetime during the catalysis. This is also evident from the longevity experiment, which shows that the catalyst stays live for successive four catalytic cycles. We anticipate that this general phenalenyl radical based transition metal-free catalytic arylation reaction will offer direct access to various biaryl motifs in aromatic chemistry and that the concept should, in principle, be extended for further transition metal-free cost-effective coupling chemistry.

EXPERIMENTAL SECTION

General. All chemicals used were purchased from commercial sources and are used as received or as otherwise mentioned. The ligand 9-methylamino-phenalen-1-one (**4a**) was prepared using a literature method.[20a] Aryl halides and potassium *tert*-butoxide were purchased from commercial sources. Organic solvents used for spectroscopy are of spectroscopy grade. All NMR spectra were taken on 400 MHz or 500 MHz spectrometers. EPR analyses were done with 9.155 GHz microwave frequency, 100 kHz modulation frequency, 5 mW power, and 4 min of sweep time. Thin layer chromatography was performed on precoated silica gel 60 F254 aluminum sheets using a different solvent system.

General Procedure for the Direct Arylation of Benzene with Aryl Halides. Typically, a 25 mL sealed tube was charged with 9-methylamino-phenalen-1-one (**4a**, 4.5 mg, 0.0021 mmol), KO^{t}Bu (**3a**, 120 mg, 1.06 mmol), benzene (**2a**, 1.2 mL), and 3-iodoanisole (**1a**, 0.43 mmol). The reaction mixture was then stirred at 130 °C for 12 h. Once the reaction is complete, the reaction mixture was quenched with 1 N HCl (2 mL) and extracted with diethyl ether. The combined organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 99/1 to 95/5) to afford 3-methoxybiphenyl (**5aa**) as a yellow oil; yield, 74 mg (94%). This generalized procedure was applied to all the remaining arylation reactions, and the purified products were characterized by ^{1}H NMR

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and ^{13}C NMR spectroscopy and were compared with the literature reports.

Procedure for the Longevity Test. Typically, a 25 mL sealed tube was charged with 9-methylamino-phenalen-1-one (**4a**, 4.5 mg, 0.0021 mmol), KO^{t}Bu (**3a**, 120 mg, 1.06 mmol), benzene (**2a**, 1.2 mL), and 3-iodoanisole (**1a**, 0.43 mmol). The reaction mixture was then stirred at 130 °C for 12 h. It was then cooled, and the yield was checked via ^1H NMR spectroscopy. Another aliquot of 3-iodoanisole (**1a**, 0.43 mmol) and KO^{t}Bu (**3a**, 48 mg, 0.43 mmol) was then introduced in the reaction mixture and was again stirred at 130 °C for 12 h, and the yield was checked via ^1H NMR spectroscopy. The process was repeated up to the fourth cycle, and the conversion was calculated by ^1H NMR spectroscopy after each run.

Procedure for the Competition Reaction. A 25 mL sealed tube was charged with 9-methylamino-phenalen-1-one (**4a**, 4.5 mg, 0.0021 mmol), KO^{t}Bu (120 mg, 1.06 mmol), benzene (1.2 mL), 4-fluoroiodobenzene (95 mg, 0.43 mmol), and 4-iodoanisole (100 mg, 0.43 mmol). The reaction mixture was then stirred at 130 °C for 12 h. After completion, the reaction mixture was quenched with 1 N HCl (2 mL) and extracted with diethyl ether. The combined organic phase was concentrated under vacuum, and the crude product was purified by column chromatography (eluent: hexane/EtOAc = 99/1 to 95/5) to afford the mixture of **5ca** and **5da** as a yellow oil. The relative yields were determined by ^1H NMR spectroscopy.

Procedure for the KIE Experiment. A 25 mL sealed tube was charged with 9-methylamino-phenalen-1-one (**4a**, 4.5 mg, 0.0021 mmol), KO^{t}Bu (120 mg, 1.06 mmol), benzene (0.6 mL), benzene-d_6 (0.6 mL), and 3-iodoanisole (0.43 mmol). The reaction mixture was then stirred at 130 °C for 12 h. On completion, the reaction mixture was quenched with 1 N HCl (2 mL) and extracted with diethyl ether. The combined organic phase was concentrated under vacuum, and the crude product was purified by column chromatography (eluent: hexane/EtOAc = 99/1 to 95/5) to give a mixture of **5aa** and its deuterated analogue as a dense yellow oil.

