Nickel-Catalyzed Alkyl-arylation of 3,3,3-Trifluoropropene

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Supplementary Methods

1. Materials and Methods

General Information: $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AM400, AM500 or Agilent 400 spectrometer and are calibrated using residual undeuterated solvent (CHCl$_3$ at 7.26 ppm $^1$H NMR, 77.00 ppm $^{13}$C NMR; CD$_3$OD at 3.34 ppm $^1$H NMR, 49.86 ppm $^{13}$C NMR). $^{19}$F NMR was recorded on a Bruker AM400 spectrometer (CFCl$_3$ as an external standard and low field is positive). Chemical shifts ($\delta$) are reported in ppm, and coupling constants ($J$) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. NMR yield was determined by $^{19}$F NMR using fluorobenzene as an internal standard before working up the reaction.

Materials: All reagents were used as received from commercial sources and used without further purification. Superdry solvents, DMF, DMA and MeCN were purchased from commercial sources. 1,4-Dioxane, THF, DCM and toluene were taken from solvent purification system (PureSolv MD5, inert technology) and stored in 500 mL storage flasks with high vacuum valve. trans-NiCl$_2$(PCy$_2$Ph)$_2$ and NiCl$_2$·6H$_2$O were purchased from Strem chemicals and used as received. 4,4'-diMeO-2,2'-bpy was purchased from Aladdin Chemicals, PCy$_2$Ph (P1) and PBu$_3$Me·HBF$_4$ (P2) were purchased from Adamas-beta Chemicals, and all used as received. 3,3,3-Trifluoropropene (TFP) 1 was purchased from Shangfluoro chemicals and used as received.

Preparation of 3,3,3-Trifluoropropene (TFP) Stock Solution

Anhydrous DMA (300 mL) was added to a 500 mL Schlenk flask under argon atmosphere (Ar). TFP gas was then slowly bubbled through DMA with stirring until the total volume of the solution reaches the maximum (generally 2 hours). The concentration of the TFP stock solution was determined by $^{19}$F NMR using benzotrifluoride as an internal standard (generally 0.9 ~ 1.0 mol/L). This solution could be stored at room temperature for one month without obvious loss of TFP.
2. Preparation of Tertiary Alkyl Iodides and Bromides

Tertiary alkyl halide 2b was purchased from commercial source. Compounds 2c, 2e, 2d, and 2l are known compounds and were prepared according to the literatures.

![Supplementary Figure 1 Structure of Tertiary Alkyl Iodides and Bromides](image)

The general procedure for the preparation of tertiary alkyl halides is according to the literature. To a 500 mL round-bottom flask were added tertiary alcohol (1 equiv) and MeCN (0.2 M for tertiary alcohol) with stirring. The clear solution was cooled to 0 °C with an ice-water bath, and NaI (2 equiv) was added in one portion. MeSO₃H (2.0 equiv) was added dropwise to the solution under vigorous stirring with precipitate formed. The reaction was stirred for 4 h at room temperature. After the consumption of the alcohol monitored by TLC, the reaction was concentrated and diluted with Et₂O, washed by water, saturated NaHCO₃, saturated Na₂S₂O₃, and brine, dried over Na₂SO₄, and concentrated on a rotary evaporator. The residue was purified by flash column chromatography to give the corresponding tertiary alkyl iodide. The iodides were unstable and would slowly become deteriorated during column chromatography. The product must be stored at -20 °C away from light to prevent its decomposition.
2-(3-Iodo-3-methylbutyl)isoindoline-1,3-dione (2a). The product (13.7 mmol scale, 3.7 g, 79% yield) as a white solid (m.p. 88.4 – 89.7 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.87 – 7.81 (m, 2H), 7.74 – 7.67 (m, 2H), 3.94 – 3.87 (m, 2H), 2.03 – 1.98 (m, 8H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.1, 133.9, 132.1, 123.2, 47.5, 45.2, 38.0, 37.7. MS (DART): m/z (%) 344.0 ([M+H]$^+$), 361.0 ([M+NH$_4]^+$, 100). HRMS (DART): Calculated for C$_{13}$H$_{15}$INO$_2$ ([M+H]$^+$): 344.0142; Found: 344.0139.

3-Iodo-3-methylbutyl 4-chlorobenzoate (2f). The product (34 mmol scale, 8.0 g, 67% yield) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 15/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.94 (d, $J$ = 8.5 Hz, 2H), 7.38 (d, $J$ = 8.5 Hz, 2H), 4.53 (t, $J$ = 6.8 Hz, 2H), 2.14 (t, $J$ = 6.8 Hz, 2H), 1.99 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.5, 139.4, 130.9, 128.7, 128.5, 65.2, 48.0, 45.76, 38.5. MS (DART): m/z (%) 353.0 ([M+H]$^+$), 370.0 ([M+NH$_4]^+$, 100). HRMS (DART): Calculated for C$_{12}$H$_{15}$ClIO$_2$ ([M+H]$^+$): 352.9800; Found: 352.9799.

3-Iodo-3-methylbutyl 4-cyanobenzoate (2g). The product (46 mmol scale, 9.5 g, 60% yield) as a yellow solid (m.p. 60.3 – 61.5 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.11 (d, $J$ = 3.0 Hz, 1H), 7.50 (d, $J$ = 4.8 Hz, 1H), 7.29 (dd, $J$ = 5.1 Hz, 3.1 Hz, 1H), 4.49 (t, $J$ = 6.8 Hz, 2H), 2.13 (t, $J$ = 6.8 Hz, 2H), 2.00 (s, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 164.9, 134.0, 132.4, 130.2, 118.0, 116.6, 66.0, 48.0, 45.5, 38.6. MS (FI): m/z (%) 216 ([M-HI]$^+$), 130, 69 (100). HRMS (FI): Calculated for C$_{13}$H$_{13}$NO$_2$ ([M-HI]$^+$): 215.0941; Found: 215.0940.

3-Iodo-3-methylbutyl thiophene-3-carboxylate (2h). The product (31.7 mmol scale, 5.0 g, 49% yield) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.08 (d, $J$ = 3.0 Hz, 1H), 7.50 (d, $J$ = 4.8 Hz, 1H), 7.29 (dd, $J$ = 5.1 Hz, 3.1 Hz, 1H), 4.49 (t, $J$ = 6.8 Hz, 2H), 2.13 (t, $J$ = 6.8 Hz, 2H), 2.00 (s, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 162.4, 133.4, 132.7, 127.2, 126.0, 64.6, 48.0,
3-Iodo-3-methylbutyl 6-bromohexanoate (2i). The product (45 mmol scale, 10.0 g, 57% yield) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 20/1). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.29 (t, \(J = 7.0\) Hz, 2H), 3.40 (t, \(J = 6.7\) Hz, 2H), 2.31 (t, \(J = 7.4\) Hz, 2H), 2.00 (t, \(J = 7.0\) Hz, 2H), 1.96 (s, 6H), 1.90 – 1.82 (m, 2H), 1.69 – 1.59 (m, 2H), 1.51 – 1.41 (m, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 173.2, 64.4, 47.9, 46.0, 38.4, 34.0, 33.4, 32.3, 27.5, 23.9. MS (DART): m/z (%) 408.0 ([M+NH\(_4\)]\(^+\), 100). HRMS (DART): Calculated for C\(_{11}\)H\(_{21}\)BrIO\(_2\) ([M+H]+): 390.9764; Found: 390.9763.

3-Iodo-3-methylbutyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (2j). The product (20 mmol scale, 4.0 g, 37% yield) as a yellow viscous oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.65 (d, \(J = 8.5\) Hz, 2H), 7.46 (d, \(J = 8.5\) Hz, 2H), 6.95 (d, \(J = 9.0\) Hz, 2H), 6.86 (d, \(J = 9.0\) Hz, 2H), 4.33 (t, \(J = 6.9\) Hz, 2H), 3.83 (s, 3H), 3.66 (s, 2H), 2.38 (s, 3H), 2.04 (t, \(J = 6.9\) Hz, 2H), 1.91 (s, 6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 170.5, 168.1, 155.9, 139.1, 135.8, 133.7, 131.0, 130.6, 130.4, 129.0, 114.8, 112.3, 111.5, 101.1, 65.0, 55.6, 47.8, 45.8, 38.2, 30.2, 13.3. MS (DART): m/z (%) 554.1 ([M+H]+), 571.1 ([M+NH\(_4\)]\(^+\), 100). HRMS (DART): Calculated for C\(_{24}\)H\(_{26}\)ClINO\(_4\) ([M+H]+): 554.0590; Found: 554.0579.

3-Iodo-3-methylbutyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (2k). The product (27 mmol scale, 6.0 g, 50% yield) as a yellow viscous oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.03 (d, \(J = 7.4\) Hz, 1H), 6.69 (d, \(J = 7.5\) Hz, 1H), 6.64 (s, 1H), 4.33 (t, \(J = 6.8\) Hz, 2H), 3.97 – 3.91 (m, 2H), 2.34 (s, 3H), 2.22 (s, 3H), 2.04 (t, \(J = 6.8\) Hz, 2H), 2.00 (s, 6H), 1.80 – 7.13 (m, 4H), 1.26 (s, 6H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 177.6, 156.9, 136.4, 130.3, 123.5, 120.8, 67.8, 64.6, 48.1, 46.3, 42.0, 38.5, 37.1, 25.24,
25.20, 21.5, 15.9. MS (DART): m/z (%) 319.2 ([M-I]+), 447.1 ([M+H]+, 100), 464.2 ([M+NH₄]+).
HRMS (DART): Calculated for C₂₀H₃₂IO₃ ([M+H]+): 447.1391; Found: 447.1387.

3. General Procedure for the Preparation of Arylzinc Reagents from Aryl Bromides

All arylzinc reagents are known compounds⁶–⁸ and were prepared from the corresponding aryl bromides or iodides using Knochel’s method. 3a-3f, 3i-3q were prepared by magnesium insertion-transmetallation process (Method A). 3g and 3h were prepared by iodine-magnesium exchange followed by transmetallation (Method B).

Method A

The synthesis of arylzinc reagents was according to the literature.⁹ To a dry 100 mL Schlenk flask were added magnesium turnings (3 g, 125 mmol, 2.5 equiv) and LiCl (2.7 g, 62.5 mmol, 1.25 equiv).
The flask was evacuated and heated with a heatgun. The flask was evacuated again and backfilled with argon for 3 times. Upon cooling, tetrahydrofuran (anhydrous, 50 mL) was added, and the mixture was stirred vigorously for 5 min. DIBAL-H (1.0 M in hexane, 0.5 mL, 0.01 equiv) was added via syringe, and the mixture was stirred vigorously for 5 min. The flask was then cooled to 0 °C with an ice/water bath, and aryl bromide (50 mmol, 1.0 equiv) was added via a syringe. After 10 minutes, the ice/water bath was removed, and the mixture was stirred at room temperature for 3-5 h until all aryl bromide was consumed (the reaction was monitored by GC). After the reaction was completed, the resulting solution of Grignard reagent ArMgBr•LiCl was titrated with I₂ according to Knochel’s method\textsuperscript{10} to afford Grignard reagents with concentration typically ranging 0.3-0.5 M in THF. To a separate oven-dried 100 mL Schlenk tube, ZnCl₂ (1.0 M in THF) (\textit{Note:} the loading amount of ZnCl₂ (1 equiv) depends on the amount of Grignard reagents used for the reaction) was added. To this tube ArMgBr•LiCl was transferred via a syringe with stirring. After stirring for at least 10 min, the solution of ArZnCl•LiCl was titrated with I₂ according to Knochel’s method. The Schlenk tube was sealed with a Teflon cap and the resulting aryl zinc reagents can be stored under argon at room temperature for several weeks.

