Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supplementary Information for:

Sc(OTf)$_3$-catalyzed diastereoselective Friedel-Crafts reactions of arenes and hetarenes with 3-phenylglycidates

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Content

1. General

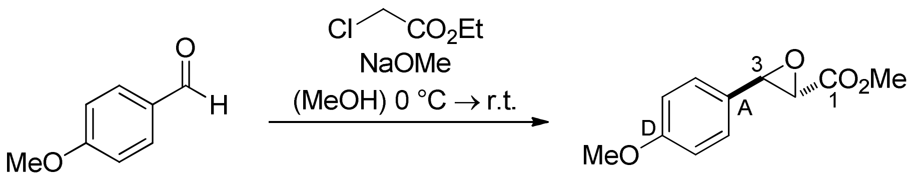
All reactions involving moisture-sensitive chemicals were carried out in flame-dried glassware in dried solvents with magnetic stirring under argon. Diethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were purified by using a SPS-800 solvent purification system (M. Braun). All other chemicals were used as received. TLC was performed on silica coated glass plates (silica gel 60 F_{254}) with detection by UV (254 nm) or ceric ammonium molybdate (CAM) with subsequent heating. Flash chromatography was performed on silica gel 60 (Merck, 230-400 mesh) with the indicated eluent. All solvents for chromatography [Pentane (P) and diethyl ether (Et_2O)] were distilled prior to use. IR-spectra were recorded on a JASCO IR-4100 (ATR), MS/HRMS-measurements were performed on a Finnigan MAT 8200 (EI), a Finnigan MAT 95S (HR-EI), a Finnigan LCQ classic (ESI) and a Thermo Scientific LTQ Orbitrap XL (HRMS-ESI). ^{1}H-and ^{13}C-NMR-spectra were recorded in $CDCl_3$ at 303 K either on a Bruker AV-250, a Bruker AV-360 or a Bruker AV-500 spectrometer. The chemical shifts are reported relative to $CHCl_3$ (δ = 7.26 ppm). Apparent multiplets that occur as a result of the accidental equality of coupling constants to those of magnetically nonequivalent protons are marked as virtual (*virt*). The multiplicities of the ^{13}C-NMR signal were determined by DEPT experiments, assignments are based on COSY, HMBC and HMQC experiments. Melting points were measured on a Koffler Thermopan and are uncorrected. Elemental analyses were carried out on a Elementar Vario EL in the Department Chemie at the Technische Universität München.

2. Substrate Synthesis

General procedure 1: *Darzens* reactions for the synthesis of compounds *trans*-2a-c

Methanol (150 mL) was carefully added to sodium (3.45 g, 150 mmol, 1.50 eq.) under an atmosphere of argon at 0 °C. After the complete dissolution of sodium, a mixture of the respective aldehyde (100 mmol, 1.00 eq.) and ethyl chloroacetate (16.0 mL, 150 mmol, 1.50 eq.) was added slowly to the alkoxide solution. The reaction mixture was stirred at ambient temperature over night, subsequently neutralised with glacial acetic acid and poured into ice water (500 mL). The mixture was extracted with CH_2Cl_2 (3 × 300 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified under the given conditions.

Methyl 3-(4-methoxyphenyl)oxirane-2-carboxylate (*trans*-2a)[1]



$C_{11}H_{12}O_4$

M = 208.21 g/mol

Following the **general procedure 1**, reaction of *p*-anisaldehyde (12.2 mL, 100 mmol, 1.00 eq.) and purification of the crude product by recrystallization from methanol yielded *trans*-**2a** (8.21 g, 39.4 mmol, 39%) as a colourless solid (d.r. *trans*/*cis* > 95/5).

TLC: R_f = 0.34 (P/Et_2O = 2/1) [UV, CAM].

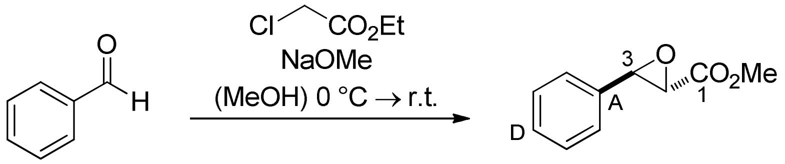
trans-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.51 (d, ^3J = 1.8 Hz, 1 H, H-2), 3.81 (s, 3 H, H_D-OMe), 3.82 (s, 3 H, COOMe), 4.05 (d, ^3J = 1.8 Hz, 1 H, H-3), 6.88-6.90 (m, 2 H, H-C), 7.20-7.22 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 52.5 (q, COO*Me*), 55.3 (q, C_D-O*Me*), 56.5 (d, C-2), 57.9 (d, C-3), 114.1 (d, C-C), 126.7 (s, C-A), 127.2 (d, C-B), 160.2 (s, C-D), 168.8 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 208 (25) [M^+], 121 (100) [$(M-C_3H_3O_3)^+$].

Methyl 3-phenyloxirane-2-carboxylate (*trans*-2b)[2]



$C_{10}H_{10}O_3$
M = 178.18 g/mol

Following the **general procedure 1**, reaction of benzaldehyde (10.1 mL, 100 mmol, 1.00 eq.) and purification of the crude product by flash chromatography (P/Et_2O = 9/1 → 2/1) yielded *trans*-**2b** (8.03 g, 45.1 mmol, 45%) as a colourless solid (d.r. *trans*/*cis* > 95/5).

TLC: R_f = 0.60 (P/Et_2O = 1/1) [UV, CAM].

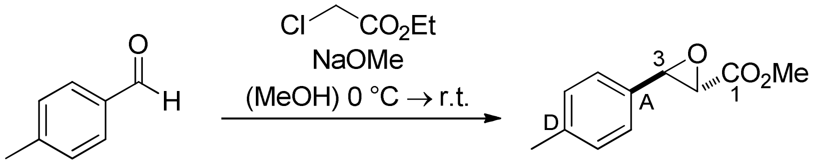
trans-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 3.52 (d, ^3J = 1.7 Hz, 1 H, H-2), 3.83 (s, 3 H, COOMe), 4.10 (d, ^3J = 1.7 Hz, 1 H, H-3), 7.28-7.31 (m, 2 H, H-B), 7.35-7.38 (m, 3 H, H-C + H-D).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 52.6 (q, COO*Me*), 56.6 (d, C-2), 58.0 (d, C-3), 125.8 (d, C-B), 128.7 (d, C-C), 129.0 (d, C-D), 134.9 (s, C-A), 168.6 (s, C-1).

MS (ESI): *m/z* (%) = 357 [$(2M+H)^+$].

Methyl 3-(*p*-tolyl)oxirane-2-carboxylate (*trans*-2c)[2]



$C_{11}H_{12}O_3$
M = 192.21 g/mol

Following the **general procedure 1**, reaction of *p*-tolualdehyde (11.8 mL, 100 mmol, 1.00 eq.) and purification of the crude product by flash chromatography (P/Et_2O = 8/1 → 2/1) yielded *trans*-**2c** (10.8 g, 56.2 mmol, 56%) as a colourless solid (d.r. *trans*/*cis* > 95/5).

TLC: R_f = 0.63 (P/Et_2O = 1/1) [UV, CAM].

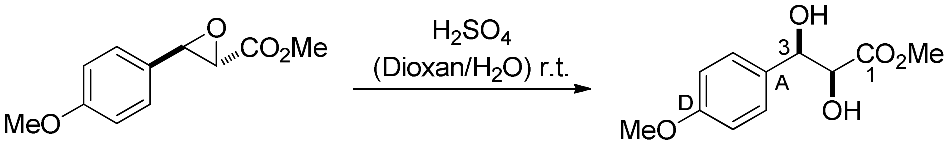
trans-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.36 (s, 3 H, H_D-Me), 3.51 (d, ^3J = 1.8 Hz, 1 H, H-2), 3.83 (s, 3 H, COOMe), 4.07 (d, ^3J = 1.8 Hz, 1 H, H-3), 7.17-7.7.18 (m, 4 H, H-B+H-C).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 21.2 (q, C_D-Me), 52.6 (q, COO*Me*), 56.6 (d, C-2), 58.0 (d, C-3), 125.8 (d, C-B), 129.3 (d, C-C), 131.8 (s, C-A), 139.0 (s, C-D), 168.8 (s, C-1).

MS (ESI): *m/z* (%) = 385 (100) [$(2M+H)^+$].

Methyl 2,3-dihydroxy-3-(4-methoxyphenyl)propanoate[3,4]



$C_{11}H_{14}O_5$
M = 226.23 g/mol

Methyl 3-(4-methoxyphenyl)oxirane-2-carboxylate (*trans*-**2a**) (2.08 g, 10.0 mmol, d.r. *trans*/*cis* > 95/5, 1.00 eq.) was dissolved in dioxane (60 mL) and water (15 mL). Conc. H_2SO_4 (250 µL, 4.69 mmol, 0.47 eq.) was added and the reaction mixture was stirred at ambient temperature over night. The solution was concentrated *in vacuo* and sat. aqueous $NaHCO_3$ (40 mL) and CH_2Cl_2 (40 mL) were subsequently added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography [P/Et_2O = 1/1 → Et_2O (100%)] to afford 1.94 g (8.57 mmol, 86%) of methyl 2,3-dihydroxy-3-(4-methoxyphenyl)propanoate as a colourless solid (d.r. *anti*/*syn* =32/68).

TLC: R_f = 0.14 (P/Et_2O = 1/3) [UV, CAM].

anti-Diastereoisomer:

^{1}H-NMR (250 MHz, $CDCl_3$): δ [ppm] = 3.10 (bs, 2 H, OH), 3.71 (s, 3 H, COOMe), 3.80 (s, 3 H, H_D-OMe), 4.47 (d, ^3J = 4.4 Hz, 1 H, H-2), 4.94 (d, ^3J = 4.4 Hz, 1 H, H-3), 6.86-6.89 (m, 2 H, H-C), 7.22-7.26 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 52.4 (q, COO*Me*), 55.2 (q, C_D-O*Me*), 74.6 (d, C-3), 74.7 (d, C-2), 113.8 (d, C-C), 127.6 (d, C-B), 130.7 (s, C-A), 159.5 (s, C-D), 172.5 (s, C-1).

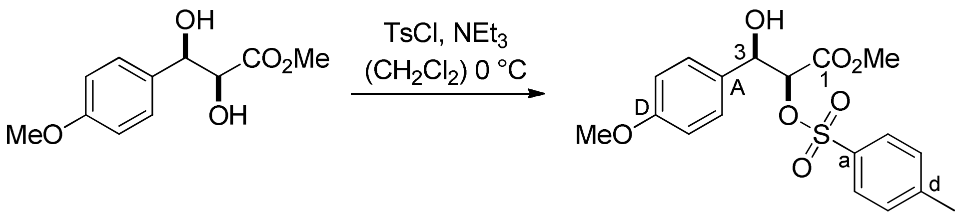
syn-Diastereoisomer:

^{1}H-NMR (250 MHz, $CDCl_3$): δ [ppm] = 2.70 (bs, 1 H, OH), 2.88 (bs, 1 H, OH), 3.81 (s, 6 H, COOMe + H_D-OMe), 4.34 (d, ^3J = 2.9 Hz, 1 H, H-2), 4.96 (d, ^3J = 2.9 Hz, 1 H, H-3), 6.88-6.93 (m, 2 H, H-C), 7.30-7.35 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 52.8 (q, COO*Me*), 55.3 (q, C_D-O*Me*), 74.1 (d, C-3), 74.7 (d, C-2), 113.9 (d, C-C), 127.5 (d, C-B), 132.0 (s, C-A), 159.4 (s, C-D), 173.2 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 226 (1) [M^+], 208 (2) [$(M-H_2O)^+$], 170 (9), 137 (100) [$(M-C_3H_5O_3)^+$], 77 (34).

Methyl 3-hydroxy-3-(4-methoxyphenyl)-2-(tosyloxy)propanoate[3,5]



$C_{18}H_{20}O_7S$

M = 380.41 g/mol

Methyl 2,3-dihydroxy-3-(4-methoxyphenyl)propanoate (1.64 g, 7.25 mmol, d.r. *anti*/*syn* = 32/68, 1.00 eq.) was dissolved in CH_2Cl_2 (40 mL) and cooled to 0 °C. NEt_3 (1.51 mL, 10.9 mmol, 1.50 eq.) and *p*-toluenesulfonyl chloride (1.42 g, 7.47 mmol, 1.03 eq.) were subsequently added and the solution was stirred for 60 h at 0 °C. The mixture was poured into ice water (50 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography (P/Et_2O = 1/1 → 1/3) to afford 1.69 g (4.44 mmol, 61%) of methyl 3-hydroxy-3-(4-methoxyphenyl)-2-(tosyloxy)propanoate as a colourless solid (d.r. *anti*/*syn* =7/93).

TLC: R_f = 0.22 (P/Et_2O = 1/3) [UV, CAM].

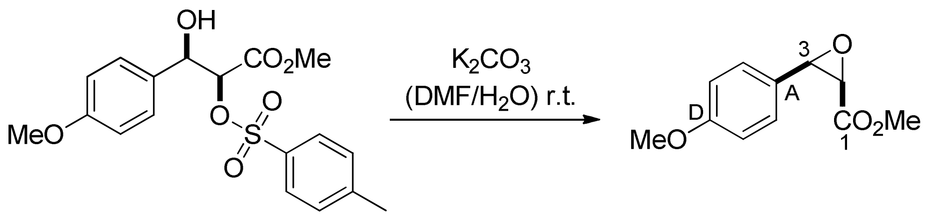
syn-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.41 (s, 3 H, H_d-Me), 2.48 (bs, 1 H, OH), 3.59 (s, 3 H, COOMe), 3.78 (s, 3 H, H_D-OMe), 4.86 (d, ^3J = 4.8 Hz, 1 H, H-2), 5.04 (d, ^3J = 4.8 Hz, 1 H, H-3), 6.74-6.76 (m, 2 H, H-C), 7.13-7.14 (m, 2 H, H-B), 7.20-7.22 (m, 2 H, H-c), 7.58-7.60 (m, 2 H, H-b).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 21.6 (q, C_d-*Me*), 52.7 (q, COO*Me*), 55.2 (q, C_D-O*Me*), 73.3 (d, C-3), 81.3 (d, C-2), 113.8 (d, C-C), 127.5 (d, C-B), 127.9 (d, C-b), 129.2 (s, C-A), 129.6 (d, C-c), 132.5 (s, C-a), 145.0 (s, C-d), 159.7 (s, C-D), 167.4 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 380 (1) [M^+], 313 (19), 171 (100) [$(M-C_{11}H_{13}O_4)^+$], 151 (19), 144 (58), 137 (70).

Methyl 3-(4-methoxyphenyl)oxirane-2-carboxylate (*cis*-2a)[3]



$C_{11}H_{12}O_4$
M = 208.21 g/mol

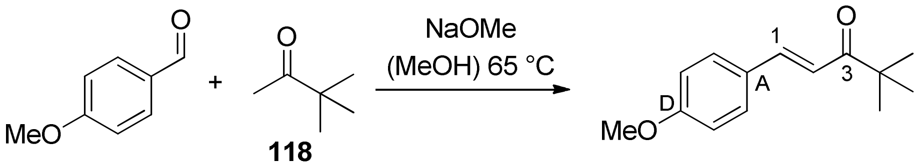
Methyl 3-hydroxy-3-(4-methoxyphenyl)-2-(tosyloxy)propanoate (1.68 g, 4.42 mmol, d.r. *anti*/*syn* = 7/93, 1.00 eq.) was dissolved in DMF (30 mL) and water (400 μL). K_2CO_3 (1.83 g, 13.4 mmol, 3.00 eq.) was added and the suspension was stirred for 20 h at ambient temperature. The mixture was poured into ice water (50 mL) and EtOAc (50 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 70 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography [P/Et_2O = 2/1 → 1/1 + 0.5% NEt_3] to afford 725 mg (3.48 mmol, 79%) of methyl 3-(4-methoxyphenyl)oxirane-2-carboxylate (*cis*-**2a**) as a colourless solid (d.r. *trans*/*cis* = 7/93).

cis-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 3.58 (s, 3 H, COOMe), 3.80 (s, 3 H, H_D-OMe), 3.81 (d, ^3J = 4.5 Hz, 1 H, H-2), 4.21 (d, ^3J = 4.5 Hz, 1 H, H-3), 6.86-6.88 (m, 2 H, H-C), 7.33-7.35 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 52.1 (q, COO*Me*), 55.2 (q, C_D-O*Me*), 56.0 (d, C-2), 57.4 (d, C-3), 113.5 (d, C-C), 124.7 (s, C-A), 127.9 (d, C-B), 159.8 (s, C-D), 167.2 (s, C-1).

1-(4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one[6]



$C_{14}H_{18}O_2$
M = 218.29 g/mol

Methanol (50 mL) was carefully added to sodium (1.59 g, 69.0 mmol, 1.15 eq.) under an atmosphere of argon at 0 °C. After the complete dissolution of sodium, a mixture of *p*-anisaldehyde (7.29 mL, 60.0 mmol, 1.00 eq.) and pinacolone 8.26 mL (66.0 mmol, 1.10 eq.) was added slowly to the alkoxide solution. The reaction mixture was heated to reflux for 24 h. After cooling to ambient temperature sat. aqueous NH_4Cl (30 mL) and Et_2O (60 mL) were added and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 80 mL).

The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography [P/Et_2O = 8/1 → 4/1] to afford 11.6 g (53.1 mmol, 88%) of 1-(4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one as a yellow oil (d.r. *trans*/*cis* > 95/5).

TLC: R_f = 0.53 (P/Et_2O = 2/1) [UV, CAM].

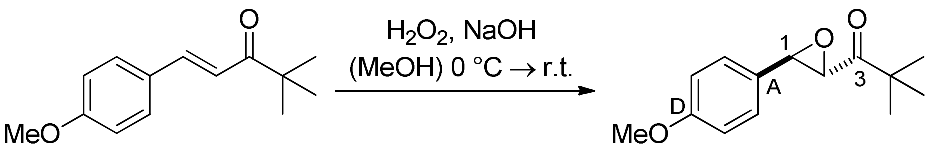
trans-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.23 [s, 9 H, $C(CH_3)_3$], 3.84 (s, 3 H, OMe), 6.90-6.92 (m, 2 H, H-C), 7.01 (d, ^3J = 15.5 Hz, 1 H, H-2), 7.52-7.54 (m, 2 H, H-B), 7.65 (d, ^3J = 15.5 Hz, 1 H, H-1).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 26.4 [q, $C(CH_3)_3$], 43.1 [s, $C(CH_3)_3$], 55.4 (q, OMe), 114.3 (d, C-C), 118.5 (d, C-2), 127.7 (s, C-A), 130.0 (d, C-B), 142.6 (d, C-1), 161.3 (s, C-D), 204.3 (s, C-3).

MS (ESI): *m/z* (%) = 219 (100) [$(M+H)^+$], 121 (8).

4,4-Dimethyl-1,2-epoxy-1-(4-methoxyphenyl)-pentan-3-one[6]



$C_{14}H_{18}O_3$
M = 234.29 g/mol

1-(4-methoxyphenyl)-4,4-dimethylpent-1-en-3-one (3.00 g, 13.7 mmol, d.r. *trans*/*cis* > 95/5, 1.00 eq.) was dissolved in methanol (20 mL) and cooled to 0 °C. H_2O_2 (3.83 mL, 44.7 mmol, 35% in H_2O, 3.25 eq.) was added over a period of 5 min and aqueous 2 M NaOH (4.00 mL, 8.00 mmol, 0.58 eq.) was subsequently added over a period of 15 min. The reaction mixture was stirred at ambient temperature over night. Sat. aqueous $Na_2S_2O_3$ (40 mL) was added and the mixture was stirred for 30 min at ambient temperature. The mixture was extracted with Et_2O (3 × 60 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by recrystallization from P/Et_2O = 4/1 to afford 1.20 g (5.12 mmol, 37%) of 4,4-Dimethyl-1,2-epoxy-1-(4-methoxyphenyl)-pentan-3-one as a colourless solid (d.r. *trans*/*cis* > 95/5).

TLC: R_f = 0.37 (P/Et_2O = 2/1 + 1% NEt_3) [UV, CAM].

