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# Base-Catalyzed H/D Exchange Reaction of Difluoromethylarenes

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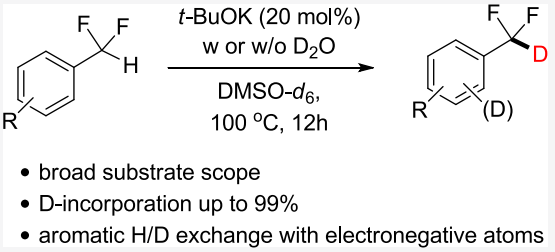
**ABSTRACT:** The budding deuteriodifluoromethyl group ($CF_2D$) is a potentially significant functional group in medicinal chemistry. Herein, we investigated *t*-BuOK-catalyzed H/D exchange reaction of difluoromethylarenes in DMSO-$d_6$ solution. The method provides excellent deuterium incorporation at the difluoromethyl group. Meanwhile, the effect of a trace amount of $D_2O$ in DMSO-$d_6$ solution on the deuteration reaction was also investigated.



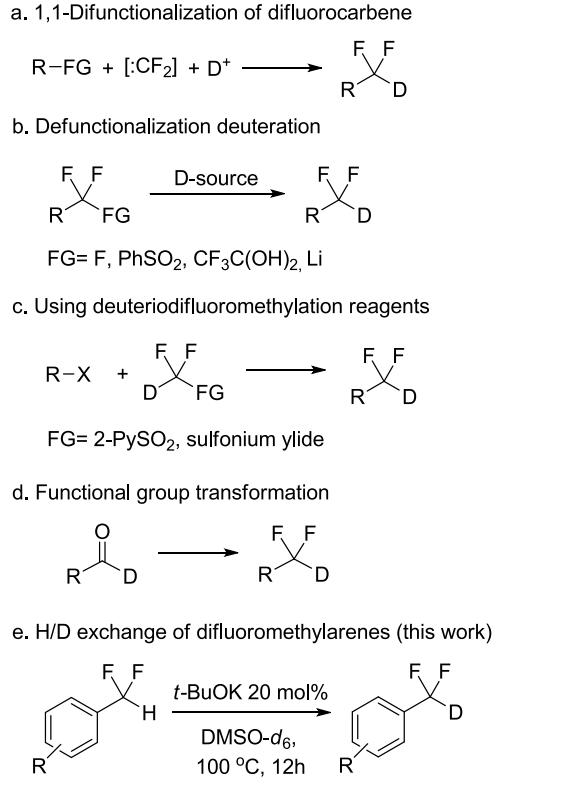

## INTRODUCTION

Deuterium-labeled compounds have substantial utilities in multiple fields, such as mechanistic study,[1] life sciences,[2] organic synthesis,[3] and optical materials.[4] Incorporation of deuterium into a molecule to generate a detection signal without changing the chemical structure, biological activity, or physical properties leads to its prevalence for further applications in the evaluation of medical materials or exploration of new biological pathways in a complicated biosystem.[5] In medicinal chemistry, deuterium incorporation has been used to modulate absorption, distribution, metabolism, and excretion (ADME) of drug candidates.[6] The first deuterated drug, deutetrabenazine (Austedo), approved by the FDA in 2017 for the treatment of Huntington's disease, seems to lead an upsurge for the development of deuterated drugs.[7]

Meanwhile, the difluoromethyl group ($CF_2H$) has received great attention in recent years[8] as its distinct biochemistry and physical properties. $CF_2H$ can serve as a H-bond donor group to establish a hydrogen-bonding reaction[9] at an active site[10] and build up the binding selectivity for biological compounds. Hence, this moiety is regarded as a possible "lipophilic bioisostere" of hydroxyl and thiol groups.[11] Meanwhile, $CF_2H$ has been introduced in drug design to alter the pharmacokinetic properties, such as membrane permeability, binding affinity, and metabolic stability.[12] This important moiety exists in many commercial pharmaceuticals, such as eflornithine, roflumilast, and bixafen.[13] In light of popular applications of deuterium and $CF_2H$ from the above descriptions, it is conceivable that the versatile and budding deuteriodifluoromethyl group ($CF_2D$) has profound significance in medical and biological fields.

To our best knowledge, present methods to synthesize deuteriodifluoromethyl compounds are limited. 1,1-Difunctionalization of difluorocarbene, in which a deuterium and another functional group can be introduced simultaneously, has been developed to give a number of deuteriodifluoromethyl molecules (Scheme 1a).[14] In addition, defunctional-

**Scheme 1. Synthetic Routes to Deuteriodifluoromethyl Compounds**

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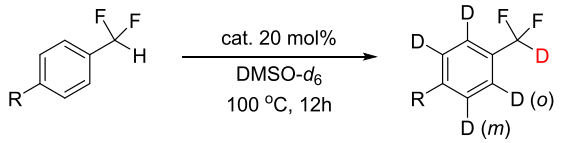
ization/deuteration of difluoromethylene compounds with α-functional groups has been reported to give deuteriodifluoromethyl complexes with moderate to high deuterium incorporation levels (Scheme 1b).[15] Furthermore, some groups have obtained deuteriodifluoromethyl compounds using deuteriodifluoromethylation regents during mechanism study (Scheme 1c).[16] Moreover, functional group transformation of deuterated precursors can also afford deuteriodifluoromethyl compounds (Scheme 1d).[17] Unfortunately, these methods have limitations of preinstallation of functional groups, low yields, or low deuteration levels.

On the other hand, H/D exchange reactions have been recognized as the most versatile way to introduce deuterium into complex molecules, especially drug molecules.[2a,18] However, the direct H/D exchange reaction of difluoromethyl compounds has been rarely investigated. It is reported that the C−H bond of $CF_2H$ on difluoromethylarenes ($ArCF_2H$) was somewhat acidic.[19] No reactions occurred in the $KN(SiMe_3)_2$/THF system,[19c] whereas LDA readily deprotonated these complexes with subsequently undesirable α-defluorination.[15f,20] Mikami et al. tried H/D exchange of $ArCF_2H$ under the condition of $K_3PO_4$/toluene/$D_2O$ unsuccessfully.[21] Lippard and co-workers reported a specific H/D exchange reaction of *o*-nitro-difluorotoluene in the $Me_4N^+OH^-$/$D_2O$/DMSO-$d_6$ system.[9b] However, the deuterium incorporation and yield were not given. Herein, we report *t*-BuOK-catalyzed H/D exchange reaction of $ArCF_2H$ in DMSO-$d_6$ solution (Scheme 1e). This reaction achieved high levels of deuterium incorporation with various $ArCF_2H$. In most cases, excellent deuterium incorporation was obtained in dry DMSO-$d_6$. The presence of a small amount of $D_2O$ would decrease the deuterated levels but increase the selectivity sometimes. It was noteworthy that $D_2O$ was necessary to achieve H/D exchange of halogen-substituted $ArCF_2H$.