\textbf{Method B}

\begin{align*}
\text{R}^1\text{B}r + \text{ZnCl}_2 & \rightarrow \text{R}^1\text{ZnCl} \\
\text{R}^1\text{B}r + \text{ArMgCLiCl} & \rightarrow \text{R}^1\text{MgCl} + \text{LiCl}
\end{align*}

The procedure was a modification to the literature.\textsuperscript{11} To a 50 mL Schlenk flask was added a THF solution of iPrMgCl•LiCl (1.5 M. 1.05 equiv) under Ar. The flask was cooled to -15 °C and a solution of aryl iodide (1 equiv) in THF was added dropwise. After complete addition, the temperature was raised to -10 °C and the reaction mixture was stirred for 30 min at this temperature. Then the resulting solution of Grignard reagent ArMgCl•LiCl was titrated with I₂ according to Knochel’s method. To a separate oven-dried 100 mL Schlenk tube, ZnCl₂ (1.0 M in THF) (\textit{Note:} the loading amount of ZnCl₂ (1 equiv) depends on the amount of Grignard reagents used for the reaction) was added. To this tube ArMgBr•LiCl was transferred via a syringe with stirring. After stirring for at least 10 min, the solution of ArZnCl•LiCl was titrated with I₂ according to Knochel’s method. The Schlenk tube was sealed with a Teflon cap and the resulting aryl zinc reagents can be stored under argon at room temperature for several weeks.
4. Optimization of Ni-Catalyzed Alkylarylation of 3,3,3-Trifluoropropene 1 with Tertiary Alkyl Iodide 2a and Arylzinc Reagent 3a

To a 25 mL of Schlenck tube were added 4,4'-diMeO-2,2'-bpy (6 mol%), NiCl₂·6H₂O (5 mol%) and the monodentate phosphine ligand (PCy₂Ph or tBu₂MeP·HBF₄, 5 mol%). The tube was evacuated and backfilled with argon for 3 times, then tertiary alkyl iodide 2a (0.4 mmol, 1.0 equiv) and TFP solution (1 M in DMA, 0.8 mmol, 2.0 equiv) were added under Ar. The resulting mixture was stirred for 20 min at room temperature, and the corresponding arylzinc reagent 3a (0.6 mmol, 1.5 equiv) was added slowly within a period of 5 min, and the tube was sealed with a Teflon cap. After stirring for 12 h at room temperature, the reaction mixture was quenched with aqueous NH₄Cl solution and diluted with EtOAc. The reaction mixture was filtered through a pad of Celite, and the filtrate was extracted with EtOAc and washed with brine. The organic layer was dried over Na₂SO₄, filtered and concentrated. The residue was purified with silica gel chromatography to give the corresponding products 4a. Isolated yields are based on the average of two runs under identical conditions.

Supplementary Table 1. Ligand effect on the nickel catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a:

\[
\begin{align*}
1 & \quad 2a & \quad 3a & \quad 4a \\
F_3C= & \quad I & \quad \text{ZnCl}_2\text{Cl} & \quad \text{NiCl}_2\text{DME} & \quad \text{Ligand}
\end{align*}
\]

\[
\begin{align*}
\text{DMA, r.t., 12h} & \quad \text{CF}_3\text{Ph}
\end{align*}
\]

Isolated yields are based on the average of two runs under identical conditions.
| Entry | Ligand | Yield [%]<sup>b</sup> | 6a | 4a | 7a |
|-------|--------|-------------------|----|----|----|
| 1     | L1     | 11                | 60 | ND |    |
| 3     | L2     | 10                | 50 | ND |    |
| 4     | L3     | 9                 | 65 | ND |    |
| 8     | L4     | 10                | 43 | ND |    |
| 9     | L5     | 7                 | 40 | 16 |    |
| 10    | L6     | 10                | 22 |  6 |    |
| 7     | L7     | ND                | 8  | 28 |    |
| 2     | L8     | 2                 | 16 | ND |    |
| 5     | L9     | 9                 | 55 | 12 |    |
| 6     | L10    | 11                | 60 | 14 |    |
| 11    | L11    | 9                 | 51 | ND |    |
| 12    | L12    | 8                 | 31 |  8 |    |
| 13    | L13    | 15                | ND | 14 |    |
| 14    | L14    | 11                | ND | 11 |    |

<sup>a</sup>Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL).<sup>b</sup>Determined by <sup>19</sup>F NMR using fluorobenzene as an internal standard.
Supplementary Table 2. Screening of the nickel catalysts for alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a

![Chemical反应式]

| Entry | [Ni]                  | Yield [%]| 6a | 4a | 7a |
|-------|-----------------------|----------|----|----|----|
| 1     | NiCl₂·DME             | 9        | 65 | ND | ND |
| 2     | NiCl₂                 | 11       | 34 | ND | ND |
| 3     | NiBr₂·DME             | 11       | 60 | ND | ND |
| 4     | NiBr₂                 | 10       | 22 | ND | ND |
| 5     | NiI₂                  | 12       | 49 | ND | ND |
| 6     | Ni(acac)₂             | 10       | 60 | 9  |    |
| 7     | NiCl₂(PPh₃)₂          | 5        | 68 | 9  |    |
| 8     | NiBr₂(PPh₃)₂          | 4        | 68 | 11 |    |
| 9     | NiCl₂(dppe)           | 6        | 19 | 5  |    |
| 10    | NiCl₂(dppf)           | ND       | 21 | ND | ND |
| 11    | trans-NiPhCl(PPh₃)₂ (Ni-1) | 5   | 73 | ND | ND |
| 12    | trans-NiCl₂(PCy₂Ph)₂ (Ni-2) | ND | 75 | ND | ND |
| 13    | Ni(TMHD)₂             | 12       | 65 | ND | ND |
| 14    | Ni(COD)₂             | 11       | 65 | ND | ND |

*Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL). *Determined by ¹⁹F NMR using fluorobenzene as an internal standard.
**Supplementary Table 3.** Solvent effects on the nickel catalysts for alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a

![Chemical structure](image)

| Entry | Solvent | Yield [%]a | 6a | 4a | 7a |
|-------|---------|------------|----|----|----|
| 1     | DMA     | ND         | 75 | ND | ND |
| 2     | DMF     | ND         | 44 | ND | ND |
| 3     | THF     | ND         | 5  | 14 |    |
| 4     | dioxane | ND         | 11 | 34 |    |
| 5     | Toluene | ND         | ND | ND | 12 |
| 6     | MeCN    | ND         | ND | ND | 18 |

aReaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and Solvent (2 mL). bDetermined by $^{19}$F NMR using fluorobenzene as an internal standard.

**Supplementary Table 4. Control experiments**

![Chemical structure](image)

| Entry | [Ni] | L3 | Yield [%]b | 6a | 4a | 7a |
|-------|------|----|------------|----|----|----|
| 1     | Ni-2 | L3 | ND         | 75 | ND | ND |
| 2     | none | L3 | ND         | ND | ND | ND |
| 3     | Ni-2 | none | ND         | ND | 47 |    |
| 4     | none | none | ND         | ND | ND | ND |

aReaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL). bDetermined by $^{19}$F NMR using fluorobenzene as an internal standard.
**Supplementary Table 5.** Screening of the nickel catalysts in the presence of phosphine ligand for nickel-catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a

![Chemical reaction diagram]

| Entry | [Ni]                        | Yield [%]³ | 6a | 4a | 7a |
|-------|-----------------------------|------------|----|----|----|
| 1     | Ni(acac)₂                   | ND         | 64 | 8  |    |
| 2     | Ni(NO₃)₂·6H₂O                | ND         | 73 | ND |    |
| 3     | NiClO₄·H₂O                  | ND         | 74 | 4  |    |
| 4     | NiBr₂·3H₂O                  | ND         | 74 | 10 |    |
| 5     | NiCl₂·6H₂O                  | ND         | 77 | ND |    |
| 6     | Ni(OTf)₂                    | ND         | 43 | 6  |    |

³Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL). Determined by ¹⁹F NMR using fluorobenzene as an internal standard.

**Supplementary Table 6.** Screening of the loading amount of PCy₂Ph for the nickel-catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a

![Chemical reaction diagram]

| Entry | x (mol%) | Yield [%]³ | 6a | 4a | 7a |
|-------|----------|------------|----|----|----|
| 1     | 2.5      | ND         | 78 | ND |    |
| 2     | 5        | ND         | 84 | ND |    |
| 3     | 10       | ND         | 77 | ND |    |
| 4     | 15       | ND         | 81 | ND |    |
| 5     | 20       | ND         | 81 | ND |    |

³Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL). Determined by ¹⁹F NMR using fluorobenzene as an internal standard.
**Supplementary Table 7.** Effects of the phosphine ligands on the nickel-catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a

| Entry | P Ligand                   | Yield [%] | 6a | 4a | 7a |
|-------|----------------------------|-----------|----|----|----|
| 1     | PCy₂Ph                     | ND        | 84 | (82) | ND |
| 2     | P(Ad₃n-Bu)·HI              | ND        | 67 |     | 8  |
| 3     | P(₃Bu₂Ph)·HBF₄             | ND        | 56 |     | 5  |
| 4     | P(2-MeO-Ph)₃               | ND        | 50 |     | 6  |
| 5     | P(4-MeO-Ph)₃               | ND        | 69 |     | 9  |
| 6     | P(2-Me-Ph)₃                | ND        | 52 |     | 6  |
| 7     | P(4-Me-Ph)₃                | ND        | 66 |     | 8  |
| 8     | P(₃Bu₂Me)·HBF₄             | ND        | 75 |     | 5  |
| 9     | PCy₃                       | ND        | 72 |     | ND |
| 10    | PCyPh₂                     | ND        | 66 |     | 7  |
| 11    | AsPh₃                      | ND        | 50 |     | 6  |
| 12    | none                       | ND        | 52 |     | ND |

*Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL). *Determined by ¹⁹F NMR using fluorobenzene as an internal standard.
Supplementary Table 8. Effects of the pyridine-based ligands on the nickel-catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a<sup>a</sup>

\[
\text{F}_3\text{C} = \text{I} + \text{ZnCl}_{2}\text{LiCl} + \text{NiCl}_2\cdot \text{H}_2\text{O} \quad \text{Py-Ligand} \quad \text{DMA, r.t., 12h} \quad \text{R = Ar or alkyl}
\]

| Entry | Py-Ligand | Yield [%]<sup>b</sup> |
|-------|-----------|------------------------|
| 1     | 4-MeO-Py  | 56                     |
| 2     | 4-Ph-Py   | 51                     |
| 3     | 4-CF<sub>3</sub>-Py | 52                     |
| 4     | DMAP      | 55                     |

<sup>a</sup>Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA (2 mL). <sup>b</sup>Determined by <sup>19</sup>F NMR using fluorobenzene as an internal standard.

