Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Evaluating Aryl Esters as Bench-Stable C(1)-Ammonium Enolate Precursors in Catalytic Enantioselective Michael Addition-Lactonisations

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SUPPORTING INFORMATION

General Information

Reactions involving moisture sensitive reagents were carried out in flame-dried glassware under an inert atmosphere (N_2) using standard vacuum line techniques. Anhydrous solvents (Et_2O, CH_2Cl_2 and THF) were obtained after passing through an alumina column (Mbraun SPS-800). Petrol is defined as petroleum ether 40–60 °C. All other solvents and commercial reagents were used as received without further purification unless otherwise stated.

Room temperature (rt) refers to 20–25 °C. Temperatures of 0 °C and –78 °C were obtained using ice/water and CO_2(s)/acetone baths, respectively. Temperatures of 0 °C to –78 °C for overnight reactions were obtained using an immersion cooler (HAAKE EK 90). Reaction involving heating were performed using DrySyn blocks and a contact thermocouple.

Under reduced pressure refers to the use of either a Büchi Rotavapor R-200 with a Büchi V-491 heating bath and Büchi V-800 vacuum controller, a Büchi Rotavapor R-210 with a Büchi V-491 heating bath and Büchi V-850 vacuum controller, a Heidolph Laborota 4001 with vacuum controller, an IKA RV10 rotary evaporator with a IKA HB10 heating bath and ILMVAC vacuum controller, or an IKA RV10 rotary evaporator with a IKA HB10 heating bath and Vacuubrand CVC3000 vacuum controller. Rotary evaporator condensers are fitted to Julabo FL601 Recirculating Coolers filled with ethylene glycol and set to –5 °C.

Analytical thin layer chromatography (tlc) was performed on pre-coated aluminium plates (Kieselgel 60 F254 silica) and visualisation was achieved using ultraviolet light (254 nm) and/or staining with either aqueous $KMnO_4$ solution followed by heating. Manual column chromatography was performed in glass columns fitted with porosity 3 sintered discs over Kieselgel 60 silica using the solvent system stated. Automated chromatography was performed on a Biotage Isolera Four running Biotage OS578 with a UV/Vis detector using the method stated and cartridges filled with Kieselgel 60 silica.

Melting points were recorded on an Electrothermal 9100 melting point apparatus, (dec) refers to decomposition.

Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell at 20 °C.

HPLC analyses were obtained on either a Shimadzu HPLC consisting of a DGU-20A5 degassing unit, LC-20AT liquid chromatography pump, SIL-20AHT autosampler, CMB-20A communications bus module, SPD-M20A diode array detector and a CTO-20A column oven or a Shimadzu HPLC consisting of a DGU-20A5R degassing unit, LC-20AD liquid chromatography pump, SIL-20AHT autosampler, SPD-20A UV/Vis detector and a CTO-20A column oven. Separation was achieved using either DAICEL CHIRALCEL OD-H and OJ-H columns or DAICEL CHIRALPAK AD-H, AS-H, IA, IB, IC and ID columns using the method stated. HPLC traces of enantiomerically enriched compounds were compared with authentic racemic spectra.

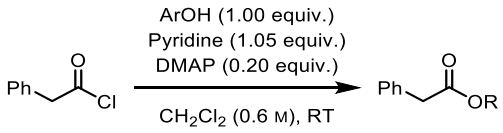
Infrared spectra were recorded on a Shimadzu IRAffinity-1 Fourier transform IR spectrophotometer fitted with a Specac Quest ATR accessory (diamond puck). Spectra were recorded of either thin films or solids, with characteristic absorption wavenumbers (ν_{max}) reported in cm^{-1}.

^{1}H, $^{13}C\{^{1}H\}$, and $^{19}F\{^{1}H\}$ NMR spectra were acquired on either a Bruker AV300 with a BBFO probe (^{1}H 300 MHz; $^{13}C\{^{1}H\}$ 75 MHz; $^{19}F\{^{1}H\}$ 282 MHz), a Bruker AV400 with a BBFO probe (^{1}H 400 MHz; $^{13}C\{^{1}H\}$ 101 MHz; $^{19}F\{^{1}H\}$ 377 MHz), a Bruker AVII 400 with a BBFO probe (^{1}H 400 MHz; $^{13}C\{^{1}H\}$ 101 MHz; $^{19}F\{^{1}H\}$ 376 MHz), a Bruker AVIII-HD 500 with a SmartProbe BBFO+ probe (^{1}H 500 MHz, $^{13}C\{^{1}H\}$ 126 MHz, $^{19}F\{^{1}H\}$ 470 MHz), or a Bruker AVIII 500 with a CryoProbe Prodigy BBO probe (^{1}H 500 MHz, $^{13}C\{^{1}H\}$ 126 MHz, $^{19}F\{1H\}$ 470 MHz) in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent peak. All coupling constants, *J*, are quoted in Hz. Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and multiples thereof. The abbreviation Ar denotes aromatic and app denotes apparent. NMR peak assignments were confirmed using 2D ^{1}H correlated spectroscopy (COSY), 2D ^{1}H–^{13}C heteronuclear multiple-bond correlation spectroscopy (HMBC), and 2D ^{1}H–^{13}C heteronuclear single quantum coherence (HSQC) where necessary.

Mass spectrometry (m/z) data were acquired by either electrospray ionisation (ESI electron impact (EI), atmospheric solids analysis probe (ASAP), atmospheric pressure chemical ionization (APCI) or nanospray ionisation (NSI) at the EPSRC UK National Mass Spectrometry Facility at Swansea University ([A]+ or [A]– quoted).

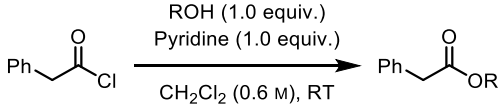
General Procedures

General Procedure A: DMAP-Catalyzed Synthesis of Esters



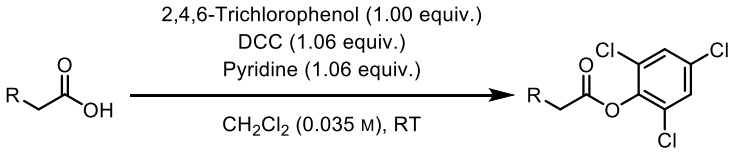
In flame-dried glassware, the alcohol (1.0 equiv.), DMAP (0.20 equiv.) and pyridine (1.05 equiv.) were dissolved in CH_2Cl_2 (0.6 M). Phenylacetyl chloride (1.0 equiv.) was added slowly and the reaction was stirred at rt under N_2 until complete by tlc. The reaction was washed with water and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified under the conditions stated.

General Procedure B: Synthesis of Esters



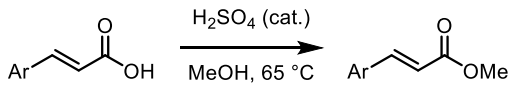
In flame-dried glassware, the alcohol (1.0 equiv.) and pyridine (1.0 equiv.) were dissolved in CH_2Cl_2 (0.6 M). Phenylacetyl chloride (1.0 equiv.) was added slowly and the reaction was stirred at rt under N_2 until complete by tlc. The solvent was removed *in vacuo* and the resulting solid was suspended in Et_2O. The solid was filtered off and washed with Et_2O. The filtrate was concentrated to dryness *in vacuo* to give the crude material, which was purified under the conditions stated.

General Procedure C: Synthesis of 2,4,6-Trichlorophenyl Esters



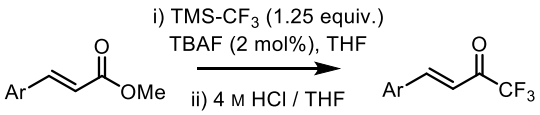
The acid (1.00 equiv.), 2,4,6-trichlorophenol (1.00 equiv.) and DCC (1.06 equiv.) were dissolved in CH_2Cl_2 (0.035 M) at rt. Pyridine (1.06 equiv.) was added and the reaction was stirred at rt until complete by tlc. The reaction was filtered and concentrated to dryness *in vacuo* to give the crude product which was purified by flash column chromatography under the conditions stated.

General Procedure D: Synthesis of Methyl Esters



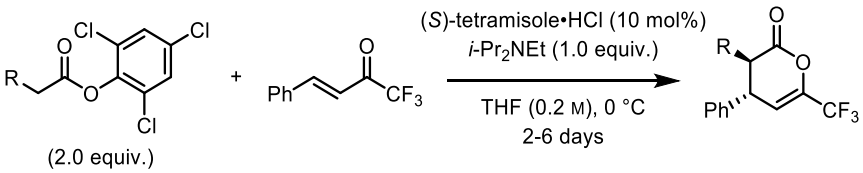
Based on a procedure reported by Brunner,[1] the α,β-unsaturated carboxylic acid was dissolved in methanol (0.5 M) and H_2SO_4 (cat.) was added. The reaction was stirred at 65 °C for 16 hours then cooled to rt. Water was added and extracted with Et_2O (3 ×). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and dried over $MgSO_4$ to give the title compound which was used without further purification unless stated.

General Procedure E: Synthesis of Trifluoromethyl Enones



Based on a procedure reported by Pedro,[2] the α,β-unsaturated methyl ester (1.0 equiv.) was dissolved in hexane (0.2 M) and cooled to 0 °C. Trifluoromethyltrimethylsilane (1.25 equiv.) and 1 M TBAF in THF (2 mol%) were added and the reaction was stirred at rt for 16 h. The solvent was removed *in vacuo* and the residue taken up in THF and 4 M aq. HCl. The mixture was stirred at rt for 10 h then Et_2O was added and washed with brine. The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified by flash column chromatography under the conditions stated to give the title compound.

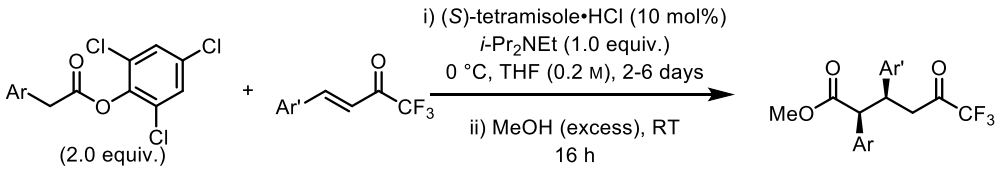
General Procedure F: Isothiourea-Catalyzed Michael Addition-Lactonization



The ester (2.0 equiv.) and **(*S*)-5·HCl** (10 mol%) were added to a flame-dried Schlenk flask cooled to 0 °C. A solution of enone **1** (1.0 equiv.) in THF (0.2 M) was then added, followed by *i*-Pr_2NEt (1.0 equiv.). The reaction was stirred at 0 °C until complete by tlc. The reaction was diluted with CH_2Cl_2 (10 mL) and washed with 1 M aq. HCl (5 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL). The organic layers were combined, dried over $MgSO_4$, filtered

and concentrated *in vacuo* to give the crude material, which was purified by flash column chromatography under the conditions stated then taken up in CH_2Cl_2 (10 mL) and washed with 1 M aq. NaOH (10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the purified material.

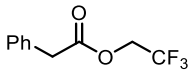
General Procedure G: Isothiourea-Catalyzed Michael Addition-Lactonization and *in situ* Methanolysis



The ester (2.0 equiv.) and **(*S*)-5·HCl** (10 mol%) were added to a flame-dried Schlenk flask cooled to 0 °C. A solution of enone (1.0 equiv) in THF (0.2 M) was then added, followed by *i*-Pr_2NEt (1.0 equiv.). The reaction was stirred at 0 °C until complete by tlc. Methanol (1 mL) was added and the reaction was stirred at rt for 16 h. The reaction was diluted with CH_2Cl_2 (10 mL) and washed with 1 M aq. HCl (5 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude material. The crude material was purified by flash column chromatography under the conditions stated then taken up in CH_2Cl_2 (10 mL) and washed with 1 M aq. NaOH (10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the purified material.

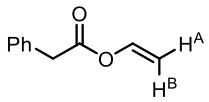
Synthesis of Esters

2,2,2-Trifluoroethyl 2-phenylacetate 6



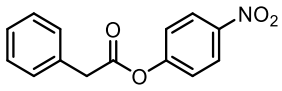
Following general procedure B, 2,2,2-trifluoroethanol (0.47 mL, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 16 h gave the crude material, which was purified by flash column chromatography (15% CH_2Cl_2 in hexane) to give **6** as a colourless oil (1.37 g, 6.25 mmol, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.66 (2H, s, C(2)H_2), 4.41 (2H, q, $^3J_{H\text{-}F}$ 8.5, OCH_2CF$_3$), 7.13–7.35 (5H, m, ArC*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F −73.8. Data in accordance with literature.[3]

Vinyl 2-phenylacetate 7



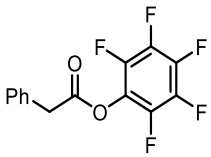
Following literature procedure,[10] phenylacetic acid (500 mg, 3.67 mmol, 1.0 equiv.) was dissolved in anhydrous THF (0.4 mL). Vinyl acetate (3.7 mL, 40.39 mmol, 11.0 equiv.) and palladium (II) acetate (8.3 mg, 0.04 mmol, 0.01 equiv.) were added. The reaction was heated to 60 °C and stirred at 60 °C under N_2 for 18 h. The reaction was cooled to rt and filtered through Celite®. The solid was rinsed with CH_2Cl_2 (20 mL) and the solvent was removed from the filtrate *in vacuo* to give the crude material, which was purified by flash column chromatography (10% CH_2Cl_2 in hexane) to give **7** as a colourless oil (242 mg, 1.49 mmol, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.71 (2H, s, C(2)H_2), 4.59 (1H, dd, *J* 6.3, 1.7, CH^AH^B), 4.91 (1H, dd, *J* 14.0, 1.7, CH^AH^B), 7.16–7.43 (6H, m, ArC*H* + OC*H*). Data in accordance with literature.[4]

4-Nitrophenyl 2-phenylacetate 8



Following general procedure B, 4-nitrophenol (0.74 g, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 16 h gave the crude material, which was purified by precipitation from CH_2Cl_2 and hexane to give **8** as a white solid (1.16 g, 4.51 mmol, 70%). mp 56–57 °C {Lit.[5] oil}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.85–4.00 (2H, m, C(2)H_2), 7.21–7.35 (2H, m, OArC(2,6)*H*), 7.32–7.50 (5H, m, C(2)ArC*H*), 8.19–8.35 (2H, m, OArC(3,5)*H*). Data in accordance with literature.[5]

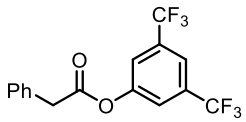
Perfluorophenyl 2-phenylacetate 9



Following general procedure A, pentafluorophenol (1.19 g, 6.47 mmol), DMAP (158 mg, 1.29 mmol), pyridine (0.55 mL, 6.79 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 for 3 h gave **9** as a colourless oil (1.72 g, 5.69 mmol, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.97 (2H, s, C(2)H_2), 7.30–7.43 (5H, m, PhC*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F −152.5–

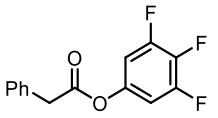
(−152.8) (m, OArC(2,6)*F*), −157.8 (t, $^{3}J_{F\text{-}F}$ 21.6, OArC(4)*F*), −162.2–(−162.4) (m, OArC(3,5)*F*). Data in accordance with literature.[5]

3,5-Bis(trifluoromethyl)phenyl 2-phenylacetate 10



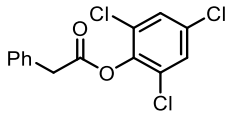
Following general procedure B, 3,5-bis(trifluoromethyl)phenol (0.99 mL, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 17 h gave the crude material, which was purified by flash column chromatography (10% Et_2O in hexane) to give **10** as a colourless oil (1.22 g, 3.50 mmol, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.91 (2H, s, C(2)H_2), 7.31–7.45 (5H, m, C(2)H$_2$ArC*H*), 7.54–7.60 (2H, m, OArC(2,6)*H*), 7.72–7.77 (1H, m, OArC(4)*H*); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ_F: −63.4 (CF_3). Data in accordance with literature. [6]

3,4,5-Trifluorophenyl 2-phenylacetate 11



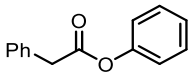
Following general procedure B, 3,4,5-trifluorophenol (948 mg, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 17 h gave the crude material, which was purified by flash column chromatography (20% Et_2O in hexane) to give **11** as a colourless oil (1.57 g, 5.90 mmol, 91%). ν_{max} (film, cm^{-1}) 1763 (C=O), 1520 (C−H), 1121 (C−O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.86 (2H, s, C(2)H_2), 6.71–6.86 (2H, m, OArC(2,6)*H*), 7.31–7.50 (5H, m, C(2)ArC*H*); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C: 41.2 (*C*(2)H_2), 106.9 (dd, $^{2,3}J_{C\text{-}F}$ 18.3, 6.2, OAr*C*(2,6)H), 127.8 (C(2)Ar*C*(4)H), 129.0 (C(2)Ar*C*(3,5)H), 129.4 (C(2)Ar*C*(2,6)H), 132.8 (C(2)Ar*C*(1)), 138.2 (dt, $^{1,2}J_{C\text{-}F}$ 250.0, 15.3, OAr*C*(4)F), 145.4 (td, $^{3,4}J_{C\text{-}F}$ 11.6, 4.3, OAr*C*(1)), 151.1 (ddd, $^{1,2,3}J_{C\text{-}F}$ 250.7, 10.7, 5.2, OAr*C*(3,5)F), 169.3 (*C*(1)=O); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F: −163.5 (t, $J_{F\text{-}F}$ 21.0, OArC(4)*F*), −132.9 (d, $J_{F\text{-}F}$ 21.0, OArC(3,5)*F*); HRMS (NSI$^+$) $C_{14}H_{10}F_3O_2$ [M+H]$^+$ found 267.0622, requires 267.0627 (−2.0 ppm).

2,4,6-Trichlorophenyl 2-phenylacetate 12



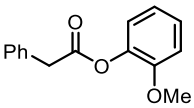
Following general procedure B, 2,4,6-trichlorophenol (1.28 g, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 16 h gave the crude material, which was purified by flash column chromatography (20% Et_2O in hexane) to give **12** as a colourless oil (1.86 g, 5.92 mmol, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.99 (2H, s C(2)H_2), 7.28–7.44 (7H, m, ArC*H*). Data in accordance with literature.[6]

Phenyl 2-phenylacetate 13



Following general procedure A, phenol (608 mg, 6.47 mmol), DMAP (158 mg, 1.29 mmol), pyridine (0.55 mL, 6.79 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 4.5 h gave the crude material, which was purified by flash column chromatography (5% EtOAc in hexane) to give **13** as a white solid (1.14 g, 5.37 mmol, 83%). mp 44–45 °C {Lit.[3] 42 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.87 (2H, s, C(2)H_2), 7.02–7.11 (2H, m, ArC*H*), 7.17–7.26 (1H, m, ArC*H*), 7.27–7.44 (7H, m, ArC*H*). Data in accordance with literature.[3]

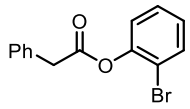
2-Methoxyphenyl 2-phenylacetate S1



Following general procedure A, 2-methoxyphenol (0.71 mL, 6.47 mmol), DMAP (158 mg, 1.29 mmol), pyridine (0.55 mL, 6.79 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 24 h gave the crude material, which was purified by flash column chromatography (10% EtOAc in hexane) to give **S1** as a colourless oil (1.42 g, 5.86 mmol, 91%). ν_{max} (film, cm^{-1}) 1759 (C=O), 1499 (C–H), 1255 (C–O), 1109 (C–O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 3.79 (3H, s, OCH_3), 3.95 (2H, s, C(2)H_2), 6.92–7.01 (2H, m, OArC(3,5)*H*), 7.06 (1H, dd, *J* 7.8, 1.7, OArC(6)*H*), 7.23 (1H, ddd, *J* 8.2, 7.4, 1.7, OArC(4)*H*), 7.31–7.37 (1H, m, C(2)ArC(4)*H*), 7.38–7.44 (2H, m, C(2)ArC(3,5)*H*), 7.43–7.50 (2H, m, C(2)ArC(2,6)*H*); ^{13}C{^{1}H} NMR (126 MHz,

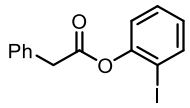
$CDCl_3$) δ_C: 41.0 (*C*(2)H_2), 55.8 (OCH_3), 112.5 (OAr*C*(3)H), 120.7 (OAr*C*(5)H), 122.7 (OAr*C*(6)H), 126.9 (OAr*C*(4)H), 127.2 (C(2)Ar*C*(4)H), 128.6 (C(2)Ar*C*(3,5)H), 129.4 (C(2)Ar*C*(2,6)H), 133.7 (C(2)Ar*C*(1)), 139.9 (OAr*C*(1)), 151.1 (OAr*C*(2)), 169.7 (*C*(1)=O); HRMS (NSI^+) $C_{15}H_{15}O_3$ $[M+H]^+$ found 243.1017, requires 243.1016 (+0.5 ppm).

2-Bromophenyl 2-phenylacetate S2



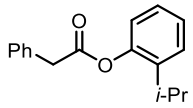
Following general procedure B, 2-bromophenol (0.74 mL, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 4 h gave the crude material, which was purified by precipitation from CH_2Cl_2 and hexane to give **S2** as a white solid (132 mg, 0.45 mmol, 7%). mp 54−55 °C; ν_{max} (film, cm^{-1}) 1761 (C=O), 1470 (C−H), 1215 (C−O), 1105 (C−O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.94 (2H, s, C(2)*H*$_2$), 7.07–7.15 (2H, m, OArC(4)*H* + OArC(6)*H*), 7.27–7.35 (2H, m, C(2)ArC(4)*H* + OArC(5)*H*), 7.35–7.45 (4H, m, C(2)ArC(2,6)*H* + C(2)ArC(3,5)*H*), 7.59 (1H, dd, *J* 8.1, 1.4, OArC(3)*H*); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C: 41.3 (*C*(2)H_2), 116.3 (OAr*C*(2)), 123.8 (OAr*C*(6)H), 127.5 (OAr*C*(4)H), 127.6 (C(2)Ar*C*(4)H), 128.6 (OAr*C*(5)H), 128.8 (C(2)Ar*C*(3,5)H), 129.7 (C(2)Ar*C*(2,6)H), 133.2 (C(2)Ar*C*(1)), 133.5 (OAr*C*(3)H), 148.4 (OAr*C*(1)), 169.2 (*C*(1)=O); HRMS (NSI^+) $C_{14}H_{15}{}^{79}BrNO_2$ $[M+NH_4]^+$ found 308.0285, requires 308.0281 (+1.4 ppm).

2-Iodophenyl 2-phenylacetate S3



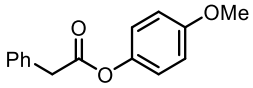
Following general procedure B, 2-iodophenol (1.42 g, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 4 h gave **S3** as a pale yellow oil (2.18 g, 6.45 mmol, 100%). ^{1}H (400 MHz, $CDCl_3$) δ_H: 3.94 (2H, s, C(2)*H*$_2$), 6.96 (1H, td, *J* 7.8, 1.5, OArC(4)*H*), 7.06 (1H, dd, *J* 7.8, 1.5, OArC(6)*H*), 7.31–7.48 (6H, m, C(2)ArC*H* + OArC(5)*H*), 7.81 (1H, dd, *J* 7.9, 1.5, OArC(3)*H*). Data in accordance with literature.[8]

2-Isopropylphenyl 2-phenylacetate S4



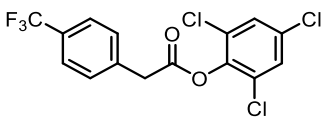
Following general procedure B, 2-isopropylphenol (0.87 mL, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 4 h gave the crude material, which was purified by flash column chromatography (5% EtOAc in hexane) to give **S4** as a colourless oil (1.54 g, 6.04 mmol, 93%). ν_{max} (film, cm^{-1}) 2963 (C−H), 1749 (C=O), 1119 (C−O); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 1.00 (6H, d, *J* 6.9, CH(C*H*$_3$)$_2$), 2.73 (1H, sept, *J* 7.0, C*H*(CH$_3$)$_2$), 3.81 (2H, s, C(2)*H*$_2$), 6.87–6.91 (1H, m, OArC(6)*H*), 7.05–7.15 (2H, m, OArC*H*) 7.15–7.38 (6H, m, C(2)ArC*H* + OAr*CH*); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ_C: 22.9 (CH(*C*H$_3$)$_2$), 27.3 (*C*H(CH)$_2$), 41.8 (*C*(2)H$_2$), 122.3 (OAr*C*(6)H), 126.4 (C(2)Ar*C*(4)H), 126.7 (C(2)Ar*C*(3,5)H), 126.7 (C(2)Ar*C*(2,6)H), 127.5 (OArCH), 128.8 (OArCH), 129.5 (OArCH), 133.7 (C(2)Ar*C*(1)), 140.3 (OAr*C*(2)), 148.2 (OAr*C*(1)), 170.2 (*C*(1)=O); HRMS (NSI$^+$) $C_{17}H_{19}O_2$ $[M+H]^+$ found 255.1383, requires 255.1380 (+1.3 ppm).

4-Methoxyphenyl 2-phenylacetate S5



Following general procedure B, 4-methoxyphenol (803 mg, 6.47 mmol), pyridine (0.52 mL, 6.47 mmol) and phenylacetyl chloride (0.86 mL, 6.47 mmol) in CH_2Cl_2 (11 mL) for 17 h the crude material, which was purified by flash column chromatography (20% CH_2Cl_2 in hexane) to give **S5** as a colourless oil (1.55 g, 6.47 mmol, 100%). ^1H NMR (400 MHz, $CDCl_3$) δ_H: 3.81 (3H, s, OC*H*$_3$), 3.87 (2H, s, C(2)*H*$_2$), 6.86–7.43 (2H, m, OArC(3,5)*H*), 6.97–7.03 (2H, m, OArC(2,6)*H*), 7.30–7.43 (5H, m, C(2)ArC*H*). Data in accordance with literature.[5]

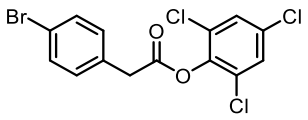
2,4,6-Trichlorophenyl 2-(4-(trifluoromethyl)phenyl)acetate S6



Following general procedure C, 4-trifluorophenylacetic acid (510 mg, 2.50 mmol, 1.00 equiv.), 2,4,6-trichlorophenol (489 mg, 2.50 mmol, 1.00 equiv.), DCC (547 mg, 2.65 mmol, 1.06 equiv.)

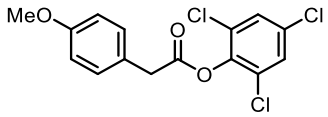
and pyridine (214 μL, 2.65 mmol, 1.06 equiv.) in CH_2Cl_2 (71 mL, 0.035 M) at rt for 7 hours gave the crude material, which was purified by flash column chromatography (0 to 4% Et_2O in petrol) to give **S6** as a white solid (758 mg, 1.98 mmol, 79%). mp 71–73 °C; ν_{max} (film, cm^{-1}) 3084 (C-H), 2930 (C-H), 2849 (C-H), 1771 (C=O), 1562 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.03 (2H, s, C(2)H_2), 7.37 (2H, s, OArC(3,5)*H*), 7.53 (2H, d, *J* 8.0, C(2)ArC(2,6)*H*), 7.64 (2H, d, *J* 7.9, C(2)C(3,5)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: −62.6 (CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C 40.4 (*C*(2)H_2), 124.2 (q, $^1J_{C\text{-}F}$ 272.0, *C*F_3), 125.8 (q, $^3J_{C\text{-}F}$ 3.8, C(2)Ar*C*(3,5)H), 128.8 (C(2)Ar*C*(2,6)H), 129.6 (OAr*C*(3,5)H), 130.1 (OAr*C*(2,6)Cl), 130.3 (q, $^2J_{C\text{-}F}$ 32.6, C(2)Ar*C*(4)CF_3), 132.4 (C(2)Ar*C*(1)), 136.6 (OAr*C*(4)Cl), 142.8 (OAr*C*(1)), 167.1 (*C*(1)=O); HRMS (ASAP) $C_{15}H_9{}^{35}Cl_3F_3O_2^+$ $[M+H]^+$ found: 382.9620, requires: 382.9620 (+ 0.0 ppm).