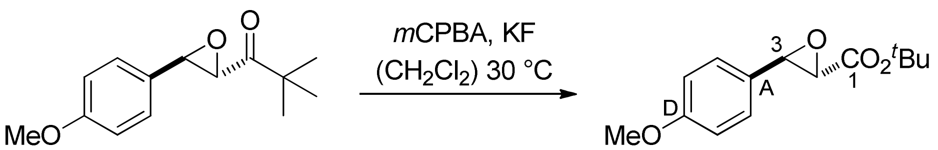
trans-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 1.23 [s, 9 H, $C(CH)_3$], 3.80 (d, ^3J = 1.9 Hz, 1 H, H-1), 3.81 (s, 3 H, OMe), 3.85 (d, ^3J = 1.9 Hz, 1 H, H-2), 6.88-6.92 (m, 2 H, H-C), 7.21-7.25 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 25.7 [q, C(*C*H)$_3$], 43.5 [s, *C*(CH)$_3$], 55.3 (q, OMe), 59.1 (d, C-2), 59.3 (d, C-1), 114.1 (d, C-C), 127.0 (d, C-B), 127.5 (s, C-A), 160.2 (s, C-D), 208.2 (s, C-3).

MS (EI, 70 eV): *m/z* (%) = 234 (35) [M^+], 177 (8) [$(M-C_4H_9)^+$], 161 (11) [$(M-C_4H_9O)^+$], 149 (19), 149 (19) [$(M-C_5H_9O)^+$], 121 (100) [$(M-C_6H_9O_2)^+$], 57 (70).

tert-Butyl 3-(4-methoxyphenyl)oxirane-2-carboxylate (*trans*-5)[6]



$C_{14}H_{18}O_4$
M = 250.29 g/mol

3-Chloroperoxybenzoic acid (3.28 g, 13.3 mmol, 70-75% in H_2O, 2.60 eq.) and KF (2.23 g, 38.4 mmol, 7.50 eq.) were dissolved in CH_2Cl_2 (60 mL) under an atmosphere of argon and stirred at ambient temperature for 30 min. Then 4,4-Dimethyl-1,2-epoxy-1-(4-methoxyphenyl)-pentan-3-one (1.20 g, 5.12 mmol, d.r. *trans*/*cis* > 95/5, 1.00 eq.), dissolved in CH_2Cl_2 (20 mL), was added and the reaction mixture was stirred at 30 °C over night. After cooling to ambient temperature 3-Chloroperoxybenzoic acid (500 mg, 2.03 mmol, 0.40 eq.) was added and the reaction mixture was stirred for another 4 h at 30 °C. The mixture was cooled to ambient temperature and filtered over Celite®. The filtrate was concentrated *in vacuo* and the crude product was purified by recrystallization from P/Et_2O = 4/1 to afford 1.07 g (4.28 mmol, 83%) of *tert*-butyl 3-(4-methoxyphenyl)oxirane-2-carboxylate (*trans*-**5**) as a colourless solid (d.r. *trans*/*cis* > 95/5).

TLC: R_f = 0.52 (P/Et_2O = 2/1 + 1% NEt_3) [UV, CAM].

trans-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.51 [s, 9 H, $C(CH)_3$], 3.40 (d, ^3J = 1.7 Hz, 1 H, H-2), 3.81 (s, 3 H, OMe), 3.97 (d, ^3J = 1.7 Hz, 1 H, H-3), 6.88-6.90 (m, 2 H, H-C), 7.20-7.22 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 28.0 [q, C(*C*H)$_3$], 55.3 (q, OMe), 57.3 (d, C-2), 57.5 (d, C-3), 82.5 [s, *C*(CH)$_3$], 114.0 (d, C-C), 127.2 (s, C-A), 127.2 (d, C-B), 160.1 (s, C-D), 167.4 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 250 (6) [M^+], 194 (27), 150 (31), 137 (39), 121 (100) [$(M-C_6H_9O_3)^+$].

3. Diastereoselective *Friedel-Crafts* alkylations

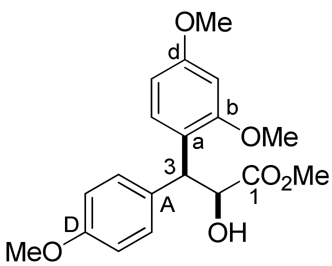
General procedure 2: *Friedel-Crafts* alkylations with glycidic esters 2

A flame-dried Schlenk flask was purged with argon and charged with the glycidic ester **2** (250 µmol, 1.00 eq.) and the aryl nucleophile (1.00 mmol, 4.00 eq.) in dry nitromethane (2 mL). The solution was cooled to 0 °C and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) was added. The resulting mixture was stirred at 0 °C for 45 min. The reaction was quenched with sat. aqueous $NaHCO_3$ (5 mL) and diluted with CH_2Cl_2 (5 mL) The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 7 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography to give the respective product.

General procedure 3: *Friedel-Crafts* alkylations with glycidic ester 5

A flame-dried Schlenk flask was purged with argon and charged with the glycidic ester **5** (37.5 mg, 150 µmol, 1.00 eq.) and the aryl nucleophile (600 µmol, 4.00 Äq.) in dry nitromethane (2 mL). The solution was cooled to −25 °C and $Sc(OTf)_3$ (3.69 mg, 7.50 µmol, 0.05 eq.) was added. The resulting mixture was stirred at −25 °C for 4 h. The reaction was quenched with sat. aqueous $NaHCO_3$ (5 mL) and diluted with CH_2Cl_2 (5 mL) The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 7 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography to give the respective product.

Methyl 3-(2,4-dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)propanoate (6a)



$C_{19}H_{22}O_6$
M = 346.37 g/mol

Following **general procedure 2**, reaction of **2a** (52.1 mg, 250 µmol, 1.00 eq.) with 1,3-dimethoxybenzene (132 µL, 1.00 mmol, 4.00 eq.) and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 2/1) **6a** (66 mg, 191 µmol, 76%) as a colourless solid (d.r. *anti*/*syn* 17/83).

TLC: R_f = 0.21 (P/Et_2O 1/1) [UV, CAM].

m.p.: 130-132 °C (d.r. *anti*/*syn* = 17/83).

IR (ATR): $\tilde{\nu}$ = 3556 (br, OH), 2954 (w, $C_{al}H$), 2837 (w, OMe), 2353 (m), 1732 (vs, C=O), 1610 (s), 1584 (s), 1501 (vs), 1473 (m, CH_3), 1246 (vs, COC), 1181 (m), 1112 (vs), 1087 (m), 1028 (s), 841 cm^{-1} (s, $C_{ar}H$).

syn-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.76 (bs, 1 H, OH), 3.67 (s, 3 H, COOMe), 3.76 + 3.77 + 3.78 (3×s, 3×3 H, H_b-OMe + H_d-OMe + H_D-OMe), 4.82-4.85 (m, 2 H, H-2 + H-3), 6.40-6.44 (m, 2 H, H-c + H-e), 6.83 (*virt*.d, $J \cong$ 8.4 Hz, 2 H, H-C), 7.11 (d, ^3J = 8.4 Hz, 1 H, H-f), 7.30 (*virt*.d, $J \cong$ 8.4 Hz, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 45.7 (d, C-3), 52.1 (q, COO*Me*), 55.2 + 55.2 + 55.5 (3×C, 3×q, C_b-O*Me* + C_d-O*Me* + C_D-O*Me*), 73.2 (d, C-2), 98.5 (d, C-c), 104.2 (d, C-e), 113.6 (d, C-C), 119.8 (s, C-a), 129.5 (d, C-B), 131.2 (d, C-f), 134.0 (s, C-A), 157.9 + 158.0 + 159.7 (3×C, 3×s, C-b + C-d + C-D), 174.4 (s, C-1).

anti-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.76 (bs, 1 H, OH), 3.69 (s, 3 H, COOMe), 3.74 + 3.77 + 3.78 (3×s, 3×3 H, H_b-OMe + H_d-OMe + H_D-OMe), 4.74 (d, ^3J = 3.8 Hz, 1 H, H-3), 4.82-4.86 (m, 1 H, H-2), 6.42-6.44 (m, 1 H, H-c), 6.45-6.47 (m, 1 H, H-e), 6.80 (*virt*.d, $J \cong$ 8.3 Hz, 2 H, H-C), 7.20 (*virt*.d, $J \cong$ 8.6 Hz, 2 H, H-B), 7.44 (d, ^3J = 8.3 Hz, 1 H, H-f).

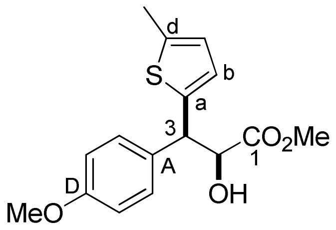
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 46.2 (d, C-3), 52.4 (q, COO*Me*), 55.1 + 55.3 + 55.4 (3×C, 3×q, C_b-O*Me* + C_d-O*Me* + C_D-O*Me*), 73.3 (d, C-2), 98.6 (d, C-c), 103.9 (d, C-e), 113.5 (d, C-C), 122.6 (s, C-a), 129.7 (d, C-f), 130.2 (d, C-B), 131.2 (s, C-A), 157.6 + 158.2 + 159.6 (3×C, 3×s, C-b + C-d + C-D), 174.4 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 346 (1) [M^+], 328 (3) [$(M-H_2O)^+$], 257 (75) [$(M-C_3H_5O_3)^+$], 196 (94), 165 (84), 135 (100).

HRMS (EI): $C_{19}H_{20}O_5$ [$(M-H_2O)^+$]: calcd.: 328.1305; found: 328.1306.

CHN ($C_{19}H_{22}O_6$):	calcd.:	C: 65.88	H: 6.40
	found:	C: 65.89	H: 6.61.

Methyl 2-hydroxy-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (7a)



$C_{16}H_{18}O_4S$
M = 306.38 g/mol

Following **general procedure 2**, reaction of **2a** (52.1 mg, 250 µmol, 1.00 eq.) with 2-methylthiophene (96.8 µL, 1.00 mmol, 4.00 eq.) and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 1/1) **7a** (64 mg, 209 µmol, 84%) as a yellow oil (d.r. *anti*/*syn* 25/75).

TLC: R_f = 0.18 (P/Et_2O: 2/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3484 (br, OH), 2928 (w, $C_{al}H$), 2837 (w, OMe), 1735 (vs, C=O), 1610 (m), 1511 (vs), 1439 (m, CH_3), 1246 (vs, COC), 1179 (s), 1113 (m), 1031 (s), 834 (m, $C_{ar}H$), 802 (m), 731 cm^{-1} (m).

syn-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.41 (d, ^4J = 1.1 Hz, 3 H, H_d-Me), 3.03 (d, ^3J = 5.8 Hz, 1 H, OH), 3.73 (s, 3 H, COOMe), 3.79 (s, 3 H, H_D-OMe), 4.63 (d, ^3J = 3.6 Hz, 1 H, H-3), 4.72 (dd, ^3J = 3.6 Hz, ^3J = 5.8 Hz, 1 H, H-2), 6.56-6.58 (m, 1 H, H-c), 6.69 (d, ^3J = 3.4 Hz, 1 H, H-b), 6.84-6.88 (m, 2 H, H-C), 7.36-7.40 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 49.5 (d, C-3), 52.6 (q, COO*Me*), 55.2 (q, C_D-O*Me*), 74.2 (d, C-2), 113.8 (d, C-C), 124.5 (d, C-c), 126.1 (d, C-b), 129.3 (d, C-B), 133.0 (s, C-A), 139.0 (s, C-a), 139.4 (s, C-d), 158.5 (s, C-D), 173.7 (s, C-1).

anti-Diastereoisomer:

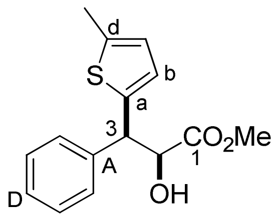
^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.43 (d, ^4J = 1.0 Hz, 3 H, H_d-Me), 2.86 (d, ^3J = 5.8 Hz, 1 H, OH), 3.72 (s, 3 H, COOMe), 3.78 (s, 3 H, H_D-OMe), 4.60 (d, ^3J = 3.4 Hz, 1 H, H-3), 4.82 (dd, ^3J = 3.4 Hz, ^3J = 5.8 Hz, 1 H, H-2), 6.58-6.60 (m, 1 H, H-c), 6.81-6.88 (m, 3 H, H-b + H-C), 7.22-7.25 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 49.4 (d, C-3), 52.5 (q, COO*Me*), 55.1 (q, C_D-O*Me*), 74.2 (d, C-2), 113.7 (d, C-C), 124.5 (d, C-c), 125.4 (d, C-b), 130.0 (d, C-B), 130.4 (s, C-A), 138.8 (s, C-d), 142.0 (s, C-a), 158.9 (s, C-D), 173.4 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 306 (1) [M^+], 217 (100) [$(M-C_3H_5O_3)^+$], 135 (34), 121 (26).

HRMS (EI): $C_{16}H_{18}O_4S$ [M^+]: calcd.: 306.0920; found: 306.0917.

Methyl 2-hydroxy-3-(5-methylthiophen-2-yl)-3-phenylpropanoate (7b)



$C_{15}H_{16}O_3S$
M = 276.35 g/mol

Following **general procedure 2**, reaction of **2b** (44.5 mg, 250 µmol, 1.00 eq.) with 2-methylthiophene (96.8 µL, 1.00 mmol, 4.00 eq.) and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 6/1 → 2/1) **7b** (36 mg, 130 µmol, 52%) as a yellow oil (d.r. *anti*/*syn* 44/56).

TLC: R_f = 0.49 (P/Et_2O: 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3493 (br, OH), 3025 (w, $C_{ar}H$), 2952 (w, $C_{al}H$), 2919 (w, $C_{al}H$), 2861 (w), 1733 (vs, C=O), 1557 (w), 1495 (m, $C=C_{ar}$), 1437 (s, CH_3), 1217 (vs, COC), 1093 (vs), 796 (m), 700 cm^{-1} (s).

syn-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.37 (d, ^4J = 0.9 Hz, 3 H, H_d-Me), 3.02 (bs, 1 H, OH), 3.69 (s, 3 H, COOMe), 4.64 (d, ^3J = 3.4 Hz, 1 H, H-3), 4.72 (d, ^3J = 3.4 Hz, 1 H, H-2), 6.53-6.56 (m, 1 H, H-c), 6.67 (d, ^3J = 3.4 Hz, 1 H, H-b), 7.19-7.44 (m, 5 H, H-B + H-C + H-D).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 50.2 (d, C-3), 52.7 (q, COO*Me*), 74.0 (d, C-2), 124.6 (d, C-c), 126.3 (d, C-b), 127.0 (d, C-D), 128.3 + 128.4 (2×C, 2×d, C-B + C-C), 138.4 (s, C-a), 139.5 (s, C-d), 140.8 (s, C-A), 173.6 (s, C-1).

anti-Diastereoisomer:

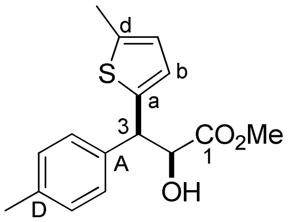
^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.39 (bs, 3 H, H_d-Me), 2.83 (bs, 1 H, OH), 3.67 (s, 3 H, COOMe), 4.59 (d, ^3J = 3.4 Hz, 1 H, H-3), 4.80 (d, ^3J = 3.4 Hz, 1 H, H-2), 6.53-6.56 (m, 1 H, H-c), 6.79 (d, ^3J = 3.4 Hz, 1 H, H-b), 7.19-7.44 (m, 5 H, H-B + H-C + H-D).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 50.3 (d, C-3), 52.5 (q, COO*Me*), 74.2 (d, C-2), 124.5 (d, C-c), 125.6 (d, C-b), 127.5 (d, C-D), 128.2 + 128.9 (2×C, 2×d, C-B + C-C), 138.3 (s, C-A), 138.9 (s, C-d), 141.5 (s, C-a), 173.3 (s, C-1).

MS (ESI): *m/z* (%) = 299 [$(M+Na)^+$], 277 [$(M+H)^+$].

HRMS (ESI): $C_{15}H_{16}O_3SNa$ [$(M+Na)^+$]: calcd.: 299.0712; found: 299.0712.

Methyl 2-hydroxy-3-(5-methylthiophen-2-yl)-3-(*p*-tolyl)propanoate (7c)



$C_{16}H_{18}O_3S$

M = 290.38 g/mol

Following **general procedure 2**, reaction of **2c** (48.1 mg, 250 µmol, 1.00 eq.) with 2-methylthiophene (96.8 µL, 1.00 mmol, 4.00 eq.) and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 1/1) **7c** (58 mg, 200 µmol, 80%) as a yellow oil (d.r. *anti*/*syn* 35/65).

TLC: R_f = 0.49 (P/Et_2O: 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3493 (br, OH), 3005 (w, $C_{ar}H$), 2952 (m, $C_{al}H$), 2912 (m, $C_{al}H$), 2861 (w), 1733 (vs, C=O), 1639 (m), 1513 (s), 1437 (s, CH_3), 1215 (vs, COC), 1092 (vs), 1021 (m), 798 (s), 723 cm^{-1} (s).

syn-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.33 (s, 3 H, H_D-Me), 2.41 (d, ^4J = 1.0 Hz, 3 H, H_d-Me), 3.02 (d, ^3J = 6.3 Hz, 1 H, OH), 3.74 (s, 3 H, COOMe), 4.65 (d, ^3J = 3.5 Hz, 1 H, H-3), 4.74 (dd, ^3J = 6.3 Hz, ^3J = 3.5 Hz, 1 H, H-2), 6.57 (dd, ^3J = 3.4 Hz, ^4J = 1.0 Hz, 1 H, H-c), 6.70 (d, ^3J = 3.4 Hz, 1 H, H-b), 7.13 (*virt*. d, $J \cong 7.9$ Hz, 2 H, H-C), 7.35 (*virt*. d, $J \cong 8.1$ Hz, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 21.0 (q, C_D-*Me*), 49.9 (d, C-3), 52.6 (q, COO*Me*), 74.2 (d, C-2), 124.6 (d, C-c), 126.2 (d, C-b), 128.1 (d, C-B), 129.1 (d, C-C), 136.7 (s, C-D), 137.9 (s, C-A), 138.7 (s, C-a), 139.4 (s, C-d), 173.7 (s, C-1).

anti-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.31 (s, 3 H, H_D-Me), 2.43 (bs, 3 H, H_d-Me), 2.83 (d, ^3J = 6.7 Hz, 1 H, OH), 3.72 (s, 3 H, COOMe), 4.60 (d, ^3J = 3.5 Hz, 1 H, H-3), 4.83 (dd, ^3J = 6.7 Hz, ^3J = 3.5 Hz, 1 H, H-2), 6.59 (dd, ^3J = 3.4 Hz, ^4J = 1.1 Hz, 1 H, H-c), 6.83

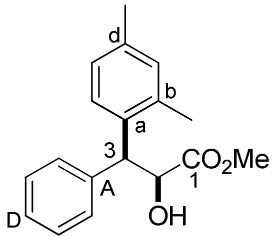
(d, ^3J = 3.4 Hz, 1 H, H-b), 7.10 (*virt*. d, $J \cong$ 8.1 Hz, 2 H, H-C), 7.19 (*virt*. d, $J \cong$ 8.1 Hz, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 21.1 (q, C_D-*Me*), 50.0 (d, C-3), 52.5 (q, COO*Me*), 74.2 (d, C-2), 124.5 (d, C-c), 125.5 (d, C-b), 128.8 (d, C-B), 129.1 (d, C-C), 135.3 (s, C-A), 137.1 (s, C-D), 138.9 (s, C-d), 141.8 (s, C-a), 173.4 (s, C-1).

MS (ESI): *m/z* (%) = 313 [$(M+Na)^+$], 291 [$(M+H)^+$].

HRMS (ESI): $C_{16}H_{19}O_3S$ [$(M+H)^+$]: calcd.: 291.1049; found: 291.1050.