Spectral Data of Biaryl Products. *3-Methoxy-biphenyl (**5aa**).*[61] Yield 74 mg, 94%. ^1H NMR (500 MHz, $CDCl_3$): δ 3.72 (s, 3H), 6.79−6.81 (m, 1H), 7.06−7.07 (m, 1H), 7.09−7.11 (m, 1H), 7.23−7.26 (m, 2H), 7.31−7.34 (m, 2H), 7.50−7.51 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.2, 112.6, 112.9, 119.6, 127.1, 127.4, 128.7, 129.7, 141.1, 142.7.

*4-Trifluoromethyl-biphenyl (**5ba**).*[61] Yield 83 mg, 87%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.59 (d, J = 7.6 Hz, 2H), 7.68 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.8 (q, J_{C-F} = 27.5 Hz), 127.4, 127.5, 128.3, 129.1, 139.9, 144.8.

*3-Fluoro-biphenyl (**5ca**).*[62] Yield 70 mg, 95%. ^1H NMR (500 MHz, $CDCl_3$): δ 7.13−7.18 (m, 2H), 7.38 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.56−7.59 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 115.6 (d, J_{C-F} = 21.2 Hz), 127.0, 127.2, 128.7 (d, J_{C-F} = 8.8 Hz), 128.8, 137.3 (d, J_{C-F} = 3.8 Hz), 162.5 (d, J_{C-F} = 243.8 Hz).

*4-Methoxy-biphenyl (**5da**).*[61] Yield 75 mg, 95%. ^1H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.98 (d, J = 9.2 Hz, 2H), 7.30 (t, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 2H), 7.54 (t, J = 9.2 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.3, 114.2, 126.6, 126.7, 128.1, 128.7, 133.7, 140.8, 159.1.

*2-Methyl-biphenyl (**5ea**).*[61] Yield 61 mg, 85%. ^1H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 7.23−7.26 (m, 4H), 7.32−7.36 (m, 3H), 7.40−7.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.4, 125.7, 126.7, 127.2, 128.0, 128.7, 129.2, 129.8, 130.3, 135.3, 142.0.

*Biphenyl (**5fa**).*[61] Yield 64 mg, 97%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.39 (m, 2H), 7.47 (t, J = 7.6 Hz, 4H), 7.62 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 127.1, 127.2, 128.7, 141.2.

*4-Methyl-biphenyl (**5ga**).*[61] Yield 66 mg, 92%. ^1H NMR (400 MHz, $CDCl_3$): δ 2.41 (s, 3H), 7.26 (d, J = 7.6 Hz, 2H), 7.31−7.35 (m, 1H), 7.41−7.45 (m, 2H), 7.50−7.51 (m, 2H), 7.58−7.60 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 127.0, 128.7, 129.5, 137.0, 138.3, 141.1.

*3,5-Dimethyl-biphenyl (**5ha**).*[63] Yield 73 mg, 94%. ^1H NMR (500 MHz, $CDCl_3$): δ 2.41 (s, 3H), 7.02 (s, 1H), 7.24 (s, 2H), 7.33−7.37 (m, 1H), 7.43−7.46 (m, 2H), 7.59−7.61 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.4, 125.1, 127.0, 127.2, 128.6, 128.9, 138.2, 141.2, 141.5.

*1-Phenyl-naphthalene (**5ia**).*[64] Yield 66 mg, 76%. ^1H NMR (500 MHz, $CDCl_3$): δ 7.43−6.7.46 (m, 3H), 7.49−7.52 (m, 5H), 7.53−7.56 (m, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 125.4, 125.7, 125.99, 126.01, 126.9, 127.2, 127.6, 128.2, 130.1, 131.6, 133.8, 140.2, 140.7.

