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Metal-Free Trifluoromethylation of Aromatic and Heteroaromatic Aldehydes and Ketones

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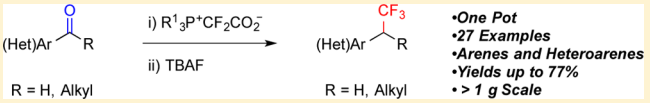
Supporting Information

ABSTRACT: The ability to convert simple and common substrates into fluoroalkyl derivatives under mild conditions remains an important goal for medicinal and agricultural chemists. One representative example of a desirable transformation involves the conversion of aromatic and heteroaromatic ketones and aldehydes into aryl and heteroaryl *β,β,β*-trifluoroethylarenes and -heteroarenes. The traditional approach for this net transformation involves stoichiometric metals and/or multistep reaction sequences that consume excessive time, material, and labor resources while providing low yields of products. To complement these traditional strategies, we report a one-pot metal-free decarboxylative procedure for accessing *β,β,β*-trifluoroethylarenes and -heteroarenes from readily available ketones and aldehydes. This method features several benefits, including ease of operation, readily available reagents, mild reaction conditions, high functional-group compatibility, and scalability.



INTRODUCTION

Recently, the synthesis of trifluoromethylated compounds has received much attention because of the great changes that the CF_3 group imparts on the physicochemical and biophysical properties of small molecules.[1] Numerous methods have been developed for the controlled incorporation of CF_3 groups into organic molecules,[2] many of which have focused on the preparation of *α,α,α*-trifluoromethylarenes and -heteroarenes.[2,3] In contrast, the ability to access other common fluorinated groups remain less well developed. For example, many *β,β,β*-trifluoroethylarenes and -heteroarenes possess medicinally relevant activity, and over 21,000 compounds bearing these substructures possess documented biological activities.[4] However, the lack of simple and general transformations to access *β,β,β*-trifluoroethylarenes and -heteroarenes limits facile access to many desired targets.

Historically, *β,β,β*-trifluoroethylarenes and -heteroarenes have been most commonly accessed from the corresponding aromatic and heteroaromatic aldehydes and ketones. This conversion generally requires a three-step sequence involving 1,2-addition of the Rupert−Prakash reagent ($TMSCF_3$),[5] functionalization of the resulting alcohol, and reduction or deoxygenation (Scheme 1A).[6] Each step of this arduous sequence requires isolation and purification of products, which diminishes the yield of final product, consumes substantial quantities of solvents and reagents, generates excessive waste, and expends an individual's time. Despite these drawbacks, this sequence still represents the most common strategy for accessing *β,β,β*-trifluoroethylarenes and -heteroarenes.[6]

Several other metal-mediated and -catalyzed strategies provide access to *β,β,β*-trifluoroethylarenes and -heteroarenes but are less commonly employed. Aryltrifluoroethanes can be accessed from benzylic electrophiles using stoichiometric Cu−CF_3 (Scheme 1B)[7] and from aryl iodides using stoichiometric Cu−CH_2CF_3" (Scheme 1C).[8] In addition, Pd-catalyzed reactions of aryl boronic acids with ICH_2CF_3 can provide *β,β,β*-trifluoroethylarenes (Scheme 1D).[9] However, few of these methods enable access to secondary trifluoromethyl products or N-containing heterocycles, the latter of which remain important for the development of therapeutic candidates and agrochemical agents. In addition, a free-radical-based C−H functionalization approach using zinc sulfonate salts can also introduce the -CH_2CF_3 group onto heteroaromatic substrates at a late stage of a synthesis (Scheme 1E).[10] However, using an innate C−H functionalization strategy, certain target molecules might be difficult to access. Therefore, the development of complementary methods to access this general substructure remains an important goal. Herein, we report a metal-free one-pot process for the trifluoromethylation of aromatic and heteroaromatic aldehydes and ketones to access privileged *β,β,β*-trifluoroethylarenes and -heteroarenes.

We sought a one-pot approach to the preparation of *β,β,β*-trifluoroethylarenes and -heteroarenes from ketones and aldehydes (Scheme 1G). Ketones and aldehydes represent attractive groups for functionalization found in many commercially available building blocks and natural products and are readily accessible by a variety of synthetic transformations. We drew inspiration from several two-step procedures involving difluoroolefination of ketones and aldehydes using Wittig reactions[11] or Julia−Kocienski reactions,[12] followed by a hydrofluorination reaction (Scheme 1F).[13] However, for "green" considerations, the ability to telescope these two reactions into a single pot process represents a desirable goal.[14]

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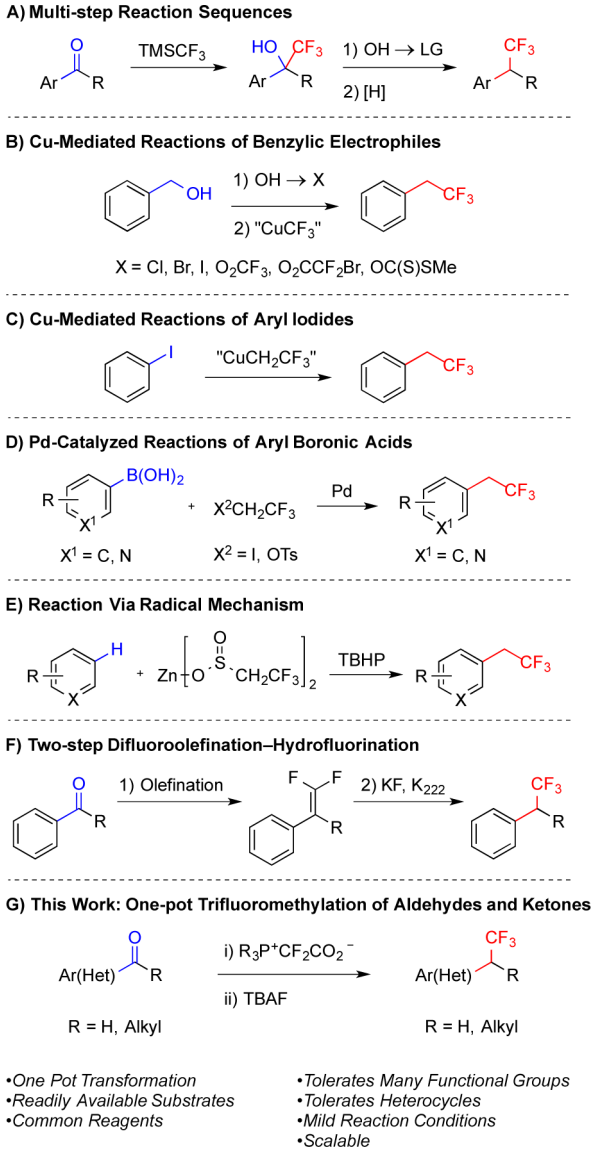
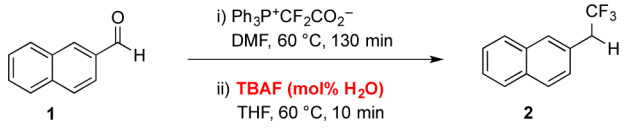
Scheme 1. Trifluoromethylation of Aryl and Heteroaryl Aldehydes and Ketones Complements Existing Methods



RESULTS AND DISCUSSION

In order to develop a practical and efficient transformation for aromatic and heteroaromatic aldehydes and ketones, we devised a one-pot difluoroolefination–hydrofluorination sequence to provide access to *β,β,β*-trifluoroethylarenes and -heteroarenes (Scheme 1G). Initially, 2-naphthaldehyde was selected as a model substrate, and quick optimization of the difluoroolefination reaction confirmed that the use of Xiao's stable $R_3P^+CF_2CO_2^-$ reagents[15] in *N,N*-dimethylformamide (DMF) at 60–100 °C provided access to the corresponding difluoroalkene. Subsequent work assessed several sources of fluoride for the hydrofluorination step of the transformation. Most commonly, hydrofluorination reactions of difluoroolefins employ metal fluorides in combination with phase-transfer catalysts (e.g., K_{222}).[16] However, the use of these reagents (KF, CsF, TBAF·3H_2O, KHF_2) in the one-pot process provided low yields of the trifluoroethylarene product in DMF. In contrast, the use of commercially available tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF), which is rarely used for this transformation, afforded good yields of product.[13b] When using

Table 1. Excess Water Decreases the Yield of *β,β,β*-Trifluoroethylarene[a]



entry	mol % H_2O	yield[b] (%)
1[c]	5.0	75
2[c]	5.2	76
3[c]	5.6	80
4[d]	8.0	75
5[c]	10.5	69
6[d]	15.0	60

[a]Reactions were performed with 0.400 mmol aldehyde, 0.800 mmol $Ph_3P^+CF_2CO_2^-$, in 1.6 mL DMF, followed by addition of 1.2 mL TBAF solution (1.0 M in THF). [b]^{19}F NMR yield using *α,α,α*-trifluorotoluene as an internal standard. [c]The content of water was determined by Karl Fischer titration. [d]The content of water was determined by adding a known quantity of deionized H_2O to the solution of TBAF employed in entry 3.

TBAF (THF), the water content of the solution was crucial for success of the reaction (Table 1). Specifically, 5–8 mol % water provided good yield of product (Table 1, entries 1–4), but increasing the water content beyond 10% decreased the yield of product (Table 1, entries 5 and 6). For all subsequent reactions, TBAF (1.0 M in THF) with 5 mol % of H_2O was employed.

