Article

Dehalogenative Deuteration of Unactivated Alkyl halides Using D2O as the Deuterium Source

Aiyou Xia, Xin Xie, Xiaoping Hu, Wei Xu, and Yuanhong Liu

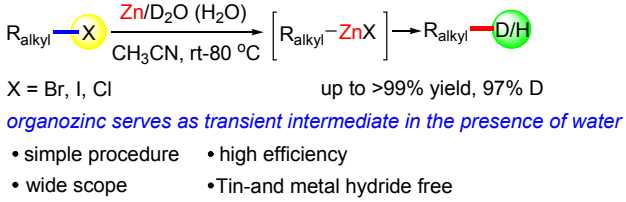
J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02026 • Publication Date (Web): 30 Sep 2019

Dehalogenative Deuteration of Unactivated Alkyl halides Using D_2O as the Deuterium Source

Aiyou Xia, Xin Xie, Xiaoping Hu, Wei Xu and Yuanhong Liu*

State Key Laboratory of Organometallic Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, People's Republic of China

Fax: (+86) 21-64166128, E-mail: yhliu@sioc.ac.cn

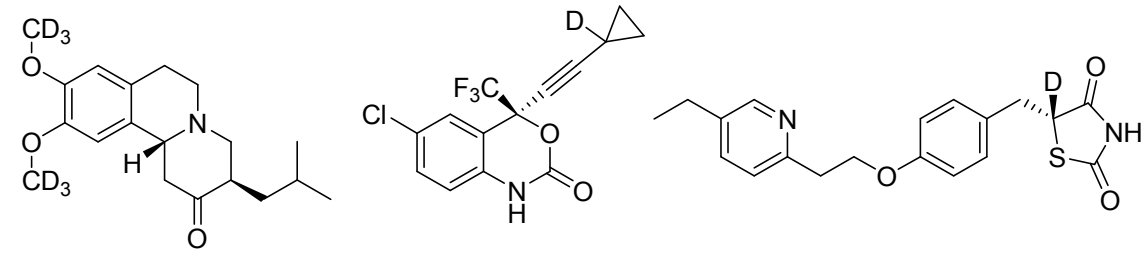


Abstract: The general dehalogenation of alkyl halides with zinc using D_2O or H_2O as a deuterium or hydrogen donor has been developed. The method provides an efficient and economic protocol for deuterium-labeled derivatives with wide substrate scope under mild reaction conditions. Mechanistic studies indicated that a radical process is involved for the formation of organozinc intermediates. The facile hydrolysis of the organozinc intermediates provides the driving force for this transformation.

INTRODUCTION

Recently, great attention has been paid to the deuteration of organic compounds due to the rapidly-growing interests in the development of deuterated drug molecules. Based on

the kinetic isotopic effect, C-D bonds are stronger than the corresponding C-H bonds toward oxidative metabolism, thus introducing the deuterium into the specific sites of the drugs may improve absorption, distribution, metabolism and excretion properties (ADME) of the drug candidates, such as slowing the drug metabolism and reducing the toxic metabolites etc.[1] A first deuterated drug of Austedo (Deutetrabenazine) for the treatment of chorea associated with Huntington's disease was approved in 2017[2a] (Figure 1)[2].



Austedo (Deutetrabenazine) Efavirenz DRX-065

Figure 1. **Representative Bioactive Deuterated Molecules**

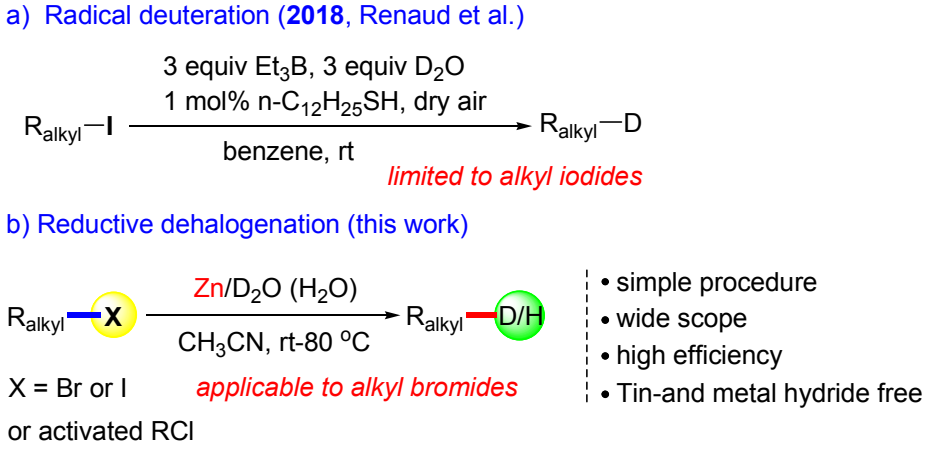
Deuteration reactions have also found wide applications in organic chemistry, organometallic chemistry, spectroscopy, mechanistic investigations of organic and bio-organic reactions, and the production of optical fibers etc.[3] Among various methods in this field, deuterodehalogenation of alkyl halides would be one of the most important strategies for the construction of C(sp^3)-D bonds, since the halide substrates are widely available or can be readily prepared from the easily-accessible alcohols. The method also enables the deuteration to occur at the well-defined positions. Despite much progress in deuteration of the aryl halides, the reactions employing alkyl halides as the substrates still

remain as a formidable task. Traditionally, these transformations have been performed through deuteration of the organometallic regents such as Grignard or organolithium reagents,[4] reduction with metal deuteride,[5] transition-metal-mediated reduction reactions,[6] or radical reductive dehalogenation with AIBN(or Et_3B)/Bu_3SnD.[7] However, these methods suffer from low functional-group tolerance, or involve the use of hazardous radical initiators (e.g., AIBN), highly toxic Bu_3SnD as the deuterium donor, and generating the tin halides byproducts which are difficult to be separated from the desired products.

Recently, dehalogenation process in the presence of D_2O as the deuterium donor emerges as one of the most promising methods since it is economic and environmentally benign. In this context, Wood et al. reported an excellent R_3B/H_2O-mediated hydrodehalogenation of xanthates[8] or alkyl iodides,[9] in which the deuterated alkyl derivatives could be produced using D_2O from xanthates. Renaud re-investigated the above reactions and disclosed that the thiol is acting as a highly active co-catalyst (Scheme 1).[10] However, these transformations are limited to alkyl iodides, and have never been applied to alkyl bromides due to the competitive deuteration of the in situ-generated ethyl radical. More recently, Loh et al reported an interesting deuteration of halogenated compounds using porous CdSe nanosheets as the catalyst under irradiation conditions in a mixed solvent of CH_3CN/D_2O, in which primary alkyl iodides were deuterated smoothly.[11] In this paper, we describe a general and attractive method for deuterodehalogenation of unactivated alkyl bromides as well as iodides using D_2O mediated by inexpensive zinc. It is realized that alkylzinc is possibly formed as an intermediate in the presence of water. Organozinc is highly sensitive to moisture and air, usually moisture free reaction media

and inert conditions are required for their preparation. Alkylzinc reagents could be prepared by oxidative insertion of zinc metal into alkyl halides. However, the method has been limited to the activated halides such as allyl halides[12] and alkyl iodides[13]. Due to the low reactivity of the alkyl bromides or chlorides, the preparation of organozinc compounds derived from these compounds usually require highly reactive Rieke-zinc[14] or activators such as 1,2-dibromoethane/Me_3SiCl/alkali iodide,[15] I_2[16] or LiCl[17] in dry solvents. It was noted that although dehalogenation by Zn in HOAc/H_2O[18] (with special substrates) or in saturated aqueous ammonium chloride and THF (with limited scope),[19] or under aqueous micellar catalysis using a designer surfactant, TMEDA and Zn,[20] have been reported, our method demonstrates that dehalogenation can occur in the presence of D_2O or water without adding any activators.[21,22]

Scheme 1. Deuterodehalogenation in the presence of D_2O



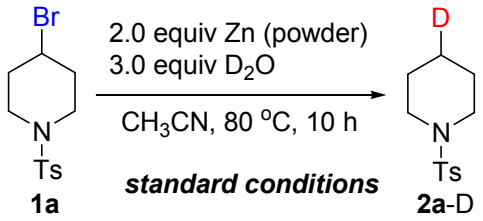
RESULTS AND DISCUSSION

During our study on Ni/Zn-catalyzed reactions of alkyl halides, we occasionally found

that alkyl halides could be reduced efficiently by Zn in the presence of water and various Lewis acid such as $Sc(OTf)_3$, $In(OTf)_3$, $Zn(OTf)_2$, etc. To our surprise, dehalogenation also proceeded efficiently even in the absence of a Lewis acid. The results prompted us to make a deep evaluation of Zn/H_2O-mediated dehalogenation, especially, to investigate the feasibility of synthesizing the deuterated products using D_2O.

Initially, the deuterodehalogenation of a secondary alkyl bromide **1a** was investigated. We were pleased to find that the desired reaction took place smoothly to afford **2a**-D in 98% yield with 92% D-incorporation at 80 ^oC in CH_3CN in the presence of 2.0 equiv zinc power (99.9% metals basis, -100 mesh) and 3.0 equiv D_2O (Table 1, entry 1). In the absence of zinc, no reaction was observed (entry 2). In the absence of D_2O, a 12% yield of non-deuterated **2a**-H (1-tosylpiperidine) was obtained (entry 3). In this case, the hydrogen source comes from trace water contained in the solvent. To our delight, the method could also be successfully applied to hydrodehalogenation using H_2O (entry 4). These results are quite remarkable, since they represent one of the most simple, inexpensive and promising protocols for dehalogenation reactions. The reaction proceeded more efficiently in polar solvents (entries 5-8). Addition of even one equiv of D_2O could also afford **2a**-D in excellent yield, albeit with lower D-incorporation (entry 9). The use of two or more than two equiv of D_2O gave the products in both high yields and high D-incorporation (entry 10). Excellent yield was also achieved using 1.5 equiv Zn (entry 12). Other reducing agents such as Mg, Al and Mn were not effective (entry 14). The purity of zinc was found to influence the D-incorporation or product yield (entries 15-16).

Table 1. Optimization of the reaction conditions[a]



Entry	Deviation from standard conditions	Yield (%)	D-inc. (%)
1	none	98	92
2	no Zn	- (97)	-
3[b]	no D_2O	- (84)	-
4	H_2O instead of D_2O	-[c]	-
5	THF instead of CH_3CN	96	88
6	dioxane instead of CH_3CN	96	82
7	toluene instead of CH_3CN	12 (86)	62
8	*n*-hexane instead of CH_3CN	42 (51)	79
9	1.0 equiv D_2O	98	81
10	2.0, 4.0 or 5.0 equiv D_2O	97->99	90-91
11	1.0 equiv Zn	82 (16)	90
12	1.5 equiv Zn	98	91
13	50 °C	69 (28)	86
14	Mg, Al, or Mn were used instead of Zn	-(>97)	-
15	Zn (99% pure, 325 mesh) was used	99	81
16	Zn (>95% pure) was used	31	78

[a]The yields of **2a**-D were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. The D-incorporation was determined by ^1H NMR. The yields of **1a** are shown in parentheses. Unless noted, zinc power (99.9% metals basis, -100 mesh) was used. [b]12% of **2a**-H (1-tosylpiperidine) was formed. [c]98% of **2a**-H was formed.

We next focused our attention on the substrate scope. The efficiency of this dehalogenation system was examined using both of the D_2O and H_2O (Scheme 2). The reactivity of the secondary alkyl halides was first investigated. In most cases, high yields and high levels of D-incorporation (up to 97%) of the desired products were achieved. Cyclic substrates bearing a fused benzene ring or with a large-sized ring afforded deuterated **2b**-**2d** in 88-97% yields. When 2-bromoadamantane was employed, only

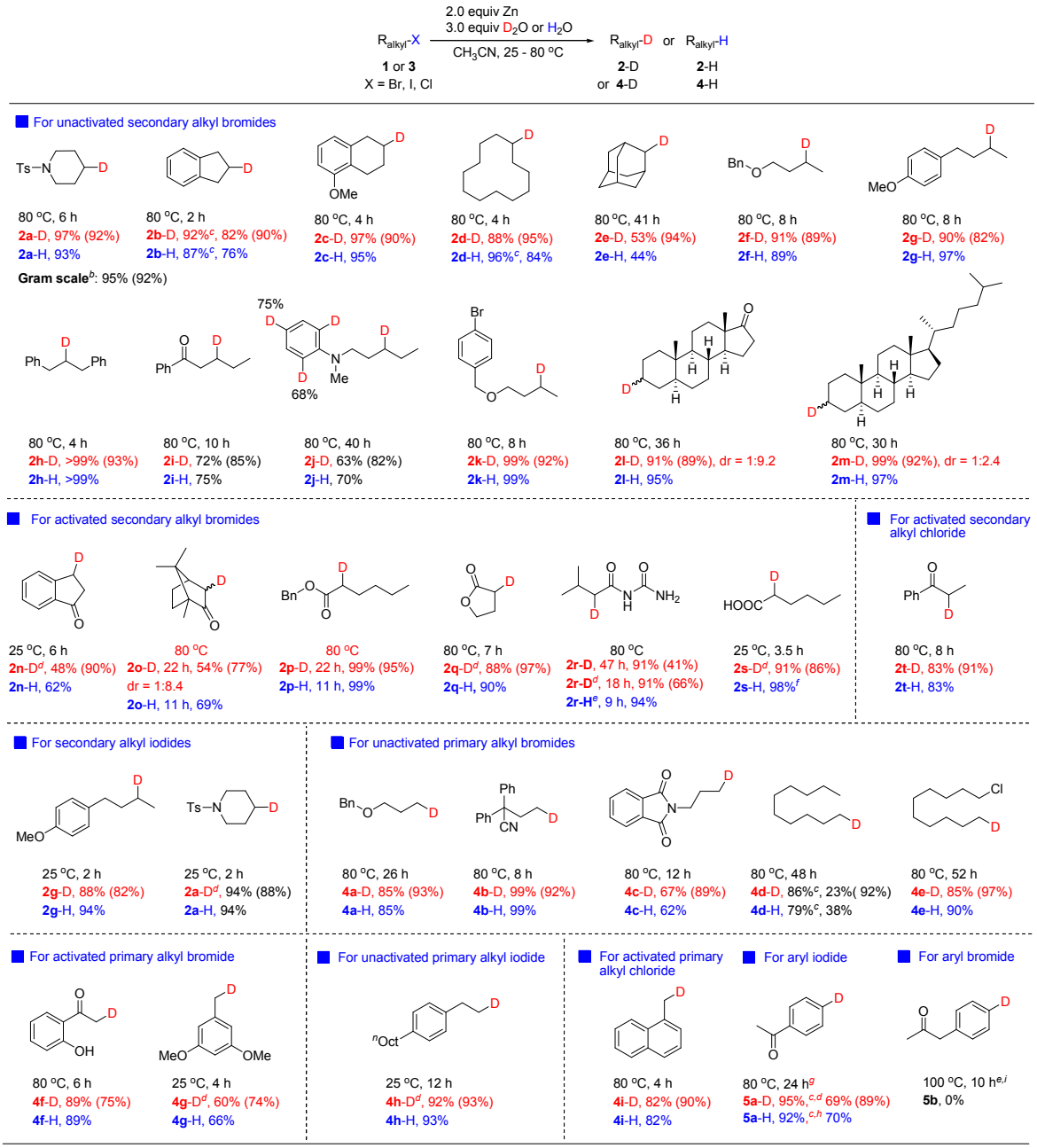
moderate yield of **2e** was obtained, probably due to the steric hindrance. Linear substrates bearing an OBn, aryl, keto or amino functional group were well compatible (**2f**-**2j**). It was noted that in the case of **2j**, deuteration also occurred at the *ortho*- and *para*-position to nitrogen of the *N*-phenyl ring, which might be promoted by a Lewis acid produced in the reaction mixture.[23,24] The reaction system was also highly chemoselective for substrate bearing an aryl and alkyl bromide moieties, in which the bromide on the aryl ring remained intact (**2k**). The method can be used for the late-stage functionalization of medicinally relevant compounds. For example, deuteration of the enantiomerically pure **1l** and **1m** derived from natural products proceeded efficiently (**2l**, **2m**). It should be noted that racemization occurred during the process. The results indicated that a radical species might be involved in the reaction.

Next, the scope of activated secondary alkyl bromides was investigated. For branched benzyl bromide **1n**, the reaction could be performed at the room temperature (**2n**). In this case, 10.0 equiv D_2O was required in order to achieve high D-incorporation (90%). The substrates bearing various functional groups at the α-position of the halide such as keto, ester, carbomyl and even free carboxyl groups were well tolerated (**2o**-**2s**). Among these examples, reduction of optically pure (+)-camphor bromide with D_2O led to the formation of a mixture of diastereoisomers of **2o**-D, emphasizing again the presence of a radical species. Notably, the deuterated γ-butyrolactone could be easily prepared with 97% D-incorporation (**2q**-D), which might be used for the preparation of deuterated polymers via ring-opening polymerization.[25] Substituted urea (bromisoval) was transformed into **2r**-D in an excellent yield, however, with a lower D-incorporation (41%) after stirring for

47 h. To our delight, the reaction rate was greatly accelerated by increasing the amount of D_2O to 10 equiv (18 h) with improved D-incorporation. We envisioned that an adequate amount of water might improve the solubility of the urea-tethered substrate and the product, which possibly formed a salt under the basic conditions. Especially, when carboxylic acid **1s** was employed, the reaction proceeded efficiently at the room temperature (**2s**-D). The ^{1}H NMR examination of the crude reaction mixture showed that the proton of the COOH moiety was also deuterated. Possibly, acid substrate could speed up the rate of the hydrolysis step involving the protonation of the in-situ-formed organozinc species. It was noted that **2s**-H could be formed without addition of water. Activated alkyl chlorides such as α-chloro ketone could also be dehalogenated (**2t**).

