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Reduced Phenalenyl in Catalytic Dehalogenative Deuteration and Hydrodehalogenation of Aryl Halides

Bhagat Singh, Jasimuddin Ahmed, Amit Biswas, Rupankar Paira,* and Swadhin K. Mandal*

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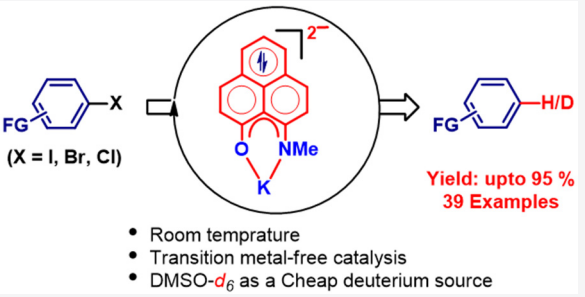
ABSTRACT: Dehalogenative deuteration reactions are generally performed through metal-mediated processes. This report demonstrates a mild protocol for hydrodehalogenation and dehalogenative deuteration of aryl/heteroaryl halides (39 examples) using a reduced odd alternant hydrocarbon phenalenyl under transition metal-free conditions and has been employed successfully for the incorporation of deuterium in various biologically active compounds. The combined approach of experimental and theoretical studies revealed a single electron transfer-based mechanism.



INTRODUCTION

Hydrodehalogenation of aryl/heteroaryl halides is a crucial reductive reaction,[1] which can be accessed by several metal-catalyzed reductions,[2−6] metal−halogen exchange,[1,7,8] reduction by hydride,[9] solid-supported metal catalysis,[10] etc. This process is well-known as a remediation strategy to convert toxic organic halides into benign chemicals in industry.[11−13] However, metal-based hydrodehalogenation suffers from toxic waste, low substrate scope, and high-temperature reaction conditions. These drawbacks led to the evolution of an alternative radical dehalogenation method,[14−21] which functions under relatively mild conditions. For example, Stephenson and co-workers successfully described a single electron transfer (SET)-based method employing an iridium-based photocatalysft *fac*-Ir(ppy)$_3$ in the presence of visible light at ambient temperature.[22] However, this method uses the rare metal-based catalyst. To avoid expensive metals in such transformation, recent reports appeared on the use of a Na-alcoholate, solvent-mediated process in the presence of a base that worked either at high temperature or under light stimulation in a noncatalytic fashion to perform a hydrodehalogenation reaction.[23−25] Murphy and co-workers explored a protocol using an organic electron donor (tetra(iminophosphorano)-substituted bispyridinylidene) under noncatalytic conditions.[26,27] Such an approach conceptually indicates the capability of an organic electron donor to function as a dehalogenative agent under a mild condition.

In this regard, König and co-workers demonstrated the first metal-free catalytic hydrodehalogenation using the perylene diimide (PDI)/Et$_3$N combination, which requires light irradiation (Scheme 1a).[28] Later on, de Alaniz et al. developed a photocatalyzed hydrodehalogenation in the presence of 10-phenylphenothiazine (PTH) (Scheme 1a).[29] A recent report by Studer and co-workers[30] utilized 1,10-phenanthroline/NaH for radical-mediated catalytic hydrodehalogenation (Scheme 1a), which operates at high temperature (140−160 °C) and requires high catalyst loading (20 mol %), leaving ample scope to establish a milder and more effective hydrodehalogenation methodology.

Furthermore, the deuterated version of this transformation, namely, dehalogenative deuteration, is of significant importance if it can be accomplished under mild and expensive transition-metal free catalytic conditions. The field of dehalogenative deuteration has drawn significant attention due to its tremendous potential in the preparation of different drug molecules with a longer lifespan in plasma, which prevents off-target site interactions and/or leads to accomplishing higher efficacy.[31−34] As a result, incorporation of deuterium in a molecule appeared as clinically highly significant. Deuterium-labeled analogues of the drug are utilized in absorption, distribution, metabolism, and excretion studies and have the potential to facilitate the discovery of new pharmacophores.[35−40] However, dehalogenative deuteration reactions[1,3,41−44] mainly involved precious transition metal catalysts/ligands and costly deuterium sources or noncatalytic methodologies using sodium amalgam[45] and lithium-halogen exchange,[46−48] which suffer from harsh conditions and require highly sensitive alkyl-lithium reagents. In 2011, Mutsumi et al.[49] demonstrated the deuterated version of this hydro-

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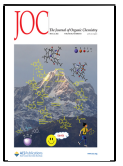
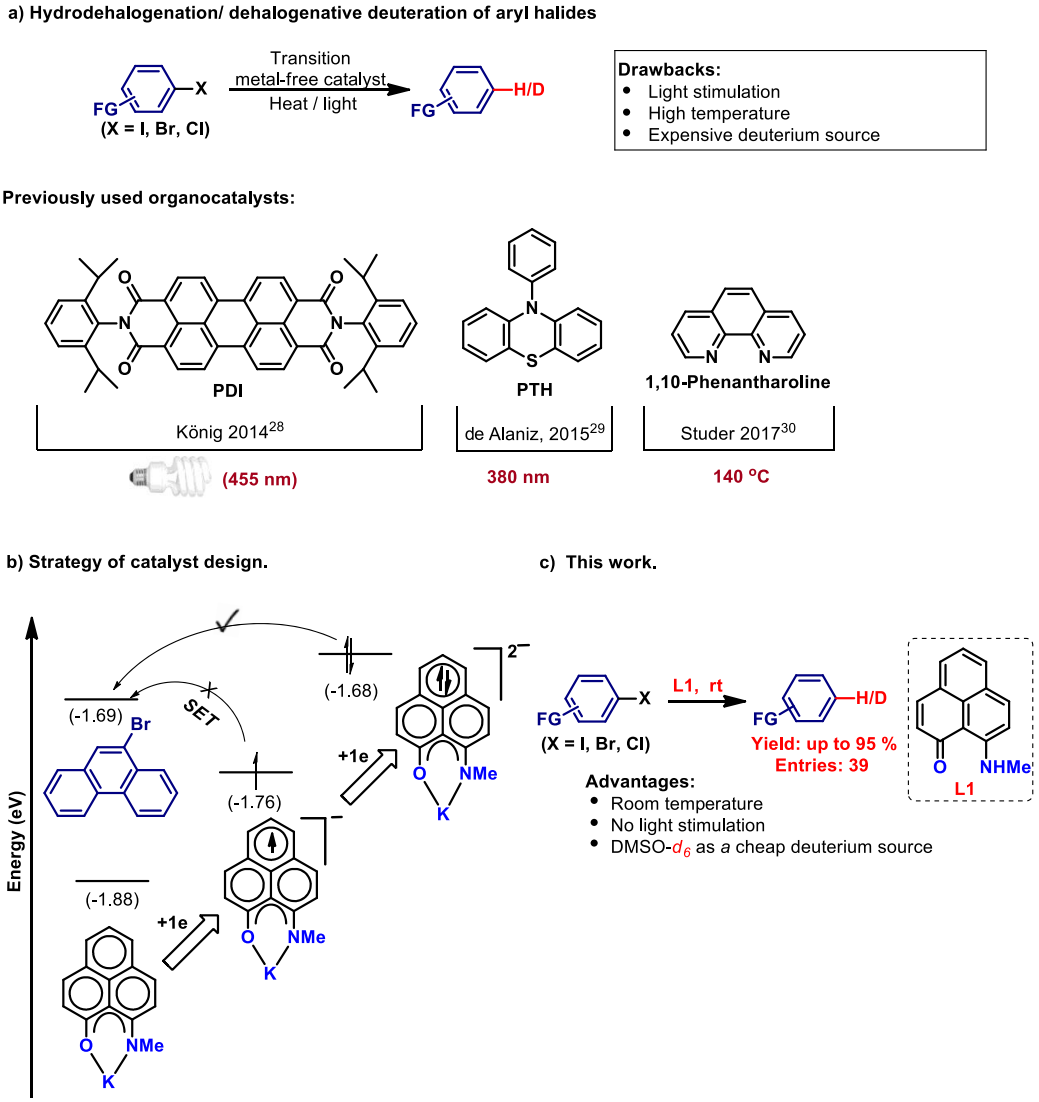


Scheme 1. Hydrodehalogenation/Dehalogenative Deuteration of Aryl Halide: (a) Previous Reports on Catalytic Organocatalytic Hydrodehalogenation; (b) Strategy of This Work; and (c) Our Catalytic Protocol



dehalogenation reaction, namely, catalytic dehalogenative deuteration of aromatic nuclei utilizing 2,2′-azobis(2,4-dimethylvaleronitrile) (V-65) in combination with an organotin reagent and THF-d_8 as deuterium sources, but the necessity of toxic Bu_3SnH, high temperature, and expensive deuterium sources (≈$630 for 10 g of THF-$d_8$, Sigma-Aldrich Cat. No. 184314-10G)[50] are considered to be the major drawbacks of this method. Recently, Liu and co-workers[51] utilized hexamethyldisilane in combination with potassium methoxide and CD_3CN as a deuterium source for dehalogenative deuteration in a noncatalytic fashion. However, this protocol also suffers from the use of an excess amount of reagents and expensive deuterium sources[52] (≈$787 for 100 g of CD_3CN, Sigma-Aldrich Cat. No. 151807-100G). Therefore, a catalytic reaction protocol using transition metal-free catalysts and cheaper deuterium sources functioning at room temperature is highly desirable for dehalogenative deuteration.

