Supplementary Information

Pd(II)-Catalyzed Decarboxylative Acylation of Phenylacetamides with α-Oxocarboxylic Acids via C–H Bond Activation

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**General methods**

Commercially available reagents were used without additional purification, unless otherwise stated. Sealed tubes (13 x100 mm²) were purchased from Fischer Scientific and dried in oven for overnight and cooled at room temperature prior to use. Thin layer chromatography was carried out using plates coated with Kieselgel 60F₂₅₄ (Merck). For flash column chromatography, E. Merck Kieselgel 60 (230-400 mesh) was used. Nuclear magnetic resonance spectra (¹H and ¹³C NMR) were recorded on a Bruker Unity 400, 500 and 700 MHz spectrometer for CDCl₃ and CD₃OD solutions and chemical shifts are reported as parts per million (ppm). Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). In addition, the notation br is used to indicate a broad signal. Coupling constants (J) are reported in hertz (Hz). IR spectra were recorded on a Varian 2000 Infrared spectrophotometer and are reported as cm⁻¹. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-600 spectrometer.
Control Experiments (1)

As the control experiment for a decarboxylation of α-oxocarboxylic acids followed by a C-H functionalization of the resulting aldehyde, we examined the coupling of 2-methoxyphenylacetamide 1e and benzaldehyde instead of phenylglyoxylic acid (2a) under standard reaction conditions (Pd(TFA)$_2$ (10 mol %), (NH$_4$)$_2$S$_2$O$_8$ (1.5 equiv.), DCE (0.3 M)). However, this reaction did not provide any acylated product and most of starting material 1e was recovered. Also, phenylglyoxylic acid (2a) was added to standard reaction conditions in the absence of 2-methoxyphenylacetamide 1e. As a result, phenylglyoxylic acid (2a) was not converted to benzaldehyde. Thus it is not possible mechanism that a decarboxylation of α-oxocarboxylic acids under palladium catalysis can provide the corresponding aldehyde, which can be inserted to palladacycle intermediate.

Control Experiments (2)

As the control experiment for a Heck type addition to a C=O bond of α-oxocarboxylic acids followed by decarboxylation rather than β-hydride elimination, we examined the coupling of 2-
methoxyphenylacetamide 1ε and methyl benzoylformate, which cannot participate in a decarboxylation process, in the presence of 1 equiv. of Pd(TFA)$_2$, to obtain Heck type addition compound to a C=O bond. However, we did not obtain any Heck type addition compound and most of starting compounds were recovered.
General procedure for the synthesis of \(N,N\)-diethylphenylacetamides 1a–j

To a stirred solution of phenylacetic acids (7.30 mmol, 100 mol %) in anhydrous CH\(_2\)Cl\(_2\) (37 mL) was added SOCl\(_2\) (11.0 mmol, 150 mol %) at 0 °C under N\(_2\). The reaction mixture was stirred for 2 h at 80 °C. After cooling to room temperature, diethylamine (21.9 mmol, 300 mol %) was added to the reaction mixture, which was stirred for 2 h at room temperature. The reaction mixture was quenched with H\(_2\)O (50 mL) and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (50 mL). The organic layer was washed with H\(_2\)O and brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc) to afford the corresponding \(N,N\)-diethylphenylacetamides.

General procedure for the synthesis of \(\alpha\)-oxocarboxylic acids

\(\alpha\)-Oxocarboxylic acids were prepared from corresponding aryl methyl ketones with SeO\(_2\) and pyridine, according to the reported procedure.\(^1\)

Typical procedure for the synthesis of acylation products (3a–j and 4b–j)

To an oven-dried sealed tube charged with N,N-diethyl-2-(2-methoxyphenyl)acetamide (1e) (66.4 mg, 0.30 mmol, 100 mol %), Pd(TFA)$_2$ (10 mg, 0.03 mmol, 10 mol %), and (NH$_4$)$_2$S$_2$O$_8$ (102.7 mg, 0.45 mmol, 150 mol %) in DCE (1 mL) was added phenylglyoxylic acid (2a) (67.6 mg, 0.45 mmol, 150 mol %). The reaction mixture was allowed to stir for 20 h at 70 °C. The reaction mixture was diluted with EtOAc (5 mL) and washed with sodium carbonate solution. The aqueous layer was extracted with EtOAc (10 mL × 3). The combined organic layer was dried over Mg$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 2:1) to afford the acylated product 3e (69.2 mg) in 71% yield.
Characterization data for acylation products (3a–j and 4b–j)

