Supporting Information

Design and Applications of N-tert-Butyl Sulfinyl Squaramide Catalysts

Yao Li,[†] Cyndi Qixin He,[‡] Fei-Xiang Gao,[†] Zhen Li,[†] Xiao-Song Xue,[†] Xin Li,[*,†] Kendall N. Houk[*,‡] and Jin-Pei Cheng[†]

[†]*State key Laboratory of Elemento-Organic Chemistry, Collaborative Innovation Center of Chemical Science and Engineering, Nankai University, Tianjin 300071 (China)*

[‡]*Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095, United States*

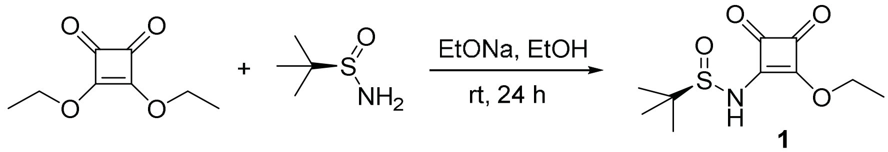
content

1. General information

Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. CH_2Cl_2 and $CHCl_3$ were purified by distillation with CaH_2. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 60-90 ^{o}C). NMR spectra were acquired on a Bruker AV400 spectrometer, running at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift mutiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. Acyl phosphonates **4** were prepared according to literature.[1]

2. Catalyst Preparation and Characterization Data

(R)-N-(2-ethoxy-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (1)

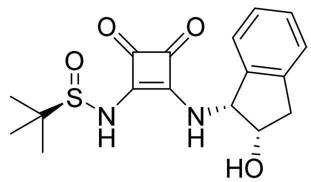


The compound was prepared according to a modified procedure for synthesis of N-sulfonyl squaramide reported by Li et al.[2] Under an atmosphere of argon, sodium ethoxide (3.40 g, 50 mmol) was added to a stirred solution of (R)-tert-butanesulfinamide (6.05 g, 50 mmol) in absolute ethanol (100 mL). The mixture was stirred for 20 min at room temperature, and then diethyl squarate (8.5 g, 50 mmol) was added dropwise. After stirring at room temperature for 24 h, the solution was concentrated *in vacuo*. H_2O (30mL) was added to dissolve the mixture. The aqueous layer was acidified to pH < 2 with saturated aqueous $NaHSO_4$ and then extracted with CH_2Cl_2 (3 x 75 mL). The combined extracts were dried over Na_2SO_4, filtered, and concentrated. Chromatography on silica gel (0% to 5% MeOH in CH_2Cl_2) followed by recrystallization from CH_2Cl_2/Hexane yielded 8.50 g (68 %) **1** as a white solid. The **ent-1** was prepared using (S)-tert-butanesulfinamide as material following the same procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (br s, 1H), 4.83 (q, J = 6.9 Hz, 2H), 1.50 (t, J = 7.0 Hz, 3H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 185.5, 181.5, 171.0, 71.0, 58.7, 22.0, 16.0. HRMS (ESI) calcd for $C_{10}H_{14}NO_4S$ $(M-H)^-$: 244.0649, found: 244.0650.

General methods for preparation of chiral N-tertiary-butyl sulfinyl squaramide catalysts (2a-2h)

To a solution of **1** or **ent-1** (2 mmol) and amine alcohol (3 mmol) in 10 mL CH_2Cl_2 was added Et_3N (2.4 mmol). The mixture was stirred at room temperature. After **1** was consumed (usually 48-72 h), H_2O (10mL) was added to the mixture. The aqueous layer was acidified to pH < 2 with saturated aqueous $NaHSO_4$ and then extracted with

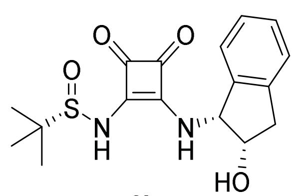
CH_2Cl_2 (3 x 20 mL). The combined extracts were dried over Na_2SO_4, filtered, and concentrated. Chromatography on silica gel (2% to 5% MeOH in CH_2Cl_2) or recrystallization from CH_2Cl_2/Hexane gave the desired product.



2a

(R)-N-(2-(((1R,2S)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2a)

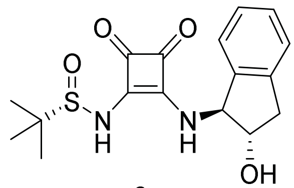
Following the general procedure, column chromatography (2% to 5% MeOH in CH_2Cl_2) afforded **2a** (592 mg, 85%) as a light yellow foam. And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (488 mg, 70%) . ^1H NMR (400 MHz, CD_3OD) δ 7.36 – 7.16 (m, 4H), 5.65 (d, J = 3.8 Hz, 1H), 4.64 (s, 1H), 3.24 – 3.13 (m, 1H), 2.96 (d, J = 16.4 Hz, 1H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD) δ 187.0, 183.9, 171.7, 166.0, 141.8, 129.6, 128.1, 126.4, 125.3, 74.3, 62.9, 59.4, 40.4, 22.1. HRMS (ESI) calcd for $C_{17}H_{19}N_2O_4S$ $(M-H)^-$: 347.1071, found: 347.1068.



2b

(S)-N-(2-(((1R,2S)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2b)

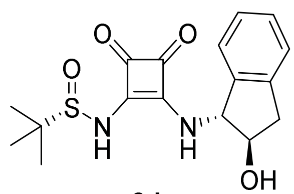
Following the general procedure, column chromatography (2% to 5% MeOH in CH_2Cl_2) afforded **2b** (627 mg, 90%) And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (522 mg, 75%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.11 (br s, 1H), 7.70 (d, J = 7.3 Hz, 1H), 7.30 – 7.26 (m, 4H), 5.63 (s, 1H), 4.69 (s, 1H), 3.20 (dd, J = 16.4, 4.9 Hz, 1H), 2.99 (d, J = 16.9 Hz, 1H), 1.25 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 182.6, 170.3, 164.3, 140.1, 128.8, 127.4, 125.7, 124.5, 74.1, 62.0, 59.0, 39.7, 21.9. HRMS (ESI) calcd for $C_{17}H_{19}N_2O_4S$ $(M-H)^-$: 347.1071, found: 347.1070.



2c

(S)-N-(2-(((1S,2S)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2c)

Following the general procedure, column chromatography (2% to 5% MeOH in CH_2Cl_2) afforded **2c** (592 mg, 85%) as a light yellow foam. And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (488 mg, 70%). ^1H NMR (400 MHz, DMSO-d_6) δ 9.67 (s, 1H), 7.95 (d, J = 9.0 Hz, 1H), 7.34 – 7.15 (m, 4H), 5.61 (s, 1H), 5.33 (t, J = 7.7 Hz, 1H), 4.29 (q, J = 6.8 Hz, 1H), 3.20 – 3.12 (m, 1H), 2.76 (dd, J = 15.3, 7.8 Hz, 1H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.7, 181.2, 170.0, 164.8, 140.4, 139.4, 128.4, 127.0, 124.9, 124.0, 79.0, 65.7, 57.5, 38.1, 21.6. HRMS (ESI) calcd for $C_{17}H_{21}N_2O_4S^+$ $(M+H)^+$: 349.1217, found: 349.1220.

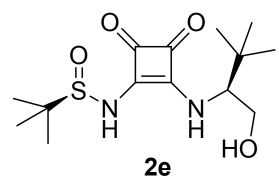


2d

(S)-N-(2-(((1R,2R)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2d)

Following the general procedure, column chromatography (2% to 5% MeOH in CH_2Cl_2) afforded **2d** (592 mg, 85%) as a light yellow foam. And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (522 mg, 75%). ^1H NMR (400 MHz, DMSO-d_6) δ 9.68 (s, 1H), 7.95 (d, J = 9.3 Hz, 1H), 7.32 – 7.16 (m, 4H), 5.63 (s, 1H), 5.34 (t, J = 8.1 Hz, 1H), 4.29 (dd, J = 14.4, 7.1 Hz, 1H), 3.16 (dd, J = 15.5, 7.2 Hz, 1H), 2.76 (dd, J = 15.5, 8.0 Hz, 1H), 1.22 (s, 9H). ^{13}C NMR

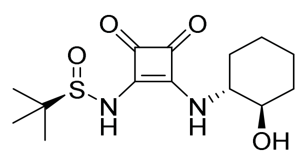
(100 MHz, DMSO-d_6) δ 185.7, 181.2, 170.0, 164.8, 140.5, 139.4, 128.4, 127.1, 125.0, 124.0, 79.0, 65.7, 57.4, 38.1, 21.6. HRMS (ESI) calcd for $C_{17}H_{21}N_2O_4S^+$ $(M+H)^+$: 349.1217, found: 349.1219.



2e

(R)-N-(2-(((S)-1-hydroxy-3,3-dimethylbutan-2-yl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2e)

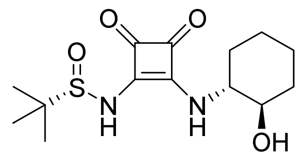
Following the general procedure, column chromatography (3% to 5% MeOH in CH_2Cl_2) afforded **2e** (506 mg, 85%) as a white foam. And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (475 mg, 75%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.57 (s, 1H), 7.57 (d, J = 10.3 Hz, 1H), 4.85 (s, 1H), 3.82 (dd, J = 12.4, 5.1 Hz, 1H), 3.68 (d, J = 11.2 Hz, 1H), 3.46 (d, J = 7.3 Hz, 1H), 1.23 (s, 9H), 0.91 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.9, 180.9, 170.6, 164.2, 64.4, 60.3, 57.4, 34.0, 26.5, 21.6. HRMS (ESI) calcd for $C_{14}H_{25}N_2O_4S+$ $(M+H)^+$: 317.1530, found: 317.1535.



2f

(R)-N-(2-(((1R,2R)-2-hydroxycyclohexyl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2f)

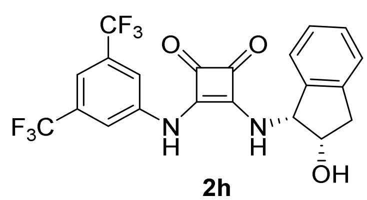
Following the general procedure, column chromatography (3% to 5% MeOH in CH_2Cl_2) afforded **2f** (566 mg, 90%) as a light yellow foam. And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (472 mg, 75%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.56 (s, 1H), 7.66 (d, J = 8.3 Hz, 1H), 4.98 (s, 1H), 3.67 – 3.52 (m, 1H), 3.26 (s, 1H), 1.98 – 1.76 (m, 2H), 1.69 – 1.55 (m, 2H), 1.38 – 1.23 (m, 4H), 1.21 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.8, 180.8, 170.1, 164.4, 72.2, 59.5, 57.3, 34.1, 32.5, 24.2, 23.8, 21.6. HRMS (ESI) calcd for $C_{14}H_{23}N_2O_4S^+$ $(M+H)^+$: 315.1373, found: 315.1375



2g

(S)-N-(2-(((1R,2R)-2-hydroxycyclohexyl)amino)-3,4-dioxocyclobut-1-en-1-yl)-2-methylpropane-2-sulfinamide (2g)

Following the general procedure, column chromatography (3% to 5% MeOH in CH_2Cl_2) afforded **2g** (566 mg, 90%) as a light yellow foam. And it could be further purified by recrystallization from CH_2Cl_2/Hexane to give a white solid (472 mg, 75%). ^1H NMR (400 MHz, DMSO-d_6) δ 9.56 (s, 1H), 7.65 (d, J = 8.5 Hz, 1H), 4.94 (s, 1H), 3.67 – 3.51 (m, 1H), 3.31 – 3.18 (m, 1H), 2.02 – 1.81 (m, 2H), 1.73 – 1.56 (m, 2H), 1.41 – 1.23 (m, 4H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.7, 180.8, 170.1, 164.5, 72.0, 59.6, 57.3, 34.1, 32.4, 24.2, 23.7, 21.6. HRMS (ESI) calcd for $C_{14}H_{23}N_2O_4S^+$ $(M+H)^+$: 315.1373, found: 315.1377



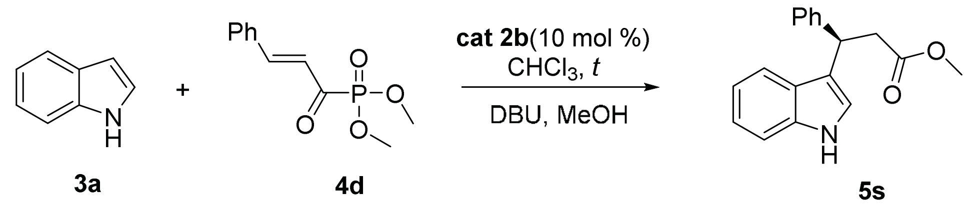
2h

3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-(((1R,2S)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)amino)cyclobut-3-ene-1,2-dione (2h)

Following the procedure reported by Rawal et al,[3] **2h** was obtained as a white solid (840 mg, 92%). ^1H NMR (400 MHz, DMSO-d_6) δ 10.49 (s, 1H), 8.19 (d, J = 9.0 Hz, 1H), 8.10 (s, 2H), 7.68 (s, 1H), 7.35 – 7.16 (m, 4H), 5.64 (s, 1H), 5.52 (dd, J = 8.8, 5.0 Hz, 1H), 4.59 (t, J = 4.1 Hz, 1H), 3.15 (dd, J = 16.4, 4.9 Hz, 1H), 2.88 (d, J = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.7, 180.5, 169.7, 162.7, 141.3, 140.6, 131.4 (q, J = 33.0 Hz), 128.1, 126.7, 125.2, 124.3, 123.2 (q, J = 273.0 Hz), 117.9, 114.7, 72.3, 61.30. The methylene signal could not be seen due to the overlap with DMSO. HRMS (ESI) calcd for $C_{21}H_{15}F_6N_2O_3^+$ (M+H)$^+$: 457.0981, found: 457.0986.

3. Optimization of Reaction Conditions of Indole 3a and β-Phenyl-substituted Acyl Phosphonates 4d

Table S1. Optimization of Reaction Conditions of Indole 3a and β-Phenyl-substituted Acyl Phosphonates 4d.[a]

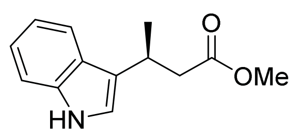


entry	*t*/°C	time	$CHCl_3$/ml	Additive	yield/%[b]	*ee*%[c]
1	-20	3 d	2.0	3 Å MS[d]	<10	43
2	0	3 d	2.0	3 Å MS[d]	20	27
3	rt	2 d	0.5	None	80	58[e]
4	rt	2 d	0.5	None	90	70
5	rt	2 d	1.0	None	68	23[e]
6	rt	2 d	0.5	3 Å MS[d]	85	55
7	0	3 d	0.5	None	75	85

[a]Unless otherwise indicated, all reactions were carried out with **3** (0.1 mmol), **4d** (0.2 mmol, 2.0 eq), 10 mol % catalyst **2b**. [b]Isolated yields. [c]Determined by HPLC analysis. [d]40 mg 3 Å MS was added. [e]Reaction was carried out with 0.1 mmol **3** and 0.1 mmol **4d**. (3 Å MS = 3 Å molecular sieves)

4. General procedure for Friedel-Crafts alkylation and Product Characterization data

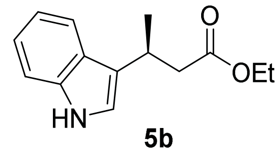
A dry, screw-capped reaction vial containing a magnetic stir bar was charged with acyl phosphonate (0.2 mmol, 2 equiv), catalyst **2b** (0.01 mmol, 0.1 equiv), 40 mg 3 Å molecular sieves and $CHCl_3$ (2.0 mL). After 10 min of stirring at -20 ˚C, the indole (0.1 mmol, 1 equiv) was added. The stirring was maintained at this temperature for the time required for almost full conversion of the indole as monitored by TLC (usually 72 h). Upon completion of the reaction, the alcohol/amine (0.1 mL) and DBU (0.2 mmol, 2 equiv) were added in the described sequence. After additionally 30 min of stirring, the crude reaction mixture was diluted with saturated aqueous NH_4Cl, extracted with EtOAc (3 x 5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purified by chromatography on silica gel afforded the desired products.



5a

(*S*)-Methyl 3-(1*H*-indol-3-yl)butanoate (5a)

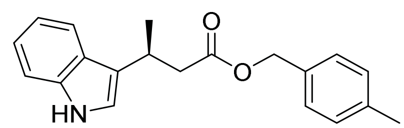
Following the general procedure **5a** was isolated by chromatography (petroleum ether /EtOAc 5:1) as a colorless oil (18.5 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 1.9 Hz, 1H), 3.66 (s, 3H), 3.64 – 3.58 (m, 1H), 2.84 (dd, *J* = 15.0, 6.2 Hz, 1H), 2.59 (dd, *J* = 15.0, 8.7 Hz, 1H), 1.42 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 136.5, 126.4, 122.1, 120.9, 120.1, 119.4, 119.3, 111.3, 51.7, 42.4, 28.1, 21.2. HRMS (ESI) calcd for $C_{13}H_{16}NO_2^+$ $(M+H)^+$: 218.1176, found: 218.1177. The enantiomeric excess was determined to be 94% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 13.4 min, t_R (major) = 19.2 min. $[\alpha]_D^{22}$:13.2 (c 1.03, $CHCl_3$). Lit. $[\alpha]_D^{28}$:7.3 (c 0.7, $CHCl_3$).[4]



5b

(S)-Ethyl 3-(1*H*-indol-3-yl)butanoate (5b)

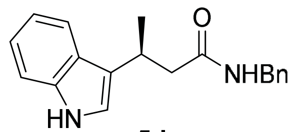
Following the general procedure **5b** was isolated by chromatography (petroleum ether /EtOAc 5:1) as a colorless oil (19.4 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 2.1 Hz, 1H), 4.12 (q, *J* = 7.1, 7.1, 7.1 Hz, 2H), 3.67 – 3.58 (m, 1H), 2.83 (dd, *J* = 14.9, 6.1 Hz, 1H), 2.58 (dd, *J* = 14.9, 8.7 Hz, 1H), 1.43 (d, *J* = 6.9 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 136.6, 126.5, 122.1, 121.0, 120.1, 119.3, 111.3, 60.4, 42.6, 28.1, 21.2, 14.3. HRMS (ESI) calcd for $C_{14}H_{18}NO_2^+$ $(M+H)^+$: 232.1332, found: 232.1336. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 10.6 min, t_R (major) = 13.6 min. $[\alpha]_D^{22}$:1.4 (c 0.57, $CHCl_3$).



5c

(S)-4-methylbenzyl 3-(1*H*-indol-3-yl)butanoate (5c)

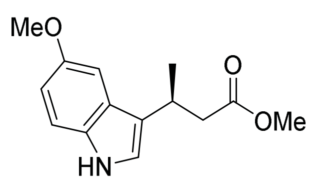
Following the general procedure **5c** was isolated by chromatography (petroleum ether /EtOAc 5:1) as a colorless oil (24.6 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (s, 1H), 7.66 (d, *J*=7.9, 1H), 7.36 (d, *J*=8.1, 1H), 7.20 (t, *J*=7.6, 1H), 7.18 – 7.08 (m, 4H), 6.97 (d, *J*=2.4, 1H), 5.05 (s, 2H), 3.64 (q, *J*=7.1, 1H), 3.04 – 2.49 (m, 2H), 2.35 (s, 3H), 1.42 (d, *J*=6.9, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 138.1, 136.5, 133.1, 129.3, 128.4, 126.5, 122.1, 120.9, 120.2, 119.4, 119.3, 111.3, 66.2, 42.6, 28.2, 21.3, 21.3. HRMS (MALDI) calcd for $C_{20}H_{21}NNaO_2$ $(M+Na)^+$: 330.1465, found: 330.1468.The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 18.2 min, tR (major) = 25.4 min. $[\alpha]_D^{22}$:-8.2 (c 0.37, $CHCl_3$).



5d

(*S*)-*N*-Benzyl-3-(1*H*-indol-3-yl)butanamide (5d)

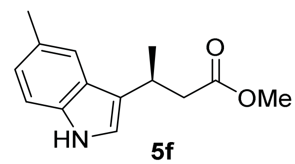
Following the general procedure **5d** was isolated by chromatography (petroleum ether /EtOAc 2:1 to 1:1) as a colorless oil (25.1 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.24 – 7.16 (m, 4H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.01 – 6.86 (m, 3H), 4.30 (d, *J* = 5.8 Hz, 2H), 3.70 – 3.55 (m, 1H), 2.71 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.54 (dd, *J* = 13.8, 6.9 Hz, 1H), 1.46 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 138.1, 136.6, 128.6, 127.5, 127.3, 126.2, 122.0, 120.7, 120.3, 119.3, 119.3, 111.4, 45.0, 43.5, 28.9, 21.3. HRMS (ESI) calcd for $C_{19}H_{21}N_2O^+$ $(M+H)^+$: 293.1648, found: 293.1654. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 20% i-PrOH in hexanes, 0.7 mL/min, 210 nm): t_R (major) = 24.2 min, t_R (minor) = 27.3 min. $[\alpha]_D^{22}$:-7.3 (c 0.93, $CHCl_3$).



5e

(S)-methyl 3-(5-methoxy-1*H*-indol-3-yl)butanoate (5e)

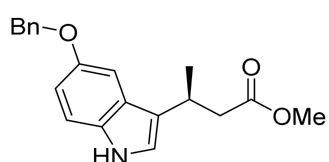
Following the general procedure **5e** was isolated by chromatography (petroleum ether /EtOAc 5:1) as a colorless oil (22.8 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.24 (d, *J*=8.8, 1H), 7.09 (d, *J*=2.4, 1H), 6.97 (d, *J*=2.5, 1H), 6.86 (dd, *J*=8.8, 2.4, 1H), 3.88 (s, 3H), 3.66 (s, 3H), 3.63 – 3.52 (m, 1H), 2.82 (dd, *J*=15.0, 6.1, 1H), 2.57 (dd, *J*=15.0, 8.8, 1H), 1.41 (d, *J*=6.9, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 153.9, 131.7, 126.8, 120.9, 120.7, 112.3, 112.0, 101.2, 56.1, 51.7, 42.3, 28.0, 21.1. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_3$ $(M+Na)^+$: 270.1101, found: 270.1103. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 15.5 min, t_R (major) = 21.3 min. $[\alpha]_D^{22}$:1.1 (c 0.73, $CHCl_3$).



5f

(S)-methyl 3-(5-methyl-1*H*-indol-3-yl)butanoate (5f)

Following the general procedure **5f** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a colorless oil (20.1 mg, 87%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.45 – 7.41 (m, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.02 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 3.66 (s, 3H), 3.63 – 3.53 (m, 1H), 2.83 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.56 (dd, *J* = 15.0, 8.8 Hz, 1H), 2.46 (s, 3H), 1.41 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 134.9, 128.6, 126.7, 123.8, 120.5, 120.2, 118.9, 111.0, 51.7, 42.4, 28.1, 21.7, 21.1. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_2$ $(M+Na)^+$: 254.1151, found: 254.1155. The enantiomeric excess was determined to be 95% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 14.1 min, t_R (major) = 28.0 min. $[\alpha]_D^{22}$:5.1 (c 0.70, $CHCl_3$).

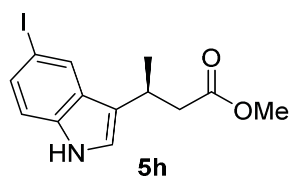


5g

(S)-methyl 3-(5-(benzyloxy)-1*H*-indol-3-yl)butanoate (5g)

Following the general procedure **5g** was isolated by chromatography (petroleum ether /EtOAc 4:1) as a colorless oil (25.2 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.53 – 7.46 (m, 2H), 7.43 – 7.36 (m, 2H), 7.36 – 7.29 (m, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.18 (d, *J* = 2.3 Hz, 1H), 7.00 – 6.90 (m, 2H), 5.12 (s, 2H), 3.66 (s, 3H), 3.61

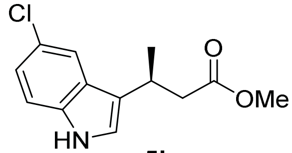
– 3.50 (m, 1H), 2.80 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.55 (dd, *J* = 15.0, 8.7 Hz, 1H), 1.39 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 153.1, 137.8, 131.9, 128.6, 127.9, 127.8, 126.9, 121.0, 120.8, 113.0, 112.0, 103.1, 71.2, 51.7, 42.2, 28.0, 21.0. HRMS (ESI) calcd for $C_{20}H_{21}NNaO_3$ $(M+Na)^+$: 346.1414, found: 346.1418. The enantiomeric excess was determined to be 92% ee by chiral HPLC analysis (ChiralCel OD-H, 20% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 11.1 min, t_R (major) = 17.7 min. $[\alpha]_D^{22}$:13.2 (c 1.03, $CHCl_3$). $[\alpha]_D^{22}$:23.0 (c 0.60, $CHCl_3$).



5h

(S)-methyl 3-(5-iodo -1*H*-indol-3-yl)butanoate (5h)

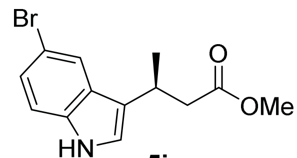
Following the general procedure **5h** was isolated by chromatography (petroleum ether /EtOAc 4:1) as a colorless oil (24.0 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.97 (d, *J* = 1.6 Hz, 1H), 7.43 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 3.65 (s, 3H), 3.54 (h, *J* = 7.1 Hz, 1H), 2.77 (dd, *J* = 15.0, 6.5 Hz, 1H), 2.57 (dd, *J* = 15.1, 8.4 Hz, 1H), 1.39 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 135.6, 130.5, 129.1, 128.1, 121.0, 120.4, 113.3, 82.9, 51.7, 42.3, 27.9, 21.2. HRMS (ESI) calcd for $C_{13}H_{13}INO_2$ $(M-H)^-$: 341.9996, found: 341.9993. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 5% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 27.7 min, t_R (major) = 36.1 min. $[\alpha]_D^{22}$:-9.2 (c 0.50, $CHCl_3$).



5i

(S)-methyl 3-(5-chloro-1*H*-indol-3-yl)butanoate (5i)

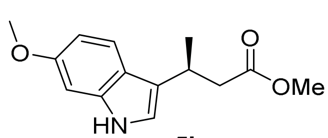
Following the general procedure **5i** was isolated by chromatography (petroleum ether /EtOAc 4:1) as a colorless oil (18.1 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.61 (d, J = 2.0 Hz, 1H), 7.26 (d, J = 6.5 Hz, 1H), 7.14 (dd, J = 8.6, 2.0 Hz, 1H), 7.02 (d, J = 2.4 Hz, 1H), 3.65 (s, 3H), 3.61 – 3.50 (m, 1H), 2.78 (dd, J = 15.1, 6.5 Hz, 1H), 2.58 (dd, J = 15.0, 8.4 Hz, 1H), 1.40 (d, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 134.9, 127.6, 125.1, 122.5, 121.6, 120.7, 118.8, 112.3, 51.7, 42.3, 28.0, 21.2. HRMS (ESI) calcd for $C_{13}H_{15}ClNO_2^+$ $(M+H)^+$: 252.0786, found: 252.0783. The enantiomeric excess was determined to be 86% ee by chiral HPLC analysis (ChiralCel OD-H, 5% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 23.9 min, tR (major) = 29.5 min. $[\alpha]_D^{22}$:-1.2 (c 1.30, $CHCl_3$).



5j

(S)-methyl 3-(5-bromo-1*H*-indol-3-yl)butanoate (5j)

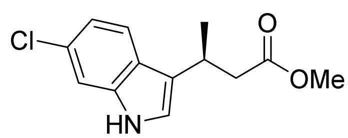
Following the general procedure **5j** was isolated by chromatography (petroleum ether /EtOAc 4:1) as a pale red oil (21.0 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.77 (d, J = 1.8 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.22 (d, J = 8.6 Hz, 1H), 7.00 (d, J = 2.3 Hz, 1H), 3.65 (s, 3H), 3.60 – 3.51 (m, 1H), 2.78 (dd, J = 15.0, 6.5 Hz, 1H), 2.57 (dd, J = 15.0, 8.4 Hz, 1H), 1.39 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 135.2, 128.3, 125.0, 121.9, 121.4, 120.7, 112.8, 112.7, 51.7, 42.3, 27.9, 21.2. HRMS (ESI) calcd for $C_{13}H_{15}BrNO_2^+$ $(M+H)^+$: 296.0281, found: 296.0278. The enantiomeric excess was determined to be 86% ee by chiral HPLC analysis (ChiralCel OD-H, 5% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 25.5min, tR (major) = 31.7 min. $[\alpha]_D^{22}$:12.5 (c 1.20, $CHCl_3$).



5k

(S)-methyl 3-(6-methoxy-1*H*-indol-3-yl)butanoate (5k)

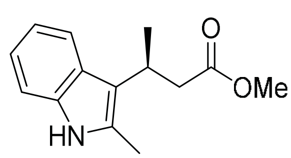
Following the general procedure **5k** was isolated by chromatography (petroleum ether /EtOAc 5:1) as a colorless oil (21.1 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 6.86 (dd, *J* = 13.7, 2.2 Hz, 2H), 6.79 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.84 (s, 3H), 3.65 (s, 3H), 3.60 – 3.53 (m, 1H), 2.81 (dd, *J* = 15.0, 6.1 Hz, 1H), 2.56 (dd, *J* = 15.0, 8.7 Hz, 1H), 1.39 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 156.6, 137.3, 121.0, 120.9, 119.9, 118.8, 109.4, 94.8, 55.8, 51.7, 42.4, 28.1, 21.2. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_3$ $(M+Na)^+$: 270.1101, found: 270.1106. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 18.2 min, t_R (major) = 24.8 min. $[\alpha]_D^{22}$:9.8 (c 0.90, $CHCl_3$).



5l

(S)-methyl 3-(6-chloro -1*H*-indol-3-yl)butanoate (5l)

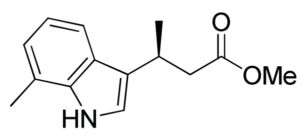
Following the general procedure **5l** was isolated by chromatography (petroleum ether /EtOAc 5:1) as a colorless oil (17.1 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 1.8 Hz, 1H), 7.08 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.98 (d, *J* = 2.3 Hz, 1H), 3.64 (s, 3H), 3.56 (m, 1H), 2.78 (dd, *J* = 15.0, 6.4 Hz, 1H), 2.57 (dd, *J* = 15.0, 8.4 Hz, 1H), 1.40 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 136.9, 128.1, 125.1, 121.1, 120.8, 120.1, 120.1, 111.2, 51.7, 42.4, 28.0, 21.2. HRMS (ESI) calcd for $C_{13}H_{13}ClNO_2$ $(M-H)^-$: 250.0640, found: 250.0638. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 5% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 17.7 min, t_R (major) = 22.4 min. $[\alpha]_D^{22}$:3.7 (c 0.60, $CHCl_3$).



5m

(S)-methyl 3-(2-methyl-1*H*-indol-3-yl)butanoate (5m)

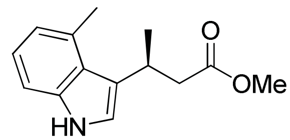
Following the general procedure **5m** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a yellow oil (13.9 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.63 – 7.58 (m, 1H), 7.28 – 7.24 (m, 1H), 7.13 – 7.02 (m, 2H), 3.60 (s, 3H), 3.59 – 3.51 (m, 1H), 2.81 (dd, *J* = 7.6, 1.6 Hz, 2H), 2.41 (s, 3H), 1.45 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 135.6, 130.5, 127.2, 120.8, 119.2, 119.1, 115.0, 110.5, 51.5, 41.5, 28.2, 20.9, 12.2. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_2$ $(M+Na)^+$: 254.1151, found: 254.1156. The enantiomeric excess was determined to be 88% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 12.7 min, t_R (major) = 21.4 min. $[\alpha]_D^{22}$:10.0 (c 0.40, $CHCl_3$).



5n

(S)-methyl 3-(7-methyl-1*H*-indol-3-yl)butanoate (5n)

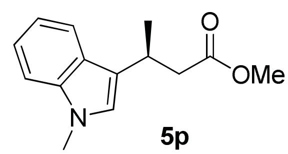
Following the general procedure **5n** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a colorless oil (16.2 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.08 – 6.97 (m, 3H), 3.65 (s, 3H), 3.64 – 3.56 (m, 1H), 2.84 (dd, *J* = 15.0, 6.1 Hz, 1H), 2.58 (dd, *J* = 15.0, 8.7 Hz, 1H), 2.48 (s, 3H), 1.42 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 136.1, 126.0, 122.7, 121.5, 120.5, 119.8, 119.7, 117.1, 51.7, 42.4, 28.2, 21.2, 16.8. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_2$ $(M+Na)^+$: 254.1151, found: 254.1156. The enantiomeric excess was determined to be 96% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 9.9 min, t_R (major) = 13.8 min. $[\alpha]_D^{22}$:10.2 (c 0.45, $CHCl_3$).



5o

(S)-methyl 3-(4-methyl-1*H*-indol-3-yl)butanoate (5o)

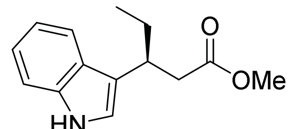
Following the general procedure **5o** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a colorless oil (16.1 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.19 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.07 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.01 (dd, *J* = 2.6, 0.8 Hz, 1H), 6.86 (dt, *J* = 7.2, 0.9 Hz, 1H), 3.96 – 3.86 (m, 1H), 3.67 (s, 3H), 2.83 (dd, *J* = 15.1, 5.5 Hz, 1H), 2.75 (s, 3H), 2.50 (dd, *J* = 15.2, 9.2 Hz, 1H), 1.38 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 136.8, 130.8, 125.1, 122.6, 122.2, 121.6, 119.9, 109.2, 51.7, 43.7, 28.5, 22.7, 20.6. HRMS (ESI) calcd for $C_{14}H_{17}NNaO_2$ $(M+Na)^+$: 254.1151, found: 254.1153. The enantiomeric excess was determined to be 92% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): t_R (minor) = 11.1 min, t_R (major) = 12.4 min. $[\alpha]_D^{22}$:5.5 (c 0.55, $CHCl_3$).



5p

(S)-methyl 3-(1-methyl-1*H*-indol-3-yl)butanoate (5p)

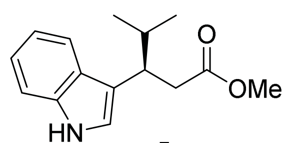
Following the general procedure **5p** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a colorless oil (9.2 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.62 (m, 1H), 7.31 – 7.27 (m, 1H), 7.25 – 7.19 (m, 1H), 7.14 – 7.07 (m, 1H), 6.85 (s, 1H), 3.74 (s, 3H), 3.65 (s, 3H), 3.63 – 3.57 (m, 1H), 2.82 (dd, J = 15.0, 6.1 Hz, 1H), 2.57 (dd, J = 15.0, 8.7 Hz, 1H), 1.41 (d, J = 6.9 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 137.1, 126.7, 124.8, 121.5, 119.3, 119.2, 118.6, 109.3, 51.5, 42.4, 32.6, 27.9, 21.2. The enantiomeric excess was determined to be 11% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 8.3 min, tR (major) = 10.0 min. $[\alpha]_D^{22}$:0.4 (c 0.57, $CHCl_3$).



5q

(S)-methyl 3-(1*H*-indol-3-yl)pentanoate (5q)

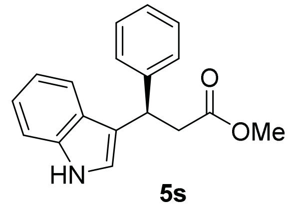
Following the general procedure **5q** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a colorless oil (18.5 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.66 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.35 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.19 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.11 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 3.60 (s, 3H), 3.48 – 3.28 (m, 1H), 2.75 (d, *J* = 7.5 Hz, 2H), 1.92 – 1.62 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 136.6, 126.8, 122.0, 121.2, 119.4, 119.3, 118.7, 111.3, 51.6, 40.7, 35.2, 28.4, 12.1. HRMS (ESI) calcd for $C_{14}H_{18}NO_2$ $(M+H)^+$: 232.1332, found: 232.1335. The enantiomeric excess was determined to be 95% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 12.1 min, tR (major) = 22.3 min. $[\alpha]_D^{26}$:5.6 (c 0.90, $CHCl_3$).