Methyl 3-(2,4-dimethylphenyl)-2-hydroxy-3-phenylpropanoate (8b)



$C_{18}H_{20}O_3$
M = 284.35 g/mol

Following **general procedure 2**, reaction of **2b** (44.5 mg, 250 µmol, 1.00 eq.) with *m*-xylene (123 µL, 1.00 mmol, 4.00 eq.) and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 1/1) **8b** (26 mg, 91.4 µmol, 37%) as a colourless oil (d.r. *anti*/*syn* 29/71).

TLC: R_f = 0.41 + 0.50 (P/Et_2O 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3469 (br, OH), 3025 (w, $C_{ar}H$), 2948 (w, $C_{al}H$), 2912 (w, $C_{al}H$), 1733 (vs, C=O), 1557 (m), 1494 (s, $C=C_{ar}$), 1451 (s), 1438 (s, CH_3), 1228 (vs, COC), 1122 (m), 1091 (vs), 802 (m, $C_{ar}H$), 699 cm^{-1} (vs).

syn-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.20 (s, 3 H, H_b-Me), 2.28 (s, 3 H, H_d-Me), 2.74 (d, ^3J = 5.1 Hz, 1 H, OH), 3.58 (s, 3 H, COOMe), 4.59 (d, ^3J = 5.9 Hz, 1 H, H-3), 4.88-4.91 (m, 1 H, H-2), 6.96 (bs, 1 H, H-c), 7.02 (d, ^3J = 7.8 Hz, 1 H, H-e), 7.18-7.27 (m, 5 H, H-B + H-C + H-D), 7.47 (d, ^3J = 7.8 Hz, 1 H, H-f).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 19.7 (q, C_b-*Me*), 20.9 (q, C_d-*Me*), 50.1 (d, C-3), 52.2 (q, COO*Me*), 74.0 (d, C-2), 126.6 + 126.7 (2×C, 2×d, C-D + C-e), 128.0 (d, C-f), 128.4 + 128.6 (2×C, 2×d, C-B + C-C), 131.6 (d, C-c), 134.5 (s, C-a), 136.4 (s, C-d), 136.5 (s, C-b), 140.5 (s, C-A), 174.2 (s, C-1).

anti-Diastereoisomer:

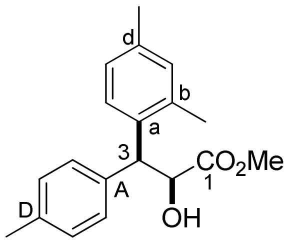
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 2.12 (s, 3 H, H_b-Me), 2.30 (s, 3 H, H_d-Me), 2.66 (d, ^3J = 7.2 Hz, 1 H, OH), 3.77 (s, 3 H, COOMe), 4.59-4.60 (m, 1 H, H-3), 4.88-4.91 (m, 1 H, H-2), 6.94 (bs, 1 H, H-c), 7.07 (d, ^3J = 8.2 Hz, 1 H, H-e), 7.12-7.14 (m, 2 H, H_{Ar}), 7.23-7.27 (m, 3 H, H_{Ar}), 7.72 (d, ^3J = 8.2 Hz, 1 H, H-f).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 19.9 (q, C_b-*Me*), 20.9 (q, C_d-*Me*), 50.4 (d, C-3), 52.5 (q, COO*Me*), 73.6 (d, C-2), 126.7 + 126.9 (2×C, 2×d, C-D + C-e), 127.8 (d, C-f), 128.3 + 129.4 (2×C, 2×d, C-B + C-C), 131.3 (d, C-c), 136.0 (s, C-b), 136.3 (s, C-d), 136.9 (s, C-a), 138.1 (s, C-A), 174.2 (s, C-1).

MS (ESI): *m/z* (%) = 307 [$(M+Na)^+$], 285 [$(M+H)^+$].

HRMS (ESI): $C_{18}H_{21}O_3$ [$(M+H)^+$]: calcd.: 285.1485; found: 285.1485.

Methyl 3-(2,4-dimethylphenyl)-2-hydroxy-3-(*p*-tolyl)propanoate (8c)



$C_{19}H_{22}O_3$
M = 298.38 g/mol

Following **general procedure 2**, reaction of **2c** (48.1 mg, 250 µmol, 1.00 eq.) with *m*-xylene (123 µL, 1.00 mmol, 4.00 eq.) and $Sc(OTf)_3$ (6.15 mg, 12.5 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 1/1) **8c** (24 mg, 80.4 µmol, 32%) as a colourless oil (d.r. *anti*/*syn* 9/91).

TLC: R_f = 0.61 (*anti*)/0.56 (*syn*) (P/Et_2O: 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3484 (br, OH), 3006 (w, $C_{ar}H$), 2952 (m, $C_{al}H$), 2919 (m, $C_{al}H$), 2861 (w), 1732 (vs, C=O), 1512 (s), 1503 (s), 1437 (s, CH_3), 1253 (vs, COC), 1126 (s), 1090 (vs), 805 (s, $C_{ar}H$), 737 cm^{-1} (m).

syn-Diastereoisomer:

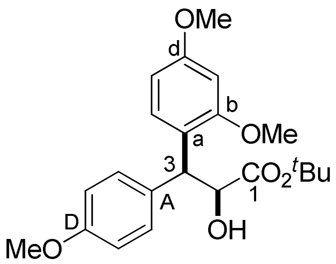
^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 2.20 (s, 3 H, H_b-Me), 2.28 (s, 3 H, H_d-Me), 2.30 (s, 3 H, H_D-Me), 2.71 (bs, 1 H, OH), 3.59 (s, 3 H, COOMe), 4.56 (d, ^3J = 5.8 Hz, 1 H, H-3), 4.88 (d, ^3J = 5.8 Hz, 1 H, H-2), 6.94-6.97 (m, 1 H, H-c), 7.00-7.03 (m, 1 H, H-e), 7.07-7.09 (m, 2 H, H-C), 7.13-7.15 (m, 2 H, H-B), 7.47 (d, ^3J = 7.9 Hz, 1 H, H-f).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 19.7 (q, C_b-*Me*), 20.9 + 21.0 (2×C, 2×q, C_d-*Me* + C_D-*Me*), 49.6 (d, C-3), 52.3 (q, COO*Me*), 74.1 (d, C-2), 126.7 (d, C-e), 127.9 (d, C-f), 128.4 (d, C-B), 129.1 (d, C-C), 131.5 (d, C-c), 134.6 (s, C-a), 136.2 (s, C-D), 136.3 (s, C-d), 136.5 (s, C-b), 137.3 (s, C-A), 174.2 (s, C-1).

MS (ESI): *m/z* (%) = 321 [$(M+Na)^+$], 299 [$(M+H)^+$].

HRMS (ESI): $C_{19}H_{23}O_3$ [$(M+H)^+$]: calcd.: 299.1642; found: 299.1642.

tert-Butyl 3-(2,4-dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)propanoate (11a)



$C_{22}H_{28}O_6$
M = 388.45 g/mol

Following **general procedure 3**, reaction of **5** (37.5 mg, 150 µmol, 1.00 eq.) with 1,3-dimethoxybenzene (79.0 µL, 600 µmol, 4.00 eq.) and $Sc(OTf)_3$ (3.69 mg, 7.50 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 1/1) **11a** (45 mg, 116 µmol, 77%) as a colourless solid (d.r. *anti*/*syn* 7/93).

TLC: R_f = 0.21 (P/Et_2O 2/1) [UV, CAM].

m.p.: 115 °C (d.r. *anti*/*syn* = 7/93).

IR (ATR): $\tilde{\nu}$ = 3490 (br, OH), 2984 (w, C_{al}H), 2939 (w), 2911 (w), 2837 (m, OMe), 1717 (vs, C=O), 1608 (s), 1507 (vs), 1469 (m, CH_3), 1260 (s, COC), 1207 (s), 1157 (vs), 1124 (s), 1034 (s), 834 (m, C_{ar}H), 737 cm^{-1} (m).

syn-Diastereoisomer:

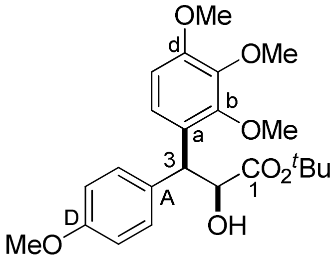
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.25 [s, 9 H, $C(CH_3)_3$], 3.01 (bs, 1 H, OH), 3.76 + 3.76 (2×s, 2×3 H, H_b-OMe + H_D-OMe), 3.77 (s, 3 H, H_d-OMe), 4.70 (d, ^3J = 5.8 Hz, 1 H, H-2), 4.77 (d, ^3J = 5.8 Hz, 1 H, H-3), 6.43 (d, ^4J = 2.5 Hz, 1 H, H-c), 6.46 (dd, ^3J = 8.5 Hz, ^4J = 2.5 Hz, 1 H, H-e), 6.80-6.82 (m, 2 H, H-C), 7.25-7.27 (m, 2 H, H-B), 7.42 (d, ^3J = 8.5 Hz, 1 H, H-f).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 27.7 [q, $C(CH_3)_3$], 45.4 (d, C-3), 55.2 + 55.3 + 55.4 (3×C, 3×q, C_b-O*Me* + C_d-O*Me* + C_D-O*Me*), 74.0 (d, C-2), 82.0 [s, $C(CH_3)_3$], 98.6 (d, C-c), 104.1 (d, C-e), 113.6 (d, C-C), 121.2 (s, C-a), 129.7 (d, C-B), 130.2 (d, C-f), 133.6 (s, C-A), 158.0 + 158.0 (2×C, 2×s, C-b + C-D), 159.5 (s, C-d), 173.2 (s, C-1).

MS (ESI): *m/z* (%) = 799 (100) [$(2M+Na)^+$], 735 (38), 411 (34) [$(M+Na)^+$], 333 (20), 225 (9).

HRMS (ESI): $C_{22}H_{28}O_6Na$ [$(M+Na)^+$]: calcd.: 411.1778; found: 411.1776.

tert-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(2,3,4-trimethoxyphenyl)propanoate (11b)



$C_{23}H_{30}O_7$
M = 418.48 g/mol

Following **general procedure 3**, reaction of **5** (37.5 mg, 150 µmol, 1.00 eq.) with 1,2,3-trimethoxybenzene (101 mg, 600 µmol, 4.00 Eq.) and $Sc(OTf)_3$ (3.69 mg, 7.50 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 1/1) **11b** (35 mg, 83.6 µmol, 56%) as a colourless oil (d.r. *anti*/*syn* < 5/95).

TLC: R_f = 0.34 (P/Et_2O 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3479 (br, OH), 2977 (w, $C_{al}H$), 2933 (w), 2837 (m, OMe), 1722 (vs, C=O), 1605 (s), 1510 (m), 1493 (m, $C=C_{ar}$), 1462 (s, CH_3), 1244 (vs, COC), 1156 (s), 1092 (vs), 838 (s, $C_{ar}H$), 803 cm^{-1} (s).

syn-Diastereoisomer:

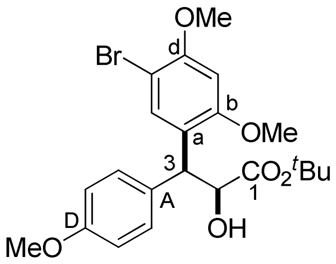
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.27 [s, 9 H, $C(CH_3)_3$], 3.07 (d, ^3J = 5.8 Hz, 1 H, OH), 3.68 (s, 3 H, H_b-OMe), 3.77 (s, 3 H, H_D-OMe), 3.82 (s, 3 H, H_c-OMe), 3.83 (s, 3 H, H_d-OMe), 4.67 (*virt.* t, $^3J \cong$ 5.6 Hz, 1 H, H-2), 4.71 (d, ^3J = 5.7 Hz, 1 H, H-3), 6.64 (d, ^3J = 8.8 Hz, 1 H, H-e), 6.82-6.84 (m, 2 H, H-C), 7.24 (d, ^3J = 8.8 Hz, 1 H, H-f), 7.26-7.27 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 27.7 [q, $C(\mathit{C}H_3)_3$], 46.3 (d, C-3), 55.2 (q, C_D-O*Me*), 55.9 (q, C_d-O*Me*), 60.6 (q, C_c-O*Me*), 60.8 (q, C_b-O*Me*), 74.1 (d, C-2), 82.3 [s, $\mathit{C}(CH_3)_3$], 107.1 (d, C-e), 113.6 (d, C-C), 123.8 (d, C-f), 126.5 (s, C-a), 129.7 (d, C-B), 133.6 (s, C-A), 142.2 (s, C-c), 151.9 (s, C-b), 152.5 (s, C-d), 158.2 (s, C-D), 173.1 (s, C-1).

MS (ESI): *m/z* (%) = 859 (100) [$(2M+Na)^+$], 441 (33) [$(M+Na)^+$], 363 (6).

HRMS (ESI): $C_{23}H_{30}O_7Na$ [$(M+Na)^+$]: calcd.: 441.1884; found: 441.1885.

tert-Butyl 3-(5-bromo-2,4-dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)propanoate (11c)



$C_{22}H_{27}BrO_6$
M = 467.35 g/mol

Following **general procedure 3**, reaction of **5** (37.5 mg, 150 µmol, 1.00 eq.) with 1-bromo-2,4-dimethoxybenzene (86.2 µL, 600 µmol, 4.00 eq.) and $Sc(OTf)_3$ (3.69 mg, 7.50 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 2/1 → 1/1) **11c** (46 mg, 98.4 µmol, 66%) as a colourless oil (d.r. *anti*/*syn* = 8/92).

TLC: R_f = 0.19 (P/Et_2O 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3484 (br, OH), 2977 (w, $C_{al}H$), 2933 (w), 2837 (w, OMe), 1720 (vs, C=O), 1600 (s), 1510 (s), 1461 (m, CH_3), 1368 (m), 1245 (s, COC), 1204 (s), 1150 (vs), 1027 (vs), 961 (m), 910 (m), 842 (s, $C_{ar}H$), 731 cm^{-1} (s).

syn-Diastereoisomer:

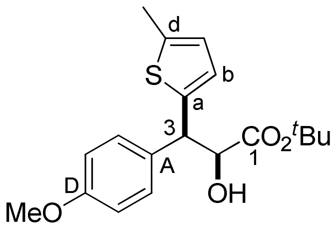
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.27 [s, 9 H, $C(CH_3)_3$], 2.98 (d, ^3J = 6.2 Hz, 1 H, OH), 3.77 (s, 3 H, H_D-OMe), 3.79 (s, 3 H, H_b-OMe), 3.87 (s, 3 H, H_d-OMe), 4.67 (*virt.* t, $^3J \cong$ 5.9 Hz, 1 H, H-2), 4.72 (d, ^3J = 5.8 Hz, 1 H, H-3), 6.44 (s, 1 H, H-c), 6.81-6.83 (m, 2 H, H-C), 7.24-7.25 (m, 2 H, H-B), 7.65 (s, 1 H, H-f).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 27.7 [q, $C(CH_3)_3$], 45.6 (d, C-3), 55.2 (q, C_D-O*Me*), 55.9 (q, C_b-O*Me*), 56.3 (q, C_d-O*Me*), 73.7 (d, C-2), 82.3 [s, $C(CH_3)_3$], 96.6 (d, C-c), 102.1 (s, C-e), 113.7 (d, C-C), 122.7 (s, C-a), 129.7 (d, C-B), 133.0 (s, C-A), 133.6 (d, C-f), 155.3 (s, C-d), 157.4 (s, C-b), 158.3 (s, C-D), 173.0 (s, C-1).

MS (ESI): *m/z* (%) = 957 (100) {[M(^{81}Br) + M(^{79}Br) + Na]$^+$}, 491 (26) {[M(^{81}Br) + Na]$^+$}, 489 (24) {[M(^{79}Br) + Na]$^+$}.

HRMS (ESI): $C_{22}H_{27}{}^{81}BrO_6Na$ {[M(^{81}Br) + Na]$^+$}: calcd.: 491.0863; found: 491.0865.

***tert*-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (11d)**



$C_{19}H_{24}O_4S$
M = 348.46 g/mol

Following **general procedure 3**, reaction of **5** (37.5 mg, 150 µmol, 1.00 eq.) with 2-methylthiophene (58.3 µL, 600 µmol, 4.00 eq.) and $Sc(OTf)_3$ (3.69 mg, 7.50 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 6/1 → 1/1) **11d** (37 mg, 106 µmol, 71%) as a pale yellow oil (d.r. *anti*/*syn* = 16/84).

TLC: R_f = 0.57 (P/Et_2O 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3483 (br, OH), 2977 (w, $C_{al}H$), 2924 (w), 2837 (w, OMe), 1716 (vs, C=O), 1610 (s), 1511 (vs), 1456 (m, CH_3), 1369 (m), 1247 (vs, COC), 1151 (vs), 1032 (s), 835 (s, $C_{ar}H$), 803 (s), 669 cm^{-1} (m).

syn-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.37 [s, 9 H, $C(CH_3)_3$], 2.41 (s, 3 H, H_d-Me), 3.04 (bs, 1 H, OH), 3.78 (s, 3 H, OMe), 4.55 (d, ^3J = 3.8 Hz, 1 H, H-3), 4.57 (d, ^3J = 3.8 Hz, 1 H, H-2), 6.55-6.56 (m, 1 H, H-c), 6.73 (d, ^3J = 3.4 Hz, 1 H, H-b), 6.84-6.86 (m, 2 H, H-C), 7.35-7.37 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 27.8 [q, $C(CH_3)_3$], 49.6 (d, C-3), 55.2 (q, OMe), 74.2 (d, C-2), 82.9 [s, $C(CH_3)_3$], 113.7 (d, C-C), 124.3 (d, C-c), 126.1 (d, C-b), 129.4 (d, C-B), 133.4 (s, C-A), 139.1 (s, C-d), 139.4 (s, C-a), 158.5 (s, C-D), 172.4 (s, C-1).

anti-Diastereoisomer:

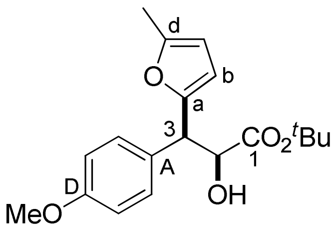
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.38 [s, 9 H, $C(CH_3)_3$], 2.42 (s, 3 H, H_d-Me), 3.04 (bs, 1 H, OH), 3.77 (s, 3 H, OMe), 4.52 (d, ^3J = 3.4 Hz, 1 H, H-3), 4.68 (d, ^3J = 3.4 Hz, 1 H, H-2), 6.56-6.57 (m, 1 H, H-c), 6.77 (d, ^3J = 3.4 Hz, 1 H, H-b), 6.81-6.83 (m, 2 H, H-C), 7.29-7.30 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 27.9 [q, $C(CH_3)_3$], 49.4 (d, C-3), 55.2 (q, OMe), 74.1 (d, C-2), 83.0 [s, $C(CH_3)_3$], 113.6 (d, C-C), 124.4 (d, C-c), 125.2 (d, C-b), 130.3 (d, C-B), 130.9 (s, C-A), 138.7 (s, C-d), 142.8 (s, C-a), 158.9 (s, C-D), 172.1 (s, C-1).

MS (ESI): *m/z* (%) = 719 (100) [$(2M+Na)^+$], 371 (52) [$(M+Na)^+$], 315 (13).

HRMS (ESI): $C_{19}H_{24}O_4SNa$ $[(M+Na)^+]$: calcd.: 371.1288; found: 371.1288.

***tert*-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(5-methylfuran-2-yl)propanoate (11e)**



$C_{19}H_{24}O_5$
M = 332.39 g/mol

Following **general procedure 3**, reaction of **5** (37.5 mg, 150 µmol, 1.00 eq.) with 2-methylfuran (54.1 µL, 600 µmol, 4.00 eq.) and $Sc(OTf)_3$ (3.69 mg, 7.50 µmol, 0.05 eq.) yielded after flash chromatography (P/Et_2O: 4/1 → 2/1) **11e** (29 mg, 87.2 µmol, 58%) as a colourless oil (d.r. *anti*/*syn* = 18/82).

