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A Continuous-Flow Protocol for Light-Induced Benzylic Fluorinations

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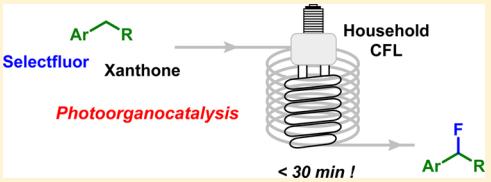
Supporting Information

ABSTRACT: A continuous-flow protocol for the light-induced fluorination of benzylic compounds is presented. The procedure uses Selectfluor as the fluorine source and xanthone as an inexpensive and commercially available photoorganocatalyst. The flow photoreactor is based on transparent fluorinated ethylene propylene tubing and a household compact fluorescent lamp. The combination of xanthone with black-light irradiation results in very efficient fluorination. Good to excellent isolated yields were obtained for a variety of substrates bearing different functional groups applying residence times below 30 min.



Incorporation of fluorine atoms to organic scaffolds has become a subject of intense research in the past few years.[1] Fluorine-enriched compounds typically exhibit enhanced biological properties and are of considerable importance in the production of agrochemicals and pharmaceuticals.[2] Compared with the dramatic development of fluorination strategies, direct selective benzylic fluorination methods have received comparatively little attention.[3] Introduction of fluorine at benzylic positions has been typically carried out by halogen exchange,[4] electrochemical methods,[5] or dehydroxyfluorination of benzyl alcohols,[6] for which two or more reaction steps and harsh, unselective reagents are required. Recently it has been shown by the groups of Grooves and Leckta that benzylic C(sp^3)−H bonds can also be selectively fluorinated under mild conditions using metal catalysts based on manganese,[7] iron,[8] or copper.[9] These reactions typically require several hours at ambient or slightly elevated temperatures. Several metal-free alternatives have also been reported,[10] using Selectfluor as the fluorine source and a suitable organocatalyst.[11,12] In this context, Chen and co-workers have recently described a simple and convenient protocol for visible-light-promoted benzylic fluorinations using diaryl ketones such as fluorenone or xanthone as photocatalysts.[12] Notably, these transformations require several hours to even a few days to reach completion for some substrates.[12] This important drawback and the problems typically associated with scaling photochemistry[13] somewhat limit the applicability of this method for large-scale preparations. In this context, we envisaged that continuous-flow technology combined with a careful optimization of the light source and reaction parameters would result in an efficient and practical fluorination protocol. It has been well-documented that microreactor/continuous-flow technology can overcome the problems associated with larger-scale photochemical transformations.[14,15] The relatively low reactor volume and in particular the high surface-to-volume ratio of capillary flow reactors assures intense and uniform irradiation of the reaction mixture for a specific time period that is very precisely controlled by the pump flow rate, thus avoiding overirradiation of the solution. Moreover, the optimized reaction conditions can be readily scaled by a simple scale-out or numbering up of the reactor.[14]

Herein we present a continuous-flow protocol for the light-induced fluorination of benzylic compounds. Our procedure utilizes xanthone as an inexpensive and commercially available photocatalyst and Selectfluor as the fluorine source. With a black-light household compact fluorescent lamp (CFL) as the photon source, the process takes places within minutes under mild conditions. The process has been successfully applied to several substrates containing benzylic positions, is scalable, and to the best of our knowledge constitutes the first example of direct benzylic fluorination under continuous-flow conditions.[16,17]

Our study commenced with a series of preliminary batch experiments to determine the most efficient catalyst and light source combination. For this purpose, the fluorination of ethylbenzene (**1a**) was selected as the model reaction (Table 1). All of the reaction mixtures were degassed prior to light exposure by purging with N_2, as the presence of oxygen inhibits the reaction (entry 1). Three different diaryl ketones (i.e., fluorenone, xanthone, and anthraquinone) were tested as catalysts (entries 2−4). Moderate conversions were observed after 2 h of light exposure (30 W cool-white CFL) in acetonitrile, with xanthone providing the best results. Other common sensitizers such as eosin or rose bengal as well as a variety of different solvents exhibited very poor performance or no reaction at all (see Table S1 in the Supporting Information). Interestingly, increasing the reaction temperature to 40 and 60 °C improved the conversion, although in the latter case several side products were observed by GC−MS, probably as a result of product decomposition after 2 h at this temperature. At this point, we turned our attention to the light source. While fluorenone has a wide UV−vis absorption band located around 400 nm, xanthone presents a maximum in the near-UV (ca. 340

