C–H Activation Dependent Pd-Catalyzed Carbonylative Coupling of (Hetero)Aryl Bromides and Polyfluoroarenes

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Supporting Information

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General Method.
All reactions were setup using the commercially available COware two chamber system, with self-sealing PTFE/silicon septa. All purchased chemicals were used as received without further purification. Chemicals were purchased from Sigma-Aldrich. All Dry solvents were afforded by adding activated 4 Å molecular sieves and purging rigorously with argon. HPLC grade solvents were purchased from Sigma-Aldrich. Flash chromatography was carried out on silica gel 60 (230–400 mesh). 

1H NMR spectra were recorded at 400 MHz, 13C NMR spectra were recorded at 100 MHz and 19F NMR spectra were recorded at 376 MHz on a Bruker Ascend 400 spectrometer. Chemical shifts were reported in ppm downfield to TMS (δ = 0) and referenced to the solvent residual peak, using the following peak pattern abbreviations: br, broad; s, single; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets; dm, doublet of multiplets; td, triplet of doublets. MS spectra were recorded on a LC TOF (ESI) apparatus.

General procedure A: Carbonylation of Polyfluoroarenes

Chamber 1: In an argon filled glovebox, to chamber 1 of a COware two-chamber system, was added aryl bromide 1 (0.50 mmol), Pd(CF₃COO)₂ (16.6 mg, 0.05 mmol), P(tBu)₃•HBF₄ (29.0 mg, 0.10 mmol), Cs₂CO₃ (355 mg, 1.075 mmol), polyfluorobenzene (2.0 mmol) and α,α,α-trifluorotoluene (0.5 mL) in that order. The chamber was sealed with a screwcap fitted with a Teflon seal. Chamber 2 (1.5 equiv CO): To chamber 2 of the two-chamber system was added 9-methylfluorene-9-carbonyl chloride (185 mg, 0.75 mmol), Pd(db)₂ (4.6 mg, 7.5×10⁻³ mmol), HBF₄•P(tBu)₃ (4.6 mg, 1.5×10⁻² mmol), α,α,α-trifluorotoluene (0.5 mL) and Cy₂NMe (0.26 mL, 1.24 mmol) in that order. The chamber was sealed with a screwcap fitted with a Teflon seal. The loaded two-chamber system was removed from the glovebox and stirred at 80 °C for 16 h. After the reaction mixture had cooled to room temperature, the solid was filtrated off and washed with ethyl acetate. The organic mixture was concentrated under vacuum, and subjected to flash column chromatography using pentane/ethyl acetate as eluent to afford the desired products 3 and 4.

(4-methoxyphenyl)(perfluorophenyl)methane (3a)

Prepared according to procedure A; isolated as white solid (108 mg, 72% from 4-bromoanisole or 107 mg, 71% from 4-idoanisole) using pentane/ethyl acetate (100:1) as eluent. 

1H NMR (400 MHz, CDCl₃) δ (ppm) 7.81 (d, J=8.8 Hz, 2H), 6.98 (d, J=8.8 Hz, 2H), 3.90 (s, 3H). 

13C NMR (100 MHz, CDCl₃) δ (ppm) 183.3, 165.1, 143.6 (dm, J=249.7 Hz, 2C), 142.2 (dm, J=255.6 Hz), 137.6 (dm, J=255.0 Hz, 2C), 132.2 (2C), 129.0,
114.3 (2C), 114.2 (m), 55.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.2 (m, 2F), -151.3 (m, 1F), -160.1 (m, 2F). HRMS C$_{14}$H$_2$F$_5$O$_2$ [M+H]$^+$; calculated 303.0444, found: 303.0441.

