JACS JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Article

Cite This: J. Am. Chem. Soc. 2018, 140, 11510−11518

pubs.acs.org/JACS

Dual Roles for Potassium Hydride in Haloarene Reduction: CS_NAr and Single Electron Transfer Reduction via Organic Electron Donors Formed in Benzene

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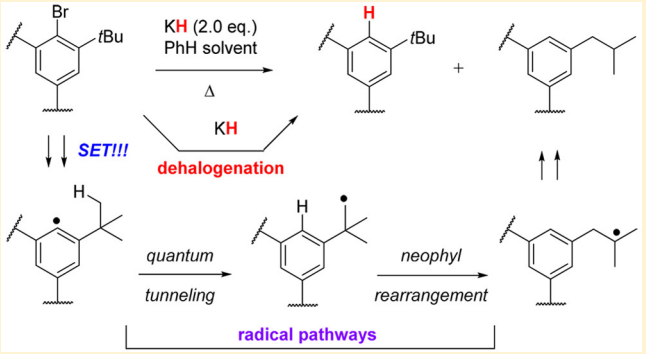
Supporting Information

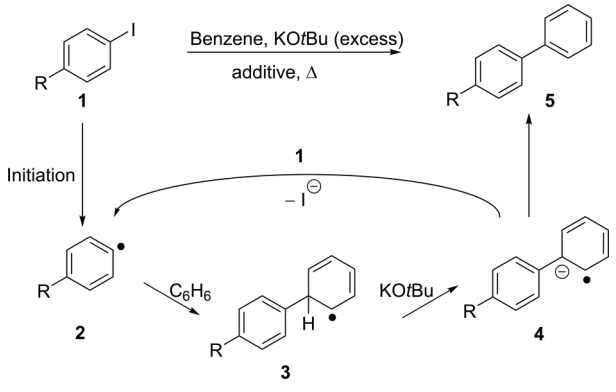
ABSTRACT: Potassium hydride behaves uniquely and differently than sodium hydride toward aryl halides. Its reactions with a range of haloarenes, including designed 2,6-dialkylhaloarenes, were studied in THF and in benzene. In THF, evidence supports concerted nucleophilic aromatic substitution, CS_NAr, and the mechanism originally proposed by Pierre et al. is now validated through DFT studies. In benzene, besides this pathway, strong evidence for single electron transfer chemistry is reported. Experimental observations and DFT studies lead us to propose organic super electron donor generation to initiate BHAS (base-promoted homolytic aromatic substitution) cycles. Organic donor formation originates from deprotonation of benzene by KH; attack on benzene by the resulting phenylpotassium generates phenylcyclohexadienylpotassium that can undergo (i) deprotonation to form an organic super electron donor or (ii) hydride loss to afford biphenyl. Until now, BHAS reactions have been triggered by reaction of a base, MO*t*Bu (M = K, Na), with many different types of organic additive, all containing heteroatoms (N or O or S) that enhance their acidity and place them within range of MO*t*Bu as a base. This paper shows that with the stronger base, KH, even a hydrocarbon (benzene) can be converted into an electron-donating initiator.



INTRODUCTION

The transition metal-free dehalogenative coupling reaction between haloarenes and arenes, mediated by a base (typically KO*t*Bu) and an organic additive is now well established in the chemical literature.[1−16] The propagation cycle of this radical chain reaction is well characterized by the base-promoted homolytic aromatic substitution (BHAS)[17] mechanism. An aryl radical **2** adds to the arene partner to yield an intermediate radical, **3**, and deprotonation yields radical anion **4**. Electron transfer from **4** to aryl halide **1** propagates the radical chain reaction, simultaneously releasing biaryl product **5** (Scheme 1). The initiation step generating the aryl radical **2** in the first instance has been a topic of much debate. Some authors have proposed single electron transfer (SET) to the haloarene from the *tert*-butoxide anion of KO*t*Bu alone, or as a complex with the organic additive. However, computational studies found these proposals to be untenable.[18,19] Our recent study critically examined the evidence presented for KO*t*Bu as a single electron donor to haloarenes in a number of different reports and found that, in each case, organic additives initiate the BHAS reaction by forming organic electron donors in situ,[20] for example, electron donor **9** from phenanthroline **6** (Scheme 2A).[18] While organic additives are not absolutely required for most substrates in this transformation,[9,10,15] they significantly enhance the yield of the coupled products, simultaneously

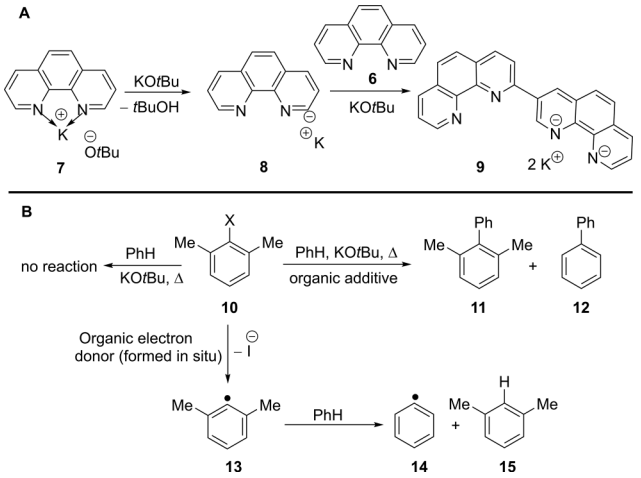
Scheme 1. Radical Chain Mechanism Depicting BHAS