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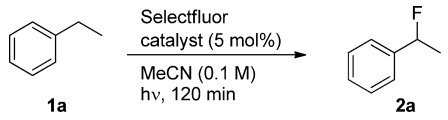
Table 1. Preliminary Batch Optimization of the Reaction Conditions for the Light-Induced Fluorination of Ethylbenzene (1a)[a,b]



entry	catalyst	equiv of Selectfluor	conv. (%)[c]	T (°C)	light source[d]
1[e]	fluorenone	2	<1	25	W
2	fluorenone	2	53	25	W
3	xanthone	2	60	25	W
4	anthraquinone	2	52	25	W
5	xanthone	2	85	40	W
6	xanthone	2	89[f]	60	W
7	fluorenone	1.2	30	25	B
8[g]	xanthone	1.2	92	25	B
9[h]	xanthone	1.2	<1	25	–

[a]Conditions: 0.2 mmol of **1a**, 2 mL of MeCN, 5 mol % catalyst. [b]Further optimization experiments are collected in Table S1 in the Supporting Information. [c]Measured by GC-FID. [d]W = 30 W cool-white lamp; B = 25 W black-light lamp. [e]The reaction mixture was not degassed. [f]Side products were observed by GC-FID. [g]Reaction time = 60 min. [h]The reaction mixture was placed in a sealed vial covered with aluminum foil, degassed, and kept at room temperature for 2 h.

nm). We therefore speculated that using black light (max. 360 nm) for these photocatalysts would have a beneficial effect. Gratifyingly, this was the case for xanthone (entry 8), and excellent conversions were obtained even when the reaction time was decreased to 1 h and the amount of Selectfluor to 1.2 equiv. Apart from the obvious advantages of decreasing the reagent stoichiometry in terms of economy and waste generation, under these conditions the reaction mixture was fully homogeneous, thus facilitating the following translation into flow. Substitution of the light source had the opposite effect for fluorenone, and only 30% conversion was observed after 2 h of irradiation (entry 7). Importantly, in the absence of light no reaction was observed, and GC-FID analysis of a reaction mixture that was kept in the dark for 2 h showed no traces of the fluorinated product (entry 9).

After the most appropriate catalyst and light source for the fluorination process were established, we decided to move forward and perform the reaction in flow. The photoreactor (Figure 1) consisted of transparent fluorinated ethylene propylene (FEP) tubing (1.6 mm inner diameter) coiled around a glass cylinder (28 mL reactor volume).[18] A commercial black light household compact fluorescent lamp (105 W) was placed inside the glass cylinder. The photoreactor

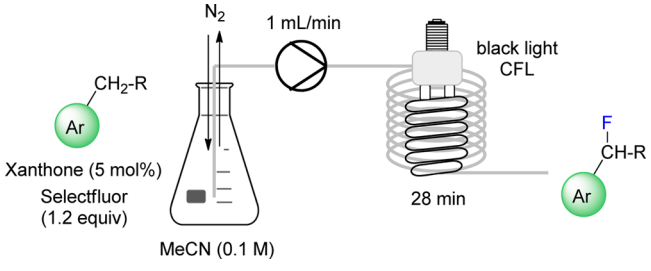


Figure 1. Schematic diagram of the continuous-flow setup employed for the light-induced fluorination of benzylic compounds.

was located inside a GC oven to enable accurate control of the temperature (see the Supporting Information for details). Both the solvent and the reaction mixture were degassed with N_2 before being pumped through the system using a commercial syringe pump (Syrris). Thus, a solution containing **1a** as a model substrate, 1.2 equiv of Selectfluor, and xanthone (5 mol %) in acetonitrile (0.1 M) was processed using this flow setup. The temperature was set to 25 °C and the pump flow rate to 1 mL min^{-1}, corresponding to a residence time of 28 min inside the photoreactor. GC-FID analysis of the crude reaction mixture revealed that 95% of the substrate had been converted into the desired 1-fluoroethylbenzene. The selectivity of the reaction was excellent, and side products were not detected in significant amounts (the corresponding GC-FID chromatogram is included as Figure S2 in the Supporting Information).