Herein, we aimed at developing a catalytic reaction protocol for dehalogenation (both hydrodehalogenation and dehalogenative deuteration) under transition metal-free conditions adopting a cost-effective approach. In this regard, we introduce an odd alternant hydrocarbon phenalenyl (PLY)[53−56] as a scaffold for designing transition metal-free catalysts to accomplish dehalogenative deuteration and hydrodehalogenation processes. The capability of a PLY-based moiety as an organic electron carrier in various organic transformations, without substantial perturbation of aromaticity of the phenalenyl core, is very well documented in recent studies.[57−59] The presence of an empty nonbonding molecular orbital of PLY cations having 12π e^- can lead to successive reduction by two electrons, transforming it into an odd 13π e^--based neutral radical and an anionic species (14π e^-).[55,60] Recently, Zeng and co-workers calculated the nuclear independent chemical shift values in pristine phenalenyl systems and found the values to be negative, which indicates that reduced PLY can retain their aromaticity upon electron acceptance.[61] Earlier, the 13π e^- radicals of PLY species have been used extensively in designing spintronics[62,63] as well as bistable materials.[64] In addition, it was also recently employed for the catalytic C−H functionalization of unactivated arenes as well as heteroarenes with aryl halides at 130 °C.[65,66] To avoid high-temperature activation of aryl halides, we recently focused on the utilization of the more reactive doubly reduced 14π e^- species.[67] It may be recalled that the 14π e^- species of

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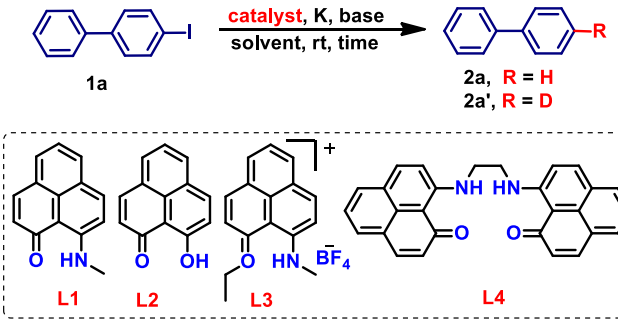
Table 1. Optimization and Control Experiments on the Hydrodehalogenation/Dehalogenative Deuteration Reaction[a]



entry	catalyst (mol %)	base (equiv)	time (h)	K (mol %)	solvent (mL)	yield (%)[b]
1	**L1** (5)	KO^{t}Bu (1.4)	24	7	DMSO (1)	47
2	**L1** (7.5)	KO^{t}Bu (1.4)	24	10	DMSO (1)	64
3	**L1** (10)	KO^{t}Bu (1.5)	24	13	DMSO (1)	77 [d]
4	**L1** (15)	KO^{t}Bu (1.6)	24	20	DMSO (1)	83
5	**L2** (10)	KO^{t}Bu (1.5)	24	13	DMSO (1)	62
6	**L3** (10)	KO^{t}Bu (1.3)	24	25	DMSO (1)	74
7	**L4** (10)	KO^{t}Bu (1.7)	24	25	DMSO (1)	71
8[c]	**L1** (10)	Cs_2CO_3 (1.3)	24	13	DMSO (1)	39
9[c]	**L1** (10)	CsF (1.3)	24	13	DMSO (1)	53
10	**L1** (10)	KO^{t}Bu (1.5)	24	13	dioxane (1)	50
11	**L1** (10)	KO^{t}Bu (1.5)	24	13	DMSO:dioxane (1.4)	93[d]
12	**L1** (10)	KO^{t}Bu (1.5)	12	13	DMSO:dioxane (1.4)	63
13		KO^{t}Bu (1.3)	24		DMSO:dioxane (1.4)	15
14		KO^{t}Bu (1.3)	24	13	DMSO:dioxane (1.4)	17
15[c]	**L1** (10)		24	13	DMSO:dioxane (1.4)	11
16	**L1** (10)	KO^{t}Bu (1.5)	24		DMSO:dioxane (1.4)	36
17	**L1** (10)	KO^{t}Bu (1.5)	24	13	DMSO-d_6 (1.3)	74[d]

[a]Reactions were performed under nitrogen atmosphere in a pressure tube with 0.15 mmol of 4-iodobiphenyl at rt. [b]Determined by ^{1}H NMR spectroscopy. [c]KO^{t}Bu, 0.2 mmol. [d]Isolated yield.

PLY, although anticipated six decades back,[55] remained practically unexplored in terms of their applications except for the recent report by us.[67] With the help of preliminary DFT calculations, we anticipated that the doubly reduced anionic state of PLY would accumulate sufficient energy to facilitate a single electron transfer to the LUMO of aryl halide (Scheme 1b), generating reactive aryl radical species that can subsequently accept hydrogen/deuterium atoms. In this work, we report the utilization of such reduced PLY species as a catalyst in combination with potassium *tert*-butoxide to execute the hydrodehalogenation and dehalogenative deuteration of aryl halides using DMSO-d_6 as a deuterium source (≈$195 for 100 g of DMSO-$d_6$, Sigma-Aldrich Cat. No. 151874-100G)[68] at room temperature (Scheme 1c).

Results and Discussion. To start with, we considered 4-iodobiphenyl (**1a**) as a model substrate for the proposed hydrodehalogenation/dehalogenative deuteration chemistry. Initially, the hydrodehalogenation of **1a** was attempted with 9-methylamino-phenalen-1-one (**L1**, 5 mol %) as a precatalyst, metallic potassium (7 mol %), potassium *tert*-butoxide (1.4 equiv), and DMSO (1 mL) in a pressure tube for 24 h at rt. (Table 1, entry 1), which produced the hydrodehalogenation product biphenyl (**2a**) with a moderate yield of 47%. The yield improved to 64% when 7.5 mol % precatalyst (**L1**) was loaded (Table 1, entry 2) and further raised to 77% (Table 1, entry 3) with 10 mol % precatalyst loading in DMSO. A further increase in precatalyst loading, however, did not improve the product yield (Table 1, entry 4).

Next, we evaluated different phenalenyl ligands **L2**–**L4** (Table 1) for their catalytic efficacy, but none of them could exhibit improved results (Table 1, entries 5–7), and **L1** turned out to be the best choice. Even screening of different bases, such as Cs_2CO_3 and CsF, as well as different solvents could not improve the yield further (Table 1, entries 8–10). However, a mixture of DMSO and dioxane in a 1:1 ratio resulted in 93% isolated yield of the desired hydrodehalogenated product (**2a**, Table 1, entry 11) under ambient conditions. The optimum reaction time was found to be 24 h, as reducing the reaction time to 12 h (Table 1, entry 12) led to a decreased yield of **2a** to 63%. Finally, in a control experiment, without using both the phenalenyl ligand and potassium metal and in another control, excluding the phenalenyl ligand only, afforded **2a** in <20% yield (Table 1, entries 13 and 14). Another control reaction with the exclusion of base resulted in only 11% yield of **2a** under optimized conditions (Table 1, entry 15). Further control reaction with PLY and potassium *tert*-butoxide yielded 36% of the product (Table 1, entry 16). All these results clearly indicated the essentiality of combining the PLY ligand, a catalytic amount of metallic potassium, and potassium tert-butoxide as a productive recipe to execute the hydrodehalogenation reaction successfully. Also, under these optimized reaction parameters, we employed DMSO-d_6, as a relatively cheap deuterium source (≈$195 for 100 g of DMSO-$d_6$), to perform the dehalogenative deuteration reaction. The desired product, 4-deuterobiphenyl (**2a′**) in this case, was successfully isolated in 74% yield (Table 1, entry 17). More importantly, the deuterated product was obtained with

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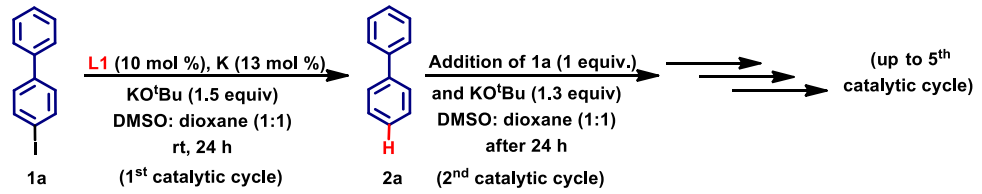


