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Deuterodechlorination of Aryl/Heteroaryl Chlorides Catalyzed by a Palladium/Unsymmetrical NHC System

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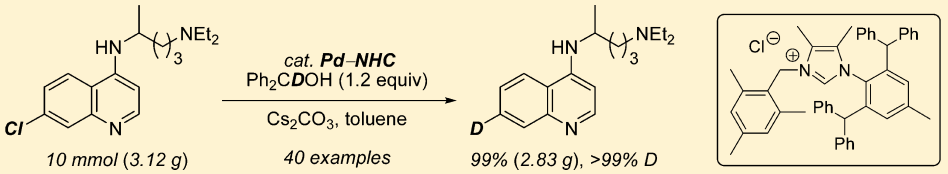
Supporting Information



ABSTRACT: The catalytic deuterodechlorination of aryl/heteroaryl chlorides was developed with a palladium/unsymmetrical NHC system, and the precisely controlled introduction of deuterium into a variety of aryl/heteroaryl compounds was achieved with a high level of efficiency, selectivity, and deuteration degree. This method was also successfully applied to the transformation of bioactive agents even in a gram-scale synthesis. The crystal structure analysis of Pd−NHC complexes led to the observation of Pd−arene interaction.

INTRODUCTION

Deuterated compounds are highly important for the metabolic analysis of bioactive agents as well as the mechanistic study of chemical and enzymatic reactions.[1,2] Moreover, the incorporation of deuterium into pharmaceutical molecules has recently attracted growing interest due to its beneficial effects to improve their therapeutic and metabolic profiles.[3] Consequently, vigorous efforts have been made to develop various catalytic deuteration reactions.[4] Particularly, the catalytic deuterium introduction into aryl/heteroaryl groups is quite significant owing to their ubiquity in pharmaceutical and bioactive agents.[5] As a typical deuteration method for this class of compounds, catalytic H/D exchange has been actively pursued.[6,7] In this process, multiple reactive sites in a molecule are basically deuterated depending on the respective reactivities. Meanwhile, deuterodehalogenation is known as a powerful transformation,[8] where catalytic methods are expected to enable a precise, efficient, and versatile deuterium introduction for fine chemical synthesis. However, catalytic Cl/D exchange has remained rather limited despite the advantages of aryl/heteroaryl chlorides, such as lower cost, wider diversity, and higher stability, because the low reactivity of chlorides demands much effort to achieve high efficiency especially in the presence of heterocycles.[9] The deuterogenative dechlorination required a deuterated solvent and suffered from difficulty in control of chemoselectivity.[10] The Pd-catalyzed method with a solid D source resulted in only moderate D content under microwave irradiation,[11] while a liquid D source was necessary as a solvent even with the dual enhancement by a high Pd catalyst loading and microwave assistance.[12] Therefore, the catalytic Cl/D exchange for aryl/heteroaryl chlorides remains a quite challenging process in spite of its high significance in light of drug development. Herein, we report the catalytic deuterodechlorination of aryl/heteroaryl chlorides with a palladium/unsymmetrical NHC system.

RESULTS AND DISCUSSION

At the outset, the effects of ligands were examined in the catalytic deuterodechlorination of aryl chloride **2a** with D source **1a** (1.2 equiv) in the presence of a Pd catalyst (1 mol %) formed in situ (Table 1). The Pd-catalyzed Cl/D exchange with no ligand gave only traces of product (entry 1). In unsymmetrical NHC precursors (Scheme 1), which were developed as stable solids with a simple two-step procedure, methyl groups at the 4- and 5-position were found to be effective (entries 2−3). While the 2,6-diisopropylphenyl group gave small improvement, a larger benzyl unit had no better influence (entries 4−5). Imidazolium chloride **L5** with the steric effect derived from benzhydryl groups led to a 92% yield and >99% D (entry 6), but a lower reaction temperature of 70 °C decreased the yield to 16%. Investigation of symmetrical NHC ligands[13] (Figure 1) was conducted only to provide low yields (entries 7−10), and the bulky aryl groups with benzhydryl units in IPr*·HCl[14] as well as methyl groups at the 4- and 5-position in ^{Me}IMes·HCl were ineffective, giving mildly reduced D content in the case of IPr*·HCl (entries 9−10). Subsequently, phosphines were also evaluated (entries 11−16). The Pd-catalyzed deuteration with Ph_3P afforded only a trace amount of desired product **3a** (entry 11). On the other hand, higher electron-donating ability and steric hindrance influenced the D content in a positive way, although chemical yields remained at a low level (entries 12−14). Therefore, bulky and electron-rich phosphines[15] were examined (entries 15−16).

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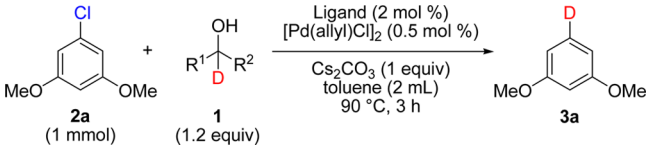
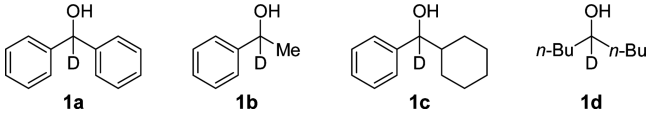
Table 1. Effect of Ligands[a]

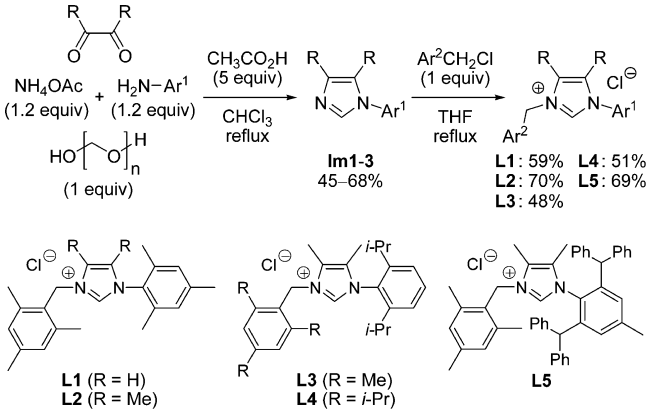


entry	ligand	1	yield (%)	D content (%)
1	none	**1a**	trace	ND
2	**L1**	**1a**	33	>99
3	**L2**	**1a**	45	>99
4	**L3**	**1a**	50	>99
5	**L4**	**1a**	43	>99
6	**L5**	**1a**	92	>99
7	IMes·HCl	**1a**	31	>99
8	SIMes·HCl	**1a**	23	99
9	^{Me}IMes·HCl	**1a**	30	99
10	IPr*·HCl	**1a**	29	93
11	Ph_3P	**1a**	trace	ND
12	$(4\text{-FPh})_3P$	**1a**	7	30
13	$(4\text{-MeOPh})_3P$	**1a**	10	41
14	$(2\text{-MePh})_3P$	**1a**	11	62
15	$t\text{-Bu}_3P\cdot HBF_4$	**1a**	26	98
16	SPhos	**1a**	28	98
17	**L5**	**1b**	85	99
18	**L5**	**1c**	43	99
19	**L5**	**1d**	26	>99

[a]Reaction conditions: **2a** (1 mmol), **1** (1.2 mmol), ligand (2 mol %), Pd (1 mol %), Cs_2CO_3 (1 mmol), toluene (2 mL), 90 °C, 3 h. D content was determined by ^{1}H NMR.



Scheme 1. Synthesis of Unsymmetrical NHC Ligand Precursors



The use of $t\text{-Bu}_3P\cdot HBF_4$ gave a low yield in spite of a high deuteration degree. SPhos[16] was also applied, but only a slight improvement was observed. Then, the investigation of α-deuterioalcohols in this reaction system[17] revealed that α-alkylated D sources **1b–d** showed a decrease in yield compared with reagent **1a** (entries 6 and 17–19). D source **1a** was readily prepared as a stable solid from benzophenone with lithium aluminum deuteride, while deuterated reagents **1b–d** were obtained as liquid-state compounds. Meanwhile, a deuterioformate salt such as DCO_2Na was not effective in affording

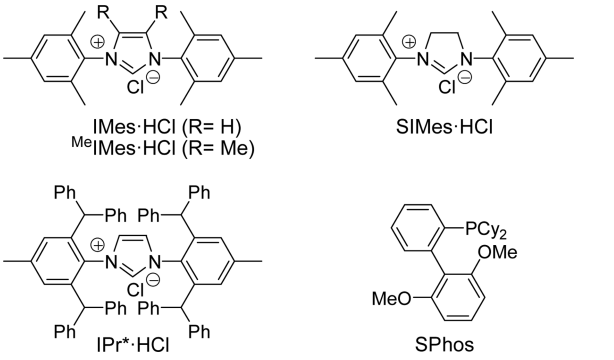
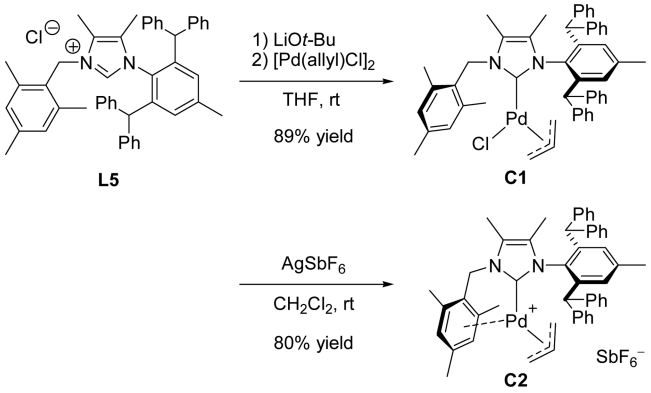


Figure 1. Symmetrical NHC precursors and SPhos.

the desired product. A screening of palladium sources, bases, and solvents was also conducted, and an allylpalladium(II) chloride dimer, cesium carbonate, and toluene proved to be most suitable (Table S1 in the Supporting Information).

To acquire more information on the catalyst system, 1:1 molar ratio complexes of Pd(II)/**L5** were prepared (Scheme 2).

Scheme 2. Synthesis of Pd–NHC Complexes



After **L5** was treated with lithium *tert*-butoxide, $[Pd(allyl)Cl]_2$ was added to the resulting reaction mixture to give neutral complex **C1** in 89% yield. In addition, cationic complex **C2** was obtained in 80% yield by the conversion of complex **C1** with $AgSbF_6$. The chemical structures of both **C1** and **C2** were determined by X-ray crystallography. In particular, the Pd–arene interaction was observed in complex **C2** (Figure 2), which was known in phosphine-based metal catalysts as a possible factor for the improvement of catalyst stability, activity, and lifetime,[15a] and the Pd center was found in the concave space formed by the aryl rings. In the X-ray crystal structure, the Pd(II)–C(10) distance was 2.376 Å. This value was marginally larger than that of a reported Pd(II)–arene distance,[15a] which could relate to the observation of slightly broad methyl signals in the ^{1}H NMR spectrum of **C2**.

While the catalysts formed in situ from Pd(II) and **L5** in 1:1 and 1:2 molar ratios, respectively, led to 76% and 94% yields with >99% D (entries 1–2 in Table 2), the chemical yields obtained with complexes **C1** and **C2** were well accorded with the result of entry 1 (entries 3 and 5) and the catalytic Cl/D exchange with the catalysts formed in situ from **C** and **L5** gave the same yields as entry 2 (entries 4 and 6). These results suggested that one NHC derived from **L5** in a complex catalyst would be required for the core formation to achieve high

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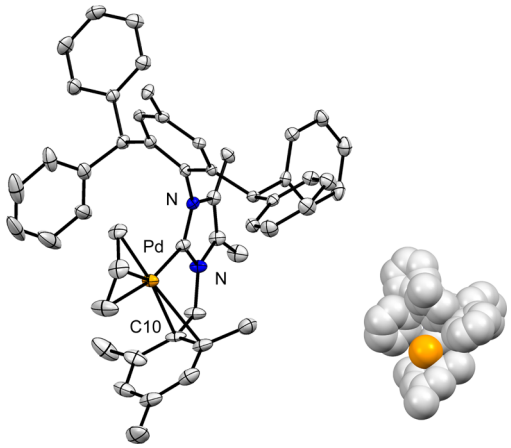
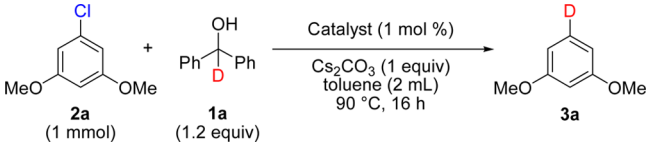


Figure 2. Crystal structure of **C2**. In the ellipsoid presentation (50% probability), H atoms and SbF_6^- were omitted for clarity. In the spacefilling presentation, an allyl anion was also omitted for clarity.