2-(2,6-Dibenzoylphenyl)-N,N-diethylacetamide (3a)

\[
\begin{align*}
\text{Ph} & \text{O} \\
\text{Ph} & \text{CONEt}_2 \\
\end{align*}
\]

\[R_f = 0.62 \text{ (n-hexanes/EtOAc = 1:1)}; \quad \text{^1H NMR (400 MHz, CDCl}_3\text{) } \delta 7.87 \text{ (d, } J = 8.4 \text{ Hz, 4H), 7.55-7.51 (m, 2H), 7.44-7.40 (m, 6H), 7.31 (t, } J = 8.3 \text{ Hz, 1H), 4.03 (s, 2H), 3.12 (q, } J = 7.2 \text{ Hz, 2H), 3.07 (q, } J = 7.1 \text{ Hz, 2H), 0.96 (t, } J = 7.2 \text{ Hz, 3H), 0.73 (t, } J = 7.1 \text{ Hz, 3H);} \quad \text{^13C NMR (100 MHz, CDCl}_3\text{) } \delta 198.2, 162.6, 140.7, 137.5, 134.4, 133.1, 130.5, 129.9, 128.3, 125.1, 42.1, 40.6, 33.3, 13.8, 12.7; \quad \text{IR (KBr) } \nu 2976, 2933, 1717, 1665, 1598, 1448, 1381, 1261, 1140, 1037, 921, 853 \text{ cm}^{-1}; \quad \text{HRMS (EI) Calcd for C}_{26}H_{25}NO_3 [M]^+ 399.1834, \text{ found 399.1833.}
\]

2-(2-Benzoylphenyl)-N,N-diethylacetamide (3aa)

\[
\begin{align*}
\text{Ph} & \text{O} \\
\text{Ph} & \text{CONEt}_2 \\
\end{align*}
\]

\[R_f = 0.41 \text{ (n-hexanes/EtOAc = 1:1)}; \quad \text{^1H NMR (500 MHz, CD}_2\text{OD) } \delta 7.86 \text{ (d, } J = 7.1 \text{ Hz, 2H), 7.69 (t, } J = 7.4 \text{ Hz, 1H), 7.60-7.55 (m, 3H), 7.47-7.44 (m, 3H), 4.02 (s, 2H), 3.46 (q, } J = 7.2 \text{ Hz, 2H), 3.34 (q, } J = 7.1 \text{ Hz, 2H), 1.24 (t, } J = 7.2 \text{ Hz, 3H), 1.04 (t, } J = 7.1 \text{ Hz, 3H);} \quad \text{^13C NMR (100 MHz, CD}_2\text{OD) } \delta 200.0, 172.1, 139.8, 139.1, 136.8, 134.2, 132.9, 131.9, 131.4, 130.8, 129.5, 127.4, 43.7, 41.9, 38.7, 14.2, 13.1; \quad \text{IR (KBr) } \nu 2973, 2930, 1713, 1642, 1453, 1314, 1271, 1136, 1074, 946 \text{ cm}^{-1}; \quad \text{HRMS (EI) Calcd for C}_{19}H_{21}NO_2 [M]^+ 295.1572, \text{ found 295.1566.}
\]

2-(2,6-Dibenzoyl-4-methoxyphenyl)-N,N-diethylacetamide (3b)
$R_f = 0.55$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.89 (d, $J = 7.4$ Hz, 4H), 7.53 (t, $J = 7.2$ Hz, 2H), 7.44-7.41 (m, 4H), 6.95 (s, 2H), 3.89 (s, 2H), 3.72 (s, 3H), 3.06 (q, $J = 6.7$ Hz, 4H), 0.83 (br s, 6H); $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta$ 199.3, 171.1, 158.5, 143.3, 138.6, 134.6, 131.5, 129.6, 126.4, 117.3, 56.1, 43.4, 41.9, 33.9, 14.0, 13.1; IR (KBr) $\nu$ 2974, 2934, 1717, 1666, 1598, 1450, 1333, 1249, 1132, 1018, 925, 862 cm$^{-1}$; HRMS (EI) Calcd for C$_{27}$H$_{27}$NO$_4$ [M]$^+$ 429.1940, found 429.1943.

2-(2-Benzoyl-4-(trifluoromethyl)phenyl)-N,N-diethylacetamide (3c)

$R_f = 0.48$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.79 (d, $J = 8.1$ Hz, 2H), 7.68 (d, $J = 8.0$ Hz, 1H), 7.57-7.56 (m, 2H), 7.49-7.43 (m, 3H), 3.92 (s, 2H), 3.28-3.23 (m, 4H), 1.12 (br s, 3H), 0.94 (br s, 3H); $^{13}$C NMR (100 MHz, CD$_3$OD) $\delta$ 198.2, 171.1, 141.4, 140.7, 138.3, 134.6, 134.1, 131.3, 130.7, 129.6, 129.4, 128.2 (q, $J_{C-F} = 3.6$ Hz), 126.9 (q, $J_{C-F} = 3.6$ Hz), 125.2 (q, $J_{C-F} = 270.2$ Hz), 43.6, 41.9, 38.5, 14.2, 13.1; IR (KBr) $\nu$ 2978, 2935, 1716, 1644, 1451, 1334, 1257, 1173, 1080, 1021, 959, 865 cm$^{-1}$; HRMS (EI) Calcd for C$_{20}$H$_{20}$F$_3$NO$_2$ [M]$^+$ 363.1446, found 363.1431.