Received: July 19, 2018
Published: August 17, 2018

DOI: 10.1021/jacs.8b07632
J. Am. Chem. Soc. 2018, 140, 11510−11518

Scheme 2. (A) Phenanthroline and KO*t*Bu; Electron Donor Precursors and (B) Reactions of 2,6-Dimethylhalobenzenes



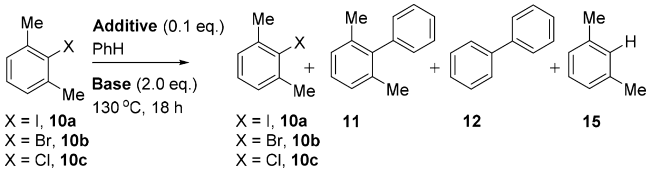
allowing reactions to be conducted at lower temperatures and for a shorter duration.[18,21−23] In the absence of suitable organic additives,[15] BHAS reactions can be initiated by arynes (benzynes), formed by base-induced elimination of HX from substrate haloarenes ArX such as **1** (see later, Scheme 4).

To separate the analysis of initiation by benzynes from initiation by organic electron donors, substrate **10** (Scheme 2B) was often employed in our studies. This haloarene cannot form benzynes, and so it undergoes coupling only when suitable single electron donors are present. Aryl radical **13**, derived from **10**, experiences competing signature reactions,[22] namely (i) addition to benzene and (ii) hydrogen atom transfer (HAT) with benzene. HAT affords the volatile *m*-xylene, **15**, as well as a phenyl radical **14**. Aryl radicals **14** and **13** add to benzene, taking the role of radical **2** in Scheme 1. This affords biaryls **12** and **11**, respectively, in a characteristic ratio of between 3:1 and 4:1. For steric reasons, the yields from substrate **10** are always lower than for substrates like iodobenzene or *p*-iodotoluene, but the mechanistic information provided by **10** is invaluable.

RESULTS AND DISCUSSION

Our original goal was to explore coupling of **10** with benzene using phenanthroline **6** as an additive with KH as a base (instead of KO*t*Bu). Successful coupling would support the idea that an alkoxide is not a necessary component of the coupling reactions and would further challenge KO*t*Bu's privileged status[20] in these reactions. Subjecting **10a**) and additive **6** to the reaction conditions using KO*t*Bu or KH as a base (Table 1, entries 2 and 3) afforded coupling in both cases, to give the characteristic ratio of **12**:**11** between 3:1 and 4:1 (note that *m*-xylene is formed in all entries except entries 1 and 5, but its yield varies due to volatility). Using KH instead of KO*t*Bu gave significantly less recovery of **10a**, but yields of biaryls **11** and **12** were similar in each case. As a control reaction, we subjected **10a** to the reaction conditions in the absence of **6**, using KH as base. Remarkably, considerable levels of biaryls **11** and **12** were still observed (Table 1, entry 4) when compared to KO*t*Bu as a control reaction which gives almost no product (Table 1, entry 1). Hence, potassium hydride behaves in a special way in its reactions with haloarenes in benzene, causing single electron transfer (SET) reduction to afford radical intermediates.

Table 1. Coupling Reactions of 2,6-Dimethylhalobenzenes with Benzene



entry	additive/base	ratio[a] **12**:**11**	**11** + **12** yield[b]	recovered **10** (%)[b]
1	−/KO*t*Bu	−	<0.5	72
2	**6**/KO*t*Bu	3.7:1	18.2	33
3	**6**/KH	3.9:1	16.3	<1
4[c]	−/KH	7.7:1	5.5	14
5	−/NaH		no reaction detected	
6[d]	−/KH	7.4:1	3.9	3
7[e]	−/KH	7.0:1	1.5	9

[a]2,6-Dimethyliodobenzene **10a** was used as a substrate unless otherwise stated. Ratios are determined by ^{1}H NMR of the crude reaction mixture (see Supporting Information). [b]Yield (%) of combined biaryls (**11** and **12**), or yield (%) of returned **10** determined by ^{1}H NMR. [c]Average of two runs. [d]**10b** was used as a substrate. [e]**10c** was used as a substrate.

We have investigated this with a range of haloarene substrates, and present experimental and computational evidence in relation to the mechanistic pathways.

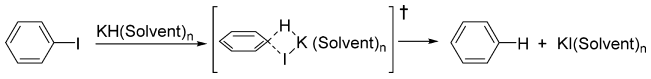
The generation of biaryls **11** and **12** in the KH control reaction reveals that SET reduction occurred. However, the high conversion of **10a** observed indicates additional pathway(s) for reaction of the substrate, and the change of ratio of **12**:**11** to ∼7:1 indicates an additional route for formation of biphenyl. The corresponding bromide **10b** (entry 6) and chloride **10c** (entry 7) showed similar results and almost identical **12**:**11** ratios. NaH gave no reaction under the same conditions (entry 5).

The high conversion of **10** in the reactions using KH can be explained by reductive dehalogenation. Dehalogenation of iodo-, bromo- and chlorobenzene with KH in THF under mild conditions was reported by Pierre et al.,[24] who found that treating iodobenzene **16** with KH (5.0 equiv)[25] in THF for 3 h at rt gave quantitative conversion to volatile benzene as product. Pierre found the order of reactivity ArI > ArBr ≫ ArCl, in contrast to the normal order of reactivity for S_NAr reactions, and so a traditional S_NAr-type mechanism was ruled out. Benzyne formation was excluded in THF as solvent due to the absence of evolved hydrogen gas.[24] Although Pierre had no access to computational chemistry, he proposed a concerted displacement from an aryl halide through a 4-centered TS; the reaction type would now be termed a CS_NAr and more examples of such reactions have recently become evident.[25a,26] Using DFT methods, we now computed an energy profile for this reaction (Table 2), that supports Pierre's proposal as an entirely reasonable mechanism. Thus, with iodobenzene as substrate, in both THF and in benzene, and using naked KH or KH solvated by two solvent molecules, the reactions are highly exergonic and feature easily achievable kinetic barriers.