Table 2. Catalytic Deuterodechlorination with C1 and C2



entry	catalyst	Pd/**L5**	yield (%)	D content (%)
1[a,b]	Pd(II) + **L5**	1/1	76	>99
2[a,c]	Pd(II) + **L5**	1/2	94	>99
3	**C1**	1/1	75	>99
4[a,d]	**C1** + **L5**	1/2	94	>99
5	**C2**	1/1	76	>99
6[a,d]	**C2** + **L5**	1/2	94	>99

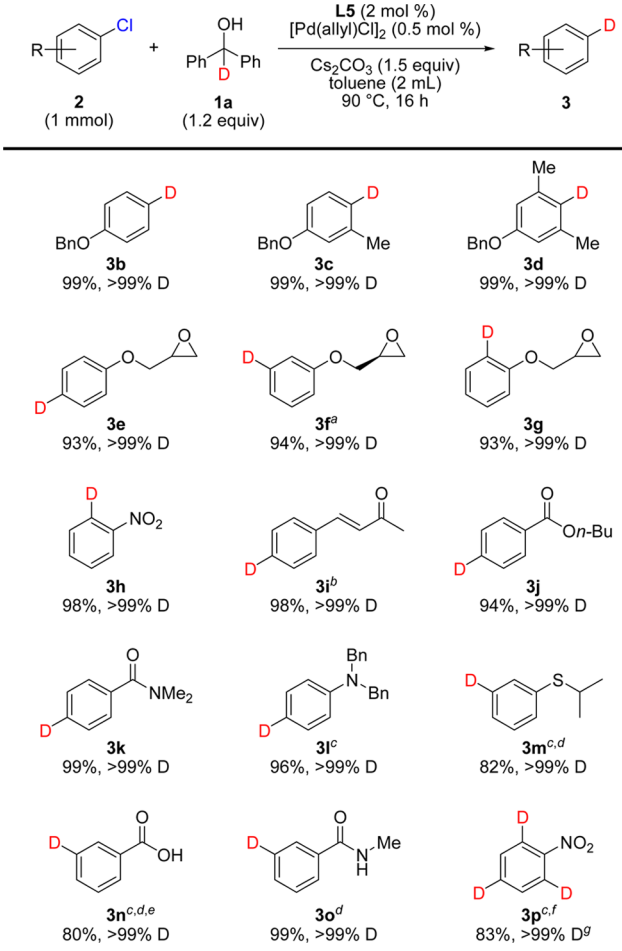
[a]The catalyst was formed in situ. [b]$[Pd(allyl)Cl]_2$ (0.5 mol %), **L5** (1 mol %). [c]$[Pd(allyl)Cl]_2$ (0.5 mol %), **L5** (2 mol %). [d]**C** (1 mol %), **L5** (1 mol %).

catalytic performance whereas the second **L5** for a Pd atom might be significant to improve the stability of precatalysts.

Investigation of aryl chlorides in the Pd-catalyzed deuterodechlorination was conducted on the basis of optimized conditions (Scheme 3). The sterically hindered as well as electron-rich substrates gave the desired products efficiently with no reductive deprotection of a benzyl group (**3b–d**). The epoxy moiety was well tolerated with high yields in spite of the concern about nucleophilic or reductive ring opening, and no racemization in a chiral epoxide was observed (**3e–g**). The electron-poor aryl chlorides with a reducible nitro or enone group also led to no side reaction (**3h–i**), and IMes·HCl and IPr*·HCl did not show adequate effects (**3i**). Both ester and amide groups proved to be suitable without problems such as transesterification (**3j–k**). This catalytic system sufficiently tolerated thioether as well as amino moieties to give high yields (**3l–m**). In the presence of a free OH or NH group, the deuteration reactions smoothly proceeded with no decrease in D content (**3n–o**). Additionally, the triple introduction of deuterium was successfully achieved (**3p**). In these examinations, quantitative D-efficiencies were observed in addition to high selectivity and functional group tolerance.

The influence of varying heteroaryl chlorides in the catalytic deuterodechlorination was investigated (Scheme 4). In a series of chlorinated pyridine and quinoline substrates, chlorine atoms

Scheme 3. Scope of Aryl Chlorides



[a]**3f** (91% ee) was obtained from **2f** (91% ee). [b]IMes·HCl, SIMes·HCl, and SPhos gave 0% yield, while IPr*·HCl led to 33% (91% D). [c]The catalyst (3 mol %). [d]100 °C. [e]Cs_2CO_3 (3 equiv). [f]**1a** (3.6 equiv), Cs_2CO_3 (4.5 equiv). [g]All the reactive sites gave >99% D.

were efficiently replaced by deuterium (**5a–f**). Electron-rich heteroaryl chlorides such as indole, benzofuran, and thiophene, as well as benzothiophene derivatives, were also found to be good reaction partners (**5g–k**). Moreover, hereroaryl chlorides bearing a few heteroatoms such as nitrogen, oxygen, and sulfur were explored. Pyrimidine, cinnoline, and benzothiazole cores were deuterated with adequate efficiency (**5l–n**). This deuteration method was successfully applied to the 6-chloro-7-azaindole derivative, as well as 6-chloroimidazopyridine (**5o–p**). The heteroaryl chloride containing oxazolopyridine moiety reacted sufficiently, leading to a 74% yield (**5q**). The double deuterated quinoline was also effectively prepared in one step (**5r**). All the various deuterated heteroaryls were obtained in quantitative D-incorporations.

To evaluate the synthetic utility[18] of this catalytic process, bioactive molecules bearing a variety of functional groups were examined as substrates (Scheme 5). In the incorporation of deuterium into oxygen-function compounds (**7a–b**), excellent chemical yields and quantitative D contents were observed, while the highly functionalized spiro molecule gave a 95% yield and 97% D (**7c**). Besides, bioactive agents with a nitrogen-containing heterocycle also led to high levels of chemical yield and deuteration degree even in the presence of a piperidine,

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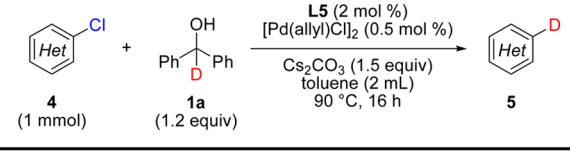
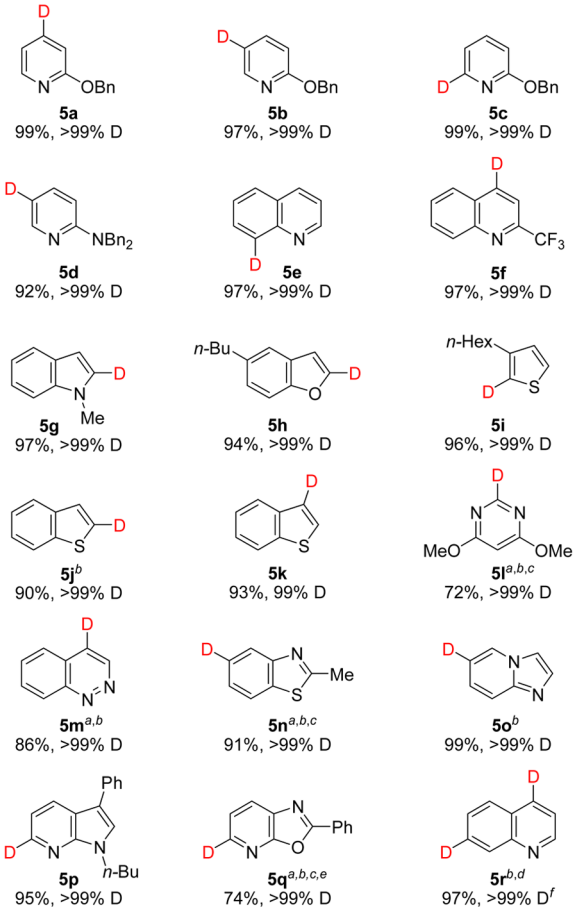
Scheme 4. Scope of Heteroaryl Chlorides





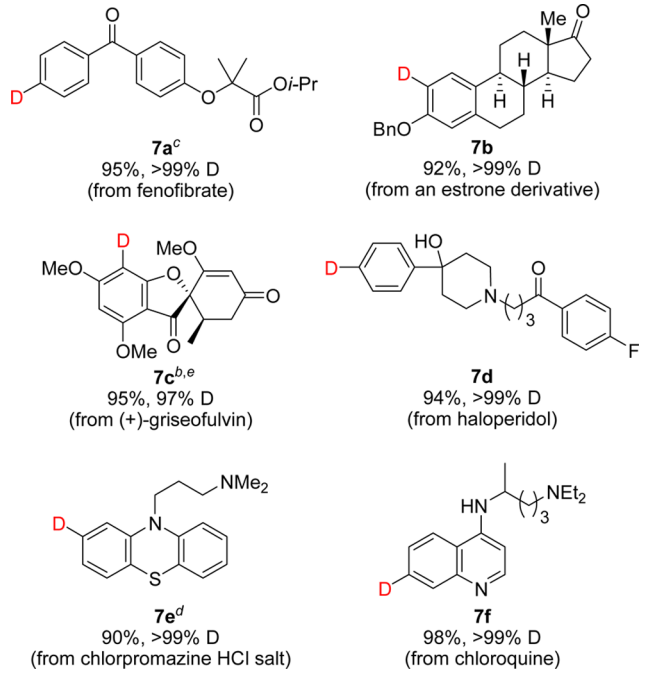
[a]The catalyst (3 mol %). [b]100 °C. [c]Cs_2CO_3 (2 equiv). [d]**1a** (2.4 equiv), Cs_2CO_3 (3 equiv). [e]32 h. [f]Both reactive sites gave >99% D.

phenothiazine, or quinoline core with additional groups such as hydroxy and amino moieties (**7d–f**).

Furthermore, gram-scale catalytic deuterodechlorination of chloroquine (**6f**) was conducted, and the desired product was obtained in 99% yield and >99% D (Scheme 6), in which the practical isolation by only back extraction was applicable in addition to the regular method by column chromatography. The quantitatively recovered benzophenone was readily converted into α-deuteriobenzhydrol (**1a**), which was applied to another deuterodechlorination without problems.

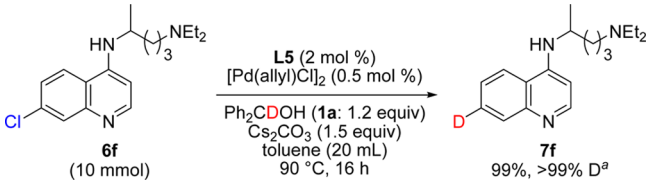
A tentative reaction mechanism for this palladium-catalyzed deuterodechlorination of aryl/heteroaryl chlorides is presented in Scheme 7. After the formation of an NHC-ligated Pd complex in the presence of a base, an aryl chloride is oxidatively added to a Pd(0) complex to give an aryl-palladium intermediate. Subsequently, base-promoted displacement of a chloride anion generates an α-deuterioalkoxy-palladium species, which undergoes β-deuterium elimination leading to an aryl–palladium–deuteride complex. Finally, reductive elimination affords a deuterated product and regenerates a Pd(0) catalyst. A similar mechanism was recently proposed in the report of a deuteration method for aryl bromides.[9c]

Scheme 5. Catalytic Deuterodechlorination of Bioactive Compounds and Their Derivatives[a]



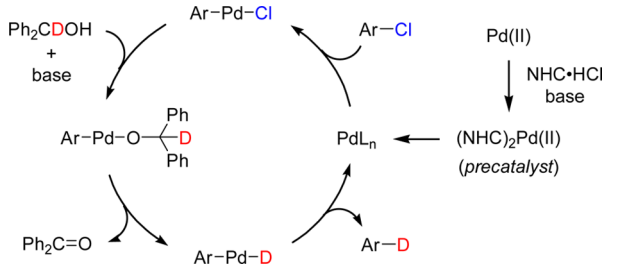
[a]Reaction conditions: substrate **6** (1 mmol), **1a** (1.2 mmol), **L5** (2 mol %), $[Pd(allyl)Cl]_2$ (0.5 mol %), Cs_2CO_3 (1.5 mmol), toluene (2 mL), 90 °C, 16 h. [b]The catalyst (3 mol %). [c]100 °C. [d]Cs_2CO_3 (2.5 equiv). [e]**1a** (1.5 equiv).

Scheme 6. Gram-Scale Catalytic Deuterodechlorination of Chloroquine



[a]The resulting benzophenone was recovered in 99% (9.9 mmol).

Scheme 7. Plausible Reaction Mechanism



CONCLUSION

In summary, the effective catalytic deuterodechlorination for aryl/heteroaryl chlorides was developed with the palladium/unsymmetrical NHC system, which required only a small excess of a deuterated chemical as a D source. NHC precursor **L5** and D source **1a** were easily prepared as stable solids.

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Investigation of the Pd−NHC complexes suggested that the Pd−arene interaction may play a key role in the catalyst performance. This process allowed for a high level of efficiency, selectivity, generality, and deuteration degree. The catalytic Cl/D exchange of bioactive molecules was also successfully achieved even in a gram-scale synthesis. We believe that this method will serve as a useful transformation in research areas requiring precisely controlled synthesis such as drug development.