2-(2,6-Dibenzoyl-4-fluorophenyl)-N,N-diethylacetamide (3d)
$R_f = 0.73$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.90 (d, $J = 7.4$ Hz, 4H), 7.58 (t, $J = 7.2$ Hz, 2H), 7.46 (t, $J = 7.6$ Hz, 4H), 7.16 (d, $J = 8.2$ Hz, 2H), 3.98 (s, 2H), 3.09 (br s, 4H), 0.96 (br s, 3H), 0.76 (br s, 3H); $^{13}$C NMR (100 MHz, CD$_3$OD) δ 197.9, 170.5, 161.2 (d, $J_{C-F} = 247.5$ Hz), 144.1 (d, $J_{C-F} = 5.8$ Hz), 138.1, 134.9, 131.5, 129.7, 129.4, 118.5 (d, $J_{C-F} = 22.6$ Hz), 43.5, 41.9, 34.1, 14.0, 13.1; IR (KBr) ν 2781, 1718, 1669, 1597, 1450, 1328, 1252, 1177, 1098, 927 cm$^{-1}$; HRMS (EI) Calcd for C$_{26}$H$_{24}$FNO$_3$ [M]$^+$ 417.1740, found 417.1737.

2-(2-Benzoyl-4-fluorophenyl)-N,N-diethylacetamide (3dd)

$R_f = 0.45$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$) δ 7.81 (d, $J = 7.4$ Hz, 2H), 7.58 (t, $J = 7.3$ Hz, 1H), 7.45 (t, $J = 7.7$ Hz, 2H), 7.35-7.32 (m, 1H), 7.16-7.14 (m, 1H), 7.05 (dd, $J = 8.7$, 2.6 Hz, 1H), 3.82 (s, 2H), 3.27 (q, $J = 6.9$ Hz, 4H), 1.10 (br s, 3H), 0.97 (br s, 3H); $^{13}$C NMR (175 MHz, CD$_3$OD) δ 198.5, 171.9, 162.2 (d, $J_{C-F} = 245.6$ Hz), 141.7, 138.5, 135.1 (d, $J_{C-F} = 7.6$ Hz), 134.6, 132.8, 131.5, 129.7, 118.4 (d, $J_{C-F} = 20.7$ Hz), 117.4 (d, $J_{C-F} = 23.5$ Hz), 43.7, 42.0, 37.9, 14.3, 13.2; IR (KBr) ν 2975, 2932, 1743, 1644, 1588, 1484, 1381, 1286, 1177, 1084, 1026, 979, 866 cm$^{-1}$; HRMS (EI) Calcd for C$_{19}$H$_{20}$FNO$_2$ [M]$^+$ 313.1478, found 313.1490.

2-(2-Benzoyl-6-methoxyphenyl)-N,N-diethylacetamide (3e)

$R_f = 0.34$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.82 (d, $J = 7.2$ Hz, 2H), 7.48 (t, $J = 7.3$ Hz, 1H), 7.37 (t, $J = 7.8$ Hz, 2H), 7.21 (t, $J = 8.0$ Hz, 1H), 6.96 (d, $J = 8.2$ Hz, 1H), 6.87 (d, $J = 7.6$ Hz, 1H), 3.85 (s, 2H), 3.80 (s, 3H), 3.30-3.22 (m, 4H), 1.12 (br s, 3H), 0.91 (br s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 198.5, 169.6, 158.0, 140.5, 137.9, 132.8, 130.5, 128.1, 126.8, 124.5, 121.3, 112.6, 55.8, 42.2, 40.5, 30.1, 14.1, 13.0; IR (KBr) ν 2973, 2933, 2838.
1661, 1580, 1461, 1321, 1278, 1138, 1080, 1040, 984, 854 \text{ cm}^{-1}; \text{HRMS (EI) Calcd for C}_{20}\text{H}_{23}\text{NO}_3 [M]^+ 325.1678, \text{found 325.1676.}

2-(2-Benzoyl-6-fluorophenyl)-N,N-diethylacetamide (3f)

