Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

DNA-cellulose: An economical, fully recyclable and highly effective chiral biomaterial for asymmetric catalysis

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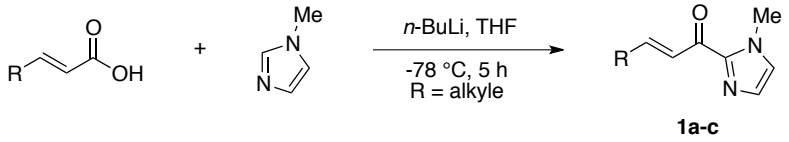
Table of Contents

General Methods

All reactions were run under argon atmosphere in oven-dried glassware unless otherwise specified. All commercially available compounds were purchased from Aldrich Chemical Co., Worthington Chemicals (CS-ct-DNA), GFS Chemicals, Strem Chemicals, Acros Organics or Alfa Aesar and used as received. Dichloromethane (DCM) was distilled from calcium hydride. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium/benzophenone. *N*,*N*-dimethylformamide (DMF) was distilled under vacuum over anhydrous $MgSO_4$. Analytical thin layer chromatography (TLC) was performed on silica gel plates (Merck $60F_{254}$) visualized either with a UV lamp (254 nm) or by using solutions of *p*-anisaldehyde/sulfuric acid/acetic acid (AcOH) in ethanol (EtOH) or $KMnO_4/K_2CO_3$/AcOH in water followed by heating. Flash chromatographies were performed on silica gel (60-230 mesh). Organic extracts were dried over anhydrous Na_2SO_4 or $MgSO_4$. Infrared spectra (IR) were recorded on a Bruker TENSORTM 27 (IRTF) and wavenumbers are indicated in cm^{-1}. ^1H NMR spectra were recorded on a Bruker AVANCE 400 at 400 MHz in $CDCl_3$ (unless otherwise specified) and the observed signals are reported as follows: chemical shift in parts per million from tetramethylsilane with the solvent as an internal indicator ($CDCl_3$ δ 7.26 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet or overlap of nonequivalent resonances), integration. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ (unless otherwise specified) and the observed signals were reported as follows: chemical shift in parts per million from tetramethylsilane with the solvent as an internal indicator ($CDCl_3$ δ 77.0 ppm), multiplicity with respect to proton (deduced from DEPT experiments, s = quaternary C, d = CH, t = CH_2, q = CH_3). Coupling constants (*J*) are reported in hertz (Hz). All NMR spectra were obtained at room temperature unless otherwise specified. Enantiomeric excess (*ees*) determinations were performed by supercritical fluid chromatography (SFC) analysis on chiral phase. The sign before the *ees* values is arbitrary. Mass spectra (MS) were recorded using a Hewlett-Packard tandem 5890A/5971 GCMS (70 eV). High-resolution mass spectra were performed by "Groupe de Spectrométrie de masse de l'Université Pierre et Marie Curie (Paris)".

Experimental and Spectral data

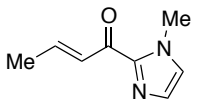
General procedure A. Synthesis of α,β-unsaturated acyl imidazoles 1a-c



1a-c

The α,β-unsaturated substrates **1a-c** were synthesized *via* a modification of the procedure originally reported by Evans and co-workers.[1] An oven-dried, 250 mL round-bottomed flask under an argon atmosphere was charged with 1-methylimidazole (24 mmol, 2.4 equiv) and dry THF (50 mL). The solution was cooled to −78 °C in a dry ice/acetone bath for 15 min, then *n*-BuLi (2.5 M in *n*-hexane, 24 mmol, 2.4 equiv) was added drop-wise over 10 min. The mixture was warmed to rt and stirred for 30 min, then cooled back to −78 °C. The desired acid (10 mmol, 1 equiv) in dry THF (10 mL) was added drop-wise over a 10 min period. The resulting solution was stirred at −78 °C for 15 min, then warmed at rt and stirred for an additional 2 h. The reaction was eventually quenched with a saturated aqueous $NaHCO_3$ solution (50 mL) and the aqueous phase was extracted with EtOAc (3 x 40 mL). The combined organic layers were washed with brine (2 x 40 mL), dried over $MgSO_4$, gravity filtered, and concentrated under reduced pressure. The reaction residue was purified by silica gel flash chromatography, eluting with EtOAc/pentane (4:6) as the eluent.

(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)but-2-en-1-one (1a)

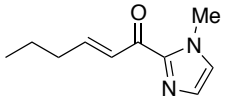


1a

Following general procedure A. 1-Methylimidazole (2 g, 2.2 mL, 27.6 mmol), *n*-BuLi (2.5 M in *n*-hexane, 11 mL, 27.6 mmol), and crotonic acid (0.95 g, 11.4 mmol) in dry THF (60 mL). The title compound (molecular formula: $C_8H_{10}N_2O$, MW = 150.18 g/mol, 0.91 g) was isolated as a colorless oil in 53% yield. **Rf**: 0.36 (EtOAc/pentane = 3:2). **IR** (neat): 3107, 2963, 1664, 1617, 1402, 1283, 1030, 909 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dq, J = 15.5, 1.8 Hz, 1H), 7.13-7.01 (m, 2H), 6.99 (s, 1H), 3.98 (s, 3H), 2.20-1.58 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.5 (s), 143.7 (d), 143.5 (s), 129.0 (d), 127.7 (d), 126.9 (d), 36.1 (q), 18.3 (q). Spectroscopic data were consistent with the literature data for this compound.[1]

[1] D. A. Evans, K. R. Fandrick, H.-J. Song *J. Am. Chem. Soc*. **2005**, *127*, 8942.

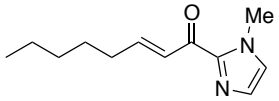
(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)hex-2-en-1-one (1b)



1b

Following general procedure A. 1-Methylimidazole (1 g, 1 mL, 12.6 mmol), *n*-BuLi (2.5 M in *n*-hexane, 5 mL, 13.7 mmol), and (2*E*)-hexenoic acid (0.65 g, 0.7 mL, 5.7 mmol) in dry THF (50 mL). The title compound (molecular formula: $C_{10}H_{14}N_2O$, MW = 178.23 g/mol, 0.505 g) was isolated as a colorless oil in 51% yield. **Rf**: 0.37 (EtOAc/pentane 3:2). **IR** (neat): 2960, 2931, 2837, 2665, 1618, 1405, 1022, 978, 917, 728 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 (dt, J = 15.6, 1.5 Hz, 1H), 7.20-7.07 (m, 2H), 7.04 (d, J = 0.5 Hz, 1H), 4.12-4.03 (m, 3H), 2.41-2.20 (m, 2H), 1.62-1.39 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.4 (s), 148.3 (d), 143.5 (s), 128.9 (d), 126.9 (d), 126.2 (d), 36.0 (q), 34.4 (t), 21.2 (t), 13.6 (q). Spectroscopic data were consistent with the literature data for this compound.[2]

(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)oct-2-en-1-one (1c)

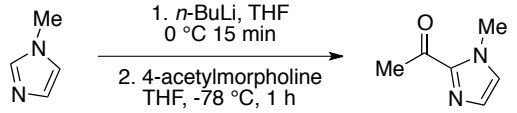


1c

Following general procedure A. 1-Methylimidazole (1 g, 1 mL, 12.2 mmol), *n*-BuLi (2.5 M in *n*-hexane, 5 mL, 13.3 mmol), and (2*E*)-oct-2-enoic acid (0.79 g, 5.5 mmol) in dry THF (50 mL). The title compound (molecular formula: $C_{12}H_{18}N_2O$, MW = 206.28 g/mol, 0.56 g) was isolated as a colorless oil in 49% yield. **Rf**: 0.39 (EtOAc/pentane 6:4). **IR** (neat): 2957, 2928, 2858, 1666, 1618, 1406, 991, 916, 732 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 (dt, J = 15.6, 1.5 Hz, 1H), 7.19-7.06 (m, 2H), 7.08-6.99 (m, 1H), 4.12-3.97 (m, 3H), 2.40-2.21 (m, 2H), 1.58-1.44 (m, 2H), 1.41-1.23 (m, 4H), 1.12-0.76 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.8 (s), 149.1 (d), 143.8 (s), 129.2 (d), 127.1 (d), 126.1 (d), 36.3 (q), 32.7 (t), 31.5 (t), 27.9 (t), 22.5 (t), 14.0 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

[2] Wang, X.; Wang, D. Z. *Tetrahedron* **2011**, *67*, 3406.
[3] Boersma, A. J.; Feringa, B. L.; Roelfes, G. *Angew. Chem, Int. Ed*. **2009**, *48*, 3346.

Synthesis of 1-(1-methyl-1*H*-imidazol-2-yl)ethanone (S1)

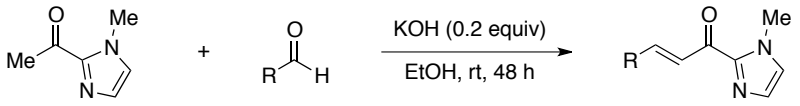


S1

Compound **S1** was synthesized *via* a modification of the procedure originally reported by Scheidt and co-workers.[3] An oven-dried 100 mL round-bottomed flask under an argon atmosphere was charged with 1-methylimidazole (4.5 g, 4.4 mL, 55.2 mmol, 1.1 equiv) and dry THF (60 mL). The solution was cooled to 0 °C in an ice bath for 15 min, then *n*-BuLi (2.5 M in *n*-hexane, 24 mL, 55.2 mmol, 1.1 equiv) was added dropwise over 10 min. The mixture was stirred at 0 °C for 15 min, then cannulated into a solution of 4-acetylmorpholine (6.5 g, 5.8 mL, 50.1 mmol, 1 equiv) in dry THF (40 mL) at −78 °C. The reaction mixture was then stirred at −78 °C for 1 h and quenched with a 1 N aqueous solution of HCl (5 mL), stirred for 5 min and diluted with a saturated aqueous solution of $NaHCO_3$ (15 mL) and brine (15 mL). The aqueous phase was extracted with EtOAc (3 x 40 mL) and the combined organic layers were dried over anhydrous $MgSO_4$, gravity filtered and concentrated under reduced pressure. The reaction residue was purified by silica gel flash chromatography, eluting with Et_2O/pentane (9:1) to provide the title compound (molecular formula: $C_6H_8N_2O$, MW = 124.14 g/mol, 6.2 g) as a colorless oil in 79% yield. **Rf**: 0.31 (Et_2O/pentane = 9:1). **IR** (neat) 3108, 2959, 1674, 1402, 915, 776 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 (d, J = 0.9 Hz, 1H), 7.02 (br, s, 1H), 3.99 (s, 3H), 2.66 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 190.2 (s), 142.9 (s), 128.7 (d), 126.7 (d), 35.9 (q), 26.8 (q). Spectroscopic data were consistent with the literature data for this compound.[4]

[4] M. C. Myers, A. R. Bharadwaj, B. C. Milgram, K. A. Scheidt *J. Am. Chem. Soc*. **2005**, *127*, 14675.

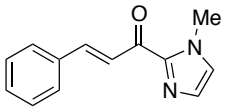
General procedure B. Synthesis of α,β-unsaturated acyl imidazoles 1d-h



S1 **1d-h**

The α,β-unsaturated substrates **1d-h** were synthesized *via* a modification of the procedure originally reported by Scheidt and co-workers.[3] An oven-dried 100 mL round-bottomed flask under an argon atmosphere was charged with 1-methylimidazole (10.0 mmol, 1.0 equiv) and EtOH (20 mL). The appropriate aromatic aldehyde (10.0 mmol, 1.0 equiv) and a catalytic amount of KOH (2 mmol, 0.2 equiv) were added and the solution was stirred at rt for 48 h. The formation of a precipitate was observed. The reaction was quenched with H_2O (50 mL) and the aqueous phase was extracted with EtOAc (3 x 40 mL). The combined organic layers were washed with brine (2 x 50 mL), dried over anhydrous $MgSO_4$, gravity filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel using EtOAc/pentane (1:1) as the eluent.

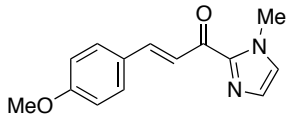
(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)-3-phenylprop-2-en-1-one (1d)



1d

Following general procedure B. Compound **S1** (1.3 g, 10.5 mmol), benzaldehyde (1.1 g, 1.1 mL, 10.5 mmol), and KOH (0.11 g, 2 mmol), in EtOH (20 mL). The title compound (molecular formula: $C_{13}H_{12}N_2O$, MW = 212.25 g/mol, 1.3 g) was isolated as a white solid in 57% yield. **Rf**: 0.40 (Et_2O/pentane = 9:1). **IR** (neat): 3124, 3100, 3022, 1655, 1603, 1400, 1017, 769 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, J = 16.0 Hz, 1H), 7.81 (d, J = 16.0 Hz, 1H), 7.73-7.64 (m, 2H), 7.44-7.32 (m, 3H), 7.20 (d, J = 0.9 Hz, 1H), 7.07 (s, 1H), 4.09 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.4 (s), 143.9 (s), 143.1 (d), 134.8 (s), 130.4 (d), 129.2 (d), 128.8 (2C, d), 128.7 (2C, d), 127.2 (d), 122.7 (d), 36.3 (q). Spectroscopic data were consistent with the literature data for this compound.[4]

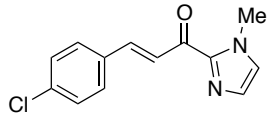
(*E*)-3-(4-Methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1e)



1e

Following general procedure B. Compound **S1** (1.3 g, 10.5 mmol), 4-methoxybenzaldehyde (1.4 g, 1.3 mL, 10.5 mmol), and KOH (0.11 g, 2 mmol), in EtOH (20 mL). The title compound (molecular formula: $C_{14}H_{14}N_2O_2$, MW = 242.27 g/mol, 1.3 g) was isolated as a yellow solid in 51% yield. **Rf**: 0.36 (Et_2O/pentane = 9:1). **IR** (neat): 3129, 3105, 2938, 2844, 1649, 1586, 1567, 1510, 1398, 1250, 1155, 1021, 990, 730 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, J = 16.0 Hz, 1H), 7.77 (d, J = 16.0 Hz, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.18 (s, 1H), 7.03 (s, 1H), 6.89 (d, J = 8.8 Hz, 2H), 4.05 (s, 3H), 3.81 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.4 (s), 161.5 (s), 144.0 (s), 143.1 (d), 130.4 (2C, d), 129.0 (d), 127.6 (s), 127.0 (d), 120.4 (d), 114.2 (2C, d), 55.3 (q), 36.3 (q). Spectroscopic data were consistent with the literature data for this compound.[4]

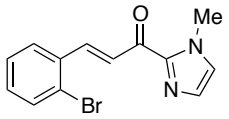
(*E*)-3-(4-Chlorophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1f)



1f

Following general procedure B. Compound **S1** (1.3 g, 10.5 mmol), 4-chlorobenzaldehyde (1.47 g, 10.5 mmol) and KOH (0.11 g, 2 mmol), in EtOH (20 mL). The title compound (molecular formula: $C_{13}H_{11}ClN_2O$, MW = 246.69 g/mol, 1.7 g) was isolated as a white solid in 67% yield. **Rf**: 0.40 (Et_2O/pentane = 9:1). **IR** (neat): 3129, 3109, 2957, 1654, 1594, 1397, 1286, 1014, 815, 783 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, J = 16.0 Hz, 1H), 7.72 (d, J = 16.0 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.19 (s, 1H), 7.06 (s, 1H), 4.06 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.1 (s), 143.8 (s), 141.7 (d), 136.2 (s), 133.3 (s), 129.8 (2C, d), 129.3 (d), 129.0 (2C, d), 127.3 (d), 123.2 (d), 36.3 (q). Spectroscopic data were consistent with the literature data for this compound.[4]

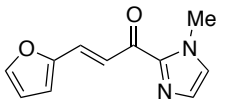
(*E*)-3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1g)



1g

Following general procedure B. Compound **S1** (1.3 g, 10.5 mmol), 2-bromobenzaldehyde (1.9 g, 1.2 mL, 10.5 mmol) and KOH (0.11 g, 2 mmol), in EtOH (20 mL). The title compound (molecular formula: $C_{13}H_{11}BrN_2O$, MW = 291.14 g/mol, 2.0 g) was isolated as a white solid in 67% yield. **Rf**: 0.37 (Et_2O/pentane = 9:1). **IR** (neat): 3128, 3102, 2954, 1654, 1599, 1402, 1019, 735 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.21 (d, J = 15.9 Hz, 1H), 8.03 (d, J = 15.9 Hz, 1H), 7.86 (dd, J = 8.0, 1.7 Hz, 1H), 7.62 (dd, J = 8.0, 1.1 Hz, 1H), 7.35-7.30 (m, 1H), 7.28-7.18 (m, 2H), 7.09 (s, 1H), 4.10 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.9 (s), 143.9 (s), 141.5 (d), 134.8 (s), 133.4 (d), 131.3 (d), 129.4 (d), 128.1 (d), 127.6 (d), 127.4 (d), 126.1 (s), 125.2 (d), 36.4 (q). Spectroscopic data were consistent with the literature data for this compound.[4]

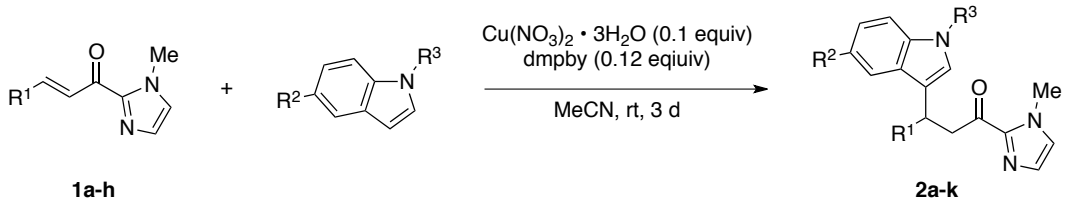
(*E*)-3-(Furan-2-yl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1h)



1h

Following general procedure B. Compound **S1** (1.3 g, 10.5 mmol), furan-2-carbaldehyde (1 g, 0.87 mL, 10.5 mmol) and KOH (0.11 g, 2 mmol), in EtOH (20 mL). The title compound (molecular formula: $C_{11}H_{10}N_2O_2$, MW = 202.21 g/mol, 0.95 g) was isolated as a brown solid in 45% yield. **Rf**: 0.30 (EtOAc/pentane = 1:1). **IR** (neat): 3129, 3109, 2957, 1654, 1594, 1397, 1286, 1014, 815, 783 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, J = 15.8 Hz, 1H), 7.56 (d, J = 15.8 Hz, 1H), 7.48 (d, J =1.7 Hz, 1H), 7.17 (s, 1H), 7.04 (s, 1H), 6.70 (d, J = 3.4 Hz, 1H), 6.46 (dd, J = 3.4, 1.7 Hz, 1H), 4.04 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.2 (s), 151.8 (s), 144.9 (d), 143.9 (s), 129.4 (d), 129.2 (d), 127.1 (d), 120.7 (d), 115.6 (d), 112.4 (d), 36.2 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

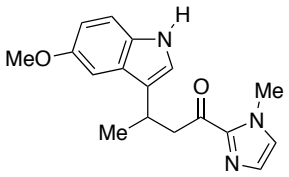
General Procedure C. Racemic Friedel-Crafts alkylations



1a-h **2a-k**

An oven-dried 25 mL round-bottomed flask was charged with $Cu(NO_3)_2 \cdot 3H_2O$ (0.035 mmol, 0.1 equiv), 4,4'-dimethyl-2,2'-bipyridyl (dmbpy, 0.042 mmol, 0.12 equiv), and MeCN (5 mL). The mixture was stirred at rt for 10 min then the α,β-unsaturated substrate (0.35 mmol, 1.0 equiv) and the desired indole (0.53 mmol, 1.5 equiv) were added. The solution was stirred at rt for 3 d. The reaction was eventually diluted with brine (10 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layers dried over anhydrous $MgSO_4$, gravity filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel using EtOAc/pentane (1:1) as the eluent.

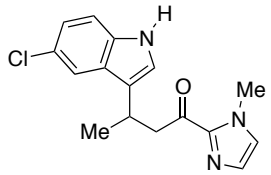
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2a)



2a

Following general procedure C. Compound **1a** (0.053 g, 0.35 mmol), 5-methoxyindole (0.078 g, 0.53 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.008 g, 0.035 mmol), dmbpy (0.008 g, 0.042 mmol), and MeCN (5 mL). The title compound (molecular formula: $C_{17}H_{19}N_3O_2$, MW = 297.35 g/mol, 0.094 g) was isolated as a brown solid in 91% yield. **Rf**: 0.29 (EtOAc/pentane = 1:1). **IR** (neat): 3047, 2958, 2926, 1671, 1484, 1405, 1215, 923, 795 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (br, s, 1H), 7.20 (d, J = 8.8 Hz, 1H), 7.17-7.15 (m, 2H), 7.02 (d, J = 2.5 Hz, 1H), 7.00 (s, 1H), 6.82 (dd, J = 8.8, 2.5 Hz, 1H), 3.94 (s, 3H), 3.86 (s, 3H), 3.83–3.72 (m, 1H), 3.58 (dd, J = 15.6, 6.5 Hz, 1H), 3.40 (dd, J = 15.6, 8.8 Hz, 1H), 1.40 (d, J = 6.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.3 (s), 153.7 (s), 143.3 (s), 131.5 (s), 128.8 (d), 126.9 (s), 126.8 (d), 121.1 (s), 120.9 (d), 112.1 (d), 111.7 (d), 101.0 (d), 55.9 (t), 46.8 (q), 36.2 (d), 27.1 (q), 21.4 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

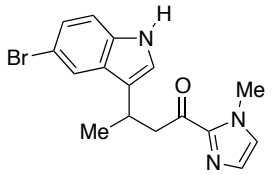
3-(5-Chloro-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2b)



2b

Following general procedure C. Compound **1a** (0.020 g, 0.133 mmol), 5-chloroindole (0.024 g, 0.160 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.0032 g, 0.013 mmol), dmbpy (0.0034 g, 0.019 mmol), and MeCN (0.5 mL). The title compound (molecular formula: $C_{16}H_{16}ClN_3O$, MW = 301.77 g/mol, 0.040 g) was isolated as a brown oil in quantitative yield. **Rf**: 0.32 (EtOAc/pentane 1:1). **IR** (neat): 3173, 2961, 2928, 2869, 1672, 1462, 1406, 1104, 986 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.56 (d, J = 2.0 Hz, 1H), 7.22 (dd, J = 8.6, 0.5Hz, 1H), 7.16 (d, J = 0.9 Hz, 1H), 7.12-7.06 (m, 1H), 7.06-6.99 (m, 2H), 3.93 (s, 3H), 3.80-3.68 (m, 1H), 3.46 (qd, J = 15.7, 7.3 Hz, 2H), 1.40 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.0 (s), 143.2 (s), 134.6 (s), 128.9 (d), 127.7 (s), 127.0 (d), 124.8 (s), 122.1 (d), 121.6 (d), 121.2 (s), 118.7 (d), 112.0 (d), 46.9 (t), 36.1 (d), 27.0 (q), 21.5 (q). **HRMS (ESI)**: m/z calcd for $C_{16}H_{16}ClN_3ONa$ $[M + Na]^+$: 324.08741, found: 324.08711.

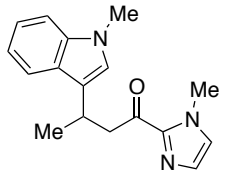
3-(5-Bromo-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2c)



2c

Following general procedure C. Compound **1a** (0.029 g, 0.19 mmol), 5-bromoindole (0.057 g, 0.29 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.004 g, 0.018 mmol), dmbpy (0.005 g, 0.026 mmol) and MeCN (1.5 mL). The title compound (molecular formula: $C_{16}H_{16}BrN_3O$, MW = 346.22 g/mol, 0.052 g) was isolated as a brown oil in 78% yield. **Rf**: 0.17 (EtOAc/pentane = 2:3). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.68 (br, s, 1H), 7.62 (s, 1H), 7.19-7.06 (m, 3H), 7.95 (s, 1H), 6.89 (s, 1H), 3.85 (s, 3H), 3.69 (m, 1H), 3.37 (d, J = 7.8 Hz, 2H), 1.30 (d, J = 1.30 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.0 (s), 143.2 (s), 135.0 (s), 128.9 (d), 128.3 (s), 127.15 (d), 124.6 (s), 121.7 (d), 121.6 (d), 121.0 (s), 112.6 (d), 112.0 (d), 47.1 (t), 36.2 (d), 27.0 (q), 21.6 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

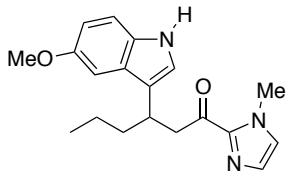
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)butan-1-one (2d)



2d

Following general procedure C. Compound **1a** (0.074 g, 0.35 mmol), *N*-methylindole (0.069 g, 0.066 mL, 0.53 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.008 g, 0.035 mmol), dmbpy (0.008 g, 0.042 mmol), and MeCN (5 mL). The title compound (molecular formula: $C_{22}H_{21}N_3O$, MW = 343.42 g/mol, 0.096 g) was isolated as a brown solid in 80% yield. **Rf**: 0.31 (EtOAc/pentane = 1:1). **IR** (neat): 3026, 2916, 1673, 1472, 1406, 1154, 915, 741 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dt, J = 8.0, 1.0 Hz, 1H), 7.44-7.38 (m, 2H), 7.29-7.20 (m, 3H), 7.20-7.08 (m, 3H), 7.04-6.94 (m, 3H), 5.05 (t, J = 7.5 Hz, 1H), 4.01 (dd, J = 16.5, 7.5 Hz, 1H), 3.88 (s, 3H), 3.86 (dd, J = 16.5, 7.5 Hz, 1H), 3.71 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 191.0 (s), 144.6 (s), 143.1 (s), 137.1 (s), 128.8 (d), 128.3 (2C, d), 127.9 (2C, d), 127.1 (s), 126.8 (d), 126.2 (d), 126.0 (d), 121.5 (d), 119.6 (d), 118.7 (d), 117.8 (s), 109.0 (d), 45.5 (t), 38.0 (d), 36.1 (q), 32.7 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)hexan-1-one (2e)

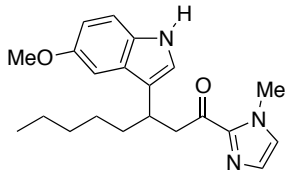


2e

Following general procedure C. Compound **1b** (0.020 g, 0.112 mmol), 5-methoxylindole (0.025 g, 0.168 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.0027 g, 0.011 mmol), dmbpy (0.0029 g, 0.016 mmol), and MeCN (0.5 mL). The title compound (molecular formula: $C_{19}H_{23}N_3O_2$, MW = 325.40 g/mol, 0.025 g) was isolated as a brown oil in 68% yield. **Rf**: 0.32 (EtOAc/pentane 1:1). **IR** (neat): 3405, 2955, 2927, 1672, 1483, 1458, 1405, 12122, 1029, 754 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.18 (d, J = 8.7 Hz, 1H), 7.13 (s, 1H), 7.08 (d, J = 2.4 Hz, 1H), 6.99 (d, J = 2.1 Hz, 1H), 6.96 (s, 1H), 6.80 (dd, J = 8.7, 2.4 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.69 (p, J = 7.2 Hz, 1H), 3.51 (d, J = 7.2 Hz, 2H), 1.84-1.67 (m, 2H), 1.37-1.22 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.4 (s), 153.6 (s),

143.3 (s), 131.4 (s), 128.7 (d), 127.4 (s), 126.7 (d), 121.8 (d), 119.3 (s), 111.8 (d), 111.6 (d), 101.1 (d), 55.9 (q), 45.5 (t), 38.4 (t), 36.0 (q), 32.0 (d), 20.6 (t), 14.1 (q). **HRMS (ESI)**: m/z calcd for $C_{19}H_{23}N_3O_2Na$ $[M + Na]^+$: 348.16825, found: 348.16772.

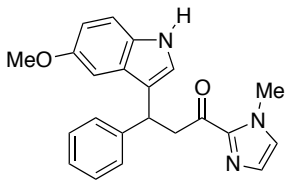
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)octan-1-one (2f)



2f

Following general procedure C. Compound **1c** (0.023 g, 0.112 mmol), 5-methoxylindole (0.025 g, 0.168 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.0027 g, 0.011 mmol), dmbpy (0.0029 g, 0.016 mmol), and MeCN (0.5 mL). The title compound (molecular formula: $C_{21}H_{27}N_3O_2$, MW = 353.46 g/mol, 0.0295 g) was isolated as a brown oil in 73% yield. **Rf**: 0.38 (EtOAc/pentane 1:1). **IR** (neat): 3049, 2954, 2926, 2855, 1672, 1484, 1459, 1407, 1214, 1032, 917, 754 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.19 (d, J = 8.7 Hz, 1H), 7.13 (d, J = 0.9 Hz, 1H), 7.07 (d, J = 2.4 Hz, 1H), 7.00 (d, J = 2.2 Hz, 1H), 6.96 (s, 1H), 6.80 (dd, J = 8.7, 2.4 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.66 (d, J = 7.2 Hz, 1H), 3.50 (dd, J = 7.3, 4.3 Hz, 2H), 1.83-1.69 (m, 2H), 1.34-1.16 (m, 6H), 0.85-0.76 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.4 (s), 153.6 (s), 143.4 (s), 131.4 (s), 128.8 (d), 127.4 (s), 126.7 (d), 121.8 (d), 119.4 (s), 111.9 (d), 111.6 (d), 101.1 (d), 55.9 (q), 45.5 (t), 36.1 (t), 36.0 (d), 32.3 (q), 31.9 (t), 27.1 (t), 22.6 (t), 14.1 (q). Spectroscopic data were consistent with the literature data for this compound.[5]

1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (2g)



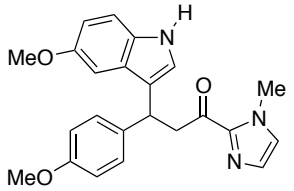
2g

Following general procedure C. Compound **1d** (0.042 g, 0.20 mmol), 5-methoxyindole (0.044 g, 0.30 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.005 g, 0.020 mmol), dmbpy (0.005 g, 0.026 mmol),

[5] Megens, R. P.; Roelfes, G. *Org. Biomol. Chem*. **2010**, *8,* 1387.

and MeCN (5 mL). The title compound (molecular formula: $C_{22}H_{21}N_3O_2$, MW = 359.42 g/mol, 0.056 g) was isolated as a brown solid in 79% yield. **Rf**: 0.31 (EtOAc/pentane = 1:1). **IR** (neat): 2919, 2830, 1672, 1511, 1401, 1247, 1030, 791, 735 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (br, s, 1H),7.27 (d, J = 7.2 Hz), 7.16-7.12 (m, 2H), 7.08-7.02 (m, 3H), 6.97 (d, J = 2.0 Hz, 1H), 6.89 (s, 1H), 6.83 (d, J = 2.4 Hz), 6.68 (dd, J = 88, 2.4 Hz, 1H), 4.92 (t, J = 7.6 Hz, 1H), 3.94-3.88 (m, 1H), 3.79 (s, 3H), 3.78-3.74 (m, 1H), 3.66 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 191.1 (s), 153.7 (s), 1.44 (s), 143.2 (s), 131.7 (s), 131.0 (d), 128.9 (d), 128.4 (2C, d), 128.0 (2C, d), 127.1 (s), 126.2 (d), 122.3 (d), 119.0 (s), 122.1 (d), 111.8 (d), 101.3 (d), 55.8 (q), 45.4 (t), 38.1 (d), 36.2 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

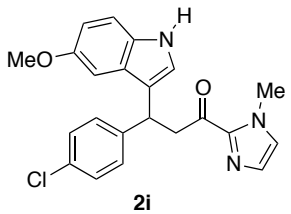
3-(5-Methoxy-1*H*-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (2h)



2h

Following general procedure C. Compound **1g** (0.085 g, 0.35 mmol), 5-methoxyindole (0.078 g, 0.53 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.008 g, 0.035 mmol), dmbpy (0.008 g, 0.042 mmol) and MeCN (5 mL). The title compound (molecular formula: $C_{23}H_{23}N_3O_3$, MW = 389.4 g/mol, 0.135 g) was isolated as a brown solid in quantitative yield. **Rf**: 0.35 (EtOAc/pentane = 1:1). **IR** (neat): 2917, 2833, 1673, 1509, 1405, 1245, 1033, 789, 734 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (br, s, 1H), 7.35-7.28 (m, 2H), 7.20 (d, J = 8.8 Hz, 1H), 7.17 (d, J = 0.9 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 7.04-6.98 (m, 1H), 6.93 (d, J = 2.4 Hz, 1H), 6.83-6.72 (m, 3H), 4.97 (t, J = 7.6 Hz, 1H), 4.00 (dd, J = 16.3, 7.6 Hz, 1H), 3.92 (s, 3H), 3.85 (dd, J = 16.3, 7.6 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 191.2 (s), 157.8 (s), 153.7 (s), 143.2 (s), 136.4 (s), 131.6 (s), 128.8 (2C, d), 128.7 (d), 127.2 (d), 126.9 (s), 122.1 (d), 119.5 (s), 113.7 (2C, d), 112.1 (d), 111.6 (d), 101.5 (d), 55.8 (q), 55.2 (q), 45.5 (t), 37.4 (d), 36.2 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

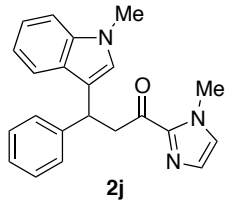
3-(4-Chlorophenyl)-3-(5-methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (2i)



2i

Following general procedure C. Compound **1f** (0.086 g, 0.35 mmol), 5-methoxyindole (0.078 g, 0.53 mmol) $Cu(NO_3)_2 \cdot 3H_2O$ (0.008 g, 0.035 mmol), dmbpy (0.008 g, 0.042 mmol) and MeCN (5 mL). The title compound (molecular formula: $C_{22}H_{20}ClN_3O_2$, MW = 393.87 g/mol, 0.137 g) was isolated as a brown solid in quantitative yield. **Rf**: 0.25 (EtOAc/pentane = 1:1). **IR** (neat): 2916, 1672, 1486, 1405, 1212, 1035, 916, 732 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.41 (br, s, 1H), 7.32-7.21 (m, 2H), 7.22-7.10 (m, 4H), 7.05 (d, J = 2.4 Hz, 1H), 7.0 (s, 1H), 6.87 (d, J = 2.4 Hz, 1H), 6.79 (dd, J = 8.8, 2.4 Hz, 1H), 4.97 (t, J = 7.6 Hz, 1H), 3.94 (dd, J = 16.5, 8.3 Hz, 1H), 3.90 (s, 3H), 3.83 (dd, J = 16.5, 8.3 Hz, 1H), 3.76 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 190.7 (s), 153.7 (s), 143.0 (s), 142.8 (s), 131.7 (s), 131.6 (s), 129.3 (2C, d), 128.9 (d), 128.4 (2C, d), 127.1 (d), 126.9 (s), 122.2 (d), 118.5 (s), 112.1 (d), 111.7 (d), 101.2 (d), 55.8 (q), 45.1 (t), 38.1 (s), 36.1 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (2j)

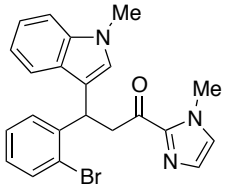


2j

Following general procedure C. Compound **1d** (0.074 g, 0.35 mmol), *N*-methylindole (0.069 g, 0.066 mL, 0.53 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.008 g, 0.035 mmol), dmbpy (0.008 g, 0.042 mmol), and MeCN (5 mL). The title compound (molecular formula: $C_{22}H_{21}N_3O$, MW = 343.42 g/mol, 0.096 g) was isolated as a brown solid in 80% yield. **Rf**: 0.31 (EtOAc/pentane = 1:1). **IR** (neat): 3026, 2916, 1673, 1472, 1406, 1154, 915, 741 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dt, J = 8.0, 1.0 Hz, 1H), 7.44-7.38 (m, 2H), 7.29-7.20 (m, 3H), 7.20-7.08 (m, 3H), 7.04-6.94 (m, 3H), 5.05 (t, J = 7.5 Hz, 1H), 4.01 (dd, J = 16.5, 7.5 Hz, 1H), 3.88 (s, 3H), 3.86 (dd, J = 16.5, 7.5 Hz, 1H), 3.71 (s, 3H). **^{13}C NMR**

(100 MHz, $CDCl_3$) δ 191.0 (s), 144.6 (s), 143.1 (s), 137.1 (s), 128.8 (d), 128.3 (2C, d), 127.9 (2C, d), 127.1 (s), 126.8 (d), 126.2 (d), 126.0 (d), 121.5 (d), 119.6 (d), 118.7 (d), 117.8 (s), 109.0 (d), 45.5 (t), 38.0 (d), 36.1 (q), 32.7 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)propan-1-one (2k)



2k

Following general procedure C. Compound **1g** (0.102 g, 0.35 mmol), *N*-methylindole (0.069 g, 0.066 mL, 0.53 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.008 g, 0.035 mmol), dmbpy (0.008 g, 0.042 mmol), and MeCN (5 mL). The title compound (molecular formula: $C_{22}H_{20}BrN_3O$, MW = 422.32 g/mol, 0.115 g) was isolated as a brown solid in 78% yield. **Rf**: 0.46 (EtOAc/pentane = 1:1). **IR** (neat): 2917, 1673, 1467, 1406, 1020, 740 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 8.0, 1.3 Hz, 1H), 7.48 (dt, J = 8.0, 0.9 Hz, 1H), 7.32-7.20 (m, 3H), 7.17-7.11 (m, 3H), 7.06-6.94 (m, 3H), 5.51 (dd, J = 9.0, 6.0 Hz, 1H), 4.20 (dd, J = 16.6, 9.0 Hz, 1H), 3.92 (s, 3H), 3.70 (s, 3H), 3.53 (dd, J = 16.6, 6.0 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 190.4 (s), 143.4 (s), 143.0 (s), 137.2 (s), 132.9 (d), 129.5 (d), 128.8 (d), 127.7 (d), 127.5 (d), 127.2 (s), 127.0 (d), 126.7 (d), 124.1 (s), 121.7 (d), 119.8 (d), 118.8 (d), 116.5 (s), 109.0 (d), 44.5 (d), 37.2 (t), 36.2 (q), 32.8 (q). Spectroscopic data were consistent with the literature data for this compound.[3]

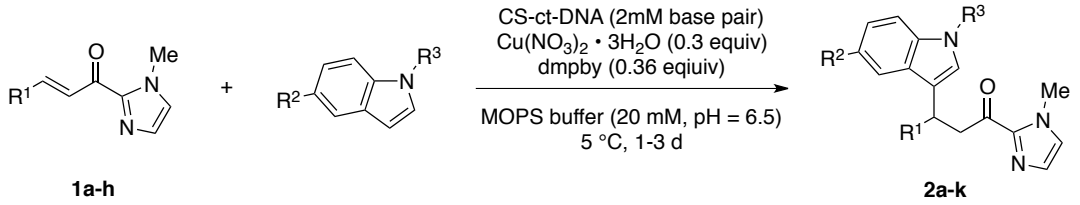
Preparation of a 20 mM MOPS buffer (pH 6.5)

209 mg of 3-(*N*-morpholino)propanesulfonic acid (MOPS, MW = 209.26 g/mol) were dissolved in 10 mL of H_2O RNase-free to obtain a 0.1 M solution. 1.9 mL of a 0.1 M solution of KOH (MW = 56.11 g/mol) in H_2O RNase-free was added followed by 38.1 mL of H_2O RNase-free.

Preparation of a 0.3 mM stock solution of [Cu(dmbpy)(NO_3)$_2$]

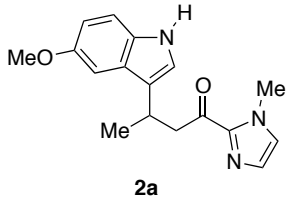
4.46 mg of $Cu(NO_3)_2$•$3H_2O$ (MW = 241.60 g/mol), and 4.24 mg of 4,4'-dimethyl-2,2'-bipyridyl (dmbpy, MW = 184.24 g/mol) were dissolved in 3.3 mL of the previously prepared 20 mM MOPS buffer (pH 6.5). The mixture was stirred at rt for 5 h in a sealed tube under air. 1.8 mL of this solution were then transferred to another vial, and diluted with 8.2 mL of the 20 mM MOPS buffer (pH 6.5).

General Procedure D. Enantioselective Friedel-Crafts alkylations



To 163 mg of cellulose-supported-ct-DNA (CS-ct-DNA, 2 mM base pair) in a 20 mM MOPS buffer (400 μL) was added the 0.3 mM stock solution of [Cu(dmbpy)(NO_3)$_2$] (200 μL). To the mixture was then added a 0.5 M solution of enone in MeCN (1.2 μL), followed by a 2.5 M solution of substituted indole in MeCN (1.2 μL). The reaction was mixed by inversion at 5 °C in a cold room. After 1-3 d, the mixture was warmed to rt. The solution was filtered, and the CS-ct-DNA was washed with Et_2O (5 mL) and H_2O MilliQ (10 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 2 mL). The combined organic layers were washed with brine (2 x 5 mL), dried over Mg_2SO_4, gravity filtered and concentrated under reduced pressure to give the crude product which was subjected to SFC analysis without further purification.

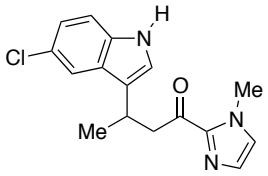
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2a)



Following general procedure D. CS-ct-DNA (2 mM base pair), **1a** (1 mM), 5-methoxyindole (5 mM), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL), 1 d. SFC analysis of the crude residue indicated a ratio between **1a** and **2a** of 0:100 and an

enantiomeric excess of (+) 82% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 8.56 min; minor enantiomer t_R = 5.78 min].

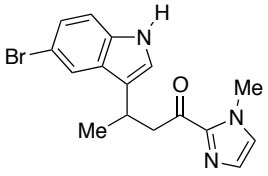
3-(5-Chloro-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2b)



2b

Following general procedure D. CS-ct-DNA (2 mM base pair), **1a** (1 mM), 5-chloroindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL), 1 d. SFC analysis of the crude residue indicated a ratio between **1a** and **2b** of 0:100 and an enantiomeric excess of (+) 66% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 7.00 min; minor enantiomer t_R = 5.80 min].

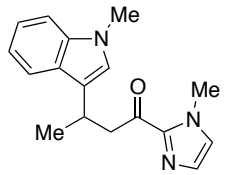
3-(5-Bromo-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2c)



2c

Following general procedure D. CS-ct-DNA (2 mM base pair), **1a** (1 mM), 5-bromoindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL), 1 d. SFC analysis of the crude residue indicated a ratio between **1a** and **2c** of 8:92 and an enantiomeric excess of (+) 66% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer tR = 7.40 min; minor enantiomer tR = 6.14 min].

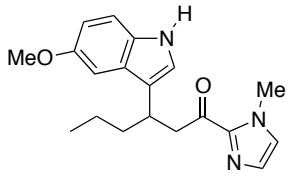
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (2d)



2d

Following general procedure D. CS-ct-DNA (2 mM base pair), **1a** (1 mM), *N*-methylindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 1 d. SFC analysis of the crude residue indicated a ratio between **1a** and **2d** of 23:77 and an enantiomeric excess of (+) 76% [DAICEL AD-H column; 100 bar; flow: 5.0 mL/min; 15% *i*-PrOH; λ = 220 nm; major enantiomer t_R = 3.33 min; minor enantiomer t_R = 4.19 min].

