Supporting information

In vitro and *in vivo* evaluation of fluorinated indanone derivatives as potential positron emission tomography agents for the imaging of monoamine oxidase B in the brain

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Chemistry

General

All chemicals and reagents were purchased from commercially available sources and used without further purification. Moisture-sensitive reactions were conducted under argon with oven-dried glassware and anhydrous solvents. Reaction progress was monitored by thin-layer chromatography (TLC) using Alugram® SIL G/UV$_{254}$ pre-coated plates (Macherey-Nagel; Düren; Germany). Column flash chromatography was carried out using silica gel 60 (40-64 µm; Merck; Darmstadt; Germany). Melting points (M. p.) were determined on a Linström capillary apparatus (Wagner & Munz GmbH; Vienna; Austria) in open capillary tubes and were not corrected. The purity of all the tested compounds was > 95% as determined by LC-MS [Dionex Ultimate 3000 system incorporating a LPG-3400SD pump, a WPS-3000 TSL autosampler, a TCC-3000SD column compartment, a DAD3000 diode array detector and a MSQ 3000 low resolution mass spectrometer (Thermo Fisher Scientific Inc.; Waltham; USA), column: Reprosil-Pur Basic HD (150 × 3 mm; 3 µm; Dr. Maisch GmbH; Ammerbuch; Germany), gradient: 10-90-10% MeCN/20 mM $NH_4OAc_{aq.}$ (*v/v*, 15 min, 0.6 mL/min]. ^{1}H, ^{13}C and ^{19}F-NMR spectra were recorded on VARIAN Mercury plus (300 MHz for ^{1}H-NMR, 75 MHz for ^{13}C-NMR, 282 MHz for ^{19}F-NMR) and BRUKER DRX-400 (400 MHz for ^{1}H-NMR, 100 MHz for ^{13}C-NMR, 377 MHz for ^{19}F-NMR); chemical shifts (δ) in parts per million (ppm) are related to internal standard tetramethylsilane and coupling constants (*J*). High resolution mass spectra (HRMS) were recorded on a FT-ICR APEX II spectrometer (Bruker Daltonics; Bruker Corporation; Billerica; USA) using electrospray ionization (ESI).

General procedure A

A solution of the corresponding fluoro-methylpyridine (100 mg, 1 eq, 0.90 mmol) in CCl_4 (2 mL) was treated with NBS (168 mg, 1.05 eq, 0.95 mmol) and AIBN (44 mg, 0.3 eq, 0.27 mmol) and stirred overnight at 80 °C. After filtration of the reaction mixture, the solvent was removed by

rotary evaporation. The remaining residue was dissolved in EA (20 mL) and the organic phase was washed with water (3 x 20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. The crude product was purified by flash chromatography (silica, gradient ethyl acetate / petroleum ether (EA/PE1:8 → 1:7 → 1:6) to give the corresponding bromomethyl-fluoropyridine (**3a**-**d**) as colorless oil.

*5-(bromomethyl)-2-fluoropyridine (**3a**).* General procedure A; colorless oil; 54% yield; TLC (EA/PE, 1:6): R_f = 0.35; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 2.6 Hz, 1H), 7.84 (td, *J* = 2.6, 7.9 Hz, 1H), 6.93 (dd, *J* = 3.0, 8.4 Hz, 1H), 4.46 (s, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 163.23 (d, *J* = 241.0 Hz), 147.61 (d, *J* = 15.3 Hz), 141.96 (d, *J* = 8.4 Hz), 131.54 (d, *J* = 4.7 Hz), 109.90 (d, *J* = 37.8 Hz), 28.38 (d, *J* = 1.8 Hz); according to *US9499537B2*.[1]

*3-(bromomethyl)-2-fluoropyridine (**3b**).* General procedure A; colorless oil; 40% yield; TLC (EA/PE, 1:6): R_f = 0.35; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 5.0 Hz, 1H), 7.83 (ddd, *J* = 2.0, 7.4, 9.6 Hz, 1H), 7.20 (ddd, *J* = 1.7, 4.9, 7.0 Hz, 1H), 4.47 (s, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 161.18 (d, *J* = 241.4 Hz), 147.92 (d, *J* = 14.8 Hz), 141.67 (d, *J* = 4.2 Hz), 121.98 (d, *J* 4.5 Hz), 120.41 (d, *J* = 29.6 Hz), 24.68 (d, *J* = 1.9 Hz); according to *US9499537B2*.[1]

*4-(bromomethyl)-2-fluoropyridine (**3c**).* General procedure A; colorless oil; 30 % yield; TLC (EA/PE, 1:6): R_f = 0.35; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 5.2 Hz, 1H), 7.18 (d, *J* = 5.2 Hz, 1H), 6.94 (s, 0H), 4.38 (s, 2H); .19 (dd, *J* = 0.8, 5.2 Hz, 1H), 7.22 – 7.06 (m, 1H), 6.94 (tt, *J* = 0.6, 1.5 Hz, 1H), 4.38 (s, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 164.21 (d, *J* = 239.5 Hz), 151.91 (d, *J* = 7.8 Hz), 148.35 (d, *J* = 15.3 Hz), 121.44 (d, *J* = 4.2 Hz), 109.60 (d, *J* = 38.6 Hz), 29.36 (d, *J* = 3.5 Hz); according to *US9499537B2*.[1]

*2-(bromomethyl)-6-fluoropyridine (**3d**).* General procedure A; colorless oil; 42% yield; TLC (EA/PE, 1:6): R_f = 0.35; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.79 (td, *J* = 7.4, 8.1 Hz, 1H), 7.32 (dd, *J* = 2.2, 7.4 Hz, 1H), 6.86 (dd, *J* = 2.7, 8.2 Hz, 1H), 4.46 (s, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 162.94 (d, *J* = 241.3 Hz), 155.61 (d, *J* = 13.4 Hz), 142.05 (d, *J* = 7.7 Hz), 120.69 (d, *J* = 4.2 Hz), 109.12 (d, *J* = 36.7 Hz), 32.29; according to *Wenzel et al*.[2]

General procedure B

To a solution of the corresponding (hetero)arene bromide (**2a-c** or **3a-d**, 1 eq, 0.34 mmol) in 1 mL DMF was added 6-hydroxy-2,3-dihydro-1*H*-inden-1-one (**1**, 50 mg, 1 eq, 0.34 mmol) and K_2CO_3 (3 eq, 1.01 mmol). The reaction mixture was then stirred overnight at room temperature. After the addition of 20 mL water, the aqueous phase was extracted with EA (3 x 20 mL) and the combined organic phases were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The crude product was purified by flash chromatography (silica, gradient EA/PE 1:2 → 1.5:2 → 1:1 for **5-10** or gradient DCM/MeOH 100:0.5 → 100:1→ 100:1.5 for **11-14**) to afford the corresponding fluorinated derivative (**5**-**11**) as tan solid.

*6-((4-fluorobenzyl)oxy)-2,3-dihydro-1H-inden-1-one (**5**).* General procedure B; tan solid; 79% yield; TLC (EA/PE, 1:1): R_f = 0.66; M. p. = 77 °C; LC-MS: t_R = 11.2 min, > 99%; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.48 – 7.35 (m, 3H), 7.31 – 7.23 (m, 2H), 7.14 – 7.03 (m, 2H), 5.07 (s, 2H), 3.12 – 3.06 (m, 2H), 2.77 – 2.69 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -113.96; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 207.02, 162.72 (d, *J* = 246.5 Hz), 158.43, 148.47, 138.40, 132.36, 129.58, 129.50, 127.67, 124.70, 115.81, 115.60, 106.25, 69.76, 37.13, 25.28; HRFT-MS (ESI+): m/z = 279.0794 (calcd. 279.0792 for $[M+H]^+$).

*6-((3-fluorobenzyl)oxy)-2,3-dihydro-1H-inden-1-one (**6**).* General procedure B; tan solid; 74% yield; TLC (EA/PE, 1:1): R_f = 0.66; M. p. = 103 °C; LC-MS: t_R = 11.4 min, > 99; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.41 (dd, *J* = 0.9, 8.2 Hz, 1H), 7.37 (td, *J* = 5.9, 8.0 Hz, 1H), 7.33 – 7.24 (m, 2H), 7.24 – 7.20 (m, 1H), 7.17 (dt, *J* = 2.1, 9.7 Hz, 1H), 7.08 – 6.96 (m, 1H), 5.11 (s, 2H), 3.15 – 3.05 (m, 2H), 2.79 – 2.67 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -112.67; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 206.87, 163.01 (d, *J* = 246.4 Hz), 158.19, 148.43, 139.06 (d, *J* = 7.4 Hz), 138.29, 130.21 (d, *J* = 8.3 Hz), 127.59, 124.52, 122.76 (d, *J* = 3.0 Hz), 114.97 (d, *J* = 21.2 Hz), 114.23 (d, *J* = 22.1 Hz), 106.13, 69.43, 37.00, 25.15; ; HRFT-MS (ESI+): m/z = 279.0794 (calcd. 279.0792 for $[M+H]^+$).

*6-((2-fluorobenzyl)oxy)-2,3-dihydro-1H-inden-1-one (**7**).* General procedure B; tan solid; 72% yield; TLC (EA/PE, 1:1): R_f = 0.66; M. p. = 130 °C; LC-MS: t_R = 11.3 min, > 99%; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.51 (td, *J* = 1.8, 7.5 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.38 – 7.26 (m, 3H), 7.19 (td, *J* = 1.2, 7.5 Hz, 1H), 7.12 (ddd, *J* = 1.2, 8.3, 9.6 Hz, 1H), 5.18 (s, 2H), 3.13 – 3.03 (m, 2H), 2.79 – 2.64 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -118.39; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 206.99, 160.67 (d, *J* = 247.5 Hz), 158.42, 148.49, 138.40, 130.03 (d, *J* = 8.2 Hz), 129.81 (d, *J* = 3.9 Hz), 127.64, 124.53, 124.38 (d, *J* = 3.6 Hz), 123.78 (d, *J* = 14.3 Hz), 115.58 (d, *J* = 21.0 Hz), 106.39, 64.28, 37.12, 25.26; HRFT-MS (ESI+): m/z = 279.0790 (calcd. 279.0792 for $[M+H]^+$).

*6-((6-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1H-inden-1-one (**8**).* General procedure B; tan solid; 62% yield; TLC (DCM/MeOH, 9:1): R_f = 0.80; M. p. = 113 °C; LC-MS: t_R = 10.1 min, > 97 %; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.30 (s, 1H), 7.89 (td, *J* = 2.4, 8.0 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.20 (m, 1H), 6.98 (dd, *J* = 2.8, 8.7 Hz, 1H), 5.08 (s, 2H), 3.17 – 3.04 (m, 2H), 2.85 – 2.67 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -68.41; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 206.75, 163.49 (d, *J* = 240.0 Hz), 157.92, 148.70, 146.91 (d, *J* = 15.2 Hz), 140.78 (d, *J* = 8.2 Hz), 138.34, 129.85, 127.73, 124.43, 109.68 (d, *J* = 37.5 Hz), 106.07, 67.05, 36.98, 25.17; HRFT-MS (ESI+): m/z = 280.0772 (calcd. 280.0744 for $[M+H]^+$).

*6-((2-fluoropyridin-4-yl)methoxy)-2,3-dihydro-1H-inden-1-one (**9**).* General procedure B; tan solid; 89 % yield; TLC (DCM/MeOH, 9:1): R_f = 0.85; M. p. = 133 °C; LC-MS: t_R = 11.3 min, > 96%; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = δ 8.23 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.28 (dd, *J* = 2.6, 8.4 Hz, 1H), 7.22 (d, *J* = 5.0 Hz, 1H), 7.20 (d, *J* = 2.6 Hz, 1H), 7.03 (s, 1H), 5.14 (s, 2H), 3.22 – 2.96 (m, 2H), 2.82 – 2.61 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -67.27; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 206.80, 164.25 (d, *J* = 239.0 Hz), 157.73, 151.80 (d, *J* = 7.8 Hz), 149.00, 148.05 (d, *J* = 13.9 Hz), 138.50, 127.97, 124.44, 119.19, 107.39 (d, *J* = 40.2 Hz), 106.15, 67.95, 37.09, 25.30; HRFT-MS (ESI+): m/z = 280.0790 (calcd. 280.0744 for $[M+H]^+$).

*6-((2-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1H-inden-1-one (**10**).* General procedure B; tan solid; 66% yield; TLC (DCM/MeOH, 9:1): R_f = 0.80; M. p. = 138 °C; LC-MS: t_R = 10.1 min, > 99 %; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1H), 8.01 – 7.90 (m, 1H), 7.41 (dq, *J* = 1.1, 7.8 Hz, 1H), 7.32 – 7.18 (m, 3H), 5.14 (s, 2H), 3.16 – 2.92 (m, 2H), 2.83 – 2.60 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -71.67; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 206.72, 160.86 (d, *J* = 239.4 Hz), 157.89, 148.69, 147.07 (d, *J* = 6.7 Hz), 139.77 (d, *J* = 4.4 Hz), 138.39, 127.72, 124.14, 121.73, 119.01 (d, *J* = 21.7 Hz), 106.38, 63.69, 36.99, 25.17; HRFT-MS (ESI+): m/z = 280.0773 (calcd. 280.0744 for $[M+H]^+$).

*6-((6-fluoropyridin-2-yl)methoxy)-2,3-dihydro-1H-inden-1-one (**11**).* General procedure B; tan solid; 75% yield; TLC (DCM/MeOH, 9:1): R_f = 0.85; M. p. = 154 °C; LC-MS: t_R = 11.3 min, > 95%; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.80 (q, *J* = 7.9 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.33 – 7.21

(m, 2H), 6.87 (dd, *J* = 2.7, 8.3 Hz, 1H), 5.14 (s, 2H), 3.14 – 2.97 (m, 2H), 2.79 – 2.63 (m, 2H); ^{19}F-NMR (377 MHz, $CDCl_3$): δ = -67.14; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 206.71, 163.09 (d, *J* = 240.7 Hz), 157.91, 155.69 (d, *J* = 13.0 Hz), 148.50, 141.85 (d, *J* = 7.8 Hz), 138.36, 127.64, 123.96, 118.38, 108.57 (d, *J* = 36.6 Hz), 106.66, 70.01, 36.99, 25.14; HRFT-MS (ESI+): m/z = 280.0771 (calcd. 280.0744 for $[M+H]^+$).

General procedure C

The corresponding benzoic acid (**4a-d**, 1.1 eq, 0.37 mmol), HATU (1.3eq, 0.44 mmol) and triethylamine (3 eq, 1.01 mmol) were dissolved in DCM (3 mL) and stirred at room temperature for 30 min. After the addition of the 6-hydroxy-2,3-dihydro-1*H*-inden-1-one (**1**, 50 mg, 1 eq, 0.34 mmol), the reaction mixture was stirred overnight at room temperature. The solvent was removed by rotatory evaporation and the remaining residue was dissolved in EA (10 mL). After the addition of 50 mL $NaHCO_3$, the aqueous phase was extracted with EA (3 x 20 mL) and the combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and evaporated to dryness. The crude product was purified by flash chromatography (silica, gradient EA/PE 1:2 → 1.5:2 → 1:1) to afford the corresponding fluorinated derivative (**12**-**15**) as tan solid.

*3-oxo-2,3-dihydro-1H-inden-5-yl 6-fluoronicotinate (**12**).* General procedure C; tan solid; 23 % yield; TLC (EA/PE, 1:2): R_f = 0.45; M. p. = 125 °C; LC-MS: t_R = 10.1 min, > 96%; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.06 (dt, *J* = 2.6, 0.8 Hz, 1H), 8.55 (ddd, *J* = 8.6, 7.4, 2.4 Hz, 1H), 7.59 (dq, *J* = 2.4, 0.6 Hz, 1H), 7.56 (dq, *J* = 8.3, 0.8 Hz, 1H), 7.44 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.10 (ddd, *J* = 8.6, 2.9, 0.7 Hz, 1H), 3.23 – 3.13 (m, 2H), 2.82 – 2.72 (m, 2H); ^{19}F-NMR (282 MHz, $CDCl_3$): δ = -59.61; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 205.73, 166.31 (d, *J* = 247.2 Hz), 162.78, 152.79, 151.09 (d, *J* = 16.9 Hz), 149.81, 143.15 (d, *J* = 9.6 Hz), 138.57, 128.12, 127.79, 123.63 (d, J = 4.6 Hz), 116.42, 109.96 (d, J = 37.5 Hz), 36.88, 25.54; HRFT-MS (ESI+): m/z = 272.0729 (calcd. 272.0717 for $[M+Na]^+$).

*3-oxo-2,3-dihydro-1H-inden-5-yl 2-fluoroisonicotinate (**13**).* General procedure C; tan solid; 76% yield; TLC (EA/PE, 1:2): R_f = 0.45; M. p. = 130 °C; LC-MS: t_R = 10.2 min, > 97%; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.46 (dt, *J* = 5.1, 0.8 Hz, 1H), 7.90 (dddd, *J* = 5.2, 1.7, 1.3, 0.5 Hz, 1H), 7.66 (ddt, *J* = 2.5, 1.3, 0.6 Hz, 1H), 7.63 – 7.48 (m, 2H), 7.44 (ddd, *J* = 8.2, 2.3, 0.5 Hz, 1H), 3.24 – 3.14 (m, 2H), 2.83 – 2.73 (m, 2H); ^{19}F-NMR (282 MHz, $CDCl_3$): δ = -65.48; ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 205.62, 164.28 (d, *J* = 240.8 Hz), 162.42 (d, *J* = 4.2 Hz), 152.98, 149.72, 149.05 (d, J = 14.5 Hz), 141.81 (d, *J* = 7.8 Hz), 138.63, 127.90, 127.84, 121.11 (d, *J* = 4.8 Hz), 116.24, 110.33 (d, *J* = 39.5 Hz), 36.87, 25.55; HRFT-MS (ESI+): m/z = 272.0725 (calcd. 272.0717 for $[M+H]^+$).

*3-oxo-2,3-dihydro-1H-inden-5-yl 2-fluoronicotinate (**14**).* General procedure C; tan solid; 92% yield; TLC (EA/PE, 1:2): R_f = 0.26; M. p. = 163 °C; LC-MS: t_R = 9.8 min, > 98%; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.60 – 8.50 (m, 1H), 8.48 (ddt, *J* = 4.8, 2.0, 0.9 Hz, 1H), 7.64 – 7.50 (m, 2H), 7.45 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.42 – 7.33 (m, 1H), 3.23 – 3.13 (m, 2H), 2.82 – 2.72 (m, 2H); ^{19}F-NMR (282 MHz, $CDCl_3$): δ = -60.39 (d, *J* = 9.0 Hz); ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 205.75, 161.79 (d, *J* = 250.9 Hz), 161.61 (d, *J* = 8.6 Hz), 152.79, 152.59 (d, *J* = 15.6 Hz), 149.80, 143.66, 138.52, 128.13, 127.75, 121.68 (d, *J* = 5.0 Hz), 116.38, 113.00 (d, *J* = 24.5 Hz), 36.88, 25.53; HRFT-MS (ESI+): m/z = 272.0737 (calcd. 272.0717 for $[M+H]^+$).

*3-oxo-2,3-dihydro-1H-inden-5-yl 6-fluoropicolinate (**15**).* General procedure C; tan solid; 61% yield; TLC (EA/PE, 1:2): R_f = 0.26; M. p. = 157 °C; LC-MS: t_R = 9.7 min, > 97%; ^{1}H-NMR (300

MHz, $CDCl_3$): δ = 8.18 (ddd, *J* = 7.4, 2.1, 0.8 Hz, 1H), 8.04 (dt, *J* = 8.2, 7.5 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.54 (dq, *J* = 8.2, 0.8 Hz, 1H), 7.45 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.29 – 7.20 (m, 1H), 3.22 – 3.12 (m, 2H), 2.81 – 2.72 (m, 2H); ^{19}F-NMR (282 MHz, $CDCl_3$): δ = -64.10 (d, *J* = 8.2 Hz); ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 205.79, 163.04 (d, *J* = 244.0 Hz), 162.60, 152.79, 150.17, 145.37 (d, *J* = 12.8 Hz), 142.35 (d, *J* = 7.6 Hz), 138.51, 128.23, 127.74, 123.60 (d, *J* = 3.9 Hz), 116.50, 114.76 (d, *J* = 36.8 Hz), 36.88, 25.53; HRFT-MS (ESI+): m/z = 272.0733 (calcd. 272.0717 for $[M+H]^+$).

Precursor synthesis

To a solution of 2-(3-(bromomethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**16**, 220 mg, 1.1 eq, 0.74 mmol) in 2 mL DMF were added 6-hydroxy-2,3-dihydro-1*H*-inden-1-one (1, 50 mg, 1 eq, 0.67 mmol) and potassium carbonate (280 mg, 3 eq, 2.02 mmol). The reaction mixture was then stirred overnight at room temperature. After filtration and washing with ethanol, the crude product was purified by flash chromatography (silica, gradient EA/PE 1:6 → 1:5 → 1:4 → 1:3 → 1:2) to afford the boronic acid pinacol ester **17** as a tan solid.

*6-((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)oxy)-2,3-dihydro-1H-inden-1-one (**17**).* 45% yield; TLC (EA/PE, 1:1): R_f = 0.69; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (tt, *J* = 0.7, 1.3 Hz, 1H), 7.78 (dt, *J* = 1.3, 7.3 Hz, 1H), 7.53 (dtd, *J* = 0.7, 1.4, 7.7 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.28 (d, *J* = 1.5 Hz, 1H), 5.07 (s, 2H), 3.18 – 3.03 (m, 2H), 2.78 – 2.67 (m, 2H), 1.36 (s, 12H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 207.09, 158.69, 148.31, 138.37, 135.82, 134.76, 134.22, 134.18, 130.75, 128.20, 127.56, 124.73, 106.27, 84.06, 70.49, 37.13, 25.26, 25.01.

