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# Mechanistic Insights into the Initiation Step of the Base Promoted Direct C−H Arylation of Benzene in the Presence of Additive

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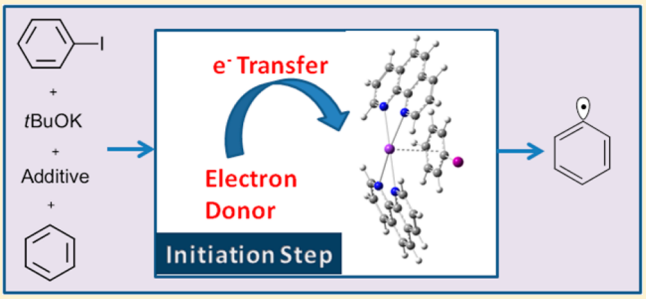
Supporting Information

**ABSTRACT:** The direct arylation of unactivated arenes is a very practical and highly convenient procedure for the construction of biaryl scaffolds. Recently, a direct arylation of unactivated benzene has been achieved in the presence of base (*t*BuOK or *t*BuONa) and organic additive such as 1,10-phenanthroline. However, details of intimate mechanism of reaction as well as the role of additive have remained elusive until date. The present work explores various mechanistic possibilities of the key electron transfer step of the reaction in order to identify a probable route for the initiation of phenyl radical from iodobenzene. A detailed DFT (M06-2X functional) investigation indicates that the reaction of additive and base can be crucial to generate an electron acceptor−donor pair that can facilitate electron transfer mechanism. This computational model provides a satisfactory explanation for experimental observations, clearly defining the roles of additive and base in the reaction.




## INTRODUCTION

The direct arylation of arene is one of the challenging frontiers in organic chemistry. Considerable efforts have been directed, especially using transition metal catalysis, in devising chemical requirements for the activation of aromatic C−H bonds and subsequent direct arylation of arene.[1] While significant advancements in the direct arylation strategies have been realized using transition metal catalysis, alternative approaches for the direct arylation are still in demand.[2] Recently, coupling of iodoarene with benzene using combination of organic additive and alkali metal *tert*-butoxide (*t*BuOK or *t*BuONa) has emerged as a transition metal free approach for the direct arylation.[3] Conceptually different from the transition metal catalyzed direct arylation, this new approach mainly relies on the generation of aryl radical intermediate in the presence of certain organic additives.[4] The choice of organic additive is found to be very crucial in order to obtain the high yields of biaryl compounds in the reaction. So far, various organic additives such as organic radicals,[5] amino acids,[6] 1,10-phenanthroline and its derivatives,[7] carbenes,[8] phenyl hydrazine,[9] alcohols[10] and small organic ligands[11] have been effectively used for the direct arylation of simple arene. To establish a coherent mechanistic picture for this novel approach, understanding of how organic additives help to generate the aryl radical is warranted. Surprisingly, very few computational studies have been devoted to investigate the role of organic additives in the reaction.[12]

Mechanism of the direct arylation of arene in the presence *t*BuOK and organic additives is also a subject of debate since the inception of the reaction. Owing to transition metal free environment, this reaction was originally referred to organo-catalyzed cross coupling reaction via aromatic C−H bond activation.[3] Concurrently, Shirakawa and Hayashi et al. based on their kinetic isotope effect and radical trapping experiments suggested a catalytic cycle for the homolytic aromatic substitution (HAS) mechanism.[3d] This mechanism involves the generation of aryl radical through a single electron transfer (SET) from potassium *tert*-butoxide-phenathroline complex to aryl halide followed by dissociation of the halide ion. The aryl radical adds to benzene to form a phenylcyclohexadienyl radical. The resulting phenylcyclohexadienyl radical on intermolecular electron transfer to the *tert*-butoxide-phenatroline complex cation radical provide a phenylcyclohexadinyl cation which on deprotonation by *tert*-butoxide leads to the biphenyl. From the perspective of the radical chemistry, Studer and Curran found two major drawbacks in this mechanism.[4] First, the oxidation of phenylcyclohexadienyl radical by a *tert*-butoxide-phenathroline complex cation radical seems to be unlikely since it involve ET between two short-lived radical species. Second, the generation of two radicals ($Ar^{\bullet}$ and $tBuO^{\bullet}$) at the initial stage of reaction might be a very endothermic process which may not fit well as one of the steps in a catalytic cycle. Alternatively, Studer and Curran suggested a radical chain mechanism within the framework of base promoted homolytic substitution reaction in which radical generation was considered as a discrete initiation step.[4] The phenyl radical then adds to benzene to form phenylcyclohexadienyl radical