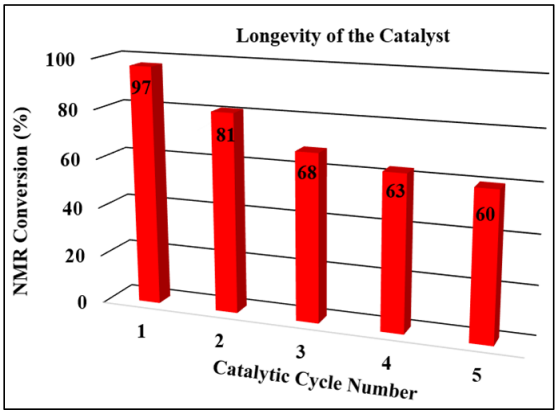
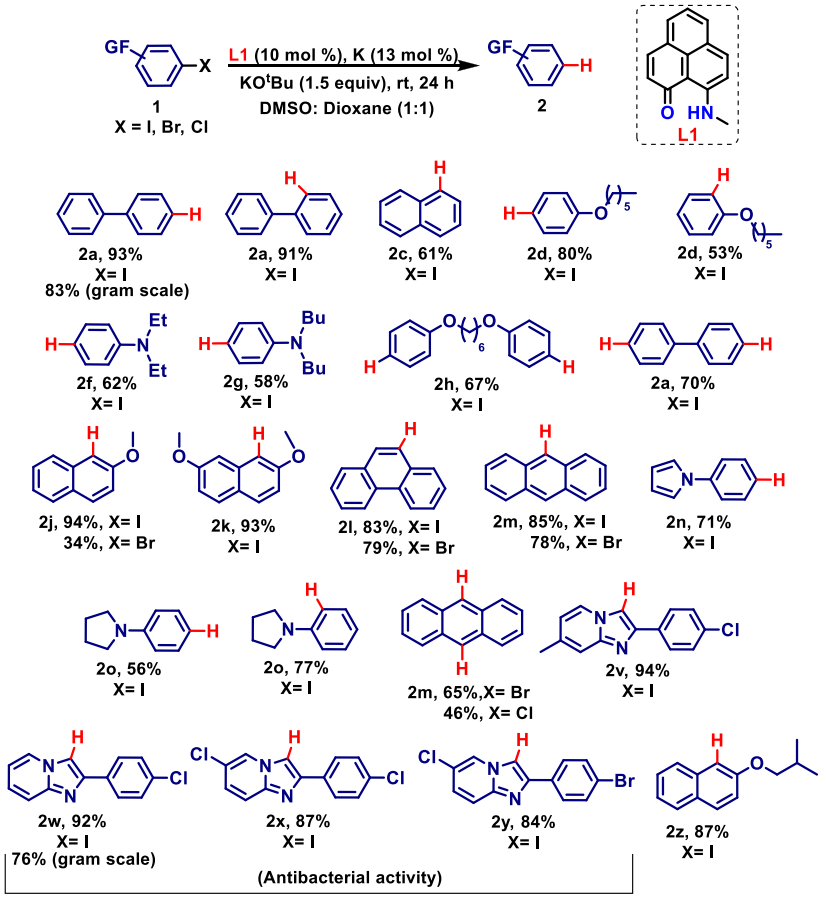


Figure 1. Longevity test of the present catalyst during the hydrodehalogenation reaction. The designated yields are NMR conversion, and the result was reproduced twice.

Scheme 2. Substrate Scope for the Hydrodehalogenation Reaction[a]



[a]Reactions were performed under nitrogen atmosphere in a pressure tube with 0.15 mmol of the substrate, 0.015 mmol of catalyst, 0.02 mmol of K, 0.225 mmol of KO^{t}Bu, and 1.4 mL of solvent. Yields reported are isolated and an average yield of two catalytic runs.

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exclusive deuterium integration in this transition metal-free approach under the ambient condition. The deuterium incorporation was confirmed by comparing the ^{1}H NMR spectra of both the deuterated product and the corresponding hydrodehalogenated product, and it was found that the corresponding proton peak was absent.[69] Next, it became obvious from our longevity experiment (see Figure 1) that the active catalyst sustains over several consecutive catalytic cycles under the optimized reaction conditions. In such an experiment, the catalyst (**L1**) was incorporated at 10 mol % loading once and executed five successive catalytic cycles with 4-iodobiphenyl (**2a**), and the catalytic efficiency was studied over several runs successively. After each catalytic run, a fresh batch of 4-iodobiphenyl (1 equiv) and potassium *tert*-butoxide (1.3 equiv) was added in the same reaction pot, but no further catalyst (**L1**) or potassium was loaded into the reaction mixture (see the Experimental Section for details). To our delight, the catalyst was found to have sustained activity even up to the fifth catalytic run. Although its efficiency declined gradually over successive catalytic cycles to a moderate yield of 60% after the fifth cycle, nevertheless, this observation clearly indicates the sustained stability of the active catalyst over consecutive catalytic runs.

With these initial results in hand, this study further advanced with the exploration of potential substrate scope. A diverse range of aryl/heteroaryl halides under the optimized reaction conditions was subjected to such hydrodehalogenation, yielding good to excellent yields of the hydrodehalogenated products. For example, 2-iodobiphenyl was efficiently reduced to biphenyl (**2a**) with an excellent yield (91%, Scheme 2). Also, 1-iodonaphthalene produced naphthalene (**2c**) with a moderate yield (61%, Scheme 2). The alkoxy and alkylamino-arenes under the optimized reaction conditions resulted in the respective hydro-deiodinated arenes, such as hexyloxy (**2d**) and dialkyl amino (**2f** and **2g**) benzenes in 53−80% yields (Scheme 2). Furthermore, diiodoarenes took part in two consecutive hydrodeiodination cycles, producing doubly reduced products (**2h** and **2a**) in good isolated yield (67−70%, Scheme 2). Moreover, 2-methoxy- and 2,7-dimethoxy-substituted iodonaphthalenes were effectively reduced under optimized conditions, and the corresponding naphthalenes (**2j** and **2k**) were isolated in excellent yields (93−94%, Scheme 2). Interestingly, 2-methoxynaphthalene (**2j**) is a crucial intermediate[70] for the synthesis of nonsteroidal anti-inflammatory drugs such as nabumetone and naproxen.[71] Even iodo-substituted polycyclic hydrocarbons such as iodophenanthrene and iodoanthracene efficiently took part in the reaction, and the corresponding arenes (**2l** and **2m**) were isolated in excellent yields (83−85%, Scheme 2). In addition, several iodo-heteroarenes (pyrroles and pyrrolidines) were successfully reduced to the corresponding hydrodeiodinated products (**2n** and **2o**), with 56−77% isolated yield (Scheme 2).

To extend the study further, more challenging substrates were next considered, such as the reduction of aryl bromides and aryl chlorides. To our delight, the present methodology worked smoothly by activating aryl chlorides and aryl bromides under ambient conditions. We successfully performed the hydrodebromination and hydrodechlorination of bromo/chloro-arenes. For example, both 9-bromophenanthrene and 9-bromoanthracene were successfully hydrodebrominated to phenanthrene (79%, **2l**) and anthracene (78%, **2m**), respectively, with very good isolated yields (Scheme 2). The yield of anthracene was notably higher than the preceding report based on PDI catalysts by light irradiation at a higher temperature (as reported with 54% yield).[28] The hydrodebromination of 1-bromo-2-methoxy-naphthalene (**1s**) was rather slow, producing 2-methoxynaphthalene (**2j**) with only 34% yield (Scheme 2). Interestingly, 9,10-dibromoanthracene smoothly proceeded through two successive debromination cycles to yield anthracene (**2m**) in 65% yield (Scheme 2). Also, the hydrodehalogenation protocol was successfully employed for the chloroarene precursor, 9,10-dichloroanthracene, which was reduced to anthracene (**2m**) with 46% yield (Scheme 2). However, the substrates with functional groups such as esters, nitro, cyano, unprotected alcohols, and amines did not undergo such hydrodehalogenation processes under our reaction conditions.

Furthermore, this methodology was successfully applied in hydrodehalogenation of a number of imidazopyridine derivatives that exhibit distinct biological activities. For example, 3-iodo-2-(aryl)imidazo[1,2-*a*]pyridine derivatives produced the corresponding deiodinated heteroarenes under the optimized reaction conditions and yielded **2v**−**2y** with excellent yields (84−94%, Scheme 2), many of which were reported to exhibit antibacterial activity against Gram-negative and Gram-positive bacteria.[72] Also, the reaction proceeded with a preferential deiodination process, instead of dechlorination/debromination at other possible sites. Finally, another important application of this protocol was found when 2-isobutoxynaphthalene (**2z**) was afforded with 87% yield (Scheme 2), which is used in perfumery as a soap perfume.[73,74] It is important to note that the present study is the first to report hydrodehalogenation of various halo-arene/heteroarene derivatives such as 1,6-bis(4-iodophenoxy)hexane, 2,7-dimethoxy-1-iodonaphthalene, 9-iodoanthracene, 9,10-dibromoanthracene, 9,10-dichloroanthracene, imidazopyridine derivatives, and 1-iodo-2-isobutoxy-naphthalene into their corresponding arenes under such transition metal-free and under ambient temperature. Next, to show the scalability of this protocol, 4-iodobiphenyl was employed under the optimized reaction conditions with a 10-fold scale-up (1.5 mmol), which was well tolerated with the current process, producing **2a** in 83% isolated yield. Furthermore, an increase in the loading of 2-(4-chlorophenyl)-3-iodoimidazo[1,2-*a*]pyridine (**1w**) by 25-fold (3.75 mmol) was also well tolerated and effectively reduced to **2w** in 76% yield.