This methodology was well extended to secondary alkyl iodides. As expected, compared to the alkyl bromides, significant difference in reactivity was observed in reduction of the alkyl iodides, since the reactions took place rapidly at the room temperature (**2g** and **2a**). In the latter case, the product yield and D-incorporation were comparable with that obtained using Et_3B/cat.dodecanethiol/D_2O.[10] Thus our method provides a cheap, convenient and practical alternative to deuterated hydrocarbons.

Scheme 2. Dehalogenation of alkyl halides[a]



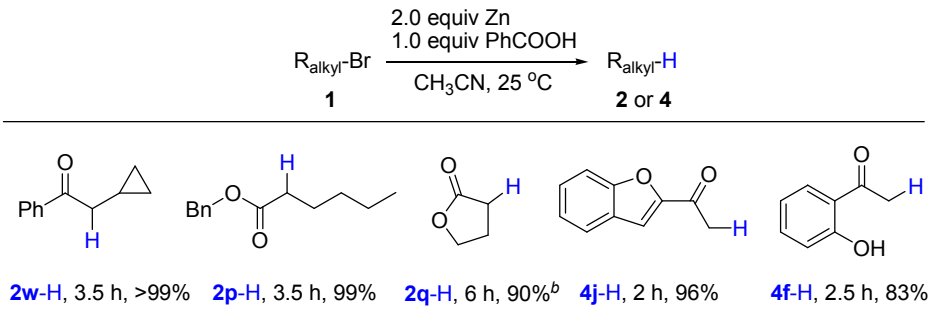
[a]Isolated yields. Deuterium incorporation is shown in parentheses. [b]1.5 equiv Zn was used. [c]^{1}H NMR yields. [d]10 equiv D_2O was used. [e]10 equiv H_2O was used. [f]Without addition of water. [g]Aryl iodide was used as the substrate. [h]20 equiv H_2O was used. [i]Aryl bromide was used as the substrate.

We next examined the scope of the primary alkyl halides. Functionalized alkyl bromides bearing benzyloxy, cyano and amide groups were all compatible (**4a**-**4c**). No further reduction of the cyano and amide groups were observed. 1-Bromodecane appeared to be reduced more slowly at 80 °C, leading to **4d**-D in 86% yield after 48 h. The results suggested that the rate of the C-Br bond cleavage process could be facilitated by the

presence of various functional groups. The system was also chemoselective for alkyl halides bearing two different halogen atoms such as Cl and Br, in which Cl remained unaltered (**4e**). Activated alkyl bromides were dehalogenated smoothly (**4f-4g**). Besides, primary alkyl iodide could be reduced at the room temperature (**4h**). Activated alkyl chloride could also be dehalogenated successfully (**4i**). The reaction is operationally simple and easily scalable, for example, gram-scale reaction of **1a** in the presence of 1.5 equiv Zn afforded **2a** without significant change of the yield and D-incorporation. The reactivity of aryl halides were also examined. To our delight, aryl iodide was also dehalogenated smoothly, however, aryl bromide failed to give the desired product (**5a**, **5b**).

It is worth to note that for α-functionalized alkyl halides, when $PhCO_2H$ was used instead of H_2O, the reaction temperature could be decreased to room temperature, and there was no evident difference on the product yields. Typical results are shown in Scheme 3. $PhCO_2H$ should also play a role in accelerating the hydrolysis of the organozinc intermediates.

Scheme 3. Dehalogenation of alkyl halides in the presence of $PhCO_2H$[a]

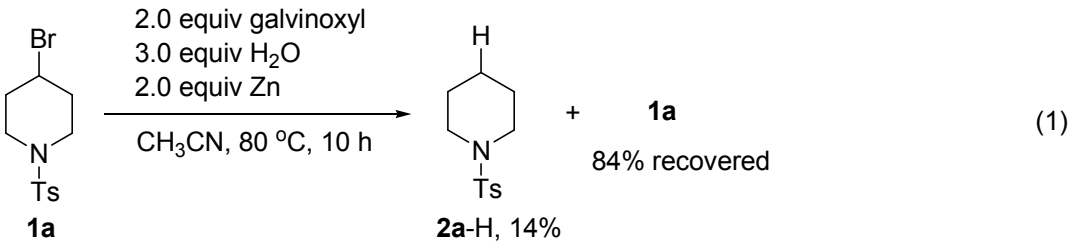


[a]Isolated yields. [b]NMR yield.

To gain a mechanistic insight into this reaction, various control experiments were performed (Scheme 4). A radical scavenger such as galvinoxyl effectively inhibited the reaction (Scheme 4, eq 1). α-Bromocyclopropane **1x** was chosen to be used as a radical clock, and the resulting ring-opening product **2x-a** was formed in 47% yield (eq 2). Both of the cyclized product **2y-a** via 5-*exo*-*trig* ring closure and uncyclized **2y** were observed in the reaction of alkene **1y** with Zn (eq 3). The above results strongly support the presence of a radical species, which are also consistent to the studies by Rieke et al. on the reaction of highly active Zn* (prepared by lithium naphthalenide reduction of $ZnCl_2$) with organic bromides.[14a] A tertiary alkyl bromide **6** reacted with zinc rapidly at room temperature, however, the desired product **7a** was obtained in only 27% yield, along with several byproducts (eq 4). The results show that the rate of halide reduction is competitive with other reaction pathways. The formation of hydroperoxide **7a-b** indicates that a tertiary radical is generated, which might be generated through the reaction of alkylzinc intermediate with O_2.[14a,26,27] A kinetic isotope effect (KIE) was measured by employing an equimolar mixture of H_2O and D_2O, which revealed a primary kinetic isotope effect of the reaction (eq 5).[28] Parallel experiments gave the similar results (k_H/k_D = 3.2). The results imply that the cleavage of the O-H/D bond is likely involved in the rate-determining step of the process.

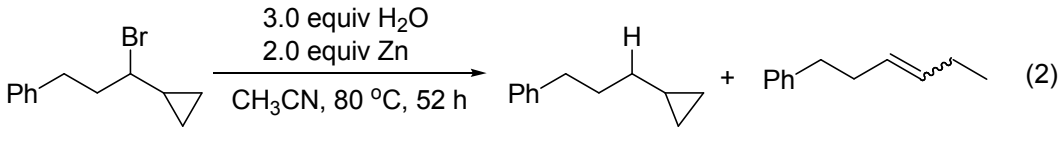
Scheme 4. Mechanistic Studies

Reaction inhibition



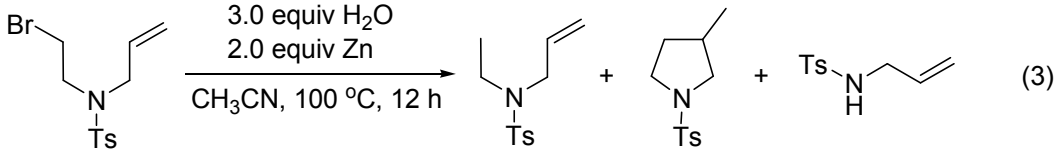
(1)

Ring-opening experiment



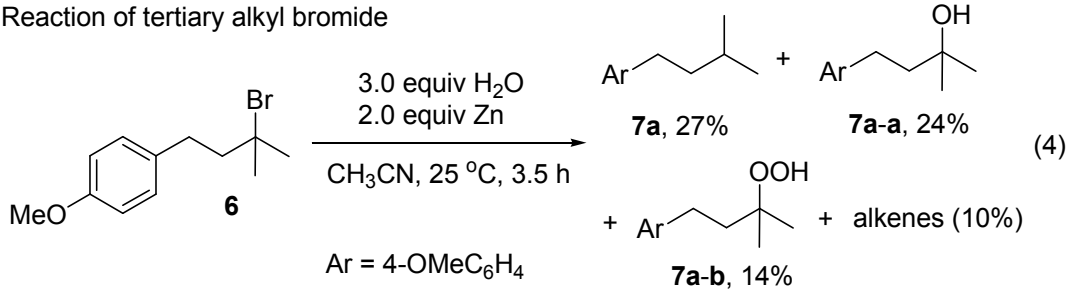
(2)

Ring-closure experiment



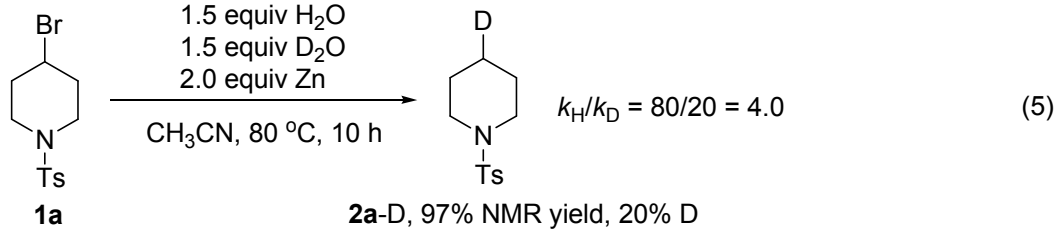
(3)

Reaction of tertiary alkyl bromide



(4)

Kinetic isotope effect

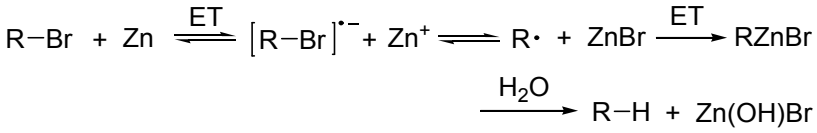


k_H/k_D = 80/20 = 4.0 (5)

Based on the above results and literature reports, we suggested that the reaction proceeds via the formation of an organozinc intermediate followed by deuteration or protonation (Scheme 5). Radical clock experiments and the stereochemical outcome of the

reaction support that the generation of organozinc takes place through a two single-electron transfer (SET) steps.[14a] Generally, organozinc is believe to be highly sensitive to moisture and air. It may be hard to understand that organozinc could be generated in water without any activators shown in the reaction mechanism. We suggest here that the intermediate of RZnBr tends to be easily protonated by H_2O. After organozinc species is formed, protonation will occur in the presence of water, which shifts the equilibrium completely to the right-hand side. Thus one of the driving force for this transformation is the facile protonation of organozinc intermediates to deliver an alkane product. It is also possible that after the protonation reaction, the soluble organic products and zinc salts are removed from the zinc surface by the solvent, thus making the zinc surface clean enough for the further reaction.[17,29]

Scheme 5. Possible Reaction Mechanism



CONCLUSION

In summary, we have developed a general dehalogenation of alkyl halides with zinc using D_2O or H_2O as the deuterium or hydrogen sources under mild reaction conditions. The results of mechanistic studies are consistent with a radical process for the formation of organozinc intermediates, and KIE experiments support that the cleavage of the O-H/D

bond might be involved in the rate-determining step of the process. The facile hydrolysis of the organozinc intermediates provides the driving force for this transformation.

EXPERIMENTAL SECTION

General Methods. Unless noted, all reactions were carried out using sealable tubes under an argon atmosphere or a dry box technique under a nitrogen atmosphere. Tetrahydrofuran and toluene were distilled from sodium and benzophenone. 1,4-Dioxane and n-hexane was distilled from sodium. D_2O (99.9 atom% D) were purchased from Sigma-Aldrich. Deionized water was used. Zinc powder (99.9% metals basis, -100 mesh) was purchased from Alfa Aesar. Zinc powder (99%, -325 mesh) was purchased from Adamas. Zinc (>95%) was purchased from Lingfeng. All zinc used in this study was activated by treatment with 1 M HCl aqueous solution, filtered and washed thoroughly with water, acetone and diethyl ether and dried under vacuum. Unless otherwise noted, all other reagents and starting materials were purchased from commercial sources. ^{1}H, and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ or d_6-DMSO (containing 0.03% TMS) solutions on Varian or Agilent XL-400 MHz spectrometer. ^{2}H NMR spectra were recorded at room temperature in CH_2Cl_2 or $CDCl_3$ solutions on Agilent XL-600 MHz spectrometer. ^{1}H NMR spectra was recorded with tetramethylsilane (0.00 ppm) or solvent residual peak ($CDCl_3$: 7.26 ppm; d_6-DMSO: 2.50 ppm) as internal reference; Unless otherwise noted, the deuterium incorporation was determined by ^{1}H NMR spectra. ^{13}C NMR spectra was recorded with $CDCl_3$ (77.00 ppm) or d_6-DMSO (39.52 ppm) as internal reference. High-resolution mass spectra was performed on a mass spectrometer with a TOF

analyzer.

Synthesis of alkyl halides.

Alkyl halides were synthesized according to the published methods.[30] For the characterization of the new substrates, see the following:

Synthesis of 2-bromo-2,3-dihydro-1*H*-indene (1b). A flame-dried flask equipped with a stirring bar were charged with 2-indanol (1.34 g, 10 mmol) and CBr_4 (3.61 g, 10.9 mmol) under argon. Anhydrous CH_2Cl_2 (50 mL) was added and the mixture was placed in an ice bath. PPh_3 (2.89 g, 11 mmol) in CH_2Cl_2 (10 mL) was added dropwise at 0 °C. The reaction mixture was warmed up to room temperature and then stirred for 8 h. After the starting material was completely consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **1b** in 77% yield (1.51 g) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 4H), 4.78-4.73 (m, 1H), 3.50 (dd, J = 16.8 Hz, 6.4 Hz, 2H), 3.33 (dd, J = 16.8 Hz, 4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.5, 126.9, 124.5, 49.6, 44.6. IR (neat): 3024, 2956, 2877, 2822, 1481, 1461, 1416, 1309, 1271, 1225, 1158, 1023, 968, 908, 808, 795, 740. HRMS (EI-TOF) calcd for C_9H_9Br $[M]^+$: 195.9888, found 195.9884.

Synthesis of 2-bromo-5-methoxy-1,2,3,4-tetrahydronaphthalene (1c). To a solution of 5-methoxy-3,4-dihydronaphthalen-2(1H)-one **s-1c** (3.52 g, 20 mmol) in MeOH (100 mL)

was added $NaBH_4$ (907.9 mg, 24 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at room temperature for 2 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was used for the next step without purification.

A flame-dried flask equipped with a stirring bar were charged with the crude product above and CBr_4 (7.23 g, 21.8 mmol) under argon. Anhydrous CH_2Cl_2 (80 mL) was added and the mixture was placed in an ice bath. PPh_3 (5.77 g, 22 mmol) in CH_2Cl_2 (20 mL) was added dropwise at 0 °C. The reaction mixture was warmed up to room temperature and then stirred for 10 h. After the starting material was completely consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: CH_2Cl_2 = 15:1) to afford **1c** (1.76 g, 36% for 2 steps) as a white solid. Mp 68-70 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, *J* = 8.0 Hz, 1H), 6.67 (dd, *J* = 13.2 Hz, 8.0 Hz, 2H), 4.53-4.47 (m, 1H), 3.81 (s, 3H), 3.38 (dd, *J* = 16.4 Hz, 4.8 Hz, 1H), 3.22 (dd, *J* = 17.2 Hz, 8.0 Hz, 1H), 2.96-2.89 (m, 1H), 2.75-2.67 (m, 1H), 2.38-2.31 (m, 1H), 2.23-2.14 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.1, 135.3, 126.5, 123.4, 120.8, 107.4, 55.2, 48.7, 40.1, 32.8, 22.5. IR (neat): 2948, 2835, 1584, 1466, 1436, 1253, 1214, 1168, 1089, 1073, 1054, 850, 775, 724, 707, 677. HRMS (EI-TOF) calcd for $C_{11}H_{13}OBr$ $[M]^+$: 240.0150, found 240.0157.

Synthesis of bromocyclododecane (1d). Cyclododecanol (3.69 g, 20.0 mmol) was heated and melted at 100 °C (oil bath) under air. PBr_3 (0.94 mL, 10.0 mmol) was then added dropwise to the solution and the mixture was stirred for 2 h. After the starting material was completely consumed, the mixture was poured into cold water, extracted with CH_2Cl_2, washed with saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: pentane) to afford **1d** in 35% isolated yield (1.74 g) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 4.29-4.22 (m, 1H), 2.09-2.00 (m, 2H), 1.93-1.84 (m, 2H), 1.56-1.34 (m, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 54.0, 34.6, 23.64, 23.62, 23.4, 22.7. IR (neat): 2928, 2862, 2850, 1468, 1444, 1345, 1244, 1206, 1183, 782, 750, 719, 699. HRMS (EI-TOF) calcd for $C_{12}H_{23}Br$ $[M]^+$: 246.0983, found 246.0981.

Synthesis of ((3-bromobutoxy)methyl)benzene (1f). Benzyl bromide (1.78 mL, 15 mmol), DIPEA (2.64 mL, 16 mmol) and 4-hydroxybutan-2-one (881.1 mg, 10 mmol) were charged in a reaction vessel under argon. The mixture was heated at 150 °C (oil bath) for 2 h. After the starting material was completely consumed, the mixture was quenched with aqueous HCl (1 M) solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 5:1) to afford a yellow oil (1.30 g), which was directly used for the next step.

To a solution of the crude product above (891.2 mg, 5 mmol) in EtOH (10 mL) was added $NaBH_4$ (227.0 mg, 6 mmol) by four portions in 15 min at room temperature under

air. The mixture was stirred at room temperature for 1 h. After the starting material was completely consumed, the mixture was quenched with saturated ammonium chloride solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was directly used for the next step.