TLC: R_f = 0.30 (P/Et_2O 2/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3484 (br, OH), 2977 (w, $C_{al}H$), 2933 (w), 2837 (w, OMe), 1724 (vs, C=O), 1610 (m), 1511 (vs), 1457 (m, CH_3), 1368 (s), 1246 (vs, COC), 1154 (vs), 1024 (s), 962 (m), 837 (s, $C_{ar}H$), 782 cm^{-1} (s).

syn-Diastereoisomer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.41 [s, 9 H, $C(CH_3)_3$], 2.23 (s, 3 H, H_d-Me), 3.02 (d, ^3J = 5.7 Hz, 1 H, OH), 3.79 (s, 3 H, OMe), 4.39 (d, ^3J = 4.0 Hz, 1 H, H-3), 4.47 (*virt.* t, $^3J \cong$ 4.2 Hz, 1 H, H-2), 5.86 (d, ^3J = 2.8 Hz, 1 H, H-c), 6.00 (d, ^3J = 2.8 Hz, 1 H, H-b), 6.86-6.87 (m, 2 H, H-C), 7.33-7.35 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 13.5 (q, C_d-*Me*), 27.8 [q, $C(CH_3)_3$], 48.3 (d, C-3), 55.2 (q, OMe), 73.7 (d, C-2), 82.6 [s, $C(CH_3)_3$], 106.1 (d, C-c), 108.8 (d, C-b), 113.7 (d, C-C), 129.8 (d, C-B), 131.2 (s, C-A), 151.0 (s, C-d), 151.6 (s, C-a), 158.7 (s, C-D), 172.5 (s, C-1).

anti-Diastereoisomer:

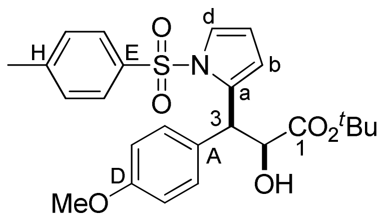
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 1.39 [s, 9 H, $C(CH_3)_3$], 2.26 (s, 3 H, H_d-Me), 2.89 (d, ^3J = 5.7 Hz, 1 H, OH), 3.78 (s, 3 H, OMe), 4.34 (d, ^3J = 3.8 Hz, 1 H, H-3), 4.73 (*virt.* t, $^3J \cong$ 4.0 Hz, 1 H, H-2), 5.88 (d, ^3J = 2.9 Hz, 1 H, H-c), 6.05 (d, ^3J = 2.9 Hz, 1 H, H-b), 6.83-6.84 (m, 2 H, H-C), 7.27-7.29 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 13.6 (q, C_d-*Me*), 27.9 [q, C(CH$_3$)$_3$], 48.1 (d, C-3), 55.2 (q, OMe), 72.6 (d, C-2), 82.8 [s, *C*(CH_3)$_3$], 106.1 (d, C-c), 108.2 (d, C-b), 113.6 (d, C-C), 128.9 (s, C-A), 130.5 (d, C-B), 151.0 (s, C-d), 152.9 (s, C-a), 158.9 (s, C-D), 172.3 (s, C-1).

MS (ESI): *m/z* (%) = 687 (100) [$(2M+Na)^+$], 355 (42) [$(M+Na)^+$], 299 (8).

HRMS (ESI): $C_{19}H_{24}O_5Na$ [$(M+Na)^+$]: calcd.: 355.1516; found: 355.1517.

tert-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(1-tosyl-1*H*-pyrrol-2-yl)propanoate (11f)



$C_{25}H_{29}NO_6S$
M = 471.57 g/mol

Following **general procedure 3**, reaction of **5** (37.5 mg, 150 μmol, 1.00 eq.) with *N*-tosylpyrrole (133 mg, 600 μmol, 4.00 eq.) and $Sc(OTf)_3$ (3.69 mg, 7.50 μmol, 0.05 eq.) at 0 °C yielded after flash chromatography (P/Et_2O: 4/1 → 1/1) **11f** (26 mg, 55.1 μmol, 37%) as a colourless solid (d.r. *anti*/*syn* = 7/93).

TLC: R_f = 0.30 (P/Et_2O 1/1) [UV, CAM].

m.p.: 122 °C (d.r. *anti*/*syn* = 7/93).

IR (ATR): $\tilde{\nu}$ = 3489 (br, OH), 2981 (w, C_{al}H), 2928 (w), 2832 (w, OMe), 1712 (vs, C=O), 1610 (m), 1511 (s), 1460 (m, CH_3), 1352 (s), 1249 (vs, COC), 1138 (vs), 1035 (m), 835 (m, C_{ar}H), 810 (s), 734 (s), 667 cm^{-1} (vs).

syn-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 1.33 [s, 9 H, C(CH_3)$_3$], 2.26 (s, 3 H, H_H-Me), 3.02 (bs, 1 H, OH), 3.75 (s, 3 H, OMe), 4.44 (d, ^3J = 4.8 Hz, 1 H, H-2), 5.26 (d, ^3J = 4.8 Hz, 1 H, H-3), 6.26 (*virt*. t, ^3J ≅ 3.4 Hz, 1 H, H-c), 6.62-6.64 (m, 3 H, H-b + H-C), 6.88-6.90 (m, 2 H, H-G), 6.92-6.95 (m, 2 H, H-B), 7.15-7.18 (m, 2 H, H-F), 7.31 (dd, ^3J = 3.4 Hz, ^4J = 1.7 Hz, 1 H, H-d).

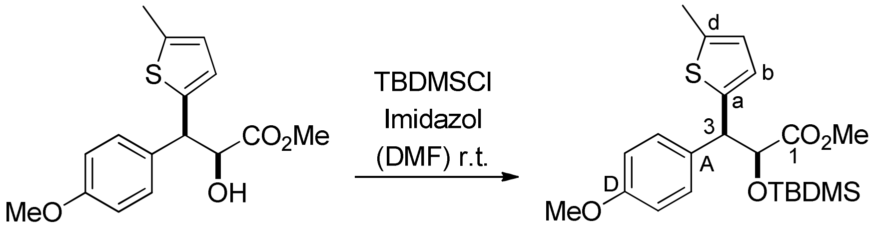
^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 21.4 (q, C_H-*Me*), 27.7 [q, C(CH$_3$)$_3$], 44.3 (d, C-3), 55.2 (q, OMe), 75.1 (d, C-2), 83.1 [s, *C*(CH_3)$_3$], 111.4 (d, C-c), 113.5 (d, C-C), 114.7 (d, C-b), 122.6 (d, C-d), 126.6 (d, C-F), 129.2 (d, C-G), 129.8 (d, C-B), 130.4 (s, C-A), 132.8 (s, C-a), 135.7 (s, C-E), 144.0 (s, C-H), 158.4 (s, C-D), 172.3 (s, C-1).

MS (ESI): *m/z* (%) = 965 (100) [$(2M+Na)^+$], 494 (52) [$(M+Na)^+$], 416 (12).

HRMS (ESI): $C_{25}H_{29}NO_6SNa$ [$(M+Na)^+$]: calcd.: 494.1608; found: 494.1609.

4. Determination of the relative configuration

Methyl 2-[(tert-butyldimethylsilyl)oxy]-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (9)



$C_{22}H_{32}O_4SSi$
M = 420.64 g/mol

Methyl 2-hydroxy-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (**7a**) (160 mg, 522 µmol, d.r. *anti*/*syn* = 25/75, 1.00 eq.) was dissolved in DMF (1.5 mL) under an atmosphere of argon. Imidazole (71.1 mg, 1.04 mmol, 2.00 eq.) and TBDMSCl (320 mg, 2.13 mmol, 4.07 eq.) were subsequently added and the solution was stirred at ambient temperature over night. Water (7 mL) and Et_2O (10 ml) were added and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography [P/Et_2O = 6/1 → 4/1] to afford **9** (196 mg, 466 µmol, 89%) as a colourless oil (d.r. *anti*/*syn* = 24/76).

TLC: R_f = 0.68 (P/Et_2O 2/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3001 (w, $C_{ar}H$), 2952 (m, $C_{al}H$), 2928 (m), 2856 (m), 1756 (s, C=O), 1610 (m), 1511 (s), 1466 (m, CH_3), 1437 (w), 1248 (vs, COC), 1131 (s), 1036 (s), 831 (vs, $C_{ar}H$), 777 (s), 727 (m), 674 cm^{-1} (w).

syn-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = –0.28 (s, 3 H, SiMe), –0.06 (s, 3 H, SiMe), 0.83 [s, 9 H, $SiC(CH_3)_3$], 2.41 (d, ^4J = 0.9 Hz, 3 H, H_d-Me), 3.55 (s, 3 H, COOMe), 3.77 (s, 3 H, H_D-OMe), 4.56 (d, ^3J = 5.7 Hz, 1 H, H-2), 4.60 (d, ^3J = 5.7 Hz, 1 H, H-3), 6.55 (dd, ^3J = 3.4 Hz, ^4J = 0.9 Hz, 1 H, H-c), 6.80-6.83 (m, 3 H, H-b + H-C), 7.22-7.24 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = −5.8 (q, SiMe), −5.4 (q, SiMe), 15.2 (q, C_d-*Me*), 18.1 [s, Si*C*(CH_3)$_3$], 25.6 [q, SiC(*C*H_3)$_3$], 50.6 (d, C-3), 51.7 (q, COO*Me*), 55.3 (q, C_D-O*Me*), 77.1 (d, C-2), 113.7 (d, C-C), 124.3 (d, C-c), 126.3 (d, C-b), 129.6 (d, C-B), 132.9 (s, C-A), 138.7 (s, C-d), 139.9 (s, C-a), 158.5 (s, C-D), 172.4 (s, C-1).

anti-Diastereoisomer:

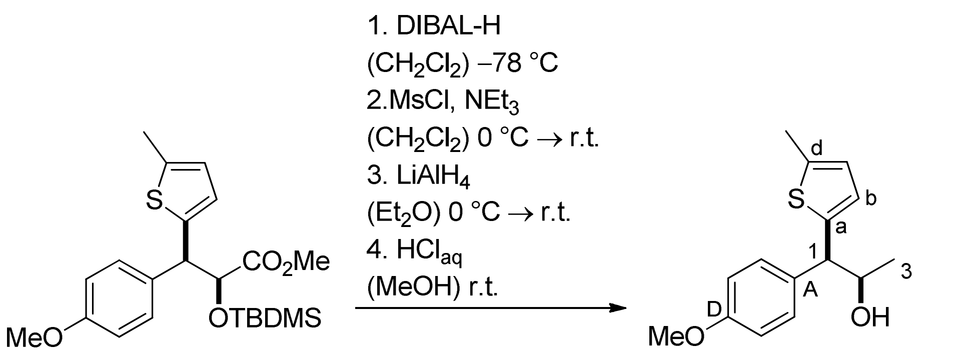
^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = −0.29 (s, 3 H, SiMe), 0.02 (s, 3 H, SiMe), 0.92 [s, 9 H, SiC(CH_3)$_3$], 2.39 (d, ^4J = 0.9 Hz, 3 H, H_d-Me), 3.57 (s, 3 H, COOMe), 3.78 (s, 3 H, H_D-OMe), 4.49 (d, ^3J = 7.1 Hz, 1 H, H-3), 4.63 (d, ^3J = 7.1 Hz, 1 H, H-2), 6.52 (dd, ^3J = 3.4 Hz, ^4J = 0.9 Hz, 1 H, H-c), 6.63 (d, ^3J = 3.4 Hz, 1 H, H-b), 6.80-6.83 (m, 2 H, H-C), 7.31-7.34 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = −5.7 (q, SiMe), −5.4 (q, SiMe), 15.2 (q, C_d-*Me*), 18.1 [s, Si*C*(CH_3)$_3$], 25.6 [q, SiC(*C*H_3)$_3$], 50.5 (d, C-3), 51.7 (q, COO*Me*), 55.2 (q, C_D-O*Me*), 77.1 (d, C-2), 113.6 (d, C-C), 124.5 (d, C-c), 125.1 (d, C-b), 130.1 (d, C-B), 132.3 (s, C-A), 138.6 (s, C-d), 141.6 (s, C-a), 158.6 (s, C-D), 172.4 (s, C-1).

MS (ESI): *m/z* (%) = 443 (100) [$(M+Na)^+$], 323 (25), 289 (10).

HRMS (ESI): $C_{22}H_{32}O_4SSiNa$ [$(M+Na)^+$]: calcd.: 443.1683; found: 443.1683.

1-(4-methoxyphenyl)-1-(5-methylthiophen-2-yl)propan-2-ol (10)[7,8]



$C_{15}H_{18}O_2S$

M = 262.37 g/mol

Methyl 2-[(tert-butyldimethylsilyl)oxy]-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)-propanoate (**9**) (42.1 mg, 100 μmol, d.r. *anti*/*syn* = 24/76, 1.00 eq.) was dissolved in CH_2Cl_2 (1 mL) under an atmosphere of argon and cooled to −78 °C. DIBAL-H (300 μL, 300 μmol, 1.0 M in cyclohexane, 3.00 eq.) was added dropwise and the mixture was stirred for 1 h at −78 °C. Then, another two equivalents of DIBAL-H (200 μL, 200 μmol, 1.0 M in cyclohexane, 2.00 eq.) were added and after stirring for an additional hour at −78 °C another two equivalents of DIBAL-H (200 μL, 200 μmol, 1.0 M in cyclohexane, 2.00 eq.) were given to the reaction mixture. After stirring for 30 min at −78 °C the reaction was quenched by adding sat. aqueous K/Na tartrate (3 mL) and the mixture was stirred at ambient temperature over night. The mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was dissolved in CH_2Cl_2 (1 mL) under an atmosphere of argon and cooled to 0 °C. Methanesulfonyl chloride (8.52 µL, 110 µmol) and NEt_3 (20.8 µL, 150 µmol) were subsequently added and the reaction was stirred at ambient temperature for 1.5 h. Water (5 mL) and CH_2Cl_2 (5 mL) were added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting product was dried under high vacuum and subsequently dissolved in Et_2O (1.5 mL). The solution was given to a suspension of $LiAlH_4$ (15.2 mg, 400 µmol) in Et_2O (0.5 mL) under an atmosphere of argon at 0 °C. The mixture was stirred for 1h at 0 °C and for another hour at ambient temperature. The reaction was quenched by adding sat. aqueous K/Na tartrate (5 mL) and the mixture was stirred for 30 min at ambient temperature and diluted with Et_2O (5 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was dissolved in methanol (2 mL). Two drops of conc. HCl were added and the solution was stirred vigorously at ambient temperature for 1 h. Sat. aqueous $NaHCO_3$ (10 mL) and Et_2O (10 mL) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by flash chromatography [P/Et_2O = 2/1 → 1/1] to afford **10** (21 mg, 80.0 µmol, 80%) as a colourless oil (d.r. *anti*/*syn* = 25/75).

TLC: R_f = 0.23 (P/Et_2O 7/3) [UV, CAM].

IR (ATR): $\tilde{\nu}$ = 3484 (br, OH), 2962 (w, $C_{al}H$), 2924 (w, $C_{al}H$), 2837 (w, OMe), 1609 (m), 1511 (vs), 1455 (m, CH_3), 1246 (vs, COC), 1177 (s), 1109 (m), 1030 (s), 797 cm^{-1} (vs).

syn-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 1.15 (d, ^3J = 6.1 Hz, 3 H, H-3), 1.83 (bs, 1 H, OH), 2.42 (d, ^4J = 0.9 Hz, 3 H, H_d-Me), 3.78 (s, 3 H, OMe), 3.93 (d, ^3J = 8.1 Hz, 1 H, H-1), 4.28 (dq, ^3J = 8.1 Hz, ^3J = 6.1 Hz, 1 H, H-2), 6.60 (dd, ^3J = 3.4 Hz, ^4J = 0.9 Hz, 1 H, H-c), 6.77 (d, ^3J = 3.4 Hz, 1 H, H-b), 6.84-6.86 (m, 2 H, H-C), 7.21-7.23 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 21.1 (q, C-3), 55.2 (q, OMe), 55.3 (d, C-1), 71.2 (d, C-2), 114.2 (d, C-C), 124.8 (d, C-c), 125.2 (d, C-b), 129.0 (d, C-B), 134.2 (s, C-A), 139.1 (s, C-d), 142.7 (s, C-a), 158.4 (s, C-D).

anti-Diastereoisomer:

^{1}H-NMR (360 MHz, $CDCl_3$): δ [ppm] = 1.24 (d, ^{3}J = 6.1 Hz, 3 H, H-3), 1.83 (bs, 1 H, OH), 2.41 (d, ^{4}J = 0.9 Hz, 3 H, H_d-Me), 3.79 (s, 3 H, OMe), 3.94 (d, ^{3}J = 7.5 Hz, 1 H, H-1), 4.35 (dq, ^{3}J = 7.5 Hz, ^{3}J = 6.1 Hz, 1 H, H-2), 6.56 (dd, ^{3}J = 3.4 Hz, ^{4}J = 0.9 Hz, 1 H, H-c), 6.67 (d, ^{3}J = 3.4 Hz, 1 H, H-b), 6.87-6.89 (m, 2 H, H-C), 7.30-7.32 (m, 2 H, H-B).

^{13}C-NMR (90.6 MHz, $CDCl_3$): δ [ppm] = 15.2 (q, C_d-*Me*), 21.2 (q, C-3), 54.9 (d, C-1), 55.2 (q, OMe), 71.0 (d, C-2), 114.2 (d, C-C), 124.4 (d, C-b), 124.6 (d, C-c), 129.7 (d, C-B), 132.9 (s, C-A), 138.3 (s, C-d), 143.6 (s, C-a), 158.7 (s, C-D).

MS (ESI): *m/z* (%) = 263 (4) [$(M+H)^+$], 245 (100) [$(M-OH)^+$], 233 (10), 196 (18), 165 (49).

HRMS (ESI): $C_{15}H_{19}O_2S$ [$(M+H)^+$]: calcd.: 263.1100; found: 263.1100.