Supplementary Table 9. Effects of DME on the nickel-catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and arylzinc reagent 3a<sup>a</sup>

\[
\text{F}_3\text{C} = \text{I} + \text{ZnCl}_{2}\text{LiCl} + \text{NiCl}_2\cdot \text{H}_2\text{O} \quad \text{DMA+DME, r.t., 12h} \quad \text{R = Ar or alkyl}
\]

| Entry | DMA/DME (v/v) | Yield [%]<sup>b</sup> |
|-------|---------------|------------------------|
| 1     | 10:1          | 54                     |
| 2     | 5:1           | 56                     |
| 3     | 2:1           | 60                     |
| 4     | 1:1           | 66                     |
| 5     | 1:2           | 73                     |
| 6     | 1:3           | 71                     |

<sup>a</sup>Reaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3a (1.5 equiv), and DMA+DME (2 mL). <sup>b</sup>Determined by <sup>19</sup>F NMR using fluorobenzene as an internal standard.
**Supplementary Table 10.** Effects of the phosphine ligands on the nickel-catalyzed alkylation of TFP 1 with alkyl iodide 2a and electron-deficient arylzinc reagent 3d

![Chemical Structure]

| Entry | P Ligand                        | Yield [%] |
|-------|---------------------------------|-----------|
|       |                                 | 6d | 4d | 7a |
| 1     | PCy₂Ph                           | ND | 41 | 5  |
| 2     | P(Ad₂n-Bu)·HI                    | ND | 54 | 4  |
| 3     | P(η-Bu₂Ph)·HBF₄                  | ND | 27 | 3  |
| 4     | P(2-MeO-Ph)₃                     | ND | 25 | 4  |
| 5     | P(4-MeO-Ph)₃                     | ND | 41 | 2  |
| 6     | P(2-Me-Ph)₃                      | ND | 26 | 4  |
| 7     | P(4-Me-Ph)₃                      | ND | 50 | 4  |
| 8     | P(η-Bu₂Me)·HBF₄                  | ND | 60 (58) | ND |
| 9     | PCy₃                             | ND | 56 | 4  |
| 10    | PCyPh₂                           | ND | 46 | 3  |

*aReaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3d (1.5 equiv), and DMA (2 mL). †Determined by ¹⁹F NMR using fluorobenzene as an internal standard.*
**Supplementary Table 11.** Effects of DME on the nickel-catalyzed alkylarylation of TFP 1 with alkyl iodide 2a and electron-deficient arylzinc reagent 3d

\[ 
\begin{array}{c|c|c|c}
\text{Entry} & \text{DMA/DME (v/v)} & \text{Yield [\%]}^b & \text{4d} & \text{7a} \\
\hline
1 & 10:1 & 30 & 3 \\
2 & 5:1 & 31 & 3 \\
3 & 2:1 & 30 & 3 \\
4 & 1:1 & 34 & 3 \\
5 & 1:2 & 48 & 9 \\
6 & 1:3 & 50 & 11 \\
\end{array}
\]

*aReaction conditions (unless otherwise specified): 2a (0.4 mmol, 1.0 equiv), 1 (2.0 equiv, 1 M in DMA, 0.8 mL), 3d (1.5 equiv), and DMA+DME (2 mL). bDetermined by \(^{19}\text{F} \) NMR using fluorobenzene as an internal standard.

5. **General Procedure for the Ni-Catalyzed Alkylarylation of 3,3,3-Trifluoropropene 1 with Tertiary Alkyl Iodides 2 and Arylzinc Reagents 3**

To a 25 mL of Schlenck tube were added 4,4'-diMeO-2,2'-bpy (6 mol%), NiCl\(_2\)-6H\(_2\)O (5 mol%) and the monodentate phosphine ligand (PCy\(_2\)Ph or P'Bu\(_2\)Me-HBF\(_4\), 5 mol%). The tube was evacuated and backfilled with argon for 3 times, then tertiary alkyl iodide 2 (0.4 mmol, 1.0 equiv) and TFP solution (1 M in DMA, 0.8 mmol, 2.0 equiv) were added under Ar. The resulting mixture was stirred for 20 min at room temperature, and the corresponding arylzinc reagent 3 (0.6 mmol, 1.5 equiv) was added slowly within a period of 5 min, and the tube was sealed with a Teflon cap. After stirring for 12 h at room temperature, the reaction mixture was quenched with aqueous NH\(_4\)Cl solution and diluted with EtOAc. The reaction mixture was filtered through a pad of Celite, and the filtrate was extracted with
EtOAc and washed with brine. The organic layer was dried over Na₂SO₄, filtered and concentrated. The residue was purified with silica gel chromatography to give the corresponding products 4 or 5. Isolated yields are based on the average of two runs under identical conditions.

6. Characterization Data for Compounds 4 and 5

2-(5-([1,1'-Biphenyl]-4-yl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4a). The product (standard reaction conditions: 153 mg, 82% yield using P1; using 2.5 mol% nickel catalyst on 0.4 mmol scale: 55% determined by ¹⁹F NMR) as a yellow solid (m.p. 108.4 – 109.7 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). ¹H NMR (400 MHz, CDCl₃) δ 7.88 – 7.77 (m, 2H), 7.74 – 7.65 (m, 2H), 7.63 – 7.52 (m, 4H), 7.49 – 7.39 (m, 4H) 7.37 – 7.30 (m, 1H), 3.75 – 3.60 (m, 2H), 3.59 – 3.46 (m, 1H), 2.17 – 1.97 (m, 2H), 1.69 – 1.58 (m, 1H), 1.58 – 1.46 (m, 1H), 0.91 (s, 3H), 0.87 (s, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -70.1 (d, J = 9.6 Hz, 3F). ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 140.7, 140.3, 135.3, 133.8, 132.0, 129.7, 128.7, 127.3, 127.2, 127.1 (q, J = 281.3 Hz), 126.9, 123.0, 46.0 (q, J = 26.4 Hz), 39.9, 39.8, 33.8, 32.8, 27.3, 27.1. MS (DART): m/z (%) 466.2 ([M+H]+), 483.2 ([M+NH₄]+, 100). HRMS (DART): Calculated for C₂₈H₂₇F₃NO₂ ([M+H]+): 466.1988; Found: 466.1985.

Gram-scale synthesis of compound 4a

To a 100 mL of Schlenck tube were added 4,4'-diMeO-2,2'-bpy (3 mol%), NiCl₂·6H₂O (2.5 mol%) and the monodentate phosphine ligand PCy₂Ph (2.5 mol%). The tube was evacuated and backfilled with argon for 3 times, then tertiary alkyl iodide 2a (6 mmol, 1.0 equiv) and TFP solution (1 M in DMA, 25 mL) were added under Ar. The resulting mixture was stirred for 20 min at room temperature, and the corresponding arylzinc reagent 3a (9 mmol, 1.5 equiv) was added slowly within a period of 5 min, and the tube was sealed with a Teflon cap. After stirring for 12 h at room temperature, the reaction mixture was quenched with aqueous NH₄Cl solution and diluted with EtOAc. The reaction mixture was filtered through a pad of Celite, and the filtrate was extracted with EtOAc and washed with brine. The organic layer was dried over Na₂SO₄, filtered and concentrated. The residue was purified with
silica gel chromatography (Hexane/Ethyl Acetate = 15/1) to give compound 4a as a yellow solid (1.4 g, 50% yield).

2-(6,6,6-Trifluoro-3,3-dimethyl-5-phenylhexyl)isoindoline-1,3-dione (4b). The product (107 mg, 69% yield using P2) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 – 7.77 (m, 2H), 7.69 – 7.63 (m, 2H), 7.37 – 7.23 (m, 5H), 3.68 – 3.56 (m, 2H), 3.51 – 3.38 (m, 1H), 2.04 – 1.95 (m, 2H), 1.63 – 1.53 (m, 1H), 1.53 – 1.44 (m, 1H), 0.83 (s, 3H), 0.79 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.2 (d, $J$ = 9.8 Hz, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.1, 136.3, 133.8, 132.0, 129.3, 128.5, 127.9, 127.1 (q, $J$ = 281.3 Hz) 123.0, 46.3 (q, $J$ = 26.3 Hz), 39.9, 39.8, 33.8, 32.7, 27.3, 27.0. MS (DART): m/z (%) 390.2 ([M+H$^+$]), 407.2 ([M+NH$_4^+$], 100). HRMS (DART): Calculated for C$_{22}$H$_{23}$F$_3$NO$_2$ ([M+H$^+$]): 390.1675; Found: 390.1673.

2-(5-(4-(tert-Butyl)phenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4c). The product (standard reaction conditions: 142.6 mg, 80% yield using P2; using L2 instead of L3 as the ligand: 71% determined by $^{19}$F NMR) as a white solid (m.p. 114.8 – 116.2$^\circ$C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 15/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.76 – 7.70 (m, 2H), 7.62 – 7.55 (m, 2H), 7.28 (d, $J$ = 8.3 Hz, 2H), 7.23 (d, $J$ = 8.2 Hz, 2H), 3.64 – 3.52 (m, 2H), 3.47 – 3.34 (m, 1H), 2.00 – 1.92 (m, 2H), 1.58 – 1.47 (m, 1H), 1.47 – 1.35 (m, 1H), 1.21 (s, 9H), 0.82 (s, 3H), 0.79 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.1 (d, $J$ = 9.9 Hz, 3F). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 168.0, 150.9, 133.8, 133.2, 132.2, 129.0, 127.3 (q, $J$ = 280.1 Hz), 125.5, 123.0, 46.0 (q, $J$ = 26.1 Hz), 40.1, 39.9, 34.4, 33.9, 32.8, 31.2, 27.1, 27.1. MS (ESI): 468.2 ([M+Na$^+$]). HRMS (ESI): Calculated for C$_{26}$H$_{30}$F$_3$NNaO$_2$ ([M+Na$^+$]): 468.2121; Found: 468.21208.

2-(6,6,6-Trifluoro-5-(4-fluorophenyl)-3,3-dimethylhexyl)isoindoline-1,3-dione (4d). The product (94 mg, 58% yield using P2) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 15/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 – 7.79 (m, 2H),

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7.73 – 7.66 (m, 2H), 7.36 – 7.28 (m, 2H), 7.02 (t, J = 8.5 Hz, 2H), 3.70 – 3.56 (m, 2H), 3.53 – 3.40 (m, 1H), 2.05 – 1.89 (m, 2H), 1.64 – 1.43 (m, 3H), 0.85 (s, 3H), 0.80 (s, 3H). 19F NMR (376 MHz, CDCl3) δ -70.5 (d, J = 9.7 Hz, 3F), -114.1 – -114.2 (m, 1F). 13C NMR (101 MHz, CDCl3) δ 168.1, 162.4 (q, J = 248.1 Hz), 133.9, 132.0, 130.9 (d, J = 8.1 Hz), 126.9 (q, J = 281.79 Hz), 123.1, 115.6 (d, J = 21.5 Hz), 45.6 (q, J = 26.6 Hz), 40.0, 39.7, 33.8, 32.7, 27.3, 27.1. MS (DART): m/z (%) 408.2 ([M+H]+, 100), 425.2 ([M+NH4]+). HRMS (DART): Calculated for C22H22F4NO2 ([M+H]+): 408.1581; Found: 408.1577.