## RESULTS AND DISCUSSION

We initiated our study of the H/D exchange reaction with *para*-bromo-(difluoromethyl)benzene **1a** using *t*-BuOK as the catalyst in DMSO-$d_6$ at 100 °C for 12 h. However, the poor repeatability of experimental results for deuterium incorporation in $CF_2H$ possibly indicated that commercial DMSO-$d_6$ exposed to air might contain a quantity of moisture because of high hygroscopicity. To confirm our speculation, dry and $D_2O$-diluted DMSO-$d_6$ were employed in the reaction system. With dry DMSO-$d_6$, no deuterium incorporation was observed, and 20% of **1a** was consumed and converted to the unidentified complex[22] (Table 1, entry 1). When 5 μL of $D_2O$ (2.5 equiv) was employed (Table 1, entry 2), 50% deuterium incorporation of $CF_2H$ was obtained and side reactions were completely suppressed. With an increase of the quantity of $D_2O$, the deuterium incorporation of $CF_2H$ increased (Table 1, entries 3−7). After 30 μL of $D_2O$ (15 equiv) was added, 88% deuterium incorporation of $CF_2H$ with excellent yield was obtained (Table 1, entry 6). When more $D_2O$ was added, the deuterium incorporation decreased (Table 1, entry 7). Other protic additives such as MeOD and EtOD provided inferior results (Table 1, entries 8−9). When the catalyst was changed to *t*-BuONa, lower deuterium incorporation was afforded (Table 1, entries 10), but no deuterium incorporation of $CF_2H$ was detected when weaker bases or no base were used in the reaction system (Table 1, entries 11−16). Moreover, attempts involving lower reaction temperature and decreased catalyst provided lower deuterium incorporation (Table 1, entries 17 and 18). In all cases, deuteration of aromatic C−H bonds was also observed, while meta-position was deuterated in high levels. Shortening the reaction time did not increase the selectivity but lead to a decrease of deuteration level in all positions (Table 1, entries 19 and 20). Unfortunately, the optimized reaction conditions were unsuitable for *para*-methoxy-(difluoromethyl)benzene **1b**, and only 40% deuterium incorporation was obtained (Table 1, entry 21).

**Table 1. Optimization of the Reaction Conditions**[a]




R= Br **1a**
R= OMe **1b**

**2a/2b**

| entries | catalysts (equiv) | solvents | additives (μL) | D% of $CF_2H$[b] | D% of Ar-H(*o*/*m*)[b] | yields[b] |
|---|---|---|---|---|---|---|
| 1 | *t*-BuOK | DMSO-$d_6$ | | 0 | 0 | 80 |
| 2 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (5) | 50 | 0/39 | >95 |
| 3 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (10) | 64 | 30/64 | >95 |
| 4 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (15) | 76 | 41/80 | >95 |
| 5 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (20) | 88 | 54/91 | >95 |
| 6 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (30) | 88 | 58/90 | >95 |
| 7 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (50) | 84 | 47/93 | >95 |
| 8 | *t*-BuOK | DMSO-$d_6$ | MeOD (30) | 48 | 44/72 | 85 |
| 9 | *t*-BuOK | DMSO-$d_6$ | EtOD (30) | 36 | 36/70 | 80 |
| 10 | *t*-BuONa | DMSO-$d_6$ | $D_2O$ (30) | 80 | 50/87 | >95 |
| 11 | *t*-BuOLi | DMSO-$d_6$ | $D_2O$ (30) | 0 | 0 | >95 |
| 12 | $Cs_2CO_3$ | DMSO-$d_6$ | $D_2O$ (30) | 10 | 0 | >95 |
| 13 | $K_2CO_3$ | DMSO-$d_6$ | $D_2O$ (30) | 0 | 0 | >95 |
| 14 | $KHCO_3$ | DMSO-$d_6$ | $D_2O$ (30) | 0 | 0 | >95 |
| 15 | LiOH | DMSO-$d_6$ | $D_2O$ (30) | 0 | 0 | >95 |
| 16 | | DMSO-$d_6$ | $D_2O$ (30) | 0 | 0 | >95 |
| 17[c] | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (30) | 79 | 52/81 | >95 |
| 18[d] | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (30) | 80 | 50/88 | >95 |
| 19[e] | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (30) | 73 | 42/79 | >95 |
| 20[f] | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (30) | 58 | 30/72 | >95 |
| 21 | *t*-BuOK | DMSO-$d_6$ | $D_2O$ (30) | 40 | 10/23 | >95 |
| 22 | *t*-BuOK | DMSO-$d_6$ | | 99 | 25/87 | >95 |

[a]Reaction conditions: **1a** (0.1 mmol) for entries 1−20, **1b** (0.1 mmol) for entries 21 and 22, catalysts (20 mol %), and DMSO-$d_6$ (anhydrous, 0.5 mL) in a sealed tube, 100 °C, 12 h. [b]Deuterium incorporation and NMR yields were determined by $CH_2Br_2$ as an internal standard. [c]The reaction was conducted at 80 °C. [d]10 mol % *t*-BuOK was used. [e]Reaction time, 3 h. [f]Reaction time, 1 h.