(3-methoxyphenyl)(perfluorophenyl)methanone (3b)

Prepared according to procedure A; isolated as white solid (92 mg, 61%) using pentane/ethyl acetate (100:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.44-7.40 (m, 2H), 7.31 (d, J=8.0 Hz, 1H), 7.22 (d, J=8.0 Hz, 1H), 3.87 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 159.0, 160.1, 143.8 (dm, J=250.4 Hz, 2C), 142.4 (dm, J=256.2 Hz), 137.6 (dm, J=255.5 Hz, 2C), 137.2, 130.0, 122.8, 121.6, 114.1 (t, J=18.7 Hz), 113.1, 55.5. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -150.9 (m, 2F), -142.3 (dm, J=8.4 Hz, 2C), 135.9, 131.3, 126.4, 121.1, 117.5 (t, J=18.7 Hz), 111.9, 55.7. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -142.4 (m, 2F), -152.2 (m, 1F), -161.6 (m, 2F). HRMS C$_{14}$H$_2$F$_5$O$_2$ [M+H]$^+$; calculated 303.0444, found: 303.0441.

(2-methoxyphenyl)(perfluorophenyl)methanone (3c)

Prepared according to procedure A; isolated as white solid (87 mg, 58%) using pentane/ethyl acetate (100:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.82 (d, J=7.6 Hz, 1H), 7.59 (t, J=7.2 Hz, 1H), 7.08 (t, J=7.6 Hz, 1H), 6.96 (d, J=8.4 Hz, 1H), 3.70 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 184.0, 159.6, 143.8 (dm, J=250.4 Hz, 2C), 141.9 (dm, J=254.8 Hz), 137.2 (dm, J=252.8 Hz, 2C), 135.9, 131.3, 126.4, 121.1, 117.5 (t, J=18.7 Hz), 111.9, 55.7. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -142.4 (m, 2F), -152.2 (m, 1F), -161.6 (m, 2F). HRMS C$_{14}$H$_2$F$_5$O$_2$ [M+H]$^+$; calculated 303.0444, found: 303.0441.

(perfluorophenyl)(p-tolyl)methanone (3d)

Prepared according to procedure A; isolated as yellow solid (85 mg, 60%) using pentane/ethyl acetate (100:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.74 (d, J=8.0 Hz, 2H), 7.32 (d, J=8.0 Hz, 2H), 2.45 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 184.7, 146.4, 143.7 (dm, J=250.1 Hz, 2C), 142.3 (dm, J=255.8 Hz), 137.6 (dm, J=255.0 Hz, 2C), 133.5, 129.9 (2C), 129.8 (2C), 114.2 (t, J=17.0 Hz), 21.8. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.1 (m, 2F), -150.9 (m, 1F), -160.0 (m, 2F). HRMS C$_{14}$H$_2$F$_5$O [M+H]$^+$; calculated 287.0495, found: 287.0490.
(perfluorophenyl)(m-tolyl)methanone (3e)

Prepared according to procedure A; isolated as yellow solid (78 mg, 55%) using pentane/ethyl acetate (200:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.67 (s, 1H), 7.61 (d, $J$=7.6 Hz, 1H), 7.49 (d, $J$=7.6 Hz, 1H), 7.40 (t, $J$=7.6 Hz, 1H), 2.43 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 185.3, 143.8 (dm, $J$=250.3 Hz, 2C), 142.4 (dm, $J$=256.0 Hz), 139.1, 137.6 (dm, $J$=255.4 Hz, 2C), 136.0, 135.9, 129.9, 128.9, 127.1, 114.2 (t, $J$=22.5 Hz), 21.2. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.0 (m, 2F), -150.7 (m, 1F), -159.9 (m, 2F). HRMS C$_{14}$H$_7$F$_5$O [M+H]$^+$; calculated 287.0495, found: 287.0490.

(perfluorophenyl)(o-tolyl)methanone (3f)

Prepared according to procedure A; isolated as white solid (81 mg, 57%) using pentane/ethyl acetate (100:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.41 (td, $J$=7.6, 1.2 Hz, 1H), 7.35 (d, $J$=7.6 Hz, 1H), 7.27 (d, $J$=7.6 Hz, 1H), 7.19 (t, $J$=7.6 Hz, 1H), 2.57 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 186.7, 143.8 (dm, $J$=250.3 Hz, 2C), 142.5 (dm, $J$=256.0 Hz), 140.8, 137.6 (dm, $J$=255.4 Hz, 2C), 135.3, 133.6, 132.5, 131.8, 126.1, 115.6 (t, $J$=23.8 Hz), 21.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.7 (m, 2F), -150.8 (m, 1F), -160.1 (m, 2F). HRMS C$_{14}$H$_7$F$_5$O [M+H]$^+$; calculated 287.0495, found: 287.0490.