5. References

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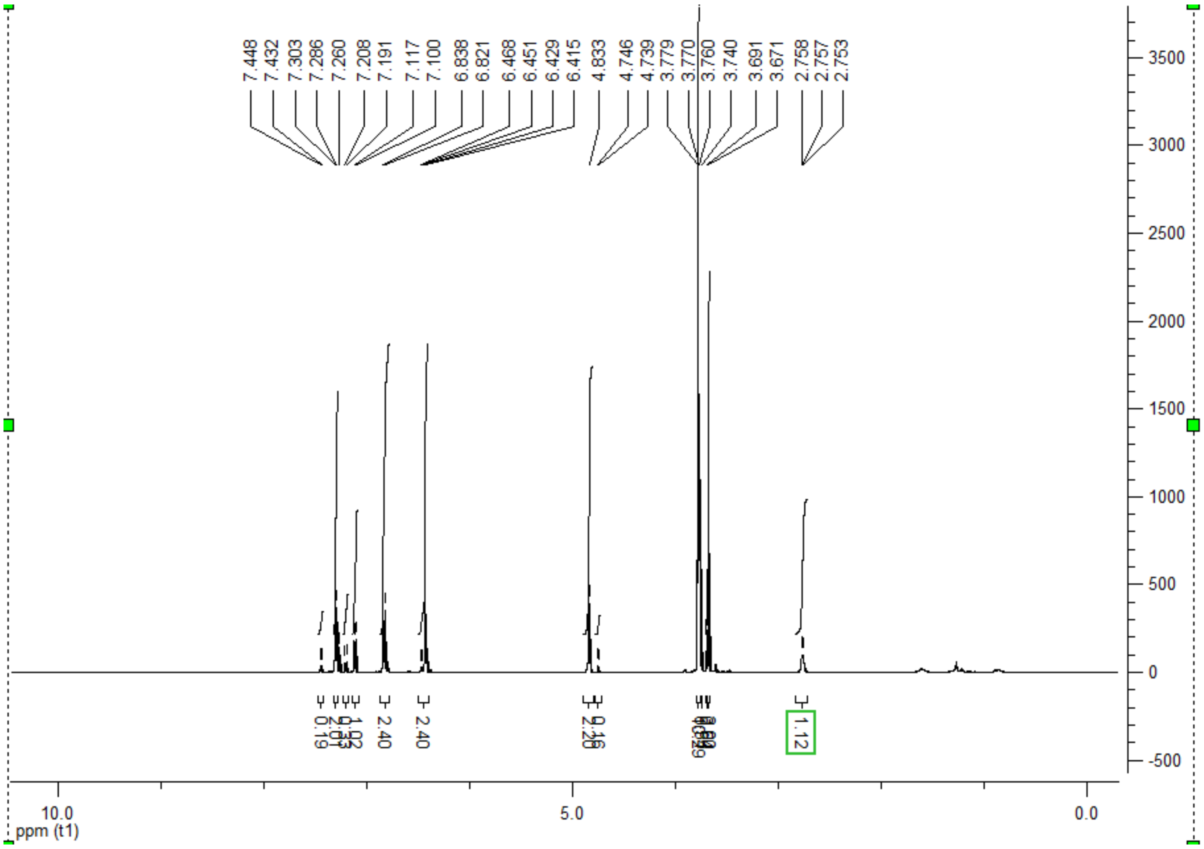
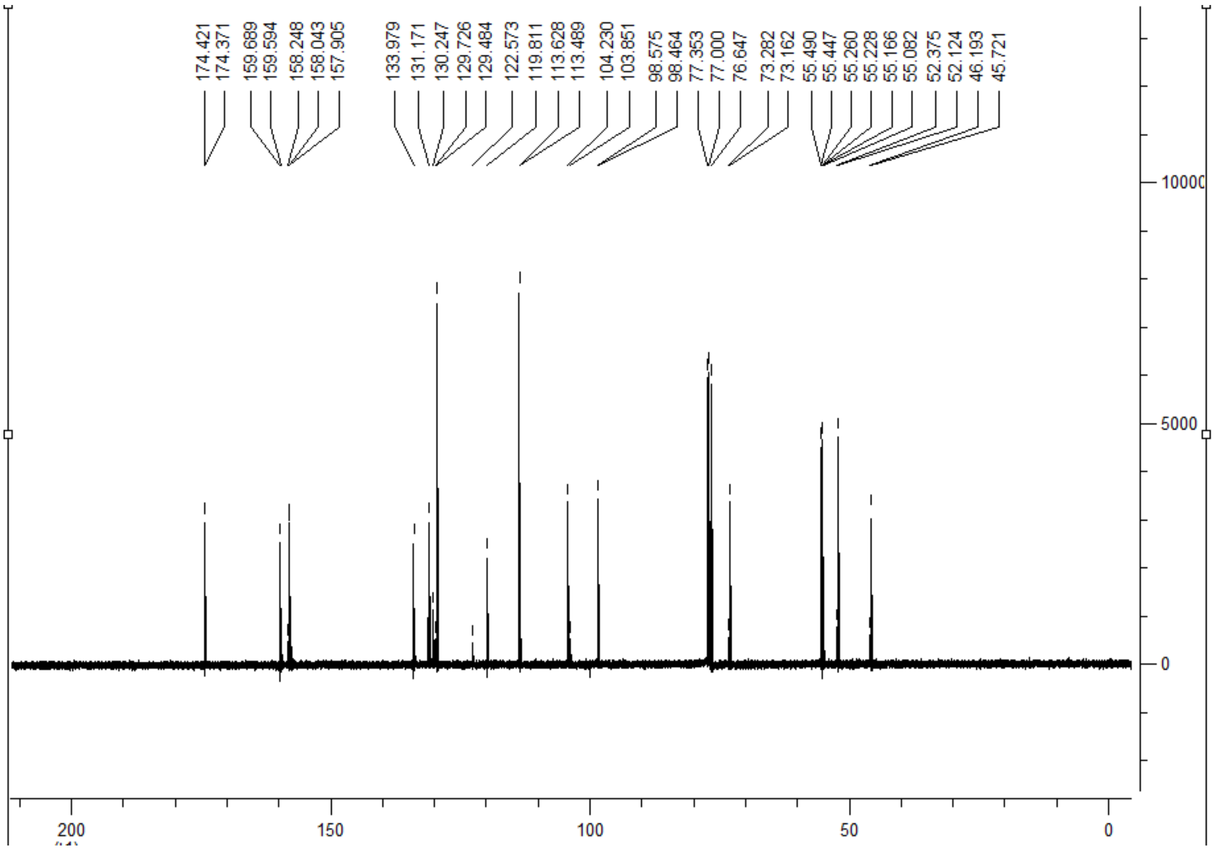
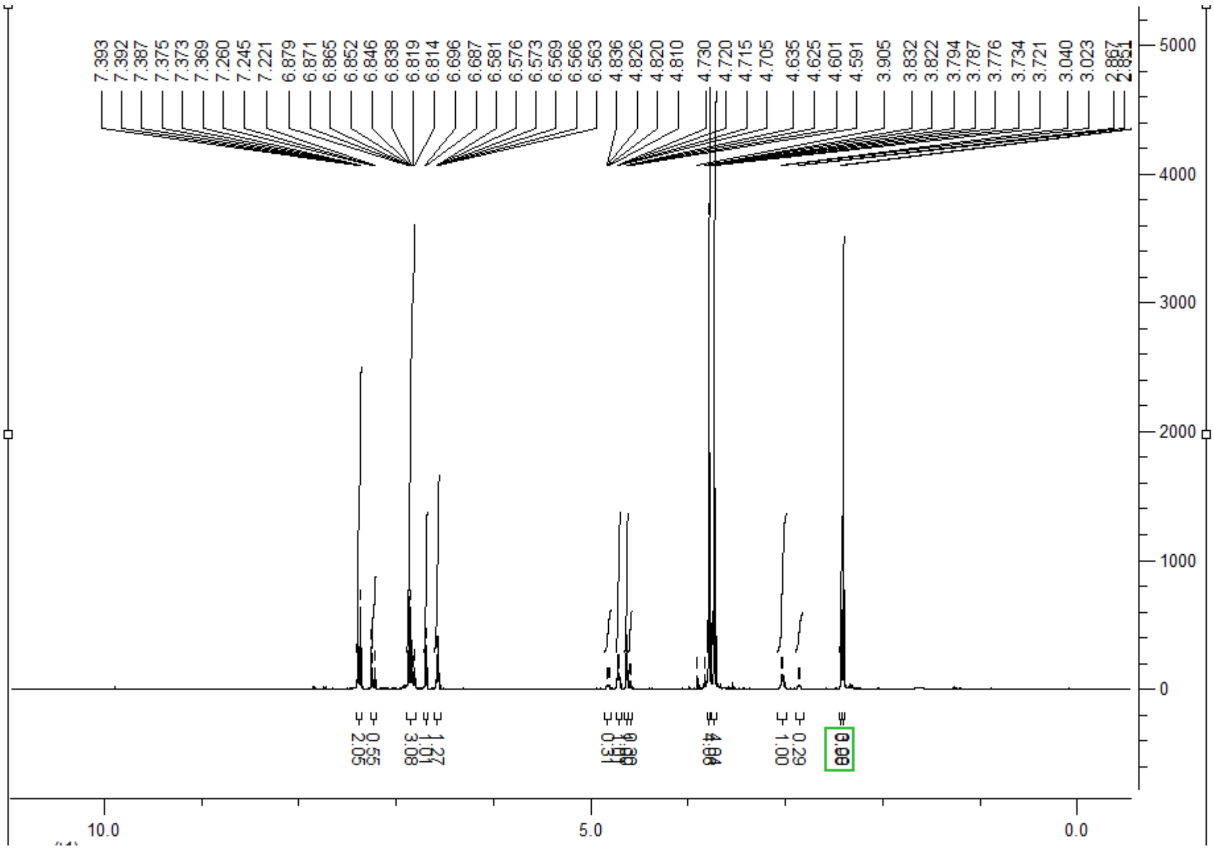
6. ^{1}H- and ^{13}C-NMR spectra

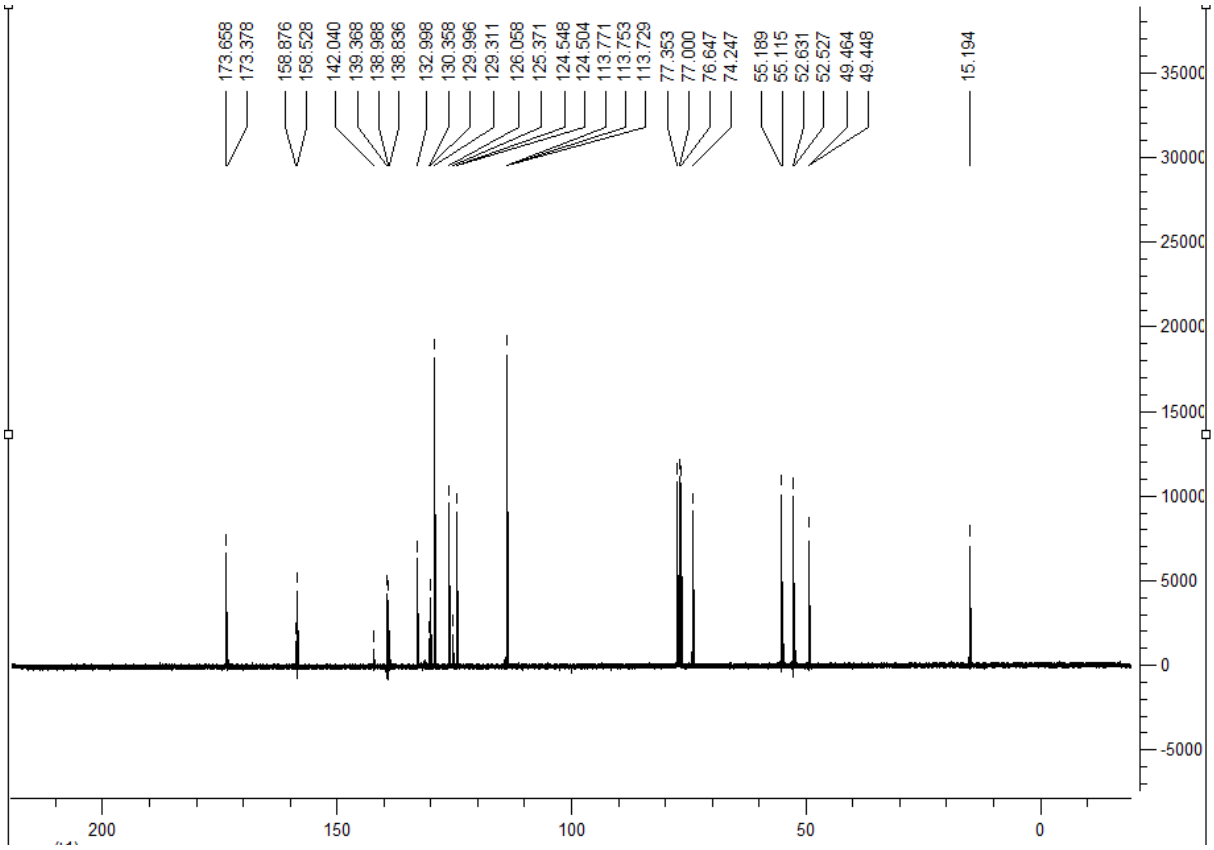
Methyl 3-(2,4-dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)propanoate (6a)



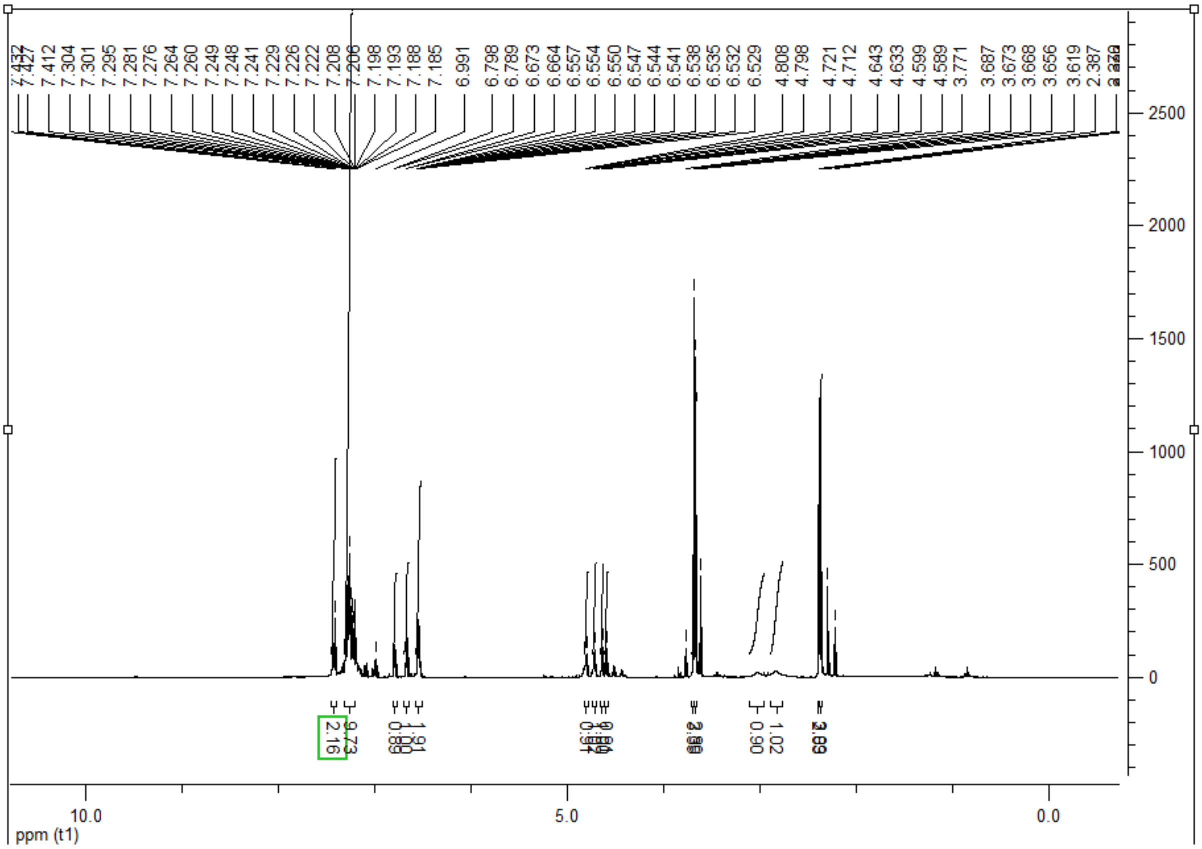


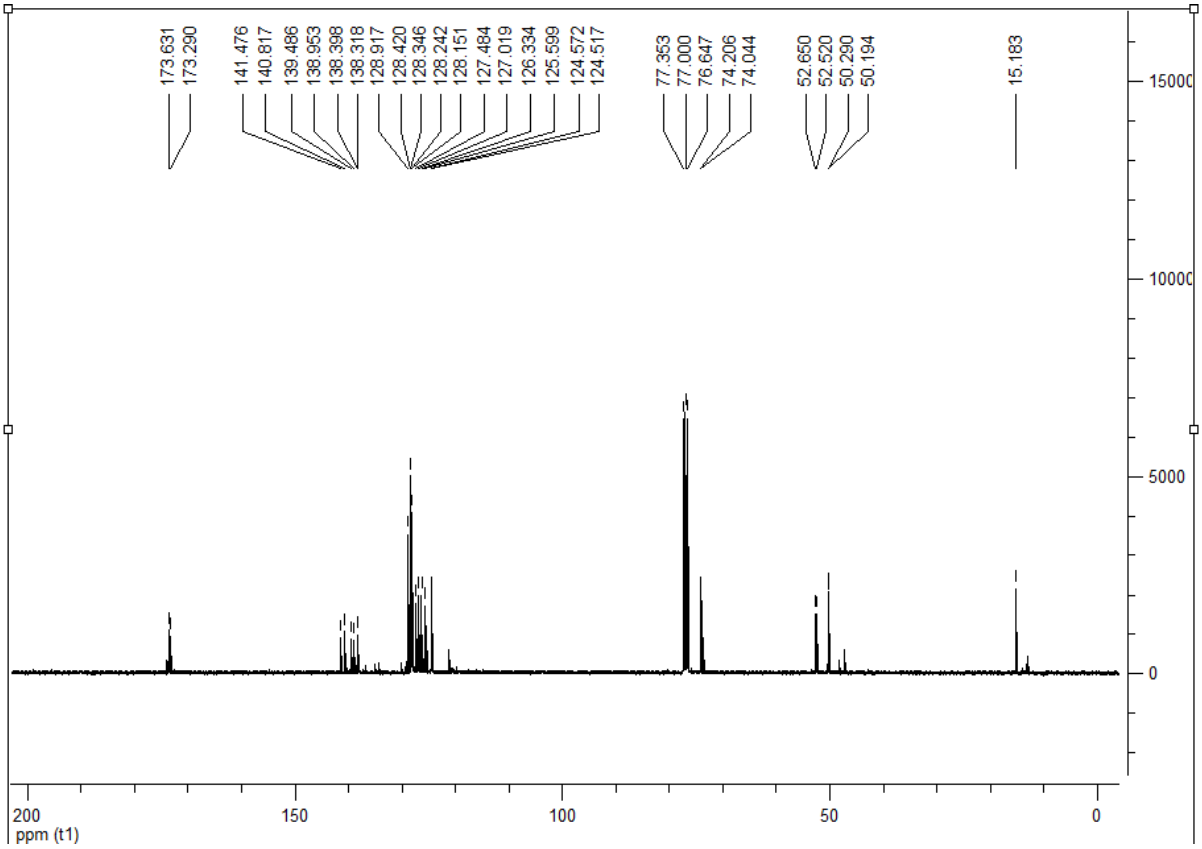
Methyl 2-hydroxy-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (7a)





Methyl 2-hydroxy-3-(5-methylthiophen-2-yl)-3-phenylpropanoate (7b)