5r

(R)-methyl 3-(1*H*-indol-3-yl)-4-methylpentanoate (5r)

Following the general procedure **5r** was isolated by chromatography (petroleum ether /EtOAc 6:1) as a colorless oil (14.7 mg, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (s, 1H), 7.64 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.34 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.17 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.10 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 6.98 (d, *J* = 2.4 Hz, 1H), 3.52 (s, 3H), 3.43 – 3.26 (m, 1H), 2.82 (dd, *J* = 15.0, 5.7 Hz, 1H), 2.70 (dd, *J* = 15.0, 9.6 Hz, 1H), 2.17 – 2.00 (m, 1H), 0.91 (dd, *J* = 11.5, 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 136.3, 127.5, 121.9, 121.6, 119.7, 119.3, 117.8, 111.2, 51.6, 39.9, 37.8, 32.5, 20.5, 20.4. HRMS (ESI) calcd for $C_{15}H_{20}NO_2$ $(M+H)^+$: 246.1489, found: 246.1493. The enantiomeric excess was determined to be 93% ee by chiral HPLC analysis (ChiralCel OD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 8.8 min, tR (major) = 13.4 min. $[\alpha]_D^{26}$:4.2 (c 1.05, $CHCl_3$).

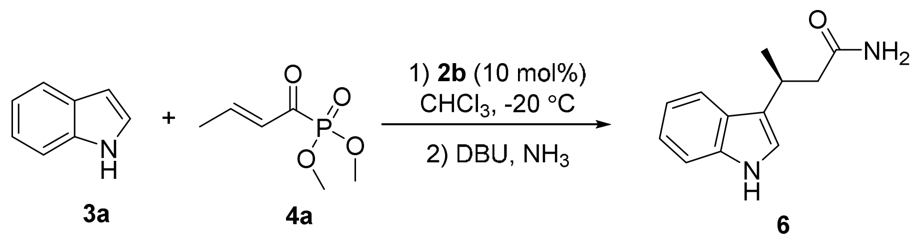


5s

(R)-methyl 3-(1*H*-indol-3-yl)-3-phenylpropanoate (5s)

Following the general procedure **5s** was isolated by chromatography (petroleum ether /EtOAc 4:1) as a white solid (21.0 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 3H), 7.28 – 7.23 (m, 2H), 7.20 – 7.10 (m, 2H), 7.04 – 6.98 (m, 2H), 4.81 (t, *J* = 7.9 Hz, 1H), 3.58 (s, 3H), 3.16 (dd, *J* = 15.2, 7.7 Hz, 1H), 3.02 (dd, *J* = 15.2, 8.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 143.8, 136.7, 128.6, 127.8, 126.7, 126.6, 122.3, 121.3, 119.6, 119.5, 118.9, 111.2, 51.8, 41.4, 39.3. HRMS (ESI) calcd for $C_{18}H_{18}NO_2$ $(M+H)^+$: 280.1332, found: 280.1327. The enantiomeric excess was determined to be 85% ee by chiral HPLC analysis (ChiralCel AD-H, 10% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 18.9 min, tR (major) = 16.0 min. $[\alpha]_D^{26}$:-24.0 (c 1.20, $CHCl_3$).

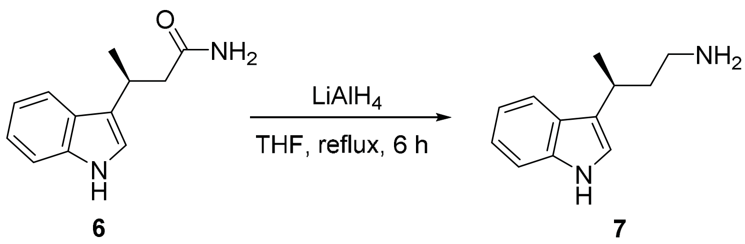
5. Procedure for the transformation of product and Characterization Data



(S)-3-(1*H*-indol-3-yl)butanamide (6)

A dry 100 ml flask containing a magnetic stir bar was charged with acyl phosphonate **4a** (356 mg, 2 mmol, 2 equiv), catalyst **2b** (34.5 mg, 0.1 mmol, 0.1 equiv), 400 mg 3 Å molecular sieves and $CHCl_3$ (20.0 mL). After 10 min of stirring at -20 ˚C, indole **3a** (117 mg, 1 mmol, 1 equiv) was added. After stirring was at this temperature for 72 h, a solution of 0.4 M NH_3 in 1,4-dioxane (40 ml, 16 mmol) was added to the mixture. Then DBU(304 mg, 2 mmol, 2 equiv) was added dropwise. The reaction mixture was warmed up to room temperature and stirred for 1 h. After 1 h, the resulting suspension was filtered and concentrated *in vacuo*. Chromatography on silica gel (petroleum ether /EtOAc 1:2 to EtOAc) gave the desired product **6** as a white solid (121.4 mg, 60%).

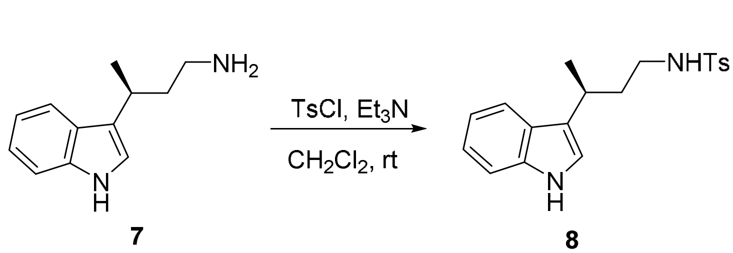
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.67 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.37 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.20 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H), 7.12 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.00 (d, *J* = 2.4 Hz, 1H), 5.38 (s, 1H), 5.32 (s, 1H), 3.58 (q, *J* = 7.1 Hz, 1H), 2.75 (dd, *J* = 14.3, 7.0 Hz, 1H), 2.51 (dd, *J* = 14.3, 7.5 Hz, 1H), 1.45 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.7, 136.7, 126.2, 122.3, 120.6, 120.6, 119.5, 119.3, 111.5, 44.1, 28.6, 21.3. HRMS (ESI) calcd for $C_{12}H_{15}N_2O$ $(M+H)^+$: 203.1179, found: 203.1178. The enantiomeric excess was determined to be 94% ee by chiral HPLC analysis (ChiralCel OD-H, 20% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 15.5 min, tR (major) = 19.1 min. $[\alpha]_D^{26}$:4.7 (c 0.60, $CHCl_3$).



(S)-3-(1*H*-indol-3-yl)butan-1-amine (7)

To the solution of **6** (101 mg, 0.5 mmol) in tetrahydrofuran (5 mL) is added lithium aluminum hydride (190 mg, 2.5 mmol) at 0 °C. The resulting mixture was warmed to room temperature and then refluxed for 6 h. The mixture was then cooled to room temperature and quenched by slow addition of water (1 mL) followed by aqueous 15% sodium hydroxide (1 mL) and water (1 mL). The resulting suspension was filtered. The aqueous layer was acidified to pH<2 with 1 M aqueous HCl and washed with AcOEt (20 mL). The aqueous solution was then basified with 6 M NaOH and extracted with CH_2Cl_2 (3 x 20 mL). The combined CH_2Cl_2 was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The desired product **7** was obtained as a pale yellow solid (70.5 mg, 75%).

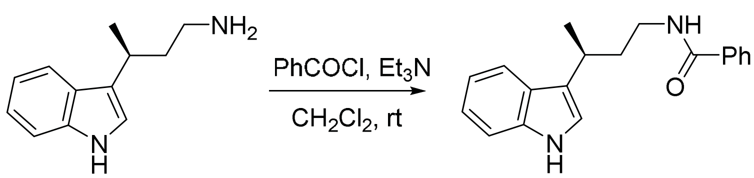
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.15 (m, 1H), 7.15 – 7.06 (m, 1H), 6.95 (d, *J* = 1.8 Hz, 1H), 3.15 (q, *J* = 7.0 Hz, 1H), 2.84 – 2.67 (m, 2H), 1.96 (dq, *J* = 14.4, 7.4 Hz, 1H), 1.81 (dq, *J* = 13.6, 7.0 Hz, 1H), 1.38 (d, *J* = 7.0 Hz, 3H), 1.50 – 1.27 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6, 126.8, 121.9, 121.9, 120.2, 119.4, 119.1, 111.3, 41.6, 40.7, 28.8, 21.9. HRMS (ESI) calcd for $C_{12}H_{17}N_2$ $(M+H)^+$: 189.1386, found: 189.1390. $[\alpha]_D^{26}$:-6.3 (c 0.60, $CHCl_3$).



(S)-N-(3-(1*H*-indol-3-yl)butyl)-4-methylbenzenesulfonamide (8)

To a stirred solution of **7** (19 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL), were sequentially added Et_3N (16 mg, 0.12 mmol) and TsCl (23 mg, 0.12 mmol). The reaction mixture was then stirred for 24 h at room temperature. Chromatography on silica gel (petroleum ether /EtOAc 4:1 to 2:1) gave the desired product **8** as a white solid (30 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.20 (dd, *J* = 18.7, 7.9 Hz, 3H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 2.3 Hz, 1H), 4.39 (t, *J* = 6.2 Hz, 1H), 3.15 – 3.01 (m, 1H), 3.01 – 2.86 (m, 2H), 2.40 (s, 3H), 1.98 – 1.75 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 137.0, 136.7, 129.7, 127.1, 126.4, 122.1, 120.6, 120.5, 119.3, 119.3, 111.5, 42.0, 37.1, 28.8, 21.7, 21.6. HRMS (ESI) calcd for $C_{19}H_{23}N_2O_2S$ $(M+H)^+$: 343.1475, found: 343.1469. The enantiomeric excess was determined to be 94% ee by chiral HPLC analysis (ChiralCel AD-H, 20% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 24.4 min, tR (major) = 22.6 min. $[\alpha]_D^{26}$:4.5 (c 0.85, $CHCl_3$).

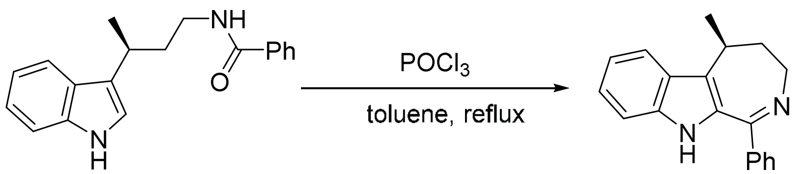


7 9

(S)-N-(3-(1H-indol-3-yl)butyl)benzamide (9)

To a stirred solution of **7** (28 mg, 0.15 mmol) in CH_2Cl_2 (1.0 mL), were sequentially added Et_3N (24 mg, 0.18 mmol) and PhCOCl (25 mg, 0.18 mmol). The reaction mixture was then stirred at room temperature overnight. Chromatography on silica gel (petroleum ether /EtOAc 2:1) gave the desired product **9** as a white solid (37.3 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.68 (dq, *J* = 8.0, 0.9 Hz, 1H), 7.44 – 7.33 (m, 4H), 7.32 – 7.26 (m, 2H), 7.21 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.12 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.01 (d, *J* = 2.3 Hz, 1H), 5.95(s, 1H), 3.59 – 3.48 (m, 1H), 3.42 (dtd, *J* = 13.7, 6.9, 5.3 Hz, 1H), 3.18 (h, *J* = 7.0 Hz, 1H), 2.08 (qd, *J* = 6.8, 1.7 Hz, 2H), 1.43 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 136.8, 134.6, 131.2, 128.5, 126.7, 126.4, 122.3, 121.0, 120.8, 119.6, 119.4, 111.6, 39.0, 36.8, 30.0, 21.9. HRMS (ESI) calcd for $C_{19}H_{21}N_2O$ $(M+H)^+$: 293.1648, found: 293.1650. The enantiomeric excess was determined to be 95% ee by chiral HPLC analysis (ChiralCel AD-H, 20% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 9.4 min, tR (major) = 11.8 min. $[\alpha]_D^{26}$:-4.4 (c 0.55, $CHCl_3$).

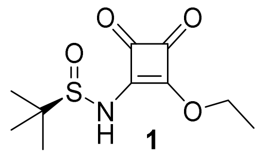


(S)-5-methyl-1-phenyl-3,4,5,10-tetrahydroazepino[3,4-b]indole (10)

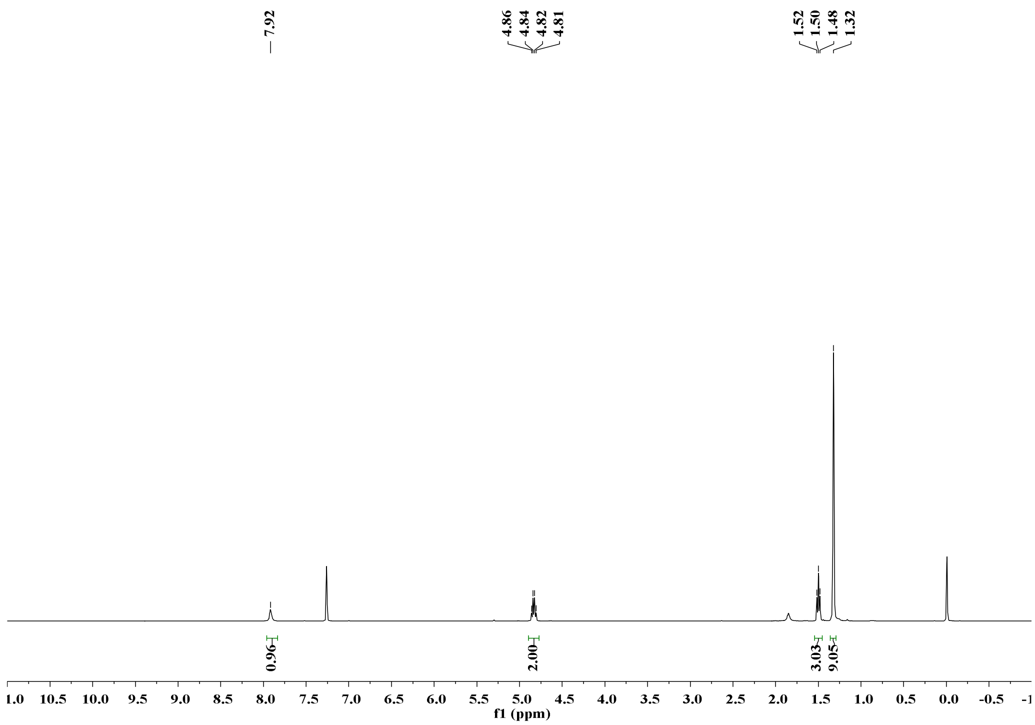
To a stirred solution of **9** (29 mg, 0.1 mmol) in toluene (2.0 mL), were added $POCl_3$ (0.1 ml). The reaction mixture was reflux overnight. The mixture was then cooled to room temperature and quenched by slow addition of water, basified with 6M NaOH, and extracted with CH_2Cl_2 (3 x 10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purified by chromatography on silica gel (petroleum ether /EtOAc 2:1 to 1:1) afforded the desired product **10** as a yellow solid (17.6 mg, 64%).

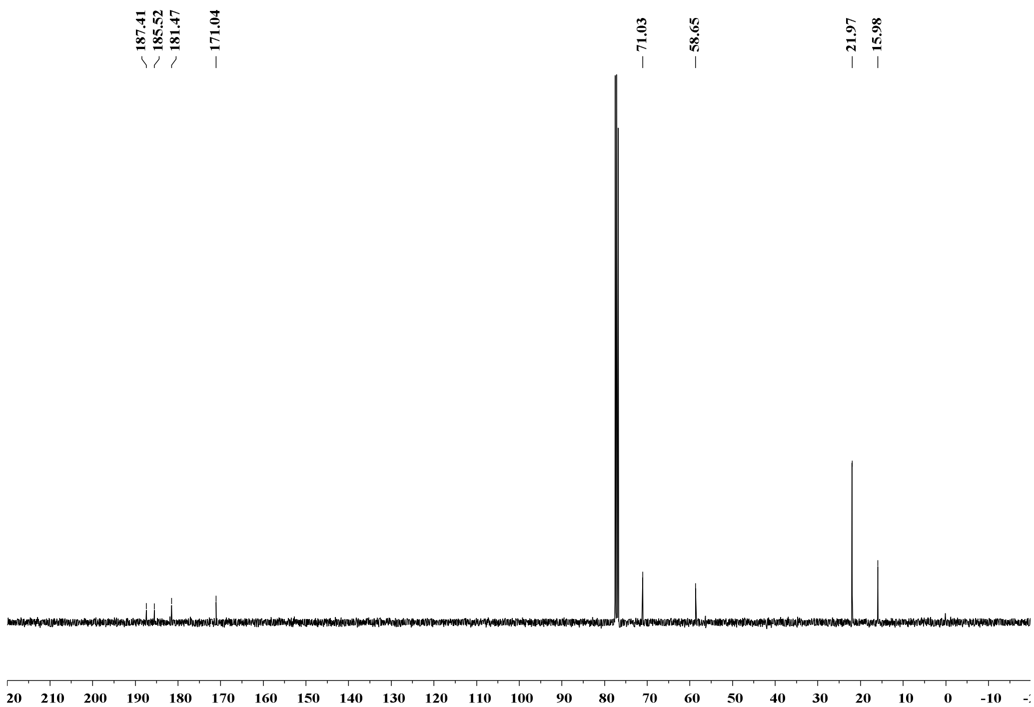
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.45 (qd, J = 8.7, 7.6, 3.6 Hz, 3H), 7.31 – 7.24 (m, 2H), 7.17 (ddd, J = 8.1, 5.9, 2.1 Hz, 1H), 4.13 (dd, J = 12.7, 7.7 Hz, 1H), 3.76 (dd, J = 12.6, 8.6 Hz, 1H), 3.70 – 3.58 (m, 1H), 2.33 (dt, J = 14.7, 7.4 Hz, 1H), 1.86 (dt, J = 14.5, 8.4 Hz, 1H), 1.47 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 140.2, 135.7, 129.8, 128.8, 128.6, 127.8, 127.7, 126.5, 124.7, 120.8, 119.9, 111.7, 50.6, 36.7, 31.9, 23.4. HRMS (ESI) calcd for $C_{19}H_{19}N_2$ $(M+H)^+$: 275.1543, found: 275.1547. The enantiomeric excess was determined to be 94% ee by chiral HPLC analysis (ChiralCel AD-H, 20% i-PrOH in hexanes, 1 mL/min, 210 nm): tR (minor) = 5.3 min, tR (major) = 8.5 min. $[\alpha]_D^{26}$:89.6 (c 0.50, $CHCl_3$).

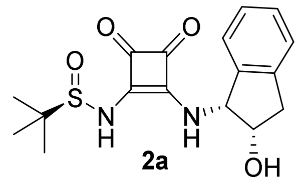
6. NMR spectra of new compounds



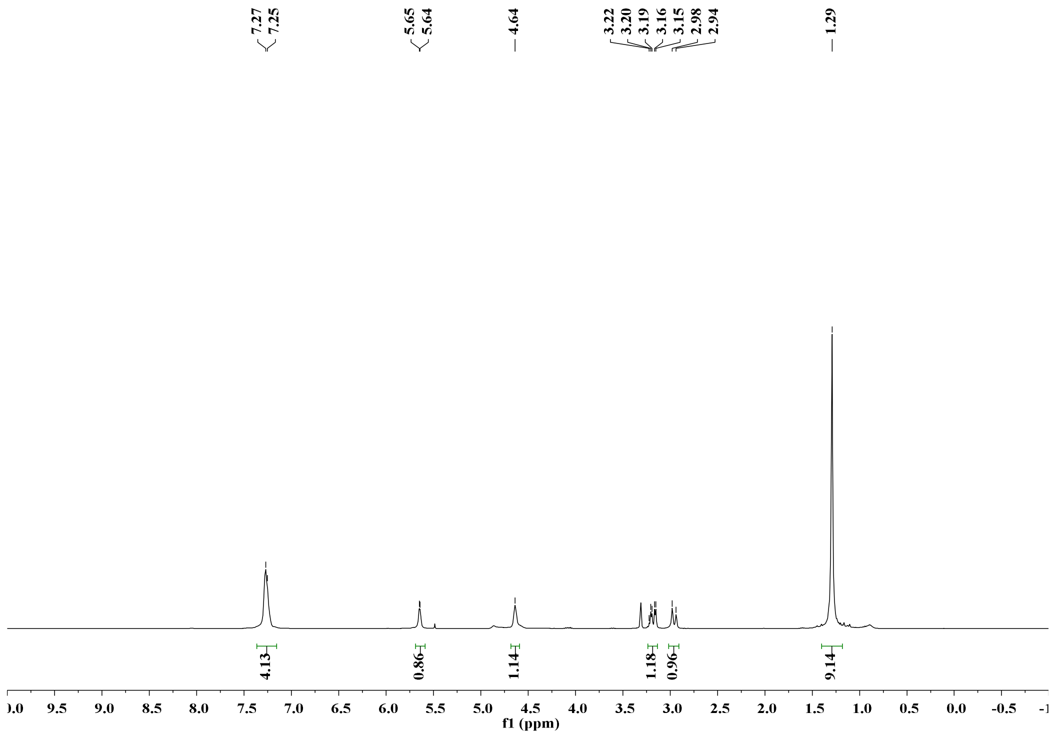
1

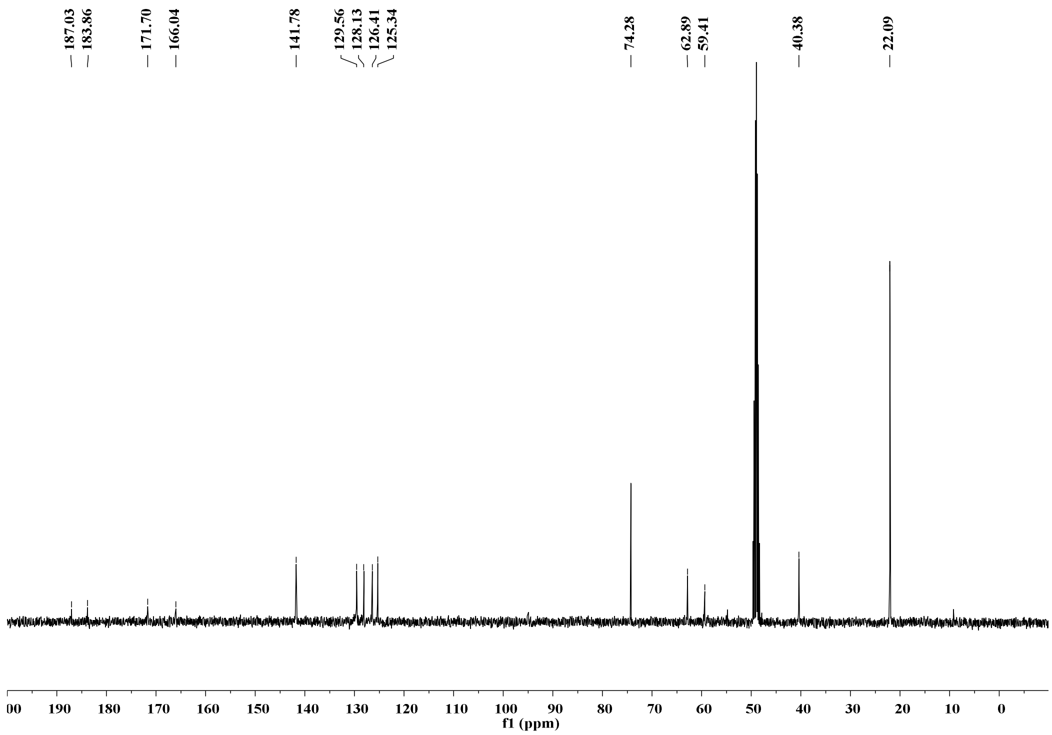


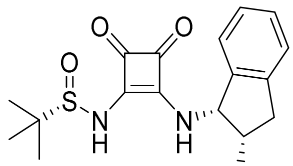




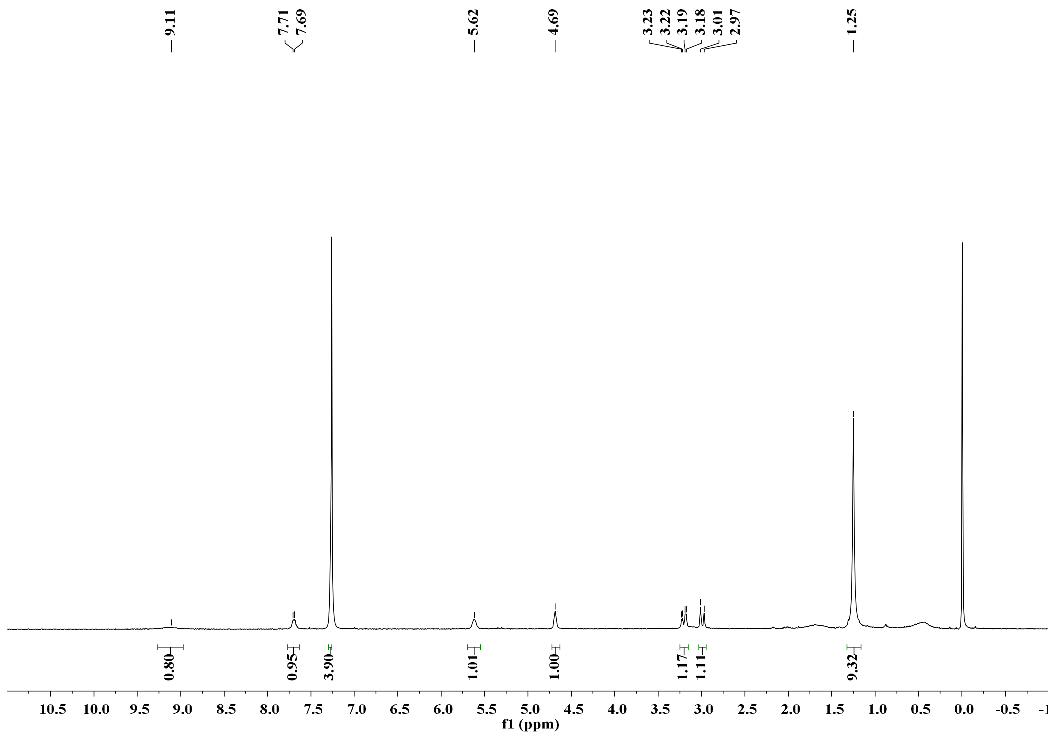
2a

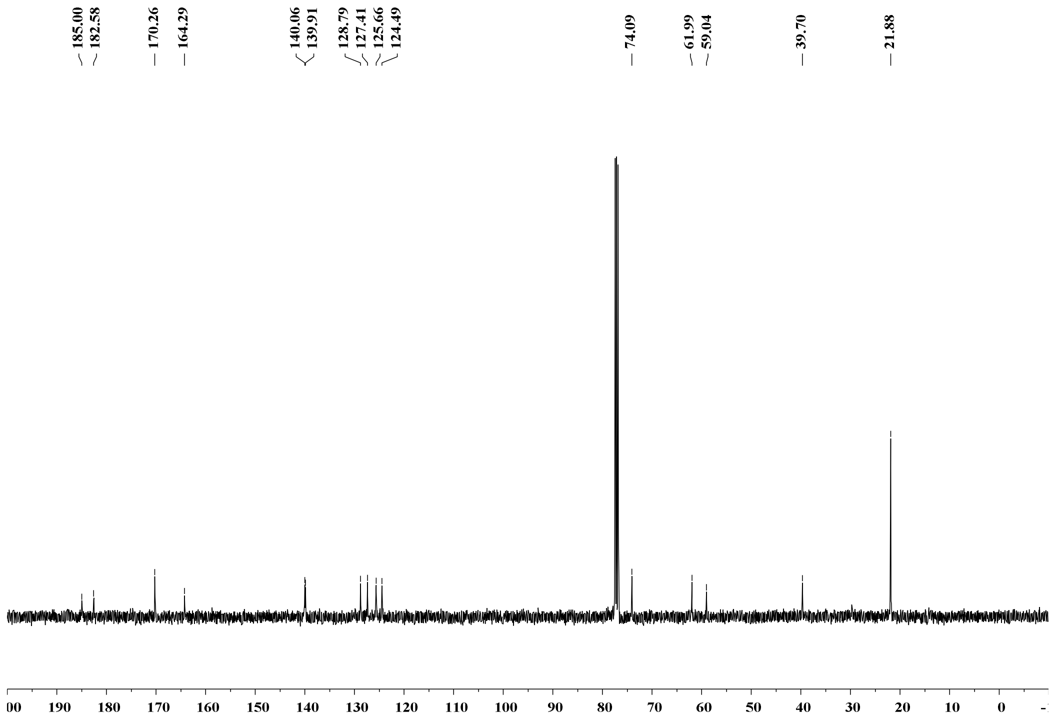

7.27
7.25
5.65
5.64
4.64
3.22
3.20
3.19
3.16
3.15
2.98
2.94
1.29
4.13
0.86
1.14
1.18
0.96
9.14
f1 (ppm)

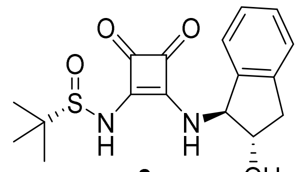

187.03
183.86
171.70
166.04
141.78
129.56
128.13
126.41
125.34
74.28
62.89
59.41
40.38
22.09
f1 (ppm)


O
O
O
S
N
H
N
H
HO

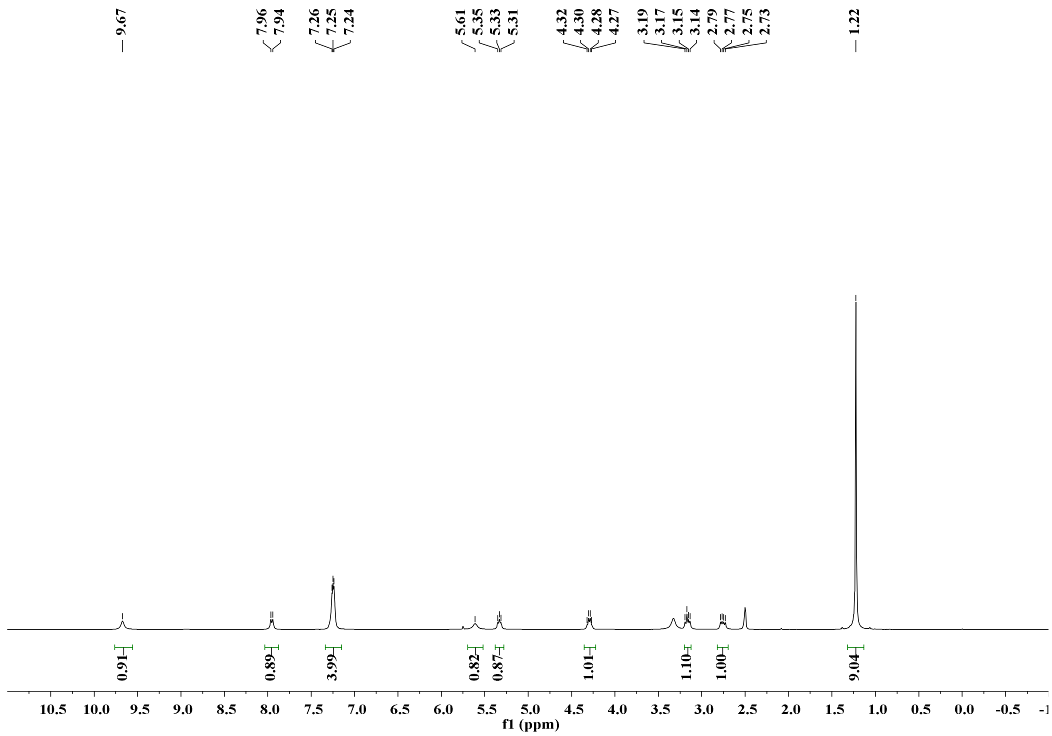
2b

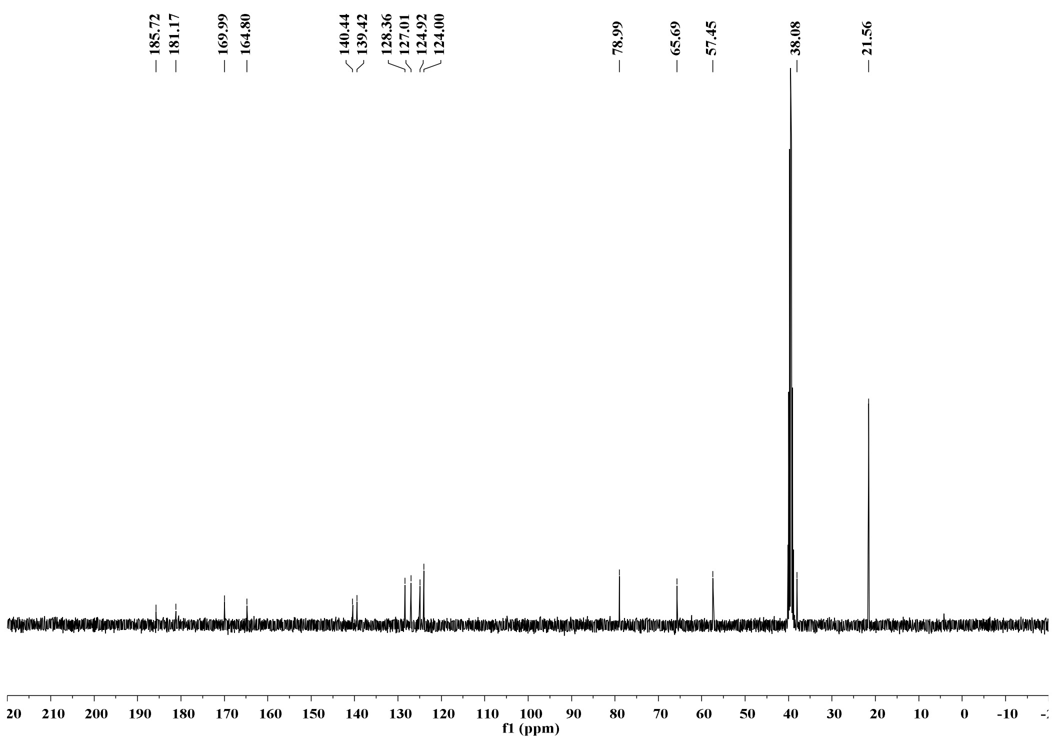

9.11
7.71
7.69
5.62
4.69
3.23
3.22
3.19
3.18
3.01
2.97
1.25
0.80
0.95
3.90
1.01
1.00
1.17
1.11
9.32
f1 (ppm)

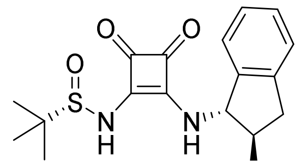

185.00
182.58
170.26
164.29
140.06
139.91
128.79
127.41
125.66
124.49
74.09
61.99
59.04
39.70
21.88
f1 (ppm)