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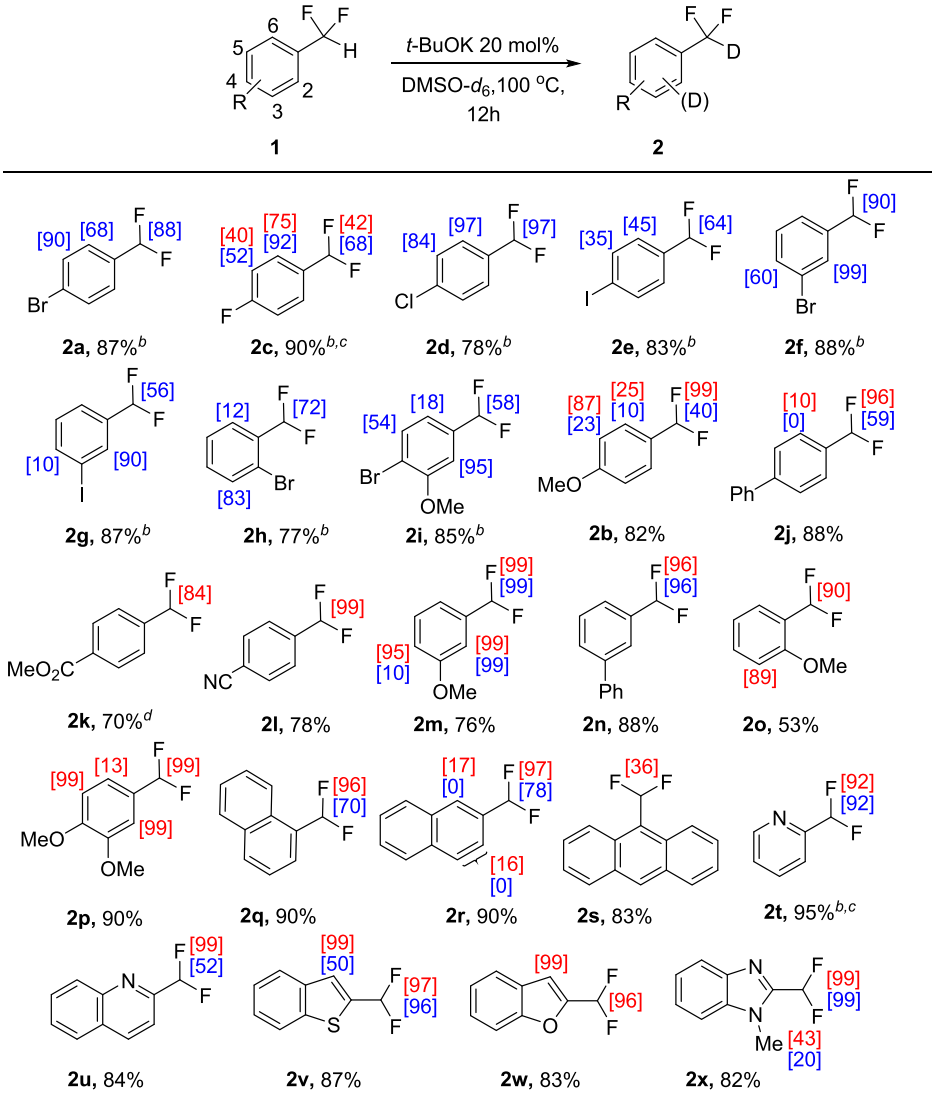
**Scheme 2. Substrate Scope for the H/D Exchange of $ArCF_2H$**[a]




[a]Standard reaction conditions: $ArCF_2H$ **1** (0.1 mmol), *t*-BuOK (20 mol %), DMSO-$d_6$ (anhydrous, 0.5 mL) in a sealed tube, 100 °C, 12 h. Isolated yields were given. Deuterium incorporation levels were determined by $^1H$ NMR spectroscopy. Deuterium incorporation with $D_2O$ (15 equiv, 30 $\mu$L) or without $D_2O$ was indicated in blue font or red font, respectively. [b]$CH_2Br_2$ was used as an internal standard for deuteration analysis. [c]NMR yield. [d]50 mol % KOMe.

Particularly, the deuterium level increased to 99% in the absence of $D_2O$ (Table 1, entry 22). In addition, the meta-position of **1b** was deuterated in 87% and the ortho-position was deuterated in 25%.[23]

With these optimized reaction conditions in hand, we investigated the substrate scope for the H/D exchange reaction (Scheme 2). For halogen-substituted substrates, the reactions were conducted in a mixture of dry DMSO-$d_6$ and $D_2O$. *para*-Halogen-substituted substrates **1a**, **1c**, **1d**, and **1f**, smoothly underwent H/D exchange with 64−97% deuterium incorporation. In the absence of $D_2O$, no deuterium incorporation was detected for **1a**, **1d**, and **1f**, while a significant decrease of deuteration level occurred for **1c**. For *meta*-halogen-substituted substrates **1f−g**, high deuterium incorporation levels were achieved both at the $CF_2H$ position and the acidic C2 position. Lower deuterium incorporation was observed for *ortho*-bromodifluoromethylbenzene **1h** due to the steric hindrance. The reaction also proceeded well for multisubstituted substrate **1i**. For other substituted substrates, the reactions were conducted in dry DMSO-$d_6$. *para*-Substituted substrates **1b** and **1j−1l** gave 84−99% deuterium incorporation and 70−88% isolated yield. *meta*-Methoxy-substituted substrate **1m** gave high deuterium incorporation at $CF_2H$, C2, and C4 positions. Only $CF_2H$ was deuterated for *meta*-phenyl-substituted substrate **1n**. *ortho*-Methoxy-substituted substrate **1o** gave high deuterium incorporation at $CF_2H$ and C3 positions. For multisubstituted substrate **1p**, deuteration occurred at $CF_2H$, C2, and C5 positions. High deuterium incorporation levels were observed for 1- and 2-difluoromethylnaphthalene, **1q** and **1r**. However, much lower deuterium incorporation levels were achieved for 9-(difluoromethyl)-anthracene **1s** due to steric hindrance. The reaction was tolerant to heterocyclic arenes, while **1t−1x** underwent the deuteration reaction with 92−99% deuterium incorporation. Addition of $D_2O$ decreased deuteration levels in both $CF_2H$ and aromatic C−H bonds and increased selectivity in some cases (**1j**, **1q**), whereas no deuteration reaction was observed for **1k**, **1l**, **1o**, **1p**, **1s**, and **1w**. In general, high deuterated incorporation levels at the



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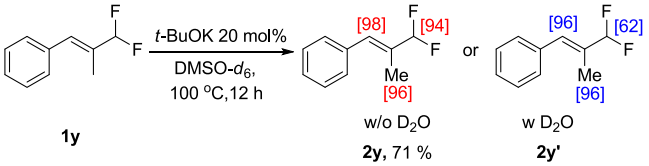
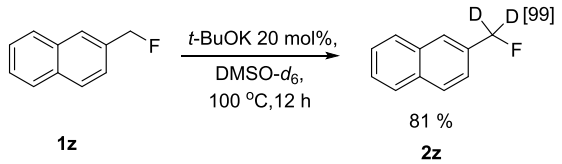
$CF_2H$ group were achieved due to the superior $CF_2$−H acidity compared with aromatic C−H bonds. Thus, good selectivity was observed in many examples. However, with electronegative-atom substituents in arenes, such as F, Cl, Br, I, and O, the acidity of aromatic C−H bonds increases significantly, resulting in deuteration at both $CF_2H$ and aromatic C−H bonds. Particularly, when a small amount of $D_2O$ were added, the basicity of the reaction solution decreased, which distinguished the difference between aromatic C−H bonds and $CF_2H$ in some cases, resulting in high selectivity (**2j**, **2q**).

Encouraged by the successful H/D exchange reaction of $ArCF_2H$, we then examined the vinyl-substituted compound **1y**. High deuterium incorporation levels were detected at $CF_2H$, vinyl C−H, and methyl groups. When $D_2O$ was added, the deuterium incorporation levels decreased to 62% at $CF_2H$ (Scheme 3). Furthermore, monofluoroarene **1z** was also applied to give excellent deuterium incorporation and yield (Scheme 4).