The present one-pot trifluoromethylation reaction of aromatic aldehydes tolerated a broad variety of useful and important functional groups, including nitro, ester, amide, aliphatic ether, and aliphatic amine groups (Table 2). Mono-, di-, and trisubstituted aromatic aldehydes with distinct electronic characters all underwent trifluoromethylation under mild conditions (60–80 °C) and in short reaction times (<2 h). Electron-neutral and -rich substrates (Table 2, entries 5–9) typically required the use of higher temperatures and longer reaction times than substrates bearing strong electron-withdrawing groups (Table 2, entries 1–3). Using this procedure on a larger scale, 1.33 g of material could be obtained in 74% yield (Table 2, entry 7). The trifluoromethylation of polysubstituted aromatic aldehydes and an ortho-substituted aldehyde also proceeded efficiently (Table 2, entries 8–10).

Heteroaryltrifluoroethanes also represent important structural motifs found in many pharmaceutical candidates and agrochemicals,[4] and the ability to access these substructures from the respective heteroaryl aldehydes would complement other approaches.[7] To this end, a variety of heteroaromatic aldehydes were subjected to the optimized reaction conditions (Table 3). Trifluoromethylation of electron-rich heteroaryl aldehydes including 2-furan, 7-benzothiophene, 5-pyrazole, and 3-indole provided products in good yields (Table 3, entries 1–5). Reactions of electron-deficient quinoline and pyridine-based aldehydes also generated the corresponding products (Table 3, entries 6 and 7). Again, these reactions demonstrated compatibility with important protecting groups (Bn and Boc) and aryl halides (Br and Cl), all of which might be useful for further synthetic elaboration (Table 3, entries 1, 3, 4, 6, and 7). In order to further demonstrate the potential for larger-scale application of this process, a trifluoromethylation reaction of a 3-formyl indole was conducted on a 1 g scale and provided 77% yield (Table 3, entry 5). However, on this scale, each step of the reaction required slightly longer time to reach full conversion

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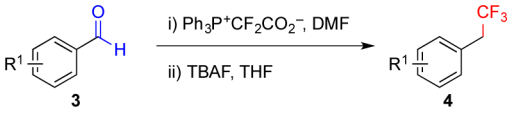
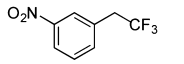
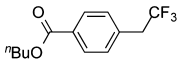
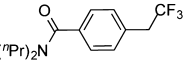
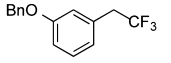
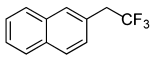
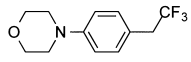
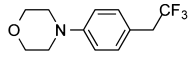
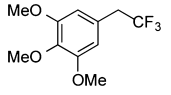
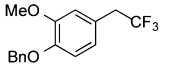
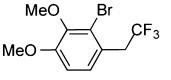
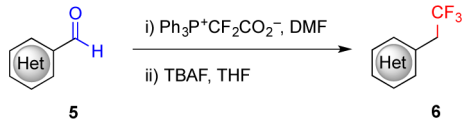
Table 2. Trifluoromethylation of Aldehydes Tolerates Many Important Functional Groups[a]

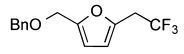
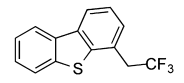
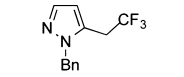
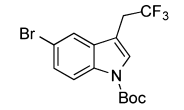
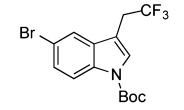
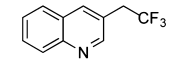
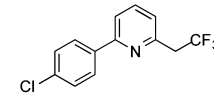


entry	1st step	2nd step	product	yield (%)[b]
1[c]	60 °C, 40 min	60 °C, 10 min		52 (45)
2[c]	60 °C, 60 min	60 °C, 10 min		61 (50)
3	60 °C, 60 min	60 °C, 10 min		67 (57)
4	60 °C, 120 min	60 °C, 10 min		67 (56)
5	60 °C, 130 min	60 °C, 10 min		76 (63)
6	60 °C, 120 min	90 °C, 120 min		83 (76)
7[d]	60 °C, 180 min	90 °C, 160 min		(74) ***1.33 g***
8	60 °C, 120 min	60 °C, 60 min		84 (68)
9	60 °C, 120 min	68 °C, 120 min		82 (72)
10[e]	80 °C, 100 min	60 °C, 10 min		78 (68)

[a]Reactions were performed with 0.400 mmol aldehyde, 0.800 mmol $Ph_3P^+CF_2CO_2^-$, in 1.6 mL DMF, followed by addition of 1.2 mL TBAF (1.0 M in THF). Times and temperatures for each step are reported in the table. [b]^{19}F NMR yield using α,α,α-trifluorotoluene as an internal standard; the number in parentheses indicates the yield. [c]5.4 mL DMF was employed. [d]Large-scale reaction, 1.33 g product was obtained. [e]0.80 mL DMF was employed.

Table 3. Trifluoromethylation of Aldehydes Tolerates Many Important Heterocycles[a]



entry	1st step	2nd step	product	yield (%)[b]
1	80 °C, 40 min	60 °C, 15 min		63 (58)
2	80 °C, 110 min	60 °C, 40 min		55 (53)
3	60 °C, 40 min	60 °C, 60 min		66 (61)
4	60 °C, 60 min	60 °C, 10 min		81 (71)
5[c]	60 °C, 80 min	60 °C, 45 min		93 (77) ***Gram Scale***
6	90 °C, 50 min	60 °C, 10 min		49 (40)
7	60 °C, 60 min	60 °C, 10 min		47 (47)

[a]Reactions were performed with 0.400 mmol aldehyde, 0.800 mmol $Ph_3P^+CF_2CO_2^-$, in 1.6 mL DMF, followed by addition of 1.2 mL TBAF (1.0 M in THF). Times and temperatures for each step are reported in the table. [b]^{19}F NMR yield using α,α,α-trifluorotoluene as an internal standard; the number in parentheses indicates the yield. [c]Reaction conducted on 1.00 g starting material.

(Table 3, entry 4 vs entry 5). Thus, this one-pot procedure enabled easy access to a variety of heteroaryl trifluoromethanes and demonstrated useful potential for drug and agrochemical applications.

Extension of the present method to trifluoromethylation reactions of aromatic and heteroaromatic ketones required thorough reoptimization, and future users of this method are encouraged to consider the attached flow diagram to assist in the optimization of their own reactions (Scheme 2). Attempts to optimize the difluoromethylenation reaction of acetophenones using $Ph_3P^+CF_2CO_2^-$ provided low yields of intermediate **8**. However, employment of a more reactive reagent, [tris(dimethylamino)phosphonio]difluoroacetate [$(Me_2N)_3P^+CF_2CO_2^-$],[15] in DMF helped overcome this problem, but the previously reported conditions provided low yields of product. Though reevaluation of the reaction conditions identified toluene (PhMe) as an optimal solvent for the difluoroolefination reaction using $(Me_2N)_3P^+CF_2CO_2^-$, although DMA also provided good yield of the difluoroalkene. Further optimization using PhMe identified lower concentration, shorter reaction time, and 100 °C as improved conditions. After successfully optimizing the first step of the transformation, efforts focused on

Scheme 2. Strategy for Troubleshooting Trifluoromethylation of Substituted Acetophenone

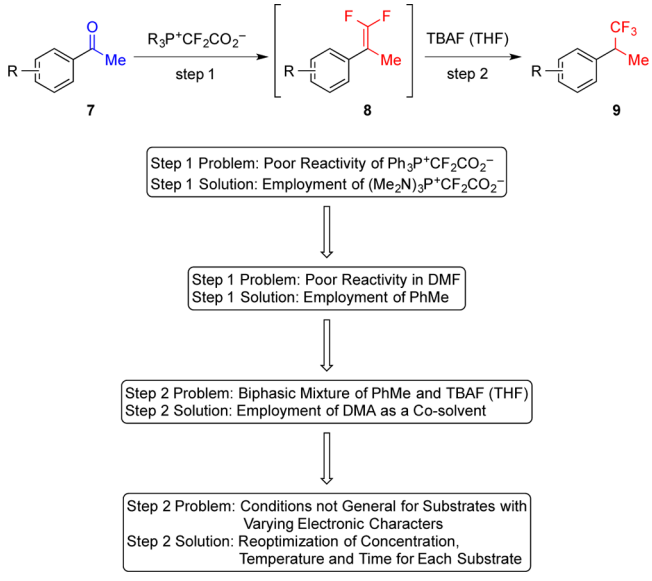


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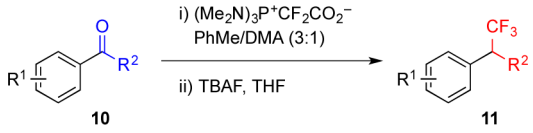
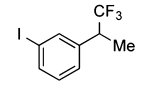
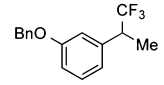
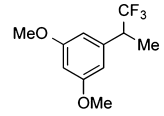
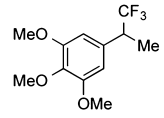
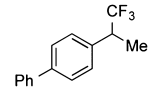
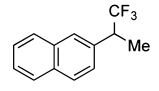
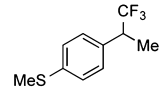
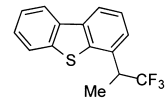
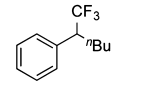
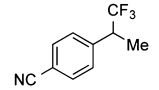
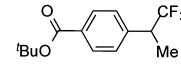
Table 4. Trifluoromethylation of Ketones Tolerates Many Important Functional Groups[a]



entry	1st step	2nd step	concentration	product	yield (%)[b]
1	100 °C, 1 h	100 °C, 2 h	0.074 M		58 (46)
2	100 °C, 1 h	100 °C, 20 h	0.25 M		70 (62)
3	100 °C, 2 h	100 °C, 14 h	0.25 M		68 (58)
4	100 °C, 2 h	100 °C, 26 h	0.50 M		67 (57)
5	100 °C, 3 h	100 °C, 30 h	0.074 M		61 (59)
6	100 °C, 3 h	100 °C, 24 h	0.074 M		62 (53)
7	100 °C, 3 h	100 °C, 30 h	0.074 M		54 (46)
8	100 °C, 1.5 h	100 °C, 24 h	0.25 M		75 (70)
9	100 °C, 3 h	100 °C, 78 h	0.50 M		42 (27)
10[c]	60 °C, 1.33 h	60 °C, 0.5 h	0.25 M		59 (46)
11[c]	60 °C, 8 h	60 °C, 1 h	0.25 M		55 (47)