A flame-dried flask equipped with a stirring bar were charged with the crude product above and CBr_4 (1.81 g, 5.45 mmol) under air. Anhydrous CH_2Cl_2 (25 mL) was added and the mixture was placed in an ice bath. PPh_3 (1.44 g, 5.5 mmol) in CH_2Cl_2 (15 mL) was added dropwise at 0 °C. The reaction mixture was warmed up to room temperature and then stirred for 5.5 h. After the starting material was completely consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **1f** (981.5 mg, 81% for 2 steps) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.24 (m, 5H), 4.51 (t, J = 13.2 Hz, 2H), 4.39-4.31 (m, 1H), 3.63 (t, J = 6.0 Hz, 2H), 2.11-2.01 (m, 2H), 1.73 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.2, 128.4, 127.63, 127.61, 73.1, 68.1, 48.3, 41.0, 26.6. IR (neat): 3030, 2861, 1496, 1453, 1359, 1240, 1186, 1113, 1093, 1057, 1028, 812, 734, 696. HRMS (EI-TOF) calcd for $C_{11}H_{15}OBr$ $[M]^+$: 242.0306, found 242.0311.

Synthesis of (2-bromopropane-1,3-diyl)dibenzene (1h). To a solution of 1,3-diphenylpropan-2-one (2.10 g, 10 mmol) in EtOH (20 mL) was added $NaBH_4$ (454.0 mg, 12 mmol) by four portions in 15 min at room temperature under air. The mixture was

stirred at room temperature for 1 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1) to afford a yellow oil, which was directly used for the next step.

A flame-dried flask equipped with a stirring bar were charged with the crude product above and CBr_4 (3.61 g, 10.9 mmol) under argon. Anhydrous CH_2Cl_2 (50 mL) was added and the mixture was placed in an ice bath. PPh_3 (2.89 g, 11 mmol) in CH_2Cl_2 (10 mL) was added dropwise at 0 °C. The reaction mixture was warmed up to room temperature and then stirred for 24 h. After the starting material was completely consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate = 20:1) to afford **1h** (788.5 mg, 29% for 2 steps) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.19 (m, 10H), 4.40-4.33 (m, 1H), 3.22 (dd, J = 14.0 Hz, 5.6 Hz, 2H), 3.14 (dd, J = 14.4 Hz, 8.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.4, 129.1, 128.4, 126.8, 57.1, 44.9. IR (neat): 3060, 3028, 1602, 1496, 1453, 1155, 1078, 1029, 928, 742, 696. HRMS (EI-TOF) calcd for $C_{15}H_{15}Br$ $[M]^+$: 274.0357, found 274.0356.

Synthesis of 3-bromo-1-phenylpentan-1-one (1i). To a solution of ^{i}Pr$_2$NH (3.10 mL, 22 mmol) in THF (50 mL) was added dropwise *n*-BuLi (12.5 mL, 1.6 M in hexane, 20 mmol)

at -78 °C under argon. After stirring for 0.5 h, acetophenone (2.34 mL, 20 mmol) was then added to the mixture. The mixture was stirred for 0.5 h and propionaldehyde (2.86 mL, 40 mmol) was then added dropwise to the mixture. The mixture was stirred at -78 °C for 2 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1 to 5:1) to afford 3-hydroxy-1-phenylpentan-1-one (**s-1i**) in 71% isolated yield (2.52 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.94 (m, 2H), 7.60-7.55 (m, 1H), 7.48-7.44 (m, 2H), 4.16-4.12 (m, 1H), 3.37 (d, *J* = 3.2 Hz, 1H), 3.17 (dd, *J* = 17.6 Hz, 2.8 Hz, 1H), 3.04 (dd, *J* = 17.6, 8.8 Hz, 1H), 1.67-1.55 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.9, 136.7, 133.4, 128.6, 128.0, 69.0, 44.5, 29.3, 9.9. The spectroscopic data is in agreement with that previously reported.[31]

To a solution of **s-1i** (1.78 g, 10 mmol) in $CHCl_3$ (30 mL) was added dropwise PBr_3 (0.47 mL, 5 mmol) at 0 °C under air. The mixture was warmed to room temperature and stirred for 20 h. After the starting material was completely consumed, the mixture was quenched with water, extracted with ethyl acetate, washed with saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1) to afford **1i** in 78% isolated yield (1.88 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.95 (m, 2H), 7.61-7.57 (m, 1H), 7.50-7.46 (m, 2H), 4.61-4.54 (m, 1H), 3.73 (dd, *J* = 17.2 Hz, 7.6 Hz, 1H), 3.41 (dd, *J* = 17.2 Hz, 6.0 Hz, 1H),

2.05-1.83 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 196.8, 136.5, 133.4, 128.7, 128.1, 51.7, 47.3, 32.0, 12.1. IR (neat): 2963, 2934, 2871, 1685, 1595, 1578, 1449, 1373, 1293, 1269, 1208, 1182, 1158, 1001, 978, 915, 783, 753, 689, 658. HRMS (EI-TOF) calcd for $C_{11}H_{14}BrO$ $[M+H]^+$: 241.0223, found 241.0224.

Synthesis of *N*-(3-bromopentyl)-*N*-methylaniline (1j). To a solution of *N*-methylaniline (2.17 ml, 20 mmol) in H_2O (20 mL) was added dropwise ethyl vinyl ketone (2.52 g, 30 mmol) at room temperature under air. The mixture was stirred at 70 °C (oil bath) for 18 h. After the starting material was completely consumed, the mixture was extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1) to afford the crude product, which was directly used for the next step.

To a solution of the crude product above in EtOH (40 mL) was added $NaBH_4$ (908 mg, 24 mmol) at room temperature under air. The mixture was stirred at room temperature for 3 h. After the starting material was completely consumed, the mixture was quenched with saturated ammonium chloride solution, extracted with ethyl acetate, dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 8:1 to 5:1) to afford 1-(methyl(phenyl)amino)pentan-3-ol (s-**1j**) in 83% overall yield for two steps (3.21 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.21 (m, 2H), 6.80-6.78 (m, 2H), 6.75-6.71 (m, 1H), 3.66-3.60 (m, 1H), 3.48-3.41 (m, 2H), 2.90 (s, 3H),

2.20 (bs, 1H), 1.76-1.71 (m, 1H), 1.66-1.62 (m, 1H), 1.52-1.47 (m, 2H), 0.94 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.8, 129.1, 117.0, 113.3, 72.1, 50.7, 38.5, 33.3, 30.7, 9.8. IR (neat): 3382, 2961, 2932, 2875, 1598, 1505, 1464, 1370, 1225, 1192, 1119, 1074, 1034, 990, 931, 864, 746, 691. HRMS (ESI-TOF) calcd for $C_{12}H_{20}NO$ $[M+H]^+$: 194.1539, found 194.1546.

To a solution of **s-1j** (966.0 mg, 5 mmol) in $CHCl_3$ (20 mL) was added dropwise PBr_3 (235.0 μL, 2.5 mmol) at 0 °C under air. The mixture was warmed to room temperature and stirred for 18 h. After the starting material was completely consumed, the mixture was quenched with water, extracted with ethyl acetate, washed with saturated $NaHCO_3$ solution, brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **1j** in 65% isolated yield (833.0 mg) as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.22 (m, 2H), 6.74-6.68 (m, 3H), 4.02-3.98 (m, 1H), 3.65-3.58 (m, 1H), 3.50-3.43 (m, 1H), 2.95 (s, 3H), 2.12-1.99 (m, 2H), 1.91-1.83 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.0, 129.2, 116.3, 112.2, 57.8, 51.0, 38.6, 35.5, 32.6, 12.0. IR (neat): 2966, 1598, 1505, 1452, 1434, 1368, 1276, 1210, 1117, 1034, 990, 802, 746, 691. HRMS (ESI-TOF) calcd for $C_{12}H_{19}BrN$ $[M+H]^+$: 256.0695, found 256.0702.

Synthesis of 1-bromo-4-((3-bromobutoxy)methyl)benzene (1k). 4-Bromobenzyl bromide (2.50 g, 10 mmol), 4-hydroxybutan-2-one (1.32 g, 15 mmol) and DIPEA (3.64 mL, 22 mmol) were charged in a reaction vessel under argon. The mixture was heated at

150 °C (oil bath) for 7 h. After the starting material was completely consumed, the mixture was quenched with aqueous HCl (1 M) solution, extracted with ethyl acetate, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 2:1) to afford 4-((4-bromobenzyl)oxy)butan-2-one as a yellow oil, which was directly used for the next step.

To a solution of the crude product above in EtOH (20 mL) was added $NaBH_4$ (454.0 mg, 12 mmol) by four portions in 15 min at room temperature under air. The mixture was stirred at room temperature for 5 h. After the starting material was completely consumed, the mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 5:1 to 2:1) to afford 4-((4-bromobenzyl)oxy)butan-2-ol as a yellow oil, which was directly used for the next step.

To a solution of the crude product above in DCM (50 mL) was added CBr_4 (3.61 g, 10.9 mmol) at room temperature under air. PPh_3 (2.89 g, 11 mmol) in CH_2Cl_2 (30 mL) was then added to the mixture at 0 °C. The mixture was warmed to room temperature and stirred for 16 h. After the starting material was consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1 to 20:1) to afford **1k** (1.42 g, 44% for 3 steps) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J*

= 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.46 (s, 2H), 4.37-4.29 (m, 1H), 3.66-3.60 (m, 2H), 2.13-1.98 (m, 2H), 1.73 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 137.2, 131.5, 129.2, 121.4, 72.4, 68.3, 48.1, 40.9, 26.6. IR (neat): 2862, 1593, 1487, 1443, 1396, 1378, 1357, 1239, 1186, 1089, 1070, 1011, 801. HRMS (EI-TOF) calcd for $C_{11}H_{14}Br_2O$ $[M]^+$: 319.9406, found 319.9406.

Synthesis of (3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-3-bromo-10,13-dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (1l). A flame-dried flask equipped with a stirring bar were charged with androsterone (1.45 g, 5 mmol) and CBr_4 (2.49 g, 7.5 mmol) under argon. Anhydrous CH_2Cl_2 (50 mL) was added and the mixture was placed in an ice bath. PPh_3 (1.97 g, 7.5 mmol) in CH_2Cl_2 (10 mL) was added dropwise at 0 °C. The reaction mixture was warmed up to room temperature and then stirred for 12 h. After the starting material was completely consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate = 20:1) to afford **1l** in 42% isolated yield (733.4 mg) as a white solid. Mp 165-167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06-4.00 (m, 1H), 2.44 (dd, *J* = 18.8 Hz, 8.8 Hz, 1H), 2.17-0.93 (m, 20H), 0.88 (s, 3H), 0.86 (s, 3H), 0.73-0.71 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 221.1, 54.2, 52.1, 51.3, 47.9, 47.7, 40.4, 39.6, 35.7, 35.4, 34.8, 34.0, 31.4, 30.7, 28.0, 21.7, 20.2, 13.7, 12.2. IR (neat): 2915, 2846, 1737, 1453, 1389, 1273, 1159, 1151, 1053, 1011, 800, 699. HRMS (EI-TOF) calcd for $C_{19}H_{29}OBr$ $[M]^+$: 352.1402, found

352.1400.

Synthesis of 2-bromo-2-cyclopropyl-1-phenylethan-1-one (1w). To a solution of PhMgBr (10.7 mL, 3M in Et_2O, 32.1 mmol) was added dropwise cyclopropylacetonitrile (2.0 g, 24.7 mmol) in Et_2O (30 mL) at 0 °C under argon. The mixture was stirred for 2 h at 0 °C and then warmed to room temperature. After stirring for 9 h at room temperature, THF (30 mL) and aqueous HCl (1 M) solution (30 mL) were added dropwise to the mixture at 0 °C sequentially. The reaction mixture was warmed up to room temperature and then stirred for 12 h. After the starting material was completely consumed, the mixture was extracted with ethyl acetate and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1 to 20:1) to afford a yellow oil, which was directly used for the next step.

To a solution of the crude product above and $TsOH{\cdot}H_2O$ (939.7 mg, 4.94 mmol) in CH_2Cl_2 (150 mL) was added dropwise NBS (5.72 g, 32.11 mmol) under air. The reaction mixture was refluxed for 8 h. After the starting material was completely consumed, the mixture was quenched with saturated $NaHCO_3$ solution, extracted with CH_2Cl_2 and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: CH_2Cl_2 = 5:1) to afford **1w** in 65% isolated yield (3.81 g) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01-7.99 (m, 2H), 7.61-7.57 (m, 1H), 7.50-7.46 (m, 2H), 4.48 (d, J = 10.0 Hz, 1H), 1.89-1.80 (m, 1H), 0.96-0.88 (m, 2H), 0.62-0.41 (m, 2H); ^{13}C{^{1}H} NMR (100

MHz, $CDCl_3$) δ 192.4, 134.1, 133.6, 128.8, 128.7, 53.9, 14.6, 9.4, 6.5. IR (neat): 3084, 3063, 3003, 1683, 1596, 1448, 1293, 1233, 1004, 942, 910, 833, 811, 781, 715, 685, 656. HRMS (EI-TOF) calcd for $C_{11}H_{11}OBr$ $[M]^+$: 237.9993, found 237.9991.

General procedure for optimization studies.

In a nitrogen-filled glove box, zinc powder (26.2 mg, 0.4 mmol), 4-bromo-1-tosylpiperidine **1a** (63.6 mg, 0.2 mmol), CH_3CN or other solvents (1 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. D_2O (10.9 μL, 0.6 mmol) or H_2O (10.8μL, 0.6 mmol) was added to the vial and the reaction mixture was stirred at 80 °C (oil bath) for 10 h. After the starting material was completely consumed, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2. The solvent was evaporated under the reduced pressure and the residue was dissolved in $CDCl_3$. The NMR yields and deuterium incorporation were determined by ^1H NMR analysis of the crude mixture (for NMR yields, 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) was used as an internal standard). For the results, see Table 1.

Zinc-mediated dehalogenation reactions.

Typical procedure for dehalogenation of alkyl halides in the presence of D_2O. To a sealable tube were added zinc powder (65.4 mg, 1.0 mmol), 4-bromo-1-tosylpiperidine **1a** (159.1 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) under argon (If the alkyl bromide is a liquid, it is added after CH_3CN). The tube was sealed and immersed into

an oil bath preheated at 80 °C. After stirring for 6 h, the mixture was cooled down to room temperature. Then the reaction mixture was filtered through a short silica gel column and washed with dichloromethane. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afforded **2a**-D in 97% yield (116.1 mg) with 92% deuterium incorporation as a white solid.

1-Tosylpiperidine-4-*d* (2a-D**).** Mp 98-100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 2.97 (t, *J* = 5.2 Hz, 4H), 2.43 (s, 3H), 1.65-1.61 (m, 4H), 1.44-1.36 (m, 1.08H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.2, 132.9, 129.4, 127.5, 46.8, 24.9, 23.3 (C-H), 22.9 (t, *J* = 19.4 Hz, C-D), 21.4. IR (neat): 2922, 2825, 1450, 1353, 1345, 1334, 1327, 1305, 1290, 1164, 1092, 1051, 1018, 930, 813, 800, 722, 705. HRMS (ESI-TOF) calcd for $C_{12}H_{17}DNO_2S$ $[M+H]^+$: 241.1116, found 241.1117.

2,3-Dihydro-1*H*-indene-2-*d* (2b-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-bromo-2,3-dihydro-1*H*-indene **1b** (98.5 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 2 h. With 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as internal standard, the NMR yield was 92%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2b**-D in 82% isolated yield (48.9 mg) with 90% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.21 (m, 2H), 7.14-7.11 (m, 2H), 2.90 (d, *J* = 7.2 Hz, 4H), 2.09-2.00 (m, 1.10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.1, 125.9, 124.3, 32.7, 25.3 (C-H), 25.0 (t, *J* = 20.2 Hz, C-D). IR (neat): 3020, 2939, 2845, 1482, 1458, 1305, 1025, 740. HRMS

(EI-TOF) calcd for C_9H_9D $[M]^+$: 119.0845, found 119.0839.

5-Methoxy-1,2,3,4-tetrahydronaphthalene-2-*d* (2c-D**).** Zinc powder (65.4 mg, 1.0 mmol), 2-bromo-5-methoxy-1,2,3,4-tetrahydronaphthalene **1c** (120.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1) to afford **2c**-D in 97% isolated yield (79.1 mg) with 90% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (t, J = 8.0 Hz, 1H), 6.69 (d, J = 7.6 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 3.80 (s, 3H), 2.74 (d, J = 5.6 Hz, 2H), 2.64 (t, J = 6.4 Hz, 2H), 1.80-1.71 (m, 3.10H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.3, 138.4, 125.8, 125.6, 121.3, 106.6, 55.1, 29.5, 23.0, 22.7, 22.8 (C-H), 22.4 (t, J = 19.3 Hz, C-D). IR (neat): 2920, 2835, 1584, 1467, 1437, 1337, 1253, 1224, 1093, 1074, 791, 780, 758, 708, 668. HRMS (EI-TOF) calcd for $C_{11}H_{13}DO$ $[M]^+$: 163.1107, found 163.1109.

Cyclododecane-*d* (2d-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), bromocyclododecane **1d** (123.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2d**-D in 88% isolated yield (74.6 mg) with 95% deuterium incorporation (determined by GC-MS) as a white solid. Mp 58-60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 23H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 23.7, 23.6, 23.6, 23.2 (t, J = 18.9 Hz, C-D). IR (neat): 2926, 2901, 2860, 2847, 1470, 1439, 716, 700. HRMS (EI-TOF) calcd for $C_{12}H_{23}D$ $[M]^+$: 169.1941, found 169.1949.