**Scheme 3. H/D Exchange of Vinyl-Substituted Compound 1y**



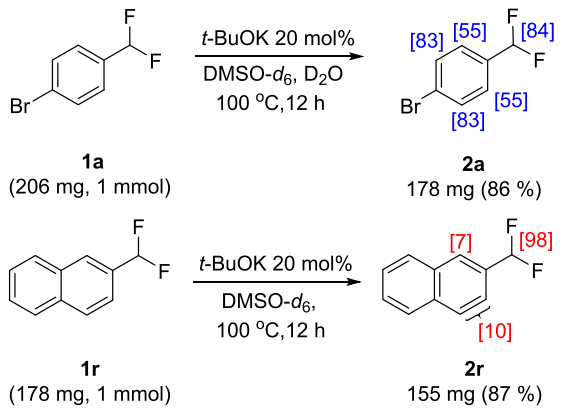

**Scheme 4. H/D Exchange of $ArCH_2F$**



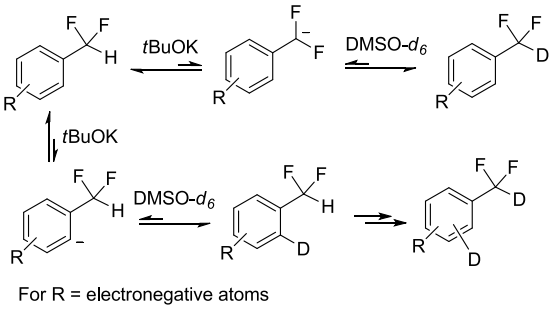

To probe the practicality of this reaction, two scale-up reactions were performed. The H/D exchange reaction of **1a** and **1r** afforded the desired products in 86% and 87% yields with slightly decreased deuteration levels (Scheme 5).

Based on the experimental results and literature reports, we proposed a plausible mechanism for the base-catalyzed H/D exchange reaction of difluoromethylarenes. *t*-BuOK/DMSO has been well recognized as the superbase system.[24] In *t*-BuOK/DMSO, the acidic $CF_2$−H bond can be deprotonated in equilibrium. Deuteriolysis by DMSO-$d_6$ gave the deuterated products. With electronegative-atom substituents in arenes, the aromatic C−H bonds can be deprotonated in equilibrium as well, resulting in deuteration at both $CF_2H$ and aromatic C−H bonds (Scheme 6).

**Scheme 5. Scale-Up Reactions of 1a and 1r**




**Scheme 6. Plausible Mechanism for the H/D Exchange Reaction in the *t*-BuOK/DMSO-$d_6$ System**




## CONCLUSIONS

In summary, we have investigated the *t*-BuOK-catalyzed H/D exchange reaction of $ArCF_2H$ in DMSO-$d_6$ solution. A number of $ArCF_2H$ with various substituents, such as methoxy, cyano, ester, halogen, and heterocycles, were studied in this reaction. In most cases, high levels of deuterium incorporation were obtained in dry DMSO-$d_6$. The presence of a small amount of $D_2O$ would decrease the deuterated levels but increase the selectivity sometimes. It is noteworthy that $D_2O$ was necessary to achieve H/D exchange of halogen-substituted $ArCF_2H$. Further, DMSO-$d_6$ was frequently used in organic reactions as a solvent and deuteration reagent without drying. We demonstrated here the dramatic influence of a trace amount of water in the base-DMSO system on basicity. Further H/D exchange reactions are currently ongoing in this area.

## EXPERIMENTAL SECTION

**General Information.** All commercial reagents were purchased from Alfa Aesar, TCI, J&K, and Energy Chemical and were used without further purification. $CH_2Cl_2$ was dried using an inert solvent purification system. DMSO-$d_6$, MeOD, and EtOD were dried and distilled prior to use according to the standard protocols and stored over molecular sieves (4 Å). Silica gel (200−300 meshes) was used for column chromatography. $^1H$, $^{13}C\{^1H\}$ NMR and $^{19}F\{^1H\}$ NMR spectra were recorded on a Bruker 400 or 600 MHz spectrometer. $CDCl_3$ and DMSO-$d_6$ were used as the NMR solvent. The solvent peak was used as a reference value, for $^1H$ NMR: $CDCl_3$ = 7.26 ppm and DMSO-$d_6$, = 2.50 ppm, for $^{13}C$ NMR: $CDCl_3$ = 77.00 ppm and DMSO-$d_6$, = 39.52 ppm. The coupling constants, *J*, are reported in hertz (Hz). Splitting patterns were denoted as s (singlet), d (doublet), t (triplet), m (multiplet), and br (broad). High-resolution mass spectra were acquired on a Thermo Q Exactive Focus Hybrid Quadrupole-Orbitrap mass spectrometer using electrospray ionization mode (ESI).

**General Procedure for Preparation of Ar-$CF_2H$.** $ArCF_2H$ was prepared according to a literature report.[25] Aldehyde (0.4 mmol, 1 equiv), diethylaminosulfur trifluoride (129.0 mg, 0.8 mmol, 2 equiv), 2 mL of $CH_2Cl_2$, and a drop of EtOH were added to an oven-dried flask under a nitrogen atmosphere. The reaction mixture was stirred under 80 °C in oil bath for 12 h under a nitrogen atmosphere. When the reaction was complete and cooled to room temperature, the reaction mixture was quenched with saturated $NaHCO_3$ (10 mL) and extracted with $CH_2Cl_2$ (10 mL × 3) three times. The organic phase was collected, dried over $Na_2SO_4$, filtered, and concentrated in vacuo.



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The crude product was purified by column chromatography (eluent: petroleum ether/ethyl acetate, 1:0 → 200:1). 2-(Fluoromethyl)-naphthalene (**1z**) was prepared according to the literature.[26]

*1-(Difluoromethyl)-3-iodobenzene (1g).* The crude mixture was purified by flash column chromatography (petroleum ether), yellow oil (303 mg, 76% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.86 (s, 1H), 7.82 (d, $J$ = 7.9 Hz, 1H), 7.48 (d, $J$ = 7.7 Hz, 1H), 7.20 (t, $J$ = 7.8 Hz, 1H), 6.58 (t, $J$ = 56.2 Hz, 1H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −111.5. $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 139.8, 136.3 (t, $^2J_{C\text{-}F}$ = 22.7 Hz), 134.6 (t, $^3J_{C\text{-}F}$ = 6.2 Hz), 130.4, 124.8 (t, $^3J_{C\text{-}F}$ = 6.0 Hz), 113.5 (t, $^1J_{C\text{-}F}$ = 240.1 Hz), 94.0. HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_7H_5FI$ 234.9414; found 234.9418.