*o-Terphenyl (**5ja**).*[62] Yield 91 mg, 92%. ^1H NMR (500 MHz, $CDCl_3$): δ 7.37−7.40 (m, 2H), 7.46−7.50 (m, 4H), 7.66−7.68 (m, 4H), 7.70 (s, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 127.0, 127.3, 127.5, 128.8, 140.1, 140.7.

*2-Phenyl-naphthalene (**5ka**).*[62] Yield 67 mg, 77%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 (t, J = 7.6 Hz, 1H), 7.48−7.54 (m, 4H), 7.73−7.78 (m, 3H), 7.87−7.94 (m, 3H), 8.06 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.6, 125.8, 125.9, 126.3, 127.3, 127.4, 127.6, 128.2, 128.4, 128.9, 132.6, 138.6, 141.1.

*4-Bromo-biphenyl (**5la**).*[65] Yield 78 mg, 78%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.39 (m, 1H), 7.43−7.47 (m, 4H), 7.55−7.58 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 121.5, 126.9, 127.6, 128.7, 128.9, 131.8, 140.0, 140.1.

*4-Iodo-biphenyl (**5ma**).*[65] Yield 66 mg, 55%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32−7.38 (m, 3H), 7.42−7.46 (m, 2H), 7.54−7.56 (m, 2H), 7.75−7.78 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 93.0, 126.9, 127.7, 128.9, 129.0, 137.8, 140.0, 140.7.

*Spectral Data of **5ab** and **5ab′** (A Mixture of α/β = 1:0.3).* Yield 87 mg, 87%. Ratio of the isomers were determined from the ^1H NMR spectroscopy, by comparing the signals from the methoxy groups of both isomers. 1-(3-Methoxy-phenyl)-naphthalene (**5ab**):[64] ^1H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3 H), 7.01 (dd, J = 8.0, 2.5 Hz, 1 H), 7.07−7.08 (m, 1 H), 7.11 (dt, J = 7.5 Hz, 2.0 Hz, 1 H). However, the following peaks were not precisely distinguishable due to the overlap with peaks of the other isomer **5ab′** at δ 7.40−7.48 (m, 3H), 7.50−7.56 (m, 2H), 7.91 (dd, 2H), 7.96 (d, 1H). Formation of such a regioisomeric mixture and overlap of their signals in the ^1H NMR spectrum were reported in the literature.[66]

*2-(3-Methoxy-phenyl)-naphthalene (**5ab′**).*[67] ^1H NMR (500 MHz, $CDCl_3$): δ 3.92 (s, 3 H), 6.96 (dd, J = 8.5, 2.5 Hz, 1 H), 7.29 (t, J = 2.0 Hz, 1 H), 7.34 (dt, J = 7.5 Hz, 2.5 Hz, 1 H), 7.77 (dd, J = 8.5, 2.0 Hz, 1 H), 8.07 (s, 1 H). However, the following peaks were not precisely distinguishable due to overlap with peaks of the other isomer **5ab**: δ 7.42 (t, 1 H), 7.50 (t, 1 H), 7.53 (t, 1 H), 7.88 (d, 1 H), 7.91 (d, 1 H), 7.93 (d, 1H). Formation of the regioisomeric mixture under similar organocatalysis and overlap of their signals in ^1H NMR spectrum were reported in the literature.[66]

*Spectral Data of **5ac** (A Mixture of o/m/p = 3:2.3:2.1).* Yield 102 mg, 92%. Ratio of the isomers were determined from the ^1H NMR spectroscopy, by comparing the signals from methoxy groups of the three isomers. 3″-Methoxy-[1,1′;2′,1″]terphenyl:[68] ^1H NMR (500 MHz, $CDCl_3$) δ 3.62 (s, 3H), 6.68 (m, 1H), 6.78 (m, 2H). However, they were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 7.13−7.26 (m, 6H), 7.42−7.48 (m, 4H). Formation of regioisomeric mixtures under similar organocatalysis and overlap of their signals in ^1H NMR spectrum were also reported in the literature.[66]

3-Methoxy-[1,1′;3′,1″]terphenyl.[69] ^1H NMR (500 MHz, $CDCl_3$): δ 3.89 (s, 3H). The following peaks, which are reported in the literature,[69] were also observed in the NMR spectra. However, they were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 6.92−7.82 (m, 13H). Formation of the regioisomeric mixture and overlap of their signals in ^1H NMR spectrum, were also reported in the literature.[66]