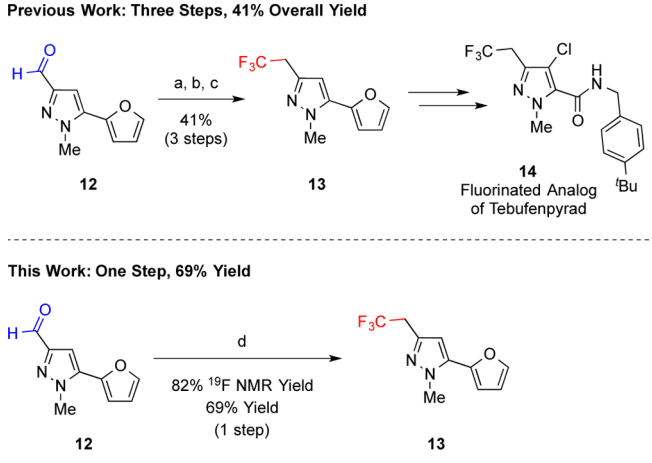
[a]Reactions were performed with 0.400 mmol aldehyde and 0.800 mmol $(Me_2N)_3P^+CF_2CO_2^-$ in PhMe/DMA (3:1), followed by addition of 1.2 mL TBAF (1.0 M in THF). Times and temperatures for each step are reported in the table. [b]^{19}F NMR yield using α,α,α-trifluorotoluene as an internal standard; the number in parentheses indicates the yield. [c]$Ph_3P^+CF_2CO_2^-$ was used instead of $(Me_2N)_3P^+CF_2CO_2^-$, DMF was used as solvent.

hydrofluorination of the difluoroolefin intermediate **8**. Evaluation of different sources and equivalents of TBAF revealed that 3 equiv of commercially available TBAF (1.0 M in THF) provided partial conversion to product. However, the biphasic combination of PhMe/TBAF/THF inhibited efficient conversion to the trifluoroethane product. In order to overcome the problem, the use of co-solvents was investigated. Specifically, studies focused on employment of PhMe/DMA (DMA also facilitated the first step of the reactions), and eventually use of a solvent mixture of PhMe/DMA (3:1) more effectively converted difluoroalkenes **8** to trifluoromethane **9**. On the basis of subsequent optimization, three parameters (concentration, temperature and solvent system) proved crucial for successful reactions, and future users of the method are encouraged to reevaluate these parameters for any particular substrate.

The one-pot trifluoromethylation reaction of ketones demonstrated high functional group tolerance, but the success of individual substrates generally required optimization of concentration and reaction time (Table 4). In general, the difluoroolefination reactions using $(Me_2N)_3P^+CF_2CO_2^-$ completed in less than 3 h at 100 °C, whereas the hydrofluorination of the difluoroalkene required extended reaction times (generally 20−30 h) at 100 °C. For the preparation of branched trifluoroethanes, extended heating did not generally decompose the final products. Electron-neutral (aromatic), inductively electron-deficient (3-iodo, 3-alkoxy), and electron-rich (3-SMe) aryl ketones readily underwent trifluoromethylation in moderate yields (Table 4, entries 1−7); however, reoptimization of the concentrations of each reaction was required to provide reasonable yields. A ketone containing a dibenzothiophene ring system also provided the trifluoromethylated product in good yield (Table 4, entry 8), and an extended chain ketone, valerophenone, also generated the desired trifluoromethylated product in lower yield, possibly because of the increased steric hindrance of the aliphatic chain (Table 4, entry 9). Finally, reactions of activated acetophenones bearing strong resonance-destabilized electron-withdrawing groups (4-CN, 4-$CO_2{}^t$Bu) did not provide product using $(Me_2N)_3P^+CF_2CO_2^-$, but the use of $Ph_3P^+CF_2CO_2^-$ at short reaction times and reduced temperature afforded moderate yields of the desired products (Table 4, entries 10 and 11). For these last two examples, reduced reaction times and decreased temperatures for both steps helped avoid decomposition of the intermediates and the products.

The proposed efficiency, functional group compatibility, and operational simplicity of the trifluoromethylation of aldehydes and ketones should provide rapid access to important target compounds. For example, the present transformation provides

Scheme 3. Improved Protocol for Trifluoromethylation of Heteroaromatic Aldehydes[a]



[a]Reagents and conditions: (a) Me_3SiCF_3, TBAF (cat.), THF, rt. (b) PhOCSCl, DMAP, PhMe, 50−60 °C. (c) Bu_3SnH, AIBN (cat.), PhMe, 80 °C. (d) (i) $Ph_3P^+CF_2CO_2^-$, DMF, 60 °C, 1 h; (ii) TBAF (1.0 M in THF), 6 h, 60 °C.

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an improved route to fluorinated compound **14**, a Tebufenpyrad analogue with acaricidal activity (Scheme 3). Previously, aldehyde **12** was converted to fluorinated intermediate **13** in 3 steps and 41% overall yield.[6a] However, using the present reaction, **13** was readily accessed in 69% yield in a one-pot transformation. Benefits of the present approach include: (1) an improved overall yield, (2) decreased operational costs associated with time and labor, (3) generation of less waste from workup and purification of multistep sequences, (4) no metal contamination, (5) operational simplicity, and (6) usage of stable and nontoxic reagents. Because of these beneficial features, this reaction should provide improved access to a wide variety of aryl and heteroaryltrifluoroethyl analogues of target molecules.

CONCLUSION

A practical one-pot protocol was developed for converting aryl and heteroaryl aldehydes and ketones into *β,β,β*-trifluoroethylarenes and -heteroarenes. This transformation should provide rapid and efficient access to fluorinated analogues of agricultural chemicals and therapeutic candidates. The benefits of the present reaction (ease of operation, mild reaction conditions, inexpensive and readily available substrates and reagents, tolerance of many functional groups and heterocycles, potential for application on larger scales) should be useful for the discovery of therapeutics and agrochemical agents.

EXPERIMENTAL SECTION

All reactions were performed under an atmosphere of dry N_2 using oven-dried glassware. Unless otherwise stated, trifluoromethylation reactions were performed in resealable 15 mL test tubes with PTFE septa. Reactions were monitored by thin-layer chromatography (TLC), visualizing by quenching of fluorescence or by use of a $KMnO_4$ stain. Flash column chromatography was performed using an automated system.

Solvents including DMF, PhMe, CH_2Cl_2, THF, CH_3CN, and MeOH were used directly from a solvent purification system in which solvent was dried by passage through two columns of activated alumina under argon. Anhydrous DMA was purchased from a commercial source and used directly from an air-free bottle. The solvents were transferred via syringe from the solvent purification system to the reaction vial. Tetrabutylammonium fluoride solution 1.0 M in THF (TBAF) was purchased from in an air-free bottle, and the water content of the solution was routinely measured to 5−6 mol % using a Karl Fischer coulometer. Unless otherwise noted, all other commercially available substrates and reagents were used without further purification.

Infrared spectra were measured using a Fourier transform infrared spectrometer. Melting points (mp, uncorrected) were measured on a capillary melting point apparatus. High-resolution mass data were recorded on a magnetic and electrostatic sector mass analyzer set to electron impact ionization mode or a quadrupole and time-of-flight tandem mass analyzer with an electrospray ion source, and all samples were prepared in MeOH. ^{1}H NMR spectra were recorded on a 400 MHz (at 400 MHz) instrument and are reported relative to the residual solvent signal ($CHCl_3$ at 7.27 ppm). ^{13}C NMR spectra were recorded on a 500 MHz (at 125 MHz) instrument and are reported relative to the solvent signal ($CDCl_3$ at 77.16 ppm). Fluorine nuclear magnetic resonance (^{19}F NMR) spectra were recorded on a 400 MHz (at 376 MHz) instrument and are reported relative to *α,α,α*-trifluorotoluene (δ = −63.72 ppm). NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, q = quartet, sept = septet, m = multiplet), and coupling constants (Hz).

Synthesis of New Substrates. 3-Benzyloxybenzaldehyde,[17] 2-bromo-3,4-dimethoxybenzaldehyde,[18] dibenzo[*b,d*]thiophen-e-4-carbaldehyde,[7k] 1-phenylmethylpyrazole-5-carboxaldehyde,[19] and 5-(furan-2-yl)-1-methyl-1*H*-yrazole-3-carbaldehyde[6a] were prepared according to known procedures.