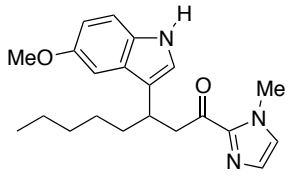
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)hexan-1-one (2e)



2e

Following general procedure D. CS-ct-DNA (2 mM base pair), **1b** (1 mM), 5-methoxyindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 1 d. SFC analysis of the crude residue indicated a ratio between **1b** and **2e** of 1:99 and an enantiomeric excess of (+) 83% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm; major enantiomer t_R = 6.76 min; minor enantiomer t_R = 5.47 min].

3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)octan-1-one (2f)

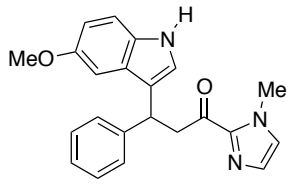


2f

Following general procedure D. CS-ct-DNA (2 mM base pair), **1c** (1 mM), 5-methoxyindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 1 d. SFC analysis of the crude residue indicated a ratio between **1c** and **2f** of 1:99 and an enantiomeric excess of (+) 72 % [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12%

MeOH; λ = 220 nm; major enantiomer t_R = 6.50 min; minor enantiomer t_R = 5.35 min].

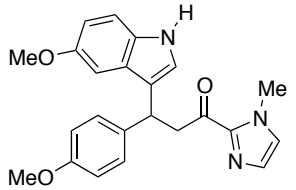
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(5-methoxy-1*H*-indol-3-yl)-3-phenylpropan-1-one (2g)



2g

Following general procedure D. CS-ct-DNA (2 mM base pair), **1d** (1 mM), 5-methoxyindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 3 d. SFC analysis of the crude residue indicated a ratio between **1d** and **2g** of 1:99 and an enantiomeric excess of (+) 62% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm; major enantiomer t_R = 8.67 min; minor enantiomer t_R = 4.92 min].

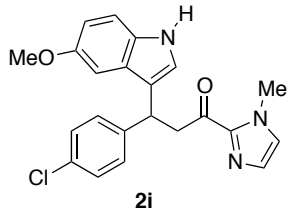
3-(5-Methoxy-1*H*-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (2h)



2h

Following general procedure D. CS-ct-DNA (2 mM base pair), **1e** (1 mM), 5-methoxyindole (5 mM), [Cu(dmbpy)$(NO_3)_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 3 d. SFC analysis of the crude residue indicated a ratio between **1e** and **2h** of 10:90 and an enantiomeric excess of (+) 54% [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm; major enantiomer t_R = 6.56 min; minor enantiomer t_R = 4.07 min].

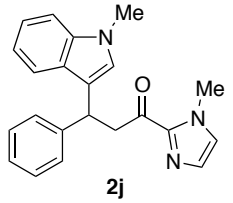
3-(4-Chlorophenyl)-3-(5-methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (2i)



2i

Following general procedure D. CS-ct-DNA (2 mM base pair), **1f** (1 mM), 5-methoxyindole (5 mM), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 3 d. SFC analysis of the crude residue indicated a ratio between **1f** and **2i** of 1:99 and an enantiomeric excess of (+) 48% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm; major enantiomer t_R = 11.77 min; minor enantiomer t_R = 6.69 min].

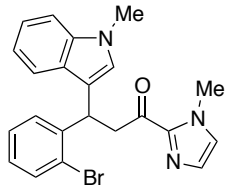
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (2j)



2j

Following general procedure D. CS-ct-DNA (2 mM base pair), **1d** (1 mM), *N*-methylindole (5 mM), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 3 d. SFC analysis of the crude residue indicated a ratio between **1d** and **2j** of 1:99 and an enantiomeric excess of (+) 76% [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm; major enantiomer t_R = 14.80 min; minor enantiomer t_R = 12.33 min].

3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)propan-1-one (2k)

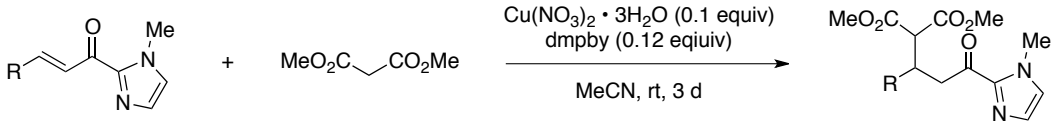


2k

Following general procedure D. CS-ct-DNA (2 mM base pair), **1g** (1 mM), N-methylindole (5 mM), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 μL); 3 d.

SFC analysis of the crude residue indicated a ratio between **1g** and **2k** of 39:61 and an enantiomeric excess of (+) 65% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm; major enantiomer t_R = 11.36 min; minor enantiomer t_R = 9.74].

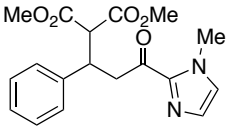
General Procedure E. Racemic Michael Additions



1d-h **3a-e**

An oven-dried 10 mL round-bottomed flask was charged with $Cu(NO_3)_2$•$3H_2O$ (0.066 mmol, 0.2 equiv), 4,4'-dimethyl-2,2'-bipyridyl (dmbpy, 0.073 mmol, 0.22 equiv), and MeCN (1 mL). The mixture was stirred at rt for 10 min then the α,β-unsaturated substrate (0.33 mmol, 1.0 equiv), and dimethylmalonate (6.65 mmol, 20 equiv) were added. The resulting solution was stirred at rt for an additional 3 d. The reaction was then diluted with brine (10 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, gravity filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel using EtOAc/pentane (1:1) as the eluent.

Dimethyl 2-(3-(1-methyl-1*H*-imidazol-2-yl)-3-oxo-1-phenylpropyl)malonate (3a)

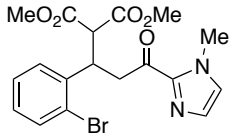


3a

Following general procedure E. Compound **1d** (0.070 g, 0.33 mmol), dimethylmalonate (0.878 g, 0.760 mL, 6.65 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.016 g, 0.066 mmol), dmbpy (0.013 g, 0.073 mmol) and MeCN (1 mL). The title compound (molecular formula: $C_{18}H_{20}N_2O_5$, MW = 344.36 g/mol, 0.046 g) was isolated as a colorless oil in 40% yield. **Rf**: 0.47 (EtOAc/pentane = 1:1). **IR** (neat): 3030, 2954, 1733, 1676, 1408, 1255, 1153, 736, 701 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32-7.20 (m, 4H), 7.19-7.13 (m, 1H), 7.07 (d, J = 0.9 Hz, 1H), 6.94 (s, 1H), 4.16 (td, J = 10.0, 4.4 Hz, 1H), 3.85 (s, 3H), 3.84-3.74 (m, 2H), 3.71 (s, 3H), 3.49-3.40 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.6 (s), 168.5 (s), 168.0 (s), 142.8 (s), 140.4 (s), 128.9 (d), 128.3 (2C, d), 128.2 (2C, d), 127.0 (d), 126.8 (d), 57.6 (d), 52.6 (q), 52.3 (q), 42.7 (t), 40.3 (d), 36.0 (q). Spectroscopic data were consistent with the

literature data for this compound.[6]

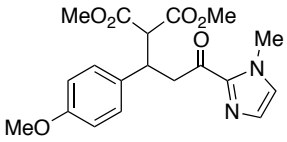
Dimethyl 2-(1-(2-bromophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3b)



3b

Following general procedure E. Compound **1g** (0.096 g, 0.33 mmol), dimethylmalonate (0.878 g, 0.760 mL, 6.65 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.016 g, 0.066 mmol), dmbpy (0.013 g, 0.073 mmol), and MeCN (1 mL). The title compound (molecular formula: $C_{18}H_{19}BrN_2O_5$, MW = 423.26 g/mol, 0.061 g) was isolated as a colorless oil in 44% yield. **Rf**: 0.45 (EtOAc/pentane = 1:1). **IR** (neat): 2953, 1735, 1677, 1409, 1254, 1155, 1022, 761 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (dd, J = 8.0, 1.0 Hz, 1H), 7.30 (dd, J = 7.8, 1.4 Hz, 1H), 7.23-7.11 (m, 1H), 7.07 (s, 1H), 7.01 (td, J = 7.8, 1.4 Hz, 1H), 6.95 (s, 1H), 4.62 (td, J = 8.9, 4.6 Hz, 1H), 4.05-3.88 (m, 2H), 3.86 (s, 3H), 3.66 (s, 3H), 3.62 (dd, J = 17.8, 4.6 Hz, 1H), 3.55 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.5 (s), 168.3 (s), 168.0 (s), 142.7 (s), 139.6 (s), 133.3 (d), 128.9 (d), 128.5 (2C, d), 127.5 (d), 126.9 (d), 125.0 (s), 55.6 (d), 52.5 (q), 52.4 (q), 41.3 (t), 38.9 (d), 36.1 (q). Spectroscopic data were consistent with the literature data for this compound.[6]

Dimethyl 2-(1-(4-methoxyphenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl) malonate (3c)



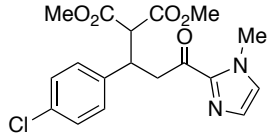
3c

Following general procedure E. Compound **1e** (0.080 g, 0.33 mmol), dimethylmalonate (0.878 g, 0.760 mL, 6.65 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (0.016 g, 0.066 mmol), dmbpy (0.013 g, 0.073 mmol) and MeCN (1 mL). The title compound (molecular formula: $C_{19}H_{22}N_2O_6$, MW = 374.39 g/mol, 0.053 g) was isolated as a colorless oil in 43% yield. **Rf**: 0.49 (EtOAc/pentane = 1:1). **IR** (neat): 3002, 2954, 2838, 1735, 1675, 1514, 1410, 1250, 1030, 776 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25-7.17 (m, 2H), 7.09 (d, J = 0.9 Hz, 1H), 6.95 (d,

[6] Coquiere, D.; Feringa, B. L.; Roelfes, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 9308-9311.

J = 0.9 Hz, 1H), 6.81-6.74 (m, 2H), 4.11 (td, *J* = 10.1, 4.4 Hz, 1H), 3.87 (s, 3H), 3.79-3.74 (m, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 3.47 (s, 3H), 3.41 (dd, *J* = 17.4, 4.4 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.7 (s), 168.6 (s), 168.2 (s), 158.4 (s), 142.8 (s), 132.4 (s), 129.3 (2C, d), 128.8 (d), 126.8, (d) 113.8 (2C, d), 57.8 (q), 55.1 (d), 52.6 (q), 52.3 (q), 42.9 (t), 39.6 (q), 36.0 (d). Spectroscopic data were consistent with the literature data for this compound.[6]

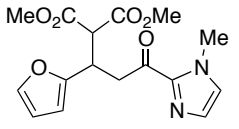
Dimethyl 2-(1-(4-chlorophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3d)



3d

Following general procedure E. Compound **1f** (0.081 g, 0.33 mmol), dimethylmalonate (0.878 g, 0.760 mL, 6.65 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.016 g, 0.066 mmol), dmbpy (0.013 g, 0.073 mmol), and MeCN (1 mL). The title compound (molecular formula: $C_{18}H_{19}ClN_2O_5$, MW = 378.81 g/mol, 0.051 g) was isolated as a colorless oil in 41% yield. **Rf**: 0.42 (EtOAc/pentane = 1:1). **IR** (neat): 2953, 1733, 1674, 1408, 1255, 1154, 1014, 914, 730 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26- 7.18 (m, 4H), 7.08 (d, *J* = 0.9 Hz, 1H), 6.98-6.94 (m, 1H), 4.13 (td, *J* = 10.1, 4.3 Hz, 1H), 3.86 (s, 3H), 3.86-3.74 (m, 2H), 3.72 (s, 3H), 3.48 (s, 3H), 3.41 (dd, *J* = 17.5, 4.3 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.3 (s), 168.3 (s), 167.9 (s), 142.7 (s), 139.0 (s), 132.8 (s), 129.7 (2C, d), 129.0 (d), 128.5 (2C, d), 127.0 (d), 57.3 (d), 52.7 (q), 52.4 (q), 42.6 (t), 39.7 (d), 36.0 (q). Spectroscopic data were consistent with the literature data for this compound.[6]

Dimethyl 2-(1-(furan-2-yl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3f)

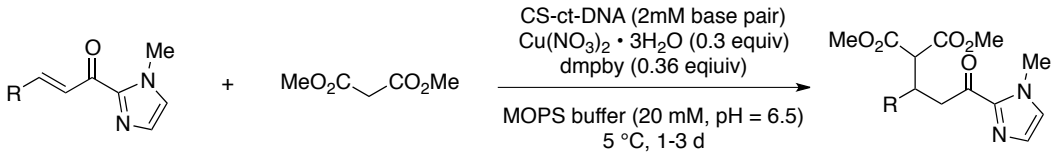


3e

Following general procedure E. Compound **1h** (0.067 g, 0.33 mmol), dimethylmalonate (0.878 g, 0.760 mL, 6.65 mmol), $Cu(NO_3)_2$•$3H_2O$ (0.016 g, 0.066 mmol), dmbpy (0.013 g, 0.073 mmol), and MeCN (1 mL). The title compound (molecular formula: $C_{16}H_{18}N_2O_6$, MW = 334.32 g/mol, 0.039 g) was isolated as a colorless oil in 35% yield. **Rf**: 0.44

(EtOAc/pentane = 1:1). **IR** (neat): 3115, 2955, 1736, 1677, 1411, 1257, 1157, 1014, 915, 741 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29-7.24 (m, 1H), 7.12 (d, J = 0.9 Hz, 1H), 7.00 (s, 1H), 6.22 (dd, J = 3.2, 1.8 Hz, 1H), 6.14 (dt, J = 3.2, 0.7 Hz, 1H), 4.29 (td, J = 9.2, 4.4 Hz, 1H), 3.94 (s, 3H), 3.91-3.80 (m, 2H), 3.72 (s, 3H), 3.62 (s, 3H), 3.45 (dd, J = 17.7, 4.4 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.4 (s), 168.2 (s), 168.1 (s), 153.5 (s), 142.7 (s), 141.7 (d), 129.1 (d), 126.9 (d), 110.1 (d), 106.9 (d), 55.2 (d), 52.7 (q), 52.6 (q), 40.2 (t), 36.1 (q), 33.9 (d). Spectroscopic data were consistent with the literature data for this compound.[6]

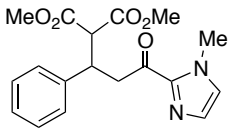
General Procedure F. Enantioselective Michael Additions



1d-h **3a-e**

To 163 mg of CS-ct-DNA in a 20 mM MOPS buffer (400 µL) was added the 0.3 mM stock solution of [Cu(dmbpy)(NO_3)$_2$] (200 µL). To the resulting mixture was added a 0.5 M solution of enone in MeCN (1.2 µL), followed by dimethyl malonate (6.9 µL). The reaction was mixed by inversion at 5 °C in a cold room. After 1-3 d, the solution was filtered, and the CS-ct-DNA was washed with Et_2O (5 mL), and H_2O MilliQ (10 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 2 mL). The combined organic layers were washed with brine (2 x 5 mL), dried over Mg_2SO_4, gravity filtered and concentrated under reduced pressure to give the crude product which was subjected to SFC analysis without further purification.

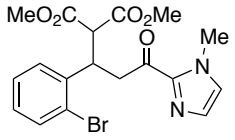
Dimethyl 2-(3-(1-methyl-1*H*-imidazol-2-yl)-3-oxo-1-phenylpropyl)malonate (3a)



3a

Following general procedure F. CS-ct-DNA (2 mM base pair), **1d** (1 mM), dimethyl malonate (6.9 µL), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 µL); 3 d. SFC analysis of the crude residue indicated a ratio between **1d** and **3a** of 2:98 and an enantiomeric excess of (+) 97% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm; major enantiomer t_R = 3.55 min; minor enantiomer t_R = 2.85 min].

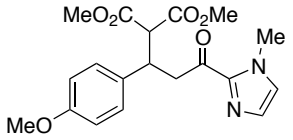
Dimethyl 2-(1-(2-bromophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl) malonate (3b)



3b

Following general procedure F. CS-ct-DNA (2 mM base pair), **1g** (1 mM), dimethyl malonate (6.9 µL), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 µL); 3 d. SFC analysis of the crude residue indicated a ratio between **1g** and **3b** of 2:98 and an enantiomeric excess of (+) 96% [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 7% MeOH; λ = 220 nm; major enantiomer t_R = 7.40 min; minor enantiomer t_R = 8.70 min].

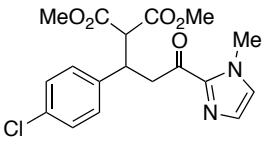
Dimethyl 2-(1-(4-methoxyphenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl) malonate (3c)



3c

Following general procedure F. CS-ct-DNA (2 mM base pair), **1e** (1 mM), dimethyl malonate (6.9 µL), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 µL); 3 d. SFC analysis of the crude residue indicated a ratio between **1e** and **3c** of 1:99 and an enantiomeric excess of (+) 81% [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm; major enantiomer t_R = 7.44 min; minor enantiomer t_R = 6.83 min].

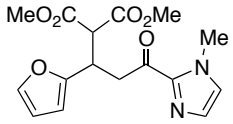
Dimethyl 2-(1-(4-chlorophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl) malonate (3d)



3d

Following general procedure F. CS-ct-DNA (2 mM base pair), **1f** (1 mM), dimethyl malonate (32 µL), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM), and MOPS buffer (20 mM, pH 6.5, 600 µL); 1 d. SFC analysis of the crude residue indicated a ratio between **1f** and **3d** of 11:89 and an enantiomeric excess of (+) 93% [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm; major enantiomer t_R = 3.73 min; minor enantiomer t_R = 3.03 min].

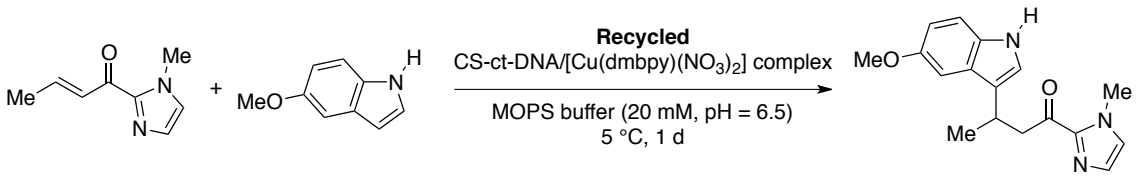
Dimethyl 2-(1-(furan-2-yl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3e)



3e

Following general procedure F. CS-ct-DNA (2 mM base pair), **1h** (1 mM), dimethyl malonate (6.9 µL), [Cu(dmbpy)(NO_3)$_2$] (0.3 mM) and MOPS buffer (20 mM, pH 6.5, 600 µL); 3 d. SFC analysis of the crude residue indicated a ratio between **1h** and **3e** of 72:28 and an enantiomeric excess of (+) 89% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 1.99 min; minor enantiomer t_R = 1.73 min].

General Procedure G. Enantioselective Friedel Crafts alkylations - Recycling of CS-ct-DNA with MOPS buffer



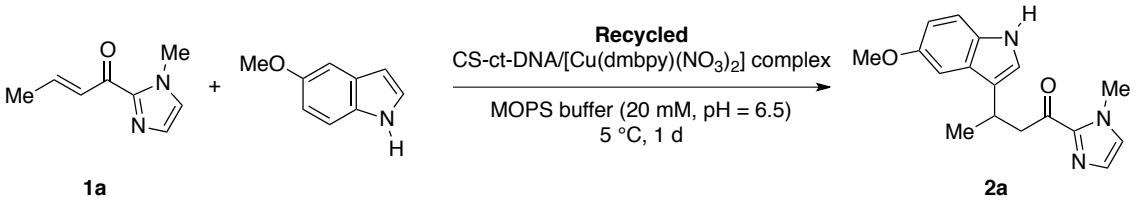
1a **2a**

To 163 mg of CS-ct-DNA in a 20 mM MOPS buffer (400 µL) was added the 0.3 mM stock solution of [Cu(dmbpy)(NO_3)$_2$] (200 µL). To the resulting mixture was added a 0.5 M solution of **1a** in MeCN (1.2 µL), followed by a 2.5 M solution of 5-methoxyindole (1.2 µL). The reaction was mixed by inversion at 5 °C in a cold room. After 1 d, the solution was warmed to rt. The CS-ct-DNA was filtered off, and washed with a 20 mM MOPS buffer (3 x 5 mL). The aqueous solution was then extracted with Et_2O (2 x 5 mL), the combined organic layers were washed with brine (2 x 5 mL), dried over Mg_2SO_4, gravity filtered, and concentrated under reduced pressure. The crude product was subjected to SFC analysis without further purification. The CS-ct-DNA was recovered and used without any further treatment in the next run simply by adding a 20 mM MOPS buffer (600 µL), compound **1a** (0.5 M solution in MeCN, 1.2 µL), and 5-methoxyindole (2.5 M solution in MeCN, 1.2 µL). Every recycling run was performed with no additional [Cu(dmbpy)(NO_3)$_2$]. The reaction was achieved ten times, and the SFC analyses of the crude residues indicated a complete conversion of the starting material into the product. The observed enantiomeric excesses are reported in the following table.

Number of runs	*ees* (%)
1st run	80
2nd run	81
3rd run	80
4th run	79
5th run	79
6th run	79
7th run	78
8th run	77
9th run	76
10th run	76

SFC conditions: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm].

General Procedure H. Enantioselective Friedel Crafts alkylations – Recycling of CS-ct-DNA with a MOPS buffer/MeOH 30:1 solution



1a **2a**

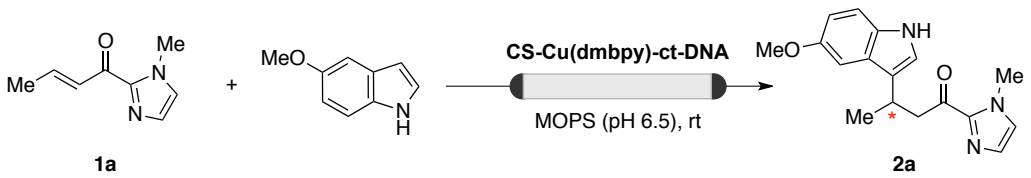
To 163 mg of CS-ct-DNA in a 20 mM MOPS buffer/MeOH 20:1 solution (400 µL) was added the 0.3 mM stock solution of [Cu(dmbpy)(NO_3)$_2$] (200 µL). To the resulting mixture was added a 0.5 M solution of **1a** in MeCN (1.2 µL), followed by a 2.5 M solution of 5-methoxyindole (1.2 µL). The reaction was mixed by inversion at 5 °C in a cold room. After 1 d, the solution was warmed to rt. The CS-ct-DNA was filtered off, and washed with a 20 mM MOPS buffer/MeOH 30:1 solution (3 x 5 mL). The aqueous solution was then extracted with Et_2O (2 x 5 mL), the combined organic layers were washed with brine (2 x 5 mL), dried over Mg_2SO_4, gravity filtered, and concentrated under reduced pressure. The crude product was subjected to SFC analysis without further purification. The CS-ct-DNA was recovered and used without any further treatment in the next run simply by adding a 20 mM MOPS buffer/MeOH 30:1 solution (600 µL), compound **1a** (0.5 M solution in MeCN, 1.2 µL), and 5-methoxyindole (2.5 M solution in MeCN, 1.2 µL). Every recycling run was performed with no additional [Cu(dmbpy)(NO_3)$_2$]. The reaction was achieved ten times, and the SFC analyses of the crude

residues indicated a complete conversion of the starting material into the product. The observed enantiomeric excesses are reported in the following table.

Number of runs	*ees* (%)
1st run	82
2nd run	82
3rd run	80
4th run	80
5th run	76
6th run	74
7th run	76
8th run	75
9th run	75
10th run	75

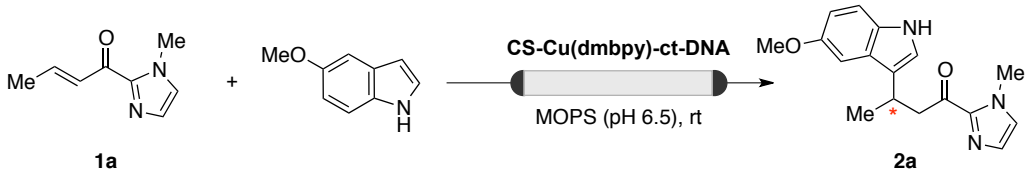
SFC conditions: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm].

General Procedure I. Enantioselective Friedel Crafts alkylations in a continuous flow process.



In a 4 g MPLC plastic cartridge (L = 65 mm, ∅ = 13 mm) was packed 1.1 g of the preformed CS-ct-DNA-Cu(dmbpy) biohybrid catalyst [prepared by mixing CS-ct-DNA with a 0.3 mM solution of [Cu(dmbpy)$(NO_3)_2$] in a 20 mM MOPS buffer (1.35 mL)]. The cartridge was connected to a syringe-pump and washed with a 20 mM MOPS buffer (50 mL) at a 1 mL/min flow-rate. The syringe-pump was then loaded with a 5:1 mixture of 5-methoxyindole (0.15 mmol) and **1a** (0.03 mmol) in a 20 mM MOPS buffer/MeOH 30:1 solution (31 mL). The reagents were then passed through the column at a 0.25 mL/min flow-rate followed by a 20 mM MOPS buffer/MeOH 30:1 solution (25 mL). The resulting solution was then extracted with Et_2O (3 x 15 mL), the combined organic layers were washed with brine (2 x 10 mL), dried over anhydrous $MgSO_4$, gravity filtered, and concentrated under reduced pressure to afford a crude residue that was subjected to SFC analysis without further purification.

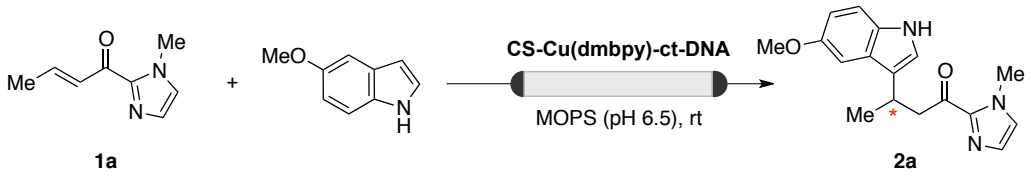
(2a): 0.25 mL/min flow rate, 1.1 g of CS-ct-DNA



1a 2a

Following general procedure I. CS-ct-DNA (2 mM base pair) (1.1 g), **1a** (0.03 mmol), 5-methoxyindole (0.15 mmol) in a MOPS/MeOH 30:1 solution (31 mL); $[Cu(dmbpy)(NO_3)_2]$ (0.3 mM) in a MOPS buffer (20 mM, pH 6.5, 1.35 mL). Flow rate: 0.25 mL/min. SFC analysis of the crude residue indicated a ratio between **1a** and **2a** of 50:50 and an enantiomeric excess of (+) 81% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 8.58 min; minor enantiomer t_R = 5.74 min].

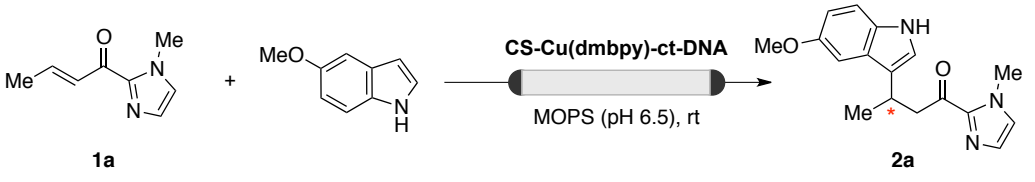
(2a): 0.125 mL/min flow rate, 2.2 g of CS-ct-DNA



1a 2a

Following general procedure I. CS-ct-DNA (2 mM base pair) (2.2 g), **1a** (0.03 mmol), 5-methoxyindole (0.15 mmol) in a MOPS/MeOH 30:1 solution (31 mL); $[Cu(dmbpy)(NO_3)_2]$ (0.3 mM) in a MOPS buffer (20 mM, pH 6.5, 2.70 mL). Flow rate: 0.125 mL/min. SFC analysis of the crude residue indicated a ratio between **1a** and **2a** of 10:90 and an enantiomeric excess of (+) 82% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 8.47 min; minor enantiomer t_R = 5.68 min].

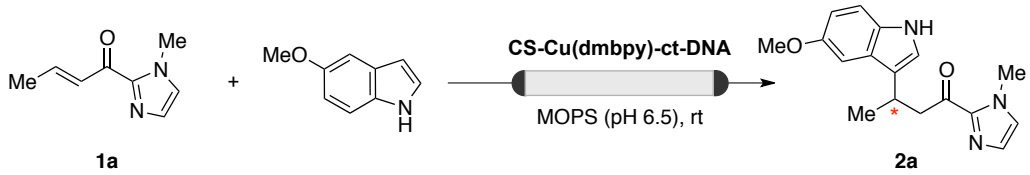
(2a): 0.125 mL/min flow rate, 4.4 g of CS-ct-DNA



1a 2a

Following general procedure I. CS-ct-DNA (2 mM base pair) (4.4 g), **1a** (0.03 mmol), 5-methoxyindole (0.15 mmol) in a MOPS/MeOH 30:1 solution (31 mL); [Cu(dmbpy)$(NO_3)_2$] (0.3 mM) in a MOPS buffer (20 mM, pH 6.5, 5.40 mL). Flow rate: 0.125 mL/min. SFC analysis of the crude residue indicated a ratio between **1a** and **2a** of 1.5:98.5 and an enantiomeric excess of (+) 79% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 9.41 min; minor enantiomer t_R = 6.28 min]. The crude was purified using petroleum ether/EtOAc (3:2). The title compound was obtained as a brownish oil (9.1 mg, 92 %).

(2a): 0.125 mL/min flow rate, 4.4 g of CS-ct-DNA

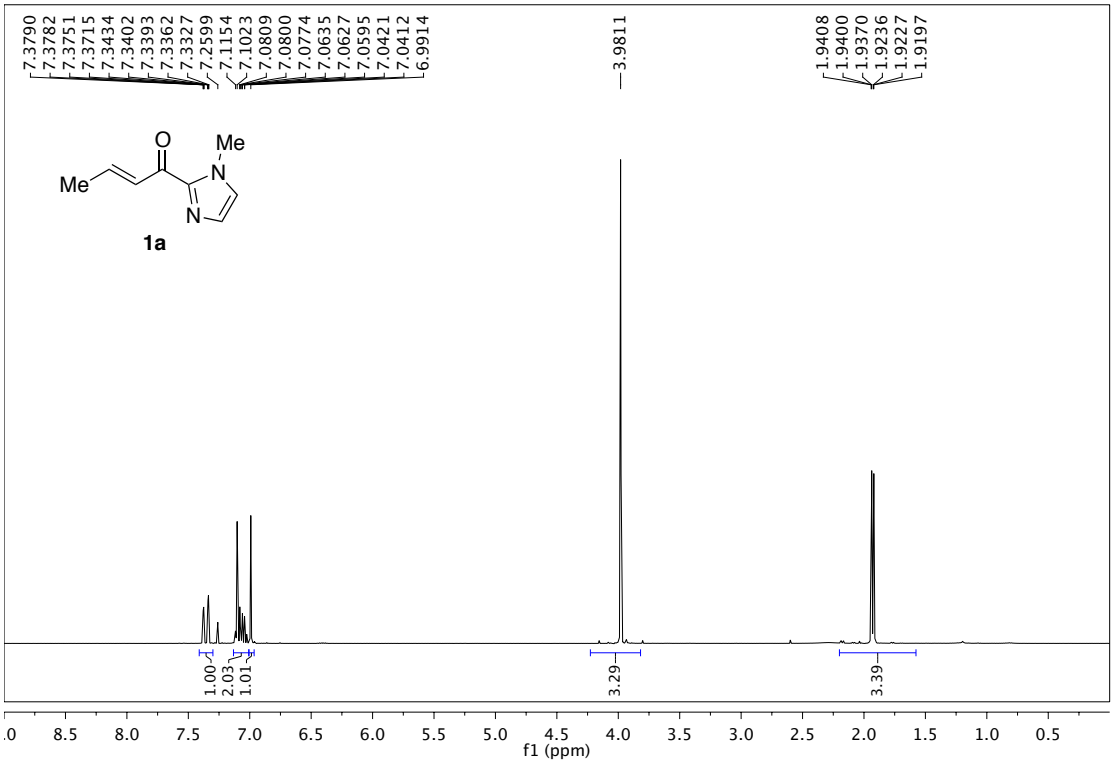


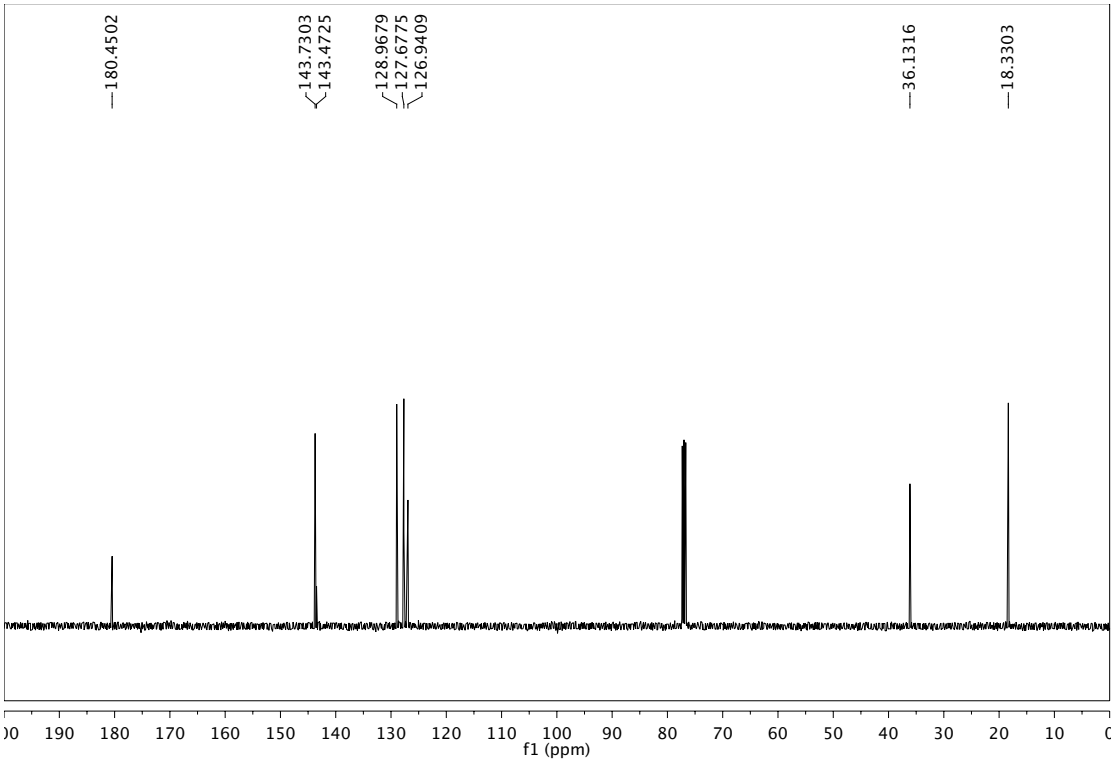
1a **2a**

Following general procedure I. CS-ct-DNA (2 mM base pair) (4.4 g), **1a** (0.3 mmol), 5-methoxyindole (1.5 mmol) in a MOPS/MeOH 30:1 solution (310 mL); [Cu(dmbpy)$(NO_3)_2$] (0.3 mM) in a MOPS buffer (20 mM, pH 6.5, 5.40 mL). Flow rate: 0.125 mL/min. SFC analysis of the crude residue indicated a ratio between **1a** and **2a** of 2:98 and an enantiomeric excess of (+) 78% [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; major enantiomer t_R = 8.51 min; minor enantiomer t_R = 5.76 min]. The crude was purified using petroleum ether/EtOAc (3:2). The title compound was obtained as a brownish oil (79.2 mg, 89 %).

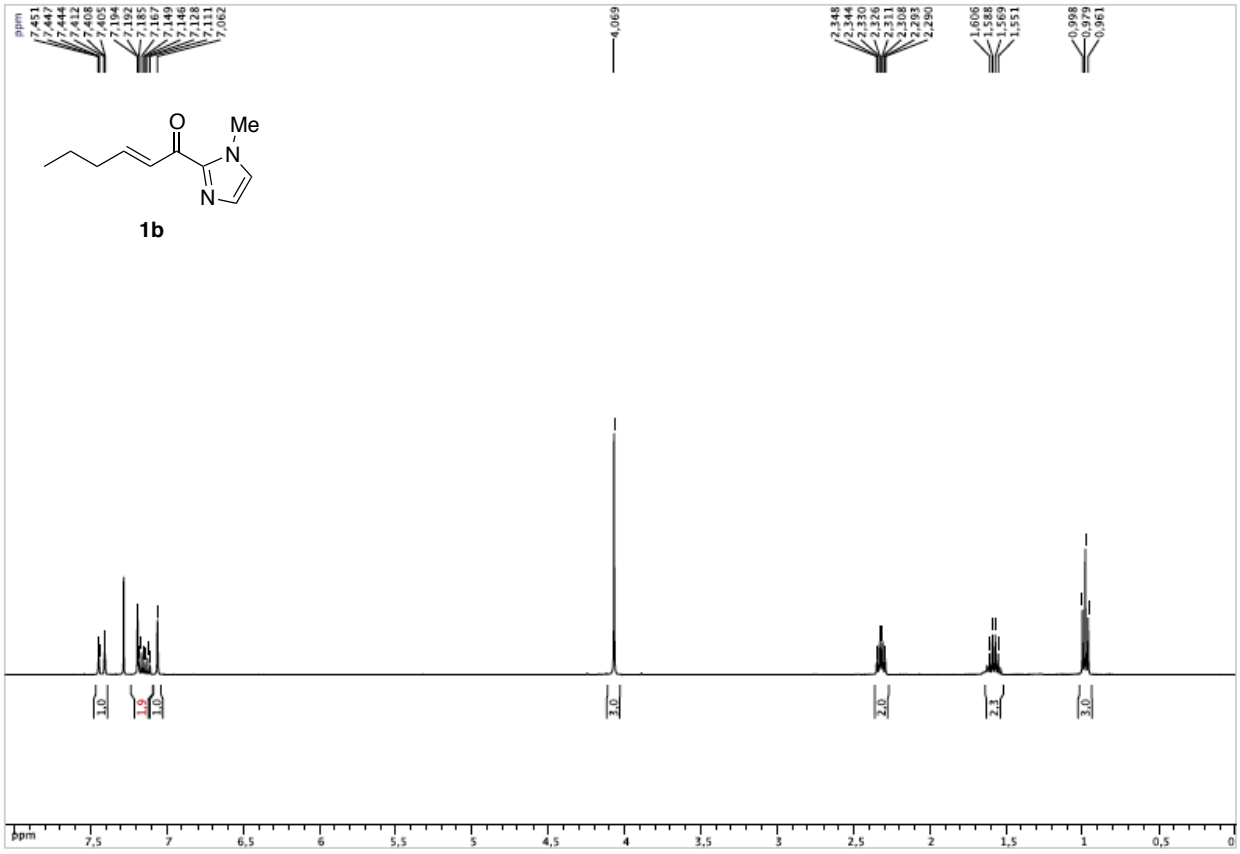
Copies of ^{1}H and ^{13}C NMR Spectra

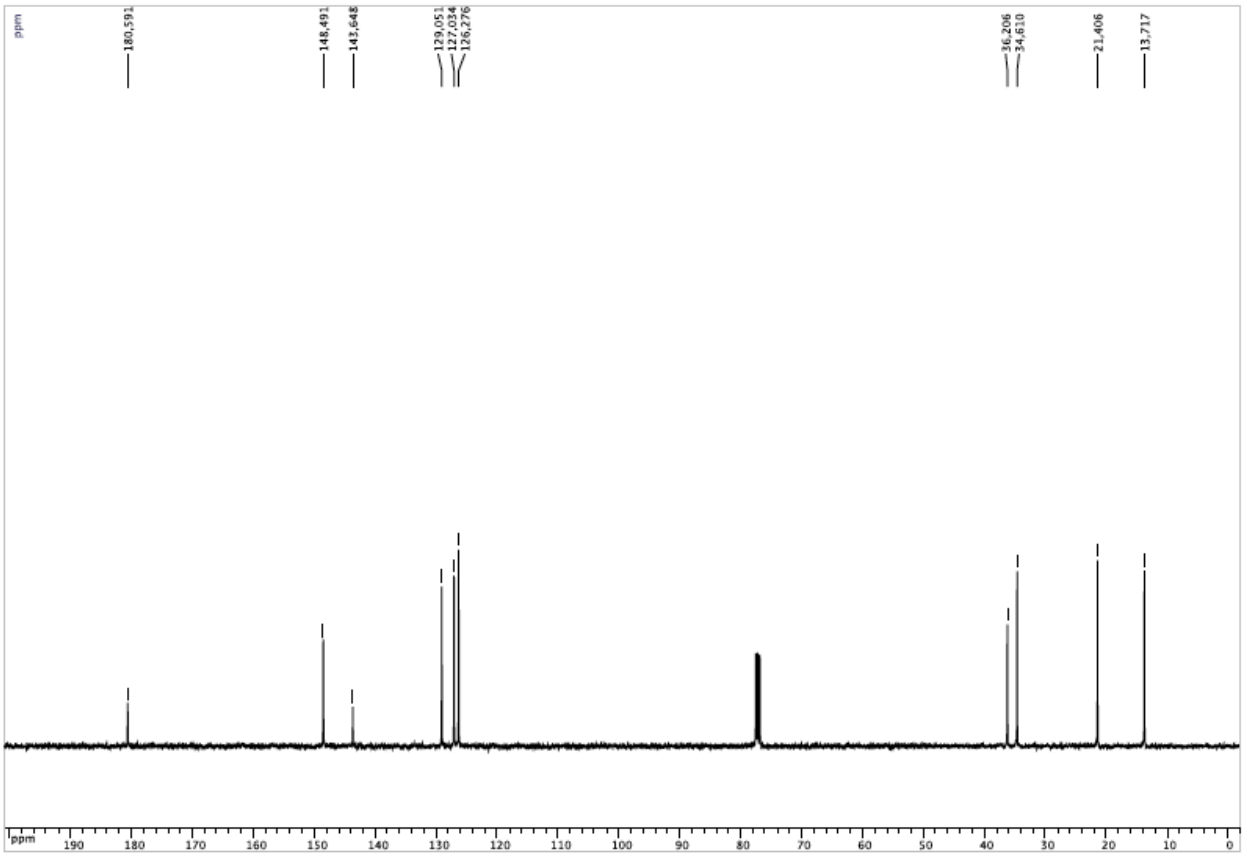
(E)-1-(1-Methyl-1*H*-imidazol-2-yl)but-2-en-1-one (1a)