2-(5-(3,5-Dimethoxyphenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4e). The product (108 mg, 60% yield using P2) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). 1H NMR (400 MHz, CDCl3) δ 7.83 – 7.76 (m, 2H), 7.70 – 7.63 (m, 2H), 6.49 (s, 2H), 6.37 (s, 1H), 3.77 (s, 6H), 3.68 – 3.56 (m, 2H), 3.45 – 3.30 (m, 1H), 1.96 (d, J = 6.0 Hz, 2H), 1.67 – 1.45 (m, 2H), 0.87 (s, 3H), 0.84 (s, 3H). 19F NMR (376 MHz, CDCl3) δ -70.0 (d, J = 9.7 Hz, 3F). 13C NMR (101 MHz, CDCl3) δ 168.1, 160.6, 138.5, 133.8, 132.0, 127.0 (q, J = 281.6 Hz), 123.0, 107.6, 99.5, 55.2, 46.5 (q, J = 26.4 Hz), 39.9, 39.8, 33.8, 32.7, 27.2, 26.9. MS (DART): m/z (%) 450.2 ([M+H]+, 100), 467.2 ([M+NH4]+). HRMS (DART): Calculated for C24H27F3NO4 ([M+H]+): 450.1887; Found: 450.1884.

2-(6,6,6-Trifluoro-5-(3-methoxyphenyl)-3,3-dimethylhexyl)isoindoline-1,3-dione (4f). The product (117 mg, 70% yield using P1) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). 1H NMR (400 MHz, CDCl3) δ 7.83 – 7.76 (m, 2H), 7.69 – 7.63 (m, 2H), 7.23 (t, J = 7.9 Hz, 1H), 6.97 – 6.87 (m, 2H), 6.81 (dd, J = 8.1 Hz, 2.2 Hz, 1H), 3.78 (s, 3H), 3.67 – 3.57 (m, 2H), 3.51 – 3.36 (m, 1H), 1.99 (d, J = 5.9 Hz, 2H), 1.66 – 1.44 (m, 2H), 0.85 (s, 3H), 0.82 (s, 3H). 19F NMR (376 MHz, CDCl3) δ -70.1 (d, J = 9.7 Hz, 3F). 13C NMR (101 MHz, CDCl3) δ 168.1, 159.5, 137.8, 133.8, 132.0, 129.5, 127.0 (q, J = 281.2 Hz), 123.0, 121.7, 115.2, 113.0, 55.0, 46.3 (q, J = 26.4 Hz), 39.9, 39.8, 33.8, 32.7, 27.2, 26.9. MS (DART): m/z (%) 420.2 ([M+H]+), 437.2 ([M+NH4]+, 100). HRMS (DART): Calculated for C23H25F3NO3 ([M+H]+): 420.1781; Found: 420.1176.
2-(6,6,6-Trifluoro-5-(4-methoxyphenyl)-3,3-dimethylhexyl)isoindoline-1,3-dione (4g). The product (96 mg, 57% yield using P1) as a white solid (m.p. 88.7 – 89.9 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 – 7.76 (m, 2H), 7.71 – 7.62 (m, 2H), 7.25 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.3$ Hz, 2H), 3.75 (s, 3H), 3.68 – 3.56 (m, 2H), 3.48 – 3.33 (m, 1H), 2.02 – 1.89 (m, 2H), 1.66 – 1.40 (m, 2H), 0.84 (s, 3H), 0.80 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.6 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.1, 159.2, 133.8, 132.0, 130.2, 128.1, 127.2 (q, $J = 281.3$ Hz), 123.0, 113.9, 55.0, 45.4 (q, $J = 281.3$ Hz), 39.8, 33.8, 32.6, 27.3, 27.0. MS (DART): m/z (%) 420.2 ([M+H]$^+$), 437.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{23}$H$_{25}$F$_3$NO$_3$ ([M+H]$^+$): 420.1781; Found: 420.1778.

Ethyl 3-(6-(1,3-dioxoisoinolin-2-yl)-1,1,1-trifluoro-4,4-dimethylhexan-2-yl)benzoate (4h). The product (74 mg, 40% yield using P2) as a colorless oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 – 7.94 (m, 2H), 7.82 – 7.76 (m, 2H), 7.69 – 7.63 (m, 2H), 7.54 (d, $J = 7.7$ Hz, 1H), 7.40 (t, $J = 7.7$ Hz, 1H), 4.35 (q, $J = 7.1$ Hz, 2H), 3.68 – 3.58 (m, 2H), 3.57 – 3.45 (m, 1H), 2.07 – 1.97 (m, 2H), 1.63 – 1.43 (m, 2H), 1.37 (t, $J = 7.1$ Hz, 3H), 0.82 (s, 3H), 0.79 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.2 (d, $J = 9.6$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.0, 166.0, 136.8, 133.8, 133.6, 132.0, 130.9, 130.4, 129.2, 128.7, 126.8 (q, $J = 281.3$ Hz), 123.0, 61.0, 46.2 (q, $J = 26.7$ Hz), 39.9, 39.9, 33.8, 32.8, 27.3, 26.9, 14.2. MS (DART): m/z (%) 462.2 ([M+H]$^+$, 100), 479.2 ([M+NH$_4$]$^+$); HRMS (DART): Calculated for C$_{25}$H$_{27}$F$_3$NO$_4$ ([M+H]$^+$): 462.1887; Found: 462.1879.

Ethyl 4-(6-(1,3-dioxoisoinolin-2-yl)-1,1,1-trifluoro-4,4-dimethylhexan-2-yl)benzoate (4i). The product (105 mg, 57% yield using P2) as a colorless oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.98 (d, $J = 8.2$ Hz, 2H), 7.79 – 7.73 (m, 2H), 7.67 – 7.60 (m, 2H), 7.41 (d, $J = 8.2$ Hz, 2H), 4.31 (q, $J = 7.1$ Hz, 2H), 3.68 – 3.46 (m, 3H), 2.06 – 1.92 (m, 2H), 1.62 – 1.40 (m, 2H), 1.33 (t, $J = 7.1$ Hz, 3H), 0.81 (s, 3H), 0.75
The product (131 mg, 69% yield using P2) as a yellow solid (m.p. 115.5 – 117.6 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 – 7.75 (m, 2H), 7.70 – 7.61 (m, 2H), 7.21 (d, $J = 8.3$ Hz, 2H), 6.83 (d, $J = 8.3$ Hz, 2H), 3.85 – 3.74 (m, 4H), 3.68 – 3.53 (m, 2H), 3.44 – 3.28 (m, 1H), 3.15 – 3.05 (m, 4H), 1.99 – 1.87 (m, 2H), 1.64 – 1.38 (m, 2H), 0.84 (s, 3H), 0.80 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.5 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 165.9, 141.2, 133.7, 132.0, 130.2, 129.7, 129.3, 126.7 (q, $J = 282.2$ Hz), 123.0, 60.8, 46.3 (q, $J = 26.5$ Hz), 39.8, 39.7, 33.7, 32.7, 27.2, 27.0, 14.1. MS (DART): m/z (%) 408.1 (100), 462.2 ([M+H]$^+$). HRMS (DART): Calculated for C$_{25}$H$_{27}$F$_3$NO$_4$ ([M+H]$^+$): 462.1887; Found: 462.1886.

2-(6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl)isoindoline-1,3-dione (4j). The product (131 mg, 69% yield using P2) as a yellow solid (m.p. 115.5 – 117.6 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 – 7.75 (m, 2H), 7.70 – 7.61 (m, 2H), 7.21 (d, $J = 8.3$ Hz, 2H), 6.83 (d, $J = 8.3$ Hz, 2H), 3.85 – 3.74 (m, 4H), 3.68 – 3.53 (m, 2H), 3.44 – 3.28 (m, 1H), 3.15 – 3.05 (m, 4H), 1.99 – 1.87 (m, 2H), 1.64 – 1.38 (m, 2H), 0.84 (s, 3H), 0.80 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.5 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 150.6, 133.7, 131.9, 129.9, 127.2 (q, $J = 281.2$ Hz), 127.0, 122.9, 115.2, 66.6, 48.7, 45.3 (q, $J = 26.4$ Hz), 39.7, 39.7, 33.8, 32.6, 27.2, 27.0. MS (DART): m/z (%) 475.2 ([M+H]$^+$, 100). HRMS (DART): Calculated for C$_{26}$H$_{30}$F$_3$N$_2$O$_3$ ([M+H]$^+$): 475.2203; Found: 475.2197.

2-(5-(4-(Diphenylamino)phenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4k). The product (169 mg, 76% yield using P2) as a dark green oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.85 – 7.77 (m, 2H), 7.70 – 7.62 (m, 2H), 7.25 – 7.15 (m, 6H), 7.09 – 6.94 (m, 8H), 3.73 – 3.56 (m, 2H), 3.50 – 3.33 (m, 1H), 2.04 – 1.91 (m, 2H), 1.68 – 1.45 (m, 2H), 0.91 (s, 3H), 0.88 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.2 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 147.4, 133.7, 132.1, 130.0, 129.7, 129.14, 127.1 (q, $J = 281.2$ Hz), 124.4, 123.1, 123.0 122.9, 45.6 (q, $J = 26.5$ Hz), 40.0, 39.8, 33.9, 32.7, 27.1, 27.1. MS (DART): m/z (%) 557.2 ([M+H]$^+$, 100). HRMS (DART): Calculated for C$_{34}$H$_{32}$F$_3$N$_2$O$_2$ ([M+H]$^+$): 557.2410; Found: 557.2396.
2-(6,6,6-Trifluoro-3,3-dimethyl-5-(4-methylthio)(phenyl)hexyl)isoindoline-1,3-dione (4l). The product (97 mg, 56% yield using P2) as a yellow solid (m.p. 88.9 – 90.4 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.81 – 7.74 (m, 2H), 7.68 – 7.61 (m, 2H), 7.24 (d, $J = 8.4$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H), 3.67 – 3.54 (m, 2H), 3.48 – 3.34 (m, 1H), 2.41 (s, 3H), 2.02 – 1.92 (m, 2H), 1.61 – 1.41 (m, 2H), 0.83 (s, 3H), 0.79 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.3 (d, $J = 9.7$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 138.4, 133.7, 132.8, 132.0, 129.6, 127.0 (q, $J = 281.4$ Hz), 126.3, 122.9, 45.7 (q, $J = 26.4$ Hz), 39.7, 33.8, 32.6, 27.2, 27.0, 15.3. MS (DART): m/z (%) 436.2 ([M+H]$^+$), 453.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{23}$H$_{25}$F$_3$NO$_2$ ([M+H]$^+$); 436.1553; Found: 436.1549.

2-(5-(4-(1,3-Dioxolan-2-yl)phenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4m). The product (129 mg, 70% yield using P1) as a colorless oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). (Note: this compound is prone to deterioration during silica gel chromatography) $^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 – 7.77 (m, 2H), 7.70 – 7.64 (m, 2H), 7.45 (d, $J = 8.2$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 2H), 5.77 (s, 1H), 4.12 – 4.06 (m, 2H), 4.02 – 3.96 (m, 2H), 3.67 – 3.58 (m, 2H), 3.54 – 3.40 (m, 1H), 2.05 – 1.97 (m, 2H), 1.64 – 1.43 (m, 2H), 0.83 (s, 3H), 0.79 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.1 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.1, 137.7, 137.3, 133.8, 132.0, 129.3, 126.9 (q, $J = 281.3$ Hz), 126.7, 123.0, 103.2, 65.2, 46.1 (q, $J = 26.4$ Hz), 39.9, 39.8, 33.8, 32.7, 27.3, 27.0. MS (DART): m/z (%) 462.2 ([M+H]$^+$), 479.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{25}$H$_{27}$F$_3$NO$_4$ ([M+H]$^+$); 462.1887; Found: 462.1882.