EXPERIMENTAL SECTION

General. All melting points are not corrected. IR spectra were expressed in cm^{-1}. ^1H and ^{13}C NMR spectra were taken at 500 and 100 MHz, respectively. Chemical shift values are expressed in ppm relative to internal or external TMS. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. A double-focusing magnetic sector mass spectrometer was used for low- and high-resolution EI-MS and FAB-MS. The products were isolated by silica gel column chromatography. The degree of deuterium incorporation was determined by ^1H NMR (500 MHz). All reactions were performed under an argon atmosphere unless otherwise specified. Toluene was distilled from sodium benzophenone ketyl under argon. Aryl chlorides **2b−g**, **2j**, **2l−m**, **2o**, **4c−d**, **4h**, **4k**, and **6b** were synthesized as new compounds. **4a**,[19a] **4b**,[19b] **4g**,[19c] **4j**,[19c] **4m**,[19d] **4o**,[19e] **4p**,[19f] **4q**,[19g] ^{Me}IMes·HC,[20a] IPr*·HCl,[20b] and 2,6-bis(diphenylmethyl)-4-methylaniline[20b] for **Im3** were prepared as previously reported. Chloroquine **6f** was obtained from purchased chloroquine diphosphate salt by treatment with aqueous 10% NaOH solution. All other chemicals were used as received.

General Synthetic Procedure of 1-Arylimidazoles. This modified procedure for synthesis of 1-arylimidazoles was optimized on the basis of Orru's method.[21] Exceptionally, 1-(2,4,6-trimethylphenyl)-1*H*-imidazole was prepared according to Waymouth's report.[22] To a aniline derivative (12 mmol) in dry $CHCl_3$ (20 mL), diacetyl (861 mg, 10 mmol), acetic acid (3.0 g, 50 mmol), NH_4OAc (925 mg, 12 mmol), paraformaldehyde (480 mg, 10 mmol), and H_2O (0.5 mL) were added and the mixture was refluxed for 48 h. After removal of the solvent, the dark residue was dissolved in Et_2O and basified to pH 14 in an ice bath with aqueous 40% KOH solution. The resulting mixture was extracted with Et_2O, and the combined organic layers were washed with H_2O and dried over Na_2SO_4. Concentration and purification through silica gel column chromatography gave a 1-arylimidazole.

1-Mesityl-4,5-dimethyl-1*H*-imidazole (Im1). Silica gel chromatography (hexane/AcOEt = 3/1) gave 1.46 g of the product (6.8 mmol, 68% yield) as pale brown solids of mp 130−131 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.84 (s, 3H), 1.93 (s, 6H), 2.24 (s, 3H), 2.34 (s, 3H), 6.97 (s, 2H), 7.25 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.0 (CH_3), 12.8 (CH_3), 17.2 (CH_3), 20.9 (CH_3), 122.5 (C), 128.9 (CH), 132.4 (C), 133.8 (C), 134.4 (CH), 136.0 (C), 138.6 (C). IR (ATR): 770, 1490 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{14}H_{18}N_2$: 214.1470; found: 214.1461.

1-(2,6-Diisopropylphenyl)-4,5-dimethyl-1*H*-imidazole (Im2). Silica gel chromatography (hexane/AcOEt = 1/2) gave 1.59 g of the product (6.2 mmol, 62% yield) as a brown oil. ^1H NMR (500 MHz, $CDCl_3$): δ 1.09 (d, J = 7.1 Hz, 6H), 1.14 (d, J = 7.1 Hz, 6H), 1.85 (s, 3H), 2.26 (s, 3H), 2.32−2.40 (m, 2H), 7.24 (s, 1H), 7.27 (d, J = 7.8 Hz, 2H), 7.42 (t, J = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.1 (CH_3), 12.6 (CH_3), 22.8 (CH_3), 24.8 (CH_3), 27.6 (CH), 123.3 (C), 123.5 (CH), 129.5 (CH), 131.5 (C), 133.4 (C), 135.3 (CH), 146.7 (C). IR (ATR): 770, 1490 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{17}H_{24}N_2$: 256.1939; found: 256.1933.

1-(2,6-Dibenzhydryl-4-methylphenyl)-4,5-dimethyl-1*H*-imidazole (Im3). This 1-arylimidazole was prepared with 2.5 mmol of diacetyl. Silica gel chromatography (hexane/AcOEt = 2/1) gave 585 mg of the product (1.13 mmol, 45% yield) as pale yellow solids of mp 87−88 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.30 (s, 3H), 2.15 (s, 3H), 2.26 (s, 3H), 4.99 (s, 2H), 6.61 (s, 1H), 6.86 (s, 2H), 6.89 (d, J = 7.2 Hz 4H), 6.95 (d, J = 7.2 Hz, 4H), 7.15−7.25 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.6 (CH_3), 12.8 (CH_3), 21.7 (CH_3), 51.3 (CH), 123.3 (C), 126.5 (CH), 128.3 (CH), 128.4 (CH), 129.2 (CH), 129.5 (CH), 129.6 (CH), 132.3 (C), 133.8 (C), 135.6 (CH), 138.8 (C), 142.4 (C), 142.78 (C), 142.85 (C). IR (ATR): 700, 1490 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{38}H_{34}N_2$: 518.2722; found: 518.2719.

General Synthetic Procedure of Imidazolium Chlorides. To a 1-arylimidazole (2.0 mmol) in dry THF (2 mL) was added an arylmethyl chloride (2.0 mmol). The mixture was refluxed for 15 h and then evaporated until THF was moderately reduced without complete drying. The resulting solids were filtered and washed with THF giving a desired imidazolium chloride.

3-Mesityl-1-(2,4,6-trimethylbenzyl)imidazolium Chloride (L1). The desired product was obtained in 59% yield (414 mg, 1.17 mmol) as white solids of mp 286−287 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 2.08 (s, 6H), 2.30 (s, 3H), 2.349 (s, 3H), 2.354 (s, 6H), 6.05 (s, 2H), 6.94 (s, 2H), 7.01 (s, 2H), 7.03 (t, J = 1.8 Hz, 1H), 7.11 (t, J = 1.8 Hz, 1H), 11.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.2 (CH_3), 19.5 (CH_3), 20.70 (CH_3), 20.72 (CH_3), 48.0 (CH_2), 121.3 (CH), 123.6 (CH), 125.7 (C), 129.6 (CH), 129.7 (CH), 130.6 (C), 133.9 (C), 137.9 (C), 138.1 (CH), 139.5 (C), 141.0 (C). IR (ATR): 760, 1190, 1540 cm^{-1}. HRMS (FAB) *m/z*: $[M-Cl]^+$ calcd for $C_{22}H_{27}N_2$: 319.2174; found: 319.2157.

3-Mesityl-4,5-dimethyl-1-(2,4,6-trimethylbenzyl)-imidazolium Chloride (L2). The desired product was obtained in 70% yield (535 mg, 1.40 mmol) as white solids of mp 285−286 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.91 (s, 3H), 2.01 (s, 6H), 2.13 (s, 3H), 2.28 (s, 3H), 2.34 (s, 6H), 2.35 (s, 3H), 5.99 (s, 2H), 6.89 (s, 2H), 7.02 (s, 2H), 9.92 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.8 (CH_3), 8.8 (CH_3), 17.1 (CH_3), 19.6 (CH_3), 20.5 (CH_3), 20.6 (CH_3), 47.1 (CH_2), 125.4 (C), 127.5 (C), 128.1 (C), 128.6 (C), 129.6 (CH), 129.7 (CH), 134.3 (C), 135.1 (CH), 137.3 (C), 138.9 (C), 141.0 (C). IR (ATR): 850, 1550 cm^{-1}. HRMS (FAB) *m/z*: $[M-Cl]^+$ calcd for $C_{24}H_{31}N_2$: 347.2487; found: 347.2488.

3-(2,6-Diisopropylphenyl)-4,5-dimethyl-1-(2,4,6-trimethylbenzyl)imidazolium Chloride (L3). The desired product was obtained in 48% yield (403 mg, 0.95 mmol) as white solids of mp 267−268 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.17 (d, J = 6.9 Hz, 6H), 1.19 (d, J = 6.9 Hz, 6H), 1.92 (s, 3H), 2.21 (septet, J = 6.9 Hz, 2H), 2.23 (s, 3H), 2.27 (s, 3H), 2.34 (s, 6H), 6.04 (s, 2H), 6.89 (s, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 8.0 Hz, 1H), 9.71 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.2 (CH_3), 9.2 (CH_3), 19.6 (CH_3), 20.7 (CH_3), 22.7 (CH_3), 24.8 (CH_3), 28.4 (CH), 47.3 (CH_2), 124.7 (CH), 125.3 (C), 128.0 (C), 128.5 (C), 128.6 (C), 129.9 (CH), 131.8 (CH), 134.8 (CH), 137.7 (C), 139.4 (C), 145.5 (C). IR (ATR): 810, 1460 cm^{-1}. HRMS (FAB) *m/z*: $[M-Cl]^+$ calcd for $C_{27}H_{37}N_2$: 389.2957; found: 389.2955.

1-(2,4,6-Triisopropylbenzyl)-3-(2,6-diisopropylphenyl)-4,5-dimethylimidazolium Chloride (L4). The desired product was obtained in 51% yield (515 mg, 1.01 mmol) as white solids of mp 208−209 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.07 (d, J = 6.8 Hz, 6H), 1.18 (d, J = 6.8 Hz, 6H), 1.22−1.25 (m, 18H), 2.02 (s, 3H), 2.24 (septet, J = 6.8 Hz, 2H), 2.69 (s, 3H), 2.88 (septet, J = 6.8 Hz, 1H), 3.16 (septet, J = 6.8 Hz, 2H), 5.79 (s, 2H), 7.08 (s, 2H), 7.29 (d, J = 7.8 Hz, 2H), 7.51 (t, J = 7.8 Hz, 1H), 8.00 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.5 (CH_3), 9.8 (CH_3), 23.1 (CH_3), 23.5 (CH_3), 24.1 (CH_3), 24.7 (CH_3), 28.2 (CH), 29.6 (CH), 34.0 (CH), 45.0 (CH_2), 121.5 (C), 122.1 (CH), 124.8 (CH), 127.9 (C), 129.4 (C), 129.7 (C), 131.9 (CH), 132.1 (CH), 145.6 (C), 148.7 (C), 151.4 (C). IR (ATR): 760, 1540 cm^{-1}. HRMS (FAB) *m/z*: $[M-Cl]^+$ calcd for $C_{33}H_{49}N_2$: 473.3896; found: 473.3901.

3-(2,6-Dibenzhydryl-4-methylphenyl)-4,5-dimethyl-1-(2,4,6-trimethylbenzyl)imidazolium Chloride (L5). The desired product was obtained in 69% yield (941 mg, 1.37 mmol) as white solids of mp 214−215 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.26 (s, 3H), 2.15 (s, 6H), 2.23 (s, 6H), 2.28 (s, 3H), 4.99 (s, 2H), 5.66 (s, 2H), 6.80 (s, 2H), 6.83 (s, 2H), 6.92−6.95 (m, 8H), 7.20−7.28 (m, 12H), 8.63 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.6 (CH_3), 9.1 (CH_3), 19.8 (CH_3), 20.7 (CH_3), 21.5 (CH_3), 47.0 (CH_2), 51.4 (CH), 125.2 (C), 127.0 (CH), 127.1 (CH), 128.2 (C), 128.5 (CH), 128.6 (CH), 128.7

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(CH), 129.2 (CH), 129.7 (CH), 130.4 (CH), 134.7 (CH), 137.4 (C), 139.2 (C), 140.7 (C), 141.1 (C), 141.4 (C). IR (ATR): 700, 1490 cm^{-1}. HRMS (FAB) *m/z*: $[M-Cl]^+$ calcd for $C_{48}H_{47}N_2$: 651.3739; found: 651.3743. Anal. calcd for $C_{48}H_{47}N_2Cl$: C, 83.87; H, 6.89; N, 4.08. found C, 83.77; H, 7.04; N, 4.01.

Typical Synthetic Procedure of α-Deuterioalcohols. Benzophenone (546 mg, 3 mmol) in THF (5 mL) was added to the suspension of lithium aluminum deuteride (63 mg, 1.5 mmol) in THF (4.2 mL) at 0 °C. After the reaction mixture was stirred for 30 min at 0 °C, water was added. The resulting mixture was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography gave α-deuteriobenzhydrol (**1a**).

α-Deuteriobenzhydrol (1a). Silica gel chromatography (hexane/AcOEt = 5/1) gave 531 mg of the product (2.87 mmol, 96% yield) as white solids of mp 64−65 °C. >99% D (D content was judged with the peak at 5.80 ppm (a deuterated site) compared to the peak at 7.32−7.40 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 2.20 (s, 1H), 7.25−7.28 (m, 2H), 7.32−7.35 (m, 4H), 7.37−7.40 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 75.4 (t, J_{C-D} = 22.4 Hz, C), 126.5 (CH), 127.3 (CH), 128.3 (CH), 143.7 (C). IR (ATR): 730, 1040, 1190, 1490, 1600, 3260 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{13}H_{11}DO$: 185.0951; found: 185.0958.

α-Deuterio-α-phenylethanol (1b). This compound was prepared from acetophenone (4 mmol). Silica gel chromatography (hexane/AcOEt = 7/1) gave 468 mg of the product (3.80 mmol, 95% yield) as a colorless oil. >99% D (D content was judged with the peak at 4.90 ppm (a deuterated site) compared to the peak at 7.34−7.39 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 1.50 (s, 3H), 1.76 (s, 1H), 7.26−7.29 (m, 1H), 7.34−7.39 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 (CH_3), 69.6 (t, J_{C-D} = 21.5 Hz, C), 125.3 (CH), 127.3 (CH), 128.3 (CH), 145.8 (C). IR (ATR): 700, 750, 1130, 1450, 2970, 3330 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for C_8H_9DO: 123.0794; found: 123.0796.