(perfluorophenyl)(phenyl)methanone (3g)

Prepared according to procedure A (46 mg, 34%) or at 70 °C (58 mg, 43%); isolated as yellow solid (58 mg, 43%) using pentane/ethyl acetate (50:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.85 (d, $J$=8.0 Hz, 2H), 7.72-7.63 (m, 1H), 7.53 (t, $J$=8.0 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 185.2, 143.8 (dm, $J$=250.5 Hz, 2C), 142.5 (dm, $J$=256.3 Hz), 137.6 (dm, $J$=255.5 Hz, 2C), 135.9, 135.0, 129.6 (2C), 129.0 (2C), 114.0 (t, $J$=22.5 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -139.9 (m, 2F), -150.4 (m, 1F), -159.8 (m, 2F). HRMS C$_{13}$H$_5$F$_5$O [M+H]$^+$; calculated 273.0339, found: 273.0333.
(4-diphenyl)(perfluorophenyl)methanone (3h)

\[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{F}_5
\end{align*}
\]

Prepared according to procedure A (37 mg, 21%) or at 70 °C (64 mg, 37%); isolated as white solid using pentane/ethyl acetate (50:1) as eluent. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.92 (d, \(J=8.0\) Hz, 2H), 7.74 (d, \(J=8.0\) Hz, 2H), 7.64 (d, \(J=7.2\) Hz, 2H), 7.55-7.39 (m, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 184.7, 147.8, 143.8 (dm, \(J=250.6\) Hz, 2C), 142.5 (dm, \(J=256.2\) Hz), 139.3, 137.7 (dm, \(J=255.4\) Hz, 2C), 134.6, 130.3 (2C), 129.0 (2C), 128.7, 127.7 (2C), 127.3 (2C), 114.0 (t, \(J=18.6\) Hz). \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) (ppm) -139.8 (m, 2F), -150.4 (m, 1F), -159.7 (m, 2F). HRMS C\(_{19}\)H\(_9\)F\(_5\)O [M+H]\(^+\); calculated 349.0652, found: 349.0645.

(perfluorophenyl)(4-phenoxyphenyl)methanone (3i)

\[
\begin{align*}
\text{PhO} & \quad \text{O} \\
\text{Ph} & \quad \text{F}_5
\end{align*}
\]

Prepared according to procedure A; isolated as white solid (96 mg, 53%) using pentane/ethyl acetate (30:1) as eluent. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.73 (d, \(J=8.8\) Hz, 2H), 7.33 (t, \(J=8.0\) Hz, 2H), 7.15 (t, \(J=7.6\) Hz, 1H), 7.01 (d, \(J=8.0\) Hz, 2H), 6.94 (d, \(J=8.8\) Hz, 2H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 183.4, 163.9, 154.7, 143.7 (dm, \(J=250.0\) Hz, 2C), 142.3 (dm, \(J=255.9\) Hz), 137.6 (dm, \(J=255.4\) Hz, 2C), 132.2 (2C), 130.3, 130.2 (2C), 125.2, 120.6 (2C), 117.3 (2C), 114.1 (t, \(J=18.9\) Hz). \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) (ppm) -140.0 (m, 2F), -150.8 (m, 1F), -159.8 (m, 2F). HRMS C\(_{19}\)H\(_9\)F\(_5\)O [M+H]\(^+\); calculated 365.0601, found: 365.0596.