Binding affinities

The binding affinities of the synthesized compounds towards MAO-B were determined in radioligand competition binding assays developed in-house.[3] The assays were performed using rat brain membrane homogenates and the MAO-B specific radioligand L-[^{3}H]**deprenyl** (Novandi Chemistry AB, NT1063, Södertälje, Sweden). Membrane suspension was incubated with 2 nM L-**[^{3}H]deprenyl** and various concentrations (10^{-12}-10^{-5} M) of the test compound in 50 mM tris(hydroxymethyl)aminomethane–HCl (Tris−HCl), pH 7.4 buffer containing 120 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$, at room temperature for 60 min. Non-specific binding was determined in the presence of 10 μM of **rasagiline**. The reaction was terminated by rapid filtration using Whatman GF/B glass-fibre filters, pre-soaked in 0.3% polyethyleneimine, and a 48-channel harvester (Biomedical Research and Development Laboratories, Gaithersburg, MD, USA) followed by washing four times with ice-cold TRIS-HCl buffer. Filter-bound radioactivity was quantified by liquid scintillation counting. At least four separate experiments in triplicate were performed for determination of K_i values. The data was analysed with GraphPad Prism, version 4.1 (GraphPad Inc., La Jolla, CA) according to the Cheng-Prusoff equation. For the most potent compounds (**6**, **9** and **13**) the binding affinities towards the MAO-A isoform and the histamine H_3 receptor (H_3R) were determined by Cerep (France, Item 443 and Item1332, respectively). The selected compounds were tested at a concentration of 100 nM. The MAO-A assay was performed with [^{3}H]**Ro 41-1049** on rat brain homogenates and the human H_3R GPCR binding with [^{3}H]***N*-alpha-Me-histamine**.

Manual radiosynthesis of [^{18}F]6

No-carrier-added (n.c.a.) [^{18}F]fluoride was produced via the ^{18}O(p,n)^{18}F nuclear reaction by irradiation of a [^{18}O]H_2O target (Hyox 18 enriched water; Rotem Industries Ltd, Mishor Yamin,

Israel) on a Cyclone®18/9 (IBA RadioPharma Solutions, Louvain-la-Neuve, Belgium) with 18 MeV proton beam using a Nirta® [^{18}F]fluoride XL target or [^{18}O]H_2O recycled by the established in-house method[4] Starting with 1–2 GBq of n.c.a. [^{18}F]fluoride, [^{18}F]F^--containing anion resin [Sep-Pak® Accell Plus QMA Carbonate Plus light cartridge (Waters GmbH, Eschborn, Germany)] was eluted with a solution composed of 100 μL of tetra-*n*-butylammonium hydrogen carbonate ($TBAHCO_3$, 0.075 M, ABX advanced biochemical compounds GmbH, Radeberg, Germany) and K_2CO_3 (20 mg/mL solution, 0.6 mg, 4.3 μmol) in H_2O/MeCN (1:4, *v/v*) in a total volume of 1.2 mL. The solution was transferred directly into a 5 mL microwave V-vial (CEM® Corporation, Matthews, NC, USA) and azeotropically dried under vacuum and argon flow in the microwave cavity (Discover PETwave microwave CEM® corporation, 50–60 °C, 75 W) for 8–10 min. Additional aliquots of MeCN (2 × 1.0 mL) were added during the drying process. After complete dryness, a solution containing the pinacol ester precursor **17** (3 mg, 8.2 μmol) and tetrakis(pyridine)copper(II) triflate [$Cu(py)_4(OTf)_2$] (~ 10 mg, 15 μmol) in *N,N*-dimethylacetamide (DMA, 600 μL) and *tert*-BuOH (300 μL) was added to the reactive anhydrous [^{18}F]TBAF. The reaction was monitored in different time points (up to 15 min) at 110°C via radio-thin layer chromatography (radio-TLC) and high performance liquid chromatography (HPLC, see quality control section). After the completion of the reaction, the crude reaction mixture was diluted with 18 mL H_2O and passed through a Sep-Pak® C18 Plus cartridge (Waters GmbH, Eschborn, Germany) to remove the excess of $Cu(py)_4(OTf)_2$ and some UV impurities. The cartridge was then eluted with 2.5 mL of MeCN and further diluted with 2.5 mL of H_2O. This solution was directly applied onto a semi-preparative HPLC system composed by a Reprosil-Pur C18-AQ column (Dr. Maisch HPLC GmbH, Germany) with an eluent of 58% MeCN/20 mM $NH_4OAc_{aq.}$ at a flow rate of 3.8 mL·min^{-1}. [^{18}F]**6** was collected and diluted in 40 mL of H_2O. Final purification was performed using a Sep-Pak® C18 Light cartridge (Waters, Milford, MA, USA) followed by elution with 1.2 mL of EtOH. To obtain an injectable solution, the solvent was concentrated under a gentle nitrogen stream at 70 °C and [^{18}F]**6** was formulated in a sterile isotonic saline solution (5–10% EtOH, *v/v*). The identity of [^{18}F]**6** was verified by radio-HPLC analysis of an aliquot of the radiotracer solution co-injected with the corresponding reference compound **6**. Radiochemical and chemical purities were assessed by radio-TLC and analytical HPLC. Molar activities were determined based on aliquots taken from the formulation, and the mass determination for the corresponding reference standard was performed via a calibration curve obtained under the same analytical HPLC conditions (see quality control section).

Automated radiosynthesis of [^{18}F]6

Remote controlled radiosynthesis was performed using a Synchrom R&D EVO III automated synthesizer (Elysia-Raytest, Germany). The setup of the automat is depicted in the supplemental information (Figure S2) and the reagents and conditions used as described for the manual synthesis. Briefly, [^{18}F]fluoride (4-6 GBq) was trapped on a Waters QMA cartridge (Trap 1) and eluted with a solution (vial SC1) containing 100 μL of $TBAHCO_3$ and 30 μL K_2CO_3 dissolved in a mixture of H_2O/MeCN (1:4, *v/v*) into the reaction vessel and dried via azeotropic distillation. Additional 1.5 mL of dried MeCN was added (vial SC2). After complete dryness, a solution containing 8.2 μmol of boronic acid pinacol ester **17** and 15 μmol $Cu(py)_4(OTf)_2$ in DMA/*tert*-BuOH (2:1, *v/v*, vial SC3) was added, and the reaction mixture was stirred at 120 °C for 10 min. To remove the excess of copper catalyst and some UV impurities a C18 light cartridge (Trap 2) was applied prior to the semi-preparative HPLC isolation of [^{18}F]**6**. For that purpose, the reaction mixture was diluted with 18 mL H_2O (vial SC4) and the cartridge eluted

with 2.5 mL MeCN (vial SC5). After further dilution with 2.5 mL H_2O (vial SC7), the solution was transferred to the semi-preparative HPLC. [^{18}F]**6** was collected in the HPLC collection vial containing 40 mL of H_2O and trapped in the Sep-Pak® C18 light cartridge (Trap 4). The cartridge was washed with 2 mL H_2O (vial SC10), and [^{18}F]**6** eluted with 1.3 mL EtOH (vial SC11). The ethanolic solution containing [^{18}F]**6** was transferred outside of the hotcell, the solvent was evaporated at 70 °C in a gentle stream of nitrogen for 5-10 min, and [^{18}F]**6** was reconstituted in a saline solution (0.9 % NaCl). [^{18}F]**6** was then ready for further biological characterization in a total synthesis time of about 60 min.

Quality control

Radio-thin layer chromatography (radio-TLC) of [^{18}F]**6** was performed on Alugram® SIL G/UV_{254} pre-coated plates (Macherey-Nagel; Düren; Germany) with PE:EA (1:1, *v*/*v*). The plates were exposed to storage phosphor screens (BAS IP MS 2025 E, GE Healthcare Europe GmbH, Freiburg, Germany) and recorded using the Amersham Typhoon RGB Biomolecular Imager (GE Healthcare Life Sciences). Images were quantified with the ImageQuant TL8.1 software (GE Healthcare Life Sciences). Analytical chromatographic separations were performed on a JASCO LC-2000 system, incorporating a PU-2080*Plus* pump, AS-2055*Plus* auto injector (100 μL sample loop), and a UV-2070*Plus* detector coupled with a gamma radioactivity HPLC flow detector (Gabi Star, Raytest Isotopenmessgeräte GmbH). Data analysis was performed with the Galaxie chromatography software (Agilent Technologies, USA) using the chromatograms obtained at 254 nm. Radiochemical yield from aliquots of the reaction mixture, radiochemical purities and *in vivo* metabolism analysis of plasma and brain samples were assessed via reverse phase – high performance liquid chromatography (RP-HPLC) in gradient mode (0–10 min: 10% MeCN/20 mM $NH_4OAc_{aq.}$, 10–30 min: 10%→90% MeCN/20 mM $NH_4OAc_{aq.}$, 30–35 min: 90% MeCN/20 mM $NH_4OAc_{aq.}$, 35–36 min: 90%→10% MeCN/20 mM $NH_4OAc_{aq.}$ 36–45 min: 10% MeCN/20 mM $NH_4OAc_{aq.}$). The molar activity was determined using analytical radio-HPLC with a Reprosil-Pur C18-AQ column (250 × 4.6 mm, 5 μm) and 54% MeCN/20 mM $NH_4OAc_{aq.}$ as eluent at a flow rate of 1 mL·min^{-1} obtained at 254 nm.

Determination of in vitro stability and lipophilicity (Log$D_{7.4}$)

In vitro radiochemical stability of [^{18}F]**6** was investigated in 0.9% NaCl solution, PBS (pH 7.2) at 40 °C and in EtOH at room temperature for up to 90 min. Samples were taken at 30 min and 90 min of incubation time and analysed by radio-TLC and radio-HPLC. Log$D_{7.4}$ of [^{18}F]**6** was experimentally determined in *n*-octanol/phosphate-buffered saline (PBS; 0.01 M, pH 7.4) at room temperature by the shake-flask method. The measurement was performed twice in triplicate.

Biological evaluation

All experimental work including animals has been conducted in accordance with the national legislation on the use of animals for research [Tierschutzgesetz (TierSchG), Tierschutz-Versuchstierverordnung (TierSchVersV)] and were approved by the Animal Care and Use Committee of Saxony (TVV 18/18; TVV 36/18 Landesdirektion Sachsen). Female CD-1 mice and Fischer rats F344 were obtained from the Medizinisch-Experimentelles Zentrum at Universität Leipzig (Leipzig, Germany) and from Janvier Labs (Le Genest-Saint-Isle, France) respectively.

In vitro autoradiography

Cryosections of brains obtained from female CD1 mice (10–12 weeks old, 25-38 g), SPRD rats (10-12 weeks, 250-300 g) and domestic piglets (Sus s. domestica, 6 weeks, 12–14 kg)) were thawed, dried in a stream of cold air, and pre-incubated in 50 mM TRIS-HCl buffer (pH 7.4, 120 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$) 2x5 min at ambient temperature. Afterwards, brain sections were incubated with either 10 nM L-[^{3}H]**deprenyl** or 0.1-0.2 MBq/mL **[^{18}F]6** in buffer for 60 min at room temperature. Non-specific binding was determined in the presence of 10 µM of L**-deprenyl**, rasagiline or compound **6**, respectively. Subsequently, the sections were washed 2 x 5 min in ice-cold TRIS-HCl buffer, and dipped for 5 s in ice-cold deionized water. The sections were rapidly dried in a stream of cold air before being exposed for three weeks or overnight on an imaging plate (Fujifilm Corporation, Tokyo, Japan). Developed autoradiographs were analysed in a phosphor imager (HD-CR 35; Duerr NDT GmbH, Bietigheim Bissingen, Germany). The quantification was performed by using 2D-densitometric analysis (AIDA 2.31 software; Raytest Isotopenmessgeräte GmbH, Germany) and presented in intensity/area (QL/pixel).

PET Scanning Protocol

For the time of the experiments, female CD-1 mice (n = 3; 10 weeks; 30-35 g) were kept in a dedicated climatic chamber with free access to water and food under a 12:12h dark:light cycle at a constant temperature (24 °C). The animals were anaesthetized (Anaesthesia Unit U-410, agntho's, Lidingö, Sweden) with isoflurane (1.8%, 0.35 L/min) delivered in a 60% oxygen/40% air mixture (Gas Blender 100 Series, MCQ instruments, Rome, Italy) and maintained at 37 °C with a thermal bed system. [^{18}F]**6** was injected into the tail vein (CD-1 mice; 5.3 ± 2.6 MBq in 150 µL isotonic saline; A_m: 13-20 GBq/µmol, EOS) followed by a 60 min PET/MR scan (Mediso nanoScan®, Hungary). Each mouse was used as its own control, undergoing a baseline and then the blocking experiment. Blocking studies (n = 3) were performed with an intravenous (i.v.) injection of 1 mg/kg L**-deprenyl** (Tocris Bioscience, Bristol, UK) 10 min prior to injection of [^{18}F]**6**. Each PET image was corrected for random coincidences, dead time, scatter and attenuation (AC), based on a whole body (WB) MR scan. The reconstruction parameters for the list mode data were 3D-ordered subset expectation maximization (OSEM), 4 iterations, 6 subsets, energy window: 400-600 keV, coincidence mode: 1-5, ring difference: 81. The mice were positioned prone in a special mouse bed (heated up to 37 °C), with the head fixed to a mouth piece for the anaesthetic gas supply with isoflurane in 40% air and 60% oxygen. The PET data were collected by a continuous WB scan during the entire investigation. Following the 60 min PET scan a T1 weighted WB gradient echo sequence (TR/TE: 20/6.4 ms, NEX: 1, FA: 25, FOV: 64 x 64 mm, Matrix: 128 x 128, STh: 0.5 mm) was performed for AC and anatomical orientation. Image registration and evaluation of the region of interest (ROI) was done with PMOD (PMOD Technologies LLC, v. 3.9, Zurich, Switzerland). The respective brain regions were identified using the mouse brain atlas template Ma-Benveniste-Mirrione-FDG. The activity data is expressed as mean SUV of the overall ROI.

In vivo metabolite analysis

From the same animals used in the PET studies, brain and blood samples were obtained at 30 min p.i., plasma was separated by centrifugation (14,000 × g, 1 min), and brain homogenized in ~ 1 mL isotonic saline on ice [10 strokes of a polytetrafluoroethylene (PTFE) plunge at 1000 rpm in a borosilicate glass cylinder; Potter S Homogenizer, B. Braun Melsungen AG, Melsungen, Germany]. Two consecutive extractions were performed as duplicate for

plasma and brain determinations. Plasma and brain samples were added to an ice-cold MeOH/H_2O mixture (8:2, *v/v*). The samples were vortexed for 3 min, incubated on ice for 5 min and centrifuged at 12,000 rpm for 5 min. Supernatants were collected and the precipitates were re-dissolved in 100 µL of extraction solvent and the extracted procedure was repeated. The extraction efficiencies were calculated by the ratio of radioactivity in the supernatant by the total radioactivity in the sample (precipitate + supernatant) measured in an automated gamma counter (1480 WIZARD, Fa. Perkin Elmer). The supernatants from both extractions were combined, concentrated at 70 °C under argon stream up to a remaining volume of 100 µL, and subsequently quantified by analytical radio-HPLC with a gradient system (see quality control section).

In vitro liver microsome studies

Incubations with MLM and HLM had a final volume of 250 µL and were performed in PBS (pH 7.4) as follows,[5] with final concentrations as stated in brackets. PPS, MLM or HLM (1 mg/mL respectively), and [^{18}F]**6** (~3 MBq) were mixed vigorously and pre-incubated for 3 min at 37°C. Analogously pre-incubated NADPH (2 mM) in PBS was added and mixtures were shaken gently at 37 °C. After termination at 15, 30, and 60 min by addition of 250 µL ice-cold MeCN and vigorous mixing for 30 s, samples were cooled on ice for 5 min, and centrifuged at 14,000 rpm for 10 min. Supernatants were immediately analysed by fast radio-HPLC. For each time point incubations were performed in duplicate, containing small amounts of EtOH (0.025%), resulting from formulation of [^{18}F]**6**. Extraction efficiencies were determined as described for ”*In vivo metabolite analyses*” and accounted for 91.5% (mean, n = 10, SD = 2.2%). Incubations without MLM or HLM, and NADPH, respectively, were performed for 60 min as negative controls. Similar to the protocol described above positive controls were performed using testosterone (20 µM) instead of [^{18}F]**6** as substrate, whereby after 90 min complete conversion by MLM and HLM was respectively confirmed by RP-HPLC analyses with UV detection. For monitoring of metabolic depletion [^{18}F]**6** the HPLC system (X-LC, JASCO) with radioactivity detection was used as previously described.[5] A ReproSil-Pur 120 C18-AQ column, (150 x 3 mm, 3 µm, incl. 10 x 3 mm pre-column - both Dr. Maisch GmbH) was used as stationary phase. At a flow rate of 0.7 mL·min^{-1} and a column oven temperature of 25 °C, a semi-isocratic elution was performed (0–4 min 67.5% MeCN/20 mM $NH_4OAc_{aq.}$, 4–5.5 min 90% MeCN/20 mM NH_4OAc_{aq}, 5.5–9 min 67.5% MeCN/20 mM NH_4OAc_{aq}), whereby unchanged [^{18}F]**6** eluted at 3.9 min and radiometabolites in the range of 0.7-4.5 min. For microsome experiments, the following instruments were used: a BioShake iQ (QUANTIFOIL Instruments, Jena, Germany) and Centrifuge 5424 (Eppendorf, Hamburg, Germany).

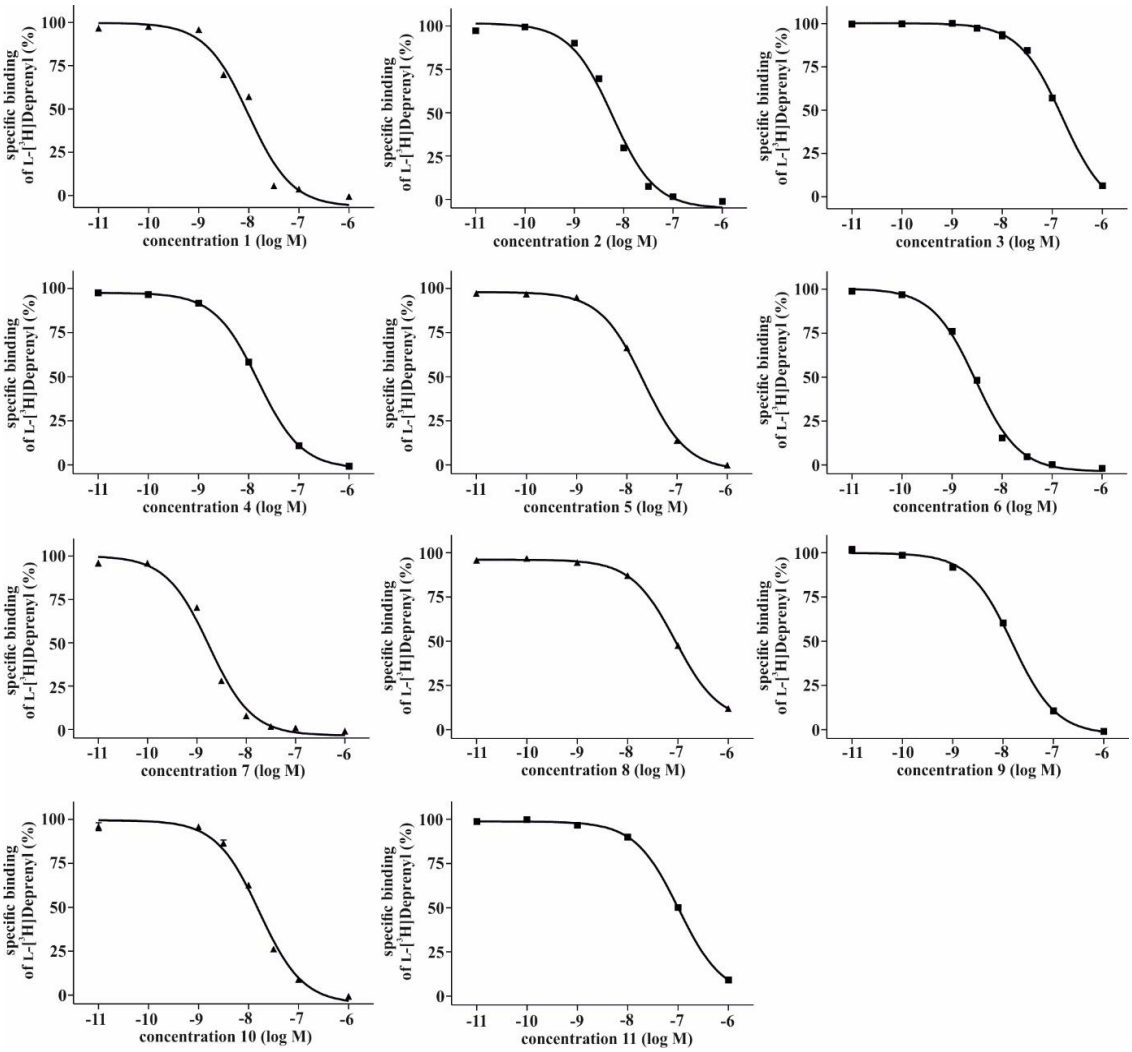

Figure S 1: Representative competition binding curves for compounds **5**-**15**.

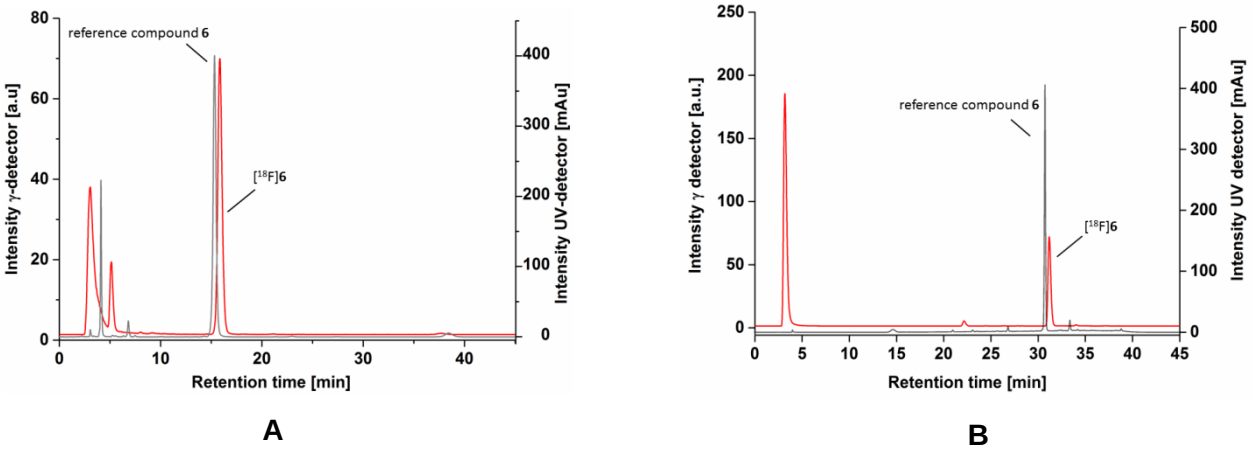

Figure S 2: Representative radio (red line)- and UV (gray line)- HPLC chromatograms of the crude reaction mixtures of [^{18}F]6 co-eluted with the reference compound 6. (**A**) manual synthesis (RCY: 49%) [Reprosil-Pur C18-AQ column (250 x 4.6 mm, 5 µm), 58% MeCN/20 mM NH_4OAc, Flow rate: 1 mL·min^{-1}] and (**B**) automated radiosynthesis (RCY: 25%) [Reprosil-Pur C18-AQ (250 x 4.6 mm; 5 µm); gradient (eluent A 10% ACN/aq. 20 mM NH_4OAc; eluent

B 90% ACN/aq. 20 mM NH_4OAc; 0–10 min 100% A, 10–30 min up to 100% B, 30–35 min 100% B, 35-36 min 100% A, 36–45 min 100% A); Flow: 1 mL·min^{-1}].