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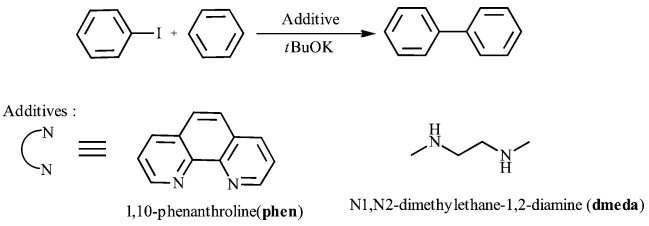
which on deprotonation by *tert*-butoxide provides the phenylcyclohexadienyl radical anion. The phenylcyclohexadienyl radical anion is thought to be a powerful reducing agent which may readily transfer an electron to aryl halide and thus can generate a new phenyl radical, potassium iodide and the final product, biphenyl. Although this mechanistic proposal closely resembles to the established radical mechanisms, issues related to the source of radical initiation and participation of organic additives in the reaction mechanism remain unresolved. Recently, Tuttle and Murphy et al. evidently demonstrated that the homocoupling of the phenanthroline (additive) can be possible in the presence of *t*BuOK resulting into a $\pi$-electron rich species.[12] Furthermore, they have proposed that in situ generated $\pi$-electron rich species termed as super electron donors (SED) play a key role in electron transfer (ET) step of the reaction. Similarly, attempts were made by the same group to identify the probable SEDs derived from the other organic additives such as 1,2-diols, 1,2-diamines and amino acids.[13] Meanwhile, two interesting reports by different research groups have appeared in the literature. In one of the reports, Wilden and co-workers have proposed that dissociation of *t*BuOK can be crucial step in the reaction since it provides the *tert*-butoxide which can supply electron to aryl halide.[14] In the second report, Jutand and Lei et al. speculated that the additive (phenanthroline) can act as a mediator in ET between *t*BuOK and aryl halide.[15] Despite these efforts to unveil the mechanism of ET step, without computational evidence, the underlying mechanism of the radical initiation has remained somewhat obscure.

The surge of interest in transition metal-free direct arylation of arene, and evidently unanswered questions regarding mechanism of the reaction prompted us to carry out a detailed computational investigation on the reaction shown in Scheme 1. In this report, the density functional theory (DFT) calculations were employed to establish the mechanism of reaction, and to investigate the role of organic additives in the transition metal-free direct arylation reaction.

**Scheme 1. Cross Coupling Reaction of Iodobenzene and Benzene in the Presence of Organic Additive and Base**




## COMPUTATIONAL METHODS

All calculations were performed with the Gaussian09 quantum chemical programs.[16] Density functional theory (DFT) was applied using the M06-2X functional (UM06-2X functional for open shell systems)[17] in combination with the 6-311G** basis set for C, H, O, K, and N[18] and the LANL2DZ effective core potential and the associated double-$\zeta$ basis set for I.[19] Furthermore, basis set such as 6-311+G(2df,p) for the atoms other than I was also tested to examine the basis set effect on the trends in the relative free energies. The selection of M06-2X functional for the present investigations, is based on the available computational reports on the radical chemistry which show that the M06-2X functional provide a reliable method for the mechanistic studies involving organic radicals.[20] Solvent effects were incorporated in the calculations using the polarizable continuum model (PCM) and benzene (dielectric constant: 2.27) as solvent.[21] This approach will be designated simply as "M062X" in the text. In UM06-2X calculations for the open shell systems, $\langle S2 \rangle$ operator expectation values were close to the idea value of 0.75 for radicals (typically were $0.75 \leq \langle S2 \rangle \geq 0.78$).

Geometry optimizations were carried out in the solvent phase without any constraints. The optimized stationary points were characterized as local minima or transition structures by harmonic force constant analysis, and intrinsic reaction coordinate (IRC) calculations were performed to verify the transition state structures.[22] The lowest energy conformer of the reactants and intermediate structures are reported in the text. Free energies of all stationary points were obtained from the calculated thermal and entropic corrections at 298 K using the unscaled vibrational frequencies. Relative free energies of all stationary points such as reactants, intermediates and transition states were also calculated at the following three DFT levels, (1) L1: PCM(benzene)/(U)M06-2*X*/6-311+G(2df,p), LANL2DZ, (2) L2: SMD(benzene)/(U)M06-2*X*/6-311G**, LANL2DZ (3) L3: SMD-(benzene)/(U)M06-2*X*/6-311+G(2df,p), LANL2DZ. The SMD solvation model was used for the calculations at the L2 and L3 levels of theory.[23] All these results are documented in the Supporting Information.