2-(5-(4-Chlorophenyl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4n). The product (93 mg, 55% yield using P1) as a white solid (m.p. 75.2 – 76.6 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 15/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.83 – 7.76 (m, 2H), 7.70 – 7.63 (m, 2H), 7.31 – 7.26 (m, 4H), 3.69 – 3.54 (m, 2H), 3.52 – 3.38 (m, 1H), 2.05 – 1.87 (m, 2H), 1.63 – 1.42 (m, 2H), 0.84 (s, 3H), 0.79 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.3 (d,
$J = 9.7 \text{ Hz}$. $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.1, 134.8, 133.9, 133.8, 132.0, 130.6, 128.8, 126.8 (q, $J = 281.3 \text{ Hz}$), 123.0, 45.7 (q, $J = 26.6 \text{ Hz}$), 39.8, 39.7, 33.7, 32.7, 27.3. 27.1. MS (DART): m/z (%) 424.1 ([M+H]$^+$), 441.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{22}$H$_{22}$ClF$_3$NO$_2$ ([M+H]$^+$): 424.1286; Found: 424.1283.

![Chemical structure](image)

2-(5-(Benzo[d][1,3]dioxol-5-yl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4o). The product (97 mg, 56% yield using P2) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 – 7.76 (m, 2H), 7.70 – 7.63 (m, 2H), 6.86 – 6.70 (m, 3H), 5.92 (s, 2H), 3.70 – 3.54 (m, 2H), 3.47 – 3.31 (m, 1H), 2.03 – 1.83 (m, 2H), 1.65 – 1.42 (m, 2H), 0.86 (s, 3H), 0.82 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.5 (d, $J = 9.7 \text{ Hz}$). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 1681, 147.8, 147.3, 133.8, 132.0, 129.8, 127.0 (q, $J = 281.3 \text{ Hz}$), 123.0, 109.1, 108.2, 101.1, 45.9 (q, $J = 26.5 \text{ Hz}$), 39.8, 39.7, 33.8, 32.7, 27.3. MS (DART): m/z (%) 434.2 ([M+H]$^+$), 451.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{23}$H$_{23}$F$_3$NO$_4$ ([M+H]$^+$): 434.1574; Found: 434.1568.

![Chemical structure](image)

2-(6,6,6-Trifluoro-3,3-dimethyl-5-(naphthalen-2-yl)hexyl)isoindoline-1,3-dione (4p). The product (99 mg, 56% yield using P1) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.88 – 7.78 (m, 6H), 7.69 – 7.61 (m, 2H), 7.54 – 7.62 (m, 3H), 3.75 – 3.61 (m, 3H), 2.23 – 2.08 (m, 2H), 1.74 – 1.51 (m, 2H), 0.88 (s, 3H), 0.84 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -69.8 (d, $J = 9.8 \text{ Hz}$). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.1, 133.7, 133.1, 132.9, 132.0, 128.8, 128.3, 127.8, 127.5, 127.2 (q, $J = 281.6 \text{ Hz}$), 126.6, 126.2, 126.1, 123.0, 46.4 (q, $J = 26.4 \text{ Hz}$), 39.9, 39.8, 33.8, 32.8, 27.3, 27.0. MS (DART): m/z (%) 440.2 ([M+H]$^+$), 457.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{26}$H$_{25}$F$_3$NO$_2$ ([M+H]$^+$): 440.1832; Found: 440.1830.
**2-(5-(Dibenzo[b,d]thiophen-2-yl)-6,6,6-trifluoro-3,3-dimethylhexyl)isoindoline-1,3-dione (4q).** The product (105 mg, 53% yield using P1) as a yellow viscous oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.23 – 8.13 (m, 2H), 7.86 – 7.79 (m, 2H), 7.79 – 7.73 (m, 2H), 7.66 – 7.56 (m, 2H), 7.53 – 7.39 (m, 3H), 3.78 – 3.59 (m, 3H), 2.17 (d, $J$ = 5.8 Hz, 2H), 1.75 – 1.51 (m, 2H), 0.90 (s, 3H), 0.86 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -69.9 (d, $J$ = 9.7 Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 139.7, 139.1, 135.7, 135.0, 133.6, 132.7, 131.9, 127.7, 127.1 (q, $J$ = 281.4 Hz), 126.8, 124.3, 122.9, 122.7, 122.3, 121.6, 46.3 (q, $J$ = 26.5 Hz), 40.2, 39.8, 33.8, 32.8, 27.4, 27.1. MS (DART): m/z (%) 496.2 ([M+H]$^+$), 513.2 ([M+NH$_4$]$^+$, 100). HRMS (DART): Calculated for C$_{28}$H$_{25}$F$_3$NO$_2$S ([M+H]$^+$): 496.1553; Found: 496.1549.

**2-(6,6,6-Trifluoro-3,3-dimethyl-5-(1-methyl-1H-indol-5-yl)hexyl)isoindoline-1,3-dione (4r).** The product (92 mg, 52% yield using P2) as a yellow solid (m.p. 92.0 – 93.2 ℃) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.86 – 7.79 (m, 2H), 7.71 – 7.62 (m, 3H), 7.33 – 7.19 (m, 2H), 7.03 (d, $J$ = 3.0 Hz, 1H), 6.48 (d, $J$ = 3.0 Hz, 1H), 3.73 (s, 3H), 3.69 (t, $J$ = 8.3 Hz, 2H), 3.65 – 3.54 (m, 1H), 2.21 – 2.04 (m, 2H), 1.75 – 1.51 (m, 2H), 0.88 (s, 3H), 0.85 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.2 (d, $J$ = 9.9 Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 168.0, 136.2, 133.7, 132.0, 129.3, 128.4, 127.6 (q, $J$ = 281.4 Hz), 126.9, 122.9, 122.6, 121.7, 109.1, 100.8, 46.3 (q, $J$ = 26.1 Hz), 40.2, 39.9, 33.9, 32.7, 32.6, 27.3, 26.9. MS (DART): m/z (%) 443.2 ([M+H]$^+$). HRMS (DART): Calculated for C$_{25}$H$_{26}$F$_3$N$_2$O$_2$ ([M+H]$^+$): 443.1941; Found: 443.1931.

**4-(4-(1,1,1-Trifluoro-4,4-dimethylpentan-2-yl)phenyl)morpholine (5a).** The product (68 mg, 54% yield using P2) as a yellow oil was purified with silica gel chromatography (DCM). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.29 – 7.16 (m, 2H), 6.86 (d, $J$ = 8.5 Hz, 2H), 3.90 – 3.77 (m, 4H), 3.33 – 3.19 (m, 1H), 3.18 – 3.10 (m, 4H), 1.91 – 1.83 (m, 2H), 0.80 (s, 9H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.6 (d, $J$ = 10.2 Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 150.7, 130.0, 127.6, 127.4 (q, $J$ = 281.1 Hz), 115.2, 66.8, 48.9, 46.0 (q, $J$ = ...
= 26.2 Hz), 41.8, 30.7, 29.7. MS (ESI): m/z (%) 316.2 ([M+H]+). HRMS (ESI): Calculated for C\textsubscript{17}H\textsubscript{25}F\textsubscript{3}NO ([M+H]+): 316.1883; Found: 316.1883.

**4-(4-(1,1,1-Trifluoro-4,4-dimethyldodecan-2-yl)phenyl)morpholine (5b).** The product (65 mg, 39% yield using P1 at 0 °C) as a yellow oil was purified with silica gel chromatography (DCM). \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.22 (d, \(J = 8.4\) Hz, 2H), 6.87 (d, \(J = 8.6\) Hz, 2H), 3.89 – 3.82 (m, 4H), 3.30 – 3.19 (m, 1H), 3.19 – 3.12 (m, 4H), 1.93 – 1.80 (m, 2H), 1.31 – 1.02 (m, 14H), 0.89 (t, \(J = 6.9\) Hz, 3H), 0.76 (s, 3H), 0.74 (s, 3H). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -70.6 (d, \(J = 10.2\) Hz, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 150.7, 130.1, 127.8, 127.8, 127.5 (q, \(J = 281.0\) Hz), 115.3, 66.8, 49.0, 45.7 (q, \(J = 281.0\) Hz), 42.1, 39.7, 33.1, 31.9, 30.4, 29.6, 29.3, 27.7, 27.5, 23.8, 22.7, 14.1. MS (ESI): m/z (%) 414.3 ([M+H]+). HRMS (ESI): Calculated for C\textsubscript{24}H\textsubscript{39}F\textsubscript{3}NO ([M+H]+): 414.2980; Found: 414.2980.

**4-(4-(7-Chloro-1,1,1-trifluoro-4,4-dimethylheptan-2-yl)phenyl)morpholine (5c').** The product (30 mg, 20% yield using P1) as a yellow oil was purified with silica gel chromatography (DCM). 5c' was obtained from 5c (reaction run with 2d as alkyl iodide) during silica gel chromatography. 5c can only be observed on the TLC. \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.21 (d, \(J = 8.5\) Hz, 2H), 6.87 (d, \(J = 8.6\) Hz, 2H), 3.88 – 3.82 (m, 4H), 3.30 (t, \(J = 6.8\) Hz, 2H), 3.27 – 3.20 (m, 1H), 3.19 – 3.13 (m, 4H), 1.95 – 1.79 (m, 2H), 1.71 – 1.59 (m, 1H), 1.59 – 1.46 (m, 1H), 1.32 – 1.21 (m, 1H), 1.20 – 1.10 (m, 1H), 0.79 (s, 3H), 0.78 (s, 3H). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -70.6 (d, \(J = 10.0\) Hz, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 151.0, 130.1, 127.5, 127.5 (q, \(J = 280.0\) Hz), 115.5, 66.9, 49.1, 45.7 (q, \(J = 26.5\) Hz), 45.6, 39.7, 39.2, 33.1, 27.7, 27.5, 27.5. MS (ESI): m/z (%) 378.1 ([M+H]+). HRMS (ESI): Calculated for C\textsubscript{19}H\textsubscript{28}ClF\textsubscript{3}NO ([M+H]+): 378.1806; Found: 378.1804.
6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl benzoate (5d). The product (95 mg, 53% yield using P2) as a brown oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.0 (d, $J = 7.5$ Hz, 2H), 7.58 – 7.51 (m, 1H), 7.46 – 7.39 (m, 2H), 7.23 (d, $J = 8.5$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 4.35 – 4.15 (m, 2H), 3.83 – 3.77 (m, 4H), 3.39 – 3.24 (m, 1H), 3.12 – 3.06 (m, 4H), 2.06 – 1.92 (m, 2H), 1.71 – 1.55 (m, 2H), 0.91 (s, 3H), 0.87 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.5 (d, $J = 9.8$ Hz, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.3, 150.7, 132.7, 130.2, 129.9, 128.2, 127.2 (q, $J = 281.3$ Hz), 127.0, 115.2, 66.6, 61.7, 48.6, 45.5 (q, $J = 26.4$ Hz), 40.2, 39.9, 32.6, 27.4, 27.3. MS (ESI): m/z (%) 450.2 ([M+H]$^+$). HRMS (ESI): Calculated for C$_{25}$H$_{31}$F$_3$NO$_3$ ([M+H]$^+$): 450.2251; Found: 450.2253.