To demonstrate the general applicability of this continuous-flow protocol, a series of benzylic compounds **1a–k** were transformed into the corresponding fluorinated derivatives using the above-described conditions (Figure 2). Notably, we

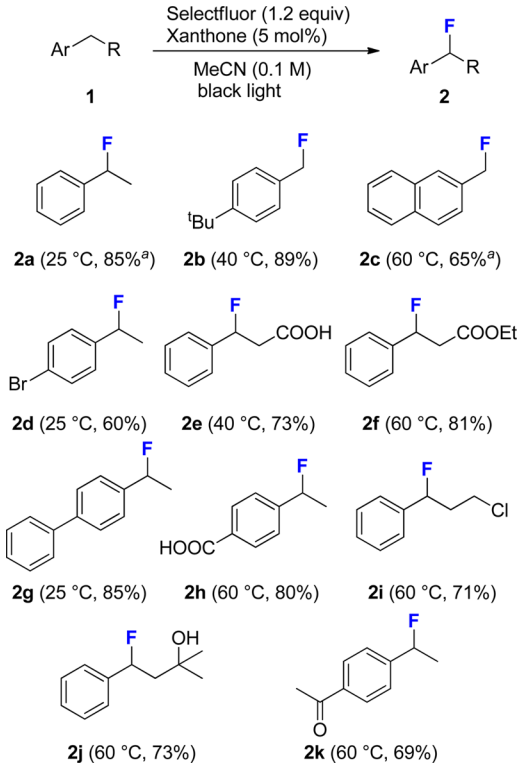


Figure 2. Continuous-flow visible-light-induced fluorination of benzylic compounds. Reactor temperatures and isolated yields are included in parentheses. [a]The yields of the volatile compounds **2a** and **2c** were determined by ^{19}F NMR spectroscopy.

were able to keep the pump flow rate (and therefore the residence time and productivity) constant by tuning the reactor temperature for each of the substrates. As described above (cf. Table 1), increased temperatures led to faster fluorinations for the model reaction, and therefore, unreactive substrates could be successfully fluorinated simply by increasing the reaction temperature.[19] Thus, a variety of benzylic substrates bearing halogen, alcohol, carboxylic acid, ester, and ketone functional groups could be fluorinated (Figure 2) with good to excellent conversions. The crude reaction mixtures obtained from the reactor output were diluted with CH_2Cl_2 and filtered through a

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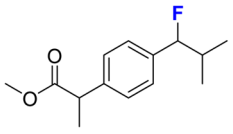
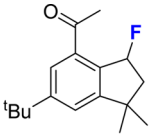
plug of silica. Evaporation of the solvent and purification by column chromatography provided the pure fluorinated products **2a**–**k** in good to excellent isolated yields.

Motivated by the good conversions and selectivities obtained, we turned our attention to two biologically active molecules with more challenging selectivity issues, namely, the anti-inflammatory ibuprofen methyl ester and the musk compound celestolide. Ibuprofen methyl ester contains two benzylic positions, and in principle a mixture of different fluorinated products could be obtained. Moderate conversions were achieved at 25 °C. Thus, the reactor temperature was set at 60 °C, and the substrate was processed using the general protocol described above. Very good selectivity (>90%) was obtained for the product **2l** fluorinated at a single position, and an isolated yield of 80% was achieved after column chromatography.



F-ibuprofen methyl ester (**2l**)



F-celestolide (**2m**)

Celestolide is a common ingredient utilized for fragrance compositions. Fluorination at 25 °C under our general conditions to give F-celestolide (**2m**) was very fast, but the product then started to decompose within minutes in the reaction mixture, ultimately leading to a mixture of several compounds. Interestingly, we observed that quenching the reaction mixture by dilution with CH_2Cl_2 followed by filtration through a plug of silica prevented the decomposition process, and the product was stable in solution for several days. The flow setup was accordingly modified by incorporating a feed of dichloromethane immediately after the photoreactor for inline dilution. Then the reaction mixture was directly collected from the output in a filter loaded with silica gel for filtration (for a detailed description of the modified flow setup, see the Supporting Information). In this way, the reaction mixture was quenched within seconds after the desired reaction time inside the photoreactor. With the modified flow reactor, a reaction mixture containing celestolide was processed at 25 °C and a flow rate of 3 mL min^{-1}, corresponding to a residence time of only ca. 9 min. Full conversion and excellent selectivity were observed for the reaction, and notably, the fluorinated product **2m** was stable in the obtained crude solution for further purification. Evaporation of the solvent and purification by chromatography yielded the desired F-celestolide **2m** (88%). Under the exact same conditions, 100 mL of the reaction mixture was processed, producing 2.3 g (87% yield) of fluorinated product, which corresponds to a productivity of ca. 0.016 mol h^{-1}.

