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KO*t*Bu: A Privileged Reagent for Electron Transfer Reactions?

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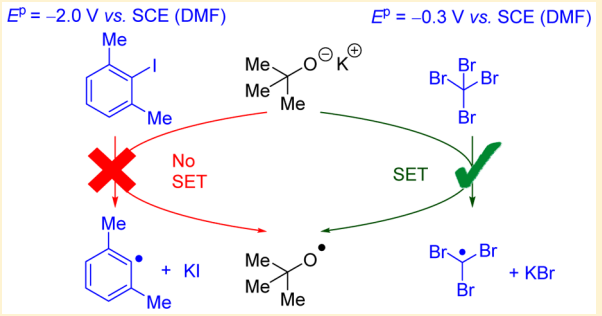
Supporting Information

ABSTRACT: Many recent studies have used KO*t*Bu in organic reactions that involve single electron transfer; in the literature, the electron transfer is proposed to occur either directly from the metal alkoxide or indirectly, following reaction of the alkoxide with a solvent or additive. These reaction classes include coupling reactions of halobenzenes and arenes, reductive cleavages of dithianes, and $S_{RN}1$ reactions. Direct electron transfer would imply that alkali metal alkoxides are willing partners in these electron transfer reactions, but the literature reports provide little or no experimental evidence for this. This paper examines each of these classes of reaction in turn, and contests the roles proposed for KO*t*Bu; instead, it provides new mechanistic information that in each case supports the *in situ* formation of organic electron donors. We go on to show that direct electron transfer from KO*t*Bu can however occur in appropriate cases, where the electron acceptor has a reduction potential near the oxidation potential of KO*t*Bu, and the example that we use is CBr_4. In this case, computational results support electrochemical data in backing a direct electron transfer reaction.



1. INTRODUCTION

Alkali metal *tert*-butoxides (KO*t*Bu, NaO*t*Bu) play key roles in numerous organic transformations, acting as powerful bases. In recent years, they have seen widespread use in transition metal-free coupling reactions of haloarenes **1** with arenes to afford biphenyls **2** (here the arene is the solvent)[1−9] or with styrenes to afford stilbenes.[2e,3a,6c] The mechanism for biaryl formation is shown in Scheme 1A.[10] Here, KO*t*Bu has a dual role: (i) acting in combination with a wide variety of organic additives to initiate the process by converting aryl halides **1** into aryl radicals **3** and (ii) deprotonating radical **4** to form the radical anion **5**; this radical anion transfers an electron to another molecule of aryl halide **1** (shown in blue), thereby propagating a chain reaction. The role of KO*t*Bu in the activation of the aryl halides **1** is the subject of wide discussion, with some authors proposing electron transfer from the *tert*-butoxide anion, alone or as part of a complex, to the aryl halide.[5e,6e,7] A related but different class of reactions arises from KO*t*Bu in DMSO as solvent. Peñéñory et al. reported[11] reductive cleavage of dithianes, for example, **6**, with KO*t*Bu in DMSO under photoactivated conditions, proposing that the reaction was triggered by direct electron transfer from KO*t*Bu to the dithiane within a charge-transfer complex (Scheme 1B). In 2015 using KO*t*Bu in DMF as solvent, Taillefer et al. reported[12] $S_{RN}1$ coupling reactions between potassium enolates **10** and aryl radicals **3**, the latter being formed from aryl halides **1**.

These reactions afforded ketones **12** as the final products (Scheme 1C). DMF was uniquely useful in accomplishing these reactions. Through computational studies, they proposed that, following deprotonation of DMF to form carbamoyl anion **8**, electron transfer occurred to the aryl halide **1**, thereby generating an aryl radical **3** and carbamoyl radical **9**, although no experimental evidence for electron transfer was presented. Whereas KO*t*Bu worked well, the corresponding sodium and lithium salts were not effective. Thus, it appears that KO*t*Bu is deeply implicated in a wide variety of electron transfer reactions, either directly or indirectly. This paper examines, in turn, the evidence in each of these cases.

2. TRANSITION METAL-FREE COUPLING REACTIONS

The coupling reactions of Scheme 1A are accomplished in the presence of different classes of organic additives. In two recent papers,[5b,f] we made a proposal, backed by experimental evidence, that these reactions generically involve reaction between KO*t*Bu and the organic additive to form an organic electron donor[8,13] and that this species, rather than a *tert*-butoxide anion, is responsible for electron transfer to aryl halides.

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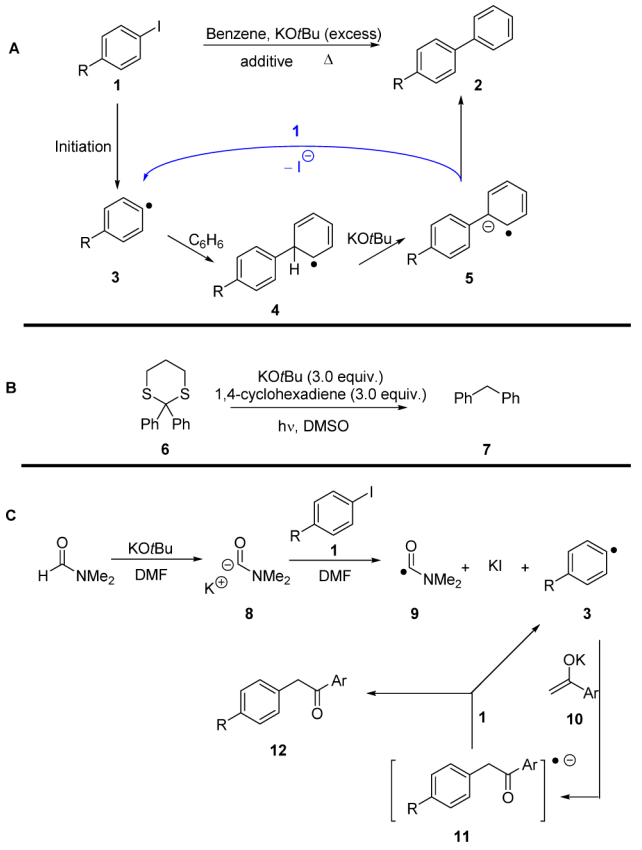
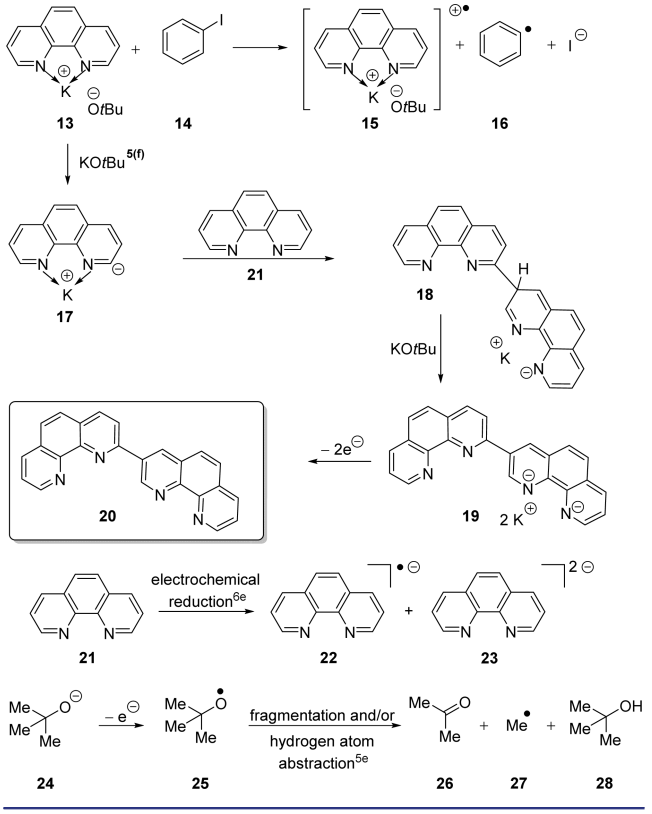
Scheme 1. KO*t*Bu Implicated in SET Processes