\[ R_f = 0.59 \ (n\text{-hexanes/EtOAc} = 1:1); \]  
\[^1\text{H NMR (400 MHz, CDCl}_3) \delta 7.82 \ (d, J = 7.0 \text{ Hz, 2H}), 7.54 \ (t, J = 7.4 \text{ Hz, 1H}), 7.43 \ (t, J = 7.8 \text{ Hz, 2H}), 7.25-7.17 \ (m, 2H), 7.13 \ (d, J = 7.4 \text{ Hz, 1H}), 3.93 \ (s, 2H), 3.33-3.25 \ (m, 4H), 1.17 \ (br s, 3H), 0.94 \ (br s, 3H); \]  
\[^{13}\text{C NMR (100 MHz, CDCl}_3) \delta 197.3, 168.2, 161.5 \ (d, J_{\text{C-F}} = 244.8 \text{ Hz}), 140.8 \ (d, J_{\text{C-F}} = 3.3 \text{ Hz}), 137.5, 132.9, 130.4, 128.2, 127.2 \ (d, J_{\text{C-F}} = 8.7 \text{ Hz}), 125.1 \ (d, J_{\text{C-F}} = 3.1 \text{ Hz}), 123.3 \ (d, J_{\text{C-F}} = 16.1 \text{ Hz}), 117.4 \ (d, J_{\text{C-F}} = 23.4 \text{ Hz}), 42.1, 40.6, 29.3, 14.1, 12.9; \]  
\[ \text{IR (KBr) \nu 2975, 2933, 1662, 1579, 1459, 1276, 1129, 1074, 922, 848 \text{ cm}^{-1}; \]  
\[ \text{HRMS (EI) Calcd for C}_{19}\text{H}_{20}\text{FNO}_2 [M]^+ 313.1478, \text{found 313.1478.} \]

2-(2-Benzoyl-6-chlorophenyl)-N,N-diethylacetamide (3g)

\[ R_f = 0.68 \ (n\text{-hexanes/EtOAc} = 1:1); \]  
\[^1\text{H NMR (500 MHz, CDCl}_3) \delta 7.84 \ (d, J = 7.4 \text{ Hz, 2H}), 7.56-7.50 \ (m, 2H), 7.42 \ (t, J = 7.7 \text{ Hz, 2H}), 7.23-7.20 \ (m, 2H), 4.06 \ (s, 2H), 3.32-3.27 \ (m, 4H), 1.18 \ (br s, 3H), 0.94 \ (br s, 3H); \]  
\[^{13}\text{C NMR (175 MHz, CD}_3\text{OD) \delta 197.4, 169.1, 141.1, 137.2, 136.3, 133.2, 133.1, 131.1, 130.1, 128.1, 127.4, 127.2, 42.2, 40.5, 33.9, 12.8, 11.7; \]  
\[ \text{IR (KBr) \nu 2975, 2933, 1664, 1596, 1446, 1380, 1271, 1176, 1097, 1027, 971, 852 \text{ cm}^{-1}; \]  
\[ \text{HRMS (EI) Calcd for C}_{19}\text{H}_{20}\text{ClNO}_2 [M]^+ 329.1183, \text{found 329.1181.} \]

2-(2-Benzoyl-6-bromophenyl)-N,N-diethylacetamide (3h)

S10
$R_f = 0.67$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (700 MHz, CD$_3$OD) $\delta$ 7.82-7.80 (m, 3H), 7.64 (t, $J = 7.4$ Hz, 1H), 7.49 (t, $J = 7.8$ Hz, 2H), 7.33-7.29 (m, 2H), 4.12 (s, 2H), 3.42 (q, $J = 7.1$ Hz, 2H), 3.26 (q, $J = 7.1$ Hz, 2H); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.79 (d, $J = 7.7$ Hz, 2H), 7.59-7.54 (m, 3H), 7.43 (t, $J = 7.8$ Hz, 3H), 3.91 (s, 2H), 3.25 (br s, 4H), 1.11 (br s, 3H), 0.94 (br s, 3H); $^{13}$C NMR (175 MHz, CD$_3$OD) $\delta$ 198.7, 171.3, 143.6, 138.2 (d, $J_{C-F} = 27.5$ Hz), 134.6, 133.2 (d, $J_{C-F} = 31.4$ Hz), 131.6, 130.9, 129.9 (d, $J_{C-F} = 3.9$ Hz), 129.7, 125.2 (q, $J_{C-F} = 270.0$ Hz), 124.43 (d, $J_{C-F} = 3.7$ Hz), 43.8, 42.1, 38.4, 14.3, 13.2; IR (KBr) $\nu$ 2977, 2935, 1667, 1645, 1598, 1449, 1364, 1287, 1221, 1129, 1077, 1026, 942, 842 cm$^{-1}$; HRMS (EI) Calcd for C$_{19}$H$_{20}$BrNO$_2$ [M]$^+$ 373.0677, found 373.0679.

2-(2-Benzoyl-5-(trifluoromethyl)phenyl)-N,N-diethylacetamide (3i)

$R_f = 0.72$ (n-hexanes/EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.79 (d, $J = 7.7$ Hz, 2H), 7.59-7.54 (m, 3H), 7.43 (t, $J = 7.8$ Hz, 3H), 3.91 (s, 2H), 3.25 (br s, 4H), 1.11 (br s, 3H), 0.94 (br s, 3H); $^{13}$C NMR (175 MHz, CD$_3$OD) $\delta$ 198.7, 171.3, 143.6, 138.2 (d, $J_{C-F} = 27.5$ Hz), 134.6, 133.2 (d, $J_{C-F} = 31.4$ Hz), 131.6, 130.9, 129.9 (d, $J_{C-F} = 3.9$ Hz), 129.7, 125.2 (q, $J_{C-F} = 270.0$ Hz), 124.43 (d, $J_{C-F} = 3.7$ Hz), 43.8, 42.1, 38.4, 14.3, 13.2; IR (KBr) $\nu$ 2977, 2935, 1667, 1645, 1598, 1449, 1364, 1287, 1221, 1129, 1077, 1026, 942, 842 cm$^{-1}$; HRMS (EI) Calcd for C$_{20}$H$_{20}$F$_3$NO$_2$ [M]$^+$ 363.1446, found 363.1433.