Selecting a precursor to a less volatile product, we subjected *p*-iodobiphenyl **17** to Pierre's conditions, affording biphenyl **12** in 87% isolated yield (Scheme 3). Importantly, in THF-d_8 the reaction proceeded in similar yield, but no D-incorporation was observed, revealing that the H atom is derived from KH and not from solvent. This is consistent with a CS_NAr-type

DOI: 10.1021/jacs.8b07632
J. Am. Chem. Soc. 2018, 140, 11510−11518

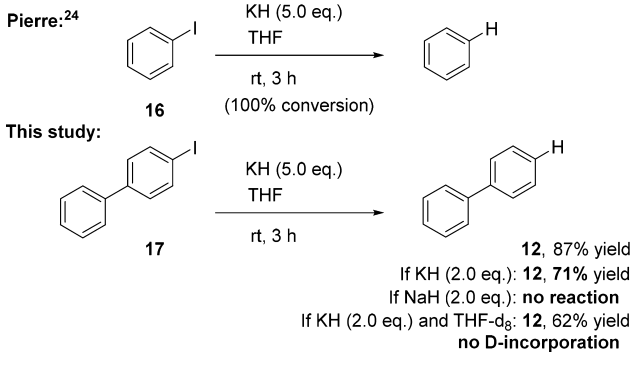
Table 2. CS_NAr Substitution Reactions[a]



entry	solvent	n	$\Delta G^{\ddagger}$ kcal/mol	ΔG_{rel} kcal/mol
1	THF	0	17.0	−91.2
2	Benzene	0	17.0	−88.1
3	THF	2	22.4	−93.9
4	Benzene	2	23.5	−90.3

[a]DFT calculations were performed[27−30] with details as in SI.

Scheme 3. Reductive Dehalogenation of Iodobenzene 16 and 4-Iodobiphenyl 17 in THF, Mediated by KH



mechanism via direct displacement of iodide by hydride described above.

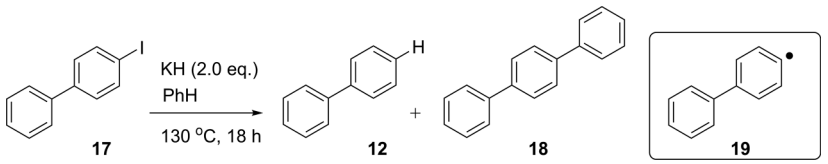
In benzene at rt, no reaction occurred with KH (Table 3, entry 1). At 130 °C in benzene as solvent, reactions gave biphenyl **12** and terphenyl **18** in a ∼3:1 **12**:**18** ratio. Studies using D_2O quench and C_6D_6 as solvent (Table 3, entries 3 and 4) confirmed that any deuterated biphenyl (**12**-d_1) arose by deuterium abstraction from the solvent, rather than from the quench with D_2O, ruling out formation of aryl anions. In entry 4, the level of labeling with deuterium was not high (**12**:**12**-d_1 was 8:1). Product **12** can arise either from a Pierre reaction (with KH, affording unlabeled **12**) or from quenching of biphenyl radical **19** (affording **12**-d_1 when C_6D_6 is solvent). On the other hand, product **18** arises from BHAS chemistry, where biphenyl radicals **19** are also intermediates.[31]

The interesting comparison in Table 3 is between entries 3 and 4. The only difference between these experiments lies in the choice of solvent−benzene in entry 3 and deuterated benzene in entry 4. Of the two mechanisms in operation, the Pierre reaction should not be affected by the change in solvent, while the BHAS mechanism will likely be significantly affected. Entry 4 shows a lower yield of terphenyl **18** and, particularly, of biphenyl **12**, compared with entry 3. The established routes to radicals in these BHAS reactions either involve the presence of an electron donor as in Scheme 2(b) or of a benzyne intermediate, generated from the haloarene substrate. As there is no apparent electron donor (but see below for the presence of electron donors), the benzyne route is shown in Scheme 4, and features benzyne **20**.

Addition of the benzyne, as a biradical,[18] to benzene affords biradical **21**. This biradical has one very reactive radical, the aryl radical, and one highly delocalized radical (the cyclohexadienyl radical). Of these, the reactive aryl radical should undergo rapid reaction (addition to, or hydrogen atom abstraction from, a molecule of benzene are likely reactions), affording **22**, followed by deprotonation to afford radical anion **23**, which can then transfer an electron to substrate **17** to begin a BHAS cycle by generating biphenyl radical **19**. This radical can then add to the solvent, benzene, as in Scheme 1, ultimately to afford terphenyl **18**, or can abstract a hydrogen atom from benzene to afford biphenyl **12**.[31] In deuterated benzene, the conversion of **22**-d_6 to electron donor **23**-d_5 would require that a C−D bond be broken (Scheme 4, inset). But this step of BHAS reactions is routinely not the rate-determining step, and so no isotope effect is likely to be seen in this step. However, the conversion of biphenyl radical **19** to biphenyl **12** involves a hydrogen atom transfer from solvent benzene in the unlabeled case, and from deuterated benzene when that is used as the solvent, and these reactions may show a substantial kinetic isotope effect. This is reflected in the significant drop in yield for biphenyl **12** on going from entry 3 to entry 4.