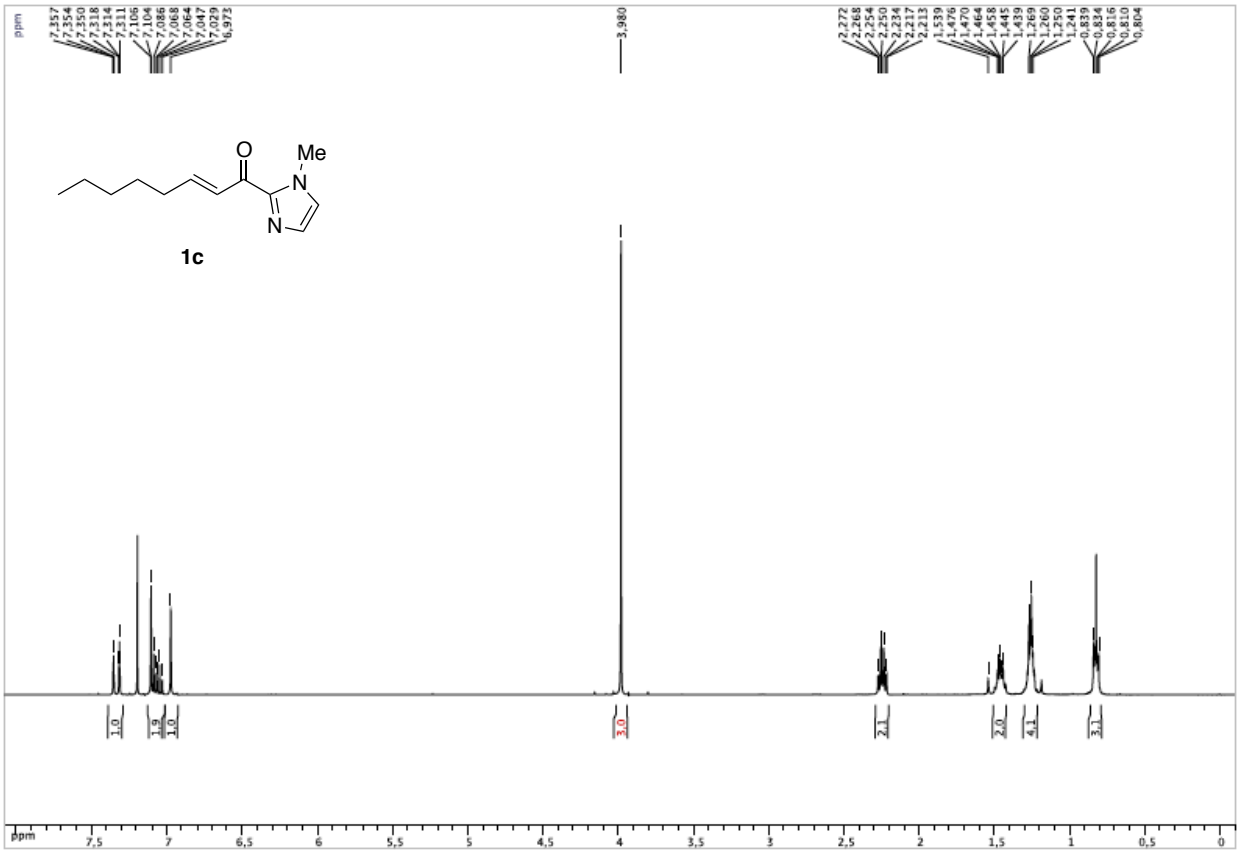


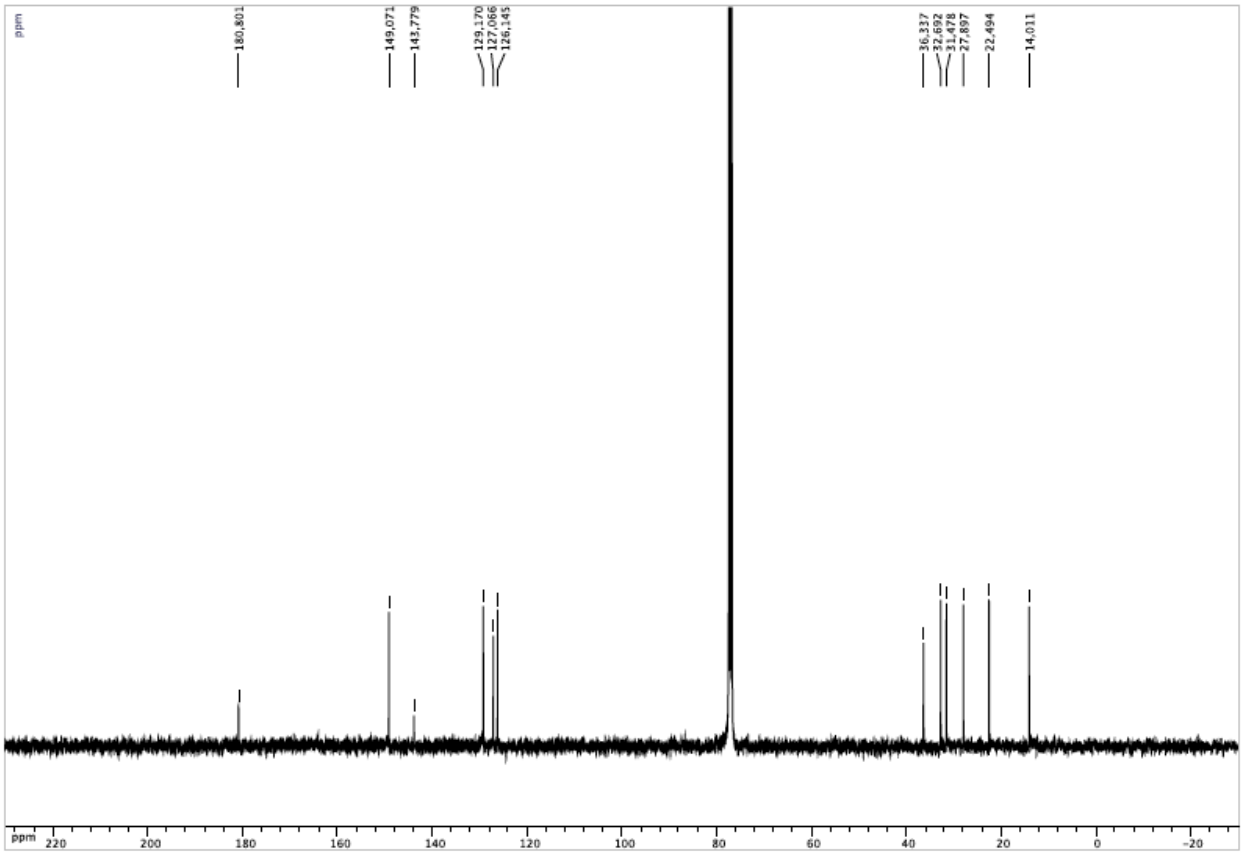
(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)hex-2-en-1-one (1b)



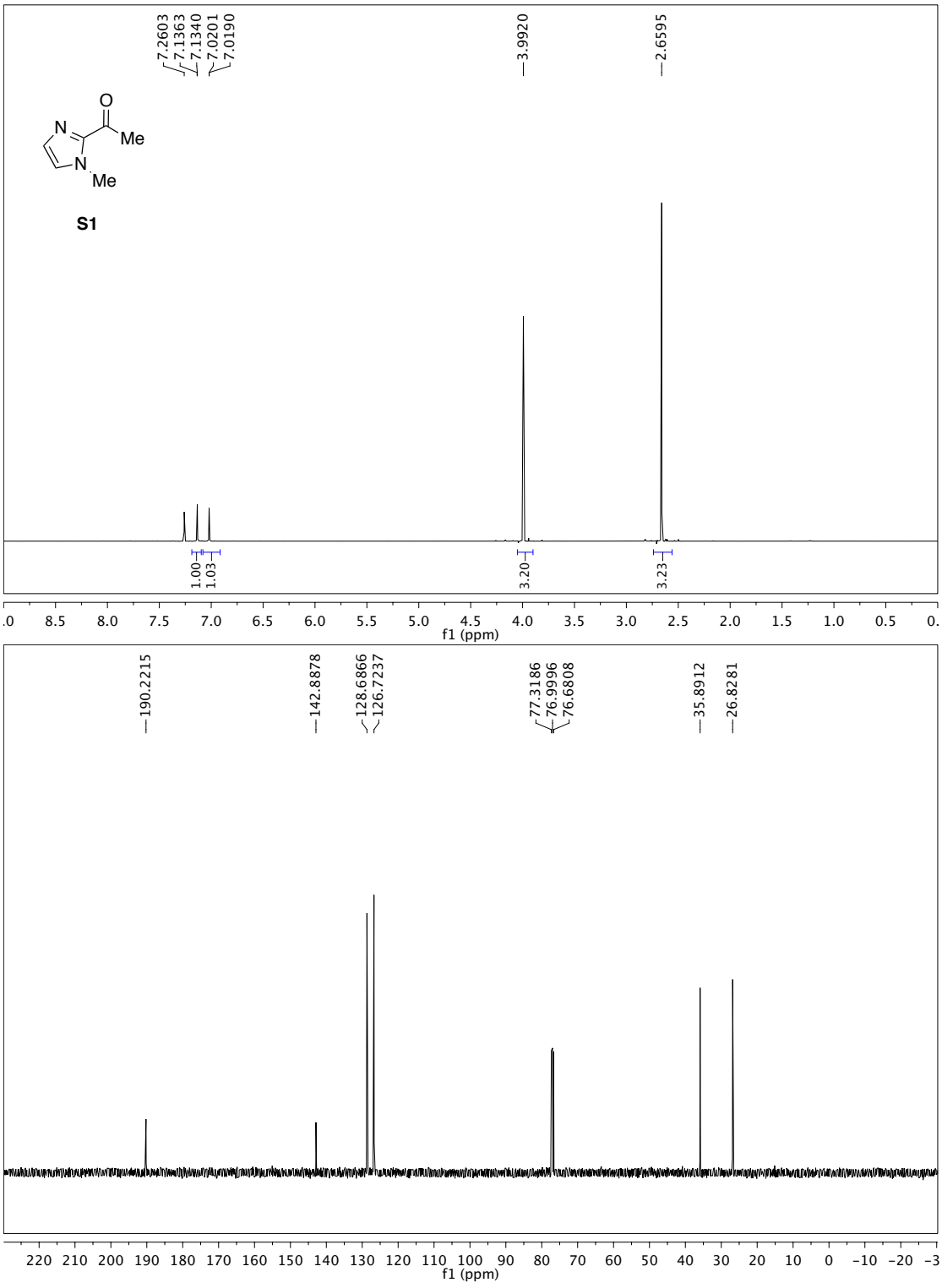


(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)oct-2-en-1-one (1c)

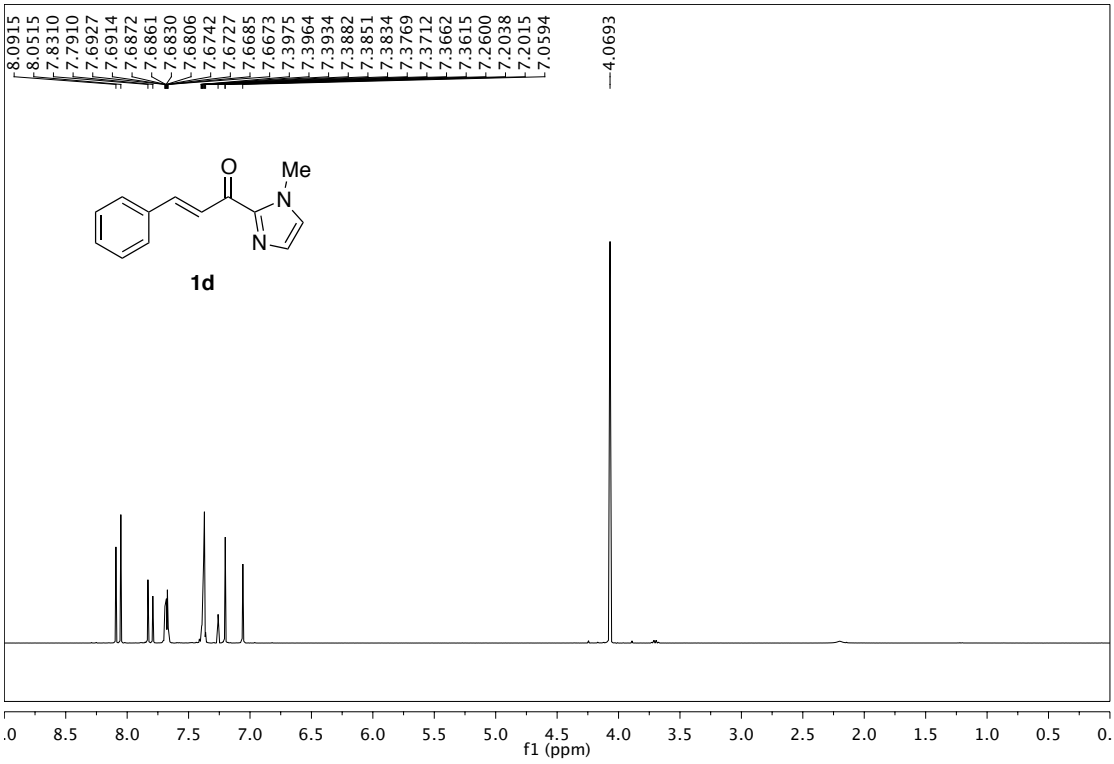


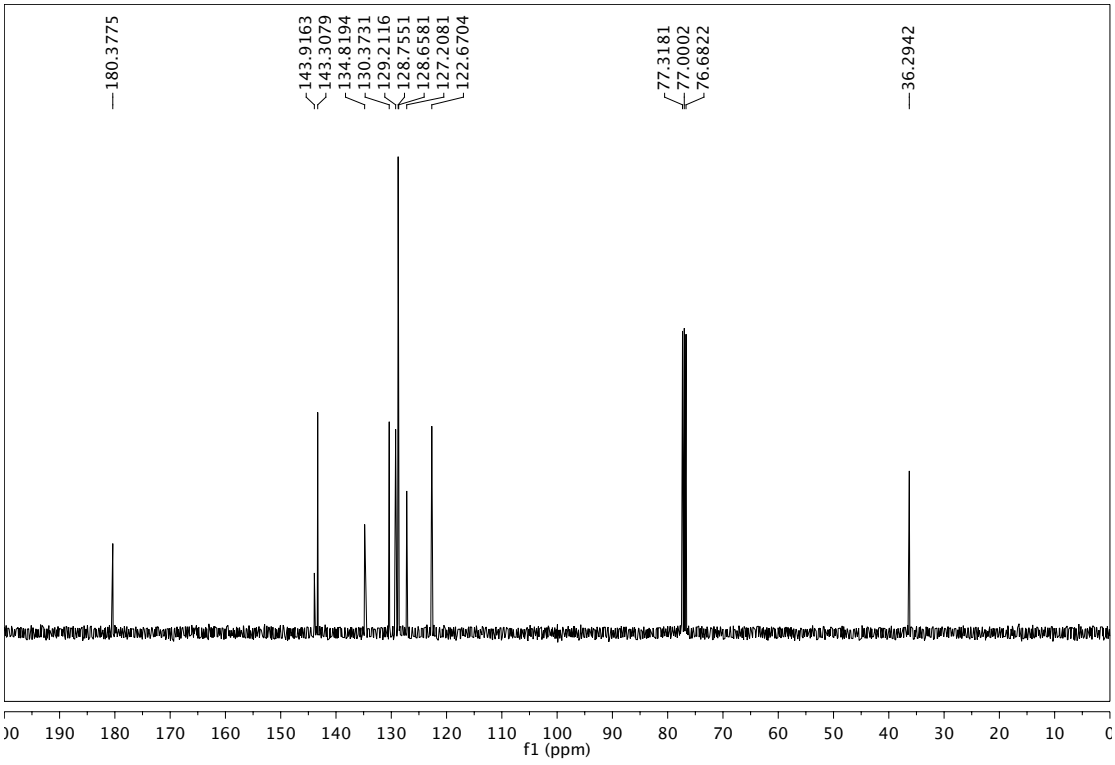


1-(1-methyl-1*H*-imidazol-2-yl)ethanone (S1)

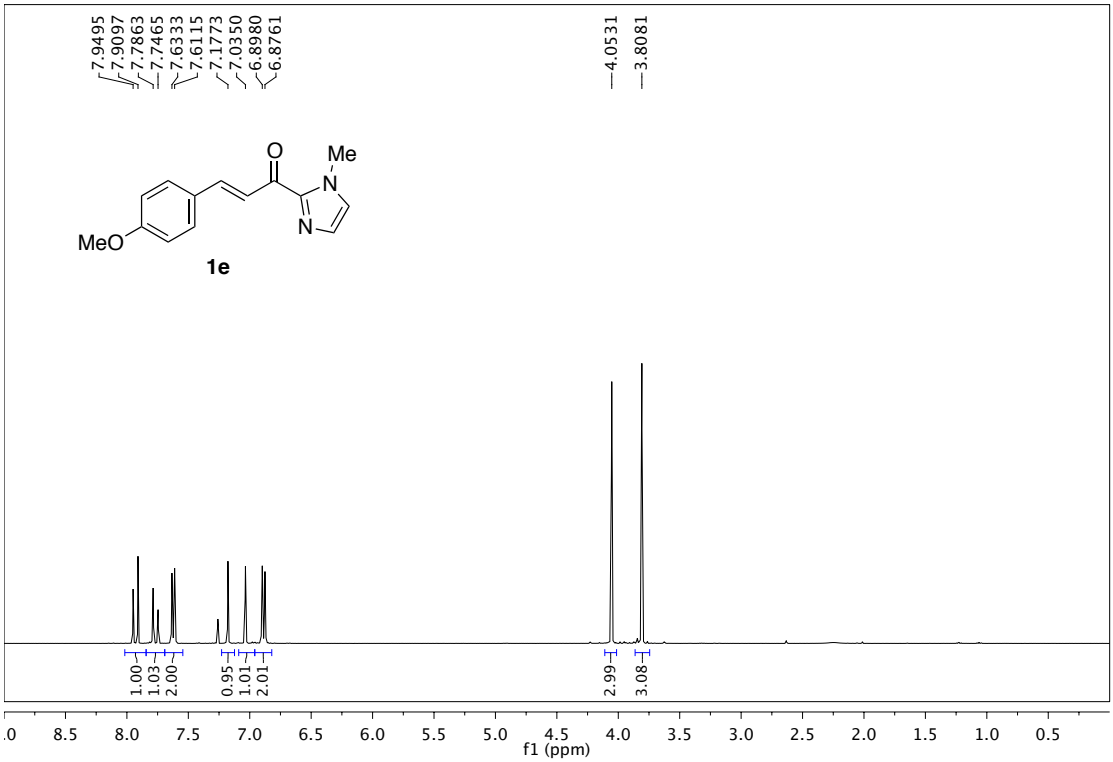


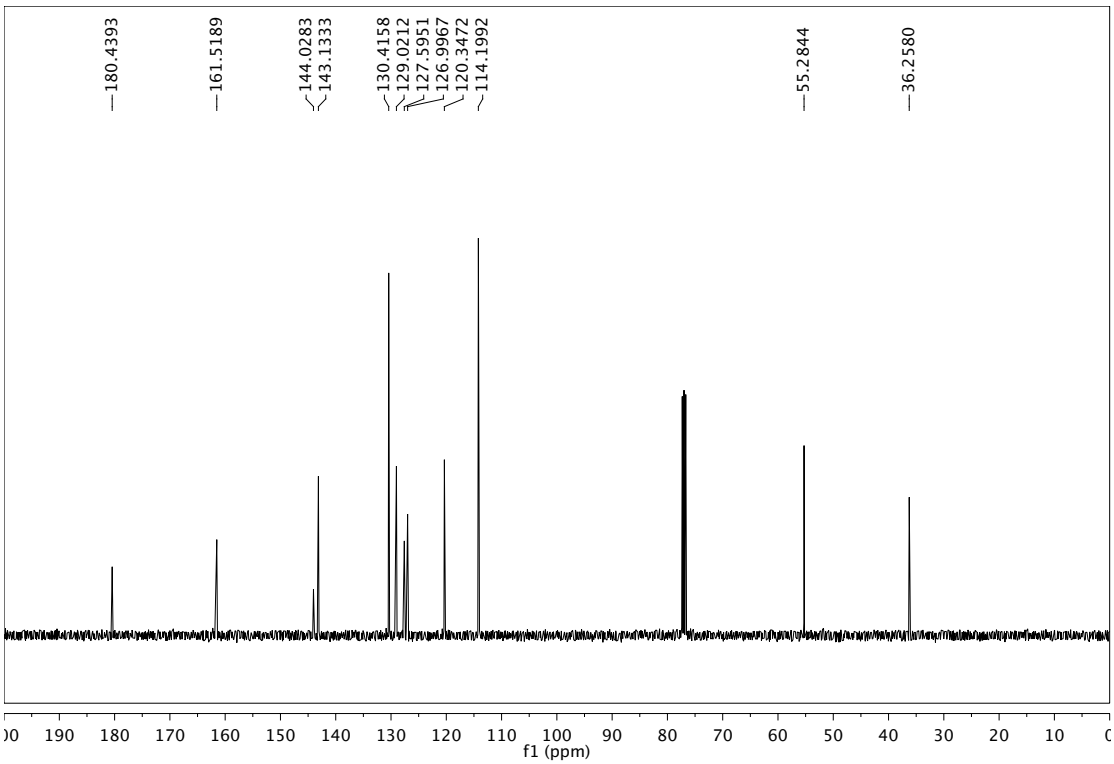
(*E*)-1-(1-Methyl-1*H*-imidazol-2-yl)-3-phenylprop-2-en-1-one (1d)



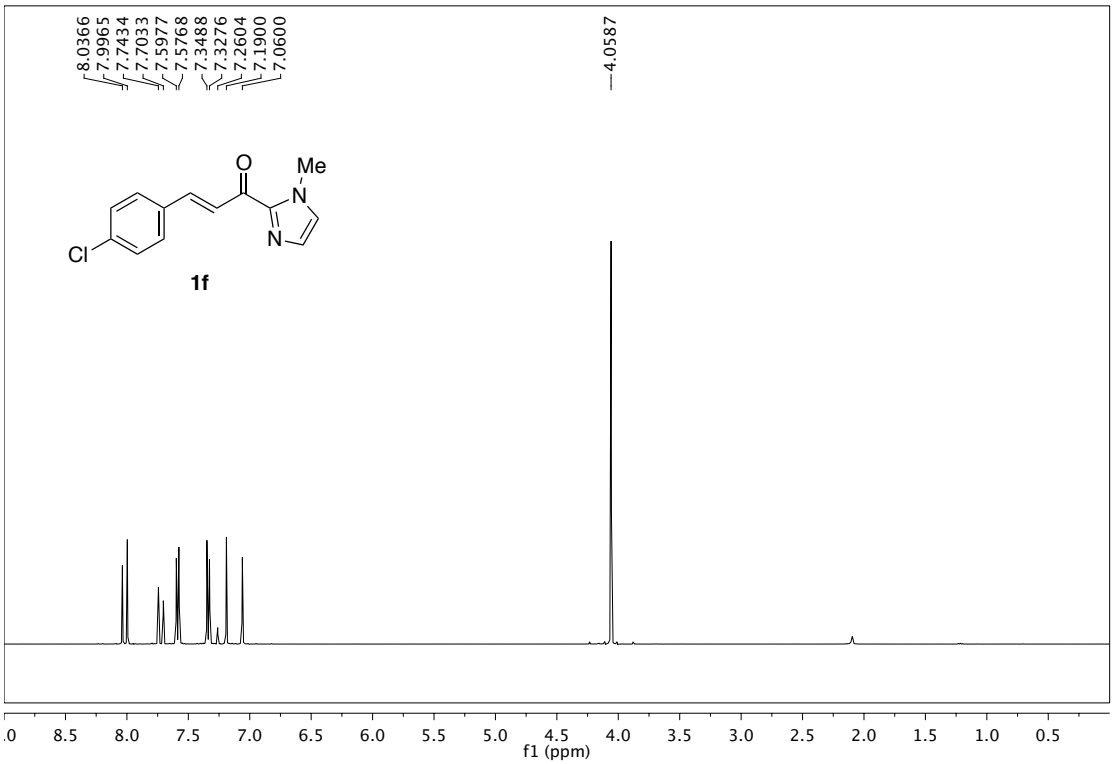


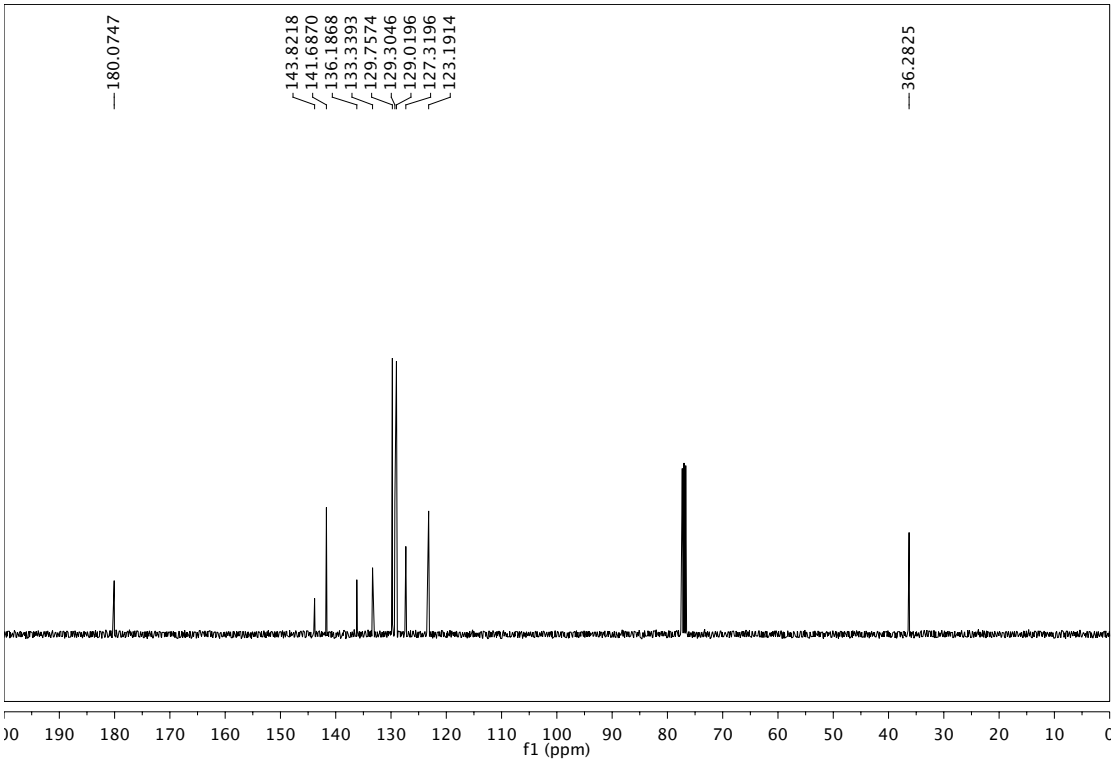
(*E*)-3-(4-Methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1e)



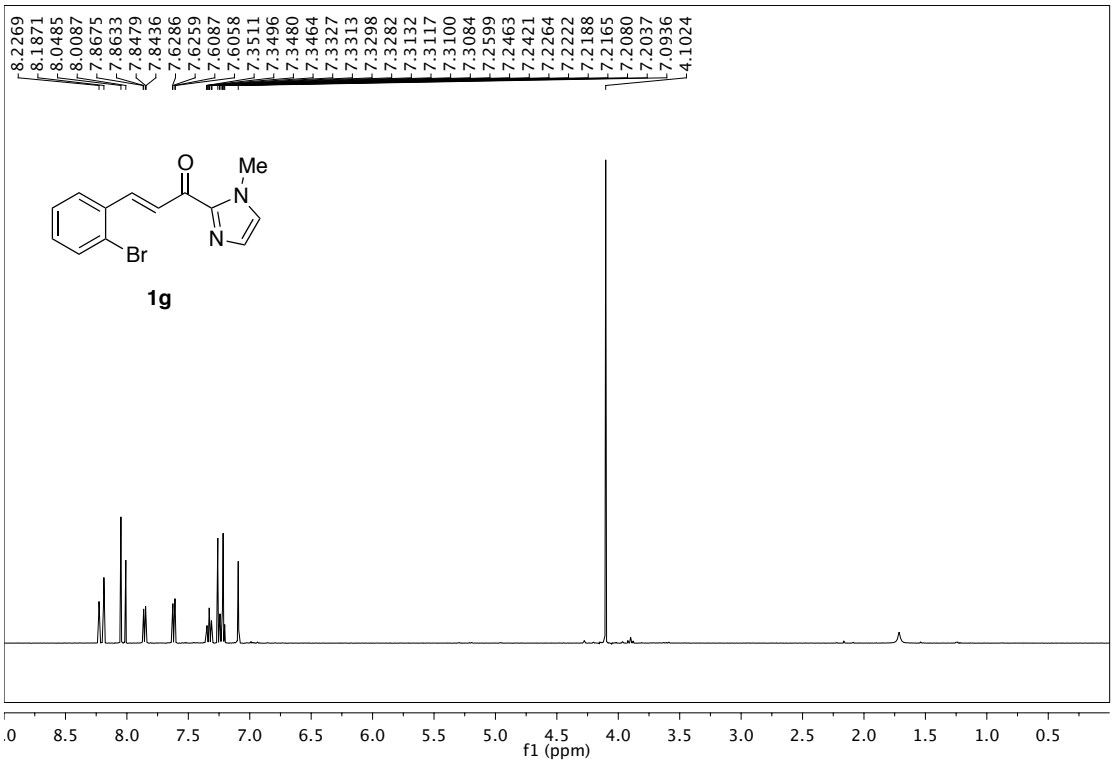


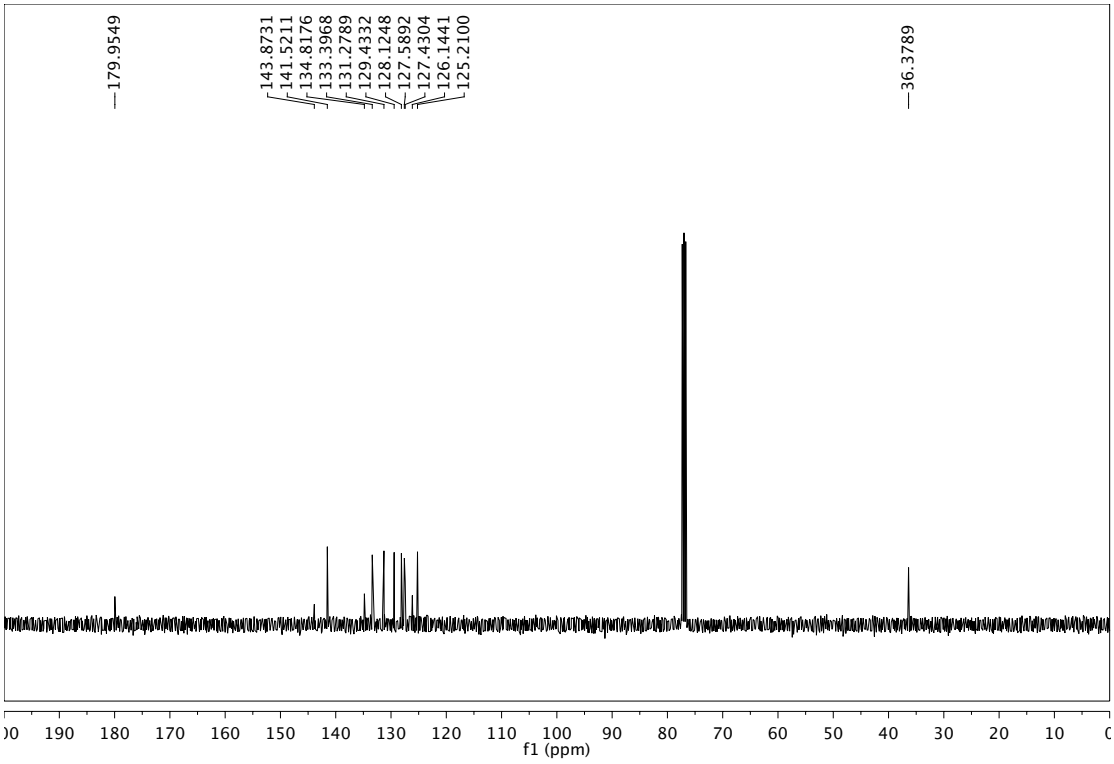
(*E*)-3-(4-Chlorophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1f)



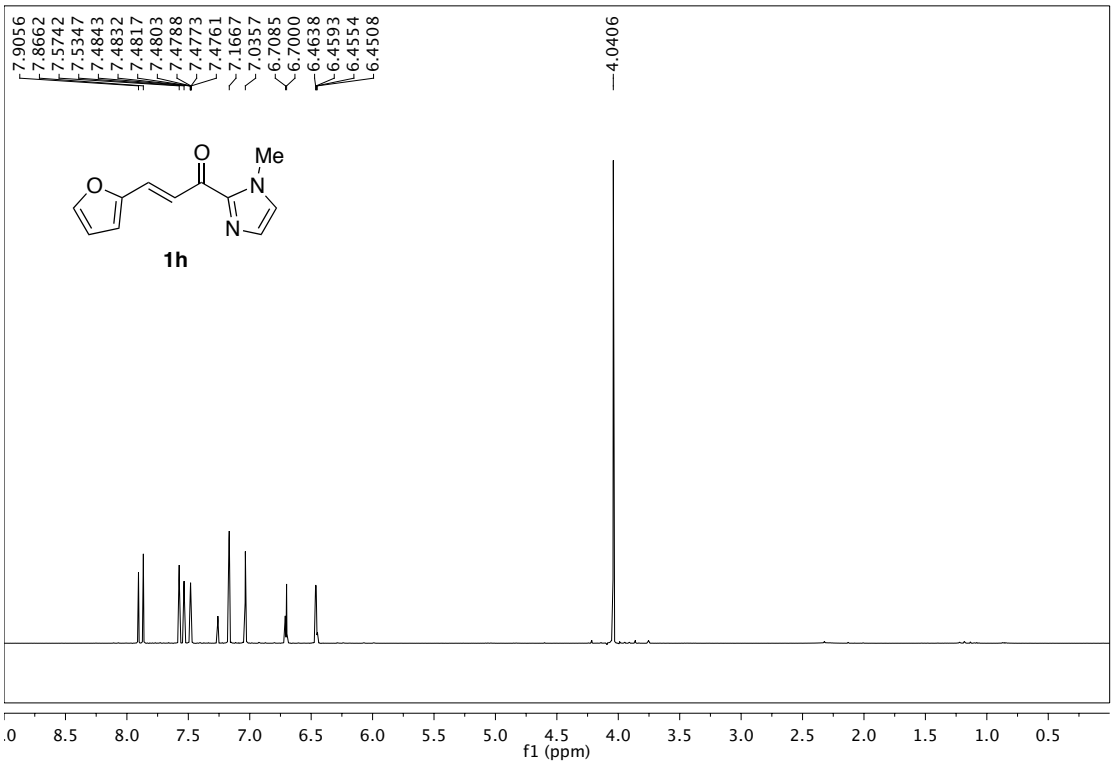


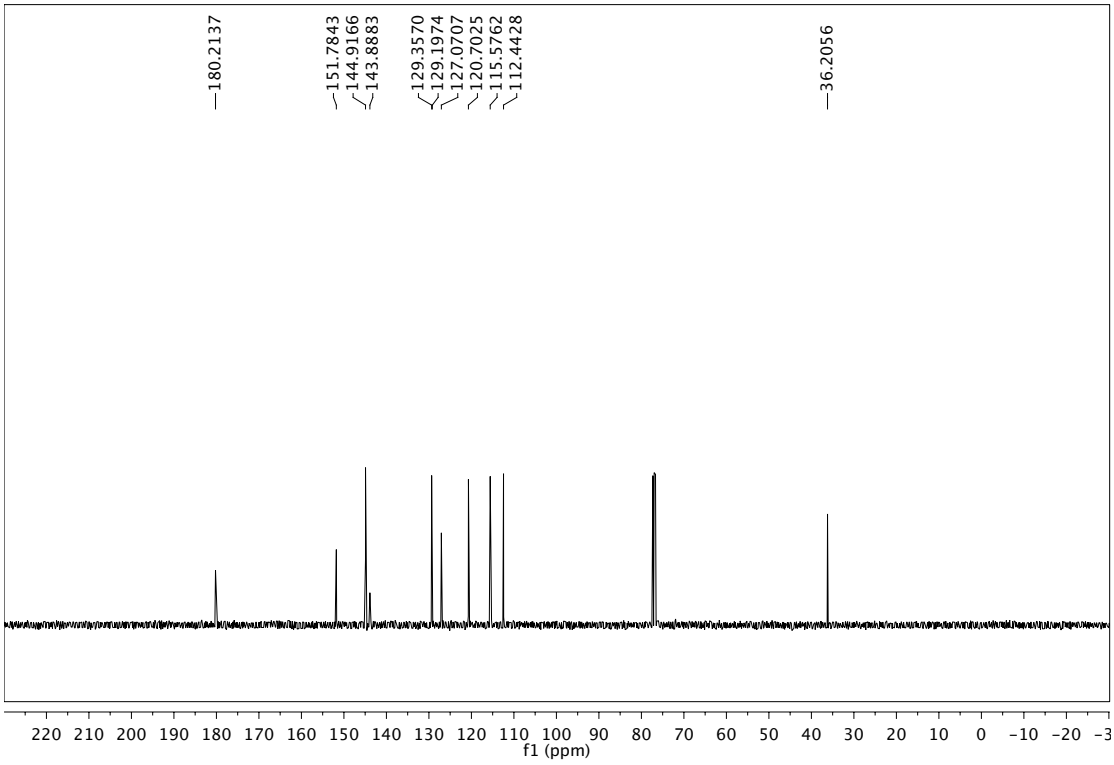
(*E*)-3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1g)



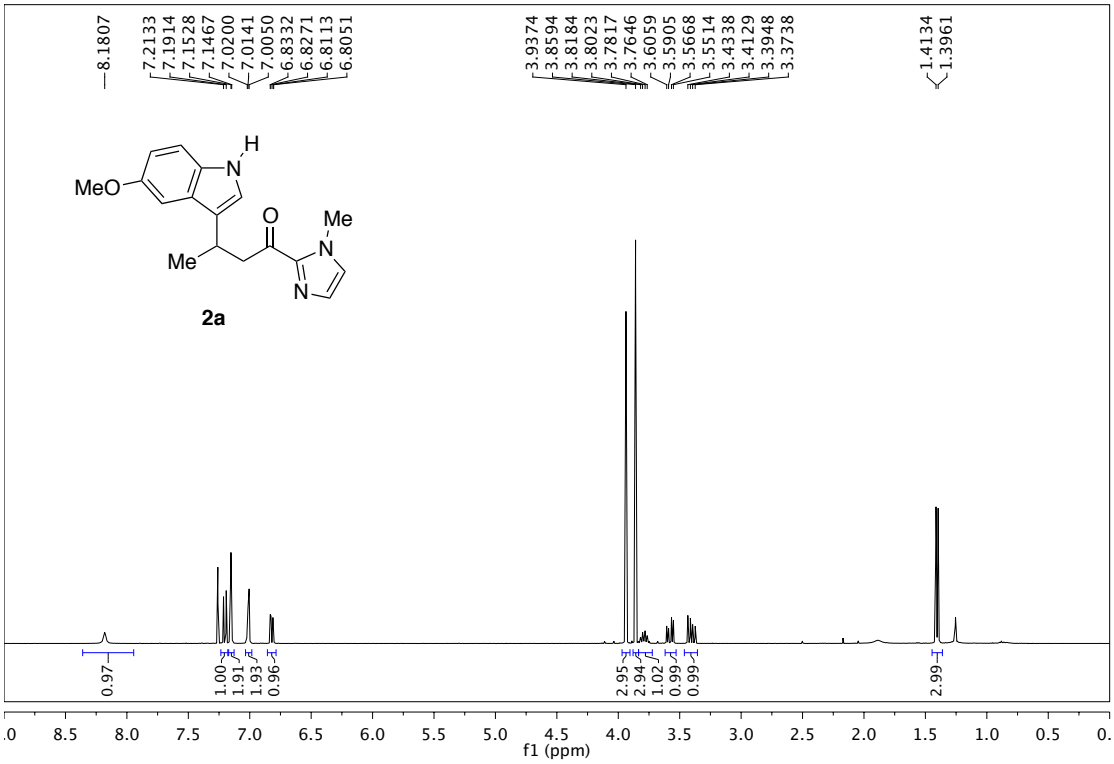


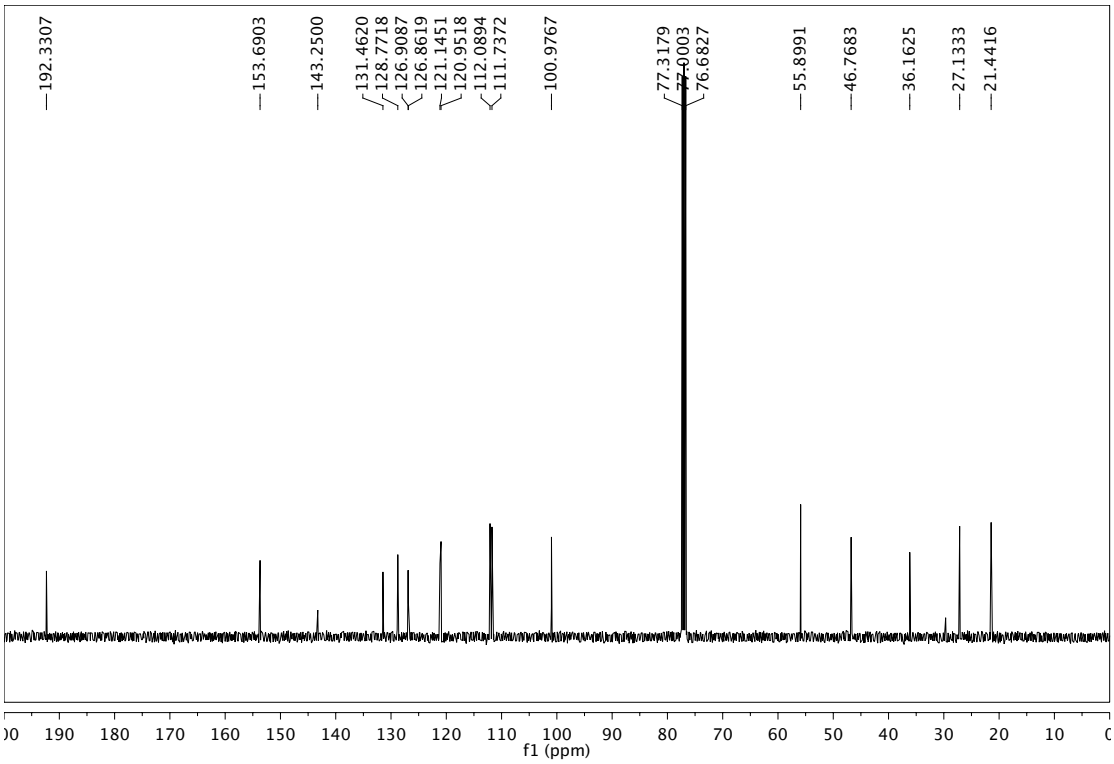
(*E*)-3-(Furan-2-yl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (1h)