The optimization of $PhI^{\bullet -}$ at the M06-2X level leads to a first order saddle point and hence, optimization of $PhI^{\bullet -}$ was carried out using the M06 functional with the standard basis set (as mentioned above). The solvent-phase single-point energy calculation at the M062X level was performed on the geometry of $PhI^{\bullet -}$ optimized at the M06 level. The ionization energies (IEs) and electron affinities (EAs) of electron donor (D) and acceptor (A) discussed in the text were calculated using eqs 1 and 2, respectively.

$$E(D^{+}) - E(D) \quad (1)$$

$$E(A^{-}) - E(A) \quad (2)$$

## RESULTS AND DISCUSSION

The key steps such as phenyl radical initiation, addition of phenyl radical to benzene and deprotonation step involved in the cross-coupling reaction between the iodobenzene (PhI) and benzene (Scheme 1) are investigated and discussed below. The 1,10-phenathroline and $N^1$,$N^2$-dimethylethane-1,2-diamine which represent typical organic additive employed in the reaction are included in the computational study. These two additives have shown similar reactivity in the cross-coupling reaction between iodobenzene and benzene under same reaction conditions.[3b−d] The 1,10-phenathroline and $N^1$,$N^2$-dimethylethane-1,2-diamine are abbreviated as "**phen**" and "**dmeda**", respectively.

A radical trapping experiment using suitable radical scavengers such as TEMPO and 1,1-diphenylethylene have confirmed the formation of radical intermediate in the reaction.[3] The key question raised here, as also highlighted in the Introduction how aryl radical could be generated in the metal free environment. In order to shed light on this issue, different pathways for the phenyl radical initiation are considered as shown in Scheme 2a. These pathways presume different electron donors to generate a radical anion $PhI^{\bullet -}$. For instances, the pathway **P−I** involves a single electron transfer (SET) between *t*BuOK and PhI whereas in **P−II**, a SET occurs between additive-coordinated *t*BuOK and PhI. For **P−III**, two consecutive SET steps are considered. In the first step of **P−III**, a SET between *t*BuOK and additive provides additive radical anion, which in the subsequent step, activates the PhI via SET to generate a $PhI^{\bullet -}$. In **P−IV**, organic super electron donor (SED) derived from the additive donates a single electron to PhI. The SED derived from **phen** and **dmeda** are shown in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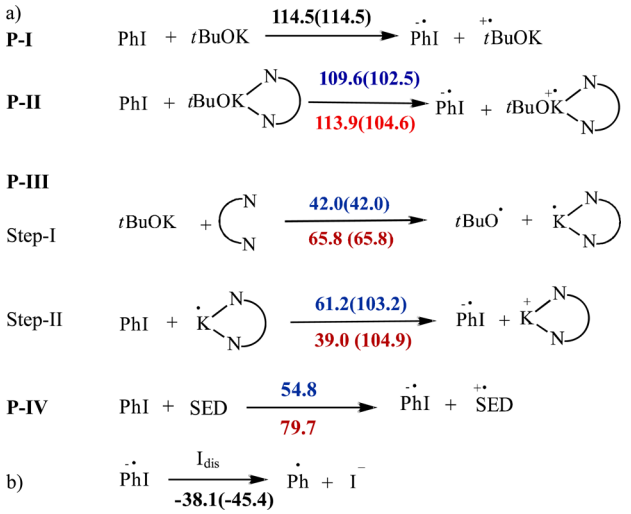
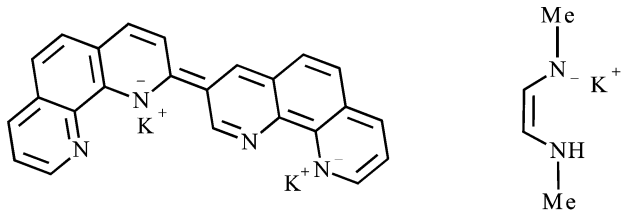
**Scheme 2. (a) Different Pathways for the ET to PhI; (b) Dissociation of Phenyl Radical Anion**[a]




[a]Values in blue and red refer to the free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) for the pathway involving **phen** and **dmeda**, respectively. Parentheses values indicate free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) relative to separated reactants.

Figure 1. The radical anion $PhI^{\bullet-}$ thus formed, can dissociate iodide ion to generate a phenyl radical (Scheme 2b).




**SED-phen** **SED-dmeda**

**Figure 1.** SED derived from phen and dmeda.

The different ET pathways discussed in the text are compared based on the reaction driving force which is related to standard Gibbs free energy change of the ET reaction. The free energies of reactions ($\Delta G_{rxn}$) for the different pathways involving SET are provided in Scheme 2. It has been suggested that the reaction can be best described as a series of radical reactions rather than as a catalytic cycle involving radical intermediates[24] and hence, free energy changes of individual steps of the reaction are reported in the text. For a sake of clarity, free energies of reactions calculated relative to separated reactants viz. PhI, *t*BuOK and additive (**phen** or **dmeda**) are also provided in the parentheses.