Scheme 2. Phenanthroline and KO*t*Bu as Precursors to Electron Donors



One of the popular organic additives in these reactions is phenanthroline **21** (Scheme 2). It was originally proposed[1b,c] that the complex **13** might directly donate an electron to an aryl iodide **14** to form complex **15**, together with an aryl radical **16** and iodide anion. Our recent paper[5b] reported that such an electron transfer reaction from KO*t*Bu–phenanthroline complex **13** to iodobenzene was endergonic by about 60 kcal mol^{-1} in benzene as solvent and hence unlikely to play a role.[7,12] Rather, we reacted KO*t*Bu with phenanthroline **21** and identified organic electron donor activity. Quenching with iodine as an electron acceptor afforded a dimer **20** in 38% yield.[5b] This implicated **19** as the *in situ*-formed electron donor to iodobenzene **14**. Since that time, papers have emerged from Wilden et al.,[5e] and from Jutand and co-workers[6e] that add to the debate. In addition, Patil has just published a computational paper[7] that examines a wide range of potential electron donors.[14]

The Jutand and co-workers[6e] paper used EPR spectroscopy to identify formation of phenanthroline-type radical anions, when phenanthroline was treated with KO*t*Bu in organic solvents. Their finding was unexpected and led them to propose that *tert*-butoxide anion **24** must be donating an electron to phenanthroline[5e] to afford the delocalized phenanthroline radical anion **22**. Such delocalized radical anions are relatively long-lived and so could be detected by EPR.

Examination of their EPR spectrum resulting from reaction of KO*t*Bu with phenanthroline in DMF as solvent (Figure 2a in that paper[6e]) shows fine structure, but the spectrum is not a symmetrical spectrum, with the possibility that more than one phenanthroline-related radical anion may be present, with superposition of the similar spectra causing the asymmetry.

We repeated the reaction of Jutand and Lei, and from EPR spectra, we confirm that radicals are indeed formed. However, given the fact that we have demonstrated that electron donor **19** is formed from phenanthroline and KO*t*Bu,[5b] we propose that, in the absence of a better electron acceptor (i.e., unlike the coupling reactions, no aryl halide is present in the EPR experiments), **19** donates an electron to phenanthroline to form two radical anions, that is, the radical anions of phenanthroline **21** and of **20**, and these species together could contribute to the reported EPR spectrum. As will be seen below, the reduction potential of phenanthroline **21** and the oxidation potential of dianion **19** are compatible with electron transfer between the species.[15]

Jutand and Lei's paper[6e] also investigated the electrochemical properties of phenanthroline. From cyclic voltammetry (CV), reduction of phenanthroline gave rise to phenanthroline dianion **23** and phenanthroline radical anion **22**. They demonstrated that **23** is a strong enough electron donor to reduce bromobenzene and that **23** can also reduce phenanthroline **21** to its radical anion **22**. They also showed that radical anion **22** was able to activate PhBr. They observed that the electrochemical reduction of phenanthroline **21** was inhibited in the presence of KO*t*Bu due to a chemical reaction between KO*t*Bu and phenanthroline. This latter finding is entirely consistent with our picture (Scheme 2, formation and reaction of **17**). The difference between our viewpoints is that our evidence points toward dianion **19** as the reactive electron donor, formed from reaction of KO*t*Bu with phenanthroline, and backed by the isolation and characterization of **20** following electron transfer.[5b]

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To gain insight, we explored the CV of **20** for comparison with phenanthroline **21**. Operating under Jutand and Lei's conditions[6e] (0.3 M nBu$_4$NBF$_4$ in DMF, 0.5 V s^{-1} scan rate, Pt wire electrode), our CV for phenanthroline **21** matched theirs (E^p = −2.05, −2.24 V vs. SCE); the dimer **20** exhibited three peaks (E^p = −1.70, −1.94, −2.19 V vs. SCE (see Figure 1).

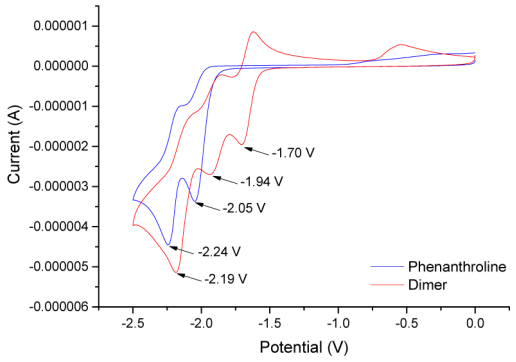


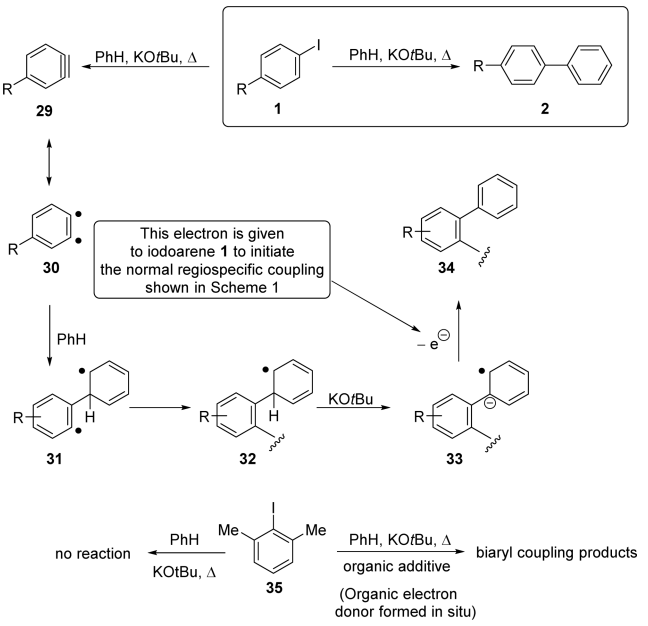
Figure 1. Cyclic voltammograms of phenanthroline **21** and dimer **20**.

Calibration with Fc/Fc$^+$ showed that these reductions of **20** corresponded, respectively, to 1e$^-$, 1e$^-$, and 2e$^-$, with all steps being reversible (see SI for analysis). Considering the first and second potentials for reduction of dimer **20**, respectively, associated with the formation of the radical anion (structure not shown here) and dianion **19**, both these species are significantly more reducing than all our previous neutral organic electron donors, which easily reduce aryl iodides (ArI, E^p = −2.0 V vs. SCE in DMF), and hence are competent electron donors to achieve the previously reported coupling reactions of iodoarenes with arenes.[13] Importantly, Jutand and Lei record the oxidation potential of *tert*-butoxide anion from KO*t*Bu at +0.10 V vs. SCE in DMF,[6e] and they show by cyclic voltammetry that it does not directly reduce aryl halides. This would also make it very unlikely to reduce phenanthroline **21** or its derived complex **13**. In contrast, the close matching of potentials for oxidation of dianion **19** and for reduction of phenanthroline **21** indicates that reduction of phenanthroline to its radical anion by dianion **19** should be possible, thereby forming two phenanthroline-related radical anions, and providing a rationalization for the EPR spectrum reported in the Jutand and Lei paper.[6e]

Although their paper proposes electron transfer from *tert*-butoxide anion to phenanthroline thereby affording a reducing species, in fact no evidence is present to support electron transfer specifically from *tert*-butoxide anion.