(1*r*,3*r*,5*r*,7*r*)-Adamantane-2-*d* (2e-**D).** Zinc powder (65.4 mg, 1.0 mmol), 2-bromoadamantane **1e** (107.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 41 h. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **2e**-D in 53% isolated yield (36.6 mg) with 94% deuterium incorporation as a white solid. Mp 124-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (s, 4H), 1.75 (s, 11.06H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 37.73, 37.72, 37.3 (t, J = 19.0 Hz, C-D), 28.3, 28.2. IR (neat): 2896, 2847, 1448, 1352, 1100, 797. HRMS (EI-TOF) calcd for $C_{10}H_{15}D$ $[M]^+$: 137.1315, found 137.1318.

((Butoxy-3-*d*)methyl)benzene (2f-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), ((3-bromobutoxy)methyl)benzene **1f** (121.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2f**-D in 91% isolated yield (75.6 mg) with 89% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 4.49 (s, 2H), 3.46 (t, J = 6.8 Hz, 2H), 1.62-1.56 (m, 2H), 1.40-1.34 (m, 1.11H), 0.91 (d, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.6, 128.3, 127.5, 127.4, 72.8, 70.1, 31.7, 19.3 (C-H), 18.9 (t, J = 19.3 Hz, C-D), 13.8. IR (neat): 2957, 2929, 2855, 1496, 1454, 1363, 1098, 1028, 733, 696. HRMS (EI-TOF) calcd for $C_{11}H_{15}DO$ $[M]^+$: 165.1264, found 165.1267.

1-(Butyl-3-*d*)-4-methoxybenzene (2g-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5

mL), 1-(3-bromobutyl)-4-methoxybenzene **1g** (121.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2g**-D in 90% isolated yield (74.4 mg) with 82% deuterium incorporation (determined by ^1H NMR of the crude reaction mixture) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 3.76 (s, 3H), 2.54 (t, J = 7.6 Hz, 2H), 1.58-1.52 (m, 2H), 1.38-1.26 (m, 1H), 0.90 (d, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.5, 134.9, 129.2, 113.6, 55.1, 34.7, 33.8, 22.3 (C-H), 21.9 (t, J = 19.0 Hz, C-D), 13.8. IR (neat): 2954, 2923, 2854, 2834, 1612, 1584, 1511, 1457, 1441, 1300, 1243, 1176, 1113, 1037, 831, 805, 746, 661. HRMS (EI-TOF) calcd for $C_{11}H_{15}DO$ $[M]^+$: 165.1264, found 165.1271.

(Propane-1,3-diyl-2-*d*)dibenzene (2h-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), (2-bromopropane-1,3-diyl)dibenzene **1h** (137.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2h**-D in >99% isolated yield (98.6 mg) with 93% deuterium incorporation as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.15 (m, 10H), 2.63 (d, J = 7.6 Hz, 4H), 1.99-1.89 (m, 1.07H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 142.2, 128.4, 128.3, 125.7, 35.3, 32.9 (C-H), 32.5 (t, J = 19.4 Hz, C-D). IR (neat): 3025, 2923, 2848, 1603, 1495, 1453, 1080, 1029, 740, 696. HRMS (EI-TOF) calcd for $C_{15}H_{15}D$ $[M]^+$: 197.1315, found 197.1320.

1-Phenylpentan-1-one-3-*d* **(2i**-D**)**. Zinc powder (65.4 mg, 1.0 mmol),

3-bromo-1-phenylpentan-1-one **1i** (120.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **2i**-D in 72% isolated yield (59.0 mg) with 85% deuterium incorporation as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.95 (m, 2H), 7.57-7.52 (m, 1H), 7.47-7.43 (m, 2H), 2.96 (d, *J* = 7.2 Hz, 2H), 1.76-1.66 (m, 1.15H), 1.44-1.37 (m, 2H), 0.95 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.5, 137.0, 132.8, 128.5, 128.0, 38.2, 26.4 (C-H), 26.0 (t, *J* = 19.3 Hz, C-D), 22.3, 13.8. IR (neat): 2958, 2929, 2872, 1683, 1597, 1581, 1448, 1362, 1345, 1283, 1214, 1179, 1018, 1002, 963, 746, 689. HRMS (EI-TOF) calcd for $C_{11}H_{13}DO$ $[M]^+$: 163.1102, found 163.1102.

***N*-Methyl-*N*-(pentyl-3-*d*)aniline-2,4,6-d_3 (2j-D).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), *N*-(3-bromopentyl)-*N*-methylbenzenamine **1j** (128.1 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 40 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1) to afford **2j**-D in 63% isolated yield (57.0 mg) as a light yellow oil. Deuterium incorporation (alkyl): 82%; Deuterium incorporation (*ortho* position of the *N*-phenyl ring): 68%; Deuterium incorporation (*para* position of the *N*-phenyl ring): 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.22 (m, 2H), 6.70-6.65 (m, 0.85H), 3.29 (t, *J* = 7.6 Hz, 2H), 2.91 (s, 3H), 1.59-1.53 (m, 2H), 1.37-1.25 (m, 3.18H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.2 (d, *J* = 6.0 Hz), 129.0 (t, *J* = 11.2 Hz), 115.7, 112.0, 52.7, 38.2, 29.4 (C-H), 28.9 (t, *J* = 19.3 Hz, C-D), 26.2, 22.5, 14.1; ^{2}H NMR (92 MHz, CH_2Cl_2) δ

6.68-6.62 (m), 1.24 (s). IR (neat): 2955, 2926, 2870, 1590, 1487, 1456, 1417, 1361, 1199, 1081, 970, 914, 816, 762, 746, 672. HRMS (ESI-TOF) calcd for $C_{12}H_{17}D_3N$ $[M+H]^+$: 181.1779, found 181.1783.

1-Bromo-4-((butoxy-3-*d*)methyl)benzene (2k-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-bromo-4-((3-bromobutoxy)methyl)benzene **1k** (161.0 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2k**-D in 99% isolated yield (121.0 mg) with 92% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.43 (s, 2H), 3.45 (t, *J* = 6.8 Hz, 2H), 1.61-1.56 (m, 2H), 1.42-1.32 (m, 1.08H), 0.91 (d, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.7, 131.3, 129.1, 121.2, 72.0, 70.3, 31.6, 19.3 (C-H), 18.9 (t, *J* = 19.3 Hz, C-D), 13.7. IR (neat): 2956, 2929, 2857, 1593, 1487, 1457, 1395, 1360, 1094, 1070, 1011, 801. HRMS (EI-TOF) calcd for $C_{11}H_{14}DBrO$ $[M]^+$: 243.0364, found 243.0365.

(5*R*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-Dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one-3-*d* (2l-D).** Zinc powder (65.4 mg, 1.0 mmol), (3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-3-bromo-10,13-dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one **1l** (176.7 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 36 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2l**-D as two

diastereoisomers with a ratio of 1:9.2 (determined by ^{2}H NMR) in 91% isolated yield (125.3 mg) with 89% deuterium incorporation (determined by GC-MS) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$), two isomers: δ 2.43 (dd, *J* = 19.2 Hz, 8.8 Hz, 1H), 2.11-2.01 (m, 1H), 1.96-1.90 (m, 1H), 1.80-1.19 (m, 16H), 1.09-0.86 (m, 6H), 0.81 (s, 3H), 0.76-0.69 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$), two isomers: δ 221.4, 54.7, 51.4, 47.7, 46.9, 38.5, 36.3, 35.7, 34.9, 31.5, 30.9, 28.8, 28.6, 26.6 (C-H), 26.2 (t, *J* = 19.4 Hz, C-D), 21.9, 21.6, 20.0, 13.7, 12.1; ^{2}H NMR (92 MHz, $CDCl_3$) δ 1.65 (s), 1.18 (s). IR (neat): two isomers: 2968, 2948, 2917, 2851, 2834, 1743, 1444, 1376, 1058, 1023, 1009. HRMS (EI-TOF) calcd for $C_{19}H_{29}DO$ $[M]^+$: 275.2359, found 275.2365.

(5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3-*d* (2m-D).** Zinc powder (65.4 mg, 1.0 mmol), (3*R*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-bromo-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene **1m** (225.8 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 30 h. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **2m**-D as two diastereoisomers with a ratio of 1:2.4 (determined by ^{2}H NMR) in 99% isolated yield (184.5 mg) with 92% deuterium incorporation (determined by GC-MS) as a white solid. Mp 76-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$), two isomers: δ 1.96 (dt, *J* = 12.4 Hz, 3.2 Hz, 1H), 1.85-1.76 (m, 1H), 1.67-0.85 (m, 38H), 0.77 (s, 3H), 0.68-0.62 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$), two isomers: δ 56.6, 56.3, 54.8, 47.0, 42.6, 40.1, 39.6, 38.7, 36.2, 35.9, 35.5, 32.2, 29.1, 29.0, 28.3, 28.0, 26.9 (C-H), 26.5 (t, *J* = 16.6 Hz, C-D), 24.2, 23.9,

22.9, 22.6, 22.1, 20.8, 18.7, 12.2, 12.1; ^{2}H NMR (92 MHz, $CDCl_3$) δ 1.69 (s), 1.22 (s). IR (neat): two isomers: 2940, 2926, 2910, 2866, 2848, 1467, 1443, 1382, 955, 929, 730. HRMS (EI-TOF) calcd for $C_{27}H_{47}D$ $[M]^+$: 373.3819, found 373.3827.

2,3-Dihydro-1*H*-inden-1-one-3-*d* (2n-D**).** Zinc powder (65.4 mg, 1.0 mmol), 3-bromo-1-indanone **1n** (105.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (90.5 μL, 5 mmol) were stirred at 25 °C for 6 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2n**-D in 48% isolated yield (31.9 mg) with 90% deuterium incorporation as a white solid. Mp 38-40 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 3.16-3.12 (m, 1.10H), 2.69 (d, *J* = 6.0 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 207.1, 155.1, 137.0, 134.5, 127.2, 126.6, 123.6, 36.0, 25.7 (C-H), 25.4 (t, *J* =20.5 Hz, C-D). IR (neat): 2924, 2853, 1707, 1608, 1588, 1462, 1398, 1316, 1272, 1241, 1202, 1147, 1094, 1048, 1016, 809, 752. HRMS (ESI-TOF) calcd for C_9H_8DO $[M+H]^+$: 134.0711, found 134.0712.

(1*S*,4*R*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one-3-*d* (2o-D**).** Zinc powder (65.4 mg, 1.0 mmol), (+)-camphor bromide **1o** (115.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 22 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **2o**-D as two diastereoisomers with a ratio of 1:8.4 in 54% isolated yield (41.4 mg) with 77% deuterium incorporation as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$), two

isomers: δ 2.39-2.32 (m, 0.23H), 2.09 (d, J = 4.0 Hz, 1H), 1.98-1.91 (m, 1H), 1.87-1.82 (m, 1H), 1.72-1.65 (m, 1H), 1.44-1.31 (m, 2H), 0.96 (s, 3H), 0.91 (s, 3H), 0.84 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$), two isomers: δ 219.6, 57.6, 46.7, 43.2 (C-H), 42.92 (t, J = 20.2 Hz, C-D), 42.89, 29.8, 26.9, 19.7, 19.1, 9.2; ^2H NMR (92 MHz, $CDCl_3$) δ 2.34 (d), 1.84 (d). IR (neat), two isomers: 2959, 2924, 2873, 2854, 1742, 1456, 1373, 1261, 1073, 1041, 1021, 800. HRMS (EI-TOF) calcd for $C_{10}H_{15}DO$ $[M]^+$: 153.1264, found 153.1260.

Benzyl hexanoate-2-*d* (2p-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), benzyl 2-bromohexanoate **1p** (142.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 22 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2p**-D in 99% isolated yield (102.6 mg) with 95% deuterium incorporation as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.29 (m, 5H), 5.11 (s, 2H), 2.36-2.31 (m, 1.05H), 1.67-1.61 (m, 2H), 1.34-1.29 (m, 4H), 0.88 (t, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.6, 136.1, 128.4, 128.08, 128.06, 65.9, 34.2 (C-H), 33.9 (t, J = 19.8 Hz, C-D), 31.2, 24.5, 22.2, 13.8. IR (neat): 2956, 2931, 2872, 1734, 1498, 1456, 1378, 1252, 1217, 1171, 1131, 1108, 1003, 734, 696. HRMS (ESI-TOF) calcd for $C_{13}H_{18}DO_2$ $[M+H]^+$: 208.1442, found 208.1447.

Dihydrofuran-2(3*H*)-one-3-*d* (2q-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-bromo-4-butanolide **1q** (82.5 mg, 0.5 mmol) and D_2O (90.5 μL, 5 mmol) were stirred at 80 °C for 7 h. The crude product was filtered by a short silica gel column (eluent:

CH_2Cl_2) to afford **2q**-D in 88% isolated yield (38.4 mg) with 97% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.37 (t, J = 6.8 Hz, 2H), 2.53-2.47 (m, 1.03H), 2.31-2.25 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.1, 68.6, 27.5 (t, J = 20.5 Hz, C-D), 21.9. IR (neat): 2990, 2914, 1758, 1459, 1375, 1217, 1162, 1106, 1031, 1003, 959, 816, 676. HRMS (EI-TOF) calcd for $C_4H_5DO_2$ $[M]^+$: 87.0431, found 87.0434.

***N*-Carbamoyl-3-methylbutanamide (2r-D).** Zinc powder (65.4 mg, 1.0 mmol), bromisoval **1r** (111.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 47 h. The mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 1:1 to 1:2) to afford **2r**-D in 91% isolated yield (65.8 mg) with 41% deuterium incorporation as a white solid.

The following procedure involves the use of 10.0 equiv D_2O: zinc powder (65.4 mg, 1.0 mmol), bromisoval **1r** (111.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (90.5 μL, 5 mmol) were stirred at 80 °C for 18 h. The mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 1:1 to 1:2) to afford **2r**-D in 91% isolated yield (65.8 mg) with 66% deuterium incorporation as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (bs, 1H), 7.80 (bs, 1H), 7.19 (bs, 1H), 2.15-2.12 (m, 1.34 H), 2.04-1.94 (m, 1H), 0.87 (d, J = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 174.7, 154.4, 45.1 (C-H), 44.8 (t, J = 19.3 Hz,

C-D), 25.5, 22.4. IR (neat): 3382, 3334, 3211, 2953, 2870, 1685, 1592, 1469, 1403, 1365, 1328, 1287, 1260, 1220, 1196, 1097, 1050, 967, 810, 672. HRMS (ESI-TOF) calcd for $C_6H_{12}DN_2O_2$ $[M+H]^+$: 146.1034, found 146.1031.

Hexanoic-2-*d* acid (2s-D). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-bromohexanoic acid **1s** (97.5 mg, 0.5 mmol) and D_2O (90.5 μL, 5 mmol) were stirred at 25 °C for 3.5 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1) to afford **2s**-D in 91% isolated yield (53.1mg) with 86% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (br, 1H), 2.37-2.31 (m, 1.14H), 1.66-1.61 (m, 2H), 1.34-1.29 (m, 4H), 0.90 (t, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.7, 34.1 (C-H), 33.8 (t, *J* = 19.4 Hz, C-D), 31.2, 24.3, 22.3, 13.8. IR (neat): 2958, 2932, 2874, 1704, 1466, 1415, 1291, 1235, 1201, 934. HRMS (EI-TOF) calcd for C_6H_9DO $[M-H_2O]^+$: 99.0794, found 99.0807.

1-Phenylpropan-1-one-2-*d* (2t-D). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-chloro-1-phenylpropan-1-one **1t** (84.3 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **2t**-D in 83% isolated yield (56.0 mg) with 91% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.95 (m, 2H), 7.56-7.53 (m, 1H), 7.47-7.43 (m, 2H), 3.03-2.94 (m, 1.09H), 1.22 (d, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.8, 136.8, 132.8, 128.5, 127.9, 31.7 (C-H), 31.4 (t, *J* = 19.0 Hz, C-D), 8.1. IR (neat): 2977, 2935, 1683, 1597, 1582,

1449, 1331, 1265, 1220, 1075, 951, 771, 745, 721, 688. HRMS (ESI-TOF) calcd for $C_9H_{10}DO$ $[M+H]^+$: 136.0867, found 136.0863.

1-(Butyl-3-*d*)-4-methoxybenzene (2g-D). This product was synthesized from 1-(3-iodobutyl)-4-methoxybenzene **1u**. Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), **1u** (145.1 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 25 °C for 2 h. The crude product was purified by column chromatography on silica gel (eluent: pentane : ethyl acetate = 40:1) to afford **2g**-D in 88% isolated yield (73.1 mg) with 82% deuterium incorporation (determined by ^1H NMR of the crude reaction mixture) as a colourless oil.

1-Tosylpiperidine-4-*d* (2a-D). This product was synthesized from 4-iodo-1-tosylpiperidine **1v**. Zinc powder (65.4 mg, 1.0 mmol), **1v** (182.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (90.5 μL, 5 mmol) were stirred at 25 °C for 2 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: CH_2Cl_2 = 5:1 to petroleum ether: ethyl acetate = 5:1) to afford **2a**-D in 94% isolated yield (112.4 mg) with 88% deuterium incorporation as a white solid.

((Propoxy-3-*d*)methyl)benzene (4a-D). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), benzyl-3-bromopropyl ether **3a** (114.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 26 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1) to afford **4a**-D in 85% isolated yield (64.3 mg) with 93% deuterium incorporation as a colourless oil. ^1H NMR (400 MHz,

$CDCl_3$) δ 7.34-7.25 (m, 5H), 4.50 (s, 2H), 3.43 (t, *J* = 6.4 Hz, 2H), 1.66-1.60 (m, 2H), 0.96-0.90 (m, 2.07H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.7, 128.3, 127.5, 127.4, 72.8, 72.1, 22.8, 10.6 (C-H), 10.3 (t, *J* = 18.9 Hz, C-D). IR (neat): 3029, 2935, 2854, 1495, 1454, 1363, 1097, 1028, 733, 696. HRMS (EI-TOF) calcd for $C_{10}H_{13}DO$ $[M]^+$: 151.1107, found 151.1103.