The electron transfer from the bare *t*BuOK to PhI in **P−I** is predicted to be endoergic process with $\Delta G_{rxn}$ of 114.5 kcal/mol. Similarly, the electron transfer from the additive bound *t*BuOK to PhI as shown in the **P−II** is also found to be highly endoergic in nature. The computed $\Delta G_{rxn}$ for the pathway involving **phen** and **dmeda** coordinated *t*BuOK are 110.0 and 114.0 kcal/mol, respectively. The **P−III** involves two steps ET, in which additive acts as a mediator for the ET between *t*BuOK and PhI. This pathway originally proposed by Jutand and Lei et al. based on their electron paramagnetic resonance and cyclic voltammetry studies on the reaction of bromobenzene and benzene in the presence of **phen**.[15] In the first step, the interaction between **phen** and *t*BuOK furnishes $\textbf{phen}^{\bullet-}$ and $t\text{BuO}^{\bullet}$ radical. This step is found to be endoergic by 42.0 kcal/mol. In the next step, it was expected that $\textbf{phen}^{\bullet-}$ readily transfer a single electron to the PhI to generate a $PhI^{\bullet-}$.[25] However, a SET from $\textbf{phen}^{\bullet-}$ to PhI is estimated to be endoergic by 61.2 kcal/mol. The free energy changes for these SET steps in **P−III** involving **dmeda** as an additive are also calculated. The $\Delta G_{rxn}$ for the step-I and step-II in **P−III** involving **dmeda** as an additive are 65.8 and 39.0 kcal/mol, respectively. Recently, Tuttle and Murphy et al. has shown that the organic additives such as **phen** and **dmeda** in the presence of *t*BuOK can produce the electron rich species during the reaction.[12,13] These electron rich species termed as SED can act as an electron donor to the PhI. The **P−IV** shown in Scheme 2a employs the SED derived from additives (**SED-phen** or **SED-dmeda**) as an electron donor in the ET mechanism. A SET in P-**IV** involving **SED-phen** and **SED-dmeda** are also found to be endoergic by 54.8 and 79.7 kcal/mol, respectively. The dissociation of iodide form radical anion $PhI^{\bullet-}$ formed in the ET step is predicted to be exoergic by 38.1 kcal/mol (Scheme 2b).

A comparison of the free energies of reactions of different pathways, it appears that ET as shown in **P−I** and **P−II** is least likely to occur in the cross-coupling reaction between iodobenzene and benzene. While the free energy changes for the ET in **P−III** and **P−IV** are substantially lower than the free energy changes in **P−I** and **P−II**, these changes are not entirely uniform for the **phen** and **dmeda**. For instances, the $\Delta G_{rxn}$ for the step-I in **P−III** involving **phen** is found to be lower by about 20 kcal/mol as compared to the $\Delta G_{rxn}$ for the step-I involving **dmeda**. The large difference in the free energies of reactions for **P−III** involving two different additives can be attributed to the stabilization of radical species obtained in the two different scenarios. Analysis of spin density distribution of the **phen-K** radical obtained in the step-I of **P−III** shows that the unpaired spin densities are delocalized over the aromatic rings of the **phen**. While in the case of **dmeda-K** radical, unpaired spin densities are mainly located on the K. The radical stabilization because of delocalization of unpaired spin densities in the **phen-K** radical may lower the endoergicity of the step-I of **P−III** involving **phen** as an additive. Somewhat opposite trend in the $\Delta G_{rxn}$ of step-II of **P−III** for the **phen** and **dmeda** is noticed. This may be because of ET in step-II from the stabilized **phen-K** radical to PhI is less facile than the **dmeda-K** radical. Similarly, the $\Delta G_{rxn}$ for ET from SEDs to PhI in **P−IV** are also not in the comparable range. The difference of about 25 kcal/mol in $\Delta G_{rxn}$ for **P−IV** involving **SED-Phen** and **SED-dmeda** is estimated. It worth noting here that the cross coupling reactions between aryl halide and benzene using these two additives (**phen** and **dmeda**) were successfully carried out under similar reaction conditions and with a wide range of aryl halides.[3b−d]