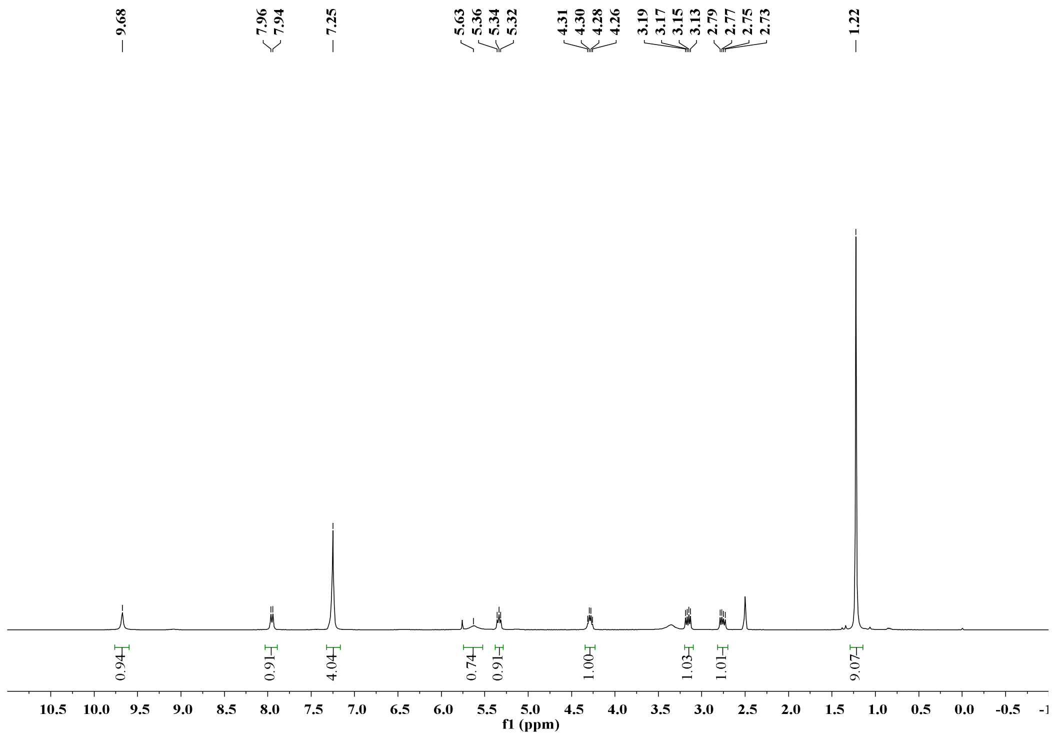
2c

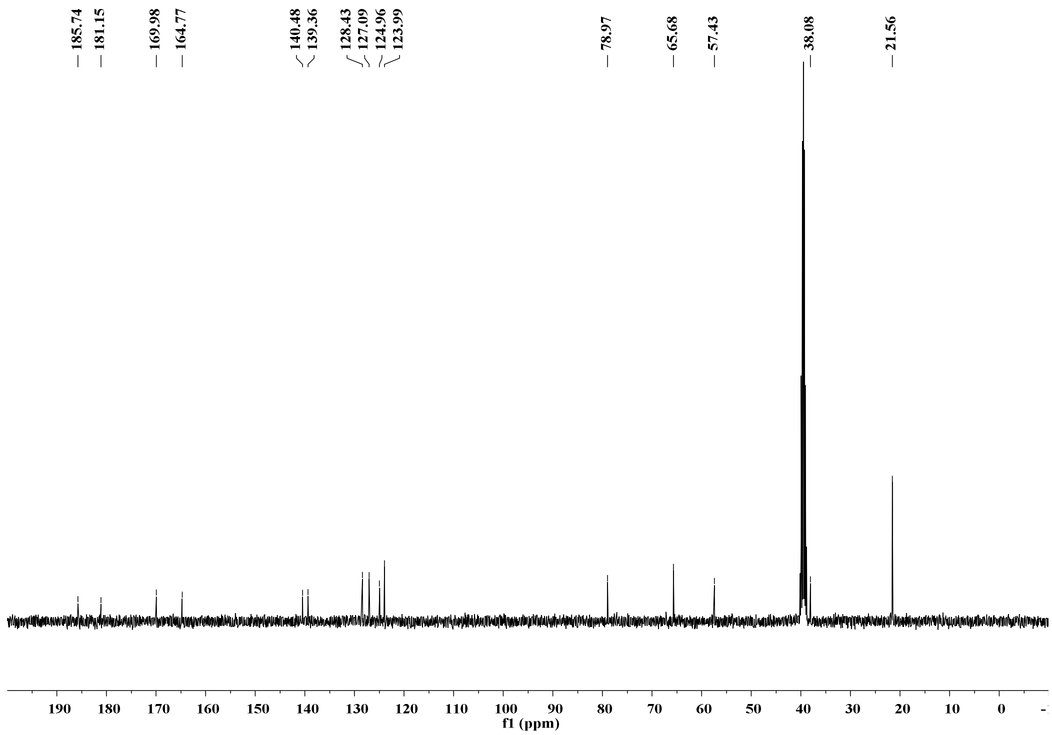

9.67
7.96
7.94
7.26
7.25
7.24
5.61
5.35
5.33
5.31
4.32
4.30
4.28
4.27
3.19
3.17
3.15
3.14
2.79
2.77
2.75
2.73
1.22
0.91
0.89
3.99
0.82
0.87
1.01
1.10
1.00
9.04
f1 (ppm)

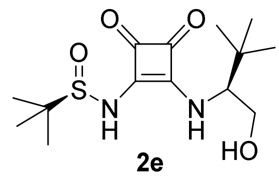

185.72
181.17
169.99
164.80
140.44
139.42
128.36
127.01
124.92
124.00
78.99
65.69
57.45
38.08
21.56
f1 (ppm)


O
O
O
S
N
H
N
H
OH

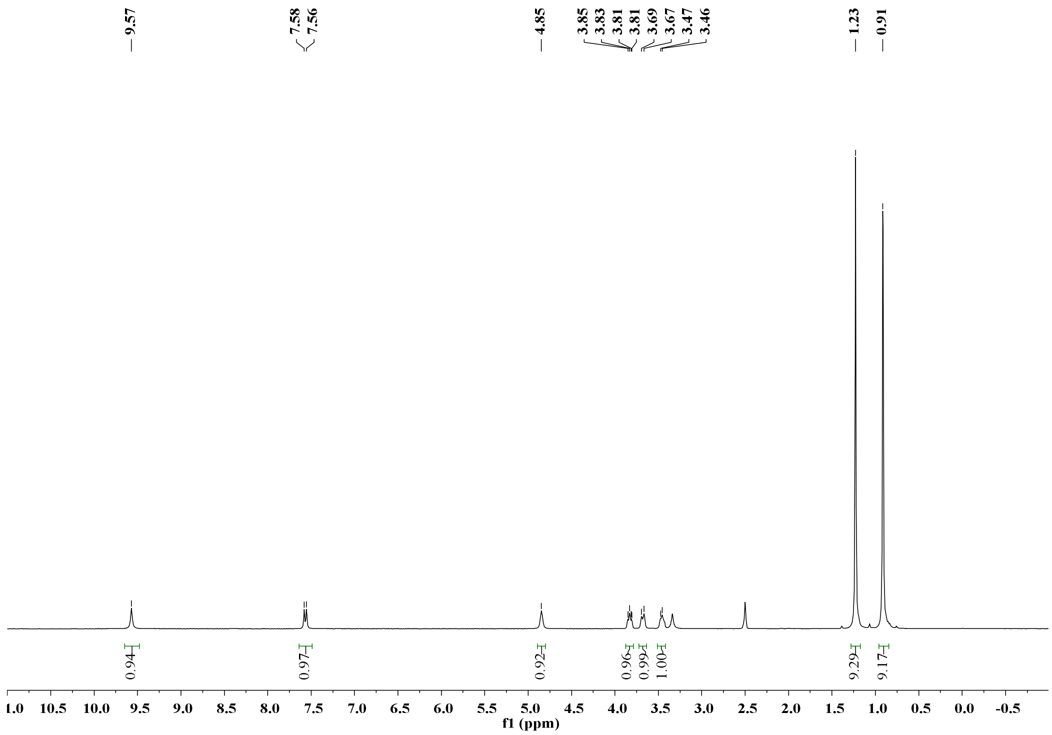
2d


9.68
7.96
7.94
7.25
5.63
5.36
5.34
5.32
4.31
4.30
4.28
4.26
3.19
3.17
3.15
3.13
2.79
2.77
2.75
2.73
1.22
0.94
0.91
4.04
0.74
0.91
1.00
1.03
1.01
9.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

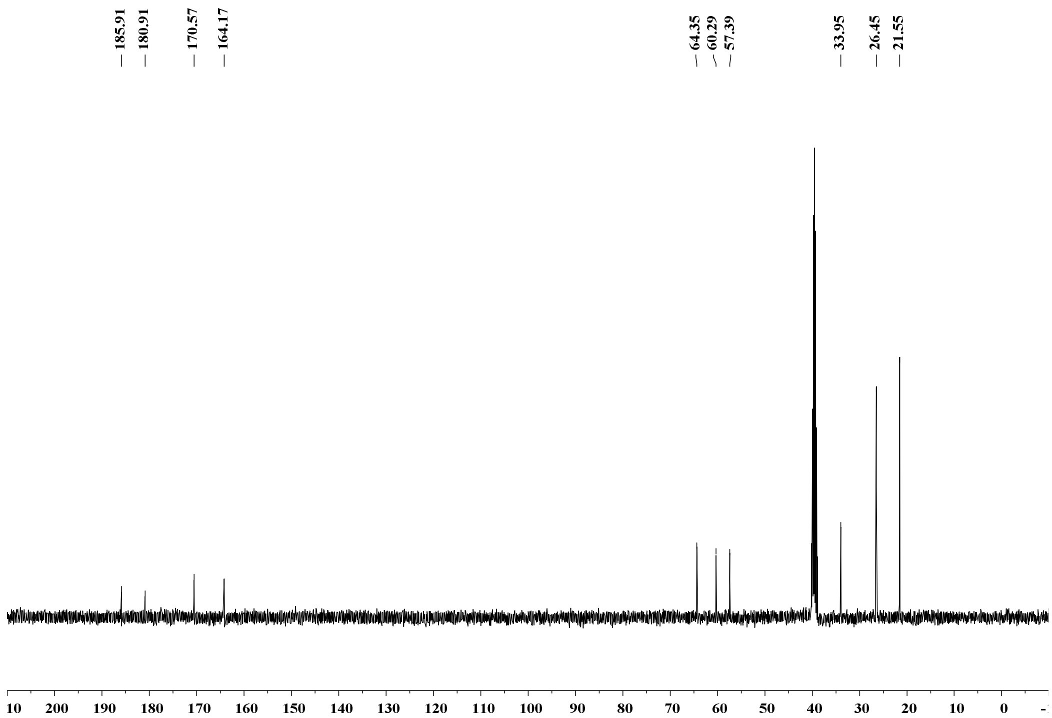

185.74
181.15
169.98
164.77
140.48
139.36
128.43
127.09
124.96
123.99
78.97
65.68
57.43
38.08
21.56
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



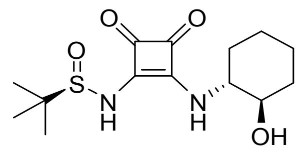
2e



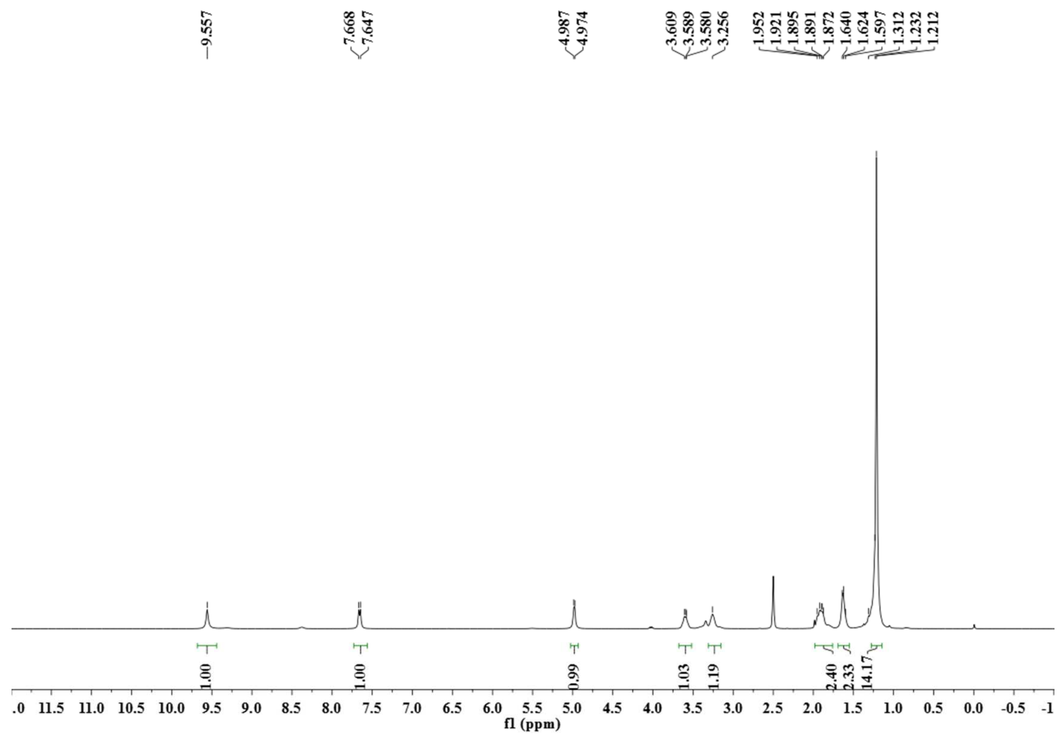
9.57
7.58
7.56
4.85
3.85
3.83
3.81
3.81
3.69
3.67
3.47
3.46
1.23
0.91
0.94
0.97
0.92
0.96
0.99
1.00
9.29
9.17
f1 (ppm)

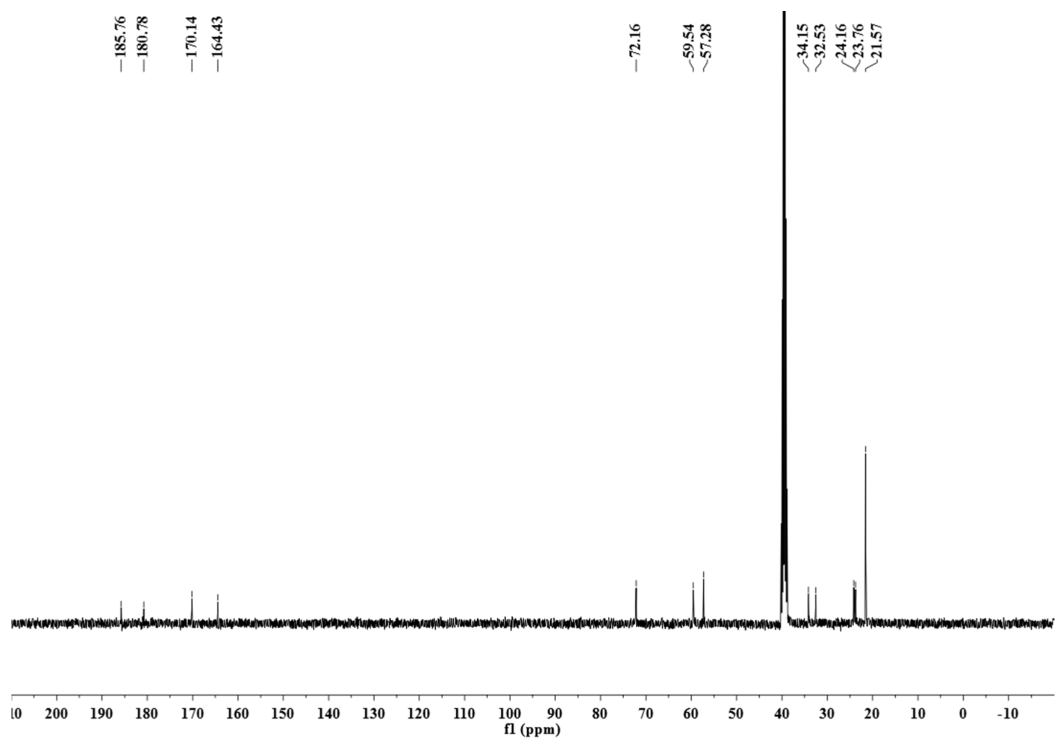


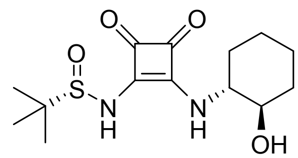
185.91
180.91
170.57
164.17
64.35
60.29
57.39
33.95
26.45
21.55
f1 (ppm)


O
O
O
S
N
H
N
H
OH

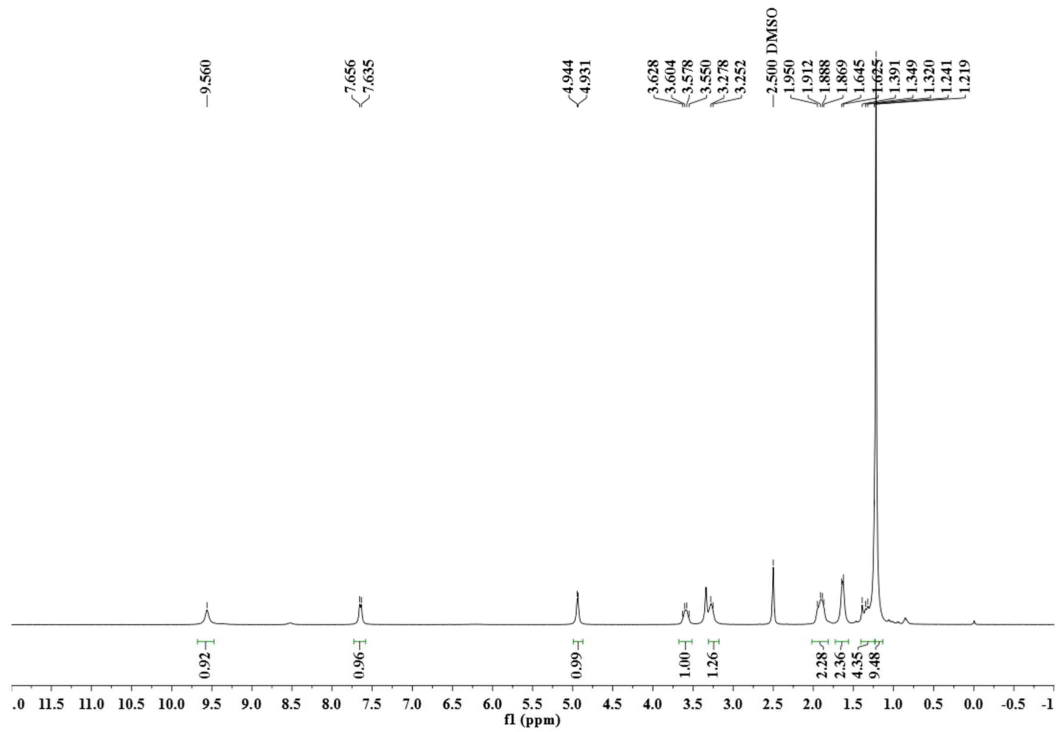
2f


9.557
7.668
7.647
4.987
4.974
3.609
3.589
3.580
3.256
1.952
1.921
1.895
1.891
1.872
1.640
1.624
1.597
1.312
1.232
1.212
1.00
1.00
0.99
1.03
1.19
2.40
2.33
14.17
f1 (ppm)

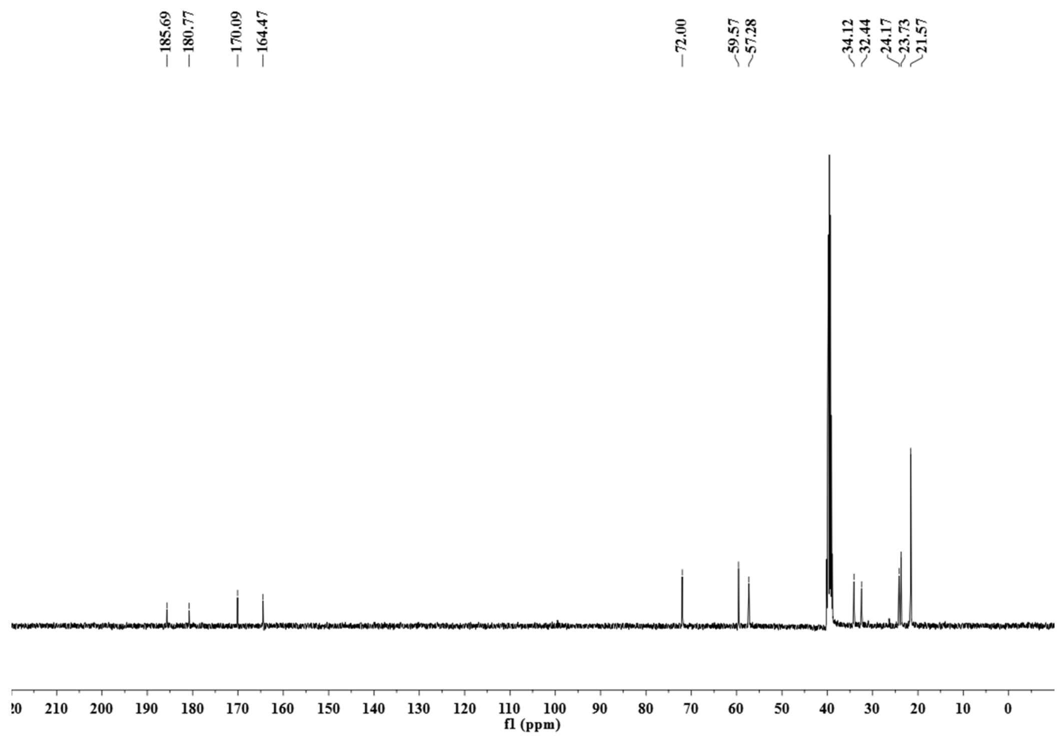

185.76
180.78
170.14
164.43
72.16
59.54
57.28
34.15
32.53
24.16
23.76
21.57
f1 (ppm)



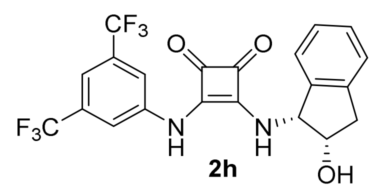
2g



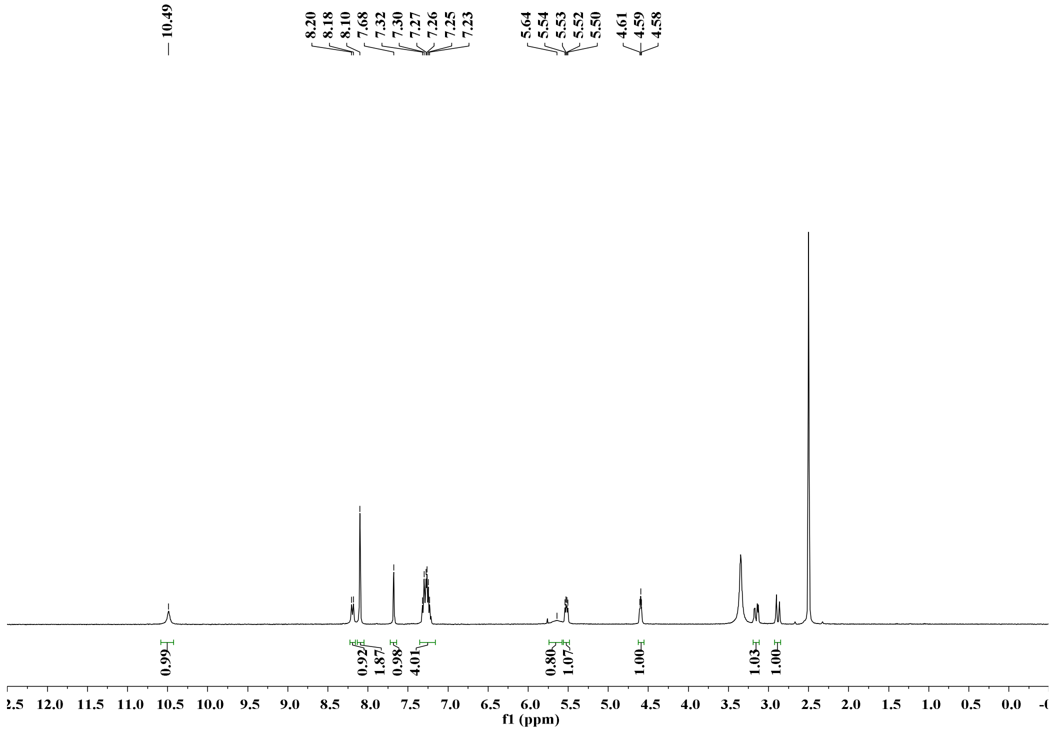
9.560
7.656
7.635
4.944
4.931
3.628
3.604
3.578
3.550
3.278
3.252
2.500 DMSO
1.950
1.912
1.888
1.869
1.645
1.625
1.391
1.349
1.320
1.241
1.219
0.92
0.96
0.99
1.00
1.26
2.28
2.36
4.35
9.48
f1 (ppm)

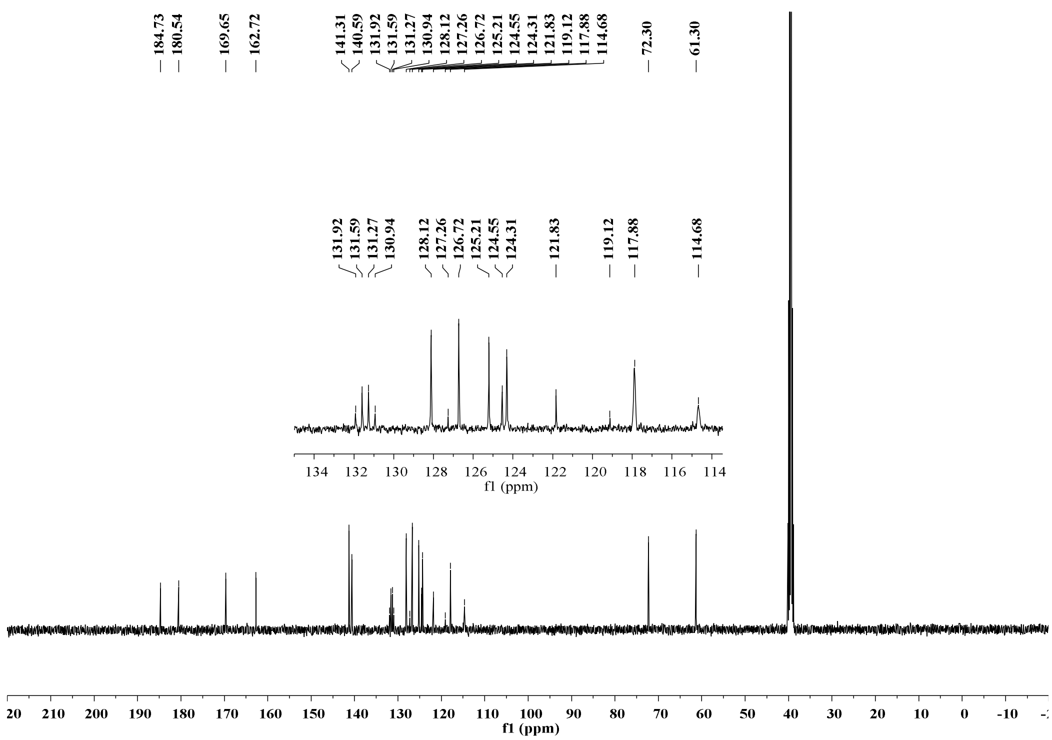


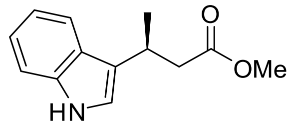
185.69
180.77
170.09
164.47
72.00
59.57
57.28
34.12
32.44
24.17
23.73
21.57
f1 (ppm)


CF3
O
O
F3C
N
H
N
H
OH

2h

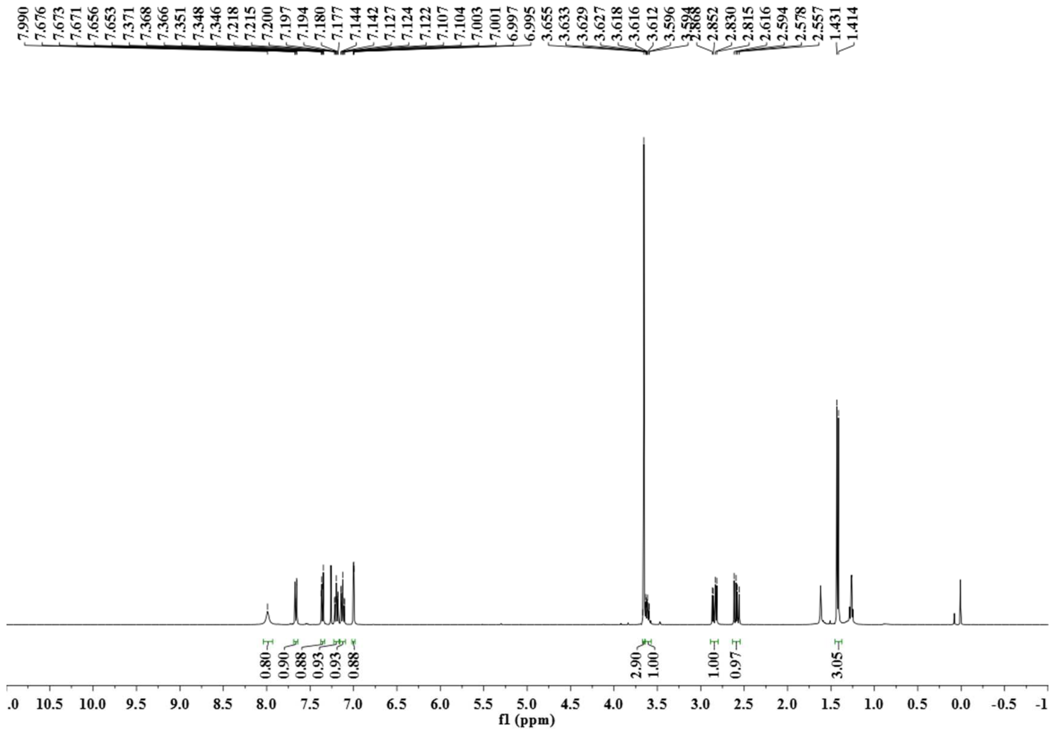

10.49
8.20
8.18
8.10
7.68
7.32
7.30
7.27
7.26
7.25
7.23
5.64
5.54
5.53
5.52
5.50
4.61
4.59
4.58
0.99
0.92
1.87
0.98
4.01
0.80
1.07
1.00
1.03
1.00
f1 (ppm)


184.73
180.54
169.65
162.72
141.31
140.59
131.92
131.59
131.27
130.94
128.12
127.26
126.72
125.21
124.55
124.31
121.83
119.12
117.88
114.68
72.30
61.30
f1 (ppm)
f1 (ppm)

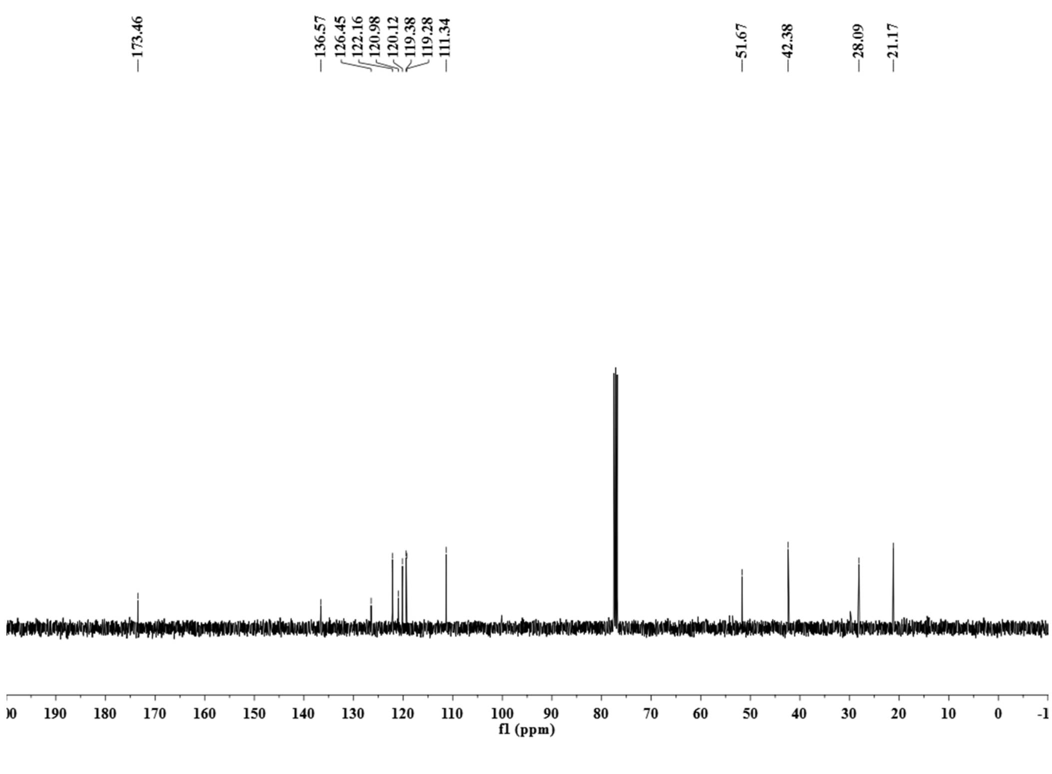


O
OMe
HN

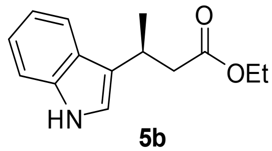
5a



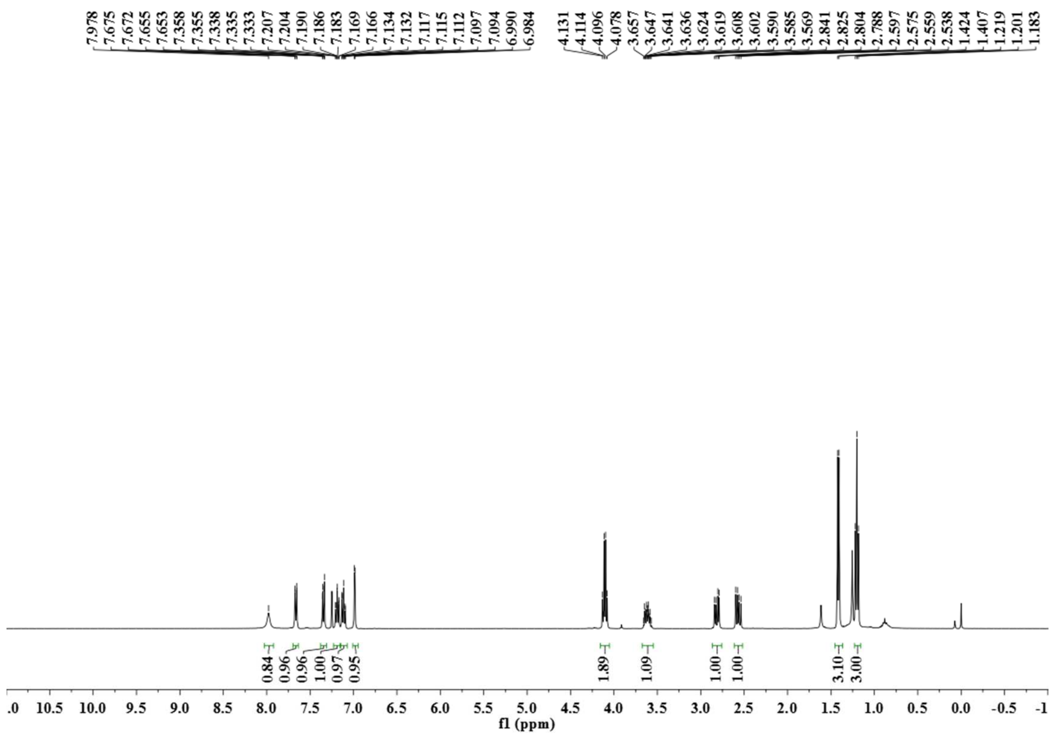
7.990 7.676 7.673 7.671 7.656 7.653 7.371 7.368 7.366 7.351 7.348 7.346 7.218 7.215 7.200 7.197 7.194 7.180 7.177 7.144 7.142 7.127 7.124 7.122 7.107 7.104 7.003 7.001 6.997 6.995 3.655 3.633 3.629 3.627 3.618 3.616 3.612 3.596 3.594 2.868 2.852 2.830 2.815 2.616 2.594 2.578 2.557 1.431 1.414
0.80 0.90 0.88 0.93 0.93 0.88 2.90 1.00 1.00 0.97 3.05
f1 (ppm)