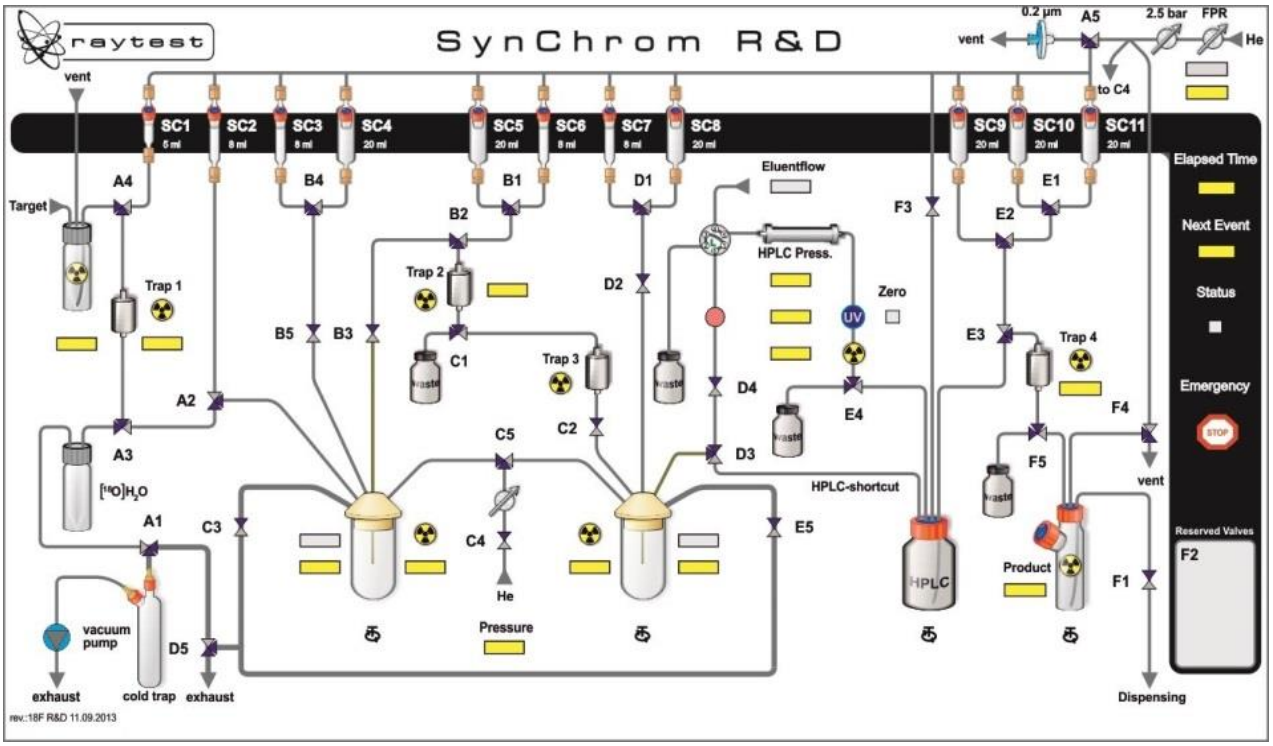

Figure S 3: Schematic representation of the setup for the automated radiosynthesis of [^{18}F]6 using the Synchrom R&D EVO III automated synthesizer (Elysia-Raytest, Germany). ^{18}F]Fluoride (4-6 GBq) was trapped on a Waters QMA cartridge (Trap 1) and eluted with a solution (vial SC1) containing 100 µL of $TBAHCO_3$ and 30 µL K_2CO_3 dissolved in a mixture of H_2O/MeCN (1:4, *v/v*) into the reaction vessel and dried via azeotropic distillation. Additional 1.5 mL of dried MeCN was added (vial SC2). After complete dryness, a solution containing 8.2 µmol of boronic acid pinacol ester **17** and 15 µmol $Cu(py)_4(OTf)_2$ in DMA/*t*-BUOH (2:1, *v/v*, vial SC3) was added, and the reaction mixture was stirred at 120 °C for 10 min. To remove the excess of copper catalyst and some UV impurities a C18 light cartridge (Trap 2) was applied prior to semi-preparative the HPLC isolation. For that purpose, the reaction mixture was diluted with 18 mL H_2O (vial SC4) and the cartridge eluted with 2.5 mL MeCN (vial SC5). After further dilution with 2.5 mL H_2O (vial SC7), the solution was transferred to the semi-preparative HPLC. [^{18}F]**6** was collected in the HPLC collection vial containing 40 mL of H_2O and trapped in the Sep-Pak® C18 light cartridge (Trap 4). The cartridge was washed with 2 mL H_2O (vial SC10), and [^{18}F]**6** eluted with 1.3 mL EtOH (vial SC11).

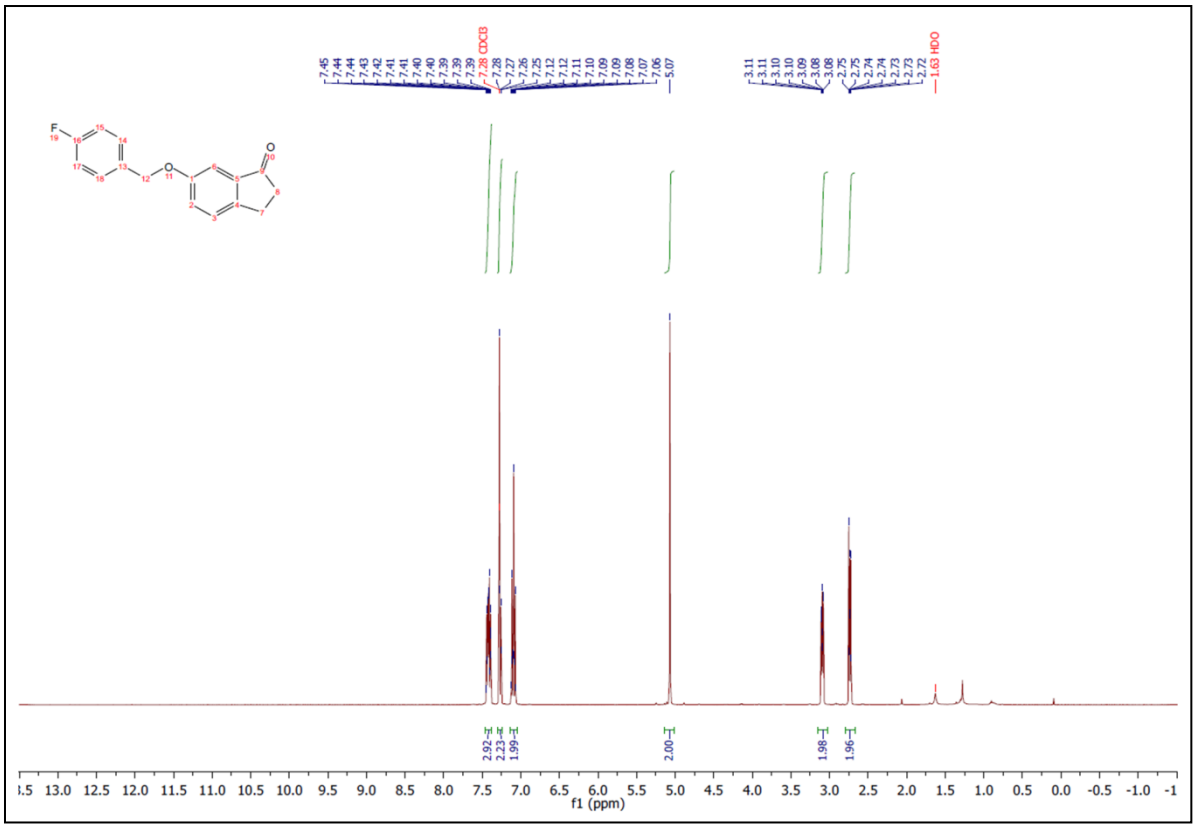

Figure S 4: ^{1}H-NMR of 6-((4-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (5).

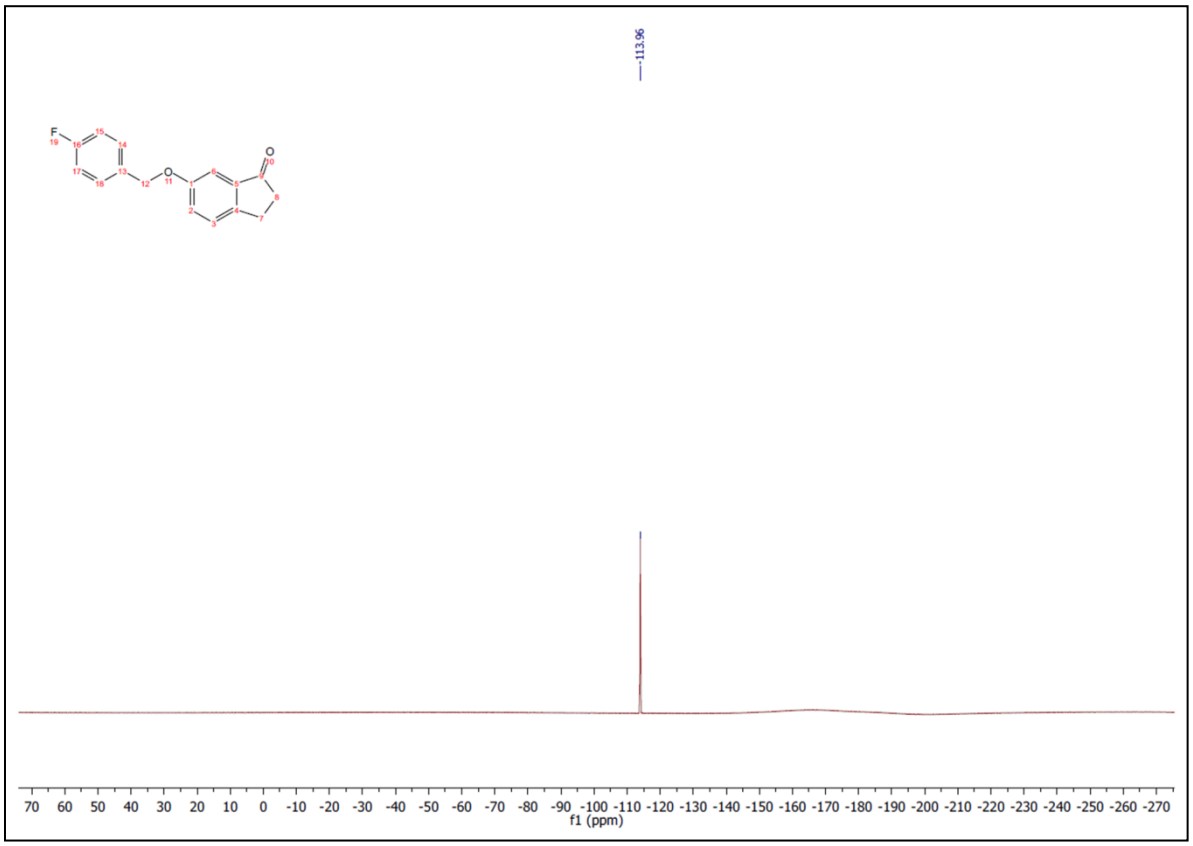

Figure S 5: ^{19}F-NMR of 6-((4-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (5).

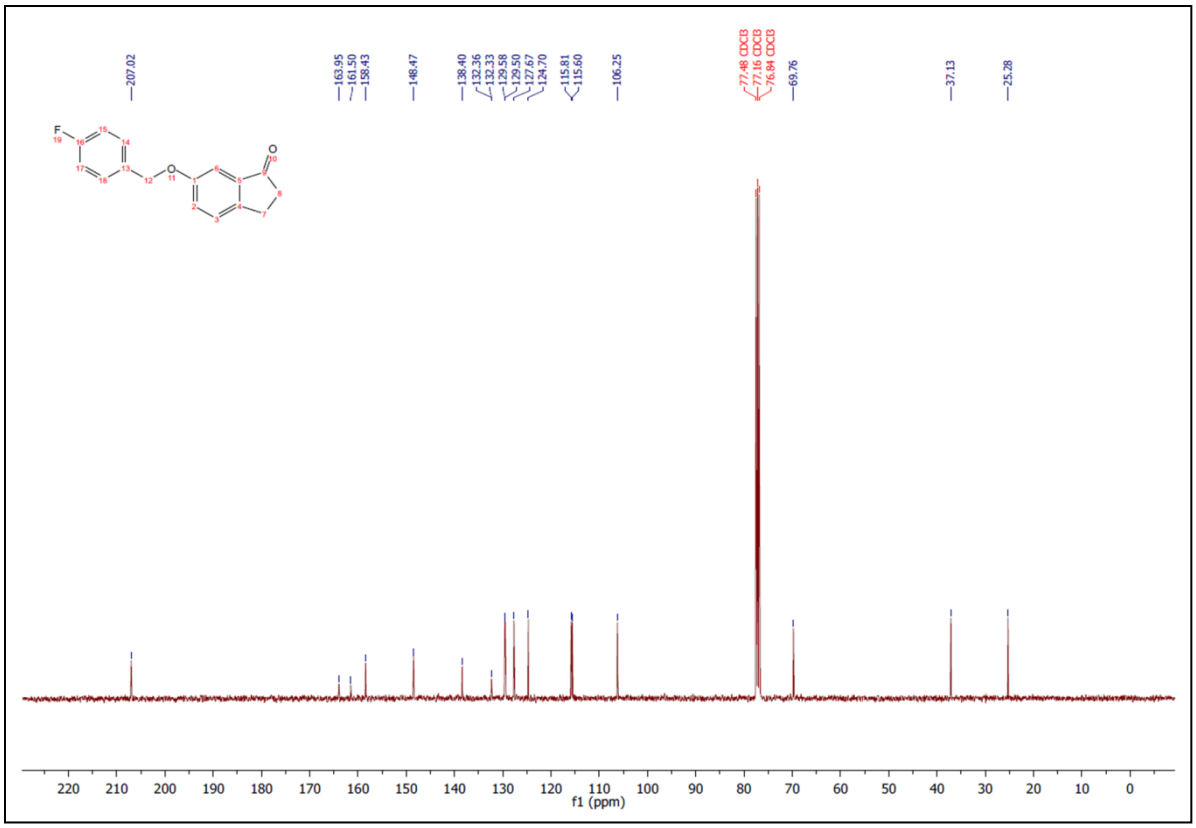

Figure S 6: ^{13}C-NMR of 6-((4-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**5**).

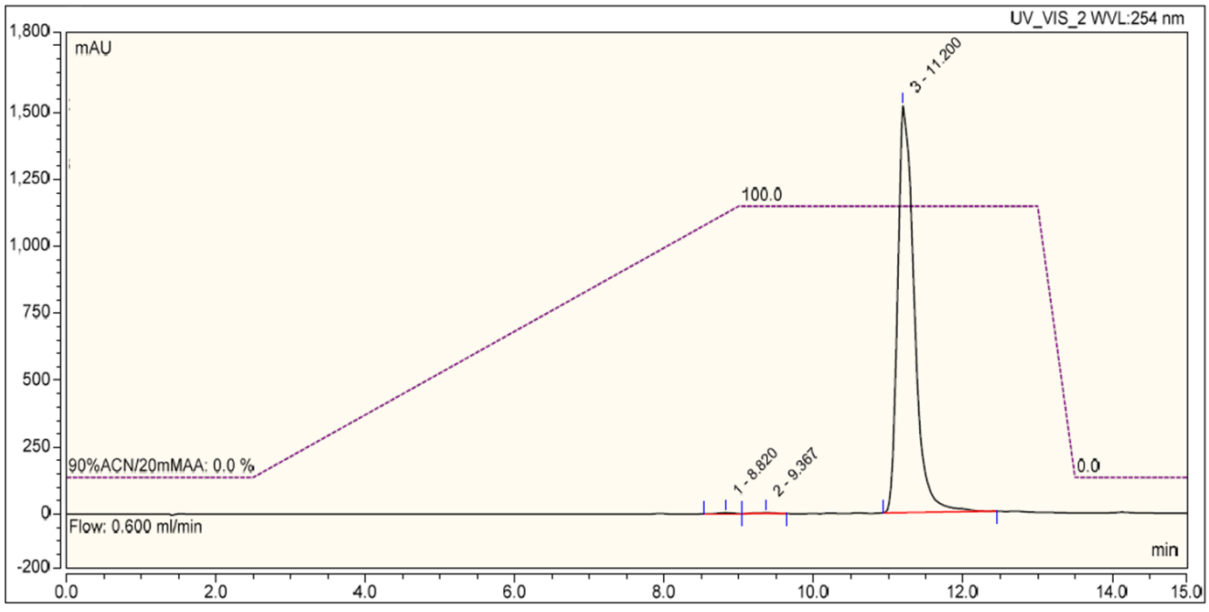

Figure S 7: LC-MS chromatogram of 6-((4-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (5).

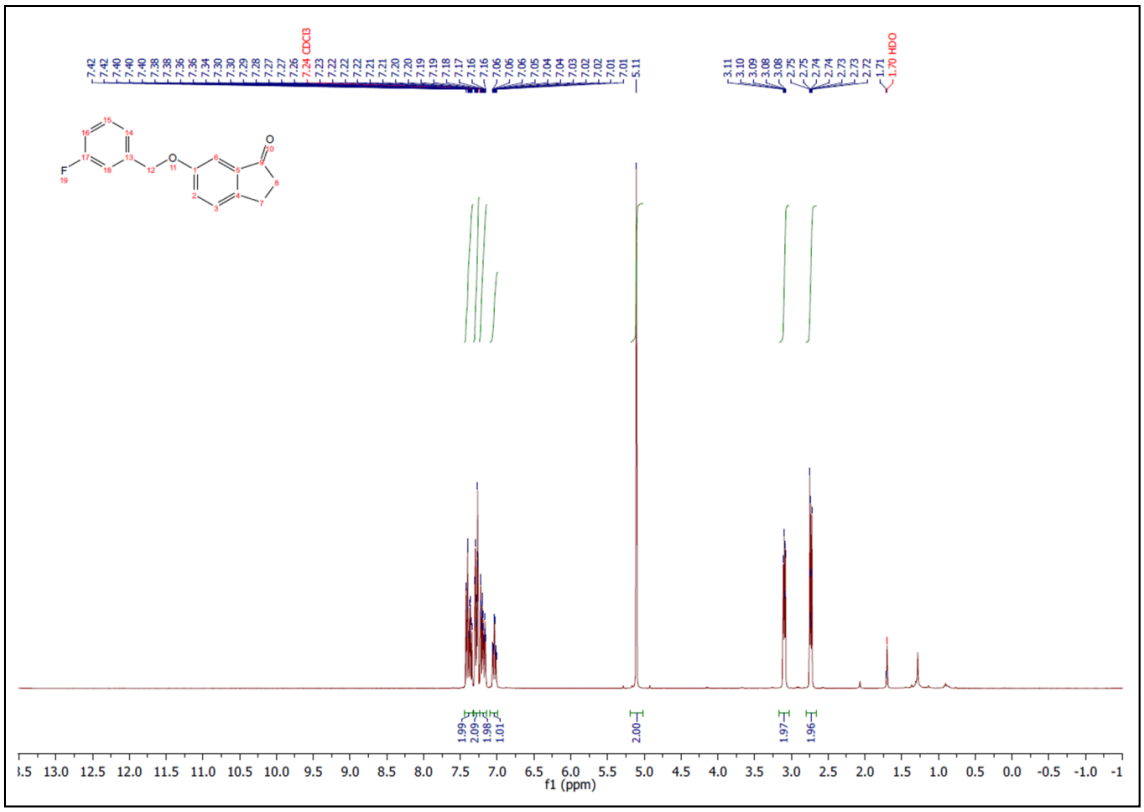

Figure S 8: ^{1}H-NMR of 6-((3-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**6**).