2,2-Diphenylbutanenitrile-4-*d* (4b-D**).** Zinc powder (65.4 mg, 1.0 mmol), 4-bromo-2,2-diphenylbutyronitrile **3b** (150.1 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **4b**-D in 99% isolated yield (110.4 mg) with 92% deuterium incorporation as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.24 (m, 10H), 2.41 (t, *J* = 6.8 Hz, 2H), 1.06-1.01 (m, 2.08H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.0, 128.7, 127.7, 126.8, 122.2, 52.4, 32.6, 10.0 (C-H), 9.7 (t, *J* = 18.9 Hz, C-D). IR (neat): 3060, 3026, 2969, 2937, 2236, 1598, 1493, 1448, 1031, 750, 695. HRMS (ESI-TOF) calcd for $C_{16}H_{15}DN$ $[M+H]^+$: 223.1340, found 223.1342.

2-(Propyl-3-*d*)isoindoline-1,3-dione (4c-D**).** Zinc powder (65.4 mg, 1.0 mmol), *N*-(3-bromopropyl)phthalimide **3c** (134.0 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 12 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **4c**-D in 67% isolated yield (64.1 mg) with 89% deuterium incorporation as a white solid. ^1H

NMR (400 MHz, $CDCl_3$) δ 7.86-7.82 (m, 2H), 7.74-7.70 (m, 2H), 3.66 (t, J = 7.2 Hz, 2H), 1.74-1.67 (m, 2H), 0.97-0.92 (m, 2.11H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.3, 133.7, 132.1, 123.0, 39.5, 21.7, 11.2 (C-H), 10.9 (t, J = 19.0 Hz, C-D). IR (neat): 2958, 2930, 2848, 1765, 1703, 1466, 1443, 1395, 1367, 1337, 1259, 1186, 1153, 1086, 1042, 1001, 885, 868, 796, 709. HRMS (EI-TOF) calcd for $C_{11}H_{10}DNO_2$ $[M]^+$: 190.0853, found 190.0859.

Decane-1-*d* (4d-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-bromodecane **3d** (110.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 48 h. **4d**-D was obtained in 86% yield using 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as an internal standard. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **4d**-D in 23% isolated yield (16.5 mg) with 92% deuterium incorporation (determined by ^1H NMR of the crude reaction mixture) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 1.32-1.26 (m, 16H), 0.90-0.86 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 31.9, 29.7, 29.4, 22.7, 14.1 (C-H), 13.8 (t, J = 18.6 Hz, C-D). The spectroscopic data are in agreement with that previously reported.[32]

1-Chlorodecane-10-*d* (4e-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-bromo-10-chlorodecane **3e** (127.8 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 52 h. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **4e**-D in 85% isolated yield (75.4 mg) with 97% deuterium incorporation (determined by ^1H NMR of the crude reaction mixture) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 3.53 (t, J = 6.8 Hz, 2H), 1.80-1.73 (m, 2H),

1.44-1.39 (m, 2H), 1.27 (s, 12H), 0.88-0.85 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 45.1, 32.7, 31.8, 29.50, 29.47, 29.3, 28.9, 26.9, 22.6, 14.1 (C-H), 13.8 (t, *J* = 19.3 Hz, C-D). IR (neat): 2924, 2854, 1464, 1289, 723, 654. HRMS (EI-TOF) calcd for $C_{10}H_{20}DCl$ $[M]^+$: 177.1395, found 177.1396.

1-(2-Hydroxyphenyl)ethan-1-one-2-*d* (4f-D). Zinc powder (65.4 mg, 1.0 mmol), 2-bromo-2'-hydroxyacetophenone **3f** (107.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 6 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **4f**-D in 89% isolated yield (61.0 mg) with 75% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.27 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.4 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 2.62-2.60 (m, 2.25H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 204.5, 162.3, 136.4, 130.7, 119.6, 118.8, 118.3, 26.5 (C-H), 26.3 (t, *J* =19.8 Hz, C-D). IR (neat): 3047, 1637, 1615, 1581, 1486, 1447, 1365, 1322, 1300, 1243, 1218, 1157, 1033, 1023, 961, 836, 799, 750, 734, 711. HRMS (EI-TOF) calcd for $C_8H_7DO_2$ $[M]^+$: 137.0587, found 137.0585.

1,3-Dimethoxy-5-(methyl-*d*)benzene (4g-D). Zinc powder (65.4 mg, 1.0 mmol), 3,5-dimethoxybenzyl bromide **3g** (115.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and D_2O (90.5 μL, 5 mmol) were stirred at 25 °C for 4 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **4g**-D in 60% isolated yield (45.6 mg) with 74% deuterium incorporation as a colourless oil. ^{1}H

NMR (400 MHz, $CDCl_3$) δ 6.33 (s, 2H), 6.28 (s, 1H), 3.76 (s, 6H), 2.30-2.28 (m, 2.26H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.7, 140.1, 107.0, 97.4, 55.1, 21.8 (C-H), 21.5 (t, *J* = 18.9 Hz, C-D). IR (neat): 2998, 2935, 2835, 1593, 1458, 1428, 1345, 1324, 1203, 1146, 1058, 825, 684. HRMS (EI-TOF) calcd for $C_9H_{11}DO_2$ $[M]^+$: 153.0900, found 153.0901.

1-(Ethyl-2-*d*)-4-octylbenzene (4h-D). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-(2-iodoethyl)-4-octylbenzene **3h** (172.1 mg, 0.5 mmol) and D_2O (90.5 μL, 5 mmol) were stirred at 25 °C for 12 h. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **4h**-D in 92% isolated yield (101.4 mg) with 93% deuterium incorporation (determined by GC-MS) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.11-7.07 (m, 4H), 2.63-2.54 (m, 4H), 1.63-1.55 (m, 2H), 1.30-1.18 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.3, 140.1, 128.3, 127.7, 35.6, 31.9, 31.7, 29.5, 29.4, 29.3, 28.4, 22.7, 15.7 (C-H), 15.4 (t, *J* = 19.0 Hz, C-D), 14.1. IR (neat): 2957, 2924, 2854, 1515, 1456, 815, 722. HRMS (EI-TOF) calcd for $C_{16}H_{25}D$ $[M]^+$: 219.2097, found 219.2093.

1-(Methyl-*d*)naphthalene (4i-D). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-chloromethyl naphthalene **3i** (88.3 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **4i**-D in 82% isolated yield (58.4 mg) with 90% deuterium incorporation as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97-7.95 (m, 1H), 7.83-7.80 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.51-7.43 (m, 2H), 7.36-7.32 (m, 1H),

7.29-7.27 (m, 1H), 2.66-2.64 (m, 2.10H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 134.2, 133.5, 132.6, 128.5, 126.5, 126.3, 125.7, 125.53, 125.50, 124.1, 19.3 (C-H), 19.1 (t, J = 19.4 Hz, C-D). IR (neat): 3043, 2919, 1596, 1509, 1397, 1164, 1019, 784, 771, 764, 731, 697. HRMS (EI-TOF) calcd for $C_{11}H_9D$ $[M]^+$: 143.0845, found 143.0851.

1-(Phenyl-4-*d*)ethan-1-one (5a-D**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 4-iodoacetophenone (123.0 mg, 0.5 mmol) and D_2O (90.5 μL, 5 mmol) were stirred at 80 °C for 24 h. The NMR yield was 95%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate = 30:1) to afford **5a**-D in 69% isolated yield (41.8 mg) with 89% deuterium incorporation as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 2H), 7.58-7.54 (m, 0.11H), 7.46 (d, J = 8.0 Hz, 2H), 2.60 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 198.1, 137.0, 133.0 (C-H), 132.7 (t, J = 23.9 Hz, C-D), 128.4, 128.2, 26.5. IR (neat): 1681, 1594, 1407, 1357, 1301, 1263, 1178, 1022, 957, 863, 761, 735, 692. HRMS (EI-TOF) calcd for C_8H_7OD $[M]^+$: 121.0638, found 121.0640.

Typical procedure for dehalogenation of alkyl halides in the presence of H_2O. To a sealable tube was added zinc powder (65.4 mg, 1.0 mmol), 4-bromo-1-tosylpiperidine **1a** (159.1 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) under argon (If the alkyl bromide is a liquid, it is added after CH_3CN). The tube was sealed and immersed into an oil bath preheated at 80 °C. After stirring for 6 h, the mixture was cooled down to room temperature. Then the reaction mixture was filtered through a short silica gel column and

washed with dichloromethane. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afforded **2a**-H in 93% yield (111.0 mg) as a white solid.

1-Tosylpiperidine (2a-H**).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* =8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.96 (t, *J* = 5.6 Hz, 4H), 2.43 (s, 3H), 1.66-1.61 (m, 4H), 1.44-1.38 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.2, 133.0, 129.4, 127.6, 46.8, 25.0, 23.4, 21.4. The spectroscopic data are in agreement with that previously reported.[33]

2,3-Dihydro-1*H*-indene (2b-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-bromo-2,3-dihydro-1*H*-indene **1b** (98.5 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 2 h. With 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as internal standard, the NMR yield was 87%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2b**-H in 76% isolated yield (45.0 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.21 (m, 2H), 7.13-7.11 (m, 2H), 2.91 (t, *J* = 7.6 Hz, 4H), 2.10-2.02 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.1, 125.9, 124.3, 32.8, 25.3. The spectroscopic data are in agreement with that previously reported.[34]

5-Methoxy-1,2,3,4-tetrahydronaphthalene (2c-H**).** Zinc powder (65.4 mg, 1.0 mmol), 2-bromo-5-methoxy-1,2,3,4-tetrahydronaphthalene **1c** (120.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was

purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1) to afford **2c**-H in 95% isolated yield (77.4 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (t, J = 8.0 Hz, 1H), 6.68 (d, J = 7.6 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 3.78 (s, 3H), 2.75-2.72 (m, 2H), 2.65-2.62 (m, 2H), 1.80-1.71 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.3, 138.4, 125.8, 125.6, 121.3, 106.6, 55.1, 29.6, 23.0, 22.8. The spectroscopic data are in agreement with that previously reported.[35]

Cyclododecane (2d-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), bromocyclododecane **1d** (123.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 4 h. With 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as internal standard, the NMR yield was 96%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2d**-H in 84% isolated yield (71.0 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6. The spectroscopic data are in agreement with that previously reported.[36]

Adamantane (2e-H**).** Zinc powder (65.4 mg, 1.0 mmol), 2-bromoadamantane **1e** (107.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 41 h. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **2e**-H in 44% isolated yield (29.9 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (s, 4H), 1.75 (s, 12H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 37.7, 28.3. The spectroscopic data are in agreement with that previously reported.[37]

(Butoxymethyl)benzene (2f-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), ((3-bromobutoxy)methyl)benzene **1f** (121.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2f**-H in 89% isolated yield (73.2 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 5H), 4.49 (s, 2H), 3.46 (t, J = 6.4 Hz, 2H), 1.63-1.56 (m, 2H), 1.44-1.35 (m, 2H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.6, 128.3, 127.5, 127.4, 72.8, 70.1, 31.8, 19.3, 13.9. The spectroscopic data are in agreement with that previously reported.[38]

1-Butyl-4-methoxybenzene (2g-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-(3-bromobutyl)-4-methoxybenzene **1g** (121.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **2g**-H in 97% isolated yield (79.4 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 3.76 (s, 3H), 2.54 (t, J = 7.6 Hz, 2H), 1.60-1.52 (m, 2H), 1.38-1.26 (m, 2H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.5, 134.9, 129.2, 113.6, 55.1, 34.7, 33.9, 22.3, 13.9. The spectroscopic data are in agreement with that previously reported.[39]

1,3-Diphenylpropane (2h-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), (2-bromopropane-1,3-diyl)dibenzene **1h** (137.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was purified by column

chromatography on silica gel (eluent: petroleum ether) to afford **2h**-H in >99% isolated yield (98 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.15 (m, 10H), 2.62 (t, *J* = 8.0 Hz, 4H), 1.98-1.90 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.2, 128.4, 128.3, 125.7, 35.4, 32.9. The spectroscopic data are in agreement with that previously reported.[40]

1-Phenylpentan-1-one (**2i**-H). Zinc powder (65.4 mg, 1.0 mmol), 3-bromo-1-phenylpentan-1-one **1i** (120.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 10 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **2i**-H in 75% isolated yield (61.0 mg) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.95 (m, 2H), 7.56-7.52 (m, 1H), 7.47-7.43 (m, 2H), 2.96 (t, *J* = 7.2 Hz, 2H), 1.76-1.68 (m, 2H), 1.46-1.36 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.5, 137.0, 132.8, 128.5, 128.0, 38.2, 26.4, 22.4, 13.9. The spectroscopic data are in agreement with that previously reported.[41]

***N*-Methyl-*N*-pentylaniline** (**2j**-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), *N*-(3-bromopentyl)-*N*-methylbenzenamine **1j** (128.1 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 40 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1) to afford **2j**-H in 70% isolated yield (62.0 mg) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.19 (m, 2H), 6.70-6.64 (m, 3H), 3.29 (t, *J* = 7.6 Hz, 2H), 2.91 (s, 3H), 1.60-1.53 (m,

2H), 1.38-1.26 (m, 4H), 0.90 (t, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.4, 129.1, 115.7, 112.0, 52.8, 38.2, 29.4, 26.3, 22.6, 14.1. The spectroscopic data are in agreement with that previously reported.[42]

1-Bromo-4-(butoxymethyl)benzene (**2k**-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-bromo-4-((3-bromobutoxy)methyl)benzene **1k** (161.0 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2k**-H in 99% isolated yield (120.9 mg) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 4.43 (s, 2H), 3.45 (t, J = 6.4 Hz, 2H), 1.62-1.55 (m, 2H), 1.43-1.34 (m, 2H), 0.91 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 137.7, 131.3, 129.1, 121.2, 72.0, 70.3, 31.8, 19.3, 13.9. The spectroscopic data are in agreement with that previously reported.[43]

(5*R*,8*R*,9*S*,10*S*,13*S*,14*S*)-10,13-Dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (2l-H). Zinc powder (65.4 mg, 1.0 mmol), (3*S*,5*S*,8*R*,9*S*,10*S*,13*S*,14*S*)-3-bromo-10,13-dimethylhexadecahydro-17*H*-cyclopenta[*a*]phenanthren-17-one **1l** (176.7 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 36 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2l**-H in 95% isolated yield (130.7 mg) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 2.43 (dd, J = 19.2 Hz, 8.8 Hz, 1H), 2.11-2.01 (m, 1H), 1.96-1.90 (m, 1H), 1.80-1.19 (m, 17H), 1.10-0.86 (m, 6H),

0.81 (s, 3H), 0.76-0.69 (m, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 221.4, 54.7, 51.4, 47.7, 46.9, 38.5, 36.3, 35.7, 34.9, 31.5, 30.9, 28.9, 28.6, 26.6, 22.0, 21.6, 19.9, 13.7, 12.1. The spectroscopic data are in agreement with that previously reported.[44]

(5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene (2m-H). Zinc powder (65.4 mg, 1.0 mmol), (3*R*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-bromo-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene **1m** (225.8 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 30 h. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **2m**-H in 97% isolated yield (180.7 mg) as a white solid. Mp 77-79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 (dt, *J* = 12.4 Hz, 2.8 Hz, 1H), 1.85-1.76 (m, 1H), 1.67-0.85 (m, 39H), 0.78 (s, 3H), 0.68-0.62 (m, 4H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 56.6, 56.3, 54.8, 47.0, 42.6, 40.1, 39.5, 38.7, 36.23, 36.22, 35.9, 35.5, 32.2, 29.1, 29.1, 28.3, 28.0, 26.9, 24.2, 23.9, 22.9, 22.6, 22.2, 20.8, 18.7, 12.2, 12.1. IR (neat): 2925, 2910, 2866, 2848, 1467, 1442, 1381, 1172, 958, 929, 732. HRMS (EI-TOF) calcd for $C_{27}H_{48}$ $[M]^+$: 372.3756, found 372.3747.