2,4,6-Trichlorophenyl 2-(4-bromophenyl)acetate S7



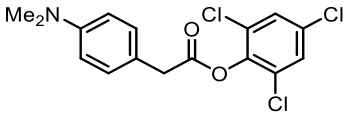
Following general procedure C, 4-bromophenylacetic acid (538 mg, 2.50 mmol, 1.00 equiv.), 2,4,6-trichlorophenol (489 mg, 2.50 mmol, 1.00 equiv.), DCC (547 mg, 2.65 mmol, 1.06 equiv.) and pyridine (214 μL, 2.65 mmol, 1.06 equiv.) in CH_2Cl_2 (71 mL, 0.035 M) at rt for 20 hours gave the crude material, which was purified by flash column chromatography (0 to 5% Et_2O in petrol) to give **S8** as a white solid (636 mg, 1.61 mmol, 65%). mp 80–81 °C; ν_{max} (film, cm^{-1}) 3084 (C-H), 2930 (C-H), 1767 (C=O), 1564 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.92 (2H, s, C(2)H_2), 7.24–7.32 (2H, m, C(2)ArC(2,6)*H*), 7.36 (2H, s, OArC(3,5)*H*), 7.47–7.55 (2H, m, C(2)ArC(3,5)*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 40.1 (*C*H_2), 121.9 (C(2)Ar*C*(4)Br), 128.7 (OAr*C*(3,5)H), 129.6 (C(2)Ar*C*(1)), 131.4 (C(2)Ar*C*(2,6)H), 131.6 (OAr*C*(2,6)Cl), 132.0 (C(2)Ar*C*(3,5)H), 132.3 (OAr*C*(4)Cl), 142.9 (OAr*C*(1)), 167.3 (*C*(1)=O). HRMS could not be obtained.

2,4,6-Trichlorophenyl 2-(4-methoxyphenyl)acetate S8



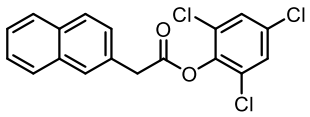
Following general procedure C, 4-methoxyphenylacetic acid (415 mg, 2.50 mmol, 1.00 equiv.), 2,4,6-trichlorophenol (489 mg, 2.50 mmol, 1.00 equiv.), DCC (547 mg, 2.65 mmol, 1.06 equiv.) and pyridine (214 μL, 2.65 mmol, 1.06 equiv.) in CH_2Cl_2 (71 mL, 0.035 M) at rt for 7 hours gave the crude material, which was purified by flash column chromatography (0 to 5% Et_2O in petrol) to give **S7** as a white solid (536 mg, 1.55 mmol, 62%). mp 56–58 °C; ν_{max} (film, cm^{-1}) 3084 (C-H), 2916 (C-H), 2833 (C-H), 1767 (C=O), 1512 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 3.81 (3H, s, OC*H*$_3$), 3.90 (2H, s, C(2)*H*$_2$), 6.90 (2H, d, *J* 8.7, C(2)ArC(3,5)*H*), 7.29–7.33 (2H, d, *J* 8.7, C(2)ArC(2,6)*H*), 7.35 (2H, s, OC(3,5)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 39.8 (*C*(2)H$_2$), 55.4 OCH$_3$), 114.3 (C(2)Ar*C*(3,5)H), 124.7 (C(2)Ar*C*(1)), 128.7 (OAr*C*(2,6)H), 129.7 (OAr*C*(2,6)Cl), 130.7 (C(2)Ar*C*(2,6)H), 132.1 (OAr*C*(4)Cl), 143.1 (OAr*C*(1)), 159.2 (C(2)Ar*C*(4)), 168.1 (*C*(1)=O); HRMS (ASAP) $C_{15}H_{12}Cl_3O_3^+$ $[M+H]^+$ found: 344.9851, requires: 344.9852 (−0.3 ppm).

2,4,6-Trichlorophenyl 2-(4-(dimethylamino)phenyl)acetate S9



Following general procedure C, 4-dimethylaminophenylacetic acid (448 mg, 2.50 mmol, 1.00 equiv.), 2,4,6-trichlorophenol (489 mg, 2.50 mmol, 1.00 equiv.), DCC (547 mg, 2.65 mmol, 1.06 equiv.) and pyridine (214 μL, 2.65 mmol, 1.06 equiv.) in CH_2Cl_2 (71 mL, 0.035 M) at rt for 20 hours gave the crude material, which was purified by flash column chromatography (0 to 5% Et_2O in petrol) to give **S9** as a yellow oil (757 mg, 2.11 mmol, 84%). ν_{max} (film, cm^{-1}) 3078 (C-H), 2887 (C-H), 2803 (C-H), 1769 (C=O), 1522 (C=C); ^1H NMR (400 MHz, $CDCl_3$) δ_H: 2.95 (6H, s, N(C*H*$_3$)$_2$), 3.86 (2H, s, C(2)*H*$_2$), 6.72 (2H, d, *J* 8.7, C(2)ArC(3,5)*H*), 7.27 (2H, d, *J* 8.7, C(2)ArC(2,6)*H*), 7.34 (2H, s, OArC(3,5)*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 39.7 (*C*H$_2$), 40.8 (N(*C*H$_3$)$_2$), 112.8 (C(2)Ar*C*(3,5)H), 120.2 (C(2)Ar*C*(1)), 128.6 (OAr*C*(3,5)H), 129.8 (OAr*C*(2,6)Cl), 130.3 (C(2)Ar*C*(2,6)H), 132.0 (OAr*C*(4)Cl), 143.2 (OAr*C*(1)), 150.11 (C(2)Ar*C*(4)N(CH$_3$)$_2$), 168.5 (*C*(1)=O); HRMS (NSI$^+$) $C_{16}H_{15}Cl_3NO_2^+$ $[M+H]^+$ found: 358.0160, requires: 358.0163. (−0.8 ppm).

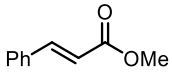
2,4,6-Trichlorophenyl 2-(naphthalen-2-yl)acetate S10



Following general procedure C, 2-(naphthalen-2-yl)acetic acid (465 mg, 2.50 mmol, 1.00 equiv.), 2,4,6-trichlorophenol (489 mg, 2.50 mmol, 1.00 equiv.), DCC (547 mg, 2.65 mmol, 1.06 equiv.) and pyridine (214 μL, 2.65 mmol, 1.06 equiv.) in CH_2Cl_2 (71 mL, 0.035 M) at rt for 20 hours gave the crude material, which was purified by flash column chromatography (0 to 5% Et_2O in petrol) to give **S10** as a white solid (898 mg, 2.45 mmol, 98%). mp 80–81 °C; ν_{max} (film, cm^{-1}) 3084 (C-H), 3019 (C-H), 2903 (C-H), 1776 (C=O), 1564 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 4.02 (2H, s, C(2)H_2), 7.23 (2H, s, OArC(3,5)*H*), 7.33–7.46 (3H, m, NapC*H*), 7.67–7.79 (4H, m, Nap*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 40.8 (*C*(2)H_2), 126.1 (Nap*C*(1)H), 126.4 (Nap*C*(5)H), 127.4 (Nap*C*(4)H), 127.8 (Nap*C*(7)H), 127.6 (Nap*C*(6)H), 128.5 (Nap*C*(3)H), 128.5 (Nap*C*(8)H), 128.6 (OAr*C*(3,5)H), 129.6 (OAr*C*(2,6)Cl), 130.0 (Nap*C*(8a)), 132.1 (OAr*C*(4)Cl), 132.7 (Nap*C*(4a)), 133.5 (Nap*C*(2)), 143.0 (OAr*C*(1)), 167.7 (*C*(1)=O). HRMS could not be obtained.

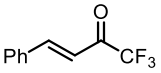
Synthesis of Electrophiles

Methyl cinnamate S11



Following general procedure D, cinnamic acid (1.70 g, 11.5 mmol, 1.0 equiv.) and H_2SO_4 (1 mL) in methanol (25 mL) gave **S11** as a white solid (1.87 g, 11.5 mmol, quant.) mp 34–35 °C {Lit.[11] 32 °C}; δ_H (400 MHz, $CDCl_3$) 3.81 (3H, s, CH_3), 6.45 (1H, d, *J* 16.0, C(2)*H*), 7.35–7.43 (3H, m, Ar*H*), 7.49–7.55 (2H, m, Ar*H*), 7.70 (1H, d, *J* 16.0, C(3)*H*). Data in accordance with literature.[9]

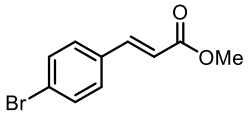
(*E*)-1,1,1-Trifluoro-4-phenylbut-3-en-2-one 1



Following general procedure E, methyl cinnamate **S11** (1.0 g, 6.2 mmol, 1.0 equiv.) was dissolved in hexane (30 mL, 0.2 M) and cooled to 0 °C. Trifluoromethyltrimethylsilane (1.1 mL, 7.7 mmol, 1.25 equiv.) and 1 M TBAF in THF (0.1 mL, 0.12 mmol, 2 mol%) were added and the

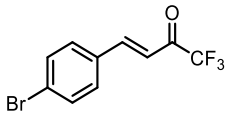
reaction was stirred at rt for 16 h. The solvent was removed *in vacuo* and the residue taken up in THF (4 mL) and 4 M aq. HCl (4 mL). The mixture was stirred at rt for 10 h then Et_2O (80 mL) was added and washed with brine (40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified by flash column chromatography (5 to 10% CH_2Cl_2 in hexane) to give **2** as a yellow oil (1.16 g, 5.5 mmol, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 7.02 (1H, dd, *J* 16.0, 1.0, C(3)*H*), 7.42–7.54 (3H, m, Ph*H*), 7.60–7.68 (2H, m, Ph*H*), 7.98 (1H, d, *J* 16.0, C(4)*H*); ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ_F: −77.6 (C*F*$_3$). Data in accordance with literature.[10]

Methyl (*E*)-3-(4-bromophenyl)acrylate S12



Following general procedure D, (*E*)-3-(4-bromophenyl)acrylic acid (2.60 g, 11.5 mmol, 1.0 equiv.) and H_2SO_4 (1 mL) in methanol (25 mL) gave **S12** as a white solid (2.48 g, 10.3 mmol, 89%). mp 86–87 °C {Lit.[1] 88 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.80 (3H, s, C*H*$_3$), 6.42 (1H, d, *J* 16.0, C(2)*H*), 7.38 (2H, d, *J* 8.5, ArC(2,6)*H*), 7.51 (2H, d, *J* 8.5, ArC(3,5)*H*), 7.62 (1H, d, *J* 16.0, C(3)*H*). Data in accordance with literature.[1]

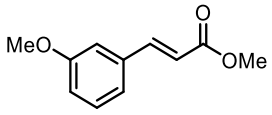
(*E*)-4-(4-Bromophenyl)-1,1,1-trifluorobut-3-en-2-one S13



Following general procedure E, methyl ester **S12** (1.67 g, 6.6 mmol, 1.0 equiv.) was dissolved in hexane (35 mL, 0.2 M) and cooled to 0 °C. Trifluoromethyltrimethylsilane (1.1 mL, 7.1 mmol, 1.25 equiv.) and 1 M TBAF in THF (0.1 mL, 0.1 mmol, 2 mol%) were added and the reaction was stirred at rt for 16 h. The solvent was removed *in vacuo* and the residue taken up in THF (4 mL) and 4 M aq. HCl (4 mL). The mixture was stirred at rt for 10 h then Et_2O (80 mL) was added and washed with brine (40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified by flash column chromatography (5 to 20% CH_2Cl_2 in hexane) to give **S13** as a white solid (769 mg, 2.76 mmol, 42%). mp 43–46 °C {Lit.[15] 56–57 °C}; ν_{max} (film, cm^{-1}) 1715 (C=O), 1603, 1585, 1123;

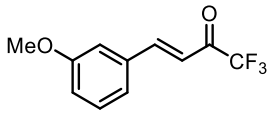
^{1}H NMR δ_H (400 MHz, $CDCl_3$) 7.00 (1H, d, *J* 15.9, C(3)*H*), 7.51 (2H, d, *J* 8.5, ArC(2,6)*H*), 7.60 (2H, d, *J* 8.5, ArC(3,5)*H*), 7.90 (1H, d, *J* 15.9, C(4)*H*); ^{19}F NMR (471 MHz, $CDCl_3$) δ_F: –77.7 (CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C: 116.4 (q, *J* 290.5 Hz, *C*(1)F_3) 117.2 (*C*(3)H), 127.1 (Ar*C*(4)Br), 130.6 (Ar*C*(2,6)H), 132.3 (Ar*C*(1)), 132.7 (Ar*C*(3,5)H), 148.8 (*C*(4)H), 180.0 (q, *J* 35.5 Hz, *C*(2)=O); HRMS (ASAP$^+$) $C_{10}H_7{}^{79}BrF_3O^+$ $[M+H]^+$ found: 278.9639, requires: 278.9627 (+4.3 ppm). Data in accordance with literature.[15]

Methyl (*E*)-3-(3-methoxyphenyl)acrylate S14



Following general procedure D, (*E*)-3-(3-methoxyphenyl)acrylic acid (663 mg, 3.7 mmol, 1.0 equiv.) and H_2SO_4 (0.5 mL) in methanol (12 mL) gave **S14** as a pale yellow oil (636 mg, 3.3 mmol, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.81 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 6.43 (1H, d, *J* 16.0, C(2)*H*), 6.94 (1H, ddd, *J* 8.2, 2.6, 0.9, ArC(4)*H*), 7.04 (1H, dd, *J* 2.6, 1.6, ArC(2)*H*), 7.12 (1H, app. d, *J* 7.7, ArC(6)*H*), 7.30 (1H, t, *J* 7.9, ArC(5)*H*) 7.66 (1H, d, *J* 16.0, C(3)*H*). Data in accordance with literature.[1]

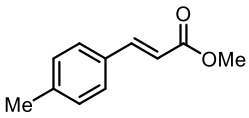
(*E*)-1,1,1-Trifluoro-4-(3-methoxyphenyl)but-3-en-2-one S15



Following general procedure E, methyl ester **S14** (677 mg, 3.3 mmol, 1.0 equiv.) was dissolved in hexane (20 mL, 0.2 M) and cooled to 0 °C. Trifluoromethyltrimethylsilane (0.6 mL, 3.6 mmol, 1.25 equiv.) and 1 M TBAF in THF (0.05 mL, 0.05 mmol, 2 mol%) were added and the reaction was stirred at rt for 16 h. The solvent was removed *in vacuo* and the residue taken up in THF (4 mL) and 4 M aq. HCl (4 mL). The mixture was stirred at rt for 10 h then Et_2O (80 mL) was added and washed with brine (40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified by flash column chromatography (5 to 20% CH_2Cl_2 in hexane) to give **S15** as a yellow oil (216 mg, 0.94 mmol, 28%). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 3.86 (3H, s, OCH_3), 6.99 (1H, dd, *J* 16.0, 0.7, C(3)*H*), 7.05 (1H, ddd, *J* 8.2, 2.6, 0.6, ArC(4)*H*), 7.11–7.16 (1H, m, ArC(2)*H*), 7.24 (1H, dt, *J* 7.7, 1.1,

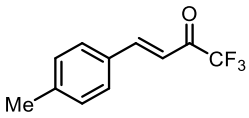
ArC(6)*H*), 7.37 (1H, t, *J* 7.9, ArC(5)*H*), 7.94 (1H, d, *J* 16.0, C(4)*H*); ^{19}F NMR (471 MHz, $CDCl_3$) δ_F: –77.6 (CF_3). Data in accordance with literature.[12]

Methyl (E)-3-(p-tolyl)acrylate S16



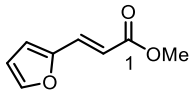
Following general procedure D, (*E*)-3-(*p*-tolyl)acrylic acid (1.87 g, 11.5 mmol, 1.0 equiv.) and H_2SO_4 (1 mL) in methanol (25 mL) gave **S16** as a white solid (1.98 g, 11.2 mmol, 98%). mp 57–59 °C {Lit.[13] 55 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.37 (3H, s, ArCH_3), 3.79 (3H, s, OCH_3), 6.40 (1H, d, *J* 16.0,), 7.19 (4H, d, *J* 7.7), 7.42 (3H, d, *J* 8.1), 7.67 (1H, d, *J* 15.8). Data in accordance with literature.[13]

(E)-1,1,1-Trifluoro-4-(p-tolyl)but-3-en-2-one S17



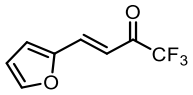
Following general procedure E, methyl ester **S16** (1.0 g, 5.7 mmol, 1.0 equiv.) was dissolved in hexane (28 mL, 0.2 M) and cooled to 0 °C. Trifluoromethyltrimethylsilane (1.1 mL, 7.1 mmol, 1.25 equiv.) and 1 M TBAF in THF (0.1 mL, 0.1 mmol, 2 mol%) were added and the reaction was stirred at rt for 16 h. The solvent was removed *in vacuo* and the residue taken up in THF (4 mL) and 4 M aq. HCl (4 mL). The mixture was stirred at rt for 10 h then Et_2O (80 mL) was added and washed with brine (40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified by flash column chromatography (7% CH_2Cl_2 in hexane) to give **S17** as a white solid (1.18 g, 5.5 mmol, 96%). mp 33–34 °C {lit.[14] 35 °C}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.44 (3H, s, CH_3), 7.00 (1H, d, *J* 16.0, C(3)*H*), 7.28 (2H, d, *J* 8.1, ArC(3,5)*H*), 7.56 (2H, d, *J* 8.1, ArC(2,6)*H*), 7.97 (1H, d, *J* 16.0, C(4)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: –77.6 (CF_3). Data in accordance with literature.[14]

Methyl (*E*)-3-(furan-2-yl)acrylate S19



Following general procedure D, (*E*)-3-(furan-2-yl)acrylic acid (1.59 g, 11.5 mmol, 1.0 equiv.) and H_2SO_4 (1 mL) in methanol (25 mL) gave **S19** as a brown oil (1.57 g, 10.3 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.78 (3H, s, C*H*$_3$), 6.31 (1H, d, *J* 15.7, C(2)*H*), 6.46 (1H, dd, *J* 3.4, 1.8, ArC(4)*H*), 6.60 (1H, d, *J* 3.4, ArC(3)*H*), 7.43 (1H, d, *J* 15.7, C(3)*H*), 7.47 (1H, d, *J* 1.8, ArC(5)*H*). Data in accordance with literature.[15]

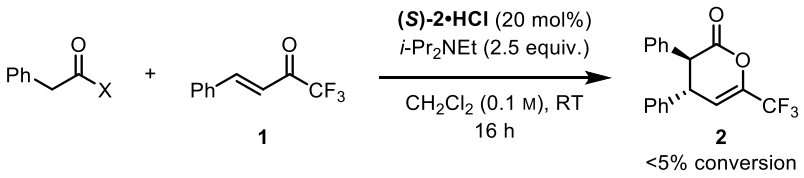
(*E*)-1,1,1-Trifluoro-4-(furan-2-yl)but-3-en-2-one S20



Following general procedure E, methyl ester **S19** (1.00 g, 6.6 mmol, 1.0 equiv.) was dissolved in hexane (30 mL, 0.2 M) and cooled to 0 °C. Trifluoromethyltrimethylsilane (1.2 mL, 8.2 mmol, 1.25 equiv.) and 1 M TBAF in THF (0.1 mL, 0.1 mmol, 2 mol%) were added and the reaction was stirred at rt for 16 h. The solvent was removed *in vacuo* and the residue taken up in THF (4 mL) and 4 M aq. HCl (4 mL). The mixture was stirred at rt for 10 h then Et_2O (80 mL) was added and washed with brine (40 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to dryness *in vacuo* to give the crude material, which was purified by flash column chromatography (5 to 20% CH_2Cl_2 in hexane) to give **S20** as a yellow oil (327 mg, 1.7 mmol, 21%). ν_{max} (film, cm^{-1}) 1714 (C=O), 1603, 1553, 1055; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H: 6.58 (1H, dd, *J* 3.5, 1.8, ArC(4)*H*), 6.89 (1H, d, *J* 15.6, C(3)*H*), 6.90 (1H, d, *J* 3.5, ArC(3)*H*), 7.61 (1H, d, *J* 1.7, ArC(5)*H*), 7.69 (1H, d, *J* 15.6, C(4)*H*); ^{19}F NMR (471 MHz, $CDCl_3$) δ_F: –77.6 (C*F*$_3$); ^{13}C{^{1}H} NMR (400 MHz, $CDCl_3$) δ_C: 113.6 (ArC(4)H), 114.1 (ArC(5)H), 116.6 (q, *J* 290.6 *C*F$_3$), 120.1 (*C*(3)H), 134.9 (ArC(3)H) , 147.1 (*C*(4)H), 150.7 (ArC(1)), 180.0 (q, *J* 35.3, *C*(2)=O); HRMS (ESI$^+$) $C_8H_5F_3O_2^+$ [M]$^+$ found: 190.0244, requires: 190.0236 (+4.2 ppm). Data in accordance with literature.[16]

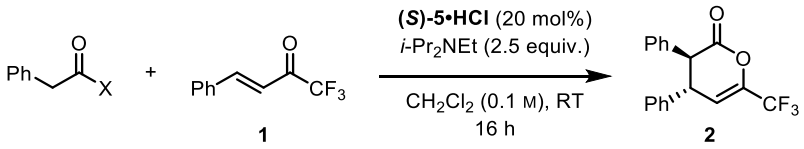
Precursor Screen

Procedure for Ester Screen



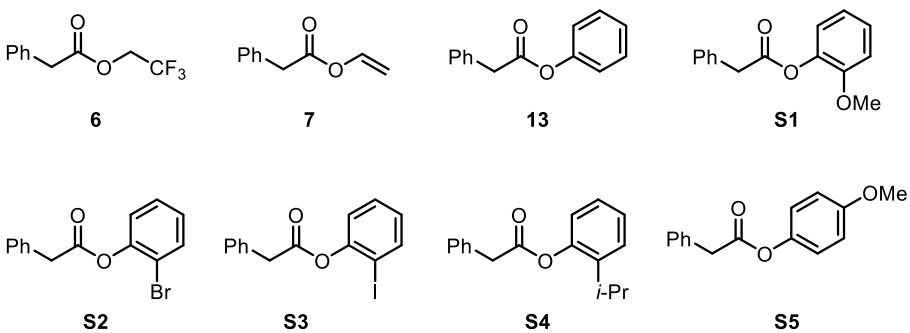
In a method related to General Procedure F, the ester (1.0 equiv.) and **(*S*)-5·HCl** (20 mol%) were added to a flame-dried Schlenk flask. A solution of enone **1** (1.0 equiv) in CH_2Cl_2 (0.2 M) was then added, followed by *i*-Pr_2NEt (2.5 equiv.). The reaction was stirred at RT for 16 hours. The reaction was diluted with CH_2Cl_2 (10 mL) and washed with 1 M aq. HCl (5 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude material. The crude material was analysis by ^1H NMR spectroscopic analysis to determine NMR yield and dr. Purification by preperative tlc gave a small amount of material suitable for er determination by chiral HPLC (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*R*,4*R*): 8.8 min, t_R (3*S*,4*S*): 9.4 min).

Table 1: Substrate screen

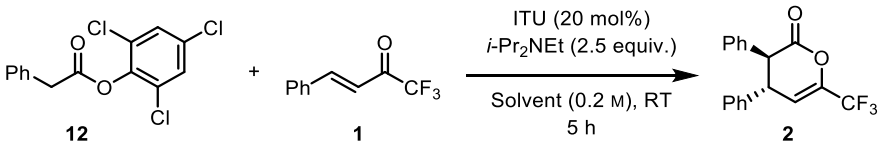


Entry	R	NMR Yield (%)[a]	dr[b]	er[c]
1	4-$NO_2C_6H_4$ **8**	32	87:13	83:17
2	C_6F_5 **9**	26	87:13	85:15
3	3,5- $(CF_3)_2C_6H_3$ **10**	16	88:12	81:19
4	3,4,5-FC_6H_2 **11**	11	87:13	81:19
5	2,4,6-ClC_6H_2 **12**	63	84:16	87:13

<5% conversion

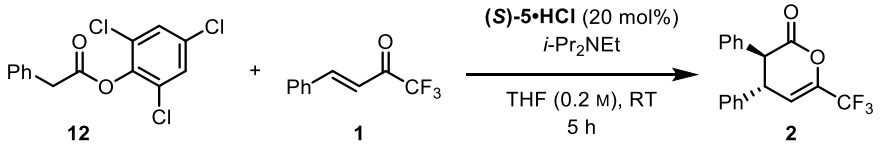


Optimisation Details



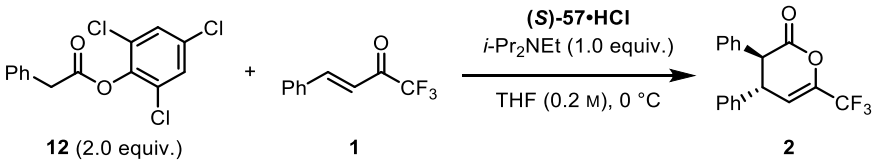
Entry	Solvent	ITU	NMR Yield (%)[a]	dr[b]	er[c]
1	CH_2Cl_2	**(*S*)-5·HCl**	53	87:13	88:12
2	CH_2Cl_2	-	0	n/d	n/d
3	Toluene	**(*S*)-5·HCl**	35	87:13	95:5
4	Et_2O	**(*S*)-5·HCl**	12	86:14	95:5
5	CH_3CN	**(*S*)-5·HCl**	56	91:9	89:11
6	THF	**(*S*)-5·HCl**	55	84:16	97:3
7	THF	**(*R*)-4**	53	86:14	4:96
8	THF	**(2*S*,3*R*)-3**	41	88:12	10:90

Table 1: Results of ITU and solvent screen using **12**. [a] Determined by ^{1}H NMR spectroscopic analysis using 1,4-dinitrobenzene as internal standard. [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] (3*S*,4*S*):(3*R*,4*R*). Determined by chiral HPLC analysis



Entry	*i*-Pr$_2$NEt Equiv.	Ester Equiv.	Yield (%)[a]	dr[b]	er[c]
1	2.5	1.0	95	89:11	96:4
2	1.5	1.0	82	87:13	96:4
3	1.0	1.0	70	89:11	97:3
4	1.0	1.5	72	89:11	96.5:3.5
5	1.0	2.0	95	88:12	96.5:3.5
6[d]	1.0	2.0	95	92:8	98:2
7[d]	1.0	2.0	79[e]	89:11	98:2

Table 2: Results of base and ester equivalency trials. [a] Isolated yield (some phenol present). [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] (3*S*,4*S*):(3*R*,4*R*). Determined by chiral HPLC analysis. [d] Reaction performed at 0 °C for 16 h. [e] Isolated yield (after wash with 1 M NaOH to removed residual phenol contaminant).

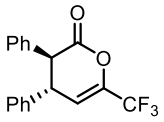


Entry	Catalyst Loading (mol%)	Time (h)	Yield(%)[a]	dr[b]	er[c]
1	20	16	79	89:11	98:2
2	10	48	96	89:11	98:2
3	5	48	76	91:9	95:5

Table 3: Results of ITU loading screen. [a] Isolated yield (after wash with 1 M NaOH). [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] (3*S*,4*S*):(3*R*,4*R*). Determined by chiral HPLC analysis.