The case of celestolide fluorination is an example highlighting the potential of continuous-flow chemistry for processes where the reaction time must be carefully controlled. Tuning of the flow rate and/or reactor volume allows very accurate control of the irradiation time as well as the application of a rapid in-line quench of the photolyzate, thus preventing product decomposition. Such reaction control is difficult to achieve in batch mode, especially when working on a larger scale, while the continuous-flow protocol can be very easily scaled as needed simply by running the reactor for longer periods.

In summary, we have developed a continuous-flow procedure for the light-induced selective fluorination of benzylic compounds. The process is based on the use of Selectfluor as the fluorine source and xanthone as the photocatalyst. The photochemical reactor has been designed using readily available materials such as transparent FEP tubing and a household CFL lamp. The combination of black light with xanthone as the catalyst resulted in very efficient fluorination. Less reactive substrates can also be successfully fluorinated by tuning the reactor temperature. Thus, several benzylic substrates could be transformed into their corresponding fluorinated derivatives in less than 30 min, including the biologically active compounds ibuprofen methyl ester and celestolide. Product decomposition in the case of the fluorinated celestolide could be avoided by installing a second feed immediately after the photoreactor for in-line dilution with CH_2Cl_2 and rapid filtration through a plug of silica. Thus, the reaction mixture could be pumped with a flow rate of 3 mL min^{-1} (ca. 9 min residence time) while obtaining full conversion and an isolated yield of 87%. This corresponds to a productivity of approximately 0.016 mol h^{-1}.

EXPERIMENTAL SECTION

General Experimental Details. ^1H NMR spectra were recorded on a 300 MHz instrument. Chemical shifts (δ) are expressed in parts per million downfield from TMS as an internal standard. The letters s, d, t, q, and m are used to indicate singlet, doublet, triplet, quadruplet, and multiplet, respectively. Analytical HPLC analysis was carried out on a C18 reversed-phase (RP) analytical column (150 mm × 4.6 mm, particle size 5 mm) at 25 °C using mobile phases A (water/acetonitrile 90:10 (v/v) + 0.1% TFA) and B (MeCN + 0.1% TFA) at a flow rate of 1.5 mL min^{-1}. The following gradient was applied: linear increase from 30% B to 100% B in 8 min, hold at 100% solution B for 2 min. GC-FID analysis was performed on a standard GC instrument with a flame ionization detector using an HP5 column (30 m × 0.250 mm × 0.025 mm). After 1 min at 50 °C, the temperature was increased in steps of 25 °C min^{-1} up to 300 °C and kept at 300 °C for 4 min. The detector gas for the flame ionization was H_2 and compressed air (5.0 quality). GC–MS monitoring was based on electron impact ionization (70 eV) using an HP/5MS column (30 m × 0.250 mm × 0.025 μm). After 1 min at 50 °C, the temperature was increased in 25 °C min^{-1} steps up to 300 °C and kept at 300 °C for 1 min. The carrier gas was helium, and the flow rate was 1.0 mL min^{-1} in constant-flow mode. HPLC-grade acetonitrile was used in all of the experiments. Selectfluor (>95% in F+ active, lot no. BCBK5355V) and xanthone (97%, lot no. 06005BOV) were purchased from Aldrich. All other chemicals were obtained from standard commercial vendors and were used without any further purification. In all of the flow experiments the lamp, was turned on at least 15 min prior use to ensure maximum and constant irradiation, and the reactor solvent container was degassed with a stream of N_2 for 1 h. All of the compounds synthesized herein are known in the literature. Proof of purity and identity was obtained by ^1H, ^{13}C , and ^{19}F NMR spectroscopy and mass spectrometry.

CAUTION: Some of the fluorinated compounds are not stable in contact with glassware when concentrated and/or decompose in $CDCl_3$ solution.[7b] Compounds **2g** and **2m** were especially sensitive to contact with glassware. Thus, during purification of these compounds, the solutions should be evaporated using suitable polymeric materials (polyethylene, PTFE). Furthermore, chromatography methods should be kept as short as possible to avoid prolonged contact with silica in all cases.