(4-(dimethylamino)phenyl)(perfluorophenyl)methanone (3j)

\[
\begin{align*}
\text{N} & \quad \text{O} \\
\text{Ph} & \quad \text{F}_5
\end{align*}
\]

Prepared according to procedure A; isolated as yellow solid (111 mg, 71%) using pentane/ethyl acetate (20:1) as eluent. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.61 (d, \(J=8.8\) Hz, 2H), 6.56 (d, \(J=8.8\) Hz, 2H), 3.00 (s, 6H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 181.9, 154.6, 143.5 (dm, \(J=248.3\) Hz, 2C), 141.7 (dm, \(J=254.1\) Hz), 137.5 (dm, \(J=253.8\) Hz, 2C), 132.2 (2C), 123.6, 115.1 (t, \(J=25.4\) Hz), 110.8 (2C), 39.9 (2C). \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) (ppm) -140.7 (m, 2F), -152.7 (m, 1F), -160.6 (m, 2F). HRMS C\(_{19}\)H\(_{10}\)F\(_5\)NO [M+H]\(^+\); calculated 316.0761, found: 316.0757.
(3,4-dimethoxyphenyl)(perfluorophenyl)methanone (3k)

Prepared according to procedure A; isolated as white solid (91 mg, 55%) using pentane/ethyl acetate (10:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.50 (d, J=2.0 Hz, 1H), 7.18 (d, J=8.0 Hz, 1H), 6.81 (d, J=8.0 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 183.4, 155.1, 149.7, 143.6 (dm, J=249.7 Hz, 2C), 142.2 (dm, J=255.5 Hz), 137.6 (dm, J=255.0 Hz, 2C), 129.2, 126.1, 114.3 (t, J=19.1 Hz), 110.2, 110.1, 56.2, 56.0. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.2 (m, 2F), -151.1 (m, 1F), -160.0 (m, 2F). HRMS C$_{15}$H$_9$F$_5$O$_3$ [M+H]$^+$; calculated 333.0550, found: 333.0547.

(perfluorophenyl)(3,4,5-trimethoxyphenyl)methanone (3l)

Prepared according to procedure A; isolated as white solid (90 mg, 50%) using pentane/ethyl acetate (from 50:1 to 20:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.07 (s, 2H), 3.95 (s, 3H), 3.87 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 183.8, 153.4 (2C), 144.6, 143.7 (dm, J=250.3 Hz, 2C), 142.4 (dm, J=256.2 Hz), 137.6 (dm, J=255.5 Hz, 2C), 130.9, 114.0 (t, J=20.7 Hz), 107.3 (2C), 61.0, 56.4 (2C). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.0 (m, 2F), -150.5 (m, 1F), -159.7 (m, 2F). HRMS C$_{16}$H$_{11}$F$_5$O$_4$ [M+H]$^+$; calculated 363.0656, found: 363.0650.

(4-chlorophenyl)(perfluorophenyl)methanone (3m)

Prepared according to procedure A; isolated as white solid (48 mg, 32%) using pentane/ethyl acetate (50:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.72 (d, J=8.4 Hz, 2H), 7.44 (d, J=8.4 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 184.0, 143.8 (dm, J=251.0 Hz, 2C), 142.7 (dm, J=257.0 Hz), 137.7 (dm, J=249.9 Hz, 2C), 141.8, 134.3, 130.9 (2C), 129.5 (2C), 113.5 (t, J=22.2 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -139.6 (m, 2F), -149.6 (m, 1F), -159.3 (m, 2F). HRMS C$_{13}$H$_4$ClF$_5$O [M+H]$^+$; calculated 306.9949, found: 306.9941.
(4-fluorophenyl)(perfluorophenyl)methanone (3n)

Prepared according to procedure A; isolated as white solid (61 mg, 42%) using pentane/ethyl acetate (100:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.90-7.86 (m, 2H), 7.24-7.13 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 183.5, 166.9 (d, J=257.1 Hz), 143.8 (dm, J=250.7 Hz, 2C), 142.6 (dm, J=256.7 Hz), 137.7 (dm, J=256.0 Hz, 2C), 132.5, 132.4 (2C), 116.5 (d, J=22.2 Hz, 2C), 113.7 (t, J=20.3 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -101.1 (m, 1F), -139.8 (m, 2F), -150.1 (m, 1F), -159.6 (m, 2F). HRMS C$_{13}$H$_6$F$_5$O [M+H]$^+$; calculated 291.0245, found: 291.0235.