2-(3-Benzoylnaphthalen-2-yl)-N,N-diethylacetamide (3j)
**N,N-Diethyl-2-(2-methoxy-6-(4-methoxybenzoyl)phenyl)acetamide (4b)**

\[
\text{Ph} \quad \text{CONEt}_2
\]

\[R_f = 0.28 \ (n\text{-hexanes/EtOAc} = 1:1); \quad ^1H \text{ NMR (400 MHz, CDCl}_3) \ \delta \ 7.78 \ (d, \ J = 8.8 \text{ Hz}, 2H), \ 7.19 \ (t, \ J = 8.0 \text{ Hz}, 1H), \ 6.92 \ (d, \ J = 8.2 \text{ Hz}, 1H), \ 6.82 \ (d, \ J = 8.7 \text{ Hz}, 3H), \ 3.78 \ (s, 8H), \ 3.24 \ (br \ s, 4H), \ 1.01-0.97 \ (m, 6H); \quad ^{13}C \text{ NMR (175 MHz, CD}_3\text{OD)} \ \delta \ 199.1, \ 172.1, \ 165.7, \ 159.8, \ 142.4, \ 134.2, \ 133.5, \ 131.7, \ 129.2, \ 128.6, \ 124.7, \ 121.8, \ 116.1, \ 115.2, \ 114.8, \ 113.6, \ 109.3, \ 56.4, \ 56.2, \ 43.8, \ 42.0, \ 31.7, \ 14.3, \ 13.4; \quad \text{IR (KBr)} \ \nu \ 2973, \ 2933, \ 2839, \ 1653, \ 1509, \ 1461, \ 1380, \ 1281, \ 1223, \ 1159, \ 1139, \ 1079, \ 984, \ 922, \ 847 \text{ cm}^{-1}; \quad \text{HRMS (EI)} \ \text{Calcd for C}_{21}\text{H}_{23}\text{NO}_4 \ [M]^+ 355.1784, \ \text{found} \ 355.1788. \]

**N,N-Diethyl-2-(2-methoxy-6-(3-methoxybenzoyl)phenyl)acetamide (4c)**

\[
\text{OMe} \quad \text{CONEt}_2 \quad \text{OMe}
\]
**N,N-Diethyl-2-(2-methoxy-6-(4-(trifluoromethyl)benzoyl)phenyl)acetamide (4d)**

\[ R_f = 0.35 \ (n\text{-hexanes/EtOAc} = 1:1) \]

$^1$H NMR (500 MHz, CD$_3$OD) $\delta$ 7.59 (t, $J = 8.8$ Hz, 2H), 7.41 (d, $J = 7.5$ Hz, 1H), 7.35-7.32 (m, 2H), 7.15 (d, $J = 8.2$ Hz, 1H), 6.89 (d, $J = 7.6$ Hz, 1H), 3.87 (s, 3H), 3.83 (s, 2H), 3.38 (q, $J = 7.2$ Hz, 2H), 3.24 (q, $J = 7.1$ Hz, 2H), 2.36 (s, 3H), 1.14 (t, $J = 7.2$ Hz, 3H), 0.97 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CD$_3$OD) $\delta$ 200.2, 172.0, 159.6, 141.8, 139.5, 139.2, 135.1, 132.0, 129.3, 128.7, 128.4, 125.0, 122.2, 113.9, 56.4, 43.6, 41.9, 31.5, 21.3, 14.2, 13.3; IR (KBr) $\nu$ 2973, 2934, 2837, 1714, 1647, 1602, 1584, 1462, 1321, 1282, 1259, 1138, 1081, 985, 821 cm$^{-1}$; HRMS (EI) Calcd for C$_{21}$H$_{25}$NO$_3$ [M]$^+$ 339.1834, found 339.1833.