6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl 4-cyanobenzoate (5e). The product (118 mg, 62% yield using P1) as a yellow oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.04 (d, $J = 8.2$ Hz, 2H), 7.67 (d, $J = 8.2$ Hz, 2H), 7.20 (d, $J = 8.4$ Hz, 2H), 6.82 (d, $J = 8.5$ Hz, 2H), 4.34 – 4.25 (m, 1H), 4.24 – 4.15 (m, 1H), 3.83 – 3.71 (m, 4H), 3.36 – 3.21 (m, 1H), 3.12 – 2.99 (m, 4H), 2.01 – 1.88 (m, 2H), 1.69 – 1.52 (m, 2H), 0.87 (s, 3H), 0.83 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.4 (d, $J = 9.9$ Hz, 3F). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 164.7, 150.8, 134.0, 132.1, 129.9, 127.2 (q, $J = 279.8$ Hz), 126.9, 66.6, 62.5, 48.6, 45.5 (q, $J = 26.4$ Hz), 40.2, 39.8, 32.6, 27.5, 27.3. MS (ESI): m/z (%) 475.1 ([M+H]$^+$). HRMS (ESI): Calculated for C$_{26}$H$_{30}$F$_3$N$_2$O$_3$ ([M+H]$^+$): 475.2203; Found: 475.2201.

5-(3,5-Dimethoxyphenyl)-6,6,6-trifluoro-3,3-dimethylhexyl 4-chlorobenzoate (5f). The product (125 mg, 68% yield using P2) as a white solid (m.p. 71.8 – 73.0 °C) was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.91 (d, $J = 8.3$ Hz, 2H), 7.38 (d, $J = 8.3$ Hz, 2H), 6.50 (s, 2H), 6.37 (s, 1H), 4.36 – 4.14 (m, 2H), 3.74 (s, 6H), 3.38 – 3.24 (m, 1H), 2.07 – 1.90 (m, 2H), 1.71 – 1.56 (m, 2H), 0.91 (s, 3H), 0.88 (s,
6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl thiophene-3-carboxylate (5g). The product (120 mg, 66% yield using P2) as a purple oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.05 – 8.02 (m, 1H), 7.51 – 7.45 (m, 1H), 7.28 – 7.24 (m, 1H), 7.22 (d, $J = 8.5$ Hz, 2H), 6.84 (d, $J = 8.7$ Hz, 2H), 4.30 – 4.09 (m, 2H), 3.83 – 3.77 (m, 4H), 3.38 – 3.22 (m, 1H), 3.12 – 3.06 (m, 4H), 2.04 – 1.89 (m, 2H), 1.67 – 1.49 (m, 2H), 0.88 (s, 3H), 0.84 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.4 (d, $J = 10.2$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 162.4, 150.7, 133.6, 132.3, 129.8, 127.7, 127.1 (q, $J = 281.3$ Hz), 126.9, 125.8, 115.1, 66.6, 61.3, 48.6, 45.5 (q, $J = 26.5$ Hz), 40.1, 39.8, 32.5, 27.4, 27.3. MS (ESI): m/z (%) 456.1 ($[M+H]^+$). HRMS (ESI): Calculated for C$_{23}$H$_{29}$F$_3$NO$_3$ ($[M+H]^+$): 456.1815; Found: 456.1816.

6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl 6-bromohexanoate (5h). The product (120 mg, 62% yield using P2) as a colorless oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.17 (d, $J = 8.4$ Hz, 2H), 6.83 (d, $J = 8.5$ Hz, 2H), 4.08 – 3.90 (m, 2H), 3.84 – 3.75 (m, 4H), 3.48 (t, $J = 6.6$ Hz, 2H), 3.31 – 3.18 (m, 1H), 3.15 – 3.06 (m, 4H), 2.23 (t, $J = 7.4$ Hz, 2H), 1.92 – 1.84 (m, 2H), 1.78 – 1.68 (m, 2H), 1.64 – 1.54 (m, 2H), 1.52 – 1.36 (m, 4H), 0.79 (s, 3H), 0.75 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.5 (d, $J = 9.9$ Hz, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 173.1, 150.6, 129.8, 127.1 (q, $J = 281.3$ Hz), 126.9, 115.1, 66.6, 60.9, 48.6, 45.3 (q, $J = 26.3$ Hz), 44.5, 40.1, 39.8, 33.8, 32.4, 31.9, 27.3, 27.1, 26.1, 23.9. MS (ESI): m/z (%) 478.2 (100), 524.1 ($[M+H]^+$). HRMS (ESI): Calculated for C$_{24}$H$_{36}$BrF$_3$NO$_3$ ($[M+H]^+$): 522.1825; Found: 522.1829.
**6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (5i).** The product (113 mg, 41% yield using P2) as a yellow viscous oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.64 (d, $J = 8.3$ Hz, 2H), 7.44 (d, $J = 8.3$ Hz, 2H), 6.97 (d, $J = 2.0$ Hz, 1H), 6.91 – 6.80 (m, 3H), 6.71 – 6.64 (m, 1H), 4.15 – 3.97 (m, 2H), 3.85 – 3.78 (m, 7H), 3.63 (s, 2H), 3.31 – 3.18 (m, 1H), 3.16 – 3.08 (m, 4H), 2.37 (s, 3H), 1.93 – 1.85 (m, 2H), 1.59 – 1.42 (m, $J = 7.3$ Hz, 2H), 0.79 (s, 3H), 0.76 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.5 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 170.6, 168.0, 155.9, 150.7, 139.0, 135.7, 133.7, 131.0, 130.6, 130.5, 129.8, 128.9, 127.1 (q, $J = 281.4$ Hz), 126.9, 115.1, 114.8, 112.4, 111.4, 101.2, 66.6, 61.7, 55.4, 48.6, 45.4 (q, $J = 26.5$ Hz), 40.3, 39.8, 32.5, 30.2, 27.2, 27.1, 13.2. MS (ESI): m/z (%) 685.2 ([M+H]$^+$, 100). HRMS (ESI): Calculated for C$_{37}$H$_{41}$ClF$_3$N$_2$O$_5$ ([M+H]$^+$): 685.2651; Found: 685.2658.

**6,6,6-Trifluoro-3,3-dimethyl-5-(4-morpholinophenyl)hexyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (5j).** The product (113 mg, 49% yield using P1) as a colorless viscous oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.23 (d, $J = 8.4$ Hz, 2H), 7.04 (d, $J = 7.4$ Hz, 1H), 6.87 (d, $J = 8.6$ Hz, 2H), 6.69 (d, $J = 7.5$ Hz, 1H), 6.64 (s, 1H), 4.14 – 3.97 (m, 2H), 3.97 – 3.91 (m, 2H), 3.89 – 3.83 (m, 4H), 3.38 – 3.23 (m, 1H), 3.20 – 3.12 (m, 4H), 2.34 (s, 3H), 2.21 (s, 3H), 1.99 – 1.91 (m, 2H), 1.78 – 1.69 (m, 4H), 1.57 – 1.44 (m, 2H), 1.22 (s, 6H), 0.89 (s, 3H), 0.82 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.5 (d, $J = 9.8$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 177.6, 156.8, 150.7, 136.3, 130.2, 129.9, 127.2 (q, $J = 281.2$ Hz), 127.1, 123.4, 120.6, 115.2, 111.8, 67.7, 66.7, 61.2, 48.7, 45.5 (q, $J = 26.3$ Hz), 41.8, 40.3, 40.2, 36.9, 32.6, 27.3, 27.2, 25.1, 25.0, 21.3, 15.7. MS (ESI): m/z (%) 578.3 ([M+H]$^+$, 100). HRMS (ESI): Calculated for C$_{33}$H$_{47}$F$_3$NO$_4$ ([M+H]$^+$): 578.3452; Found: 578.3440.
Di-tert-butyl 3a-(3,3,3-trifluoro-2-(4-methoxyphenyl)propyl)-2,3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1,8-dicarboxylate (5k). The product (115 mg, 51% yield using P2) as a colorless viscous oil was purified with silica gel chromatography (Hexane/Ethyl Acetate = 10/1). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.28 – 7.19 (m, 2H), 7.12 – 7.01 (m, 2H), 6.91 (d, $J$ = 8.4 Hz, 2H), 6.82 (d, $J$ = 8.6 Hz, 2H), 3.81 – 3.70 (m, 4H), 2.98 – 2.84 (m, 1H), 2.68 – 2.51 (m, 2H), 2.42 – 2.27 (m, 1H), 2.00 – 1.92 (m, 1H), 1.84 – 1.74 (m, 1H), 1.58 – 1.53 (m, 2H), 1.48 (s, 2H), 1.43 (s, 15H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.4 (d, $J$ = 9.4 Hz). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 159.5, 153.9, 151.5, 143.7, 131.8, 130.0, 128.7, 126.8 (q, $J$ = 281.7 Hz), 125.2, 123.0, 122.8, 114.7, 114.2, 81.0, 79.7, 79.1, 54.8, 54.7, 46.7 (q, $J$ = 27.1 Hz), 44.5, 41.9, 37.0, 28.2, 28.1. MS (ESI): m/z (%) 451.1 (100), 563.2 ([M+H]$^+$). HRMS (ESI): Calculated for C$_{30}$H$_{38}$F$_3$N$_2$O$_5$ ([M+H]$^+$): 563.2727; Found: 563.2736.

(6,6-Dimethyl-4-(trifluoromethyl)heptyl)benzene (5l). The reaction was conducted using NiCl$_2$-DME as the catalyst without L3 and phosphine ligand. (Note: the standard reaction conditions failed to provide the desired product). The product (28.3 mg, 26% yield) as a colorless viscous oil was purified with silica gel chromatography (Hexane). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37 – 7.28 (m, 2H), 7.25 – 7.18 (m, 3H), 2.69 – 2.61 (m, 2H), 2.15 – 2.00 (m, 1H), 1.90 – 1.66 (m, 3H), 1.65 – 1.58 (m, 1H), 1.58 – 1.46 (m, 1H), 1.26 – 1.17 (m, 1H), 0.93 (s, 9H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -70.2 (d, $J$ = 10.0 Hz, 3F). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 141.9, 129.0 (q, $J$ = 279.8 Hz), 128.4, 125.9, 41.8 (d, $J$ = 1.9 Hz), 39.2 (q, $J$ = 24.9 Hz), 36.1, 30.9 (q, $J$ = 2.2 Hz), 30.7, 29.4, 28.9. MS (FI): m/z (%) 272 ([M]$^+$). HRMS (FI): Calculated for C$_{16}$H$_{23}$F$_3$ ([M]$^+$): 272.1750; Found: 272.1746.
7. Transformations of Compound 4a

Deprotection of compound 4a

5-([1,1'-Biphenyl]-4-yl)-6,6,6-trifluoro-3,3-dimethylhexan-1-amine (8). To a suspension of 4a (6 mmol, 1 equiv) in 40 mL ethanol was added hydrazine monohydrate (2 mL, 18 mmol, 6 equiv) at room temperature. The mixture was heated under reflux for 8 hours. The reaction was cooled to room temperature, and the resulting precipitate was filtered off and washed by ethyl acetate. The filtrate was concentrated and the residue was purified with silica gel chromatography (DCM/MeOH = 30/1) to give compound 8 as a yellow solid (1.44g, 72% yield, m.p. 77.0 – 78.0 ℃). ¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.52 (m, 4H), 7.50 – 7.30 (m, 5H), 5.01 (s, 2H), 3.52 – 3.36 (m, 1H), 2.91 – 2.62 (m, 2H), 2.05 – 1.89 (m, 2H), 1.67 – 1.37 (m, 2H), 0.82 (s, 3H), 0.79 (s, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -70.0 (d, J = 9.5 Hz). ¹³C NMR (126 MHz, CDCl₃) δ 141.0, 140.4, 129.8, 128.9, 127.5, 127.3, 127.3 (q, J = 279.9 Hz), 127.1, 46.1 (q, J = 26.7 Hz), 43.0, 40.1, 36.8, 32.9, 27.6, 27.2. MS (ESI): m/z (%) 336.1 ([M+H]+). HRMS (ESI): Calculated for C₂₀H₂₅F₃N ([M+H]+): 336.1934; Found: 336.1932.