To find out more information about these electron transfer reactions, we turned to 2,6-disubstituted haloarene probes, in

Table 3. Coupling Reactions of 4-Iodobiphenyl with Benzene[a]



			yield (%)[b]			
entry	base	solvent/quench	**12**	**18**	**17**	D-incorp
1[c]	KH	C_6H_6/H_2O	no reaction detected			N/A
2[d]	KH	C_6H_6/H_2O	54	16	3	N/A
3[e]	KH	C_6H_6/D_2O	58	24	4	no[f]
4	KH	C_6D_6/D_2O	18	15	34	yes[g]
5[h]	KO*t*Bu	C_6H_6/H_2O	11	76	7	N/A
6[i]	KO*t*Bu (+**6**)	C_6H_6/H_2O	9	87	<1	N/A

[a]D-incorp = Deuterium incorporation, N/A (not applicable). [b]Yields determined by ^{1}H NMR of the crude reaction mixture. [c]Reaction conducted at rt with KH (5 eq.). [d]Average of three replicates. [e]Average of two replicates. [f]No D-incorporation detected by GC−MS. [g]D-incorporated: **18**-d_5 and **12**-d_1 detected by GC−MS but not **12**-d_{10}. Here, a 2% yield of **12**-d_1 is observed. [h]*tert*-Butoxide adducts to the aryne were observed to give a 1:1 ratio of regioisomers in 6% combined yield. [i]20 mol % of phenanthroline **6** was used as an additive.

DOI: 10.1021/jacs.8b07632
J. Am. Chem. Soc. 2018, 140, 11510−11518

Scheme 4. In Substrates That Can Form Benzynes, e.g., Iodobiphenyl 17, an Alternative and Slower Initiation Route for BHAS Cycles from the Benzyne (in this case, 20′), Can Occur

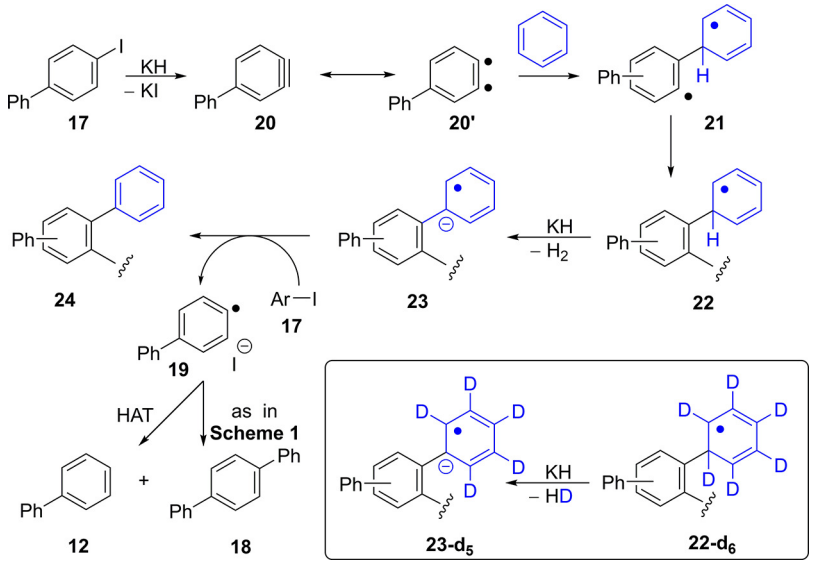
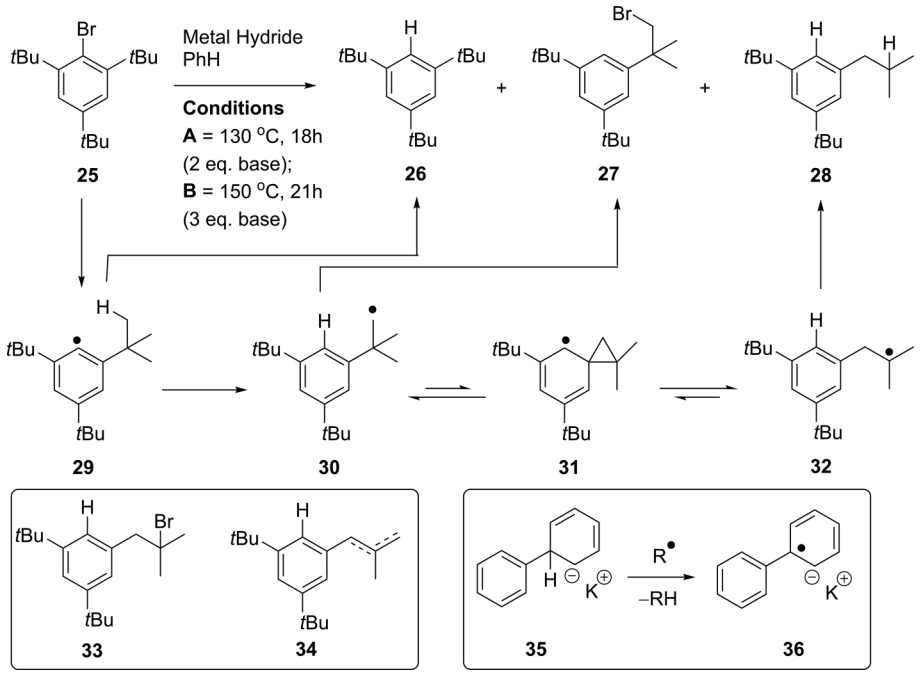