α-Deuterio-α-cyclohexylbenzenemethanol (1c). This compound was prepared from cyclohexyl(phenyl)methanone (8 mmol). Silica gel chromatography (hexane/AcOEt = 8/1) gave 1.52 g of the product (7.94 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 4.37 ppm (a deuterated site) compared to the peak at 1.97−2.01 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 0.89−0.97 (m, 1H), 1.01−1.27 (m, 4H), 1.36−1.40 (m, 1H), 1.59−1.68 (m, 3H), 1.75−1.79 (m, 2H), 1.97−2.01 (m, 1H), 7.25−7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.8 (CH_2), 25.9 (CH_2), 26.2 (CH_2), 28.6 (CH_2), 29.0 (CH_2), 44.6. (CH), 78.6 (t, J_{C-D} = 21.5 Hz, C), 126.6 (CH), 127.2 (CH), 128.0 (CH), 143.6 (C). IR (ATR): 700, 760, 1450, 2850, 2920, 3370 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{13}H_{17}DO$: 191.1420; found: 191.1420.

5-Deuterio-5-nonanol (1d). This compound was prepared from nonan-5-one (8 mmol). Silica gel chromatography (hexane/AcOEt = 10/1) gave 1.15 g of the product (7.92 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 3.59 ppm (a deuterated site) compared to the peak at 0.91 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 0.91 (t, *J* = 7.1 Hz, 6H), 1.25 (s, 1H), 1.27−1.50 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7 (CH_3), 22.5 (CH_2), 27.6 (CH_2), 36.8 (CH_2), 71.0 (t, J_{C-D} = 21.5 Hz, C). IR (ATR): 2860, 2870, 2930, 2960, 2970, 3340 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_9H_{19}DO$: 145.1577; found: 145.1571.

Allylchloro{4,5-dimethyl-3-[2,6-bis(diphenylmethyl)-4-methylphenyl]-1-(2,4,6-trimethylbenzyl)imidazol-2-ylidene}-palladium(II) (C1). A reaction flask was charged with ligand precursor **L5** (289 mg, 0.42 mmol) and LiO*t*-Bu (39 mg, 0.49 mmol). After dry THF (28 mL) was added, the reaction mixture was stirred for 4 h at room temperature. Then, $[Pd(allyl)Cl]_2$ (77 mg, 0.21 mmol) was added. After the mixture was stirred for 3 h at room temperature, the resulting mixture was filtered through Celite. Concentration and purification through silica gel chromatography (hexane/AcOEt = 4/1) gave 311 mg of the product (0.37 mmol, 89% yield) as pale yellow solids of mp 205−206 °C, which were recrystallized from CH_2Cl_2/hexane. ^1H NMR (500 MHz, $CDCl_3$): δ −0.07 (s, 3H), 1.56−1.57 (m, 1H), 1.61 (s, 3H), 2.28 (s, 3H), 2.29 (s, 3H), 2.44 (s, 6H), 2.66 (d, *J* = 6.7 Hz, 1H), 3.06 (d, *J* = 13.5 Hz, 1H), 4.18 (dd, *J* = 1.5, 7.5 Hz, 1H), 4.75−4.83 (m, 1H), 5.75 (d, *J* = 15.7 Hz, 1H), 5.77 (s, 2H), 5.86 (d, *J* = 15.7 Hz, 1H), 6.85 (s, 2H), 6.96−7.25 (m, 22H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.21, 8.93, 20.8, 21.1, 21.7, 49.6, 50.0, 50.7, 50.9, 71.9, 114.4, 125.8, 126.2, 126.3, 128.03, 128.05, 128.08, 129.4, 129.56, 129.63, 129.7, 129.8, 129.9, 130.0, 130.7, 135.2, 137.3, 137.5, 138.0, 142.1, 142.3, 142.4, 142.5, 143.1, 143.4, 181.3. IR (ATR): 700, 1450, 1490 cm^{-1}. HRMS (FAB) *m/z*: $[M-Cl]^+$ calcd for $C_{51}H_{51}N_2{}^{106}Pd$: 797.3082; found: 797.3095. Anal. calcd for $C_{51}H_{51}ClN_2Pd$: C, 73.46; H, 6.16; N, 3.36. found C, 73.36; H, 5.83; N, 3.26.

Allyl{4,5-dimethyl-3-[2,6-bis(diphenylmethyl)-4-methylphenyl]-1-(2,4,6-trimethylbenzyl)imidazol-2-ylidene}-palladium(II) Hexafluoroantimonate (C2). Complex **C1** (50 mg, 0.06 mmol) in dry CH_2Cl_2 (16 mL) was treated with $AgSbF_6$ (21 mg, 0.06 mmol) for 1 h at room temperature. The resulting mixture was filtered through Celite. Concentration and purification through silica gel chromatography (hexane/AcOEt = 1/1.5) gave 50 mg of the product (0.048 mmol, 80% yield) as pale yellow solids of mp 147−148 °C, which were recrystallized from CH_2Cl_2/pentane. ^1H NMR (500 MHz, $CDCl_3$): δ 1.02 (s, 3H), 1.20 (d, *J* = 11.7 Hz, 1H), 1.77−1.78 (m, 1H), 2.32 (s, 3H), 2.34 (s, 3H), 2.32−2.34 (m, 1H), 2.41 (s, 3H), 2.51 (s, 3H), 2.69 (s, 3H), 2.90 (d, *J* = 13.7, Hz, 1H), 4.67−4.77 (m, 1H), 4.93−5.04 (m, 4H), 6.90 (t, *J* = 7.3 Hz, 4H), 6.97 (d, *J* = 7.8 Hz, 2H), 7.04 (s, 1H), 7.09−7.12 (m, 3H), 7.20−7.28 (m, 13H), 7.39 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.19, 9.10, 20.77, 20.84, 21.8, 46.4, 51.6, 51.7, 52.1, 90.2, 112.8, 118.1, 126.1, 126.9, 127.0, 127.16, 127.19, 128.49, 128.55, 128.6, 128.82, 128.83, 129.0, 129.1, 129.5, 129.6, 129.7, 140.0, 141.50, 141.53, 141.58, 141.61, 141.65, 141.70, 142.1, 174.2. IR (ATR): 700, 1450, 1490 cm^{-1}. HRMS (FAB) *m/z*: $[M-SbF_6]^+$ calcd for $C_{51}H_{51}N_2{}^{106}Pd$: 797.3082; found: 797.3090. Anal. calcd for $C_{51}H_{51}F_6N_2PdSb$: C, 59.23; H, 4.97; N, 2.71. found C, 59.36; H, 4.82; N, 2.74.

Typical Procedure for the Palladium-Catalyzed Deuterodechlorination of Aryl/Heteroaryl Chlorides. A reaction tube was charged with ligand precursor **L5** (13.7 mg, 0.02 mmol), $[Pd(allyl)Cl]_2$ (1.83 mg, 0.005 mmol), and Cs_2CO_3 (489 mg, 1.5 mmol). After toluene (2.0 mL) was added, the mixture was stirred for 15 min at 80 °C. Then, aryl chloride **2b** (219 mg, 1.0 mmol) and α-deuterioalcohol **1a** (222 mg, 1.2 mmol) were added at room temperature. The reaction mixture was stirred for 16 h at 90 °C and cooled to room temperature. Water was added, and then the resulting mixture was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$. Concentration and purification through silica gel column chromatography gave desired product **3b**.

1-Deuterio-3,5-dimethoxybenzene (3a). Silica gel chromatography (hexane/Et_2O = 100/1) gave 131 mg of the product (0.94 mmol, 94% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.19 ppm (a deuterated site) compared to the peak at 6.47 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 3.80 (s, 6H), 6.47 (t, *J* = 2.4 Hz, 1H), 6.51−6.52 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.2 (CH_3), 100.5 (CH), 106.1 (CH), 129.6 (t, J_{C-D} = 24.0 Hz, C), 160.9 (C). IR (ATR): 1200, 1430, 1600 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_8H_9DO_2$: 139.0744; found: 139.0756.

1-Benzyloxy-4-deuteriobenzene (3b). Silica gel chromatography (hexane/Et_2O = 100/1) gave 184 mg of the product (0.99 mmol, 99% yield) as white solids of mp 38−39 °C. >99% D (D content was judged with the peak at 6.97−7.00 ppm (a deuterated site) compared to the peak at 5.07 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 5.07 (s, 2H), 6.97−7.00 (m, 2H), 7.28−7.34 (m, 3H), 7.37−7.40 (m, 2H), 7.44 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.8 (CH_2), 114.8 (CH), 120.7 (t, J_{C-D} = 24.0 Hz, C), 127.5 (CH), 127.9 (CH), 128.6 (CH), 129.4 (CH), 137.1 (C), 158.9 (C). IR (ATR): 1010, 1240, 1590 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{13}H_{11}DO$: 185.0951; found: 185.0938.

1-Benzyloxy-4-deuterio-3-methylbenzene (3c). Silica gel chromatography (hexane/Et_2O = 100/1) gave 198 mg of the product (0.99 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.77−6.82 ppm (a deuterated site) compared to the peak at 2.33 ppm by ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$): δ 2.33 (s, 3H), 5.05 (s, 2H), 6.78 (dd, *J* = 2.5, 8.2 Hz, 1H), 6.82 (d, *J* =

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2.5 Hz, 1H), 7.17 (d, J = 8.2 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.43 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4 (CH_3), 69.8 (CH_2), 111.6 (CH), 115.7 (CH), 121.5 (t, $J_{C\text{-}D}$ = 24.0 Hz, C), 127.5 (CH), 127.9 (CH), 128.6 (CH), 129.1 (CH), 137.2 (C), 139.4 (C), 158.9 (C). IR (ATR): 730, 1030, 1240, 1600 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{14}H_{13}DO$: 199.1107; found: 199.1112.

1-Benzyloxy-4-deuterio-3,5-dimethylbenzene (3d). Silica gel chromatography (hexane/Et_2O = 100/1) gave 211 mg of the product (0.99 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.62 ppm (a deuterated site) compared to the peak at 7.30−7.44 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.29 (s, 6H), 5.03 (s, 2H), 6.62 (s, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.43 (d, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3 (CH_3), 69.7 (CH_2), 112.6 (CH), 122.4 (t, $J_{C\text{-}D}$ = 23.2 Hz, C), 127.5 (CH), 127.8 (CH), 128.5 (CH), 137.3 (C), 139.1 (C), 159.0 (C). IR (ATR): 850, 1060, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{15}H_{15}DO$: 213.1264; found: 213.1262.

2-[(4-Deuteriophenoxy)methyl]oxirane (3e). Silica gel chromatography (hexane/Et_2O = 10/1) gave 141 mg of the product (0.93 mmol, 93% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.96 ppm (a deuterated site) compared to the peak at 2.84 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.71 (dd, J = 2.7, 5.1 Hz, 1H), 2.84 (dd, J = 4.3, 5.1 Hz, 1H), 3.31−3.34 (m, 1H), 3.82 (dd, J = 6.5, 11.3 Hz, 1H), 4.31 (dd, J = 2.7, 11.3 Hz, 1H), 6.96 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 8.7 Hz, 2H). ^{2}H NMR (61 MHz, $CHCl_3$): δ 6.95 (brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.6 (CH_2), 50.1 (CH), 68.6 (CH_2), 114.6 (CH), 120.9 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 129.4 (CH), 158.5 (C). IR (ATR): 840, 1040, 1240, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_9DO_2$: 151.0744; found: 151.0730.

(*S*)-(+)-2-[(3-Deuteriophenoxy)methyl]oxirane (3f). Silica gel column chromatography (hexane/benzene = 1/1) gave 142 mg (0.94 mmol, 94% yield) of the product as a colorless oil. >99% D (D content was judged with the peak at 7.28−7.31 ppm (a deuterated site) compared to the peak at 4.31 ppm by ^{1}H NMR). $[\alpha]^{21}_D$ +11.8 (c 1.58, EtOH). 91% *ee* (HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, 0.8 mL/min, 220 nm, (*S*)-isomer 14.3 min and (*R*)-isomer 9.0 min). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.71 (dd, J = 2.7, 5.1 Hz, 1H), 2.84 (dd, J = 4.3, 5.1 Hz, 1H), 3.31−3.34 (m, 1H), 3.82 (dd, J = 6.5, 11.4 Hz, 1H), 4.31 (dd, J = 2.7, 11.4 Hz, 1H), 6.94−6.97 (m, 3H), 7.28−7.31 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.3 (CH_2), 49.9 (CH), 68.5 (CH_2), 114.4 (CH), 114.5 (CH), 121.0 (CH), 129.1 (t, $J_{C\text{-}D}$ = 24.0 Hz, C), 129.4 (CH), 158.4 (C). IR (ATR): 790, 840, 1050, 1220, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_9DO_2$: 151.0744; found: 151.0737.