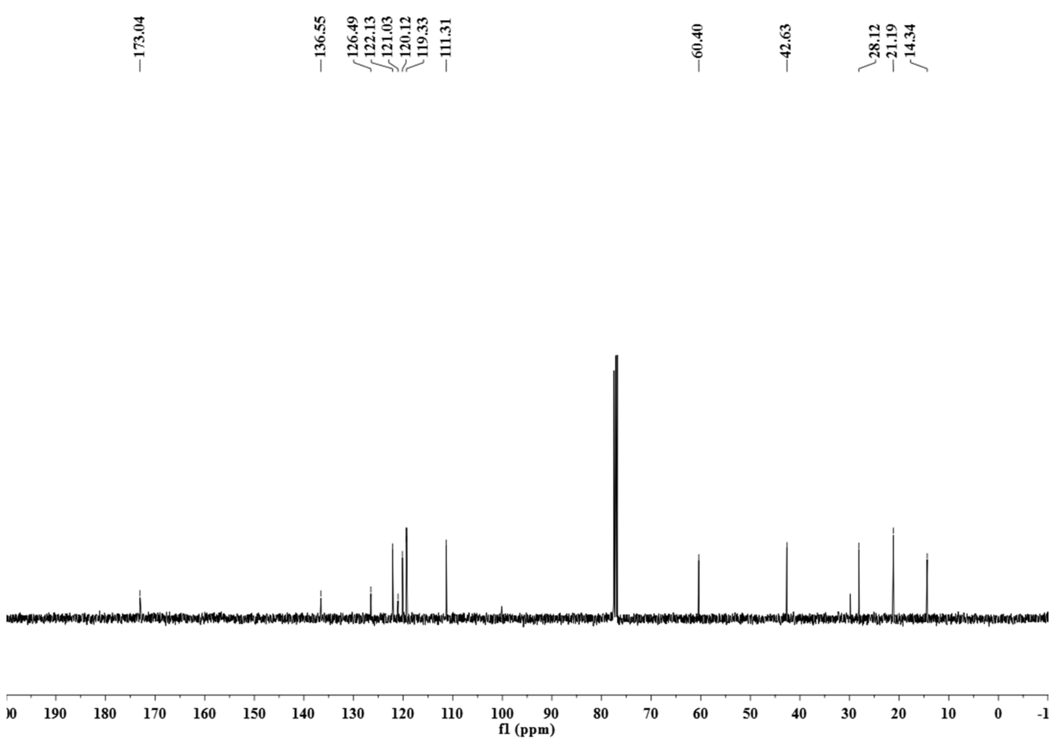


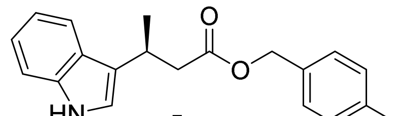
173.46 136.57 126.45 122.16 120.98 120.12 119.38 119.28 111.34 51.67 42.38 28.09 21.17
f1 (ppm)



5b

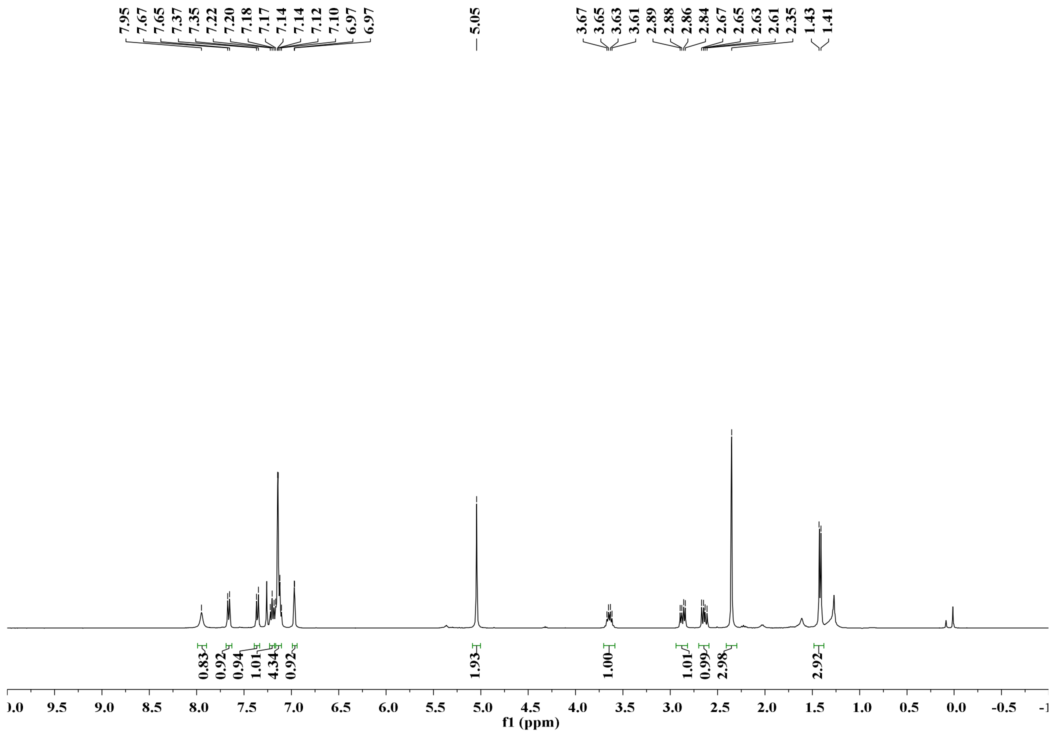

7.978
7.675
7.672
7.655
7.653
7.358
7.355
7.338
7.335
7.333
7.207
7.204
7.190
7.186
7.183
7.169
7.166
7.134
7.132
7.117
7.115
7.112
7.097
7.094
6.990
6.984
4.131
4.114
4.096
4.078
3.657
3.647
3.641
3.636
3.624
3.619
3.608
3.602
3.590
3.585
3.569
2.841
2.825
2.804
2.788
2.597
2.575
2.559
2.538
1.424
1.407
1.219
1.201
1.183
0.84
0.96
0.96
1.00
0.97
0.95
1.89
1.09
1.00
1.00
3.10
3.00
f1 (ppm)


173.04
136.55
126.49
122.13
121.03
120.12
119.33
111.31
60.40
42.63
28.12
21.19
14.34
f1 (ppm)

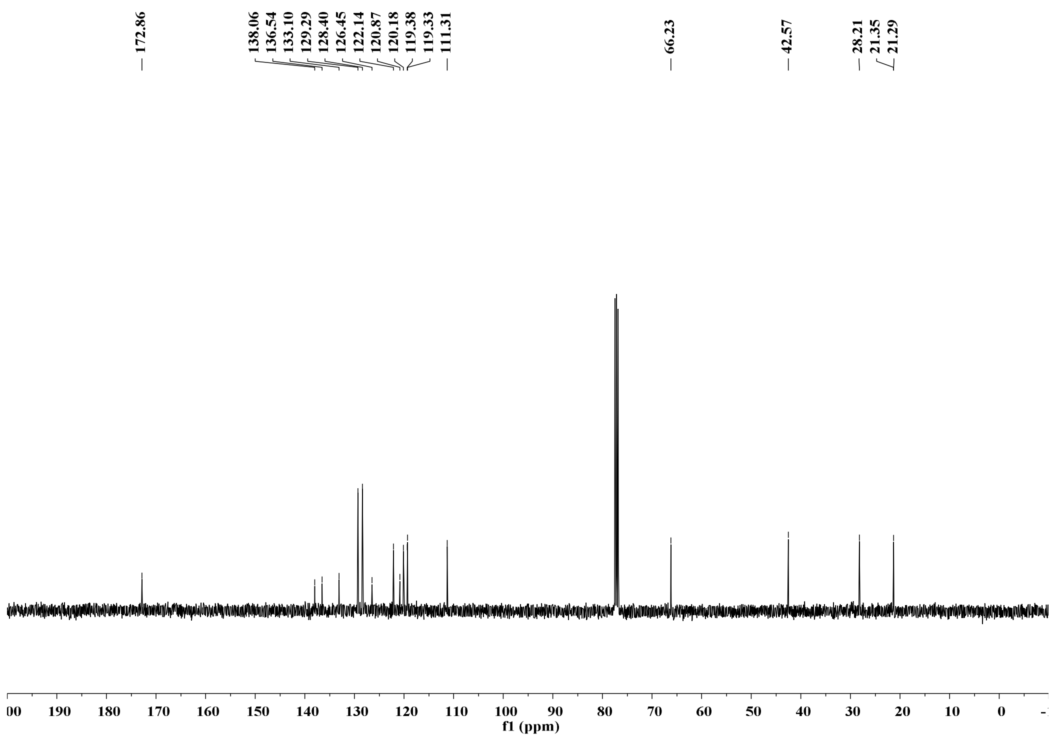


O
HN

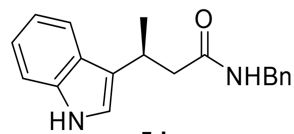
5c



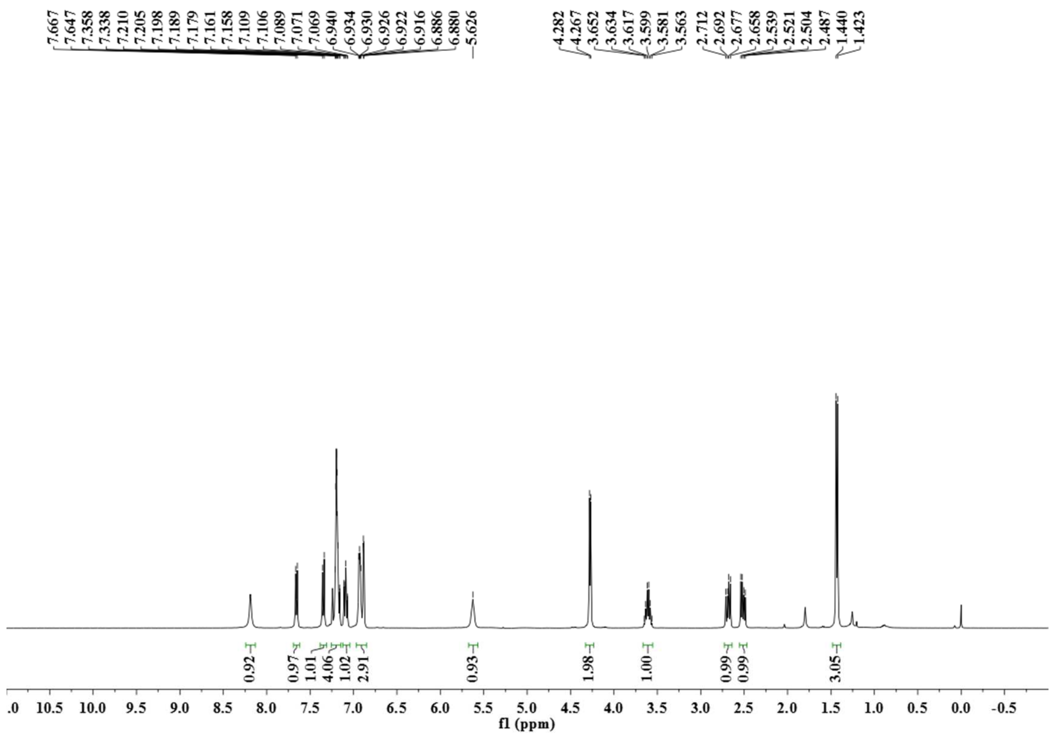
7.95 7.67 7.65 7.37 7.35 7.22 7.20 7.18 7.17 7.14 7.14 7.12 7.10 6.97 6.97
5.05
3.67 3.65 3.63 3.61 2.89 2.88 2.86 2.84 2.67 2.65 2.63 2.61 2.35 1.43 1.41
0.83 0.92 0.94 1.01 4.34 0.92
1.93
1.00
1.01 0.99 2.98
2.92
f1 (ppm)

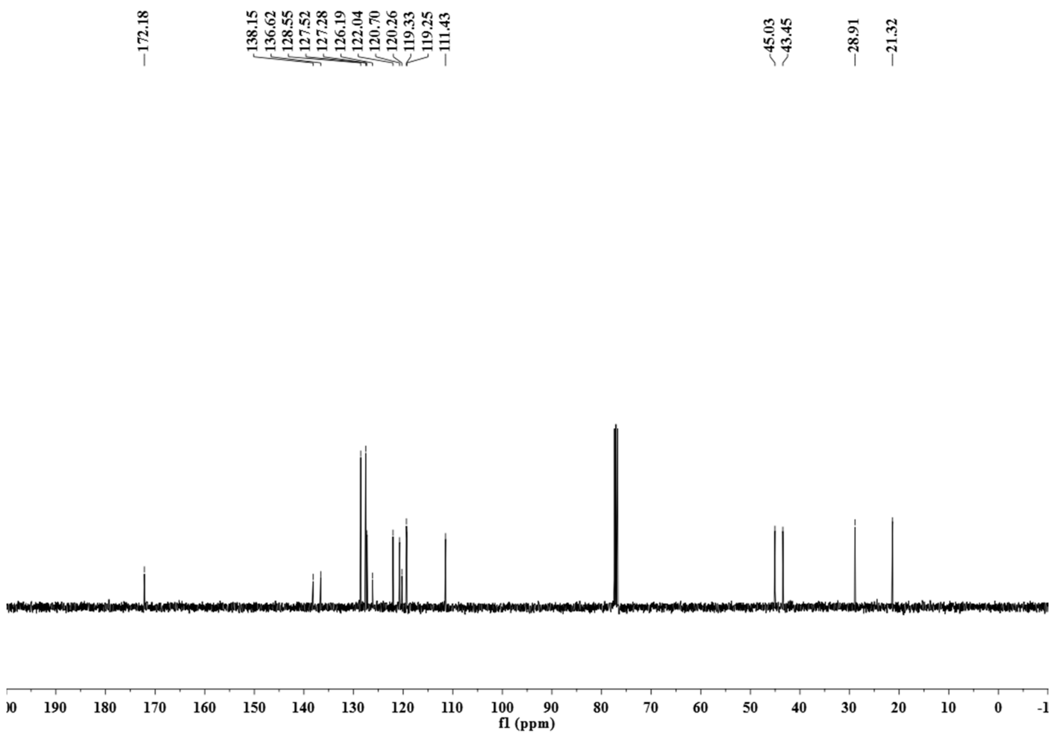


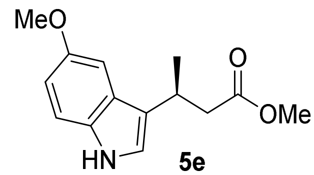
172.86
138.06 136.54 133.10 129.29 128.40 126.45 122.14 120.87 120.18 119.38 119.33 111.31
66.23
42.57
28.21 21.35 21.29
f1 (ppm)


O
NHBn
HN

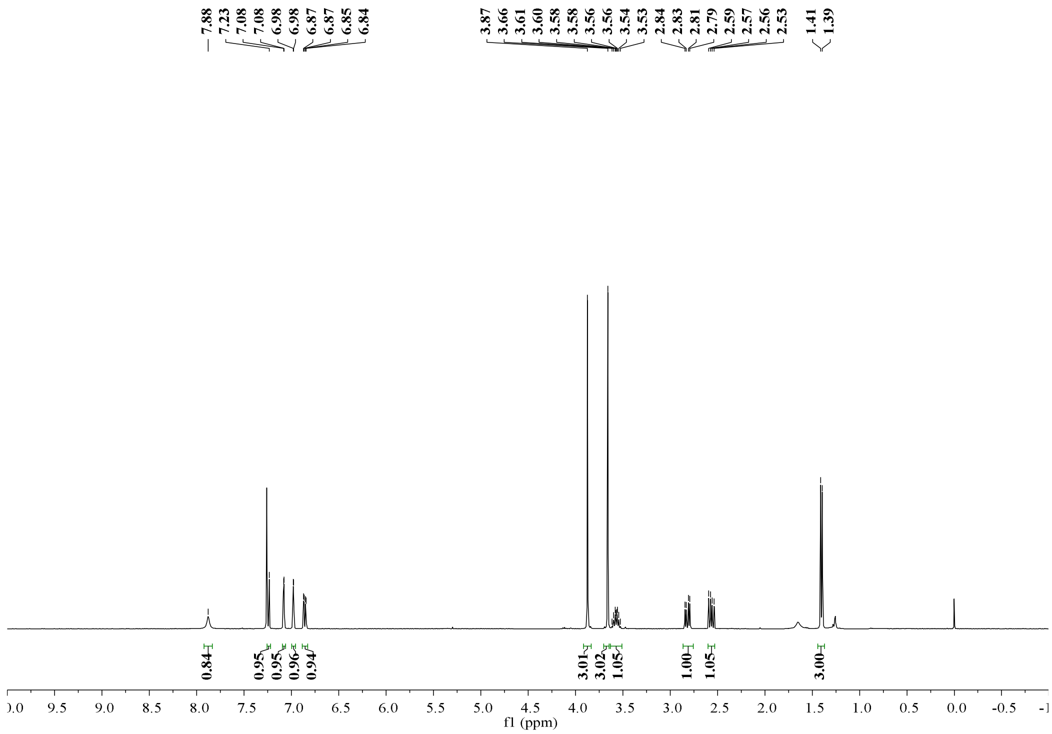
5d

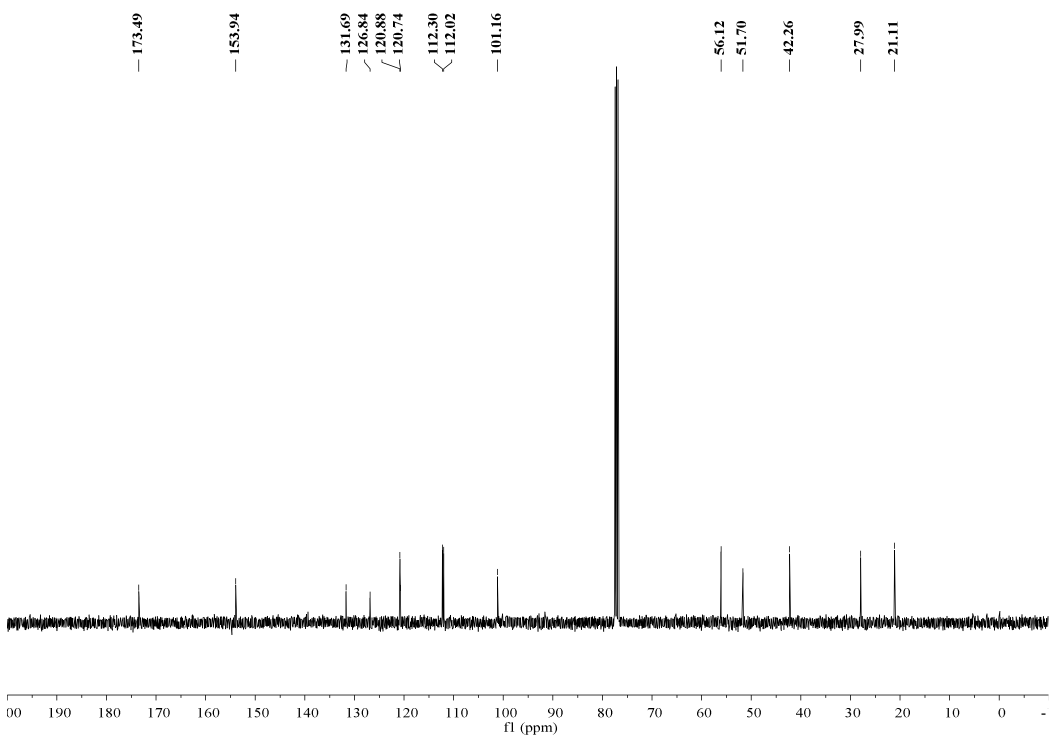

7.667
7.647
7.358
7.338
7.210
7.205
7.198
7.189
7.179
7.161
7.158
7.109
7.106
7.089
7.071
7.069
6.940
6.934
6.930
6.926
6.922
6.916
6.886
6.880
5.626
4.282
4.267
3.652
3.634
3.617
3.599
3.581
3.563
2.712
2.692
2.677
2.658
2.539
2.521
2.504
2.487
1.440
1.423
0.92
0.97
1.01
4.06
1.02
2.91
0.93
1.98
1.00
0.99
0.99
3.05
f1 (ppm)

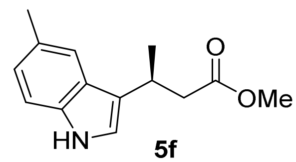

172.18
138.15
136.62
128.55
127.52
127.28
126.19
122.04
120.70
120.26
119.33
119.25
111.43
45.03
43.45
28.91
21.32
f1 (ppm)



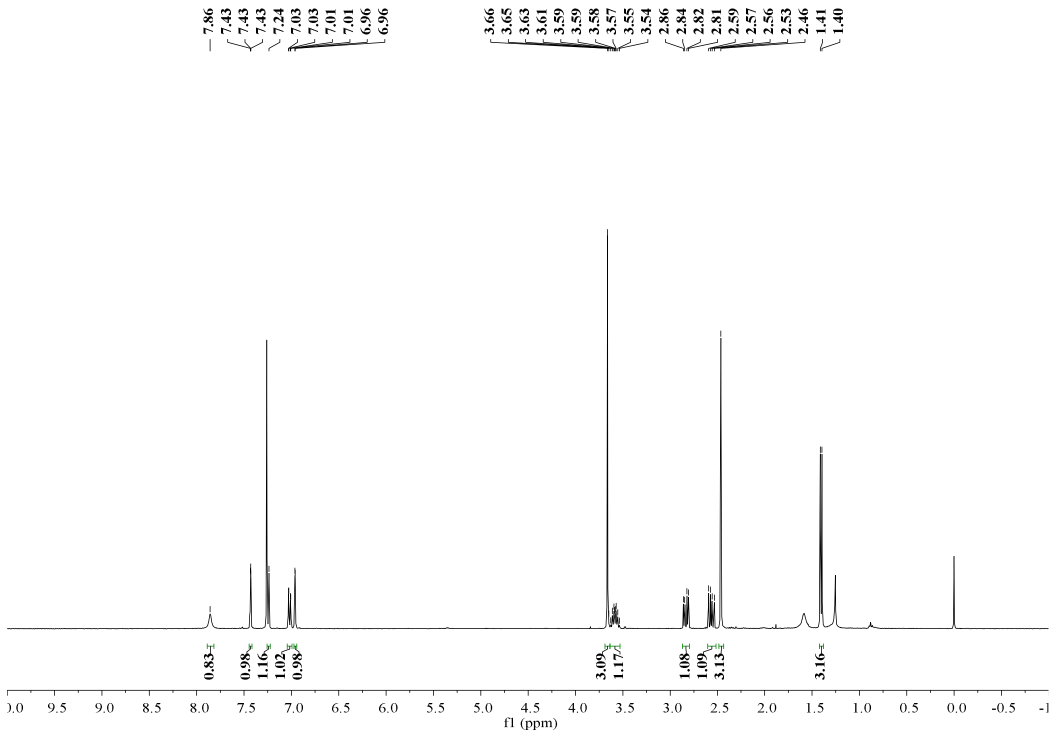
5e

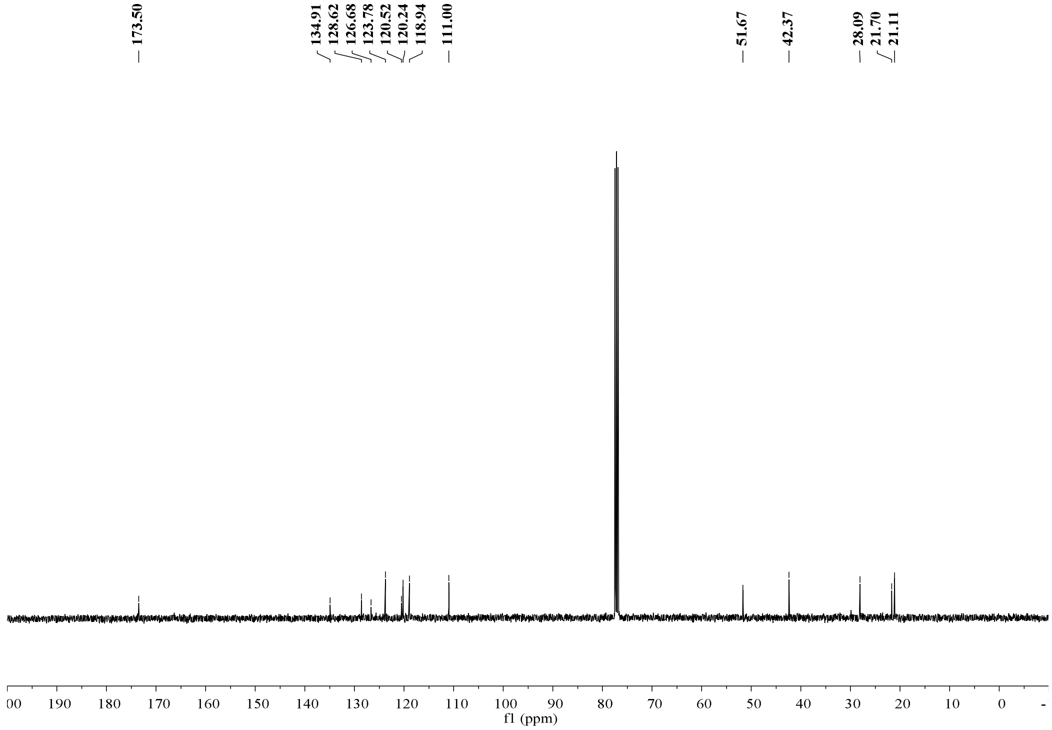


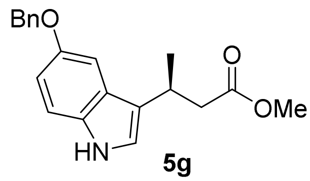



OMe
HN

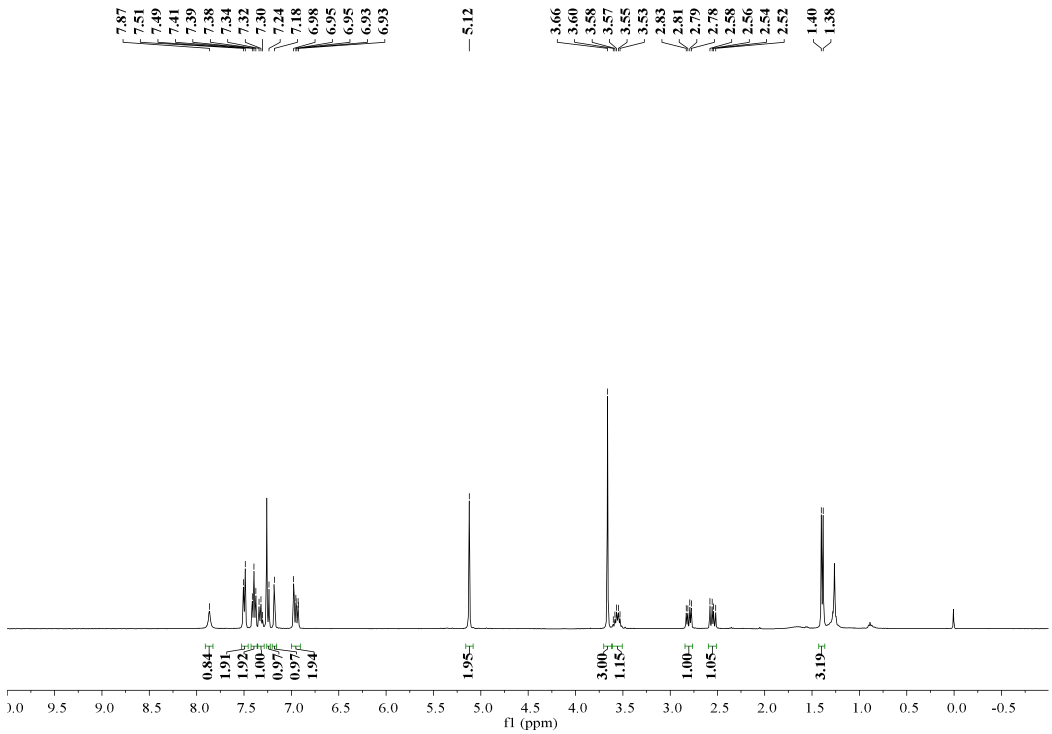
5f

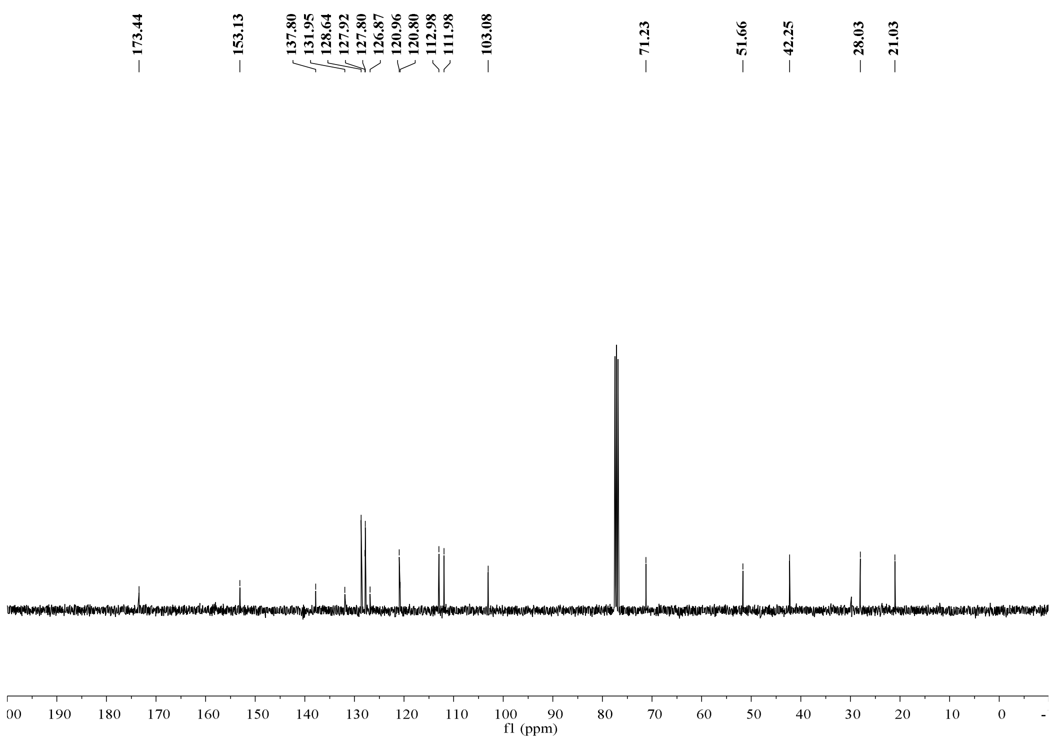

7.86 7.43 7.43 7.43 7.24 7.03 7.03 7.01 7.01 6.96 6.96
3.66 3.65 3.63 3.61 3.59 3.59 3.58 3.57 3.55 3.54 2.86 2.84 2.82 2.81 2.59 2.57 2.56 2.53 2.46 1.41 1.40
0.83 0.98 1.16 1.02 0.98 3.09 1.17 1.08 1.09 3.13 3.16
f1 (ppm)

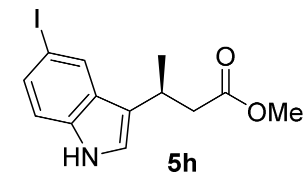

173.50
134.91 128.62 126.68 123.78 120.52 120.24 118.94 111.00
51.67 42.37 28.09 21.70 21.11
f1 (ppm)


BnO
O
OMe
HN

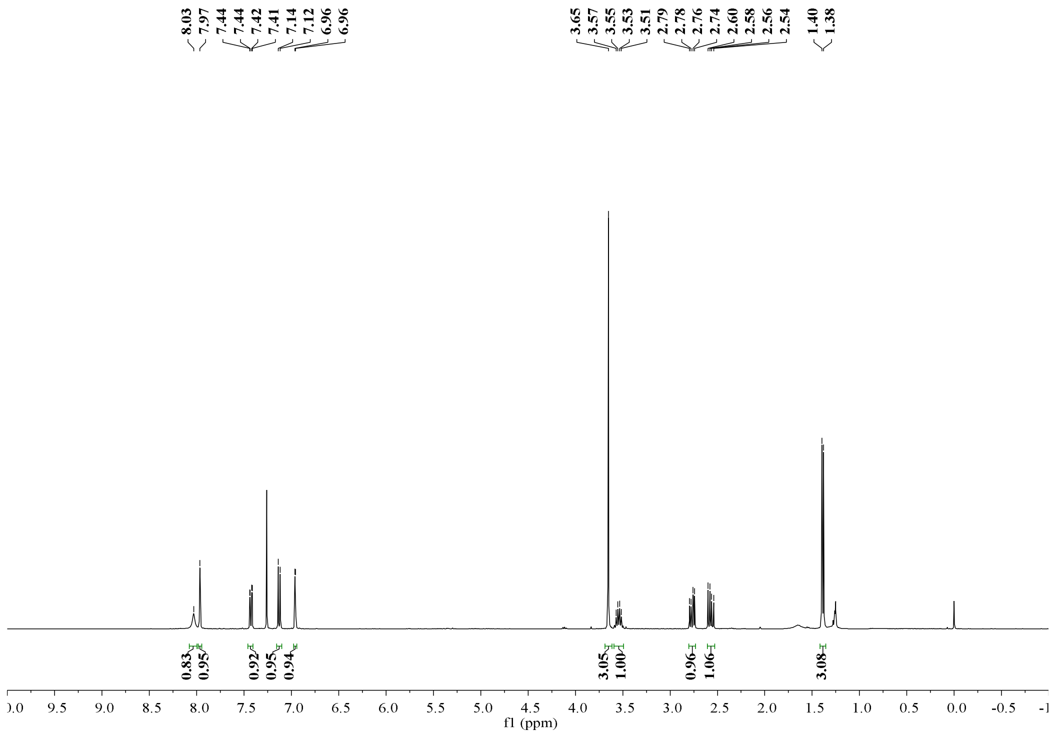
5g


7.87
7.51
7.49
7.41
7.39
7.38
7.34
7.32
7.30
7.24
7.18
6.98
6.95
6.95
6.93
6.93
5.12
3.66
3.60
3.58
3.57
3.55
3.53
2.83
2.81
2.79
2.78
2.58
2.56
2.54
2.52
1.40
1.38
0.84
1.91
1.92
1.00
0.97
0.97
1.94
1.95
3.00
1.15
1.00
1.05
3.19
f1 (ppm)

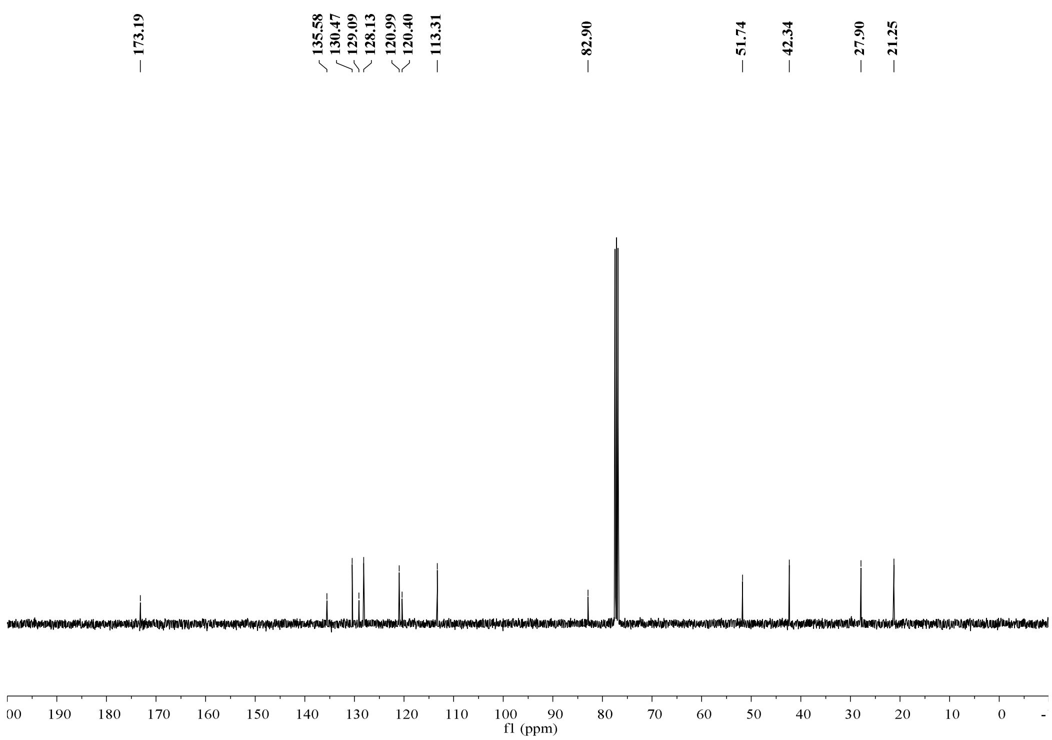

173.44
153.13
137.80
131.95
128.64
127.92
127.80
126.87
120.96
120.80
112.98
111.98
103.08
71.23
51.66
42.25
28.03
21.03
f1 (ppm)