Moreover, to demonstrate the potential application of this protocol, a range of aryl and heteroaryl halides was investigated for dehalogenative deuteration. It is worth mentioning that an alternative approach for deuterium labeling is a C−H/C−D exchange protocol,[75] which enables direct incorporation of deuterium by the addition of a deuterium source without the requirement of the starting material prefunctionalization or any significant structural modification of the chemical entity. However, this approach suffers from various limitations, such as difficulty to directly activate the C−H bonds,[76] low functional group acceptance, requirement of high temperature, etc.[77] Recently, the direct hydrogen isotope exchange (HIE) protocol was explored utilizing D_2 by Kerr[78] and Chirik[79] groups, and they successfully employed iridium and iron catalysis, respectively. Also, the Macmillan[80] group utilized iridium photoredox catalysts for the HIE protocol and D_2O as a deuterium source. In spite of the efficiency of these methods, these protocols are limited by the use of transition metal catalysts, the requirement of directing groups, light irradiation, low deuterium content in the product, high cost, and poor site

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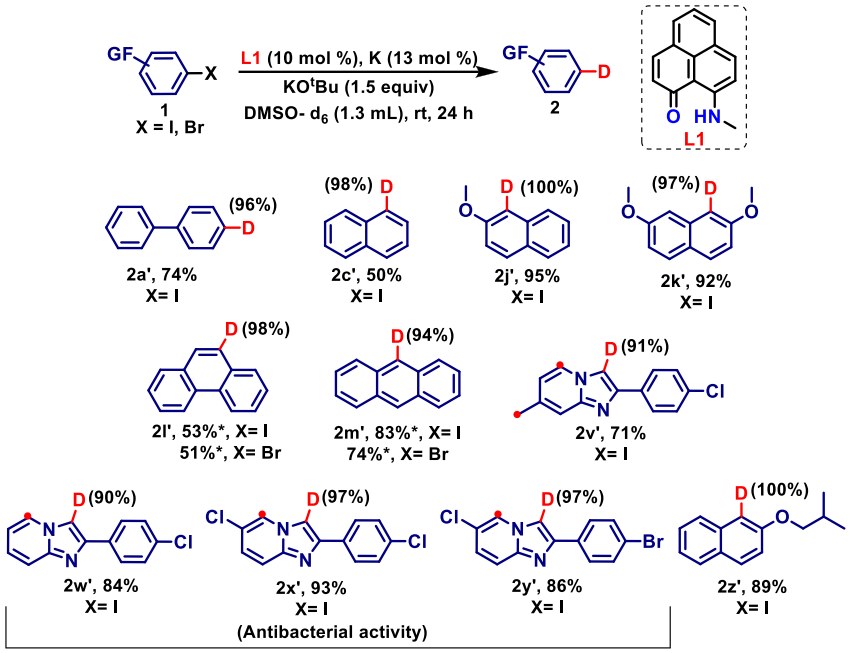
Scheme 3. Substrate Scope for the Dehalogenative Deuteration Reaction[a]



[a]Reactions were performed under nitrogen atmosphere in a pressure tube with 0.15 mmol of substrate, 0.015 mmol of catalyst, 0.02 mmol of K, 0.225 mmol of KO^{t}Bu, and 1.3 mL of DMSO-d_6. Yields are isolated yield. *0.037 mmol of catalyst, 0.049 mmol of K, and 0.232 mmol of KO^{t}Bu. Deuterium incorporation is given in the parentheses.

selectivity. On the contrary, the present method consists of a transition metal-free dehalogenative protocol under ambient temperature with DMSO-d_6 as a cheap deuterium source,[68] and the reactions were found to proceed with the excellent deuterium incorporation. For example, 4-iodobiphenyl (**1a**) led to the desired deuterated product (**2a′**) in 74% isolated yield (Scheme 3) and the reduction of 1-iodonaphthalene (**1c**) afforded the deuterated naphthalene (**2c′**) with 50% yield (Scheme 3) under the optimized reaction conditions of dehalogenative deuteration. Excellent yields were observed in the cases of 1-iodo-2-methoxynaphthalene and 1-iodo-2,7-dimethoxynaphthalene, which were efficiently reduced to 2-methoxynaphthalene-1-*d* (**2j′**, 95%) and 2,7-dimethoxynaphthalene-1-*d* (**2k′**, 92%), respectively, with this protocol (Scheme 3). Phenanthrene-9-*d* (**2l′**), on the other hand, was obtained from 9-iodophenantharene with 53% yield (Scheme 3), and anthracene-9-*d* (**2m′**) was obtained from 9-iodoanthracene in 83% yield (Scheme 3). Interestingly, the yields of debrominative deuteration of their bromo analogues were only marginally diminished from those of the iodo compounds. For example, 9-bromophenantharene was dehalogenatively deuterated to phenanthrene-9-*d* (**2l′**) with 51% yield and 9-bromoanthracene to anthracene-9-*d* (**2m′**) with 74% isolated yield (Scheme 3). Moreover, when we shifted toward the deuteration of pharmaceutically important heterocyclic moieties, such as imidazopyridine derivatives, clean deuterodeiodination at room temperature was observed. As demonstrated in Scheme 3, 2-(4-chlorophenyl)-3-iodo-7-methylimidazo[1,2-*a*]pyridine (**1v**) effectively produced the deuterated product (**2v′**) in 71% yield. Also, the deuterated versions (**2w′**−**2y′**) of the antibacterial imidazopyridine derivatives (**2w**−**2y**) were afforded from the corresponding iodo-imidazopyridines with excellent yields (84−93%, Scheme 3) under this deuterodeiodination protocol. It is noteworthy that, similar to hydrodehalogenation, chloride and bromide substituents in imidazopyridine derivatives are also well tolerated during the course of the catalytic deuteration. Furthermore, we reduced 1-iodo-2-isobutoxynaphthalene to a deuterated version of 2-isobutoxynaphthalene (**2z′**), with 89% yield (Scheme 3), which is used in the perfumery/flavoring industry. It is worth mentioning that, in the case of hydrodehalogenation, the productivity of this mild reaction protocol at room temperature runs parallel to the existing transition metal-free methodologies that uses either stoichiometric reactants[23] and/or harsh reaction parameters[24] (such as high temperature[30]). For dehalogenative deuteration, the existing literature is enriched in metal-catalyzed reactions, except one report, catalyzed by an organotin reagent and operates at high temperature, utilizing an expensive deuterium source (THF-d_8).[49] However, in this study, we utilized the catalyst under transition metal-free methodology, which runs at room temperature using a cheap deuterium source (DMSO-d_6) and produces the corresponding arenes and deuterated arenes in good yield. To the best of our knowledge, this work reports the first catalytic hydrodehalogenation and dehalogenative deuteration protocol of aryl/heteroaryl halides together using a transition metal-free approach without the assistance of any external stimuli such as heat or light.

Next, to gain an insight into the underlying mechanism of the catalytic process, we resorted to a series of control experiments along with DFT calculations. Keeping in mind the idea of utilizing the reduced 14π e$^-$ anionic state of a phenalenyl moiety, we hypothesized that such species would accumulate sufficiently high energy to accomplish a SET process to the LUMO of aryl halides, splitting it into a reactive aryl radical and halide and generating the radical species having 13π e$^-$. To confirm the involvement of radical species, we performed the radical quenching studies, where a radical scavenger, galvinoxyl, was utilized under the optimized conditions, and the catalysis was efficiently shut down with