The other paper that gives a different mechanistic picture than ours on the coupling reactions is presented by Wilden et al.,[5e] who employ KO*t*Bu with phenanthroline **21** to effect couplings but who also observed coupling in the absence of phenanthroline. The authors attributed this latter phenomenon to electron transfer from KO*t*Bu directly to the aryl iodide, when conducted in the absence of phenanthroline; in contrast, when phenanthroline is present, they propose electron transfer from *tert*-butoxide anion to phenanthroline. Coupling in the presence of KO*t*Bu and in the absence of additives had previously been reported by Bisai et al.[3g,4e] We went on to propose that, while organic additives in the presence of KO*t*Bu form organic electron donors that convert aryl iodides to aryl radicals,[5b,f] a second and more sluggish activation can occur in the background in the absence of additives via benzyne **29** (Scheme 3). (We have repeated the reaction under the Wilden conditions in the absence of phenanthroline and find

Scheme 3. Evidence for Initiation by Benzyne[5b]



unambiguous evidence for benzyne formation. See SI file.[16]) Benzyne can function as a diradical, **30**, that initiates the coupling reactions by occasionally adding to the benzene solvent to form distal diradical **31**.[5f] Some of these radicals react further (e.g., by addition of the reactive aryl radical to a further molecule of benzene) to form arylcyclohexadienyl radical **32**, and this suffers deprotonation by KO*t*Bu to afford electron donor **33**, which donates an electron to iodoarene **1** to start the much faster cycle shown in Scheme 1A leading to biaryl **2**. When the propagation cycle in Scheme 1A is much faster than the benzyne initiation, the isolated products arise overwhelmingly from the reaction cycle in Scheme 1A and show apparent site-specific arylation at the iodine-bearing carbon of **1**. This is in line with observed outcomes from these coupling reactions.

An important piece of evidence to support our benzyne proposal was that reaction of 2,6-dimethyliodobenzene **35** in benzene, in the presence of KO*t*Bu but in the absence of any organic additive, gave no coupled product.[5f] For this substrate, formation of benzyne would not be possible. However, in the presence of a range of organic additives (that give rise to organic electron donors *in situ* on reaction with KO*t*Bu), coupling is seen with substrate **35**.

A number of interesting observations from Wilden et al. appear to provide support for their proposals, and so we address these. One of the outcomes that would arise from conversion of *tert*-butoxide ion **24** to *tert*-butoxyl radical **25** would be the known fragmentation of this radical to acetone **26** and methyl radical **27** (Scheme 2).[17]

To model this, Wilden added 1,3-dinitrobenzene **36** (Scheme 4) to a dilute THF solution of an equimolar mixture of potassium *tert*-pentoxide (an analogue of KO*t*Bu) and phenanthroline **21**, and this resulted in an intense purple color. This was regarded as a positive Janovsky test, which reports the presence of an enolizable ketone or aldehyde.[18] This result was taken as evidence for the presence of a significant amount of

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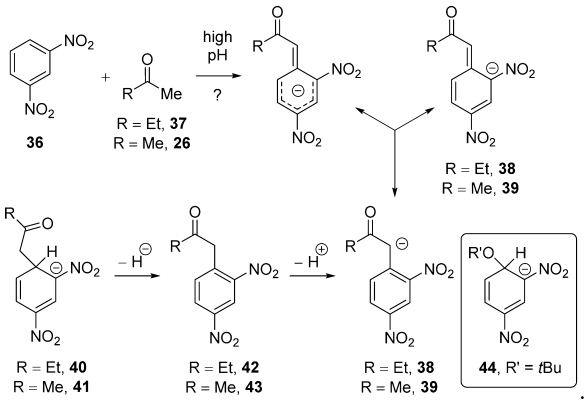
Scheme 4. Mechanistic Considerations in the Formation of Janovsky Adducts



butanone **37**, which was proposed to result from the collapse of a *tert*-pentoxyl radical, itself arising from the transfer of an electron from the *tert*-pentoxide anion (analogous to what is shown for *tert*-butoxide anion **24** in Scheme 2) to phenanthroline.

It was proposed that, under alkaline conditions, the enolate of butanone adds to 1,3-dinitrobenzene **36** to give a colored adduct that was represented as **38** (Scheme 4).[5e] In alkaline conditions (high pH), if any ketone were present, the product resulting from the addition of the same enolate of butanone to 1,3-dinitrobenzene would initially be adduct **40**, and this would require oxidation to afford **38**.[18]

We now performed a number of experiments. Experiment a, when KO*t*Bu (1 equiv), acetone (1 equiv), and 1,3-dinitrobenzene (1 equiv) were combined in THF, a purple color and UV–vis absorption at 552 nm resulted (Figure 2, blue trace). The result was always the same, regardless of the order of addition (see SI for full details). Previous NMR studies by Fyfe and Foster[18d] disclosed the ^{1}H NMR spectrum of adduct **41** when treating 1,3-dinitrobenzene in acetone solution with NaOMe, and current NMR studies mirrored those findings (See Supporting Information), so this is the normal Janovsky test outcome.

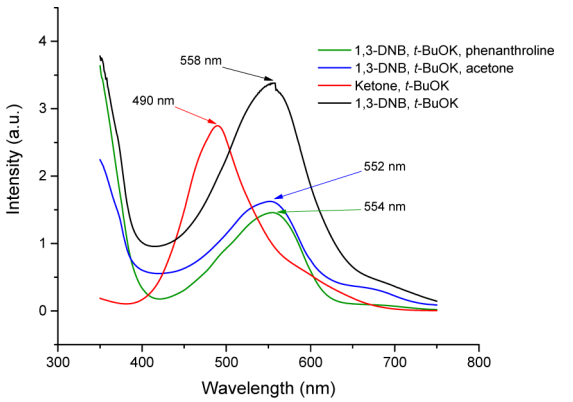


Figure 2. UV–visible spectroscopy of Janovsky tests.

Experiment b, when we dissolved phenanthroline (1 equiv) and KO*t*Bu (1 equiv) in THF and stirred at room temperature for 2 h and then 1,3-dinitrobenzene **36** (1 equiv) was added, a purple coloration was again observed and an absorption at 554 nm detected (Figure 2, green trace).

To probe further, we prepared ketone **43** by an independent route. In experiment c, when this ketone (1 equiv) was dissolved in THF and KO*t*Bu (1 equiv) was added, a purple color was again seen. However, this color was slightly different than in the previous cases, and the UV–vis spectrum of the solution showed a different absorption, at 490 nm (red trace), attributable to **39**, rather than the 552–554 nm previously seen. This clearly demonstrated that the purple coloration mentioned above, resulting from the reaction of KO*t*Bu with phenanthroline mixture in experiment b was not due to the presence of adduct **39**.