*1-Bromo-4-(difluoromethyl)-2-methoxybenzene (1i).* The crude mixture was purified by flash column chromatography (petroleum ether), colorless oil (251 mg, 53% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.61 (d, $J$ = 8.1 Hz, 1H), 7.03 (s, 1H), 6.96 (d, $J$ = 8.1 Hz, 1H), 6.60 (t, $J$ = 56.4 Hz, 1H), 3.93 (s, 3H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −110.8. $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 155.6, 134.9 (t, $^2J_{C\text{-}F}$ = 22.5 Hz), 133.6, 118.9 (t, $^3J_{C\text{-}F}$ = 6.5 Hz), 114.5 (t, $^4J_{C\text{-}F}$ = 2.1 Hz), 114.0 (t, $^1J_{C\text{-}F}$ = 239.5 Hz), 108.6 (t, $^3J_{C\text{-}F}$ = 5.8 Hz), 56.3. HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_8H_7BrFO$ 216.9659; found 216.9657.

*(3,3-Difluoro-2-methylprop-1-en-1-yl)benzene (1y).* The crude mixture was purified by flash column chromatography (petroleum ether), colorless oil (223 mg, 66% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.42−7.40 (m, 2H), 7.36−7.32 (m, 3H), 6.73 (s, 1H), 6.12 (t, $J$ = 56.3 Hz, 1H), 2.00 (s, 3H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −114.2. $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 135.3, 131.9 (t, $^3J_{C\text{-}F}$ = 10.7 Hz), 131.1 (t, $^2J_{C\text{-}F}$ = 21.5 Hz), 129.1, 128.4, 127.9, 118.2 (t, $^1J_{C\text{-}F}$ = 236.6 Hz), 10.7. HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_{10}H_{10}F$ 149.0761; found 149.0761.

**Procedure for Preparation of 1x.** A 25 mL flask was charged with 2-(difluoromethyl)-1*H*-benzimidazole (2 mmol, 336 mg), $K_2CO_3$ (4 mmol, 552 mg), $CH_3I$ (6 mmol, 852 mg), and 5 mL of $CH_3CN$. The mixture was allowed to stir at 65 °C for 4 h. The reaction was indicated by TLC before completion. The mixture was filtered after cooled to room temperature and purified by column chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford a white solid, **1x** (321 mg, 88% yield); mp: 65−66 °C. $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.82 (d, $J$ = 8.1 Hz, 1H), 7.45−7.40 (m, 2H), 7.34 (t, $J$ = 7.5 Hz, 1H), 6.92 (t, $J$ = 52.5 Hz, 1H), 3.98 (s, 3H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −113.8. $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 144.8 (t, $^2J_{C\text{-}F}$ = 27.1 Hz), 141.7, 136.3, 124.8, 123.1, 121.1, 111.2 (t, $^1J_{C\text{-}F}$ = 237.3 Hz), 109.9, 30.5. HRMS (ESI) $m/z$: [M + H]$^+$ calcd for $C_9H_9F_2N_2$ 183.0728; found 183.0728.

**General Procedure for H/D Exchange of ArCF$_2$H.** In a 25 mL sealed tube, $ArCF_2H$ **1** (0.1 mmol, 1.0 equiv), *t*-BuOK (0.02 mmol, 0.2 equiv), and anhydrous DMSO-$d_6$ (0.5 mL) were added and stirred at 100 °C for 12 h. The reaction was cooled to room temperature, then water (5 mL) was added. The mixture was extracted with petroleum ether (5 mL × 3). The organic layers were combined, dried over $Na_2SO_4$, and filtered. The volatiles were removed in vacuo, and the crude product was purified by silica gel chromatography: petroleum ether/ethyl acetate, 1:0 → 100:1. For some specific examples, $D_2O$ (30 $\mu$L, 1.5 mmol, 15 equiv) was added to obtained high yields (for detailed information, see the text).

(**2a**) Purified by flash column chromatography (petroleum ether), colorless oil (18 mg, 87% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.59 (d, $J$ = 8.3 Hz, 0.20H), 7.38 (s, 0.64H), 6.61 (t, $J$ = 56.3 Hz, 0.12H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −111.8 (t, $J$ = 8.8 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 133.2 (t, $^2J_{C\text{-}F}$ = 22.6 Hz), 131.6 (t, $J_{C-D}$ = 25.7 Hz), 127.1,126.8 (tt, $J_{C-D}$ = 24.9 Hz, $^3J_{C\text{-}F}$ = 6.0 Hz), 113.8 (tt, $^1J_{C\text{-}F}$ = 236.5 Hz, $J_{C-D}$ = 28.4 Hz). HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_7D_3BrF$ 191.9867; found 191.9875.

(**2b**) Purified by flash column chromatography (petroleum ether), colorless oil (13 mg, 82% yield). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.44 (d, $J$ = 8.4 Hz, 1.50H), 6.96 (d, $J$ = 8.9 Hz, 0.26H), 3.84 (s, 3H); $^{19}$F{$^1$H} NMR (375 MHz, $CDCl_3$): $\delta$ −109.0 (t, $J$ = 9.0 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 161.3, 127.0 (t, $^3J_{C\text{-}F}$ = 5.9 Hz), 126.6 (t, $^2J_{C\text{-}F}$ = 22.5 Hz), 114.6 (tt, $^1J_{C\text{-}F}$ = 236.5 Hz, $J_{C-D}$ = 28.5 Hz), 113.7 (t, $J_{C-D}$ = 24.5 Hz), 55.3. HRMS (ESI) $m/z$: [M + H]$^+$ calcd for $C_8H_6D_3F_2O$ 162.0804; found 162.0801.

(**2c**) Not isolated due to high volatility, and in situ NMR data were given. $^1$H NMR (600 MHz, DMSO-$d_6$): $\delta$ 7.65 (d, $J$ = 5.0 Hz, 0.96H), 7.35 (t, $J$ = 9.0 Hz, 0.16H), 7.04 (t, $J$ = 55.8 Hz, 0.32H). $^{19}$F{$^1$H} NMR (565 MHz, DMSO-$d_6$): $\delta$ −108.5, −109.2 (t, $J$ = 9.2 Hz). $^{13}$C{$^1$H} NMR (150 MHz, DMSO-$d_6$): $\delta$ 163.4 (d, $^1J_{C\text{-}F}$ = 247.8 Hz), 128.3 (tt, $^1J_{C\text{-}F}$ = 235.5 Hz, $J_{C-D}$ = 25.9 Hz), 128.3−128.2 (m), 128.1−128.0(m), 116.0−115.4(m). HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_7D_5F_2$ 132.0668; found 132.0658.

(**2d**) Purified by flash column chromatography (petroleum ether), colorless oil (13 mg, 78% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.45 (s, 0.32H), 7.44 (s, 0.06H), 6.63 (t, $J$ = 56.4 Hz, 0.03H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −111.6 (t, $J$ = 8.8 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 136.7, 132.6 (t, $J_{C-D}$ = 23.1 Hz), 128.6 (t, $^2J_{C\text{-}F}$ = 25.5 Hz), 126.6 (tt, $J_{C-D}$ = 24.8 Hz, $^3J_{C\text{-}F}$ = 5.8 Hz), 113.7 (tt, $^1J_{C\text{-}F}$ = 238.0, $J_{C-D}$ = 28.8 Hz). HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_7D_5ClF$ 148.0372; found 148.0371.