General Procedure for Continuous-Flow Benzylic Fluorination (Figure 2). Selectfluor (850 mg, 2.4 mmol, 1.2 equiv), HPLC-grade acetonitrile (10 mL), and 10 mL of a 0.01 M stock solution of xanthone (5 mol %) in the same solvent were placed into a vial covered with aluminum foil, and the mixture was sonicated in an ultrasound bath until it was completely homogeneous. The corresponding substrate **1a**–**m** (2 mmol) was added, and the vial

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was capped with a septum. The mixture was degassed with N_2 for 10 min, and then the solution was pumped through the reactor at a flow rate of 1 mL min^{-1} (3 mL min^{-1} for **1m**). The reaction mixture collected from the reactor output was diluted with CH_2Cl_2 and filtered through a plug of silica, and the solvent was evaporated under reduced pressure. The crude mixture was then purified by flash column chromatography using petroleum ether/dichloromethane or petroleum ether/ethyl acetate as the eluent.

Determination of ^{19}F NMR Yields for Volatile Compounds 2a and 2c. Fluorination of **1a** and **1c** was carried out using the above-described general procedure. Subsequently, 2 mmol of fluorobenzene (internal standard) was added to the crude reaction mixture collected from the reactor output. A 0.3 mL aliquot of the resulting solution was diluted in DMSO-d_6 and analyzed by ^{19}F NMR spectroscopy.

1-*tert*-Butyl-4-(fluoromethyl)benzene (2b). Yield 295 mg, 89%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 9.0 Hz, 2H), 7.36 (d, J = 9.0 Hz, 2H), 5.47 (s, 1H), 5.30 (s, 1H), 1.37 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 152.0, 133.3, 133.1, 127.7, 127.6, 125.6, 125.6, 85.7, 83.5, 34.7, 31.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ −204.3 (t, J = 47.9 Hz); MS-EI m/z 166 (20%), 151 (100%), 123 (40%).

1-Bromo-4-(1-fluoroethyl)benzene (2d). Yield 243 mg, 60%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, J = 9.0 Hz, 2H), 7.24 (d, J = 9.0 Hz, 2H), 5.60 (dq, J = 48, 6 Hz, 1H), 1.64 (dd, J = 24, 6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6, 140.4, 131.6, 127.0, 126.9, 122.1, 91.4, 89.2, 23.0, 22.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ −168.0 (dq, J = 22.6, 45.1 Hz); MS-EI m/z 204 (45%), 202 (50%), 189 (90%), 187 (100%).

3-Fluoro-3-phenylpropanoic Acid (2e). Yield 246 mg, 73%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.39 (m, 5H), 5.95 (ddd, J = 45.0, 9.0, 3.0 Hz, 1H), 3.18−2.80 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 176.0, 138.4, 138.1, 129.0, 129.0, 128.8, 125.7, 125.6, 91.4, 89.1, 42.4, 42.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −172.91 (ddd, J = 46.5, 32.5, 13.6 Hz).

Ethyl 3-Fluoro-3-phenylpropanoate (2f). Yield 318 mg, 81%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.35 (m, 5H), 5.95 (ddd, J = 46.9, 9.1, 4.2 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.11−2.72 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.69, 169.63, 138.81, 138.55, 128.83, 128.81, 128.65, 125.66, 125.57, 91.79, 89.54, 60.99, 42.70, 42.34, 14.14; ^{19}F NMR (282 MHz, $CDCl_3$) δ −172.91 (ddd, J = 46.5, 32.5, 13.6 Hz); MS-EI m/z 196 (15%), 167 (10%), 151 (15%), 125 (40%), 122 (40%), 109 (100%).

4-(1-Fluoroethyl)biphenyl (2g). Yield 340 mg, 85%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66−7.62 (m, 4H), 7.49 (t, J = 9.0 Hz, 4H), 7.39 (t, J = 6.0 Hz, 1H), 5.72 (dq, J = 47.7, 6.4 Hz, 1H), 1.73 (dd, J = 23.8, 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.3, 141.2, 140.7, 140.6, 140.3, 128.8, 127.5, 127.3, 127.2, 125.8, 125.7, 91.9, 89.7, 23.1, 22.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ −166.6 (dq, J = 47.7, 23.8 Hz); MS-EI m/z 200 (40%), 185 (100%).