Finally, we ran a test in the absence of acetone **26** and in the absence of phenanthroline **21**: in experiment d, KO*t*Bu (1 equiv) was dissolved in THF and 1,3-dinitrobenzene **36** (1 equiv) was added. The result was striking; a purple color was obtained and a UV–vis absorption at 558 nm (black trace in Figure 2) was detected. This result was indistinguishable from that when a ketone was present in the mixture and indicates that observation of a purple color in the Janovsky test is not sufficient to confirm the presence of a ketone. Having confirmed that the species giving rise to a purple color in experiment b when KO*t*Bu, phenanthroline, and 1,3-dinitrobenzene are simply mixed cannot be **39**, we propose **44** as a more likely candidate. Indeed, in the absence of added acetone, instantaneous addition of alkoxides to 1,3-dinitrobenzene **36** was observed by ^{1}H NMR, and this was accompanied by the same purple color (See Supporting Information).

Wilden's paper had also reported that when a mixture of phenanthroline and KO*t*Bu was prepared and observed by NMR, the intensity of the *t*Bu signal dramatically decreased almost immediately, indicating that KO*t*Bu was rapidly consumed in a reaction. In our hands, phenanthroline and KO*t*Bu were mixed in THF-d_8 at room temperature under an inert atmosphere for 2 h, and then the mixture was analyzed directly by ^{1}H NMR (Figure 3). Importantly, and in contrast to the reported observations, we saw no collapse of the *tert*-butoxide signal, and the two reagents were unchanged.

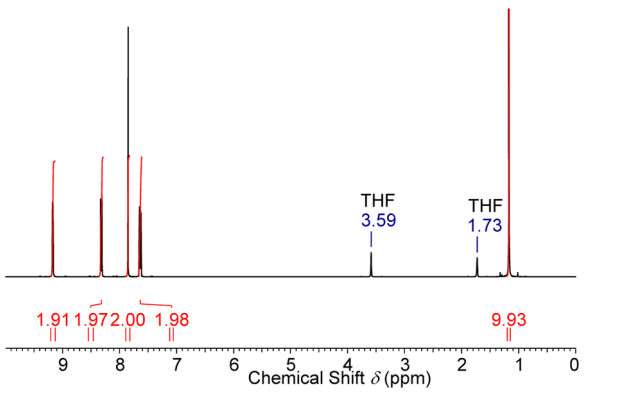


Figure 3. ^{1}H NMR of phenanthroline and KO*t*Bu (1:1) in THF-d_8 after 2 h at room temperature, showing unchanged reagents and no collapse of the *tert*-butoxide peak at 1.2 ppm.

Examination of the spectrum published by Wilden et al.[5e] shows a singlet signal at 7.28 ppm that could be due to residual $CHCl_3$. If this arose from use of $CDCl_3$ as NMR solvent, we considered that this would be potentially reactive to KO*t*Bu.[19] Indeed, when we mixed phenanthroline and KO*t*Bu in THF at room temperature for 2 h and then diluted with $CDCl_3$, the ^{1}H

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NMR showed almost total collapse of the *tert*-butoxide signal (Figure 4).

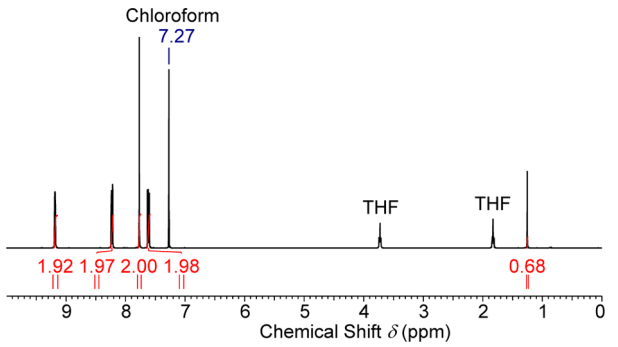


Figure 4. ^{1}H NMR of phenanthroline and KO*t*Bu in THF after the addition of $CDCl_3$ as the NMR solvent, showing collapse of the *tert*-butoxide peak.

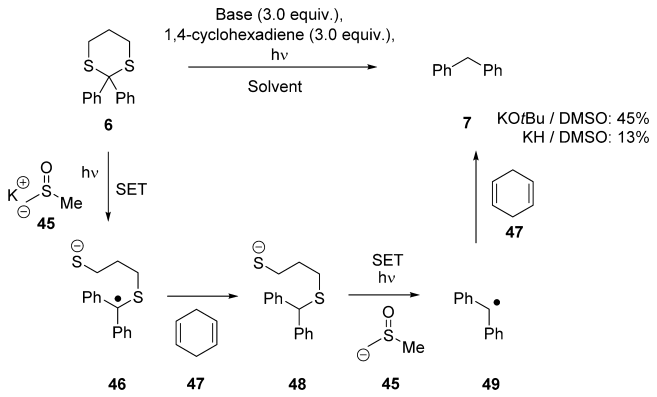
Wilden further noted that analyzing a mixture of potassium pentoxide and phenanthroline by mass spectrometry suggests that butanone is a major component of the reaction mixture. However, since the mixture was handled in THF and since THF has the same molecular formula as butanone, reassurance would be needed about this experiment. Moreover, DiRocco reports[20] that the fragmentation of *tert*-pentoxyl radical does not afford butanone together with the methyl radical in significant amounts but rather gives rise to acetone and the (more stable) ethyl radical.

Hence it is seen that these reports do not provide convincing evidence of any direct electron transfer from the butoxide anion of KO*t*Bu.

3. REDUCTIVE FRAGMENTATION OF DITHIANES

Quite aside from the coupling reactions, potassium *tert*-butoxide has also been proposed as an electron donor in a number of other reactions, among them the photoinduced cleavage of dithianes reported by Peñéñory et al. (Scheme 5).[11]

Scheme 5. Photo-induced Cleavage Reaction of 2,2-Diphenyl-1,3-dithiane, 6



In this reaction, a charge-transfer complex had been reported as characterized by UV−vis spectroscopy between KO*t*Bu and the dithiane, and so this appeared to be the best documented case where electron transfer from *tert*-butoxide might be observed, albeit with photochemical assistance. Indeed, when a solution of 2,2-diphenyl-1,3-dithiane, **6**, in DMSO was treated by us with KO*t*Bu and 1,4-cyclohexadiene and exposed to UV irradiation, diphenylmethane **7** was the major product (45% isolated yield), in agreement with the literature findings.

The reported stable charge transfer complex between dithiane **6** and KO*t*Bu had been assigned to a peak at 467 nm in the UV−visible spectrum.[11] On mixing dithiane **6** in DMSO with KO*t*Bu, we also observed a similar absorption at 466 nm (Figure 5, red trace). However, in view of our

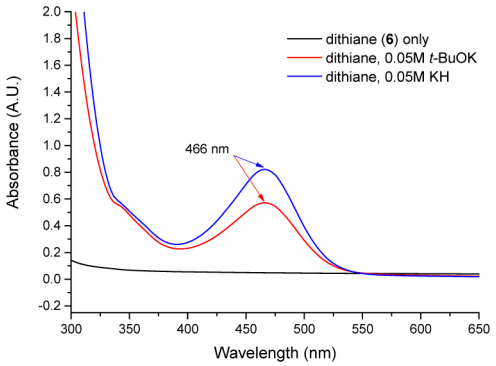


Figure 5. UV−visible spectra of 2,2-diphenyl-1,3-dithiane, **6**, in DMSO without base (black trace), of **6** in DMSO with KO*t*Bu (red trace), and of **6** in DMSO with KH as base (blue trace).

misgivings about the role of KO*t*Bu as a single electron donor, we considered whether there might be an alternative role for the KO*t*Bu. Repetition of the reaction using KH as the base rather than KO*t*Bu also led to the isolation of **7**, albeit in a lower yield of 13%.[21] Most interestingly, the UV−vis spectrum of the mixture of **6**, DMSO, and KH also showed an absorption at 466 nm, while a mixture of **6**, DMF, and KO*t*Bu gave no such absorption (See SI for UV−vis traces). These results suggest that rather than a charge transfer complex between dithiane **6** and KO*t*Bu, a charge transfer complex between dithiane **6** and the dimsyl salt **45** is the likely source of the UV absorptions measured. Therefore, even under photoactivated conditions, evidence supporting direct electron transfer from KO*t*Bu is lacking.