(**2e**) Purified by flash column chromatography (petroleum ether), white solid (21 mg, 83% yield); mp: 37−38 °C. $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.82−7.80 (m, 1.10H), 7.25 (s, 1.3H), 6.79 (t, $J$ = 56.3 Hz, 0.36H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −112.1 (t, $J$ = 8.0 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 137.6 (t, $J_{C-D}$ = 25.6 Hz), 133.8 (t, $^2J_{C\text{-}F}$ = 22.8 Hz), 127.2 (tt, $J_{C-D}$ = 24.7 Hz, $^3J_{C\text{-}F}$ = 5.9 Hz), 113.9 (tt, $^1J_{C\text{-}F}$ = 238.4 Hz, $J_{C-D}$ = 28.5 Hz), 97.0. HRMS (ESI) $m/z$: [M − I]$^+$ calcd for $C_7D_5F_2$ 132.0668; found 132.0657.

(**2f**) Purified by flash column chromatography (petroleum ether), colorless oil (18 mg, 88% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.61 (d, $J$ = 8.0 Hz, 0.40H), 7.44 (d, $J$ = 7.7 Hz, 1H), 7.36−7.31 (m, 1H), 6.61 (t, $J$ = 56.2 Hz, 0.10H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −112.2 (t, $J$ = 8.5 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 136.2 (t, $^2J_{C\text{-}F}$ = 22.8 Hz), 133.6 (t, $J_{C-D}$ = 25.0 Hz), 130.2, 128.5 (tt, $J_{C-D}$ = 26.0 Hz, $^3J_{C\text{-}F}$ = 6.5 Hz), 124.2 (t, $^3J_{C\text{-}F}$ = 6.0 Hz), 122.5, 113.3 (tt, $^1J_{C\text{-}F}$ = 238.8 Hz, $J_{C-D}$ = 28.5 Hz). HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_7H_2D_3BrF$ 189.9741; found 189.9746.

(**2g**) Purified by flash column chromatography (petroleum ether), colorless oil (22 mg, 87% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.86 (s, 0.10H), 7.82 (d, $J$ = 7.9 Hz, 0.90H), 7.48 (d, $J$ = 7.7 Hz, 1H), 7.20 (t, $J$ = 7.7 Hz, 1H), 6.58 (t, $J$ = 56.2 Hz, 0.44H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −112.1 (t, $J$ = 8.7 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 139.8, 136.2 (t, $^2J_{C\text{-}F}$ = 22.7 Hz), 134.3 (tt, $J_{C-D}$ = 25.8 Hz, $^3J_{C\text{-}F}$ = 6.2 Hz), 130.4, 124.8 (t, $^3J_{C\text{-}F}$ = 6.0 Hz), 113.2 (tt, $^1J_{C\text{-}F}$ = 238.9, $J_{C-D}$ = 28.6 Hz), 93.9. HRMS (ESI) $m/z$: [M + H]$^+$ calcd for $C_7H_4D_2F_2I$ 256.9602; found 256.9601.

(**2h**) Purified by flash column chromatography (petroleum ether), colorless oil (16 mg, 77% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.67 (d, $J$ = 7.7 Hz, 0.88H), 7.61 (d, $J$ = 8.0 Hz, 0.17H), 7.43 (t, $J$ = 7.5 Hz, 1H), 7.34 (d, $J$ = 7.2 Hz, 1H), 6.92 (t, $J$ = 54.9 Hz, 0.28H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −115.3 (t, $J$ = 8.3 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 133.2 (t, $^2J_{C\text{-}F}$ = 25.4 Hz), 132.8 (t, $J_{C-D}$ = 25.4 Hz), 132.0, 127.8, 127.2 (t, $^3J_{C\text{-}F}$ = 6.1 Hz), 121.5 (t, $^3J_{C\text{-}F}$ = 6.4 Hz), 113.5 (tt, $^1J_{C\text{-}F}$ = 237.3 Hz, $J_{C-D}$ = 28.4 Hz). HRMS (ESI) $m/z$: [M − F]$^+$ calcd for $C_7H_3D_2BrF$ 188.9679; found 188.9682.

(**2i**) Purified by flash column chromatography (petroleum ether), colorless oil (20 mg, 85% yield). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 7.61 (d, $J$ = 8.0 Hz, 0.46H), 7.03 (s, 0.05H), 6.98−6.95 (m, 0.82H), 6.61 (t, $J$ = 56.4 Hz, 0.42H), 3.93 (s, 3H). $^{19}$F{$^1$H} NMR (565 MHz, $CDCl_3$): $\delta$ −111.6 (t, $J$ = 8.7 Hz). $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$): $\delta$ 156.2, 134.8 (t, $^2J_{C\text{-}F}$ = 22.6 Hz), 133.3 (t, $J_{C-D}$ = 25.5 Hz), 118.8 (t, $^3J_{C\text{-}F}$ = 6.4 Hz), 114.4, 113.7 (tt, $^1J_{C\text{-}F}$ = 238.4 Hz, $J_{C-D}$ = 28.3 Hz), 108.4 (tt, $J_{C-D}$ = 24.5 Hz, $^3J_{C\text{-}F}$ = 5.7 Hz), 56.3. HRMS (ESI) $m/z$: [M + H]$^+$ calcd for $C_8H_5D_3BrF_2O$ 239.9909; found 239.9907.

(**2j**) Purified by flash column chromatography (petroleum ether), white solid (18 mg, 88% yield); mp 76−78 °C. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.69 (d, $J$ = 8.3 Hz, 2H), 7.65−7.57 (m, 3.80H), 7.49 (dd, $J$ = 10.2, 4.7 Hz, 2H), 7.44−7.38 (m, 1H), 6.72 (t, $J$ = 56.5 Hz, 0.04H). $^{19}$F{$^1$H} NMR (375 MHz, $CDCl_3$): $\delta$ −110.0 (t, $J$ = 8.7 Hz).


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$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): $\delta$ 143.7, 140.2, 133.2 (t, $^2J_{C-F}$ = 22.5 Hz), 128.9, 127.9, 127.5, 127.3,126.1 (t, $^3J_{C-F}$ = 5.9 Hz), 114.4 (tt, $^1J_{C-F}$ = 238.4 Hz, $J_{C-D}$ = 28.7 Hz). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{10}DF_2$ 206.0886; found 206.0881.