\[ N,N\text{-Diethyl-2-(2-methoxy-6-(4-(trifluoromethyl)benzoyl)phenyl)}\text{acetamide (4e)} \]

\[ R_f = 0.48 (n\text{-hexanes/EtOAc} = 1:1); \]  
\[ ^1H \text{ NMR (400 MHz, CD}_3\text{OD} \delta 7.98 (d, } J = 8.1 \text{ Hz, 2H), 7.79 (d, } J = 8.1 \text{ Hz, 2H), 7.37 (t, } J = 7.9 \text{ Hz, 1H), 7.22 (d, } J = 8.3 \text{ Hz, 1H), 6.94 (d, } J = 7.6 \text{ Hz, 1H), 3.96 (s, 2H), 3.90 (s, 3H), 3.46 (q, } J = 7.1 \text{ Hz, 2H), 3.26 (q, } J = 7.1 \text{ Hz, 2H), 1.22 (t, } J = 7.1 \text{ Hz, 3H), 0.98 (t, } J = 7.1 \text{ Hz, 3H); }^{13}C \text{ NMR (125 MHz, CD}_3\text{OD) } \delta 198.6, 172.0, 159.6, 142.4, 140.7, 135.0 (q, } J_{C,F} = 32.2 \text{ Hz), 131.9, 128.5, 126.3 (q, } J_{C,F} = 3.8 \text{ Hz), 125.5, 125.2 (q, } J_{C,F} = 270.0 \text{ Hz), 122.5, 114.5, 56.4, 43.6, 30.9, 14.2, 13.2; \text{ IR (KBr) } \nu 2975, 2936, 2839, 1719, 1643, 1582, 1463, 1380, 1325, 1278, 1169, 1132, 1065, 986, 947, 862 \text{ cm}^{-1}; \text{ HRMS (EI) Calcd for } C_{21}H_{22}F_3NO_5 [M]^+ 393.1552, \text{ found 393.1554.} \]

\[ N,N\text{-Diethyl-2-(2-methoxy-6-(3-nitrobenzoyl)phenyl)}\text{acetamide (4f)} \]

\[ R_f = 0.29 (n\text{-hexanes/EtOAc} = 1:1); \]  
\[ ^1H \text{ NMR (500 MHz, CDCl}_3 \delta 8.71 (s, 1H), 8.37 (d, } J = 8.2 \text{ Hz, 1H), 8.17 (d, } J = 7.7 \text{ Hz, 1H), 7.60 (t, } J = 8.0 \text{ Hz, 1H), 7.28 (t, } J = 8.0 \text{ Hz, 1H), 7.06 (d, } J = 8.2 \text{ Hz, 1H), 6.87 (d, } J = 7.6 \text{ Hz, 1H), 4.01 (s, 2H), 3.87 (s, 3H), 3.33 (br s, 4H), 1.10 (br s, 6H); }^{13}C \text{ NMR (100 MHz, CD}_3\text{OD) } \delta 197.3, 172.1, 159.7, 149.6, 140.7, 140.3, 137.1, 130.9, 128.6, 128.2, 125.8, 125.6, 122.5, 114.7, 56.5, 43.7, 41.9, 30.7, 14.3, 13.3; \text{ IR (KBr) } \nu 2975, 2935, 2839, 2237, 1581, 1532, 1463, 1380, 1321, 1297, 1273, 1141, 1075, 1000, 913, 827 \text{ cm}^{-1}; \text{ HRMS (EI) Calcd for } C_{20}H_{22}N_2O_5 [M]^+ 370.1529, \text{ found 370.1524.} \]
**N,N-Diethyl-2-(2-(3-fluorobenzoyl)-6-methoxyphenyl)acetamide (4g)**

\[
\begin{align*}
\text{OMe} & \quad \text{CONEt}_2 \\
\text{CONEt}_2 & \quad \text{OMe}
\end{align*}
\]

\[R_f = 0.38 \text{ (n-hexanes/EtOAc = 1:1); } ^1\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 7.62-7.56 \text{ (m, 2H), 7.39-7.38 \text{ (m, 1H), 7.28-7.22 \text{ (m, 2H), 7.01 (d, } J = 8.2 \text{ Hz, 1H), 6.91 (d, } J = 7.7 \text{ Hz, 1H), 3.93 (s, 2H), 3.86 (s, 3H), 3.33 (br s, 4H), 1.12 (br s, 6H); } ^{13}\text{C NMR (100 MHz, CD}_3\text{OD) } \delta 198.4 \text{ (d, } J_{\text{C-F}} = 2.1 \text{ Hz), 172.0, 163.6 \text{ (d, } J_{\text{C-F}} = 244.9 \text{ Hz), 159.6, 141.4 \text{ (d, } J_{\text{C-F}} = 6.2 \text{ Hz), 141.0, 131.3 \text{ (d, } J_{\text{C-F}} = 7.5 \text{ Hz), 128.5, 127.6, 127.5, 125.3, 122.3, 121.0 \text{ (d, } J_{\text{C-F}} = 21.6 \text{ Hz), 117.6 \text{ (d, } J_{\text{C-F}} = 22.5 \text{ Hz), 114.3, 56.4, 43.6, 41.9, 31.1, 14.2, 13.3; IR (KBr) } \nu 2973, 2934, 2838, 1718, 1644, 1586, 1440, 1380, 1323, 1272, 1136, 1051, 994, 884 \text{ cm}^{-1}; \text{ HRMS (EI) Calcd for C}_{29}H_{22}FNO_3 [M]^+ 343.1584, \text{ found 343.1577.}}
\]