(perfluorophenyl)(3-(trifluoromethyl)phenyl)methanone (3o)

Prepared according to procedure A; isolated as yellow syrup (39 mg, 23%) using pentane/ethyl acetate (100:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 8.12 (s, 1H), 8.00 (d, J=8.0 Hz, 1H), 7.94 (d, J=8.0 Hz, 1H), 7.69 (t, J=8.0 Hz, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 184.0, 144.0 (dm, J=251.7 Hz, 2C), 143.0 (dm, J=257.6 Hz), 137.8 (dm, J=250.5 Hz, 2C), 136.5, 132.7, 132.0 (q, J=32.2 Hz), 131.3 (q, J=3.5 Hz), 129.8, 126.2 (q, J=3.5 Hz), 123.3 (q, J=271.0 Hz), 113.0 (t, J=21.5 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -62.9 (s, 3F), -139.3 (m, 2F), -148.7 (m, 1F), -159.0 (m, 2F). HRMS C$_{14}$H$_4$F$_6$O [M+H]$^+$; calculated 341.0213, found: 341.0210.

(1-methyl-1H-indol-5-yl)(perfluorophenyl)methanone (3p)

Prepared according to procedure A; isolated as white solid (61 mg, 38%) using pentane/ethyl acetate (10:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 8.06 (d, J=0.4 Hz, 1H), 7.85 (dd, J=8.8, 1.6 Hz, 1H), 7.39 (d, J=8.8 Hz, 1H), 7.15 (d, J=3.2 Hz, 1H), 6.61 (dd, J=3.2, 0.8 Hz, 1H), 3.84 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 184.8, 143.6 (dm, J=249.1 Hz, 2C), 142.0 (dm, J=254.7 Hz), 137.5 (dm, J=254.5 Hz, 2C), 140.1, 131.1, 128.2, 128.1, 125.7, 122.6, 115.1 (t, J=23.3 Hz), 109.8, 103.6, 33.1. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.3 (m, 2F), -152.0 (m, 1F), -160.3 (m, 2F). HRMS C$_{16}$H$_6$F$_5$NO [M+H]$^+$; calculated 326.0604, found: 326.0605.
benzyl 5-(perfluorobenzoyl)-1H-indole-1-carboxylate (3q)

![Chemical Structure](image)

Prepared according to procedure A; isolated as white solid (80 mg, 36%) using pentane/ethyl acetate (50:1) as eluent. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 8.31 (d, \(J=8.8\) Hz, 1H), 8.05 (s, 1H), 7.86 (dd, \(J=8.8, 1.6\) Hz, 1H), 7.57 (d, \(J=3.6\) Hz, 1H), 7.50 (dd, \(J=8.0, 2.0\) Hz, 2H), 7.43 (m, 3H), 6.69 (d, \(J=3.6\) Hz, 1H), 5.49 (s, 2H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 184.8, 150.3, 143.7 (dm, \(J=249.9\) Hz, 2C), 142.3 (dm, \(J=255.7\) Hz), 139.0, 137.6 (dm, \(J=255.1\) Hz, 2C), 134.5, 131.3, 130.7, 129.0, 128.8 (2C), 128.6 (2C), 127.7, 125.8, 124.0, 115.7, 114.4 (t, \(J=22.6\) Hz), 108.7, 69.4. \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) (ppm) -139.9 (m, 2F), -150.9 (m, 1F), -159.8 (m, 2F). HRMS C\(_{23}\)H\(_{12}\)F\(_3\) NO\(_3\) [M+H]\(^+\); calculated 446.0816, found: 446.0811.