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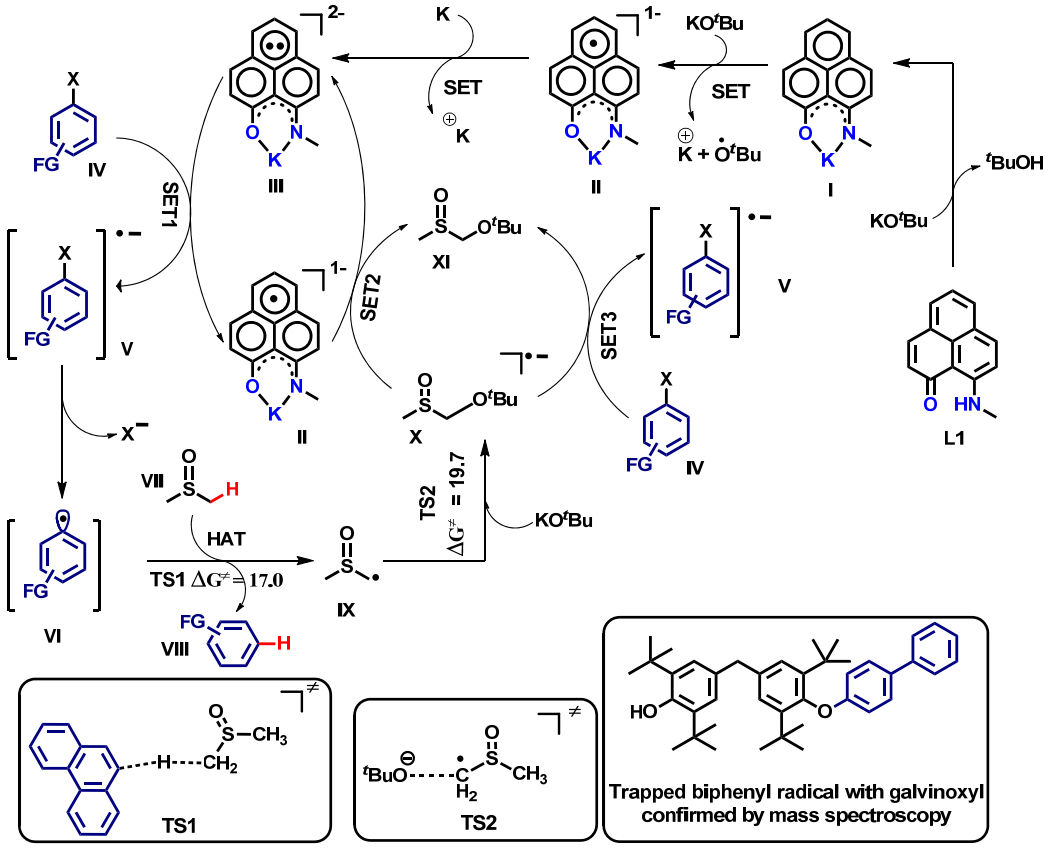
Scheme 4. Plausible Reaction Mechanism



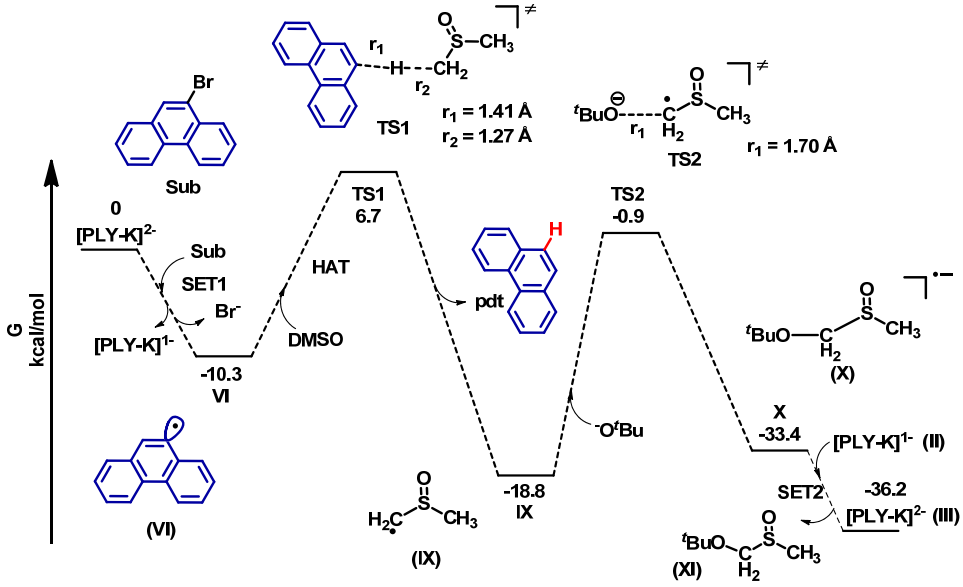


Figure 2. Energy profile diagram for aryl halide dehalogenation, considering DMSO as one of the reactants.

no detectable hydrodehalogenative product, even after 24 h (Scheme S1, Supporting Information). Based on this finding and on the basis of theoretical calculations and previous observations[67] on the generation of doubly reduced PLY species upon reaction with K, a mechanistic cycle was proposed, as illustrated in Scheme 4 and Figure 2. Initially, a PLY-K complex **I** was formed by the interaction of the phenalenyl ligand and KO^{t}Bu and such observation was established in previous studies.[57,59,65] A SET from $^-$O^{t}Bu to **I** generates a monoreduced phenalenyl radical-K complex **II** (13π electron species) along with a *tert*-butoxy radical. Such a monoreduced phenalenyl radical has been trapped and characterized earlier.[81] A further reduction of this monoreduced PLY-K complex **II** by metallic potassium produced a doubly reduced PLY-K complex **III** (the anionic 14π electron species). Such doubly reduced species, upon reduction by

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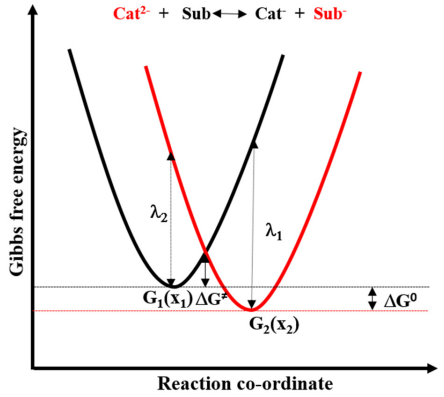
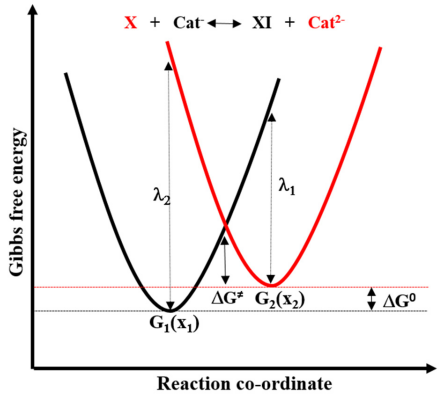
a) Substrate activation (9-bromophenanthrene) with **III** (SET1):



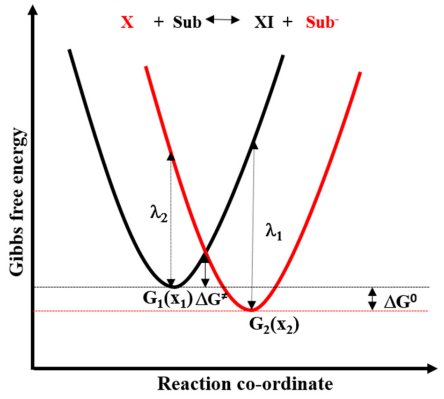
Reorganization energy (eV)	Driving force ΔG^0 (kcal/mol)	Activation energy barrier $\Delta G^{\neq}$ (kcal/mol)
$\lambda_1 = 0.31$	-0.584	$\Delta G^{\neq}_{\lambda 1} = 1.3$
$\lambda_2 = 0.36$	-0.584	$\Delta G^{\neq}_{\lambda 2} = 0.8$

b) Catalyst regeneration with **X** (SET2):



Reorganization energy (eV)	Driving force ΔG^0 (kcal/mol)	Activation energy barrier $\Delta G^{\neq}$ (kcal/mol)
$\lambda_1 = 3.32$	0.406	$\Delta G^{\neq}_{\lambda 1} = 24.1$
$\lambda_2 = 0.76$	0.406	$\Delta G^{\neq}_{\lambda 2} = 10.3$

c) Radical chain propagation (SET3).



Reorganization energy (eV)	Driving force ΔG^0 (kcal/mol)	Activation energy barrier $\Delta G^{\neq}$ (kcal/mol)
$\lambda_1 = 3.29$	-0.177	$\Delta G^{\neq}_{\lambda 1} = 17.1$
$\lambda_2 = 1.59$	-0.177	$\Delta G^{\neq}_{\lambda 2} = 7.2$

Figure 3. Parabolic PESs for reactants (blue) and products (red) in an electron self-exchange process as a function of the reaction coordinate along with the theoretically calculated reorganization energies λ_1 and λ_2, which represent the reorganization energies of forward and backward reactions, respectively. $\Delta G^{\neq}_{\lambda 1}$ and $\Delta G^{\neq}_{\lambda 2}$ represent the activation energy barriers of forward and backward reactions, respectively. (a) Electron transfer from the doubly reduced PLY moiety to aryl halides. (b) Catalyst regeneration at the final step of product formation. (c) Radical chain propagation process.

metallic potassium, has also been trapped and characterized very recently.[67] The doubly reduced PLY-K complex **III** having high HOMO energy (−1.68 eV) transfers an electron through SET to the LUMO of aryl/heteroaryl halide (−1.69 eV for 9-bromophenanthrene) at room temperature and leads to the formation of aryl halide radical anion **V**, oxidizing itself to the monoreduced PLY-K complex **II**.