**N,N-Diethyl-2-(2-(4-fluorobenzoyl)-6-methoxyphenyl)acetamide (4h)**

\[
\begin{align*}
\text{OMe} & \quad \text{CONEt}_2 \\
\text{CONEt}_2 & \quad \text{OMe}
\end{align*}
\]

\[R_f = 0.40 \text{ (n-hexanes/EtOAc = 1:1); } ^1\text{H NMR (500 MHz, CD}_3\text{OD) } \delta 7.94-7.91 \text{ (m, 2H), 7.39 \text{ (t, } J = 8.0 \text{ Hz, 1H), 7.26-7.21 \text{ (m, 3H), 6.95 (d, } J = 7.7 \text{ Hz, 1H), 3.93 (s, 3H), 3.92 (s, 2H), 3.46 (q, } J = 7.2 \text{ Hz, 2H), 3.30 (q, } J = 7.1 \text{ Hz, 2H), 1.23 (t, } J = 7.2 \text{ Hz, 3H), 1.02 (t, } J = 7.1 \text{ Hz, 3H); } ^{13}\text{C NMR (175 MHz, CD}_3\text{OD) } \delta 196.9, 170.6, 165.8 \text{ (d, } J_{\text{C-F}} = 251.9 \text{ Hz), 158.2, 140.0, 134.2, 133.0 \text{ (d, } J_{\text{C-F}} = 9.4 \text{ Hz), 127.1, 123.6, 120.6, 114.9 \text{ (d, } J_{\text{C-F}} = 22.0 \text{ Hz), 112.6, 55.0, 42.2, S15}}
\]
40.5, 29.8, 12.5, 11.8; IR (KBr) ν 2974, 2935, 2838, 1713, 1644, 1598, 1462, 1380, 1279, 1226, 1153, 1079, 986, 922, 856 cm⁻¹; HRMS (EI) Calcd for C₂₀H₂₂FNO₃ [M]+ 343.1584, found 343.1584.

2-(2-(4-Chlorobenzoyl)-6-methoxyphenyl)-N,N-diethylacetamide (4i)

\[
\begin{align*}
\text{RF} &= 0.41 \text{ (n-hexanes/EtOAc = 1:1); } ^1H \text{ NMR (500 MHz, CD}_3\text{OD) } \delta 7.87 \text{ (d, J = 8.6 Hz, 2H), 7.56 \text{ (d, J = 8.6 Hz, 2H), 7.43 \text{ (t, J = 8.0 Hz, 1H), 7.26 \text{ (d, J = 8.2 Hz, 1H), 6.99 \text{ (d, J = 7.6 Hz, 1H), 3.97 \text{ (s, 2H), 3.96 \text{ (s, 3H), 3.51 \text{ (q, J = 7.2 Hz, 2H), 3.34 \text{ (q, J = 7.1 Hz, 2H), 1.28 \text{ (t, J = 7.2 Hz, 3H), 1.06 \text{ (t, J = 7.1 Hz, 3H); }} } ^{13}C \text{ NMR (175 MHz, CD}_3\text{OD) } \delta 197.2, 170.6, 158.2, 139.8, 139.1, 136.2, 131.7, 128.2, 127.1, 123.8, 120.8, 112.6, 54.9, 42.2, 40.5, 29.7, 12.8, 11.8; } \text{IR (KBr) } \nu 2973, 2934, 2837, 1644, 1584, 1462, 1323, 1277, 1138, 1078, 985, 921, 846 \text{ cm}^{-1}; } \text{HRMS (EI) } \text{Calcd for C}_20\text{H}_{22}\text{ClNO}_3 [M]^+ 359.1288, \text{found 359.1284.}
\end{align*}
\]

2-(2-(2-Naphthoyl)-6-methoxyphenyl)-N,N-diethylacetamide (4j)

\[
\begin{align*}
\text{RF} &= 0.35 \text{ (n-hexanes/EtOAc = 1:1); } ^1H \text{ NMR (400 MHz, CDCl}_3\text{) } \delta 8.35 \text{ (s, 1H), 8.04 \text{ (d, J = 8.6 Hz, 1H), 7.94-7.87 \text{ (m, 3H), 7.61 \text{ (t, J = 7.2 Hz, 1H), 7.54 \text{ (d, J = 7.2 Hz, 1H), 7.34-7.28}}}
\end{align*}
\]
(m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.01 (d, J = 7.6 Hz, 1H), 3.94 (s, 2H), 3.90 (s, 3H), 3.29 (br s, 4H), 1.16-0.93 (m, 6H); $^{13}$C NMR (175 MHz, CD$_3$OD) δ 200.1, 172.0, 159.8, 142.1, 137.3, 136.4, 134.8, 133.8, 131.0, 130.0, 129.4, 128.9, 128.7, 128.0, 126.0, 125.1, 122.3, 114.0, 56.5, 43.6, 41.9, 31.7, 14.3, 13.3; IR (KBr) υ 2972, 2933, 1655, 1581, 1463, 1321, 1238, 1139, 1076, 989, 921 cm$^{-1}$; HRMS (EI) Calcd for C$_{24}$H$_{25}$NO$_3$ [M]$^+$ 375.1834, found 375.1831.
Experimental procedure and characterization data for the synthesis of 3-isochromanone 6