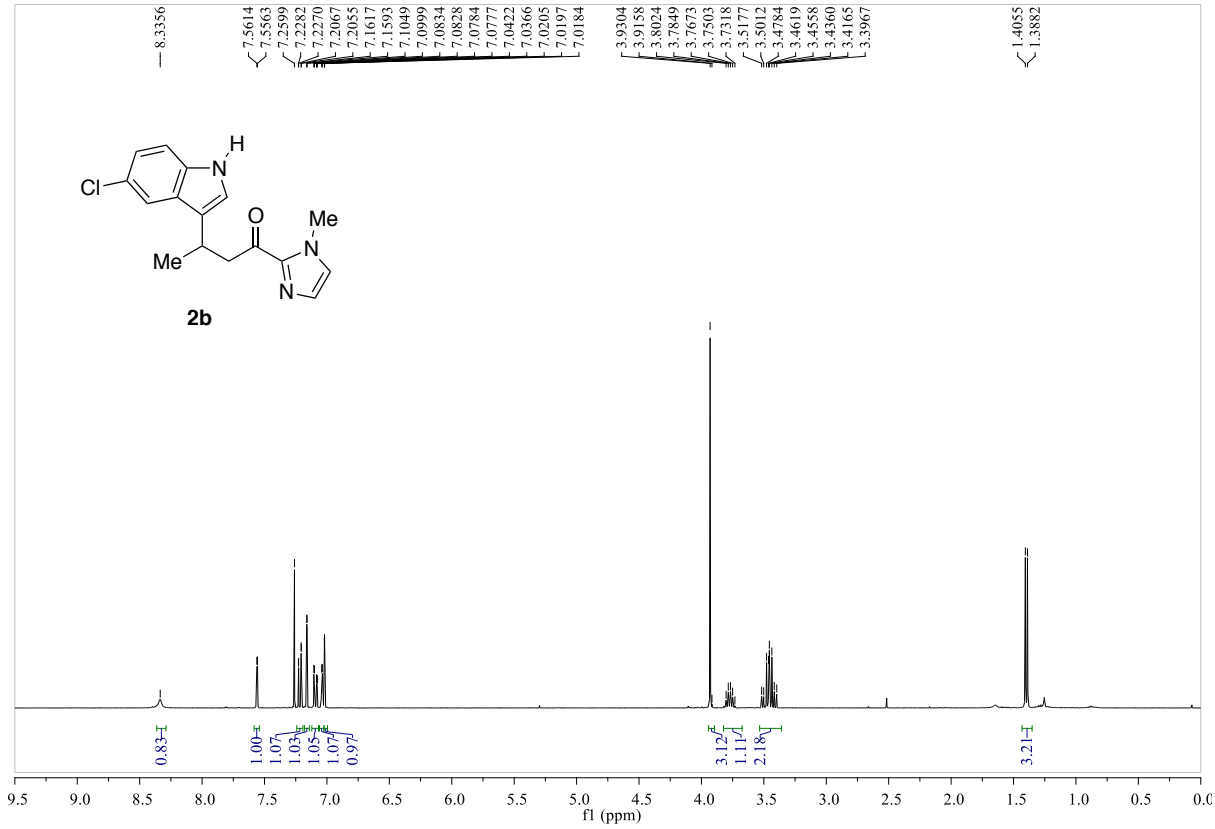


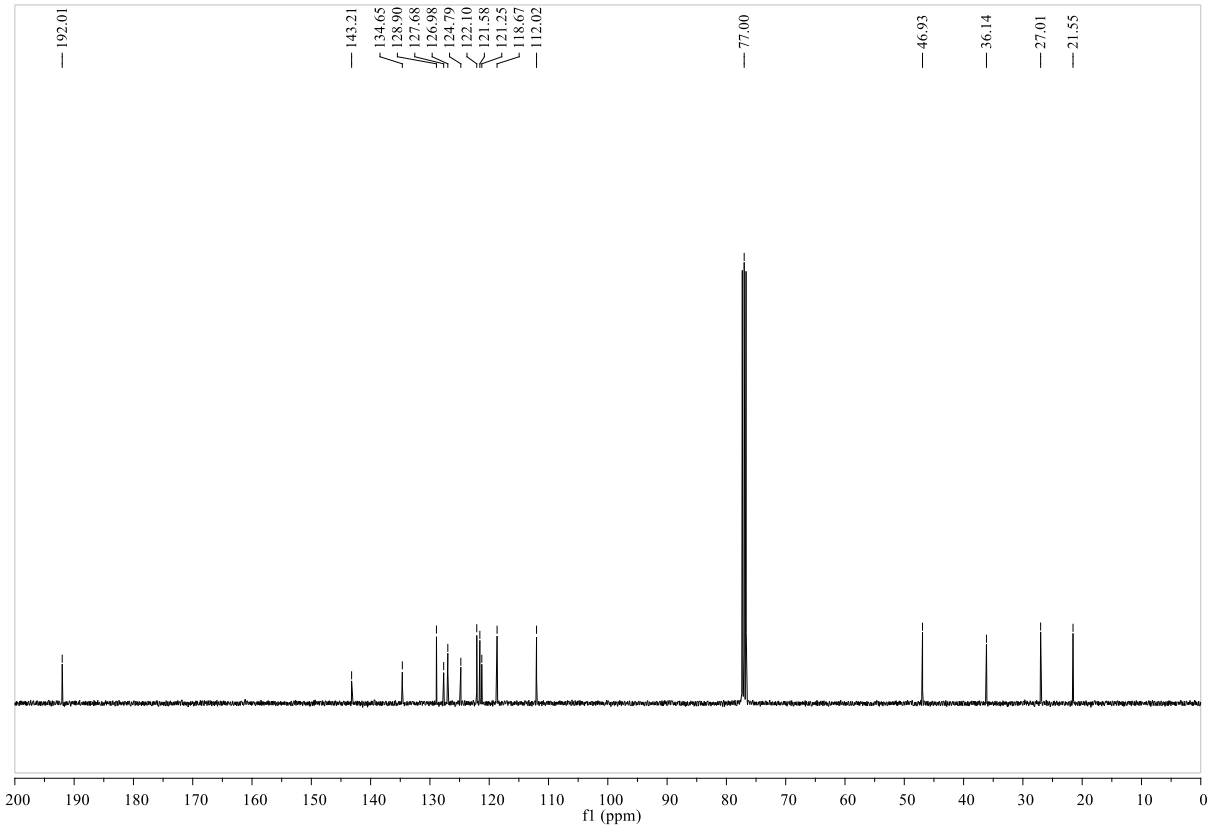
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2a)



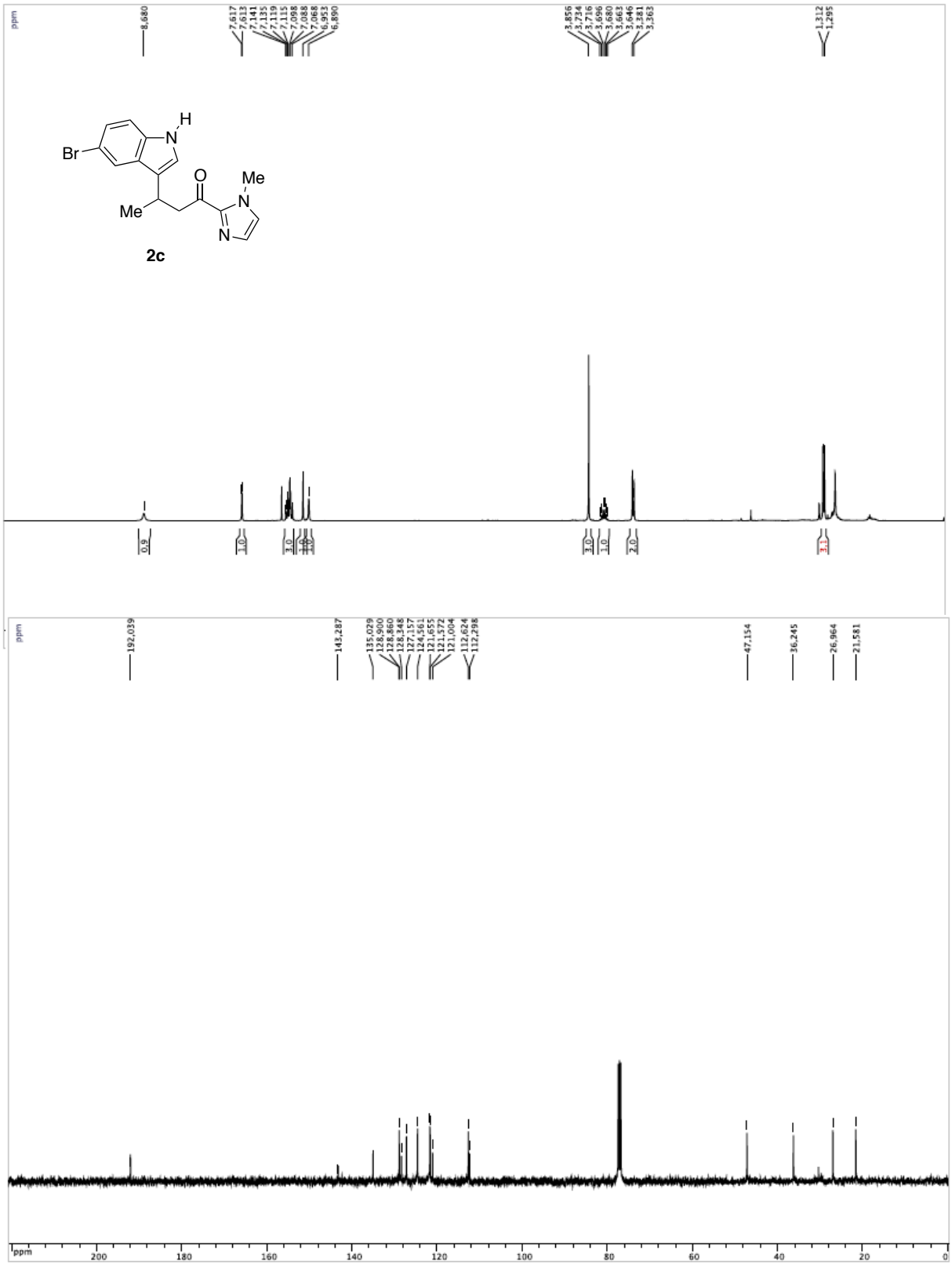


3-(5-Chloro-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2b)

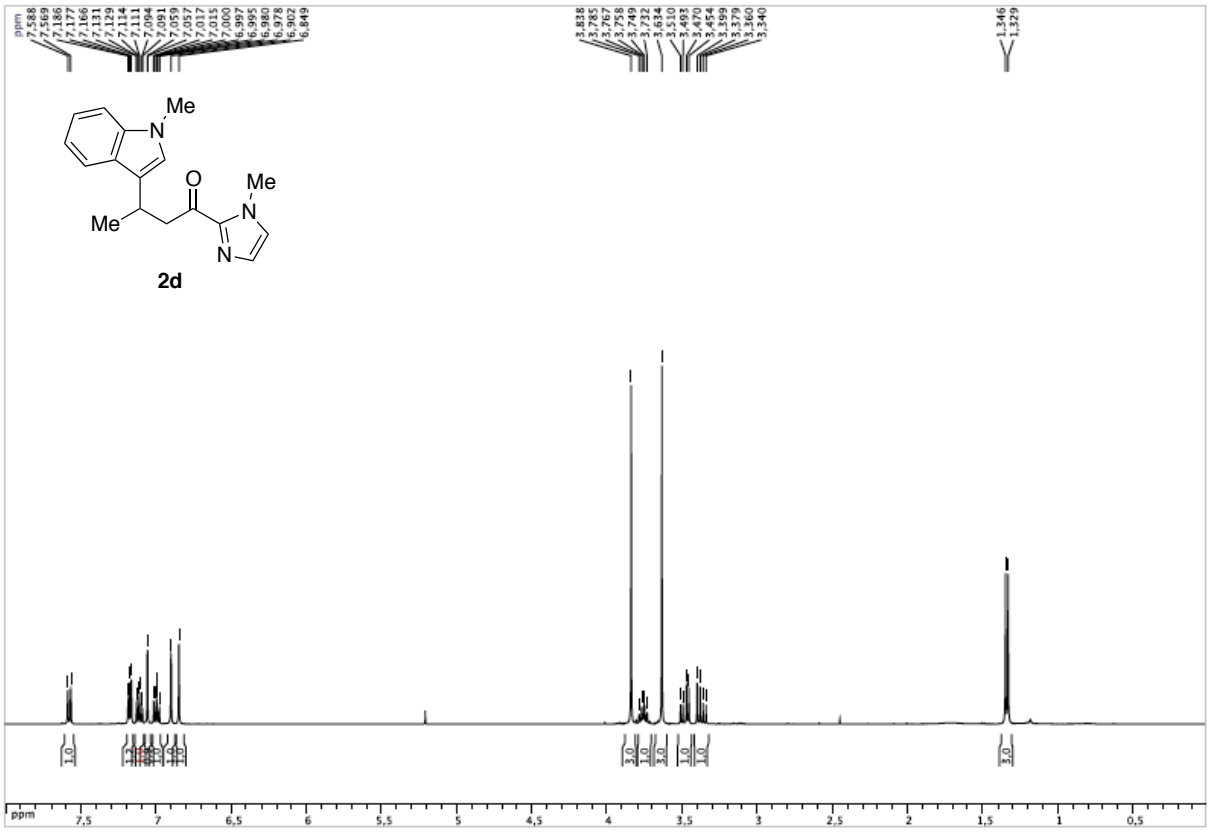


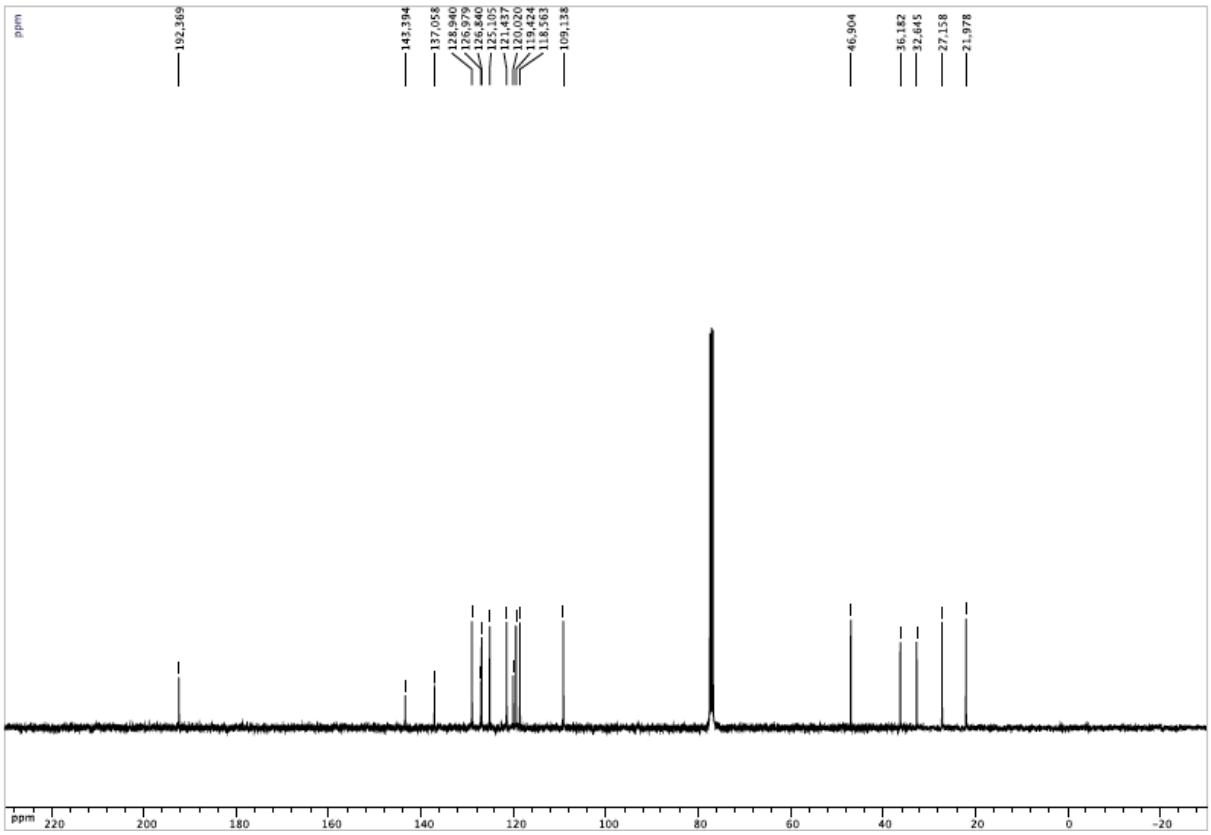


3-(5-Bromo-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2c)

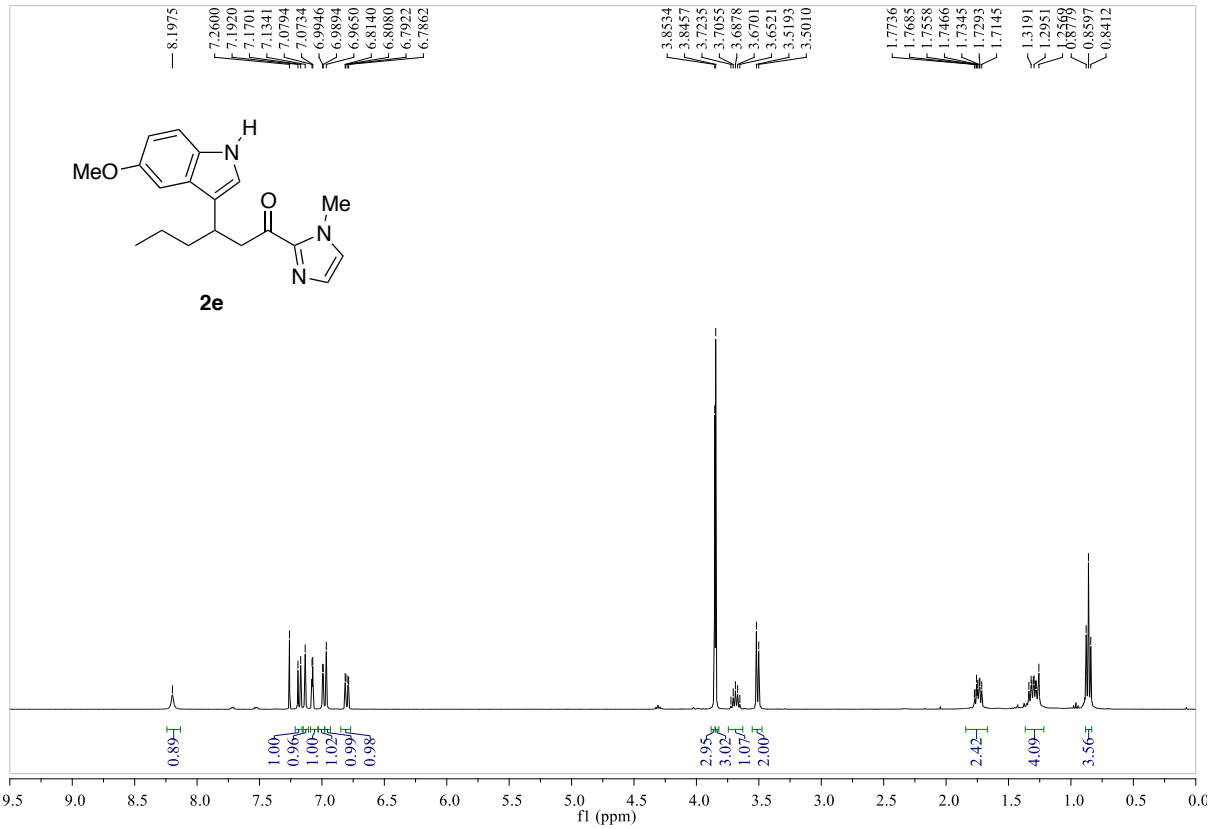


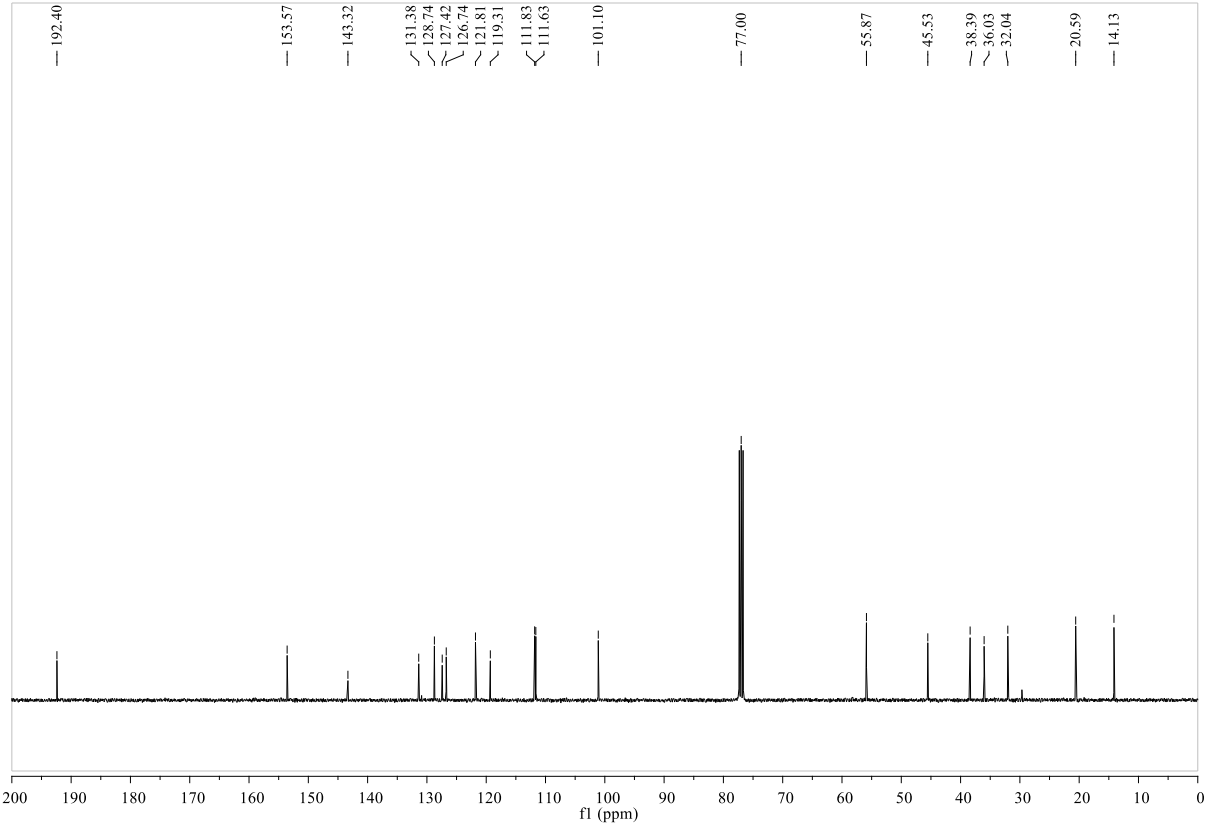
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)butan-1-one (2d)



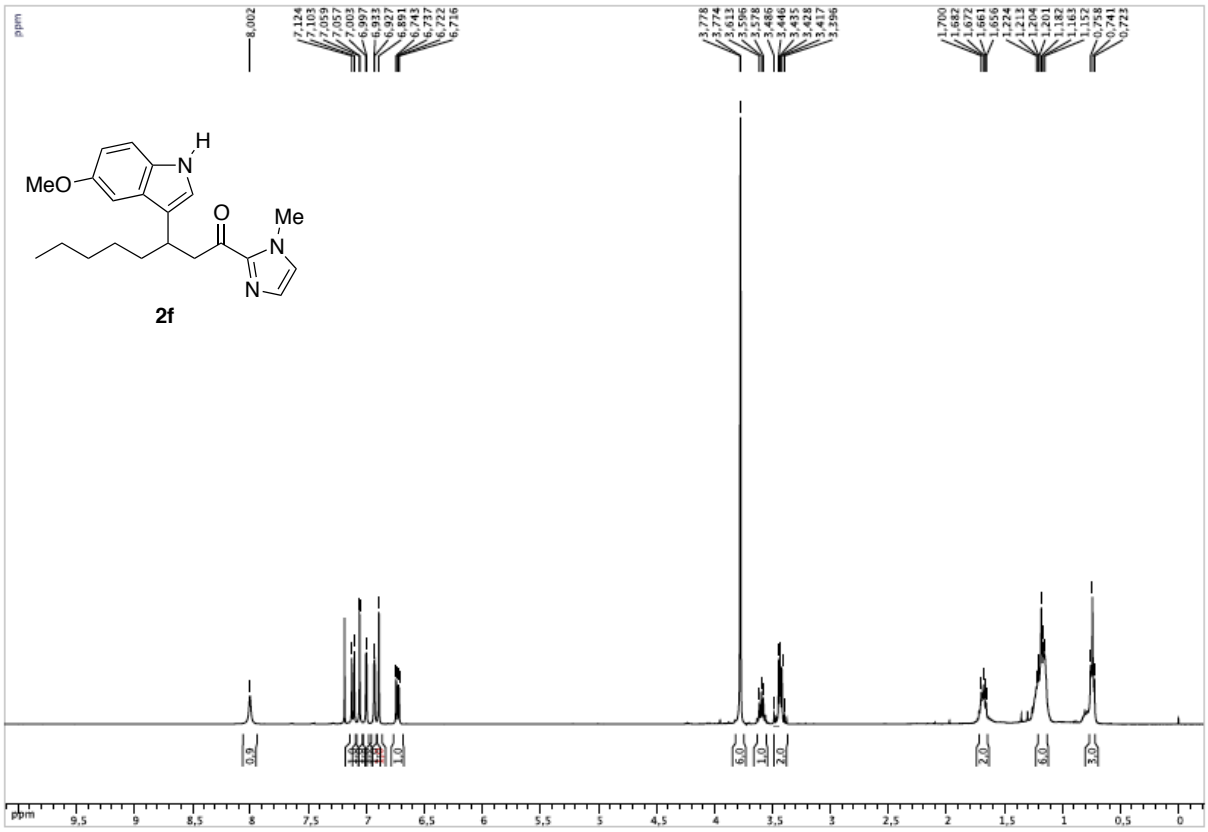


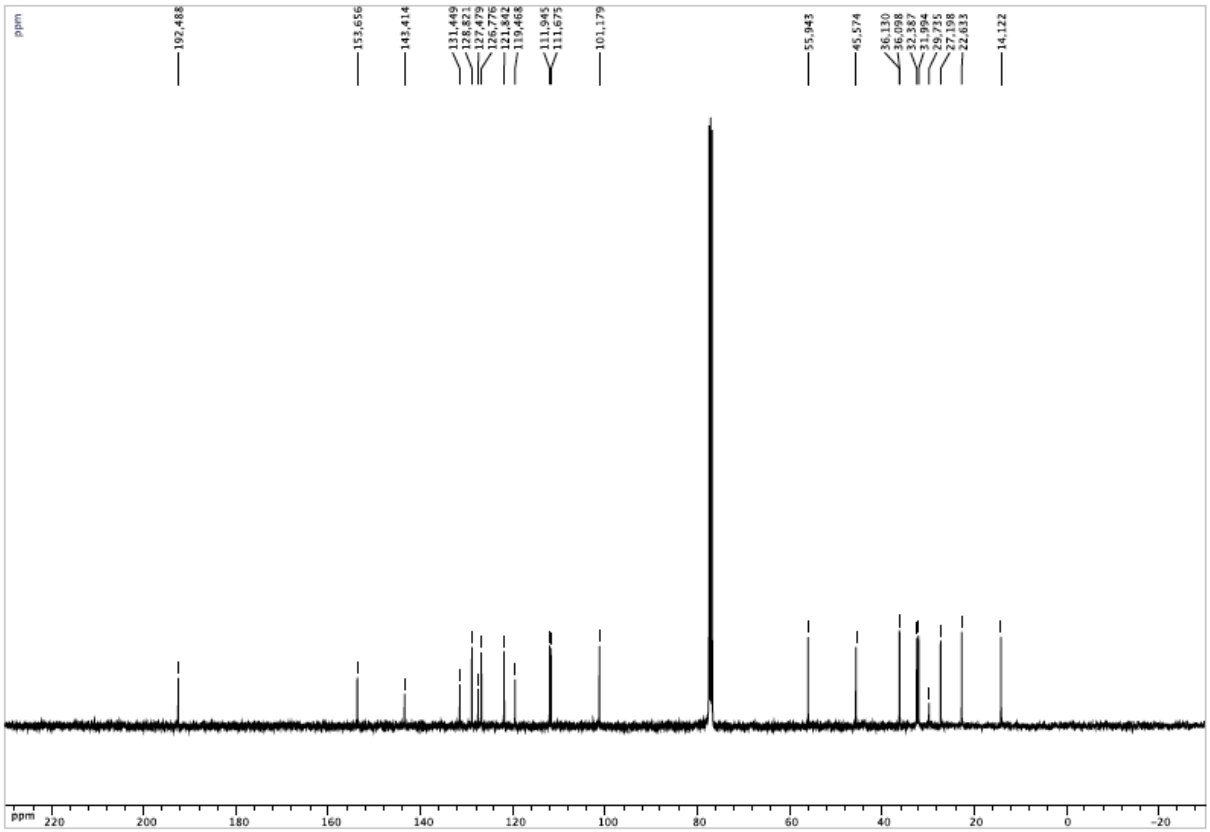
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)hexan-1-one (2e)



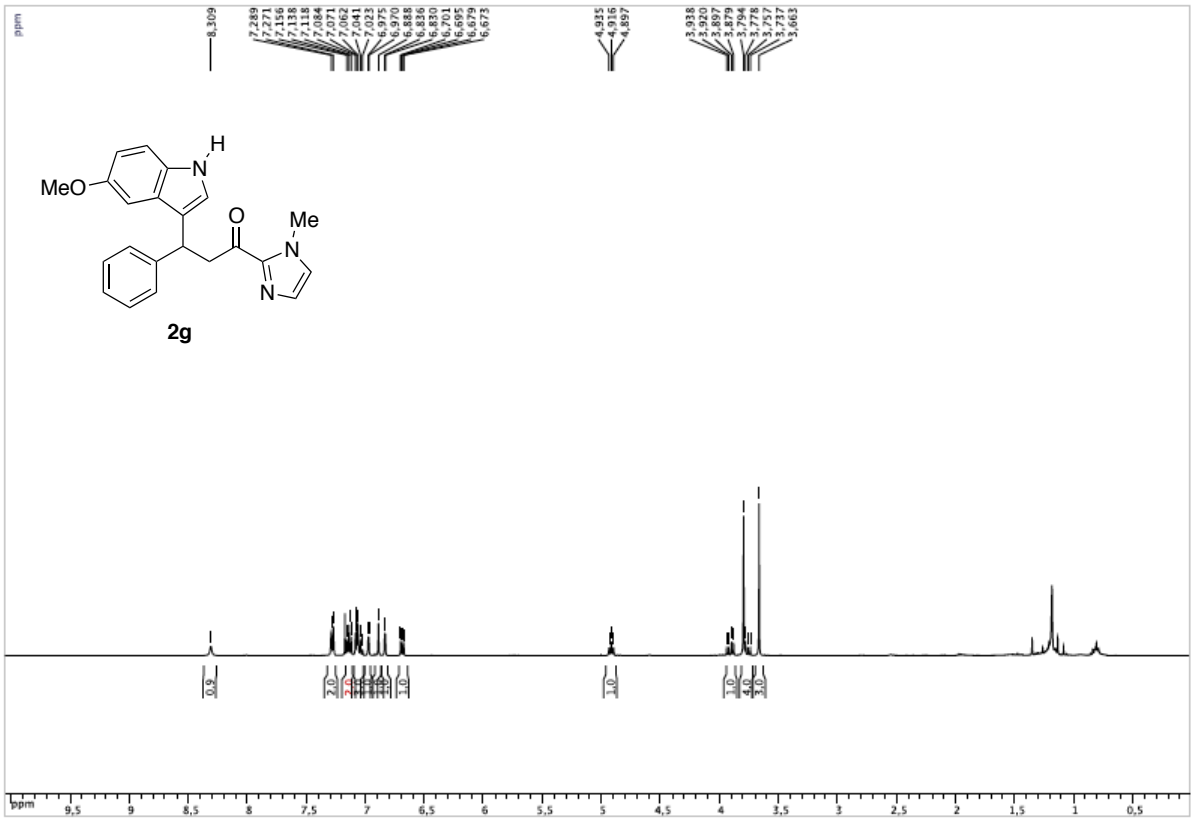


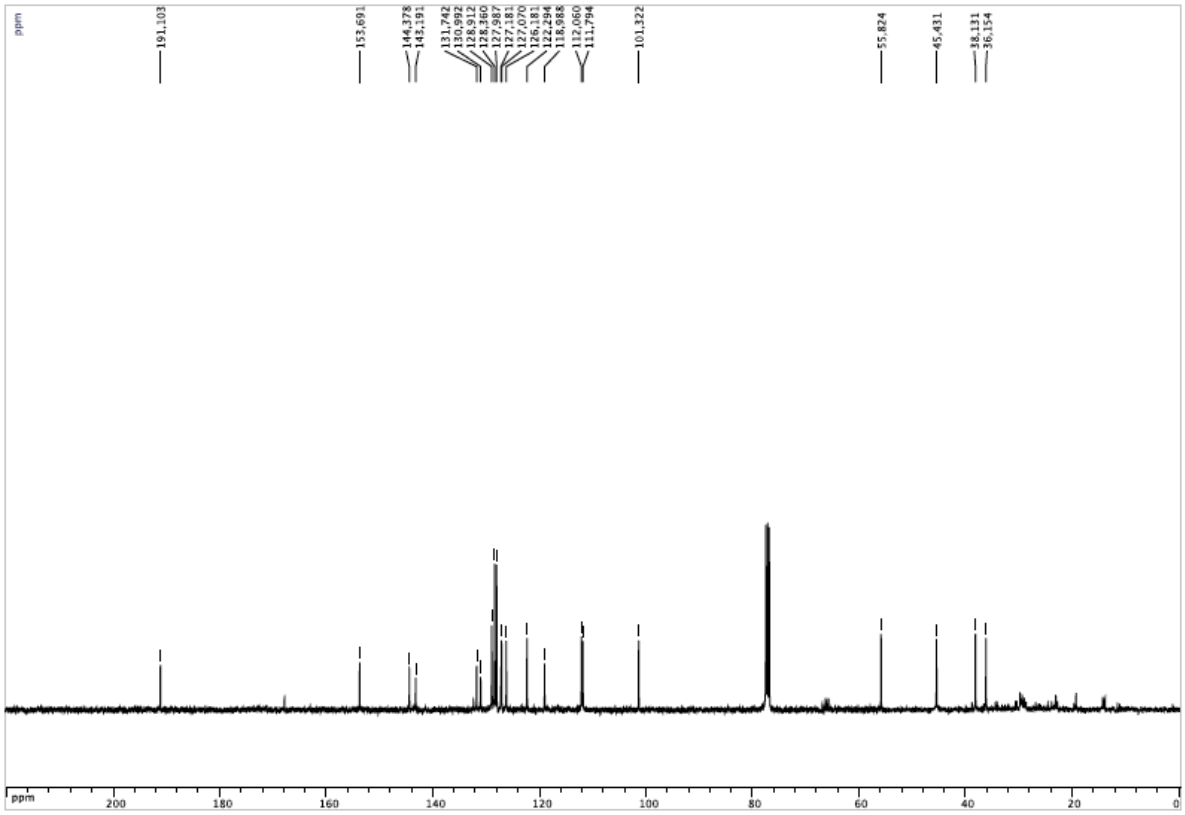
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)octan-1-one (2f)



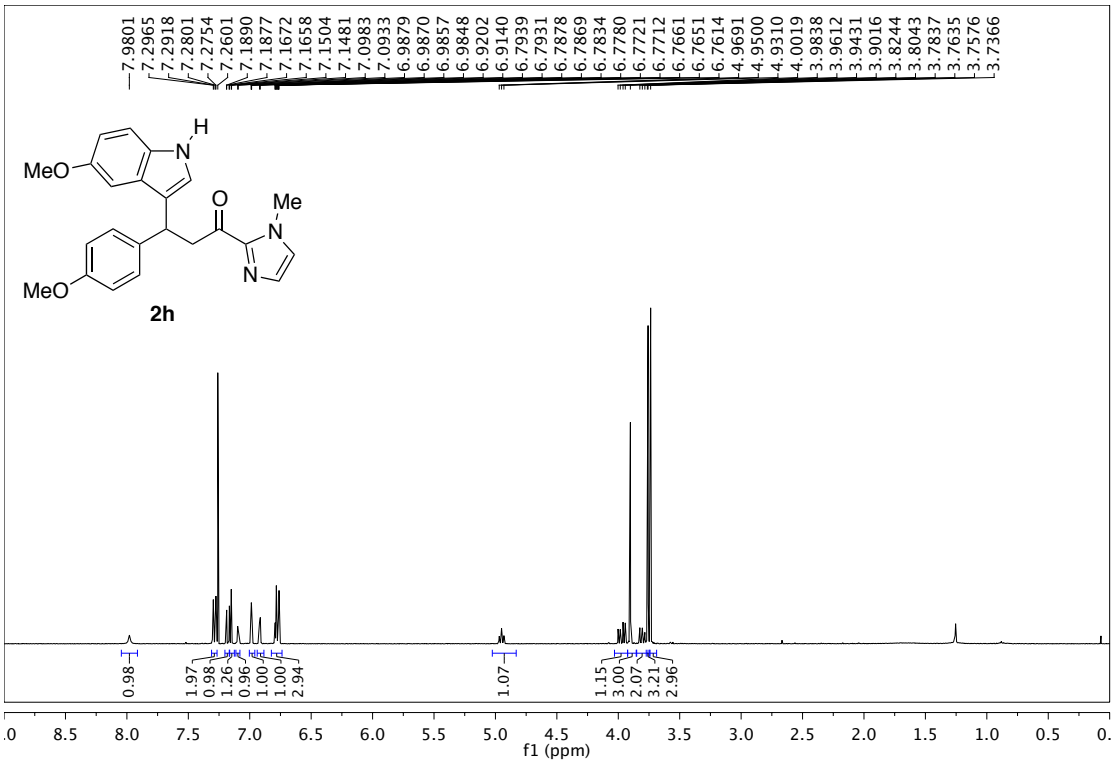


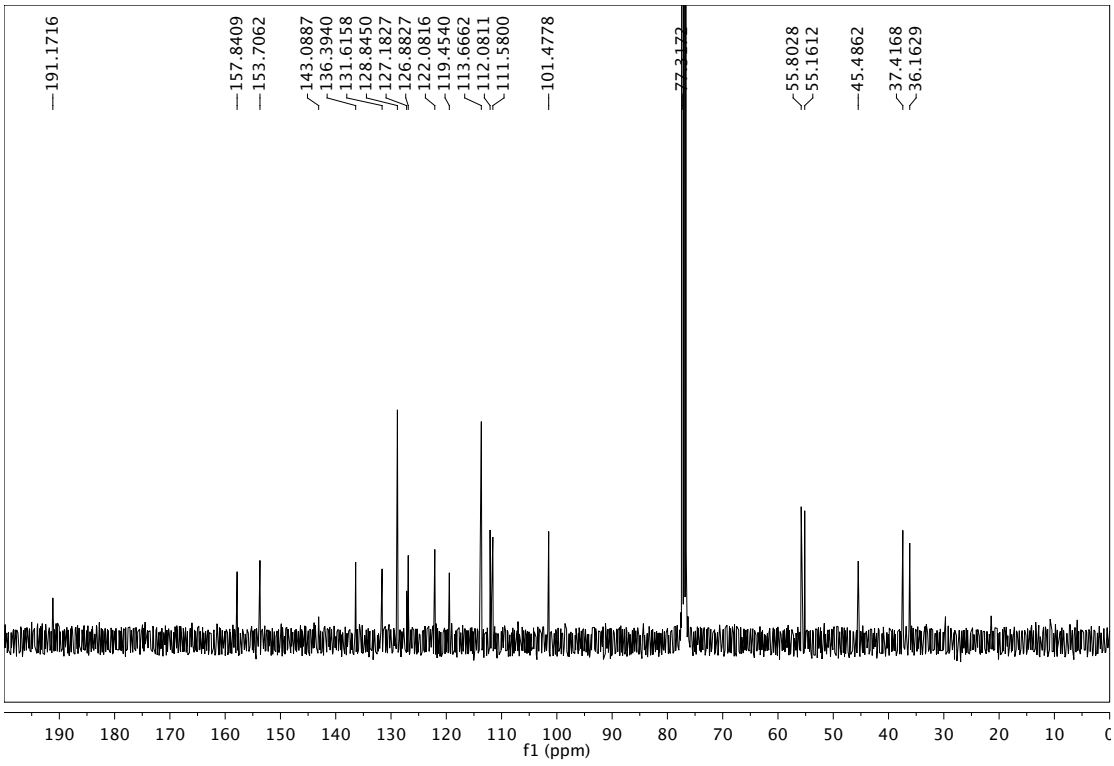
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(5-methoxy-1*H*-indol-3-yl)-3-phenylpropan-1-one (2g)



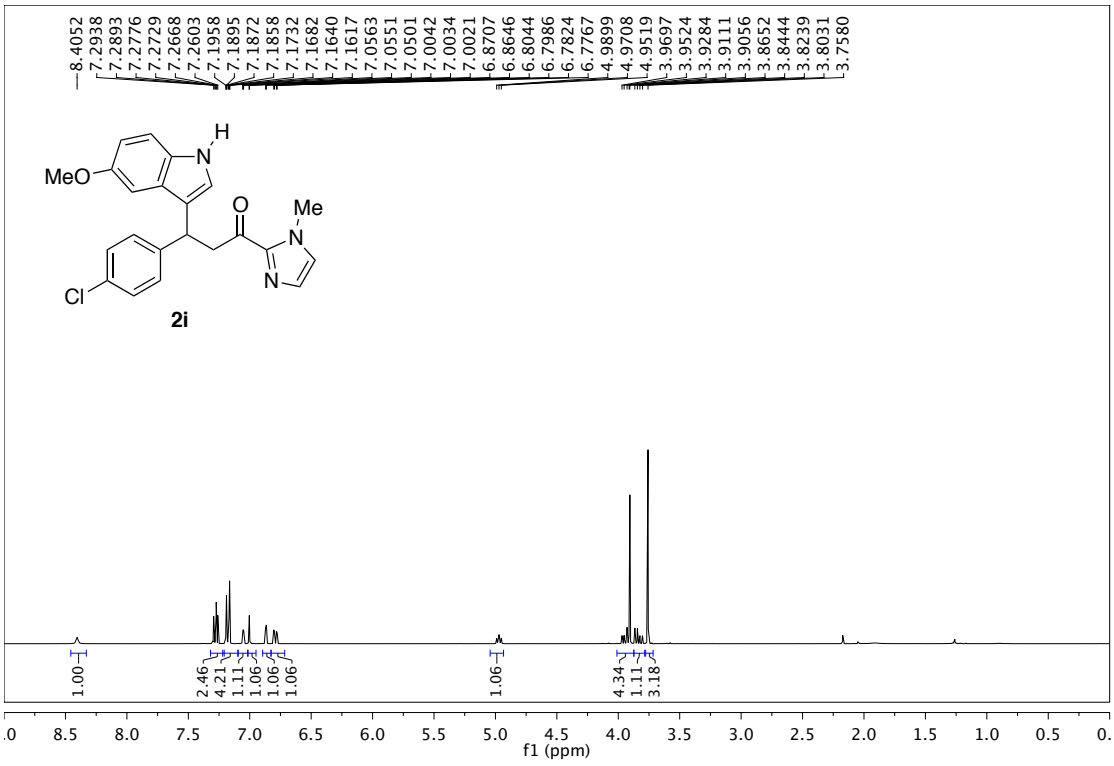


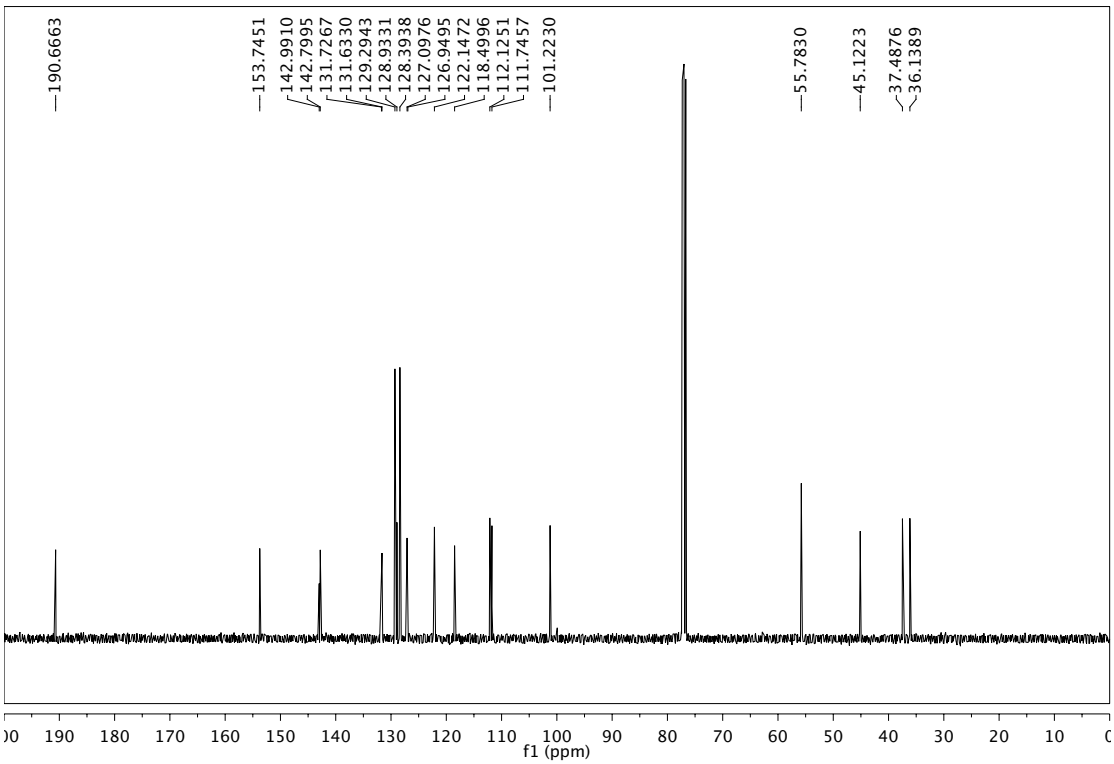
3-(5-Methoxy-1*H*-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (2h)