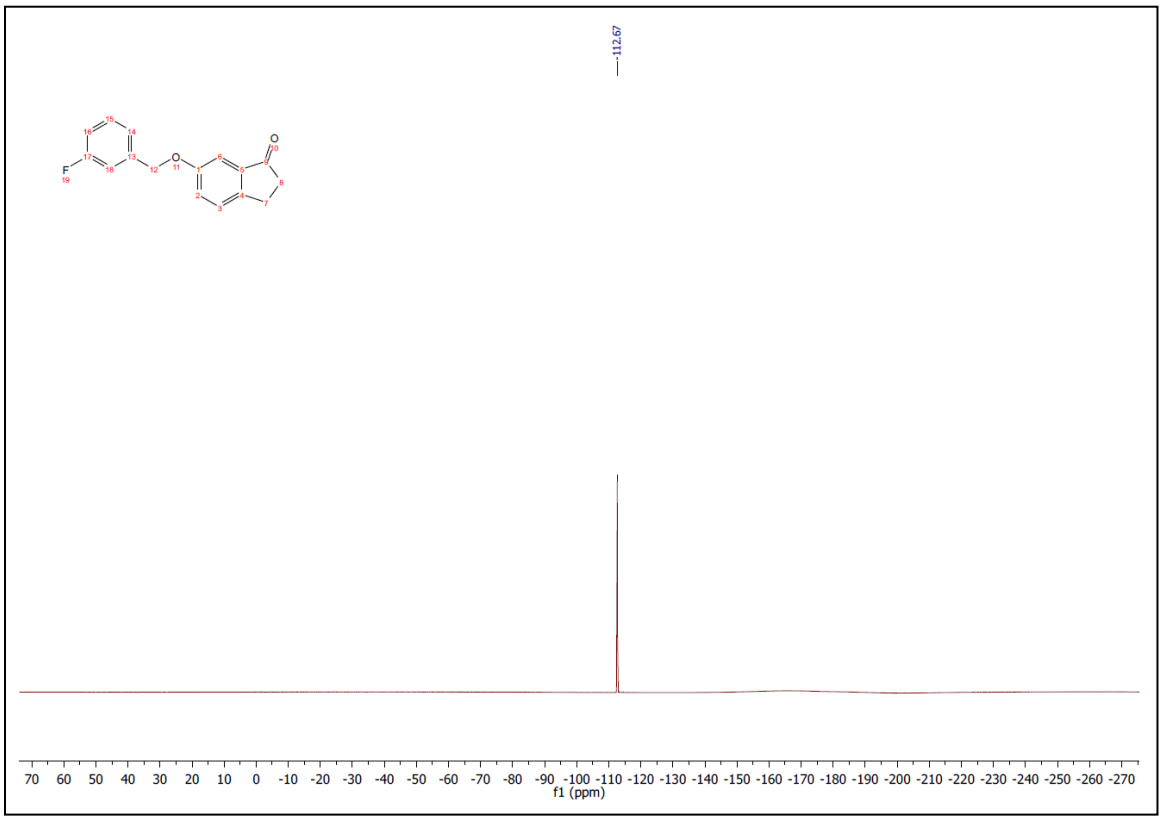

Figure S 9: ^{19}F-NMR of 6-((3-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**6**).

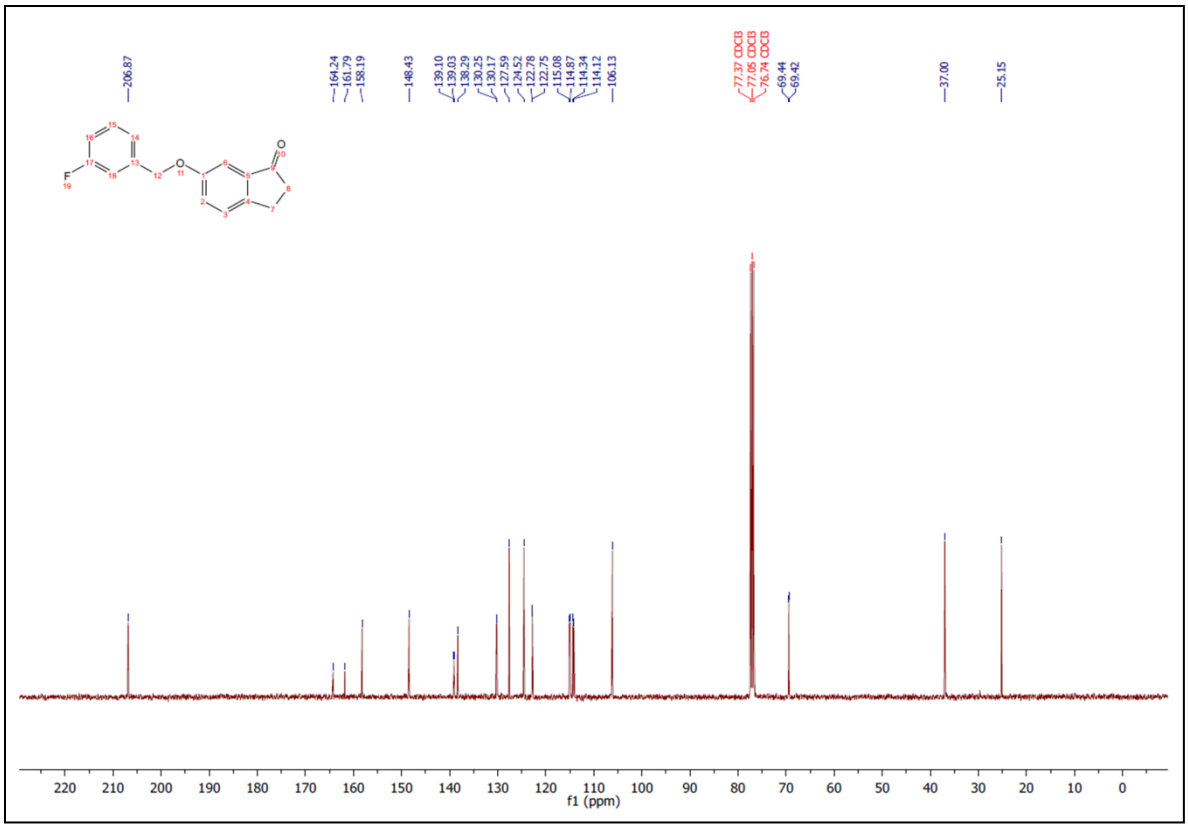

Figure S 10: ^{13}C-NMR of 6-((3-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**6**).

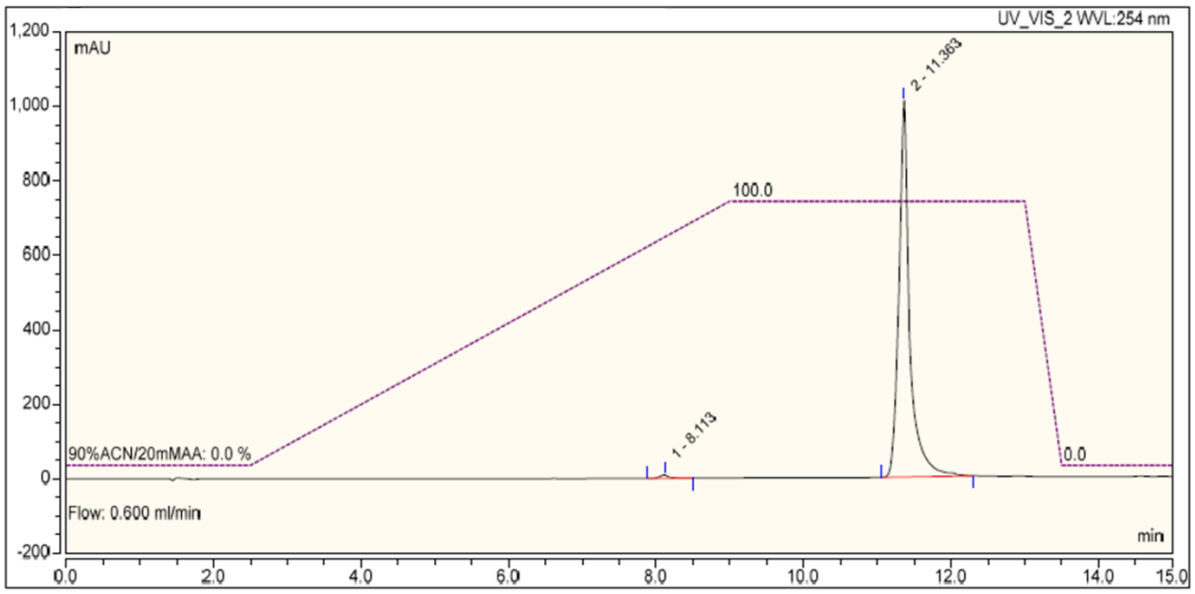

Figure S 21: LC-MS chromatogram of 6-((3-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**6**).

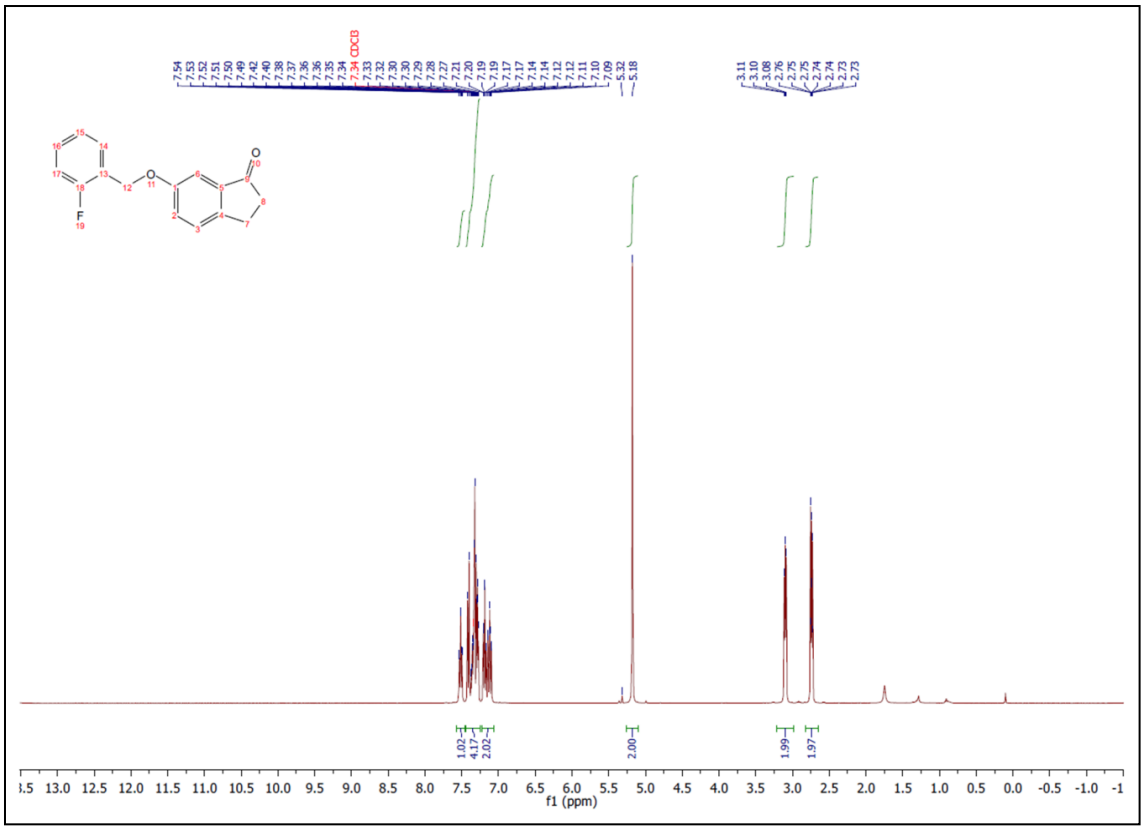

Figure S 12: ^{1}H-NMR of 6-((2-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**7**).

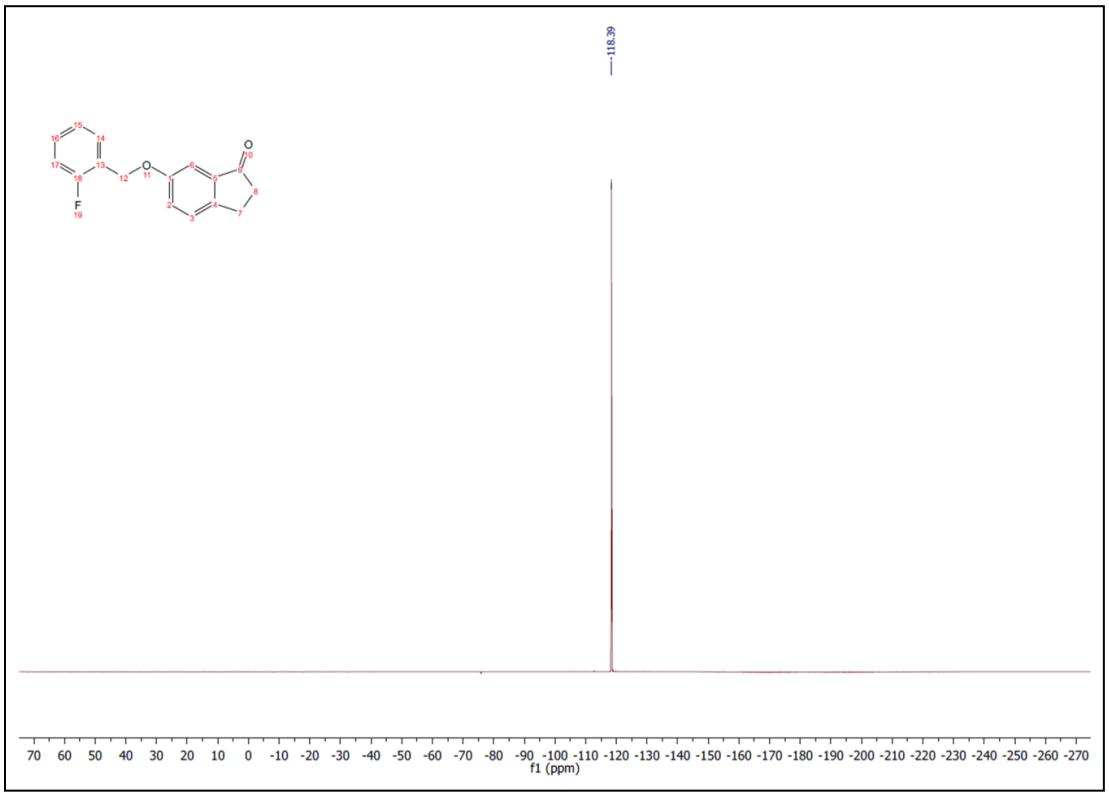

Figure S 13: ^{19}F-NMR of 6-((2-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**7**).

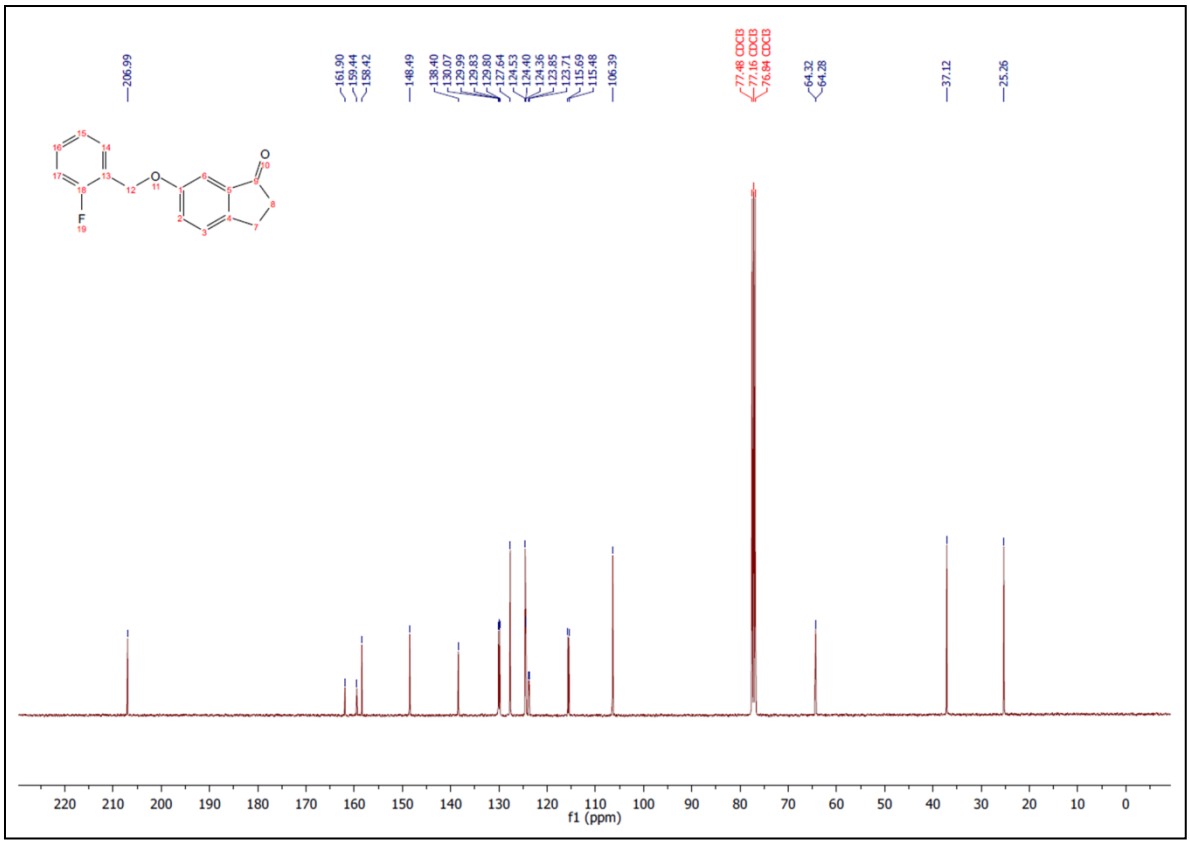

Figure S 34: ^{13}C-NMR of 6-((2-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**7**).

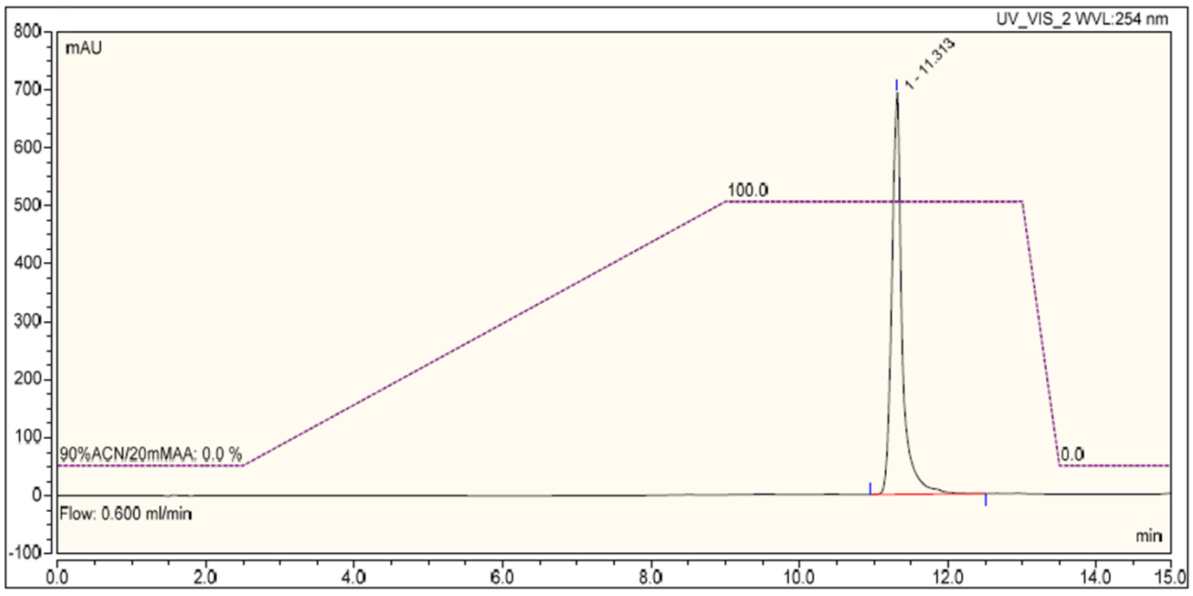

Figure S 45: LC-MS chromatogram of 6-((2-fluorobenzyl)oxy)-2,3-dihydro-1*H*-inden-1-one (**7**).

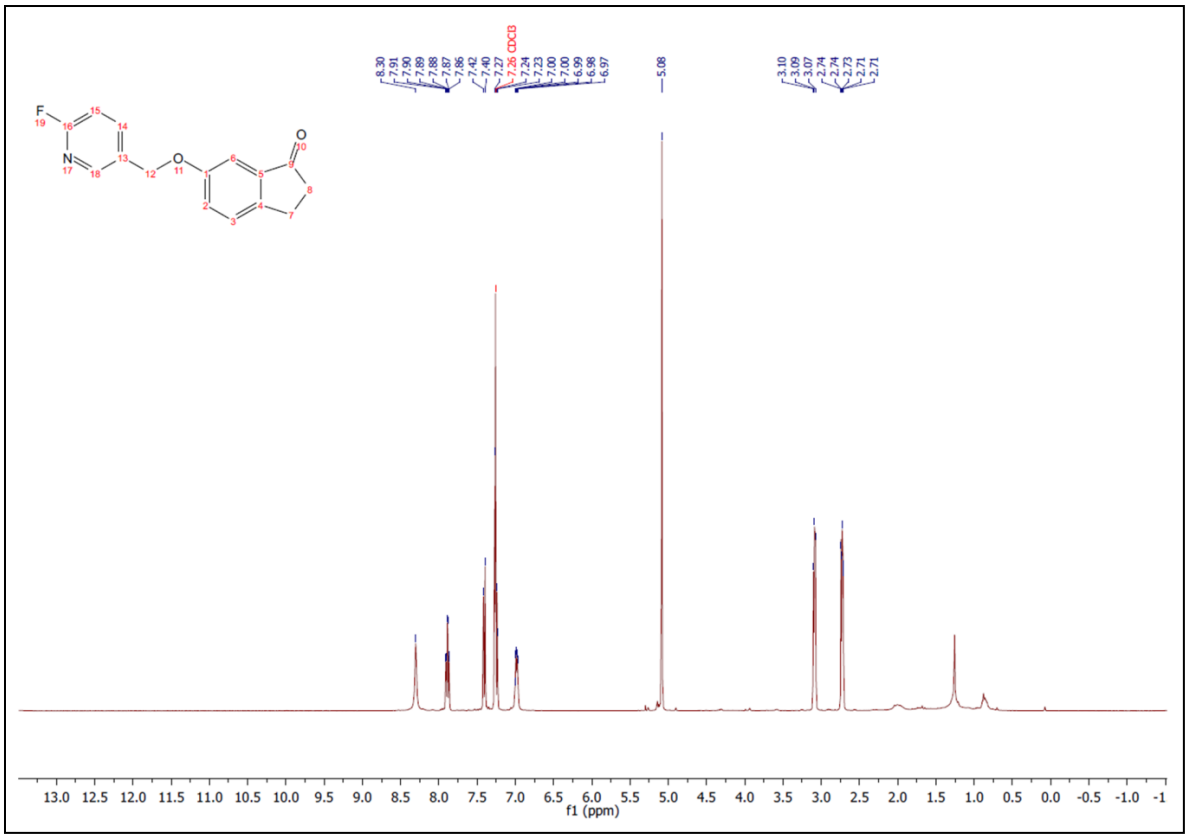

Figure S 16: ^{1}H-NMR of 6-((6-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**8**).