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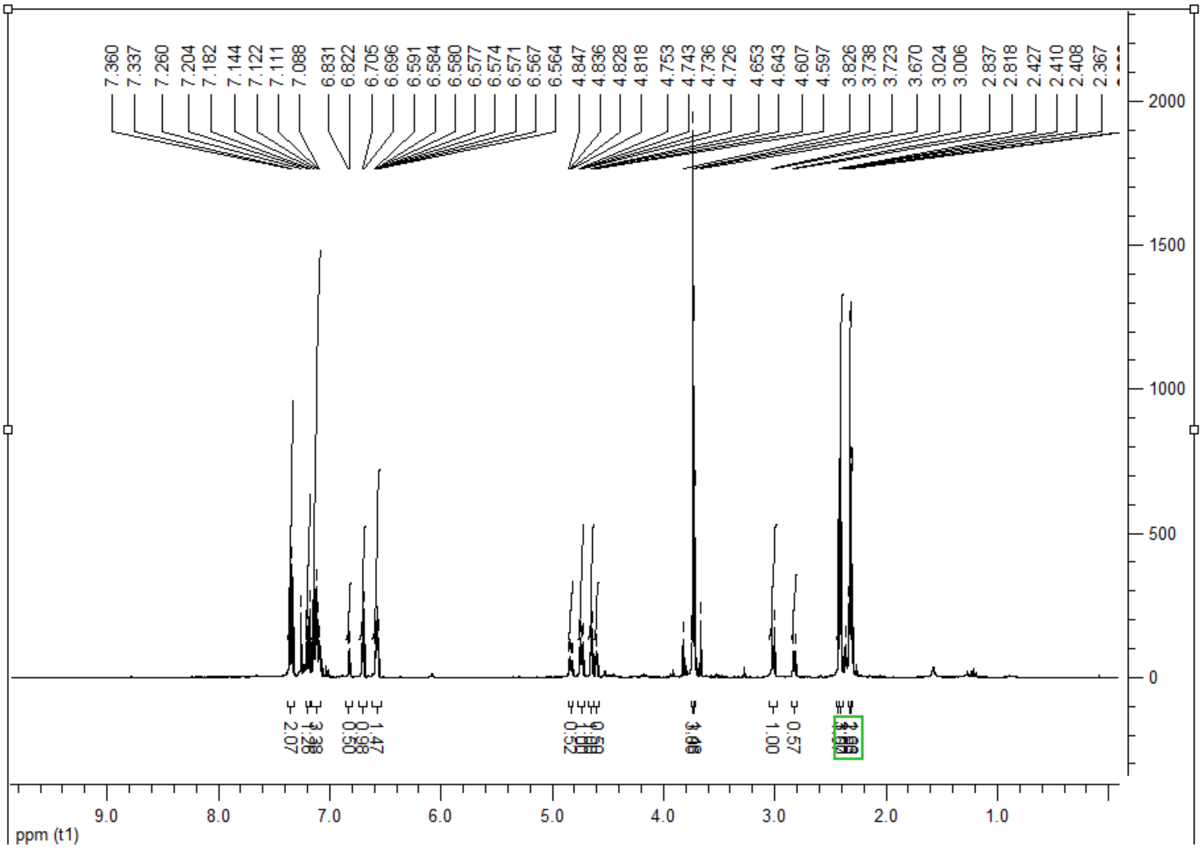
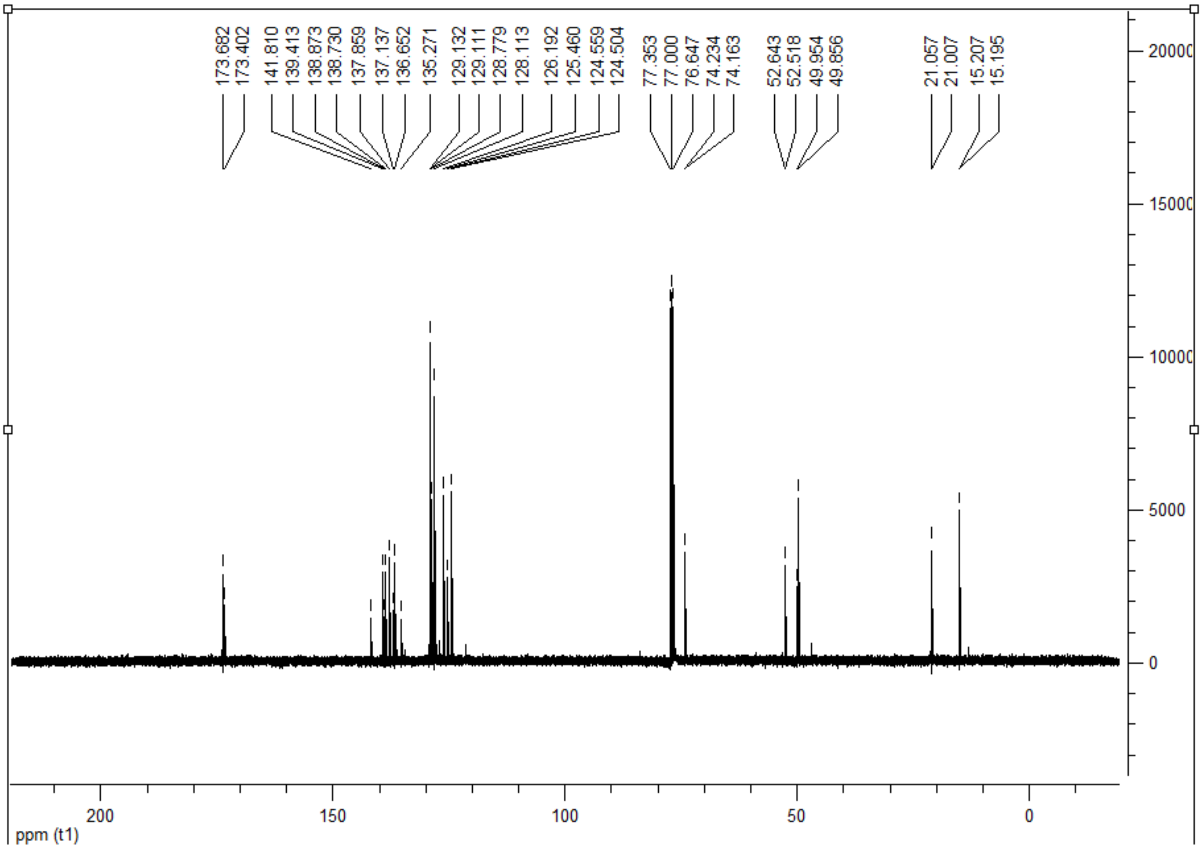
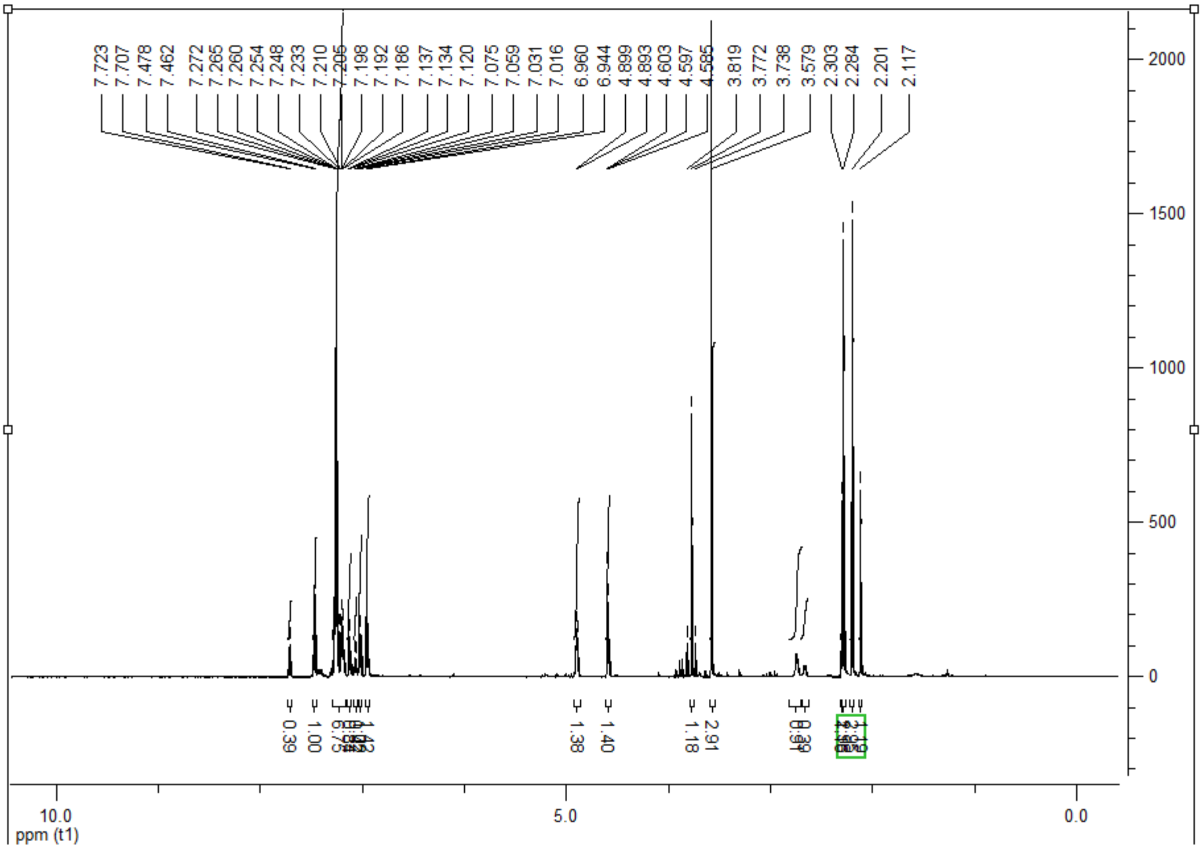
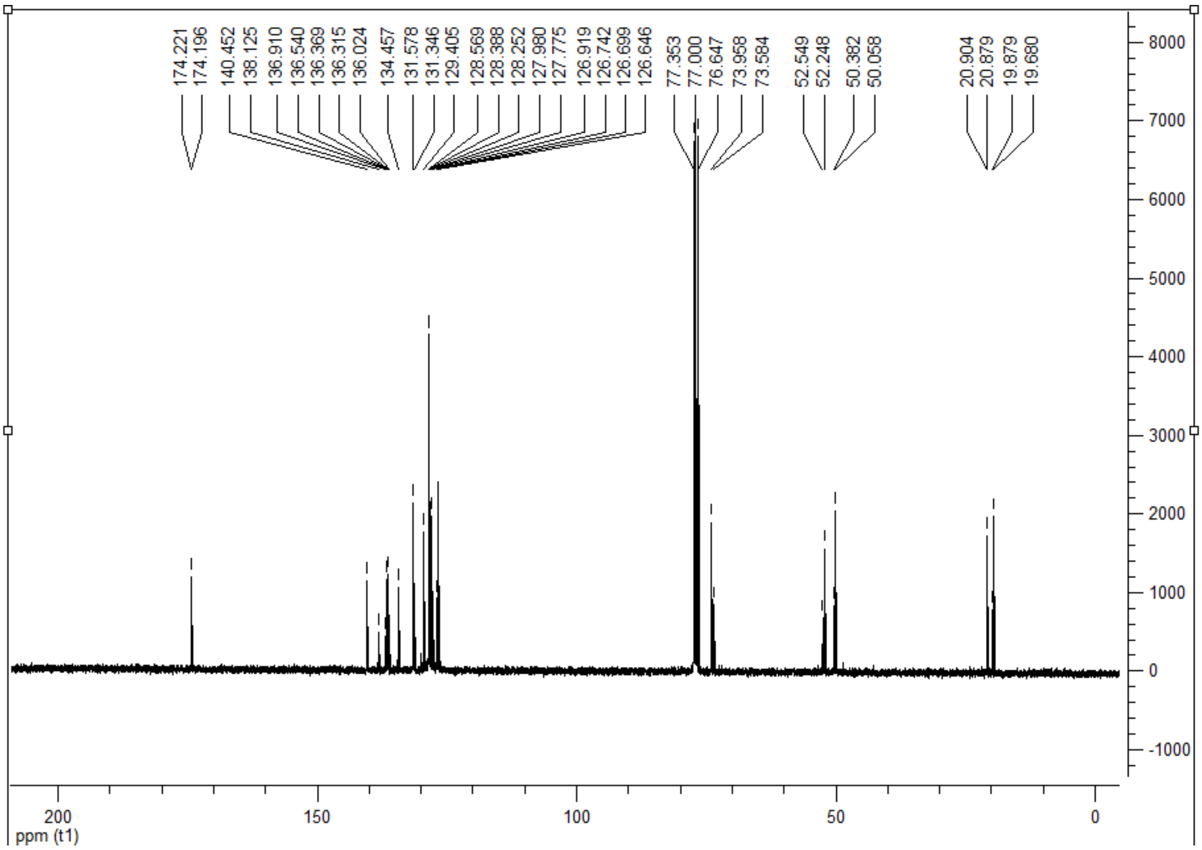
Methyl 2-hydroxy-3-(5-methylthiophen-2-yl)-3-(*p*-tolyl)propanoate (7c)



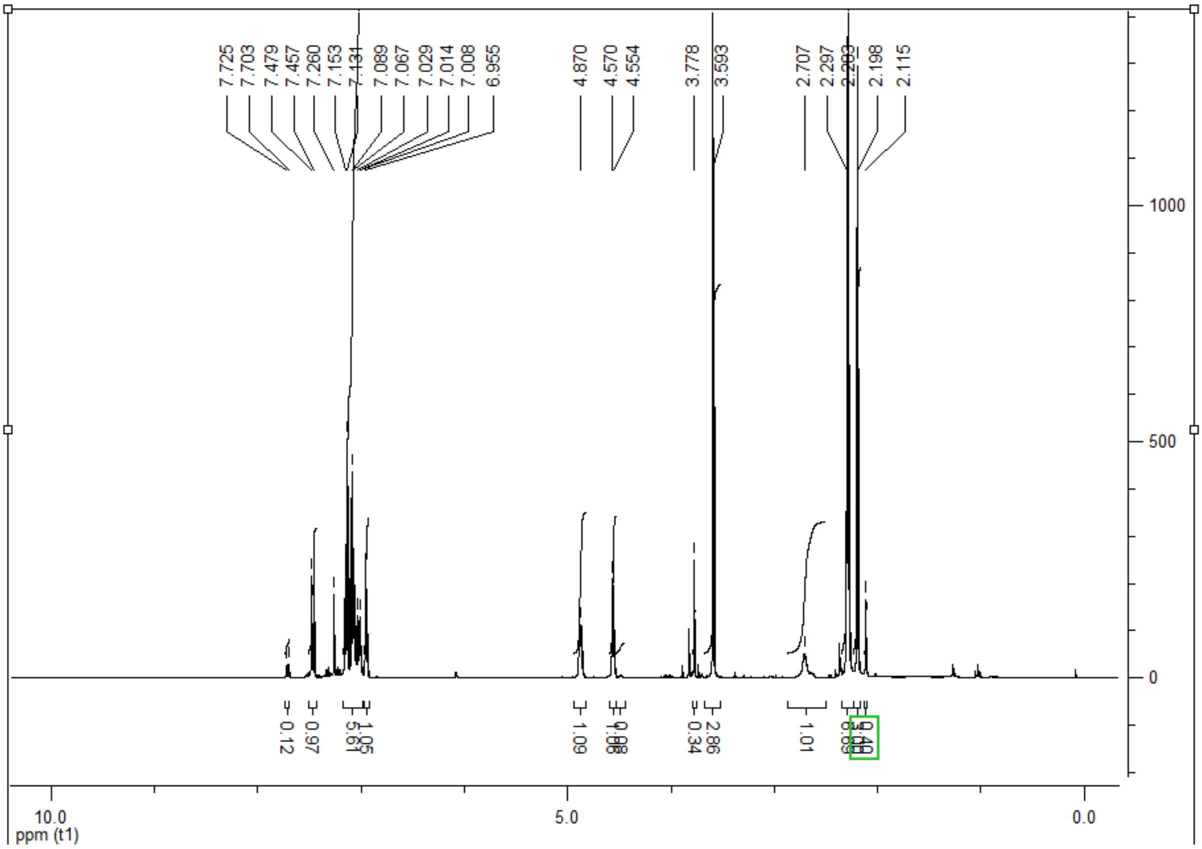


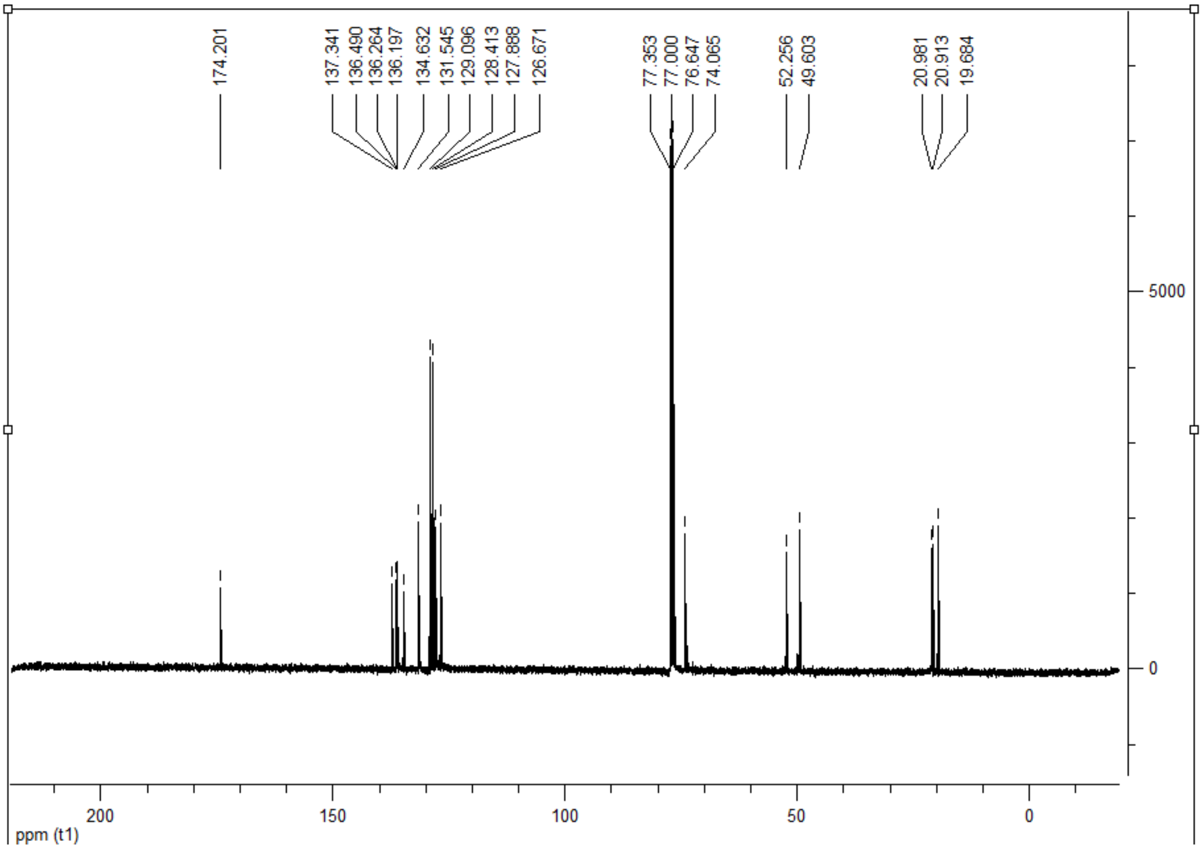
Methyl 3-(2,4-dimethylphenyl)-2-hydroxy-3-phenylpropanoate (8b)



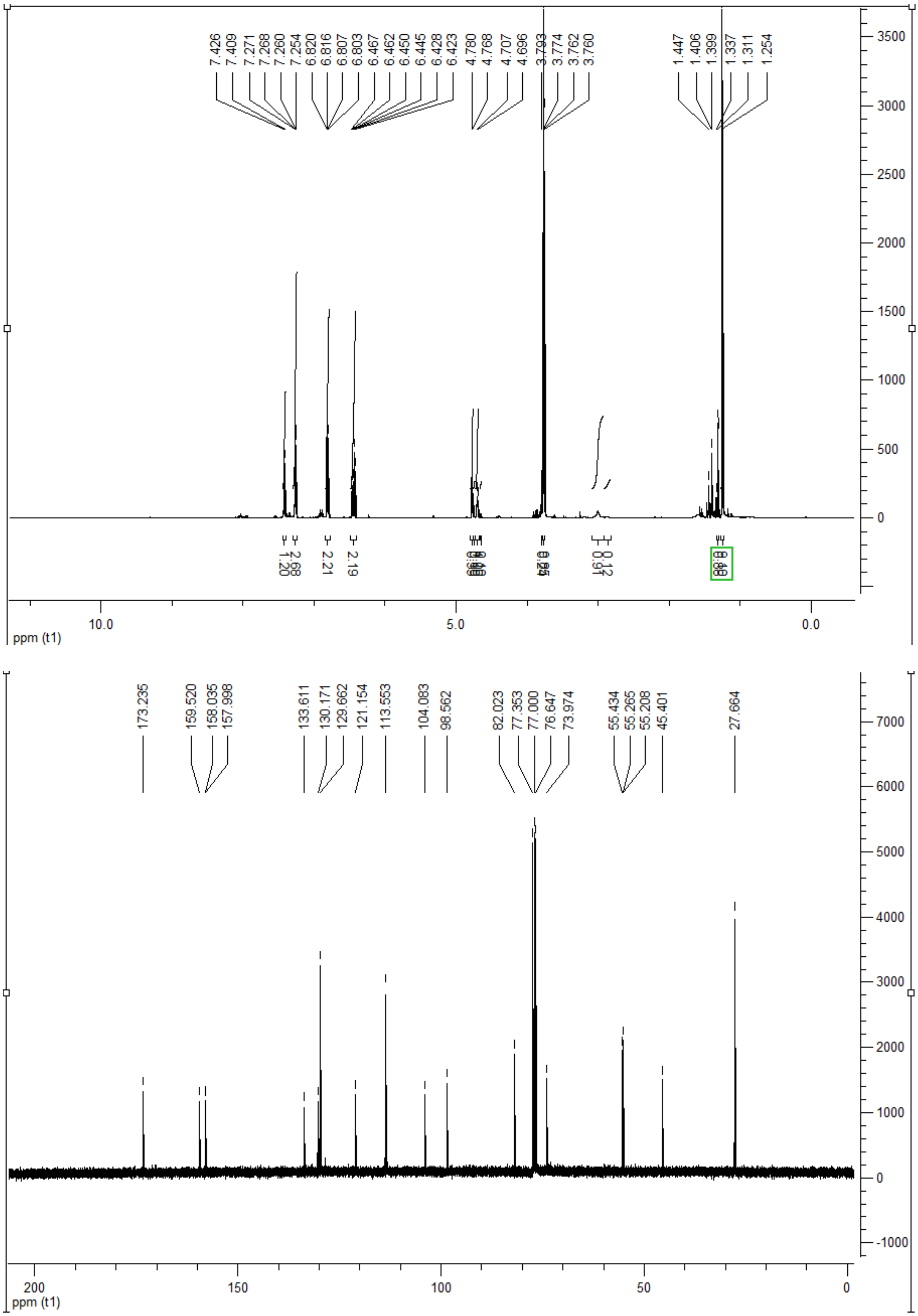


Methyl 3-(2,4-dimethylphenyl)-2-hydroxy-3-(*p*-tolyl)propanoate (8c)