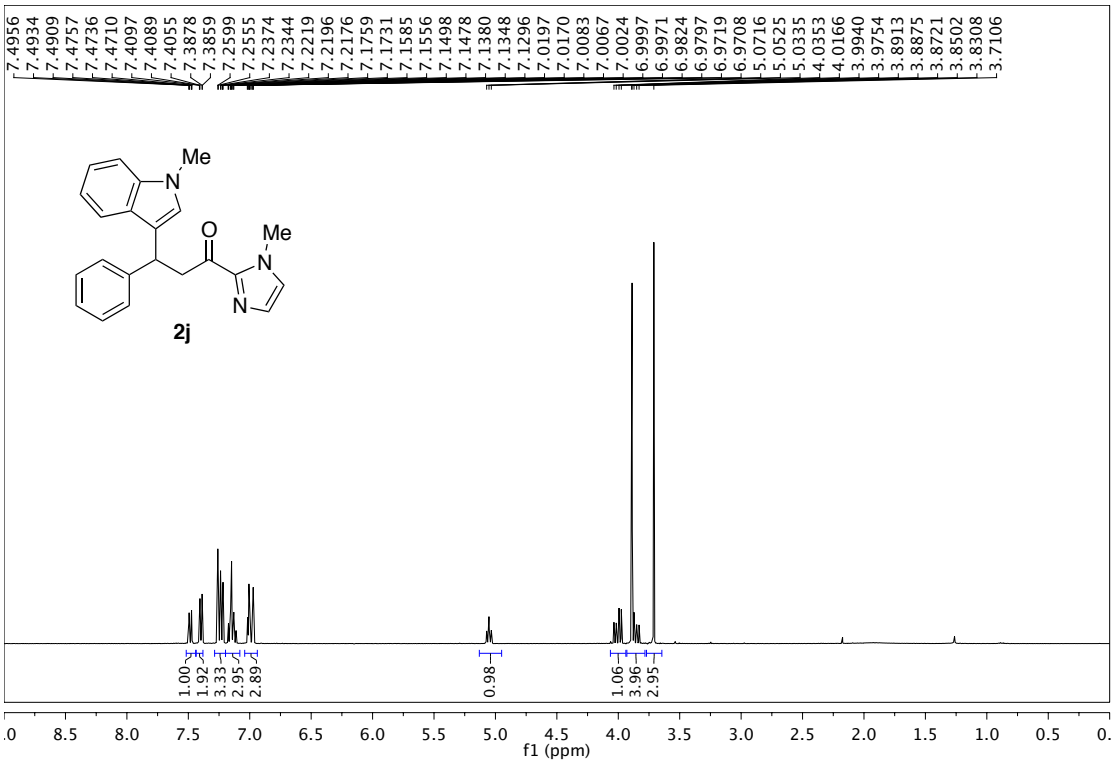


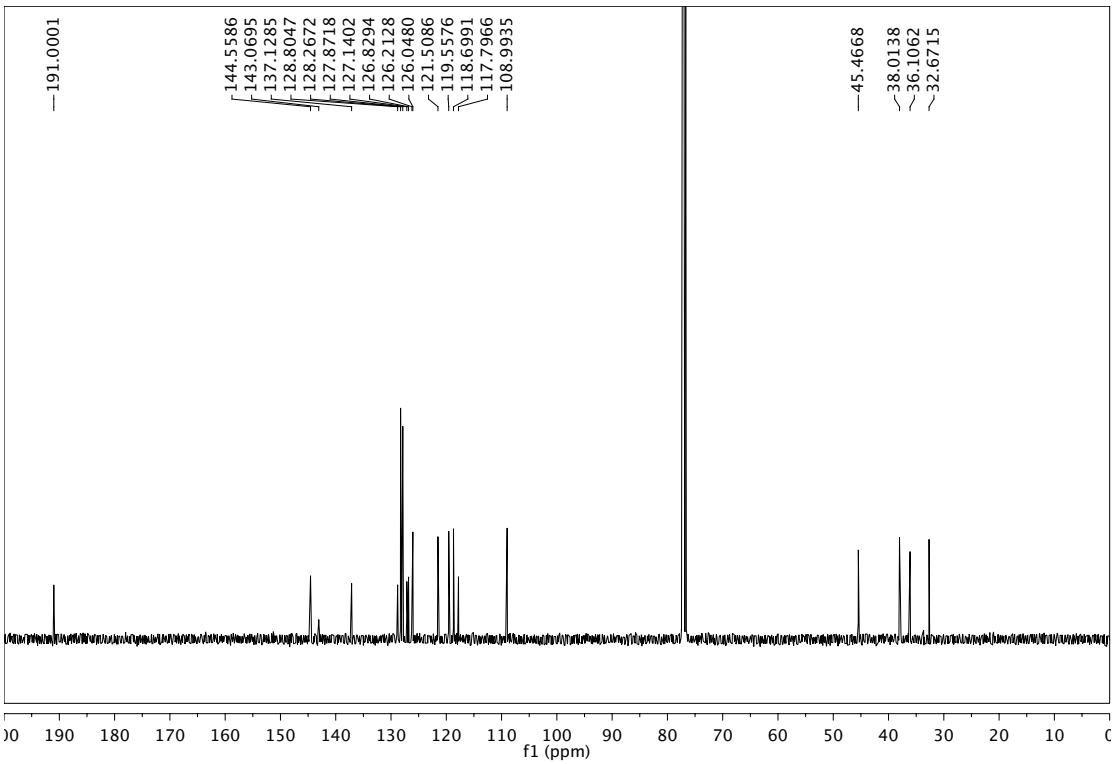
3-(4-Chlorophenyl)-3-(5-methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)propan-1-one (2i)



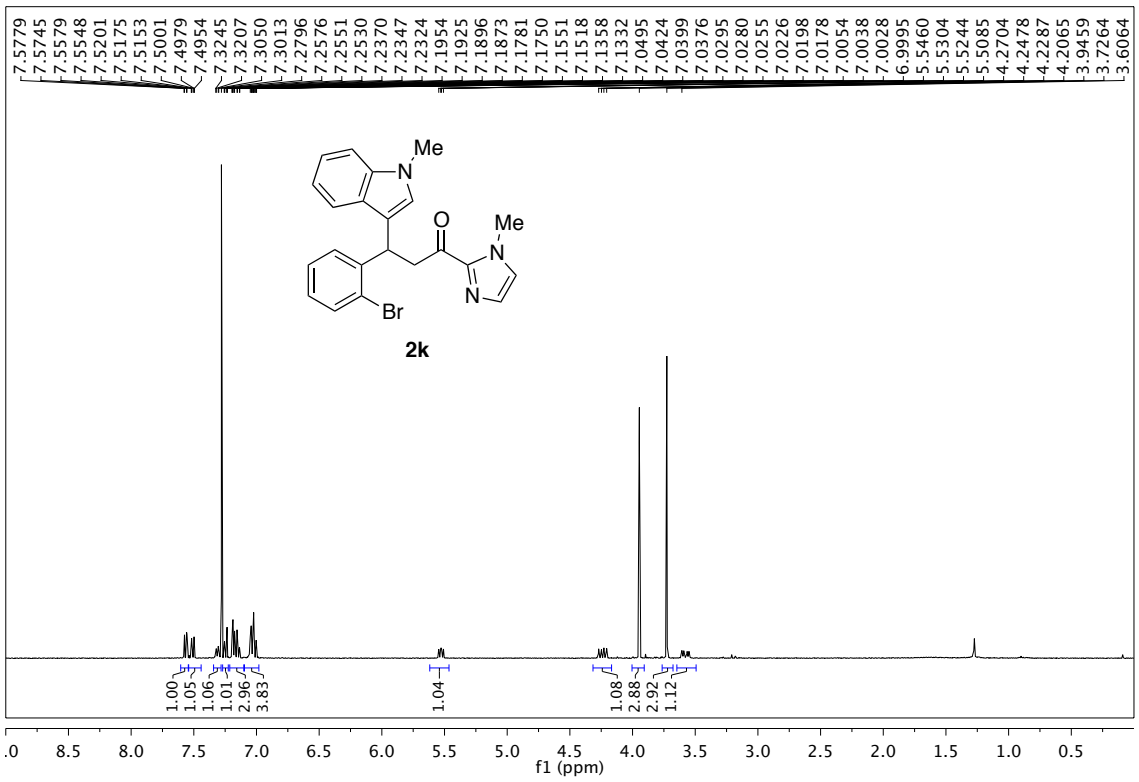


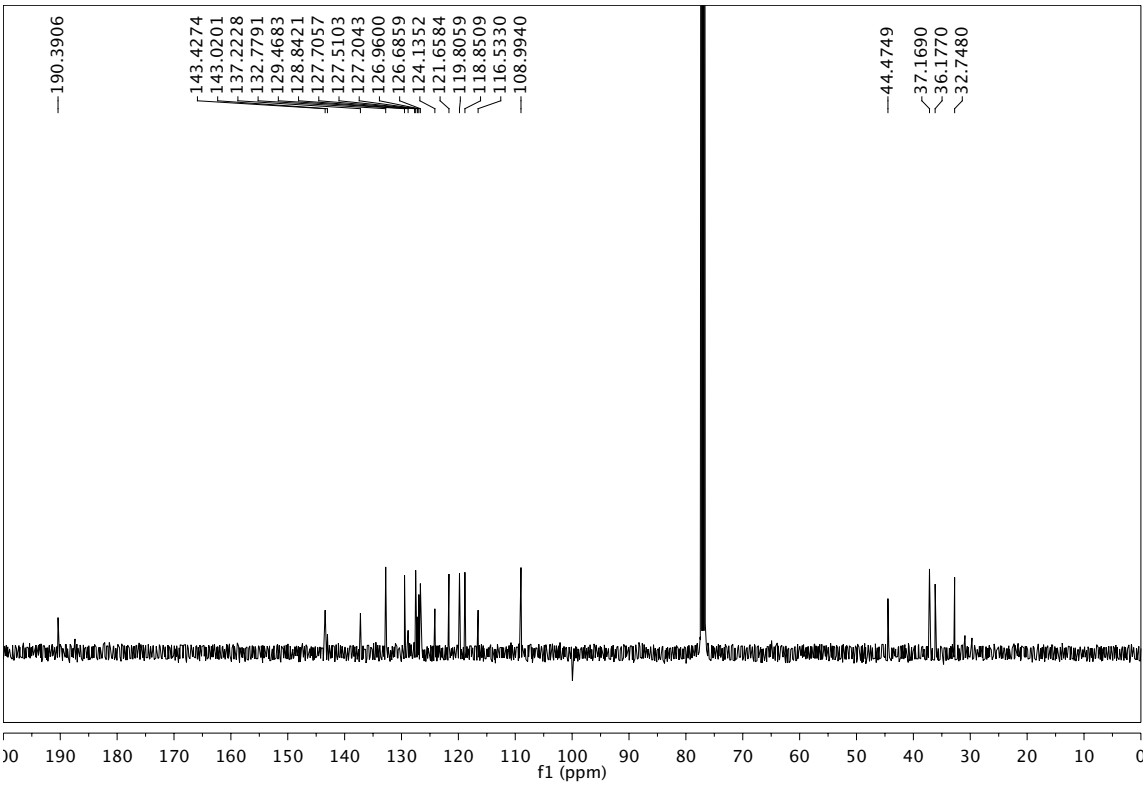
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (2j)



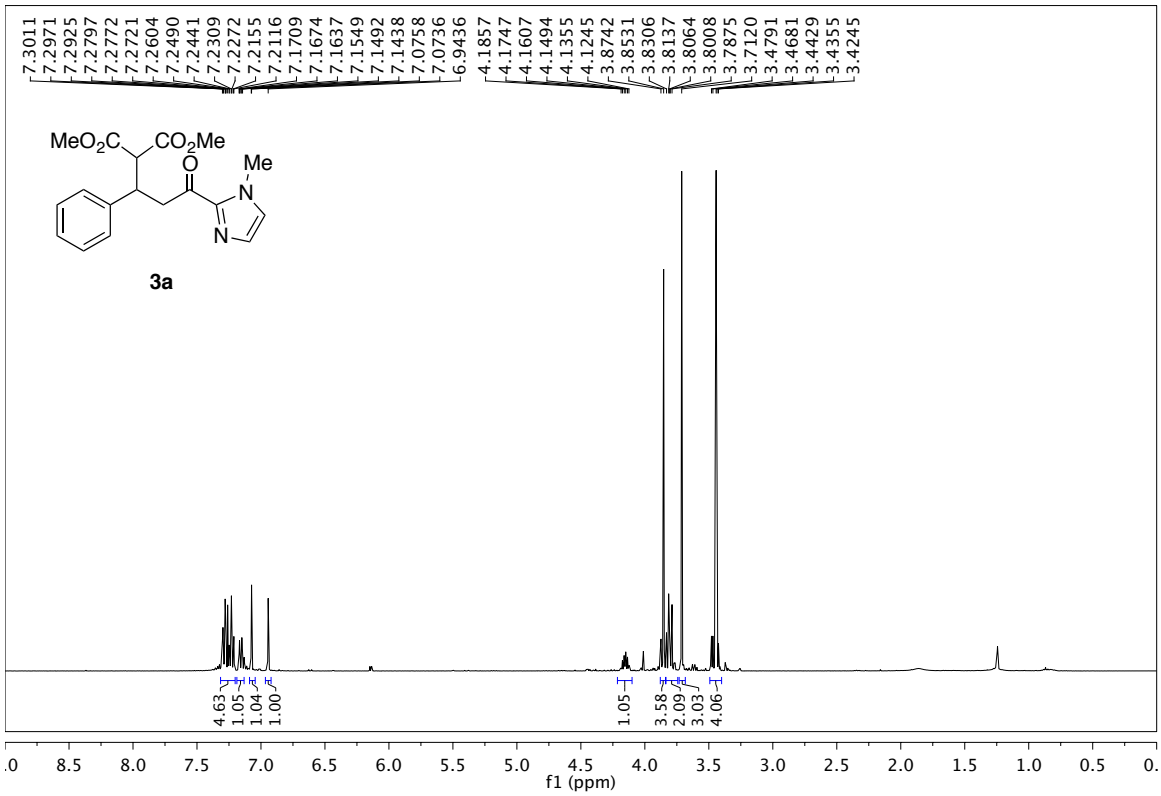


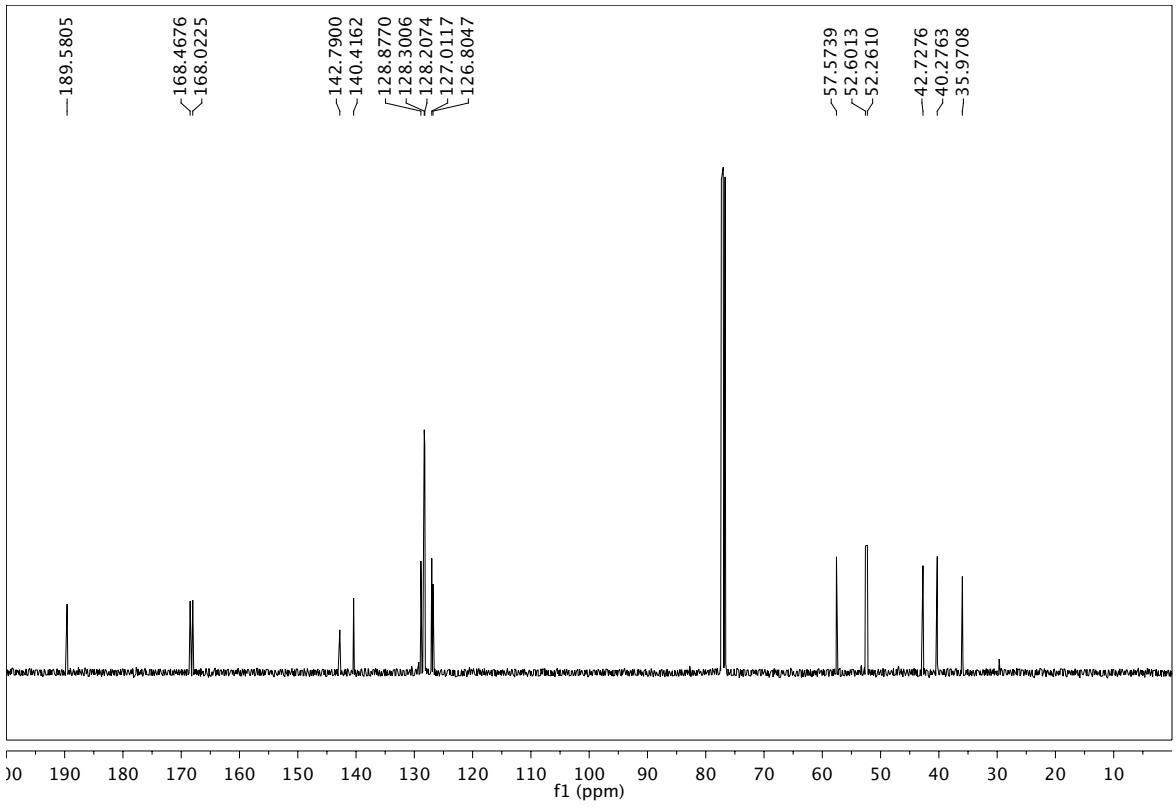
3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)propan-1-one (2k)



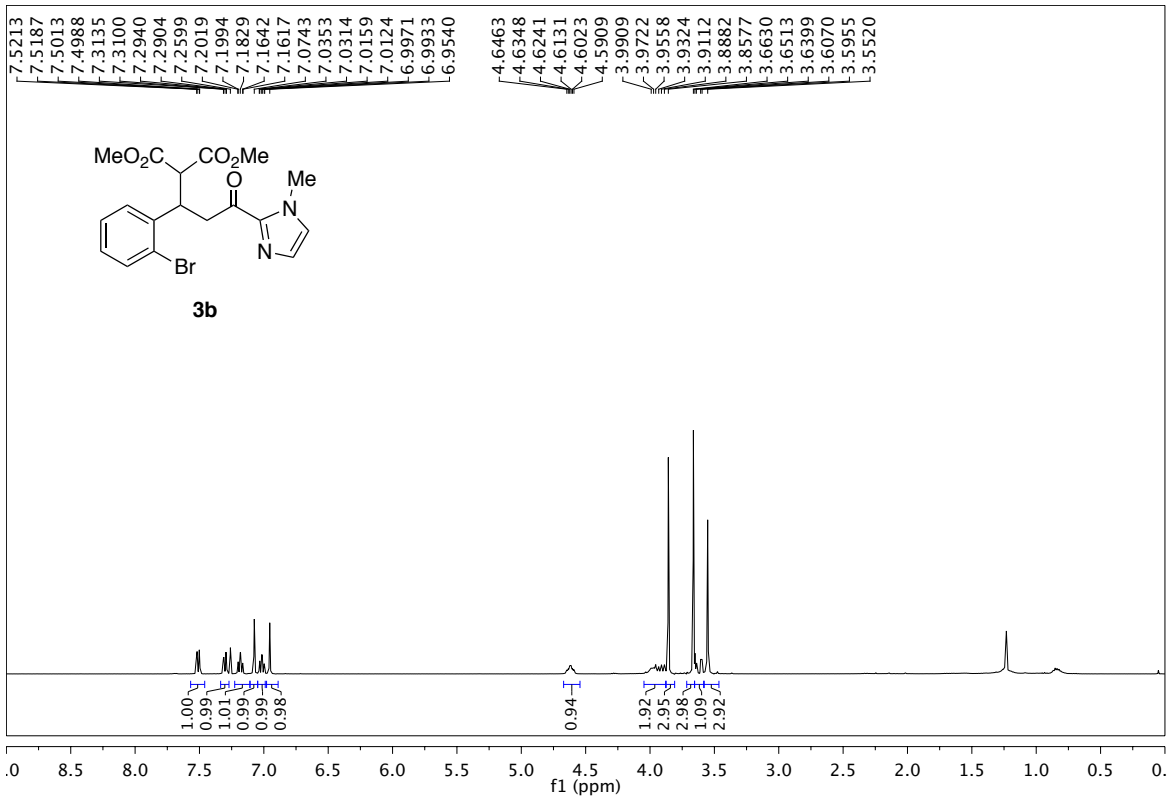


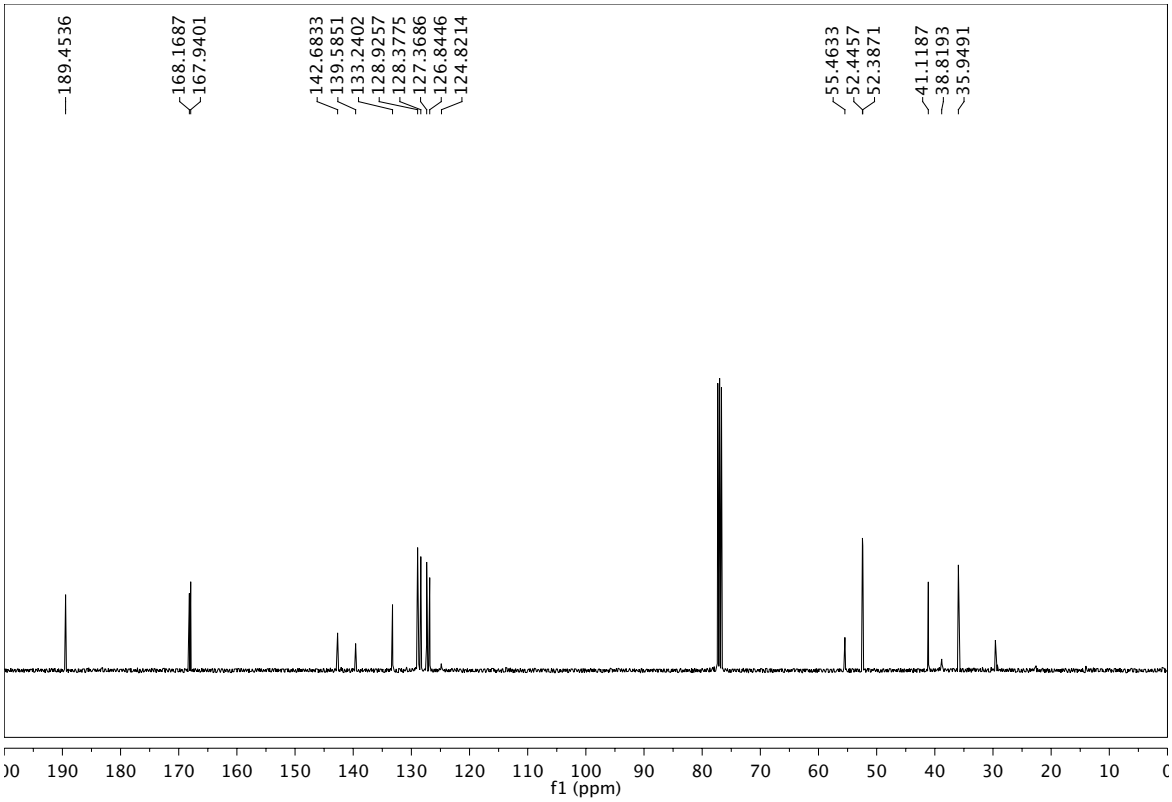
Dimethyl 2-(3-(1-methyl-1*H*-imidazol-2-yl)-3-oxo-1-phenylpropyl)malonate (3a)



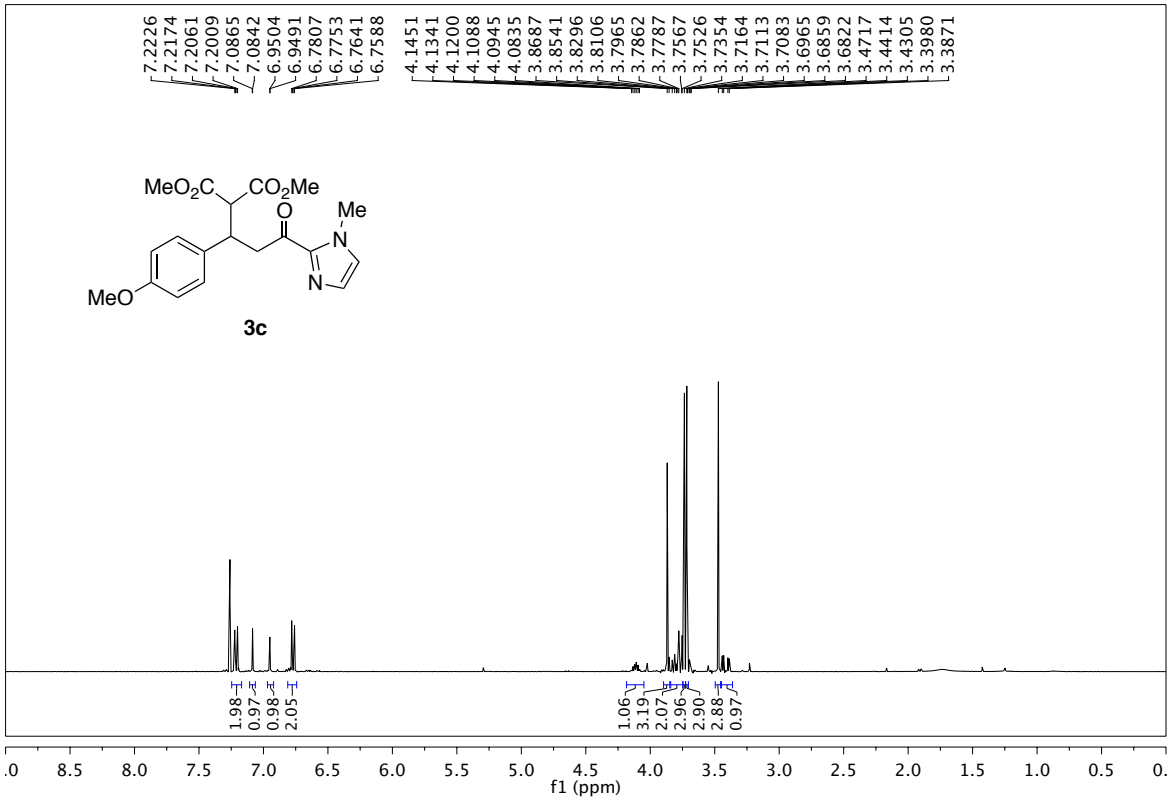


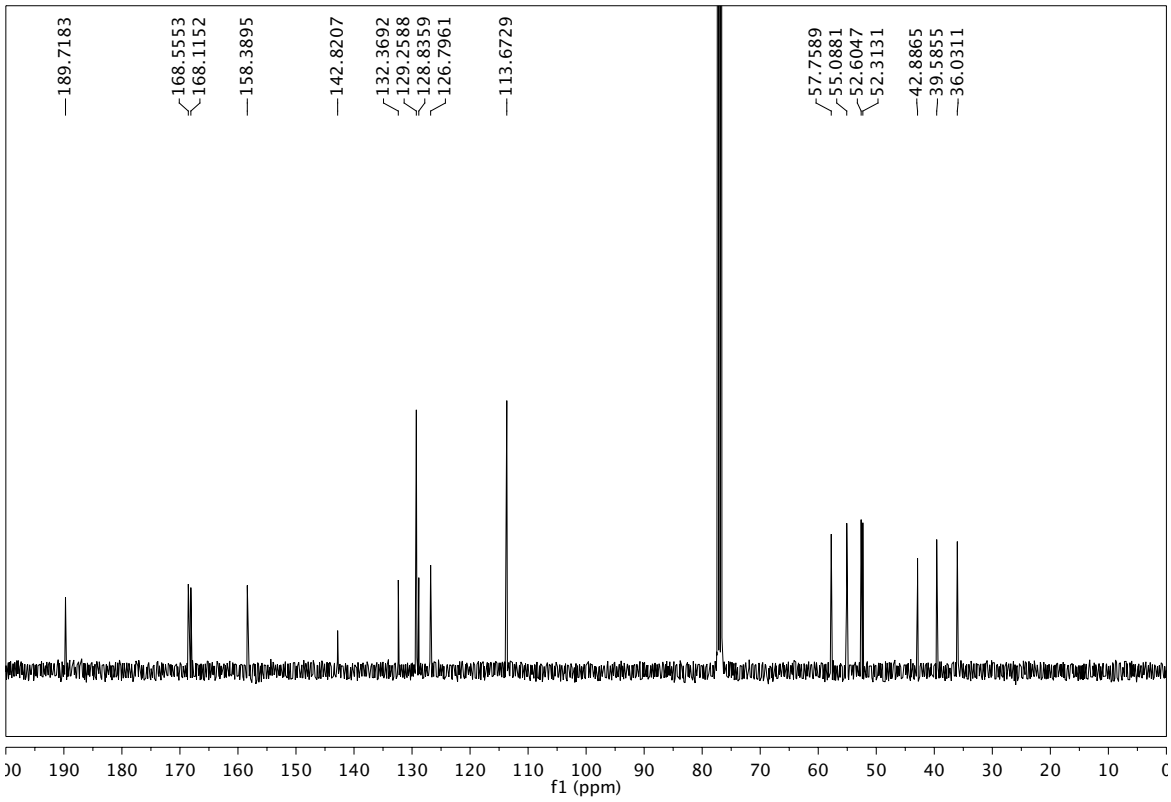
Dimethyl 2-(1-(2-bromophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3b)



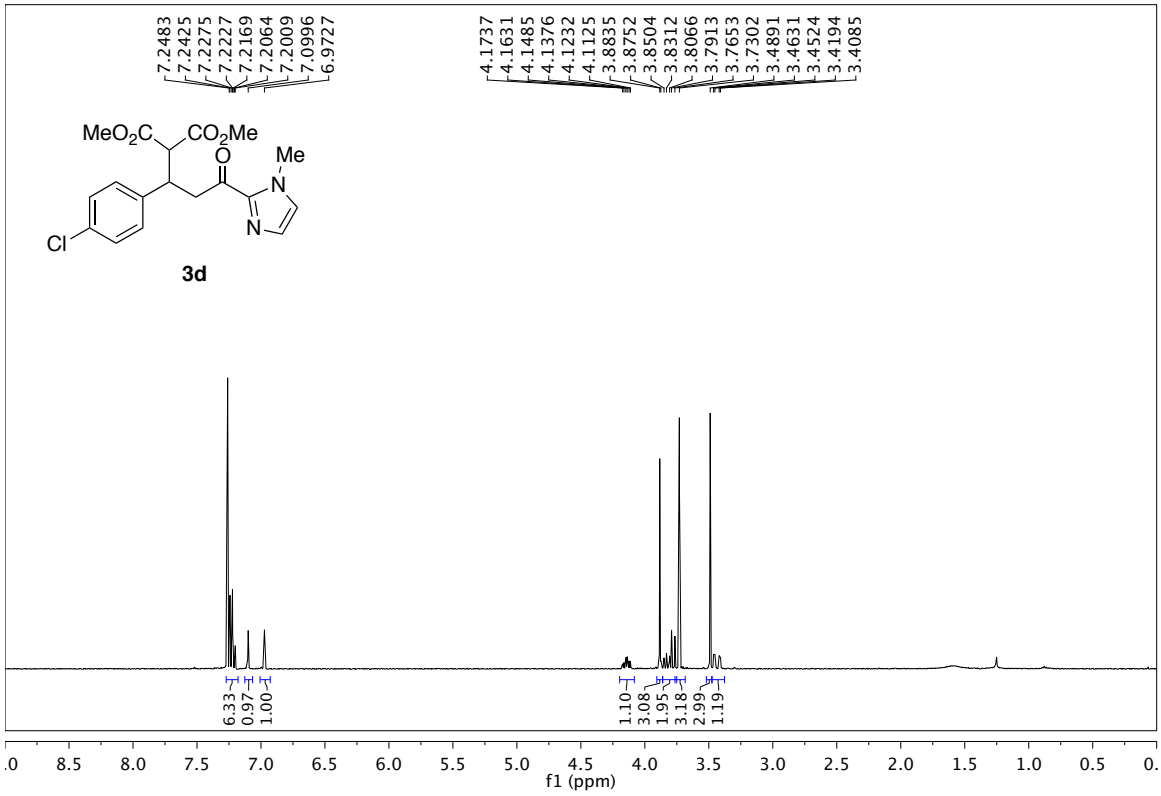


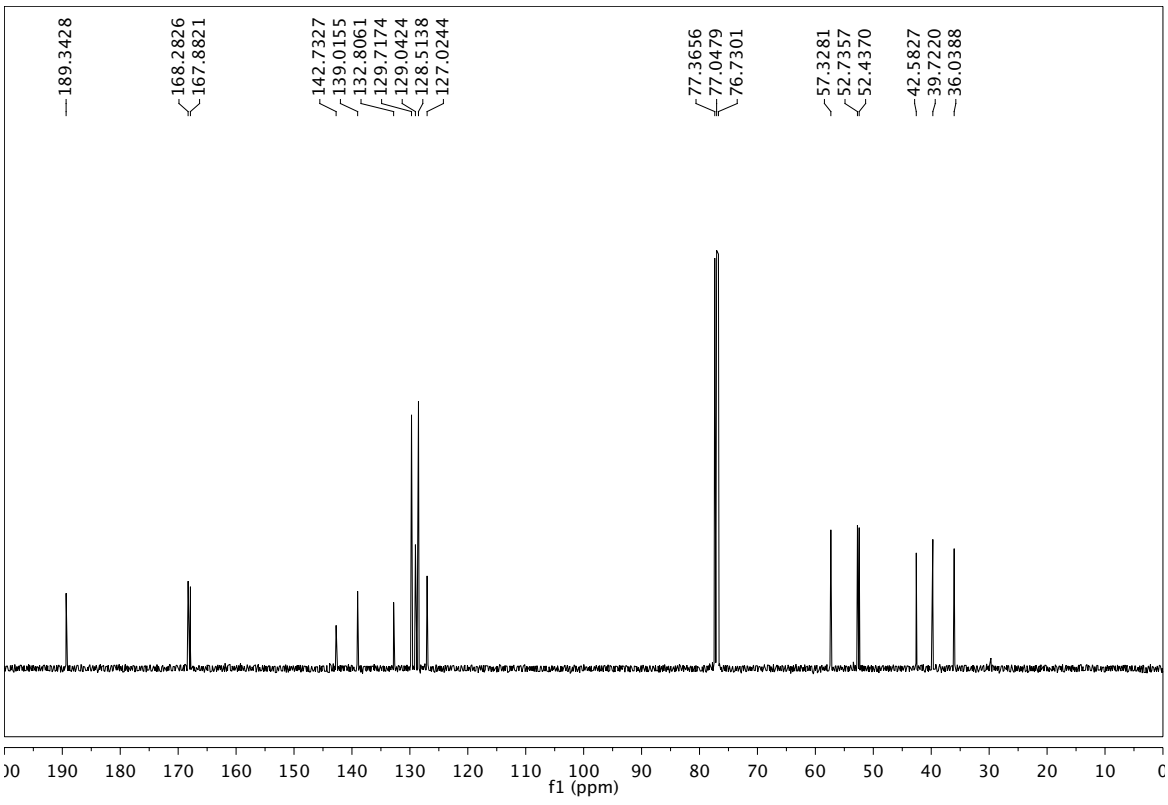
Dimethyl 2-(1-(4-methoxyphenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3c)



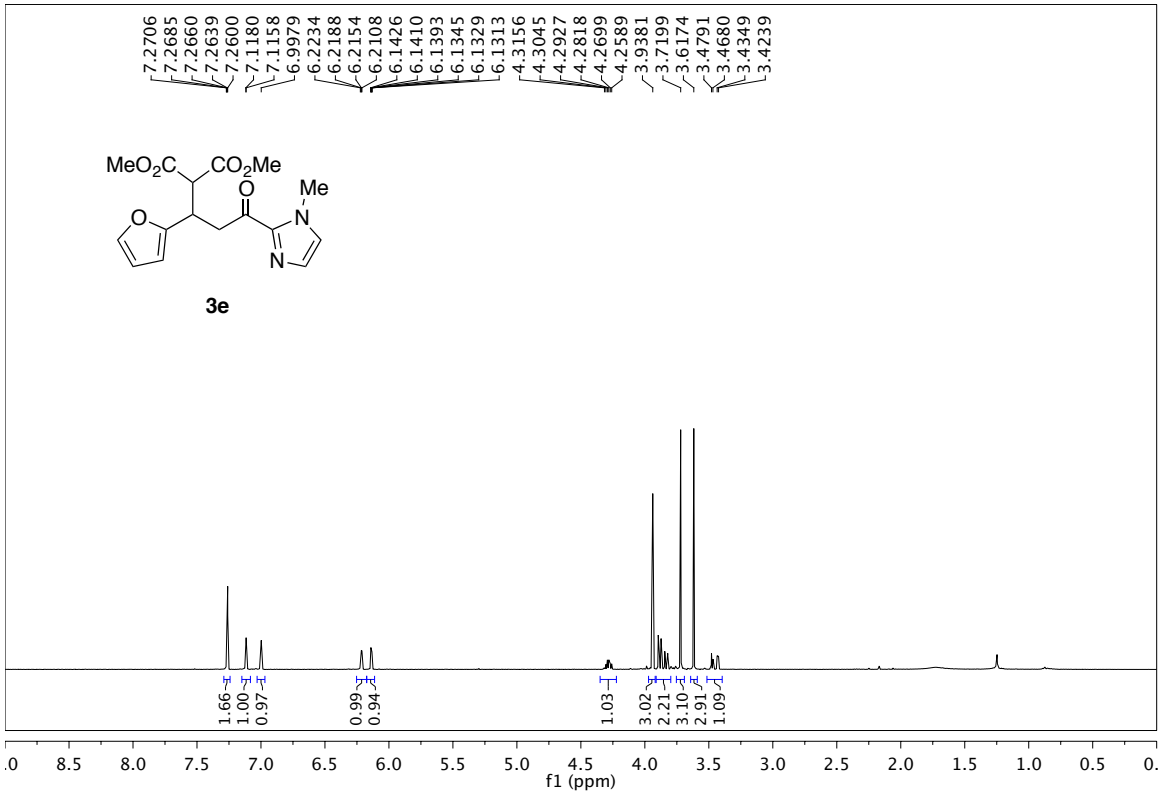


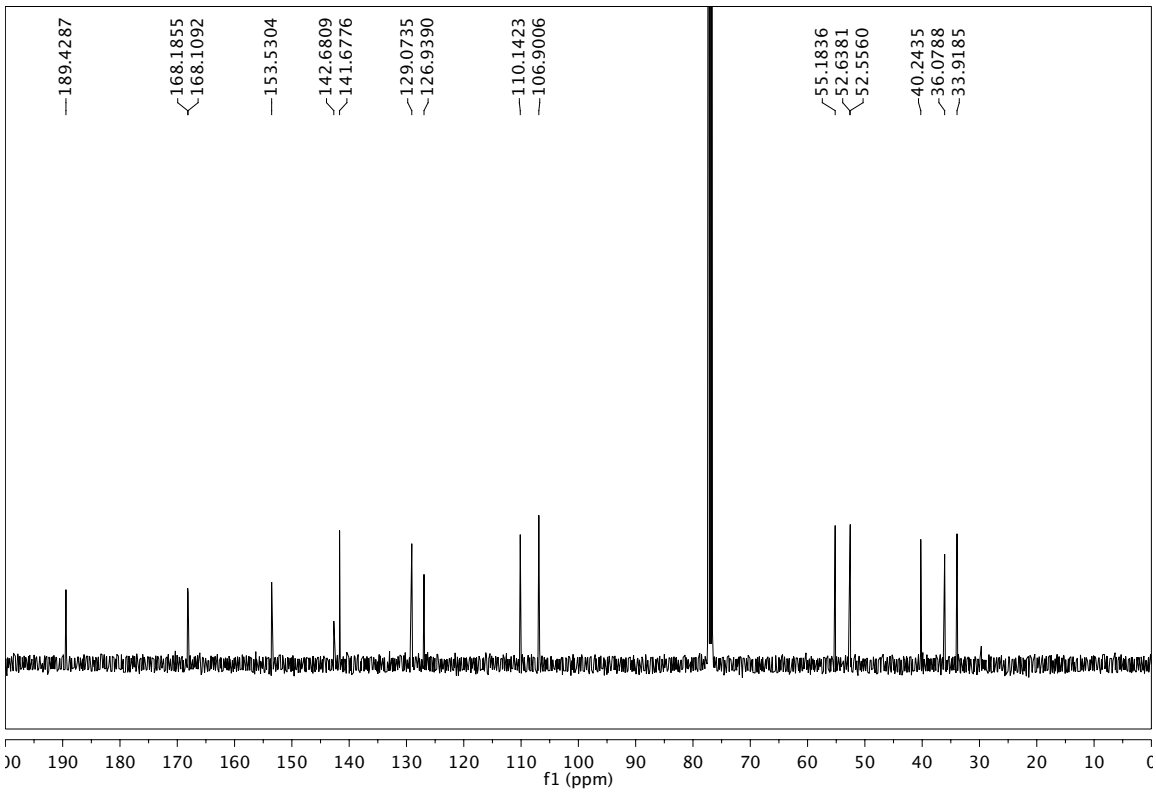
Dimethyl 2-(1-(4-chlorophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3d)





Dimethyl 2-(1-(furan-2-yl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3e)

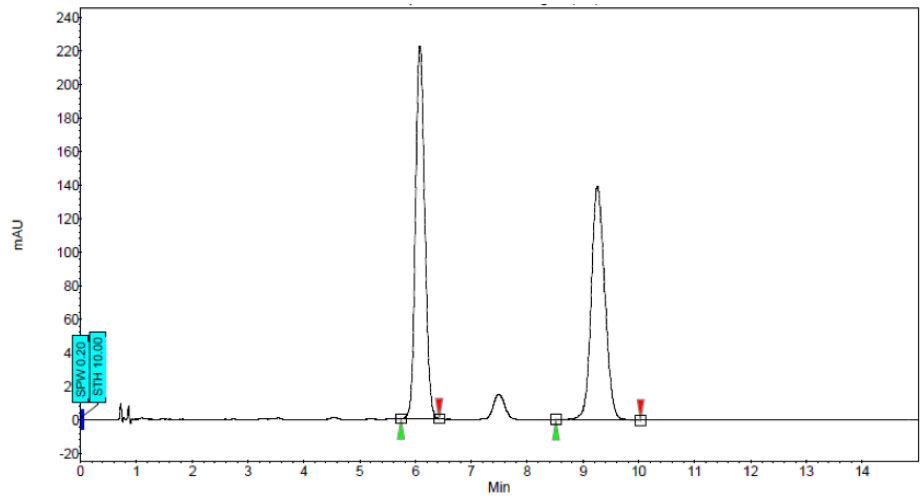




SFC Chromatograms

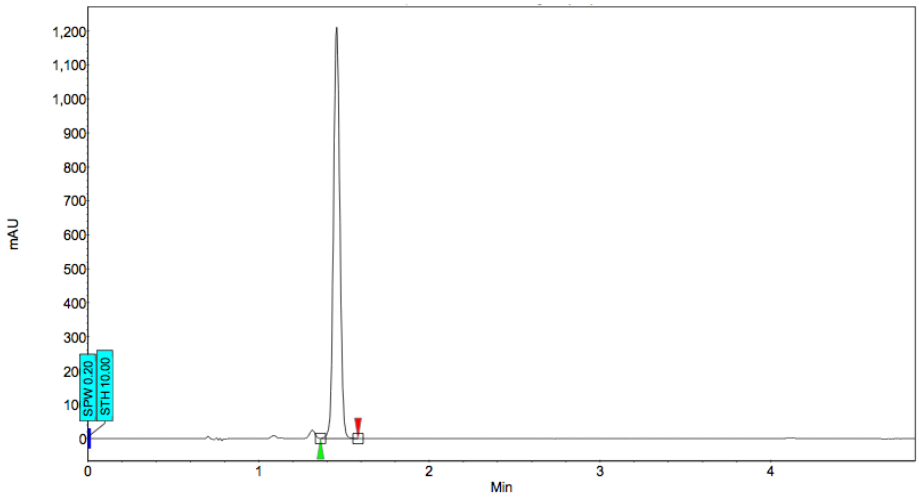
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2a)

Racemic (2a) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; first enantiomer t_R = 6.07; second enantiomer t_R = 9.26 min].