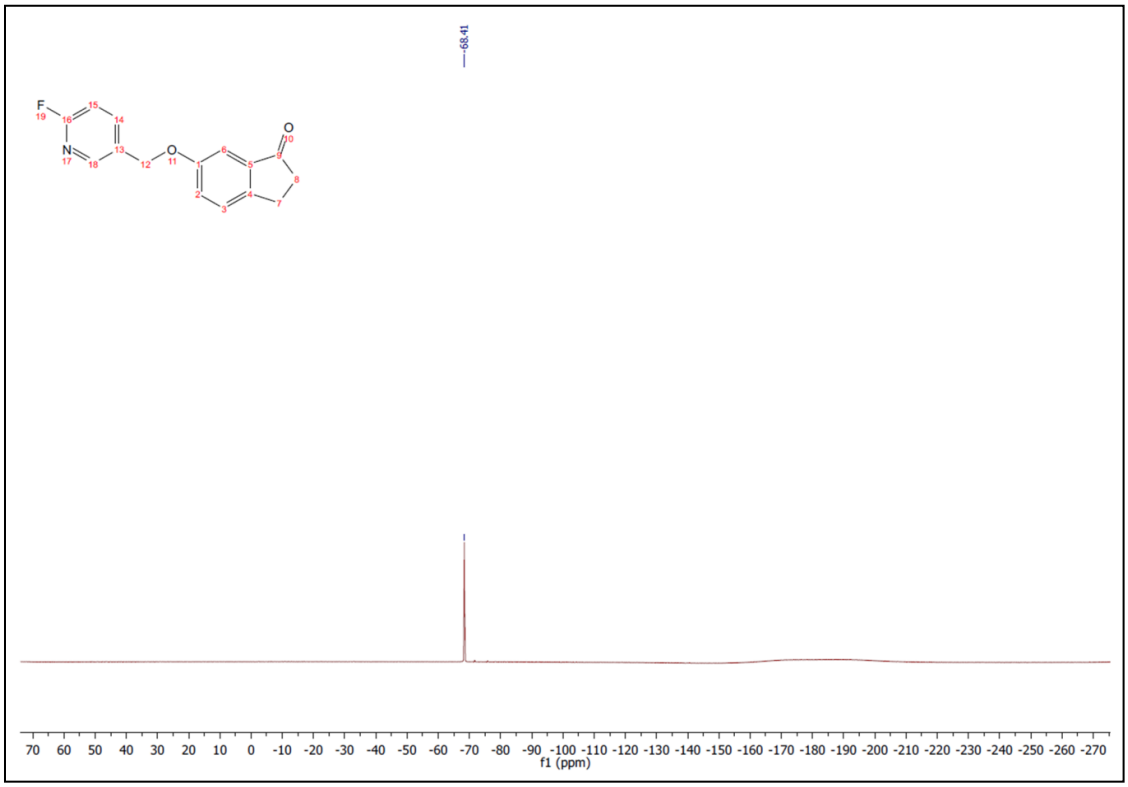

Figure S 57: ^{19}F-NMR of 6-((6-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**8**).

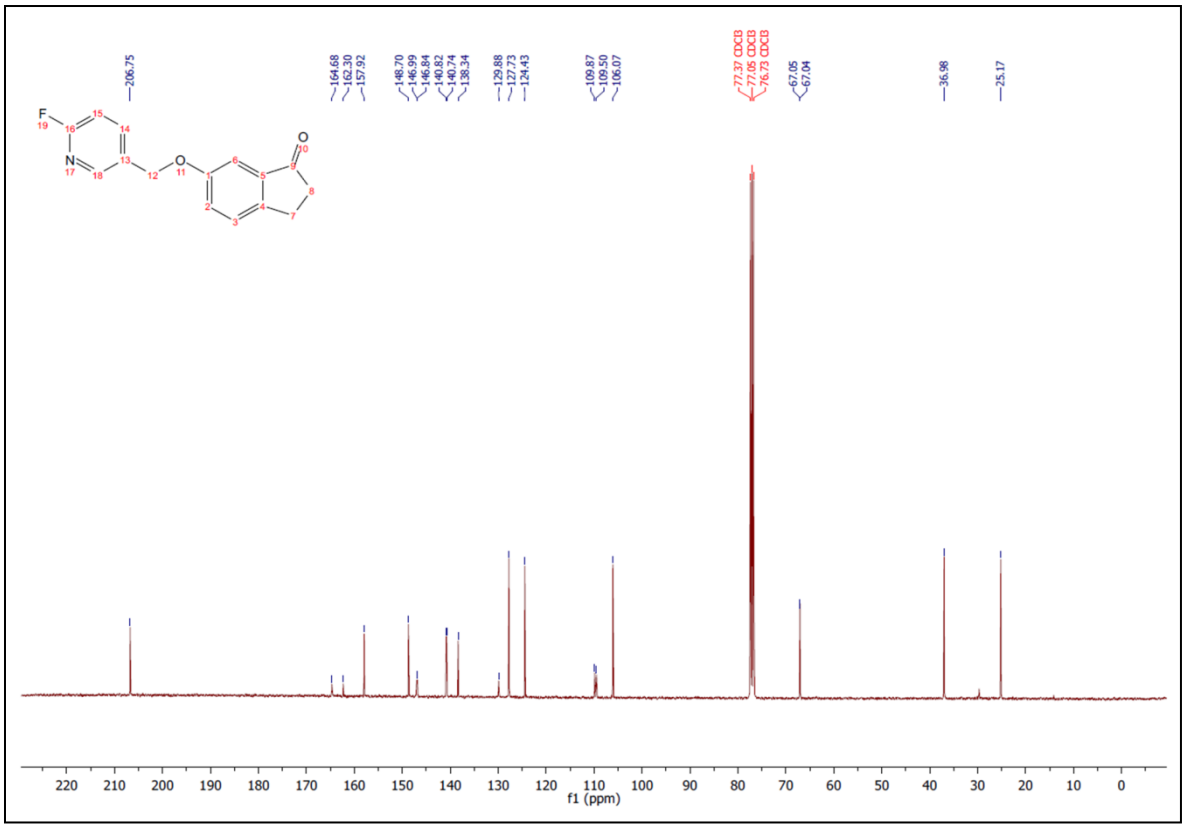

Figure S 68: ^{13}C-NMR of 6-((6-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**8**).

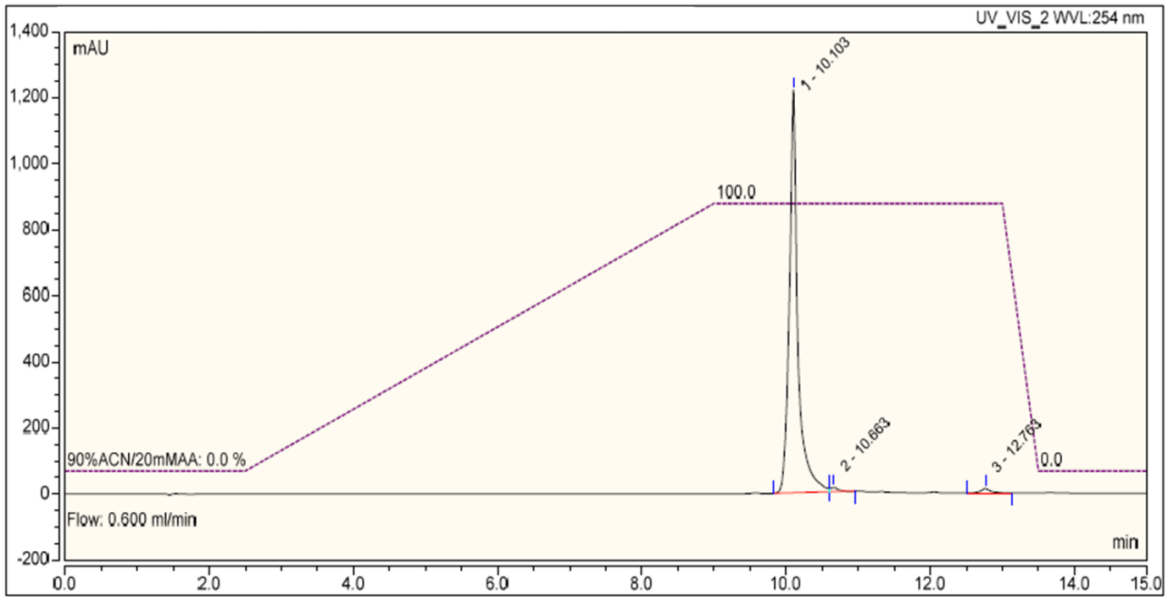

Figure S 19: LC-MS chromatogram of 6-((6-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**8**).

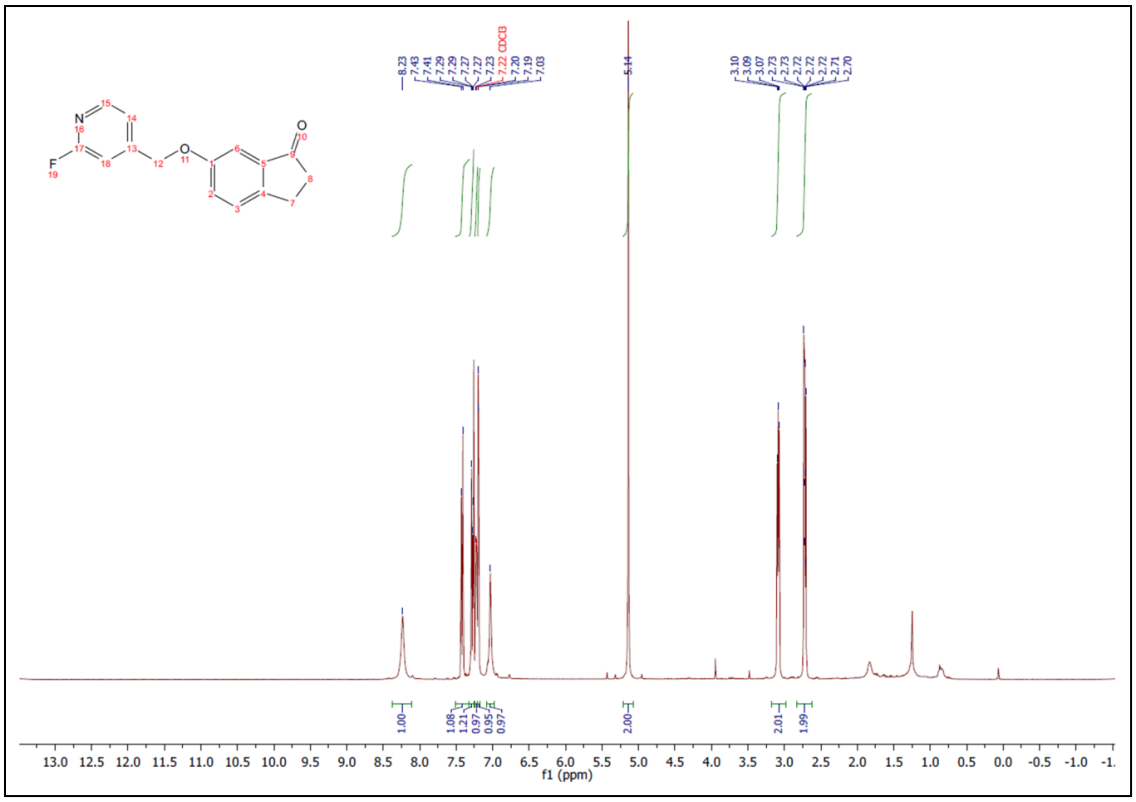

Figure S 7: ^{1}H-NMR of 6-((2-fluoropyridin-4-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**9**).

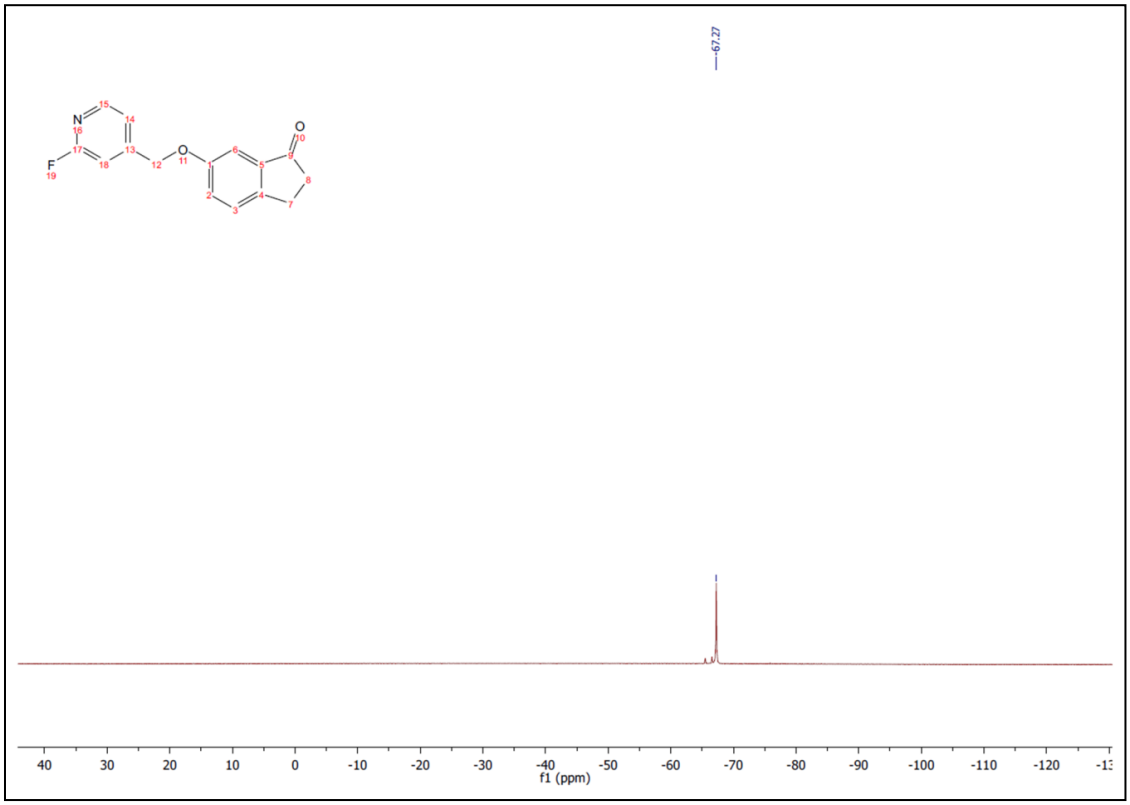

Figure S 81: ^{19}F-NMR of 6-((2-fluoropyridin-4-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**9**).

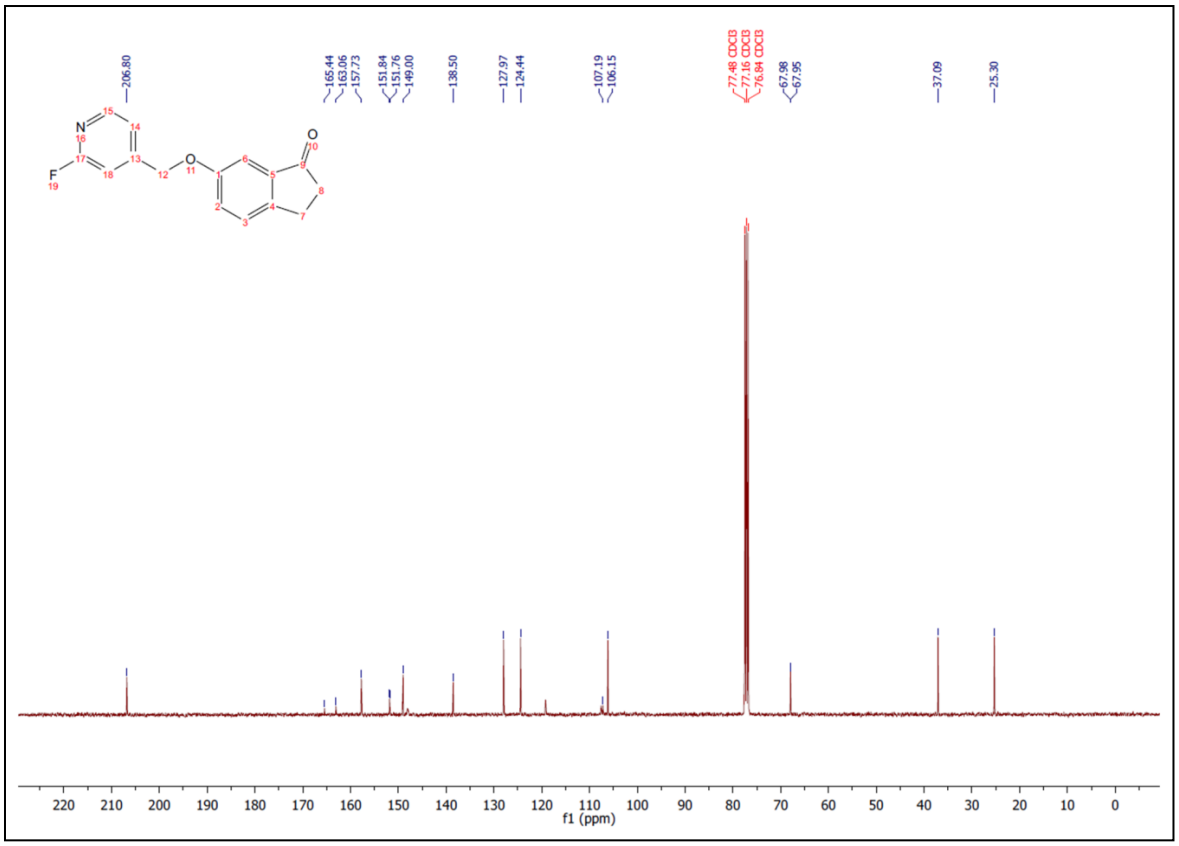

Figure S 92: ^{13}C-NMR of 6-((2-fluoropyridin-4-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**9**).

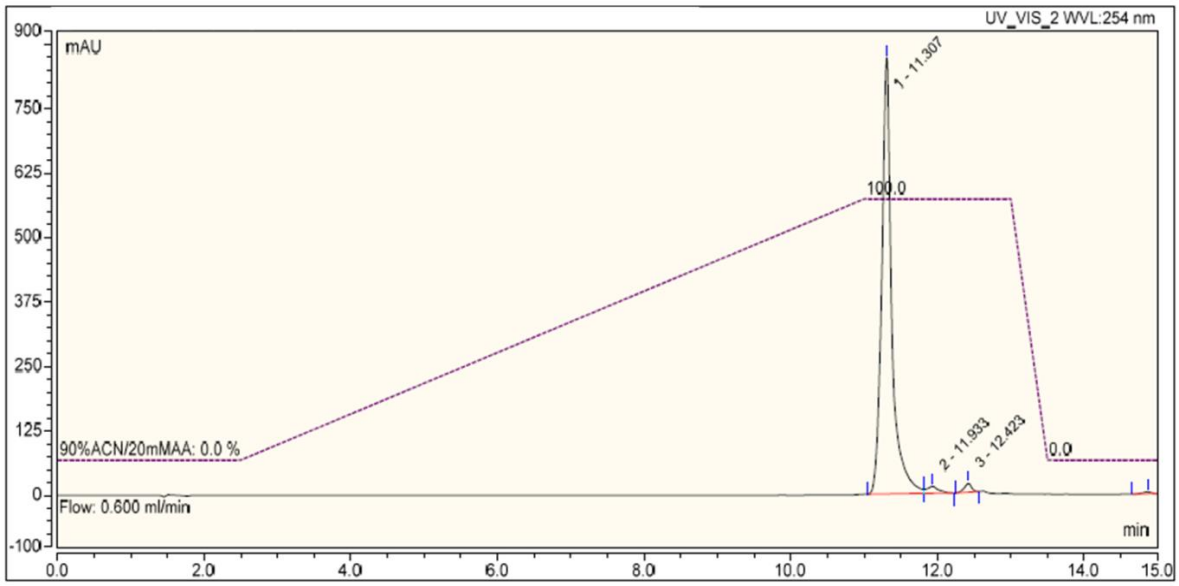

Figure S 103: LC-MS chromatogram of 6-((2-fluoropyridin-4-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**9**).

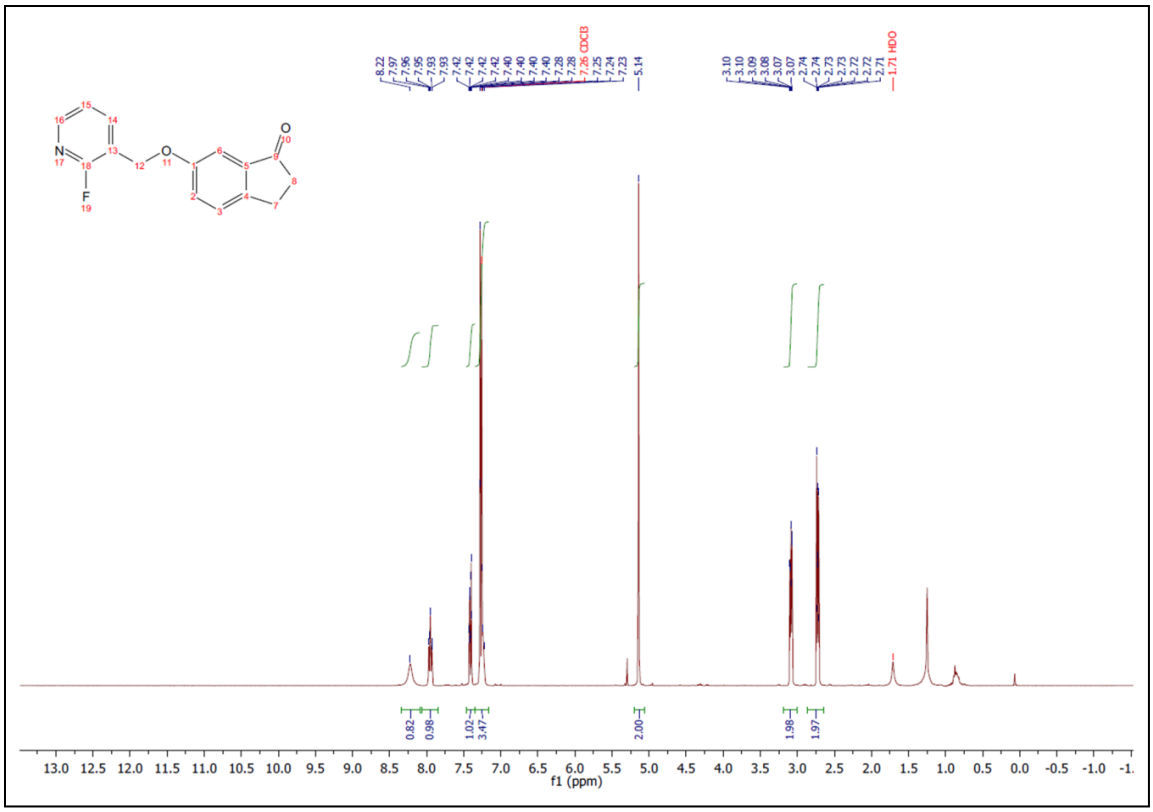

Figure S 114: ^{1}H-NMR of 6-((2-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**10**).