\(\text{\(N,N\)-Diethyl-2-(2-(hydroxy(phenyl)methyl)-6-methoxyphenyl)acetamide (5)}\)

To a stirred solution of 3e (79 mg, 0.243 mmol, 100 mol %) in EtOH (1.2 mL) was added NaBH\(_4\) (13.8 mg, 150 mol %) at room temperature. The reaction mixture was stirred for 30 min at 50 °C, and quenched with a saturated solution of NH\(_4\)Cl (1.2 mL). The aqueous layer was extracted with EtOAc (15 mL \(\times\) 2). The organic layer was washed with H\(_2\)O, dried over MgSO\(_4\) and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 1:1) to afford 59.8 mg of 5 in 75% yield.

\(R_f = 0.37\) (n-hexanes/EtOAc = 1:1); \(^1\text{H} \text{NMR (700 MHz, CD\(_3\)OD}) \delta 7.35-7.31\) (m, 4H), 7.26-7.22 (m, 2H), 6.91 (t, \(J = 8.2\) Hz, 2H), 5.96 (s, 1H), 3.86 (d, \(J = 16.0\) Hz, 1H), 3.81 (s, 3H), 3.71 (d, \(J = 16.0\) Hz, 1H), 3.51 (q, \(J = 7.1\) Hz, 2H), 3.38 (q, \(J = 7.1\) Hz, 2H), 1.24 (t, \(J = 7.1\) Hz, 3H), 1.11 (t, \(J = 7.1\) Hz, 3H); \(^{13}\text{C} \text{NMR (175 MHz, CD\(_3\)OD}) \delta 171.6, 157.8, 144.0, 143.4, 127.8, 127.4, 126.8, 126.6, 122.8, 120.1, 109.4, 72.7, 54.7, 42.4, 40.7, 29.7, 13.0, 11.9; IR (KBr) \(\nu\) 3270, 2974, 2934, 1615, 1469, 1321, 1264, 1144, 1070, 1038, 949, 859 cm\(^{-1}\); HRMS (EI) Calcd for C\(_{20}\)H\(_{25}\)NO\(_3\) \([M]^+\) 327.1834, found 327.1832.

5-Methoxy-1-phenylisochroman-3-one (6)
To a stirred solution of 5 (41 mg, 0.161 mmol, 100 mol %) in THF (0.8 mL) was added 1 M HCl (0.8 mL) at room temperature. The reaction mixture was stirred for 12 h at 100 ºC, and quenched with a saturated solution of Na2CO3 (1.2 mL). The aqueous layer was extracted with EtOAc (10 mL × 2). The organic layer was washed with H2O, dried over MgSO4 and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc = 4:1) to afford 39.3 mg of 6 in 96% yield.

Rf = 0.36 (n-hexanes/EtOAc = 3:1); 1H NMR (700 MHz, CDCl3) δ 7.41-7.37 (m, 3H), 7.31-7.25 (m, 3H), 6.91 (d, J = 8.2 Hz, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.41 (s, 1H), 3.89 (s, 3H), 3.79 (d, J = 19.4 Hz, 1H), 3.62 (d, J = 19.4 Hz, 1H); 13C NMR (175 MHz, CDCl3) δ 170.7, 156.0, 137.5, 135.5, 128.8, 128.7, 128.0, 127.4, 119.0, 118.1, 110.2, 82.0, 55.6, 29.6; IR (KBr) ν 2938, 2839, 1740, 1480, 1367, 1329, 1267, 1230, 1151, 1078, 1015, 974, 845 cm⁻¹; HRMS (EI) Calcd for C16H14O3 [M]+ 254.0943, found 254.0941.
SpinWorks 3: JH574M

file: ...
file: ...

freq. of 0 ppm: 495.558043 MHz
processed size: 65536 complex points
LB: 0.000
GF: 0.000
H/axioms: 179.509
ppm/axiom: 0.35103

number of scans: 36
width: 1611.02 Hz = 19.2523 ppm = 0.264267 Hz/pt

draw: "SpinWorks"

SpinWorks 3: JH574M

file: ...
file: ...

freq. of 0 ppm: 100.62626 MHz
processed size: 32768 complex points
LB: 0.000
GF: 0.000
H/axioms: 877.614
ppm/axiom: 8.69200

number of scans: 1004
width: 2639.46 Hz = 238.8967 ppm = 0.36678 Hz/pt

PPM

3aa
Electronic Supplementary Material (ESI) for Chemical Communications
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SpinWorks 3: JH554-H

SpínWorks 3: JH-5S4_13C
SpinWorks 3: 3H-546-1H

SpinWorks 3: 3H-546-13C