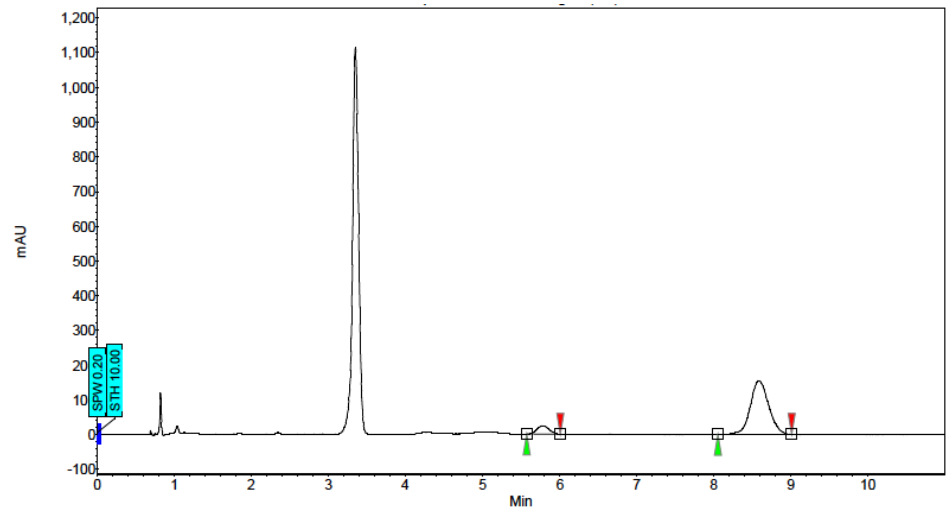
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	6.07	52.020
2	UNKNOWN	9.26	47.980
Total			100.000

Starting material (1a) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; t_R = 1.46 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.46	100.000
Total			100.000

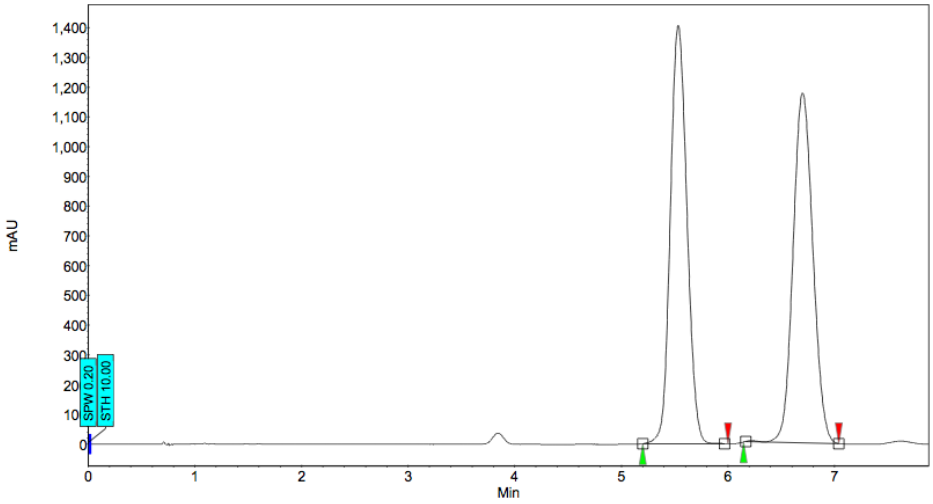
Following general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.56 min; minor enantiomer t_R = 5.78 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.78	23.9	4.3	9.170	0.00	0.00
2	UNKNOWN	8.58	155.0	42.4	90.830	1.49	7.85
Total			178.9	46.7	100.000		

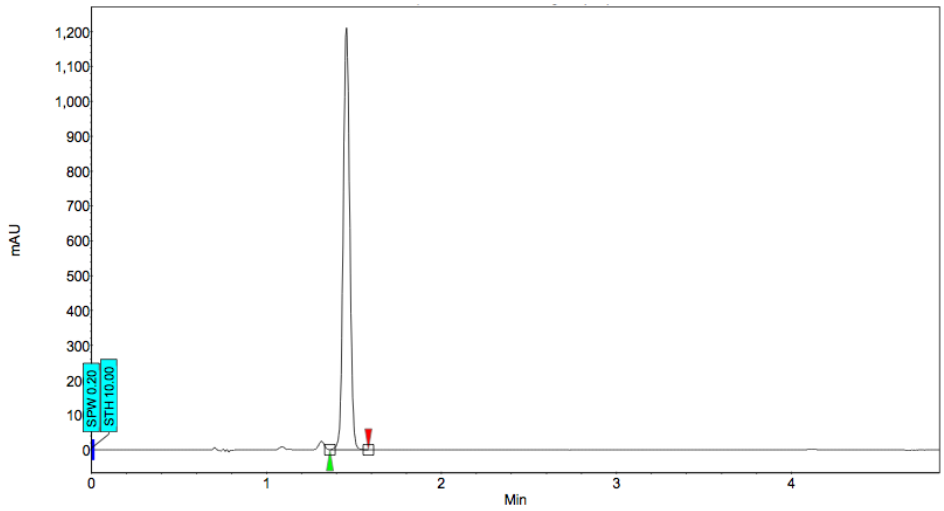
3-(5-Chloro-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2b)

Racemic 2b: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; first enantiomer t_R = 5.53 min; second enantiomer t_R = 6.70 min].



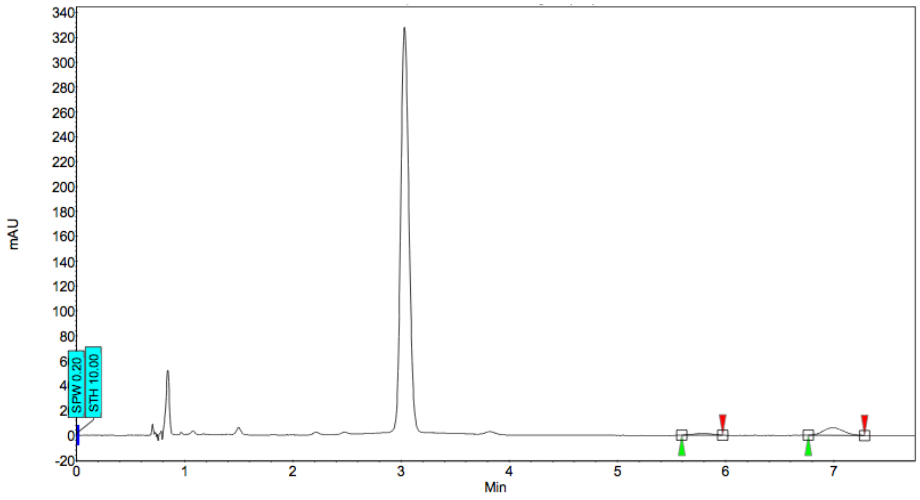
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.53	50.045
2	UNKNOWN	6.70	49.955
Total			100.000

Starting material 1a: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; t_R = 1.46 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.46	100.000
Total			100.000

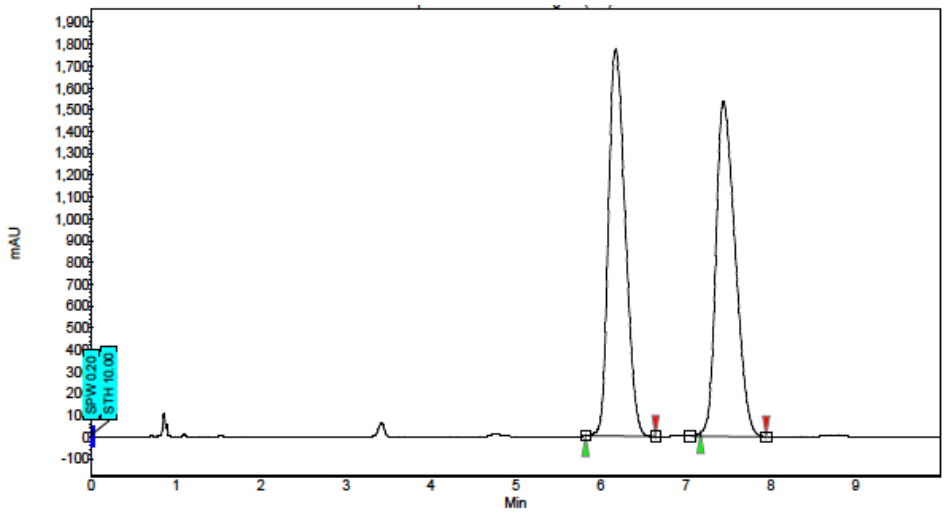
Following general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 7.00 min; minor enantiomer t_R = 5.80 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.80	16.698
2	UNKNOWN	7.00	83.302
Total			100.000

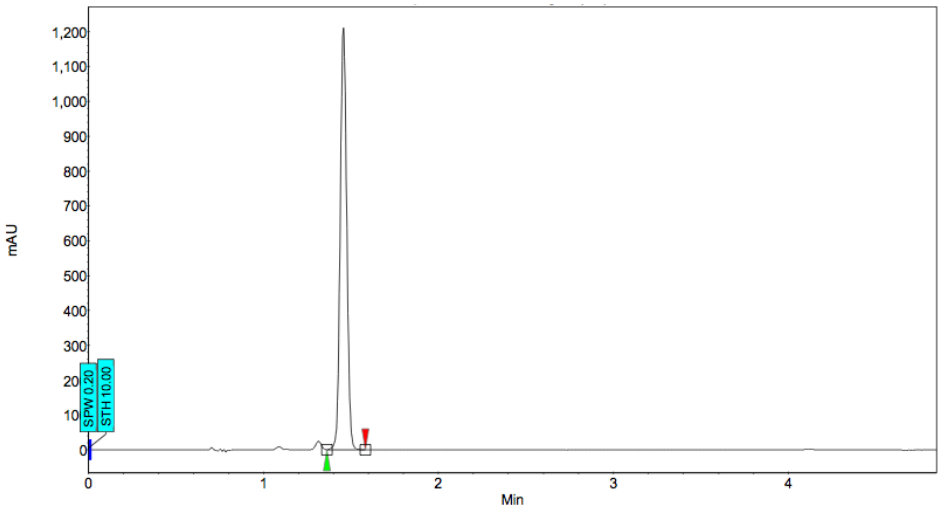
3-(5-Bromo-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)butan-1-one (2c)

Racemic (2c) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; first enantiomer t_R = 6.18 min; second enantiomer t_R = 7.44 min].



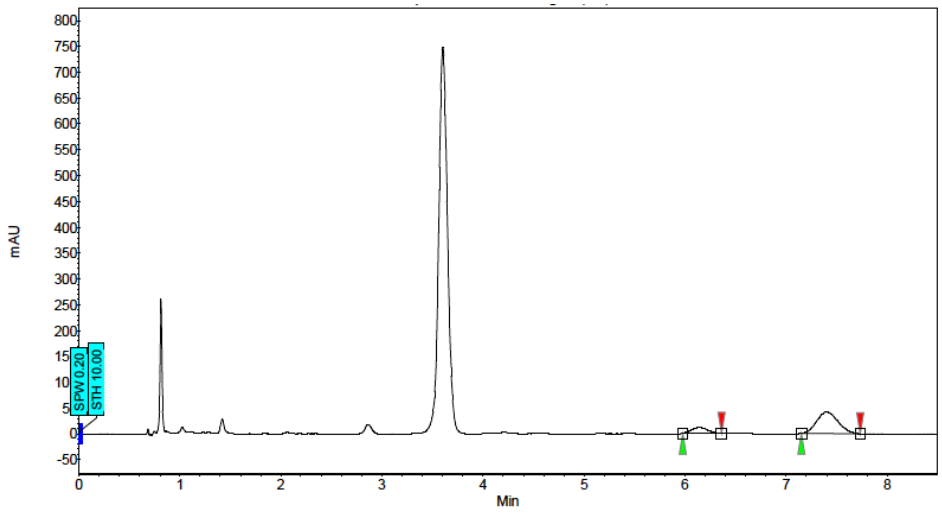
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	6.18	1777.1	403.4	49.966	0.00	0.00
2	UNKNOWN	7.44	1535.8	403.9	50.034	1.21	3.22
Total			3312.9	807.3	100.000		

Starting material (1a) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; t_R = 1.46 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.46	100.000
Total			100.000

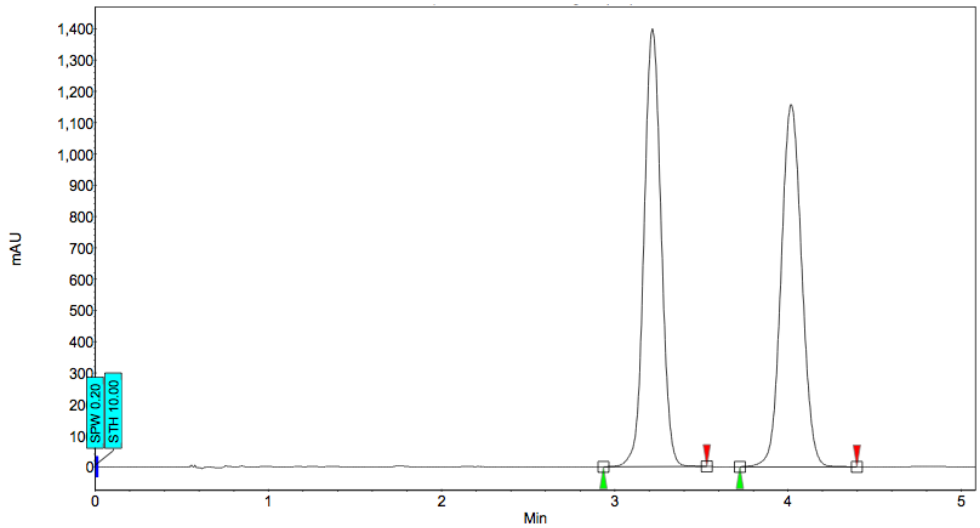
Following general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 7.40 min; minor enantiomer t_R = 6.14 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	6.14	11.2	2.1	16.985	0.00	0.00
2	UNKNOWN	7.40	41.5	10.1	83.015	1.21	3.62
Total			52.8	12.2	100.000		

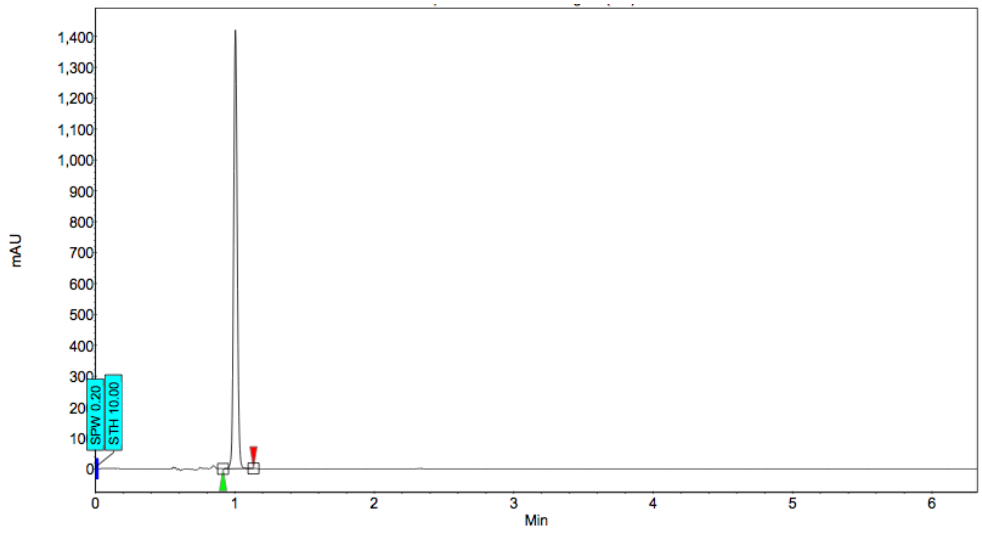
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)butan-1-one (2d)

Racemic (2d) [DAICEL AD-H column; 100 bar; flow: 5.0 mL/min; 15% *i*-PrOH; λ = 220 nm; first enantiomer t_R = 3.22 min; second enantiomer t_R = 4.02 min].



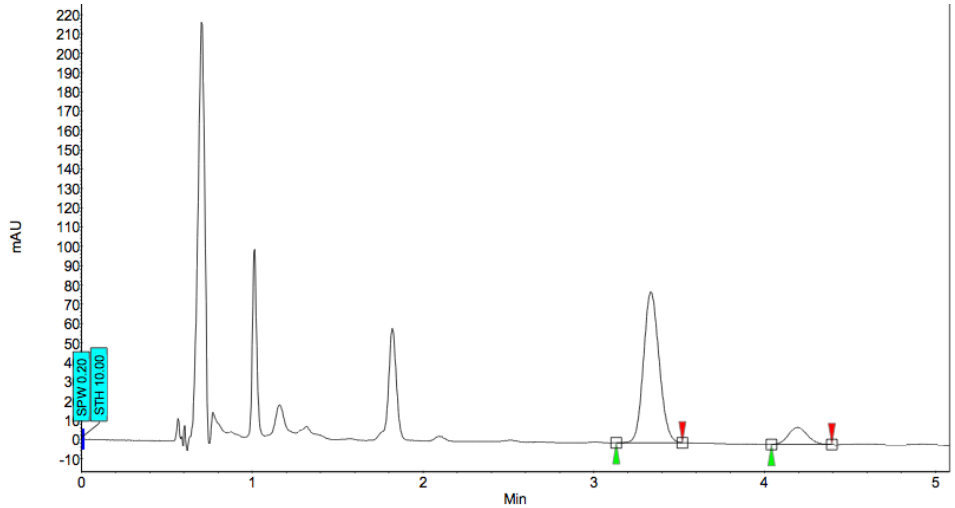
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	3.22	49.967
2	UNKNOWN	4.02	50.033
Total			100.000

Starting material (1a) [DAICEL AD-H column; 100 bar; flow: 15.0 mL/min; 15% *i*-PrOH; λ = 220 nm; t_R = 1.00 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.00	100.000
Total			100.000

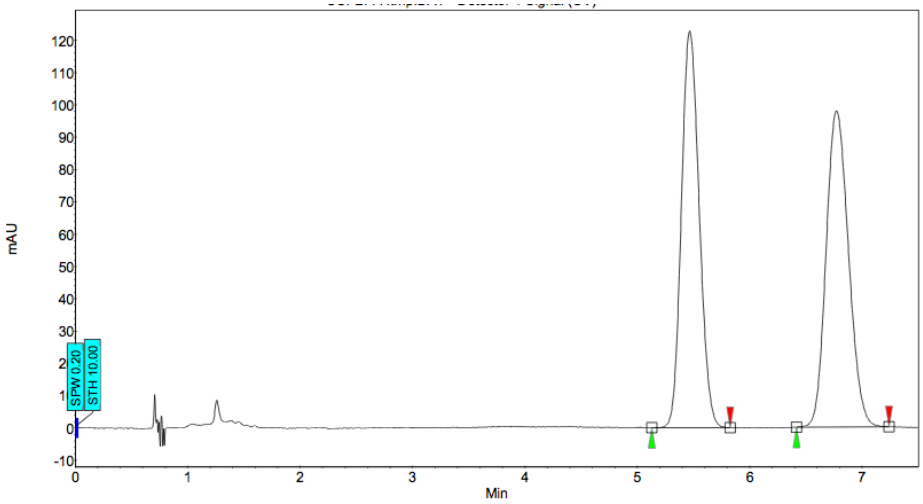
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 15.0 mL/min; 15% *i*-PrOH; λ = 220 nm, major enantiomer t_R = 3.33 min; minor enantiomer t_R = 4.19 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	3.33	87.814
2	UNKNOWN	4.19	12.186
Total			100.000

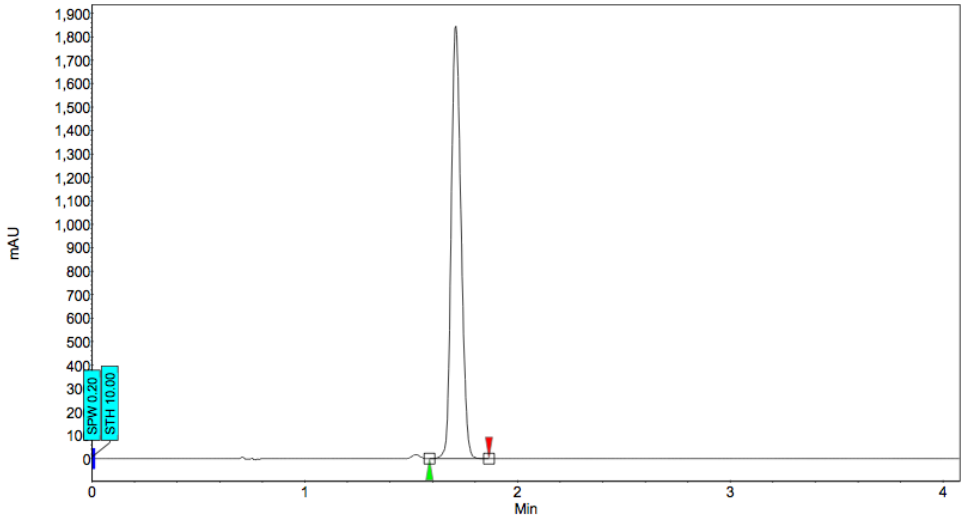
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)hexan-1-one (2e)

Racemic 2e: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm; first enantiomer t_R = 5.47 min; second enantiomer t_R = 6.77 min].



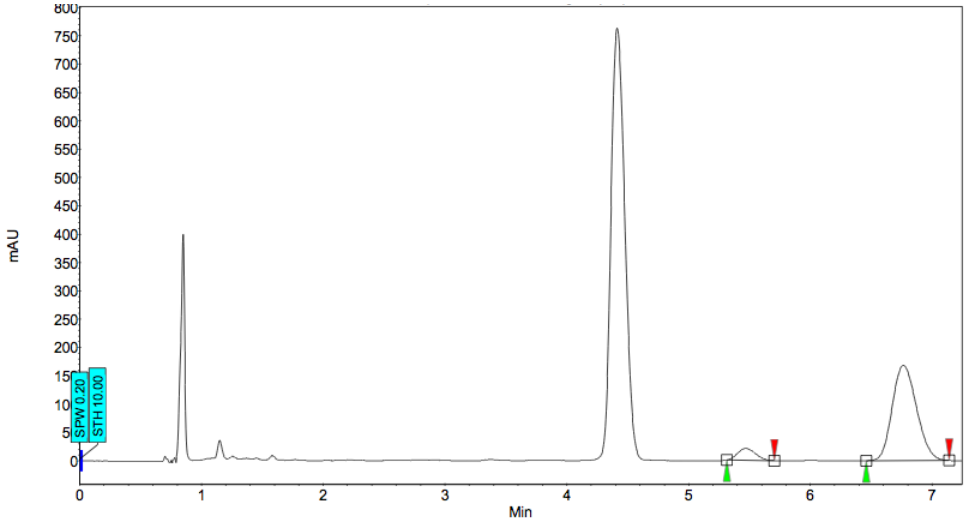
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.47	49.898
2	UNKNOWN	6.77	50.102
Total			100.000

Starting material 1b: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm; t_R = 1.71 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.71	100.000
Total			100.000

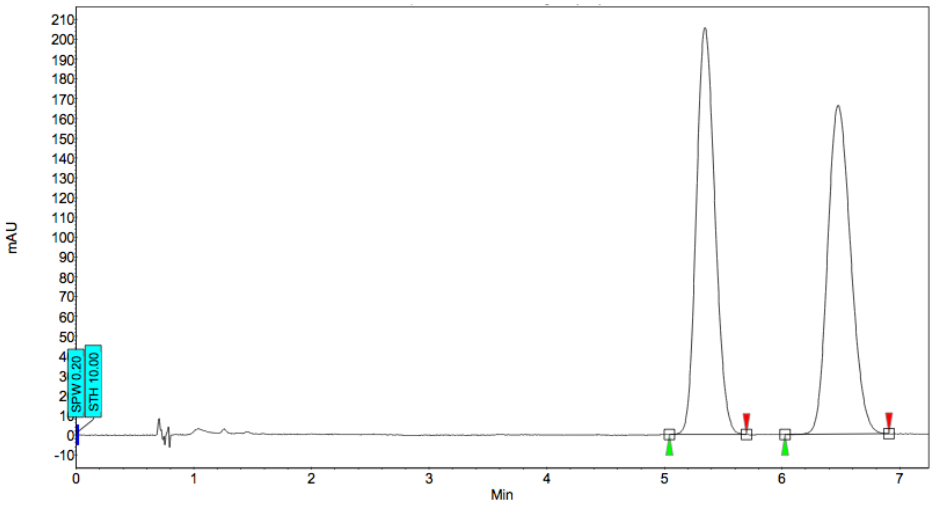
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm, major enantiomer t_R = 6.76 min; minor enantiomer t_R = 5.47 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.47	8.490
2	UNKNOWN	6.76	91.510
Total			100.000

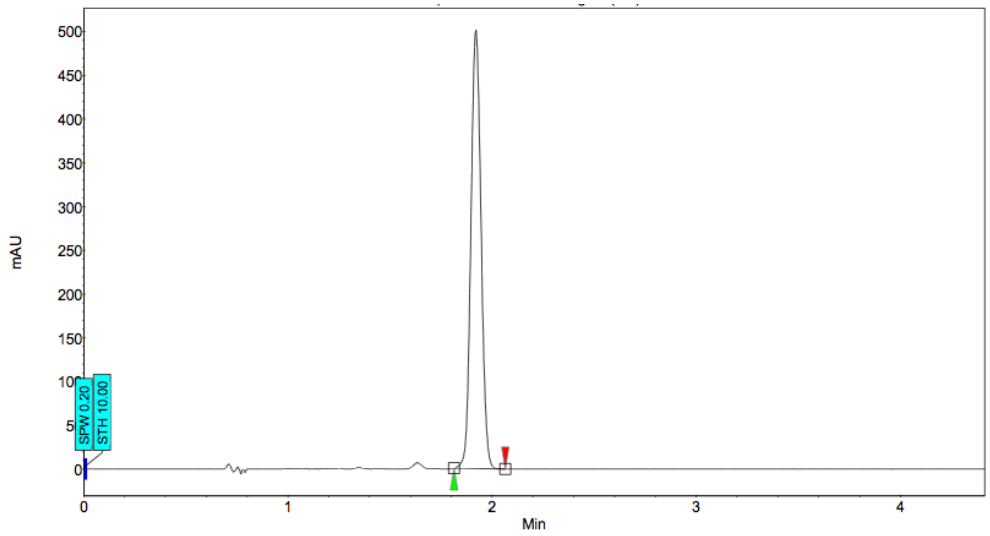
3-(5-Methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl)octan-1-one (2f)

Racemic **2f**: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm; first enantiomer t_R = 5.34 min; second enantiomer t_R = 6.48 min].



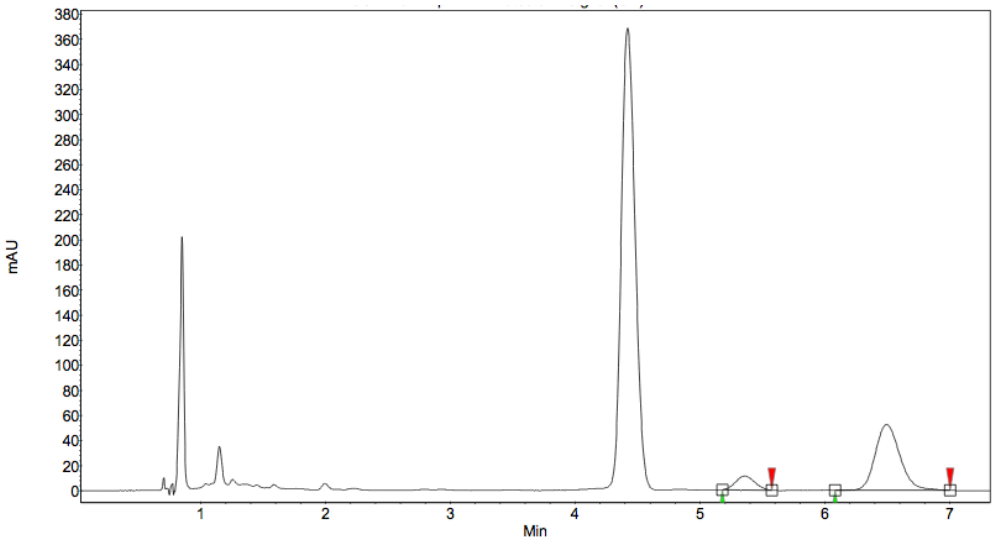
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.34	49.990
2	UNKNOWN	6.48	50.010
Total			100.000

Starting material (1c) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm; tR = 1.92 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.92	100.000
Total			100.000

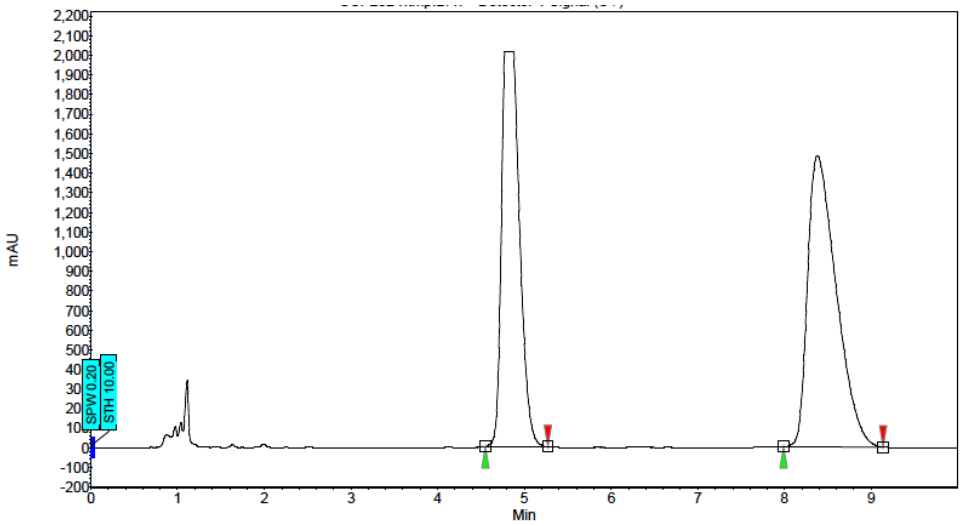
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 12% MeOH; λ = 220 nm; major enantiomer; t_R = 6.50 min; minor enantiomer; t_R = 5.35 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.35	13.998
2	UNKNOWN	6.50	86.002
Total			100.000

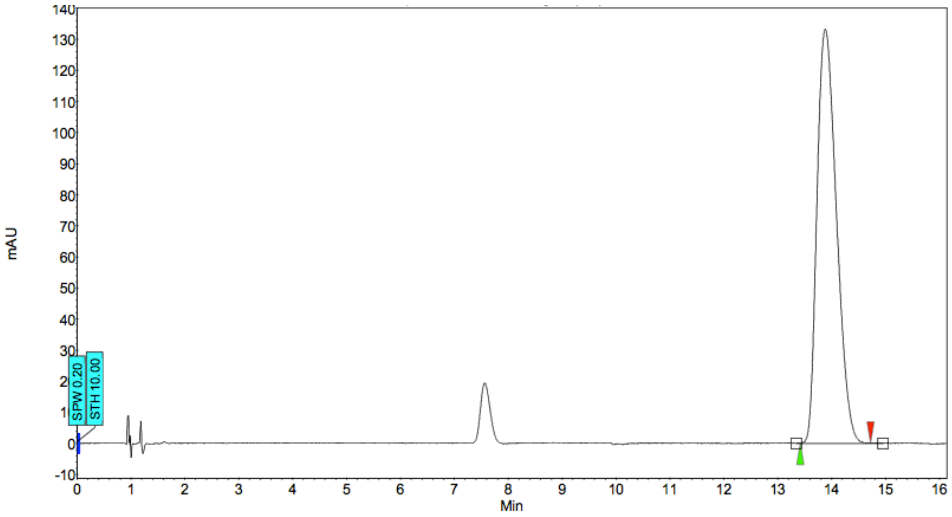
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(5-methoxy-1*H*-indol-3-yl)-3-phenylpropan-1-one (2g)

Racemic (2g) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm; first enantiomer t_R = 4.87 min; second enantiomer t_R = 8.38 min]



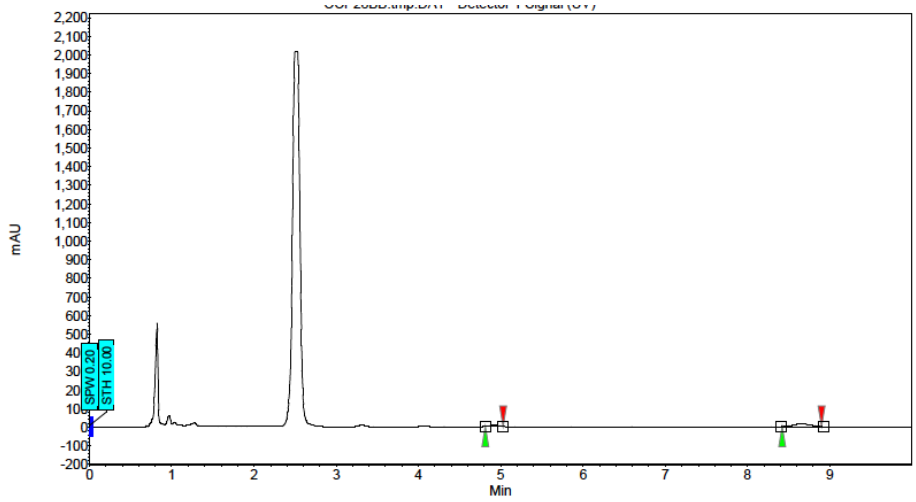
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	4.87	2014.3	489.8	46.299	0.00	0.00
2	UNKNOWN	8.38	1484.4	568.1	53.701	1.72	7.08
Total			3498.8	1058.0	100.000		

Starting material (1d) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm; t_R = 13.88 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	13.88	100.000
Total			100.000

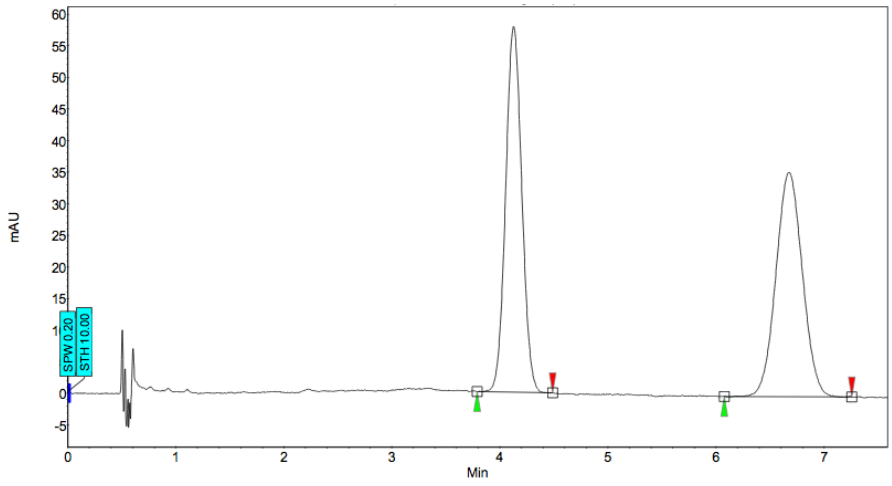
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm, major enantiomer t_R = 8.67 min; minor enantiomer t_R = 4.92 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	4.92	6.8	0.9	18.927	0.00	0.00
2	UNKNOWN	8.67	13.3	3.7	81.073	1.76	11.00
Total			20.1	4.5	100.000		

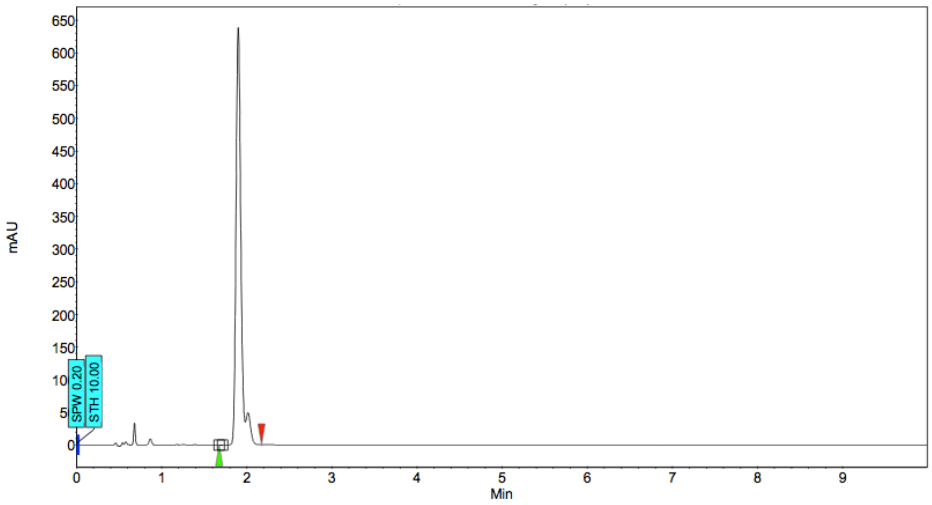
3-(5-Methoxy-1*H*-indol-3-yl)-3-(4-methoxyphenyl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one (2h)

Racemic (2h) [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm; first enantiomer t_R = 4.13 min; second enantiomer t_R = 6.68 min]



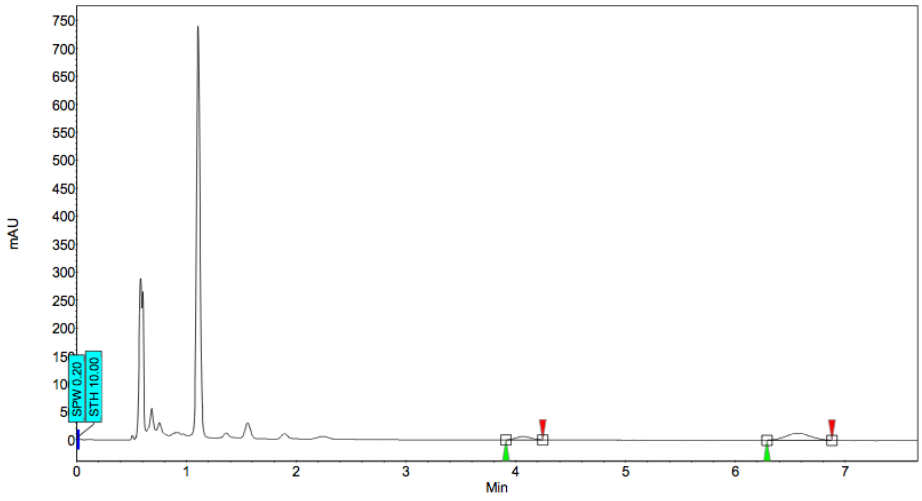
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	4.13	49.963
2	UNKNOWN	6.68	50.037
Total			100.000

Starting material (1e) [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm; t_R = 1.90 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	1.90	100.000
Total			100.000

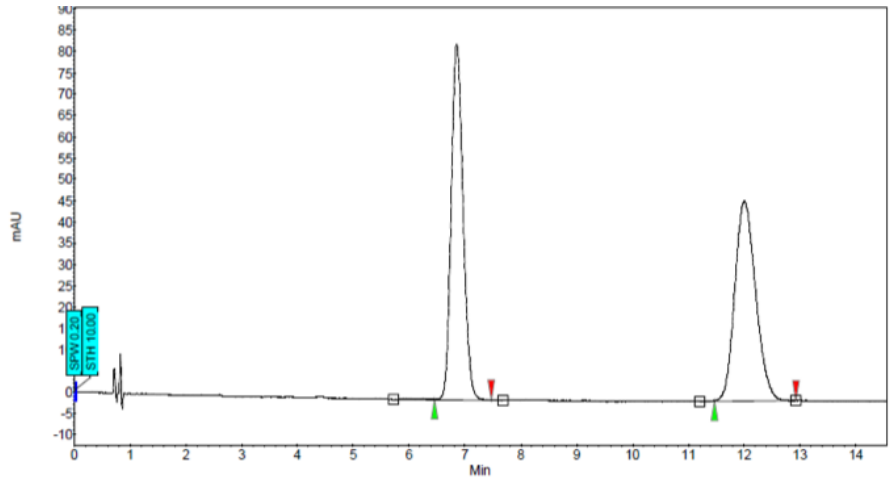
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm, major enantiomer t_R = 6.56 min; minor enantiomer t_R = 4.07 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	4.07	22.720
2	UNKNOWN	6.56	77.280
Total			100.000