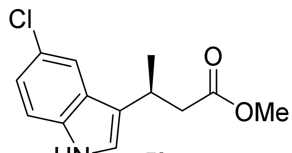
5h



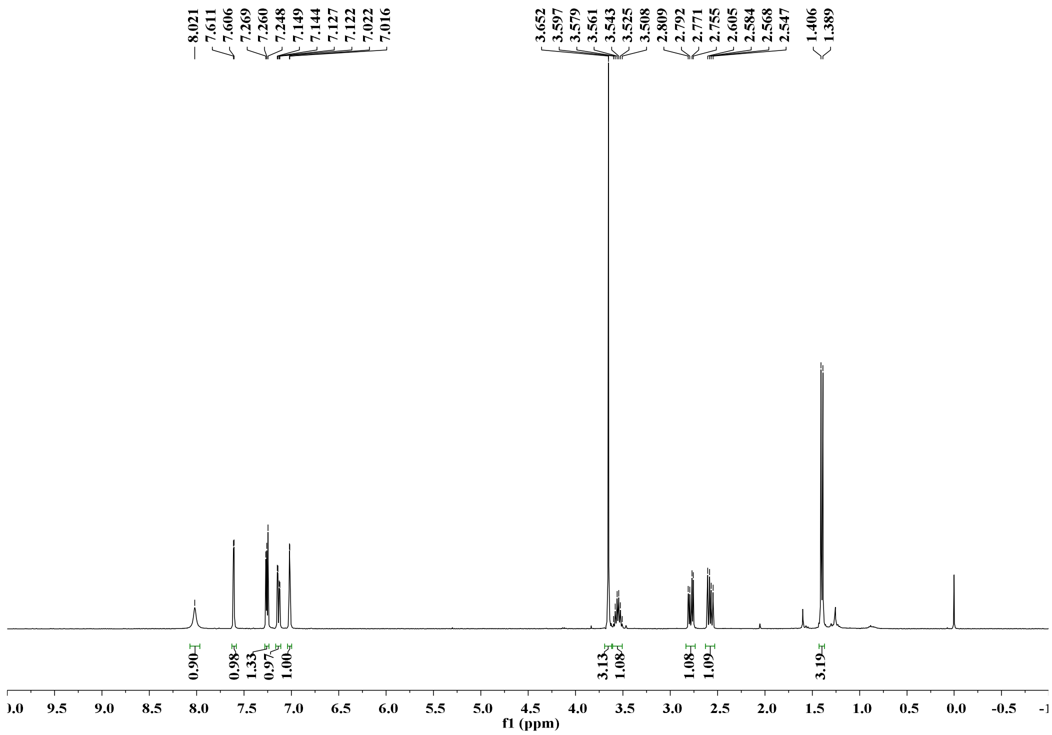
8.03
7.97
7.44
7.44
7.42
7.41
7.14
7.12
6.96
6.96
3.65
3.57
3.55
3.53
3.51
2.79
2.78
2.76
2.74
2.60
2.58
2.56
2.54
1.40
1.38
0.83
0.95
0.92
0.95
0.94
3.05
1.00
0.96
1.06
3.08
f1 (ppm)

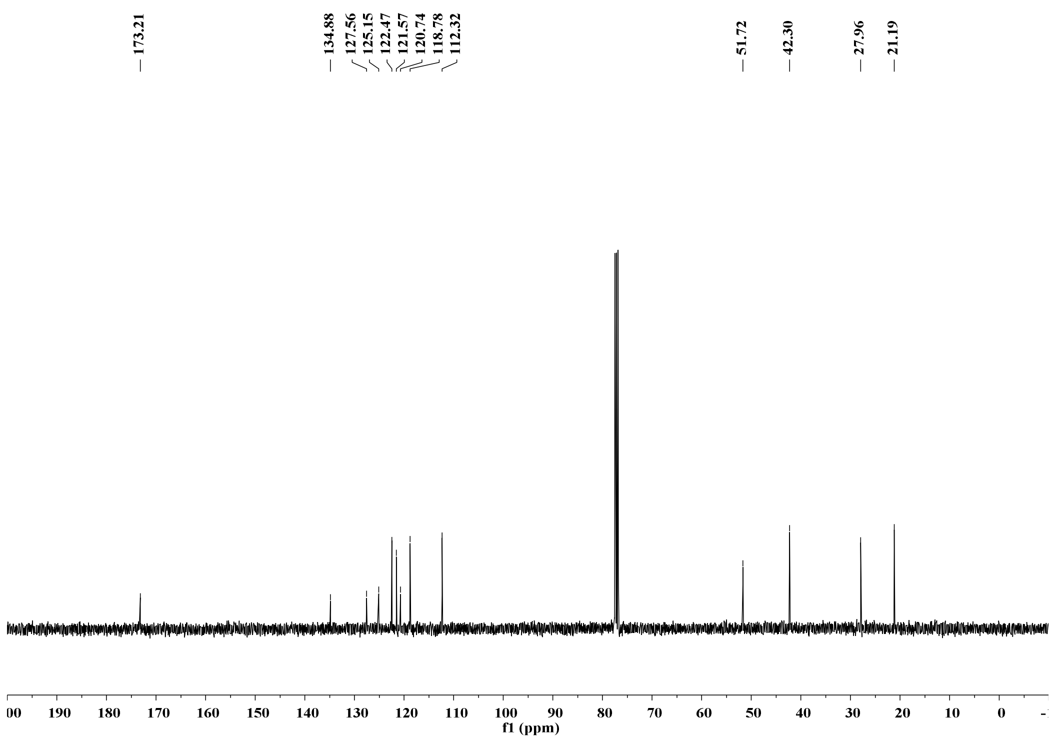


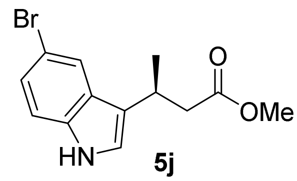
173.19
135.58
130.47
129.09
128.13
120.99
120.40
113.31
82.90
51.74
42.34
27.90
21.25
f1 (ppm)


Cl
O
OMe
HN

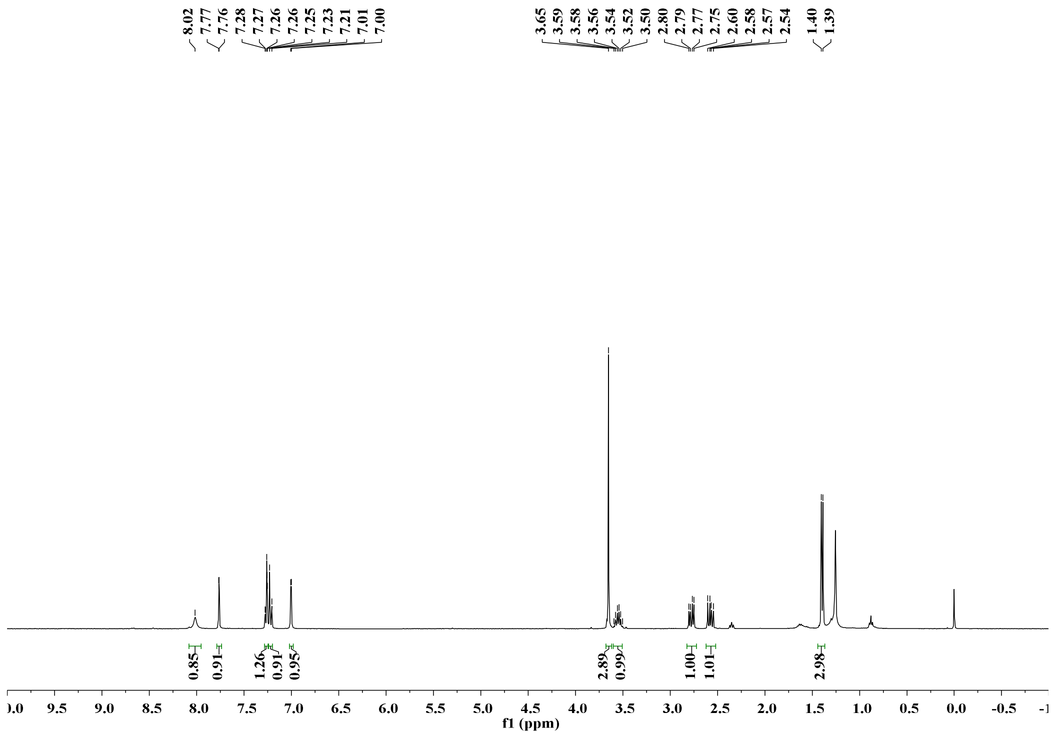
5i

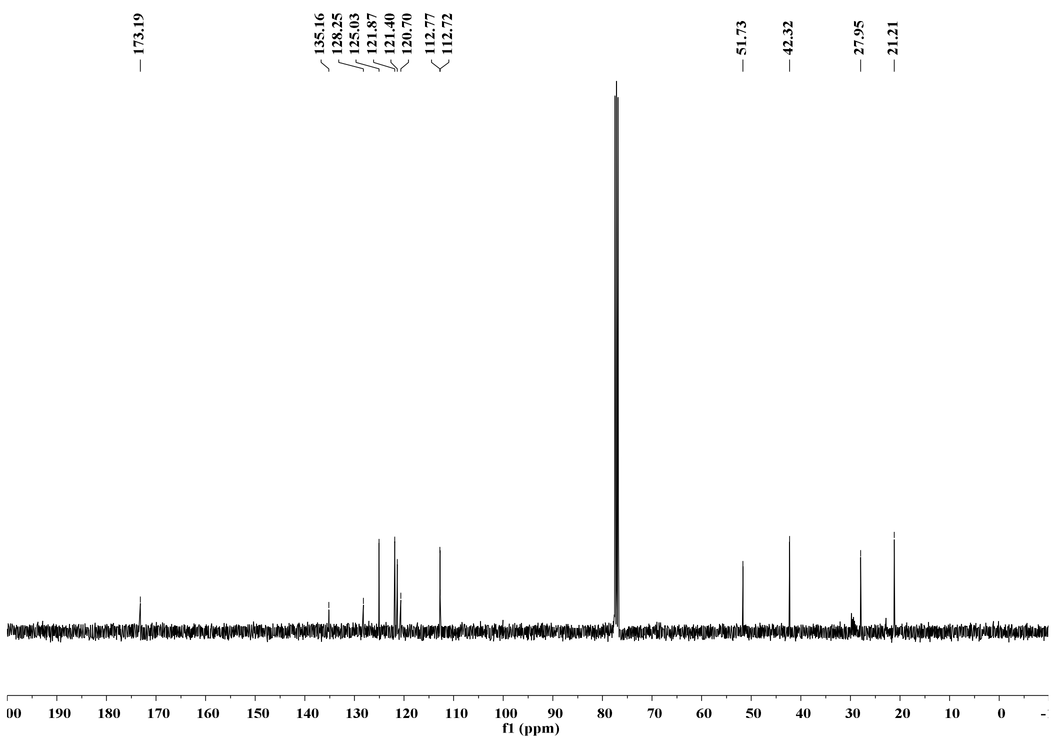

8.021
7.611
7.606
7.269
7.260
7.248
7.149
7.144
7.127
7.122
7.022
7.016
3.652
3.597
3.579
3.561
3.543
3.525
3.508
2.809
2.792
2.771
2.755
2.605
2.584
2.568
2.547
1.406
1.389
0.90
0.98
1.33
0.97
1.00
3.13
1.08
1.08
1.09
3.19
f1 (ppm)

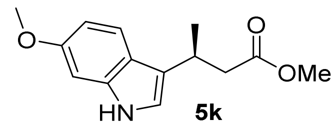

173.21
134.88
127.56
125.15
122.47
121.57
120.74
118.78
112.32
51.72
42.30
27.96
21.19
f1 (ppm)


Br
O
OMe
HN

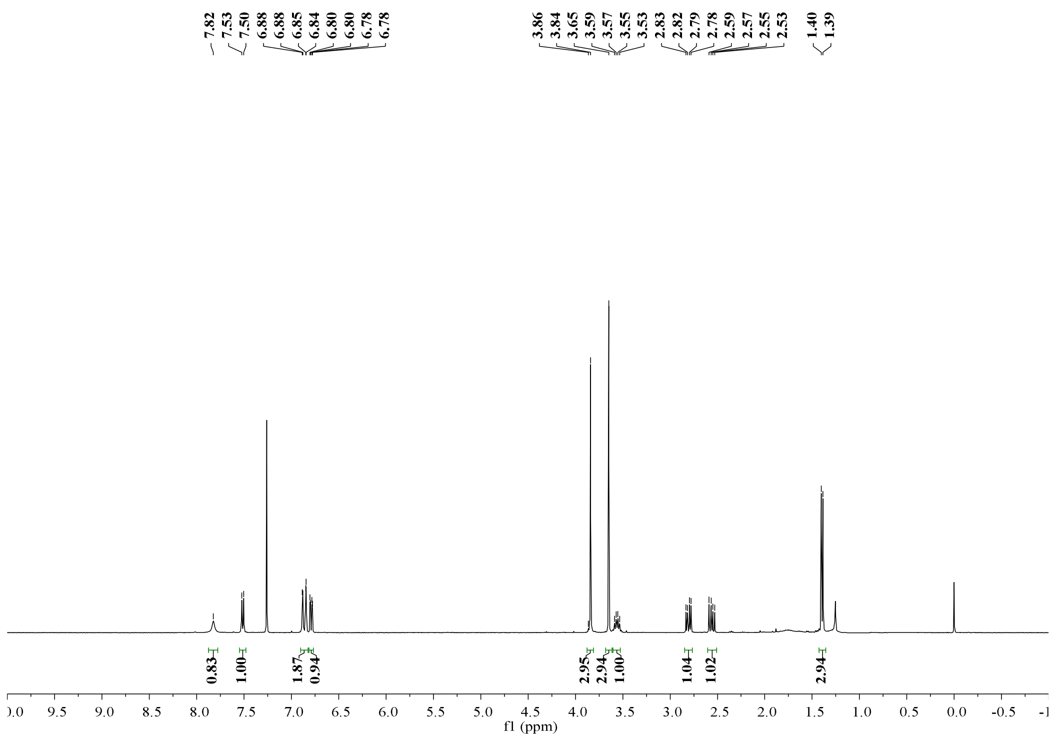
5j

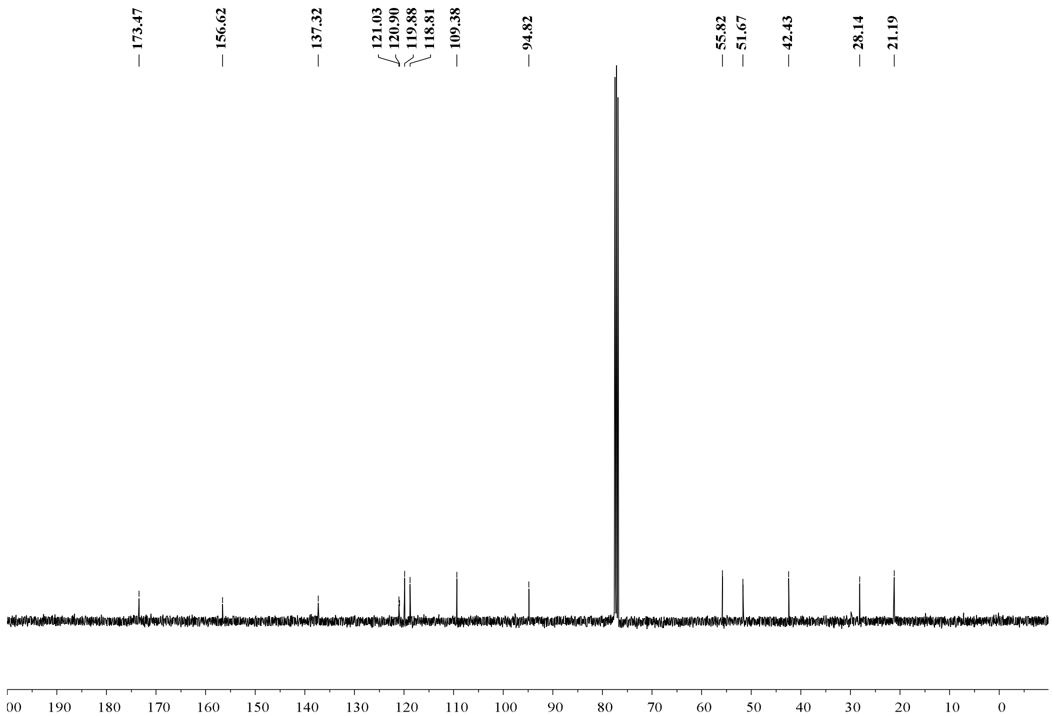

8.02
7.77
7.76
7.28
7.27
7.26
7.26
7.25
7.23
7.21
7.01
7.00
3.65
3.59
3.58
3.56
3.54
3.52
3.50
2.80
2.79
2.77
2.75
2.60
2.58
2.57
2.54
1.40
1.39
0.85
0.91
1.26
0.91
0.95
2.89
0.99
1.00
1.01
2.98
f1 (ppm)

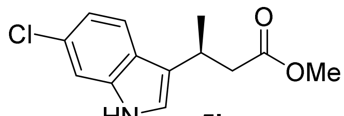

173.19
135.16
128.25
125.03
121.87
121.40
120.70
112.77
112.72
51.73
42.32
27.95
21.21
f1 (ppm)


HN
OMe
O

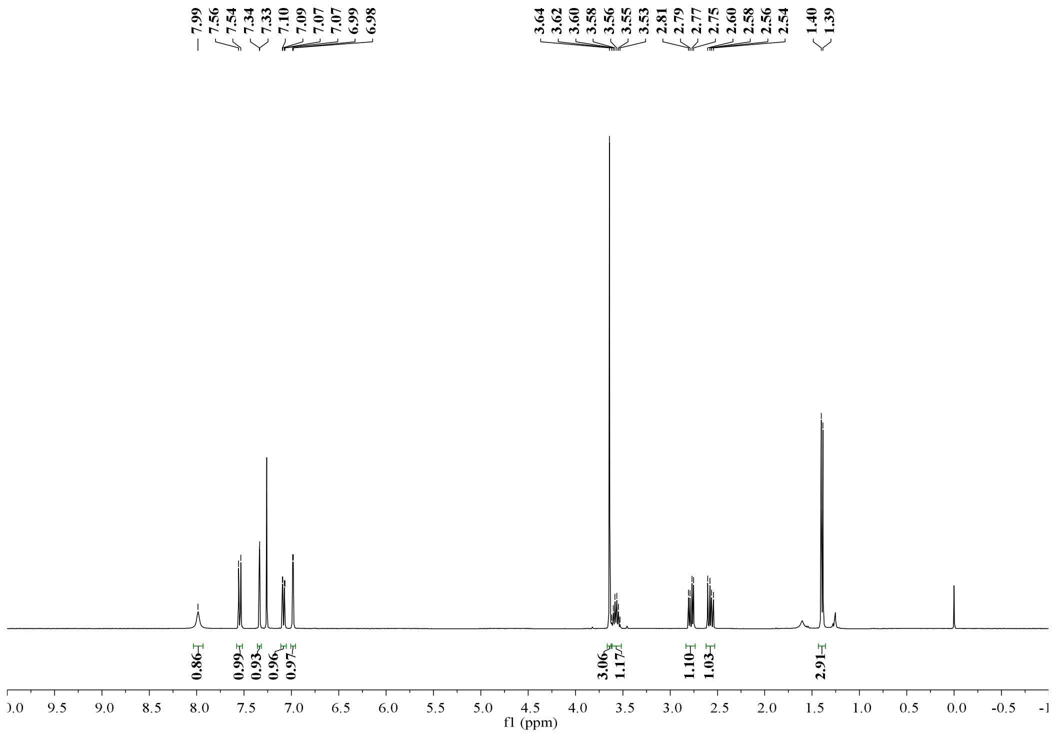
5k

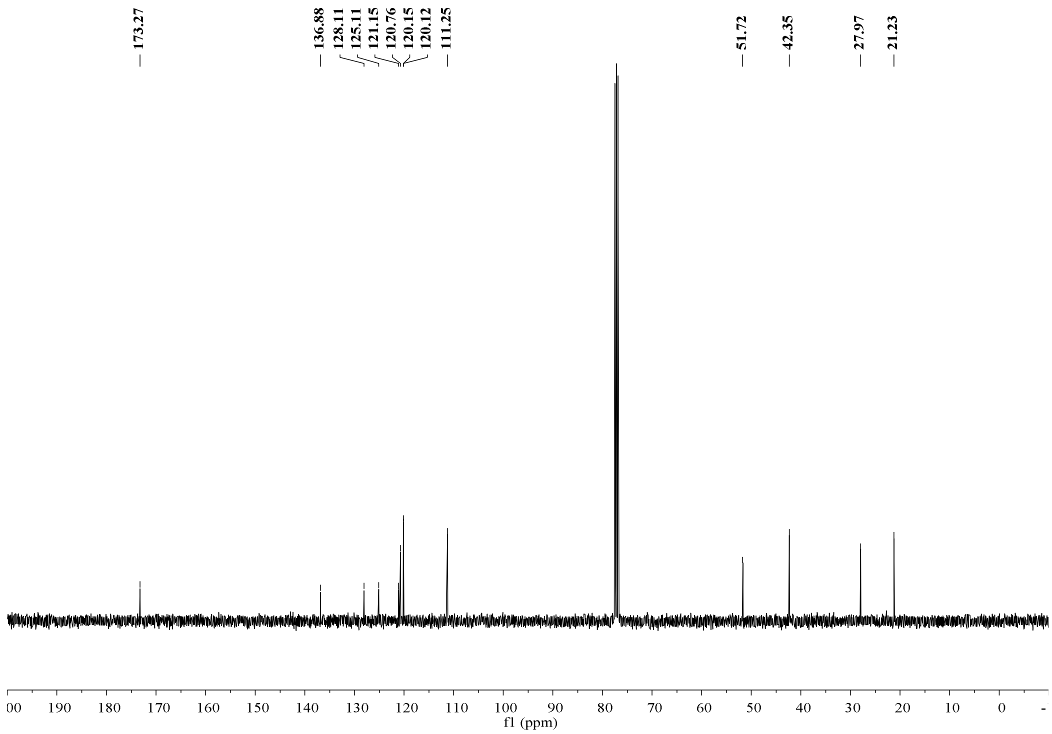

7.82
7.53
7.50
6.88
6.88
6.85
6.84
6.80
6.80
6.78
6.78
3.86
3.84
3.65
3.59
3.57
3.55
3.53
2.83
2.82
2.79
2.78
2.59
2.57
2.55
2.53
1.40
1.39
0.83
1.00
1.87
0.94
2.95
2.94
1.00
1.04
1.02
2.94
f1 (ppm)

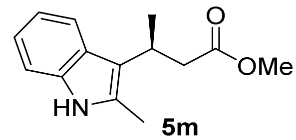

173.47
156.62
137.32
121.03
120.90
119.88
118.81
109.38
94.82
55.82
51.67
42.43
28.14
21.19
f1 (ppm)


Cl
O
OMe
HN

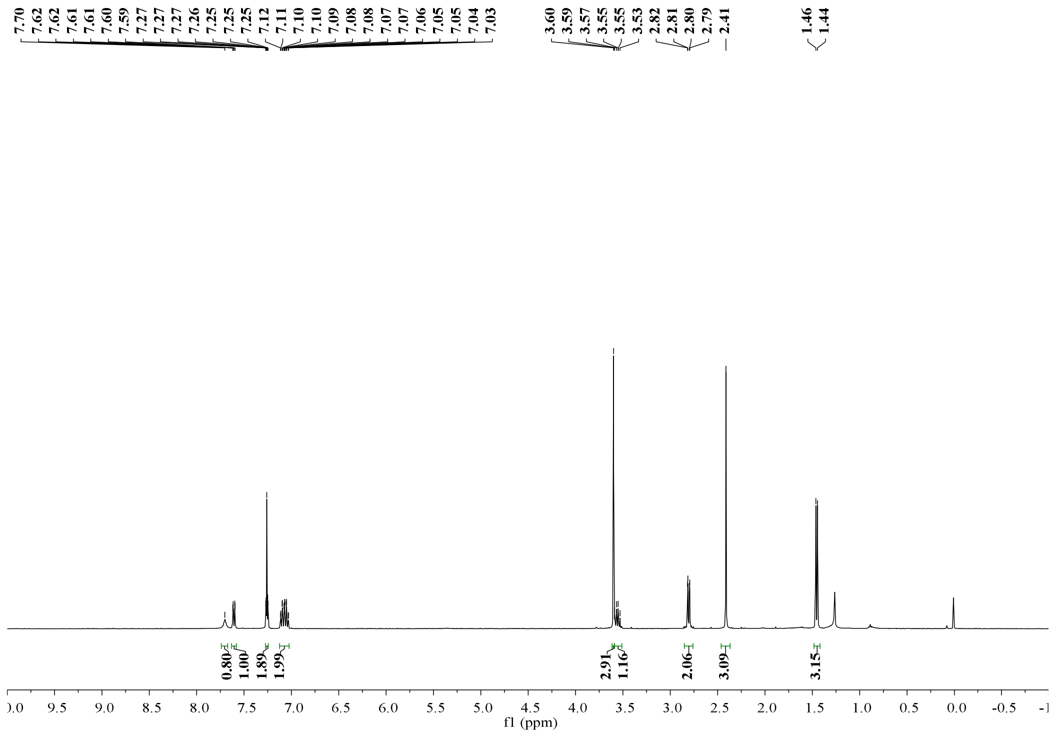
5l

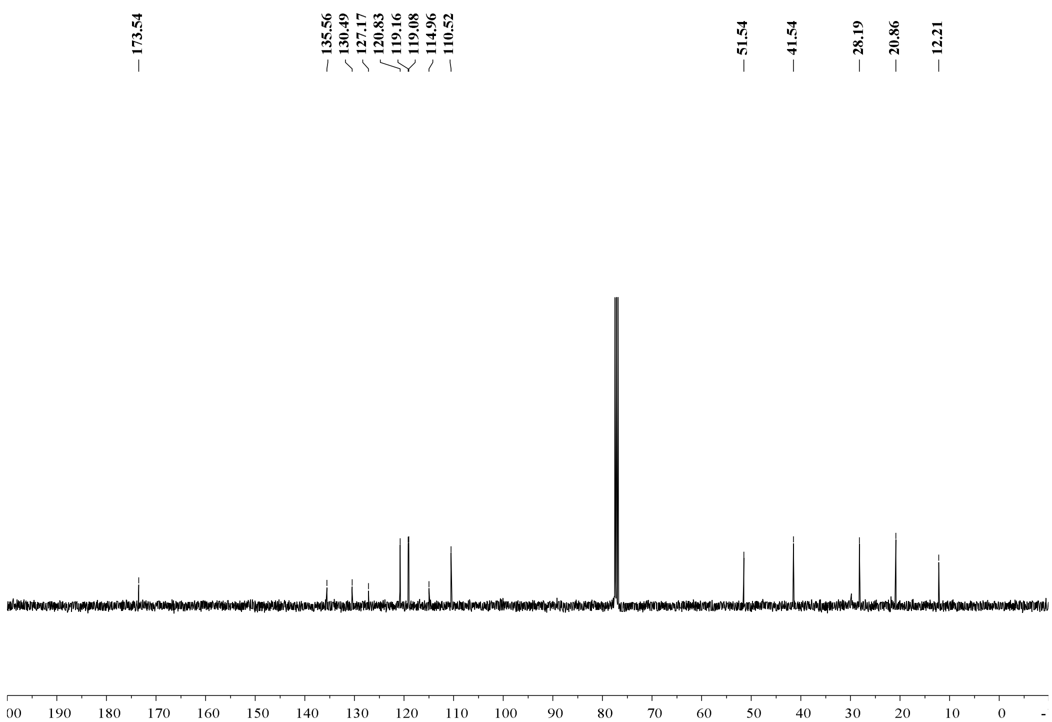

7.99
7.56
7.54
7.34
7.33
7.10
7.09
7.07
7.07
6.99
6.98
3.64
3.62
3.60
3.58
3.56
3.55
3.53
2.81
2.79
2.77
2.75
2.60
2.58
2.56
2.54
1.40
1.39
0.86
0.99
0.93
0.96
0.97
3.06
1.17
1.10
1.03
2.91
f1 (ppm)

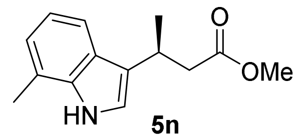

173.27
136.88
128.11
125.11
121.15
120.76
120.15
120.12
111.25
51.72
42.35
27.97
21.23
f1 (ppm)



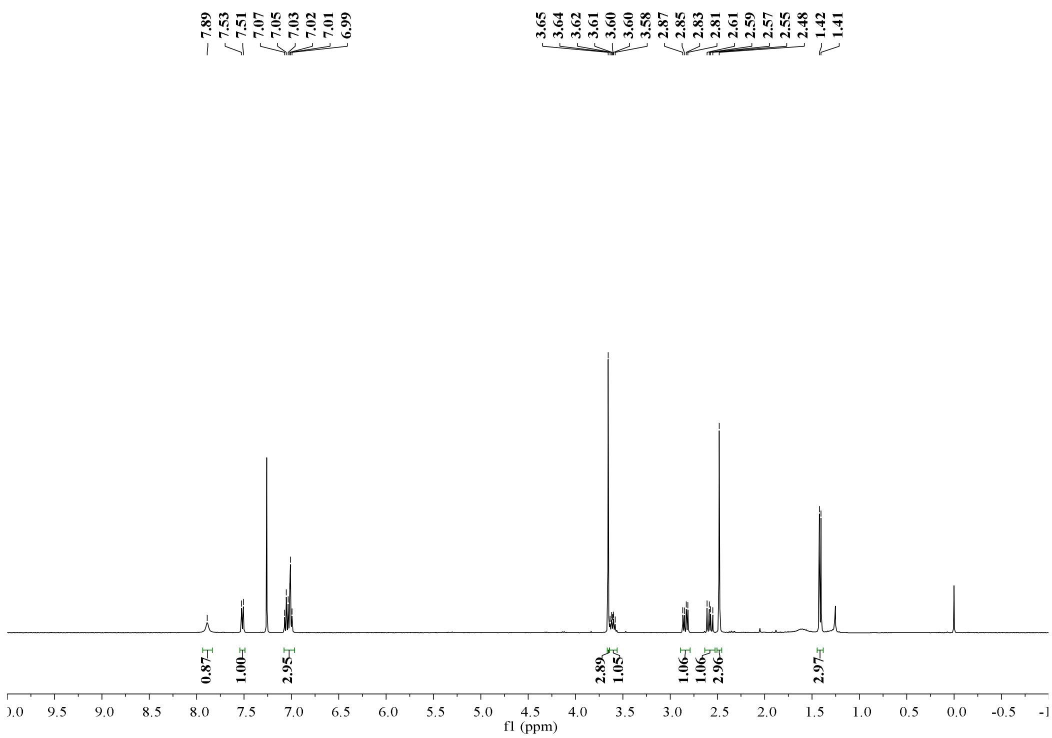
5m


7.70
7.62
7.61
7.61
7.60
7.59
7.27
7.27
7.27
7.26
7.25
7.25
7.25
7.12
7.11
7.10
7.09
7.08
7.08
7.07
7.07
7.06
7.05
7.05
7.04
7.03
3.60
3.59
3.57
3.55
3.55
3.53
2.82
2.81
2.80
2.79
2.41
1.46
1.44
0.80
1.00
1.89
1.99
2.91
1.16
2.06
3.09
3.15
f1 (ppm)

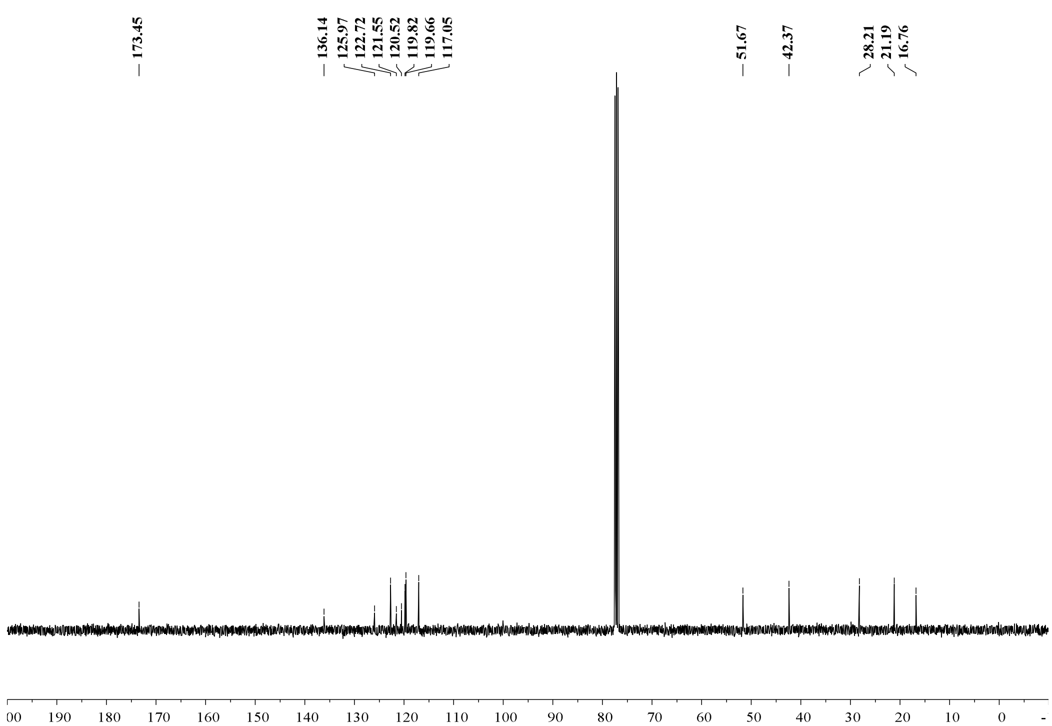

173.54
135.56
130.49
127.17
120.83
119.16
119.08
114.96
110.52
51.54
41.54
28.19
20.86
12.21
f1 (ppm)



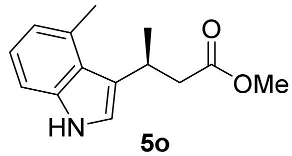
5n



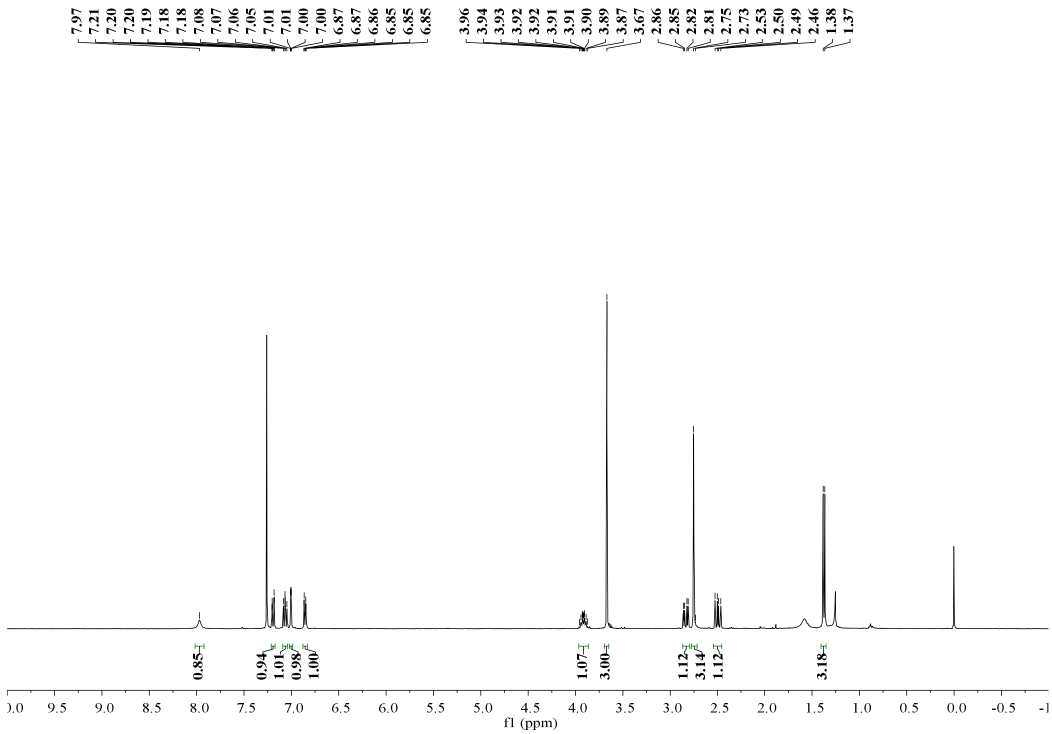
7.89
7.53
7.51
7.07
7.05
7.03
7.02
7.01
6.99
3.65
3.64
3.62
3.61
3.60
3.60
3.58
2.87
2.85
2.83
2.81
2.61
2.59
2.57
2.55
2.48
1.42
1.41
0.87
1.00
2.95
2.89
1.05
1.06
1.06
2.96
2.97
f1 (ppm)