Butyl 4-Formylbenzoate. Prepared according to the analogous procedure for the synthesis of octadecyl 4-formylbenzoate.[20] 4-Formylbenzoic acid (3.00 g, 20.0 mmol), 1-butanol (1.48 g, 20.0 mmol), DMAP (0.240 g, 2.00 mmol) and DCC (4.10 g, 20.0 mmol) were dissolved in anhydrous CH_2Cl_2 (0.050 L), and the mixture was stirred at rt for 24 h. The suspension was filtered, and the filtrate was concentrated *in vacuo*. Chromatography on silica gel (hexane/EtOAc = 90:10) produced the desired product (2.80 g, 68% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.19 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.2 Hz, 2H), 4.36 (t, J = 6.6 Hz, 2H), 1.81−1.74 (m, 2H), 1.53−1.44 (m, 2H,), 0.99 (t, J = 7.4 Hz, 3H). Spectroscopic data are consistent with the previous report.[21]

4-Formyl-N,N-dipropylbenzamide. Prepared according to the analogous procedure for the synthesis of diethyl 2,2′-(4-formylbenzoylazanediyl)diacetate.[22] $SOCl_2$ (32 mL) was added dropwise to a cooled solution of 4-formylbenzoic acid (2.00 g, 13.3 mmol) in PhMe (0.030 L) at 0 °C. The solution was refluxed for 1 h and then cooled to rt. The solvents were removed *in vacuo*, and the crude product was used immediately without further purification. A solution of dipropylamine (2.7 mL, 0.020 mol) and DIEA (9.0 mL, 52 mmol) in CH_2Cl_2 (15 mL) was added dropwise to a solution of the above acyl chloride in CH_2Cl_2 (0.040 L) at 0 °C. The solution was warmed to rt and stirred for 4 h. When TLC showed complete consumption of the acyl chloride, CH_2Cl_2 (10 mL) was added, and the organic phase was washed with 2 N HCl (2 × 80 mL) and brine (2 × 80 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by column chromatography over silica gel (hexane/EtOAc = 85:15) to afford the title compound as a colorless oil (2.24 g, 72% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.04 (s, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 3.46 (t, J = 7.6 Hz, 2H), 3.11 (t, J = 7.6 Hz, 2H), 1.69 (sept, J = 7.5 Hz, 2H), 1.52 (sept, J = 7.4 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H), 0.73 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 191.8, 170.5, 143.2, 136.6, 130.0, 127.2, 50.7, 46.5, 22.0, 20.8, 11.5, 11.1; HRMS (ESI, m/z) calcd for $C_{14}H_{19}NO_2Na$ $[M + Na]^+$ 256.1313, found 256.1327; IR (film) υ = 3060, 2964, 2933, 2873, 2837, 2731, 1629, 1608, 1506, 1465, 1427, 1382, 1303, 842, 831 cm^{-1}.

5-((Benzyloxy)methyl)furan-2-carbaldehyde.[23] A solution of ^{n}BuLi (2.5 M, 7.7 mL, 19 mmol) in hexane was added to a stirred solution of 2-((benzyloxy)methyl)furan[24] (2.41 g, 12.8 mmol) in dry THF (0.050 L) at −78 °C. The reaction mixture was warmed to −10 °C and stirred for 30 min. The mixture was cooled to −78 °C, and DMF (2.0 mL) was added slowly. The mixture was allowed to warm to rt and stirred for 6 h. The mixture was poured into a solution of saturated aqueous ammonium chloride (40 mL), and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The organic layer was washed sequentially with water and brine (40 mL each), dried over anhydrous Na_2SO_4, and concentrated. Chromatography on silica gel (hexane/EtOAc = 85:15) afforded the desired product (0.390 g, 14% yield) as a brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.63 (s, 1H), 7.38−7.29 (m, 5H), 7.22 (d, J = 3.5 Hz, 1H), 6.55 (d, J = 3.6 Hz, 1H), 4.62 (s, 2H), 4.58 (s, 2H). Spectroscopic data are consistent with the previous report.[25]

tert-Butyl 5-Bromo-3-formyl-1H-indole-1-carboxylate. Prepared according to the analogous procedure for the synthesis of *tert*-butyl 5,6-dibromo-3-formyl-1*H*-indole-1-carboxylate.[26] 5-Bromo-1*H*-indole-3-carbaldehyde (2.00 g, 8.90 mmol) was dissolved in THF (0.050 mL), and the solution was cooled to 0 °C. Sodium hydride (60% dispersion in mineral oil, 0.690 g, 17.3 mmol) was added in one portion, and the mixture was stirred for 30 min. After this time, a solution of di-*tert*-butyl dicarbonate (2.34 g, 14.3 mmol) in THF (0.010 mL) was added dropwise, and the reaction mixture was stirred for a further 90 min while warming to rt. When TLC showed complete consumption of the starting material, the reaction was quenched by the careful addition of water (6 mL). The mixture was diluted with ethyl acetate (30 mL), and the organic layer was washed with water (2 × 30 mL) and brine (2 × 30 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 80:20) to afford the desired product as a white solid (2.70 g, 93% yield), mp 162−163 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.06 (s, 1H), 8.45 (d,

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J = 2.0 Hz, 1H), 8.22 (s, 1H), 8.02 (d, J = 8.9 Hz, 1H), 7.51 (dd, J = 8.9, 2.0 Hz, 1H), 1.71 (s, 9H). Spectroscopic data are consistent with the previous report.[27]

6-(4-Chlorophenyl)-2-pyridinecarboxaldehyde.[28] Trifluoroacetic acid (0.709 mL, 9.30 mmol) and 4-chlorophenylboronic acid (2.18 g, 14.0 mmol) were sequentially added to a solution of 2-pyridinecarboxaldehyde (1.00 g, 9.30 mmol) in CH_2Cl_2 (46 mL). Water (28 mL) was added, followed by a solution of silver(I)nitrate (0.317 g, 1.86 mmol) in water (19 mL). Potassium persulfate (7.50 g, 27.9 mmol) was added, and the solution was stirred vigorously at rt for 6 h and monitored by TLC. The reaction was diluted with CH_2Cl_2 (30 mL) and washed with 5% sodium bicarbonate (30 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL), dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 80:20) to afford the desired product in 8% yield in a 1:1.7 ratio (C4:C6) as a pale yellow solid, mp 91−93 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.15 (s, 1H), 8.06−8.03 (m, 2H), 7.94−7.89 (m, 3H), 7.50−7.47 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 193.9, 156.8, 152.9, 138.1, 136.6, 136.0, 129.3, 128.4, 124.3, 120.1. HRMS (ESI, m/z) calcd for $C_{12}H_8ClNNaO$ $[M + Na]^+$ 240.0192, found 240.0185. IR (film) υ = 3058, 2842, 1735, 1708, 1589, 1492, 1450, 1392, 1350, 1298, 1217, 1188, 1163, 1091, 1008, 991, 867, 840, 796, 763, 688, 640, 592 cm^{-1}.

1-(3-Benzyloxy-phenyl)-ethanone. Prepared according to the analogous procedure for the synthesis of 1-(4-benzyloxy-phenyl)-ethanone.[29] K_2CO_3 (3.00 g, 22.0 mmol) and benzyl bromide (1.44 mL, 12.0 mmol) were added to a solution of 3-hydroxyacetophenone (1.50 g, 11.0 mmol) in acetone (15 mL). The resulting suspension was refluxed for 12 h and then cooled to rt. The K_2CO_3 was removed by filtration, and the acetone was removed *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with water (3 × 15 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4, and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (hexane/EtOAc = 90:10) to afford the desired product as a colorless oil (1.98 g, 79% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61−7.56 (m, 2H), 7.47−7.34 (m, 6H), 7.21−7.19 (m, 1H), 5.13 (s, 2H), 2.60 (s, 3H). Spectroscopic data are consistent with the previous report.[30]

General Procedure A. Under an atmosphere of nitrogen, a solution of methylmagnesium bromide (3.0 M in diethyl ether, 6.0 mL, 18 mmol) was added to a solution of aldehyde (12.0 mmol) in anhydrous THF (0.020 L) at 0 °C. The ice bath was removed, and the reaction was stirred for 2 h. The reaction was quenched with a solution of saturated aqueous ammonium chloride. The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 30 mL). The organic layers were combined, washed with brine (45 mL), dried over Na_2SO_4, and filtered. The solvent was removed *in vacuo*. Column chromatography afforded the intermediate alcohol.

General Procedure B. DMSO (0.030 mol, 2.1 mL) was added dropwise to a solution of oxalyl chloride (15 mmol, 1.3 mL) in CH_2Cl_2 (5.0 mL) at −78 °C. After 30 min of stirring, a solution of the intermediate alcohol (10.9 mmol) was added via syringe at −78 °C, and the reaction was stirred for an additional 30 min. Triethylamine (50 mmol, 7.0 mL) was added dropwise, and the reaction was stirred for 20 min at −78 °C. The reaction was quenched with a solution of saturated ammonium chloride (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to produce the desired ketone.