4. $S_{RN}1$ REACTIONS IN DMF

Recently, a number of authors have proposed electron transfer reactions when KO*t*Bu was reacted in DMF with various types of substrate. In particular, the team of Yan suggested that a complex of KO*t*Bu with DMF could act as an electron donor to another molecule of DMF.[22] The most recent was an intriguing study by Taillefer et al. which investigated $S_{RN}1$ reactions of aryl radicals **3** with potassium enolates **10** in the absence of photoexcitation (Scheme 1C).[12] They found that DMF was unique among solvents in promoting these reactions. It is known that KO*t*Bu can deprotonate DMF,[23] but their proposal was that the anion of the resulting salt **8** behaves as an electron donor to aryl halides, affording the corresponding carbamoyl radical **9** and an aryl radical **3**. Radical **3** then combines with enolate **10** to give radical anion **11**. Electron transfer to another molecule of **1** continues the chain process and affords product **12**. Their computational studies show that their proposal follows an energetically viable pathway, in which potassium ions play a special role, although there is no experimental support for their proposal from anion **8**.[24]

Our experience with probing electron transfer reactions using substrate **35** attracted us to test for an electron transfer pathway using DMF and KO*t*Bu (2 equiv) in benzene under previously

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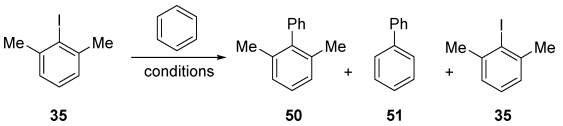
tested conditions. This substrate cannot undergo side-reactions via formation of benzyne but is converted to the corresponding aryl radical following electron transfer. This aryl radical is hindered and undergoes competing signature reactions, namely, (i) addition to benzene, leading to substituted biphenyl **50** (see drawing above Table 1) and (ii) hydrogen abstraction from benzene affording a phenyl radical that leads to the volatile *m*-xylene, as well as biphenyl **51**, where the ratio of **50**/**51** is ca. 1:3.5.[5f,8] This substrate has given very valuable mechanistic information in studies to date.

Table 1. Comparison of Reactivity of DMF and Diformamides in Coupling Reactions That Use KO*t*Bu as Base



35 50 51 35

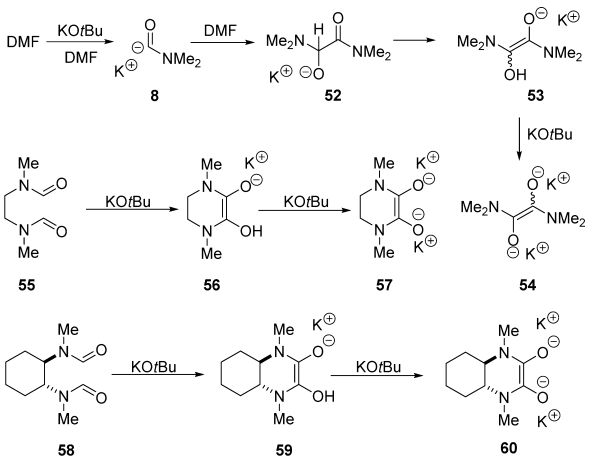
entry	additive	**50** + **51**[d] (%)
1[a]	none	0.5
2[a]	DMF (1%[c])	2.6
3[a]	DMF (0.1 mmol)	0.6
4[a]	**55** (0.05 mmol)	8.0
5[a]	**58** (0.05 mmol)	16.1
6[b]	DMF (1%[c])	0.4
7[b]	**55** (0.5%[c])	19.6
8[b]	**58** (0.5%[c])	31.6

[a]Substrate **35** (0.5 mmol), 1 mmol KO*t*Bu, benzene as solvent, 130 °C, 18 h. [b]Reaction at 110 °C, 4 h. [c]Relative to benzene (v/v) as solvent. [d]As determined by internal standard (^{1}H NMR, see SI).

With this substrate, when the reaction was conducted in the absence of DMF, only a barely detectable amount of biphenyls was seen (entry 1). In contrast, using DMF (1% v/v wrt the solvent benzene) and KO*t*Bu (2 equiv) for 18 h at 130 °C, coupling was observed to afford a mixture of biphenyls **50** and **51**, in their characteristic ratio, in a small, but measurable amount (entry 2). This clearly indicated that an electron donor was being produced from the reaction involving KO*t*Bu and DMF.

As mentioned, Scheme 1C is the current working hypothesis proposed by Taillefer for the reductions observed with KO*t*Bu in DMF. However, in Scheme 6, we suggest an alternative electron donor. The DMF-derived anion **8** is known to act as a nucleophile;[23] if it attacks a neutral DMF molecule, this forms anion **52**. Proton transfer affords the enolate **53**, which is a candidate electron donor. Alternatively, further deprotonation should afford the dianion **54**, an even better electron donor.[8] These species could then initiate electron transfer to aryl iodides to form aryl radicals, after which an $S_{RN}1$ chain reaction would follow. Checking the literature shows that reaction of carbamoyl anions with formamides has already been reported, affording dianions similar to those shown in Scheme 6.[25]

Scheme 6. Forming Electron Donors from Formamides



To distinguish between the two proposals for DMF, we made use of the effective concentration of electron donor for initiating the coupling of iodoarenes to benzene. Our plan was to compare the abilities of **55** with DMF in triggering the reactions in benzene as solvent. Specifically, we would compare (i) the reaction in the presence of a fixed concentration of **55** with (ii) the reaction with *twice* this concentration of DMF. If the acyl anion **8** were the electron donor, then a fixed concentration, *x*, of **55** might work equally as well as twice that concentration, 2*x*, of DMF, since equal concentrations of formyl groups would be present in both reactions. But if the electron transfer agents are **53** or **54** (when DMF is used), which requires a dimerization to form an organic electron donor, then the fixed concentration of additive **55** should work much better than twice that concentration of DMF, since the positioning of the formyl groups [1,6] to each other in **55** would give a massive advantage for formation of such an electron donor by intramolecular reaction in terms of effective molarity, compared with intermolecular dimerization of two molecules of DMF. Formation of higher concentrations of electron donors would lead to higher conversion of substrate **35** over a defined time period.