2-[(2-Deuteriophenoxy)methyl]oxirane (3g). Silica gel chromatography (hexane/benzene =1/1) gave 140 mg of the product (0.93 mmol, 93% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.93−6.97 ppm (a deuterated site) compared to the peak at 4.31 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.71 (dd, J = 2.7, 5.1 Hz, 1H), 2.84 (t, J = 5.1 Hz, 1H), 3.31−3.37 (m, 1H), 3.82 (dd, J = 6.3, 11.2 Hz, 1H), 4.31 (dd, J = 2.7, 11.2 Hz, 1H), 6.93−6.97 (m, 2H), 7.28−7.31 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.4 (CH_2), 49.9 (CH), 68.5 (CH_2), 114.2 (t, $J_{C\text{-}D}$ = 24.2 Hz, C), 114.5 (CH), 121.1 (CH), 129.3 (CH), 129.4 (CH), 158.4 (C). IR (ATR): 760, 840, 1050, 1230, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_9DO_2$: 151.0744; found: 151.0746.

1-Deuterio-2-nitrobenzene (3h). Silica gel chromatography (hexane/benzene = 3/1) gave 121 mg of the product (0.98 mmol, 98% yield) as a pale yellow oil. >99% D (D content was judged with the peak at 8.23−8.25 ppm (a deuterated site) compared to the peak at 7.54−7.57 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.57 (m, 2H), 7.71 (dt, J = 1.0, 7.5 Hz, 1H), 8.23−8.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.2 (t, $J_{C\text{-}D}$ = 25.7 Hz, C), 123.5 (CH), 129.2 (CH), 129.3 (CH), 134.6 (CH), 148.2 (C). IR (ATR): 1340, 1520 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_6H_4DNO_2$: 124.0383; found: 124.0362.

(*E*)-4-(4-Deuteriophenyl)but-3-en-2-one (3i). Silica gel chromatography (hexane/AcOEt = 10/1) gave 144 mg of the product (0.98 mmol, 98% yield) as pale yellow solids of mp 39−40 °C. >99% D (D content was judged with the peak at 7.40 ppm (a deuterated site) compared to the peak at 6.73 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.39 (s, 3H), 6.73 (d, J = 16.4 Hz, 1H), 7.40 (d, J = 8.1 Hz, 2H), 7.52 (d, J = 16.4 Hz, 1H), 7.55 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.4 (CH_3), 127.2 (CH), 128.3 (CH), 128.9 (CH), 130.2 (t, $J_{C\text{-}D}$ = 24.0 Hz, C), 134.5 (C), 143.5 (CH), 198.5 (C). IR (ATR): 990, 1190, 1680 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{10}H_9DO$: 147.0794; found: 147.0771.

Butyl 4-Deuteriobenzoate (3j). Silica gel chromatography (hexane/benzene = 5/1) gave 168 mg of the product (0.94 mmol, 94% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.55 ppm (a deuterated site) compared to the peak at 7.45 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.99 (t, J = 7.5 Hz, 3H), 1.45−1.52 (m, 2H), 1.73−1.79 (m, 2H), 4.33 (t, J = 6.5 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 8.05 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 19.1 (CH_2), 30.6 (CH_2), 64.7 (CH_2), 128.1 (CH), 129.5 (CH), 130.5 (C), 132.4 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 166.6 (C). IR (ATR): 1100, 1270, 1720, 2960 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{11}H_{13}DO_2$: 179.1057; found: 179.1056.

4-Deuterio-*N*,*N*-dimethylbenzamide (3k). Silica gel chromatography (benzene/AcOEt = 2/1) gave 149 mg of the product (0.99 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.04 ppm (a deuterated site) compared to the peak at 7.32 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, benzene-d_6): δ 2.29 (brs, 3H), 2.76 (brs, 3H), 7.04 (d, J = 7.8 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.9 (CH_3), 39.2 (CH_3), 126.8 (CH), 128.0 (CH), 128.9 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 136.2 (C), 171.4 (C). IR (ATR): 860, 1080, 1620 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_{10}DNO$: 150.0903; found: 150.0906.

4-Deuterio-*N*,*N*-dibenzylbenzeneamine (3l). Silica gel chromatography (hexane/benzene = 10/1) gave 263 mg of the product (0.96 mmol, 96% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.73−6.75 ppm (a deuterated site) compared to the peak at 4.65 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.65 (s, 4H), 6.73−6.75 (m, 2H), 7.16 (d, J = 8.8 Hz, 2H), 7.23−7.26 (m, 6H), 7.31−7.34 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.1 (CH_2), 112.4 (CH), 116.5 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 126.6 (CH), 126.9 (CH), 128.6 (CH), 129.1 (CH), 138.6 (C), 149.2 (C). IR (ATR): 730, 1350, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{20}H_{18}DN$: 274.1580; found: 274.1576.

3-Deuteriophenyl Isopropyl Sulfide (3m). Silica gel chromatography (hexane/*i*-Pr_2O = 200/1) gave 126 mg of the product (0.82 mmol, 82% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.30−7.33 ppm (a deuterated site) compared to the peak at 3.43 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, CD_3CN): δ 1.26 (d, J = 6.5 Hz, 6H), 3.43 (septet, J = 6.5 Hz, 1H), 7.24 (dt, J = 1.0, 7.5 Hz, 1H), 7.30−7.33 (m, 1H), 7.38−7.40 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0 (CH_3), 38.1 (CH), 126.6 (CH), 128.5 (t, $J_{C\text{-}D}$ = 24.0 Hz, C), 128.8 (CH), 131.8 (CH), 131.9 (CH), 135.5 (C). IR (ATR): 660, 1580, 2960 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_{11}DS$: 153.0722; found: 153.0726.

3-Deuteriobenzoic Acid (3n). Deuterated product **3n** was directly converted into allyl 3-deuteriobenzoate (**3n′**) for purification. 3-Deuteriobenzoic acid (**3n**) was allylated according to the reported procedure.[23] To the reaction mixture was added water, and the mixture was acidified with 10% HCl. The resulting mixture was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated to give the crude product. The solution of crude product in THF (1 mL) was added to the mixture of *n*-Bu_4NHSO_4 (20 mg, 0.05 mnol) and KF (290 mg, 5.0 mmol) in THF (1 mL). Subsequently, allyl bromide (133 mg, 1.1 mmol) was added, and then the reaction mixture was stirred for 3 h at room temperature. After water was added, the resulting mixture was extracted with *i*-Pr_2O. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/benzene = 5/1) gave 131 mg of allyl 3-deuteriobenzoate (**3n′**) (0.80 mmol, 80% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.43−7.46 ppm (a deuterated site) compared to the peak at 4.83 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.83

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(dt, J = 1.0, 5.6 Hz, 2H), 5.29 (dd, J = 1.0, 10.5 Hz, 1H), 5.42 (dd, J = 1.5, 17.3 Hz, 1H), 6.01−6.09 (m, 1H), 7.43−7.46 (m, 1H), 7.56 (d, J = 7.5 Hz, 1H), 8.06−8.08 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 65.4 (CH_2), 118.2 (CH_2), 128.1 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 128.4 (CH), 129.5 (CH), 129.6 (CH), 130.2 (C), 132.3 (CH), 132.9 (CH), 166.3 (C). IR (ATR): 640, 1090, 1110, 1250, 1430, 1720, 3080 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{10}H_9DO_2$: 163.0744; found: 163.0747.

3-Deuterio-*N*-methylbenzamide (3o). Silica gel chromatography (benzene/AcOEt = 3/1) gave 135 mg of the product (0.99 mmol, 99% yield) as white solids of mp 74−75 °C. >99% D (D content was judged with the peak at 7.42−7.50 ppm (a deuterated site) compared to the peak at 7.75−7.77 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.03 (d, J = 4.8 Hz, 3H), 7.43 (dd, J = 7.5, 8.2 Hz, 1H), 7.49 (d, J = 7.5 Hz, 1H), 7.75−7.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5 (CH_3), 126.8 (CH), 126.9 (CH), 128.0 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 128.2 (CH), 131.0 (CH), 134.4 (C), 168.5 (C). IR (ATR): 690, 1550, 1630, 2930, 3320 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for C_8H_8DNO: 136.0747; found: 136.0749.

2,4,6-Trideuteriontrobenzene (3p). Silica gel chromatography (hexane/benzene = 8/1) gave 105 mg of the product (0.83 mmol, 83% yield) as a pale yellow oil. >99% D (D content was judged with the peak at 7.71 and 8.25 ppm (deuterated sites) compared to the peak at 7.56 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.1 (t, J = 25.7 Hz, C), 129.0 (CH), 134.3 (t, J = 25.7 Hz, C), 148.0 (C). IR (ATR): 690, 860, 1340, 1510 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_6H_2D_3NO_2$: 126.0509; found: 126.0507.

2-Benzyloxy-4-deuteriopyridine (5a). Silica gel chromatography (hexane/benzene = 1/1.5) gave 185 mg of the product (0.99 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.62 ppm (a deuterated site) compared to the peak at 8.18 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.38 (s, 2H), 6.81 (s, 1H), 6.88 (d, J = 5.1 Hz, 1H), 7.32 (t, J = 7.3 Hz, 1H), 7.38 (t, J = 7.3 Hz, 2H), 7.46−7.48 (m, 2H), 8.18 (d, J = 5.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.3 (CH_2), 111.0 (CH), 116.6 (CH), 127.7 (CH), 127.8 (CH), 128.3 (CH), 137.3 (C), 138.2 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 146.8 (CH), 163.5 (C). IR (ATR): 700, 990, 1220, 1560 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{12}H_{10}DNO$: 186.0903; found: 186.0902.

2-Benzyloxy-5-deuteriopyridine (5b). Silica gel chromatography (hexane/benzene = 1/1) gave 181 mg of the product (0.97 mmol, 97% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.88 ppm (a deuterated site) compared to the peak at 8.18 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.38 (s, 2H), 6.81 (dd, J = 1.5, 8.4 Hz, 1H), 7.30−7.33 (m, 1H), 7.36−7.39 (m, 2H), 7.46−7.48 (m, 2H), 7.58 (dd, J = 1.5, 8.4 Hz, 1H), 8.18 (d, J = 1.5 Hz 1H). ^{2}H NMR (61 MHz, $CHCl_3$): δ 6.86 (brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.3 (CH_2), 111.2 (CH), 116.5 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 127.7 (CH), 127.9 (CH), 128.3 (CH), 137.3 (C), 138.4 (CH), 146.7 (CH), 163.6 (C). IR (ATR): 740, 990, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{12}H_{10}DNO$: 186.0903; found: 186.0899.

2-Benzyloxy-6-deuteriopyridine (5c). Silica gel chromatography (hexane/benzene = 1.5/1) gave 185 mg of the product (0.99 mmol, 99% yield) as a colorless oil. >99% D (D content was judged with the peak at 8.18 ppm (a deuterated site) compared to the peak at 6.88 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.38 (s, 2H), 6.81 (dd, J = 1.0, 8.3 Hz, 1H), 6.88 (d, J = 7.1 Hz, 1H), 7.30−7.33 (m, 1H), 7.36−7.39 (m, 2H), 7.46−7.48 (m, 2H), 7.58 (dd, J = 7.1, 8.3 Hz 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 67.3 (CH_2), 111.2 (CH), 116.7 (CH), 127.7 (CH), 127.9 (CH), 128.4 (CH), 137.4 (C), 138.5 (CH), 146.5 (t, $J_{C\text{-}D}$ = 27.3 Hz, C), 163.6 (C). IR (ATR): 1250, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{12}H_{10}DNO$: 186.0903; found: 186.0907.

2-(Dibenzylamino)-5-deuteriopyridine (5d). Silica gel chromatography (hexane/benzene = 1.5/1) gave 254 mg of the product (0.92 mmol, 92% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.58 ppm (a deuterated site) compared to the peak at 7.38 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.80 (s, 4H), 6.46 (dd, J = 0.8, 8.5 Hz, 1H), 7.23−7.26 (m, 6H), 7.29−7.32 (m, 4H), 7.38 (dd, J = 2.0, 8.5 Hz, 1H), 8.20−8.21 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 50.8 (CH_2), 105.7 (CH), 111.9 (t, $J_{C\text{-}D}$ = 25.7 Hz, C), 126.9 (CH), 127.0 (CH), 128.5 (CH), 137.3 (CH), 138.4 (C), 148.0 (CH), 158.6 (C). IR (ATR): 1240, 1490, 1580 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{19}H_{17}DN_2$: 275.1533; found: 275.1530.

8-Deuterioquinoline (5e). Silica gel chromatography (benzene/AcOEt = 10/1) gave 126 mg of the product (0.97 mmol, 97% yield) as a colorless oil. >99% D (D content was judged with the peak at 8.12 ppm (a deuterated site) compared to the peak at 7.73 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (dd, J = 4.2, 8.3 Hz, 1H), 7.56 (dd, J = 7.0, 8.1 Hz, 1H), 7.73 (d, J = 7.0 Hz, 1H), 7.83 (dd, J = 1.7, 8.1 Hz, 1H), 8.17 (dd, J = 1.7, 8.3 Hz, 1H), 8.93 (dd, J = 1.7, 4.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.8 (CH), 126.2 (CH), 127.5 (CH), 128.0 (C), 128.9 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 129.0 (CH), 135.7 (CH), 148.0 (C), 150.1 (CH). IR (ATR): 790, 1490 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for C_9H_6DN: 130.0641; found: 130.0645.