1-(3,5-Dimethoxyphenyl)ethanone. Prepared by subjection of 3,5-dimethoxybenzaldehyde to general procedure A to provide the intermediate alcohol (1.83 g, 90% yield), followed by subjection of the alcohol to the conditions described in general procedure B (1.46 g, 81% yield). Brown solid, mp 38−40 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.08 (d, J = 2.3 Hz, 2H), 6.64 (t, J = 2.3 Hz, 1H), 3.83 (s, 6H), 2.57 (s, 3H). Spectroscopic data are consistent with the previous report.[31]

1-(Dibenzo[b,d]thiophen-4-yl)ethanone. Prepared by subjection of dibenzo[b,d]thiophene-4-carbaldehyde to general procedure A to provide the intermediate alcohol (1.20 g, 97% yield), followed by subjection of the alcohol to the conditions described in general procedure B (1.10 g, 96% yield). Pale yellow solid, mp 129−131 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38 (dd, J = 7.8, 1.1 Hz, 1H), 8.20−8.17 (m, 1H), 8.10 (dd, J = 7.6, 1.1 Hz, 1H), 7.96−7.94 (m, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.54−7.47 (m, 2H), 2.79 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 197.6, 142.4, 139.3, 137.5, 133.8, 130.9, 129.2, 127.3, 126.2, 124.7, 124.24, 122.9, 121.5, 26.6; HRMS (ESI, m/z) calcd for $C_{14}H_{10}OSNa$ $[M + Na]^+$ 249.0350, found 249.0352; IR (film) υ = 3058, 3047, 2995, 1666, 1556, 1454, 1444, 1394, 1355, 1319, 798, 752 cm^{-1}.

tert-Butyl 4-Acetylbenzoate. Prepared by subjection of *tert*-butyl 4-formylbenzoate[32] to general procedure A to provide the intermediate alcohol (1.36 g, 91% yield), followed by subjection of the alcohol to the conditions described in general procedure B (1.20 g, 89% yield). White solid, mp 56−58 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.07 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 8.5 Hz, 2H), 2.65 (s, 3H), 1.62 (s, 9H). Spectroscopic data are consistent with the previous report.[33]

General Procedure C: Trifluoromethylation of Aldehydes. A 15 mL screw-top vial was charged with aldehyde (0.400 mmol), $Ph_3P^+CF_2CO_2^-$ (285 mg, 0.800 mmol) and a stir bar, sealed, evacuated and backfilled with N_2, DMF (1.6 mL) was added via syringe. The vial was placed in a 60 °C heating block, and the reaction mixture was stirred for the time indicated in Table 2 or 3 (Step 1). A solution of TBAF (1.2 mL, 1.0 M THF) was added, and the reaction mixture was stirred for the time indicated in Table 2 or 3 (Step 2). The vial was allowed to cool to rt, and the mixture was diluted with EtOAc (3 mL). α,α,α-Trifluorotoluene (49 μL, 0.40 mmol) was injected as an internal standard, and an aliquot was removed for ^{19}F NMR analysis. After determination of the ^{19}F yield, the aliquot was recombined with the reaction mixture. H_2O (6 mL) was added to the vial, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic solvents were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by automated flash chromatography to provide the desired trifluoroethylated products (Note: many of the products are volatile, and special care was taken not to evaporate lower MW compounds).

1-Nitro-3-(2,2,2-trifluoroethyl)benzene (Table 2, entry 1). General procedure C was followed using butyl 3-nitrobenzaldehyde (60.4 mg, 0.400 mmol) in DMF (5.4 mL); first step: 60 °C, 40 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane/EtOAc = 95:5) yielded the title compound as a white solid (36.9 mg, 45%), mp 43−44 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.26−8.23 (m, 1H), 8.21 (s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 3.51 (q, J = 10.4 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.9 (t, J = 10.4 Hz, 3F); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 148.5, 136.4, 132.1 (q, J = 2.8 Hz), 129.9, 125.3, 125.3 (q, J = 276.9 Hz), 123.5, 40.0 (q, J = 30.4 Hz); Spectroscopic data are consistent with the previous report.[9a,13a]

Butyl 4-(2,2,2-Trifluoroethyl)benzoate (Table 2, entry 2). General procedure C was followed using butyl 4-formylbenzoate (82.5 mg, 0.400 mmol) in DMF (5.4 mL); first step: 60 °C, 60 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane/EtOAc = 95:5) yielded the title compound as a colorless oil (52.1 mg, 50%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 7.88 Hz, 2H), 4.34 (t, J = 6.6 Hz, 2H), 3.44 (q, J = 10.7 Hz, 2H), 1.80−1.73 (m, 2H), 1.53−1.44 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.6 (t, J = 10.5 Hz, 3F); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 166.4, 135.1 (q, J = 2.9 Hz), 130.6, 130.3, 130.0, 125.6 (q, J = 276.9 Hz), 65.1, 40.3 (q, J = 29.9 Hz), 30.9, 19.4, 13.9; HRMS (ESI, m/z) calcd for $C_{13}H_{15}F_3O_2Li$ $[M + Li]^+$ 267.1184, found 267.1168; IR (film) υ = 3043, 2962, 2937, 2875, 1722, 1616, 1579, 1512, 1467, 1433, 14221, 1386, 1361, 1280, 1259, 1207, 1182, 1141, 1108, 1080, 1022, 964, 943, 912, 867, 837, 819, 763, 709, 667, 634 cm^{-1}.

N,N-Dipropyl-4-(2,2,2-trifluoroethyl)benzamide (Table 2, entry 3). General procedure C was followed using 4-formyl-*N*,*N*-dipropylbenzamide (93.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 60 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane/EtOAc = 70:30) yielded the title compound as a colorless oil (65.5 mg, 57%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37−7.35 (m, 2H), 7.32 (d, J = 8 Hz, 2H), 3.46 (t, J = 8 Hz, 2H), 3.39 (q, J = 10.7 Hz, 2H), 3.15 (t, J = 6 Hz, 2H), 1.72−1.67 (m, 2H), 1.56−1.51 (m, 2H), 0.99 (t, J = 6 Hz, 3H), 0.76 (t, J = 6 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.1 (t, J = 10.7 Hz, 3F); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ

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171.3, 137.4, 131.1 (q, J = 3.2 Hz), 130.4, 127.0, 125.7 (q, J = 276.9 Hz), 50.8, 46.4, 40.2 (q, J = 29.8 Hz), 22.0, 20.8, 11.6. 11.1; HRMS (ESI, m/z) calcd for $C_{15}H_{20}F_3NONa$ $[M + Na]^+$ 310.1389, found 310.1373; IR (film) υ = 3033, 2966, 2937, 2877, 1631, 1466, 1427, 1361, 1259, 1137, 1116, 1099, 1080, 1022, 912, 844, 818 cm^{-1}.

1-(Benzyloxy)-3-(2,2,2-trifluoroethyl)benzene (Table 2, entry 4). General procedure C was followed using 3-(benzyloxy)benzaldehyde (84.8 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 120 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (59.6 mg, 56%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.46−7.29 (m, 6H), 6.98−6.90 (m, 3H), 5.08 (s, 2H), 3.35 (q, J = 10.8 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.0 (t, J = 10.8 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 159.1, 136.9, 131.7 (q, J = 2.9 Hz), 129.8, 128.8, 128.2, 127.7, 125.9 (q, J = 276.9 Hz), 122.9, 117.1, 114.4, 70.2, 40.4 (q, J = 29.7 Hz). Spectroscopic data are consistent with the previous report.[34]

2-(2,2,2-Trifluoroethyl)naphthalene (Table 2, entry 5). General procedure C was followed using 2-naphthaldehyde (62.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 130 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane) yielded the title compound as a white solid (53.0 mg, 63%), mp 53−54 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.87−7.84 (m, 3H), 7.79 (s, 1H), 7.54−7.49 (m, 2H), 7.42 (d, J = 8.4 Hz, 1H), 3.55 (q, J = 10.8 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.8 (t, J = 10.8 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 133.4, 133.0, 129.6, 128.5, 127.9, 127.8, 127.7, 127.7, 126.6, 126.5, 126.0 (q, J = 277.0 Hz), 40.5 (q, J = 29.7 Hz). Spectroscopic data are consistent with the previous report.[34]

4-(4-(2,2,2-Trifluoroethyl)phenyl)morpholine (Table 2, entry 6). General procedure C was followed using 4-morpholinobenzaldehyde (76.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 120 min; second step: 90 °C, 120 min; workup and chromatographic purification (hexane/EtOAc = 90:10) yielded the title compound as a white solid (74.6 mg, 76%), mp 77−78 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.21 (d, J = 8.5 Hz, 2H), 6.91−6.89 (m, 2H), 3.88−3.86 (m, 4H), 3.30 (q, J = 10.9 Hz, 2H), 3.19−3.16 (m, 4H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −66.3 (t, J = 11.3 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 151.1, 131.1, 126.1 (q, J = 276.8 Hz), 121.3 (q, J = 2.9 Hz), 115.7, 67.0, 49.2, 39.5 (q, J = 29.6 Hz); HRMS (ESI, m/z) calcd for $C_{12}H_{14}F_3NONa$ $[M + Na]^+$ 268.0925, found 268.0931; IR (film) υ = 2983, 2948, 2925, 2900, 2866, 2837, 1614, 1523, 1450, 1380, 1363, 1336, 1305, 1261, 1234, 1132, 1070, 935, 923, 906, 808 cm^{-1}.