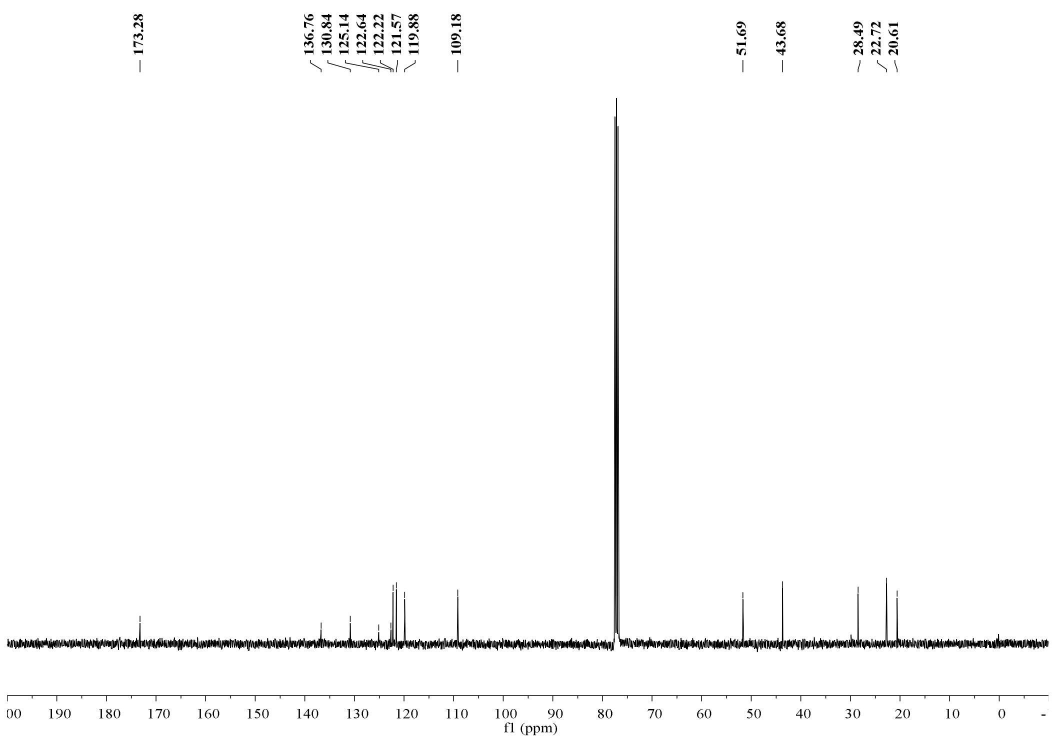


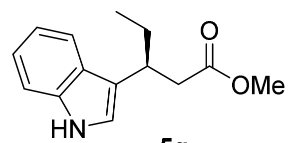
173.45
136.14
125.97
122.72
121.55
120.52
119.82
119.66
117.05
51.67
42.37
28.21
21.19
16.76
f1 (ppm)


O
OMe
HN

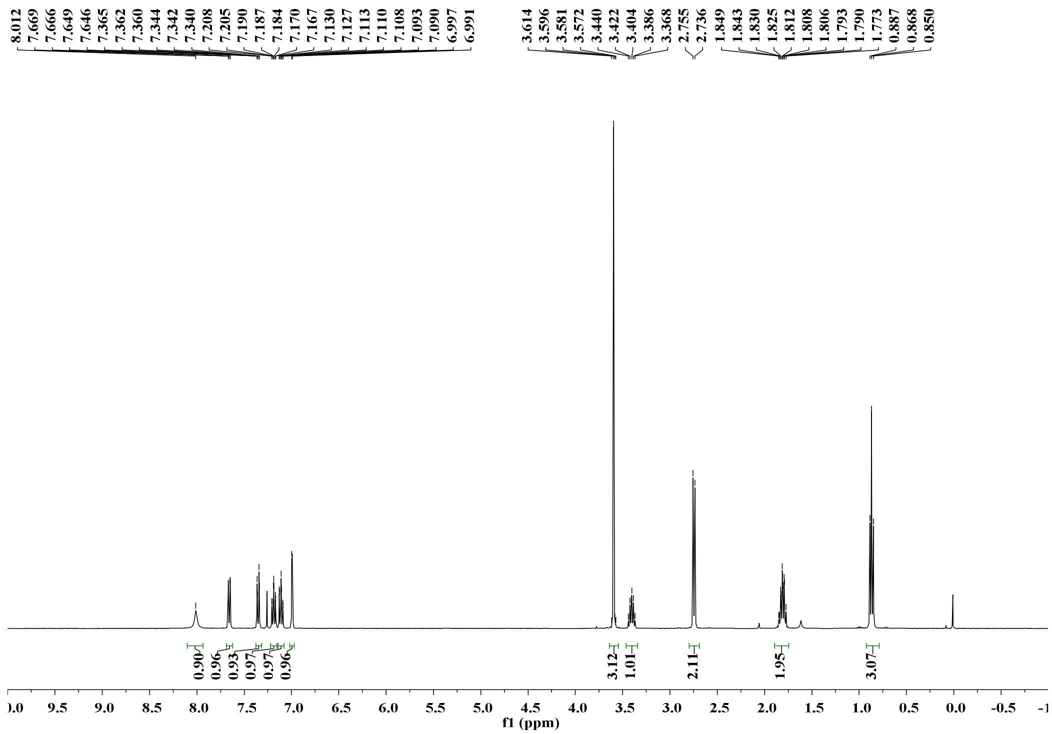
5o

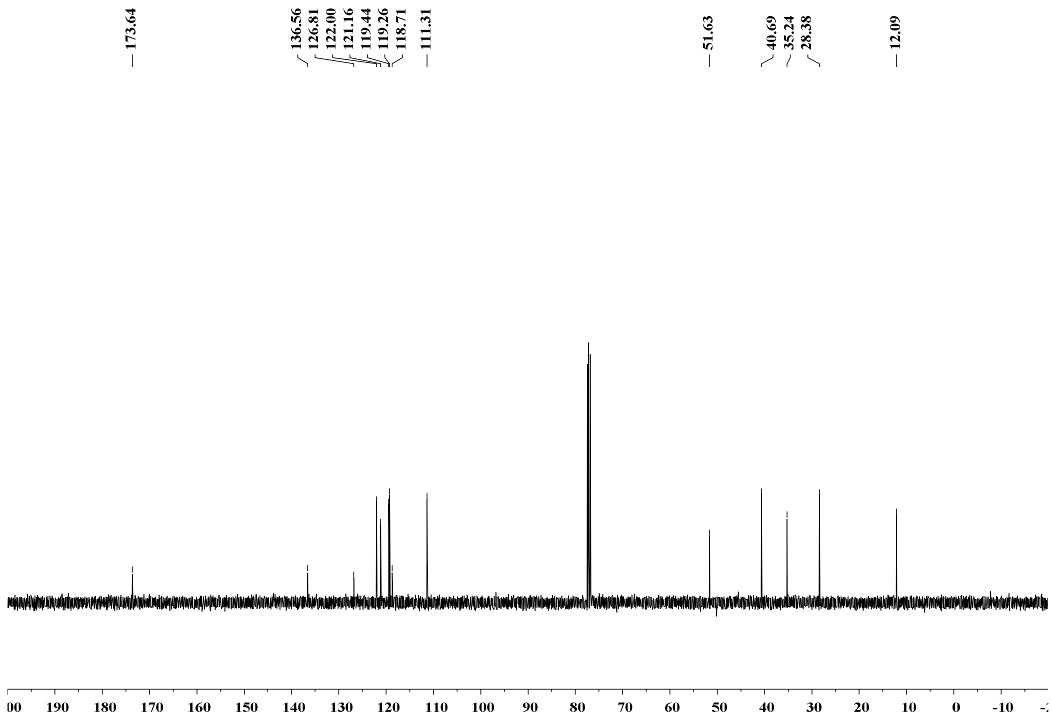

7.97
7.21
7.20
7.20
7.19
7.18
7.18
7.08
7.07
7.06
7.05
7.01
7.01
7.00
6.87
6.87
6.86
6.85
6.85
6.85
3.96
3.94
3.93
3.92
3.92
3.91
3.91
3.90
3.89
3.87
3.67
2.86
2.85
2.82
2.81
2.75
2.73
2.53
2.50
2.49
2.46
1.38
1.37
0.85
0.94
1.01
0.98
1.00
1.07
3.00
1.12
3.14
1.12
3.18
f1 (ppm)

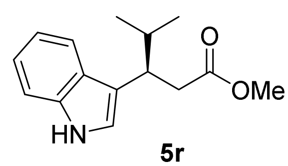

173.28
136.76
130.84
125.14
122.64
122.22
121.57
119.88
109.18
51.69
43.68
28.49
22.72
20.61
f1 (ppm)


O
OMe
HN

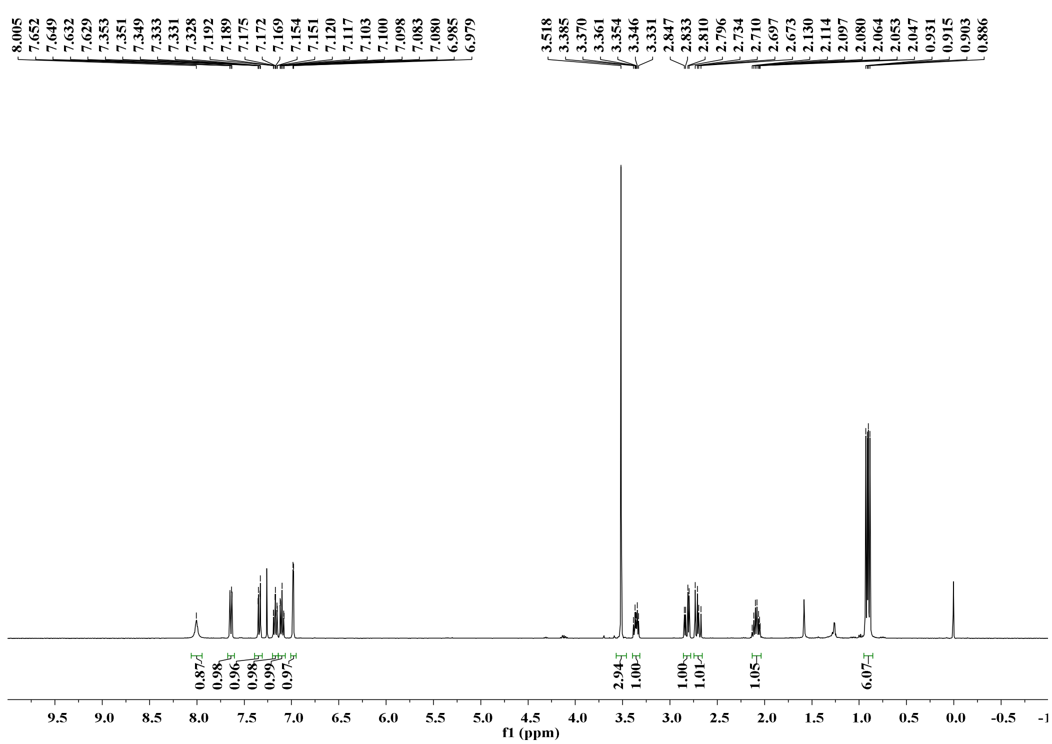
5q

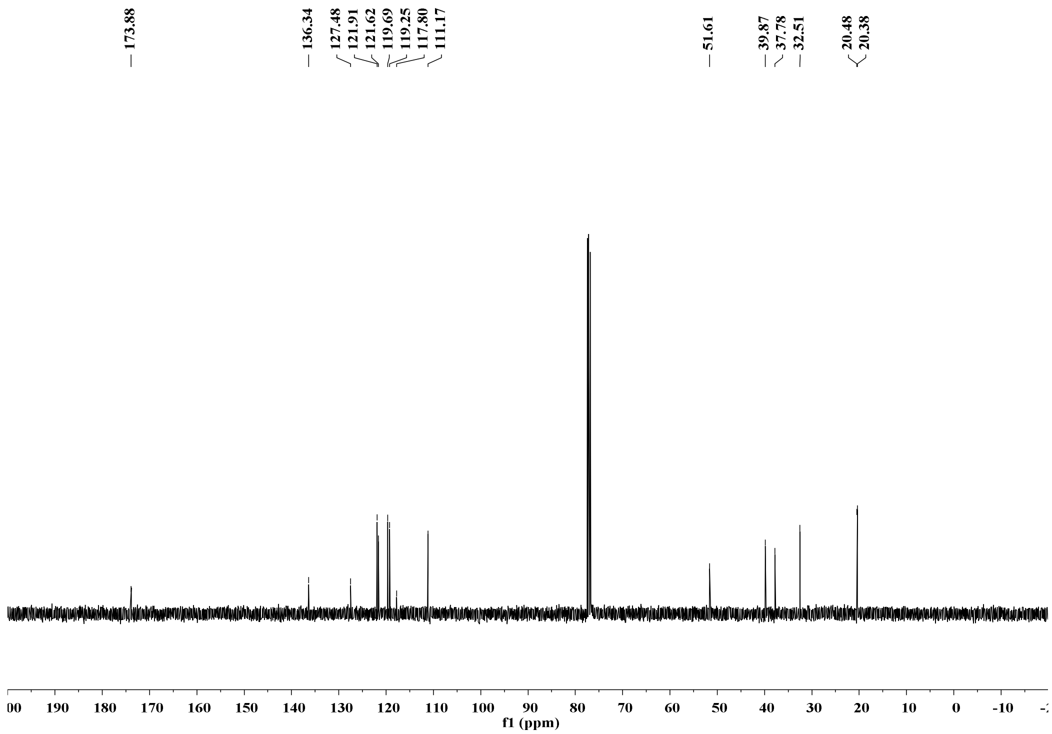

8.012
7.669
7.666
7.649
7.646
7.365
7.362
7.360
7.344
7.342
7.340
7.208
7.205
7.190
7.187
7.184
7.170
7.167
7.130
7.127
7.113
7.110
7.108
7.093
7.090
6.997
6.991
3.614
3.596
3.581
3.572
3.440
3.422
3.404
3.386
3.368
2.755
2.736
1.849
1.843
1.830
1.825
1.812
1.808
1.806
1.793
1.790
1.773
0.887
0.868
0.850
0.90
0.96
0.93
0.97
0.97
0.96
3.12
1.01
2.11
1.95
3.07
f1 (ppm)

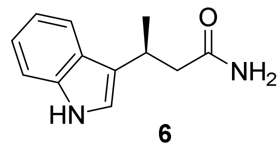

173.64
136.56
126.81
122.00
121.16
119.44
119.26
118.71
111.31
51.63
40.69
35.24
28.38
12.09
f1 (ppm)



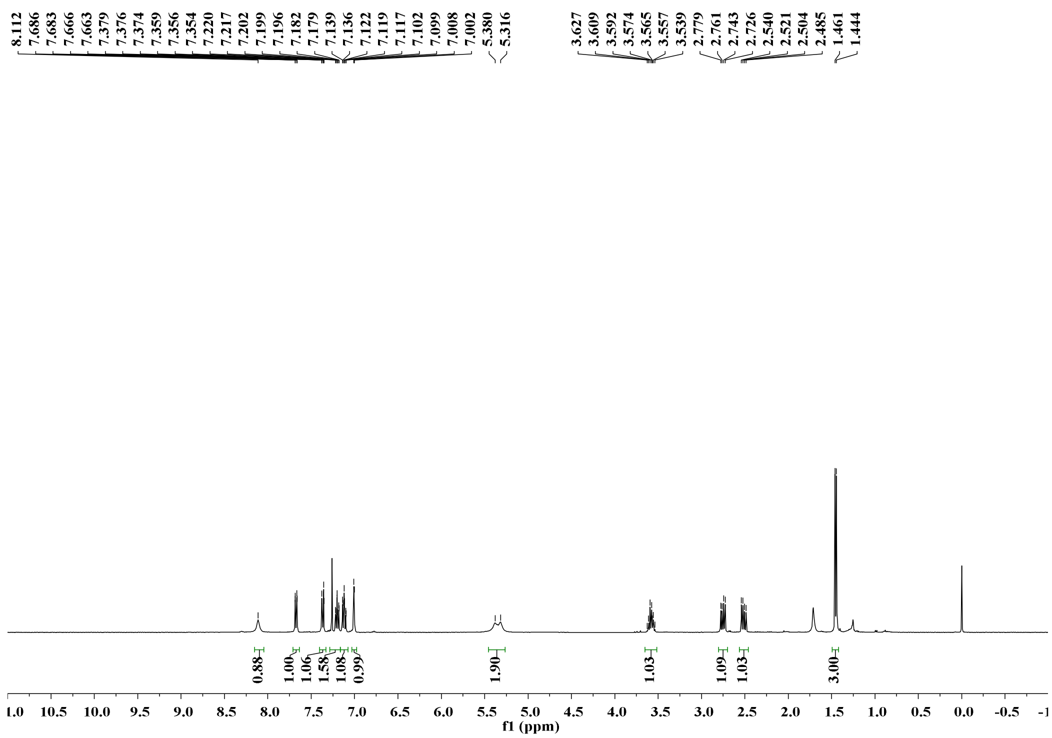
5r

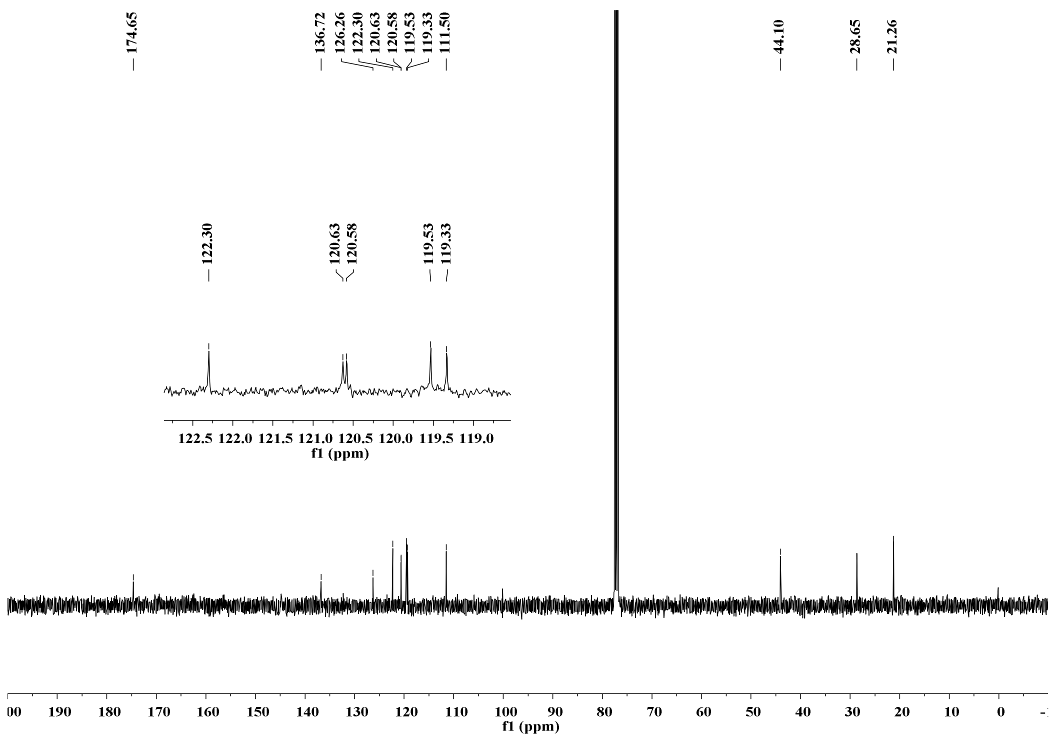


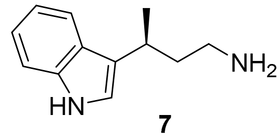




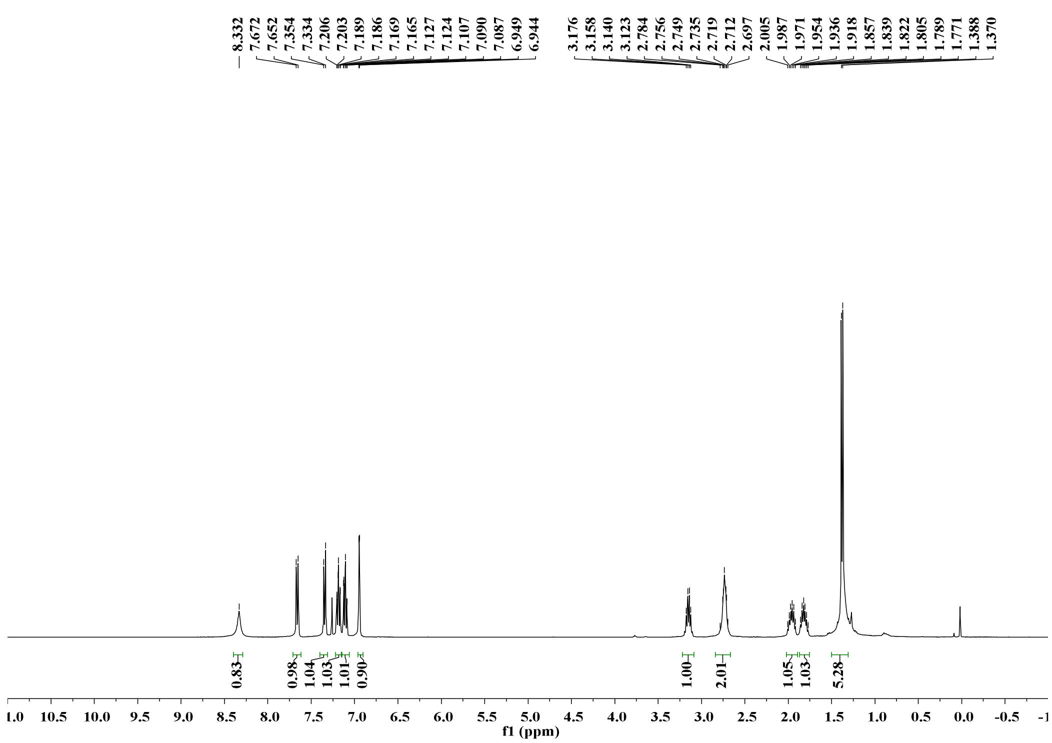
6

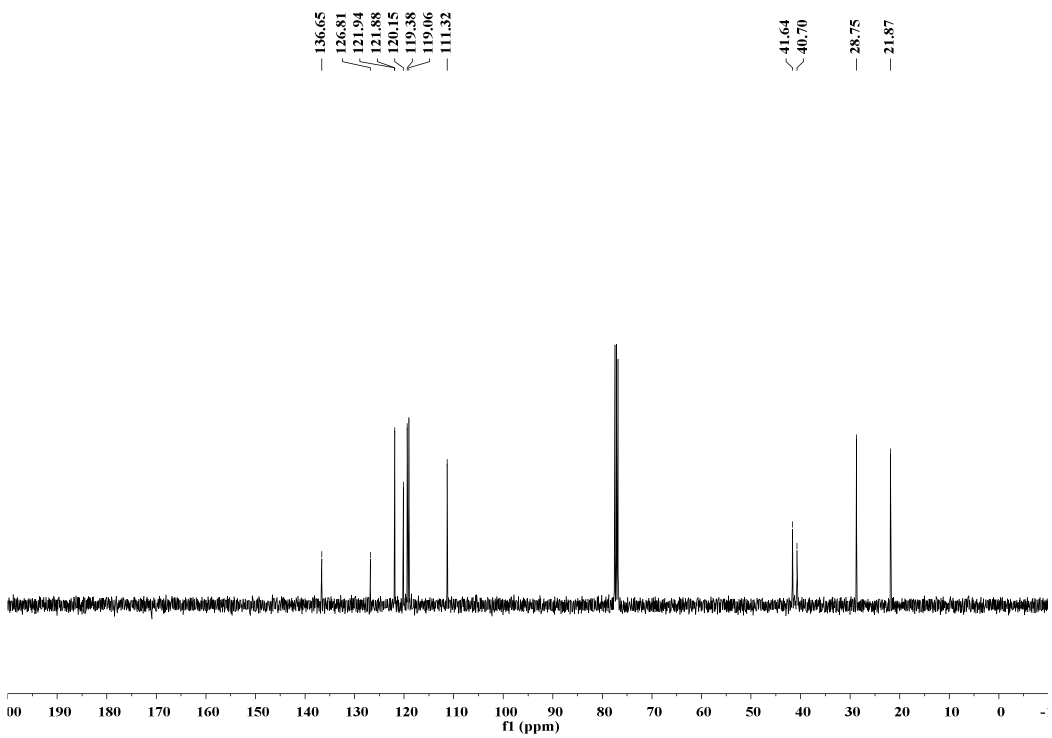


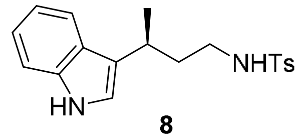



NH2
HN

7

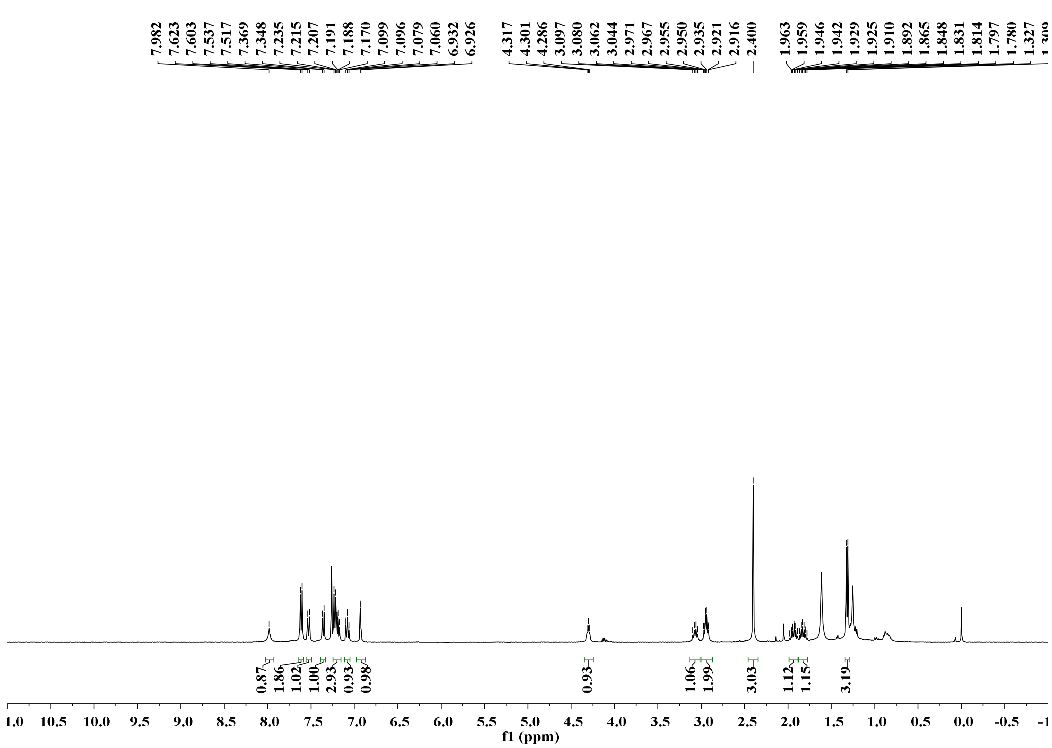

8.332
7.672
7.652
7.354
7.334
7.206
7.203
7.189
7.186
7.169
7.165
7.127
7.124
7.107
7.090
7.087
6.949
6.944
3.176
3.158
3.140
3.123
2.784
2.756
2.749
2.735
2.719
2.712
2.697
2.005
1.987
1.971
1.954
1.936
1.918
1.857
1.839
1.822
1.805
1.789
1.771
1.388
1.370
0.83
0.98
1.04
1.03
1.01
0.90
1.00
2.01
1.05
1.03
5.28
f1 (ppm)


136.65
126.81
121.94
121.88
120.15
119.38
119.06
111.32
41.64
40.70
28.75
21.87
f1 (ppm)

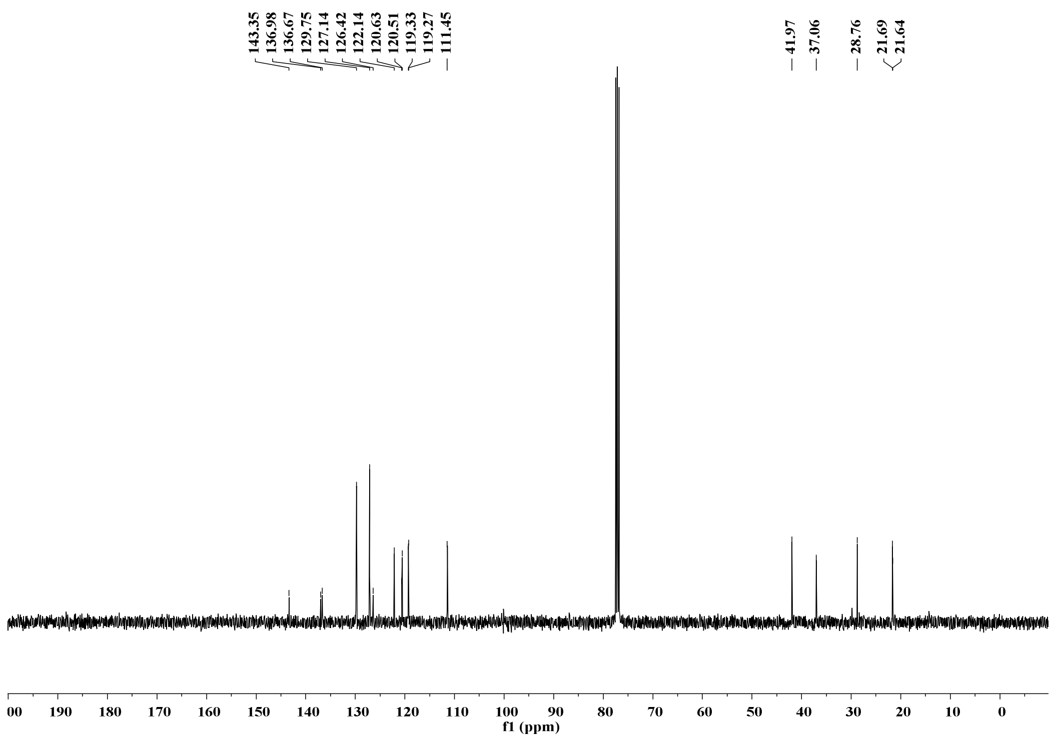


HN
NHTs

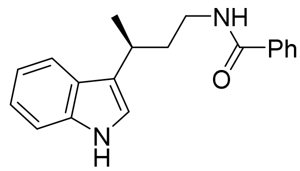
8



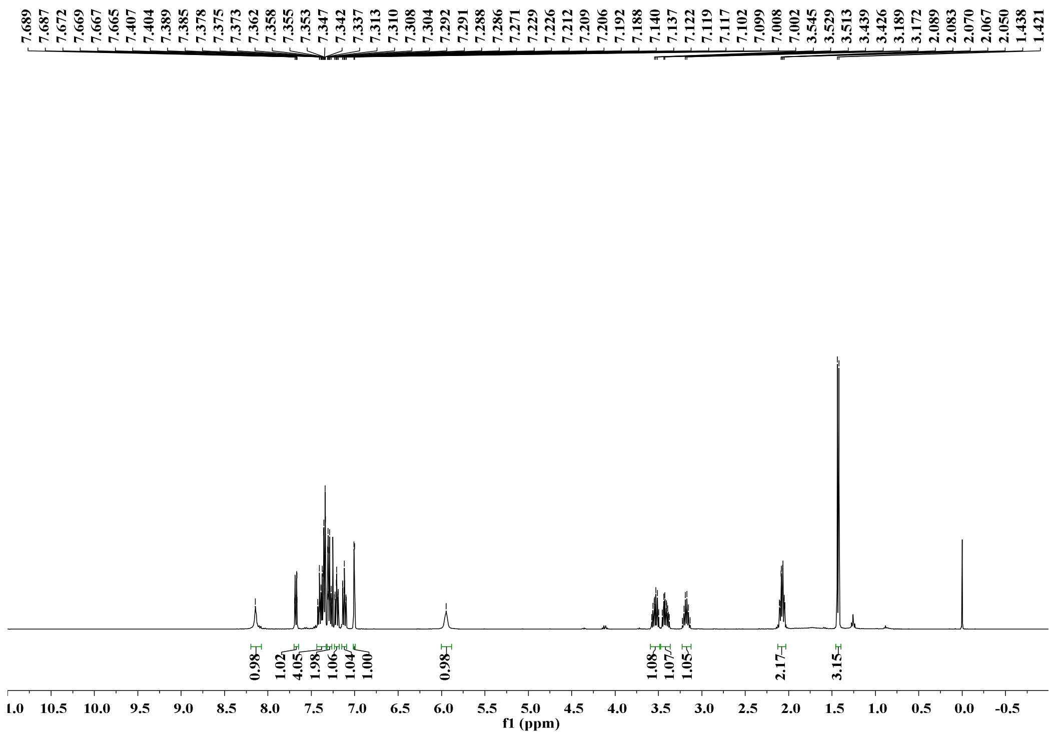
7.982
7.623
7.603
7.537
7.517
7.369
7.348
7.235
7.215
7.207
7.191
7.188
7.170
7.099
7.096
7.079
7.060
6.932
6.926
4.317
4.301
4.286
3.097
3.080
3.062
3.044
2.971
2.967
2.955
2.950
2.935
2.921
2.916
2.400
1.963
1.959
1.946
1.942
1.929
1.925
1.910
1.892
1.865
1.848
1.831
1.814
1.797
1.780
1.327
0.87
1.86
1.02
1.00
2.93
0.93
0.98
0.93
1.06
1.99
3.03
1.12
1.15
3.19
f1 (ppm)

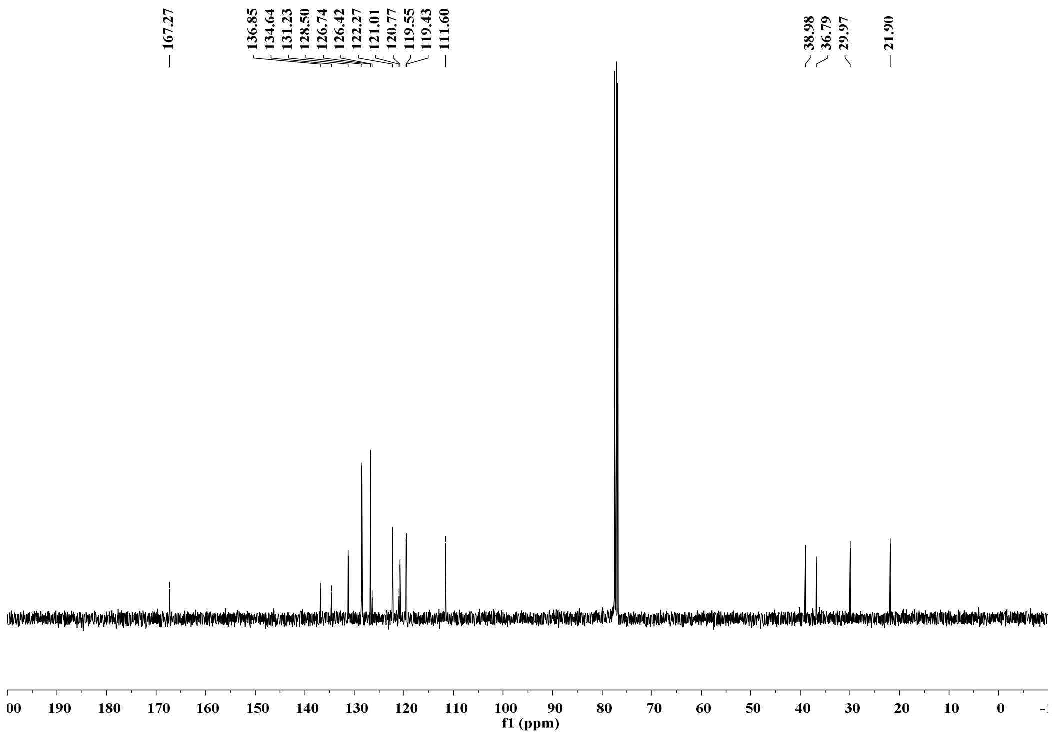


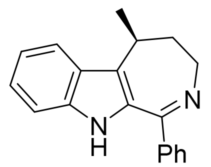
143.35
136.98
136.67
129.75
127.14
126.42
122.14
120.63
120.51
119.33
119.27
111.45
41.97
37.06
28.76
21.69
21.64
f1 (ppm)