Table 4. KH-Mediated Reactions of 2,4,6-Tri-*tert*-butyl-bromobenzene[a]



			yield (%)[b]				
entry	base	solvent/quench	**26**	**27**	**28**	**25**	D-incorp
1[c]	–	C_6H_6/H_2O		no reaction detected			N/A
2[c]	KO*t*Bu	C_6H_6/H_2O		no reaction detected			N/A
3[d]	KH	C_6H_6/H_2O	28	5	6	56	no[e]
4	KH	C_6D_6/D_2O	18	11	3	66	yes[f,g]
5[h]	KH	C_6H_6/H_2O	31	1	13	29	N/A
6[h]	NaH	C_6H_6/H_2O	4	<1	1	95	N/A
7	KO*t*Bu/NaH (1:1)	C_6H_6/H_2O	75	<1	10	<1	N/A

[a]D-incorp = Deuterium incorporation. N/A (not applicable). Unless otherwise stated, conditions **A** were used. [b]Yields determined by ^{1}H NMR of the crude reaction mixture. [c]No products were observed, **25** was recovered in quantitative (ca. 100%) yield. [d]Average of eight replicates. [e]After quenching with D_2O, D-incorporation was not detected. [f]D-incorporated was detected by ^{2}H NMR and/or GC–MS analysis of the reaction mixture (see Supporting Information). [g]After quenching with H_2O, D-incorporation was still detected. [h]Reaction conducted under conditions **B**.

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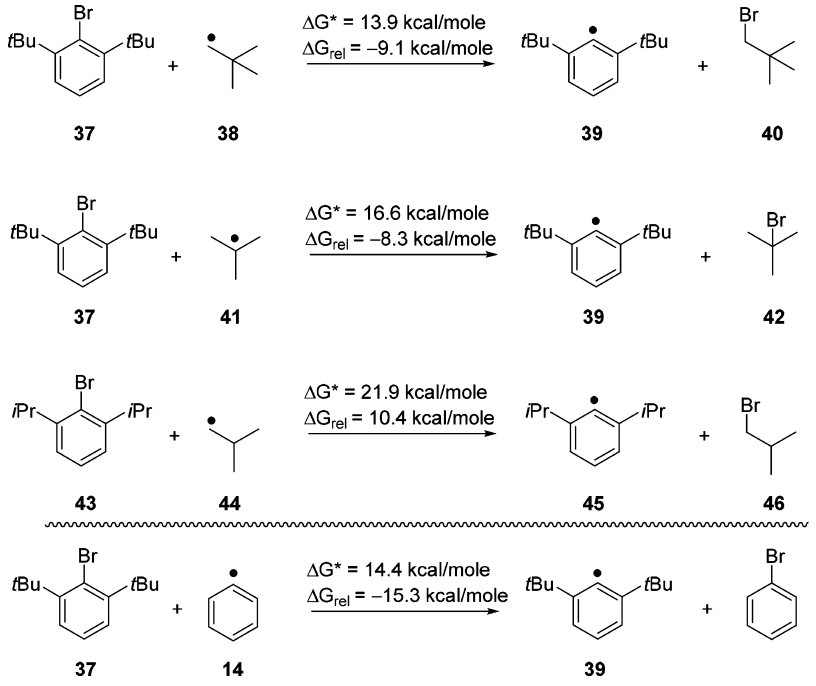
Scheme 5. Atom Transfer Reactions[a]



[a]DFT calculations were performed[27−30] with details as in SI.

benzene as solvent. As with **10**, these substrates would not be susceptible to benzyne initiation of the BHAS mechanism but, importantly and in contrast to **10**, they would form products, none of which should be volatile. 2,4,6-Tri-*tert*-butylbromobenzene **25** was employed as a probe; its derived aryl radical **29** should be so hindered that it should neither be able to undergo addition to, nor HAT with, benzene (Table 4). Ingold reported that the aryl radical **29** behaves in a very special way; it partakes in very rapid intramolecular 1,4-HAT with one of its *ortho*-*tert*-butyl groups via quantum mechanical tunneling, to give alkyl radical **30**.[32,33] Control reactions in the absence of base, or using KO*t*Bu, gave no reaction, as expected (Table 4, entries 1−2). Subjecting **25** to conditions **A** (Table 4, entry 3) gave dehalogenated product **26** (28%) and recovered **25** (56%); in addition, two other products were characterized, bromide **27** (5%) and rearranged hydrocarbon **28** (6%). When the reaction was conducted in C_6D_6, **26** was detected as the major product with only traces of **26-*d*$_1$** (Table 4, entry 4). In all reactions of **25**, neither biphenyl **12** nor biphenyl-d_{10} (**12-*d*$_{10}$**) was detected.

Bromide **27** and hydrocarbon **28** are clear reporters of a radical mechanism in this reaction. We now examine how they arise and follow this with a rationalization of how radicals are generated in this system at all, in the apparent absence of any electron donor and with a substrate, **25**, that cannot form a benzyne. Clearly, bromide **27** must arise by Br-atom abstraction by primary alkyl radical **30**. Atom transfer chemistry normally precludes transfer of a halogen from an aryl halide to an alkyl radical due to an unfavorable energy profile.[34] In this case, the Ar−Br bond is significantly weakened by steric interaction with the *ortho*-*tert*-butyl groups as shown by our DFT investigation (Scheme 5).