1,2,3-Trimethoxy-5-(2,2,2-trifluoroethyl)benzene (Table 2, entry 8). General procedure C was followed using 3,4,5-trimethoxybenzaldehyde (78.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 120 min; second step: 60 °C, 60 min; workup and chromatographic purification (hexane/EtOAc = 90:10) yielded the title compound as a colorless oil (68.1 mg, 68%). ^1H NMR ($CDCl_3$, 400 MHz) δ 6.50 (s, 2H), 3.87 (s, 6H), 3.86 (s, 3H), 3.31 (q, J = 10.7 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −64.9 (t, J = 9.4 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 153.4, 138.0, 125.9 (q, J = 276.8 Hz), 125.7 (q, J = 2.9 Hz), 107.4, 61.0, 56.3, 40.6 (q, J = 29.8 Hz); HRMS (ESI, m/z) calcd for $C_{11}H_{13}F_3NaO_3$ $[M + Na]^+$ 273.0714, found 273.0728; IR (film) υ = 3072, 2999, 2943, 2842, 1593, 1510, 1463, 1427, 1367, 1328, 1294, 1259, 1244, 1157, 1128, 1085, 1006, 981, 937, 902, 852, 819, 784, 709 cm^{-1}.

1-(Benzyloxy)-2-methoxy-4-(2,2,2-trifluoroethyl)benzene (Table 2, entry 9). General procedure C was followed using 4-(benzyloxy)-3-methoxybenzaldehyde (97.0 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 120 min; second step: 68 °C, 120 min; workup and chromatographic purification (hexane/EtOAc = 95:5) yielded the title compound as a white solid (85.3 mg, 72%), mp 59−60 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, J = 8.2 Hz, 2H), 7.40−7.36 (m, 2H), 7.34−7.30 (m, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.83 (s, 1H), 6.78 (d, J = 8 Hz, 1H), 5.17 (s, 2H), 3.91 (s, 3H), 3.30 (q, J = 10.8 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −63.4 (t, J = 10.8 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 149.7, 148.2, 137.1, 128.7, 128.0, 127.4, 126.0 (q, J = 276.8 Hz), 123.1 (q, J = 3.0 Hz), 122.67, 113.9, 113.8, 71.0, 56.2, 39.9 (q, J = 29.7 Hz); HRMS (ESI, m/z) calcd for $C_{16}H_{15}F_3O_2Na$ $[M + Na]^+$ 319.0922, found 319.0900; IR (film) υ = 3035, 2966, 2931, 2869, 1608, 1593, 1519, 1465, 1456, 1421, 1379, 1367, 1338, 1263, 1234, 1161, 1134, 1083, 1031, 1006, 918, 864, 833, 800, 792, 746, 698 cm^{-1}.

2-Bromo-3,4-dimethoxy-1-(2,2,2-trifluoroethyl)benzene (Table 2, entry 10). General procedure C was followed using 2-bromo-3,4-dimethoxybenzaldehyde (98.0 mg, 0.400 mmol) in DMF (0.80 mL); first step: 80 °C, 100 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane/EtOAc = 95:5) yielded the title compound as a colorless oil (81.4 mg, 68%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.11 (d, J = 8.5 Hz, 1H), 6.88 (d, J = 8.5 Hz, 1H), 3.88 (d, J = 9.1 Hz, 6H), 3.6 (q, J = 10.5 Hz, 2H). ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.5 (t, J = 10.5 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 153.6, 146.9, 126.98, 125.8 (q, J = 277.6 Hz), 123.1 (q, J = 2.7 Hz), 121.7, 111.3, 60.6, 56.2, 39.3 (q, J = 30.2 Hz); HRMS (ESI, m/z) calcd for $C_{10}H_{10}BrF_3O_2Li$ $[M + Li]^+$ 304.9976, found 304.9990; IR (film) υ = 3002, 2966, 2943, 2912, 2840, 1595, 1488, 1450, 1438, 1407, 1359, 1305, 1284, 1269, 1249, 1211, 1137, 1091, 1035, 946, 900, 817, 806, 781, 765, 680 cm^{-1}.

Experimental Procedures for Compounds in Table 3. *2-((Benzyloxy)methyl)-5-(2,2,2-trifluoroethyl)furan (Table 3, entry 1).* General procedure C was followed using 5-((benzyloxy)methyl)furan-2-carbaldehyde (86.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 80 °C, 40 min; second step: 60 °C, 15 min; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (62.7 mg, 58%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.28 (m, 5H), 6.31 (d, J = 3.2 Hz, 1H), 6.29 (d, J = 3.3 Hz, 1H), 4.56 (s, 2H), 4.47 (s, 2H), 3.47 (q, J = 10.2 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.8 (t, J = 10.2 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 152.3, 144.7 (q, J = 3.7 Hz), 137.9, 128.6, 128.1, 127.9, 124.7 (q, J = 277.0 Hz), 110.7, 110.6, 72.1, 63.9, 33.7 (q, J = 32.1 Hz); HRMS (ESI, m/z) calcd for $C_{14}H_{17}F_3NO_2$ $[M + NH_4]^+$ 288.1211, found 288.1197; IR (film) υ = 3089, 3066, 3033, 2927, 2864, 1774, 1720, 1701, 1602, 1560, 1496, 1454, 1417, 1369, 1263, 1220, 1139, 1083, 1026, 973, 892, 800, 742, 698 cm^{-1}.

4-(2,2,2-Trifluoroethyl)dibenzo[b,d]thiophene (Table 3, entry 2). General procedure C was followed using dibenzo[b,d]thiophene-4-carbaldehyde (85.0 mg, 0.400 mmol) in DMF (1.6 mL); first step: 80 °C, 110 min; second step: 60 °C, 40 min; workup and chromatographic purification (hexane) yielded the title compound as a white solid (56.5 mg, 53%), mp 100−102 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.19−8.15 (m, 2H), 7.91−7.87 (m, 1H), 7.52−7.47 (m, 3H), 7.45 (d, J = 7.4 Hz, 1H), 3.69 (q, J = 10.6 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −64.7 (t, J = 10.6 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 141.0, 138.9, 136.40, 135.9, 128.8, 127.2, 126.0 (q, J = 277.8 Hz), 125.0, 124.9, 124.8, 122.9, 122.0, 121.6, 39.5 (q, J = 30.6 Hz); HRMS (ESI, m/z) calcd for $C_{14}H_9F_3NaS$ $[M + Na]^+$ 289.0275, found 289.0271; Spectroscopic data are consistent with the previous report.[7k]

1-Benzyl-5-(2,2,2-trifluoroethyl)-1H-pyrazole (Table 3, entry 3). General procedure C was followed using 1-benzyl-1*H*-pyrazole-5-carbaldehyde (74.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 40 min; second step: 60 °C, 60 min; workup and chromatographic purification (hexane/EtOAc = 70:30) yielded the title compound as a colorless oil (58.6 mg, 61%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.57 (d, J = 2.1 Hz, 1H), 7.36−7.29 (m, 3H), 7.08−7.06 (m, 2H), 6.36 (s, 1H), 5.40 (s, 2H), 3.37 (q, J = 10.1 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.4 (t, J = 10.2 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 139.2, 136.5, 131.4 (q, J = 3.2 Hz), 129.1, 128.1, 126.7, 124.7 (q, J = 276.7 Hz), 108.4, 53.7, 31.1 (q, J = 32.2 Hz); HRMS (ESI, m/z) calcd for $C_{12}H_{11}F_3N_2$ $[M + H]^+$ 241.0953, found 241.0944; IR (film) υ = 3066, 3033, 2983, 2948, 1606, 1541, 1496, 1479, 1456, 1407, 1363, 1282, 1257, 1199, 1141, 1116, 1064, 933, 902, 838, 783, 719 cm^{-1}.

tert-Butyl 5-Bromo-3-(2,2,2-trifluoroethyl)-1H-indole-1-carboxylate (Table 3, entry 4). General procedure C was followed using *tert*-butyl 5-bromo-3-formyl-1*H*-indole-1-carboxylate (129.6 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 60 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane) yielded the title compound as a white solid (107.4 mg, 71%), mp 89−91 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, J = 7.9 Hz, 1H), 7.68 (s, 1H), 7.60 (s, 1H), 7.45 (dd, J = 8.7 Hz, 2.2 Hz, 1H), 3.46 (q, J = 10.5 Hz, 2H), 1.68 (s, 9H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.6 (t, J = 10.4 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 149.2, 134.2, 131.7, 127.8, 127.0, 125.7 (q, J = 276.8 Hz), 121.8, 116.9, 116.5, 108.8 (q, J = 3.3 Hz), 84.7,

30.4 (q, J = 31.9 Hz), 28.3; HRMS (ESI, m/z) calcd for $C_{15}H_{15}BrF_3NNaO_2$ $[M + H]^+$ 400.0136, found 400.0145; IR (film) υ = 2981, 2935, 1737, 1450, 1379, 1280, 1259, 1141, 1105, 1080, 1014, 916, 856, 842, 806, 796 cm^{-1}.