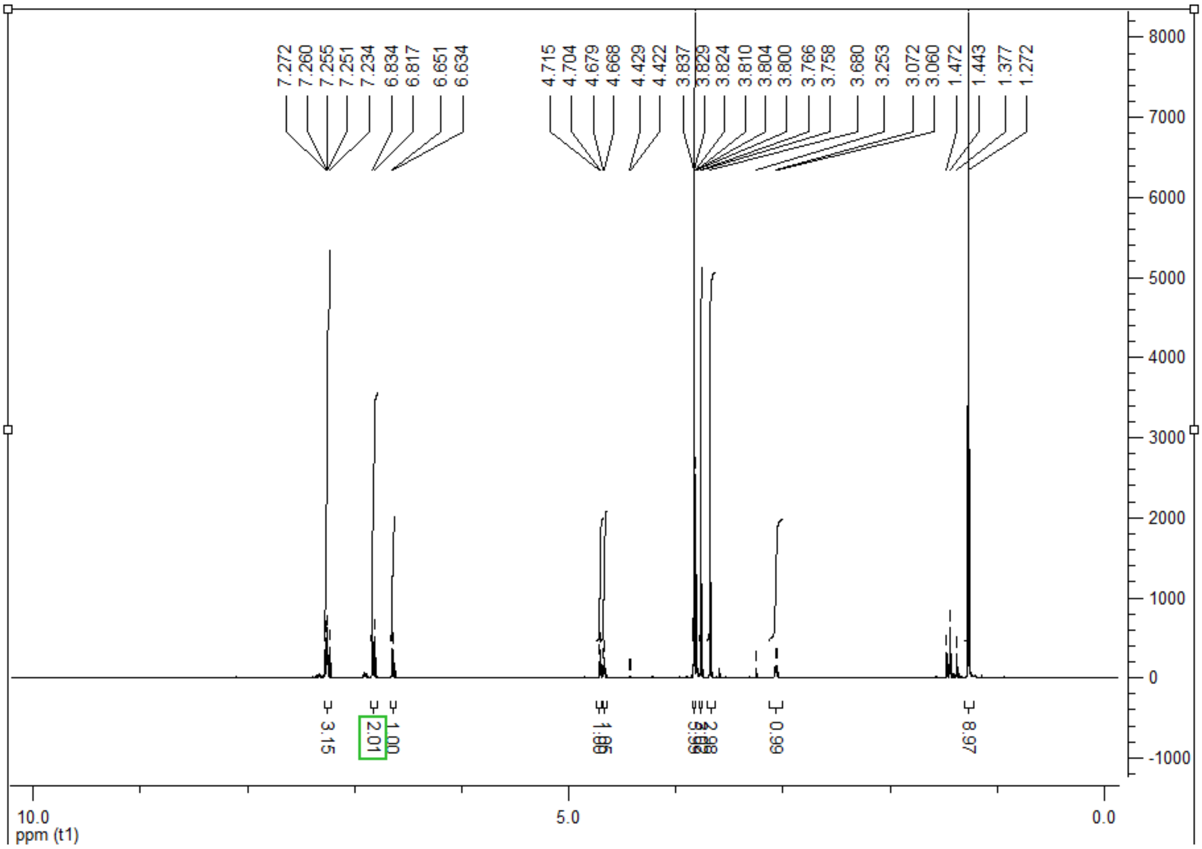


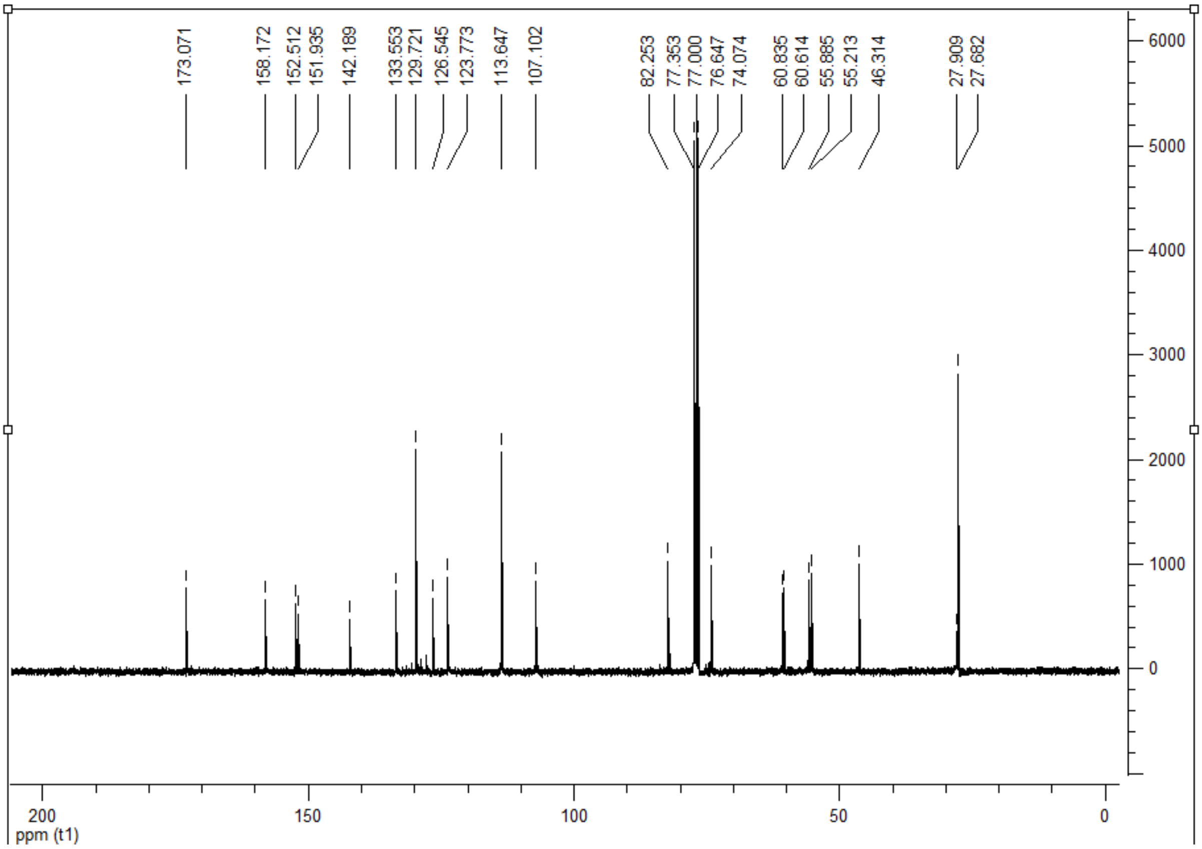


***tert*-Butyl 3-(2,4-dimethoxyphenyl)-2-hydroxy-3-(4-methoxyphenyl)propanoate (11a)**



tert-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(2,3,4-trimethoxyphenyl)propanoate (11b)





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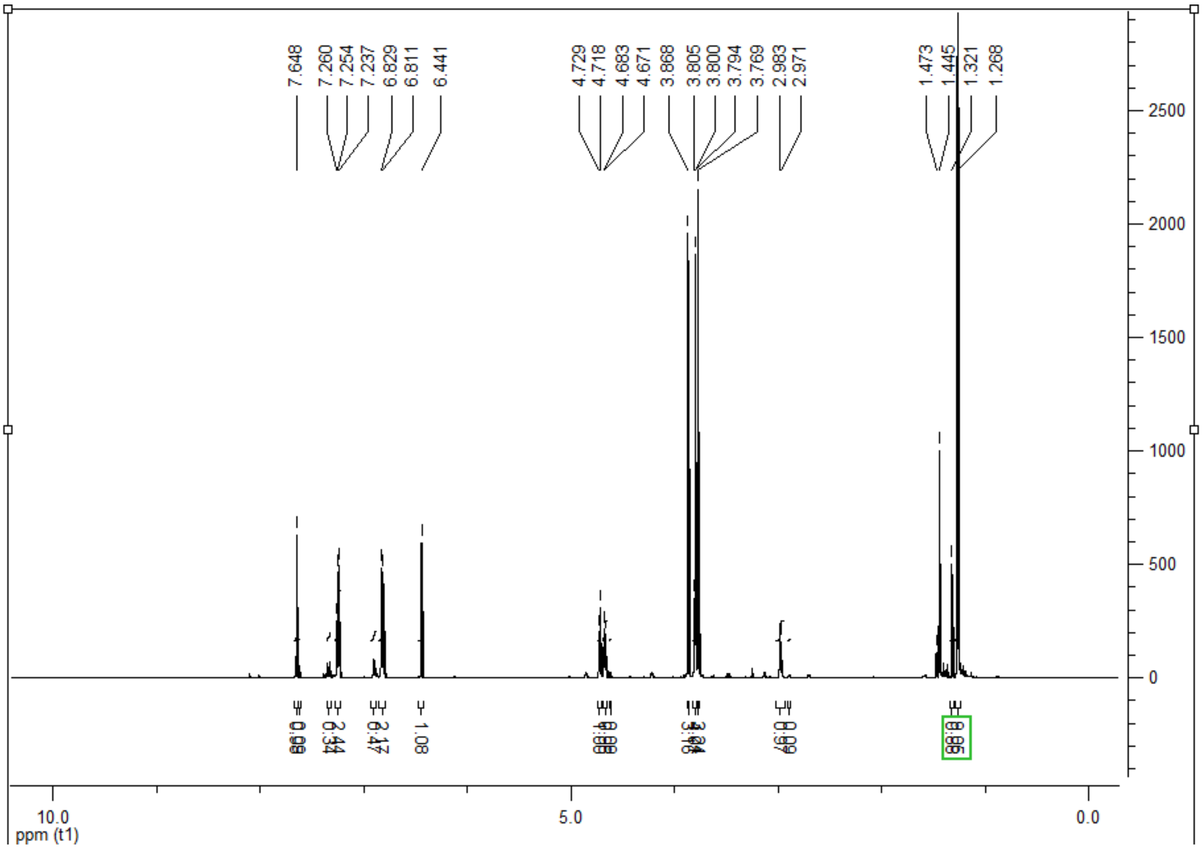
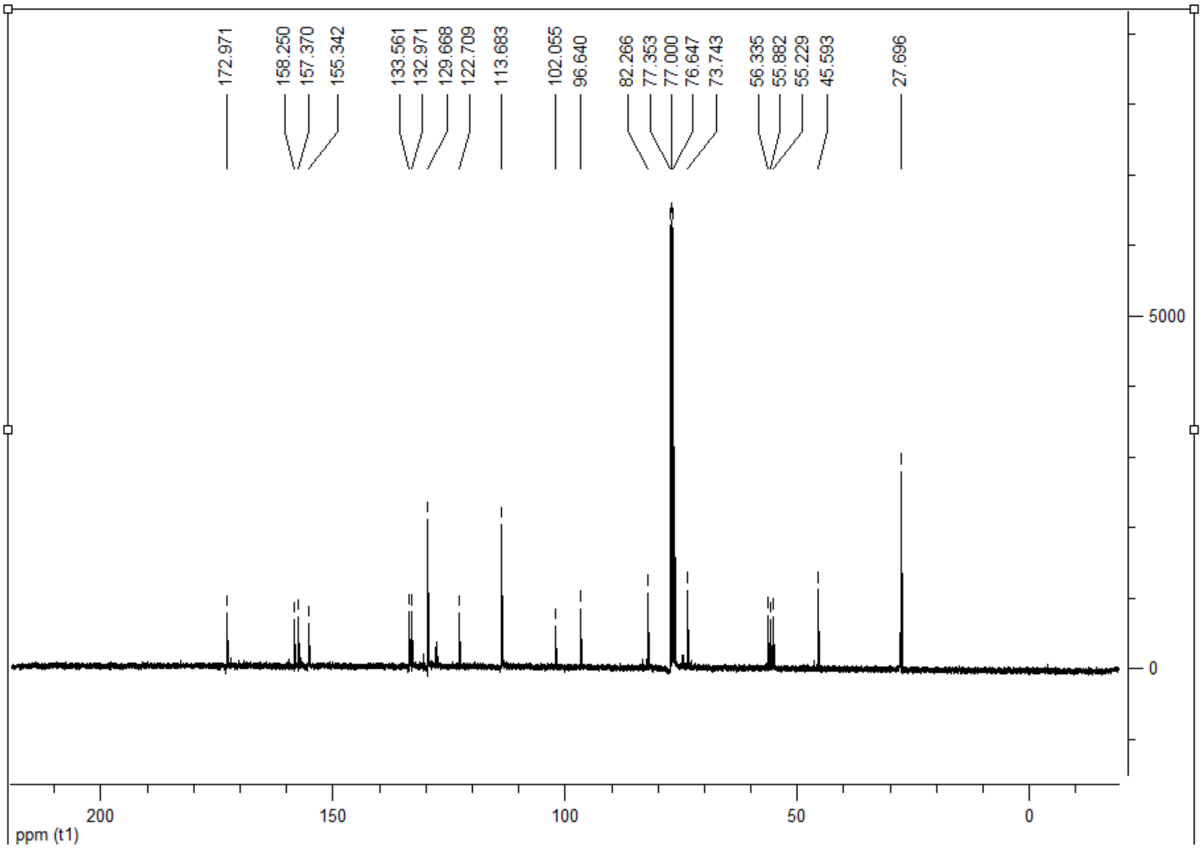
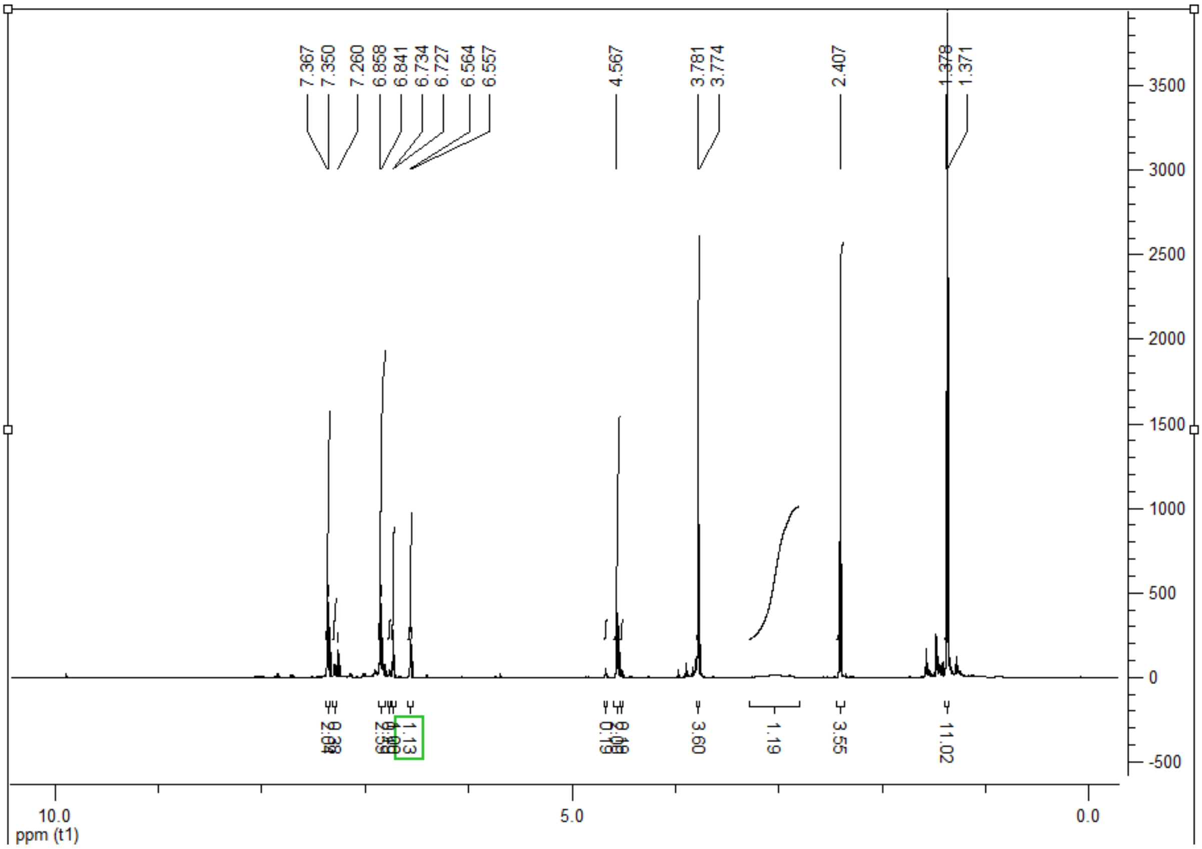
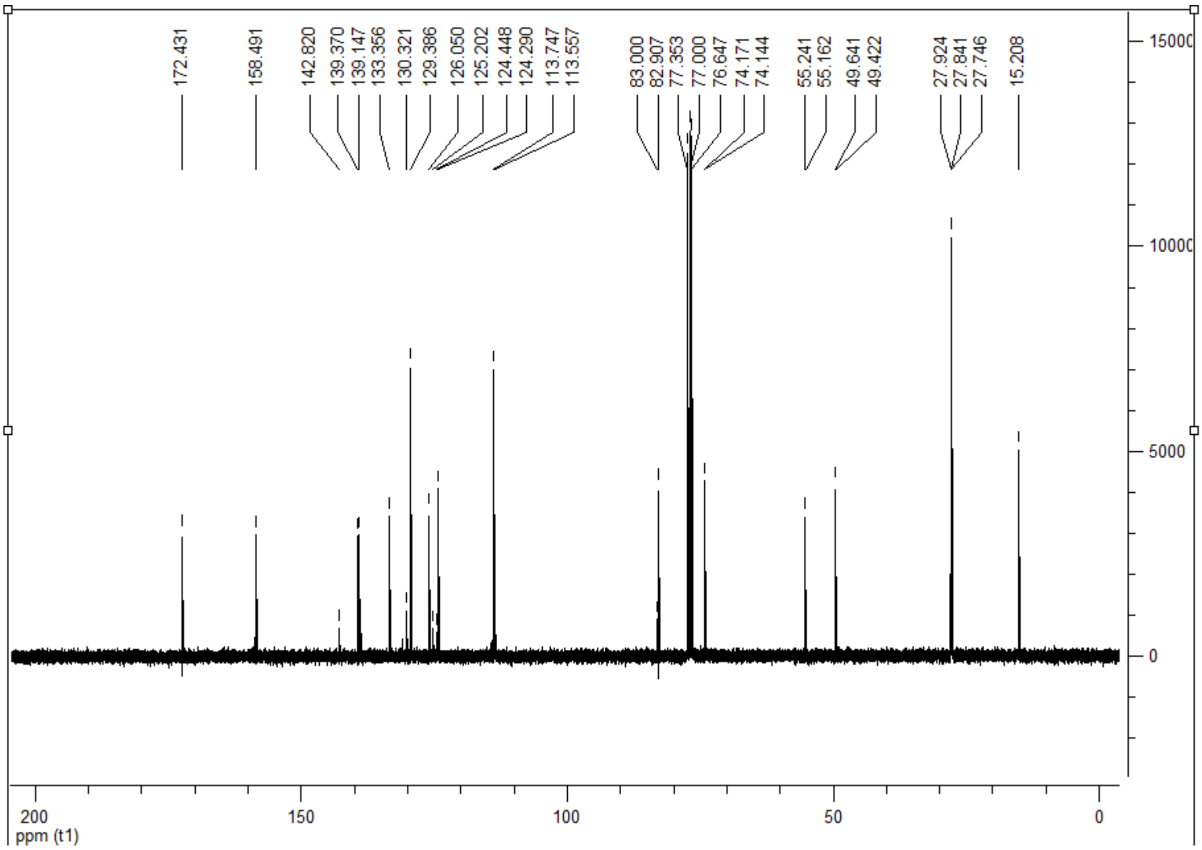




tert-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (11d)