4-Deuterio-2-(trifluoromethyl)quinoline (5f). Silica gel chromatography (hexane/benzene =3/1) gave 192 mg of the product (0.97 mmol, 97% yield) as colorless solids of mp 53−54 °C. >99% D (D content was judged with the peak at 8.37 ppm (a deuterated site) compared to the peak at 7.92 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67−7.70 (m, 1H), 7.75 (s, 1H), 7.82−7.85 (m, 1H), 7.92 (dd, J = 1.0, 8.5 Hz, 1H), 8.24 (d, J = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.5 (q, J_{C-F} = 2.5 Hz, CH), 121.6 (q, J_{C-F} = 275.6 Hz, C), 127.6 (CH), 128.5 (CH), 128.7 (C), 130.0 (CH), 130.8 (CH), 137.7 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 147.1 (C), 147.9 (q, J_{C-F} = 34.8 Hz, C). IR (ATR): 770, 1120, 1200 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{10}H_5DF_3N$: 198.0515; found: 198.0505.

2-Deuterio-1-methyl-1*H*-indole (5g). Silica gel chromatography (hexane/benzene = 10/1) gave 128 mg of the product (0.97 mmol, 97% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.31 ppm (a deuterated site) compared to the peak at 7.53 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.78 (s, 3H), 6.40 (d, J = 0.7 Hz, 1H), 7.00−7.03 (m, 1H), 7.12−7.15 (m, 1H). 7.42 (dd, J = 0.7, 8.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.4 (CH_3), 100.6 (CH), 109.1 (CH), 119.2 (CH), 120.8 (CH), 121.4 (CH), 128.4 (C), 128.5 (t, $J_{C\text{-}D}$ = 27.3 Hz, C), 136.6 (C). IR (ATR): 730, 1230, 1470 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for C_9H_8DN: 132.0798; found: 132.0801.

5-Butyl-2-deuteriobenzofuran (5h). Silica gel chromatography (hexane/*i*-Pr_2O = 400/1) gave 164 mg of the product (0.94 mmol, 94% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.58 ppm (a deuterated site) compared to the peak at 7.39−7.41 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.93 (t, J = 7.5 Hz, 3H), 1.33−1.41 (m, 2H), 1.60−1.66 (m, 2H), 2.70 (t, J = 7.5 Hz, 2H), 6.70 (d, J = 0.8 Hz, 1H), 7.11 (dd, J = 1.5, 8.3 Hz, 1H), 7.39 (s, 1H), 7.40 (d, J = 8.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (CH_3), 22.2 (CH_2), 34.2 (CH_2), 35.5 (CH_2), 106.2 (CH), 110.9 (CH), 120.4 (CH), 125.0 (CH), 127.5 (C), 137.3 (C), 144.7 (t, $J_{C\text{-}D}$ = 30.6 Hz, C), 153.5 (C). IR (ATR): 810, 1030, 1450 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{12}H_{13}DO$: 175.1107; found: 175.1107.

2-Deuterio-3-*n*-hexylthiophene (5i). Silica gel chromatography (hexane/*i*-Pr_2O = 200/1) gave 163 mg of the product (0.96 mmol, 96% yield) as a colorless oil. >99% D (D content was judged with the peak at 6.93 ppm (a deuterated site) compared to the peak at 0.88 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (t, J = 6.5 Hz, 3H), 1.30−1.35 (m, 6H), 1.62 (quintet, J = 7.5 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 6.93 (d, J = 4.8 Hz, 1H), 7.23 (d, J = 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (CH_3), 22.5 (CH_2), 29.0 (CH_2), 30.2 (CH_2), 30.5 (CH_2), 31.6 (CH_2), 119.6 (t, $J_{C\text{-}D}$ = 27.3 Hz, C), 124.9 (CH), 128.3 (CH), 143.1 (C). IR (ATR): 720, 830, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{10}H_{15}DS$: 169.1035; found: 169.1039.

2-Deuteriobenzothiophene (5j). Silica gel chromatography (hexane/benzene = 400/1) gave 122 mg of the product (0.90 mmol, 90% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.44 ppm (a deuterated site) compared to the peak at 7.82−7.90 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): 7.32−7.38 (m, 3H), 7.83 (dd, J = 1.8, 7.0 Hz, 1H), 7.88−7.90 (m, 1H). ^{13}C

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NMR (100 MHz, $CDCl_3$): 122.5 (CH), 123.6 (CH), 123.7 (CH), 124.17 (CH), 124.21 (CH), 126.1 (t, $J_{C\text{-}D}$ = 28.1 Hz, C), 139.6 (C), 139.7 (C). IR (ATR): cm^{-1} 730, 840, 1450, 2920. HRMS (EI) *m/z*: (M^+) calcd for C_8H_5DS: 135.0253; found: 135.0254.

3-Deuteriobenzothiophene (5k). Silica gel chromatography (hexane/benzene = 400/1) gave 125 mg of the product (0.93 mmol, 93% yield) as a colorless oil. 99% D (D content was judged with the peak at 6.96 ppm (a deuterated site) compared to the peak at 7.55−7.59 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, benzene-d_6): 6.91 (s, 1H), 7.04−7.07 (m, 1H), 7.12−7.15 (m, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 122.5 (CH), 123.58 (CH), 123.62 (t, $J_{C\text{-}D}$ = 25.7 Hz, C), 124.1 (CH), 124.2 (CH), 126.2 (CH), 139.5 (C), 139.7 (C). IR (ATR): 720, 860, 1460, 2920 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for C_8H_5DS: 135.0253; found: 135.0252.

2-Deuterio-4,6-dimethoxypyrimidine (5l). Silica gel chromatography (hexane/AcOEt = 15/1) gave 101 mg of the product (0.72 mmol, 72% yield) as a colorless oil. >99% D (D content was judged with the peak at 8.46 ppm (a deuterated site) compared to the peak at 6.06 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.95 (s, 6H), 6.06 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.9 (CH_3), 90.3 (CH), 157.2 (t, $J_{C\text{-}D}$ = 31.0 Hz, C), 171.3. (C). IR (ATR): 700, 1190, 1260, 1590 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_6H_7DN_2O_2$: 141.0649; found: 141.0645.

4-Deuteriocinnoline (5m). Silica gel chromatography (benzene/AcOEt = 4/1) gave 113 mg of the product (0.86 mmol, 86% yield) as pale yellpw oil. >99% D (D content was judged with the peak at 8.24 ppm (a deuterated site) compared to the peak at 9.40 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.88−7.91 (m, 1H), 7.96−8.00 (m, 1H), 8.10 (dd, *J* = 0.7, 8.5 Hz, 1H), 8.48 (dd, *J* = 0.7, 8.5 Hz, 1H), 9.40 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.0, (t, $J_{C\text{-}D}$ = 25.7 Hz, C), 125.6 (C), 126.4 (CH), 129.5 (CH), 130.4 (CH), 130.9 (CH), 144.8 (CH), 150.6 (C). IR (ATR): 770, 1140, 1570 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_8H_5DN_2$: 131.0594; found: 131.0597.

5-Deuterio-2-methylbenzo[*d*]thiazole (5n). Silica gel chromatography (benzene/*i*-Pr_2O = 20/1) gave 137 mg of the product (0.91 mmol, 91% yield) as a colorless oil. >99% D (D content was judged with the peak at 7.48 ppm (a deuterated site) compared to the peak at 7.39 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.80 (s, 3H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.91 (s, 1H), 8.03 (dd, *J* = 0.5, 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8 (CH_3), 121.2 (CH), 122.1 (CH), 124.4 (CH), 125.5 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 135.5 (C), 153.2 (C), 166.8 (C). IR (ATR): 1170, 1520 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for C_8H_6DNS: 150.0362; found: 150.0365.

6-Deuterioimidazo[1,2-*a*]pyridine (5o). Silica gel chromatography (AcOEt and AcOEt/MeOH = 10/1) gave 118 mg of the product (0.99 mmol, 99% yield) as a pale yellow oil. >99% D (D content was judged with the peak at 6.78 ppm (a deuterated site) compared to the peak at 8.14 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): 7.17 (d, *J* = 9.1 Hz, 1H), 7.58−7.60 (m, 1H), 7.62−7.64 (m, 2H), 8.14 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): 111.6 (t, $J_{C\text{-}D}$ = 25.7 Hz, C), 112.0 (CH), 117.3 (CH), 123.9 (CH), 125.4 (CH), 133.0 (CH), 145.0 (C). IR (ATR): 710, 1130, 1500, 1630 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_7H_5DN_2$: 119.0594; found: 119.0594.

1-Butyl-6-deuterio-3-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (5p). Silica gel chromatography (hexane/benzene = 1/1) gave 238 mg of the product (0.95 mmol, 95% yield) as a pale yellow oil. >99% D (D content was judged with the peak at 8.37 ppm (a deuterated site) compared to the peak at 8.22 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.96 (t, *J* = 7.4 Hz, 3H), 1.37−1.44 (m, 2H), 1.88−1.94 (m, 2H), 4.35 (t, *J* = 7.4 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 1H), 7.27−7.30 (m, 1H), 7.43−7.46 (m, 3H), 7.64 (dd, *J* = 1.2, 8.3 Hz, 2H), 8.22 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 20.0 (CH_2), 32.3 (CH_2), 44.2 (CH_2), 114.8 (C), 115.8 (CH), 118.6 (C), 125.1 (CH), 126.0 (CH), 126.9 (CH), 128.0 (CH), 128.9 (CH), 135.1 (C), 142.7 (t, $J_{C\text{-}D}$ = 27.3 Hz, C), 148.0 (C). IR (ATR): 750, 760, 1430, 1540, 1600 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{17}H_{17}DN_2$: 251.1533; found: 251.1532.

5-Deuterio-2-phenyloxazolo[5,4-*b*]pyridine (5q). Silica gel chromatography (hexane/Et_2O = 5/1) gave 146 mg of the product (0.74 mmol, 74% yield) as white solids of mp 97−98 °C. >99% D (D content was judged with the peak at 8.36 ppm (a deuterated site) compared to the peak at 8.08 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.8 Hz 1H), 7.54−7.61 (m, 3H), 8.08 (d, *J* = 7.8 Hz, 1H), 8.29−8.32 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.7 (CH), 126.4 (C), 127.7 (CH), 128.1 (CH), 128.9 (CH), 132.1 (CH), 133.8 (C), 144.2 (t, $J_{C\text{-}D}$ = 28.1 Hz, C), 159.7 (C), 163.0 (C). IR (ATR): 680, 1540, 1600, 1610 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{12}H_7DN_2O$: 197.0699; found: 197.0701.

4,7-Dideuterioquinoline (5r). Silica gel chromatography (benzene/AcOEt = 10/1) gave 127 mg of the product (0.97 mmol, 97% yield) as a colorless oil. >99% D (D content was judged with the peaks at 7.73 and 8.17 ppm (deuterated sites) compared to the peak at 8.12 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, *J* = 4.2 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 8.12 (s, 1H), 8.93 (d, *J* = 4.2 Hz 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.8 (CH), 126.3 (CH), 127.6 (CH), 128.1 (C), 129.0 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 129.2 (CH), 135.6 (t, $J_{C\text{-}D}$ = 24.8 Hz, C), 148.2 (C), 150.3 (CH). IR (ATR): 710, 1490, 1560 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_9H_5D_2N$: 131.0704; found: 131.0707.

Isopropyl 2-[4-(4-Deuteriobenzoyl)phenoxy]-2-methylpropanoate (7a). Silica gel column chromatography (benzene) gave 310 mg of the product (0.95 mmol, 95%) as off-white solids of mp 83 °C. >99% D (D content was judged with the peak at 7.56 ppm (a deuterated site) compared to the peak at 6.86 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): 1.20 (d, *J* = 6.2 Hz, 6H), 1.67 (s, 6H), 5.09 (septet, *J* = 6.3 Hz, 1H), 6.85−6.88 (m, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.74−7.78 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): 21.4 (CH_3), 25.2 (CH_3), 69.2 (CH), 79.3 (C), 117.1 (CH), 128.1 (CH), 129.7 (CH), 130.6 (C), 131.6 (t, $J_{C\text{-}D}$ = 24.0 Hz, C), 132.0 (CH), 138.1 (C), 159.6 (C), 173.2 (C), 195.5 (C). IR (ATR): 850, 1660, 1720 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{20}H_{21}DO_4$: 327.1581; found: 327.1582.

(8*R*,9*S*,13*S*,14*S*)-(+)-3-Benzyloxy-2-deuterio-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]-phenanthren (7b). This reaction was conducted in 0.5 mmol scale. Silica gel chromatography (hexane/*i*-Pr_2O = 3/1) gave 167 mg of the product (0.46 mmol, 92% yield) as white solids of mp 126−127 °C. $[\alpha]^{27}_D$ +117.6 (*c* 1.00, $CHCl_3$). >99% D (D content was judged with the peak at 6.79 ppm (a deuterated site) compared to the peak at 6.74 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.91 (s, 3H), 1.40−1.67 (m, 6H), 1.94−2.08 (m, 3H), 2.11−2.18 (m, 1H), 2.23−2.28 (m, 1H), 2.38−2.42 (m, 1H), 2.48−2.53 (m, 1H), 2.88−2.92 (m, 2H), 5.04 (s, 2H), 6.74 (s, 1H), 7.20 (s, 1H), 7.30−7.33 (m, 1H), 7.37−7.44 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7 (CH_3), 21.4 (CH_2), 25.8 (CH_2), 26.4 (CH_2), 29.5 (CH_2), 31.4 (CH_2), 35.7 (CH_2), 38.2 (CH), 43.8 (CH), 47.9 (C), 50.3 (CH), 69.8 (CH_2), 112.0 (t, $J_{C\text{-}D}$ = 24.0 Hz, C), 114.9 (CH), 126.2 (CH), 127.4 (CH), 127.8 (CH), 128.5 (CH), 132.3 (C), 137.2 (C),137.8 (C), 156.8 (C), 220.9 (C). IR (ATR): 700, 1020, 1220, 1490, 1730 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{25}H_{27}DO_2$: 361.2152; found: 361.2157.