3-(2,2,2-Trifluoroethyl)quinolone (Table 3, entry 6). General procedure C was followed using quinoline-3-carbaldehyde (62.8 mg, 0.400 mmol) in DMF (1.6 mL); first step: 90 °C, 50 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane/EtOAc = 80:20) yielded the title compound as a white solid (33.8 mg, 40%), mp 64−66 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.85 (d, J = 2.4 Hz, 1H), 8.15−8.12 (m, 2H), 7.84 (dd, J = 8.2, 1.5 Hz, 1H), 7.78−7.74 (m, 1H), 7.62−7.58 (m, 1H), 3.59 (q, J = 10.5 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.7 (t, J = 10.7 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 151.7, 147.9, 137.4, 130.1, 129.5, 127.8, 127.8, 127.3, 125.6 (q, J = 276.9 Hz), 123.3 (q, J = 2.6 Hz), 38.0 (q, J = 30.4 Hz); HRMS (ESI, m/z) calcd for $C_{11}H_9F_3N$ $[M + H]^+$ 212.0687, found 212.0674; Spectroscopic data are consistent with the previous report.[34]

2-(4-Chlorophenyl)-6-(2,2,2-trifluoroethyl)pyridine (Table 3, entry 7). General procedure C was followed using 6-(4-chlorophenyl)-2-pyridinecarboxaldehyde (87.1 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 60 min; second step: 60 °C, 10 min; workup and chromatographic purification (hexane/EtOAc = 85:15) yielded the title compound as a pale white solid (51.1 mg, 47%), mp 64−66 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.99−7.96 (m, 2H), 7.77 (m, 1H), 7.68 (dd, J = 7.8, 1.1 Hz, 1H), 7.47−7.44 (m, 2H), 7.29 (t, J = 7.6 Hz, 1H), 3.69 (q, J = 10.8 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −61.7 (t, J = 10.7 Hz, 3F). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 156.3, 151.0 (q, J = 3.3 Hz), 137.7, 137.5, 135.5, 129.1, 128.4, 125.8 (q, J = 282.6 Hz), 122.9, 119.5, 43.0 (q, J = 29.2 Hz); HRMS (ESI, m/z) calcd for $C_{13}H_{10}ClF_3N$ $[M + H]^+$ 272.0454, found 272.0421; IR (film) υ = 3074, 2954, 2927, 1593, 1494, 1456, 1429, 1390, 1355, 1301, 1284, 1255, 1236, 1224, 1132, 1085, 1058, 1012, 993, 883, 852, 831, 796, 757, 717, 690, 657, 611 cm^{-1}.

General Procedure D: Trifluoromethylation of Ketones. In an N_2-filled glovebox, a 15 mL screw-top vial equipped with a stir bar was charged with ketone (0.400 mmol) and $(Me_2N)_3P^+CF_2CO_2^-$ (206 mg, 0.800 mmol). The vial was sealed with a PTFE-lined cap and transferred outside the glovebox. A solution composed of PhMe/DMA (v/v = 3:1) was added via syringe. The vial was placed in a 100 °C heating block, and the reaction mixture was stirred for the time indicated in Table 4 (Step 1). A solution of TBAF (1.2 mL, 1.0 M THF) was added, and the reaction was stirred for the time indicated in Table 4 (Step 2). The vial was allowed to cool to rt, and the mixture was diluted with EtOAc (3 mL). α,α,α-Trifluorotoluene (49 μL, 0.40 mmol) was injected as an internal standard, and an aliquot was removed for ^{19}F NMR analysis. After determination of the ^{19}F yield, the aliquot was recombined with the reaction mixture. H_2O (6 mL) was added to the vial, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic solvents were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by automated flash chromatography, to provide the desired trifluoroethylated products (Note: many of the products are volatile, and special care was taken not to evaporate lower MW compounds).

Experimental Procedures for Compounds in Table 4. *1-Iodo-3-(1,1,1-trifluoropropan-2-yl)benzene (Table 4, entry 1).* General procedure D was followed using 3′-iodoacetophenone (98.4 mg, 0.400 mmol) in PhMe/DMAc (5.4 mL, v/v = 3/1); first step: 100 °C, 1 h; second step: 100 °C, 2 h; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (55.2 mg, 46%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.69−7.67 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.13−7.09 (m, 1H), 3.41−3.33 (m, 1H), 1.50 (d, J = 8.0 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.4 (d, J = 9.0 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 138.8 (q, J = 2.5 Hz), 137.6, 137.4, 130.5, 127.9, 126.9 (q, J = 279.6 Hz), 94.5, 43.9 (q, J = 28.0 Hz), 14.7 (q, J = 2.5 Hz); HRMS (ESI, m/z) calcd for $C_9H_8F_3ILi$ $[M + Li]^+$ 306.9783, found 306.9775; IR (film) υ = 3062, 2991, 2948, 2891, 1591, 1566, 1473, 1465, 1425, 1386, 1350, 1255, 1203, 1166, 1072, 1043, 989, 885, 838, 794, 777, 703, 617, 501 cm^{-1}.

1-(Benzyloxy)-3-(1,1,1-trifluoropropan-2-yl)benzene (Table 4, entry 2). General procedure D was followed using 3′-benzyloxyacetophenone (90.6 mg, 0.400 mmol) in PhMe/DMAc (1.6 mL, v/v = 3/1); first step: 100 °C, 1 h; second step: 100 °C, 20 h; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (69.5 mg, 62%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.47−7.45 (m, 2H), 7.43−7.39 (m, 2H), 7.37−7.33 (m, 1H), 7.30−7.28 (m, 1H), 6.97−6.93 (m, 3H), 5.08 (s, 2H), 3.47−3.35 (m, 1H), 1.51 (d, J = 7.2 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.68 (d, J = 9.0 Hz, 3F). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 159.0, 138.1 (q, J = 2.1 Hz), 136.9, 129.7, 128.8, 128.2, 127.7, 127.2 (q, J = 279.7 Hz), 121.3, 115.7, 114.1, 70.2, 44.3 (q, J = 27.5 Hz), 14.8 (q, J = 2.7 Hz); HRMS (ESI, m/z) calcd for $C_{16}H_{15}F_3LiO$ $[M + Li]^+$ 287.1235, found 287.1240; IR (film) υ = 3066, 3033, 2989, 2925, 2871, 1602, 1585, 1492, 1452, 1384, 1353, 1325, 1290, 1259, 1234, 1182, 1157, 1124, 1039, 1026, 989, 925, 910, 875, 844, 781, 756, 736, 696 cm^{-1}.

1,3-Dimethoxy-5-(1,1,1-trifluoropropan-2-yl)benzene (Table 4, entry 3). General procedure D was followed using 3′,5′-dimethoxyacetophenone (72.1 mg, 0.400 mmol) in PhMe/DMAc (1.6 mL, v/v = 3/1); first step: 100 °C, 2 h; second step: 100 °C, 14 h; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (54.3 mg, 58%). ^1H NMR ($CDCl_3$, 400 MHz) δ 6.47 (d, J = 2.3 Hz, 2H), 6.43 (t, J = 2.3 Hz, 1H), 3.81 (s, 6H), 3.42−3.30 (m, 1H), 1.49 (d, J = 7.3 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.3 (d, J = 9.1 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 160.92, 138.8 (q, J = 2.1 Hz), 127.2 (q, J = 279.7 Hz), 106.9, 99.7, 55.5, 44.5 (q, J = 27.5 Hz), 14.9 (q, J = 2.5 Hz); HRMS (ESI, m/z) calcd for $C_{11}H_{14}F_3O_2$ $[M + H]^+$ 235.0946, found 235.0949; IR (film) υ = 2995, 2945, 2914, 2840, 2331, 1610, 1600, 1463, 1433, 1386, 1344, 1330, 1294, 1261, 1207, 1176, 1161, 1124, 1058, 1041, 1000, 991, 929, 837, 715 cm^{-1}.

1,2,3-Trimethoxy-5-(1,1,1-trifluoropropan-2-yl)benzene (Table 4, entry 4). General procedure D was followed using 3′,4′,5′-trimethoxyacetophenone (84.0 mg, 0.400 mmol) in PhMe/DMAc (0.80 mL, v/v = 3/1); first step: 100 °C, 2 h; second step: 100 °C, 26 h; workup and chromatographic purification (hexane/EtOAc = 85:15) yielded the title compound as a colorless oil (60.2 mg, 57%). ^1H NMR ($CDCl_3$, 400 MHz) δ 6.52 (s, 2H), 3.86 (d, J = 7.2 Hz, 9H), 3.42−3.30 (m, 1H), 1.50 (d, J = 7.4 Hz, 3H). ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.7 (d, J = 9.2 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 153.3, 137.9, 132.1 (q, J = 2.1 Hz), 127.2 (q, J = 279.7 Hz), 105.7, 61.0, 56.3, 44.5 (q, J = 27.6 Hz), 14.9 (q, J = 2.4 Hz); HRMS (ESI, m/z) calcd for $C_{12}H_{16}F_3O_3$ $[M + H]^+$ 265.1052, found 265.1039; IR (film) υ = 2983, 2941, 2840, 1733, 1593, 1510, 1463, 1423, 1334, 1261, 1242, 1172, 1153, 1130, 1083, 1002, 929, 837, 777, 711 cm^{-1}.