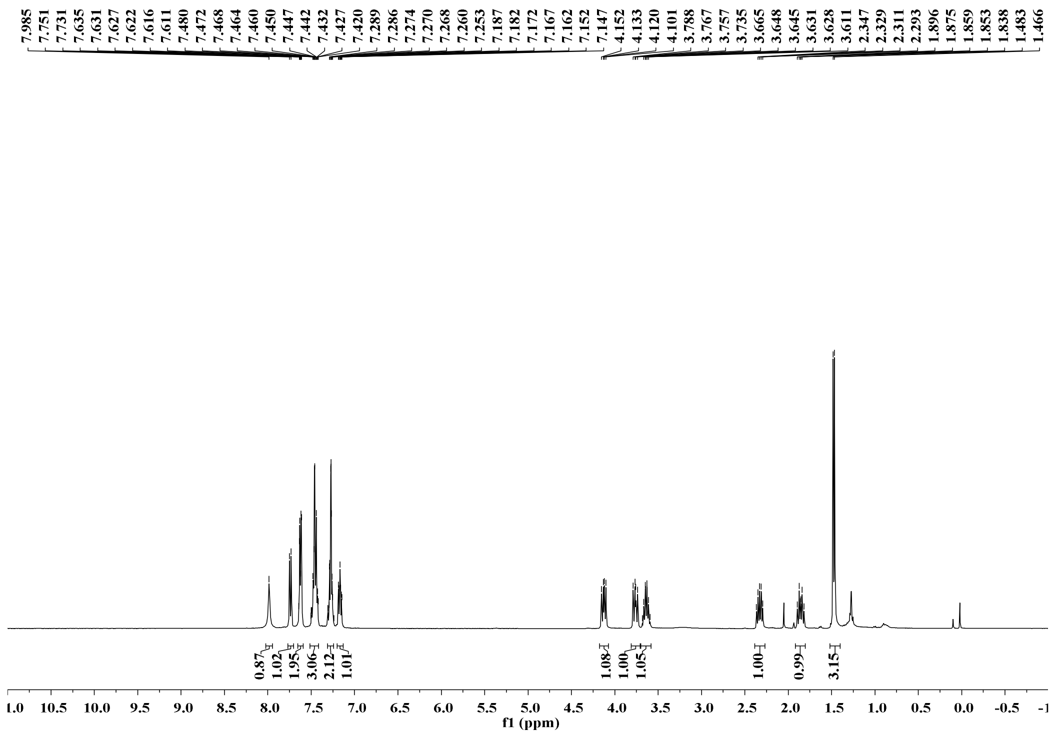
9

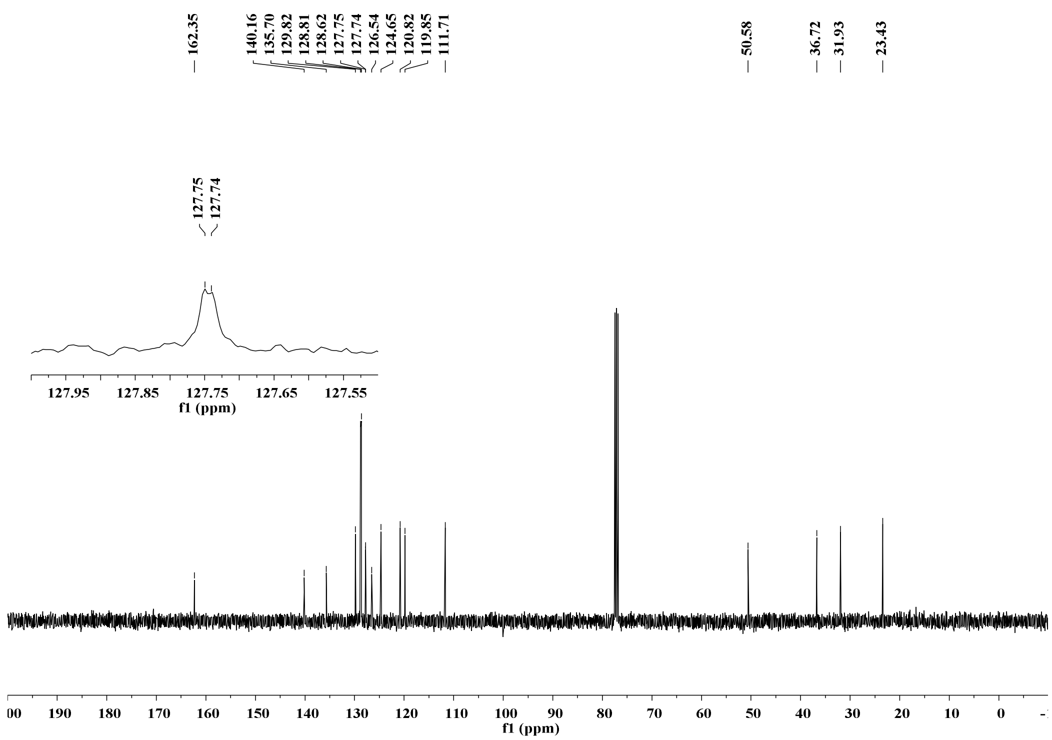




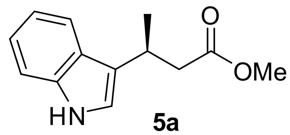


10

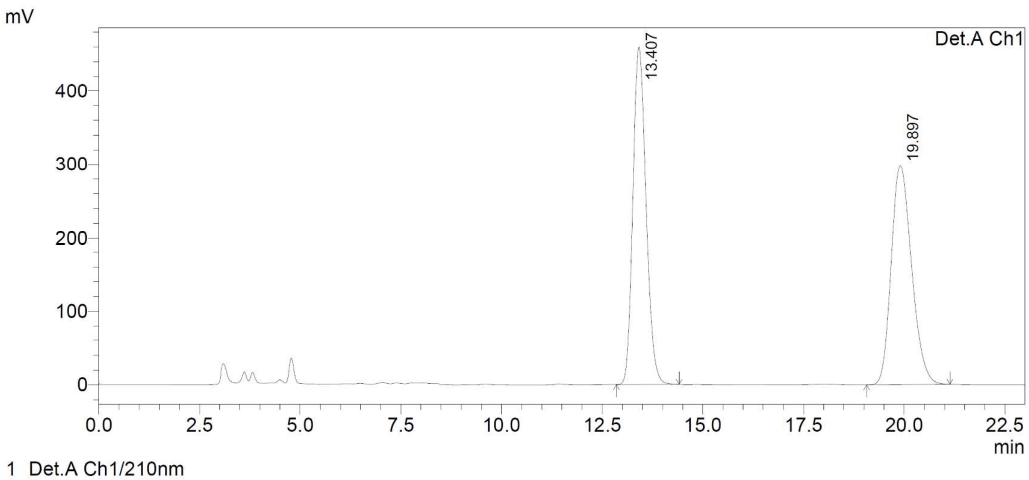




7. HPLC spectra



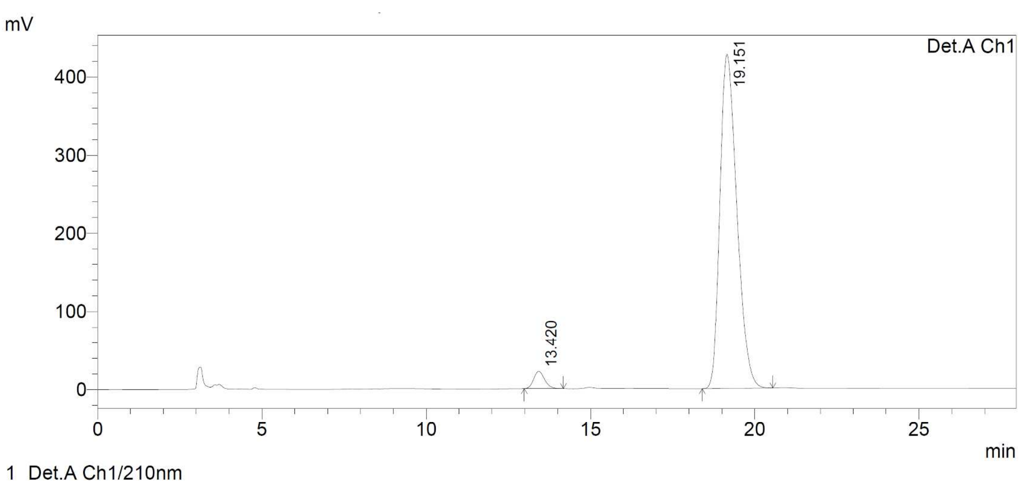
5a



PeakTable

Detector A Ch1 210nm

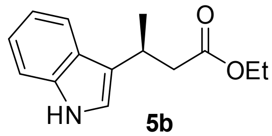
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.407	10452016	459644	49.910	60.641
2	19.897	10489778	298326	50.090	39.359
Total		20941795	757970	100.000	100.000



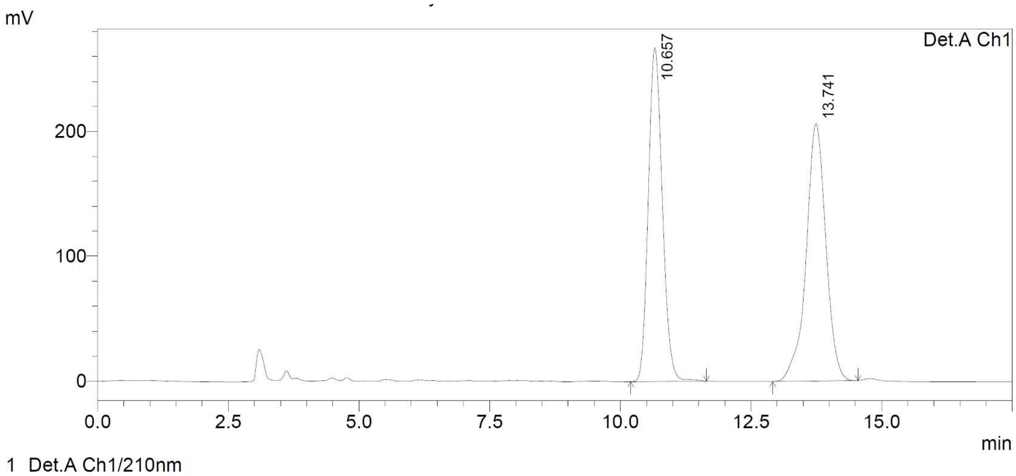
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.420	506461	22033	3.199	4.901
2	19.151	15323500	427509	96.801	95.099
Total		15829961	449542	100.000	100.000



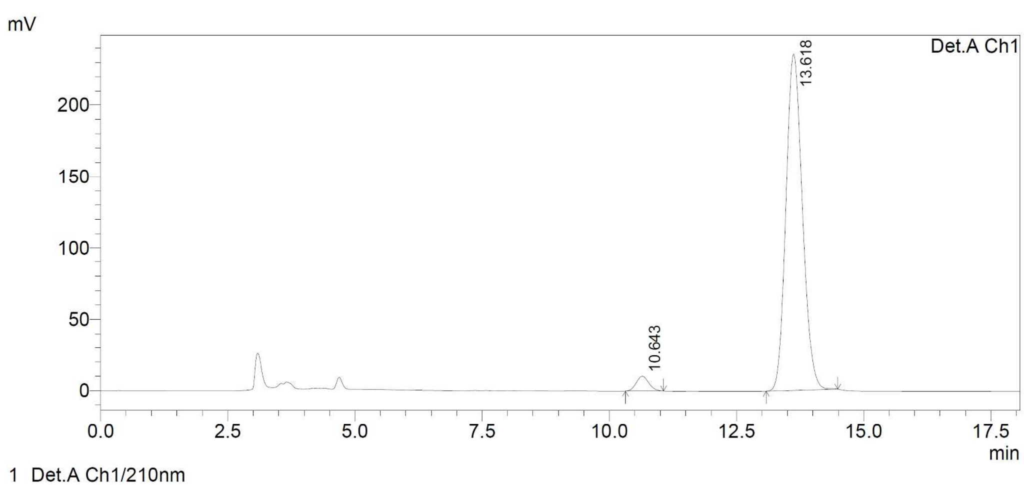
5b



PeakTable

Detector A Ch1 210nm

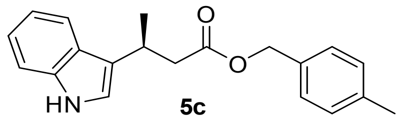
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.657	5009169	267208	48.080	56.467
2	13.741	5409309	206004	51.920	43.533
Total		10418477	473212	100.000	100.000



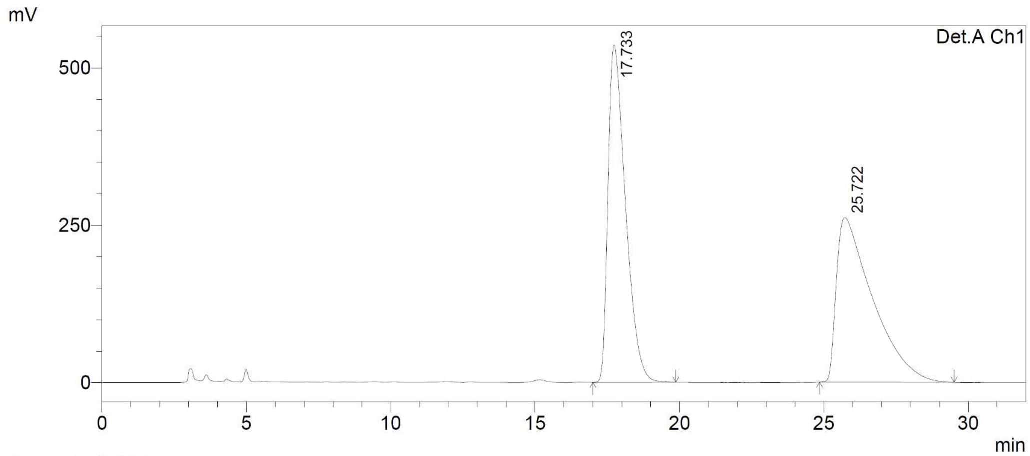
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.643	177779	10314	3.234	4.192
2	13.618	5318576	235726	96.766	95.808
Total		5496355	246040	100.000	100.000



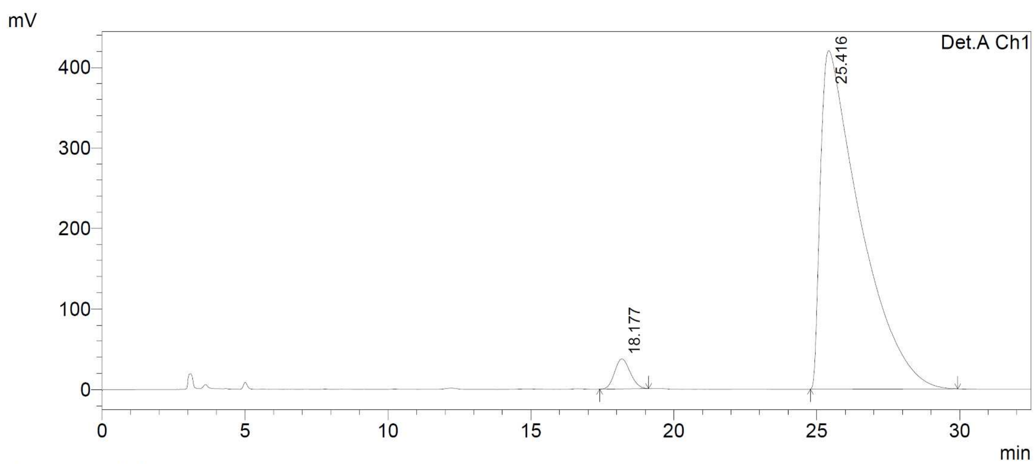
5c



PeakTable

Detector A Ch1 210nm

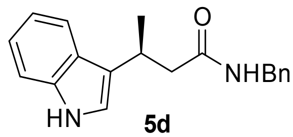
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.733	22591862	535898	49.675	67.188
2	25.722	22887480	261707	50.325	32.812
Total		45479341	797605	100.000	100.000



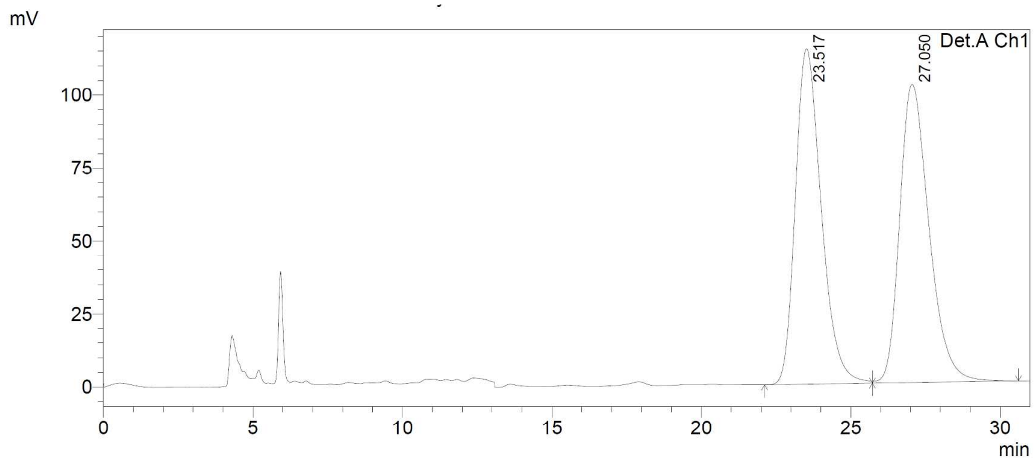
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.177	1406655	37039	3.343	8.098
2	25.416	40664887	420328	96.657	91.902
Total		42071543	457367	100.000	100.000



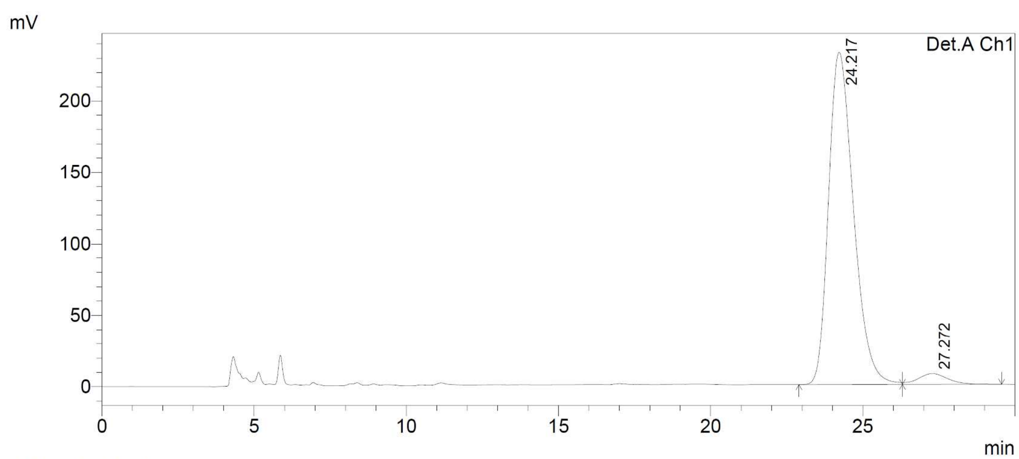
5d



PeakTable

Detector A Ch1 210nm

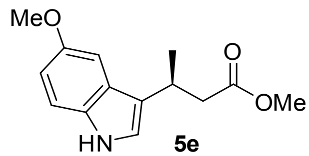
Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.517	6918067	114792	49.855	52.907
2	27.050	6958250	102179	50.145	47.093
Total		13876318	216971	100.000	100.000



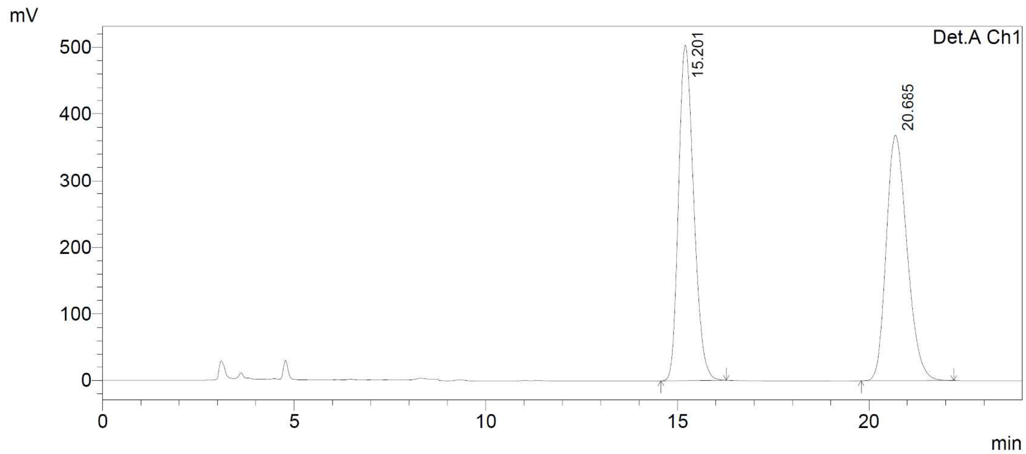
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.217	13258366	232598	96.304	96.869
2	27.272	508867	7519	3.696	3.131
Total		13767233	240117	100.000	100.000



5e

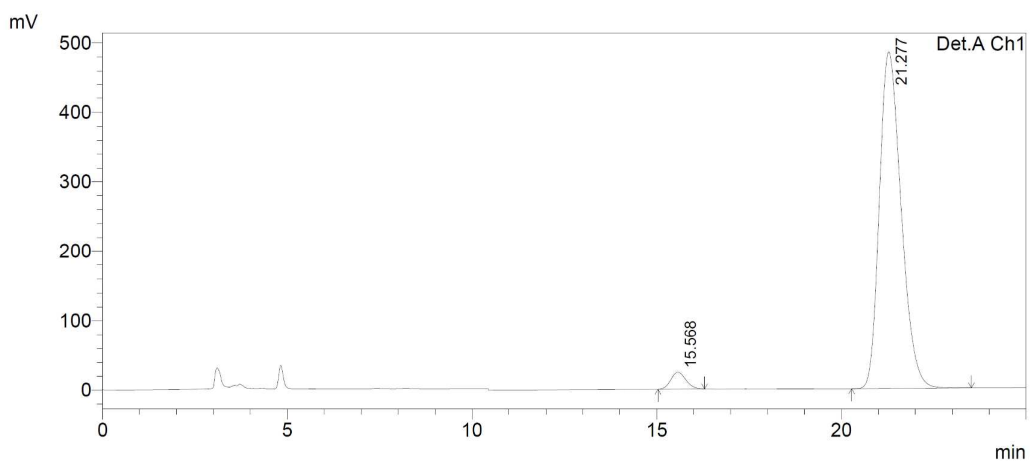


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.201	13903999	503453	49.876	57.713
2	20.685	13973205	368880	50.124	42.287
Total		27877204	872333	100.000	100.000

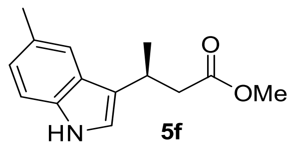


1 Det.A Ch1/210nm

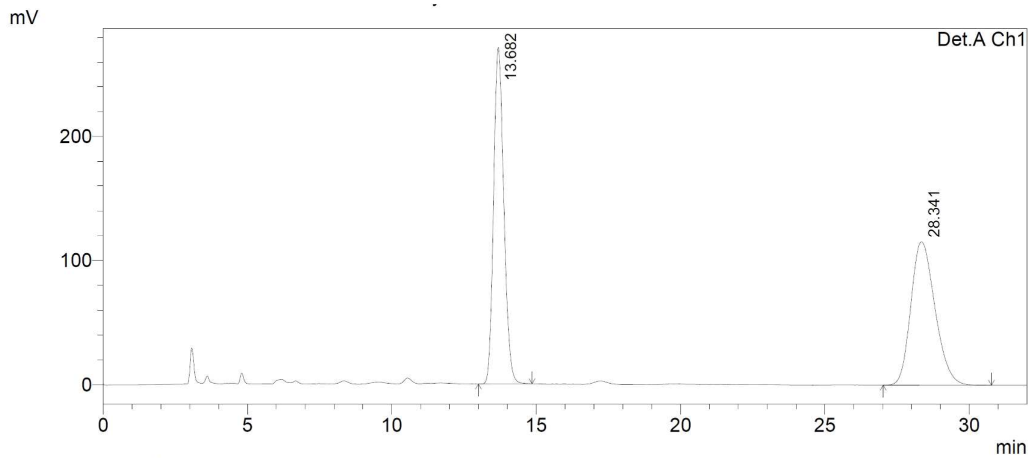
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.568	687565	24370	3.344	4.785
2	21.277	19871910	484914	96.656	95.215
Total		20559475	509285	100.000	100.000



5f

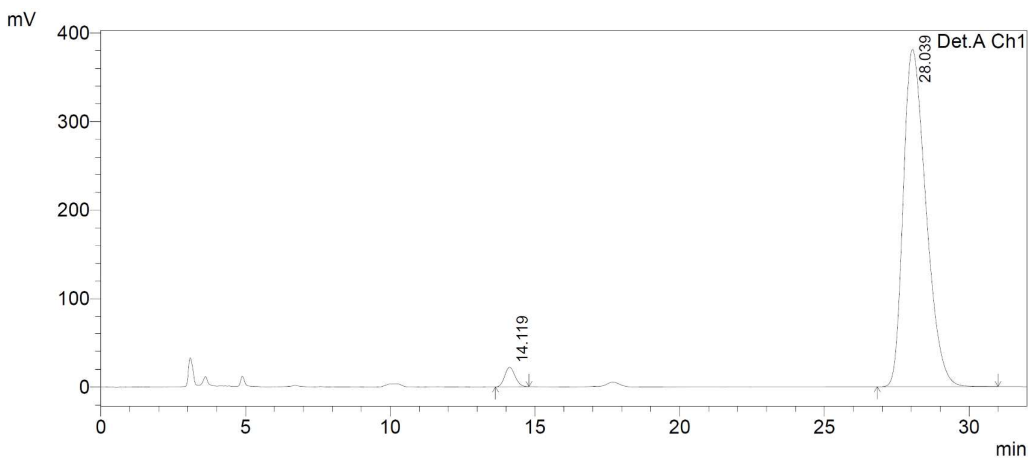


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.682	6680657	271083	49.939	70.133
2	28.341	6696910	115445	50.061	29.867
Total		13377567	386528	100.000	100.000

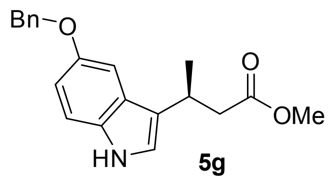


1 Det.A Ch1/210nm

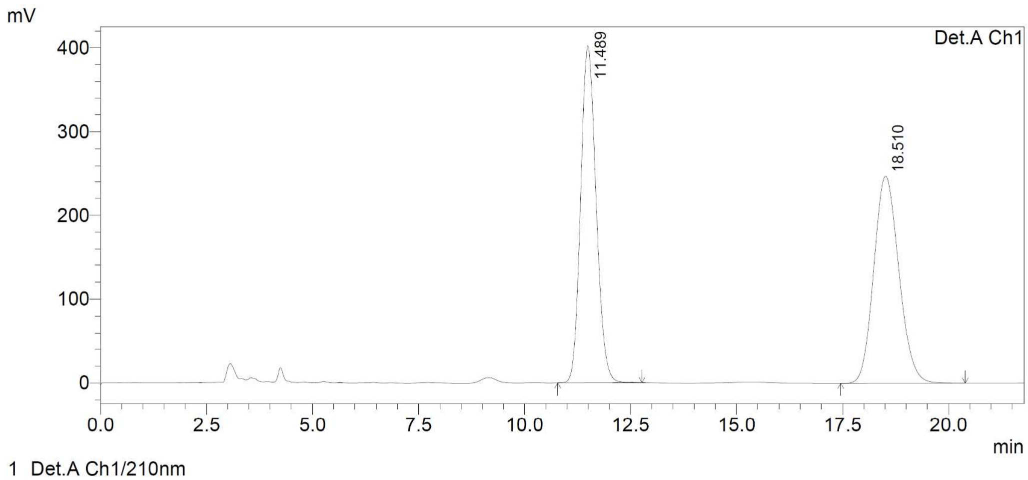
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.119	540027	21815	2.534	5.418
2	28.039	20773239	380862	97.466	94.582
Total		21313265	402677	100.000	100.000



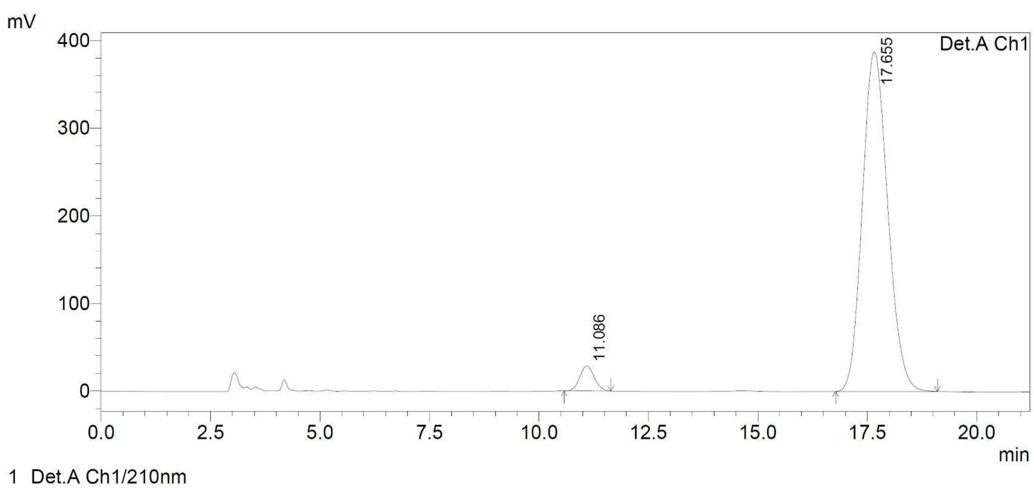
5g



PeakTable

Detector A Ch1 210nm

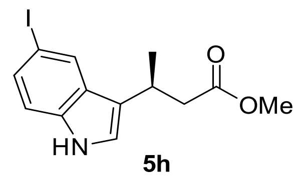
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.489	10213164	402227	50.127	61.959
2	18.510	10161352	246950	49.873	38.041
Total		20374516	649177	100.000	100.000



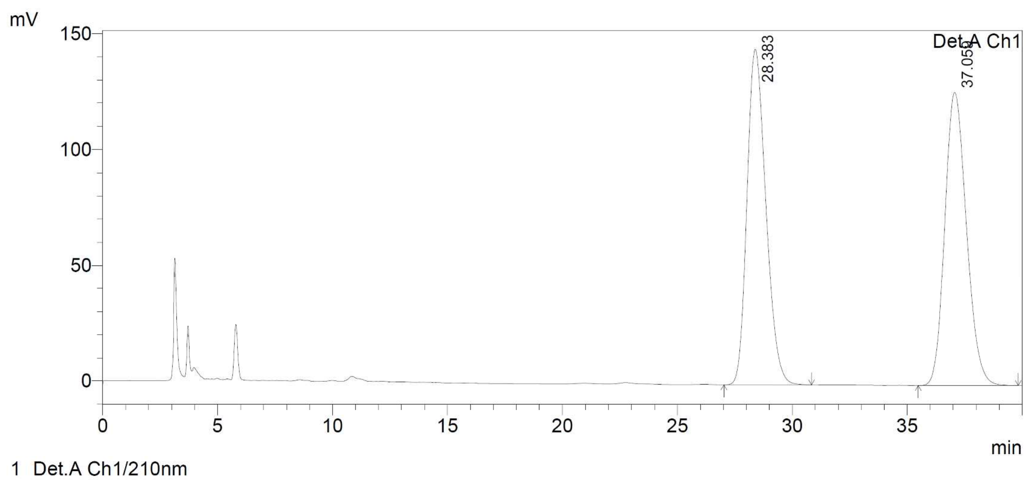
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.086	647436	28237	3.983	6.794
2	17.655	15608066	387359	96.017	93.206
Total		16255502	415597	100.000	100.000



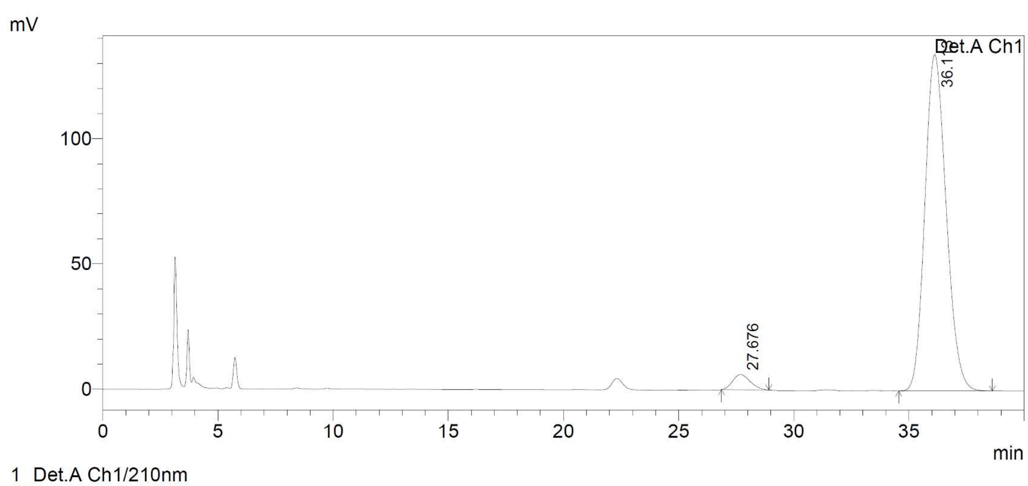
5h



PeakTable

Detector A Ch1 210nm

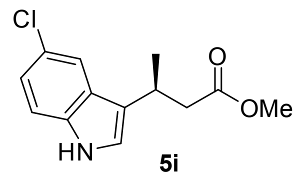
Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.383	8304885	145086	49.946	53.358
2	37.059	8322986	126825	50.054	46.642
Total		16627870	271911	100.000	100.000



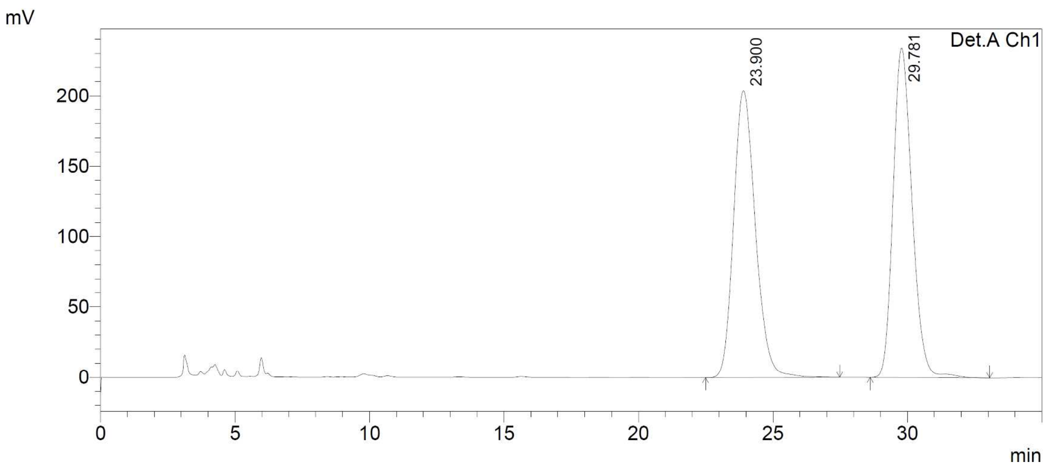
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.676	324238	6068	3.618	4.324
2	36.113	8637671	134273	96.382	95.676
Total		8961909	140341	100.000	100.000