This electron transfer step was supported by theoretical calculations (considering bromophenanthrene as the substrate), showing a free-energy change of −10.3 kcal/mol (ΔG), which indicates a thermodynamically favorable process. It is important to note that the formation of aryl radicals has been successfully demonstrated by trapping it with galvinoxyl and characterized by mass spectroscopic measurements (Scheme S2, Supporting Information).

The aryl radical next accepts a hydrogen atom from DMSO through a transition state **TS1** (Figure 2). The transition state calculations for this hydrogen atom transfer (HAT) process show that the transition state **TS1** with an energy barrier $\Delta G^{\ddagger}$ = 17.0 kcal/mol is achievable at room temperature to yield the

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desired product **VIII** and DMSO-based radical intermediate **IX** (Figure 2). In this case (Figure 2), the Gibbs free-energy change for the electron transfer from **IX** (DMSO rad) to produce the doubly reduced active catalyst was calculated as 83.4 kcal/mol, which is thermodynamically unfavorable defying its direct electron transfer to regenerate the catalyst. Alternatively, **IX** may undergo an additive interaction with a *tert*-butoxide anion *via* a radical anionic transition state **TS2**, resulting in a radical anionic intermediate **X** with an energy barrier of 19.7 kcal/mol. This intermediate **X** has a favorable SOMO energy (−1.66 eV) and can transfer an electron to the SOMO (−1.76 eV) of the monoreduced PLY-K complex **II** to regenerate the doubly reduced active catalyst along with the formation of **XI**. Such solvent−potassium *tert*-butoxide adduct has been reported in the literature.[24] The radical anionic intermediate **X** can also directly transfer one electron to the aryl halide **IV** and promote another set of reactions to deliver the desired product through a radical chain propagation process. Furthermore, to understand electron transfer energetics for all the single electron transfer process, Nelsen's four-point calculation based on the Marcus−Hush theory was carried out (Figure 3).

The energy barriers of the forward reaction for substrate activation (SET1) and catalyst regeneration considering the radical anionic DMSO−O^{t}Bu adduct, **X** (SET2), are 1.3 and 24.1 kcal/mol, respectively, for both the reactions, which can be easily accessible at room temperature (Figure 3a,b). We explored the possibility of a radical chain propagation process, where a SET takes place from **X** to another aryl halide molecule directly (9-bromophenanthrene, SET3). The activation energy barrier is 17.1 kcal/mol for the forward reaction, which indicates that the chain propagation runs parallel to the catalyst regeneration step (Figure 3c). However, a sequence of control reactions was carried out in the absence of the ligand (**L1**) using only metallic potassium (13 mol %) and potassium *tert*-butoxide (1.5 equiv), which produced the hydrodehalogenated products [**2a**, **2j**, (X = I, Br); see page S2 in the Supporting Information] only up to 33% yield. This observation shows the inefficacy of the chain propagation step to obtain the satisfactory yield of the hydrodehalogenated products, whereas the addition of the PLY ligand (10 mol %) could afford the yield up to 94%. From these experiments, it can be concluded that although the chain propagation for such a process is thermodynamically favorable along with the catalyst regeneration, the chain propagation process alone cannot offer our observed yield (94%).

In summary, we have developed a dehalogenative deuteration/reductive hydrodehalogenation methodology catalyzed by the reduced (14π e$^-$) state of a phenalenyl system. The reduced PLY species having sufficiently high energy undergoes a SET process activating the aryl/heteroaryl halides at room temperature under mild conditions. The protocol is compatible with various aryl/heteroaryl halides to access various biologically active molecules under transition metal-free catalytic conditions at room temperature. The deuterated analogues were obtained with good yields by employing DMSO-d_6 as a deuterium source.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all reactions were performed inside a nitrogen filled glovebox, with the concentration of H_2O and O_2 maintained below 0.1 ppm. All solvents were distilled from calcium hydride or Na/benzophenone under an inert atmosphere prior to use. KO^{t}Bu, potassium metal, aryl/heteroaryl halides, and all other chemicals were acquired from Sigma Aldrich or other commercial sources and used without further purification. Deuterated solvents were acquired from Cambridge Isotope Laboratories. $CDCl_3$ (99.8 atom% D), $(CD_3)_2SO$ (99.9 atom% D), and CD_3OD (99.8 atom% D) were stored inside a glovebox and used as received. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL 400 MHz or a BRUKER 500 MHz NMR spectrometer using $CDCl_3$ or $(CD_3)_2SO$ or CD_3OD as a solvent. Chemical shifts were reported in the ppm downfield to tetramethylsilane. The residual undeuterated solvent peaks were used as references for ^{13}C NMR and ^{1}H NMR spectra ($CDCl_3$: δ_C = 77.1 ppm, δ_H = 7.26 ppm; $(CD_3)_2SO$: δ_C = 39.5 ppm, δ_H = 2.50 ppm; CD_3OD: δ_C = 49.0 ppm, δ_H = 3.31 ppm). HRMS measurements were carried out on a Bruker maXis impact. Thin-layer chromatography (TLC) was carried out using precoated aluminum baked silica gel plates and visualized by UV absorbance (254 nm). Column chromatography was performed using a Merck silica gel (particle size, 230−400 mesh) and neutral alumina.

Preparation of the Substrates. 1-Hexyloxy-4-iodobenzene,[82] 1-hexyloxy-2-iodobenzene,[83] *N*,*N*-diethyl-4-iodoaniline,[84] *N*,*N*-dibutyl-4-iodoaniline,[85] 1,6-bis(4-iodophenoxy)hexane,[86] 1-iodo-2-7-dimethoxynaphthalene,[87] iodophenantharene,[88] idooanthracene,[89] 1-(4-iodophenyl)-1*H*-pyrrole,[24] 1-(4-iodophenyl)-pyrrolidine,[90] 1-(2-iodophenyl)-pyrrolidine,[91] 2-(4-chlorophenyl)-3-iodo-7-methylimidazo[1,2-*a*]pyridine,[92] 2-(4-chlorophenyl)-3-iodoimidazo[1,2-*a*]pyridine,[92] 6-chloro-2-(4-chlorophenyl)-3-iodoimidazo[1,2-*a*]pyridine,[93] 2-(4-bromophenyl)-6-chloro-3-iodoimidazo[1,2-*a*]pyridine,[93] 1-iodo-2-isobutoxynaphthalene,[94] 9-hydroxy-1*H*-phenalenone,[65] 9-(methylamino)-1*H*-phenalenone,[65] (*E*)-ethyl(9-(methylamino)-1*H*-phenalen-1-ylidene)oxonium tetrafluoroborate salt,[95] and 9,9′-(ethane-1,2-diylbis(azanediyl))bis(1*H*-phenalenone)[66] were synthesized according to the reported literature.

General Procedure for the Catalytic Hydrodehalogenation Reaction. Inside a nitrogen-filled glovebox, precatalyst **L1** (3.1 mg, 0.015 mmol), KO^{t}Bu (3.4 mg, 0.03 mmol), metallic potassium (0.76 mg, 0.02 mmol), DMSO (0.7 mL), and dioxane (0.7 mL) were charged in a 25 mL pressure tube. Subsequently, aryl/heteroaryl halide (0.15 mmol) and KO^{t}Bu (22 mg, 0.195 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature for 24 h. After completion of the reaction, the reaction mixture was extracted with diethyl ether. The organic phase was dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure to obtain the crude product, which was purified by column chromatography using hexane or a hexane/EtOAc mixture to afford the desired products.

General Procedure for the Catalytic Dehalogenative Deuteration Reaction. Inside a nitrogen-filled glovebox, precatalyst **L1** (3.1 mg, 0.015 mmol), KO^{t}Bu (3.4 mg, 0.03 mmol), metallic potassium (0.76 mg, 0.02 mmol), and DMSO-d_6 (1.3 mL) were charged in a 25 mL pressure tube. Subsequently, aryl/heteroaryl halide (0.15 mmol) and KO^{t}Bu (22 mg, 0.195 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature (25−30 °C) for 24 h. After completion of the reaction, the reaction mixture was extracted with diethyl ether. The organic phase was dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure to obtain the crude product, which was purified by column chromatography using hexane or a hexane/EtOAc mixture to afford the desired deuterated products.

Procedure for the Longevity Experiment. Inside a nitrogen-filled glovebox, precatalyst **L1** (3.1 mg, 0.015 mmol), KO^{t}Bu (3.4 mg, 0.03 mmol), metallic potassium (0.76 mg, 0.02 mmol), DMSO (0.7 mL), and dioxane (0.7 mL) were charged in a 25 mL pressure tube. Subsequently, 4-iodobiphenyl (42 mg, 0.15 mmol) and KO^{t}Bu (22 mg, 0.195 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature (25−30 °C) for 24 h. After completion of the reaction, the yield was calculated by ^{1}H NMR spectroscopy. Next, the aliquots of 4-iodobiphenyl (40.2 mg, 0.143 mmol, maintaining the catalyst substrate ratio) and KO^{t}Bu (20.8 mg, 0.186 mmol) were charged in the reaction mixture, and it was allowed to stir at room temperature (25−30 °C) for 24 h. The

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conversion was calculated by ^{1}H NMR spectroscopy. Maintaining the catalyst to substrate ratio, the procedure was replicated up to the fifth catalytic cycle, and after each run, the conversion was calculated by ^{1}H NMR spectroscopy.