The pathways **P−III** and **P−IV** exhibit very high thermodynamic barriers, rendering ET step as a rate limiting step of the reaction. However, this prediction appears to contradict experimental findings pertaining to rate-determining step of the reaction.[26] Moreover, the free energies of ET steps vary drastically for the different additives employed in these pathways. These computational results conspicuously indicate the possibility of an alternative route for the ET step in the cross-coupling reaction between PhI and benzene mediated by the *t*BuOK and organic additives.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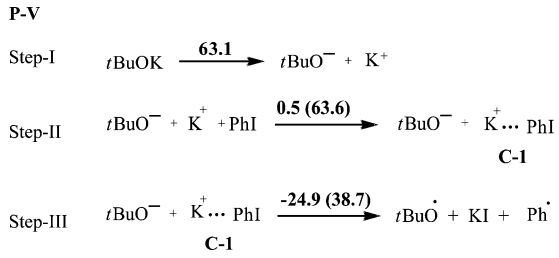
Very recently, Wilden and co-workers have performed the cross coupling reactions of aryl iodide with the benzene under different reaction conditions, and have shown that a degree of dissociation of base (alkali metal *tert*-butoxide) into the metal counterion and alkoxide ion, which may supply the electron to the aryl halide, can be a decisive factor in these reactions.[14] They have also suggested that the addition of additive facilitate the dissociation of base to provide sufficient amount of alkoxide ion needed for the ET process. Accordingly, the dissociation of *t*BuOK in the absence of additive, and subsequent ET step are considered in pathway **P−V**. The steps involved in **P−V** and the corresponding free energies of reactions are provided in Scheme 3. First step involves the dissociation of *t*BuOK into potassium cation and *tert*-butoxide which is found to be highly endoergic process ($\Delta G_{rxn}$: 63.1 kcal/mol). The ET from the *tert*-butoxide to PhI is expected to have same thermodynamic barrier as it is noticed in the case of **P−I** (Scheme 2), hence it is not discussed here. Alternatively, complexation of the potassium ion to PhI prior to the ET is considered in this pathway. Considering the fact that the base is used in the sufficiently excess in amount (almost three equivalent to the PhI), it is logical to envisage the complexation of the potassium ion to PhI through cation-pi interaction. The complexation of potassium ion to PhI (**C-1**) is found to be marginally endoergic by 0.5 kcal/mol. In the next step, ET between *tert*-butoxide and **C-1** leads to dissociation of the **C-1** to the phenyl radical, *tert*-butoxide radical and KI. This step is predicted to be exoergic by 24.9 kcal/mol. In reality, the direct arylation of benzene in the absence of organic additives were feasible only at the high range of temperature (150−180 °C).[12,14] A trend of the $\Delta G_{rxn}$ in **P−V** suggests that in additive free reaction, high temperature might be required to overcome a very high thermodynamic barrier of the dissociation step (step-I, **P−V**).[27]

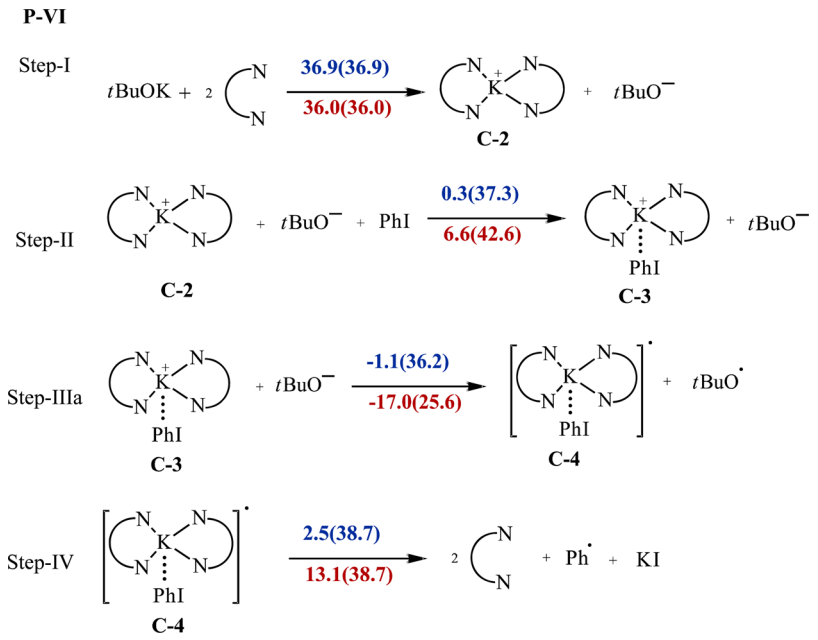
**Scheme 3. Pathway (P−V) Showing Dissociation of *t*BuOK and Subsequent ET Step**[a]




[a]The free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) are reported. Parentheses values indicate free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) relative to separated reactants.

As an extension to this pathway, a new pathway (**P−VI**) is envisioned in which, additive acts as bidentate ligand for the alkali metal cation to form a chelate complex. The steps involved in **P−VI** are shown in Scheme 4 wherein, two additive molecules are considered for the coordination to potassium ion. The **P−VI** commences with the dissociation of *t*BuOK in the presence of additive which leads to the formation of additive coordinated potassium ion (**C-2**) and *tert*-butoxide. The predicted $\Delta G_{rxn}$ for the dissociation of *t*BuOK in the presence of **phen** and **dmeda** are 36.9 and 36.0 kcal/mol, respectively. The step-II of **P−VI** involves complexation of the PhI with **C-2** through cation-pi interactions to form a complex **C-3**. This step is found to be endoergic by 0.3 and 6.6 kcal/mol for the **phen** and **dmeda**, respectively. In the subsequent step (step-IIIa), ET occurs between *tert*-butoxide and **C-3** to form a radical complex **C-4**. Unlike the ET pathways discussed in Scheme 2, ET transfer in this pathway is found to be exoergic, albeit to the different extent for the two different additives. The ET between *tert*-butoxide and **C-3(phen)** is slightly exoergic (1 kcal/mol/) whereas in the case of **C-3(dmeda)**, it is exoergic by 17 kcal/mol. In the final step of **P−VI**, the radical complex **C-4** dissociates into a phenyl radical, additive and KI, which is

**Scheme 4. Pathway (P−VI) Showing Dissociation of *t*BuOK in the Presence of Additive and Subsequent ET Step**[a]




[a]Values in blue and red refer to the free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) for the pathway involving **phen** and **dmeda**, respectively. Parentheses values indicate free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) relative to separated reactants.