The abstraction of bromine by primary radical **30** from bromoarene **25** is modeled computationally by the reaction between bromide **37** and radical **38**. The bromine atom transfer is exergonic by 9.1 kcal/mol and features a low and very accessible barrier (13.9 kcal/mol). To our knowledge, this is the first example of an exergonic halogen transfer from an aryl halide to an alkyl radical. Scheme 5 also shows that a more stabilized tertiary alkyl radical **41** could also easily abstract the bromine atom from **37**, underlining what a sterically strained system is present in substrate **37**. Radical **41** in our computational work mirrors tertiary radical **32** in our laboratory experiments. Conversion of **32** to the corresponding tertiary alkyl bromide **33** is also therefore a possibility. Under basic conditions, **33** should undergo E_2 elimination to afford alkene, **34**, and indeed this molecule was detected by mass spectrometry (see Supporting Information). For completeness, we also calculated the energy profile for reaction of a phenyl radical **14** with **37**. Table 4 shows an energy barrier (14.4 kcal/mol) very similar to those of the alkyl radicals with **37**.

The special nature of molecule **37** is seen when primary radical **44** abstracts a bromine atom from isopropyl analogue **43**; here, in the absence of bulky *tert*-butyl groups, the reaction is significantly endergonic.[33]

Hydrocarbon **28** arises from radical **29** by intramolecular 1,4-HAT via quantum mechanical tunneling, followed by neophyl rearrangement of primary alkyl radical **30**[32,35] to the more stabilized tertiary radical **32** as a thermodynamic sink (supported by computation, see Supporting Information). Besides isolation of **28**, further evidence for radical **32** as an intermediate came from detection of its dimer by GC−MS (see Supporting Information),[36] although this dimer was not produced in sufficient quantities for isolation. Alkene **34**, mentioned above, could also arise along with hydrocarbon **28** in a disproportionation reaction between two radicals **32**. Under harsher conditions **B**, conversion was higher but mass balance was poorer (Table 4, entry 5).

The formation of bromide **27** and hydrocarbon **28** depends on the generation of radicals **29**, reinforcing the conclusions arising from the reactions of substrate **10**. The absence of any recognized electron donor when using a substrate **25** that

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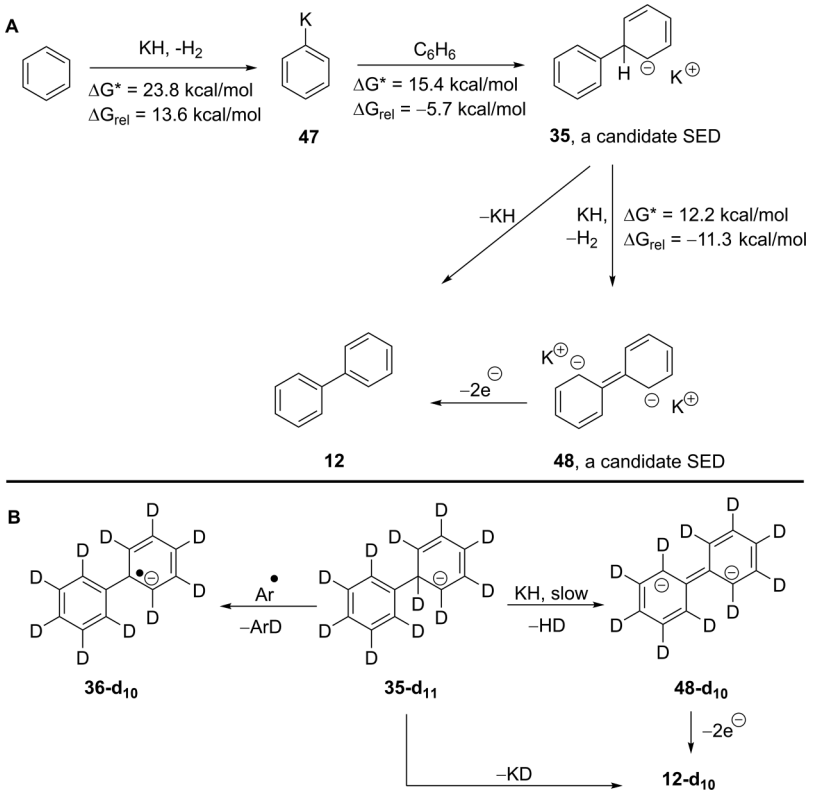
Scheme 6. (A) Proposed Pathways for Biphenyl Formation in KH/Benzene;[a] (B) Consideration of Deuterated Intermediates Arising from Benzene-d_6



[a]DFT calculations were performed[27−30] with details as in SI.

cannot form a benzyne, caused us to examine the reaction in depth. We first considered whether traces of residual potassium metal that might be present in the KH sample could trigger formation of biphenyl. However, ICP-OES analysis and control reactions with K metal ruled against this (see Supporting Information).

In our previous investigations of BHAS reactions, performing blank reactions (in the absence of substrate) led to helpful information, and the same was true here. Notably, treatment of benzene with KH in a control reaction led to small amounts of biphenyl, characterized by NMR (see SI), whereas reaction with NaH (or KO*t*Bu) afforded no biphenyl.

In a manner reminiscent of other BHAS reactions,[18] a strong organic electron donor could be formed if KH deprotonates benzene to form PhK **47** (Scheme 6). Here, PhK would attack benzene to form phenylcyclohexadienyl potassium **35**.[37] Whereas this anion might function as a mild electron donor, more likely it could be deprotonated again to form the disalt **48**, a biphenyl dianion and a known class of strong electron donors[38] This could initiate electron transfer to haloarenes to trigger radical chemistry. Indeed, sequential transfer of two electrons would form biphenyl **12**. Alternatively, biphenyl could also be formed by expelling KH from anion **35**. Indeed, it is known that phenylpotassium attacks benzene to form biphenyl and an insoluble polybenzene.[37] From our previous work on initiation of BHAS reactions, we know that the amount of initiator that needs to be present is vanishingly small, and that evidence of the electron donating initiator is generally not found in the products of these reactions.