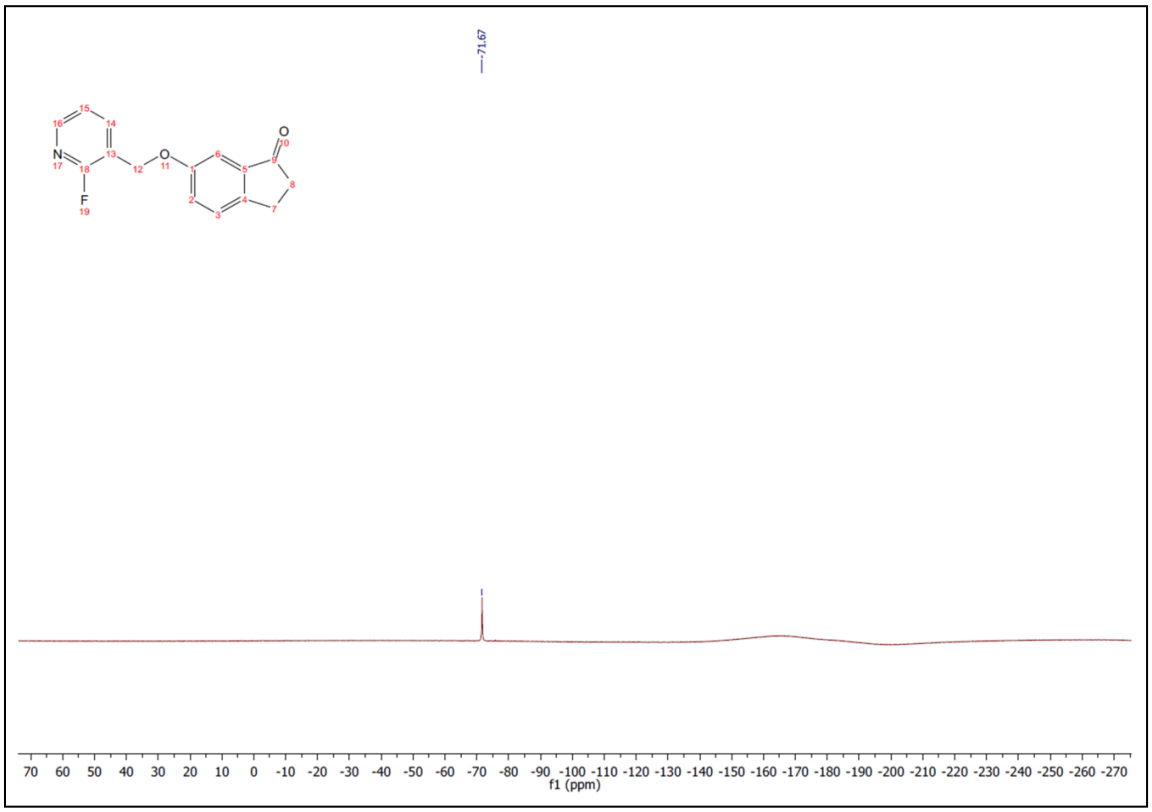

Figure S 125: ^{19}F-NMR of 6-((2-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**10**).

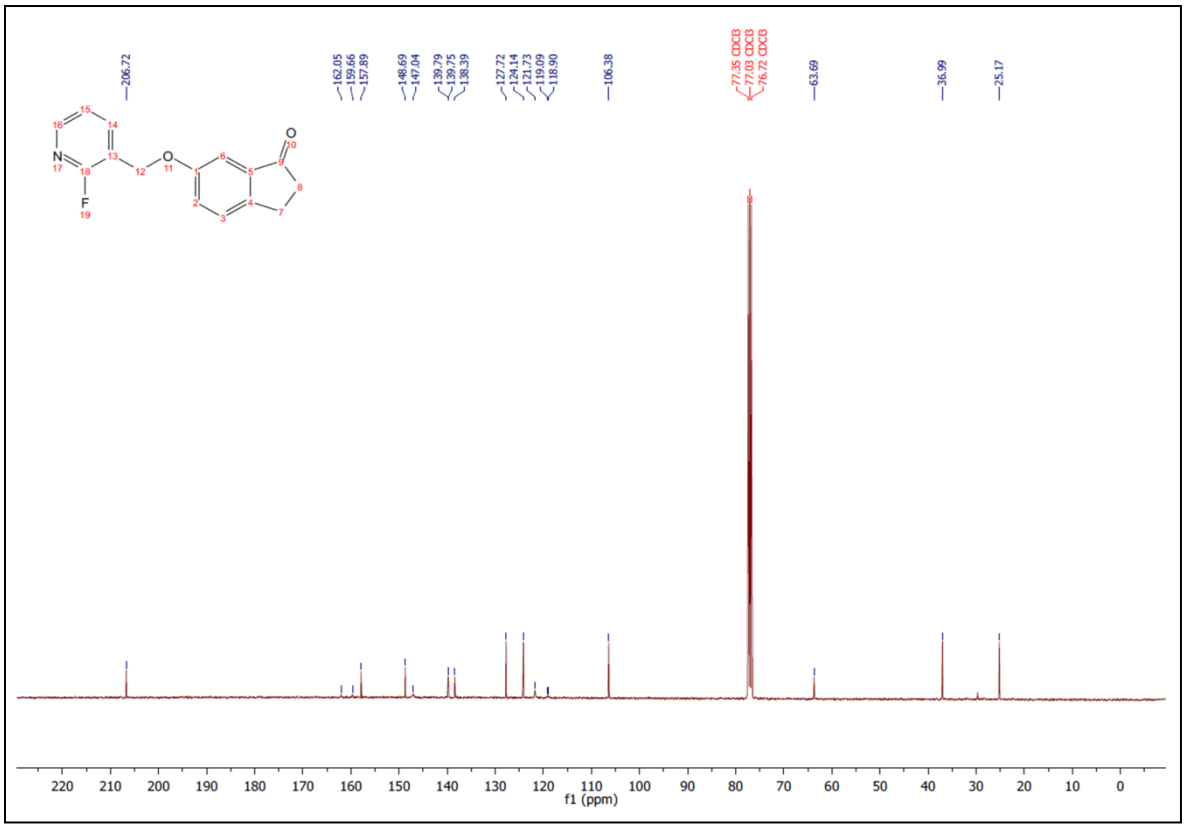

Figure S 136: ^{13}C-NMR of 6-((2-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**10**).

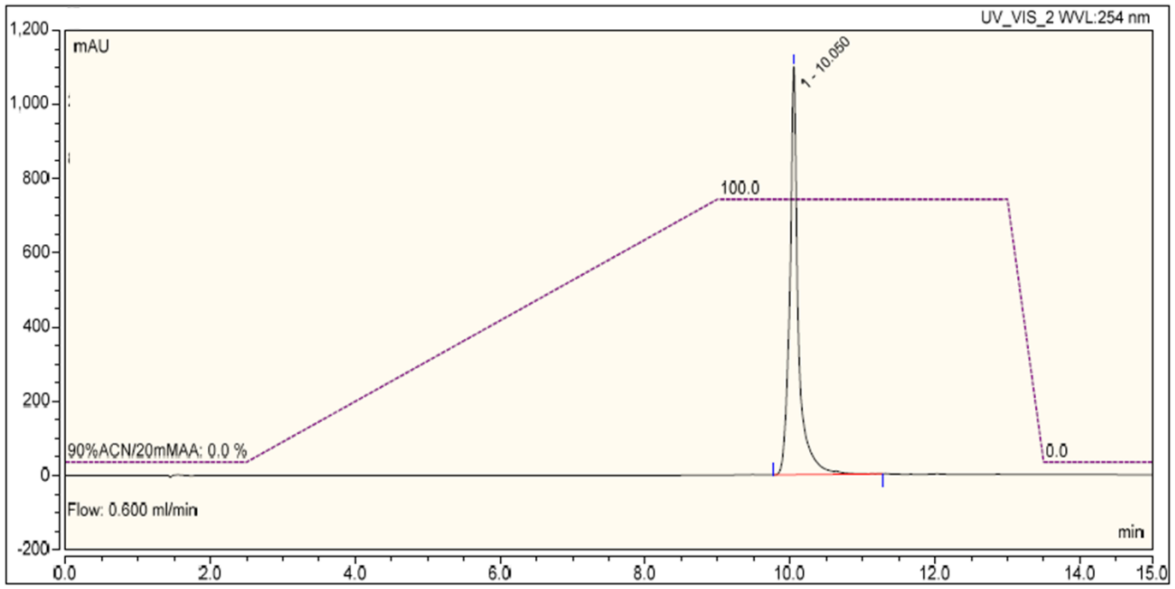

Figure S 147: LC-MS chromatogram of 6-((2-fluoropyridin-3-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**10**).

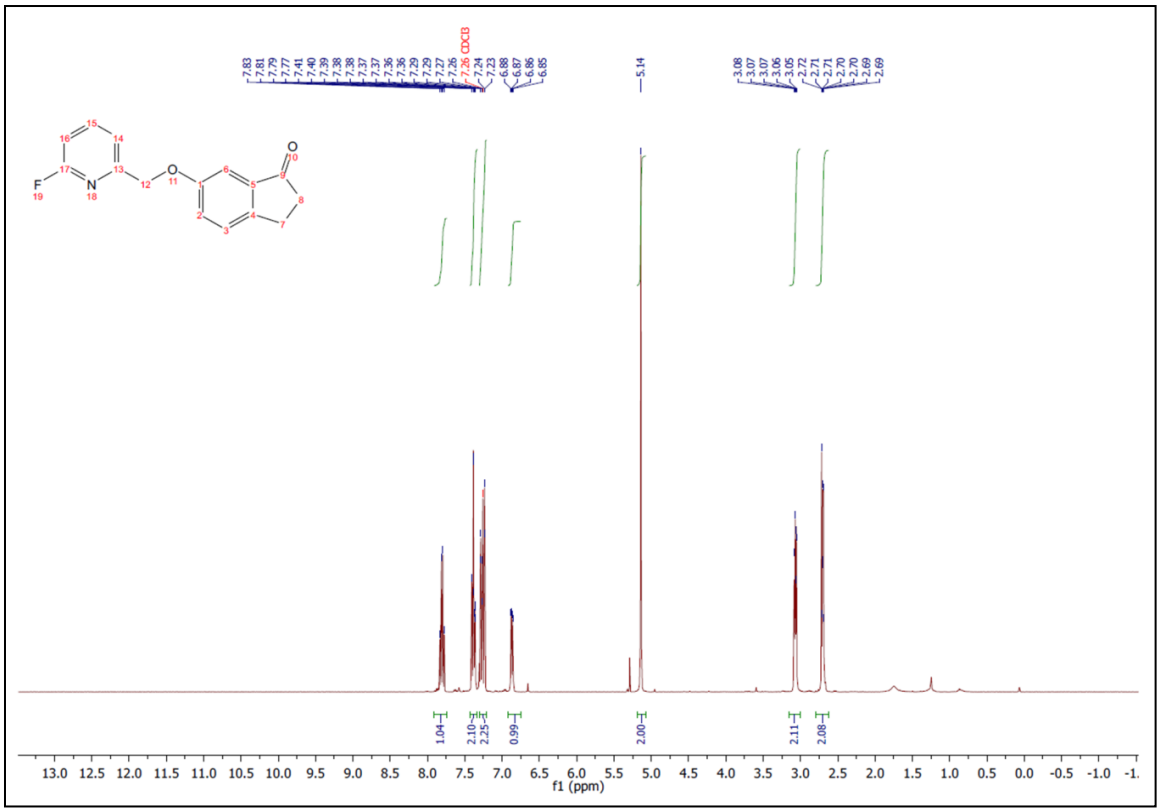

Figure S 158: ^{1}H-NMR of 6-((6-fluoropyridin-2-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**11**).

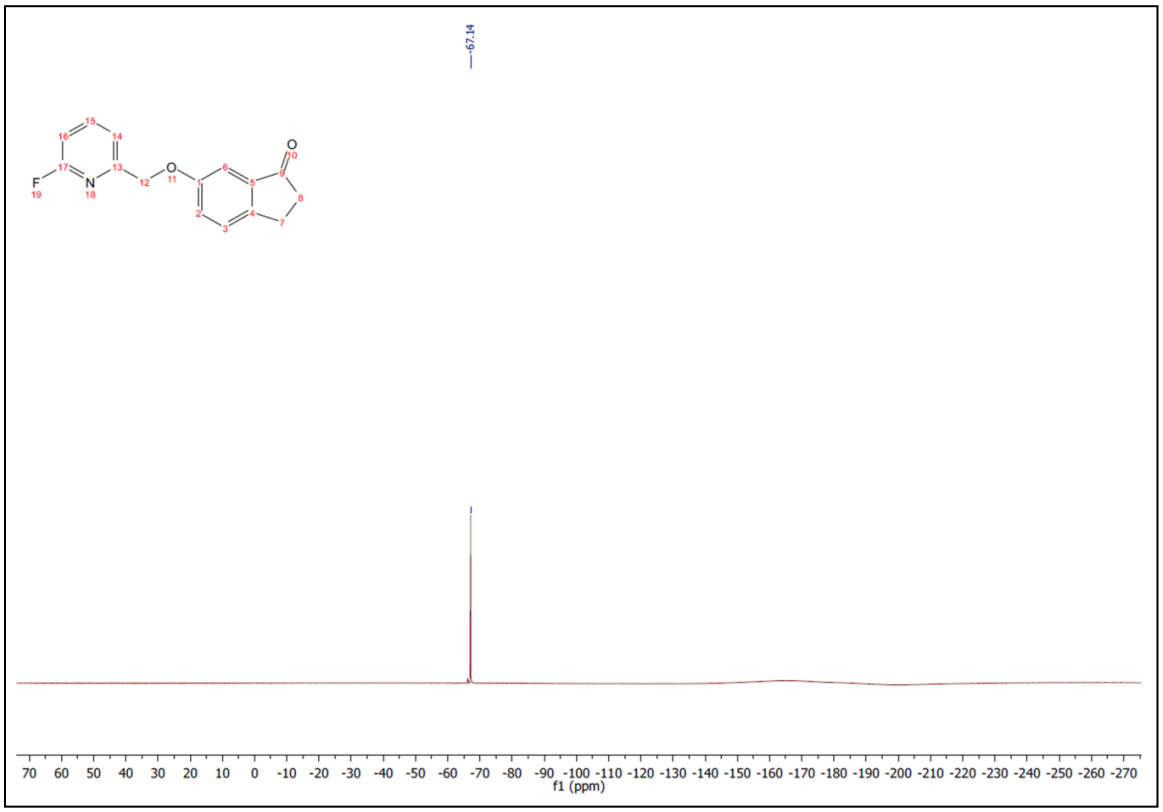

Figure S 169: ^{19}F-NMR of 6-((6-fluoropyridin-2-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**11**).

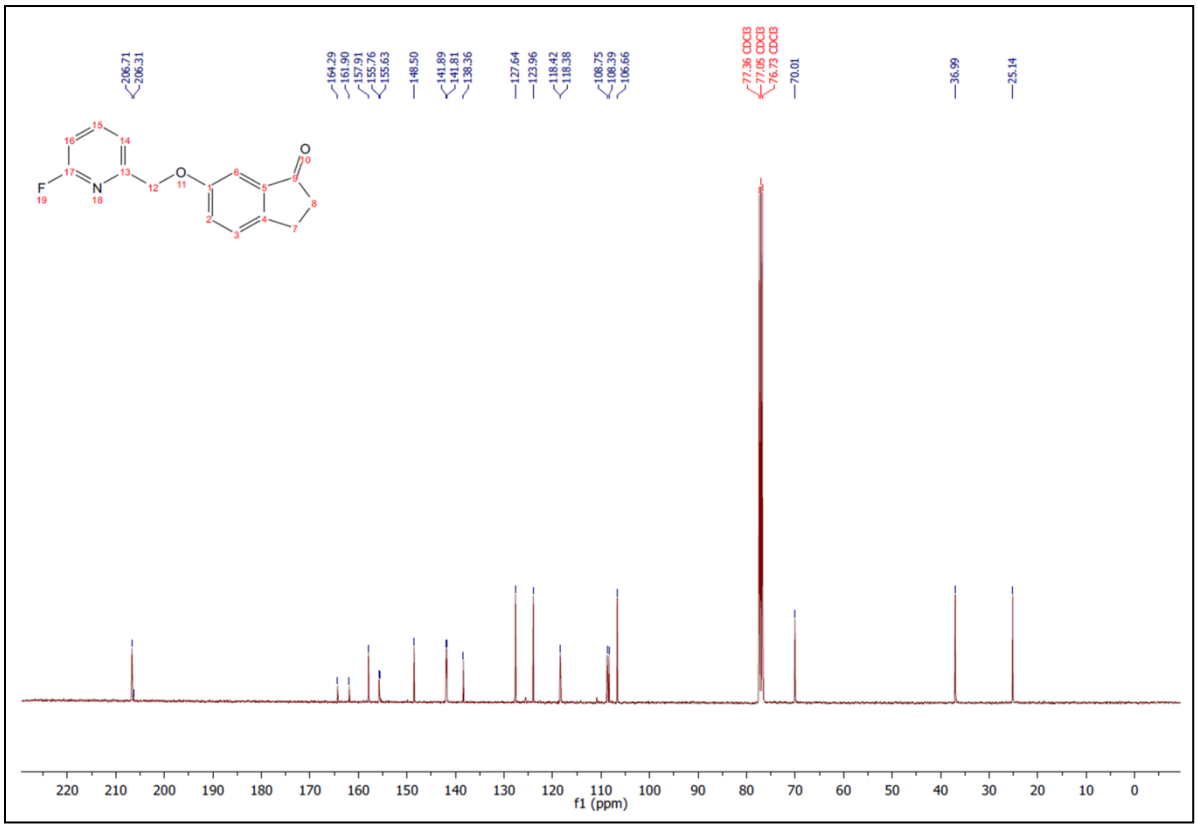

Figure S 17: ^{13}C-NMR of 6-((6-fluoropyridin-2-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**11**).

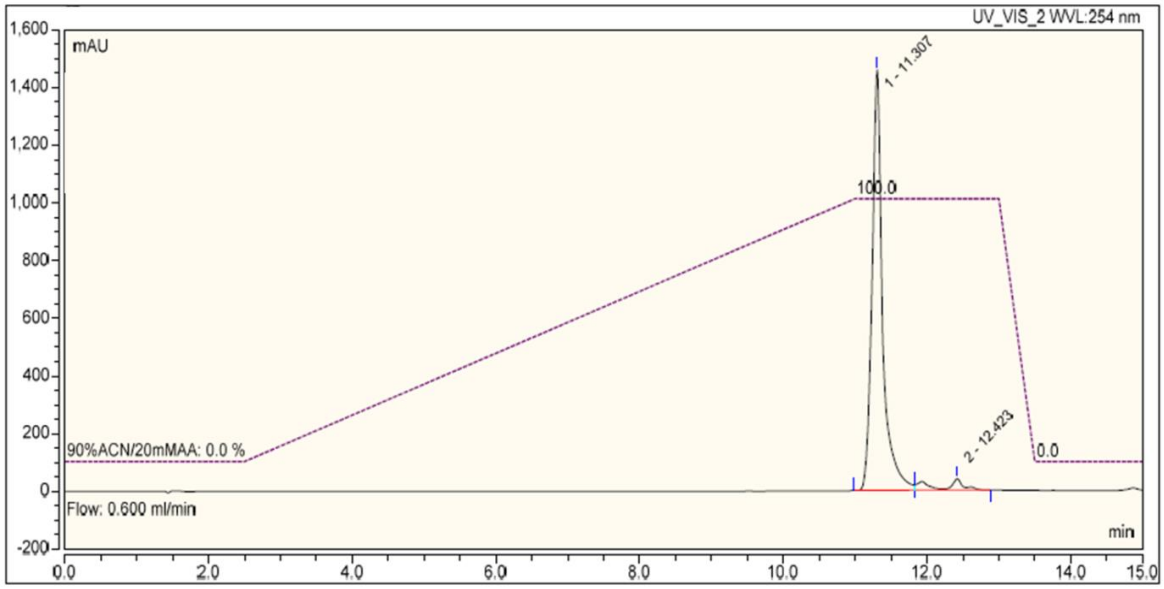

Figure S 181: LC-MS chromatogram of 6-((6-fluoropyridin-2-yl)methoxy)-2,3-dihydro-1*H*-inden-1-one (**11**).