When the amount of DMF was lowered (0.1 mmol, 0.2 equiv, Table 1, entry 3), a trace amount of biaryls was formed (0.6%). However, under the same reaction conditions using linear diformamide **55** (0.05 mmol, 0.1 equiv., entry 4), a very clear increase in the amount of biaryls formed was seen (8.0%). If our proposal about the cyclization of additive **55** is correct, then introducing the more conformationally restricted diformamide **58** should be even more successful, and this was indeed the case, providing 16.1% of biaryl products (entry 5) and reacting through electron donors **59** or **60**. At 110 °C for 4 h and using an increased amount of additive (1% DMF, 0.5% **55** or **58**) a similar trend of an increased quantity of biaryls was observed when switching from DMF to linear diformamide **55** (entries 6 and 7). A further increase in biaryl yield was observed when cyclic diformamide **58** was used (entry 8).

We explored computationally our proposed reactions between substrate **35** and (*Z*)-**54**, (*E*)-**54**, and **60** (see SI file for details). These reactions showed very achievable barriers (ΔG^*) of 30.2, 23.6, and 28.1 kcal/mol with the solvent benzene modeled as a continuum. [The M062X functional[26,27] was used with the 6-311++G(d,p) basis set[28−32] on all atoms, except for the iodine. Iodine was modeled with the MWB46 relativistic pseudopotential and associated basis set.[33] All calculations were carried out using the C-PCM implicit solvent model[34,35] as implemented in Gaussian09.[36]] The combined experimental and computational results provide strong evidence in support of the ability of formamides to dimerize in the presence of KO*t*Bu to form electron donors and hence provides an alternative to the proposals of Taillefer.

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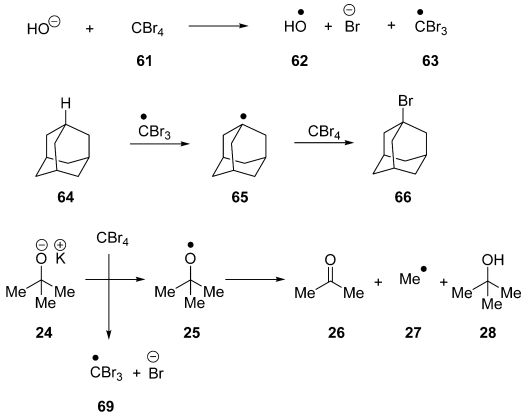
5. CAN KO*t*Bu EVER ACT AS A DIRECT ELECTRON DONOR?

The reluctance of KO*t*Bu to act as electron donor to aryl iodides in section 2 arises from the mismatch of the redox potentials. As mentioned above, aryl iodides have reduction potentials at −2.0 V vs. SCE, while the oxidation potential of KO*t*Bu is at +0.10 V vs. SCE in DMF.[6e] This does not mean that KO*t*Bu would never act as electron donor. The search for a suitable system to demonstrate this phenomenon revealed a series of studies by Schreiner and Fokin et al. on the reaction between KOH and CBr_4, **61**, in the presence of adamantane and a phase transfer agent, where selective bromination at the methine positions of adamantane was observed (Scheme 7).[37]

Scheme 7. Hydroxide[37] and *tert*-Alkoxides as Electron Donors to CBr_4



This was explained by electron transfer from hydroxide to CBr_4, to afford a bromide anion and a tribromomethyl radical, **63**. This radical is highly selective in abstracting the methine hydrogen to form the 1-adamantyl radical, **65**, which in turn abstracted a Br atom from CBr_4 to form 1-bromoadamantane **66**. Given that the reduction potential of CBr_4 is known in DMF (−0.31 V vs. SCE)[38] and that it represents a much more accessible reduction potential for *tert*-butoxide anion in KO*t*Bu, we undertook a study of the reaction of tertiary alkoxide **24** with CBr_4 under similar conditions to Schreiner, except that we did not add a phase transfer salt. Reaction of KO*t*Bu with CBr_4 in DCM, following the conditions of Schreiner, selectively afforded 1-bromoadamantane, **66**, in line with his selective reaction where he had used potassium hydroxide, KOH.[39] Our experiments were backed by computation, which showed that electron transfer from KO*t*Bu to CBr_4 featured a very achievable barrier of 23.3 kcal mol^{-1}. [The M062X functional[26,27] was used with the 6-311++G(d,p) basis set[28−32] on all atoms, except for the bromine. Bromine was modeled with the MWB28 relativistic pseudopotential and associated basis set.[33] All calculations were carried out using the C-PCM implicit solvent model[34,35] as implemented in Gaussian09.[36]] This supports the idea that KO*t*Bu can undergo electron transfer to an electrophile with a suitable reduction potential, such as CBr_4.

In summary, reports on the unique capacity of KO*t*Bu to cause unusual reactions have appeared regularly in the recent literature: (i) In the cases of transition metal-free coupling reactions, where the reactions are conducted in an arene solvent, to date there is no evidence to support KO*t*Bu acting directly as an electron donor to an aryl halide. This finding accords both with electrochemical information on the oxidation potential of KO*t*Bu and with computational evidence, as well as with our published lack of reaction between KO*t*Bu and 2-iodo-*m*-xylene, **35**.[5b,f] (ii) Reaction of KO*t*Bu with DMSO leads to the dimsyl anion, which acts as an electron donor to appropriate substrates.[40] (iii) Reaction of KO*t*Bu with DMF affords electron transfer activity also, but here, our experiments indicate a role for a dimerization of formamides to afford novel and strong organic electron donors.[25] Thus, in all these cases, it is the behavior of KO*t*Bu as a base that gives access to these electron transfer reactions. The greater basicity of the KO*t*Bu over its sodium and lithium counterparts likely results from the difference in the metal−oxygen bonding in these salts.[14]

Finally, in pursuit of likely examples of direct electron transfer from KO*t*Bu, we mirrored earlier experiments of Schreiner, who had used KOH with CBr_4. The substrate CBr_4 has a reduction potential near to the oxidation potential of KO*t*Bu and, in the presence of adamantane as a reporter molecule, leads to 1-bromoadamantane via the generation of tribromomethyl radicals. Computational studies show that in this case, electron transfer from KO*t*Bu is the likely source of these radicals. This study does address a number of cases where KO*t*Bu has been associated with electron transfer, but we are now investigating yet further cases[41] and will report on those in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b03282.

Experimental procedures including the synthesis of substrates, important NMR spectra, cyclic voltammetry and EPR studies, and computational coordinates (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Yanagisawa, S.; Ueda, K.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 4673−4676. (b) Sun, C.-L.; Li, H.; Yu, D.-G.; Yu, M.; Zhou, X.; Lu, X.-Y.; Huang, K.; Zheng, S.-F.; Li, B.-J.; Shi, Z.-J. *Nat. Chem.* **2010**, *2*, 1044−1049. (c) Shirakawa, E.; Itoh, K.-I.; Higashino, T.; Hayashi, T. *J. Am. Chem. Soc.* **2010**, *132*, 15537−15539. Note: this paper also demonstrated effective reactions with NaO*t*Bu. (d) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 16737−16740.

(2) (a) Sun, C. L.; Gu, Y.-F.; Wang, B.; Shi, Z.-J. *Chem. - Eur. J.* **2011**, *17*, 10844−10847. (b) Sun, C. L.; Gu, Y.-F.; Huang, W.-P.; Shi, Z.-J.