Using DFT methods, we have modeled the first step of the reaction, i.e., the formation of phenylpotassium **47** which has a very achievable reaction barrier of 23.8 kcal/mol, under the conditions of the reaction. The formation of **47** is endergonic by 13.6 kcal/mol, but the reaction is irreversible due to release of hydrogen. The following two steps, **47** → **35** and **35** → **48** are also accomplished easily, and feature low kinetic barriers.

Returning to Table 4, an important comparison is between entries 3, 4, and 5. In deuterated benzene, the amount of **26** is decreased relative to the reaction in C_6H_6. This can arise because less electron donor is present in the reaction with the labeled solvent. Formation of electron donor, **48**-d_{10}, (Scheme 6B) would require a difficult deprotonation from **35**-d_{11} that could be subject to an isotope effect. In C_6D_6, (compared to C_6H_6) that would lead to a lower concentration of electron donor, and so the reaction would be more sluggish. When an electron transfer occurs, bromide loss is followed by intramolecular HAT to afford **30**. This radical can then easily abstract a bromine atom from another molecule of substrate to form **27** in an atom transfer chain, or radical **30** can enter a neophyl rearrangement to afford radical **32**. Bromide **27** can react with another molecule of electron donor to afford **32**. The aliphatic radicals on this pathway may afford hydrocarbon **28**, together with **34**, by disproportionation. An alternative possibility is that an intermediate like **35**, which would have a weakened C(sp^3)−H bond, would surrender a hydrogen atom to radical **32**. This may be particularly difficult in the deuterated analogues.

Under the harsher conditions **B**, NaH gave only traces of dehalogenated product (Table 4, entry 6).

Interestingly, while KO*t*Bu and NaH gave no reaction by themselves, the combination gave full conversion, a high yield of **26** (75%) and some hydrocarbon **28** (10%) as the main

DOI: 10.1021/jacs.8b07632
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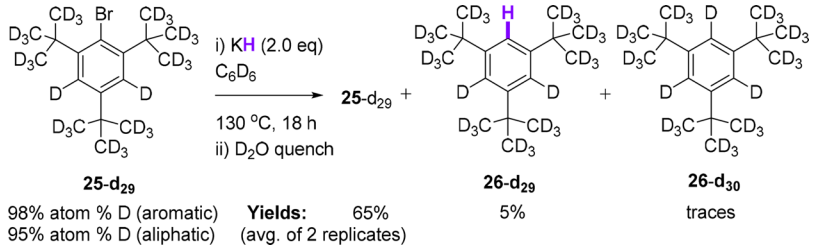
Scheme 7. H-Incorporation from KH in a Fully Deuterated Reaction System



byproduct (Table 4, entry 7); we have not investigated this in detail, but the high yield of **26** may indicate the empowerment of NaH as a nucleophile.[25] Formation of **28** indicates that some radical chemistry also occurs under those conditions.

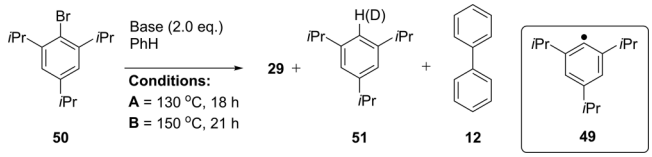
In view of the D-incorporation detected in the reaction of **25** in C_6D_6 (Table 4, entry 4) we wished to gain more information about the roles of HAT as a pathway for aromatic dehalogenation vs H-incorporation from KH. Halide **25** is a most interesting substrate because its derived aryl radical undergoes intramolecular HAT reaction. We were interested to find out whether its deuterated counterpart would behave analogously. To do so, substrate **25-d_{29}** was synthesized (with 99% aromatic atom % D and 95% aliphatic atom % D) and treated with KH in C_6D_6, quenching with D_2O. Recovered bromide starting material was the main component at the end of the reaction (65%), with hydrocarbons **26-d_{29}** (5%) and **26-d_{30}** (trace) as the new products; no products of side-chain rearrangement were detected (Scheme 7).

Product **26-d_{29}** can arise directly by the Pierre mechanism, while **26-d_{30}** would either require deuterium atom abstraction from benzene-d_6 or could arise through the Pierre mechanism through reaction with KD, generated during the reaction (Scheme 6B); (for spectra and D-incorporation calculations, see Supporting Information).[29] We compared the outcome of this experiment with that of entry 4 in Table 4. Both return similar amounts of residual starting substrate, **25** and **25-d_{29}** respectively. The Pierre reaction proceeds more easily for the unlabeled substrate. This may reflect that less steric compression of the Br atom is present in the deuterated substrate, as the C−D bonds in **25-d_{29}** are shorter than the C−H bonds in **25**.[39] With the deuterated substrate, the observation of less evidence of radicals on the side-chain is as would be expected, as this would now involve breaking a higher energy C−D bond.

Competition between H-incorporation from KH vs HAT from solvent was emphasized when 2,4,6-tri-isopropylbromobenzene **50** was employed. Given that the 2,6-dimethyl-substituted aryl radical **13** adds to benzene 4 times more slowly than it undergoes HAT with benzene, due to steric hindrance, then the aryl radical **49** derived from **50** (Table 5) should add to benzene even more slowly and HAT with benzene should also be slow. Subjecting **50** to KH under conditions **A** (Table 5, entry 1) gave dehalogenated product **51** and biphenyl **12** in a 3:1 ratio. Notably, the reactivity of **50** was significantly lower than that of **25**. This can be rationalized by the greater release of steric strain in reactions of **25**.[40] When the reaction was conducted in C_6D_6, **51-d_1** and **12-d_{10}** were now detected (Table 5, entry 2), but in very low yield. No arylation product from coupling of aryl radical **49** to benzene was observed.