2,3-Dihydro-1*H*-inden-1-one (2n-H). Zinc powder (65.4 mg, 1.0 mmol), 3-bromo-1-indanone **1n** (105.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 25 °C for 6 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2n**-H in 62% isolated yield (41.2 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d,

J = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.36 (t, *J* =7.6 Hz, 1H), 3.14 (t, *J* = 6.0 Hz, 2H), 2.68 (t, *J* = 6.0 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 207.0, 155.1, 137.0, 134.5, 127.2, 126.6, 123.6, 36.1, 25.7. The spectroscopic data are in agreement with that previously reported.[45]

(1*S*,4*R*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one (2o-H**).** Zinc powder (65.4 mg, 1.0 mmol), (+)-camphor bromide **1o** (115.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 11 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **2o**-H in 69% isolated yield (52.4 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38-2.33 (m, 1H), 2.09 (t, *J* = 4.0 Hz, 1H), 1.99-1.92 (m, 1H), 1.84 (d, *J* = 18.0 Hz, 1H), 1.72-1.66 (m, 1H), 1.44-1.31 (m, 2H), 0.96 (s, 3H), 0.91 (s, 3H), 0.84 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 219.6, 57.6, 46.7, 43.2, 43.0, 29.8, 27.0, 19.7, 19.1, 9.2. The spectroscopic data are in agreement with that previously reported.[46]

Benzyl hexanoate (2p-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), benzyl 2-bromohexanoate **1p** (142.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 11 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2p**-H in 99% isolated yield (101.9 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H), 5.11 (s, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 1.72-1.61 (m, 2H), 1.36-1.25 (m, 4H), 0.88 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 173.6, 136.1, 128.4, 128.08, 128.06, 65.9, 34.2, 31.2,

24.6, 22.2, 13.8. The spectroscopic data are in agreement with that previously reported.[47]

Dihydrofuran-2(3*H*)-one (2q-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-bromo-4-butanolide **1q** (82.5 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 7 h. The crude product was filtered by a short silica gel column (eluent: CH_2Cl_2) to afford **2q**-H in 90% isolated yield (38.8 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (t, J = 7.2 Hz, 2H), 2.53 (t, J = 8.0 Hz, 2H), 2.33-2.25 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.4, 68.7, 27.8, 22.0. The spectroscopic data are in agreement with that previously reported.[48]

***N*-Carbamoyl-3-methylbutanamide (2r**-H**).** Zinc powder (65.4 mg, 1.0 mmol), bromisoval **1r** (111.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (90.1 μL, 5 mmol) were stirred at 80 °C for 9 h. The mixture was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 1:1 to 1:2) to afford **2r**-H in 94% isolated yield (68.0 mg) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.12 (bs, 1H), 7.80 (bs, 1H), 7.21 (bs, 1H), 2.15 (d, J = 6.8 Hz, 2 H), 2.04-1.94 (m, 1H), 0.87 (d, J = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 174.3, 154.0, 44.8, 25.2, 22.1. The spectroscopic data are in agreement with that previously reported.[49]

Hexanoic acid (2s-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL),

2-bromohexanoic **1s** (97.5 mg, 0.5 mmol) were stirred at 25 °C for 3.5 h. The mixture was quenched with 3 M HCl aqueous solution, extracted with ethyl acetate, dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1) to afford **2s**-H in 98% isolated yield (56.7 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.37 (br, 1H), 2.35 (t, J = 7.6 Hz, 2H), 1.66-1.63 (m, 2H), 1.36-1.31 (m, 4H), 0.92-0.89 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 180.6, 34.1, 31.2, 24.3, 22.3, 13.8. The spectroscopic data are in agreement with that previously reported.[46]

Propiophenone (2t-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 2-chloro-1-phenylpropan-1-one **1t** (84.3 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **2t**-H in 83% isolated yield (56.0 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 3.00 (q, J = 7.2 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.7, 136.8, 132.8, 128.5, 127.9, 31.7, 8.1. The spectroscopic data are in agreement with that previously reported.[50]

1-Butyl-4-methoxybenzene (2g-H). This product was synthesized from 1-(3-iodobutyl)-4-methoxybenzene **1u**. Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), **1u** (145.1 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 25 °C for 2 h. The crude product was purified by column chromatography on silica gel (eluent: pentane :

ethyl acetate = 40:1) to afford **2g**-H in 94% isolated yield (76.9 mg) as a colourless oil.

1-Tosylpiperidine (2a-H**).** This product was synthesized from 4-iodo-1-tosylpiperidine **1v**. Zinc powder (65.4 mg, 1.0 mmol), **1v** (182.6 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 25 °C for 2 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2a**-H in 94% isolated yield (112.9 mg) as a white solid.

(Propoxymethyl)benzene (4a-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), benzyl-3-bromopropyl ether **3a** (114.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 26 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1) to afford **4a**-H in 85% isolated yield (64.0 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.25 (m, 5H), 4.50 (s, 2H), 3.43 (t, *J* = 6.8 Hz, 2H), 1.68-1.59 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 138.7, 128.3, 127.5, 127.4, 72.8, 72.1, 22.9, 10.6. The spectroscopic data are in agreement with that previously reported.[51]

2,2-Diphenylbutanenitrile (4b-H**).** Zinc powder (65.4 mg, 1.0 mmol), 4-bromo-2,2-diphenylbutyronitrile **3b** (150.1 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 8 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **4b**-H in 99% isolated yield (109.8 mg) as a colourless oil. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.39-7.24 (m, 10H), 2.41 (q, *J* = 7.2 Hz, 2H), 1.04 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 140.0, 128.7, 127.7, 126.8, 122.2, 52.4, 32.6, 10.0. The spectroscopic data are in agreement with that previously reported.[52]

2-Propylisoindoline-1,3-dione (4c-H). Zinc powder (65.4 mg, 1.0 mmol), *N*-(3-bromopropyl)phthalimide **3c** (134.0 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 12 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **4c**-H in 62% isolated yield (58.2 mg) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.82 (m, 2H), 7.73-7.69 (m, 2H), 3.66 (t, *J* = 7.2 Hz, 2H), 1.76-1.67 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.3, 133.7, 132.1, 123.0, 39.5, 21.8, 11.2. The spectroscopic data are in agreement with that previously reported.[53]

Decane (**4d**-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-bromodecane **3d** (110.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 48 h. **4d**-H was obtained in 79% yield using 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as an internal standard. The crude product was purified by column chromatography on silica gel (eluent: pentane) to afford **4d**-H in 38% isolated yield (27.3 mg) as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 1.32-1.26 (m, 16H), 0.90-0.86 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 31.9, 29.7, 29.4, 22.7, 14.1. The spectroscopic data are in agreement with that previously reported.[54]

1-Chlorodecane (**4e**-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-bromo-10-chlorodecane **3e** (127.8 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 52 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **4e**-H in 90% isolated yield (79.7 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.52 (t, J = 6.8 Hz, 2H), 1.80-1.73 (m, 2H), 1.44-1.39 (m, 2H), 1.27 (s, 12H), 0.88 (t, J = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 45.1, 32.7, 31.9, 29.52, 29.48, 29.3, 28.9, 26.9, 22.7, 14.1. The spectroscopic data are in agreement with that previously reported.[55]

1-(2-Hydroxyphenyl)ethan-1-one (4f-H**).** Zinc powder (65.4 mg, 1.0 mmol), 2-bromo-2'-hydroxyacetophenone **3f** (107.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 6 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **4f**-H in 89% isolated yield (60.5 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.26 (s, 1H), 7.74-7.71 (m, 1 H), 7.48-7.44 (m, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.91-6.87 (m, 1H), 2.62 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.5, 162.3, 136.4, 130.7, 119.63, 118.8, 118.3, 26.5. The spectroscopic data are in agreement with that previously reported.[56]

1,3-Dimethoxy-5-methylbenzene (4g-H**).** Zinc powder (65.4 mg, 1.0 mmol), 3,5-dimethoxybenzyl bromide **3g** (115.5 mg, 0.5 mmol), CH_3CN (2.5 mL) and H_2O (27.0 μL, 1.5 mmol) were stirred at 25 °C for 4 h. The crude product was purified by column

chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **4g**-H in 66% isolated yield (50.0 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33 (s, 2H), 6.28 (s, 1H), 3.76 (s, 6H), 2.30 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 160.6, 140.1, 107.0, 97.4, 55.1, 21.7. The spectroscopic data are in agreement with that previously reported.[57]

1-Ethyl-4-octylbenzene (4h-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-(2-iodoethyl)-4-octylbenzene **3h** (172.1 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 25 °C for 12 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **4h**-H in 93% isolated yield (101.2 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11-7.07 (m, 4H), 2.63-2.54 (m, 4H), 1.63-1.55 (m, 2H), 1.30-1.20 (m, 13H), 0.88 (t, J = 6.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.3, 140.1, 128.3, 127.7, 35.6, 31.9, 31.6, 29.5, 29.4, 29.3, 28.4, 22.7, 15.6, 14.1. IR (neat): 2960, 2924, 2854, 1514, 1456, 1377, 1120, 1021, 819, 722. HRMS (EI-TOF) calcd for $C_{16}H_{26}$ $[M]^+$: 218.2035, found 218.2040.

1-Methylnaphthalene (4i-H**).** Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 1-chloromethyl naphthalene **3i** (88.3 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) were stirred at 80 °C for 4 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether) to afford **4i**-H in 82% isolated yield (58.3 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 1H), 7.83-7.80 (m, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.51-7.43 (m, 2H), 7.36-7.32 (m, 1H), 7.28 (d, J = 6.8 HZ, 1H),

2.66 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 134.2, 133.5, 132.6, 128.5, 126.5, 126.3, 125.7, 125.54, 125.50, 124.1, 19.3. The spectroscopic data are in agreement with that previously reported.[58]

Typical procedure for dehalogenation of alkyl bromides in the presence of PhCOOH. A Schlenk tube was dried under vacuum using a heat gun, and evacuated and back-filled with argon for several times. Then zinc powder (65.4 mg, 1.0 mmol), PhCOOH (61.1 mg, 0.5 mmol) were added under argon. The tube was evacuated and refilled with argon for three times, and then CH_3CN (1.5 mL), 2-bromo-2-cyclopropyl-1-phenylethanone **1w** (119.6 mg, 0.5 mmol), CH_3CN (1 mL) was added (If the alkyl bromide is a solid, it is added before CH_3CN). The Schlenk tube was sealed and immersed into an oil bath preheated at 25 °C. After stirring for 3.5 h, the reaction mixture was filtered through a short pad of silica gel and washed with CH_2Cl_2. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **2w**-H in >99% yield (79.8 mg) as a colourless oil.

2-Cyclopropyl-1-phenylethan-1-one (**2w**-H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.93 (m, 2H), 7.56-7.53 (m, 1H), 7.47-7.43 (m, 2H), 2.88 (d, J = 6.8 Hz, 2H), 1.21-1.11 (m, 1H), 0.62-0.57 (m, 2H), 0.21-0.17 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 199.9, 136.8, 132.8, 128.4, 128.0, 43.7, 6.5, 4.4. The spectroscopic data are in agreement with that previously reported.[59]

Benzyl hexanoate (**2p**-H). Zinc powder (65.4 mg, 1.0 mmol), PhCOOH (61.1 mg, 0.5 mmol), CH_3CN (1.5 mL), benzyl 2-bromohexanoate **1p** (142.6 mg, 0.5 mmol) and CH_3CN (1 mL) were stirred at 25 °C for 3.5 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) to afford **2p**-H in 99% isolated yield (102.1 mg) as a colourless oil.

Dihydrofuran-2(3*H*)-one (2q-H**).** Zinc powder (65.4 mg, 1.0 mmol), PhCOOH (61.1 mg, 0.5 mmol), CH_3CN (1.5 mL), 2-bromo-4-butanolide **1q** (82.5 mg, 0.5 mmol) and CH_3CN (1 mL) were stirred at 25 °C for 6 h. **2q**-H was obtained in 90% yield using 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as an internal standard.

1-(Benzofuran-2-yl)ethan-1-one (**4j**-H). Zinc powder (65.4 mg, 1.0 mmol), PhCOOH (61.1 mg, 0.5 mmol), 1-(benzofuran-2-yl)-2-bromoethan-1-one **3j** (119.5 mg, 0.5 mmol) and CH_3CN (2.5 mL) were stirred at 25 °C for 2 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) to afford **4j**-H in 96% isolated yield (76.9 mg) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-7.69 (m, 1H), 7.59-7.56 (m, 1H), 7.50-7.45 (m, 2H), 7.33-7.29 (m, 1H), 2.60 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.6, 155.6, 152.5, 128.2, 126.9, 123.8, 123.2, 113.0, 112.4, 26.4. The spectroscopic data are in agreement with that previously reported.[60]

1-(2-Hydroxyphenyl)ethan-1-one (4f-H**).** Zinc powder (65.4 mg, 1.0 mmol), PhCOOH

(61.1 mg, 0.5 mmol), 2-bromo-2'-hydroxyacetophenone **3f** (107.5 mg, 0.5 mmol) and CH_3CN (2.5 mL) were stirred at 25 °C for 2.5 h. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **4f**-H in 83% isolated yield (56.7 mg) as a yellow oil.

Acetophenone (5a-H). Zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), 4-iodoacetophenone (123.0 mg, 0.5 mmol) and H_2O (180 μL, 10 mmol) were stirred at 80 °C for 24 h. The NMR yield was 92%. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate = 30:1) to afford **5a**-H in 70% isolated yield (42.0 mg) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.94 (m, 2H), 7.58-7.54 (m, 1H), 7.48-7.44 (m, 2H), 2.60 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.1, 137.0, 133.0, 128.5, 128.2, 26.5. The spectroscopic data are in agreement with that previously reported.[61]

When the reaction of 4-bromophenylacetone with Zn (2 equiv) was performed in the presence of 10 equiv H_2O in CH_3CN at 100 °C for 10 h, no dehalogenated product was formed and 4-bromophenylacetone was recovered in 98% NMR yield.

Gram scale study

To a Schlenk tube were added zinc powder (490.4 mg, 7.5 mmol), 4-bromo-1-tosylpiperidine **1a** (1.59 g, 5 mmol), CH_3CN (12 mL) and D_2O (271.4 μL, 15 mmol) under argon. The tube was sealed and immersed into an oil bath preheated at 80 °C. After stirring for 19 h, the mixture was cooled down to room temperature. Then the

reaction mixture was filtered through a short silica gel column and washed with dichloromethane. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afforded **2a**-D in 95% yield (1.14 g) with 92% deuterium incorporation as a white solid.

Deuteration of the *N*-phenyl ring of *N*,*N*-dimethylbenzenamine.

In a nitrogen-filled glove box, $ZnBr_2$ (112.6 mg, 0.5 mmol) was added to a sealable tube. Then the sealing cap was securely fitted and taken out of the glove box. The tube was evacuated and refilled with argon for three times. CH_3CN (2.5 mL), *N*,*N*-dimethylbenzenamine (60.6 mg, 0.5 mmol) and D_2O (27.1 μL, 1.5 mmol) was added to the tube under argon. Then the sealing cap was securely fitted and the reaction mixture was stirred at 80 °C in an oil-bath for 12 h. After the mixture was cooled down to room temperature, the crude product was filtered by a short silica gel column (eluent: CH_2Cl_2) to afford *N*,*N*-dimethylaniline-2,4,6-d_3 in 49% isolated yield (30.1 mg) as a light yellow oil. Deuterium incorporation (*ortho*-position of the phenyl ring): 55%; Deuterium incorporation (*para*-position of the phenyl ring): 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.22 (m, 2H), 6.75-6.70 (m, 1.25H), 2.93 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.5 (t, J = 5.2 Hz), 128.9 (t, J = 11.1 Hz), 116.6 (C-H), 116.3 (t, J = 26.0 Hz, C-D), 112.6 (C-H), 112.3 (t, J = 24.6 Hz, C-D), 40.6. IR (neat): 2844, 2795, 1591, 1489, 1438, 1422, 1341, 1220, 1062, 1051, 980, 970, 962, 947, 821, 750, 736. HRMS (ESI-TOF) calcd for $C_8H_{10}D_2N$ $[M+H]^+$: 124.1090, found 124.1089.

The NMR yield of *N*,*N*-dimethylaniline-2,4,6-d_3 was 99% using 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as an internal standard.

Mechanistic studies:

1) Reaction inhibition by Galvinoxyl.

In a nitrogen-filled glove box, zinc powder (26.2 mg, 0.4 mmol), 4-bromo-1-tosylpiperidine **1a** (63.6 mg, 0.2 mmol), Galvinoxyl (168.7 mg, 0.4 mmol) and CH_3CN (1 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. H_2O (10.8 μL, 0.6 mmol) was added to the vial and the reaction mixture was stirred at 80 °C (oil bath) for 10 h. After the starting material was completely consumed, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: CH_2Cl_2 = 5:1 to petroleum ether: ethyl acetate = 20:1 to 10:1) to afford 1-tosylpiperidine (**2a**-H) in 14% isolated yield (6.7 mg) and 4-bromo-1-tosylpiperidine (**1a**) in 84% isolated yield (53.2 mg) as white solids.

2) Ring-opening experiment.

To a sealable tube were added zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), (3-bromo-3-cyclopropylpropyl)benzene **1x** (119.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) under argon. Then the sealing cap was securely fitted and the mixture was stirred at 80 °C in an oil-bath for 52 h. After the mixture was cooled down to room temperature, the

mixture was filtered through $MgSO_4$ and washed with dichloromethane. With 1,3,5-trimethoxybenzene (84.1 mg, 0.5 mmol) as an internal standard, the NMR yield of (3-cyclopropylpropyl)benzene **2x** was 32%, the NMR yield of hex-3-enylbenzene **2x-a** was 47% (*Z*:*E* = 1:6.8). The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate =5:1) to afford a mixture of **2x** and hex-3-en-1-ylbenzene **2x-a** in 24% isolated yield (19.1 mg) [**2x**: **2x-a** (*trans*): **2x-a** (*cis*) = 1.5:8.2:1] as a colourless oil.

(3-Cyclopropylpropyl)benzene (2x). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 7.22-7.20 (m, 3H), 2.64 (t, J = 8.4 Hz, 2H), 1.79-1.71 (m, 2H), 1.29-1.24 (m, 2H), 0.76-0.66 (m, 1H), 0.45-0.40 (m, 2H), 0.04-0.01 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.9, 128.4, 128.3, 125.5, 35.8, 34.3, 31.4, 10.7, 4.4. The spectroscopic data are in agreement with that previously reported.[62]

(*E*)-Hex-3-en-1-ylbenzene [2x-a (trans)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 7.22-7.20 (m, 3H), 5.55-5.43 (m, 2H), 2.69 (t, *J* = 7.6 Hz, 2H), 2.35-2.30 (m, 2H), 2.05-1.99 (m, 2H), 0.98 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.2, 132.6, 132.3, 128.4, 128.2, 125.7, 36.1, 34.4, 25.6, 13.9. The ^{1}H NMR data are in agreement with that previously reported.[63]

(*Z*)-Hex-3-en-1-ylbenzene [2x-a (cis)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H),

7.22-7.20 (m, 3H), 5.42-5.39 (m, 2H), 2.69 (t, J = 7.6 Hz, 2H), 2.41-2.37 (m, 2H), 2.05-1.99 (m, 2H), 0.92 (t, J = 7.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.1, 132.6, 132.3, 128.4, 128.3, 125.7, 36.0, 29.0, 20.5, 14.2. The spectroscopic data are in agreement with that previously reported.[64]

3) Ring-closure experiment.