Procedure for the Large-Scale Catalytic Hydrodehalogenation Reaction of Aryl Halide. Inside a nitrogen-filled glovebox, catalyst **L1** (31.3 mg, 0.15 mmol), KO^{t}Bu (33.6 mg, 0.30 mmol), metallic potassium (7.8 mg, 0.20 mmol), DMSO (5 mL), and dioxane (5 mL) were charged in a 25 mL pressure tube. Subsequently, 4-iodobiphenyl (420 mg, 1.50 mmol) and KO^{t}Bu (218 mg, 1.95 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature (25−30 °C) for 24 h. After completion of the reaction, the reaction mixture was extracted with diethyl ether. The organic phase was dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure to obtain the crude product, which was purified by column chromatography using hexane, and 192 mg of biphenyl was isolated with 83% yield.

Procedure for the Large-Scale Catalytic Hydrodehalogenation Reaction for the Synthesis of Biologically Active Compounds. Inside a nitrogen-filled glovebox, catalyst **L1** (78 mg, 0.375 mmol), KO^{t}Bu (84 mg, 0.75 mmol), metallic potassium (19 mg, 0.487 mmol), DMSO (15 mL), and dioxane (15 mL) were charged in a 70 mL sealed tube. Subsequently, 2-(4-chlorophenyl)-3-iodoimidazo[1,2-*a*]pyridine (1329 mg, 3.75 mmol) and KO^{t}Bu (546 mg, 4.87 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature (25−30 °C) for 24 h. After completion of the reaction, the reaction mixture was extracted with diethyl ether. The organic phase was dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure to obtain the crude product, which was purified by column chromatography using a hexane/EtOAc mixture, and 652 mg of 2-(4-chlorophenyl)imidazo[1,2-*a*]pyridine was isolated with 76% yield.

Procedure for Inhibition of the Hydrodehalogenation Reaction in the Presence of the Radical Scavenger. Inside a nitrogen-filled glovebox, precatalyst **L1** (3.1 mg, 0.015 mmol), KO^{t}Bu (3.4 mg, 0.03 mmol), metallic potassium (0.76 mg, 0.02 mmol), DMSO (0.7 mL), and dioxane (0.7 mL) were charged in a 25 mL pressure tube. Subsequently, 4-iodobiphenyl (42 mg, 0.15 mmol), KO^{t}Bu (22 mg, 0.195 mmol), and galvinoxyl (63 mg, 0.15 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature (25−30 °C) for 24 h. After completion of the reaction, the reaction mixture was extracted with diethyl ether. The organic phase was dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure to obtain the crude product, which was purified by column chromatography using hexane to obtain a mixture of less than 8% biphenyl with remaining unreacted 4-iodobiphenyl.

Mass Spectroscopy Analysis of the Galvinoxyl Adduct. Inside a nitrogen-filled glovebox, catalyst **L1** (11.7 mg, 0.056 mmol), KO^{t}Bu (12.5 mg, 0.112 mmol), metallic potassium (2.83 mg, 0.073 mmol), DMSO (0.5 mL), and dioxane (0.5 mL) were charged in a 25 mL pressure tube. Subsequently, 4-iodobiphenyl (15.6 mg, 0.056 mmol), KO^{t}Bu (7 mg, 0.062 mmol), and galvinoxyl (20 mg, 0.048 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature (25−30 °C) for 24 h. After completion of the reaction, the reaction mixture was characterized by mass spectroscopy. The mass spectra showed exact molecular ion peaks, which correspond to the proposed galvinoxyl−biphenyl and galvinoxyl−DMSO trapped product.

Hydrodehalogenation Reactions in the Absence of Catalysts. Inside a nitrogen-filled glovebox, KO^{t}Bu (3.4 mg, 0.03 mmol), metallic potassium (0.76 mg, 0.02 mmol), DMSO (0.7 mL), and dioxane (0.7 mL) were charged in a 25 mL pressure tube. Subsequently, aryl/heteroaryl halide (0.15 mmol) and KO^{t}Bu (22 mg, 0.195 mmol) were added to the reaction mixture. The resulting reaction mixture was allowed to stir at room temperature for 24 h. After completion of the reaction, the reaction mixture was extracted with diethyl ether. The organic phase was dried over anhydrous sodium sulfate. The solvent was concentrated under reduced pressure to obtain the crude product, and the yield was calculated by ^{1}H NMR spectroscopy.

Spectral Characterization Data of the Hydrodehalogenated/Dehalogenative Deuterated Products. *Biphenyl (**2a**).*[96] White solid, yield 21 mg (93%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.80 (m, 4H), 7.59−7.64 (m, 4H), 7.51−7.55 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.2, 128.8, 127.2, 127.2.

*Naphthalene (**2c**).*[96] White solid, yield 12 mg (61%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02−8.04 (m, 4H), 7.65−7.67 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 133.5, 127.9, 125.8.

*(Hexyloxy)benzene (**2d**).*[97,98] Colorless oil, yield 15 mg (80%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29−7.33 (m, 2H), 6.93−6.98 (m, 3H), 3.99 (t, J = 6.7 Hz, 2H), 1.78−1.85 (m, 2H), 1.47−1.54 (m, 2H), 1.36−1.40 (m, 4H), 0.95 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.2, 129.4, 120.4, 114.5, 67.9, 31.7, 29.3, 25.8, 22.7, 14.1.

*N,N-Diethylaniline (**2f**).*[23] Colorless liquid, yield 14 mg (62%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24−7.28 (m, 2H), 6.68−6.75 (m, 3H), 3.40 (q, J = 14.6, 7.3 Hz, 4H), 1.21 (t, J = 7.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 147.8, 129.3, 115.4, 111.9, 44.3, 12.6.

*N,N-Dibutylaniline (**2g**).*[99] Colorless liquid, yield 18 mg (58%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (t, J = 7.3 Hz, 2H), 6.61−6.66 (m, 3H), 3.26 (t, J = 7.9 Hz, 4H), 1.54−1.61 (m, 4H), 1.31−1.41 (m, 4H), 0.96 (t, J = 7.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.3, 129.2, 115.1, 111.7, 50.8, 29.5, 20.4, 14.1.

*1,6-Diphenoxyhexane (**2h**).*[100] Colorless solid, yield 20 mg (67%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.32 (m, 4H), 6.91−6.97 (m, 6H), 3.99 (t, J = 6.1 Hz, 4H), 1.83−1.86 (m, 4H), 1.55−1.59 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.1, 129.4, 120.5, 114.5, 67.7, 29.3, 25.9.

*2-Methoxynaphthalene (**2j**).*[96] White solid, yield 22 mg (94%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74−7.79 (m, 3H), 7.45 (t, J = 7.9 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.15−7.18 (m, 2H), 3.93 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 157.6, 134.6, 129.4, 129.0, 127.7, 126.8, 126.4, 123.6, 118.8, 105.8, 55.3.

*2,7-Dimethoxynaphthalene (**2k**).*[101] White solid, yield 26 mg (93%); purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 9.1 Hz, 2H), 7.06 (d, J = 2.4 Hz, 2H), 6.99 (dd, J = 2.4, 9.1 Hz, 2H), 3.91 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 158.2, 135.9, 129.1, 124.3, 116.0, 105.3, 55.2.

*Phenanthrene (**2l**).*[23] White solid, yield 22 mg (83%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (d, J = 7.9 Hz, 2H), 7.92 (d, J = 7.9 Hz, 2H), 7.76 (s, 2H), 7.60−7.70 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 132.1, 130.3, 128.6, 127.0, 126.6, 122.7.

*Anthracene (**2m**).*[26] White solid, yield 23 mg (85%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 2H), 8.02 (dd, J = 6.7, 3 Hz, 4H), 7.48 (dd, J = 6.7, 3 Hz, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 131.7, 128.2, 126.2, 125.4.

*N-Phenylpyrrole (**2n**).*[23] Light brown solid, yield 15 mg (71%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (t, J = 2.4 Hz, 2H), 7.49 (t, J = 2.4 Hz, 2H), 7.54−7.58 (m, 1H), 7.71−7.72 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 110.4, 118.9, 119.9, 125.1, 129.2, 140.4.

*1-Phenylpyrrolidine (**2o**).*[102] Colorless oil, yield 12 mg (56%); purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.37 (m, 2H), 6.79 (t, J = 7.3 Hz, 1H), 6.69 (d, J = 7.9 Hz, 2H), 3.39 (t, J = 6.7 Hz, 4H), 2.09−2.12 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 147.9, 129.1, 115.3, 111.6, 47.5, 25.4.