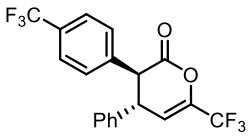
Catalysis Products

(3*S*,4*S*)-3,4-Diphenyl-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 2



Following general procedure F, 2,4,6-trichlorophenyl 2-phenylacetate **12** (126 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **2** (40 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 40 hours gave crude material of 89:11 dr. Purification by flash column chromatography (5% Et$_2$O in hexane) and base wash gave **(3*S*,4*S*)-2** as a white solid (61.3 mg, 0.19 mmol, 96%, 93:7 dr). mp 85–87 °C ($CHCl_3$) {Lit.[17] 90–92 °C}; $[\alpha]_D^{20}$ −210.7 (*c*, CH_2Cl_2) {Lit.[17] (*ent*) $[\alpha]_D^{20}$ +227.2 (*c* 0.25, CH_2Cl_2}; HPLC (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*R*,4*R*): 8.8 min, t_R (3*S*,4*S*): 9.4 min, 2:98 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.88 (1H, d, *J* 8.8, C(3)*H*), 3.94 (1H, ddd, *J* 8.8, 3.7, 2.2, C(4)*H*), 6.05 (1H, d, *J* 3.7, C(5)*H*), 6.95 (2H, dd, *J* 7.6, 1.9, ArC*H*), 7.00 (2H, dd, *J* 7.5, 2.0, ArC*H*), 7.15–7.26 (6H, m, ArC*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F:.–72.1 (C*F*$_3$). Data in accordance with literature.[17]

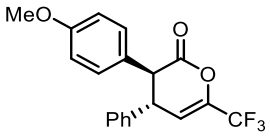
(3*S*,4*S*)-4-Phenyl-6-(trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-pyran-2-one 14



Following general procedure F, 2,4,6-trichlorophenyl 2-(4-(trifluoromethyl)phenyl)acetate **S6** (153 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 1.0 mmol) in THF (1 mL) at 0 °C for 2 days gave crude material of 88:12 dr. Purification by flash column chromatography (5% Et$_2$O in hexane) and base wash gave **(3*S*,4*S*)-14** as a white solid (50 mg, 0.15 mmol, 75%, 86:14 dr). mp 114–115 °C ($CHCl_3$) {Lit.[17] 90–92 °C}; $[\alpha]_D^{20}$ +134.0 (*c* 0.25, CH_2Cl_2) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −153.6 (*c* 0.125, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 2% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*S*,4*S*): 13.5 min, t_R (3*R*,4*R*): 15.3 min, 90:10 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.92–3.97 (2H, m, C(3)*H* and C(4)*H*), 6.08 (1H, d, *J* 2.5, C(5)*H*), 6.88–6.95 (2H, m, C(4)ArC*H*), 7.10 (2H, d, *J* 8.1, C(3)ArC(2,6)*H*), 7.15–7.24 (3H, m, C(4)ArC*H*),

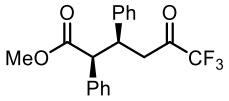
7.48 (2H, d, *J* 8.1, C(3)ArC(3,5)*H*); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ_F: −72.1 (C(6)CF_3), −62.8 (C(3)ArC(4)F_3). Data in accordance with literature.[17]

(3*S*,4*S*)-3-(4-Methoxyphenyl)-4-phenyl-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 15



Following general procedure F, 2,4,6-trichlorophenyl 2-(4-(methoxy)phenyl)acetate **S7** (138 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr_2NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 3 days gave crude material of dr 90:10. Purification by flash column chromatography (5% Et_2O in hexane) and base wash gave **(3*S*,4*S*)-15** as a white solid (34 mg, 0.1 mmol, 50%, 94:6 dr). mp 92–94 °C ($CHCl_3$) {Lit.[17] 90–92 °C}; $[\alpha]_D^{20}$ +182.8 (*c* 1.0, CH_2Cl_2) {Lit.[17] (*ent*) $[\alpha]_D^{20}$ −199.5 (*c* 0.2, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 2% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*R*,4*R*): 21.7 min, t_R (3*S*,4*S*): 23.1 min, 95:5 er; ^{1}H NMR δ_H (400 MHz, $CDCl_3$) 3.69 (3H, s, OCH_3), 3.83 (1H, d, *J* 9.1, C(3)*H*), 3.91 (1H, ddd, *J* 9.1, 3.6, 2.3, C(4)*H*), 6.05 (1H, d, *J* 3.6, C(5)*H*), 6.74 (2H, d, *J* 8.7, C(3)ArC(2,6)*H*), 6.88–6.93 (2H, m, C(3)ArC(3,5)*H*), 6.95 (2H, dd, *J* 7.7, 1.8, C(4)ArC*H*), 7.16–7.23 (3H, m, C(3)ArC*H*);$^{19}F\{^{1}H\}$ NMR (377 MHz, $CDCl_3$) δ_F: −72.2 (CF_3). Data in accordance with literature.[17]

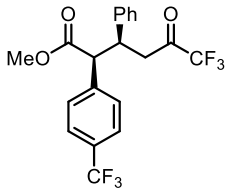
Methyl (2*S*,3*S*)-6,6,6-trifluoro-5-oxo-2,3-diphenylhexanoate 16



Following general procedure G, 2,4,6-trichlorophenyl 2-phenylacetate **12** (125 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr_2NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 2 days gave crude material of dr 88:12. Purification by flash column chromatography (15% Et_2O in hexane) and base wash gave **(2*S*,3*S*)-16** as a white solid (61 mg, 0.17 mmol, 86%, 94:6 dr). mp 83–84 °C ($CHCl_3$) {Lit.[18] 62–64 °C}; $[\alpha]_D^{20}$ +103.2 (*c* 1.00, CH_2Cl_2) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −90.4 (*c* 0.45, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 4.7 min, t_R (2*R*,3*R*): 5.2 min, 97:3 er; ^{1}H NMR δ_H: (400 MHz, $CDCl_3$) 3.08 (1H, dd, *J* 18.3, 3.8, C(4)*H*H), 3.27 (1H, dd, *J* 18.4, 9.6, C(4)*H*H), 3.61 (3H, s, OCH_3), 3.79 (1H, d, *J* 10.6, C(2)*H*), 3.88 (1H, td, *J* 10.0, 3.8, C(3)*H*), 6.88–6.96 (2H, m, ArC*H*), 6.97–7.13

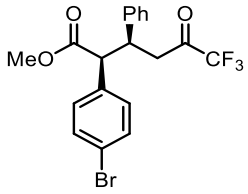
(8H, m, ArC*H*).; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ_F:.–79.5 (C(6)F_3). Data in accordance with literature.[18]

Methyl (2*S*,3*S*)-6,6,6-trifluoro-5-oxo-3-phenyl-2-(4-(trifluoromethyl)phenyl)hexanoate 17



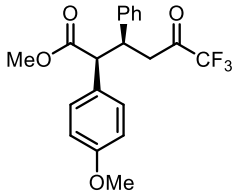
Following general procedure G, 2,4,6-trichlorophenyl 2-(4-(trifluoromethyl)phenyl)acetate **S6** (153 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr_2NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 2 days gave crude material of 89:11 dr. Purification by flash column chromatography (15% Et_2O in hexane) and base wash gave **(2*S*,3*S*)-17** as a white solid (64 mg, 0.15 mmol, 77%, 88:12 dr). mp 108–111 °C ($CHCl_3$); $[\alpha]_D^{20}$ +70.4 (*c* 0.25, CH_2Cl_2); HPLC (Chiralpak AD-H, 2% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 5.7 min, t_R (2*R*,3*R*): 6.3 min, 93:7 er; ν_{max} (film, cm^{-1}) 2961 (C-H), 1757 (C=O), 1732 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.08 (1H, dd, *J* 18.4, 3.4, C(4)*H*H), 3.26 (1H, dd, *J* 18.4, 8.5, C(4)H*H*), 3.64 (3H, s, OCH_3), 3.86 (1H, d, *J* 10.9, C(2)*H*), 3.90 (1H, dd, *J* 10.9, 7.0, C(3)*H*), 6.92 (2H, d, *J* 7.7, C(2)ArC(2,6)*H*), 7.04 (3H, app. dd, *J* 12.2, 6.9, C(3)ArC*H*), 7.12–7.20 (2H, m, C(3)ArC*H*), 7.34 (2H, d, *J* 7.7, C(2)ArC(3,5)*H*).; $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ_F: −79.5 (C(6)F_3), −62.7 (ArCF_3); ^{13}C NMR: (101 MHz, $CDCl_3$) δ_C: 41.1 (*C*(4)), 43.4 (*C*(3)), 52.7 (CH_3), 56.9 (*C*(2)), 115.4 (*C*(6)F_3) 123.9 (q, *J* 273.3, C(2)ArC(4)CF_3), 125.4 (q, *J* 4.4, C(2)Ar*C*(3,5)H), 127.7 (C(3)Ar*C*(4)H), 128.0 (C(3)Ar*C*(3,5)H), 128.7 (C(2)Ar*C*(2,6)H), 129.0 (C(3)Ar*C*(2,6)H), 130.1 (q, *J* 33.0 C(2)Ar*C*(4)CF_3), 139.0 C(2)Ar*C*(1)), 140.3 (C(3)Ar*C*(1)), 172.5 (*C*(1)=O), 188.9 (q, *J* 35.5, *C*(5)=O); HRMS (NSI^+) $C_{20}H_{20}F_6NO_3$ $[M+NH_4]^+$ found 436.1343, requires 436.1342 (+0.3 ppm). Selected data for minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.61 (1H, dd, *J* 18.4, 3.5, C(4)*H*H), 2.91 (1H, dd, *J* 18.2, 9.5, C(4)H*H*), 7.50 (2H, d, *J* 8.1, C(2)ArC(2,6)*H*), 7.58 (2H, d, *J* 8.1, C(2)ArC(3,5)*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: .40.3 (*C*(4)), 43.3 (*C*(3)), 52.3 (CH_3), 57.8 (*C*(2)).

Methyl (2*S*,3*S*)-2-(4-bromophenyl)-6,6,6-trifluoro)-5-oxo-3-phenylhexanoate 18



Following general procedure G, 2,4,6-trichlorophenyl 2-(4-bromophenyl)acetate **S8** (138 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 4 days gave crude material of 83:17 dr. Purification by flash column chromatography (15% Et$_2$O in hexane) and base wash gave **(2*S*,3*S*)-18** as a white solid (62 mg, 0.15 mmol, 73%, 91:9 dr). mp 86–88 °C {Lit.[18] 62–64 °C}; $[\alpha]_D^{20}$ +101.0 (*c* 1.00, CH_2Cl_2) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −118.5 (*c* 0.15, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 5.4 min, t_R (2*R*,3*R*): 6.3 min, 97:3 er; ^{1}H NMR δ_H: (400 MHz, $CDCl_3$) 3.05 (1H, dd, *J* 18.3, 4.0, C(4)*H*H), 3.24 (1H, dd, *J* 18.3, 9.4, C(4)H*H*), 3.62 (3H, s, C*H*$_3$), 3.76 (1H, d, *J* 10.8, C(2)*H*), 3.85 (1H, td, *J* 10.0, 4.0, C(3)*H*), 6.86–6.94 (4H, m, C(2)C(2,6)*H* + C(3)ArC*H*), 6.99–7.12 (3H, m, C(3)ArC*H*), 7.16–7.23 (2H, m, C(2)C(3,5)*H*); ^{19}F{^{1}H} NMR (377 MHz, $CDCl_3$) δ_F: −79.5 (C(6)*F*$_3$). Data in accordance with literature.[18]

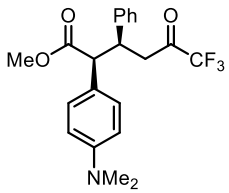
Methyl (2*S*,3*S*)-6,6,6-trifluoro-2-(4-methoxyphenyl)-5-oxo-3-phenylhexanoate 19



Following general procedure G, 2,4,6-trichlorophenyl 2-(4-methoxy)acetate **S7** (158 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 4 days gave crude material of 94:6 dr. Purification by flash column chromatography (20% Et$_2$O in hexane) and base wash gave **(2*S*,3*S*)-19** as a white solid (62 mg, 0.15 mmol, 73%, 90:10 dr). mp 78–80 °C {Lit.[18] 112–114 °C}; $[\alpha]_D^{20}$ +128.0 (*c* 1.00, CH_2Cl_2) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −125.2 (*c* 0.5, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 254 nm, 30 °C): t_R (2*S*,3*S*): 5.74 min, t_R (2*R*,3*R*): 6.8 min, 97:3 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.05 (1H, dd, *J* 18.3, 3.8, C(4)*H*H), 3.26 (1H, dd, *J* 18.3, 9.6, C(4)H*H*), 3.60 (3H, s, C*H*$_3$), 3.64 (3H, s, C*H*$_3$), 3.74 (1H, d, *J* 10.5, C(2)*H*), 3.84 (1H, td, *J* 10.0, 3.8, C(3)*H*), 6.58–6.65 (2H, m,

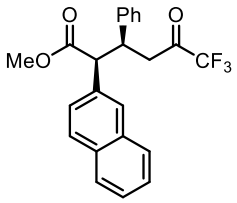
C(2)ArC(3,5)*H*), 6.90–6.96 (4H, m, C(2)ArC(2,6)*H* + C(3)ArC*H*), 6.98–7.03 (1H, m, C(3)ArC(4)*H*), 7.04–7.11 (2H, m, C(3)Ar(3,5)C*H*); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ_F: −79.5 (C(6)F_3). Data in accordance with literature.[21]

Methyl (2*S*,3*S*)-2-(4-(dimethylamino)phenyl)-6,6,6-trifluoro-5-oxo-3-phenylhexanoate 20



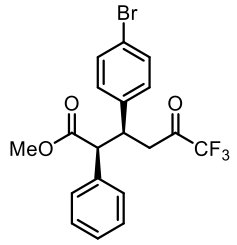
Following general procedure G, 2,4,6-trichlorophenyl 2-(4-(dimethylamino)phenyl)acetate **S9** (143 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr_2NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 5 days gave the crude material (dr could not be determined through ^{1}H NMR spectroscopic analysis). Purification by flash column chromatography (20% Et_2O in hexane) and base wash gave **(2*S*,3*S*)-20** as an off-white solid (41 mg, 0.10 mmol, 51%, 82:18 dr). mp 95–96 °C ($CHCl_3$); $[\alpha]_D^{20}$ +128.3 (*c* 0.30, CH_2Cl_2); HPLC (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 254 nm, 30 °C): t_R (2*S*,3*S*): 6.8 min, t_R (2*R*,3R): 7.4 min, 99:1 er; ν_{max} (film, cm^{-1}) 2951 (C-H), 1759 (C=O), 1726 (C=O), 1614 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.87 (6H, s, N(CH_3)$_2$), 3.15 (1H, d, *J* 18.2, 3.9, C(4)*H*H), 3.38 (2H, dd, *J* 18.2, 10.1, C(4)H*H*), 3.66 (3H, s, OCH_3), 3.82 (1H, d, *J* 10.1, C(2)*H*), 3.91 (1H, td, *J* 10.1, 3.9, C(3)*H*), 6.54 (2H, d, *J* 8.5, C(2)ArC(3,5)*H*), 7.00 (2H, d, *J* 8.5, C(2)ArC(2,6)*H*), 7.02–7.09 (2H, m, C(3)ArC(2,6)*H*), 7.07–7.16 (1H, m, C(3)ArC(4)*H*), 7.14–7.23 (2H, m, C(3)ArC(3,5)*H*); $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) δ_F: −79.5 (C(6)F_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 40.7 (N(*C*H_3)$_2$), 40.8 (*C*(4)), 43.5 (*C*(3)), 52.3 (O*C*H_3), 56.2 (*C*(2)), 112.7 (C(2)Ar*C*(3,5)H), 115.3 (q, *J* 292.0, *C*(6)F_3), 127.1 (C(3)Ar*C*(4)H), 128.1 (C(3)Ar*C*(3,5)H), 128.5 (C(2)Ar*C*(4)), 128.5 (C(2)Ar*C*(2,6)H), 129.3 (C(3)Ar*C*(2,6)H), 140.0 (C(3)Ar*C*(1)), 149.6 (C(2)Ar*C*(4)N(*C*H_2)$_3$), 173.7 (*C*(1)=O), 189.5 (q, *J* 35.2 *C*(5)=O); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: –79.5 (*C*F_3). HRMS (NSI$^+$) $C_{21}H_{23}F_3NO_3$ $[M+H]^+$ found 394.1619, requires 394.1625 (−1.4 ppm). Selected data for minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 6.72 (2H, d, *J* 8.3, C(2)ArC(3,5)*H*), 7.27–7.37 (5H, m, Ar*H*).

Methyl (2*S*,3*S*)-6,6,6-trifluoro-2-(naphthalen-2-yl)-5-oxo-3-phenylhexanoate 21



Following general procedure G, 2,4,6-trichlorophenyl 2-(naphthalen-2-yl)acetate **S10** (146 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **1** (40 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 2 days gave crude material of 92:8 dr. Purification by flash column chromatography (20% Et$_2$O in hexane) and base wash gave **(2*S*,3*S*)-21** as a white solid (58 mg, 0.14 mmol, 72%, 91:9 dr). mp 100–102 °C {Lit.[18] 86–90 °C}; $[\alpha]_D^{20}$ +123.4 (*c* 0.50, CH_2Cl_2) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −183.7 (*c* 0.3, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 1% IPA/hexane, 0.5 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 12.6 min, t_R (2*R*,3*R*): 15.1 min, 97.3 er; ^{1}H NMR δ_H (500 MHz, $CDCl_3$) 3.12 (1H, dd, *J* 18.3, 3.5, C(4)*H*H), 3.32 (1H, dd, *J* 18.3, 9.1, C(4)H*H*), 3.60 (3H, s, C*H*$_3$), 3.98 (1H, d, *J* 10.4, C(2)*H*), 4.02 (1H, td, *J* 10.4, 9.1, 3.5, C(3)*H*), 6.91–7.04 (5H, m, ArC*H*), 7.18 (1H, d, *J* 8.3, ArC*H*), 7.31–7.36 (2H, m, ArC*H*), 7.50 (1H, s, ArC*H*), 7.57 (1H, d, *J* 8.5, ArC*H*), 7.60–7.67 (2H, m, ArC*H*); ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ_F: −79.5 (C*F*$_3$). Data in accordance with literature.[18]

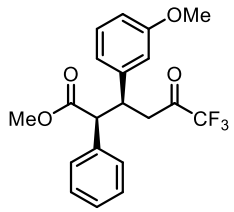
Methyl (2*S*,3*S*)-3-(4-bromophenyl)-6,6,6-trifluoro-5-oxo-2-phenylhexanoate 22



Following general procedure G, 2,4,6-trichlorophenyl 2-phenylacetate **12** (126 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **13** (56 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 3 days gave crude material of 90:10 dr. Purification by flash column chromatography (20% Et$_2$O in hexane) and base wash gave **(2*S*,3*S*)-22** as a white solid (60 mg, 0.14 mmol, 69%, 94:6 dr). mp 55–56 °C; $[\alpha]_D^{20}$ +92.1 (*c* 1.00, CH_2Cl_2); HPLC (Chiralpak OD-H, 1% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*R*,3*R*): 6.2 min, t_R (2*S*,3*S*): 6.7 min, 95:5 er; ν_{max} (film, cm^{-1}) 2963 (C-H), 1765 (C=O), 1728 (C=O), 1198, 1142, 1011; ^{1}H NMR (400 MHz,

$CDCl_3$) δ_H: 3.07 (1H, dd, *J* 18.5, 3.8, C(4)*H*H), 3.23 (1H, dd, *J* 18.5, 10.0, C(4)H*H*), 3.61 (3H, s, CH_3), 3.74 (1H, d, *J* 10.6, C(2)*H*), 3.85 (1H, td, *J* 10.0, 3.8, C(3)*H*), 6.79–6.85 (2H, m, C(3)ArC(2,6)*H*), 6.99–7.04 (2H, m, C(2)ArC(2,6)*H*), 7.05–7.13 (3H, m, C(2)ArC(3,4,5)*H*), 7.15–7.20 (2H, m, C(3)ArC(2,6)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: –79.5 (CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 40.7 (*C*(4)H_2) , 43.0 (*C*(3)H), 52.5 (*C*H_3), 56.8 (*C*(2)H), 115.4 (q, *J* 292.0, *C*(6)F_3), 121.1 (C(3)Ar*C*(4)Br), 127.9 (C(2)Ar*C*(4)H), 128.5 (C(2)Ar(3,5)*C*H), 128.8 (C(2)Ar(2,6)*C*H), 129.8 (C(3)Ar*C*(2,6)H), 131.6 (C(3)Ar*C*(3,5)H), 135.9 (C(3)Ar*C*(1)), 138.7 (C(2)Ar*C*(1)), 173.0 (*C*(1)=O), 189.1 (q, *J* 35.8, *C*(5)=O); HRMS (NSI$^+$) $C_{20}H_{20}F_6NO_3$ $[M+H]^+$ found 429.0308, requires 429.0308 (+0.0 ppm). Selected data for minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.08 (1H, dd, *J* 15.0, 2.8), 2.37 (1H, dd, *J* 14.9, 7.2), 2.62 (1H, dd, *J* 18.5, 3.5, C(4)H*H*), 2.83 (1H, dd, *J* 18.5, 10.3, C(4)H*H*), 6.85–6.95 (2H, m, ArC(2,6)*H*), 7.25–7.45 (2H, m, Ar*H*).

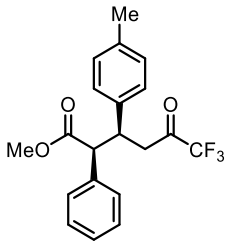
Methyl (2*S*,3*S*)-6,6,6-trifluoro-3-(3-methoxyphenyl)-5-oxo-2-phenylhexanoate 23



Following general procedure G, 2,4,6-trichlorophenyl 2-phenylacetate **12** (126 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **S15** (46 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 3 days gave crude material of 90:10 dr. Purification by flash column chromatography (20% Et_2O in hexane) and base wash gave **(2*S*,3*S*)-23** as a colourless oil (66 mg, 0.17 mmol, 86%, 90:10 dr).)}; $[\alpha]_D^{20}$ +85.3 (*c* 1.00, CH_2Cl_2); HPLC (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 5.5 min, t_R (2*R*,3*R*): 6.6 min, 94:6 er (minor diastereomer: t_R 7.1 min, 9.8 min, 85:15 er); ν_{max} (film, cm^{-1}) 2955 (C-H), 1765 (C=O), 1728 (C=O), 1140; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 3.13 (1H, dd, *J* 18.3, 3.8, C(4)*H*H), 3.35 (1H, dd, *J* 18.3, 9.6, C(4)H*H*), 3.66 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 3.84 (1H, d, *J* 10.5, C(2)*H*), 3.92 (1H, td, *J* 10.2, 3.9, C(3)*H*), 6.51 (1H, t, *J* 2.1, C(3)ArC(2)*H*), 6.57–6.65 (2H, m, ArC(3)Ar(3,6)*H*), 7.02–7.07 (1H, m, C(3)ArC(5)*H*), 7.12 (2H, dd, *J* 7.6, 2.0, C(2)ArC(2,6)*H*), 7.13–7.19 (3H, m, C(2)ArC(3,4,5)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: –79.4 (CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 40.8 (*C*(4)H_2), 43.6 (*C*(3)H), 52.5 (OCH_3), 55.2 (ArOCH_3), 57.1 (*C*(3)H), 112.5 (C(3)Ar*C*(4)H), 114.2 (C(3)Ar*C*(2)H), 115.4 (q, *J* 292.2, *C*(6)F_3) 120.2 (C(3)Ar*C*(6)H), 127.7 (C(2)Ar*C*(4)H), 128.5 (C(2)Ar*C*H), 128.6

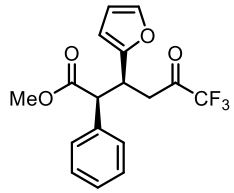
(C(2)ArCH), 129.5 (C(3)Ar*C*(5)H), 136.3 (C(2)Ar*C*(1)), 141.2 (C(3)Ar*C*(1)), 159.5 (C(2)Ar*C*(3)), 173.2 (*C*(1)=O), 189.2 (q, *J* 35.5, *C*(5)=O); HRMS (NSI$^+$) $C_{20}H_{20}F_3O_4$ $[M+H]^+$ found 381.1310, requires 381.1308 (+0.5 ppm). Selected data for minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.69 (1H, dd, *J* 18.3, 3.6, C(4)*H*H), 2.93 (1H, dd, *J* 18.3, 10.0, C(4)H*H*), 4.02 (1H, td, *J* 10.8, 3.6 ,C(3)*H*), 6.78 (1H, ddd, *J* 8.2, 2.6, 0.9, C(3)ArC(2)*H*), 6.84 (1H, t, *J* 2.1, Ar*H*), 6.89 (1H, dt, *J* 7.7, 1.2, Ar*H*), 7.32–7.46 (5H, m, Ar*H*); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C: 40.5 (*C*(4)H_2), 43.1 (*C*(3)H), 52.2 (OCH_3), 55.4 (ArOCH_3).