4-(1-Fluoroethyl)benzoic Acid (2h). Yield 269 mg, 80%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, J = 8.1 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 5.72 (dq, J = 47.6, 6.5 Hz, 1H), 1.68 (dd, J = 24.0, 6.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 147.7, 147.4, 130.5, 129.0, 125.1, 125.0, 91.4, 89.2, 23.2, 22.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −171.7 (dq, J = 47.9, 24.0 Hz); MS-EI m/z 168 (40%), 153 (60%), 123 (100%).

1-Chloro-3-fluoro-3-phenylpropane (2i). Yield 244 mg, 71%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.32 (m, 5H), 5.72 (ddd, J = 47.8, 8.9, 3.9 Hz, 1H), 3.78 (ddd, J = 11.0, 8.7, 5.6 Hz, 1H), 3.71−3.53 (m, 1H), 2.62−2.38 (m, 1H), 2.38−2.06 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 139.0, 128.7, 125.5, 125.4, 92.4, 90.1, 40.5, 40.4, 40.2, 39.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −179.4 (ddd, J = 45.6, 31.2, 14.1 Hz); MS-EI m/z 172 (10%), 109 (100%).

4-Fluoro-2-methyl-4-phenylbutan-2-ol (2j). Yield 265 mg, 73%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.33 (m, 5H), 5.82 (ddd, J = 49.0, 10.2, 2.2 Hz, 1H), 2.39−2.14 (m, 1H), 2.07−1.69 (m, 1H), 1.40 (s, 1H), 1.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.7, 140.4, 128.6, 128.4, 128.4, 125.5, 125.4, 93.8, 91.6, 70.2, 50.4, 50.1, 29.9, 29.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ −173.4 (ddd, J = 49.0, 40.6, 16.1 Hz); MS-EI m/z 164 (30%), 149 (30%), 109 (45%), 104 (70%), 59 (100%).

4-(1-Fluoroethyl)acetophenone (2k). Yield 230 mg, 69%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.3 Hz, 1H), 5.70 (dq, J = 47.6, 6.5 Hz, 1H), 2.63 (s, 2H), 1.66 (dd, J = 24.0, 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.67, 146.81, 146.55, 136.83, 128.60, 125.15, 125.05, 91.42, 89.16, 26.66, 23.17, 22.83; ^{19}F NMR (282 MHz, $CDCl_3$) δ −171.3 (dq, J = 47.9, 24.0 Hz); MS-EI m/z 166 (20%), 151 (100%).

Methyl 2-(4-(1-Fluoro-2-methylpropyl)phenyl)propanoate (2l). Yield 381 mg, 80%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.22 (m, 1H), 5.10 (dd, J = 47.0, 6.8 Hz, 1H), 3.75 (dd, J = 14.5, 7.3 Hz, 1H), 3.68 (s, 1H), 2.22−2.04 (m, 1H), 1.52 (d, J = 7.2 Hz, 1H), 1.04 (d, J = 6.7 Hz, 1H), 0.87 (d, J = 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9, 140.3, 138.4, 138.1, 127.3, 126.5, 126.4, 100.2, 97.9, 52.1, 45.2, 34.4, 34.1, 18.6, 18.4, 18.3, 17.6, 17.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −179.6 (ddd, J = 47.0, 16.9, 6.0 Hz); MS-EI m/z 238 (20%), 195 (100%), 179 (70%).

4-Acetyl-6-*tert*-butyl-3-fluoro-1,1-dimethylindane (2m). Yield 462 mg, 88%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 1.6 Hz, 1H), 7.44 (t, J = 1.5 Hz, 1H), 6.46 (ddd, J = 53.8, 5.9, 1.4 Hz, 1H), 2.67 (s, 3H), 2.42−2.08 (m, 2H), 1.39 (s, 12H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.7, 155.9, 155.8, 154.2, 154.1, 135.2, 134.9, 134.9, 125.6, 123.6, 94.9, 92.6, 48.5, 48.2, 42.7, 42.7, 35.1, 31.5, 31.4, 29.0, 28.9, 28.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ −158.6 (ddd, J = 54.3, 33.8, 23.8 Hz); MS-EI m/z 262 (70%), 247 (100%), 227 (35%).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Supplementary figures and copies of NMR spectra of all prepared compounds. 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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