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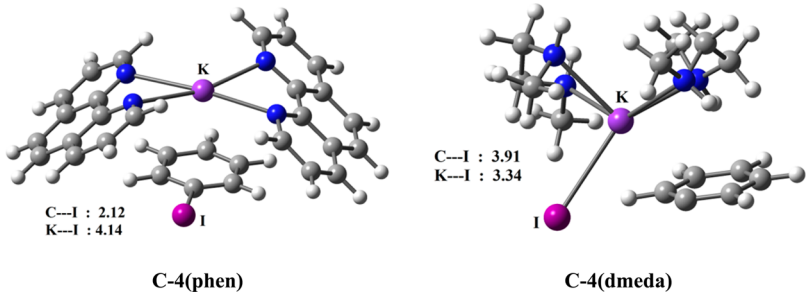
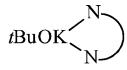
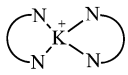



C-4(phen) C-4(dmeda)

**Figure 2.** Optimized structure of **C-4(phen)** and **C-4(dmeda)**.

**Table 1. Electron Affinities (EAs) of Electron Acceptors and Ionization Energies (IEs) of Electron Donors Computed at the PCM(Benzene)/M062X Level of Theory**

| Acceptor | Additive | EA(kcal/mol) | Donor | Additive | IE(kcal/mol) |
|---|---|---|---|---|---|
| PhI | — | −6.5 | *t*BuOK | — | 123.2 |
|  | **phen** | −67.6 |  | **phen** | 118.4 |
| | **dmeda** | −46.3 | | **dmeda** | 124.5 |
|  | **phen** | −65.4 | SED | **phen** | 61.8 |
| | **dmeda** | −36.2 | | **dmeda** | 87.8 |

predicted to be endoergic by 2.5 and 13.1 kcal/mol for the **C-4(phen)** and **C-4(dmeda)**, respectively.

It is also noticed that transfer of electron from *tert*-butoxide to **C-3** in step-IIIa (**P−VI**) is accompanied by the structural changes in **C-3**. The optimized structures of radical complexes (**C-4(phen)** and **C-4(dmeda)**) obtained in the step-III (**P−VI**) are shown in Figure 2. The analysis of optimized structures of **C-4(phen)** and **C-4(dmeda)** reveals that the key changes are in the C···I(PhI) and K···I bond distances. Interestingly, **C-4(dmeda)** exhibit fairly elongated C···I bond (PhI) and shorter K···I bond as compared to the corresponding bonds in **C-4(phen)**. The bond distances C···I and K···I in **C-4(dmeda)** are 3.91 and 3.34 Å, respectively whereas corresponding distances in **C-4(phen)** are 2.12 and 4.41 Å, respectively. A large variation in the geometry of **C-4(dmeda)** as compared to the **C-4(phen)** can be attributed to the ability of additive to delocalize the unpaired spin density in the radical complex. As explained earlier, the **phen** can effectively delocalize the unpaired spin density in **C-4(phen)**, which exhibits very small changes in the geometry, where the **dmeda** fails to delocalize the unpaired spin density in **C-4(dmeda)** resulted into cleavage of the C···I(PhI) bond in **C-4(dmeda)** to generate a radical center at the C(*ipso*) of PhI.

Cognizant of the fact that the direct arylation of unactivated benzene in the presence of base and additive is always carried out at high temperature (80 °C and above), the reaction mechanism shown in the **P−VI** for the generation of phenyl radical seems to be more practical than the pathways discussed in Scheme 2. However, this pathway mainly relies on the binding ability of additives to the metal ion which eventually, facilitates the dissociation of *t*BuOK (as shown in step-I, **P−VI**). This implies that any organic additive, which efficiently binds with the metal ions of the *t*BuOK can be effective in the coupling of PhI with the benzene. On the contrary, it has been shown that many additives, structurally similar to the **phen** and **dmeda** such as substituted **phen**, tetramethylethylene diamine (TMEDA) were not effective in the coupling reactions. Thus, the mechanism presented in **P−VI** fails to account why only certain additives were effective in the coupling reactions.