(2*S*,6′*R*)-(+)-7-Deuterio-2′,4,6-trimethoxy-6′-methyl-3*H*-spiro[1-benzofuran-2,1′-cyclohexan]-2′-ene-3,4′-dione (7c). Silica gel chromatography (hexane/AcoEt = 1/1) gave 304 mg of the product (0.95 mmol, 95% yield) as white solids of mp 180−181 °C. $[\alpha]^{17}_D$ +358.2 (*c* 1.00, acetone). 97% D (D content was judged with the peak at 6.23 ppm (a deuterated site) compared to the peak at 5.54 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.98 (d, *J* = 6.7 Hz, 3H), 2.42 (dd, *J* = 4.8, 16.8 Hz, 1H), 2.73−2.80 (m, 1H), 3.08 (dd, *J* = 13.5, 16.8 Hz, 1H), 3.64 (s, 3H), 3.91 (s, 3H), 3.92 (s, 3H), 5.55 (s, 1H), 6.06 (s, 1H). ^{2}H NMR (61 MHz, $CHCl_3$): δ 6.27 (brs). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (CH_3), 36.3 (CH), 39.8 (CH_2), 55.88 (CH_3), 55.90 (CH_3), 56.4 (CH_3), 88.2 (t, $J_{C\text{-}D}$ = 25.7 Hz, C), 89.7 (C), 93.2 (CH), 104.1 (C), 104.5 (CH), 159.0 (C), 170.3 (C), 171.3 (C), 175.9 (C), 192.4 (C), 197.2 (C). IR (ATR): 810, 1210, 1610 cm^{-1}. HRMS (EI) *m/z*: (M^+) calcd for $C_{17}H_{17}DO_6$: 319.1166; found: 319.1161.

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4-[4-(4-Deuteriophenyl)-4-hydroxypiperidino]-4′-fluorobutyrophenone (7d). Silica gel chromatography (CH_2Cl_2/MeOH = 10/1) gave 322 mg of the product (0.94 mmol, 94% yield) as white solids of mp 136−137 °C. >99% D (D content was judged with the peak at 7.21−7.25 ppm (a deuterated site) compared to the peak at 7.30−7.39 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, CD_3CN): δ 1.50−1.55 (m, 2H), 1.79 (dt, J = 4.5, 12.6 Hz, 2H), 1.88−1.94 (m, 3H), 2.34 (dt, J = 2.6, 12.6 Hz, 2H), 2.40 (t, J = 6.8 Hz, 2H), 2.64 (m, 2H), 2.97 (t, J = 6.8 Hz, 2H), 7.21−7.25 (m, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.37−7.39 (m, 2H), 8.05−8.09 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (CH_2), 36.2 (CH_2), 38.3 (CH_2), 49.3 (CH_2), 57.8 (CH_2), 71.1 (C), 115.6 (d, J_{C-F} = 21.5 Hz, CH), 124.5 (CH), 126.6 (t, J_{C-D} = 24.0 Hz, C), 128.1 (CH), 130.7 (d, J_{C-F} = 9.1 Hz, CH), 133.7 (d, J_{C-F} = 3.3 Hz, C), 148.5 (C), 165.6 (d, J_{C-F} = 254.1 Hz, C), 198.5 (C). IR (ATR): 830, 1200, 1600, 1680, 3180 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{21}H_{23}DFNO_2$: 342.1854; found: 342.1843.

2-Deuterio-10-[3-(dimethylamino)-1-propyl]phenothiazine (7e). This reaction was conducted with chlorpromazine hydrochloride as a substrate. Silica gel chromatography (AcOEt/Et_3N = 60/1) gave 258 mg of the product (0.90 mmol, 90% yield) as brown oil. >99% D (D content was judged with the peak at 7.14−7.22 ppm (a deuterated site) compared to the peak at 3.90 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.79 (quintet, J = 6.9 Hz, 2H), 2.08 (s, 6H), 2.30 (t, J = 6.9 Hz, 2H), 3.90 (t, J = 6.9 Hz, 2H), 6.92−6.95 (m, 2H), 7.02−7.03 (m, 2H), 7.15 (d, J = 7.6 Hz, 2H), 7.18−7.22 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0 (CH_2), 45.1 (CH_2), 45.4 (CH_3), 56.9 (CH_2), 115.3 (CH), 115.4 (CH), 122.1 (CH), 122.2 (CH), 124.9 (C), 126.8 (t, J_{C-D} = 24.0 Hz, C), 127.1 (CH), 127.3 (CH), 145.1 (C). IR (ATR): 740, 1220, 1240, 1450 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{17}H_{19}DN_2S$: 285.1410; found: 285.1417.

7-Deuterio-4-[4-(diethylamino)-1-methylbutylamino]-quinoline (7f). This reaction was conducted in 10 mmol scale. Silica gel chromatography (CH_2Cl_2/MeOH = 9/1 and CH_2Cl_2/MeOH/Et_3N = 10/1/0.1) gave 2.83 g of the product (9.9 mmol, 99% yield) as pale yellow solids of mp 69−70 °C. >99% D (D content was judged with the peak at 7.61 ppm (a deuterated site) compared to the peak at 7.41 ppm by ^{1}H NMR). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.01 (t, J = 7.2 Hz, 6H), 1.33 (d, J = 6.3 Hz, 3H), 1.58−1.78 (m, 4H), 2.45 (t, J = 7.2 Hz, 2H), 2.53 (q, J = 7.2 Hz, 4H), 3.70−3.77 (m, 1H), 5.10 (d, J = 7.2 Hz, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.41 (dd, J = 1.1, 8.4 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.97 (s, 1H), 8.54 (d, J = 5.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.0 (CH_3), 19.6 (CH_3), 23.3 (CH_2), 33.9 (CH_2), 46.2 (CH_2), 47.7 (CH), 52.1 (CH_2), 98.4 (CH), 118.6 (C), 119.7 (CH), 123.7 (CH), 128.1 (t, J_{C-D} = 22.4 Hz, C), 129.1 (CH), 148.3 (C), 148.9 (C), 150.5 (CH). IR (ATR): 1150, 1330, 1540, 1570, 3250 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{18}H_{26}DN_3$: 286.2268; found: 286.2265.

1-Benzyloxy-4-chlorobenzene (2b). This compound was prepared on the basis of the previous report.[24a] To a mixture of K_2CO_3 (885 mg, 6.4 mmol) and 4-chlorophenol (1.23 g, 9.6 mmol) in dry acetone (6.0 mL) was added benzyl bromide (547 mg, 3.2 mmol) followed by heating to 50 °C. After stirring for 15 h, the reaction mixture was poured into a 2 M NaOH solution and extracted with AcOEt. The organic layers were dried over $MgSO_4$. Concentration and purification through silica gel chromatography (hexane/AcOEt = 10/1) gave 698 mg of the product (3.2 mmol, 99% yield) as white solids of mp 66−67 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.04 (s, 2H), 6.89−6.91 (m, 2H), 7.22−7.26 (m, 2H), 7.32−7.35 (m. 1H), 7.37−7.42 (m. 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 70.2 (CH_2), 116.2 (CH), 125.8 (C), 127.5 (CH), 128.1 (CH), 128.7 (CH), 129.4 (CH), 136.6 (C), 157.4 (C). IR (ATR): 830, 1040, 1240, 1490, 1580 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{13}H_{11}{}^{35}ClO$: 218.0498; found: 218.0489.

1-Benzyloxy-4-chloro-3-methylbenzene (2c). This compound was prepared with the same procedure as that for **2b**. Silica gel chromatography (hexane/Et_2O = 10/1) gave 721 mg of the product (3.1 mmol, 97% yield) as white solids of mp 57−58 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.34 (s, 3H), 5.02 (s, 2H), 6.74 (dd, J = 3.1, 8.7 Hz, 1H), 6.86 (d, J = 3.1 Hz, 1H), 7.22 (d, J = 8.7 Hz, 1H), 7.33, (t, J = 7.2 Hz, 1H), 7.37−7.42 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.2 (CH_3), 70.1 (CH_2), 113.4 (CH), 117.5 (CH), 126.1 (C), 127.4 (CH), 128.0 (CH), 128.6 (CH), 129.6 (CH), 136.8 (C), 137.1 (C), 157.3 (C). IR (ATR): 820, 1020, 1240, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{14}H_{13}{}^{35}ClO$: 232.0655; found: 232.0654.

1-Benzyloxy-4-chloro-3,5-dimethylbenzene (2d). This compound was prepared from benzyl bromide (6.4 mmol) with the same procedure as that for **2b**. Silica gel chromatography (hexane/AcOEt = 10/1) gave 1.58 g of the product (6.4 mmol, 99% yield) as white solids of mp 52−53 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.34 (s, 6H), 5.01 (s, 2H), 6.72 (s, 2H), 7.31−7.34 (m, 1H), 7.37−7.42 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.8 (CH_3), 69.9 (CH_2), 114.8 (CH), 126.5 (C), 127.4 (CH), 127.9 (CH), 128.6 (CH), 136.9 (C), 137.1 (C), 156.7 (C). IR (ATR): 700, 750, 850, 1030, 1160, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{15}H_{15}{}^{35}ClO$: 246.0811; found: 246.0808.

2-[(4-Chlorophenoxy)methyl]oxirane (2e). This compound was prepared on the basis of the previous report.[25a] To a solution of 4-chlorophenol (1.00 g, 7.78 mmol) in dry acetone (20 mL) were added K_2CO_3 (3.22 g, 23.3 mmol) and epichlorohydrin (2.88 g, 31.1 mmol). The reaction mixture was refluxed for 24 h. Additional epichlorohydrin (2.88 g, 31.1 mmol) was added, and the solution was refluxed for 24 h. The mixture was cooled to room temperature, and the solids were filtered off. The solvent was removed, and the resulting oil was taken up in toluene (20 mL). The organic layer was washed with H_2O, 1 M NaOH solution, and H_2O, and then dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/Et_2O = 9/1) gave 1.17 g of the product (6.3 mmol, 81% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.75 (dd, J = 3.1, 4.9 Hz, 1H), 2.91 (dd, J = 4.2, 4.9 Hz, 1H), 3.33−3.36 (m, 1H), 3.92 (dd, J = 5.8, 11.1 Hz, 1H), 4.21 (dd, J = 3.1, 11.1 Hz, 1H), 6.84−6.87 (m, 2H), 7.22−7.25 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.0 (CH_2), 49.6 (CH), 68.8 (CH_2), 115.7 (CH), 125.7 (C), 129.1 (CH), 157.0 (C). IR (ATR): 820, 1090 1240, 1490 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_9{}^{35}ClO_2$: 184.0291; found: 184.0292.

(*S*)-(+)-2-[(3-Chlorophenoxy)methyl]oxirane (2f). This compound was prepared on the basis of the previous report.[25b] A solution of 3-chlorophenol (1.13 g, 8.8 mmol) in dry DMF (7.4 mL) was added to a suspension of NaH (60% in mineral oil, 420 mg, 10.5 mmol) in dry DMF (29 mL) at room temperature. After stirring for 30 min, a solution of (2*S*)-(+)-glycidyl tosylate (1.83 g, 8.0 mmol) in dry DMF (5.4 mL) was added. After the mixture was stirred for 15 h at room temperature, saturated NH_4Cl was added. The resulting mixture was extracted with *i*-Pr_2O. The combined organic layers were washed with saturated $NaHCO_3$ and brine, and then dried over Na_2SO_4. Concentration and purification through silica gel column chromatography (hexane/benzene = 1/1) gave 1.00 g (5.4 mmol, 68% yield) of the product as a colorless oil. $[\alpha]^{22}_D$ +11.8 (*c* 9.41, EtOH). 91% *ee* (HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 200/1, 1.0 mL/min, 254 nm, (*S*)-isomer 17.3 min and (*R*)-isomer 15.3 min). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.76 (dd, J = 3.0, 4.8 Hz, 1H), 2.92 (dd, J = 4.2, 4.8 Hz, 1H), 3.33−3.36 (m, 1H), 3.93 (dd, J = 5.8, 11.0 Hz, 1H), 4.23 (dd, J = 3.0, 11.0 Hz, 1H), 6.82 (ddd, J = 0.8, 2.0, 8.3 Hz, 1H), 6.93 (t, J = 2.0 Hz, 1H), 6.96 (ddd, J = 0.8, 2.0, 8.0 Hz, 1H), 7.20 (dd, J = 8.0, 8.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.4 (CH_2), 49.8 (CH), 68.9 (CH_2), 113.1 (CH), 115.0 (CH), 121.4 (CH), 130.3 (CH), 134.8 (C), 159.2 (C). IR (ATR): 770, 1070, 1280, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_9{}^{35}ClO_2$: 184.0291; found: 184.0289.