DOI: 10.1021/jacs.6b03282
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

Chem. Commun. **2011**, *47*, 9813−9815. (c) Shirakawa, E.; Zhang, X.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 4671−4674. (d) Yong, G.-P.; She, W.-L.; Zhang, Y.-M.; Li, Y.-Z. *Chem. Commun.* **2011**, *47*, 11766−11768. (e) Rueping, M.; Leiendecker, M.; Das, A.; Poisson, T.; Bui, L. *Chem. Commun.* **2011**, *47*, 10629−10631. (f) Qiu, Y.; Liu, Y.; Yang, K.; Hong, W.; Li, Z.; Wang, Z.; Yao, Z.; Jiang, S. *Org. Lett.* **2011**, *13*, 3556−3559. (g) Roman, D. S.; Takahashi, Y.; Charette, A. B. *Org. Lett.* **2011**, *13*, 3242−3245.

(3) (a) Shirakawa, E.; Hayashi, T. *Chem. Lett.* **2012**, *41*, 130−134. (b) Liu, H.; Yin, B.; Gao, G. Z.; Li, Y.; Jiang, H. *Chem. Commun.* **2012**, *48*, 2033−2035. (c) Chen, W.-C.; Hsu, Y.-C.; Shih, W.-C.; Lee, C.-Y.; Chuang, W.-H.; Tsai; Chen, P. P.-Y.; Ong, T.-G. *Chem. Commun.* **2012**, *48*, 6702−6704. (d) Pieber, B.; Cantillo, D.; Kappe, O. C. *Chem. - Eur. J.* **2012**, *18*, 5047−5055. (e) Bhakuni, B. S.; Kumar, A.; Balkrishna, S. J.; Sheikh, J. A.; Konar, S.; Kumar, S. *Org. Lett.* **2012**, *14*, 2838−2841. (f) Ng, Y. S.; Chan, C. S.; Chan, K. S. *Tetrahedron Lett.* **2012**, *53*, 3911−3914. (g) De, S.; Ghosh, S.; Bhunia, S.; Sheikh, J. A.; Bisai, A. *Org. Lett.* **2012**, *14*, 4466−4469. (h) Tanimoro, K.; Ueno, M.; Kirihata, M.; Tanimori, S. *J. Org. Chem.* **2012**, *77*, 7844−7849. (i) Wu, Y.; Wong, S. M.; Mao, F.; Chan, T. L.; Kwong, F. Y. *Org. Lett.* **2012**, *14*, 5306−5309.

(4) (a) Zhao, H.; Shen, J.; Guo, J.; Ye, R.; Zeng, H. *Chem. Commun.* **2013**, *49*, 2323−2325. (b) Buden, M. E.; Guastavino, J. F.; Rossi, R. A. *Org. Lett.* **2013**, *15*, 1174−1177. (c) Liu, W.; Tian, F.; Wang, X.; Yu, H.; Bi, Y. *Chem. Commun.* **2013**, *49*, 2983−2985. (d) Kumar, A.; Bhakuni, B. S.; Prasad, Ch. D.; Kumar, S.; Kumar, S. *Tetrahedron* **2013**, *69*, 5383−5392. (e) De, S.; Mishra, S.; Kakde, B. N.; Dey, D.; Bisai, A. *J. Org. Chem.* **2013**, *78*, 7823−7844. (f) Sharma, S.; Kumar, M.; Kumar, V.; Kumar, N. *Tetrahedron Lett.* **2013**, *54*, 4868−4871. (g) Dewanji, A.; Murarka, S.; Curran, D. P.; Studer, A. *Org. Lett.* **2013**, *15*, 6102−6105.

(5) (a) Wu, Y.; Choy, P. Y.; Kwong, F. Y. *Org. Biomol. Chem.* **2014**, *12*, 6820−6823. (b) Zhou, S.; Anderson, G. M.; Mondal, B.; Doni, E.; Ironmonger, V.; Kranz, M.; Tuttle, T.; Murphy, J. A. *Chem. Sci.* **2014**, *5*, 476−482. (c) Guastavino, J. F.; Buden, M. E.; Rossi, R. A. *J. Org. Chem.* **2014**, *79*, 9104−9111. (d) Bhakuni, B. S.; Yadav, A.; Kumar, S.; Patel, S.; Sharma, S.; Kumar, S. *J. Org. Chem.* **2014**, *79*, 2944−2954. (e) Cuthbertson, J.; Gray, V. J.; Wilden, J. D. *Chem. Commun.* **2014**, *50*, 2575−2578. (f) Zhou, S.; Doni, E.; Anderson, G. M.; Kane, R. G.; MacDougall, S. W.; Ironmonger, V. M.; Tuttle, T.; Murphy, J. A. *J. Am. Chem. Soc.* **2014**, *136*, 17818−17826. (g) Ghosh, D.; Lee, J.-Y.; Liu, C.-Y.; Chiang, Y.-H.; Lee, H. M. *Adv. Synth. Catal.* **2014**, *356*, 406−410. (h) Zheng, X.; Yang, L.; Du, W.; Ding, A.; Guo, H. *Chem. - Asian J.* **2014**, *9*, 439−442. Bhakuni, B. S.; Yadav, A.; Kumar, S.; Kumar, S. *New J. Chem.* **2014**, *38*, 827−836.

(6) (a) Liu, W.; Xu, L. G. *Tetrahedron* **2015**, *71*, 4974−4981. (b) Liu, W.; Liu, R.; Bi, Y. *Tetrahedron* **2015**, *71*, 2622−2628. (c) Doni, E.; Zhou, S.; Murphy, J. A. *Molecules* **2015**, *20*, 1755−1774. (d) Masters, K.-S. *RSC Adv.* **2015**, *5*, 29975−29986. (e) Yi, H.; Jutand, A.; Lei, A. *Chem. Commun.* **2015**, *51*, 545−548.

(7) Patil, M. *J. Org. Chem.* **2016**, *81*, 632−639.

(8) Barham, J. P.; Coulthard, G.; Kane, R. G.; Delgado, N.; John, M. P.; Murphy, J. A. *Angew. Chem., Int. Ed.* **2016**, *55*, 4492−4496.

(9) Sun, C. L.; Gu, Y.-F.; Wang, B.; Shi, Z.-J. *Chem. - Eur. J.* **2011**, *17*, 10844−10847.

(10) Studer, A.; Curran, D. P. *Angew. Chem., Int. Ed.* **2011**, *50*, 5018−5022.

(11) Oksdath-Mansilla, G.; Argüello, J. E.; Peñéñory, A. B. *Tetrahedron Lett.* **2013**, *54*, 1515−1518.

(12) Pichette Drapeau, M.; Fabre, I.; Grimaud, L.; Ciofini, I.; Ollevier, T.; Taillefer, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 10587−10591.

(13) (a) Murphy, J. A.; Khan, T. A.; Zhou, S.-Z.; Thomson, D. W.; Mahesh, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1356−1360. (b) Murphy, J. A.; Zhou, S.-Z.; Thomson, D. W.; Schoenebeck, F.; Mahesh, M.; Park, S. R.; Tuttle, T.; Berlouis, L. E. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5178−5183. (c) Murphy, J. A.; Garnier, J.; Park, S. R.; Schoenebeck, F.; Zhou, S.-Z.; Turner, A. T. *Org. Lett.* **2008**, *10*, 1227−1230. (d) Farwaha, H. S.; Bucher, G.; Murphy, J. A. *Org. Biomol. Chem.* **2013**, *11*, 8073−8081. (e) Hanson, S. S.; Doni, E.; Traboulsee, K. T.; Coulthard, G.; Murphy, J. A.; Dyker, C. A. *Angew. Chem., Int. Ed.* **2015**, *54*, 11236−11239.