Recently, Murphy and co-workers strongly advocated the concept of "super electron donors (SED)" to explain the role of additive in the radical coupling reactions.[28] It has been elegantly demonstrated by the same group that only those additives which can generate SED in situ were effective in the reaction.[13] In order to gain insights on the electron donating power of SEDs, ionization energies (IEs) of SEDs calculated at the M062X level are provided in Table 1. Likewise, to verify the electron accepting ability of the additive-metal ion complexes proposed in this work, electron affinities (EAs) of additive-metal ion complexes were calculated and shown in Table 1. A comparison of the IEs of SEDs with the IE of the *t*BuOK suggests that the proposed SEDs can readily donate an electron as compared to the *t*BuOK or additives.[29] However, the IEs values for electron donors are found to be in the range of 60−80 kcal/mol, indicating the need of a strong electron acceptor to compensate the large energy penalty associated with the release of electron from the donor.[30] From Table 1, it is also clear that the additive coordinated metal ions possess sufficiently high EAs to counterbalance the energy changes during ET process. Now, a new route for the ET step which involves ET between SED and additive coordinated metal ion can be speculated. In order to this ET pathway to operate, the formation of the SED as well as additive coordinated metal ion from additives is crucial. It is therefore necessary to collect details on the barriers associated with the formation of SED as well as additive coordinated metal ion from additives, to corroborate the possibility of new ET pathway in the reaction. First, the formation of **SED-dmeda** was investigated at the M062X level. A complete investigation of reaction mechanism of **SED-dmeda** formation is discussed in the Supporting Information (see Figure S1). It is noticed that the cleavage of $\alpha$C−H bond (next to the heteroatom) is a rate limiting step in the process of **SED-dmeda** formation, with the barrier of 32.5 kcal/mol. Moreover, the conversion of **dmeda** to **SED-dmeda**



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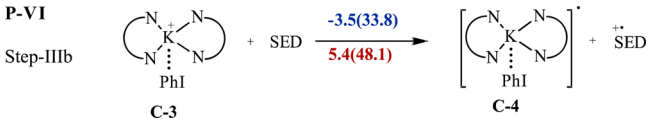
is endoergic by 27.9 kcal. These thermodynamic as well as kinetics barriers for the **SED-dmeda** formation are considerably high and the conversion of **demda** to **SED-dmeda** could only be expected at very high temperature. Interestingly, the formation of a small amount of SED is suggested even at the high temperature (80 °C and above), which was found to be sufficient to promote the coupling reaction.[12,13] In addition, using deuterium labeled analogs of **dmeda** in the coupling reaction, Tuttle and Murphy et al. have also shown that the formation of **SED** involves the cleavage of a C−H bond of **dmeda** in the rate-determining step.[13] Our computational results on the **SED-dmeda** formation are consistent with these experimental observations. Similarly, in the case **SED-phen**, it was proposed that *ortho* deprotonation of **phen** can be a rate limiting step.[12] The formation of **SED-phen** has been discussed in detail elsewhere[12] and hence, not included in this work.

Next, the formation of additive coordinated metal ion is considered. As shown in step-I of **P−VI** (Scheme 4), the dissociation of *t*BuOK in the presence of additive can provide the additive coordinated potassium ion (**C-2**). The formation of **C-2** by the dissociation of *t*BuOK is predicted to be an endoergic process and need to surmount a very high thermodynamic barrier (36−37 kcal/mol). Generally speaking, it has been observed that the rate of dissociation of metal alkoxide depends on the choice of solvent in the reaction.[31] Exner and Steiner, based on their conductometric studies, have suggested that the addition of alcohol to alkoxide solution can facilitate ion-pair dissociation because of specific alkoxide solvation by alcohol.[32] Interestingly, the initial step of SED formation involves deprotonation of $\alpha$C−H bond (next to the heteroatom) of additive by *t*BuOK to release the deprotonated additive and *t*BuOH.[6] Can *t*BuOH released in the process of SED formation assist the dissociation of *t*BuOK in the presence of additive? To find out the answer, the dissociation of *t*BuOK as shown in the step-I of **P−VI** (Scheme 4) is reexamined but this time, *tert*-butoxide ion coordinated to the three *t*BuOH molecules through hydrogen bonding interactions is considered.[33] Indeed, inclusion of specific *t*BuOH−*tert*-butoxide interactions lowers the $\Delta G_{rxn}$ of step-I of **P−VI** to 5.0 kcal/mol.[34] On the basis of this new evidence, the step-IIIa of **P−VI** (Scheme 4) is modified as shown in Scheme 5 wherein, *tert*-

**Scheme 5. Modified Step-III of P−VI Involving SED in the ET Mechanism**[a]



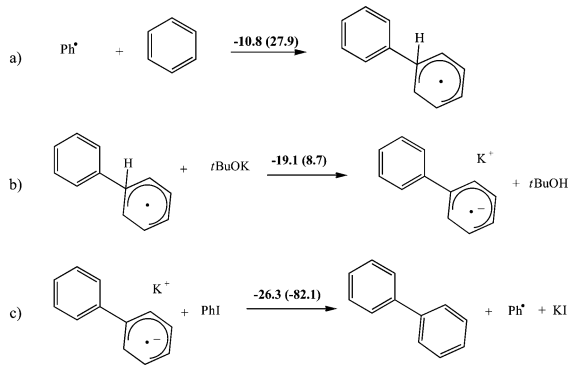

[a]Values in blue and red refer to the free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) for the pathway involving **phen** and **dmeda**, respectively. Parentheses values indicate free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) relative to separated reactants.

butoxide ion is replaced by the SED. The free energy changes for the electron transfer mechanism between the SED and **C-3** is shown in Scheme 5. The $\Delta G_{rxn}$ for the step-IIIb in **P−VI** involving **phen** and **dmeda** as an additive are −3.5 and 5.4 kcal/mol, respectively.