(4-methoxyphenyl)(2,3,5,6-tetrafluorophenyl)methanone (4b)

![Chemical Structure](image)

Prepared according to procedure A (78 mg, 55%) or at 90 °C (88 mg, 62%); isolated as white syrup using pentane/ethyl acetate (20:1) as eluent. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.84 (d, \(J=8.8\) Hz, 2H), 7.25-7.12 (m, 1H), 6.98 (d, \(J=8.8\) Hz, 2H), 3.90 (s, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 184.4, 165.0, 145.8 (dm, \(J=249.2\) Hz, 2C), 143.1 (dm, \(J=248.7\) Hz, 2C), 132.3 (2C), 129.0, 120.1 (t, \(J=20.6\) Hz), 114.3 (2C), 107.3 (t, \(J=22.4\) Hz), 55.6. \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) (ppm) -137.3 (m, 2F), -141.2 (m, 2F). HRMS C\(_{14}\)H\(_8\)F\(_5\)O\(_2\) [M+H]\(^+\); calculated 285.0539, found: 285.0536.

(4-methoxyphenyl)(2,3,5,6-tetrafloro-4-methylphenyl)methanone (4c)

![Chemical Structure](image)

Prepared according to procedure A at 90 °C; isolated as white solid (51 mg, 34%) using pentane/ethyl acetate (20:1) as eluent. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (ppm) 7.83 (d, \(J=8.8\) Hz, 2H), 6.96 (d, \(J=8.8\) Hz, 2H), 3.89 (s, 3H), 2.34 (t, \(J=2.4\) Hz, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm) 184.8, 164.9, 144.9 (dm, \(J=239.6\) Hz, 2C), 142.9 (dm, \(J=260.3\) Hz, 2C), 132.2 (2C), 129.3, 118.1 (t, \(J=18.8\) Hz), 116.5 (t, \(J=20.2\) Hz), 114.2 (2C), 55.6, 7.8. \(^19\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) (ppm) -142.1 (m, 2F), -142.5 (m, 2F). HRMS C\(_{15}\)H\(_{10}\)F\(_4\)O\(_2\) [M+H]\(^+\); calculated 299.0695, found: 299.0694.
(4-methoxyphenyl)(2,3,5,6-tetrafluoro-4-methoxyphenyl)methanone (4d)

![Chemical Structure](image)

Prepared according to procedure A at 90 °C; isolated as yellow syrup (77 mg, 49%) using pentane/ethyl acetate (20:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.83 (d, $J$=8.8 Hz, 2H), 6.97 (d, $J$=8.8 Hz, 2H), 4.15 (s, 3H), 3.89 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 144.2, 143.9 (dm, $J$=247.9 Hz, 2C), 140.6 (dm, $J$=264.5 Hz, 2C), 139.9 (m), 132.2 (2C), 129.5, 114.2 (2C), 112.3 (t, $J$=20.5 Hz), 62.2 (t, $J$=4.0 Hz), 55.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -141.8 (td, $J$=10.3, 3.2 Hz, 2F), -156.7 (ddd, $J$=8.1, 6.3, 3.9 Hz, 2F). HRMS C$_{13}$H$_{10}$F$_{2}$O$_{3}$ [M+H]$^+$; calculated 315.0644, found: 315.0641.

(4-methoxyphenyl)(2,3,4,6-tetrafluorophenyl)methanone (4e)

![Chemical Structure](image)

Prepared according to procedure A; isolated as white syrup (45 mg, 32%) using pentane/ethyl acetate (25:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.82 (d, $J$=8.8 Hz, 2H), 6.97 (d, $J$=8.8 Hz, 2H), 6.92-6.84 (m, 1H), 3.89 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 184.7, 164.9, 155.1(m), 152.7(m), 150.3(m), 148.6 (dm, $J$=252.4 Hz), 137.2 (dm, $J$=249.9 Hz), 132.2 (2C), 129.4, 114.2 (2C), 101.6(m), 55.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -115.1 (m, 1F), -128.8 (m, 1F), -132.8 (m, 1F), -163.7 (m, 1F). HRMS C$_{14}$H$_{8}$F$_{2}$O$_{2}$ [M+H]$^+$; calculated 285.0539, found: 285.0536.