Methyl (2*S*,3*S*)-6,6,6-trifluoro-5-oxo-2-phenyl-3-(p-tolyl)hexanoate 24



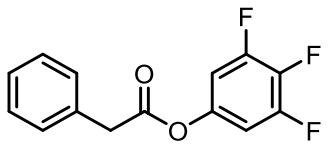
Following general procedure G, 2,4,6-trichlorophenyl 2-phenylacetate **12** (126 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **S17** (43 mg, 0.2 mmol) and *i*-Pr_2NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 3 days gave crude material of 89:11 dr. Purification by flash column chromatography (10 to 20% Et_2O in hexane) and base wash gave **(2*S*,3*S*)-24** as a white solid (45 mg, 0.12 mmol, 62%, 90:10 dr). mp 72–73 °C {Lit.[18] oil}; $[\alpha]_D^{20}$ +94.9 (*c* 1.00, $CHCl_3$) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −105.6 (*c* 0.1, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 4.9 min, t_R (2*R*,3*R*): 5.2 min, 96:4 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.20 (3H, s, ArCH_3), 3.12 (1H, dd, *J* 18.3, 3.8, C(4)*H*H), 3.34 (1H, dd, *J* 18.3, 9.4, C(4)*H*H), 3.68 (3H, s, OCH_3), 3.86 (1H, d, *J* 10.4, C(3)*H*), 3.92 (1H, td, *J* 10.0, 3.8, C(2)*H*), 6.89 (2H, d, *J* 8.2, C(3)ArC(3,5)*H*), 6.93 (2H, d, *J* 8.2, C(3)ArC(2,6)*H*), 7.06–7.21 (5H, m, C(2)Ar*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: –79.5 (CF_3). Data in accordance with literature.[21]

Methyl (2*S*,3*S*)-6,6,6-trifluoro-3-(furan-2-yl)-5-oxo-2-phenylhexanoate 25



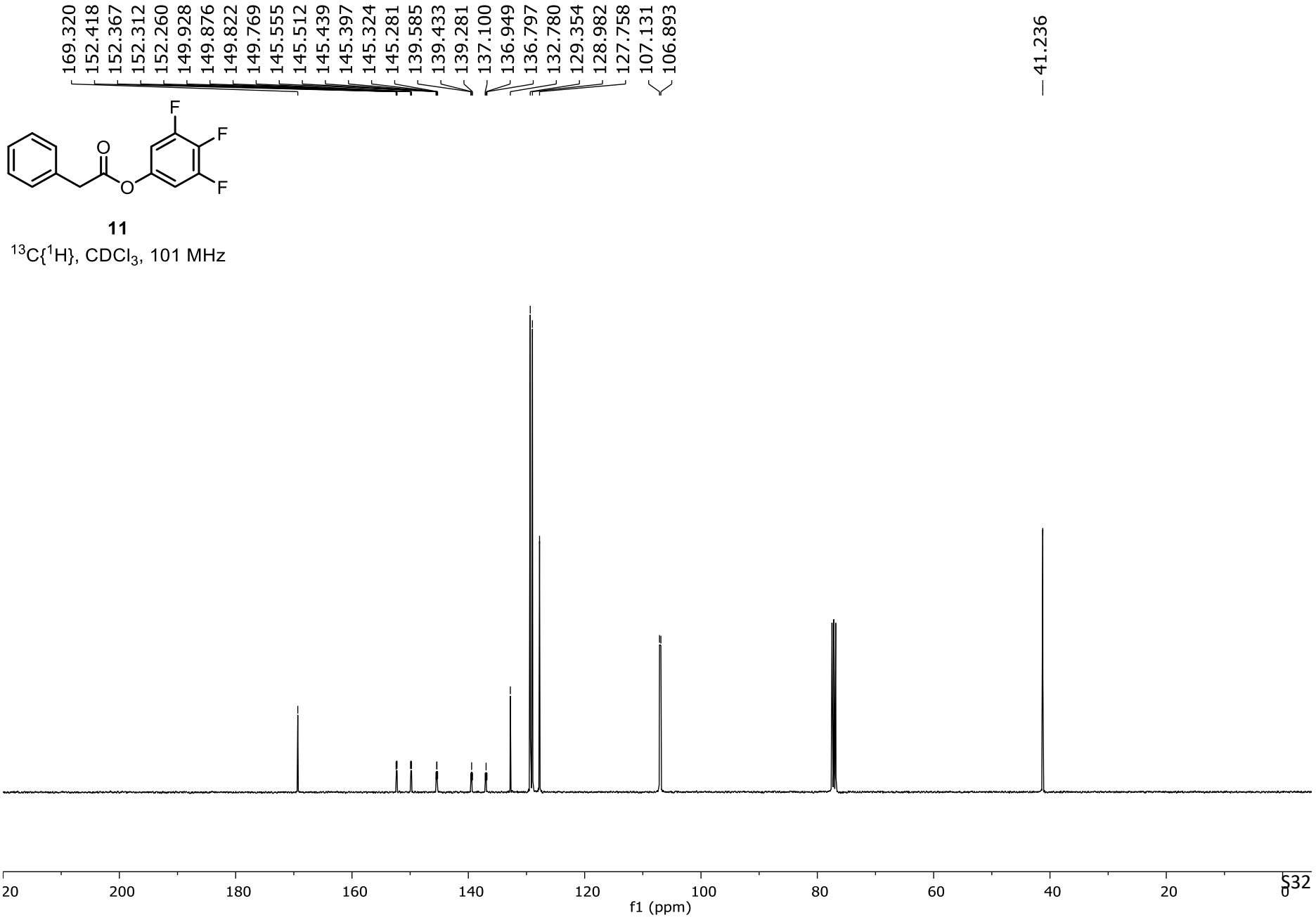
Following general procedure G, 2,4,6-trichlorophenyl 2-phenylacetate **12** (126 mg, 0.4 mmol), **(*S*)-5·HCl** (4.8 mg, 0.02 mmol), enone **S20** (38 mg, 0.2 mmol) and *i*-Pr$_2$NEt (35 μL, 0.2 mmol) in THF (1 mL) at 0 °C for 3 days gave crude material of 71:29 dr. Purification by flash column chromatography (20% Et$_2$O in hexane) and base wash gave **(2*S*,3*S*)-25** as a white solid (47 mg, 0.14 mmol, 69%, 76:24 dr). mp 80–82 °C {Lit.[18] 48–50 °C}; $[\alpha]_D^{20}$ +41.1 (*c* 1.00, CH_2Cl_2) {Lit.[18] (*ent*) $[\alpha]_D^{20}$ −89.8 (*c* 0.6, CH_2Cl_2)}; HPLC (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 4.6 min, t_R (2*R*,3*R*): 5.0 min, 98:2 er; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.96 (1H, dd, *J* 18.3, 3.7, C(4)*H*H), 3.29 (1H, dd, *J* 18.3, 9.4, C(4)H*H*), 3.62 (3H, s, OC*H*$_3$), 3.93 (1H, d, *J* 9.9, C(2)*H*), 4.00 (1H, dt, *J* 3.8, 9.8, C(3)*H*), 5.72 (1H, d, *J* 3.2, C(3)ArC(3)*H*), 6.00 (1H, dd, *J* 3.3, 1.9, C(3)ArC(4)*H*), 6.99–7.09 (2H, m, ArC*H*), 7.09–7.19 (4H, m, ArC*H*); ^{19}F NMR (376 MHz, $CDCl_3$) –79.4 (C*F*$_3$). Data in accordance with literature.[18]

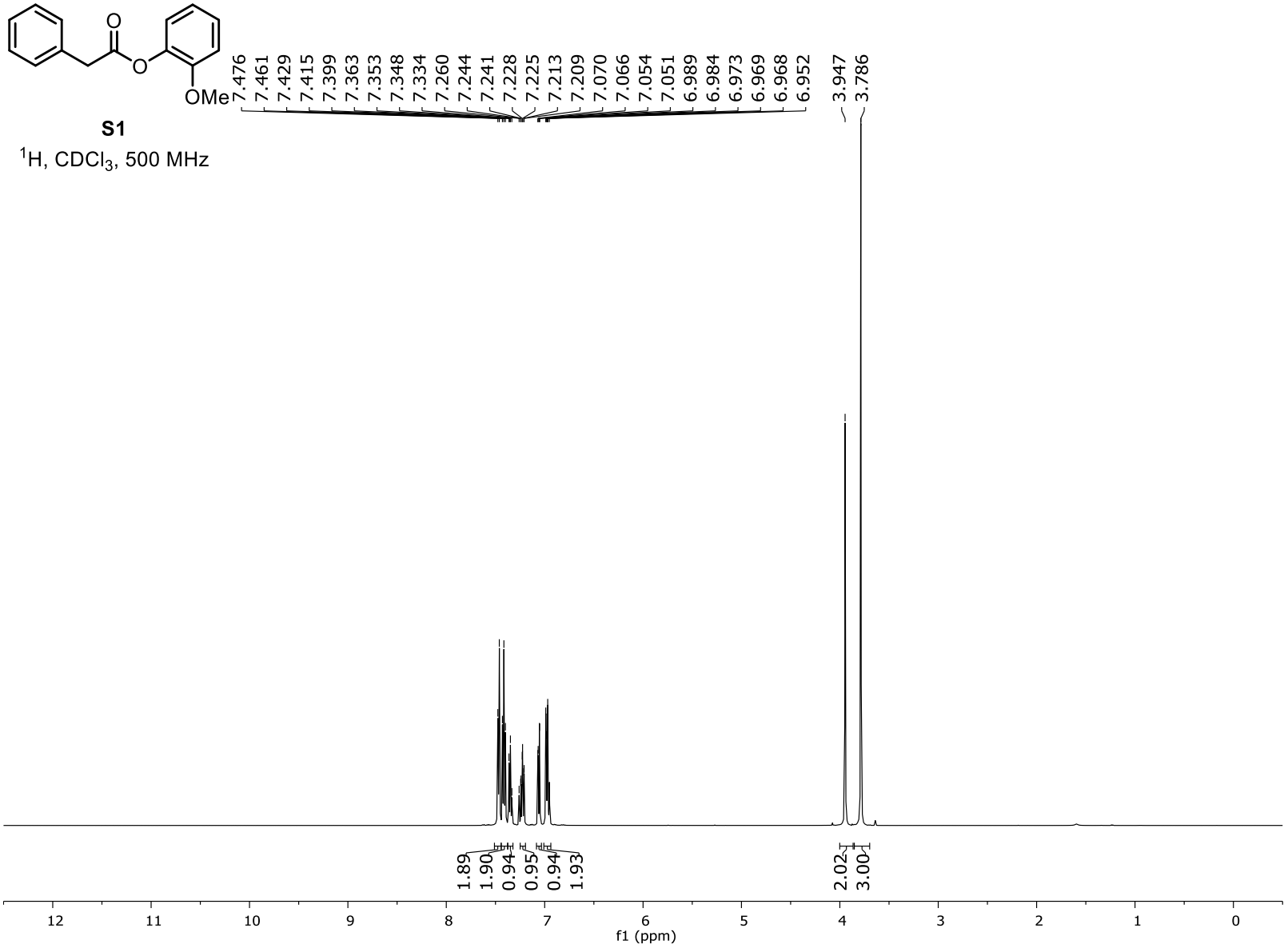
^{1}H NMR and ^{13}C {^{1}H} NMR Spectra



11

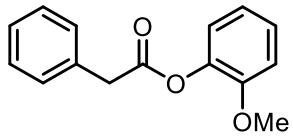
^{1}H, $CDCl_3$, 400 MHz


169.320
152.418
152.367
152.312
152.260
149.928
149.876
149.822
149.769
145.555
145.512
145.439
145.397
145.324
145.281
139.585
139.433
139.281
137.100
136.949
136.797
132.780
129.354
128.982
127.758
107.131
106.893
41.236
F
F
F
O
O
11
13C{1H}, CDCl3, 101 MHz
20
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



S1

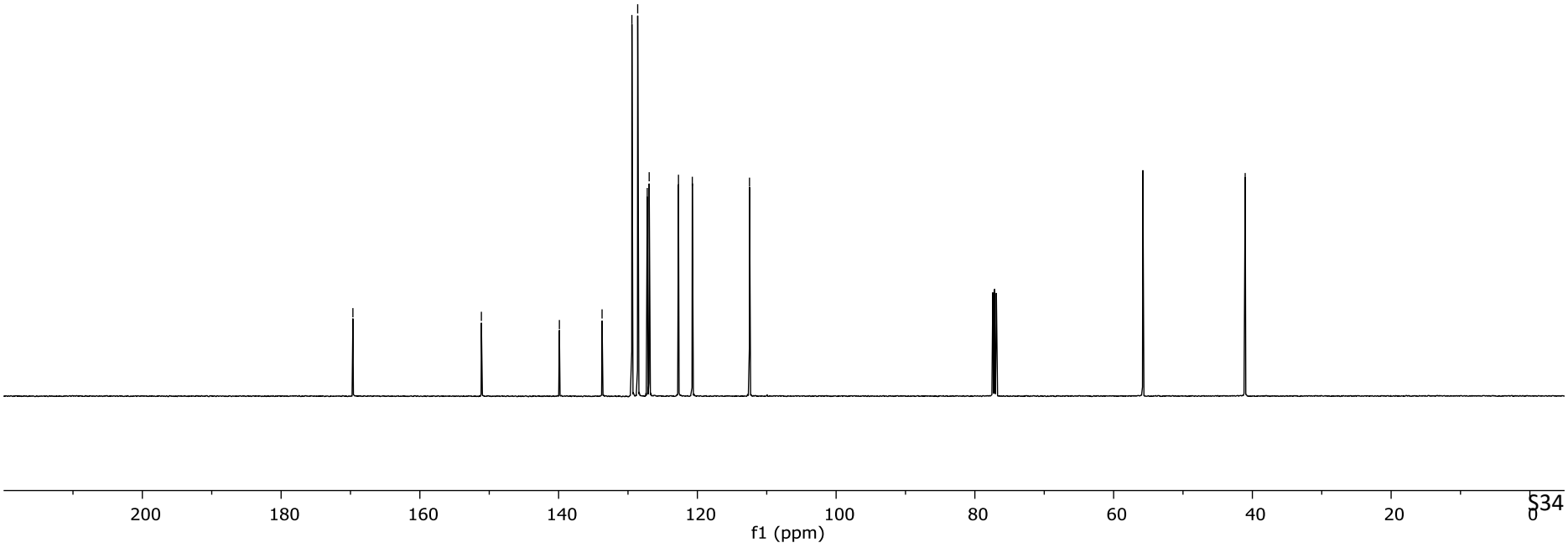
^{1}H, $CDCl_3$, 500 MHz

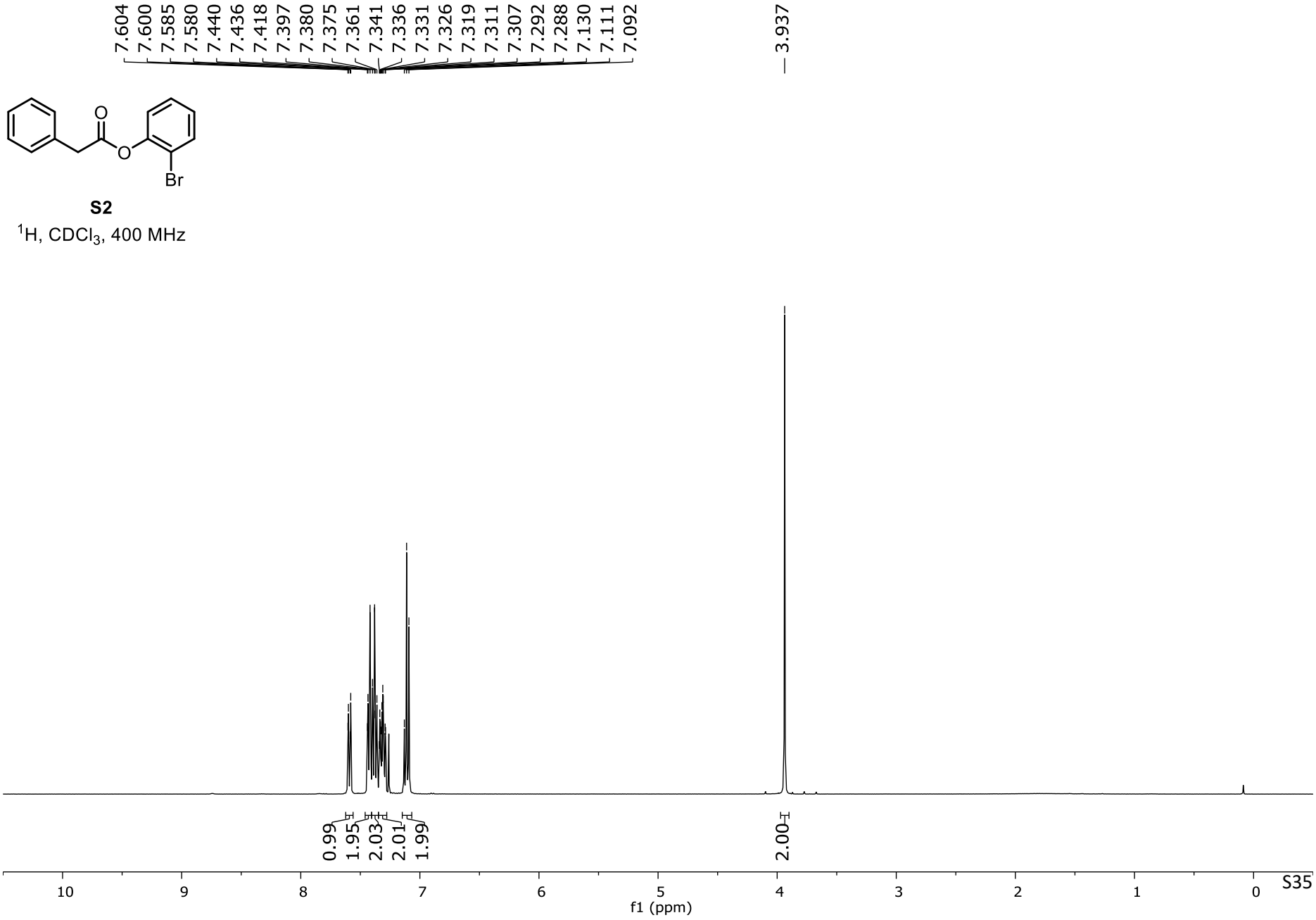


S1

$^{13}C\{^{1}H\}$, $CDCl_3$, 126 MHz

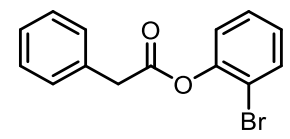
169.651
151.132
139.889
133.735
129.437
128.602
127.224
126.944
122.724
120.730
112.485
55.789
41.036





S2

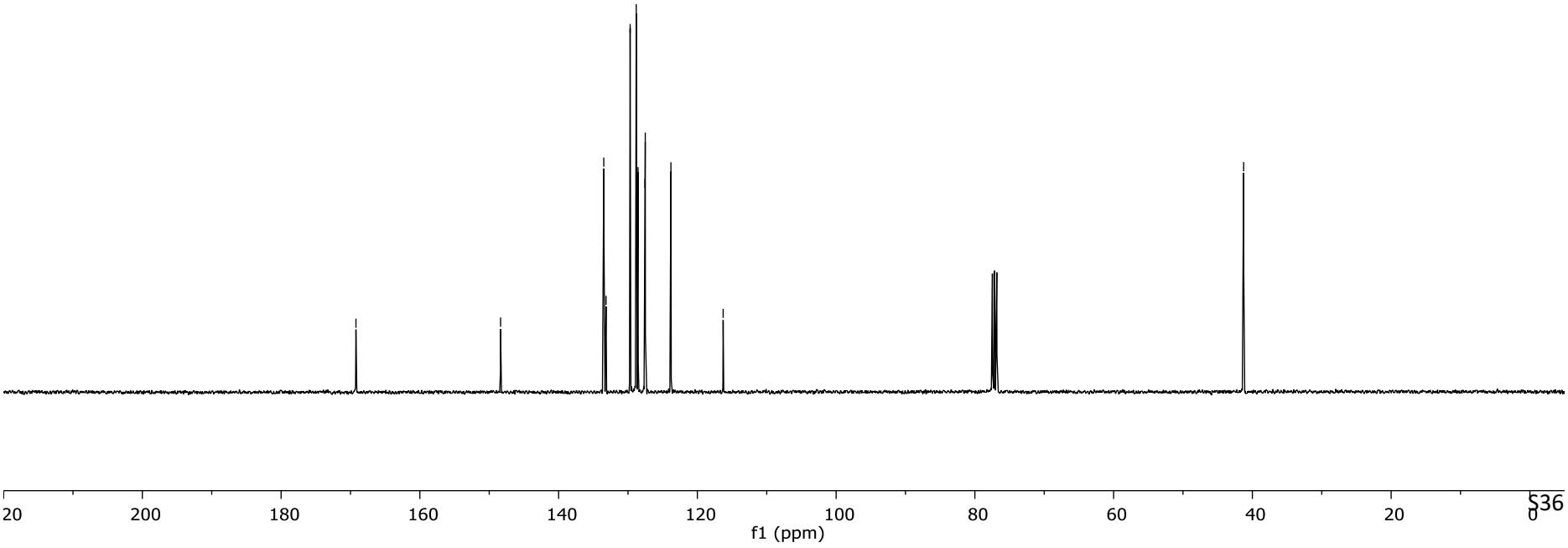
^{1}H, $CDCl_3$, 400 MHz

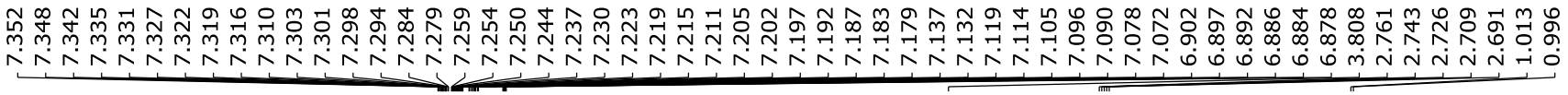


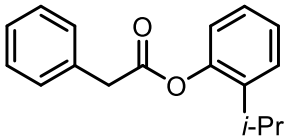
S2

$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz

169.212
148.364
133.489
133.163
129.689
128.810
128.551
127.558
127.510
123.813
116.281
41.261

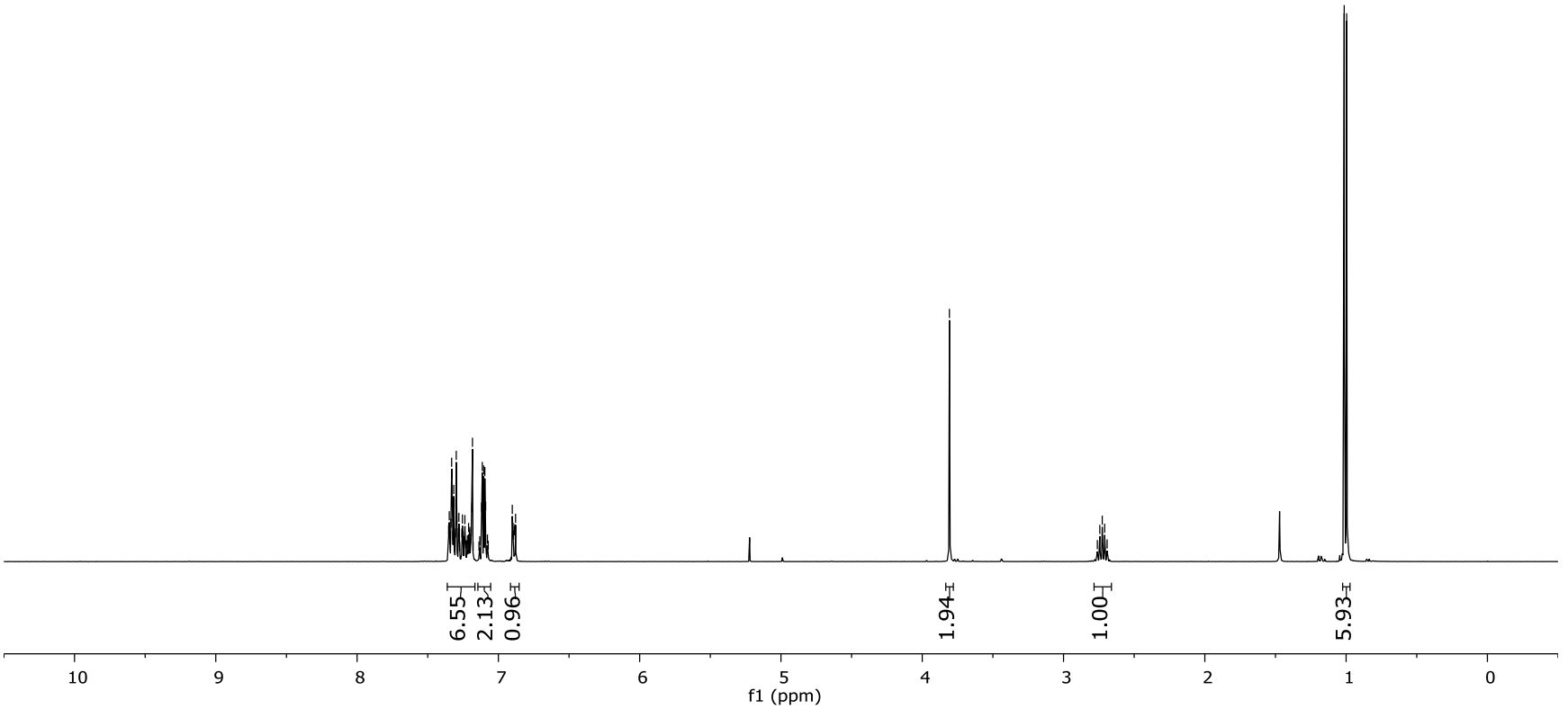


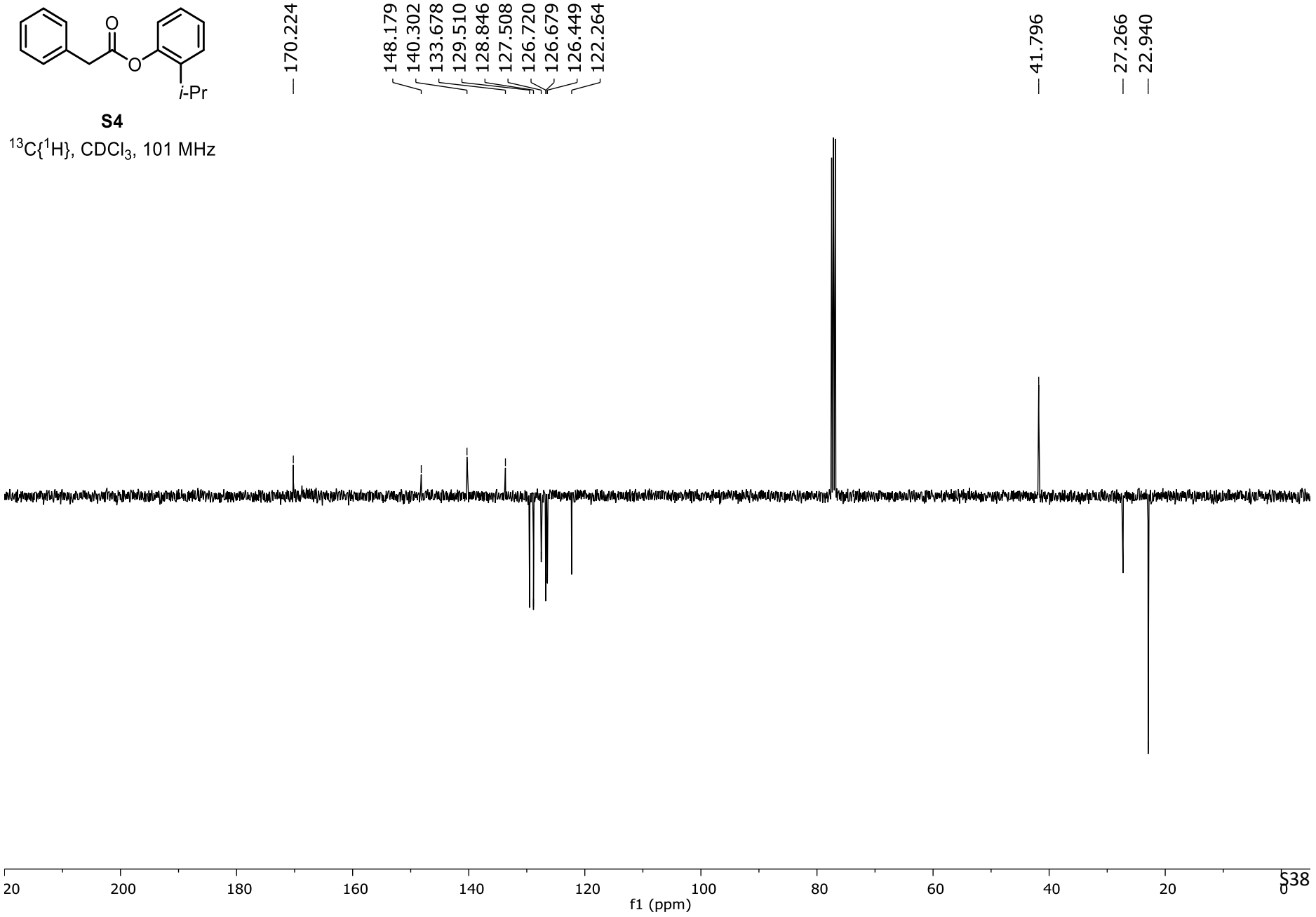


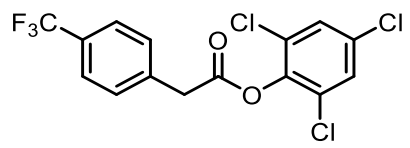


S4

^{1}H, $CDCl_3$, 400 MHz

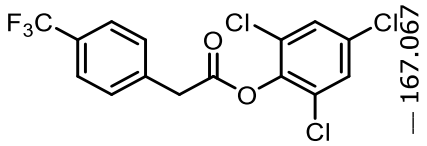


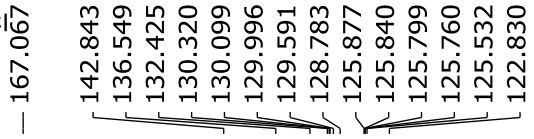

O
O
i-Pr
170.224
148.179
140.302
133.678
129.510
128.846
127.508
126.720
126.679
126.449
122.264
41.796
27.266
22.940
S4
13C{1H}, CDCl3, 101 MHz
20
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