Synthesis of compound 10a

tert-Butyl 3-([5-([1,1'-biphenyl]-4-yl]-6,6,6-trifluoro-3,3-dimethylhexyl)carbamoyl)azetidine-1-carboxylate (10a). To a mixture of 1-(t-butyloxycarbonyl)-azetidine-3-carboxylic acid (1.2 mmol, 1.2 equiv) and 4-(dimethylamino)pyridine (2 mmol, 2 equiv) in 5 mL anhydrous CH₂Cl₂ was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDCI·HCl) (1.2 mmol, 1.2 equiv) and amine 6 (1 mmol, 1 equiv) at room temperature. The mixture was then stirred at room temperature for 20 h. The solution was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated. The residue was purified with silica gel chromatography (Hexane/Ethyl Acetate = 2/1) to give compound 10a as a viscous colorless oil (451
mg, 87% yield). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.60 – 7.50 (m, 4H), 7.44 – 7.27 (m, 5H), 6.20 (s, 1H), 4.10 – 3.98 (m, 2H), 3.97 – 3.84 (m, 2H), 3.46 – 3.32 (m, 1H), 3.30 – 3.16 (m, 1H), 3.12 – 2.98 (m, 2H), 2.02 – 1.88 (m, 2H), 1.40 (s, 9H), 1.34 – 1.23 (m, 2H), 0.80 (s, 3H), 0.77 (s, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.0 (d, $\text{J} = 9.7$ Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 171.6, 156.1, 140.7, 140.1, 135.4, 129.7, 128.8, 127.5, 127.1, 127.1 (q, $\text{J} = 280.0$ Hz), 126.8, 79.6, 52.1 (br), 46.0 (q, $\text{J} = 26.3$ Hz), 41.1, 40.0, 35.6, 33.0, 32.7, 28.2, 27.4, 27.0. MS (ESI): m/z (%) 541.2 ([M+Na]$^+$, 100). HRMS (ESI): Calculated for C$_{29}$H$_{37}$F$_3$N$_2$NaO$_3$ ([M+Na]$^+$): 541.2648; Found: 541.2646.

Synthesis of compound 10b

$^{N}$-(5-((1,1'-biphenyl)-4-yl)-6,6,6-trifluoro-3,3-dimethylhexyl)-1-cyanocyclopropane-1-carboxamide (10b). To a mixture of 1-cyano-cyclopropanecarboxylic acid (1.2 mmol, 1.2 equiv) and 4-(dimethylamino)pyridine (2 mmol, 2 equiv) in 5 mL anhydrous CH$_2$Cl$_2$ was added $^{N}$-(3-dimethylaminopropyl)-$^{N'}$-ethylcarbodiimide hydrochloride (EDCI·HCl) (1.2 mmol, 1.2 equiv) and amine 6 (1 mmol, 1 equiv) at room temperature. The mixture then was stirred at room temperature for 20 h. The solution was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated. The residue was purified with silica gel chromatography (Hexane/Ethyl Acetate = 2/1) to give compound 10b as a white solid (293 mg, 68% yield, m.p. 96.7 – 97.8 °C). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.66 – 7.58 (m, 4H), 7.48 – 7.32 (m, 5H), 6.37 (t, $\text{J} = 5.0$ Hz, 1H), 3.51 – 3.37 (m, 1H), 3.33 – 3.21 (m, 1H), 3.18 – 3.06 (m, 1H), 2.08 – 1.94 (m, 2H), 1.68 – 1.55 (m, 2H), 1.49 – 1.32 (m, 4H), 0.85 (s, 6H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -70.0 (d, $\text{J} = 9.8$ Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 165.0, 140.9, 140.2, 135.3, 129.7, 128.8, 127.5, 127.2, 127.2 (q, $\text{J} = 279.6$ Hz), 127.0, 120.2, 46.1 (q, $\text{J} = 26.1$ Hz), 40.8, 39.9, 36.5, 32.8, 27.5, 27.2, 17.3, 17.3, 13.4. MS (ESI): m/z (%) 429.2 ([M+H]$^+$, 100), 451.1 ([M+Na]$^+$). HRMS (ESI): Calculated for C$_{25}$H$_{28}$F$_3$N$_2$O ([M+H]$^+$): 429.2148; Found: 429.2148.
Synthesis of compound 10c

N-(5-((1,1'-biphenyl)-4-yl)-6,6,6-trifluoro-3,3-dimethylhexyl)-6-(3-((3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)-2-naphthamide (10c). To a mixture of adapalene (1.2 mmol, 1.2 equiv) and 4-(dimethylamino)pyridine (2 mmol, 2 equiv) in 5 mL anhydrous CH$_2$Cl$_2$ was added N-(3-dimethylaminopropyl)-N’-ethylcarbodiimide hydrochloride (EDCI·HCl) (1.2 mmol, 1.2 equiv) and amine 6 (1 mmol, 1 equiv) at room temperature. The mixture then was stirred at room temperature for 20 h. The solution was diluted with ethyl acetate and washed with water and brine. The organic layer was dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated. The residue was purified with silica gel chromatography (Hexane/Ethyl Acetate = 5/1) to give compound 10c as a white solid (673 mg, 92% yield, m.p. 141.5 – 142.8 °C). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.24 (s, 1H), 8.02 (s, 1H), 7.82 (s, 2H), 7.78 (s, 2H), 7.71 – 7.65 (m, 1H), 7.62 – 7.52 (m, 5H), 7.47 – 7.32 (m, 5H), 7.01 (d, $J$ = 8.5 Hz, 1H), 6.45 (t, $J$ = 5.2 Hz, 1H), 3.91 (s, 3H), 3.64 – 3.43 (m, 2H), 3.31 – 3.18 (m, 1H), 2.28 (s, 6H), 2.19 (s, 3H), 1.90 (s, 6H), 1.68 – 1.56 (m, 1H), 1.49 – 1.28 (m, 2H), 0.93 (s, 6H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -69.8 (d, $J$ = 9.8 Hz). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 167.6, 158.8, 140.9, 140.6, 140.0, 138.9, 135.4, 135.0, 132.5, 131.3, 131.3, 129.9, 129.3, 128.8, 128.4, 127.5, 127.2 (q, $J$ = 279.9 Hz), 127.2, 127.1, 126.9, 126.4, 125.8, 125.7, 124.6, 123.9, 112.1, 55.1, 46.3 (q, $J$ = 26.7 Hz), 40.9, 40.6, 39.7, 37.2, 37.1, 36.1, 34.1, 32.9, 29.1, 27.6, 27.4, 22.4, 14.1. MS (ESI): m/z (%) 730.3 ([M+H]$^+$, 100). HRMS (ESI): Calculated for C$_{48}$H$_{51}$F$_3$NO$_2$ ([M+H]$^+$): 730.3866; Found: 730.3867.
8. Mechanistic Studies

Radical Inhibition Experiments

**Procedure:** To a 25 mL Schlenk tube were added 2a (0.4 mmol, 1.0 equiv) 4,4'-diMeO-bpy (6 mol%), Cy2PhP (5 mol%), 1,4-dinitrobenzene or TEMPO (0.2 equiv or 1.0 equiv) and NiCl2·6H2O (5 mol%) in the glovebox. Then 1 (1.6 mmol, 2.0 equiv, 2 mL) was added under Ar. The resulting mixture was stirred for 20 min at room temperature, and arylzinc reagent 3a (0.6 mmol, 1.5 equiv) was added slowly within a period of 10 min, and the tube was sealed with a Teflon cap. After stirring for 12 h, the reaction mixture was quenched with aqueous NH4Cl solution and diluted with EtOAc. The yield was determined by 19F-NMR with benzotrifluoride as the internal standard. When 0.2 equiv or 1.0 equiv of 1,4-dinitrobenzene was added, the product 4a was not detected. When 0.2 equiv of TEMPO was added, the product 4a was obtained in 16% yield; when 1.0 equiv TEMPO was added, the product 4a was not detected. In the case of using 1.0 equiv of TEMPO as the radical trapping reagent, compound 11 was detected by LC-MS. Compound 11: MS (ESI): m/z (%) 373 ([M+H]+).

**Supplementary Figure 3** LC-MS of TEMPO Trapping Product 11

Synthesis of aryl nickel complex B1
**Procedure:** Complex B1 is a known compound and the preparation is according to the literature. In a argon filled glove box, a 50 mL round bottom flask containing a stirring bar was charged with Ni(COD)₂ (550.0 mg, 2.0 mmol, 1.0 equiv), 4,4’-di-tert-butyl-2,2’-pyridine L₂ (537.0 mg, 2.0 mmol, 1.0 equiv) and dry THF (5 mL). The resulting dark purple mixture was stirred for 1h at room temperature. Then 1-chloro-4-(1,1-dimethylethyl)benzene (8.6 mL, 51.5 mmol, 25.0 equiv) was added and the reaction mixture was stirred for additional 20 minutes. The resulting dark red solution was tritivated with pentane and the precipitate was collected on a frit, rinsed with pentane and dried under vacuum to give nickel complex (B1) as a light red powder (725 mg, 73% yield). The nickel complex was used in control experiments without further purification.

**Control Experiments:**

**Stoichiometric Experiments**

\[
\begin{align*}
\text{F}_3\text{C} & \quad + \quad \text{B}1 \quad + \quad 2\text{a} \quad \xrightarrow{\text{Zn (x equiv), P2 (y equiv)}} \quad \text{DMA, rf, 12 h} \quad \xrightarrow{19\text{F} \text{-NMR}} \\
& \quad \text{4c} \quad \xrightarrow{\text{4c'}, \text{detected by GC-MS}} \quad \text{detected by 19F NMR}
\end{align*}
\]

**Procedure:** To a 25 mL of Schlenck tube were added complex B1 (0.2 mmol, 1.0 equiv), zinc powder (if needed, 0.2 mmol, 1.0 equiv) and Cy₂PhP (if needed, 0.2 mmol, 1.0 equiv). The tube was evacuated and backfilled with argon for 3 times, then anhydrous DMA was added (5 mL). The reaction mixture was stirred for 10 min. Then TFP solution (1 M in DMA, 5 mL) was added under Ar. The resulting mixture was stirred for additional 10 min at room temperature, and alkyl iodide 2a (0.2 mmol, 1.0 equiv) was added in one portion, and the tube was sealed with a Teflon cap. After stirring for 12 h at room temperature, the reaction mixture was quenched with aqueous NH₄Cl solution and diluted with EtOAc. The yield was determined by ¹⁹F-NMR with fluorobenzene as the internal standard. For all the control experiments, the biaryl 4c’ was detected by GC-MS. Compound 4c’: MS (EI): m/z (%) 266 ([M]⁺).
Complex B1 Catalyzed Reaction under Standard Reaction Conditions

Procedure: To a 25 mL of Schlenck tube were added complex B1 (x mol%) and the monodentate phosphine ligand (PCy₂Ph (P1) or PBu₃Me·HBF₄ (P2), x mol%). The tube was evacuated and backfilled with argon for 3 times, then tertiary alkyl iodide 2a (0.4 mmol, 1.0 equiv) and TFP solution (1 M in DMA, 1.6 mmol, 4.0 equiv, 2 mL) were added under Ar. The resulting mixture was stirred for 20 min at room temperature, and the corresponding arylzinc reagent 3a (0.6 mmol, 1.5 equiv) was added slowly within a period of 10 min, and the tube was sealed with Teflon cap. After stirring for 12 h at room temperature, the reaction mixture was quenched with aqueous NH₄Cl solution and diluted with EtOAc. The yield was determined by ¹⁹F-NMR using benzotrifluoride as the internal standard.