(4-methoxyphenyl)(2,2',3,3',5,5',6,6'-octafluoro-[1,1'-biphenyl]-4-yl)methanone (4f)

![Chemical Structure](image)

Prepared according to procedure A at 90 °C; isolated as white solid (108 mg, 50%) using pentane/ethyl acetate (30:1) as eluent. $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.92 (d, $J$=8.8 Hz, 2H), 7.38-7.25 (m, 1H), 7.04 (d, $J$=8.8 Hz, 2H), 3.93 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 183.7, 165.3, 146.1 (dm, $J$=244.4 Hz, 2C), 145.2 (m, 2C), 143.2 (dm, $J$=249.9 Hz, 2C), 142.8 (m, 2C), 132.4 (2C), 128.8, 121.1 (t, $J$= 21.0 Hz), 114.4 (2C), 108.6 (t, $J$= 18.1 Hz), 108.2 (t, $J$= 22.3 Hz), 107.4 (t, $J$= 18.0 Hz), 55.6. $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -136.5 (m, 2F), -137.4 (m, 2F), -137.9 (m, 2F), -140.0 (m, 2F). HRMS C$_{20}$H$_{8}$F$_{8}$O$_{2}$ [M+H]$^+$; calculated 433.0475, found: 433.0474.
\(^{13}\text{C}-\text{labelled (perfluorophenyl)(phenyl)methanone (}^{13}\text{C-3g)}\)

![Image of \(^{13}\text{C}-\text{labelled (perfluorophenyl)(phenyl)methanone (}^{13}\text{C-3g)}\)](image)

Prepared according to procedure A at 70 °C; isolated as yellow solid (58 mg, 43%) using pentane/ethyl acetate (50:1) as eluent. \(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta\) (ppm) 7.85 (dd, \(J=7.2, 4.8\) Hz, 2H), 7.69 (t, \(J=7.2\) Hz, 1H), 7.53 (t, \(J=7.6\) Hz, 2H). \(^{13}\text{C NMR (100 MHz, CDCl}_3\) \(\delta\) (ppm) 185.2 (\(^{13}\text{C}), 143.8\) (dm, \(J=250.6\) Hz, 2C), 142.4 (dm, \(J=255.9\) Hz, 2C), 135.9 (d, \(J=59.6\) Hz), 135.0 (d, \(J=0.9\) Hz), 129.6 (d, \(J=3.3\) Hz, 2C), 129.0 (d, \(J=4.6\) Hz, 2C), 114.0 (dt, \(J=41.1, 18.6\) Hz). \(^{19}\text{F NMR (376 MHz, CDCl}_3\) \(\delta\) (ppm) -139.1 (m, 2F), -150.3 (m, 1F), -159.7 (m, 2F). HRMS C\(_{12}\)\(^{13}\text{C}\)H\(_{15}\)F\(_5\)O [M+H]+; calculated 274.0372, found: 274.0366.

\(^{13}\text{C}-\text{labelled (4-(dimethylamino)phenyl)(perfluorophenyl)methanone (}^{13}\text{C-3j)}\)

![Image of \(^{13}\text{C}-\text{labelled (4-(dimethylamino)phenyl)(perfluorophenyl)methanone (}^{13}\text{C-3j)}\)](image)

Prepared according to procedure A; isolated as yellow solid (113 mg, 72%) using pentane/ethyl acetate (20:1) as eluent. \(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta\) (ppm) 7.70 (dd, \(J=8.8, 4.0\) Hz, 2H), 6.65 (d, \(J=8.8\) Hz, 2H), 3.09 (s, 6H). \(^{13}\text{C NMR (100 MHz, CDCl}_3\) \(\delta\) (ppm) 182.0 (\(^{13}\text{C}), 154.6, 143.5\) (dm, \(J=248.4\) Hz, 2C), 141.7 (dm, \(J=254.1\) Hz), 137.5 (dm, \(J=253.9\) Hz, 2C), 132.3 (d, \(J=3.7\) Hz, 2C), 123.6 (d, \(J=64.7\) Hz), 115.1 (m), 110.9 (d, \(J=4.7\) Hz, 2C), 40.0 (2C). \(^{19}\text{F NMR (376 MHz, CDCl}_3\) \(\delta\) (ppm) -140.6 (m, 2F), -152.6 (m, 1F), -160.6 (m, 2F). HRMS C\(_{14}\)\(^{13}\text{C}\)H\(_{10}\)F\(_5\)N [M+H]+; calculated 317.0794, found: 317.0793.