(**2k**) Purified by flash column chromatography (petroleum ether/ethyl acetate = 40:1), Pale-yellow solid (13 mg, 70% yield); mp: 41−42 °C. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 8.12 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 6.69 (t, *J* = 56.1 Hz, 0.16H), 3.94 (s, 3H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ −113.0 (t, *J* = 8.8 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 166.2, 138.4 (t, $^2J_{C-F}$ = 22.5 Hz), 132.3, 129.9, 125.6 (t, $^3J_{C-F}$ = 6.0 Hz), 113.7 (tt, $^1J_{C-F}$ = 238.7 Hz, $J_{C-D}$ = 28.4 Hz), 52.4. HRMS (ESI) *m/z*: $[M - F]^+$ calcd for $C_9H_7DFO_2$ 168.0566; found 168.0563.

(**2l**) Purified by flash column chromatography (petroleum ether), pale-yellow oil (13 mg, 78% yield). $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.77 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H). $^{19}F\{^1H\}$ NMR (375 MHz, $CDCl_3$): $\delta$ −113.8 (t, *J* = 8.6 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): $\delta$ 138.4 (t, $^2J_{C-F}$ = 22.9 Hz), 132.6, 126.4 (t, $^3J_{C-F}$ = 6.0 Hz), 117.8, 114.8, 113.0 (tt, $^1J_{C-F}$ = 240.7 Hz, $J_{C-D}$ = 28.8 Hz). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_8H_5DF_2N$ 155.0526; found 155.0525.

(**2m**) Purified by flash column chromatography (petroleum ether), colorless oil (12 mg, 76% yield). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.37 (d, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 0.05H), 3.84 (s, 3H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -113.4 (t, *J* = 8.6 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 159.7, 135.6 (t, $^2J_{C-F}$ = 22.3 Hz), 129.7, 117.8 (t, $^3J_{C-F}$ = 6.1 Hz), 116.3 (t, $J_{C-D}$ = 24.2 Hz), 114.3 (tt, $^1J_{C-F}$ =237.9 Hz, $J_{C-D}$ = 28.5 Hz), 110.4 (tt, $J_{C-D}$ =24.0 Hz, $^3J_{C-F}$ = 5.9 Hz), 55.4. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_8H_6D_3F_2O$ 162.0804; found 162.0798.

(**2n**) Purified by flash column chromatography (petroleum ether), colorless oil (18 mg, 88% yield). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.75 (s, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.52−7.46 (m, 3H), 7.40 (t, *J* = 7.4 Hz, 1H), 6.73 (t, *J* = 56.5 Hz, 0.04H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -111.3 (t, *J* = 8.7 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 141.9, 140.2, 134.9 (t, $^2J_{C-F}$ = 22.2 Hz), 129.5, 129.2, 128.9, 127.8, 127.2, 124.4 (t, $^3J_{C-F}$ = 5.7 Hz), 124.3 (t, $^3J_{C-F}$ = 5.7 Hz), 114.6 (tt, $^1J_{C-F}$ = 237.9 Hz, $J_{C-D}$ = 28.3 Hz). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{10}DF_2$ 206.0886; found 206.0889.

(**2o**) Purified by flash column chromatography (petroleum ether), colorless oil (10 mg, 53% yield). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.58 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 55.6 Hz, 0.10H), 6.94 (d, *J* = 8.6 Hz, 0.11H), 3.87 (s, 3H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ −116.0 (t, *J* = 8.7 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 157.2 (t, $^3J_{C-F}$ = 5.9 Hz), 131.8, 126.2 (t, $^3J_{C-F}$ = 5.8 Hz), 122.6 (t, $^2J_{C-F}$ = 22.2 Hz), 120.6, 111.3 (tt, $^1J_{C-F}$ =234.4 Hz, $J_{C-D}$ = 24.4 Hz), 110.6 (t, $J_{C-D}$ = 24.4 Hz), 55.6. HRMS (ESI) *m/z*: $[M - F]^+$ calcd for $C_8H_6D_2FO$ 141.0679; found 141.0678.

(**2p**) Purified by flash column chromatography (petroleum ether/ethyl acetate = 8:1), beige solid (17 mg, 90% yield); mp: 60−62 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.04 (s, *J* = 8.4 Hz, 0.87H), 3.91 (s, 3H), 3.90 (s, 3H). $^{19}F\{^1H\}$ NMR (375 MHz, $CDCl_3$): $\delta$ -108.9 (t, *J* = 8.6 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): $\delta$ 150.8, 149.2, 126.7 (t, $^2J_{C-F}$ = 22.7 Hz), 118.6 (t, $^3J_{C-F}$ = 6.9 Hz), 114.6 (tt, $^1J_{C-F}$ = 237.5 Hz, $J_{C-D}$ = 28.6 Hz), 110.4 (t, $J_{C-D}$ = 22.8 Hz), 107.8 (tt, $J_{C-D}$ = 24.9 Hz, $^3J_{C-F}$ = 5.3 Hz), 56.1, 56.0. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd for $C_9H_7D_3F_2NaO_2$ 214.0729; found 214.0724.

(**2q**) Purified by flash column chromatography (petroleum ether), colorless oil (17 mg, 90% yield). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 8.19 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 7.0 Hz, 1H), 7.61 (t, *J* = 7.1 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.15 (t, J = 55.2 Hz, 0.04H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -111.6 (t, *J* = 8.4 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 133.8, 131.5, 129.8, 129.5 (t, $^2J_{C-F}$ = 20.8 Hz), 128.8, 127.2, 126.4, 124.8 (t, $^3J_{C-F}$ = 8.6 Hz), 124.7, 123.6, 115.1 (tt, $^1J_{C-F}$ = 237.4 Hz, $J_{C-D}$ = 28.2 Hz). HRMS (ESI) *m/z*: $[M - F]^+$ calcd for $C_{11}H_7DF$ 160.0667; found 160.0668.

(**2r**) Purified by flash column chromatography (petroleum ether), white solid (16 mg, 90% yield); mp: 68−70 °C. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.99 (s, 0.83H), 7.96−7.88 (m, 3H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.60−7.54 (m, 1.84H). $^{19}F\{^1H\}$ NMR (375 MHz, $CDCl_3$): $\delta$ −110.5 (t, *J* = 8.7 Hz), 6.82 (t, *J* = 56.4 Hz, 0.03H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): $\delta$ 134.3, 132.6, 131.6 (t, $^2J_{C-F}$ = 22.3 Hz), 128.9, 128.5, 127.9, 127.4, 126.8, 125.9 (t, $^3J_{C-F}$ = 7.5 Hz), 122.0 (t, $^3J_{C-F}$ = 4.5 Hz), 114.7 (tt, $^1J_{C-F}$ = 237.6 Hz, $J_{C-D}$ = 28.4 Hz). HRMS (ESI) *m/z*: $[M - F]^+$ calcd for $C_{11}H_7DF$ 160.0667; found 160.0667.