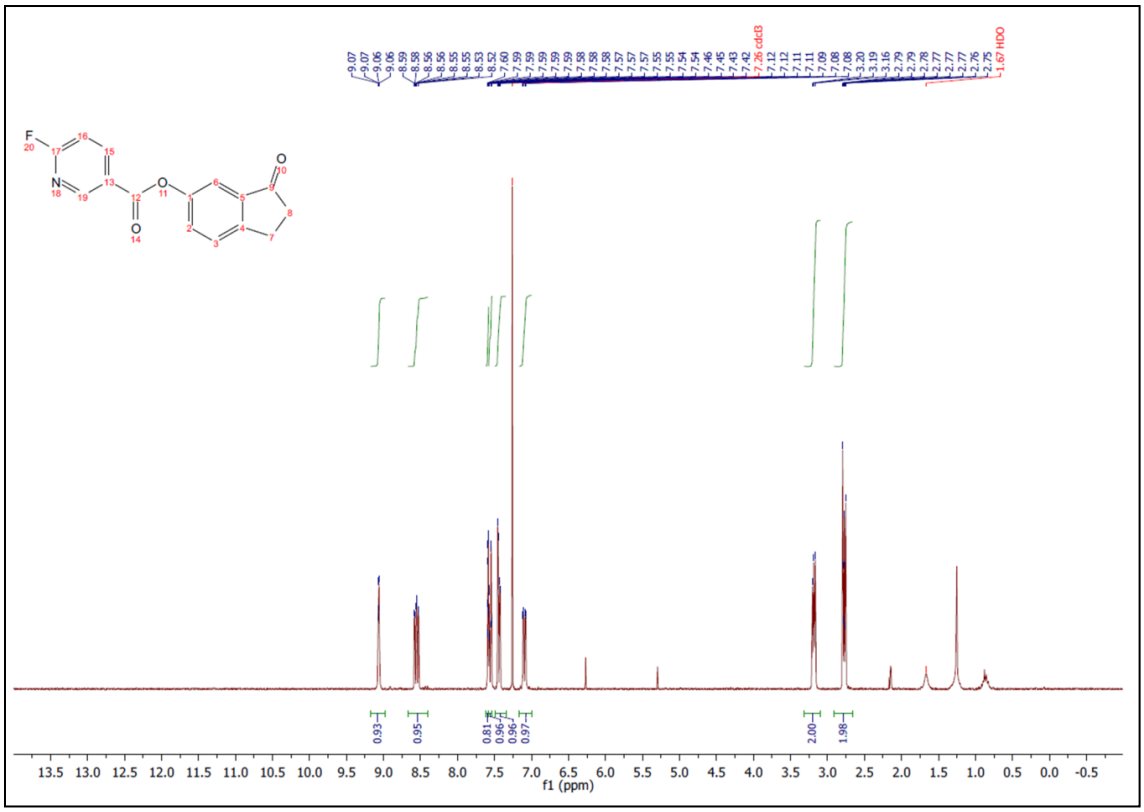

Figure S 192: ^{1}H-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoronicotinate (**12**).

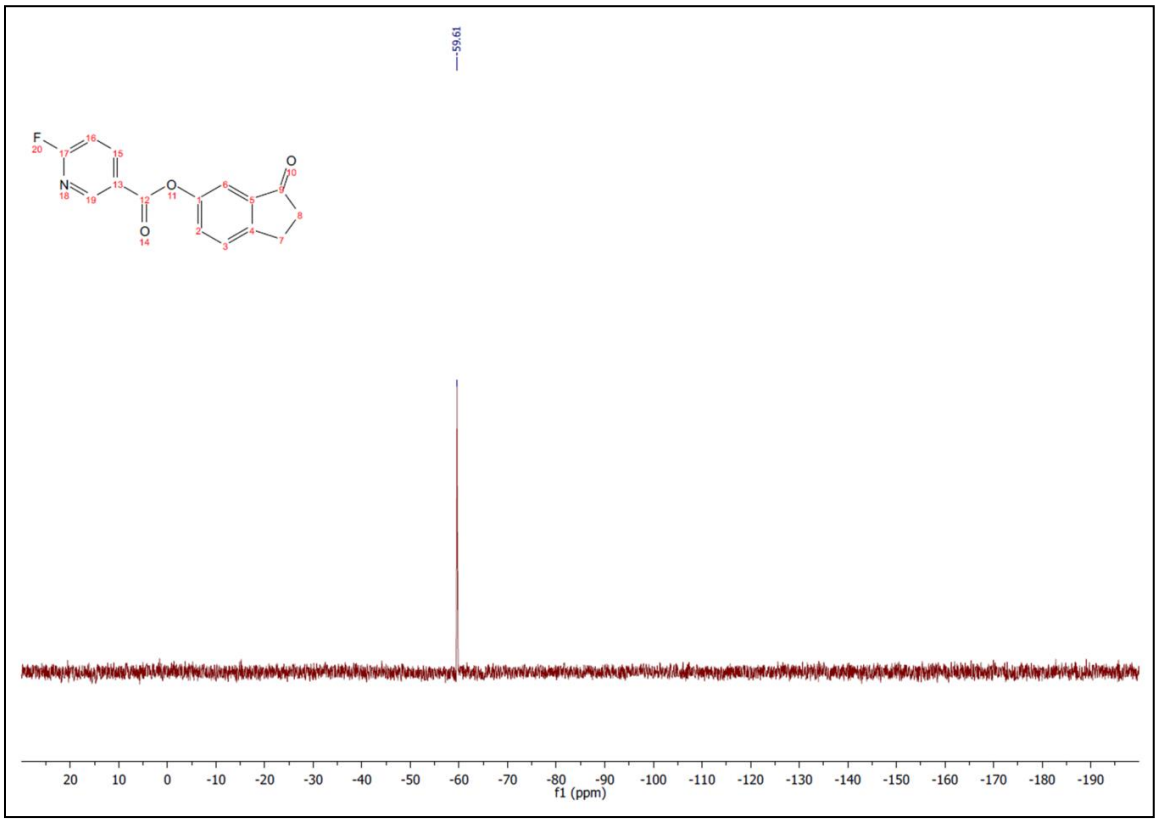

Figure S 203: ^{19}F-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoronicotinate (**12**).

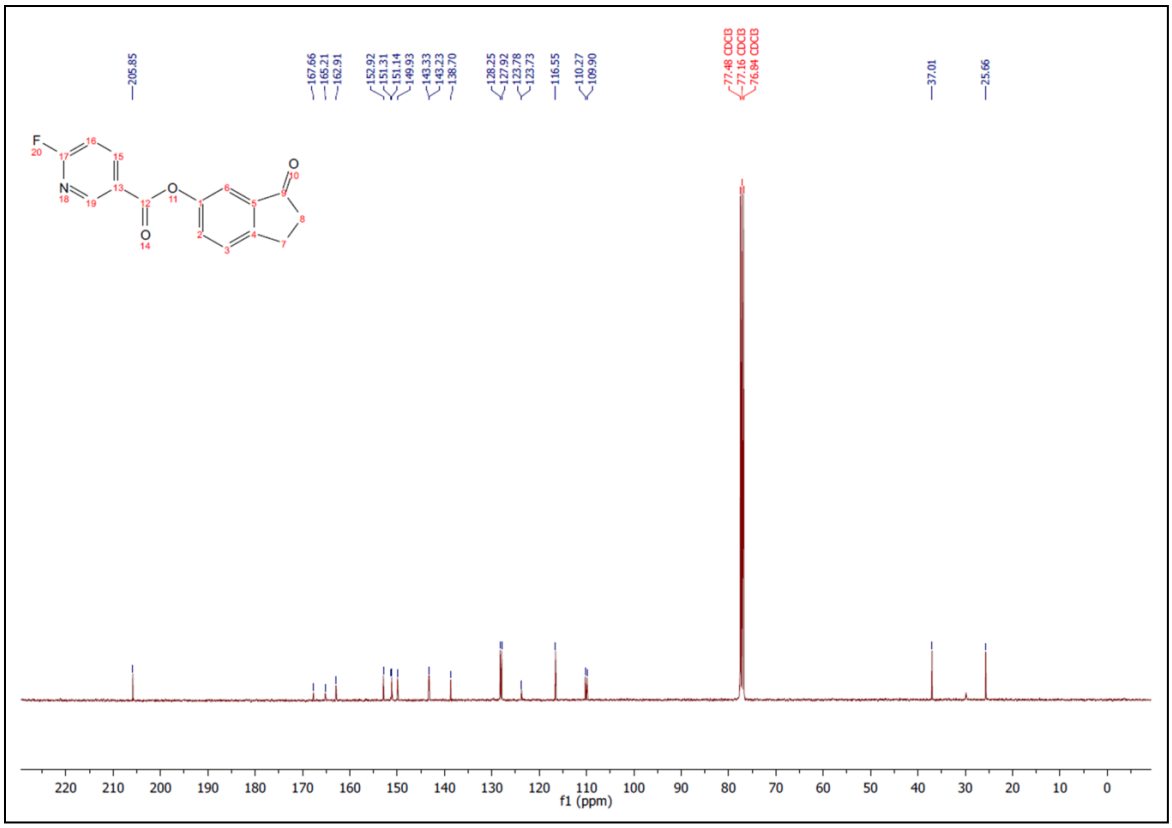

Figure S 214: ^{13}C-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoronicotinate (**12**).

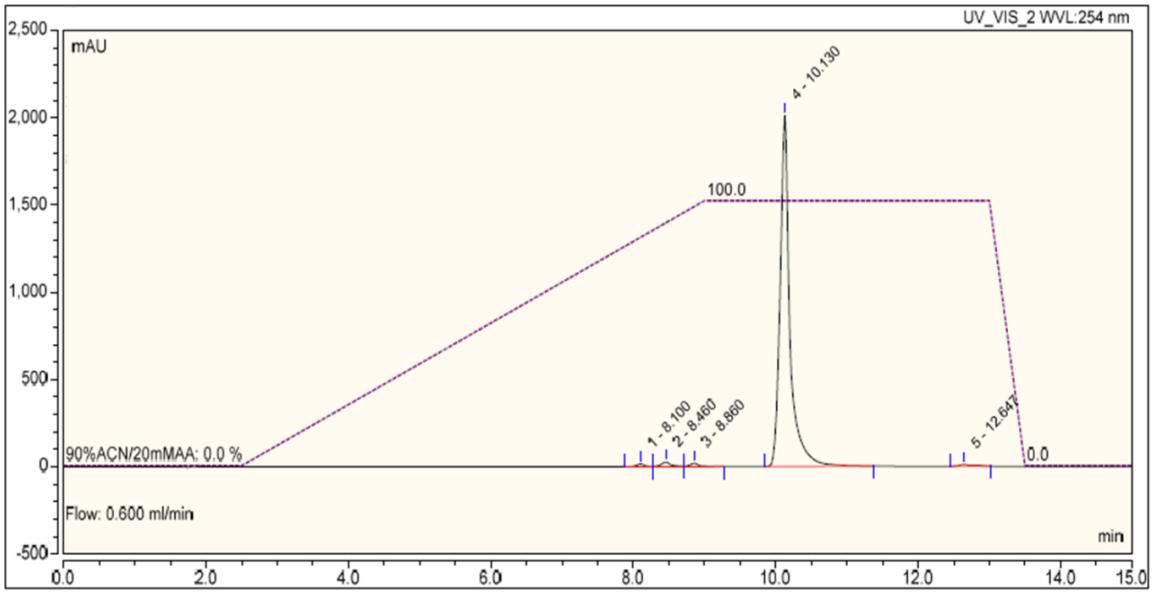

Figure S 225: LC-MS chromatogram of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoronicotinate (**12**).

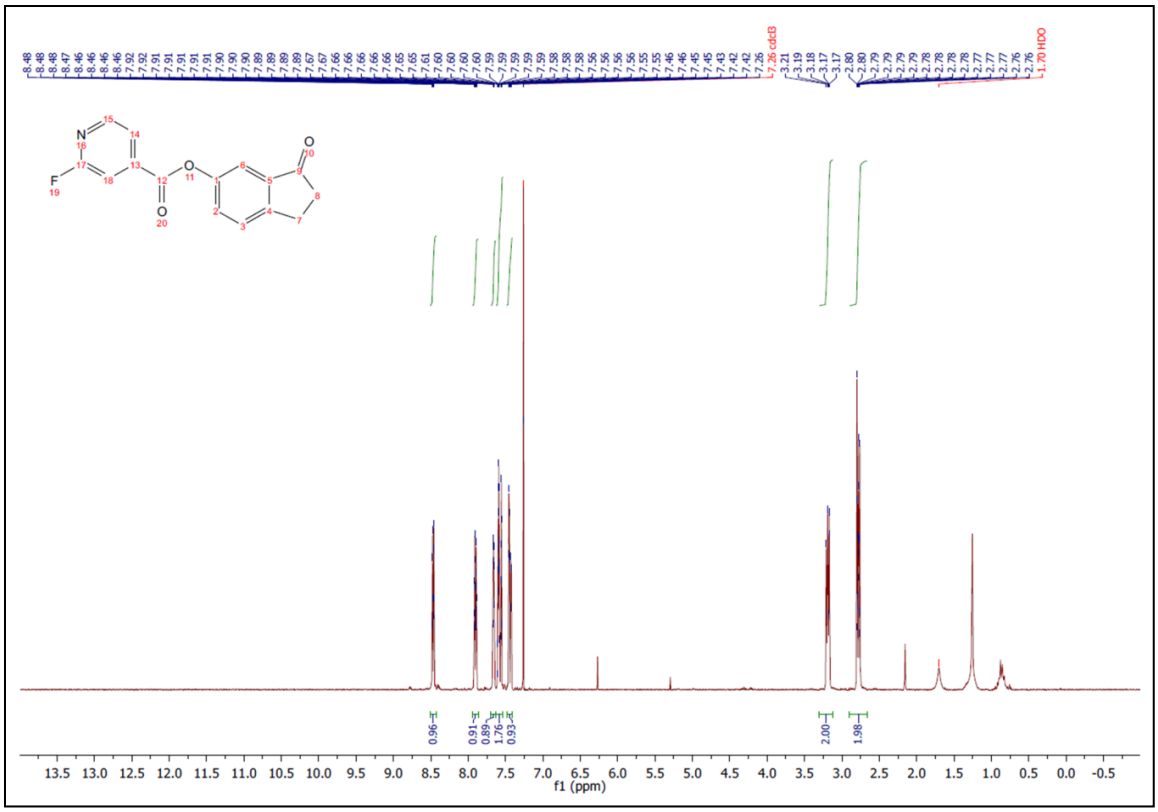

Figure S 236: ^{1}H-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoroisonicotinate (**13**).

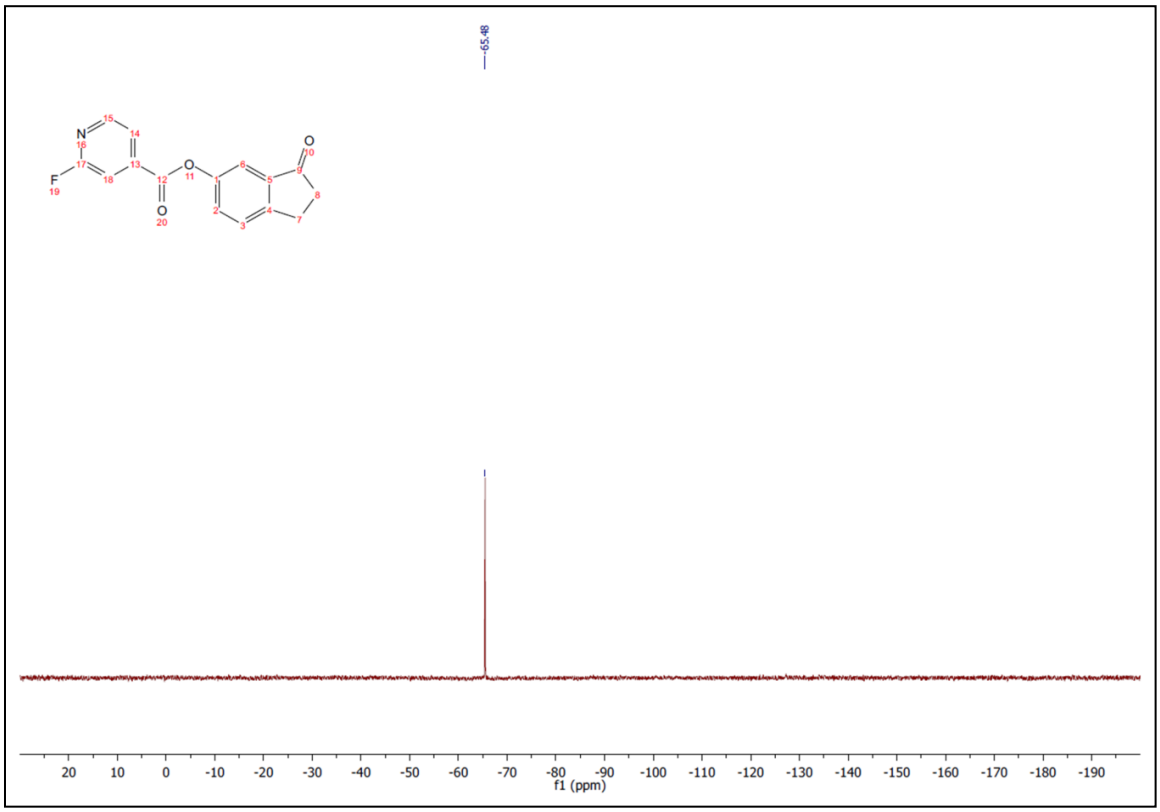

Figure S 247: ^{19}F-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoroisonicotinate (**13**).

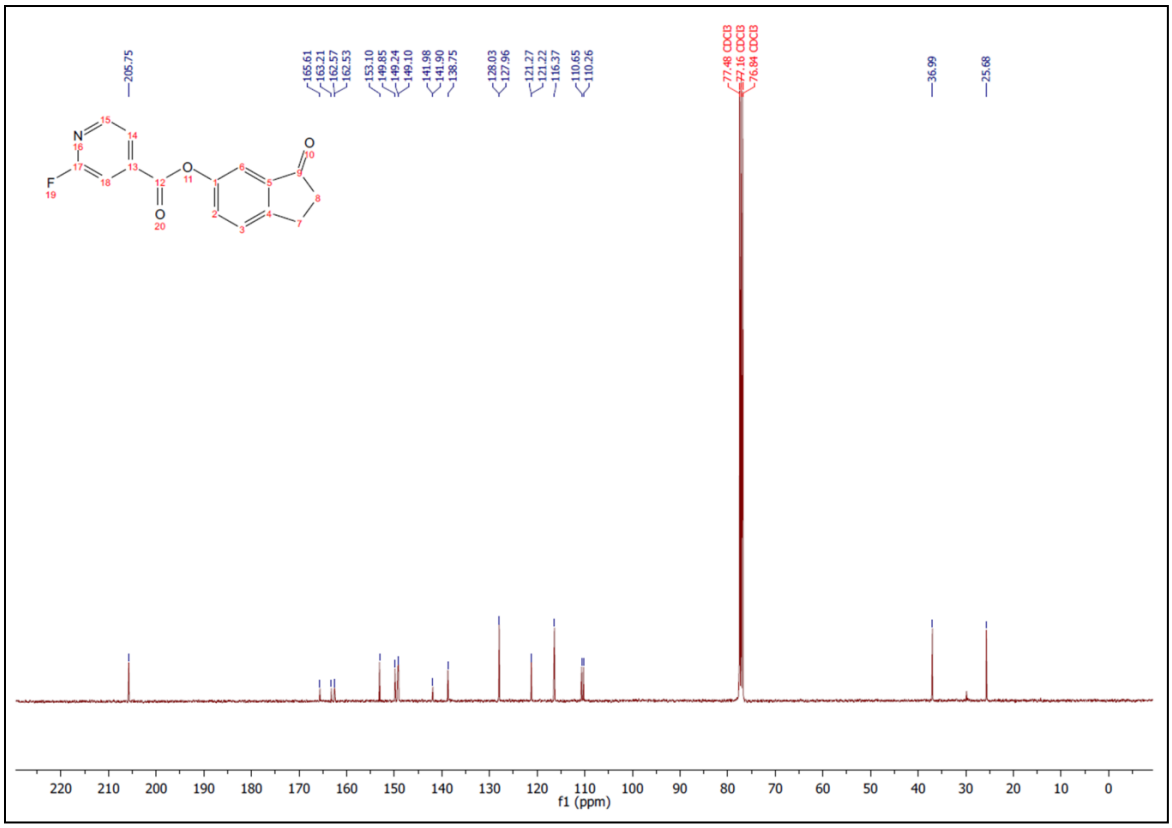

Figure S 25: ^{13}C-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoroisonicotinate (**13**).

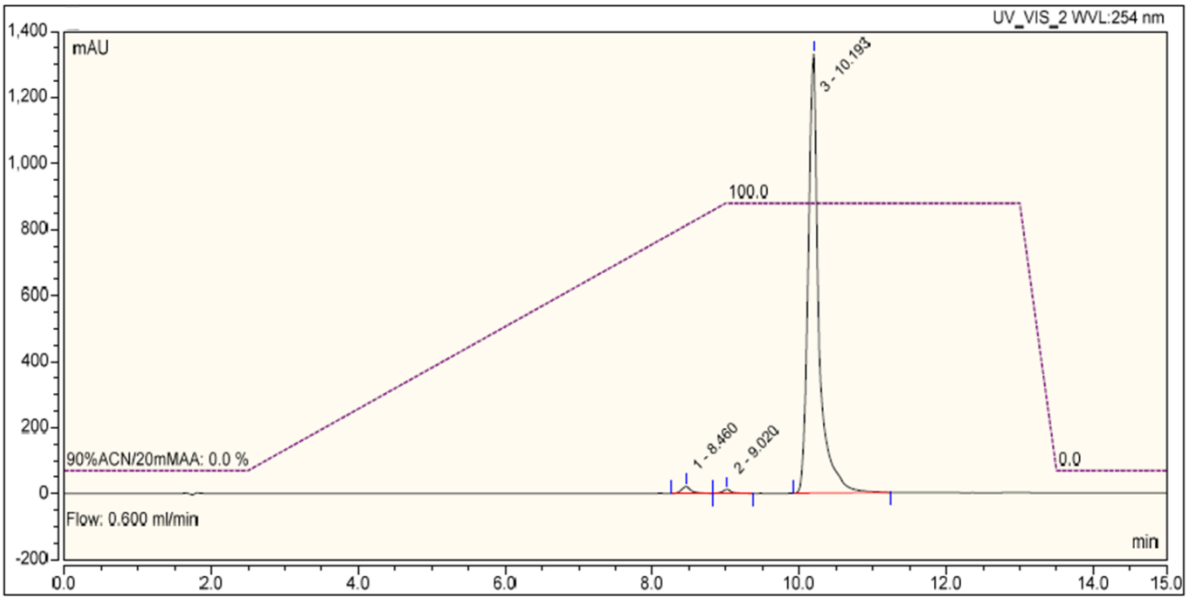

Figure S 269: LC-MS chromatogram of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoroisonicotinate (**13**).