\(4,5,6,7\)-tetrafluoro-3-phenyl-1H-indazole (5)

![Image of \(4,5,6,7\)-tetrafluoro-3-phenyl-1H-indazole (5)](image)

Based on a procedure by Dario.\(^3\) In a dry 8 mL vial, (perfluorophenyl)(phenyl)methanone (3k, 0.43 mmol, 117 mg) was dissolved in toluene (3 mL). Hydrazine monohydrate (0.12 mL) was added and the mixture was refluxed for 6 h. After this period, the mixture was cooled and the solvent was removed under reduced pressure. The product was purified by silica gel chromatography (pentane/ethyl acetate=10:1) to afford 5 as white solid (93 mg, 81%). \(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta\) (ppm) 11.52 (br, 1H), 7.90-7.73 (m,
2H), 7.56-7.34 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 146.2 (m), 139.5 (dm, J=250.6 Hz), 135.7 (dt, J=244.6, 15.9 Hz), 133.6 (m), 131.0 (m), 130.7, 129.1 (2C), 128.6 (2C), 128.4, 128.3, 107.6 (d, J=18.3 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.3 (s, 1F), -156.1 (s, 1F), -158.8 (s, 1F), -164.6 (t, J=18.2 Hz, 1F). HRMS C$_{13}$H$_6$F$_4$N$_2$ [M+H]$^+$; calculated 267.0545, found: 267.0540.

$^{13}$C-labelled 4,5,6,7-tetrafluoro-3-phenyl-1H-indazole ($^{13}$C-5)

Based on a procedure by Dario.\textsuperscript{3} In a dry 8 mL vial, (perfluorophenyl)(phenyl)methanone ($^{13}$C-3k, 0.5 mmol, 137 mg) was dissolved in toluene (3 mL). Hydrazine monohydrate (0.15 mL) was added and the mixture was refluxed for 6 h. After this period, the mixture was cooled and the solvent was removed under reduced pressure. The product was purified by silica gel chromatography (pentane/ethyl acetate=10:1) to afford $^{13}$C-5 as white solid (107 mg, 80%). $^1$H NMR (400 MHz, CDCl$_3$) δ (ppm) 11.6-10.6 (br, 1H), 7.69-7.65 (m, 2H), 7.44-7.27 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm) 146.1 (13C), 139.5 (dm, J=250.6 Hz), 135.7 (dt, J=244.6, 15.9 Hz), 133.6 (m), 131.0 (m), 130.7, 129.2 (d, J=0.6 Hz, 2C), 128.6 (d, J=4.5 Hz, 2C), 128.4 (d, J=2.3 Hz), 128.3 (d, J=2.3 Hz), 107.66 (ddd, J=59.2, 18.7, 2.8 Hz). $^{19}$F NMR (376 MHz, CDCl$_3$) δ (ppm) -140.48 (t, J=18.5 Hz, 1F), -156.03 (t, J=19.1 Hz, 1F), -158.67 (t, J=18.6 Hz, 1F), -164.57 (tdd, J=19.5, 6.1, 3.0 Hz, 1F). HRMS C$_{12}$H$_6$F$_4$N$_2$ [M+H]$^+$; calculated 268.0579, found: 268.0574.

Control Experiment:

In an argon filled glovebox, a dry 8 mL vial was added 4-methoxybenzoyl Chloride (85 mg, 0.5 mmol), Cs$_2$CO$_3$ (355 mg, 1.075 mmol), polyfluorobenzene (2.0 mmol) and α,α,α-trifluorotoluene (0.5 mL) in that order. Then the vial was removed from the glovebox and stirred at 80 °C for 16 h. After the reaction mixture had cooled to room temperature, the solid was filtrated off and washed with ethyl acetate. The organic mixture was concentrated under vacuum, and subjected to NMR.
References

1. A detailed description of how to use the COware two chamber system can be found on the www. under sytracks.com.
NMR spectra

3a
3b
3d
3h
3I
S31
3n
$^{13}$C-3j