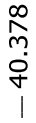


S6

^{1}H, $CDCl_3$, 400 MHz

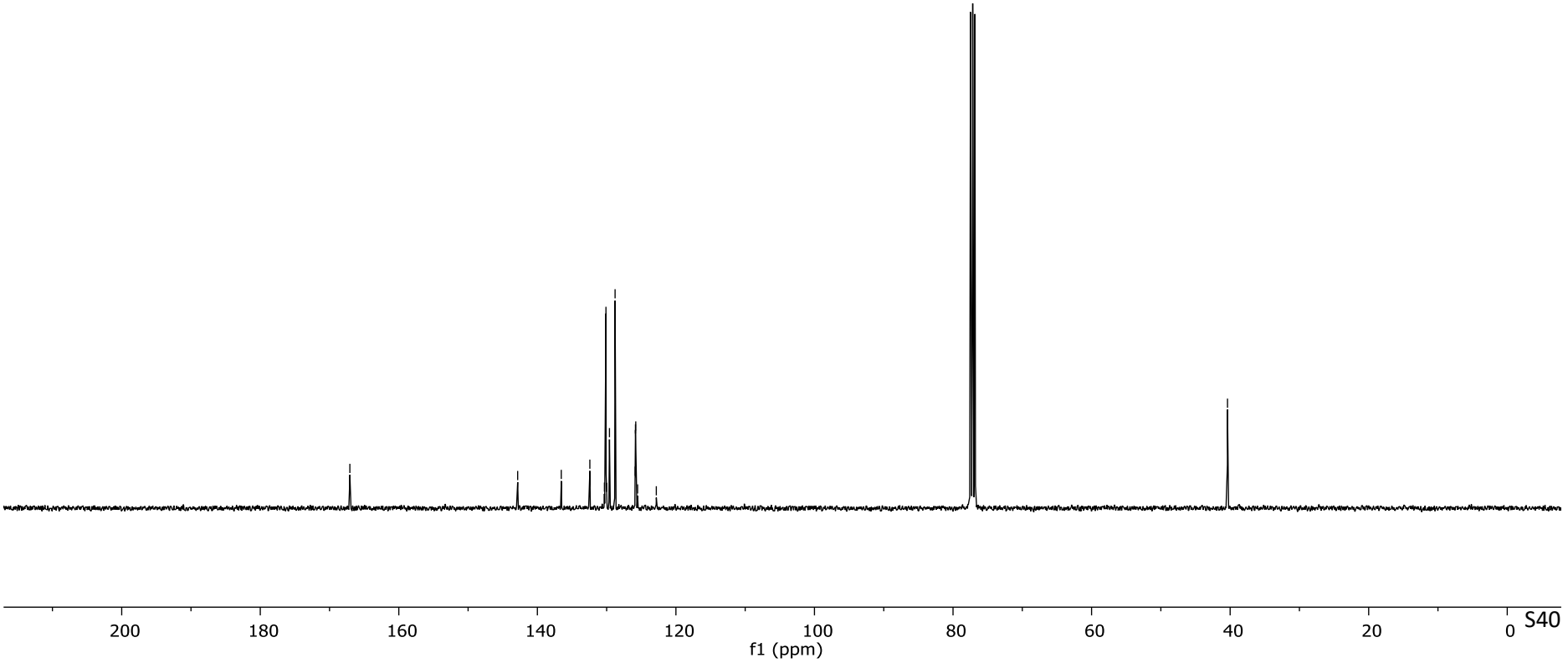


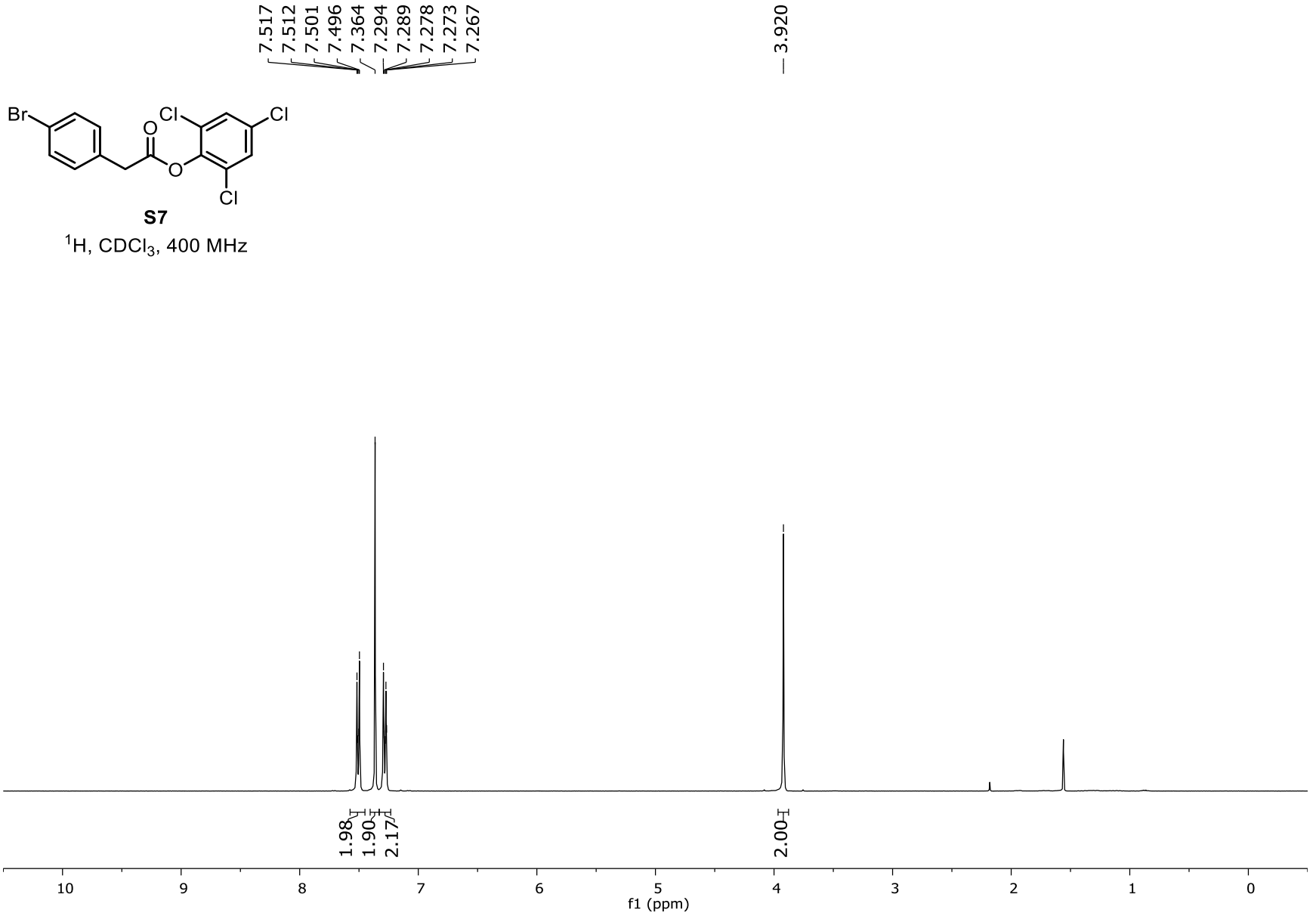




S6

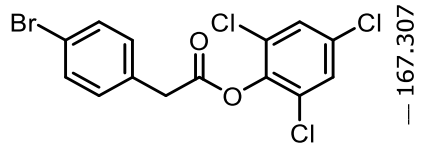
$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz





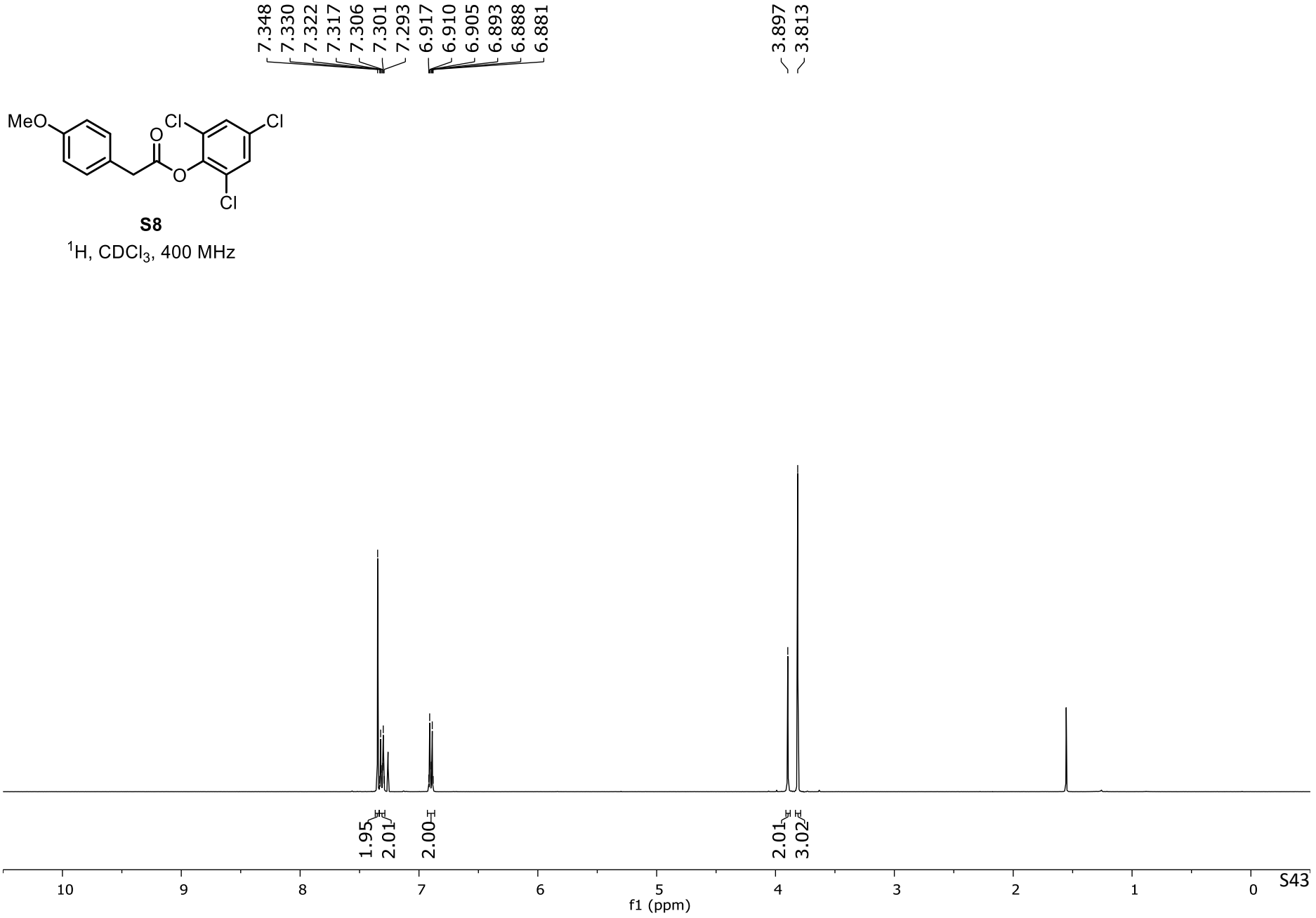
S7

^{1}H, $CDCl_3$, 400 MHz



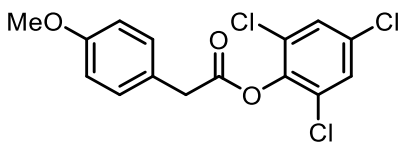
S7

$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz



S8

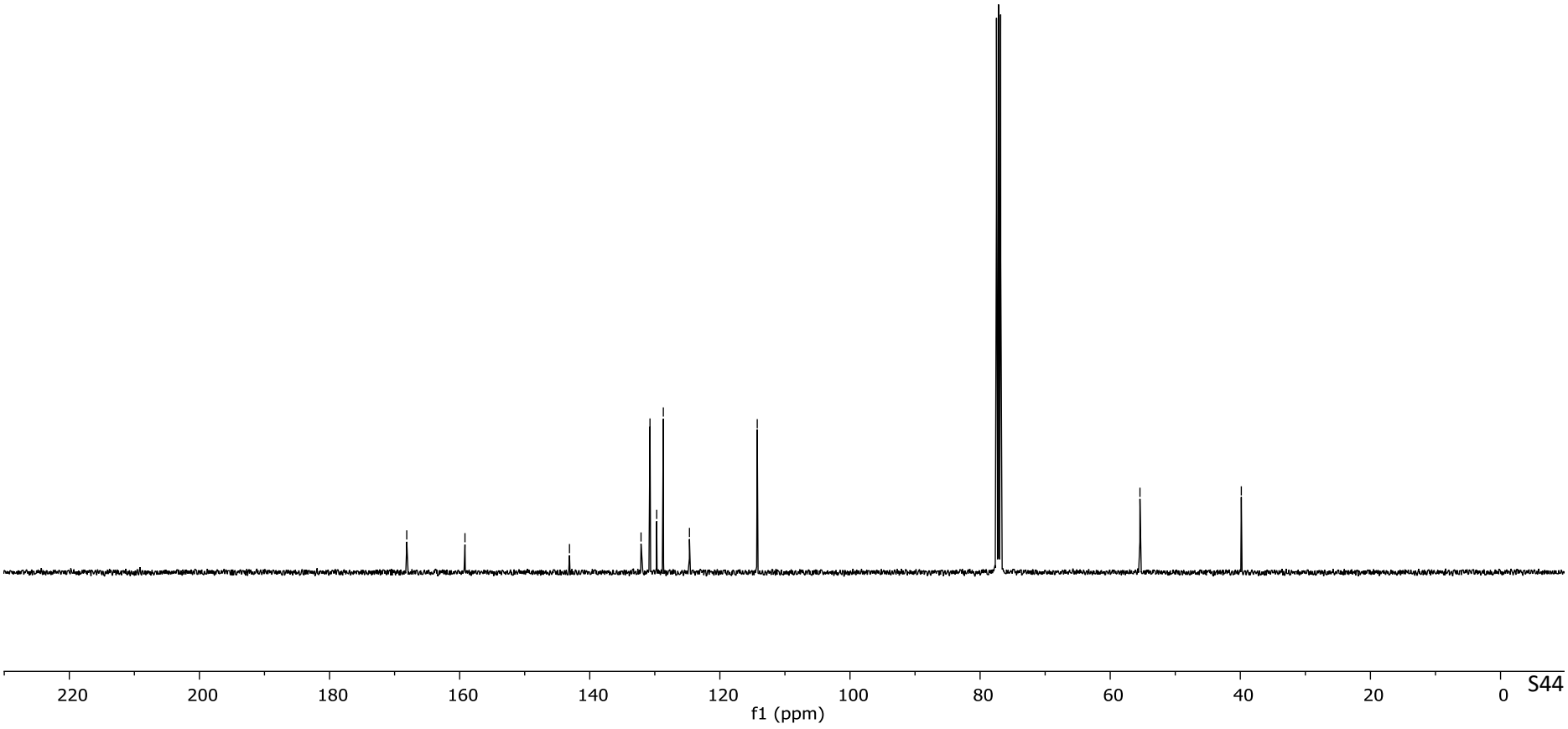
^{1}H, $CDCl_3$, 400 MHz

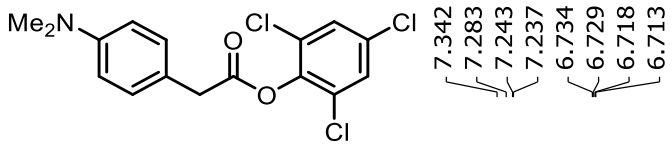


S8

$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz

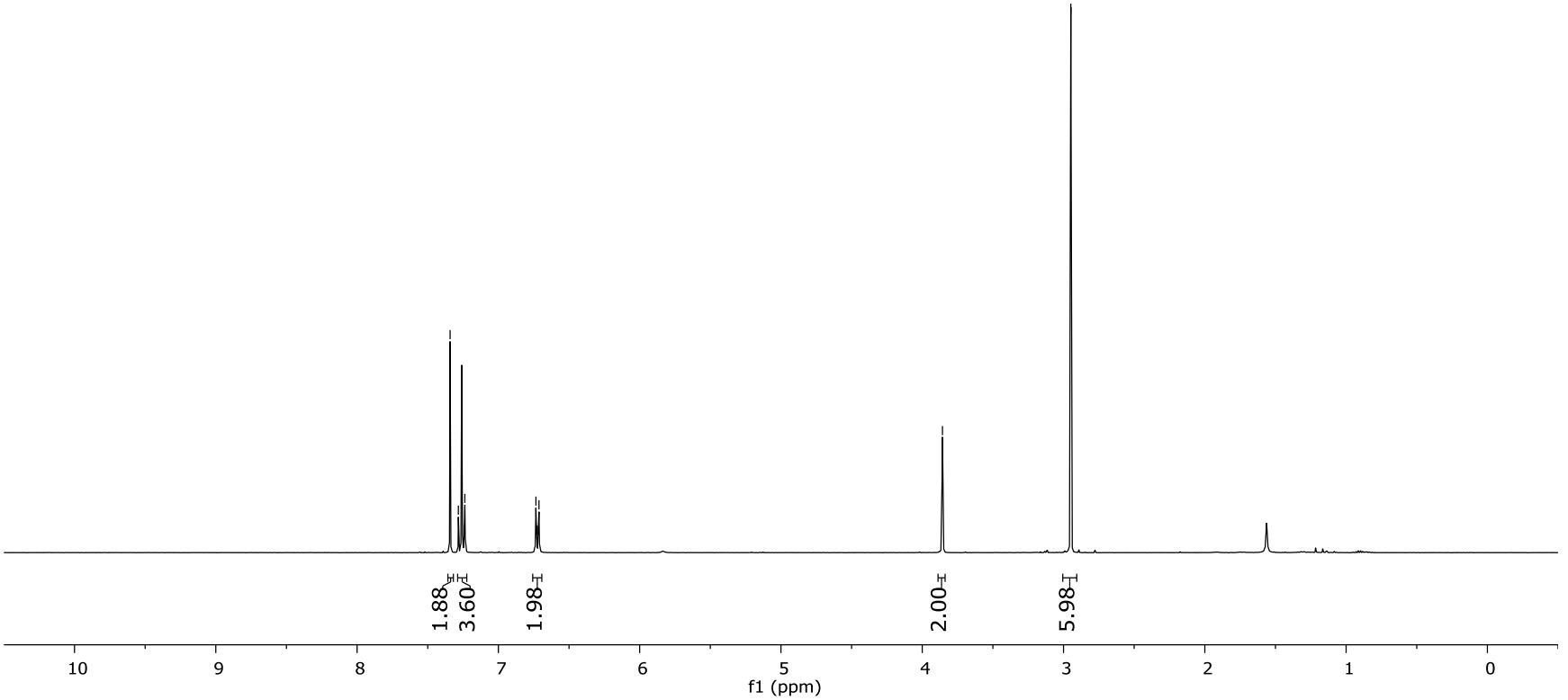
168.129
159.181
143.115
132.117
130.742
129.711
128.690
124.672
114.253
55.426
39.846

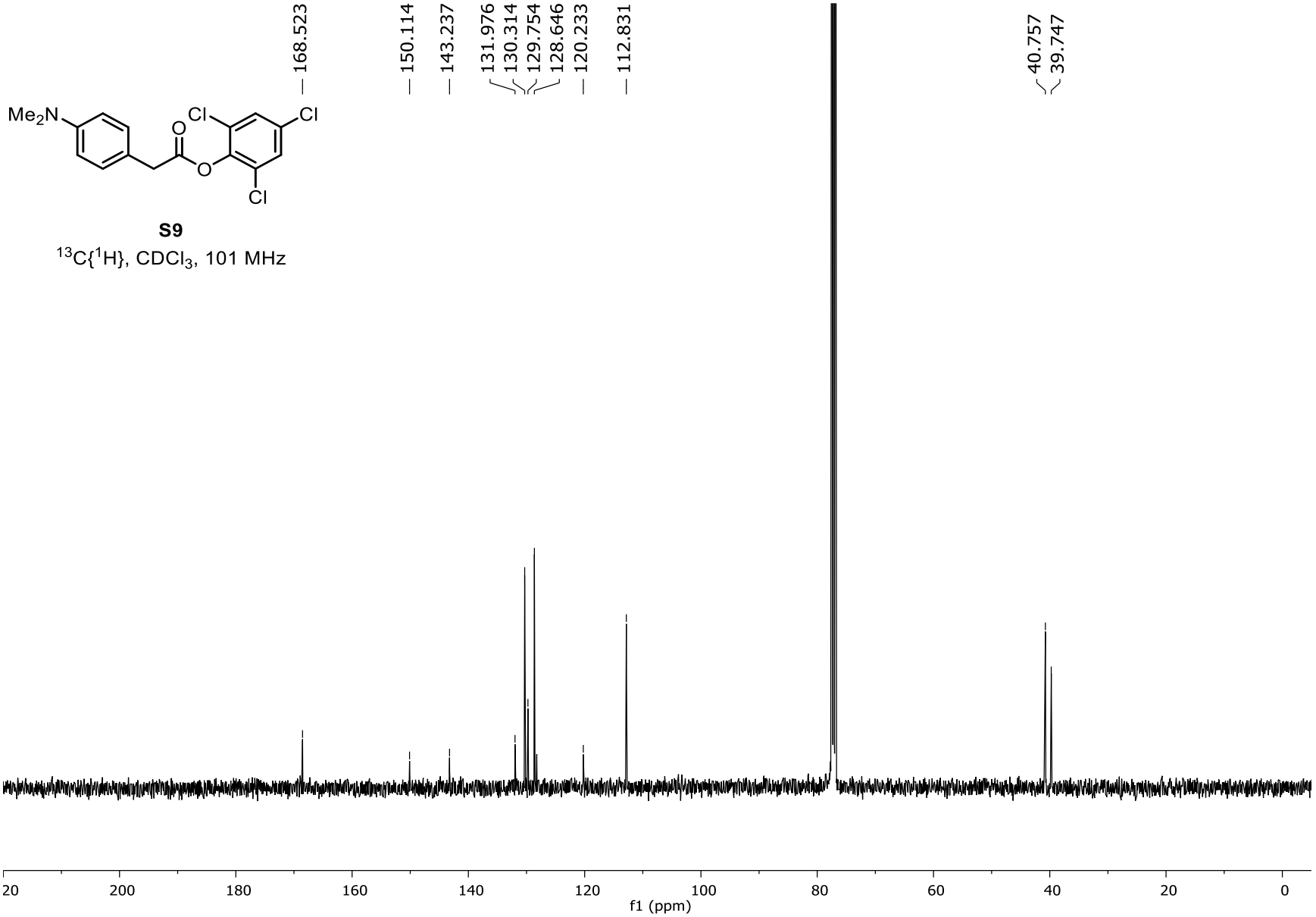


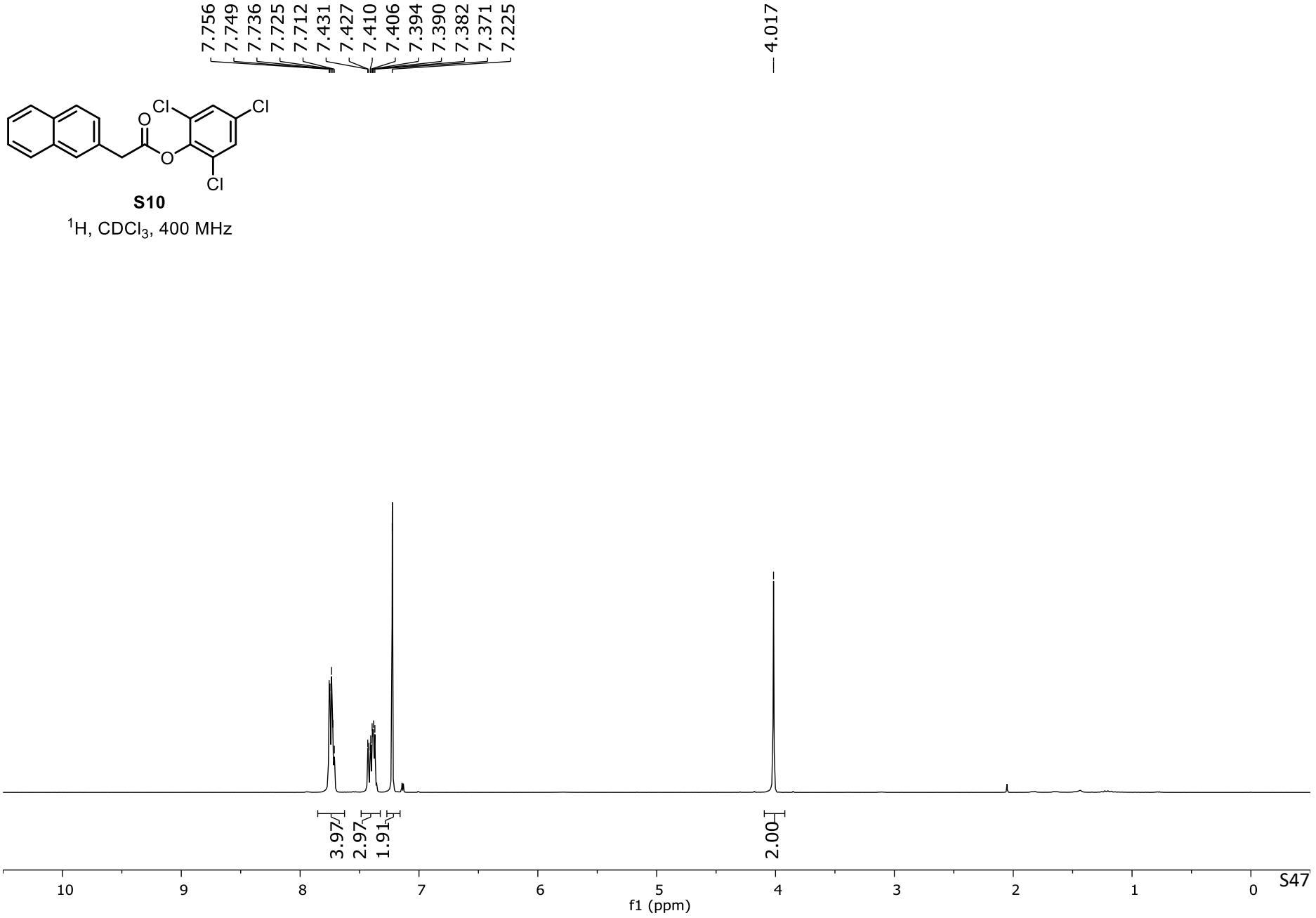


S9

^{1}H, $CDCl_3$, 400 MHz

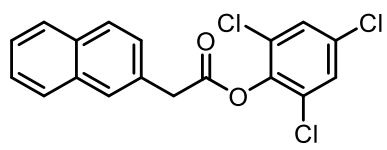



168.523
150.114
143.237
131.976
130.314
129.754
128.646
120.233
112.831
40.757
39.747
Me2N
O
O
Cl
Cl
Cl
S9
13C{1H}, CDCl3, 101 MHz
20
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



S10

^{1}H, $CDCl_3$, 400 MHz



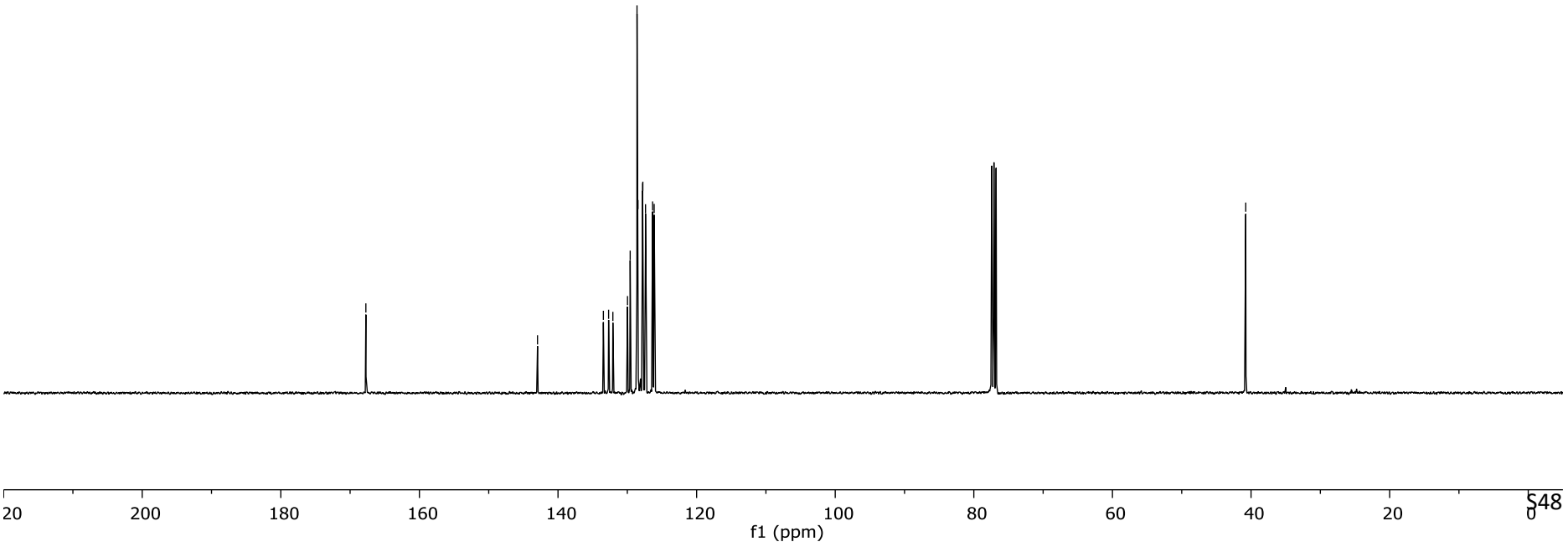
S10

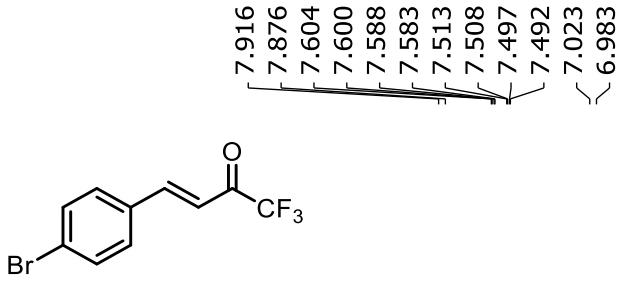
$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz

167.726

142.960
133.456
132.699
132.085
129.973
129.586
128.602
128.541
128.460
127.794
127.760
127.374
126.351
126.126

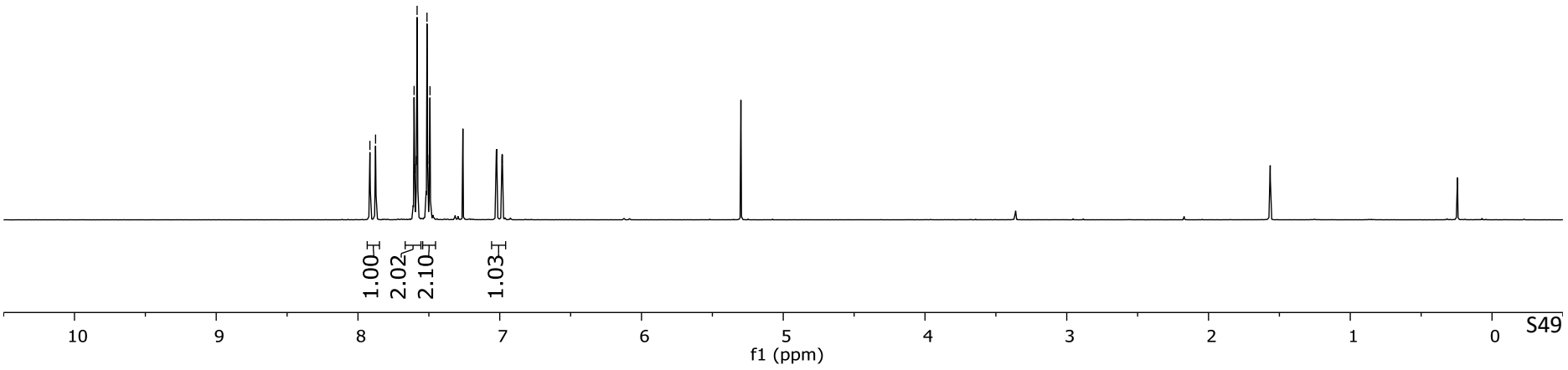
40.763

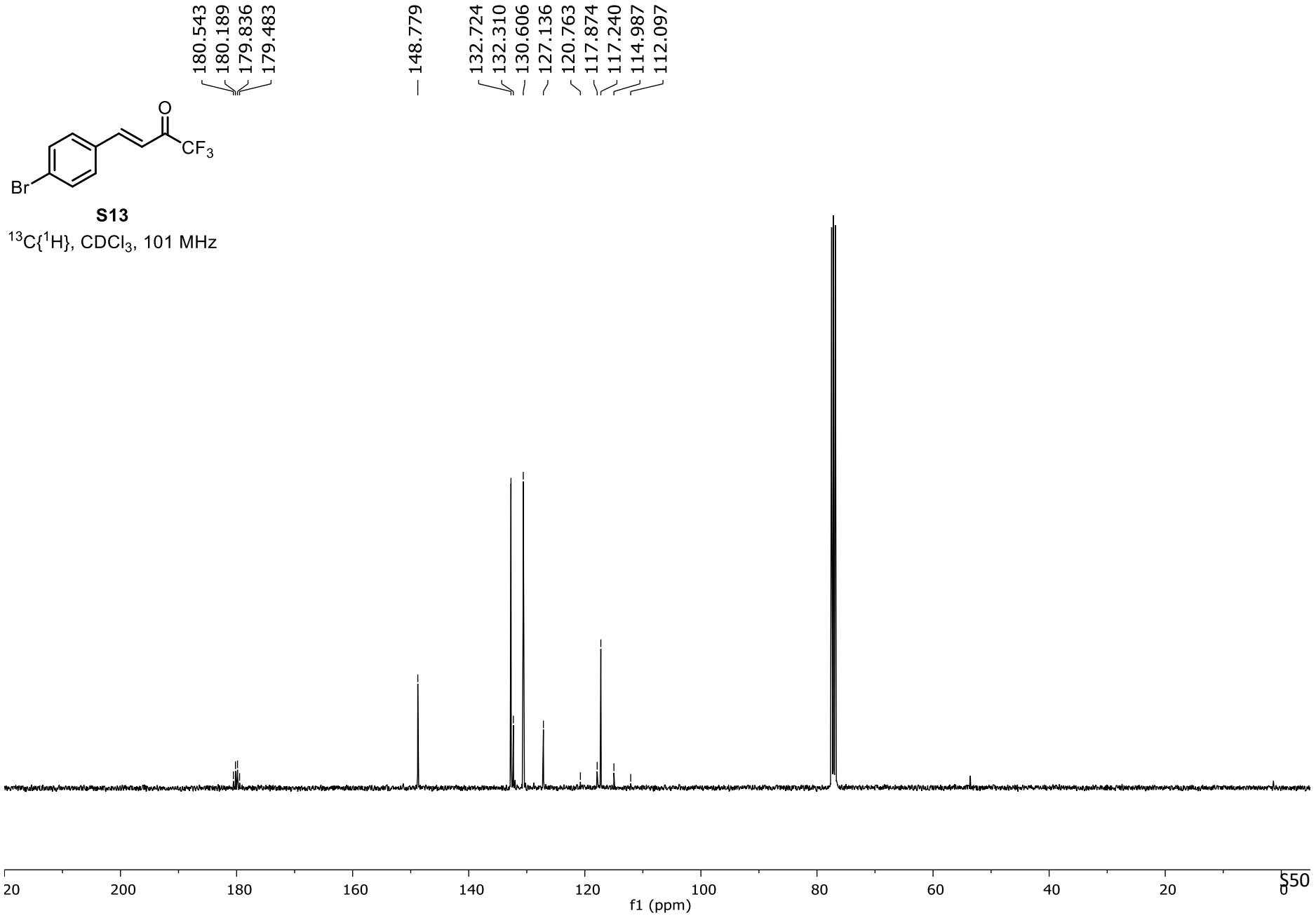


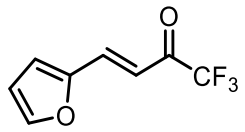


S13

^{1}H, $CDCl_3$, 400 MHz

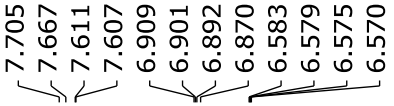


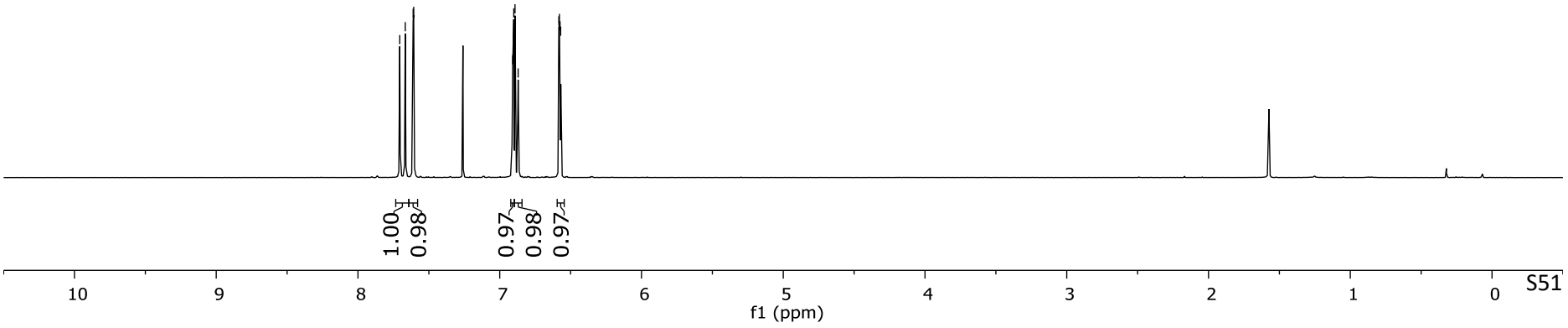

180.543
180.189
179.836
179.483
148.779
132.724
132.310
130.606
127.136
120.763
117.874
117.240
114.987
112.097
O
CF3
Br
S13
13C{1H}, CDCl3, 101 MHz
f1 (ppm)

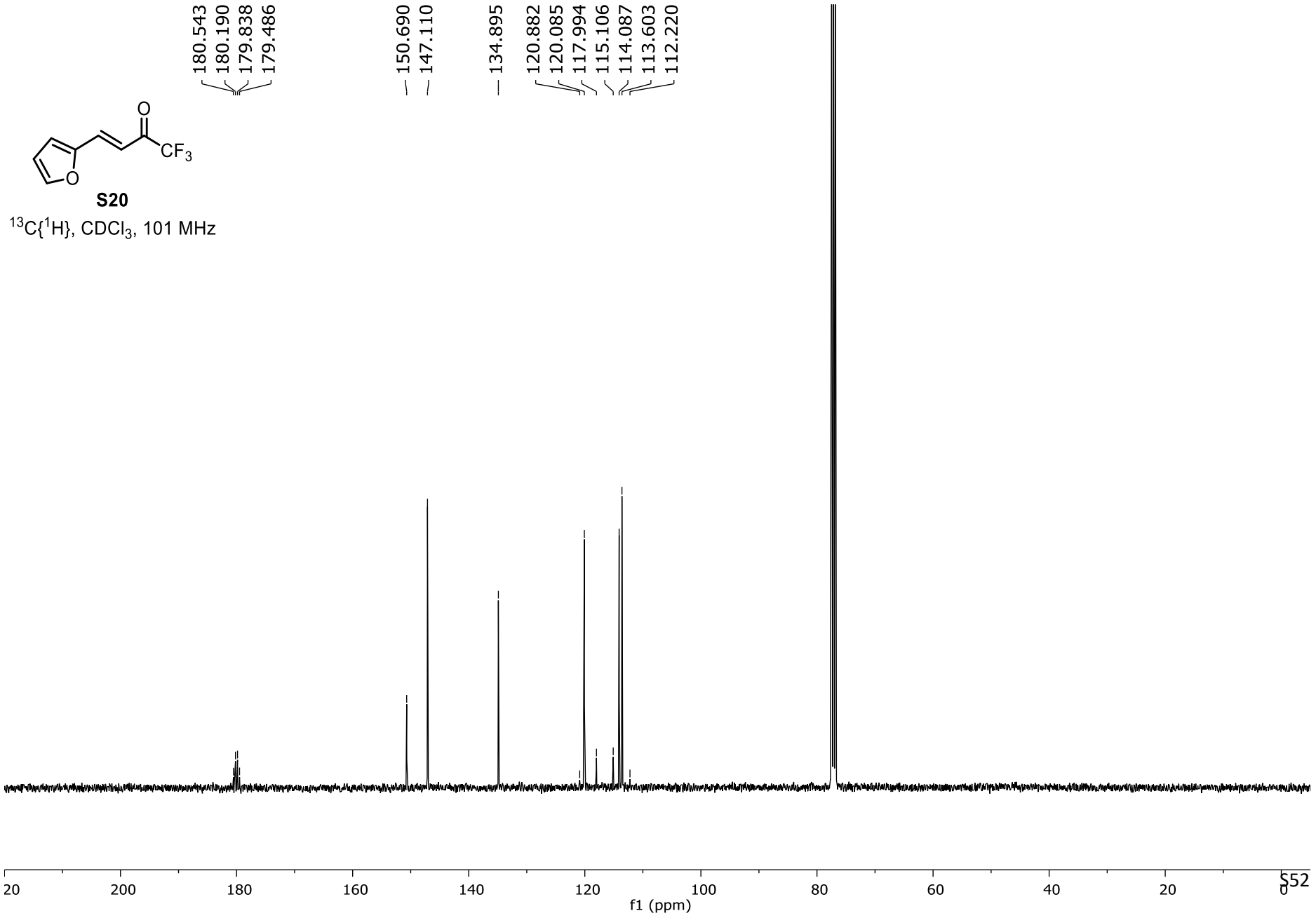


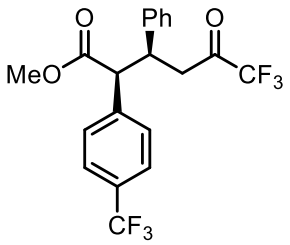
S20

^{1}H, $CDCl_3$, 400 MHz



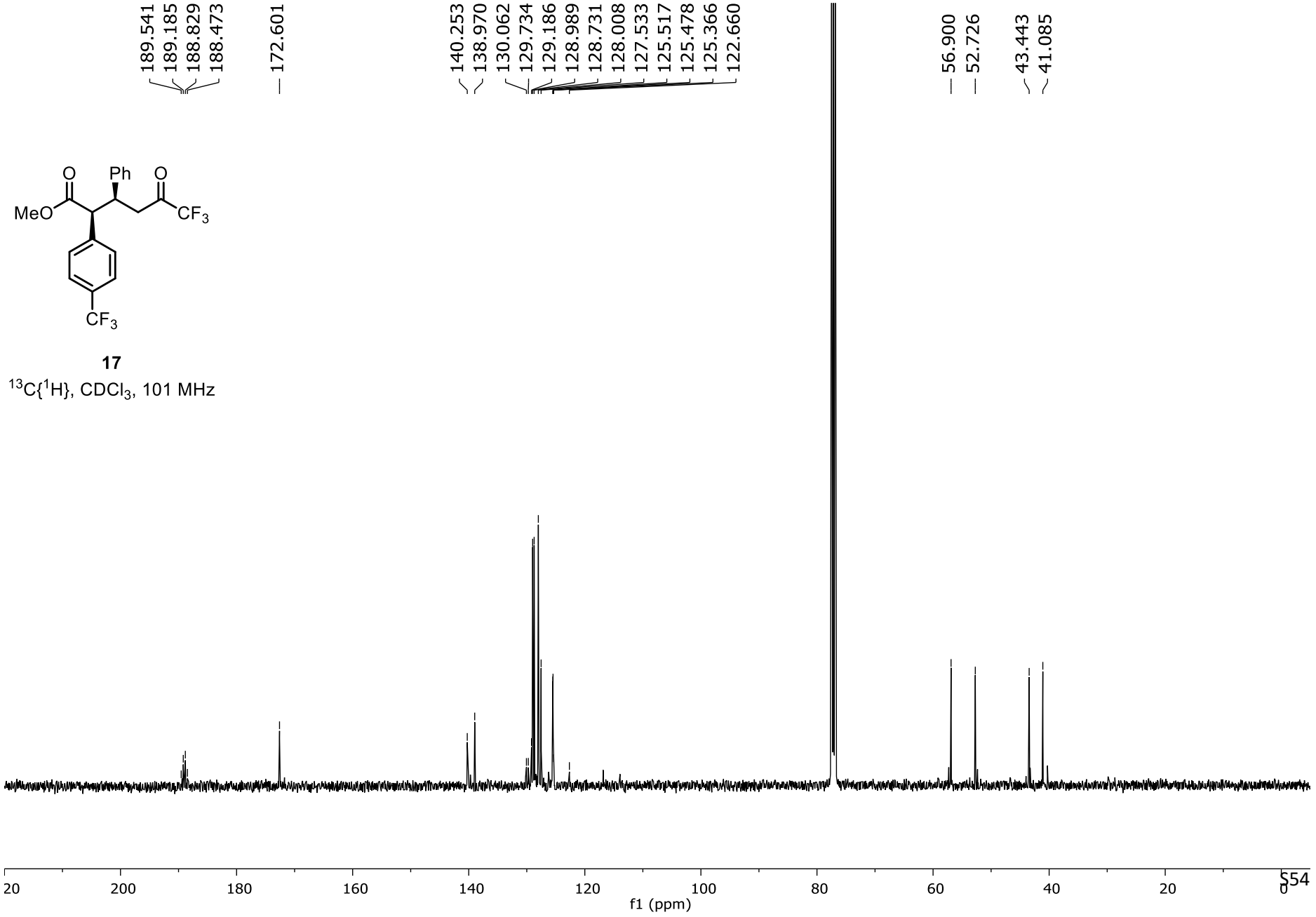



180.543
180.190
179.838
179.486
150.690
147.110
134.895
120.882
120.085
117.994
115.106
114.087
113.603
112.220
O
CF3
O
S20
13C{1H}, CDCl3, 101 MHz
f1 (ppm)



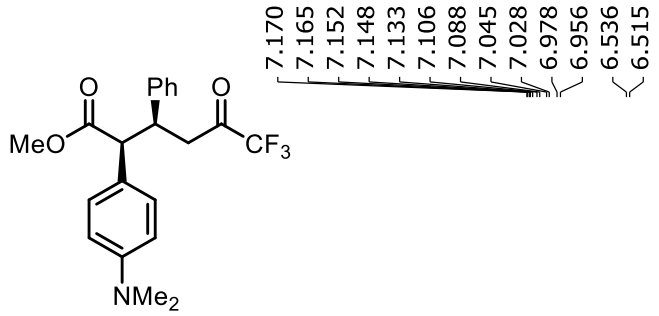
17

^{1}H, $CDCl_3$, 400 MHz



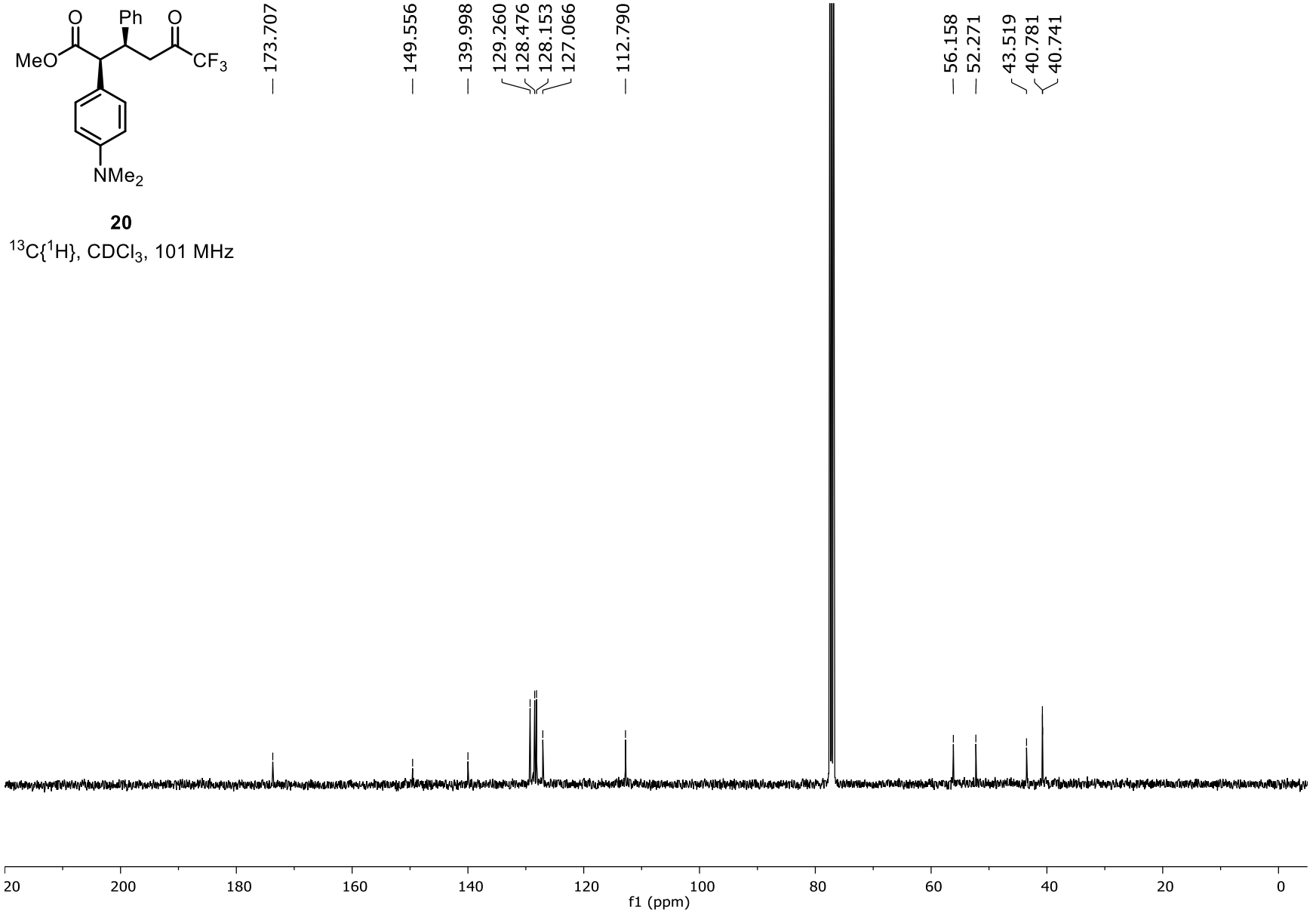
17

$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz



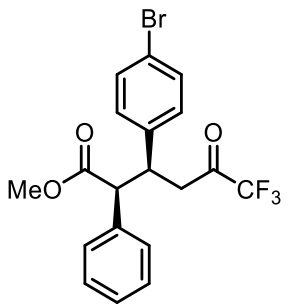
20

^{1}H, $CDCl_3$, 400 MHz



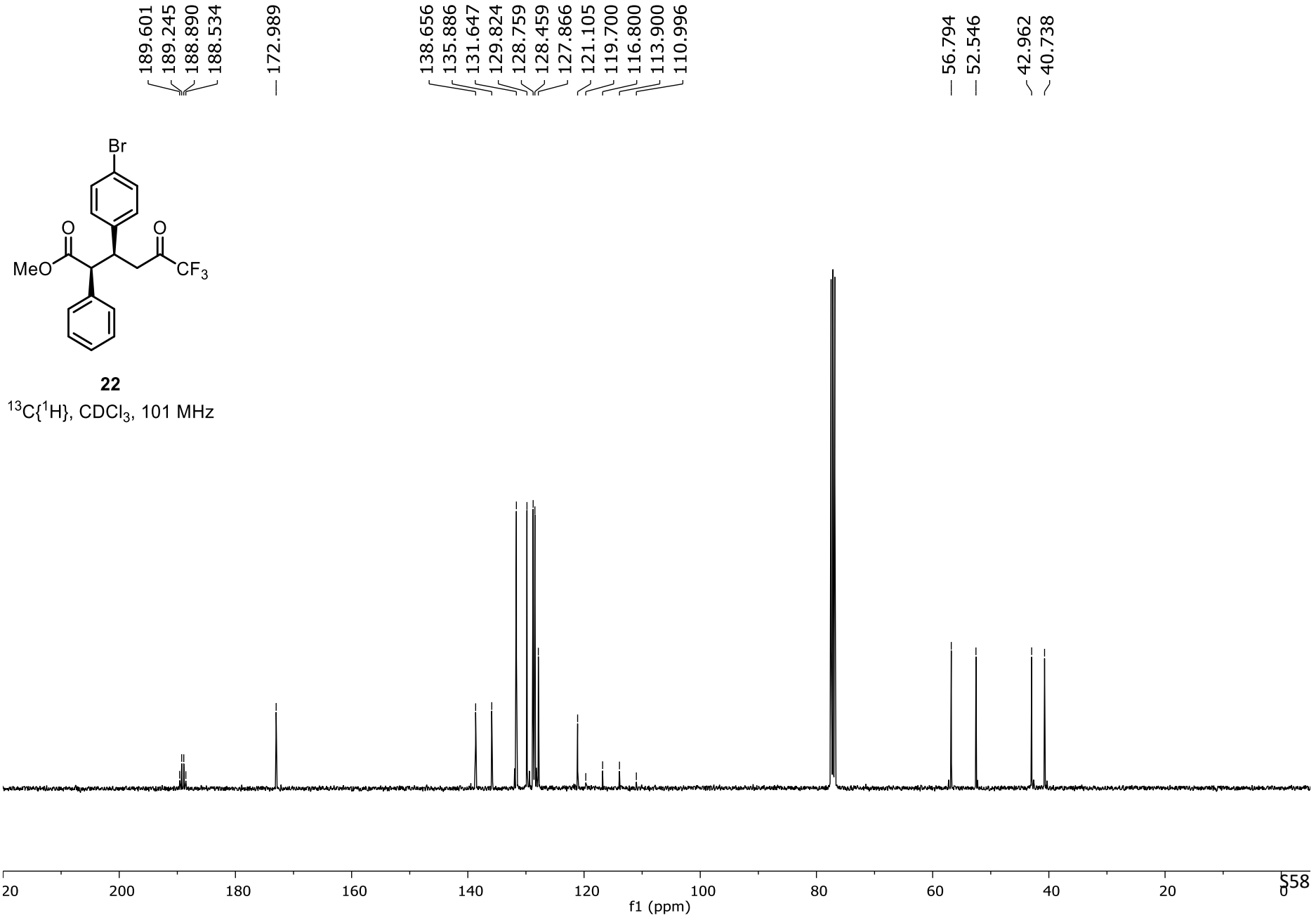
20

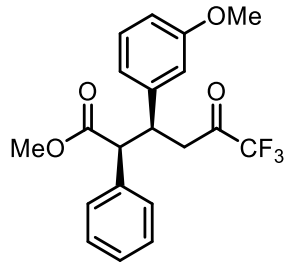
$^{13}C\{^{1}H\}$, $CDCl_3$, 101 MHz



22

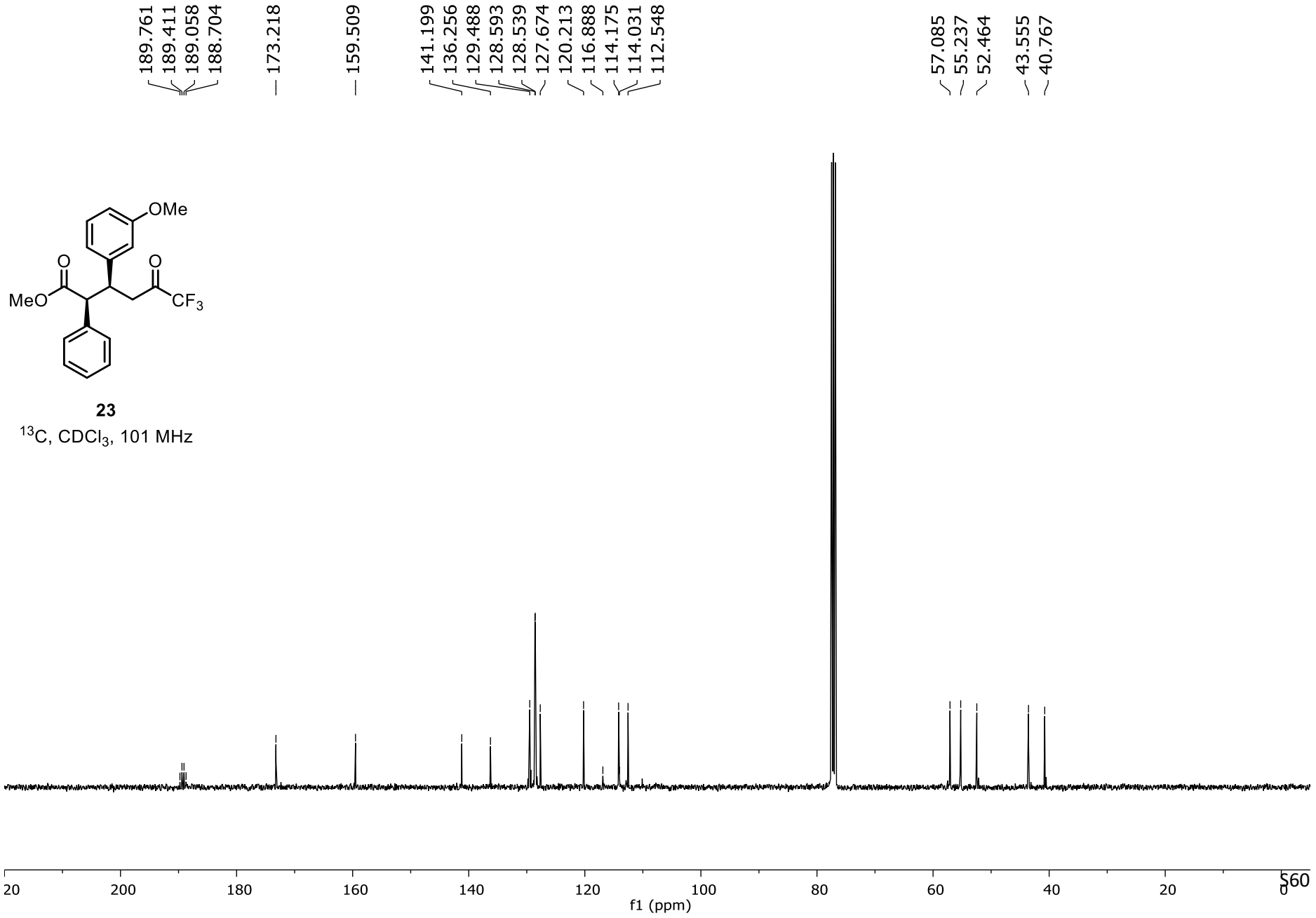
^{1}H, $CDCl_3$, 400 MHz

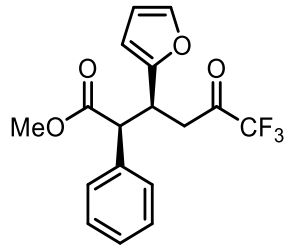

189.601
189.245
188.890
188.534
172.989
138.656
135.886
131.647
129.824
128.759
128.459
127.866
121.105
119.700
116.800
113.900
110.996
56.794
52.546
42.962
40.738
Br
O
O
MeO
CF3
22
13C{1H}, CDCl3, 101 MHz
f1 (ppm)