2-[(2-Chlorophenoxy)methyl]oxirane (2g). This compound was prepared from 2-chlorophenol (8.0 mmol) with the same procedure as that for **2e**. Silica gel chromatography (hexane/AcOEt = 10/1) gave 1.40 g of the product (7.6 mmol, 95% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.83 (dd, J = 3.1, 5.0 Hz, 1H), 2.92 (t, J = 5.0 Hz, 1H), 3.39−3.42 (m, 1H), 4.07 (dd, J = 5.3, 11.3 Hz, 1H), 4.30 (dd, J = 3.1, 11.3 Hz, 1H), 6.93 (dt, J = 1.5, 8.0 Hz, 1H), 6.97 (dd, J = 1.5, 8.0 Hz, 1H), 7.19−7.23 (m, 1H), 7.37 (dd, J = 1.5, 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.4 (CH_2), 49.9 (CH), 69.5 (CH_2), 114.0 (CH), 122.0 (CH), 123.1 (C), 127.7 (CH), 130.3 (CH), 154.0 (C). IR (ATR): 740, 1060, 1280, 1590 cm^{-1}.

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HRMS (EI) m/z: (M^+) calcd for $C_9H_9{}^{35}ClO_2$: 184.0291; found: 184.0294.

Butyl 4-Chlorobenzoate (2j). This compound was prepared on the basis of the previous report.[26a] To a solution of 4-chlorobenzoyl chloride (1.31 g, 7.5 mmol) in dry THF (24 mL) was added butanol (838 mg, 11.3 mmol). The reaction was refluxed for 12 h and cooled to room temperature. Water was added, and then the resulting mixture was extracted with i-Pr_2O. The combined organic layers were washed with water and brine, and then dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 50/1) gave 1.59 g of the product (7.4 mmol, 99% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.98 (t, J = 7.4 Hz, 3H), 1.44−1.51 (m, 2H), 1.72−1.78 (m, 2H), 4.32 (t, J = 6.7 Hz, 2H), 7.40−7.42 (m, 2H), 7.96−7.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 19.1 (CH_2), 30.6 (CH_2), 64.9 (CH_2), 128.6 (CH), 128.9 (C), 130.9 (CH), 139.2 (C), 165.8 (C). IR (ATR): 760, 1090, 1170, 1720 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{11}H_{13}{}^{35}ClO_2$: 212.0604; found: 212.0602.

4-Chloro-*N*,*N*-dibenzylaniline (2l). This compound was prepared on the basis of the previous report.[24b] To a mixture of 4-chloroaniline (1.28 g, 10 mmol) and K_2CO_3 (2.76 g, 20 mmol) in dry CH_3CN (10 mL) was added benzyl bromide (4.10 g, 24 mmol). The reaction mixture was stirred for 5 h at 120 °C. After water was added at room temperature, the resulting mixture was extracted with Et_2O. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/i-Pr_2O = 50/1) gave 2.80 g of the product (9.1 mmol, 91% yield) as white solids of mp 98−99 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.63 (s, 4H), 6.62−6.65 (m, 2H), 7.07−7.10 (m, 2H), 7.22 (d, J = 7.1 Hz, 4H), 7.24−7.27 (m, 2H), 7.31−7.34 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.4 (CH_2), 113.7 (CH), 121.5 (C), 126.6 (CH), 127.1 (CH), 128.7 (CH), 129.0 (CH), 138.1 (C), 147.7 (C). IR (ATR): 800, 1090, 1170, 1350 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{20}H_{18}{}^{35}ClN$: 307.1128; found: 307.1118.

3-Chlorophenyl Isopropyl Sulfide (2m). This compound was prepared on the basis of the previous report.[27] To a solution of NaOEt (20% in EtOH, 11 mmol) was added 3-chlorobenzenethiol (1.45 g, 10 mmol). The reaction mixture was stirred for 30 min at room temperature and treated with 2-iodopropane (2.04 g, 12 mmol). After the reaction mixture was stirred for 16 h, water was added. The resulting mixture was extracted with CH_2Cl_2. The combined organic layers were washed with a 2 M NaOH solution and brine, and then dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/i-Pr_2O = 100/1) gave 1.80 g of the product (9.6 mmol, 96% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31 (d, J = 6.7 Hz, 6H), 3.40 (septet, J = 6.7 Hz, 1H), 7.17−7.26 (m, 3H), 7.36 (t, J = 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.9 (CH_3), 37.9 (CH), 126.5 (CH), 129.2 (CH), 129.8 (CH), 130.7 (CH), 134.4 (C), 138.0 (C). IR (ATR): 680, 1080, 1580 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_9H_{11}{}^{35}ClS$: 186.0270; found: 186.0273.

3-Chloro-*N*-methylbenzamide (2o). This compound was prepared on the basis of the previous report.[26b] To a solution of 3-chlorobenzoyl chloride (1.75 g, 10 mmol) in dry Et_2O (20 mL) was added $MeNH_2$ (40% in methanol, 15 mmol) and Et_3N (2.02 g, 20 mmol). The reaction mixture was stirred for 1 h at room temperature. After water was added, the resulting mixture was extracted with Et_2O. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 1/1) gave 1.69 g of the product (9.9 mmol, 99% yield) as white solids of mp 68−69 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.02 (d, J = 4.9 Hz, 3H), 6.11 (brs, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.47 (ddd, J = 1.2, 2.0, 7.8 Hz, 1H), 7.61−7.63 (m, 1H), 7.75 (t, J = 2.0, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7 (CH_3), 125.0 (CH), 127.3 (CH), 129.6 (CH), 131.2 (CH), 134.4 (C), 136.2 (C), 167.3 (C). IR (ATR): 680, 1170, 1550, 1640, 3310 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_8H_8{}^{35}ClNO$: 169.0294; found: 169.0298.

2-Benzyloxy-6-chloropyridine (4c). This compound was prepared on the basis of the previous report.[24c] A mixture of 6-chloro-2-hydroxypyridine (4.66 g, 36 mmol) and NaH (60% in mineral oil, 1.44 g, 36 mmol) in DMF (144 mL) was stirred for 30 min. After benzyl chloride (4.56 g, 36 mmol) was added, the resulting mixture was stirred for 3 h at room temperature. Water was added, and then the mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 4/1) gave 2.53 g of the product (11.6 mmol, 32% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.36 (s, 2H), 6.70−6.72 (m, 1H), 6.91−6.93 (m, 1H), 7.32−7.35 (m, 1H), 7.37−7.40 (m, 2H), 7.46−7.47 (m, 2H), 7.51−7.54 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 68.2 (CH_2), 109.3 (CH), 116.4 (CH), 128.0 (CH), 128.2 (CH), 128.5 (CH), 136.6 (C), 140.7 (CH), 148.2 (C), 163.2 (C). IR (ATR): 790, 1160, 1260, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{12}H_{10}{}^{35}ClNO$: 219.0451; found: 219.0451.

2-(Dibenzylamino)-5-chloropyridine (4d). This compound was prepared on the basis of the previous report.[24d] NaH (60% in mineral oil, 2.72 g, 68 mmol) was suspended in dry DMF (60 mL) and cooled in an ice bath. 2-Amino-5-chloropyridine (3.86 g, 30 mmol) was added, and the mixture was stirred for 15 min. Then, benzyl bromide (1.16 g, 68 mmol) was added, and the reaction mixture was allowed to warm slowly to room temperature. After the resulting mixture was stirred for 1 h at room temperature, water was added. DMF was evaporated, and the residue was extracted with AcOEt. The combined organic layers were washed with brine and then dried over Na_2SO_4. Concentration and purification through silica gel chromatography (hexane/AcOEt = 20/1) gave 4.36 g of the product (14 mmol, 47% yield) as colorless solids of mp 83−84 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.77 (s, 4H), 6.38 (d, J = 9.1 Hz, 1H), 7.20−7.22 (m, 4H), 7.24−7.26 (m, 2H), 7.29−7.32 (m, 5H), 8.12−8.13 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.2 (CH_2), 106.7 (CH), 119.2 (C), 127.0 (CH), 127.1 (CH), 128.7 (CH), 137.1 (CH), 138.0 (C), 146.3 (CH), 157.0 (C). IR (ATR): 690, 730, 1140, 1360, 1490 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{19}H_{17}{}^{35}ClN_2$: 308.1080; found: 308.1069.

5-Butyl-2-chlorobenzofuran (4h). This compound was prepared on the basis of the previous report.[19c] To a solution of 5-butylbenzofuran[28] (888 mg, 5.1 mmol) in dry THF (27 mL) at −78 °C was added n-BuLi (1.6 M in hexane, 6.2 mmol) dropwise. After stirring for 30 min, hexachloroethane (1.21 g, 5.1 mmol) was added. The resulting mixture was warmed to room temperature over 1 h, and then saturated NH_4Cl was added. The mixture was extracted with AcOEt. The organic layers were washed with water and then dried over $MgSO_4$. Concentration and purification through silica gel chromatography (hexane/i-Pr_2O = 400/1) gave 1.04 g of the product (5.0 mmol, 98% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.93 (t, J = 7.3 Hz, 3H), 1.32−1.39 (m, 2H), 1.59−1.65 (m, 2H), 2.67 (t, J = 7.9 Hz, 2H), 6.51 (s, 1H), 7.07−7.09 (m, 1H), 7.27 (s, 1H), 7.32 (d, J = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8 (CH_3), 22.2 (CH_2), 34.1 (CH_2), 35.5 (CH_2), 103.0 (CH), 110.4 (CH), 119.5 (CH), 124.9 (CH), 128.4 (C), 138.2 (C), 141.3 (C), 152.7 (C). IR (ATR): 790, 930, 1190, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_{12}H_{13}{}^{35}ClO$: 208.0655; found: 208.0655.

3-Chlorobenzothiophene (4k). This compound was prepared on the basis of the previous report.[29] A mixture of 3-chlorobenzothiophene-2-carboxylic acid (1.70 g, 8.0 mmol), copper (254 mg, 4.0 mmol), and quinoline (19.6 g, 152 mmol) was stirred for 3 h at 150 °C. Hexane was added at room temperature, and then the copper was removed by filtration. The filtrate was washed with 6 M HCl solution, 1 M HCl solution, and brine, and then dried over $MgSO_4$. Concentration and purification through silica gel chromatography (hexane/i-Pr_2O = 400/1) gave 1.16 g of the product (6.88 mmol, 86% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): 7.31 (s, 1H), 7.40−7.44 (m, 1H), 7.45−7.49 (m, 1H), 7.83−7.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 120.7 (CH), 121.1 (C), 121.8 (CH), 122.8 (CH), 124.8 (CH), 125.3 (CH), 136.1 (C), 138.4 (C). IR (ATR): 720, 750, 1060, 1420 cm^{-1}. HRMS (EI) m/z: (M^+) calcd for $C_8H_5{}^{35}ClS$: 167.9800; found: 167.9803.

(8*R*,9*S*,13*S*,14*S*)-(+)-3-Benzyloxy-2-chloro-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]-phenanthren (6b). This compound was prepared on the basis of the previous report.[24e] To a mixture of 2-chloroestrone[30] (183 mg, 0.6 mmol) and K_2CO_3 (331 mg, 2.4 mmol) in dry acetone (3.0 mL) was

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added benzyl bromide (188 mg, 1.1 mmol). The reaction mixture was refluxed for 2 h and cooled to room temperature. The resulting mixture was filtered with CH_2Cl_2, and the filtrate was collected. Concentration and purification through silica gel chromatography (hexane/AcOEt = 8/1) gave 216 mg of the product (0.55 mmol, 91% yield) as white solids of mp 194−195 °C. $[\alpha]^{27}_D$ +116.4 (*c* 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.91 (s, 3H), 1.37−1.66 (m, 6H), 1.93−2.07 (m, 3H), 2.11−2.18 (m, 1H), 2.20−2.25 (m, 1H), 2.33−2.37 (m, 1H), 2.50 (dd, *J* = 8.1, 19.3 Hz, 1H), 2.83−2.85 (m, 1H), 5.12 (s, 2H), 6.70 (s, 1H), 7.29 (s, 1H), 7.30−7.34 (m, 1H), 7.37−7.40 (m, 2H), 7.46−7.48 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7 (CH_3), 21.4 (CH_2), 25.7 (CH_2), 26.2 (CH_2), 29.1 (CH_2), 31.3 (CH_2), 35.7 (CH_2), 37.9 (CH), 43.6 (CH), 47.8 (C), 50.2 (CH), 70.7 (CH_2), 114.4 (CH), 120.4 (C), 127.0 (CH), 127.2 (CH), 127.9 (CH), 128.5 (CH), 133.5 (C), 136.1 (C),136.8 (C), 152.0 (C), 220.7 (C). IR (ATR): 740, 1060, 1250, 1730 cm^{-1}. HRMS (EI) *m*/*z*: (M^+) calcd for $C_{25}H_{27}{}^{35}ClO_2$: 394.1700; found: 394.1686.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01609.

Table S1, ORTEP plots, charts of spectra, and HPLC chromatograms (PDF)

X-ray data for **C1** and **C2** (CIF)

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Notes

The authors declare no competing financial interest.

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