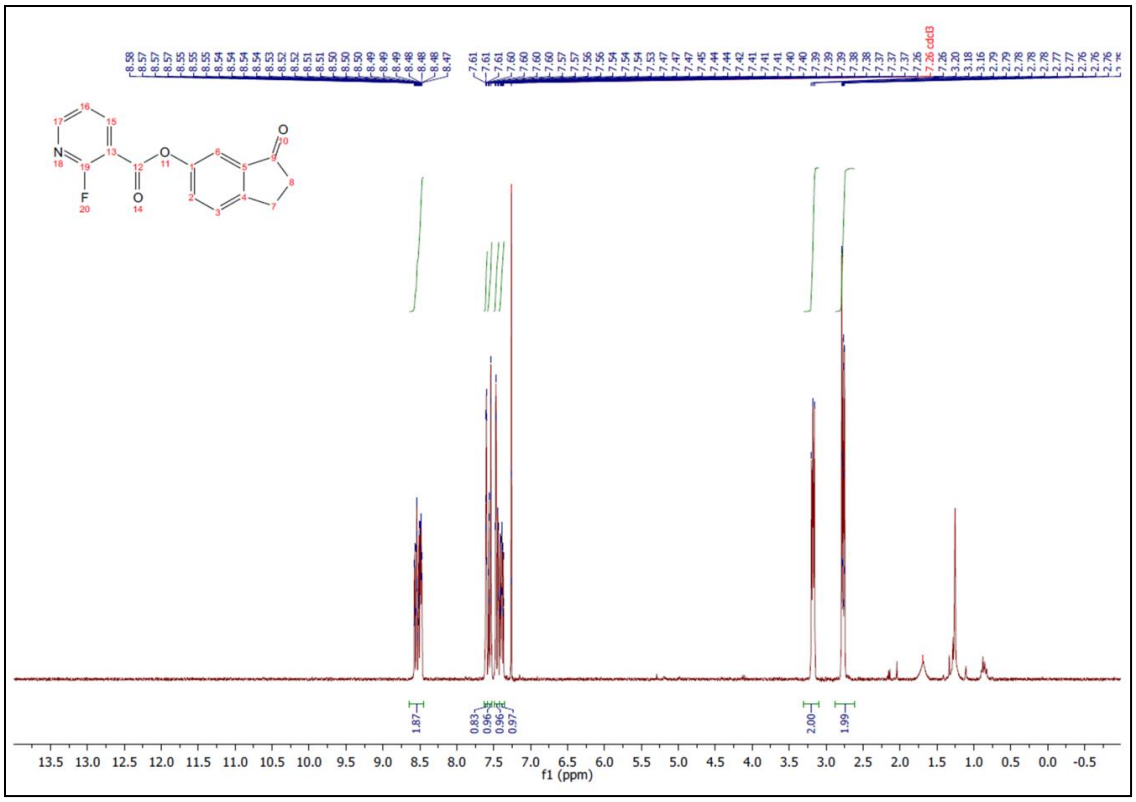

Figure S 27: ^{1}H-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoronicotinate (**14**).

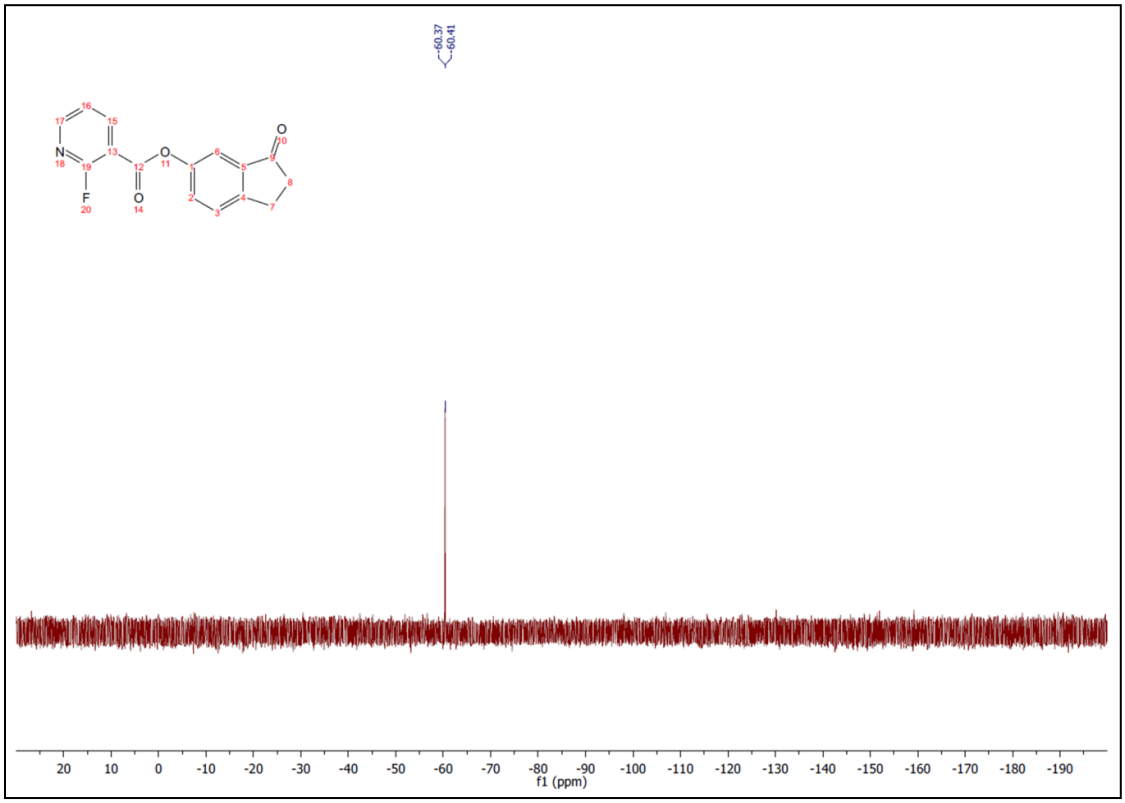

Figure S 281: ^{18}F-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoronicotinate (**14**).

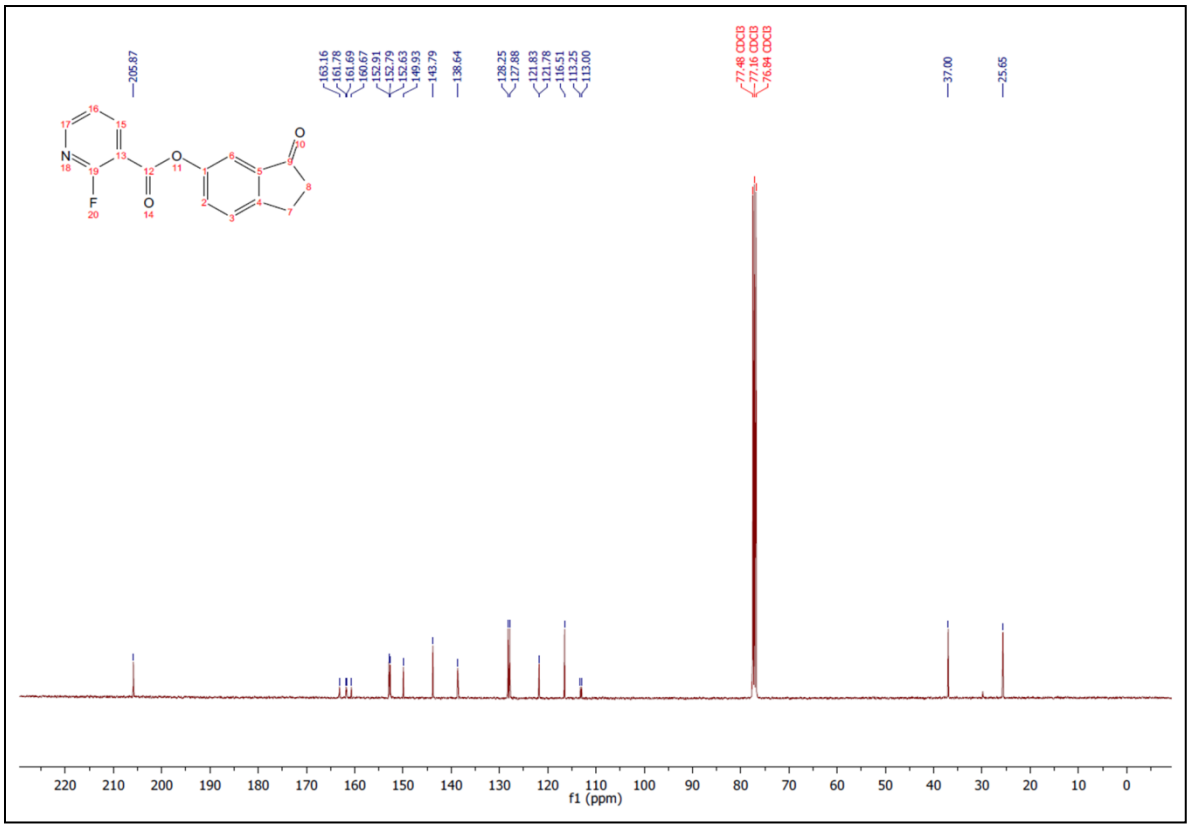

Figure S 292: ^{13}C-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoronicotinate (**14**).

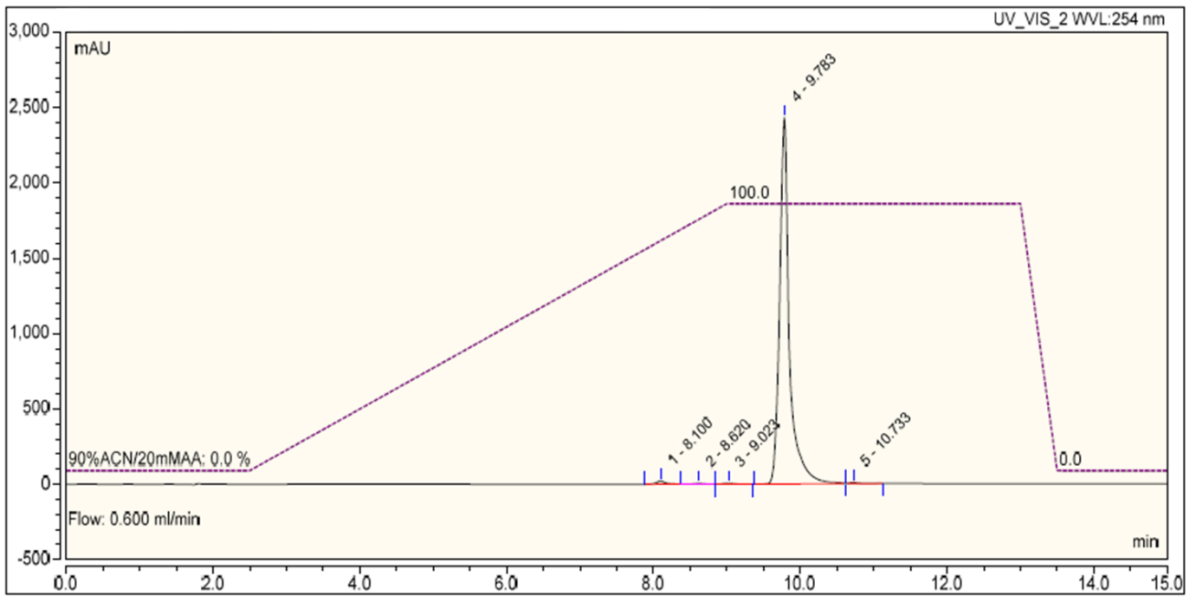

Figure S 303: LC-MS chromatogram of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 2-fluoronicotinate (**14**).

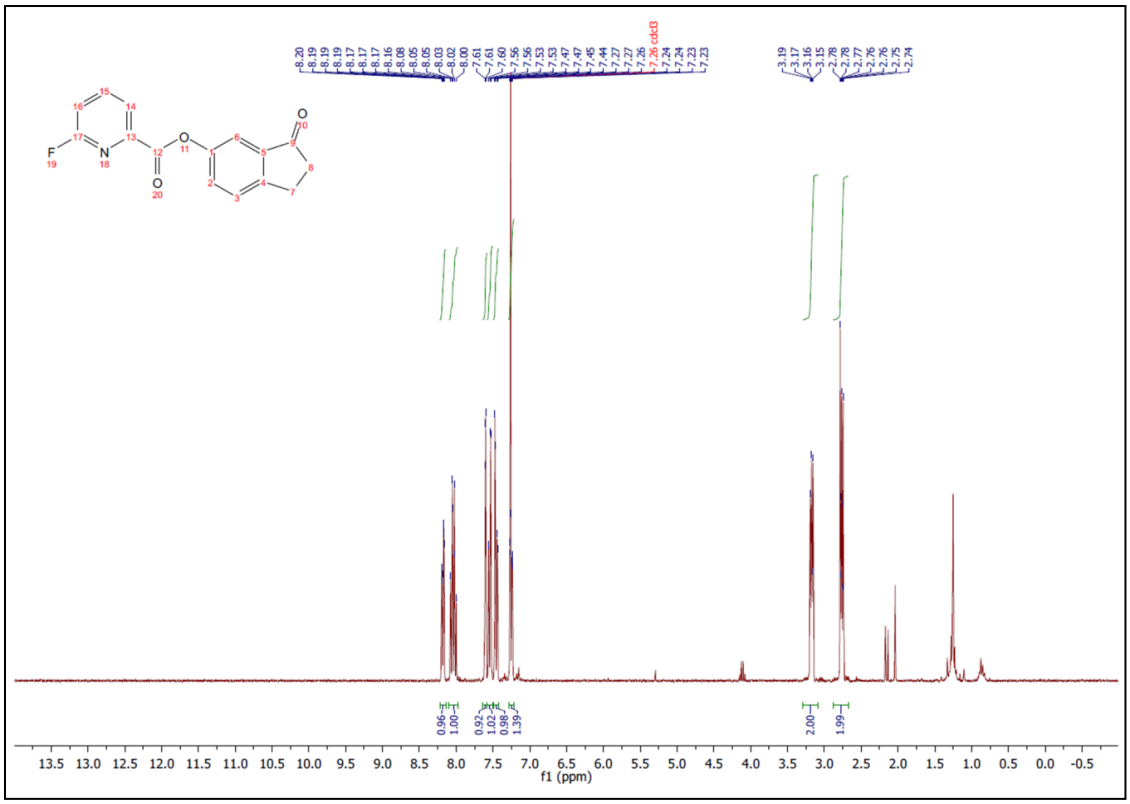

Figure S 314: ^{1}H-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoropicolinate (**15**).

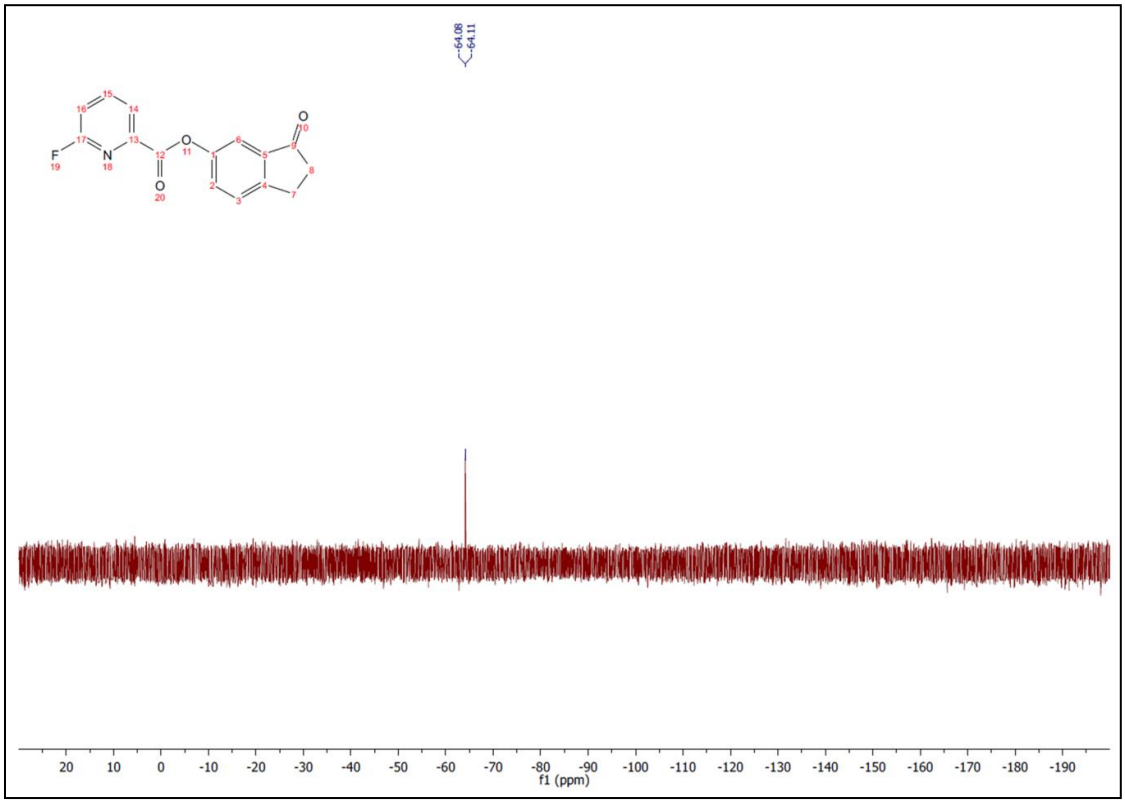

Figure S 325: ^{19}F-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoropicolinate (**15**).

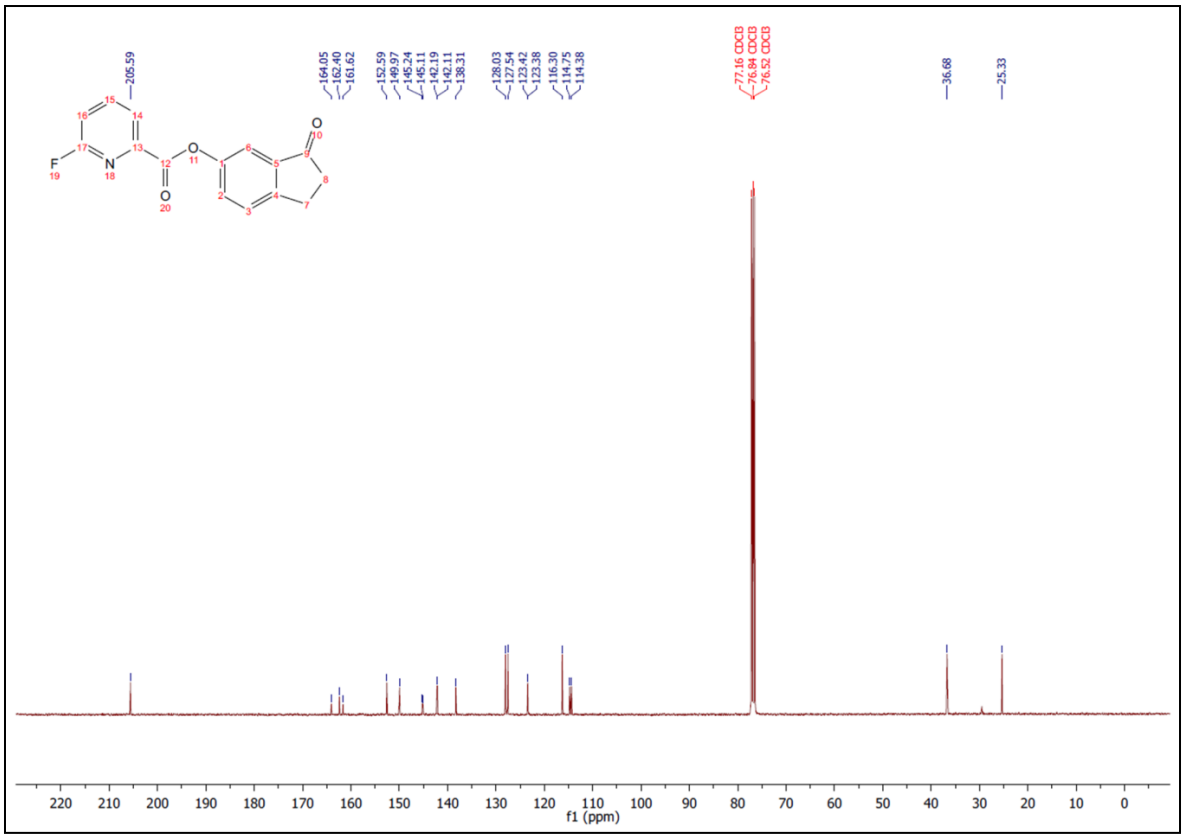

Figure S 336: ^{13}C-NMR of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoropicolinate (**15**).

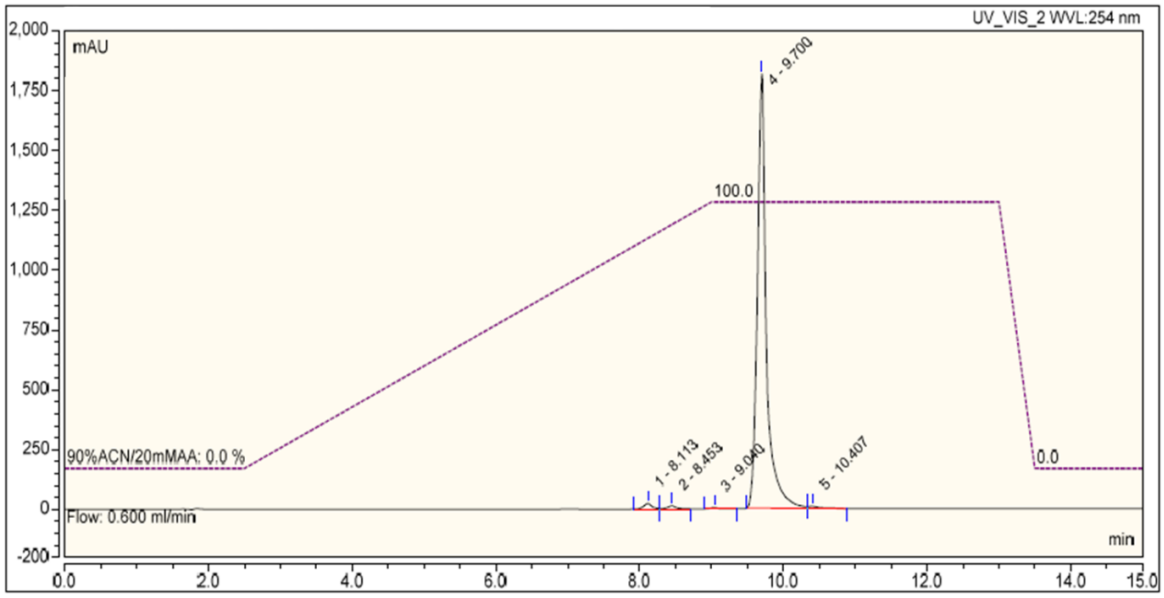

Figure S 347: LC-MS chromatogram of 3-oxo-2,3-dihydro-1*H*-inden-5-yl 6-fluoropicolinate (**15**).

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