23

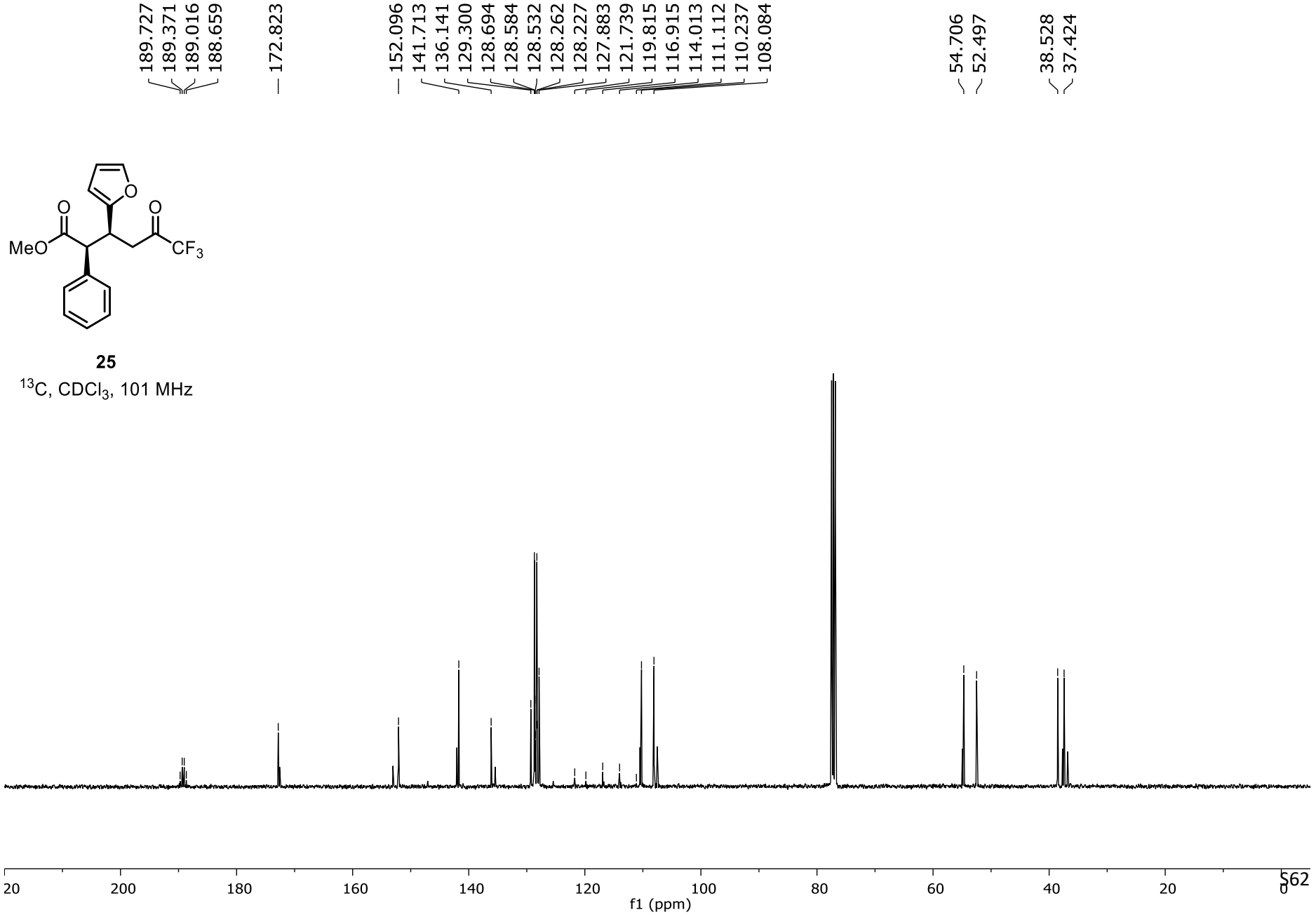
^{1}H, $CDCl_3$, 400 MHz


189.761
189.411
189.058
188.704
173.218
159.509
141.199
136.256
129.488
128.593
128.539
127.674
120.213
116.888
114.175
114.031
112.548
57.085
55.237
52.464
43.555
40.767
OMe
O
O
MeO
CF3
23
13C, CDCl3, 101 MHz
f1 (ppm)



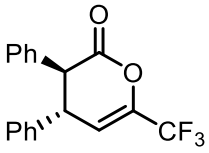
25

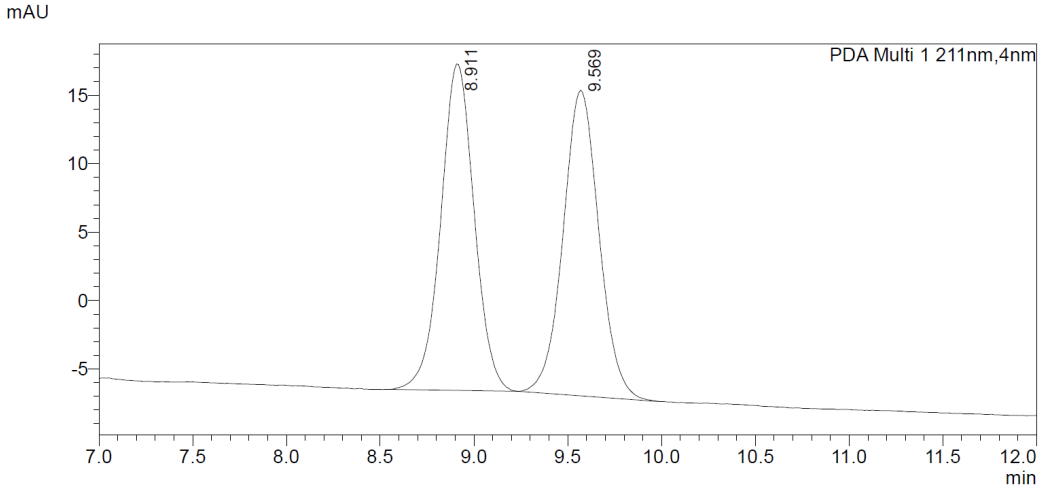
^{1}H, $CDCl_3$, 400 MHz


189.727
189.371
189.016
188.659
172.823
152.096
141.713
136.141
129.300
128.694
128.584
128.532
128.262
128.227
127.883
121.739
119.815
116.915
114.013
111.112
110.237
108.084
54.706
52.497
38.528
37.424
MeO
O
O
O
CF3
25
13C, CDCl3, 101 MHz
f1 (ppm)

HPLC Data

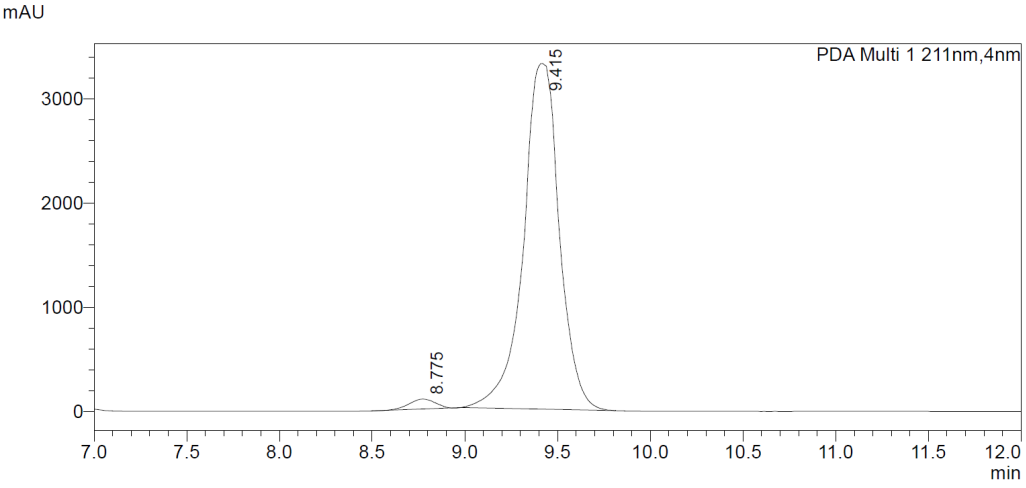
HPLC data for **2** (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*R*,4*R*): 8.8 min, t_R (3*S*,4*S*): 9.4 min, 2:98 er.





PDA Ch1 211nm

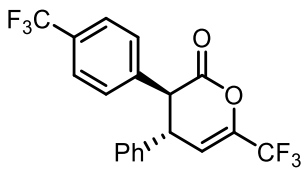
Peak#	Ret. Time	Area%
1	8.911	49.930
2	9.569	50.070
Total		100.000



PDA Ch1 211nm

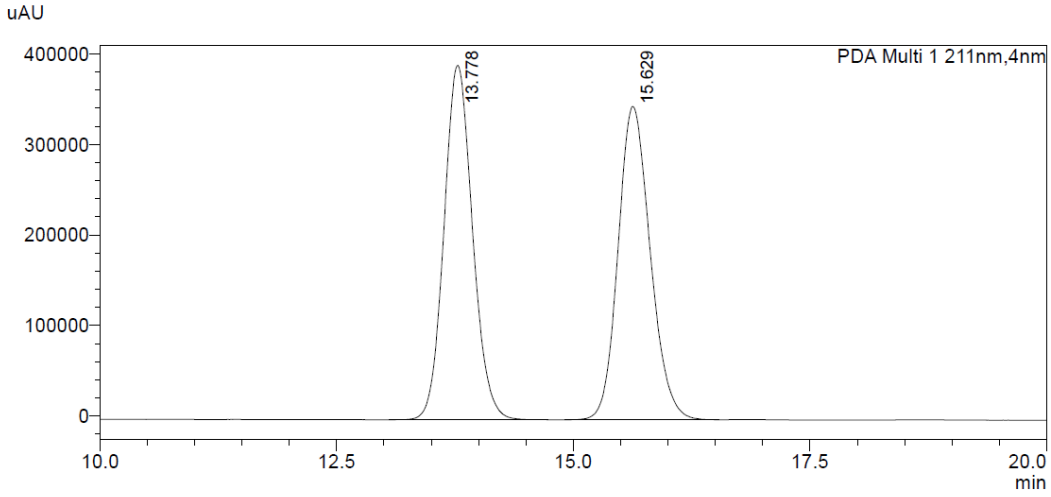
Peak#	Ret. Time	Area%
1	8.775	2.043
2	9.415	97.957
Total		100.000

HPLC data for **14**: (Chiralpak AD-H, 2% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*S*,4*S*): 13.5 min, t_R (3*R*,4*R*): 15.3 min, 90:10 er



PDA Ch1 211nm

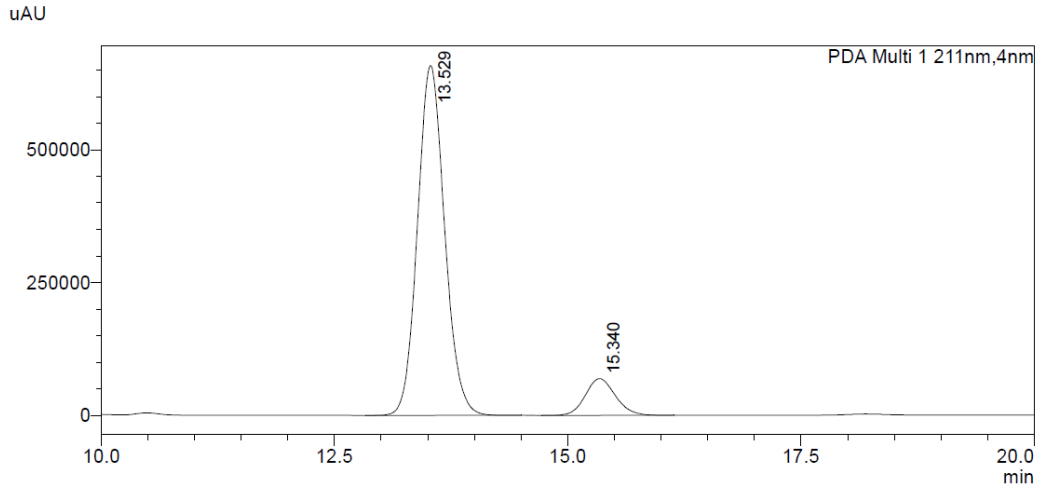
Peak#	Ret. Time	Area%
1	13.778	50.089
2	15.629	49.911
Total		100.000



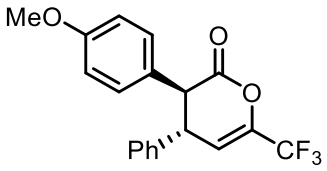
<Peak Table>

PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.529	89.575
2	15.340	10.425
Total		100.000

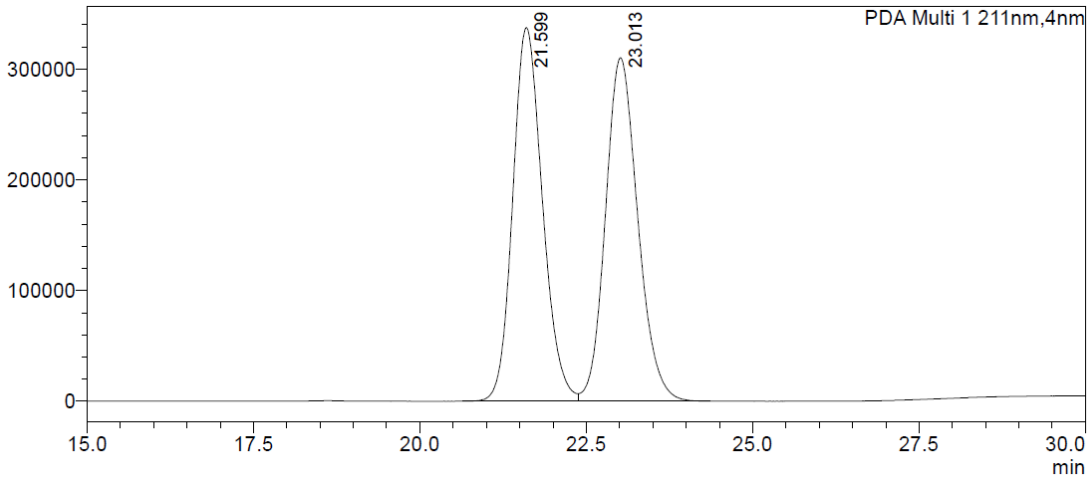


HPLC data for **15**: (Chiralpak AD-H, 2% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*R*,4*R*): 21.7 min, t_R (3*S*,4*S*): 23.1 min, 5:95 er



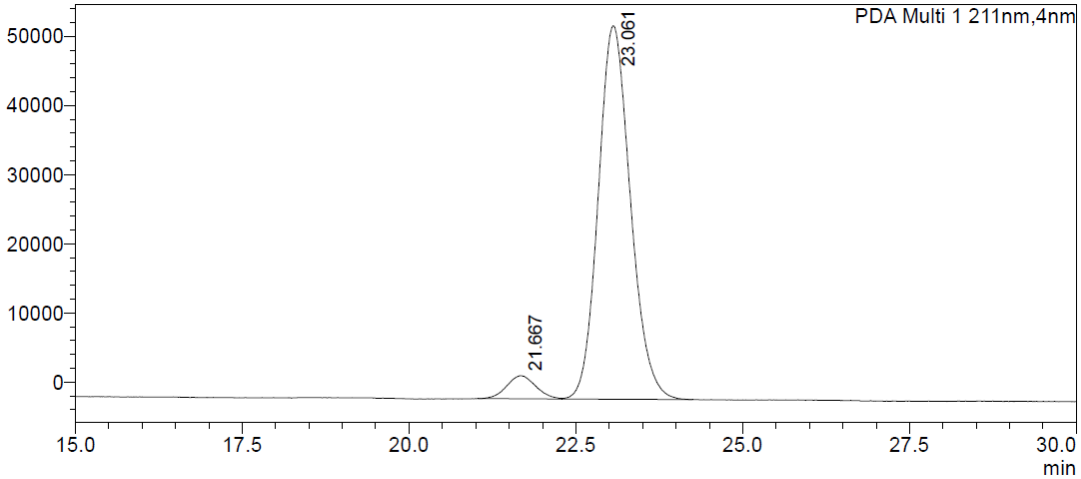
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	21.599	49.979
2	23.013	50.021
Total		100.000

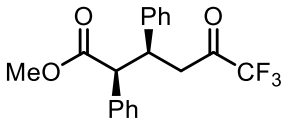


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	21.667	5.262
2	23.061	94.738
Total		100.000

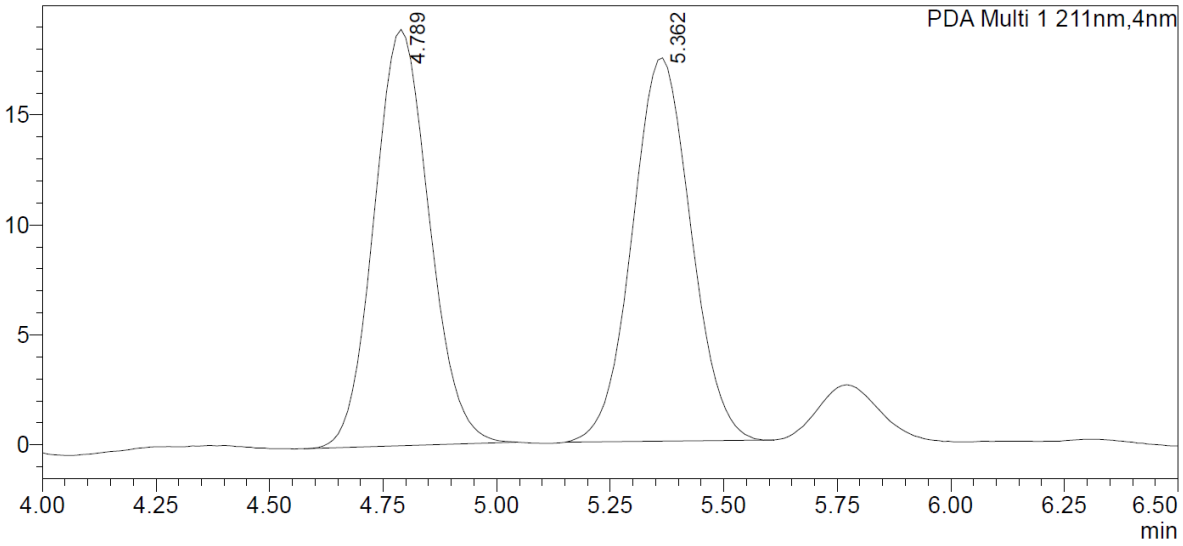


HPLC data for **16**: (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (3*S*,4*S*): 4.7 min, t_R (3*R*,4*R*): 5.2 min, 98:2 er



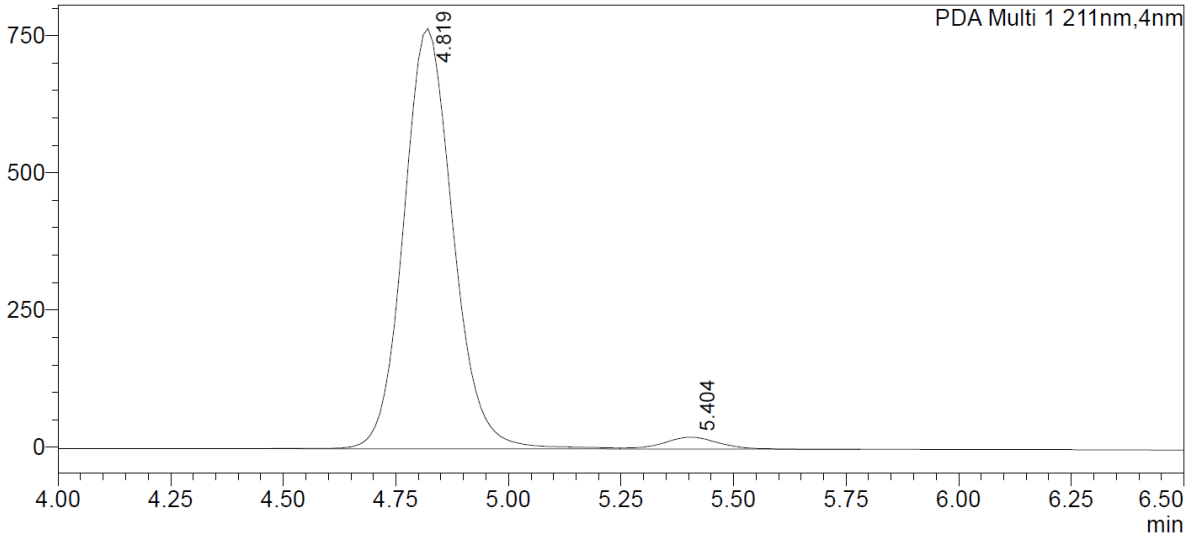
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	4.789	50.492
2	5.362	49.508
Total		100.000

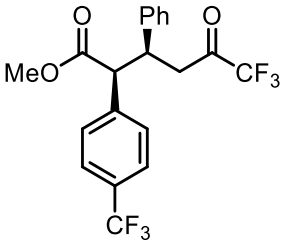


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	4.819	96.905
2	5.404	3.095
Total		100.000

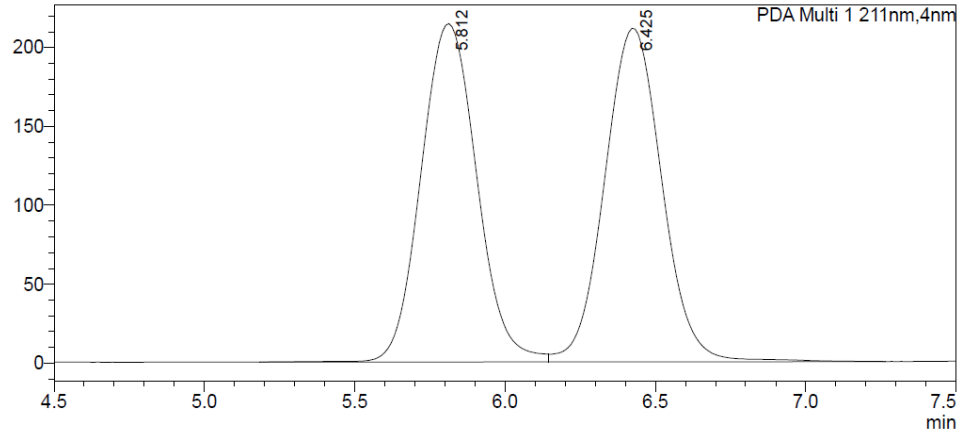


HPLC data for **17**: (Chiralpak AD-H, 2% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 5.7 min, t_R (2*R*,3*R*): 6.3 min, 93:7 er



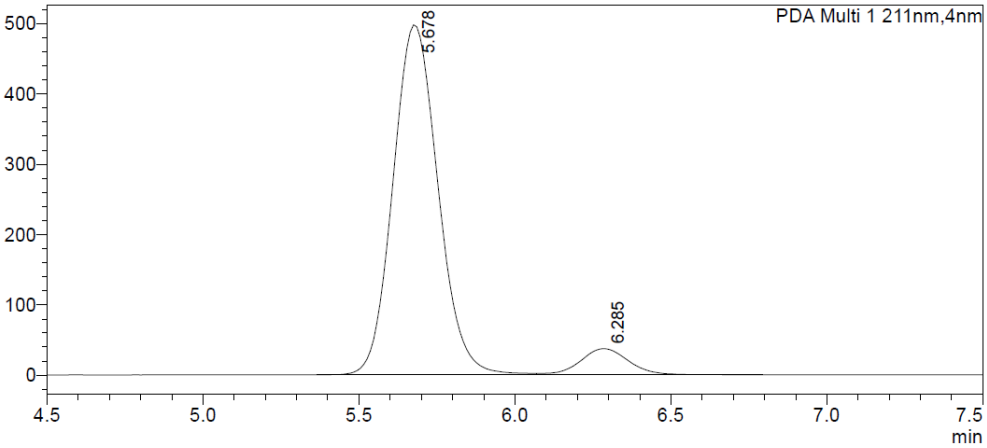
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	5.812	49.709
2	6.425	50.291
Total		100.000

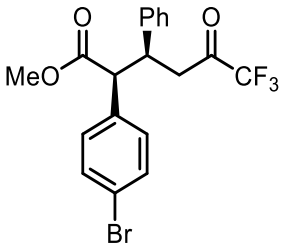


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	5.678	92.640
2	6.285	7.360
Total		100.000

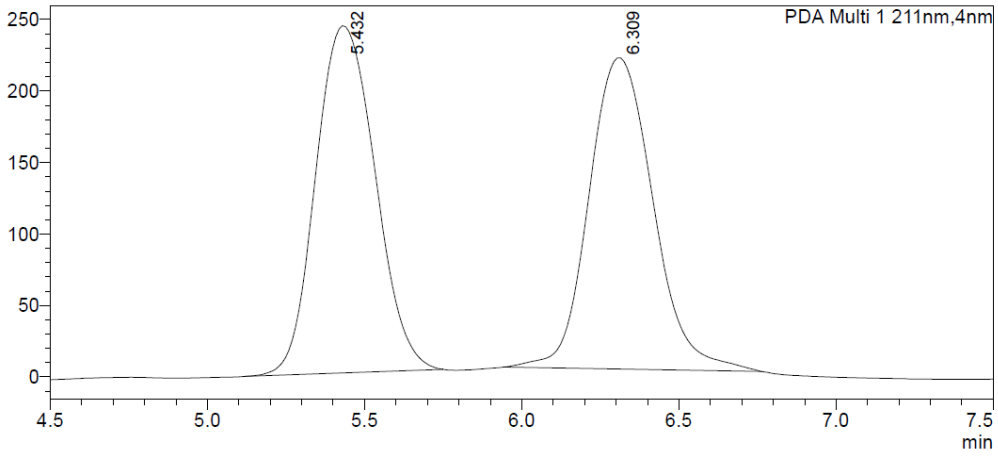


HPLC data for **18**: (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 5.4 min, t_R (2*R*,3*R*): 6.3 min, 97:3 er