(14) One facet that Patil's paper[7] addresses is a possible special role for potassium ions in assisting the activation of aryl iodides. This may explain why KO*t*Bu, is usually more successful than NaO*t*Bu in these activation reactions. See also ref 12.

(15) Following ref 6b, our electrochemistry experiments were conducted with tetralkylammonium counterions, not potassium cations; potassium complex **13** is likely to be a little more easily reducible than **21**.

(16) Our SI file shows addition of the elements of *t*BuOH to benzyne intermediates. For discussions of such reactions, see: Dong, Y.; Lipschutz, M. I.; Tilley, T. D. *Org. Lett.* **2016**, *18*, 1530−1533. Roberts, J. D.; Vaughan, W. C.; Carlsmith, L. A.; Semenow, D. A. *J. Am. Chem. Soc.* **1956**, *78*, 611−614. One reviewer has raised the question whether the immediate KO*t*Bu adduct of the benzyne, that is, an *o*-butoxyarylpotassium, might act as an electron donor. This is an interesting question because aryl Grignard reagents can sometimes act as electron donors to aryl halides. See Uchiyama, N.; Shirakawa, E.; Hayashi, T. *Chem. Commun.* **2013**, *49*, 364−366.

(17) (a) Williams, A. L.; Oberright, E. A.; Brooks, J. W. *J. Am. Chem. Soc.* **1956**, *78*, 1190−1193. (b) Thelen, M.-A.; Felder, P.; Frey, J. G.; Huber, J. R. *J. Phys. Chem.* **1993**, *97*, 6220−6225.

(18) (a) King, T. J.; Newall, C. E. *J. Chem. Soc.* **1962**, 367−369. (b) Foster, R.; Mackie, R. K. *Tetrahedron* **1962**, *18*, 1131−1135. (c) Pollitt, R. J.; Saunders, B. C. *J. Chem. Soc.* **1965**, 4615−4628. (d) Fyfe, C. A.; Foster, R. *Chem. Commun.* **1967**, 1219.

(19) von E. Doering, W.; Hoffmann, A. K. *J. Am. Chem. Soc.* **1954**, *76*, 6162−6165.

(20) Di Rocco, D. A.; Dykstra, K.; Krska, S.; Vachal, P.; Conway, D. V.; Tudge, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 4802−4806.

(21) Full conversion of dithiane **6** was observed, and a complex mixture was produced, from which the product was isolated.

(22) (a) Wei, W.-T.; Dong, X.-J.; Nie, S.-Z.; Chen, Y.-Y.; Zhang, X.-J.; Yan, M. *Org. Lett.* **2013**, *15*, 6018−6021. (b) Chen, Y.-Y.; Zhang, X.-J.; Yuan, H.-M.; Wei, W.-T.; Yan, M. *Chem. Commun.* **2013**, *49*, 10974−10976. (c) Wang, W.-J.; Zhao, X.; Tong, L.; Chen, J.-H.; Zhang, X.-J.; Yan, M. *J. Org. Chem.* **2014**, *79*, 8557−8565. (d) Wei, W.-T.; Dong, X.-J.; Nie, S.-Z.; Chen, Y.-Y.; Zhang, X.-J.; Yan, M. *Org. Lett.* **2013**, *15*, 6018−6021.

(23) (a) Reeves, J. T.; Lorenc, C.; Camara, K.; Li, Z.; Lee, H.; Busacca, C. A.; Senanayake, C. H. *J. Org. Chem.* **2014**, *79*, 5895−5902 and references therein. (b) Reeves, J. T.; Tan, Z.; Herbage, M. A.; Han, Z. S.; Marsini, M. A.; Li, Z.; Li, G.; Xu, Y.; Fandrick, K. R.; Gonnella, N. C.; Campbell, S.; Ma, S.; Grinberg, N.; Lee, H.; Lu, B. Z.; Senanayake, C. H. *J. Am. Chem. Soc.* **2013**, *135*, 5565−5568.

(24) For a case where experimental observations differ from computational predictions, see: (a) Plata, R. E.; Singleton, D. A. *J. Am. Chem. Soc.* **2015**, *137*, 3811−3826. For successful interplay of theory and experiment, see: (b) Sperger, T.; Sanhueza, I. A.; Schoenebeck, F. *Acc. Chem. Res.* **2016**, DOI: 10.1021/acs.accounts.6b00068. (c) Tsang, A. S.-K.; Sanhueza, I. A.; Schoenebeck, F. *Chem. - Eur. J.* **2014**, *20*, 16432−16441.

(25) Nudelman, N. S.; Garcia Linares, G. E. *J. Org. Chem.* **2000**, *65*, 1629−1635.

(26) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157−167.

(27) Zhao, Y.; Truhlar, D. G. *J. Chem. Phys.* **2006**, *125*, 194101.

(28) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650−654.

(29) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265−3269.

(30) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639−5648.

(31) Blaudeau, J.-P.; McGrath, M. P.; Curtiss, L. A.; Radom, L. *J. Chem. Phys.* **1997**, *107*, 5016−5021.

(32) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. V. R. *J. Comput. Chem.* **1983**, *4*, 294−301.

DOI: 10.1021/jacs.6b03282
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

(33) Bergner, A.; Dolg, M.; Küchle, W.; Stoll, H.; Preuß, H. *Mol. Phys.* **1993**, *80*, 1431−1441.
(34) Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. *J. Comput. Chem.* **2003**, *24*, 669−681.
(35) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995−2001.
(36) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, (Revision A.02)*; Gaussian, Inc.: Wallingford, CT, 2009.
(37) Schreiner, P. R.; Lauenstein, O.; Kolomitsyn, I. V.; Nadi, S.; Fokin, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 1895−1897. (b) Fokin, A. A.; Schreiner, P. R. *Adv. Synth. Catal.* **2003**, *345*, 1035−1052.
(38) Murayama, E.; Kohda, A.; Sato, T. *J. Chem. Soc., Perkin Trans. 1* **1980**, 947−949.
(39) The chemistry in this reaction mixture is not confined to electron transfer from KO*t*Bu, and we believe that a competing reaction involves the formation of hypobromites, although they are not involved in the bromination of adamantane. This forms part of a comprehensive study that we hope to publish shortly.
(40) Previous papers that discussed the possibility of dimsyl anion as a single electron donor: (a) Rajan, S.; Muralimohan, K. *Tetrahedron Lett.* **1978**, *19*, 483−486. (b) Alonso, R. A.; Rossi, R. A. *Tetrahedron Lett.* **1985**, *26*, 5763−5766. (c) Shishlov, N. M.; Khursan, S. L. *Russ. J. Phys. Chem. B* **2011**, *5*, 737−747. (d) Øpstad, C. L.; Melø, T. B.; Sliwka, H. R.; Partali, V. *Tetrahedron* **2009**, *65*, 7616−7619. (e) Zhang, M.-X.; Hu, X.-H.; Xu, Y.-H.; Loh, T.-P. *Asian J. Org. Chem.* **2015**, *4*, 1047−1049.
(41) Ashby, E. C.; Goel, A. B.; DePriest, R. N. *J. Org. Chem.* **1981**, *46*, 2429. (b) Ashby, E. C.; Argyropoulos, J. N. *J. Org. Chem.* **1986**, *51*, 3593−3597.

DOI: 10.1021/jacs.6b03282
J. Am. Chem. Soc. XXXX, XXX, XXX−XXX