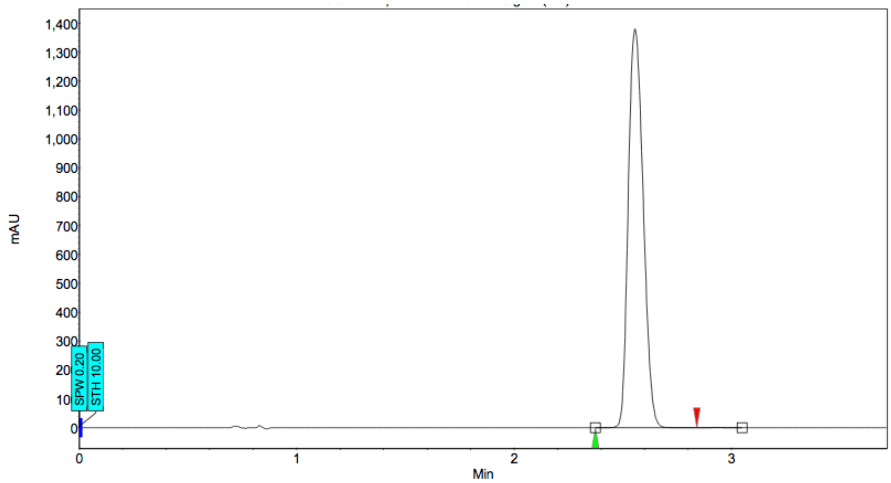
3-(4-Chlorophenyl)-3-(5-methoxy-1*H*-indol-3-yl)-1-(1-methyl-1*H*-imidazol-2-yl) propan-1-one(2i)

Racemic (2i) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm; first enantiomer t_R = 6.85 min; second enantiomer t_R = 12.00 min]



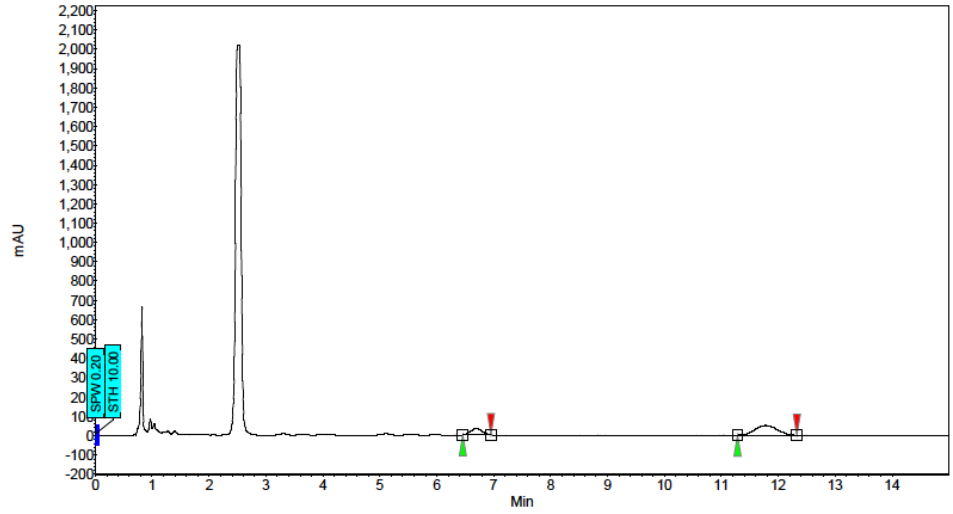
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	6.85	50.227
2	UNKNOWN	12.00	49.773
Total			100.000

Starting material **1f**: [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm; t_R = 6.11 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	2.56	100.000
Total			100.000

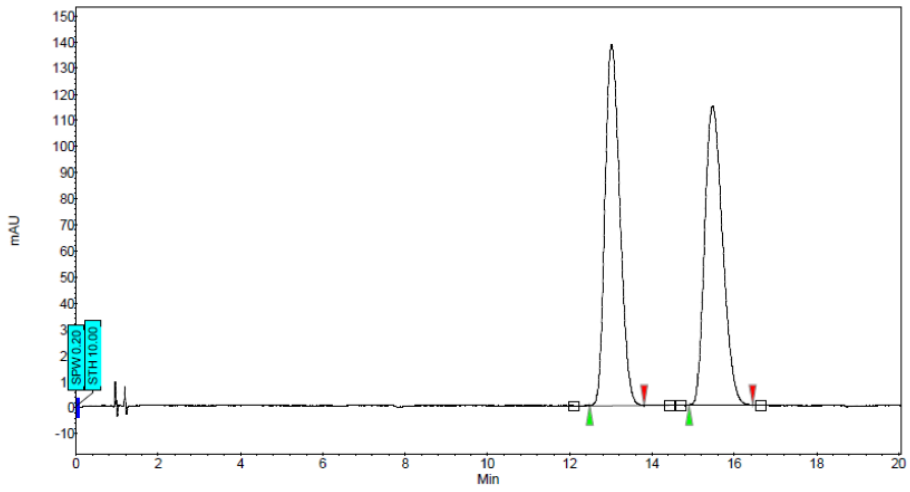
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 20% MeOH; λ = 220 nm, major enantiomer t_R = 11.77 min; minor enantiomer t_R = 6.69 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	6.69	32.9	7.8	25.760	0.00	0.00
2	UNKNOWN	11.77	51.1	22.4	74.240	1.76	9.32
Total			83.9	30.1	100.000		

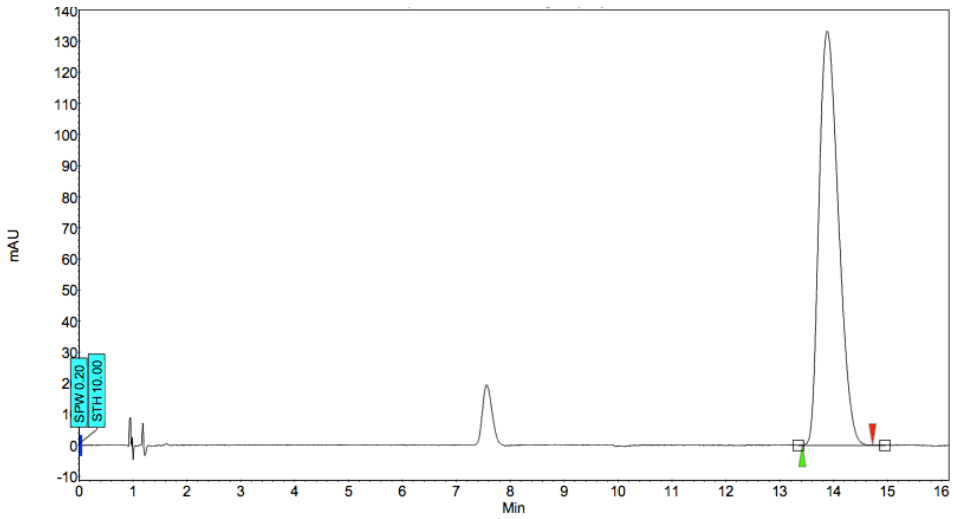
1-(1-Methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)-3-phenylpropan-1-one (2j)

Racemic (2j) [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm; first enantiomer t_R = 13.01 min; second enantiomer t_R = 15.47 min]



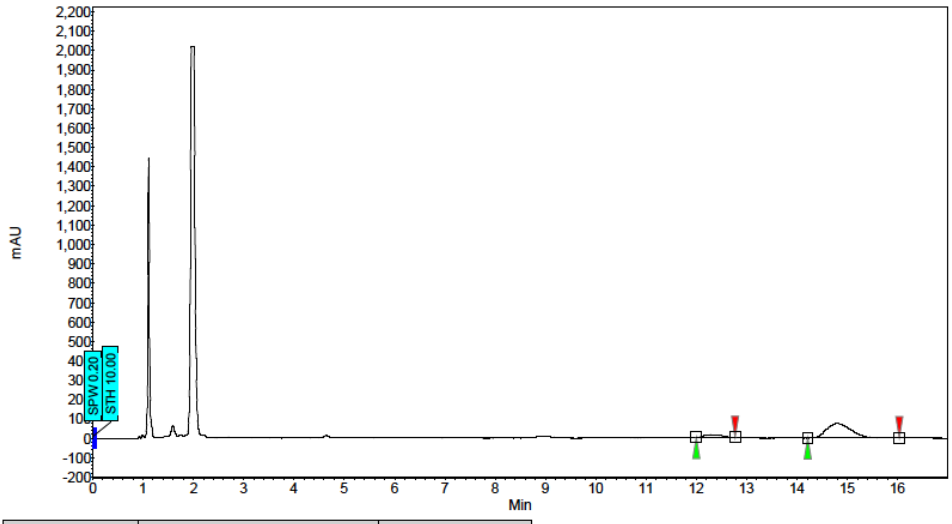
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	13.01	50.044
2	UNKNOWN	15.47	49.956
Total			100.000

Starting material (1d) [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm; t_R = 13.88 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	13.88	100.000
Total			100.000

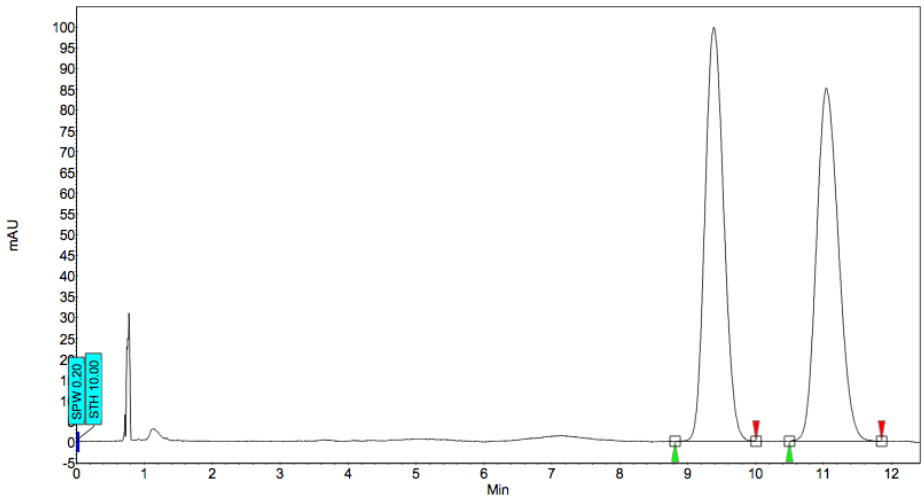
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm, major enantiomer t_R = 14.80 min; minor enantiomer t_R = 12.33 min]



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	12.33	13.4	5.7	11.821	0.00	0.00
2	UNKNOWN	14.80	73.8	42.5	88.179	1.20	2.98
Total			87.2	48.2	100.000		

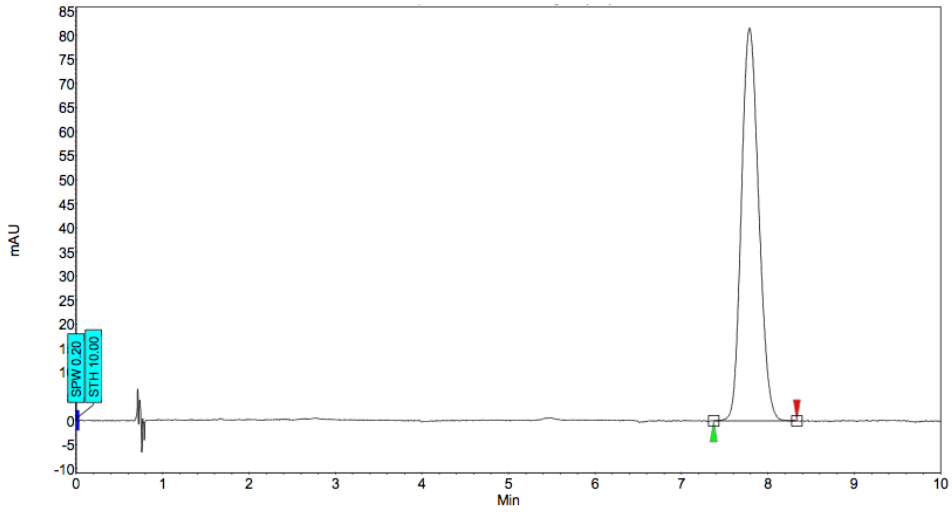
3-(2-Bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(1-methyl-1*H*-indol-3-yl)propan-1-one (2k)

Racemic (2k) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm; first enantiomer t_R = 9.39 min; second enantiomer t_R = 11.04 min]



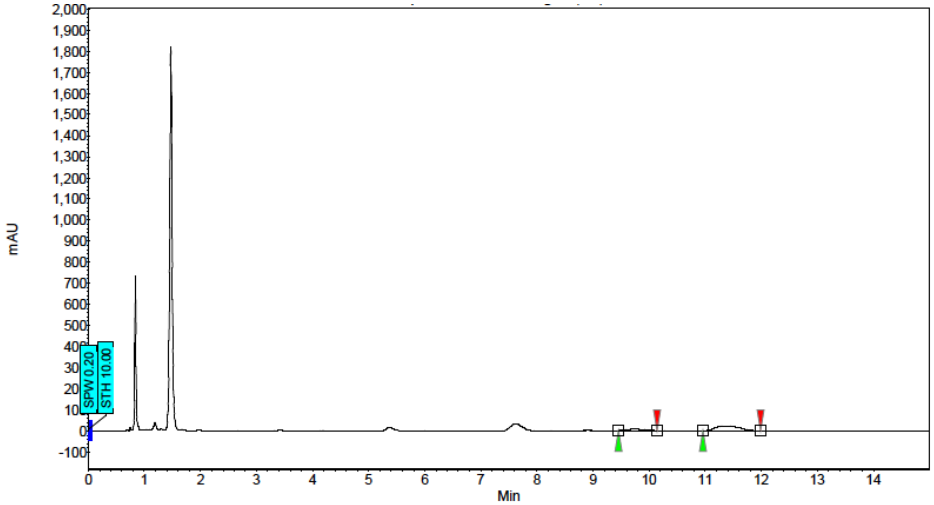
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	9.39	49.885
2	UNKNOWN	11.04	50.115
Total			100.000

Starting material (1g) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm; t_R = 7.79 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	7.79	100.000
Total			100.000

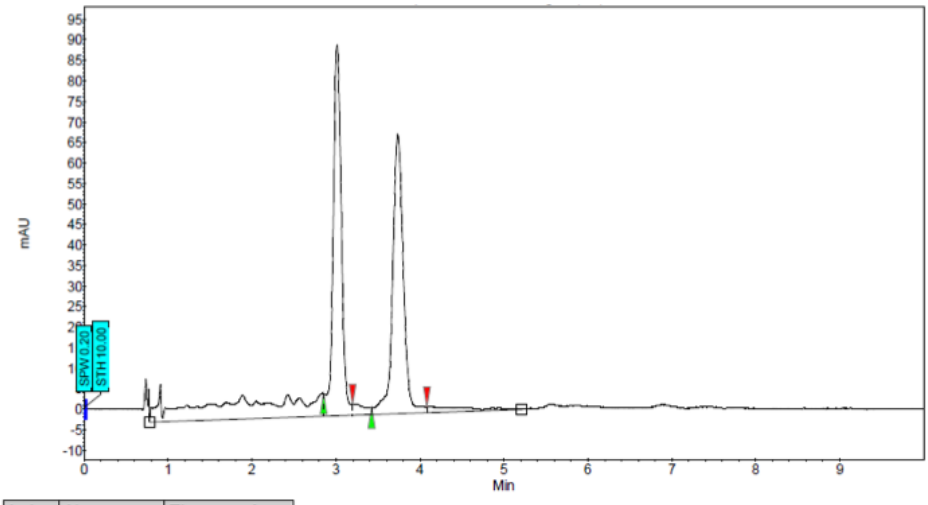
Following the general procedure **D** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm, major enantiomer t_R = 11.36 min; minor enantiomer t_R = 9.74 min]



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	9.74	7.3	2.8	19.197	0.00	0.00
2	UNKNOWN	11.36	24.1	11.7	80.803	1.17	2.23
Total			31.4	14.5	100.000		

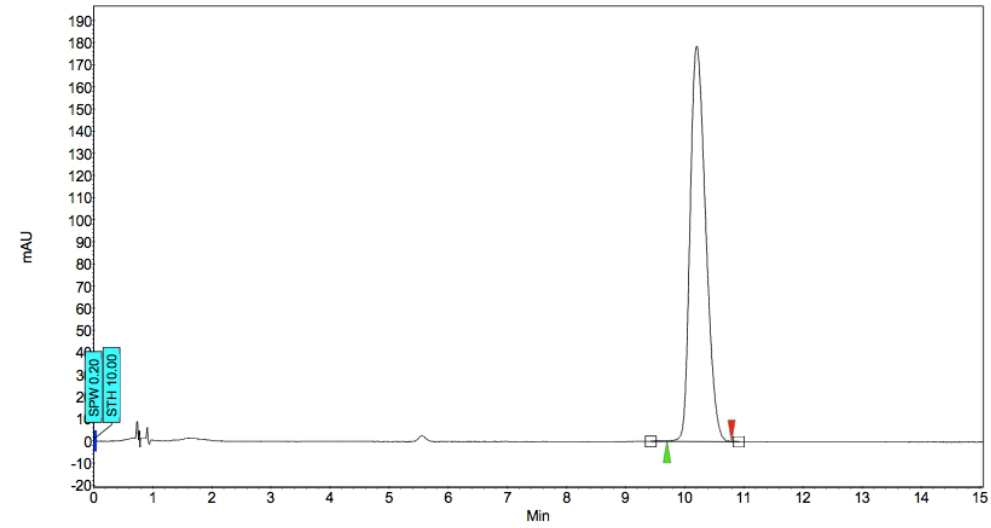
Dimethyl 2-(3-(1-methyl-1*H*-imidazol-2-yl)-3-oxo-1-phenylpropyl)malonate (3a)

Racemic (3a) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm; first enantiomer t_R = 3.01 min; second enantiomer t_R = 3.74 min]



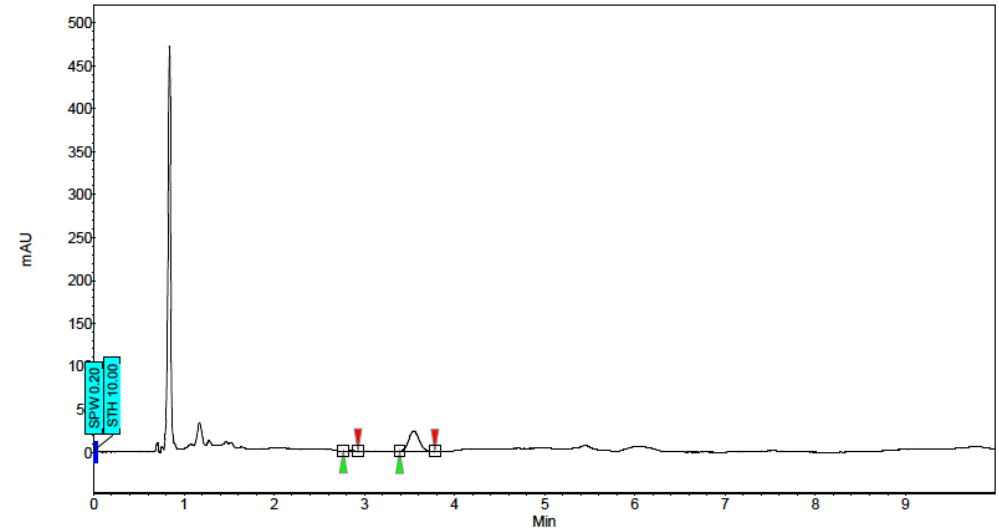
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	3.01	49.726
2	UNKNOWN	3.74	50.274
Total			100.000

Starting material (1d) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm; t_R = 10.20 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	10.20	100.000
Total			100.000

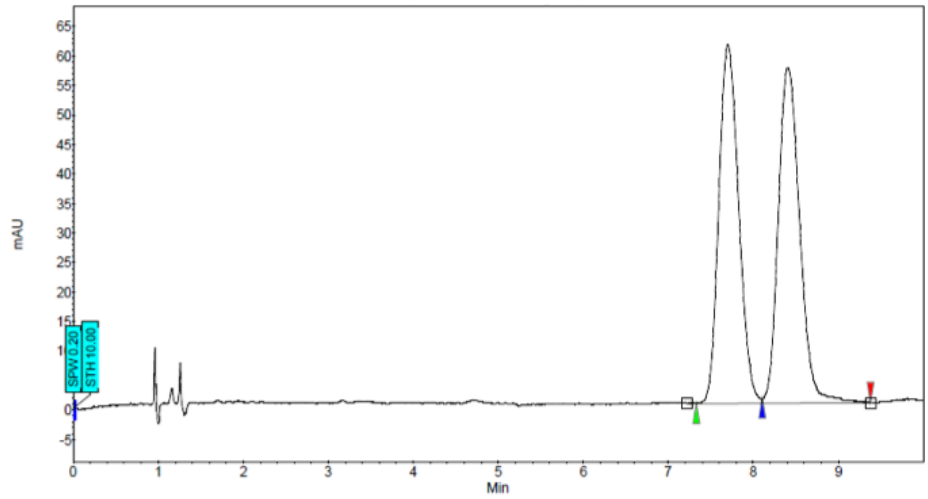
Following the general procedure **F** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 10% MeOH; λ = 220 nm, major enantiomer t_R = 3.55 min; minor enantiomer t_R = 2.85 min]



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
2	UNKNOWN	2.85	0.8	0.1	1.560	0.00	0.00
1	UNKNOWN	3.55	23.8	3.2	98.440	1.24	4.39
Total			24.5	3.3	100.000		

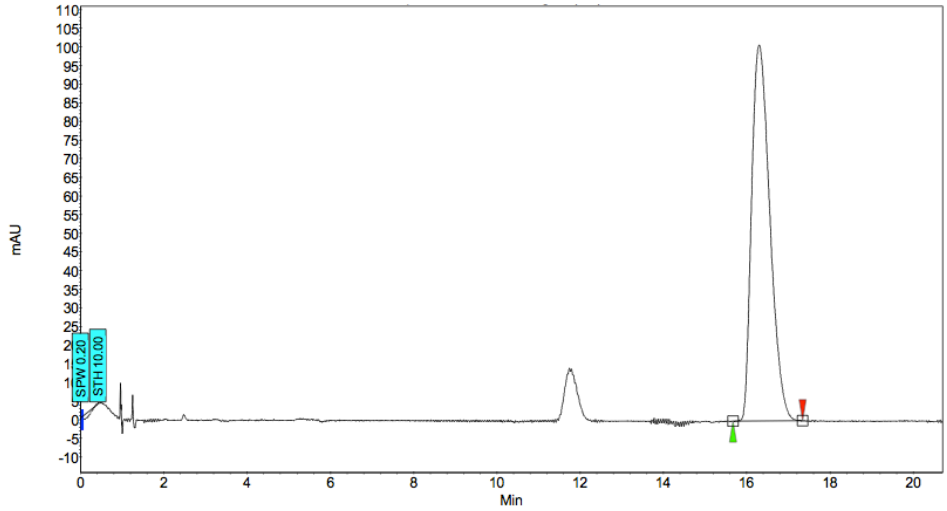
Dimethyl 2-(1-(2-bromophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3b)

Racemic (3b) [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 7% MeOH; λ = 220 nm; first enantiomer t_R = 8.41 min; second enantiomer t_R = 7.70 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	7.70	49.740
2	UNKNOWN	8.41	50.260
Total			100.000

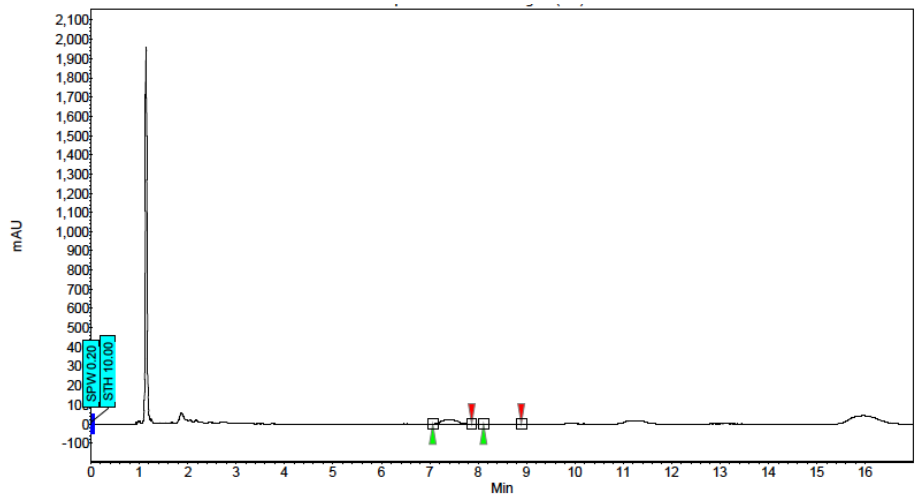
Starting material (1g) [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 7% MeOH; λ = 220 nm; t_R = 16.30 min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	16.30	100.000
Total			100.000

v

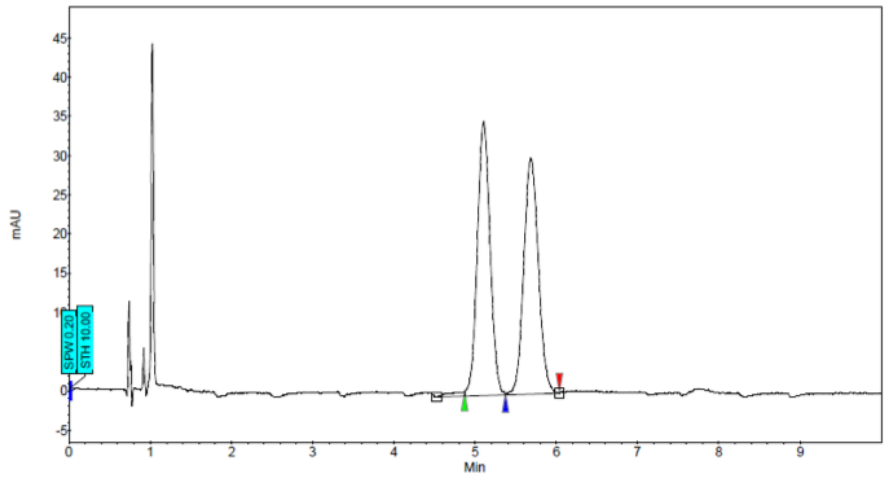
Following the general procedure **F** [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 7% MeOH; λ = 220 nm, major enantiomer t_R = 7.40 min; minor enantiomer t_R = 8.70 min]



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	7.40	22.9	8.6	98.332	0.00	0.00
2	UNKNOWN	8.70	0.7	0.1	1.668	1.18	3.13
Total			23.6	8.7	100.000		

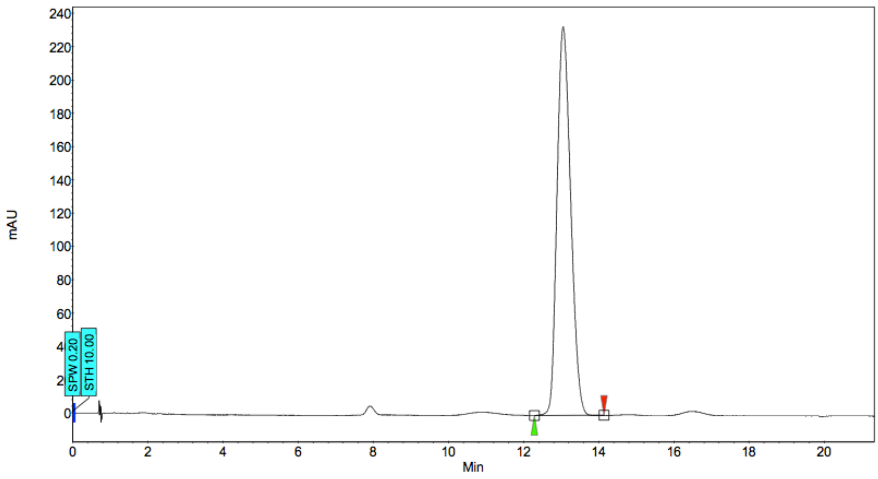
Dimethyl 2-(1-(4-methoxyphenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl) malonate (3c)

Racemic (3b) [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm; first enantiomer t_R = 5.10 min; second enantiomer t_R = 5.69 min]



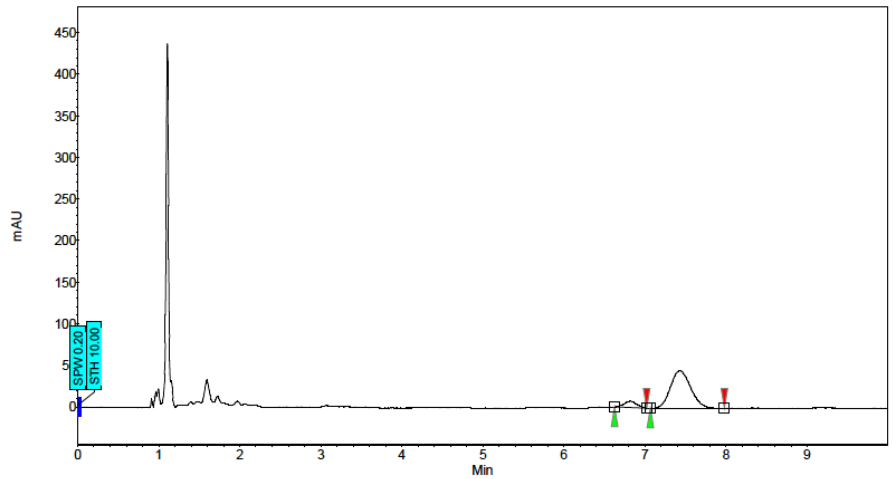
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	5.10	50.221
2	UNKNOWN	5.69	49.779
Total			100.000

Starting material (1e) [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm; t_R = min]



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	13.05	100.000
Total			100.000

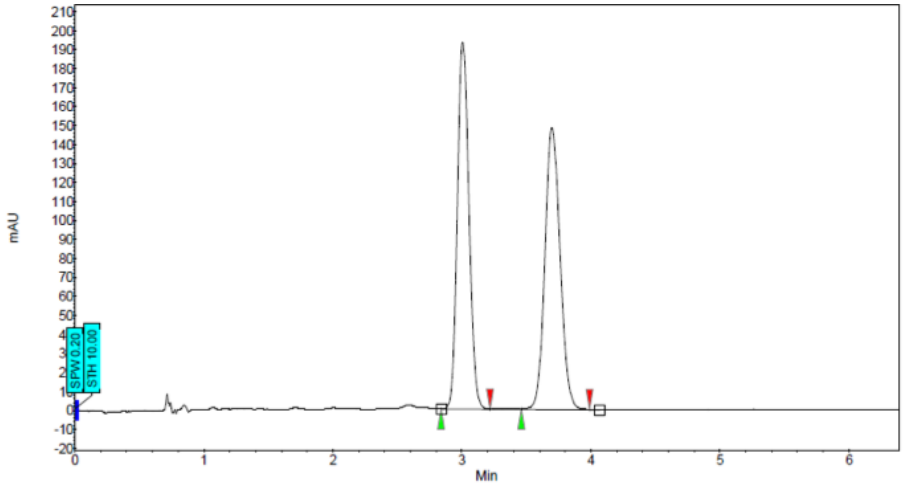
Following the general procedure **F** [DAICEL AD-H column; 100 bar; flow: 3.0 mL/min; 10% MeOH; λ = 220 nm, major enantiomer t_R = 7.44 min; minor enantiomer t_R = 6.83 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
2	UNKNOWN	6.83	7.6	1.3	9.355	0.00	0.00
1	UNKNOWN	7.44	45.2	13.1	90.645	1.09	1.64
Total			52.8	14.4	100.000		

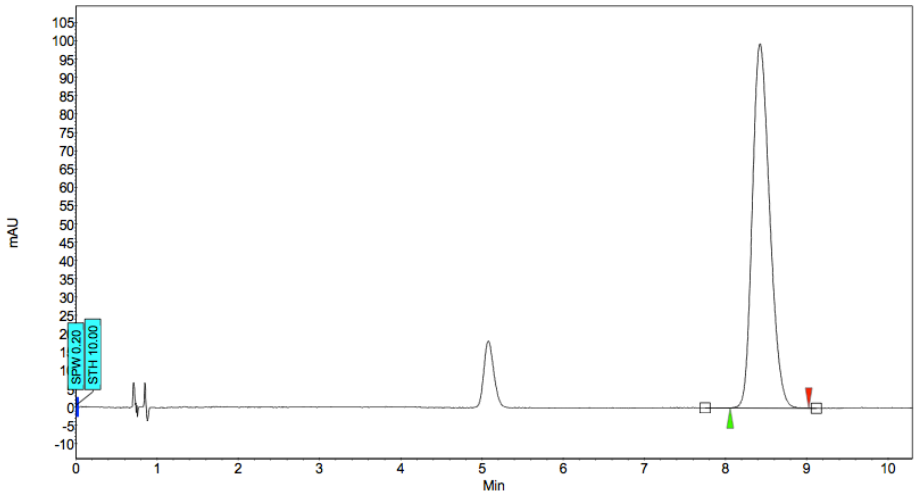
Dimethyl 2-(1-(4-chlorophenyl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl) malonate (3d)

Racemic (3d) [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm; first enantiomer t_R = 3.00 min; second enantiomer t_R = 3.70 min].



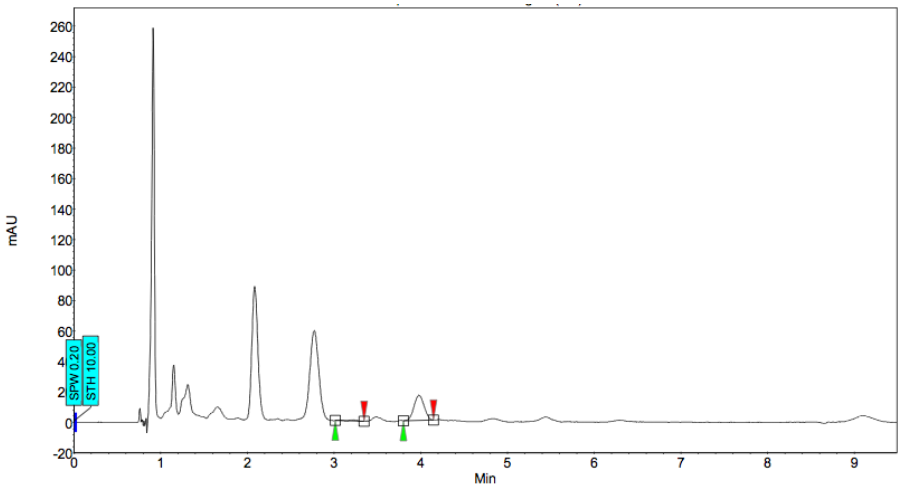
Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	3.00	49.745
2	UNKNOWN	3.70	50.255
Total			100.000

Starting material (1f) [DAICEL AD-H column; 100 bar; flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm; t_R = 8.42 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	8.42	100.000
Total			100.000

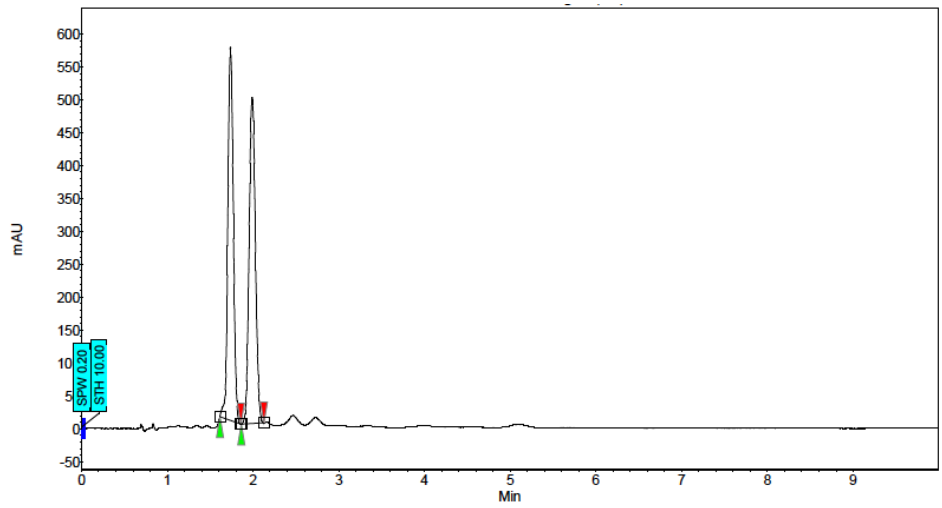
Following the general procedure **F** [DAICEL AD-H column; 100 bar flow: 6.0 mL/min; 30% *i*-PrOH; λ = 220 nm, major enantiomer t_R = 3.98 min; minor enantiomer t_R = 3.22 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	3.22	3.468
2	UNKNOWN	3.98	96.532
Total			100.000

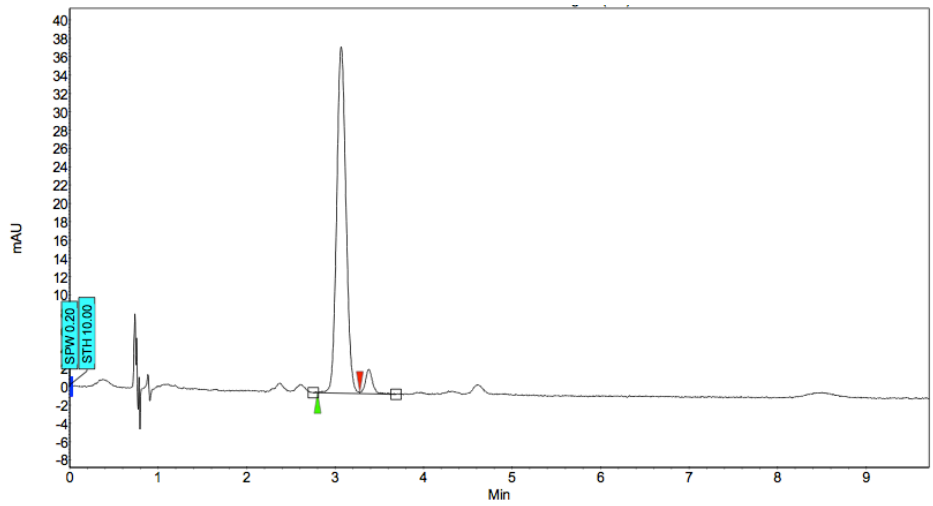
Dimethyl 2-(1-(furan-2-yl)-3-(1-methyl-1*H*-imidazol-2-yl)-3-oxopropyl)malonate (3e)

Racemic (3e) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; first enantiomer t_R = 1.74 min; second enantiomer t_R = 1.99 min].



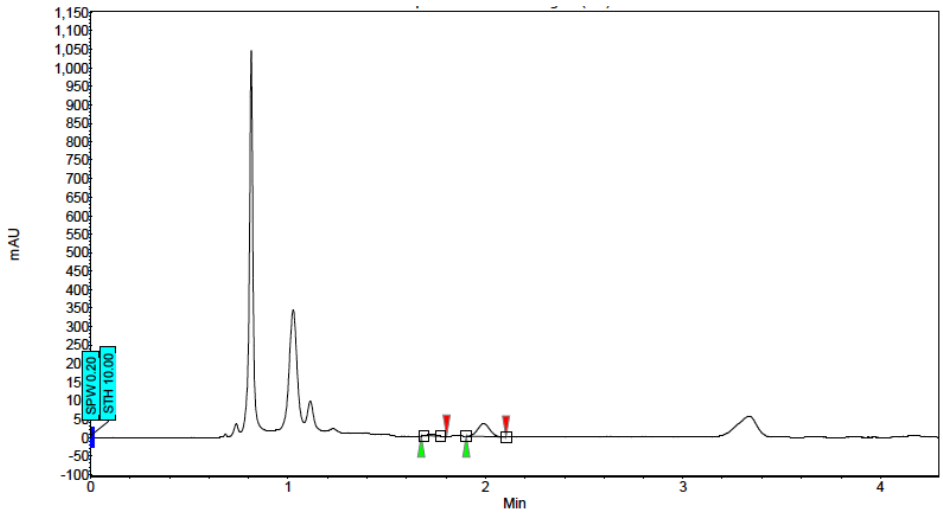
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	1.74	568.4	41.6	49.583	0.00	0.00
2	UNKNOWN	1.99	496.5	42.3	50.417	1.15	2.02
Total			1065.0	83.9	100.000		

Starting material (1h) [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm; t_R = 3.07 min].



Index	Name	Time	Area
		[Min]	[%]
1	UNKNOWN	3.07	100.000
Total			100.000

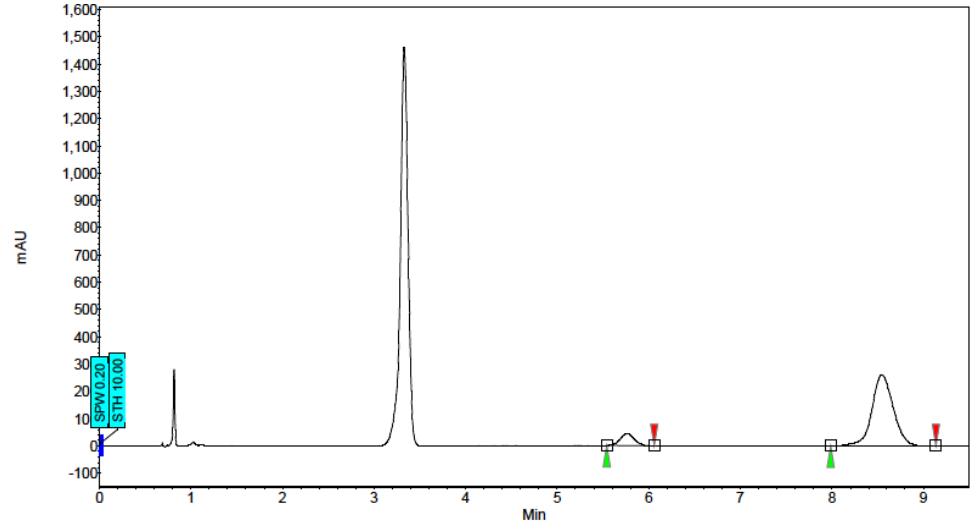
Following the general procedure **F** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 1.99 min; minor enantiomer t_R = 1.73 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	1.73	3.4	0.1	5.449	0.00	0.00
2	UNKNOWN	1.99	35.3	2.5	94.551	1.15	2.73
Total			38.6	2.6	100.000		

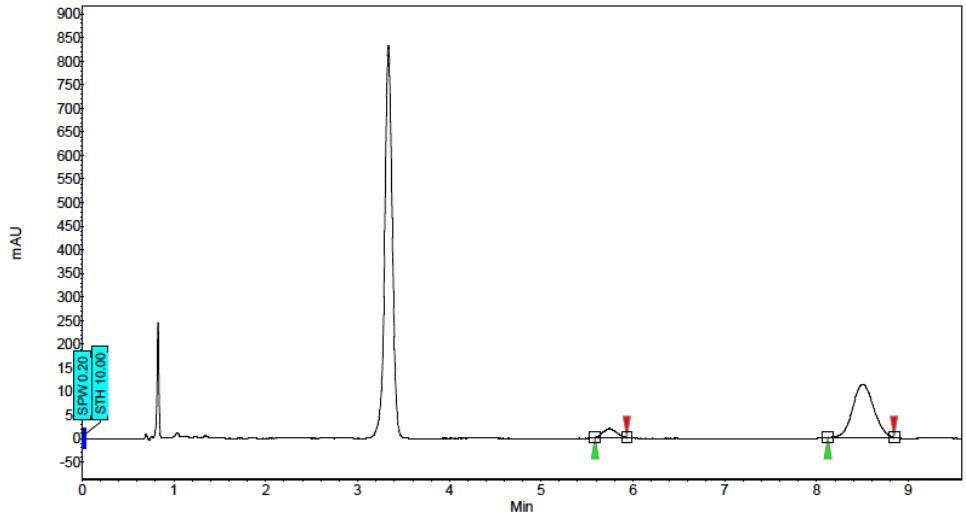
Enantioselective Recycling of Friedel Crafts alkylations

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.54 min; minor enantiomer t_R = 5.76 min].