(**2s**) Purified by flash column chromatography (petroleum ether), yellow solid (19 mg, 83% yield); mp: 59−60 °C. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 8.57 (s, 1H), 8.47 (d, *J* = 8.9 Hz, 2H), 8.04 (d, *J* = 8.5 Hz, 2H), 8.02 (t, *J* = 53.7 Hz, 0.64H), 7.61 (t, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.7 Hz, 2H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -107.3 (t, *J* = 8.2 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 131.5, 131.1, 129.6 (t, $^2J_{C-F}$ = 3.6 Hz), 129.2, 127.3, 125.2, 123.3, 123.2, 113.7 (tt, $^1J_{C-F}$ = 221.0 Hz, $J_{C-D}$ = 27.9 Hz). HRMS (ESI) *m/z*: $[M - F]^+$ calcd for $C_{15}H_9DF$ 210.0824; found 210.0823.

(**2t**) Not isolated due to high volatility, and in situ NMR data were given. $^1H$ NMR (600 MHz, DMSO-$d_6$): $\delta$ 8.69 (d, *J* = 4.4 Hz, 1H), 8.00 (t, *J* = 7.3 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 6.7, 5.3 Hz, 1H), 6.95 (t, *J* = 55.0 Hz, 0.08H). $^{19}F\{^1H\}$ NMR (565 MHz, DMSO-$d_6$): $\delta$ -116.0 (t, *J* = 8.7 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-$d_6$): $\delta$ 151.8 (t, $^2J_{C-F}$ = 24.7 Hz), 149.6, 137.9, 126.0, 120.45 (t, $^3J_{C-F}$ = 3.5 Hz), 113.5 (tt, $^1J_{C-F}$ = 237.0 Hz, $J_{C-D}$ = 29.4 Hz). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_6H_6F_2D$ 131.0526; found 131.0531.

(**2u**) Purified by flash column chromatography (petroleum ether/ethyl acetate = 80:1), white solid (15 mg, 84% yield); mp: 48−51 °C. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 8.31 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.78 (t, *J* = 7.1 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -114.9 (t, *J* = 8.4 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 152.7 (t, $^2J_{C-F}$ = 26.8 Hz), 147.2, 137.8, 130.3, 129.7, 128.7, 127.9, 127.7, 116.8, 114.3 (tt, $^1J_{C-F}$ = 239.6 Hz, $J_{C-D}$ = 29.0 Hz). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{10}H_7DF_2N$ 181.0682; found 181.0680.

(**2v**) Purified by flash column chromatography (petroleum ether/ethyl acetate = 100:1), white solid (16 mg, 87% yield); mp: 44−46 °C. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.89 (d, *J* = 8.9 Hz, 1H), 7.84 (d, *J* = 8.9 Hz, 1H), 7.47−7.40 (m, 2H), 6.94 (t, *J* = 55.8 Hz, 0.03H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -104.7 (t, *J* = 8.6 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 140.2, 138.3, 136.3 (t, $^2J_{C-F}$ = 25.7 Hz), 125.9, 126.1, 124.9, 124.7, 124.3 (tt, $J_{C-D}$ = 25.8 Hz, $^3J_{C-F}$ = 7.3 Hz), 111.6 (tt, $^1J_{C-F}$ = 236.5 Hz, $J_{C-D}$ = 28.8 Hz). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_9H_5D_2F_2S$ 187.0357; found 187.0366.

(**2w**) Purified by flash column chromatography (petroleum ether/ethyl acetate = 100:1), colorless oil (14 mg, 83% yield). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.65 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 55.8 Hz, 0.04H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ -117.2 (t, *J* = 8.3 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 155.2, 148.3 (t, $^2J_{C-F}$ = 29.1 Hz), 126.6, 126.1, 123.6, 122.1, 111.9, 108.4 (tt, $^1J_{C-F}$ = 235.0 Hz, $J_{C-D}$ = 28.6 Hz), 106.7 (tt, $J_{C-D}$ = 27.2 Hz, $^3J_{C-F}$ = 4.5 Hz). HRMS (ESI) *m/z*: $[M - F]^+$ calcd for $C_9H_4D_2FO$ 151.0523; found 151.0520.

(**2x**) Purified by flash column chromatography (petroleum ether/ethyl acetate = 5:1), white solid (15 mg, 82% yield); mp: 65−66 °C. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.82 (d, *J* = 8.1 Hz, 1H), 7.43−7.40 (m, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 4.00−3.90 (m, 1.72H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ −114.5 (t, *J* = 7.8 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 144.8 (t, $^2J_{C-F}$ = 27.4 Hz), 141.7, 136.3, 124.8, 123.1, 121.0, 111.0 (tt, Hz, $^1J_{C-F}$ = 206.6 Hz, $J_{C-D}$ = 29.4 Hz), 109.9, 30.5 (m). HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_9H_5D_4F_2N_2$ 187.0979; found 187.0975.

(**2y**) Purified by flash column chromatography (petroleum ether), colorless oil (12 mg, 71% yield). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.42−7.37 (m, 2H), 7.35−7.30 (m, 3H), 6.71 (s, 0.02H), 6.11 (t, *J* = 56.3 Hz, 0.04H), 2.06 (s, 0.06H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$):


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$\delta$ −114.9 (t, $J$ = 8.6 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 135.2, 131.6 (tt, $J_{C-D}$ = 24.2 Hz, $^3J_{C-F}$ = 11.0 Hz), 130.8 (t, $^2J_{C-F}$ = 22.5 Hz), 129.1, 128.4, 127.9, 117.8 (tt, $^1J_{C-F}$ = 237.8 Hz, $J_{C-D}$ = 28.5 Hz), 10.7(m). HRMS (ESI) $m/z$: $[M - F]^+$ calcd for $C_{10}H_5D_5F$ 154.1075; found 154.1076.

(**2z**) Purified by flash column chromatography (petroleum ether), ivory solid (13 mg, 81% yield); mp: 58−60 °C. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ 7.93−7.83 (m, 4H), 7.55−7.48 (m, 3H). $^{19}F\{^1H\}$ NMR (565 MHz, $CDCl_3$): $\delta$ 207.7 (quint, $J$ = 7.6 Hz). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): $\delta$ 133.5 (d, $^2J_{C-F}$ = 16.8 Hz), 133.3, 133.1, 128.5, 128.1, 127.7, 126.8 (d, $^3J_{C-F}$ = 7.4 Hz), 126.4, 126.3, 125.0 (d, $^3J_{C-F}$ = 4.6 Hz), 84.07 (dt, $^1J_{C-F}$ = 164.7 Hz, $J_{C-D}$ = 23.1 Hz). HRMS (ESI) $m/z$: $[M - F]^+$ calcd for. $C_{11}H_7D_2$ 143.0824; found 143.0824.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02827.

Copies of $^1H$, $^{13}C\{^1H\}$ NMR and $^{19}F\{^1H\}$ NMR spectra for all compounds (PDF)

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### Notes

The authors declare no competing financial interest.

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