For using P1 as the co-ligand, 4a was provided in 57% yield (x = 5) and 4c was formed in 3% yield (x = 5); for using P2 as the co-ligand, 4a was provided in 61% yield (x = 5) and 66% yield (x = 10), respectively; 4c was formed in 3% yield (x = 5) and 7% yield (x = 10), respectively. The structure of 4c was confirmed by its ¹⁹F, ¹H, and ¹³C NMR.
Supplementary Note

Supplementary Note 1: Characterization Spectra for Tertiary Alkyl Iodides 2

Supplementary Figure 4 $^1$H NMR Spectrum of 2a

Supplementary Figure 5 $^{13}$C NMR Spectrum of 2a
Supplementary Figure 6 $^1$H NMR Spectrum of 2f

Supplementary Figure 7 $^{13}$C NMR Spectrum of 2f
Supplementary Figure 8 $^1$H NMR Spectrum of 2g

Supplementary Figure 9 $^{13}$C NMR Spectrum of 2g
Supplementary Figure 10 $^1$H NMR Spectrum of 2h

Supplementary Figure 11 $^{13}$C NMR Spectrum of 2h
Supplementary Figure 12 $^1$H NMR Spectrum of 2i

Supplementary Figure 13 $^{13}$C NMR Spectrum of 2i
Supplementary Figure 14 $^1$H NMR Spectrum of 2j

Supplementary Figure 15 $^{13}$C NMR Spectrum of 2j
Supplementary Figure 16 $^1$H NMR Spectrum of 2k

Supplementary Figure 17 $^{13}$C NMR Spectrum of 2k
Supplementary Note 2: Characterization Spectra for Compounds 4 and 5

Supplementary Figure 18 $^1$H NMR Spectrum of 4a

Supplementary Figure 19 $^{19}$F NMR Spectrum of 4a
**Supplementary Figure 20**\(^{13}\text{C} \text{NMR Spectrum of 4a}\)

**Supplementary Figure 21** \(^1\text{H} \text{NMR Spectrum of 4b}\)
Supplementary Figure 22  $^{19}$F NMR Spectrum of 4b

Supplementary Figure 23  $^{13}$C NMR Spectrum of 4b
Supplementary Figure 24 $^1$H NMR Spectrum of 4c

Supplementary Figure 25 $^{19}$F NMR Spectrum of 4c
Supplementary Figure 26 $^{13}$C NMR Spectrum of 4c

Supplementary Figure 27 $^1$H NMR Spectrum of 4d
Supplementary Figure 28. $^{19}$F NMR Spectrum of 4d

Supplementary Figure 29. $^{13}$C NMR Spectrum of 4d
Supplementary Figure 30 $^1$H NMR Spectrum of 4e

Supplementary Figure 31 $^{19}$F NMR Spectrum of 4e
Supplementary Figure 32 $^{13}$C NMR Spectrum of 4e

Supplementary Figure 33 $^1$H NMR Spectrum of 4f
Supplementary Figure 34 $^{19}$F NMR Spectrum of 4f

Supplementary Figure 35 $^{13}$C NMR Spectrum of 4f
Supplementary Figure 36 $^1$H NMR Spectrum of 4g

Supplementary Figure 37 $^{19}$F NMR Spectrum of 4g
Supplementary Figure 38 $^{13}$C NMR Spectrum of 4g

Supplementary Figure 39 $^1$H NMR Spectrum of 4h
Supplementary Figure 40 $^{19}$F NMR Spectrum of 4h

Chemical Formula: C$_3$H$_6$F$_3$NO$_3$
Molecular Weight: 416.5

Supplementary Figure 41 $^{13}$C NMR Spectrum of 4h

Chemical Formula: C$_3$H$_6$F$_3$NO$_3$
Molecular Weight: 461.5
Supplementary Figure 42 $^1$H NMR Spectrum of 4i

Supplementary Figure 43 $^{19}$F NMR Spectrum of 4i
Supplementary Figure 44 $^{13}$C NMR Spectrum of 4i

Supplementary Figure 45 $^1$H NMR Spectrum of 4j
Supplementary Figure 46 19F NMR Spectrum of 4j

Supplementary Figure 47 13C NMR Spectrum of 4j
Supplementary Figure 48 $^1$H NMR Spectrum of 4k

Supplementary Figure 49 $^{19}$F NMR Spectrum of 4k
Supplementary Figure 50 ¹³C NMR Spectrum of 4k

Supplementary Figure 51 ¹H NMR Spectrum of 4l
Supplementary Figure 52 $^{19}$F NMR Spectrum of 4l

Supplementary Figure 53 $^{13}$C NMR Spectrum of 4l
Supplementary Figure 54 $^1$H NMR Spectrum of 4m

Supplementary Figure 55 $^{19}$F NMR Spectrum of 4m
Supplementary Figure 56 $^{13}$C NMR Spectrum of 4m

Supplementary Figure 57 $^1$H NMR Spectrum of 4n
Supplementary Figure 58 $^{19}$F NMR Spectrum of 4n

Chemical Formula: C$_7$H$_6$ClF(NO)$_2$

Exact Mass: 423.1

Supplementary Figure 59 $^{13}$C NMR Spectrum of 4n

Chemical Formula: C$_7$H$_6$ClF(NO)$_2$

Exact Mass: 423.1
Supplementary Figure 60 $^1$H NMR Spectrum of 4o

Supplementary Figure 61 $^{19}$F NMR Spectrum of 4o
Supplementary Figure 62 $^{13}$C NMR Spectrum of 4o

Supplementary Figure 63 $^1$H NMR Spectrum of 4p
Supplementary Figure 64 $^{19}$F NMR Spectrum of 4p

Supplementary Figure 65 $^{13}$C NMR Spectrum of 4p
Supplementary Figure 66 $^1$H NMR Spectrum of 4q

Supplementary Figure 67 $^{19}$F NMR Spectrum of 4q
Supplementary Figure 68 $^{13}$C NMR Spectrum of 4q

Supplementary Figure 69 $^1$H NMR Spectrum of 4r
Supplementary Figure 70 $^{19}$F NMR Spectrum of 4r

Supplementary Figure 71 $^{13}$C NMR Spectrum of 4r
Supplementary Figure 72 $^1$H NMR Spectrum of 5a

Supplementary Figure 73 $^{19}$F NMR Spectrum of 5a
Supplementary Figure 74 $^{13}$C NMR Spectrum of 5a

Supplementary Figure 75 $^1$H NMR Spectrum of 5b
Supplementary Figure 76 ¹⁹F NMR Spectrum of 5b

Supplementary Figure 77 ¹³C NMR Spectrum of 5b
Supplementary Figure 78 $^1$H NMR Spectrum of 5c'

Supplementary Figure 79 $^{19}$F NMR Spectrum of 5c'
Supplementary Figure 80 $^{13}$C NMR Spectrum of 5c'

Supplementary Figure 81 $^1$H NMR Spectrum of 5d
Supplementary Figure 82 $^{19}$F NMR Spectrum of 5d

Supplementary Figure 83 $^{13}$C NMR Spectrum of 5d
Supplementary Figure 84 $^1$H NMR Spectrum of 5e

Supplementary Figure 85 $^{19}$F NMR Spectrum of 5e
Supplementary Figure 86 $^{13}$C NMR Spectrum of 5e

Supplementary Figure 87 $^1$H NMR Spectrum of 5f
Supplementary Figure 88 $^{19}$F NMR Spectrum of 5f

Supplementary Figure 89 $^{13}$C NMR Spectrum of 5f
Supplementary Figure 90 $^1$H NMR Spectrum of 5g

Supplementary Figure 91 $^{19}$F NMR Spectrum of 5g
Supplementary Figure 92 $^{13}$C NMR Spectrum of 5g

Supplementary Figure 93 $^1$H NMR Spectrum of 5h
**Supplementary Figure 94** $^{19}$F NMR Spectrum of 5h

Chemical Formula: C$_{14}$H$_{19}$BrF$_3$JO$_2$
Molecular Weight: 522.4

**Supplementary Figure 95** $^{13}$C NMR Spectrum of 5h

Chemical Formula: C$_{14}$H$_{19}$BrF$_3$JO$_2$
Molecular Weight: 522.4
Supplementary Figure 96 $^1$H NMR Spectrum of 5i

Supplementary Figure 97 $^{19}$F NMR Spectrum of 5i
Supplementary Figure 98 ¹³C NMR Spectrum of 5i

Supplementary Figure 99 ¹H NMR Spectrum of 5j
Supplementary Figure 100 $^{19}$F NMR Spectrum of 5j

Chemical Formula: C$_{32}$H$_{23}$F$_{4}$NO$_{4}$
Molecular Weight: 577.7

Supplementary Figure 101 $^{13}$C NMR Spectrum of 5j

Chemical Formula: C$_{32}$H$_{23}$F$_{4}$NO$_{4}$
Molecular Weight: 577.7
Supplementary Figure 102 $^1$H NMR Spectrum of 5k

Supplementary Figure 103 $^{19}$F NMR Spectrum of 5k
Supplementary Figure 104 $^{13}$C NMR Spectrum of 5k

Supplementary Figure 105 $^1$H NMR Spectrum of 5l
Supplementary Figure 106 $^{19}$F NMR Spectrum of 5l

Supplementary Figure 107 $^{13}$C NMR Spectrum of 5l
Supplementary Note 3: Characterization Spectra for Compounds 8-10

**Supplementary Figure 108** $^1$H NMR Spectrum of 8

**Supplementary Figure 109** $^{19}$F NMR Spectrum of 8
Supplementary Figure 110 $^{13}$C NMR Spectrum of 8

Supplementary Figure 111 $^1$H NMR Spectrum of 10a
Supplementary Figure 112 $^{19}$F NMR Spectrum of 10a

Supplementary Figure 113 $^{13}$C NMR Spectrum of 10a
Supplementary Figure 114 $^1$H NMR Spectrum of 10b

Supplementary Figure 115 $^{19}$F NMR Spectrum of 10b
Supplementary Figure 116 $^{13}$C NMR Spectrum of 10b

Supplementary Figure 117 $^1$H NMR Spectrum of 10c
Supplementary Figure 118 $^{19}$F NMR Spectrum of 10c

Supplementary Figure 119 $^{13}$C NMR Spectrum of 10c
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