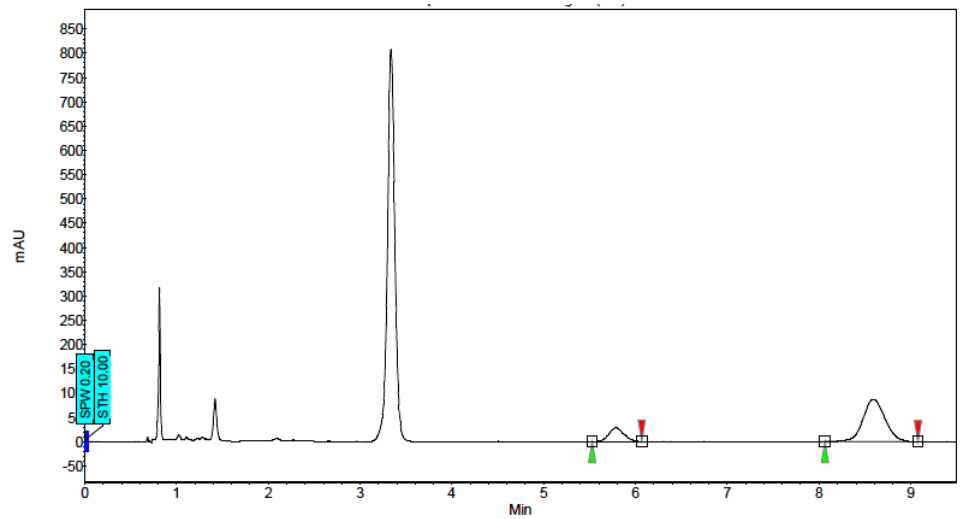
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.76	43.5	7.6	9.825	0.00	0.00
2	UNKNOWN	8.54	260.2	70.1	90.175	1.48	8.09
Total			303.7	77.7	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.50 min; minor enantiomer t_R = 5.75 min].



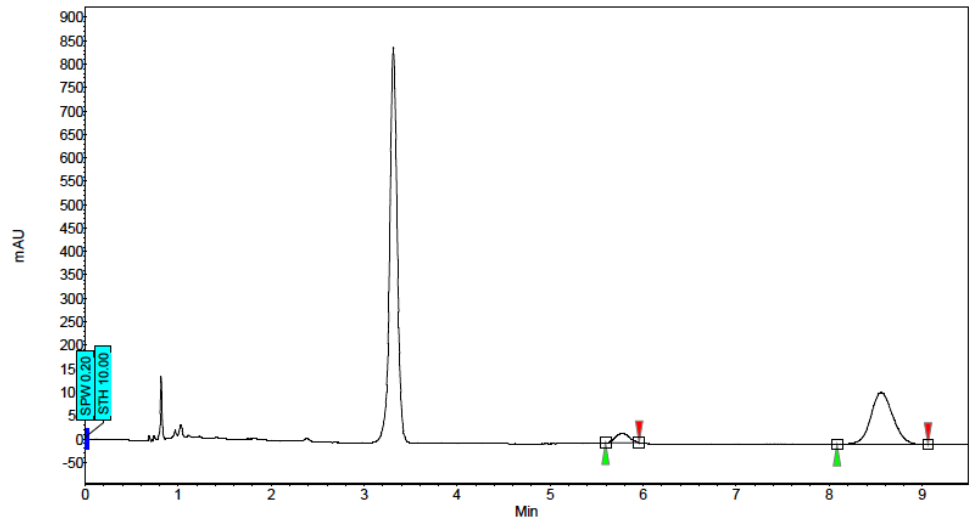
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.75	18.4	3.1	9.349	0.00	0.00
2	UNKNOWN	8.50	113.4	29.9	90.651	1.48	7.97
Total			131.8	33.0	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.59 min; minor enantiomer t_R = 5.79 min].



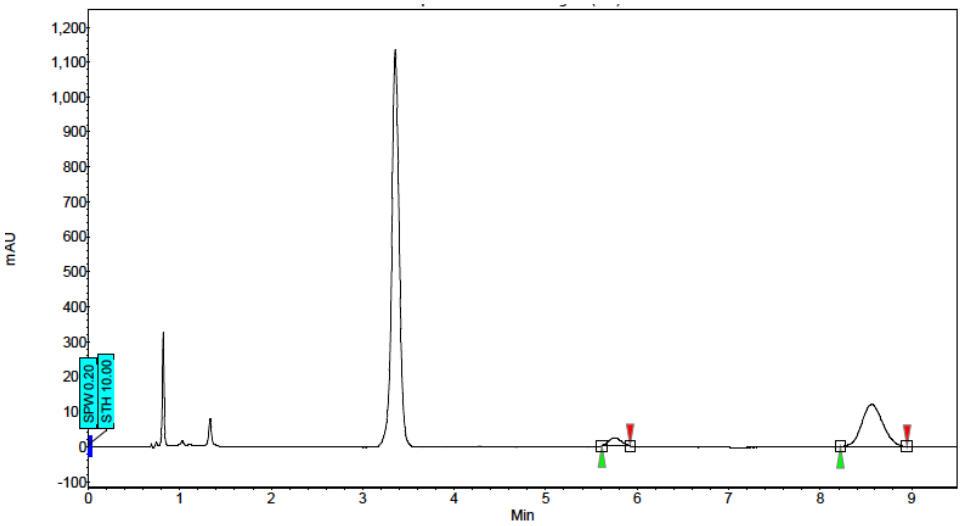
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.79	27.5	5.2	17.590	0.00	0.00
2	UNKNOWN	8.59	87.4	24.3	82.410	1.49	7.69
Total			114.8	29.5	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.56 min; minor enantiomer t_R = 5.77 min].



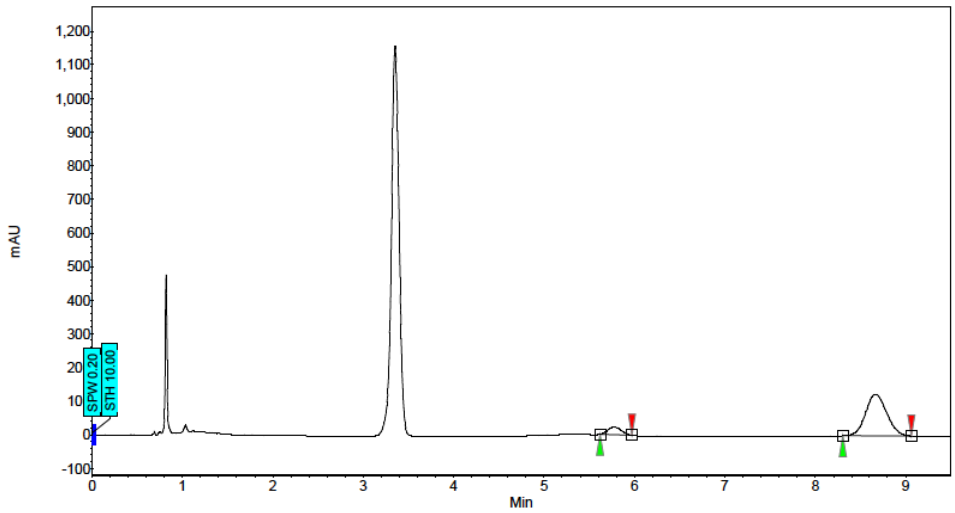
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.77	20.5	3.5	10.425	0.00	0.00
2	UNKNOWN	8.56	110.6	30.3	89.575	1.48	7.87
Total			131.1	33.8	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.56 min; minor enantiomer t_R = 5.75 min].



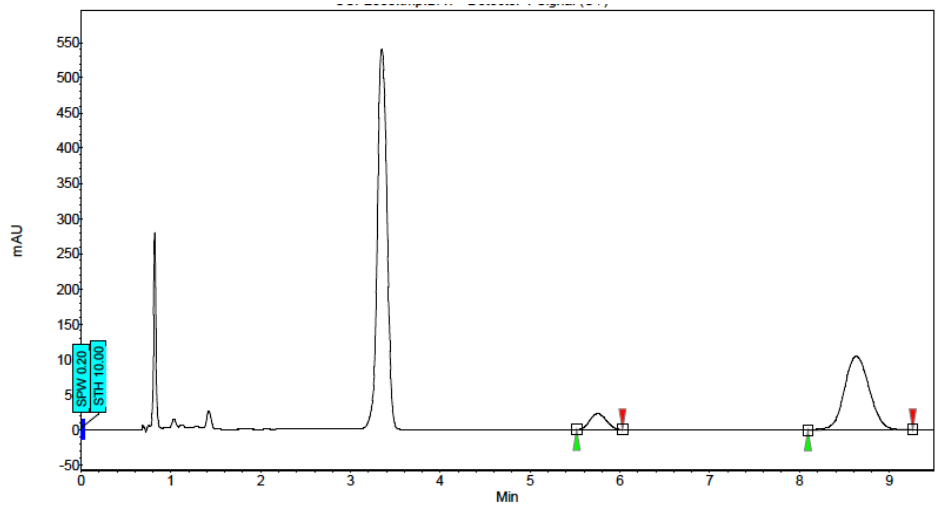
Index	Name	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]	Selectivity	Res. HW
1	UNKNOWN	5.75	23.1	3.7	10.324	0.00	0.00
2	UNKNOWN	8.56	120.8	32.3	89.676	1.49	8.14
Total			144.0	36.0	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer tR = 8.66 min; minor enantiomer tR = 5.77 min].



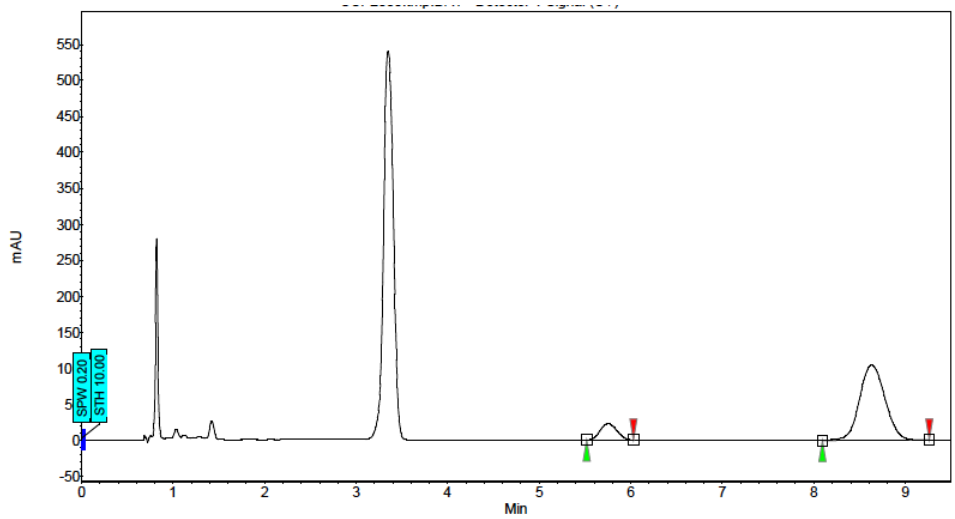
Index	Name	Time [Min]	Height [µV]	Area [µV.Min]	Area [%]	Selectivity	Res. HW
1	UNKNOWN	5.77	22.8	3.9	10.472	0.00	0.00
2	UNKNOWN	8.66	124.1	33.6	89.528	1.50	8.16
Total			147.0	37.5	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.63 min; minor enantiomer t_R = 5.75 min].



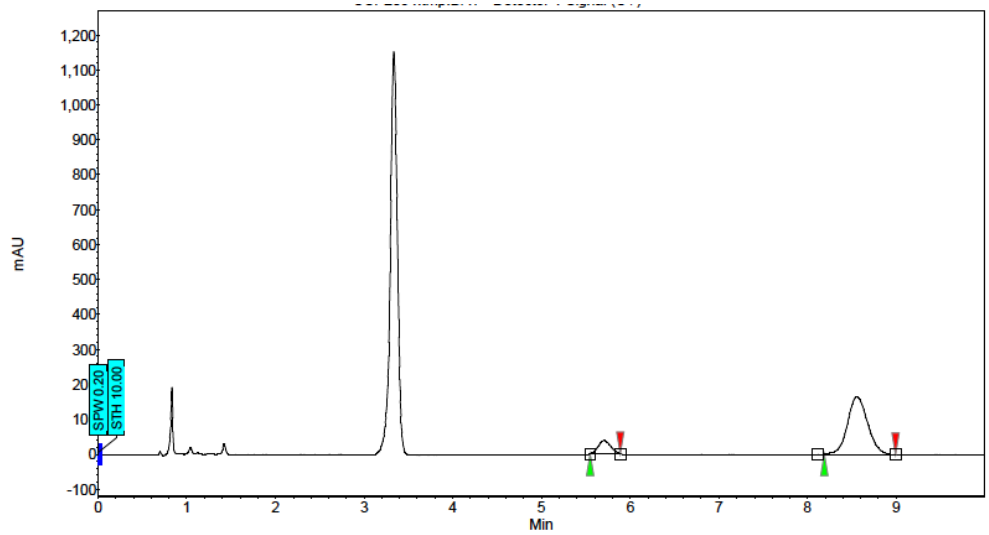
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.75	23.2	4.9	12.812	0.00	0.00
2	UNKNOWN	8.63	104.4	33.6	87.188	1.50	6.72
Total			127.6	38.5	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.63 min; minor enantiomer t_R = 5.75 min].



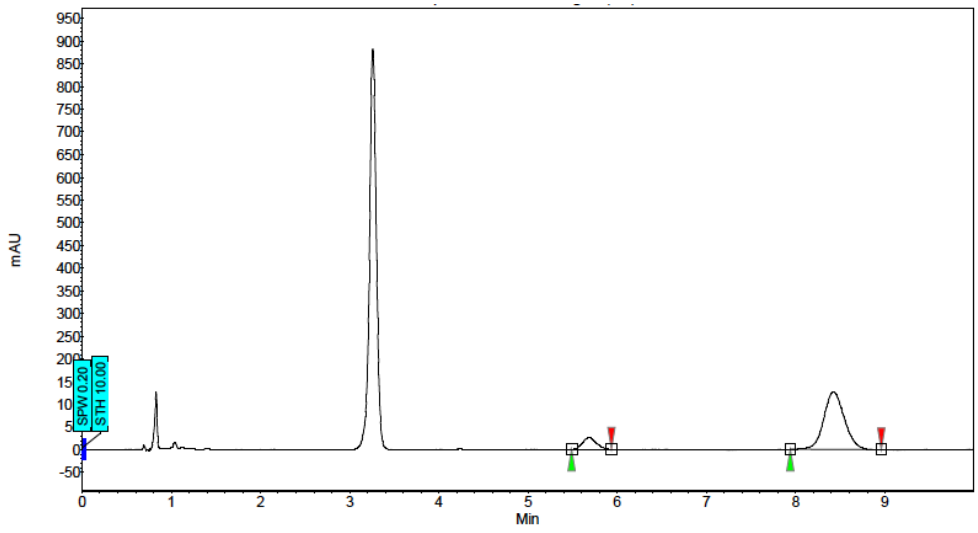
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.75	23.2	4.9	12.812	0.00	0.00
2	UNKNOWN	8.63	104.4	33.6	87.188	1.50	6.72
Total			127.6	38.5	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.56 min; minor enantiomer t_R = 5.71 min].



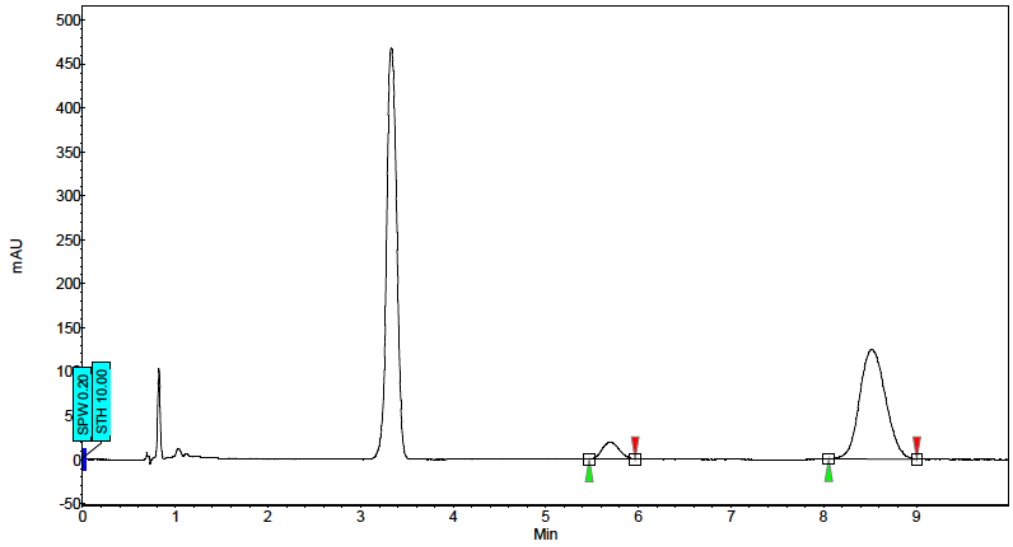
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.71	37.2	6.1	12.162	0.00	0.00
2	UNKNOWN	8.56	165.9	43.7	87.838	1.50	8.43
Total			203.1	49.8	100.000		

Following General procedure **G** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.42 min; minor enantiomer t_R = 5.68 min].



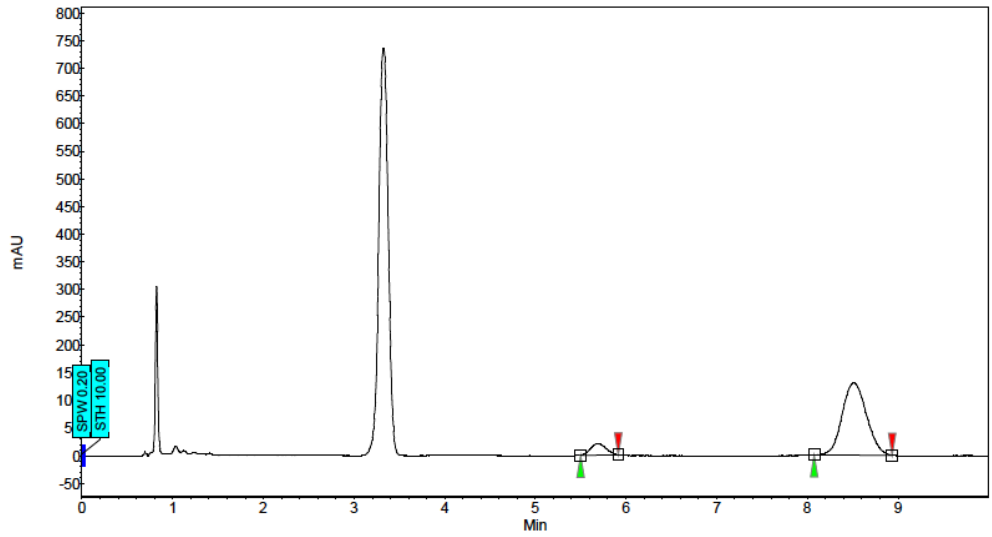
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.68	25.5	4.6	11.811	0.00	0.00
2	UNKNOWN	8.42	126.9	34.0	88.189	1.48	7.82
Total			152.3	38.6	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.52 min; minor enantiomer t_R = 5.69 min].



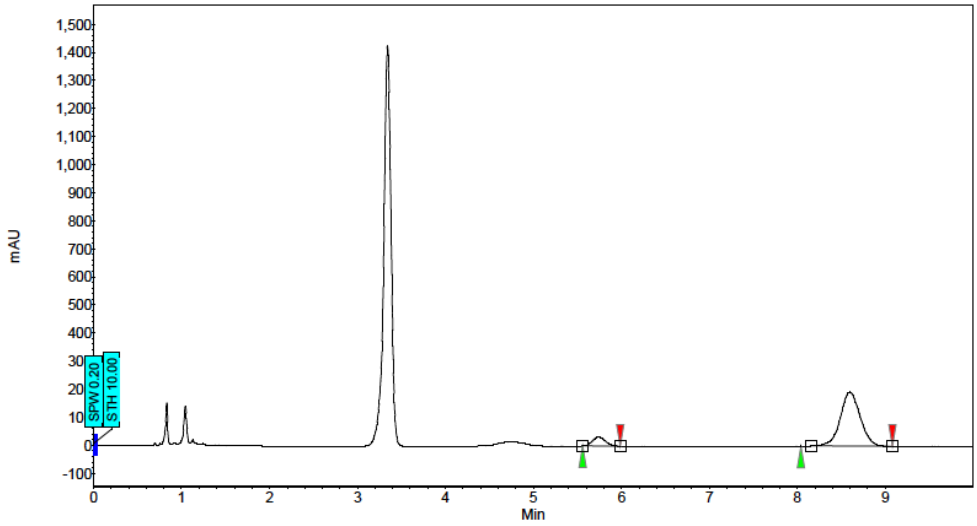
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.69	19.4	4.1	9.212	0.00	0.00
2	UNKNOWN	8.52	124.8	40.4	90.788	1.50	6.58
Total			144.2	44.5	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.51 min; minor enantiomer t_R = 5.69 min].



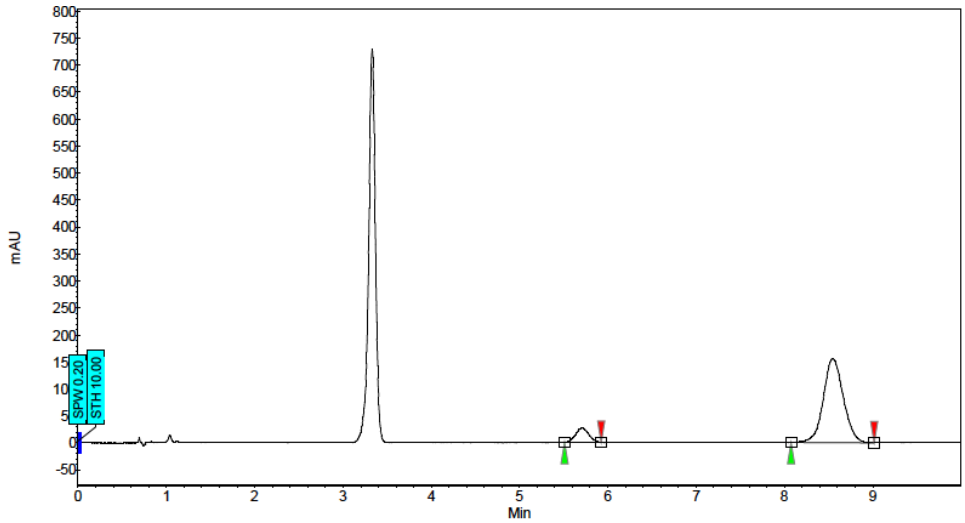
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.69	20.2	4.0	9.025	0.00	0.00
2	UNKNOWN	8.51	130.6	40.5	90.975	1.50	6.85
Total			150.9	44.5	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.49 min; minor enantiomer t_R = 5.66 min].



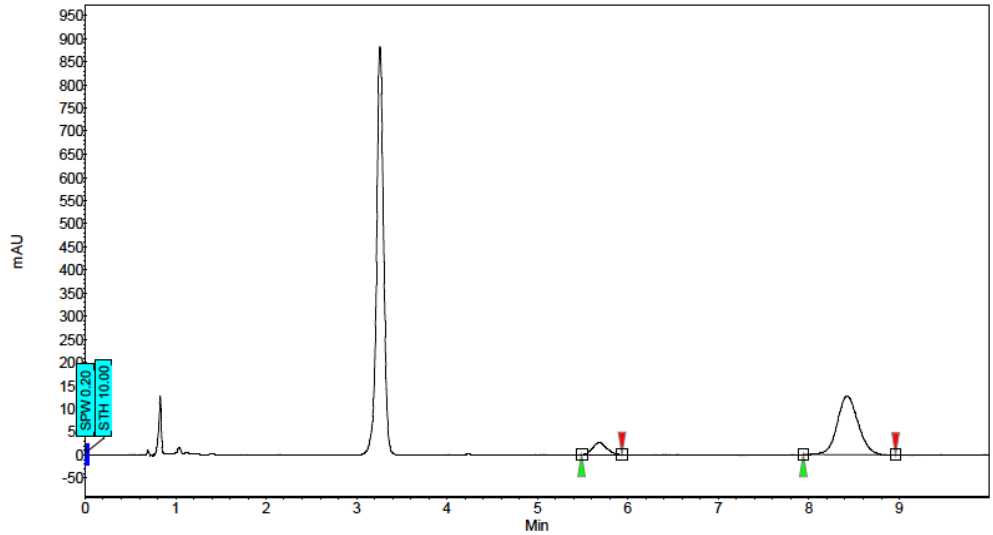
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.74	32.8	5.5	9.896	0.00	0.00
2	UNKNOWN	8.59	192.2	50.4	90.104	1.50	8.49
Total			225.0	55.9	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.55 min; minor enantiomer t_R = 5.70 min].



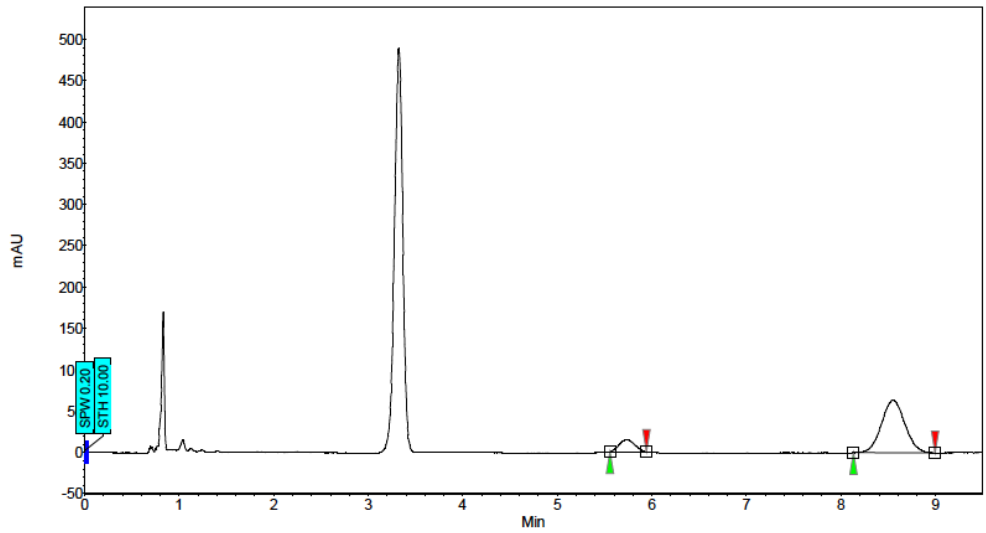
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.70	26.4	4.5	9.982	0.00	0.00
2	UNKNOWN	8.55	155.5	40.9	90.018	1.50	8.36
Total			181.9	45.4	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.42 min; minor enantiomer t_R = 5.68 min].



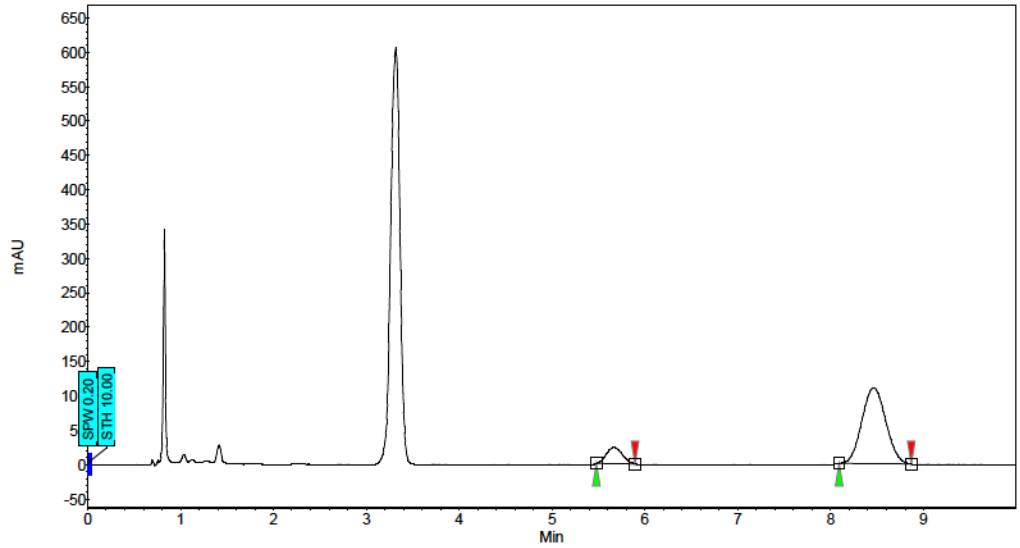
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.68	25.5	4.6	11.811	0.00	0.00
2	UNKNOWN	8.42	126.9	34.0	88.189	1.48	7.82
Total			152.3	38.6	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.55 min; minor enantiomer t_R = 5.73 min].



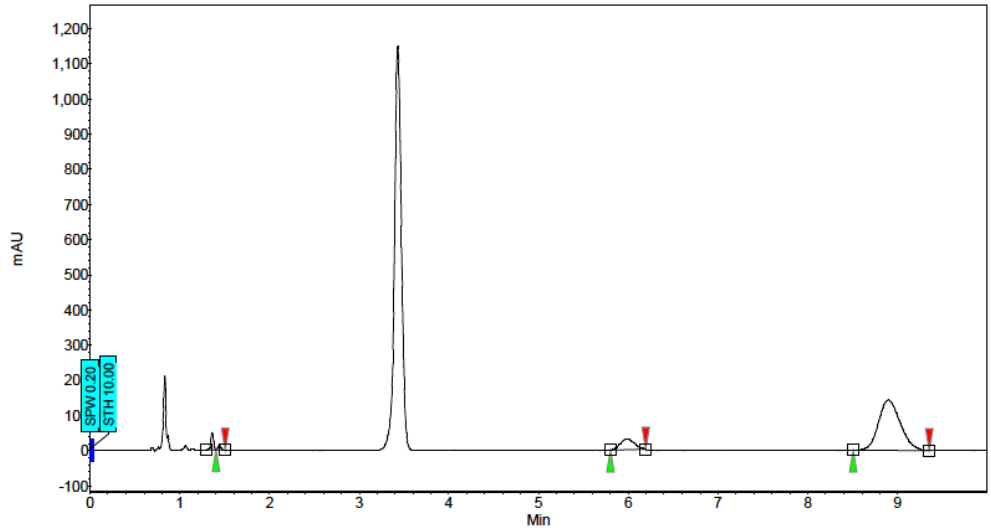
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.73	14.7	2.8	13.098	0.00	0.00
2	UNKNOWN	8.55	63.6	18.3	86.902	1.49	7.39
Total			78.3	21.0	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.47 min; minor enantiomer t_R = 5.67 min].



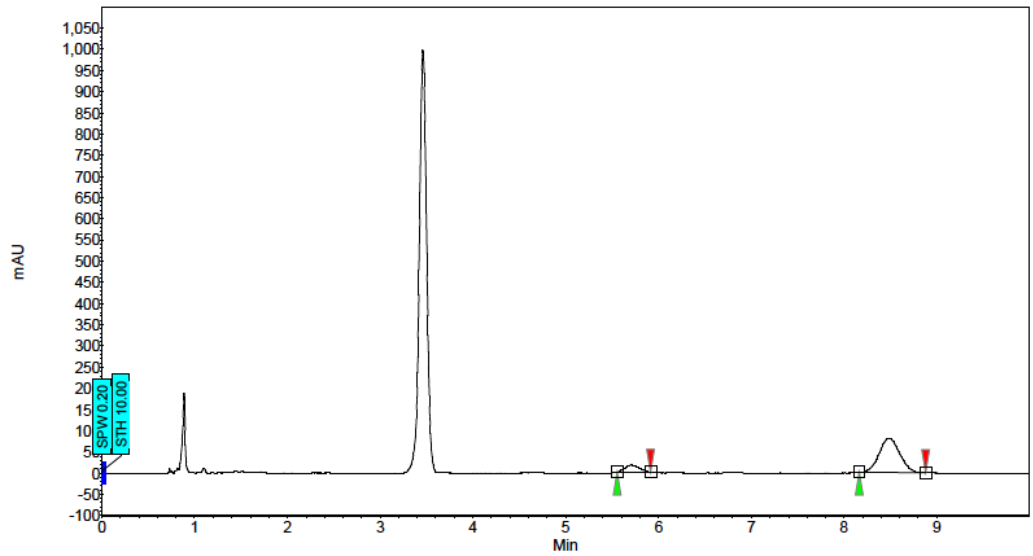
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.67	23.7	4.7	12.335	0.00	0.00
2	UNKNOWN	8.47	110.7	33.1	87.665	1.49	6.94
Total			134.5	37.7	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 890 min; minor enantiomer t_R = 5.98 min].



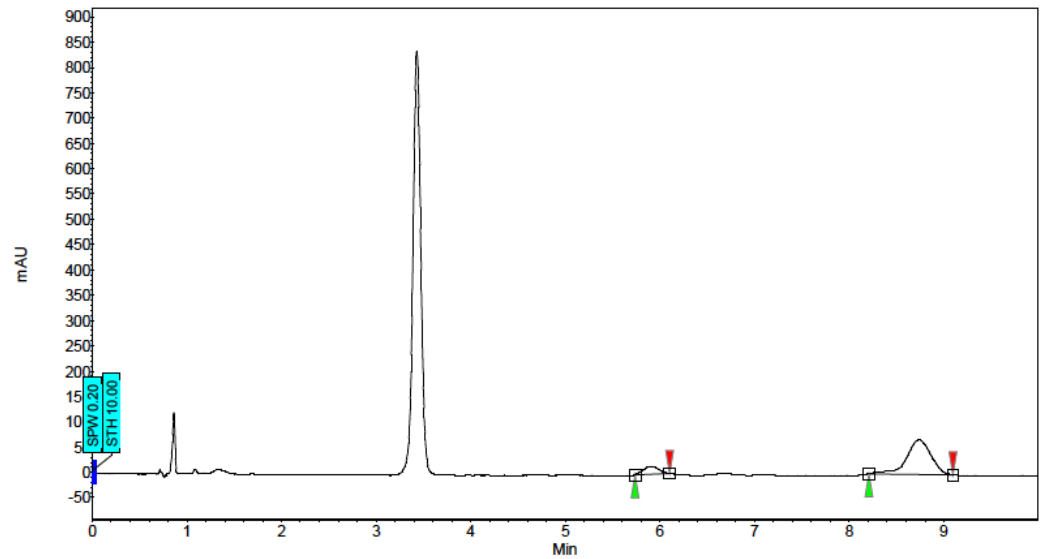
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	1.44	14.7	0.5	1.131	0.00	0.00
3	UNKNOWN	5.98	30.5	5.7	12.266	4.15	24.99
2	UNKNOWN	8.90	143.0	40.1	86.603	1.49	7.80
Total			188.2	46.3	100.000		

Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.49 min; minor enantiomer t_R = 5.71 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.71	16.7	3.1	12.852	0.00	0.00
2	UNKNOWN	8.49	81.2	20.9	87.148	1.49	7.83
Total			97.9	23.9	100.000		

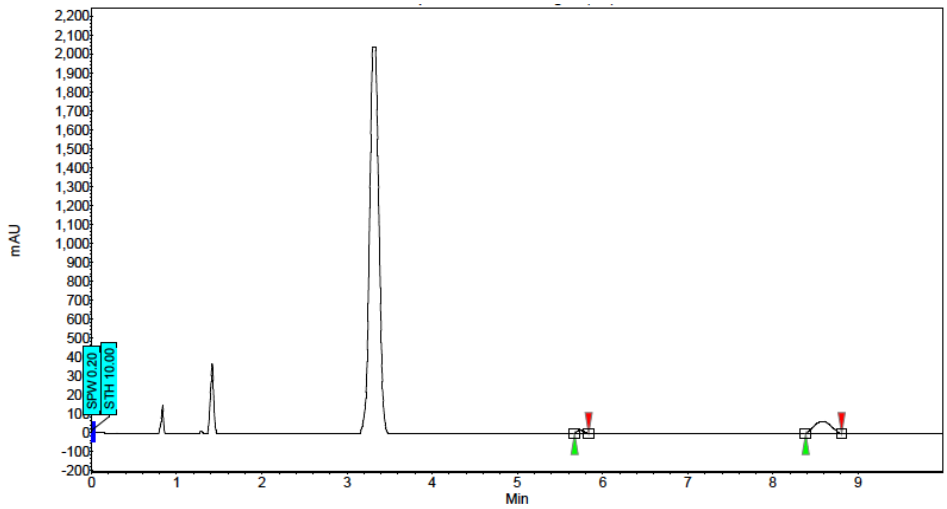
Following General procedure **H** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.74 min; minor enantiomer t_R = 5.89 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.89	15.5	3.0	12.657	0.00	0.00
2	UNKNOWN	8.74	68.3	20.4	87.343	1.48	7.36
Total			83.9	23.4	100.000		

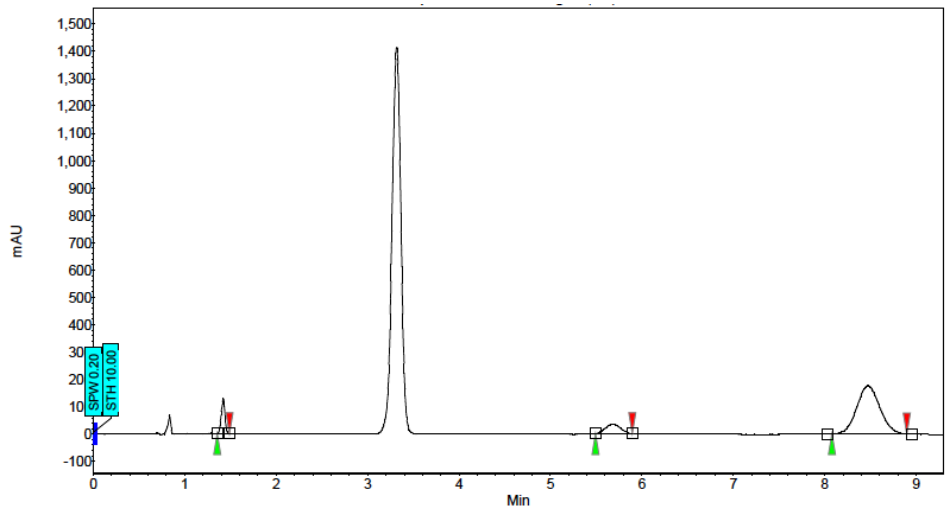
Enantioselective Friedel Crafts alkylations in a continuous flow process

(2a): 0.25 mL/min flow rate, 1.1 g of CS-ct-DNA: Following General procedure **I** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.58 min; minor enantiomer t_R = 5.74 min].



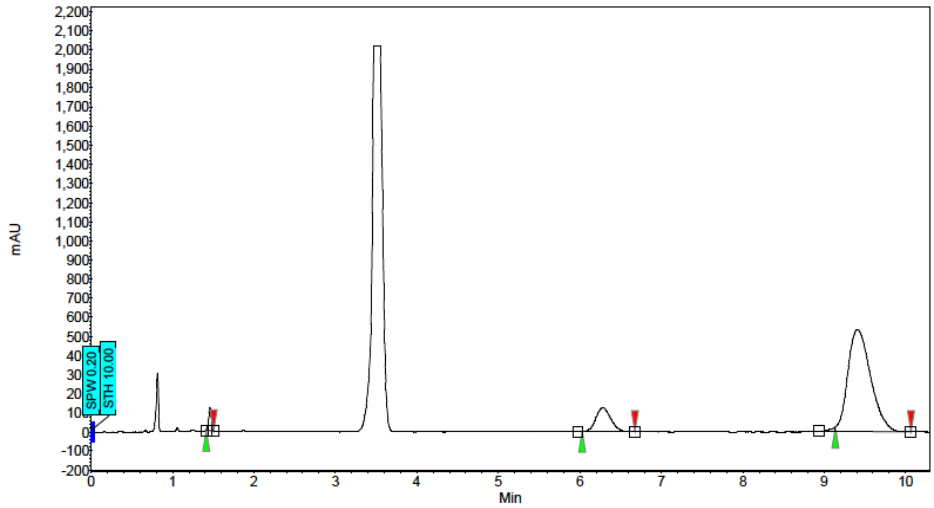
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.74	15.7	1.7	10.151	0.00	0.00
2	UNKNOWN	8.58	65.7	15.1	89.849	1.49	9.55
Total			81.4	16.8	100.000		

(2a): 0.125 mL/min flow rate, 2.2 g of CS-ct-DNA: Following General procedure **I** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.47 min; minor enantiomer t_R = 5.68 min].



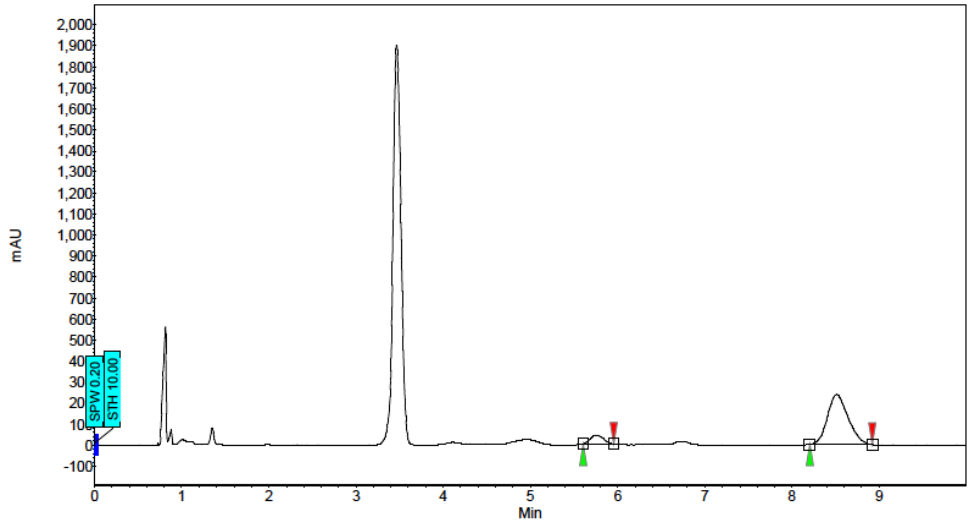
Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
3	UNKNOWN	1.42	126.9	6.0	9.348	0.00	0.00
1	UNKNOWN	5.68	35.4	6.7	10.316	3.99	22.05
2	UNKNOWN	8.47	177.0	52.0	80.336	1.49	7.23
Total			339.3	64.7	100.000		

(2a): 0.125 mL/min flow rate, 4.4 g of CS-ct-DNA: Following General procedure **I** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 9.41 min; minor enantiomer t_R = 6.28 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	1.46	122.2	4.3	2.108	0.00	0.00
2	UNKNOWN	6.28	125.9	26.7	13.068	4.30	24.85
3	UNKNOWN	9.41	533.1	173.2	84.824	1.50	7.40
Total			781.2	204.2	100.000		

(2a): 0.125 mL/min flow rate, 4.4 g of CS-ct-DNA (Large Scale): Following General procedure **I** [DAICEL AD-H column; 100 bar; flow: 4.0 mL/min; 15% MeOH; λ = 220 nm, major enantiomer t_R = 8.51 min; minor enantiomer t_R = 5.76 min].



Index	Name	Time	Height	Area	Area	Selectivity	Res. HW
		[Min]	[µV]	[µV.Min]	[%]		
1	UNKNOWN	5.76	42.2	7.3	10.134	0.00	0.00
2	UNKNOWN	8.51	237.0	64.9	89.866	1.48	7.68
Total			279.2	72.2	100.000		