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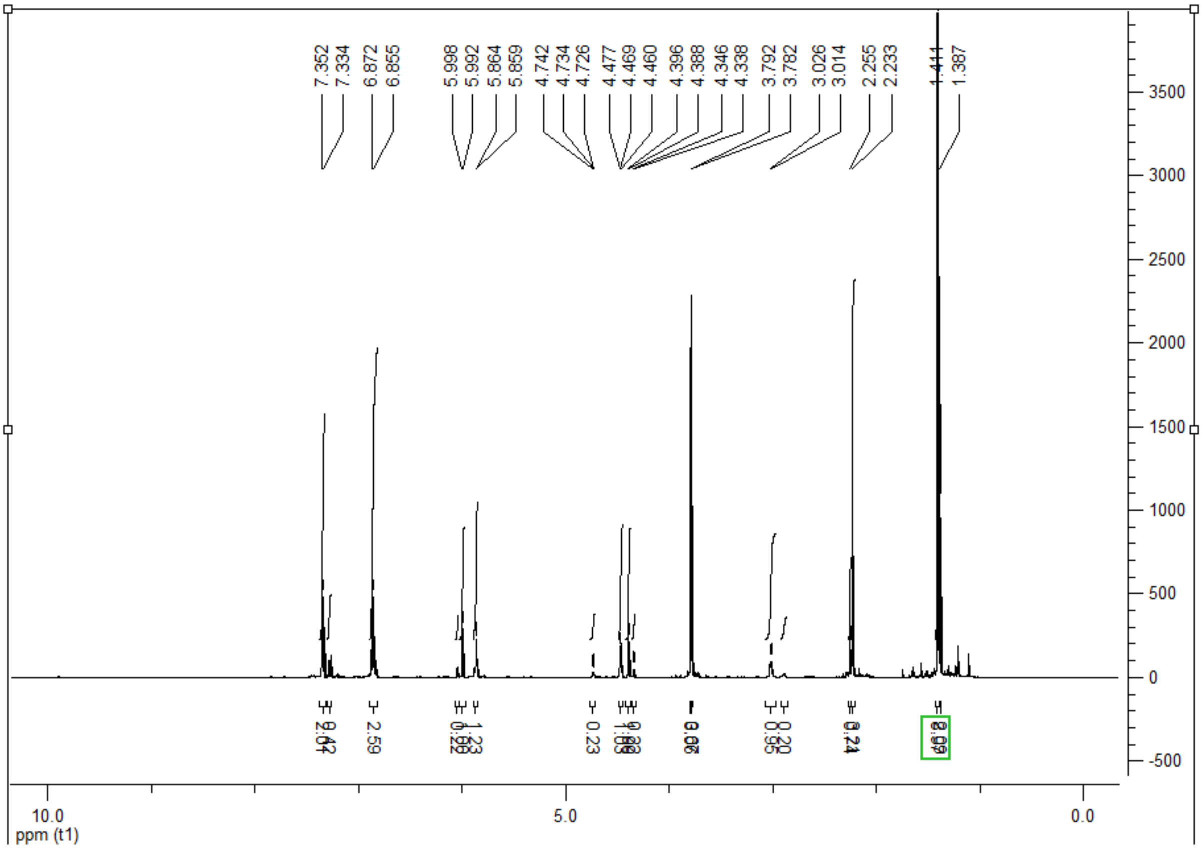
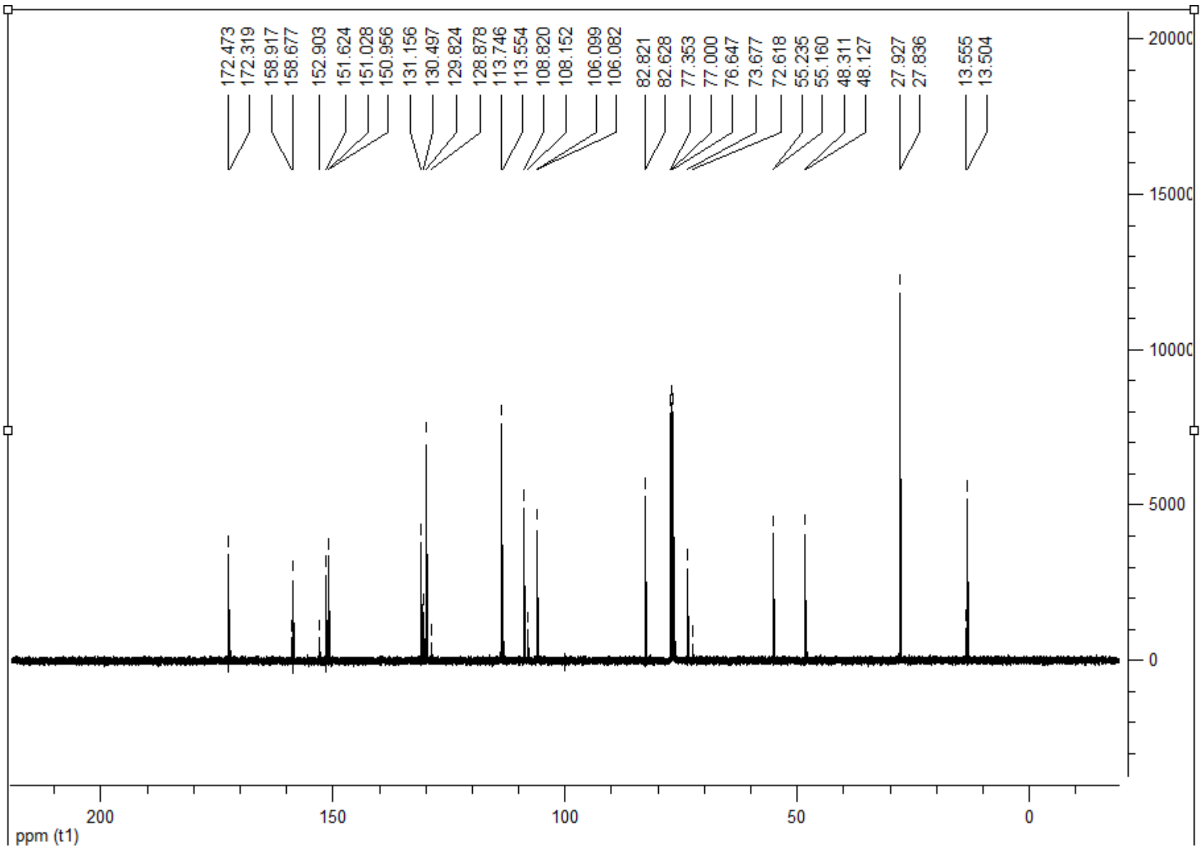
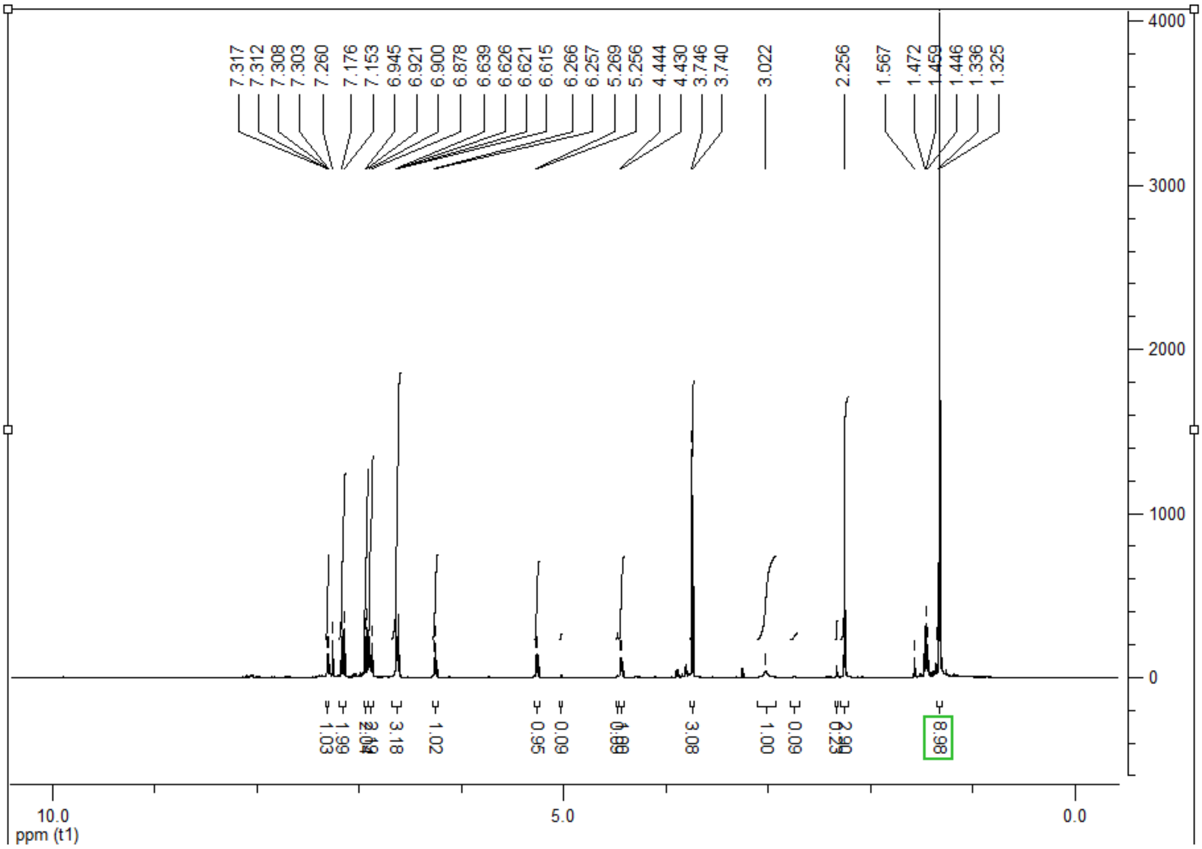
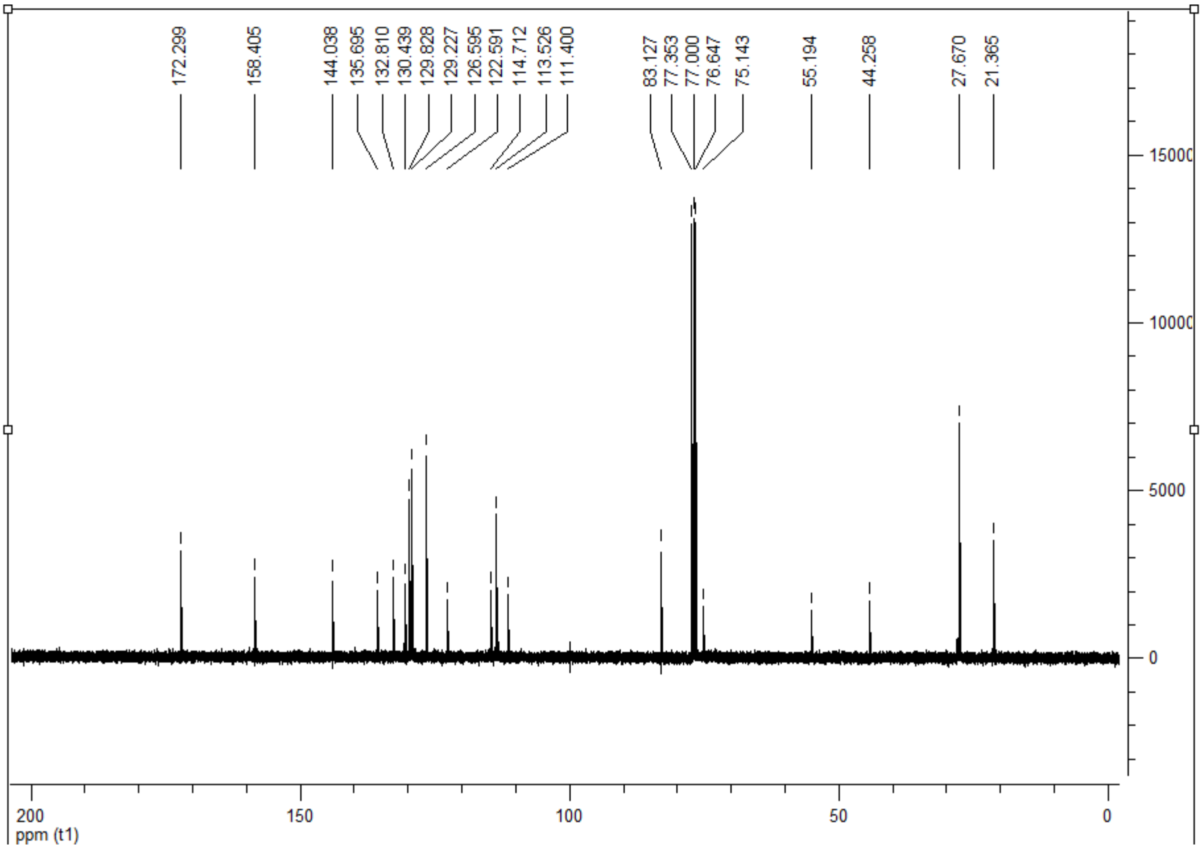


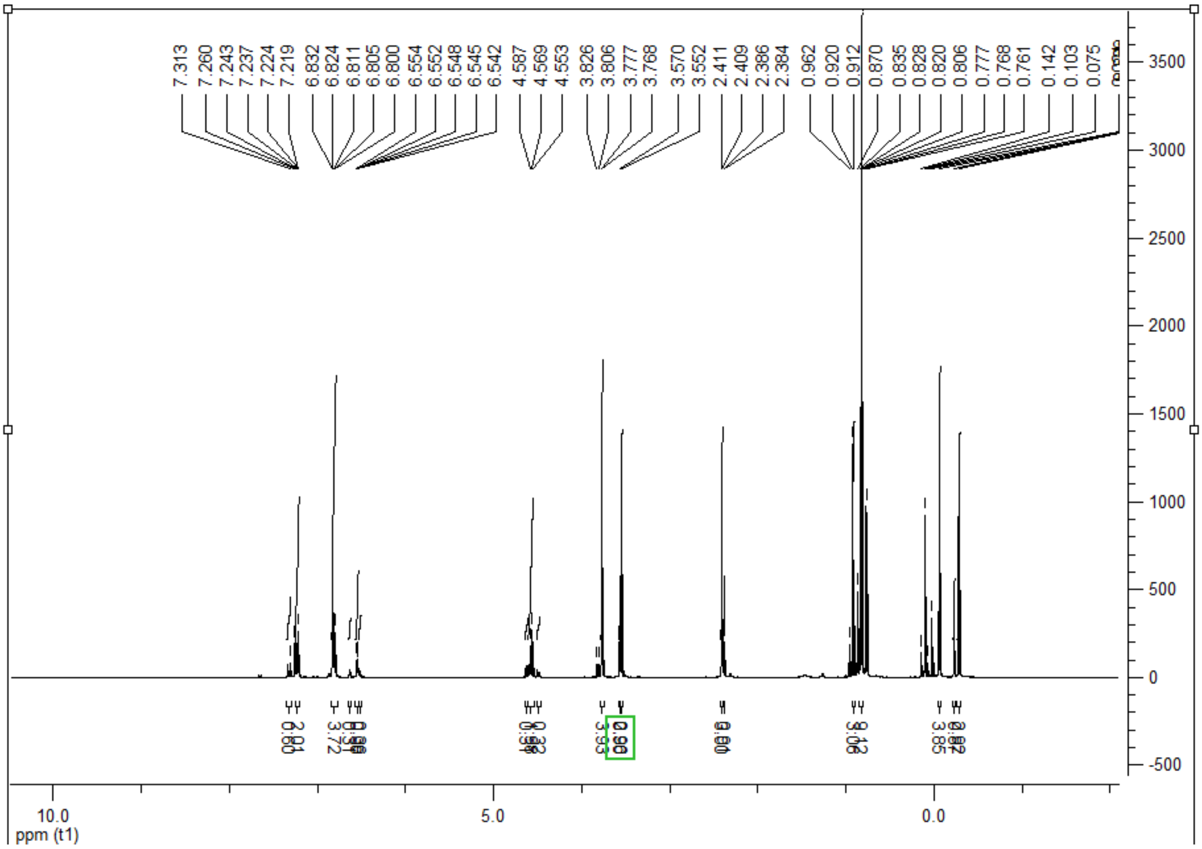


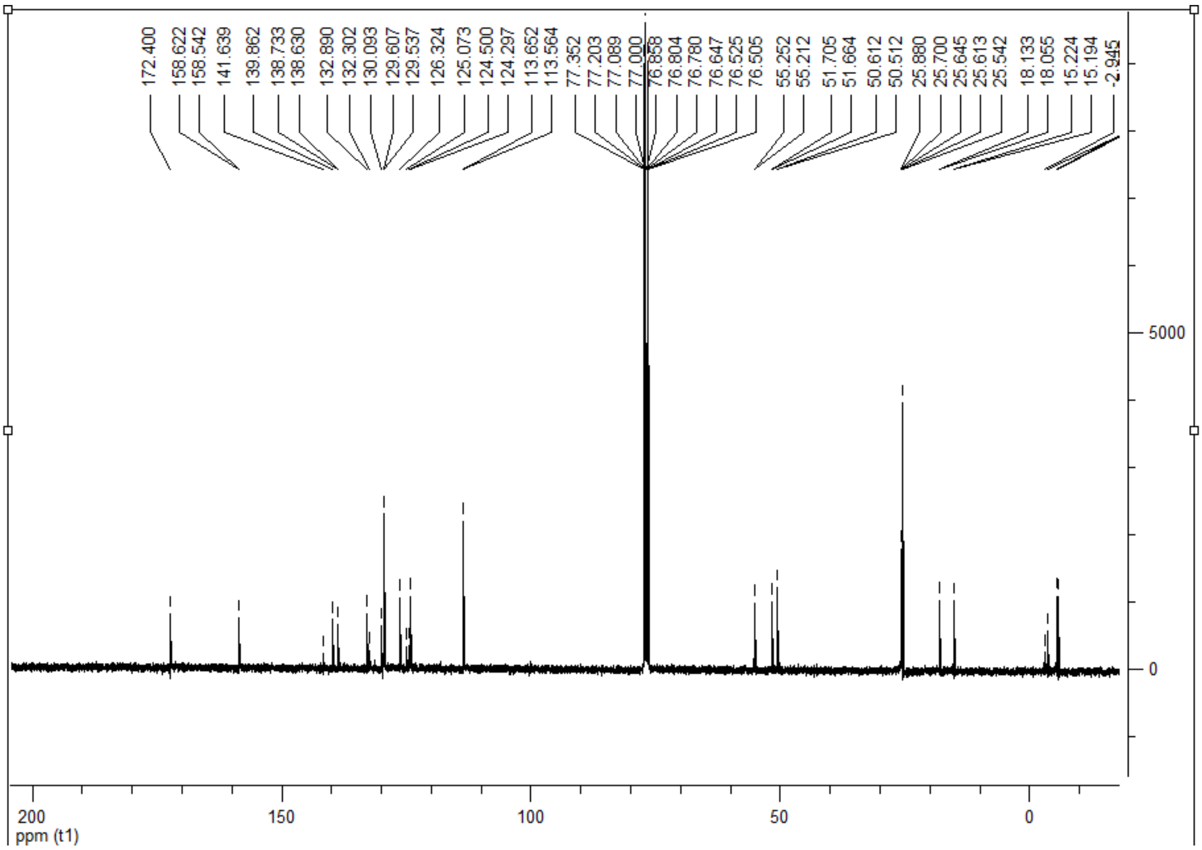
***tert*-Butyl 2-hydroxy-3-(4-methoxyphenyl)-3-(1-tosyl-1*H*-pyrrol-2-yl)propanoate (11f)**





Methyl 2-[(tert-butyldimethylsilyl)oxy]-3-(4-methoxyphenyl)-3-(5-methylthiophen-2-yl)propanoate (9)





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1-(4-methoxyphenyl)-1-(5-methylthiophen-2-yl)propan-2-ol (10)