3″-Methoxy-[1,1′;4′,1″]terphenyl.[70] ^1H NMR (500 MHz, $CDCl_3$): δ 3.90 (s, 3H), 7.70 (s, 4H). The following peaks, which are reported in the literature,[70] were also observed in the ^1H NMR spectrum. However, the following peaks were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 6.93−6.96 (m, 1H), 7.19−7.120 (m, 1H), 7.24−7.27 (m, 1H), 7.36−7.41 (m, 2H), 7.45−7.49 (m, 2H). 7.66−7.68 (m, 2H). Formation of the regioisomeric mixture and overlap of their signals in ^1H NMR spectrum were also reported in the literature.[66]

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*Spectral Data of **5cc** (A Mixture of o/m/p = 1:0.8:0.4).* Yield 94 mg, 88%. Ratio of the isomers were determined from the ^{1}H NMR spectroscopy, by comparing the signals from aromatic ring protons of the three isomers. 4″-Fluoro-[1,1′;2′,1″]terphenyl:[71] ^{1}H NMR (500 MHz, $CDCl_3$) 6.92 (m, 2H), 7.16 (m, 2H). However, the following peaks were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 7.19−7.21 (2H, m), 7.26−7.32 (3H, m), 7.47−7.49 (4H, m). Formation of the regioisomeric mixture and overlap of their signals in ^{1}H NMR spectrum were reported in the literature.[66]

4-Fluoro-[1,1′;3′,1″]terphenyl.[71] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (1H, s). However, the following peaks were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 7.16 (t, 2H), 7.39 (t, 1H), 7.48 (d, 2H), 7.52−7.54 (m, 2H), 7.58−7.63 (m, 3H), 7.66 (d, 2H). Formation of the regioisomeric mixture and overlap of their signals in ^{1}H NMR spectrum were reported in the literature.[66]

4″-Fluoro-[1,1′;4′,1″]terphenyl.[71] ^{1}H NMR (500 MHz, $CDCl_3$): The ^{1}H NMR signals for this isomer, which are reported in the literature,[14] were observed in the spectra. However, all peaks were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 7.69−7.54 (m, 8H), 7.45 (t, 2H), 7.39−7.32 (m, 1H), 7.13 (t, 2H). Formation of the regioisomeric mixture and overlap of their signals in ^{1}H NMR spectrum were reported in the literature.[66]

*Spectral Data of **5fc** (A Mixture of o/m/p = 0.9:0.8:1).* Yield 85 mg, 86%. Ratio of the isomers were determined from the ^{1}H NMR spectroscopy, by comparing the signals from aromatic ring protons of the three isomers. *o*-Terphenyl:[72] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13−7.15 (m, 4H), 7.19−7.23 (m, 6H), 7.41−7.44 (m, 4H). The NMR data are in agreement with those in the literature.[72] Formation of regioisomeric mixture and overlap of their signals in the ^{1}H NMR spectrum were also reported in the literature.[66]

m-Terphenyl.[73] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (s, 1 H), 7.58−7.59 (m, 2H). The following peaks, which are reported in the literature,[73] were also observed in the ^{1}H NMR spectrum. However, they were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 7.35 (t, 2H), 7.42−7.51 (m, 5H), 7.63 (d, 4H). Formation of regioisomeric mixtures and overlap of their signals in ^{1}H NMR spectrum were also reported in the literature.[66]

p-Terphenyl.[73] ^{1}H NMR (500 MHz, $CDCl_3$): 7.69 (s, 4H). The ^{1}H NMR signals for this isomer, which are reported in the literature,[73] were also observed in the spectra. However, they were not precisely distinguishable due to the overlap with peaks of the other isomers: δ 7.35 (t, 2H), 7.45 (t, 4H), 7.64 (d, 4H). Formation of the regioisomeric mixture and overlap of their signals in ^{1}H NMR spectrum were also reported in the literature.[66]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00002.

Experimental details, DFT calculations, and NMR characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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