It is immediate apparent form the data shown in Scheme 5 that the ET step (step-IIIb) in **P−VI**, unlike the ET pathways discussed in Scheme 2, is exergonic (marginally endergonic for **SED-dmeda**). Thus, additives may play a crucial role in the ET step, by providing electron donor as well as acceptor which facilitate transfer of a single electron to the PhI. It is also noticeable that the ET occurs in the endergonic region if the free energies of reactions are compared relative to separated reactants viz. PhI, additive, *t*BuOK and SED. The organic reactions which involve ET in the endergonic regions are known and well documented in the literature.[35]

A phenyl radical generated via **P−VI** may follow the reaction course as shown in Scheme 6, which involves three steps:

**Scheme 6. Chain Mechanism Involving (a) Radical Addition (b) Deprotonation, and (c) Dissociative Electron Transfer Step**[a]




[a]Parentheses values indicate free energies of reactions ($\Delta G_{rxn}$ in kcal/mol) relative to separated reactants.

namely, addition of phenyl radical to benzene, deprotonation of phenyl cyclohexadienyl radical and the dissociative electron transfer step. The transition state for the addition of phenyl radical to benzene was located at the M062X level. The addition of phenyl radical to the benzene requires an activation barrier of 14.4 kcal/mol, and the addition is predicted to be exoergic by 10.8 kcal/mol. The resulting phenyl cyclohexadienyl radical loses its proton to *tert*-butoxide to generate biphenyl radical anion. The deprotonation of phenyl cyclohexadienyl radical by *t*BuOK to form a biphenyl radical anion is also found to be exoergic (19.1 kcal/mol). The biphenyl radical anion may act as a strong reducing agent, and is expected to transfer an electron to the phenyl iodide to provide biphenyl and phenyl radical. This dissociative electron transfer step is predicted to be exoergic by 26.3 kcal/mol. The trend of $\Delta G_{rxn}$ for the radical addition and deprotonation step as shown in Scheme 6 suggest that the reaction can proceed spontaneously toward the final product after initiation of the phenyl radical.

In summary, this study provides a reasonable explanation to the ongoing debate about the mode of phenyl radical initiation and the role of additives in the coupling reaction of iodoarene with benzene. The possible mechanism for the generation of phenyl radical at the initial stage of the reaction can be outlined in four key steps. First step of mechanism involves dissociation of *t*BuOK in the presence of additive to release additive coordinated potassium ion and *tert*-butoxide ion. The additive coordinated potassium ion is predicted to be a strong electron acceptor, and likely to form a complex with PhI through cation−$\pi$ interaction. In the subsequent step, ET can occur between SED and additive···$K^+$···PhI complex to form a radical complex, which dissociates to produce the phenyl radical, KI and additive in the final step. Overall, this study underscores the involvement of additive···$K^+$···PhI complex and SED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derived from additive as an electron acceptor and donor, respectively, in the ET mechanism, and also provides a mechanistic route for the formation of additive···$K^+$···PhI complex. Thus, the role of additives in the ET step turned out to be much broader than experimentally projected. A proposed mechanistic model for the direct arylation of arene in the presence of *t*BuOK and additive supports the experimentally established mechanism of reaction within the framework of "homolytic aromatic substitution" reaction.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02438.

Optimized Cartesian coordinates and total energies of all computed stationary points. (PDF)

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### Notes

The authors declare no competing financial interest.

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(25) The $PhI^{\bullet-}$ could not be optimized at the M062X level. The single-point energy calculations at M062X level on the geometry optimized at the M06 level was performed. See computational methods.

(26) Hayashi and co-workers ruled out the possibility of ET step, radical addition or C−H bond cleavage (deprotonation) step as a rate determining step for the coupling reactions of a variety of aryl halide and benzene mediated by the *t*BuOK and organic additives. See ref 3d.

(27) Alternatively, Tuttle and Murphy et al. have proposed the formation of benzyne intermediate to explain the coupling reaction in the absence of additives. See ref 12.

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(29) The IE of *tert*-butoxide (IE: 85 kcal/mol) cannot be directly compared with the IEs of neutral SEDs and hence, the IE of *t*BuOK is chosen as a standard electron donor for the comparison of IEs.
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