To a sealable tube was added zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL), *N*-allyl-*N*-(2-bromoethyl)-4-methylbenzenesulfonamide **1y** (159.1 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) under argon. Then the sealing cap was securely fitted and it was stirred at 100 °C in an oil-bath for 12 h. After the mixture was cooled down to room temperature, the mixture was filtered through a short silica gel column and washed with dichloromethane. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1 to 2:1) to afforded *N*-allyl-*N*-ethyl-4-methylbenzenesulfonamide **2y** in 21% isolated yield (25.5 mg) as a colourless oil, 3-methyl-1-tosylpyrrolidine **2y-a** in 17% isolated yield (20.0 mg) and *N*-allyl-4-methylbenzenesulfonamide **2y-b** in 61% isolated yield (64.0 mg) as white solids.

***N*-Allyl-*N*-ethyl-4-methylbenzenesulfonamide (2y).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 5.72-5.62 (m, 1H), 5.19 (dd, J = 17.2 Hz, 1.6 Hz, 1H), 5.14 (dd, J = 10.0 Hz, 1.2 Hz, 1H), 3.81 (d, J = 6.0 Hz, 2H), 3.21 (q, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 143.0,

137.3, 133.3, 129.6, 127.0, 118.5, 49.8, 41.9, 21.4, 13.6. The spectroscopic data are in agreement with that previously reported.[65]

3-Methyl-1-tosylpyrrolidine (2y-a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 3.42 (dd, *J* = 9.6 Hz, 7.2 Hz, 1H), 3.37-3.32 (m, 1H), 3.25-3.19 (m, 1H), 2.75 (dd, *J* = 10.0 Hz, 7.6 Hz, 1H), 2.44 (s, 3H), 2.18-2.05 (m, 1H), 1.94-1.87 (m, 1H), 1.40-1.31 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.2, 133.9, 129.5, 127.5, 54.7, 47.6, 33.24, 33.18, 21.5, 17.6. The spectroscopic data are in agreement with that previously reported.[66]

***N*-Allyl-4-methylbenzenesulfonamide (2y-b).** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.76-5.66 (m, 1H), 5.18-5.14 (m, 1H), 5.09-5.06 (m, 2H), 3.59-3.55 (m, 2H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.4, 136.8, 132.9, 129.6, 127.0, 117.5, 45.6, 21.4. The spectroscopic data are in agreement with that previously reported.[67]

4) Reaction of tertiary alkyl bromide 6.

To a Schlenk tube were added zinc powder (65.4 mg, 1.0 mmol), CH_3CN (2.5 mL),1-(3-bromo-3-methylbutyl)-4-methoxybenzene **6** (128.6 mg, 0.5 mmol) and H_2O (27.0 μL, 1.5 mmol) under argon. Then the mixture was stirred at 25 °C in an oil-bath for 3.5 h. Then the mixture was filtered through a short silica gel column and washed with dichloromethane. The solvent was evaporated under the reduced pressure and the residue

was purified by column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate = 2:1) to afforded 1-isopentyl-4-methoxybenzene **7a** in 27% isolated yield (24.3 mg) as a colourless oil, 4-(4-methoxyphenyl)-2-methylbutan-2-ol **7a-a** in 24% isolated yield (23.6 mg) as a colourless oil, 1-(3-hydroperoxy-3-methylbutyl)-4-methoxybenzene **7a-b** in 14% isolated yield (15.1 mg) a yellow oil, and a mixture of 1-methoxy-4-(3-methylbut-3-en-1-yl)benzene **7a-c** and 1-methoxy-4-(3-methylbut-2-en-1-yl)benzene **7a-d** in 10% isolated yield (8.5 mg) (**7a-c**:**7a-d** = 2:1) as a colourless oil.

1-Isopentyl-4-methoxybenzene (7a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 3.78 (s, 3H), 2.55 (t, *J* = 8.0 Hz, 2H), 1.62-1.44 (m, 3H), 0.92 (d, *J* = 6.4 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.5, 135.1, 129.1, 113.6, 55.2, 41.1, 32.8, 27.6, 22.5. The spectroscopic data are in agreement with that previously reported.[68]

4-(4-Methoxyphenyl)-2-methylbutan-2-ol (7a-a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.78 (s, 3H), 2.67-2.62 (m, 2H), 1.78-1.74 (m, 2H), 1.28 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.6, 134.5, 129.1, 113.8, 70.9, 55.2, 45.9, 29.7, 29.2. The spectroscopic data are in agreement with that previously reported.[30e]

1-(3-Hydroperoxy-3-methylbutyl)-4-methoxybenzene (7a-b). ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.33 (bs, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 2.63-2.59 (m, 2H), 1.88-1.84 (m, 2H), 1.28 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.7, 134.5, 129.1, 113.8, 82.5, 55.2, 40.5, 29.3, 24.0. IR (neat): 3396, 2977, 2935, 1611, 1511, 1464, 1364, 1300, 1241, 1210, 1177, 1098, 1034, 820, 780, 736. HRMS (EI-TOF) calcd for $C_{12}H_{18}O_3$ $[M]^+$: 210.1250, found 210.1258.

1-Methoxy-4-(3-methylbut-3-en-1-yl)benzene (7a-c). ^1H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 6.83 Hz, 2H), 4.73 (s, 1H), 4.70 (s, 1H), 3.79 (s, 3H), 2.72-2.68 (m, 2H), 2.31-2.27 (m, 2H), 1.76 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.7, 145.5, 134.3, 129.2, 113.7, 110.1, 55.2, 39.8, 33.3, 22.6. The spectroscopic data are in agreement with that previously reported.[69]

1-Methoxy-4-(3-methylbut-2-en-1-yl)benzene (7a-d). ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 5.33-5.28 (m, 1H), 3.78 (s, 3H), 3.28 (d, J = 7.6 Hz, 2H), 1.74 (s, 3H), 1.71 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.7, 133.9, 132.2, 129.1, 123.6, 113.8, 55.3, 33.4, 25.7, 17.8. The spectroscopic data are in agreement with that previously reported.[70]

5) KIE experiment.

a) KIE experiment in the presence of equivalent H_2O and D_2O

In a nitrogen-filled glove box, zinc powder (26.2 mg, 0.4 mmol), 4-bromo-1-tosylpiperidine **1a** (63.6 mg, 0.2 mmol) and CH_3CN (1 mL) were added

sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. D_2O (5.4 μL, 0.3 mmol) and H_2O (5.4 μL, 0.3 mmol) were added to the vial and the reaction mixture was stirred at 80 °C (oil bath) for 10 h. After the starting material was completely consumed, the mixture was filtered through a pad of silica gel and washed with CH_2Cl_2. With 1,3,5-trimethoxybenzene (33.6 mg, 0.2 mmol) as internal standard, the NMR yield of **2a**-D was 97%. D-incorporation.: 20%. k_H/k_D = 80/20 = 4.0.

b) Parallel experiments.

The following two reactions were carried out at the same time. (1) In a nitrogen-filled glove box, zinc powder (26.2 mg, 0.4 mmol), 4-bromo-1-tosylpiperidine **1a** (63.6 mg, 0.2 mmol) and CH_3CN (1 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. D_2O (10.9 μL, 0.6 mmol) was added to the vial and the reaction mixture was stirred at 80 °C (oil bath) for 30 min.

(2) In a nitrogen-filled glove box, zinc powder (26.2 mg, 0.4 mmol), 4-bromo-1-tosylpiperidine **1a** (63.6 mg, 0.2 mmol) and CH_3CN (1 mL) were added sequentially to a 4 mL screw-cap vial. The vial cap was then securely fitted and taken outside the glove box. H_2O (10.8 μL, 0.6 mmol) was added to the vial and the reaction mixture was stirred at 80 °C (oil bath) for 30 min.

The two reaction mixtures were filtered through a pad of silica gel sequentially, washed with CH_2Cl_2. The combined reaction mixture was used for ^1H NMR analysis. With 1,3,5-trimethoxybenzene (67.3 mg, 0.4 mmol) as an internal standard, 4-bromo-1-tosylpiperidine **1a** was obtained in 82% yield; the mixture of **2a**-H and **2a**-D

was obtained in 17% yield. The ratio of **2a**-H and **2a**-D was determined by ^{1}H NMR, and the KIE of k_H/k_D was found to be 3.2.

Reaction of 1a in the presence Zn/LiCl.

To a sealable tube was added zinc powder (65.4 mg, 1.0 mmol), LiCl (42.4 mg, 1 mmol), **1a** (159.1 mg, 0.5 mmol) and CH_3CN (2.5 mL) under argon. Then the sealing cap was securely fitted and it was stirred at 80 ^{o}C (oil bath) in an oil-bath for 6 h. After the mixture was cooled down to room temperature, the mixture was quenched by H_2O (90.1 μL, 5 mmol) and stirred for 10 min. The crude product was then filtered through a short silica gel column and washed with dichloromethane. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1 to 1:1) to afforded **2a**-H in 88% isolated yield (105.9 mg) as a white solid.

ASSOCIATED CONTENT

Supporting Information

NMR spectra. This material is available free of charge via the internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: yhliu@sioc.ac.cn.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We thank the National Key R&D Program of China (2016YFA0202900), the Strategic Priority Research Program of the Chinese Academy of Sciences (XDB20000000), Science and Technology Commission of Shanghai Municipality (18XD1405000) and Shanghai Institute of Organic Chemistry (sioczz201807) for financial support.

REFERENCES

(1) (a) Harbeson, S. L.; Tung, R. D. Deuterium in Drug Discovery and Development. *Ann. Rep. Med. Chem.* **2011**, *46*, 403-417. (b) Kushner, D. J.; Baker, A.; Dunstall, T. G. Can. Pharmacological uses and perspectives of heavy water and deuterated compounds. *J. Physiol. Pharm.* **1999**, *77*, 79-88. (c) Foster, A. B. Deuterium isotope effects on studies of drug metabolism. *Trends. Pharmacol. Sci.* **1984**, *5*, 524-527.

(2) (a) Schmidt, C. First deuterated drug approved. *Nat. Biotechnol.* **2017**, *35*, 493-494. (b) Mutlib, A. E.; Gerson, R. J.; Meunier, P. C.; Haley, P. J.; Chen, H.; Gan, L. S.; Davies, M. H.; Gemzik, B.; Christ, D. D.; Krahn, D. F.; Markwalder, J. A.; Seitz, S. P.; Robertson, R. T.; Miwa, G. T. The Species-Dependent Metabolism of Efavirenz Produces a Nephrotoxic Glutathione Conjugate in Rats. *Toxicol. Appl. Pharm.* **2000**, *169*, 102-113. (c)

Liu, J. F.; Harbeson, S. L.; Brummel, C. L.; Tung, R.; Silverman, R.; Doller, D. A Decade of Deuteration in Medicinal Chemistry. *Annu. Rep. Med. Chem.* **2017**, *50*, 519-542.

(3) (a) Lin, G. M.; Choi, S. H.; Ruszczycky, M. W.; Liu, H. W. Mechanistic Investigation of the Radical S-Adenosyl-L-methionine Enzyme DesII Using Fluorinated Analogues. *J. Am. Chem. Soc.* **2015**, *137*, 4964-4967. (b) Kondo, A.; Ishigure, T.; Koike, Y. Fabrication Process and Optical Properties of Perdeuterated Graded-Index Polymer Optical Fiber. *J. Lightwave Technol*. **2005**, *23*, 2443-2448.

(4) (a) Mcfarland, J. W.; Coleman, G. N. Reaction of *p*-Tolylsulfonylmethylmagnesium Bromide with Ethyl Cinnamate. *J. Org. Chem.* **1970**, *35*, 1194-1195. (b) Pocker, Y.; Exner, J. H. Deuterium Isotope Effects in the Decomposition of Organometals by Proton Donors. *J. Am. Chem. Soc.* **1968**, *90*, 6764-6773.

(5) Upshur, M. A.; Chase, H. M.; Strick, B. F.; Ebben, C. J.; Fu, L.; Wang, H.; Thomson, R. J.; Geiger, F. M. Vibrational Mode Assignment of alpha-Pinene by Isotope Editing: One Down, Seventy-One To Go. *J. Phys. Chem. A* **2016**, *120*, 2684-2690.

(6) Alonso, F.; Radivoy, G.; Yus, M. Dehalogenation of Organic Halides using the $NiCl_2 \cdot 2H_2O$-Li-DTBB (cat.) Combination. *Tetrahedron* **1999**, *55*, 4441-4444.

(7) Curran, D. P.; Ramamoorthy, P. S. 1,2-Asymmetric Induction in Radical Reactions. Deuteration and Allylation Reactions of β-oxy-α-Bromo Esters. *Tetrahedron* **1993**, *49*, 4841-4858.

(8) Spiegel, D. A.; Wiberg, K. B.; Schacherer, L. N.; Medeiros, M. R.; Wood, J. L. Deoxygenation of Alcohols Employing Water as the Hydrogen Atom Source. *J. Am. Chem. Soc.* **2005**, *127*, 12513-12515.

(9) Medeiros, M. R.; Schacherer, L. N.; Spiegel, D. A.; Wood, J. L. Expanding the Scope of Trialkylborane/Water-Mediated Radical Reactions. *Org. Lett.* **2007**, *9*, 4427-4429.

(10) Soulard, V.; Villa, G.; Vollmar, D. P.; Renaud, P. Radical Deuteration with D_2O: Catalysis and Mechanistic Insights. *J. Am. Chem. Soc.* **2018**, *140*, 155-158.

(11) Liu, C.; Chen, Z.; Su, C.; Zhao, X.; Gao, Q.; Ning, G. H.; Zhu, H.; Tang, W.; Leng, K.; Fu, W.; Tian, B.; Peng, X.; Li, J.; Xu, Q. H.; Zhou, W.; Loh, K. P. Controllable deuteration of halogenated compounds by photocatalytic D_2O splitting. *Nat. Commun.* **2018,** *9*, 80.

(12) For allene formation from iodoallylic bromides using In- or Zn in THF/H_2O, see: Lin, M. H.; Tsai, W. S.; Lin, L. Z.; Hung, S. F.; Chuang, T. H.; Su, Y. J. Methods for the preparation of allenes employing indium- and zinc-mediated dehalogenation reactions in aqueous solutions. *J. Org. Chem.* **2011,** *76*, 8518-8523.

(13) (a) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. Synthesis and reactivity toward acyl chlorides and enones of the new highly functionalized copper reagents RCu(CN)ZnI. *J. Org. Chem.* **1988,** *53*, 2390-2392. (b) Erdik, E. Use of activation methods for organozinc reagents. *Tetrahedron* **1987,** *43*, 2203-2212. (c) Yeh, M. C. P.; Knochel, P. 2-Cyanoethylzinc iodide: A new reagent with reactivity umpolung. *Tetrahedron Lett.* **1988,** *29*, 2395-2396.

(14) (a) Guijarro, A.; Rosenberg, D. M.; Rieke, R. D. The Reaction of Active Zinc with Organic Bromides. *J. Am. Chem. Soc.* **1999**, *121*, 4155-4167. (b) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. The Direct Formation of Functionalized Alkyl(aryl)zinc Halides by Oxidative Addition of Highly Reactive Zinc with Organic Halides and Their Reactions

with Acid Chlorides, α,β-Unsaturated Ketones, and Allylic, Aryl, and Vinyl Halides. *J. Org. Chem.* **1991**, *56*, 1445-1453.

(15) Jubert, C.; Knochel, P. Preparation of New Classes of Aliphatic, Allylic, and Benzylic Zinc and Copper Reagents by the Insertion of Zinc Dust into Organic Halides, Phosphates, and Sulfonates. *J. Org. Chem.* **1992**, *57*, 5425-5431.

(16) Huo, S. Highly Efficient, General Procedure for the Preparation of Alkylzinc Reagents from Unactivated Alkyl Bromides and Chlorides. *Org. Lett.* **2003**, *5*, 423-425.

(17) For Zn/LiCl-mediated formation of organozinc species, see: (a) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. Efficient synthesis of functionalized organozinc compounds by the direct insertion of zinc into organic iodides and bromides. *Angew. Chem. Int. Ed.* **2006**, *45*, 6040-6044. (b) Feng, C.; Cunningham, D. W.; Easter, Q. T.; Blum, S. A. Role of LiCl in Generating Soluble Organozinc Reagents. *J. Am. Chem. Soc.* **2016**, *138*, 11156-11159.

(18) (a) Wu, J.; Liu, Z.-J.; Chen, Q.-Y.; Liu, C., An optimized condition for practical and scalable hydrodeiodination of perfluoroalkyl iodides. *J. Fluorine Chem.* **2016**, *184*, 45-49. (b) Ziegler, F. E.; Kneisley, A.; Thottathil, J. K.; Wester, R. T., 3-Methyl-.gamma.-butyrolactones as templates for the synthesis of polypropionates: the basic strategy. *J. Am. Chem. Soc.* **1988,** *110*, 5434-5442.

(19) Hekmatshoar, R.; Sajadi, S.; Heravi, M. M., Reductive Dehalogenation of Arylhalides and Alkylhalides with Zinc in THF Saturated Aqueous Ammonium Chloride. *J. Chin. Chem. Soc-Taip.* **2008**, *55,* 616-618.