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*2-(4-Chlorophenyl)-7-methylimidazo[1,2-a]pyridine (**2v**).*[103] Light brown solid, yield 34 mg (94%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 6.7 Hz, 1H), 7.83−7.87 (m, 2H), 7.72 (s, 1H), 7.36−7.39 (m, 3H), 6.60 (dd, J = 6.7, 1.2 Hz, 1H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 146.1, 144.3, 136.1, 133.5, 132.4, 128.9, 127.2, 124.8, 115.9, 115.3, 107.6, 21.4.

*2-(4-Chlorophenyl)imidazo[1,2-a]pyridine (**2w**).*[103,104] Colorless needles, yield 32 mg (92%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 6.7 Hz, 1H), 7.85−7.88 (m, 2H), 7.80 (s, 1H), 7.61 (dd, J = 9.1, 1.2 Hz, 1H), 7.36−7.40 (m, 2H), 7.14−7.18 (m, 1H), 6.76(td, J = 6.7, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.7, 144.6, 133.7, 132.3, 128.9, 127.2, 125.6, 124.9, 117.5, 112.6, 108.2.

*6-Chloro-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine (**2x**).*[105,106] White solid, yield 34 mg (87%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 1.8 Hz, 1H), 7.83−7.86 (m, 2H), 7.78 (s, 1H), 7.56 (d, J = 9.7 Hz, 1H), 7.37−7.41 (m, 2H), 7.14 (dd, J = 9.7, 2.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.5, 144.0, 134.1, 131.7, 129.0, 127.3, 126.5, 123.4, 120.9, 117.8, 108.5.

*6-Chloro-2-(4-bromophenyl)-imidazo[1,2-a]pyridine (**2y**).*[105,107] White solid, yield 39 mg (84%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15−8.16 (m, 1H), 7.78 (s, 1H), 7.77−7.81 (m, 3H), 7.54−7.59 (m, 3H), 7.16 (dd, J = 9.7, 1.8 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.5, 144.0, 132.0, 127.6, 126.6, 123.4, 122.4, 121.0, 117.8, 108.6.

*2-Isobutoxynaphthalene (**2z**).* Yellowish liquid, yield 26 mg (87%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.84 (m, 3H), 7.51 (t, J = 7.9 Hz, 1H), 7.40 (t, J = 7.9 Hz, 1H), 7.18−7.26 (m, 2H), 3.91 (d, J = 6.7 Hz, 2H), 2.21−2.27 (m, 1H), 1.16 (d, J = 6.7 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.2, 134.7, 129.3, 128.9, 127.7, 126.7, 126.3, 123.4, 119.1, 106.6, 74.4, 28.3, 19.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{17}O$ 201.1274; Found 201.1271.

*Biphenyl-4-d (**2a′**).*[69,108] White solid, yield 17 mg (74%); purified by column chromatography using hexane; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 7.7 Hz, 4H), 7.44−7.47 (m, 4H), 7.34−7.37 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 141.3, 128.8, 128.7, 127.3, 127.2.

*Naphthalene-1-d (**2c′**).*[41] Colorless solid, yield 10 mg (50%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.88 (m, 3H), 7.47−7.51 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 133.5, 133.4, 127.9, 125.9, 125.7.

*2-Methoxynaphthalene-1-d (**2j′**).*[51] White solid, yield 23 mg (95%); purified by column chromatography using 3% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.82 (m, 3H), 7.46−7.49 (m, 1H), 7.36−7.40 (m, 1H), 7.20 (d, J = 8.5 Hz, 1H), 3.95 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.6, 134.5, 129.4, 129.0, 127.7, 126.7, 126.4, 123.6, 118.7, 105.5 (t, J = 24.6 Hz), 55.3.

*2,7-Dimethoxynaphthalene-1-d (**2k′**).* White solid, yield 26 mg (92%); purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 9.1 Hz, 2H), 7.09 (d, J = 2.4 Hz, 1H), 7.02−7.04 (m, 2H), 3.93 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.2, 135.9, 129.1, 124.3, 116.0, 105.2, 105.0 (t, J = 24.6 Hz), 55.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{12}H_{12}DO_2$ 190.0973; found 190.0977.

*Phenanthrene-9-d (**2l′**).*[41] White color solid, yield 14 mg (53%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (d, J = 8.5 Hz, 2H), 7.91 (dd, J = 7.3, 1.2 Hz, 2H), 7.76 (s, 1H), 7.60−7.69 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 132.1, 132.0, 130.3, 128.6, 128.6, 126.9, 126.8, 126.6, 122.7.

*Anthracene-9-d (**2m′**).*[41] White color solid, yield 22 mg (83%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 8.01−8.04 (m, 4H), 7.46−7.50 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 131.7, 131.6, 128.2, 128.1, 126.2, 125.9 (t, J = 26.1 Hz), 125.4.

*2-(4-Chlorophenyl)-7-methy-d_3-limidazo[1,2-a]pyridine-3,5-d_2 (**2v′**).* Light brown solid, yield 26 mg (71%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79−7.83 (m, 2H), 7.66 (s, 0.08H), 7.33−7.36 (m, 3H), 6.55 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.9, 144.0, 143.8, 135.8, 133.2, 132.2, 128.6, 127.0, 124.4 (t, J = 29.2 Hz), 115.5, 114.9, 107.4, 107.2 (t, J = 27.6 Hz), 20.4 (m). HRMS (ESI-TOF) m/z: [M] Calcd for $C_{14}H_6D_5ClN_2$ 247.0919; found 247.0911.

*2-(4-Chlorophenyl)imidazo[1,2-a]pyridine-3,5-d_2 (**2w′**).* Colorless needles, yield 29 mg (84%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.90 (m, 2H), 7.83 (s, 0.12H), 7.64 (dd, J = 9.1, 1.2 Hz, 1H), 7.38−7.41 (m, 2H), 7.19 (dd, J = 9.1, 6.7 Hz, 1H), 6.80 (d, J = 6.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.6, 144.4, 133.8, 132.1, 129.0, 127.3, 125.4 (t, J = 29.2 Hz), 125.1, 117.5, 112.6, 107.9 (t, J = 29.2 Hz). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_8D_2ClN_2$ [M + H]$^+$ 231.0653; found 231.0653.

*6-Chloro-2-(4-chlorophenyl)imidazo[1,2-a]pyridine-3,5-d_2 (**2x′**).* White solid, yield 37 mg (93%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83−7.86 (m, 2H), 7.56 (d, J = 9.1 Hz 1H), 7.38−7.41 (m, 2H), 7.14 (d, J = 9.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.5, 144.0, 134.1, 131.7, 129.0, 127.3, 126.4, 123.1 (t, J = 27.6 Hz), 120.7, 117.8, 108.3 (t, J = 23 Hz). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{13}H_7D_2Cl_2N_2$ [M + H]$^+$ 265.0263; found 265.0258.

*6-Chloro-2-(4-bromophenyl)imidazo[1,2-a]pyridine-3,5-d_2 (**2y′**).* White solid, yield 40 mg (86%); purified by column chromatography using 25% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.8 (d, J = 7.9 Hz 2H), 7.55−7.59 (m, 3H), 7.16 (d, J = 8.5 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.0, 143.7, 131.9, 131.6, 127.6, 126.8, 123.2 (t, J = 26.1 Hz), 122.5, 121.0, 117.6, 108.5. HRMS (ESI-TOF) m/z: [M] Calcd for $C_{13}H_6D_2BrClN_2$ [M] 307.9679; found 307.9687.

*2-Isobutoxynaphthalene-1-d (**2z′**).* Yellowish liquid, yield 27 mg (89%); purified by column chromatography using hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79−7.84 (m, 3H), 7.50 (t, J = 7.9 Hz, 1H), 7.40 (t, J = 7.9 Hz, 1H), 7.25 (d, J = 9.1 Hz, 1H), 3.90 (d, J = 6.7 Hz, 2H), 2.20−2.27 (m, 1H), 1.15 (d, J = 6.7 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.2, 134.6, 129.3, 128.9, 127.6, 126.6, 126.3, 123.4, 119.1, 106.3 (t, J = 24.6 Hz), 74.4, 28.3, 19.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{14}H_{16}DO$ 202.1337; found 202.1345.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00573.

Experimental procedures; NMR, HRMS spectral data; and DFT calculation data (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Rupankar Paira − *Department of Chemistry, Maharaja Manindra Chandra College, Kolkata 700003, India*; Email: rupankarpaira85@gmail.com

Swadhin K. Mandal − *Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata 741246, India*; orcid.org/0000-0003-3471-7053; Email: swadhin.mandal@iiserkol.ac.in

Authors

Bhagat Singh − *Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata 741246, India*

Jasimuddin Ahmed − *Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata 741246, India*

Amit Biswas − *Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata 741246, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00573

Notes

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