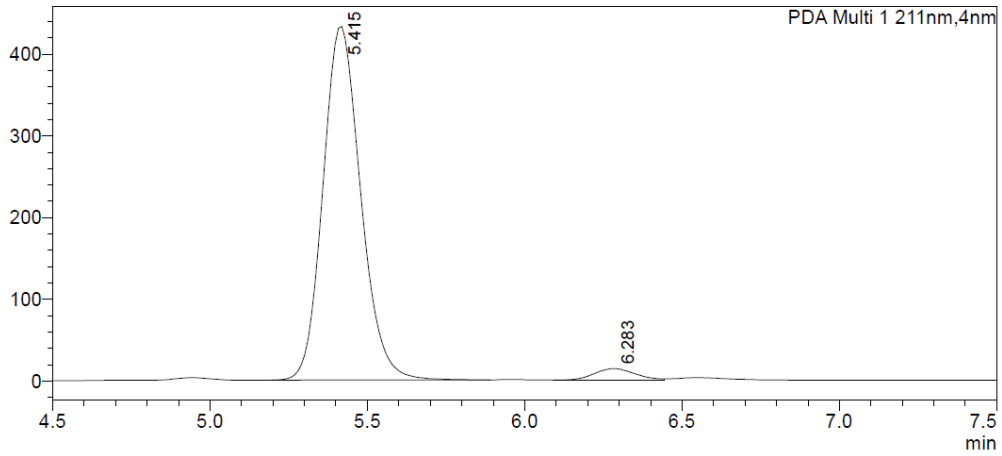
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	5.432	50.799
2	6.309	49.201
Total		100.000

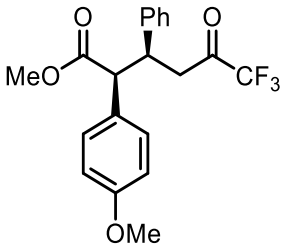


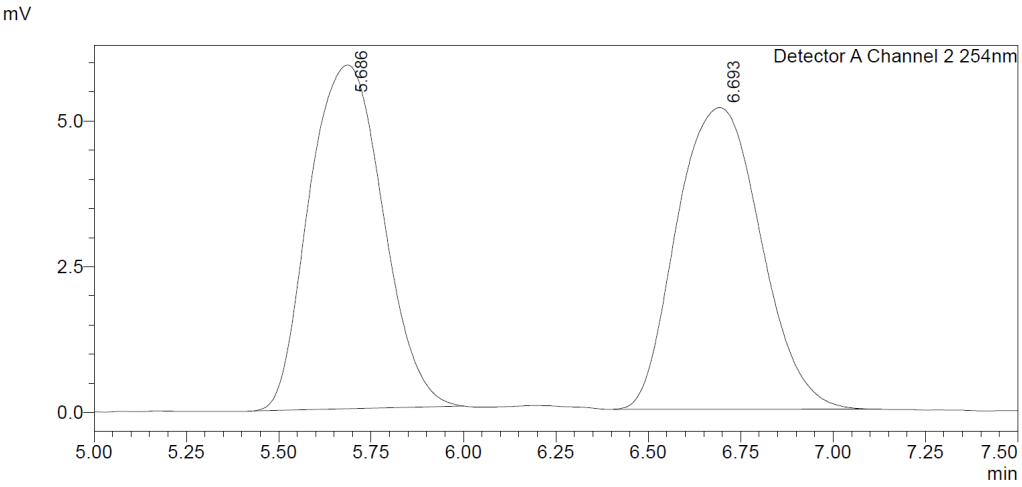
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	5.415	96.640
2	6.283	3.360
Total		100.000



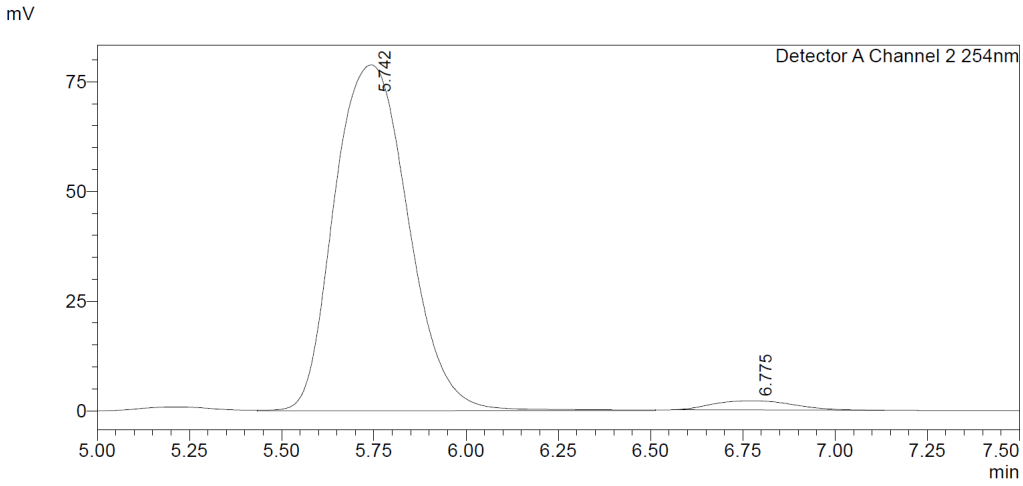
HPLC data for **19**: (Chiralpak AD-H, 5% IPA/hexane, 1.0 mL min^{-1}, 254 nm, 30 °C): t_R (2*S*,3*S*): 5.7 min, t_R (2*R*,3*R*): 6.8 min, 97:3 er.





Detector A Channel 2 254nm

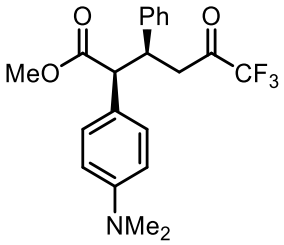
Peak#	Ret. Time	Area%
1	5.686	49.958
2	6.693	50.042
Total		100.000



Detector A Channel 2 254nm

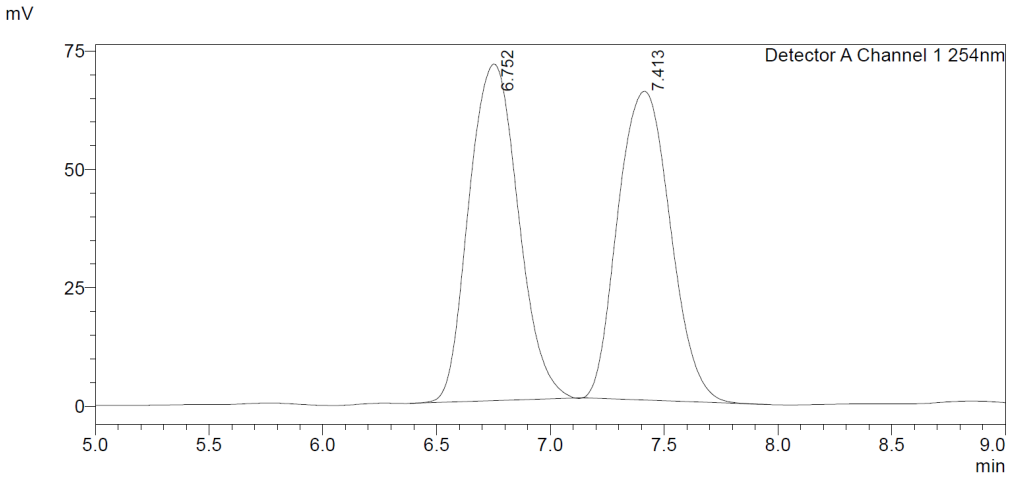
Peak#	Ret. Time	Area%
1	5.742	97.170
2	6.775	2.830
Total		100.000

HPLC data for **20**: (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 254 nm, 30 °C): t_R (2*S*,3*S*): 6.8 min, t_R (2*R*,3R): 7.4 min, 99:1 er.



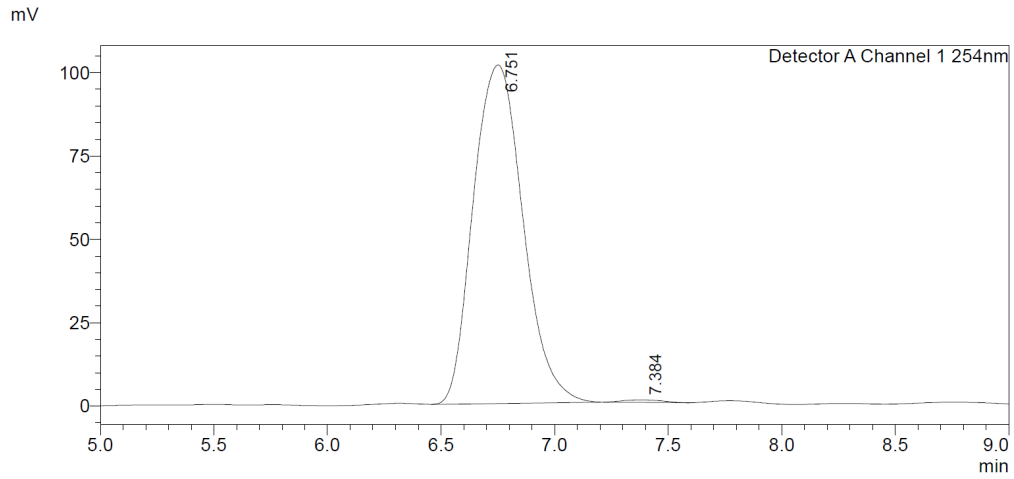
Detector A Channel 1 254nm

Peak#	Ret. Time	Area%
1	6.752	50.609
2	7.413	49.391
Total		100.000

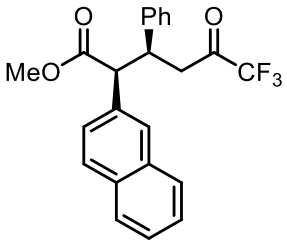


Detector A Channel 1 254nm

Peak#	Ret. Time	Area%
1	6.751	99.423
2	7.384	0.577
Total		100.000

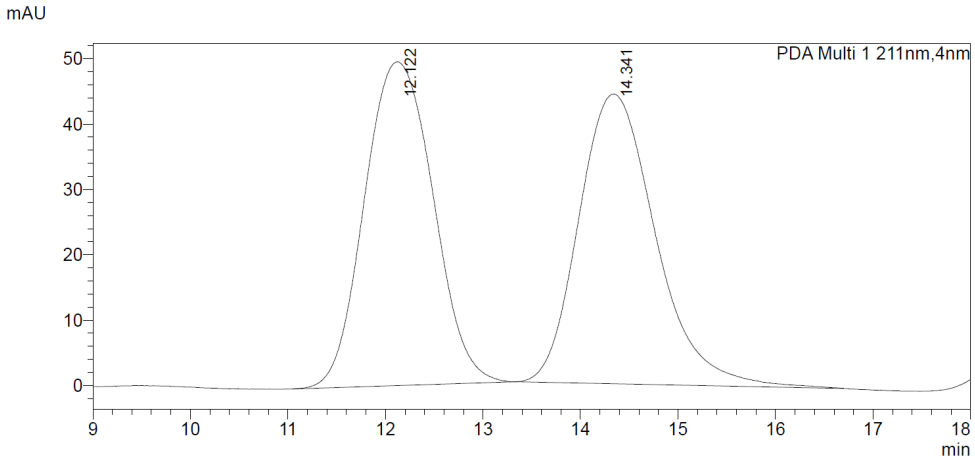


HPLC data for **21**: (Chiralpak AD-H, 1% IPA/hexane, 0.5 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 12.6 min, t_R (2*R*,3*R*): 15.1 min, 97.3 er.



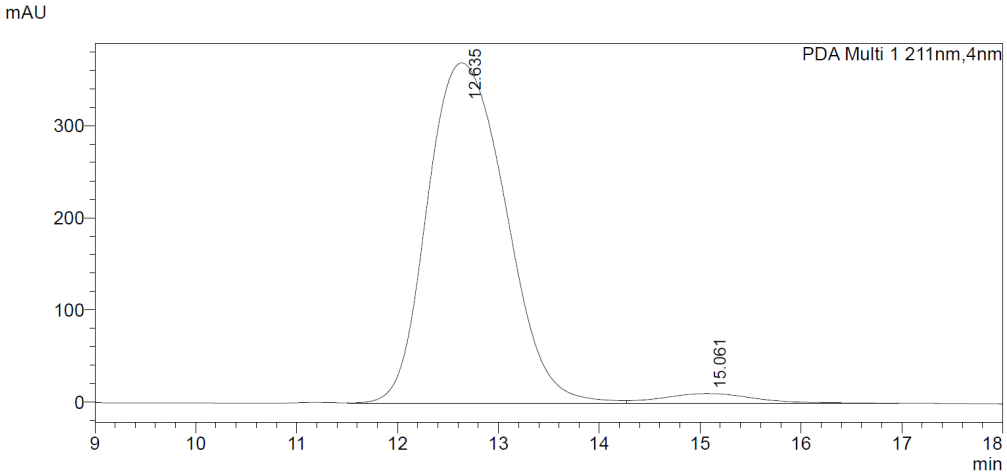
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	12.122	50.041
2	14.341	49.959
Total		100.000

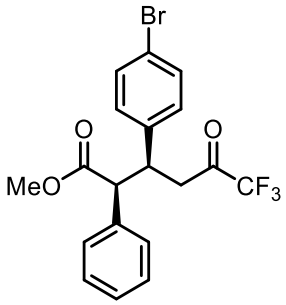


PDA Ch1 211nm

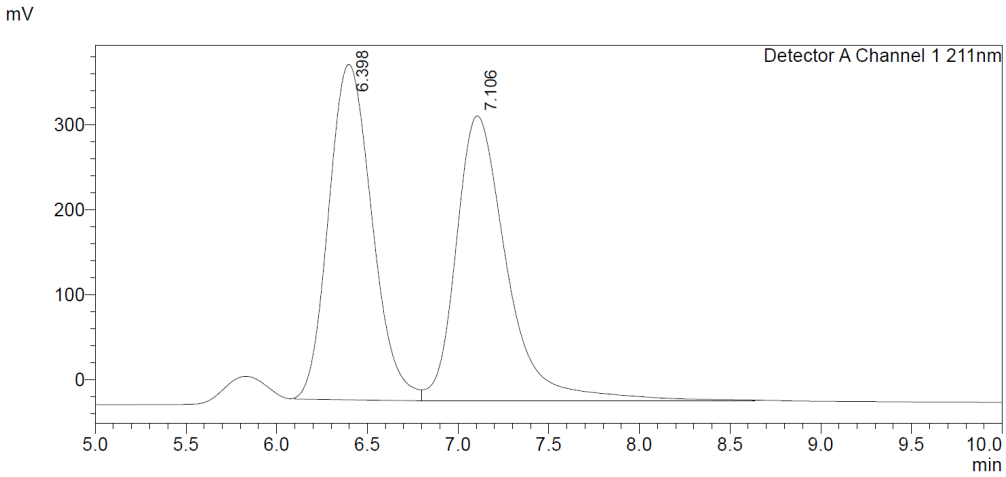
Peak#	Ret. Time	Area%
1	12.635	96.821
2	15.061	3.179
Total		100.000



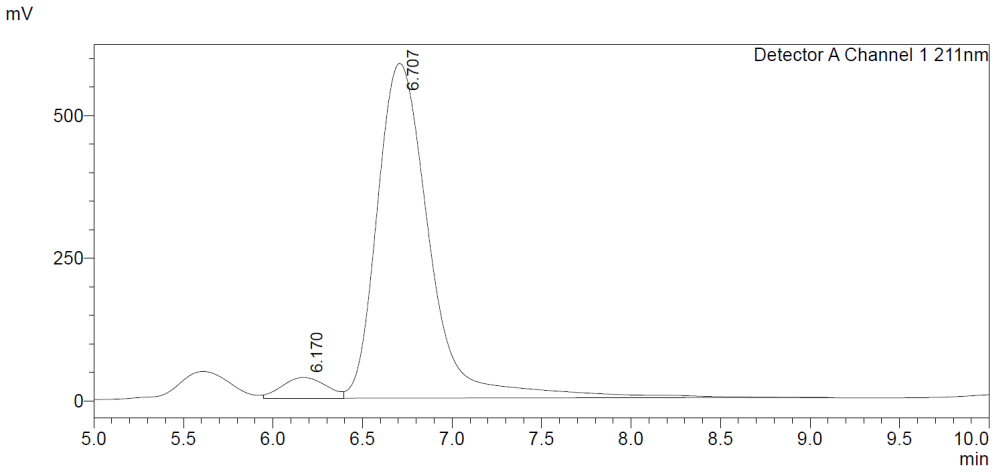
HPLC data for **22**: HPLC (Chiralpak OD-H, 1% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*R*,3*R*): 6.2 min, t_R (2*S*,3*S*): 6.7 min, 95:5 er.



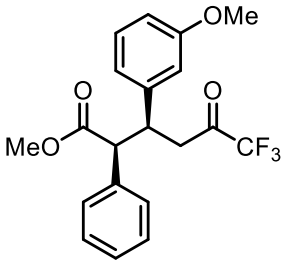
Peak#	Ret. Time	Area%
1	6.398	50.027
2	7.106	49.973
Total		100.000



Peak#	Ret. Time	Area%
1	6.170	4.926
2	6.707	95.074
Total		100.000

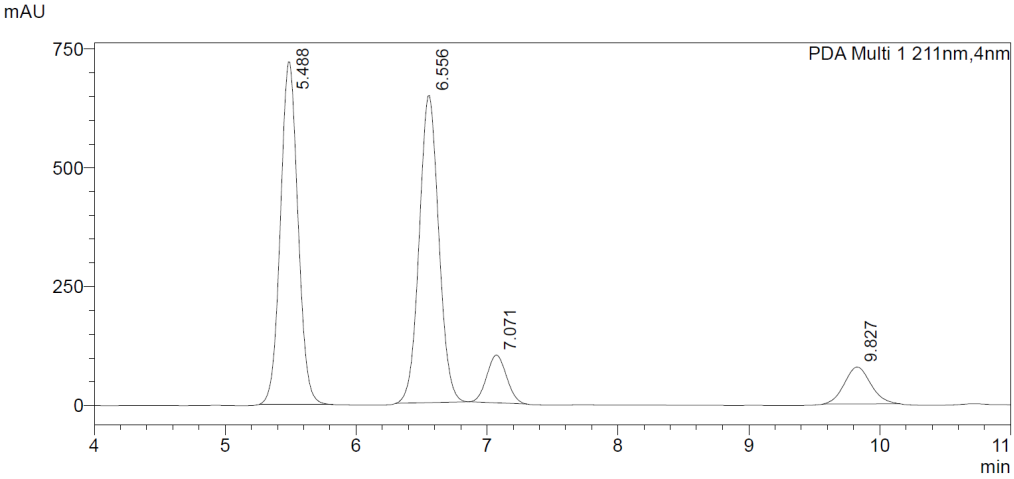


HPLC data for **23**: (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 5.5 min, t_R (2*R*,3*R*): 6.6 min, 94:6 er (minor diastereomer 85:15 er)



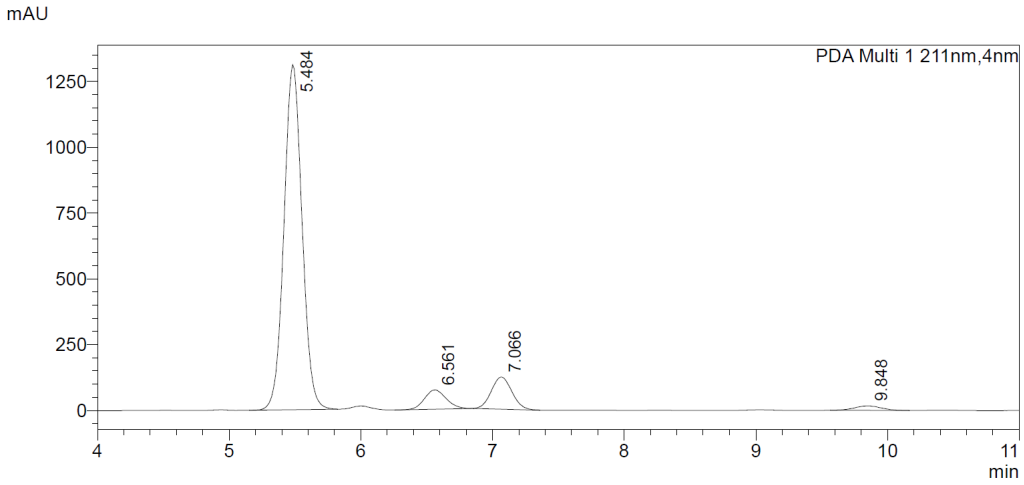
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	5.488	43.141
2	6.556	43.107
3	7.071	6.760
4	9.827	6.992
Total		100.000

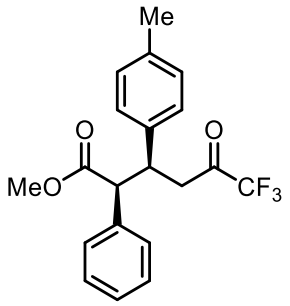


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	5.484	83.903
2	6.561	5.650
3	7.066	8.856
4	9.848	1.590
Total		100.000

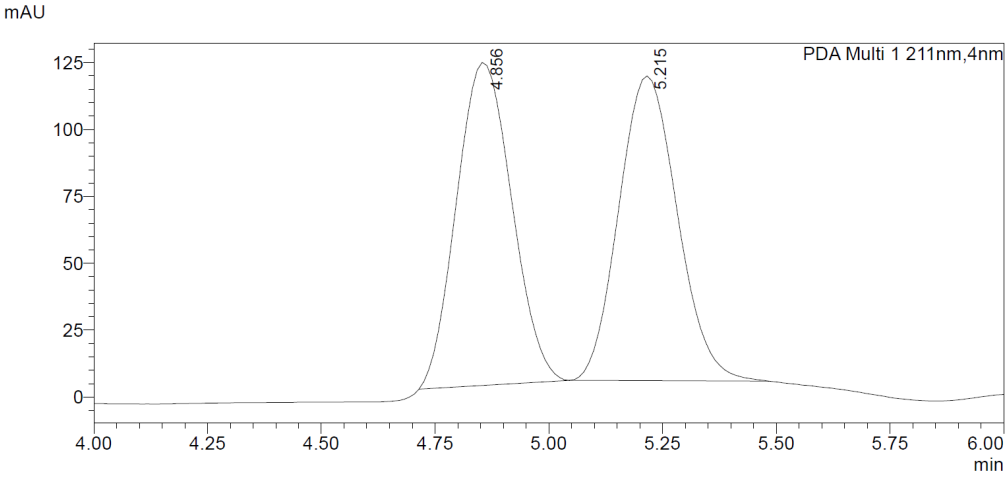


HPLC data for **24**: (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 4.9 min, t_R (2*R*,3*R*): 5.2 min, 96:4 er.



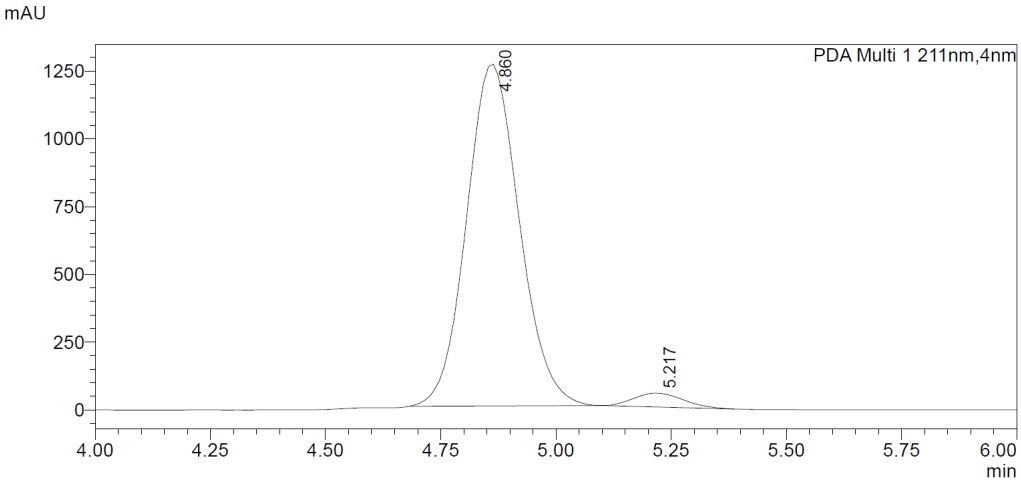
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	4.856	50.014
2	5.215	49.986
Total		100.000

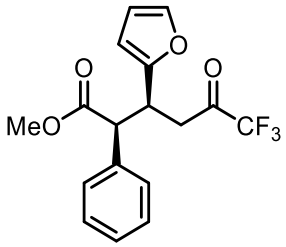


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	4.860	96.378
2	5.217	3.622
Total		100.000

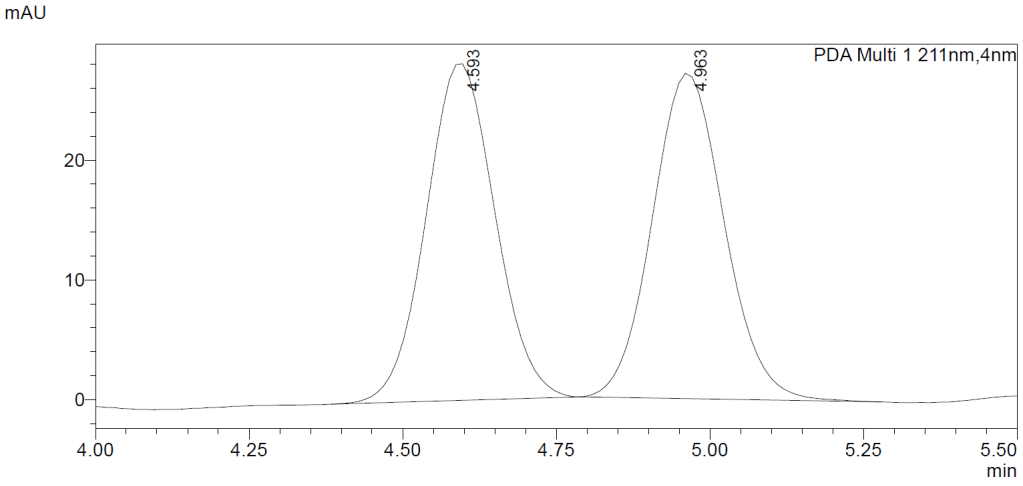


HPLC data for **25**: (Chiralpak AD-H, 4% IPA/hexane, 1.0 mL min^{-1}, 211 nm, 30 °C): t_R (2*S*,3*S*): 4.6 min, t_R (2*R*,3*R*): 5.0 min, 98:2 er.



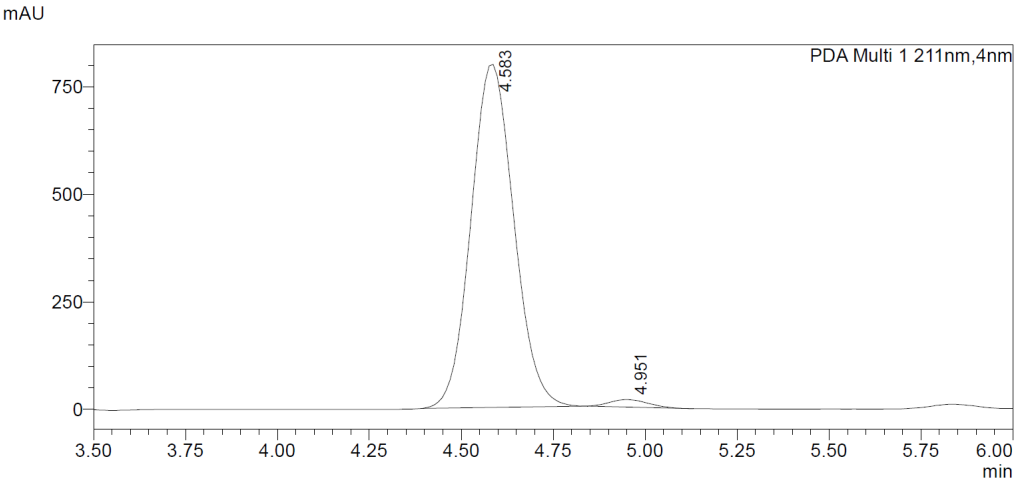
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	4.593	49.873
2	4.963	50.127
Total		100.000



PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	4.583	98.120
2	4.951	1.880
Total		100.000



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