(20) Isley, N. A.; Hageman, M. S.; Lipshutz, B. H. Dehalogenation of Functionalized Alkyl Halides in Water at Room Temperature. *Green Chem.* **2015**, *17*, 893-897.

(21) For early reports of Zn-mediated dehalogenation of carbon tetrachloride in water, see: (a) Boronina, T.; Klabunde, K. J.; Sergeev, G. Destruction of Organohalides in Water Using Metal Particles: Carbon Tetrachloride/Water Reactions with Magnesium, Tin, and Zinc. *Environ. Sci. Technol.* **1995**, *29*, 1511-1517. (b) Boronina, T. N.; Lagadic, I.; Sergeev, G. B.; Klabunde, K. J. Activated and Nonactivated Forms of Zinc Powder: Reactivity toward Chlorocarbons in Water and AFM Studies of Surface Morphologies. *Environ. Sci. Technol.* **1998**, *32*, 2614-2622; For Zn-mediated dehalogenation of 1,1,1-trichloethane, 1,1-dibromoethane, ethyl iodide, $CHCl_3$ and CCl_4 by slowly adding D_2O in a period of several hours or after formation of an organic zinc reagent to the reaction mixture, see: (c) Leblanc, M. E.; Morse, A. T.; Leitch, L. C. Organic Deuterium Compounds: Xv. Synthesis of Some Deuterated Alkanes. *Can. J. Chem.* **1956**, *34*, 354-358. For a review of metal-mediated hydrodehalogenation of organic halides, see: (d) Alonso, F.; Beletskaya, I. P.; Yus, M. Metal-Mediated Reductive Hydrodehalogenation of Organic Halides. *Chem. Rev.* **2002**, *102*, 4009-4091.

(22) It was reported that reduction of alkyl sulfonate esters could occur with zinc and sodium iodide in the presence of D_2O, see: Turecek, F.; Veres, K.; Kocovsky, P.; Pouzar, V.; Fajkos, J., Deuterium and tritium labeling with the zinc-sodium iodide method. *J. Org. Chem.* **1983**, *48*, 2233-2237.

(23) Control experiment indicated that deuteration of *N*-phenyl ring of *N*,*N*-dimethylbenzenamine took place in the presence of 1.0 equiv $ZnBr_2$ and 3.0 equiv D_2O in CH_3CN at 80 °C.

(24) For a recent report on $B(C_6F_5)_3$-catalyzed deuteration of aniline derivatives, see: Li, W.; Wang, M.-M.; Hu, Y.; Werner, T. $B(C_6F_5)_3$-Catalyzed Regioselective Deuteration of Electron-Rich Aromatic and Heteroaromatic Compounds. *Org. Lett.* **2017**, *19*, 5768-5771.

(25) Hong, M.; Chen, E. Y. X. Completely recyclable biopolymers with linear and cyclic topologies via ring-opening polymerization of γ-butyrolactone. *Nat. Chem.* **2016**, *8*, 42-49.

(26) For a recent study on indium-mediated synthesis of benzylic hydroperoxides, see: Hou, Y.; Hu, J.; Xu, R.; Pan, S.; Zeng, X.; Zhong, G., Indium-Mediated Synthesis of Benzylic Hydroperoxides. *Org. Lett.* **2019,** *21*, 4428-4432.

(27) Cohen, T.; Gibney, H.; Ivanov, R.; Yeh, E. A.-H,; Marek, I.; Curran, D. P. Intramolecular Carbozincation of Unactivated Alkenes Occurs through a Zinc Radical Transfer Mechanism. *J. Am. Chem. Soc.* **2007**, *129*, 15405-15409.

(28) For a large kinetic isotope effect (KIE = 12.0±1.5 at 298K) observed in the hydrolysis of allylindium iodide, see: Koszinowski, K. Large Solvent Isotope Effect Associated with the Hydrolysis of Allylindium Iodide. *J. Org. Chem.* **2018**, *83*, 14314-14322.

(29) As suggested by a reviewer, the reaction of **1a** with Zn (2 equiv) and LiCl (2 equiv) in CH_3CN at 80 °C for 6 h in the absence of a proton source was carried out. After quenching the reaction by water, the desired product **2a-**H was formed in 88% yield.

(30) For **1a**, see: (a) Yang, C. T.; Zhang, Z. Q.; Liang, J.; Liu, J. H.; Lu, X. Y.; Chen, H.

H.; Liu, L. Copper-catalyzed cross-coupling of nonactivated secondary alkyl halides and tosylates with secondary alkyl Grignard reagents. *J. Am. Chem. Soc.* **2012**, *134*, 11124-11127. For **1g**, see: (b) (Sargent, B. T.; Alexanian, E. J. Palladium-Catalyzed Alkoxycarbonylation of Unactivated Secondary Alkyl Bromides at Low Pressure. *J. Am. Chem. Soc.* **2016**, *138*, 7520-7523. For **1m**, see: (c) Boonyarattanakalin, S.; Martin, S. E.; Sun, Q.; Peterson, B. R. A synthetic mimic of human Fc receptors: defined chemical modification of cell surfaces enables efficient endocytic uptake of human immunoglobulin-G. *J. Am. Chem. Soc.* **2006,** *128*, 11463-11470. For **1p**, see: (d) You, T.; Wang, Z.; Chen, J.; Xia, Y. Transfer Hydro-dehalogenation of Organic Halides Catalyzed by Ruthenium(II) Complex. *J. Org. Chem.* **2017,** *82*, 1340-1346. For **1u**, see: (e) Atack, T. C.; Lecker, R. M.; Cook, S. P. Iron-Catalyzed Borylation of Alkyl Electrophiles. J. Am. Chem. Soc. 2014, 136, 9521-9523. For **1v**, see: Ref. 10. For **3e**, see: (f) Pluempanupat, W.; Chavasiri, W. An efficient method for chlorination of alcohols using PPh_3/Cl_3CCONH_2. *Tetrahedron Lett.* **2006,** *47*, 6821-6823.

(31) Tang, Y.; Fan, Y.; Zhang, Y.; Li, X.; Xu, X. Metal-Free *tert*-Butyl Hydrogenperoxide (TBHP) Mediated Radical Alkylation of Enol Acetates with Alcohols: A New Route to *β*-Hydroxy Ketones. *Synlett* **2016,** *27*, 1860-1863.

(32) Ibragimov, A. G.; Khafizova, L. O.; Zagrebel'naya, I. V.; Parfenova, L. V.; Sultanov, R. M.; Khalilov, L. M.; Dzhemilev, U. M. A new route of the reaction of $EtAlCl_2$ with α-olefins catalyzed by Ti complexes. *Russ. Chem. Bull.* **2001,** *50*, 292-296.

(33) Shavnya, A.; Hesp, K. D.; Mascitti, V.; Smith, A. C. Palladium-Catalyzed Synthesis of (Hetero)Aryl Alkyl Sulfones from (Hetero)Aryl Boronic Acids, Unactivated

Alkyl Halides, and Potassium Metabisulfite. *Angew. Chem. Int. Ed.* **2015,** *54*, 13571-13575.

(34) Kalutharage, N.; Yi, C. S. Scope and Mechanistic Analysis for Chemoselective Hydrogenolysis of Carbonyl Compounds Catalyzed by a Cationic Ruthenium Hydride Complex with a Tunable Phenol Ligand. *J. Am. Chem. Soc.* **2015,** *137*, 11105-11114.

(35) Conrad, J. C.; Kong, J.; Laforteza, B. N.; MacMillan, D. W. C. Enantioselective α-arylation of aldehydes via organo-SOMO catalysis. An ortho-selective arylation reaction based on an open-shell pathway. *J. Am. Chem. Soc.* **2009**, *131*, 11640-11641.

(36) Povie, G.; Ford, L.; Pozzi, D.; Soulard, V.; Villa, G.; Renaud, P. Catechols as Sources of Hydrogen Atoms in Radical Deiodination and Related Reactions. *Angew. Chem. Int. Ed.* **2016,** *55*, 11221-11225.

(37) Fukuyama, T.; Fujita, Y.; Miyoshi, H.; Ryu, I.; Kao, S.-C.; Wu, Y.-K. Electron transfer-induced reduction of organic halides with amines. *Chem. Commun.* **2018,** *54*, 5582-5585.

(38) Thompson, S. J.; Thach, D. Q.; Dong, G. Cyclic Ether Synthesis via Palladium-Catalyzed Directed Dehydrogenative Annulation at Unactivated Terminal Positions. *J. Am. Chem. Soc.* **2015,** *137*, 11586-11589.

(39) Nakamura, Y.; Yoshikai, N.; Ilies, L.; Nakamura, E. Nickel-Catalyzed Monosubstitution of Polyfluoroarenes with Organozinc Reagents Using Alkoxydiphosphine Ligand. *Org. Lett.* **2012,** *14*, 3316-3319.

(40) Kawamoto, T.; Oritani, K.; Curran, D. P.; Kamimura, A. Thiol-Catalyzed Radical Decyanation of Aliphatic Nitriles with Sodium Borohydride. *Org. Lett.* **2018,** *20*,

2084-2087.

(41) Xia, Y.; Wang, J.; Dong, G. Suzuki-Miyaura Coupling of Simple Ketones via Activation of Unstrained Carbon-Carbon Bonds. *J. Am. Chem. Soc.* **2018,** *140*, 5347-5351.

(42) Katritzky, A. R.; Rachwal, S.; Wu, J. A versatile method for the *N*,*N*-dialkylation of aromatic amines via Grignard reactions on *N*,*N*-bis(benzotriazolylmethyl)arylamines. *Can. J. Chem.* **1990,** *68*, 456-463.

(43) Wang, L.; Hashidoko, Y.; Hashimoto, M. Cosolvent-Promoted O-Benzylation with Silver(I) Oxide: Synthesis of 1'-Benzylated Sucrose Derivatives, Mechanistic Studies, and Scope Investigation. *J. Org. Chem.* **2016,** *81*, 4464-4474.

(44) Yusubov, M. S.; Postnikov, P. S.; Yusubova, R. Y.; Yoshimura, A.; Jürjens, G.; Kirschning, A.; Zhdankin, V. V. 2-Iodoxybenzoic Acid Tosylates: the Alternative to Dess-Martin Periodinane Oxidizing Reagents. *Adv. Synth. Catal.* **2017,** *359*, 3207-3216.

(45) Bai, C.; Li, A.; Yao, X.; Liu, H.; Li, Y. Efficient and selective aerobic oxidation of alcohols catalysed by MOF-derived Co catalysts. *Green Chem.* **2016,** *18*, 1061-1069.

(46) Saisaha, P.; Buettner, L.; van der Meer, M.; Hage, R.; Feringa, B. L.; Browne, W. R.; de Boer, J. W. Selective Catalytic Oxidation of Alcohols, Aldehydes, Alkanes and Alkenes Employing Manganese Catalysts and Hydrogen Peroxide. *Adv. Synth. Catal.* **2013,** *355*, 2591-2603.

(47) Lu, B.; Zhu, F.; Sun, H.-M.; Shen, Q. Esterification of the Primary Benzylic C-H Bonds with Carboxylic Acids Catalyzed by Ionic Iron(III) Complexes Containing an Imidazolinium Cation. *Org. Lett.* **2017,** *19*, 1132-1135.

(48) Miller, S. A.; Bobbitt, J. M.; Leadbeater, N. E. Oxidation of terminal diols using an

oxoammonium salt: a systematic study. *Org. Biomol. Chem.* **2017,** *15*, 2817-2822.

(49) Maity, R.; Naskar, S.; Das, I. Copper(II)-Catalyzed Reactions of α-Keto Thioesters with Azides via C-C and C-S Bond Cleavages: Synthesis of *N*-Acylureas and Amides. *J. Org. Chem.* **2018,** *83*, 2114-2124.

(50) Qin, Y.; Zhang, L.; Lv, J.; Luo, S.; Cheng, J.-P. Bioinspired Organocatalytic Aerobic C-H Oxidation of Amines with an ortho-Quinone Catalyst. *Org. Lett.* **2015,** *17*, 1469-1472.

(51) Lamani, M.; Guralamata, R. S.; Prabhu, K. R. Guanidine catalyzed aerobic reduction: a selective aerobic hydrogenation of olefins using aqueous hydrazine. *Chem. Commun.* **2012,** *48*, 6583-6585.

(52) You, J.; Verkade, J. G. P(*i*-BuNCH$_2$CH$_2$)$_3$N: An Efficient Ligand for the Direct α-Arylation of Nitriles with Aryl Bromides. *J. Org. Chem.* **2003,** *68*, 8003-8007.

(53) Konishi, H.; Nagase, H.; Manabe, K. Concise synthesis of cyclic carbonyl compounds from haloarenes using phenyl formate as the carbonyl source. *Chem. Commun.* **2015,** *51*, 1854-1857.

(54) Haibach, M. C.; Stoltz, B. M.; Grubbs, R. H. Catalytic Reduction of Alkyl and Aryl Bromides Using Propan-2-ol. *Angew. Chem. Int. Ed.* **2017,** *56*, 15123-15126.

(55) Wang, Y.; Huang, Z.; Leng, X.; Zhu, H.; Liu, G.; Huang, Z. Transfer Hydrogenation of Alkenes Using Ethanol Catalyzed by a NCP Pincer Iridium Complex: Scope and Mechanism. *J. Am. Chem. Soc.* **2018,** *140*, 4417-4429.

(56) Xie, Y. Acylation of Csp^2-H bond with acyl sources derived from alkynes: Rh-Cu bimetallic catalyzed C≡C bond cleavage. *Chem. Commun.* **2016,** *52*, 12372-12375.

(57) Xi, X.; Chen, T.; Zhang, J.-S.; Han, L.-B. Efficient and selective hydrogenation of C-O bonds with a simple sodium formate catalyzed by nickel. *Chem. Commun.* **2018,** *54*, 1521-1524.

(58) Zhu, D.; Shi, L. Ni-Catalyzed cross-coupling of aryl thioethers with alkyl Grignard reagents *via* C-S bond cleavage. *Chem. Commun.* **2018,** *54*, 9313-9316.

(59) Jie, X.; Shang, Y.; Zhang, X.; Su, W. Cu-Catalyzed Sequential Dehydrogenation-Conjugate Addition for β-Functionalization of Saturated Ketones: Scope and Mechanism. *J. Am. Chem. Soc.* **2016,** *138*, 5623-5633.

(60) Paizs, C.; Toşa, M.; Majdik, C.; Moldovan, P.; Novák, L.; Kolonits, P.; Marcovici, A.; Irimie, F.-D.; Poppe, L. Optically active 1-(benzofuran-2-yl)ethanols and ethane-1,2-diols by enantiotopic selective bioreductions. *Tetrahedron: Asymmetry* **2003,** *14*, 1495-1501.

(61) Miao, C. X.; He, L. N.; Wang, J. L.; Wu, F. Self-neutralizing in situ acidic CO_2/H_2O system for aerobic oxidation of alcohols catalyzed by TEMPO functionalized imidazolium salt/$NaNO_2$. *J. Org. Chem.* **2010**, *75*, 257-260.

(62) Liu, J.-H.; Yang, C.-T.; Lu, X.-Y.; Zhang, Z.-Q.; Xu, L.; Cui, M.; Lu, X.; Xiao, B.; Fu, Y.; Liu, L. Copper-Catalyzed Reductive Cross-Coupling of Nonactivated Alkyl Tosylates and Mesylates with Alkyl and Aryl Bromides. *Chem. Eur. J.* **2014,** *20*, 15334-15338.

(63) Rasappan, R.; Aggarwal, V. K. Synthesis of hydroxyphthioceranic acid using a traceless lithiation-borylation-protodeboronation strategy. *Nat. Chem.* **2014,** *6*, 810-814.

(64) O'Neil, I. A.; Bhamra, I.; Gibbons, P. D. α-Lithio quinuclidine *N*-oxide (Li-QNO):

A new base for synthetic chemistry. *Chem. Commun.* **2006,** 4545-4547.

(65) Dong, X.; Sang, R.; Wang, Q.; Tang, X.-Y.; Shi, M. Copper-Catalyzed Trifluoromethylation and Cyclization of Aromatic-Sulfonyl-Group-Tethered Alkenes for the Construction of 1,2-Benzothiazinane Dioxide Type Compounds. *Chem. Eur. J.* **2013,** *19*, 16910-16915.

(66) Qin, Q.; Yu, S. Visible-Light-Promoted Remote C(sp^3)-H Amidation and Chlorination. *Org. Lett.* **2015,** *17*, 1894-1897.

(67) Inagaki, F.; Hira, S.; Mukai, C. Silver(I)-Catalyzed Deprenylation of Allylsulfonamide Derivatives. *Synlett* **2017,** *28*, 2143-2146.

(68) Bess, E. N.; DeLuca, R. J.; Tindall, D. J.; Oderinde, M. S.; Roizen, J. L.; Du Bois, J.; Sigman, M. S. Analyzing Site Selectivity in $Rh_2(esp)_2$-Catalyzed Intermolecular C-H Amination Reactions. *J. Am. Chem. Soc.* **2014,** *136*, 5783-5789.

(69) Onodera, G.; Yamamoto, E.; Tonegawa, S.; Iezumi, M.; Takeuchi, R. Rhodium-Catalyzed Allylation of Benzyl Acetates with Allylsilanes. *Adv. Synth. Catal.* **2011,** *353*, 2013-2021.

(70) Zhang, Z.; Xu, L.; Chen, Z.; Liu, Z.; Miao, M.; Song, J.; Ren, H. Nickel-Catalyzed Regioselective Reductive Cross-Coupling of Aryl Halides with Polysubstituted Allyl Halides in the Presence of Imidazolium Salts. *Synlett* **2015**, *26*, 2784-2788.