Under conditions A, it is clear that the reaction of **50** is slow to initiate. Comparison of entries 1 and 2 shows that deuterated solvent does suppress products from the BHAS

Table 5. KH-Mediated Reactions of 2,4,6-Tri-isopropylbromobenzene[a]



			yield (%)[b]			
entry	base	solvent/quench	**51**	**12**	**50**	D-incorp
1[c]	KH	C_6H_6/H_2O	9	3	88	N/A
2	KH	C_6D_6/H_2O	1	<1	65	yes[d]
3[e]	KH	C_6H_6/H_2O	25	10	62	N/A
4[c,e,f]	KH	C_6D_6/D_2O	55	0	14	yes[g]
5[e]	NaH	C_6H_6/H_2O	4	1	95	N/A

[a]D-incorp (D-incorporation). Unless otherwise stated, reactions were conducted using conditions **A**. [b]Yields determined by ^{1}H NMR of the crude reaction mixture. [c]Average of three replicates. [d]D-incorporation (**51-d_1**) and **12-d_{10}** were detected by GC−MS analysis of the reaction mixture, but not by ^{2}H NMR. [e]Reaction conducted under conditions **B**. [f]The yield of **51** + **51-d_1** is reported, see Supporting Information. [g]Under conditions **B**, both **51-d_1** and **12-d_{10}** were observed by NMR, see Supporting Information.

process. It is clear that the extent of the Pierre mechanism with this substrate is very small. Harsher conditions **B** (Table 5, entry 3) gave higher yields of **51** and **12**; curiously, when the reaction was repeated in C_6D_6, (Table 5, entry 4) high conversions to **51** (**51** + **51-d_1**, 55%) were observed, together with some recovered **50** (14%). Only traces of product **51** and biphenyl **12** were observed when NaH was used (conditions **B**; Table 5, entry 5).

Looking at the higher yield of product **51** in C_6D_6 (entry 4) at these higher temperatures (150 °C), the spectra reveal that there is substantial monolabeling in the aromatic ring. Formation of anion **35-d_{11}** (Scheme 6B) takes place analogously to Scheme 6A; if isotope effects for conversion of **35-d_{11}** to **48-d_{10}** are large, then the concentration of **35-d_{11}** may build up in solution to a level greater than for the nondeuterated counterpart that is present when benzene is the solvent. This means that if a molecule of **48-d_{10}** forms and executes SET to the haloarene substrate to form an aryl radical, that radical can abstract D from **35-d_{11}**, thereby forming **36-d_{10}**, which in turn can donate an electron to another molecule of haloarene to initiate another cycle. The comparison between conditions **A** (entries 1 and 2) and conditions **B** (entries 3 and 4) reflects that the higher temperature selectively helps the reaction in C_6D_6, possibly either by creating a greater concentration of **35-d_{11}**, or by facilitating the conversion to **48-d_{10}**.

In summary, unlike sodium hydride, KH undergoes substitution of haloarenes in THF or benzene as proposed

DOI: 10.1021/jacs.8b07632
J. Am. Chem. Soc. 2018, 140, 11510−11518

by Pierre. DFT studies support a concerted 4-centered transition state for these substitution reactions. In benzene as solvent, 2,6-dialkyl substituted halobenzenes show clear evidence of electron transfer chemistry when KH is used, and studies with deuterated versus unlabeled benzene show a clear dependence on the solvent. Isolation of small quantities of biphenyl on reaction of KH with benzene supports the formation of phenylpotassium by deprotonation of benzene, and generation of an organic electron donor **48** in trace amounts as an initiator for BHAS cycles to rationalize the observed chemistry. 2,6-Dialkylhalobenzenes **10a−c**, **25** and **50** are particularly helpful reporters of the mechanisms of the reactions. The intramolecular hydrogen abstracting behavior of aryl radicals derived from unusual substrate **25** has previously been demonstrated. Further unusual reactivity of **25** is reported here, as the first haloarene to undergo exergonic halogen atom abstraction by alkyl radicals, including tertiary alkyl radicals.

CONCLUSION

Placing this work in context, BHAS reactions mediated by KO*t*Bu are now widely recognized in dehalogenation and in coupling chemistry,[17] where electron transfer reactions arise from organic donors formed in situ. The diversity of structures that have been shown to act as precursors of organic electron donors is quite revealing. This paper extends that range, and shows that in the presence of an appropriately strong base, organic electron donors can arise even by deprotonation of benzene. Minute amounts of donors can set up desired chain reactions, or can create undesired byproducts, and so, awareness of this chemistry is important in strategic planning of synthetic chemistry. Having demonstrated that the strong base, KH, can trigger formation of organic electron donors, a challenge for the immediate future is the generation of strong organic electron donors[41] either under nonbasic conditions or with bases that are significantly milder than either KH or KO*t*Bu.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.8b07632.

Experimental procedures, key NMR spectra, ICP-OES data, characterization data of novel compounds, computational studies and computational coordinates (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank GlaxoSmithKline, AstraZeneca, EPSRC (award ref EP/M506643/1) and the University of Strathclyde for funding. High resolution mass spectrometry data were acquired at the ESPRC UK National Mass Spectrometry Facility at Swansea University. We thank Dr. Colin Edge for helpful discussions. We thank a referee for the suggestion to compute the reaction of phenyl radical 14 with aryl bromide **37**. This paper is dedicated to the memory of Matthew P. John.

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