4-(1,1,1-Trifluoropropan-2-yl)-1,1′-biphenyl (Table 4, entry 5). General procedure D was followed using 4-acetylbiphenyl (78.5 mg, 0.400 mmol) in PhMe/DMAc (5.4 mL, v/v = 3/1); first step: 100 °C, 3 h; second step: 100 °C, 30 h; workup and chromatographic purification (hexane) yielded the title compound as a white solid (59.1 mg, 59%), mp 74−76 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.61−7.59 (m, 4H), 7.46 (t, J = 7.6 Hz, 2H), 7.42−7.35 (m, 3H), 3.55−3.43 (m, 1H), 1.56 (d, J = 7.0 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.7 (d, J = 9.1 Hz, 3F); HRMS (EI, m/z) calcd for $C_{15}H_{13}F_3$ $[M]^+$ 250.0969, found 250.0960; Spectroscopic data are consistent with the previous report.[7a]

2-(1,1,1-Trifluoropropan-2-yl)naphthalene (Table 4, entry 6). General procedure D was followed using 2-acetonaphthone (68.1 mg, 0.400 mmol) in PhMe/DMAc (5.4 mL, v/v = 3/1); first step: 100 °C, 3 h; second step: 100 °C, 24 h; workup and chromatographic purification (hexane) yielded the title compound as a white solid (47.5 mg, 53%), mp 43−45 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.87−7.84 (m, 3H), 7.80 (s, 1H), 7.54−7.49 (m, 2H), 7.46 (d, J = 8.4 Hz, 1H), 3.68−3.56 (m, 1H), 1.62 (d, J = 7.2 Hz, 3H). ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.4 (d, J = 9.6 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 134.0 (q, J = 2.1 Hz), 133.4, 133.1, 128.5, 128.1, 127.9, 127.8, 127.4 (q, J = 279.8 Hz), 126.5, 126.4, 126.2, 44.5 (q, J = 27.7 Hz), 14.9 (q, J = 2.4 Hz); HRMS (EI, m/z) calcd for $C_{13}H_{11}F_3$ $[M]^+$ 224.0813, found 224.0797; IR (film) υ = 3060, 2991, 2948, 2891, 1602, 1510, 1461, 1388, 1344, 1261, 1184, 1161, 1122, 1081, 1041, 995, 894, 858, 819, 802, 748, 682 cm^{-1}.

Methyl(4-(1,1,1-trifluoropropan-2-yl)phenyl)sulfane (Table 4, entry 7). General procedure D was followed using 4′-methylthioacetophenone (66.4 mg, 0.400 mmol) in PhMe/DMAc (5.4 mL, v/v = 3/1); first step: 100 °C, 3 h; second step: 100 °C, 30 h; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (40.5 mg, 46%). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.25 (s,

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4H), 3.46−3.34 (m, 1H), 2.49 (s, 3H), 1.50 (d, J = 7.2 Hz, 3H). ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.7 (d, J = 9.1 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 138.6, 133.2 (q, J = 2.0 Hz), 129.1, 127.2 (q, J = 279.7 Hz), 126.7, 43.8 (q, J = 27.6 Hz), 15.8, 14.6 (q, J = 2.5 Hz). HRMS (ESI, m/z) calcd for $C_{10}H_{12}F_3S$ $[M + H]^+$ 221.0612, found 221.0615; IR (film) υ = 3083, 3028, 2991, 2947, 2923, 2891, 1602, 1496, 1465, 1438, 1411, 1384, 1353, 1330, 1271, 1255, 1207, 1164, 1128, 1095, 1043, 1016, 987, 819 cm^{-1}.

4-(1,1,1-Trifluoropropan-2-yl)dibenzo[b,d]thiophene (Table 4, entry 8). General procedure D was followed using 1-(dibenzo[*b*,*d*]-thiophen-4-yl)ethanone (90.5 mg, 0.400 mmol). in PhMe/DMAc (1.6 mL, v/v = 3/1); first step: 100 °C, 1.5 h; second step: 100 °C, 24 h; workup and chromatographic purification (hexane) yielded the title compound as a white solid (78.5 mg, 70%), mp 62−64 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.18−8.13 (m, 2H), 7.90−7.88 (m, 1H), 7.53−7.48 (m, 4H), 3.87−3.75 (m, 1H), 1.67 (d, J = 7.2 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −70.9 (d, J = 11.3 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 140.5, 138.7, 136.2, 136.1, 131.4 (q, J = 2.1 Hz), 127.2, 127.3 (q, J = 280.3 Hz), 125.3, 125.2, 124.8, 122.9, 121.9, 121.4. 43.3 (q, J = 28.2 Hz), 14.7 (q, J = 2.7 Hz); HRMS (EI, m/z) calcd for $C_{15}H_{11}F_3S$ $[M]^+$ 280.0534, found 280.0523; IR (film) υ = 3064, 2991, 2947, 2920, 1463, 1456, 1444, 1407, 1348, 1259, 1180, 1164, 1128, 1095, 1064, 1033, 987, 792, 750, 725 cm^{-1}.

(1,1,1-Trifluorohexan-2-yl)benzene (Table 4, entry 9). General procedure D was followed using valerophenone (64.9 mg, 0.400 mmol) in PhMe/DMAc (1.6 mL, v/v = 3/1); first step: 100 °C, 3 h; second step: 100 °C, 78 h; workup and chromatographic purification (hexane) yielded the title compound as a colorless oil (23.4 mg, 27%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.34 (m, 3H), 7.29 (d, J = 7.7 Hz, 2H), 3.27−3.16 (m, 1H), 2.05−1.97 (m, 1H), 1.92−1.82 (m, 1H), 1.37−1.25 (m, 2H), 1.20−1.12 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −69.8 (d, J = 9.4 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 135.2 (q, J = 2.1 Hz), 129.2, 128.7, 128.2, 127.2 (q, J = 280.0 Hz), 50.2 (q, J = 26.3 Hz), 29.0, 28.5 (q, J = 2.1 Hz), 22.5, 13.9; HRMS (ESI, m/z) calcd for $C_{12}H_{19}F_3N$ $[M + NH_4]^+$ 234.1470, found 234.1483; IR (film) υ = 3091, 3068, 3035, 2958, 2937, 2875, 2864, 1496, 1469, 1456, 1377, 1365, 1321, 1259, 1163, 1124, 1093, 1074, 1027, 941, 754, 702, 686 cm^{-1}.

4-(1,1,1-Trifluoropropan-2-yl)benzonitrile (Table 4, entry 10). General procedure D was followed using 4-acetylbenzonitrile (58.0 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 1.33 h; second step: 60 °C, 0.5 h; workup and chromatographic purification (hexane/EtOAc = 95:5) yielded the title compound as a colorless oil (36.6 mg, 46%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 7.9 Hz, 2H), 3.57−3.45 (m, 1H), 1.54 (d, J = 7.2 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.4 (d, J = 9.0 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 141.7 (q, J = 2.1 Hz), 132.6, 129.5, 126.6 (q, J = 279.8 Hz), 118.5, 112.4, 44.4 (q, J = 28.0 Hz), 14.5 (q, J = 2.5 Hz); HRMS (ESI, m/z) calcd for $C_{10}H_9F_3N$ $[M + H]^+$ 200.0687, found 200.0647; IR (film) υ = 3066, 2995, 2952, 2925, 2852, 2231, 1612, 1508, 1465, 1460, 1388, 1352, 1330, 1255, 1205, 1166, 1132, 1120, 1072, 1045, 989, 846 cm^{-1}.

tert-Butyl 4-(1,1,1-Trifluoropropan-2-yl)benzoate (Table 4, entry 11). General procedure D was followed using *tert*-butyl 4-acetylbenzoate (88.1 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 8 h; second step: 60 °C, 1 h; workup and chromatographic purification (hexane/EtOAc = 96:4) yielded the title compound as a colorless oil (51.6 mg, 47%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 3.56−3.43 (m, 1H), 1.60 (s, 9H), 1.53 (d, J = 7.2 Hz, 3H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.3 (d, J = 9.1 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 165.5, 141.0 (q, J = 1.8 Hz), 132.0, 129.8, 128.5, 127.0 (q, J = 279.7 Hz), 81.3, 44.3 (q, J = 27.9 Hz), 28.3, 14.67 (q, J = 2.7 Hz); HRMS (ESI, m/z) calcd for $C_{14}H_{18}F_3O_2$ $[M + H]^+$ 275.1259, found 275.1275; IR (film) υ = 3064, 2981, 2935, 2893, 1716, 1614, 1477, 1460, 1419, 1392, 1369, 1353, 1311, 1296, 1257, 1207, 1166, 1120, 1074, 1045, 1020, 989, 860, 850, 827 cm^{-1}.

*5-(Furan-2-yl)-1-methyl-3-(2,2,2-trifluoroethyl)-1H-pyrazole (**13**).* General procedure C was followed using 5-(furan-2-yl)-1-methyl-1*H*-pyrazole-3-carbaldehyde (70.4 mg, 0.400 mmol) in DMF (1.6 mL); first step: 60 °C, 60 min; second step: 60 °C, 6 h; workup and chromatographic purification (hexane/EtOAc = 80:20) yielded the title compound as a pale yellow oil (63.5 mg, 69%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (dd, J = 1.9, 0.9 Hz, 1H), 6.57 (d, J = 3.4 Hz, 1H), 6.52−6.51 (m, 1H), 6.48 (s, 1H), 4.03 (s, 3H), 3.45 (q, J = 10.7 Hz, 2H); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −65.7 (t, J = 11.3 Hz, 3F); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 144.6, 142.9, 141.1 (q, J = 3.5 Hz), 135.5, 125.6 (q, J = 276.3 Hz), 111.6, 108.9, 105.2, 38.7, 33.8 (q, J = 31.0 Hz); HRMS (ESI, m/z) calcd for $C_{10}H_{10}F_3N_2O$ $[M + H]^+$ 231.0745, found 231.0742; IR (film) υ = 2950, 1533, 1496, 1348, 1271, 1255, 1137, 1083, 1008, 900, 885, 804, 786, 740, 667, 634 cm^{-1}. Spectroscopic data are consistent with the previous report.[6a]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H, ^{19}F, and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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