5i

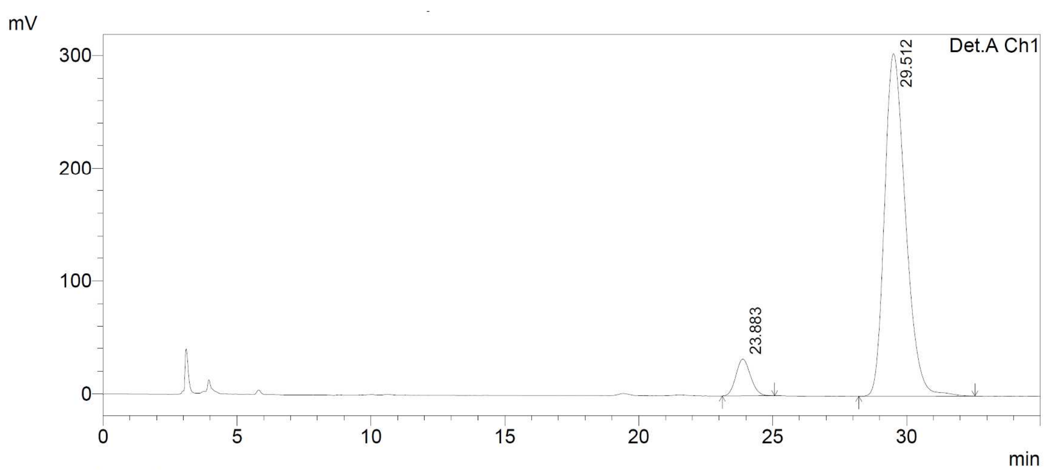


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.900	11463968	203771	50.029	46.578
2	29.781	11450896	233709	49.971	53.422
Total		22914864	437481	100.000	100.000

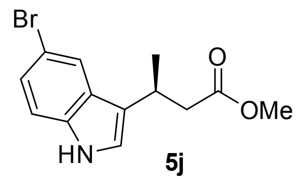


1 Det.A Ch1/210nm

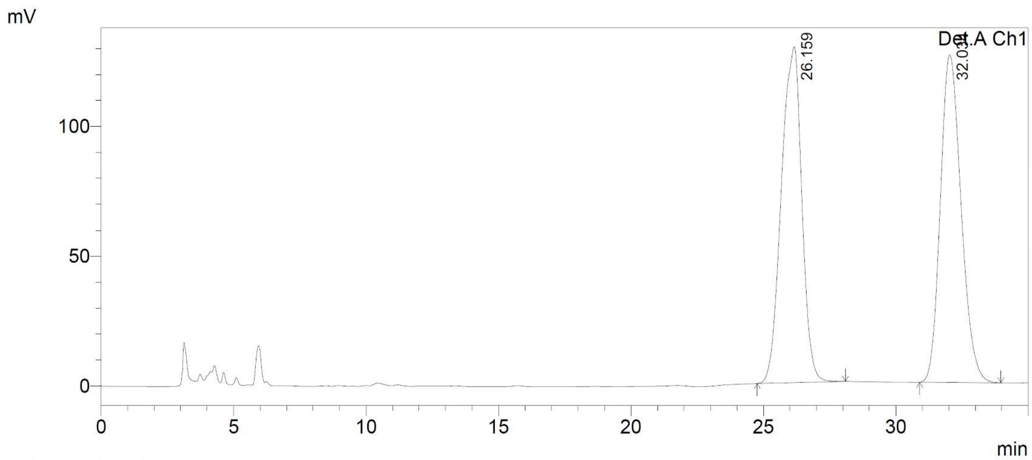
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.883	1219860	32184	6.851	9.587
2	29.512	16586751	303505	93.149	90.413
Total		17806611	335688	100.000	100.000



5j

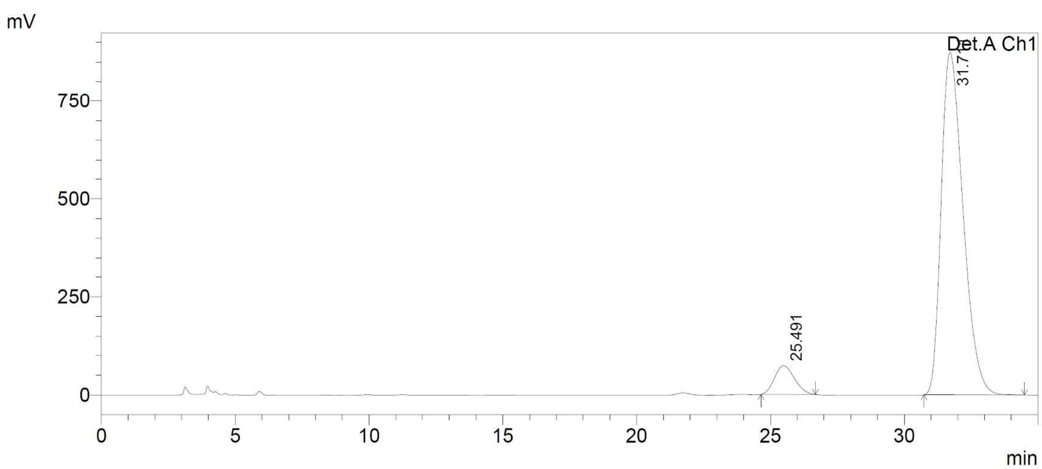


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.159	6941581	129273	50.246	50.597
2	32.034	6873638	126222	49.754	49.403
Total		13815218	255495	100.000	100.000

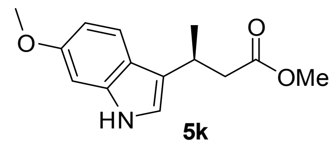


1 Det.A Ch1/220nm

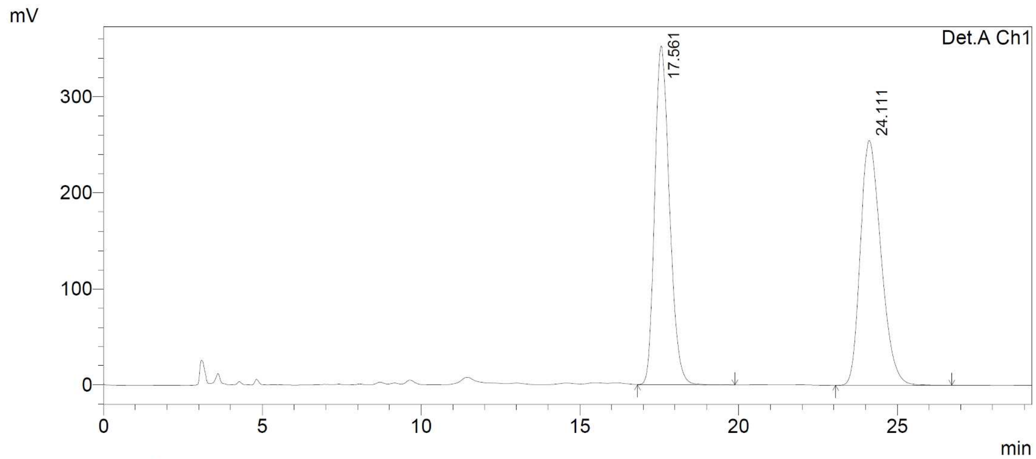
PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.491	3747141	72222	7.024	7.634
2	31.711	49600533	873778	92.976	92.366
Total		53347675	946001	100.000	100.000



5k

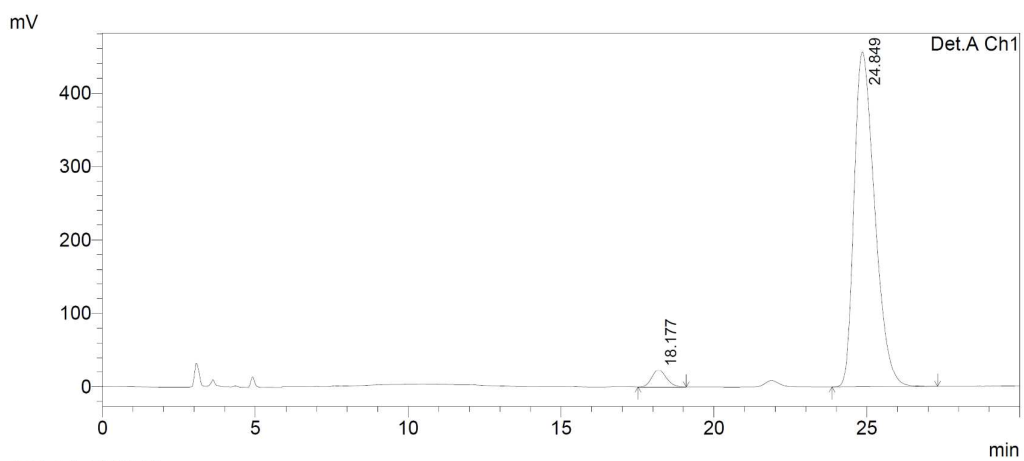


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.561	11519944	352967	49.897	58.060
2	24.111	11567530	254973	50.103	41.940
Total		23087474	607940	100.000	100.000

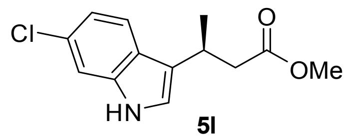


1 Det.A Ch1/210nm

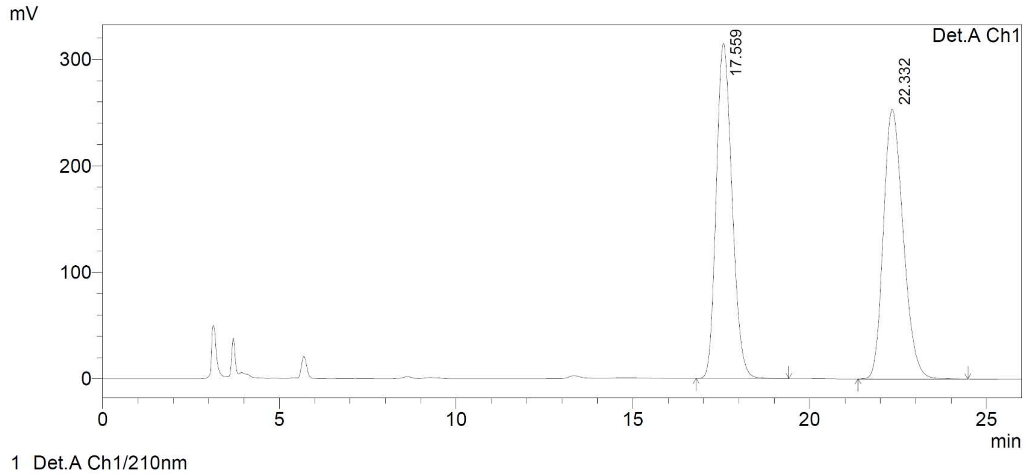
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.177	760486	23222	3.432	4.851
2	24.849	21396803	455465	96.568	95.149
Total		22157289	478688	100.000	100.000



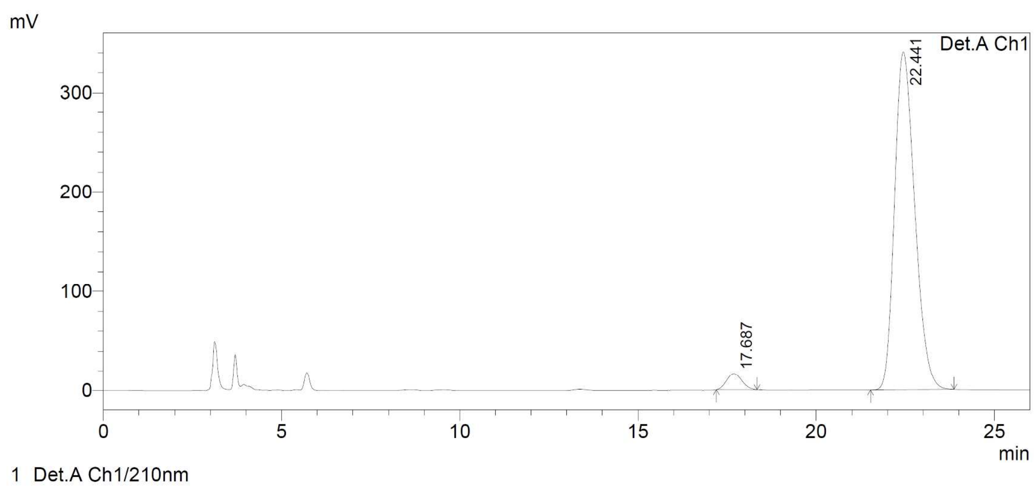
5l



PeakTable

Detector A Ch1 210nm

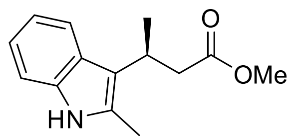
Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.559	9813825	314427	49.813	55.401
2	22.332	9887447	253118	50.187	44.599
Total		19701272	567545	100.000	100.000



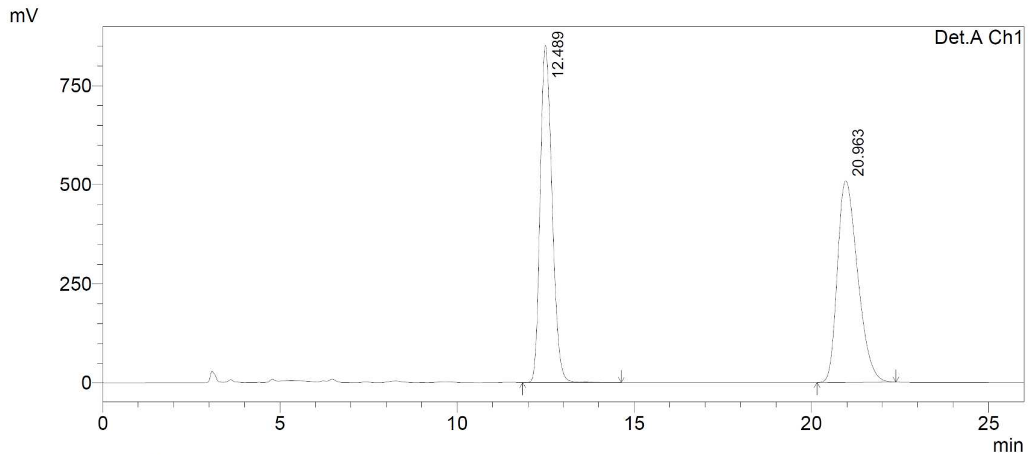
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.687	488245	16491	3.512	4.627
2	22.441	13414962	339952	96.488	95.373
Total		13903206	356443	100.000	100.000



5m

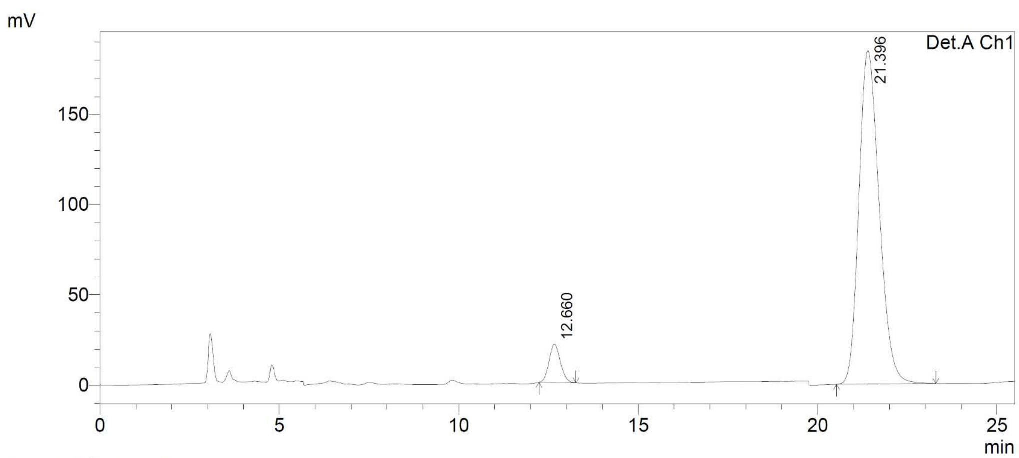


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.489	19867331	850515	49.493	62.558
2	20.963	20274204	509040	50.507	37.442
Total		40141535	1359555	100.000	100.000

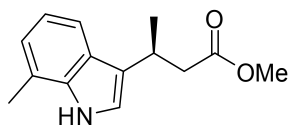


1 Det.A Ch1/210nm

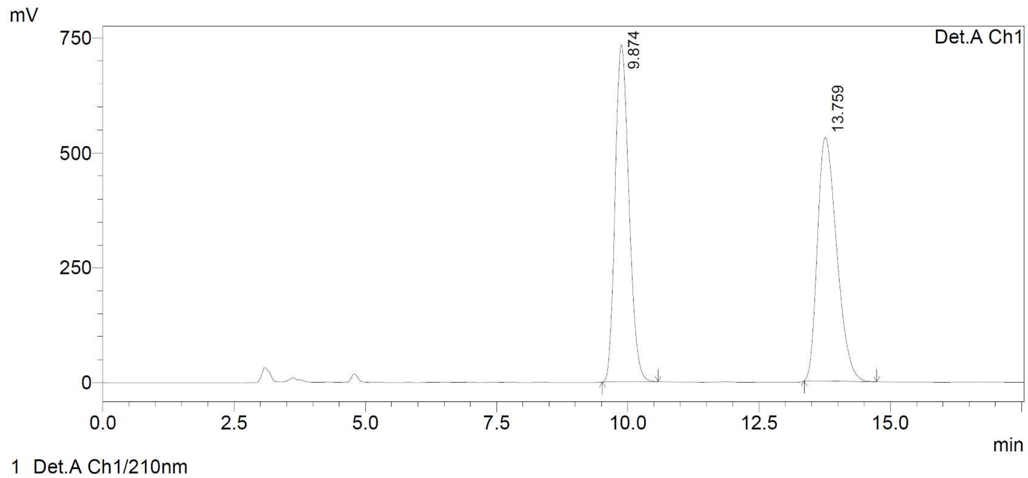
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.660	476093	21519	6.131	10.432
2	21.396	7288627	184761	93.869	89.568
Total		7764720	206280	100.000	100.000



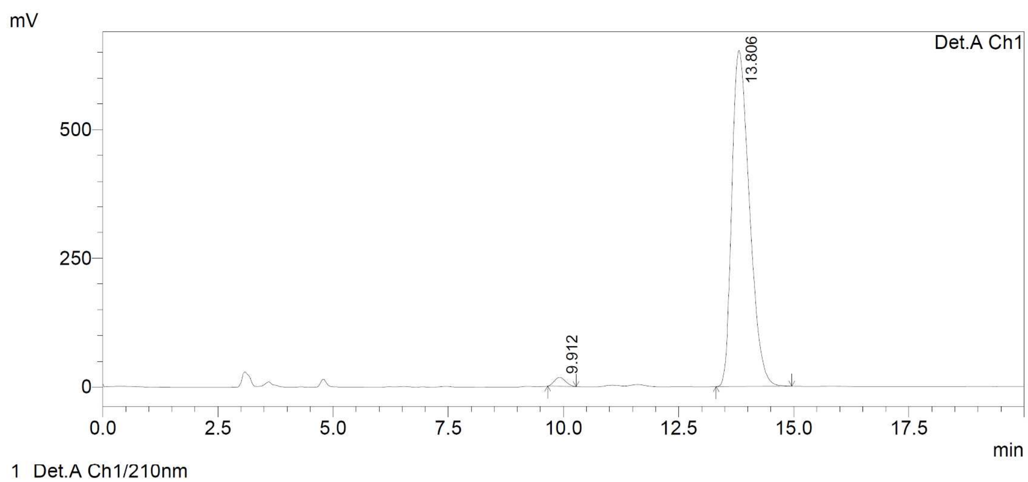
5n



PeakTable

Detector A Ch1 210nm

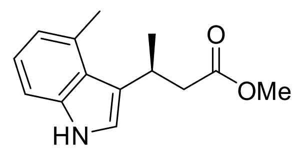
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.874	13455680	733162	49.683	57.967
2	13.759	13627471	531633	50.317	42.033
Total		27083151	1264795	100.000	100.000



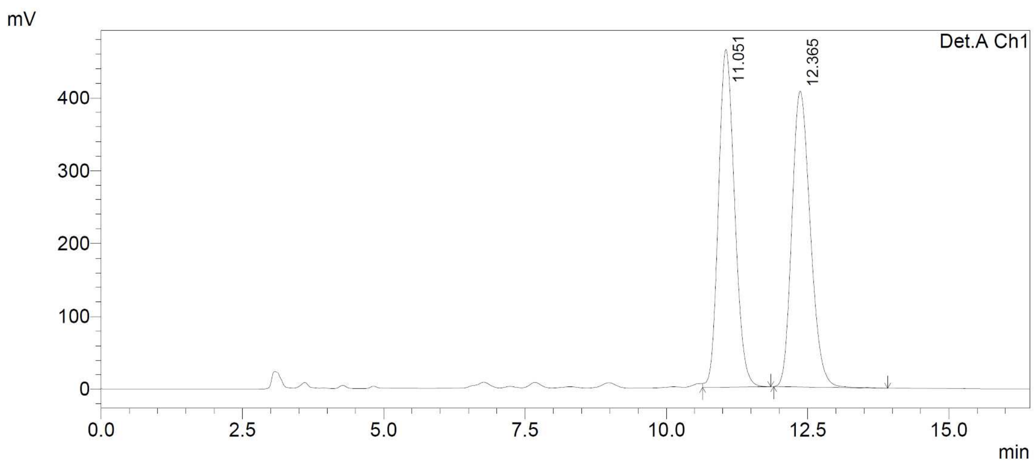
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.912	289547	17207	1.636	2.567
2	13.806	17414207	652995	98.364	97.433
Total		17703754	670202	100.000	100.000



5o

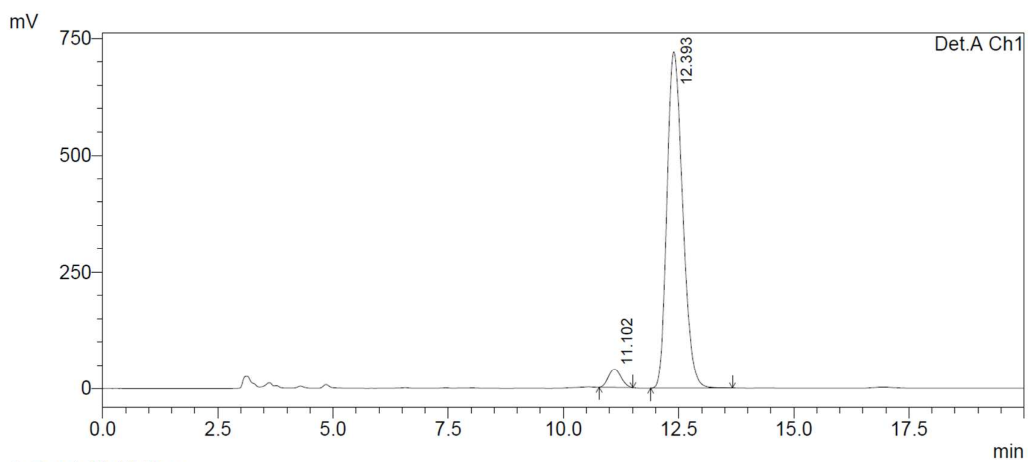


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.051	9259124	463599	50.042	53.257
2	12.365	9243549	406892	49.958	46.743
Total		18502674	870490	100.000	100.000

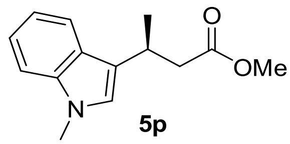


1 Det.A Ch1/210nm

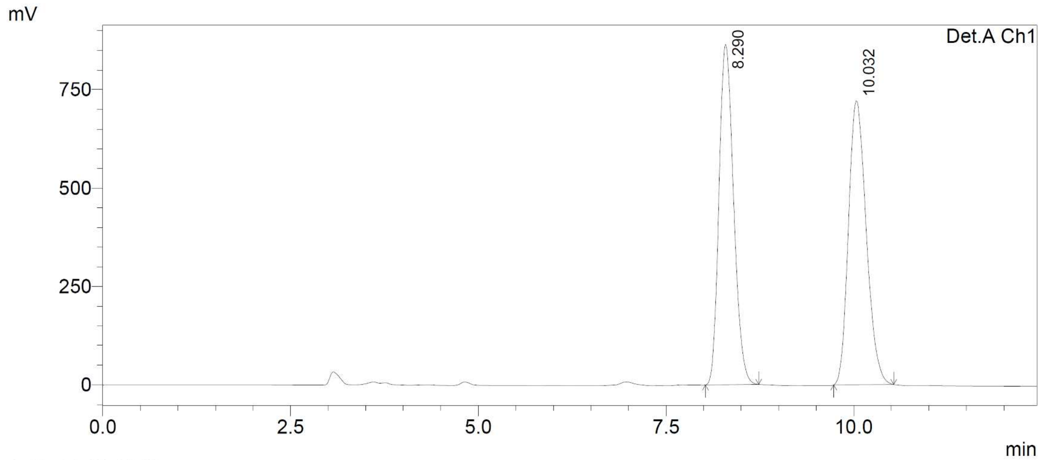
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.102	754494	39451	4.219	5.187
2	12.393	17130811	721159	95.781	94.813
Total		17885305	760610	100.000	100.000



5p

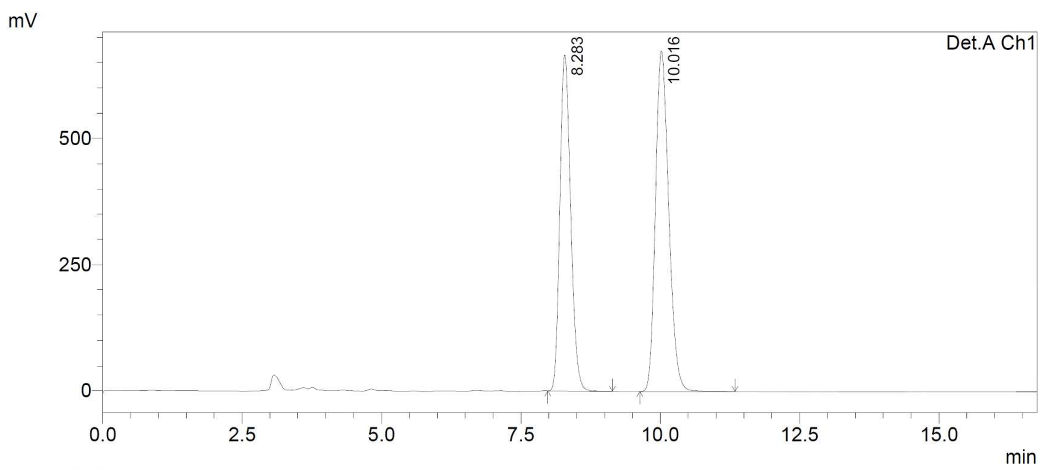


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.290	11724555	865010	49.617	54.536
2	10.032	11905422	721111	50.383	45.464
Total		23629977	1586121	100.000	100.000

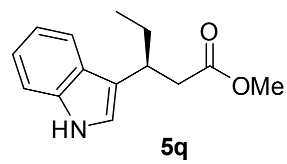


1 Det.A Ch1/210nm

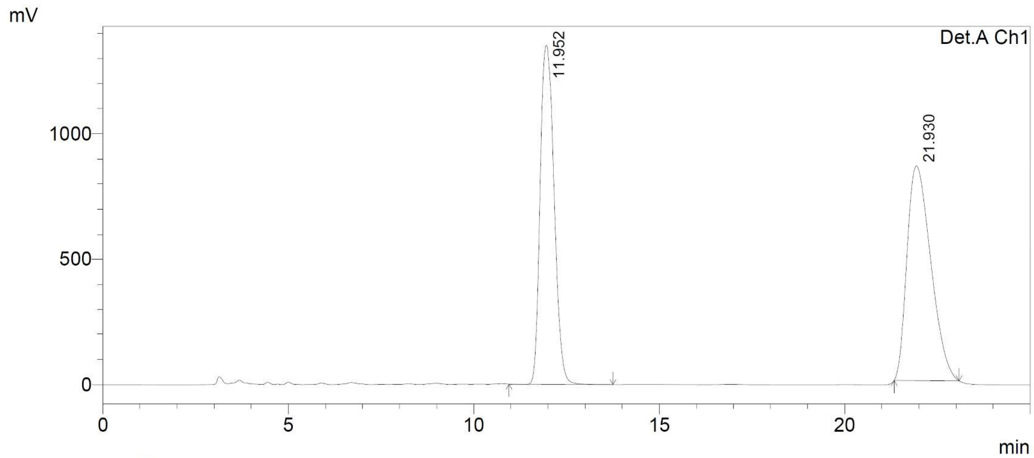
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.283	8981232	665940	44.506	49.692
2	10.016	11198475	674203	55.494	50.308
Total		20179707	1340144	100.000	100.000



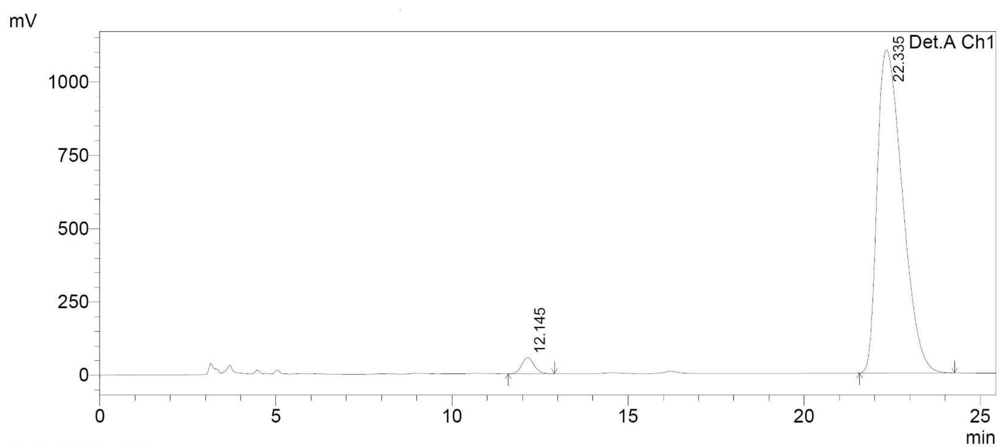
5q



PeakTable

Detector A Ch1 210nm

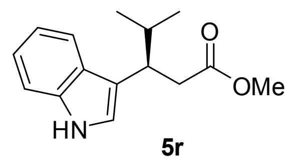
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.952	35255243	1350458	48.009	61.261
2	21.930	38179441	853986	51.991	38.739
Total		73434683	2204444	100.000	100.000



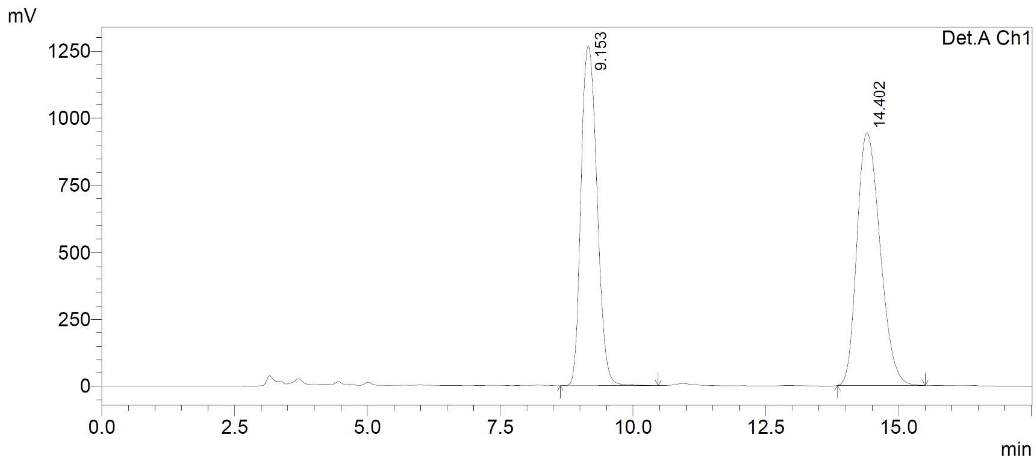
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.145	1319858	55321	2.345	4.782
2	22.335	54962574	1101589	97.655	95.218
Total		56282433	1156910	100.000	100.000



5r

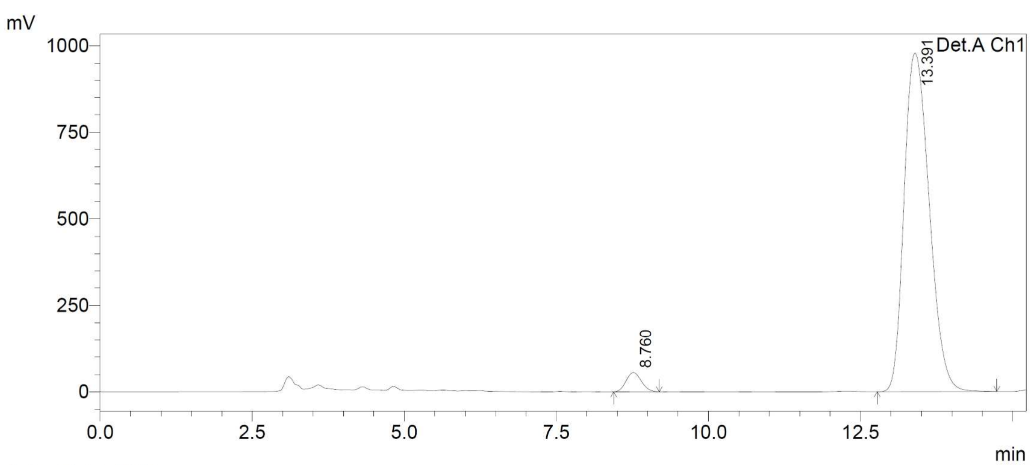


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.153	26703722	1266920	48.205	57.331
2	14.402	28692387	942905	51.795	42.669
Total		55396109	2209825	100.000	100.000

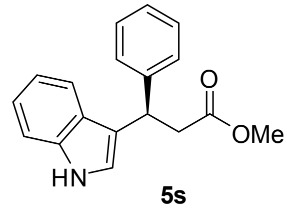


1 Det.A Ch1/210nm

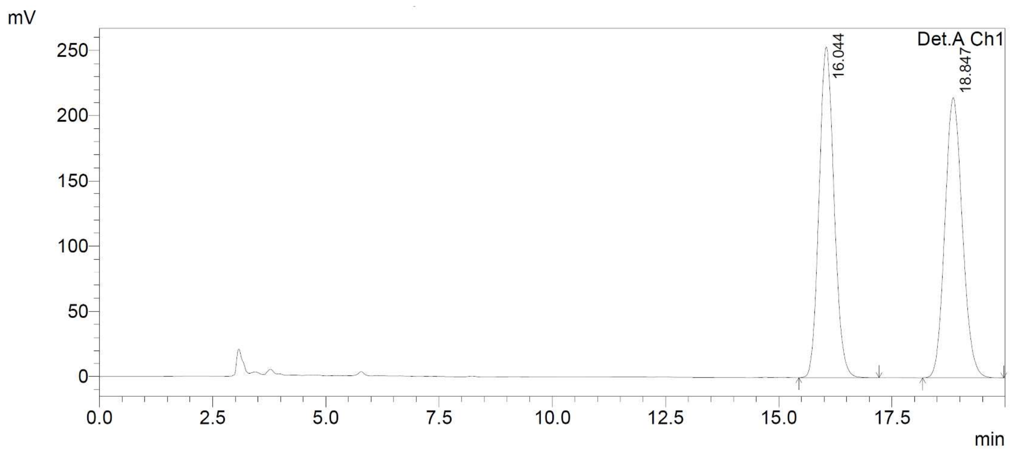
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.760	973370	55509	3.345	5.368
2	13.391	28126378	978561	96.655	94.632
Total		29099749	1034069	100.000	100.000



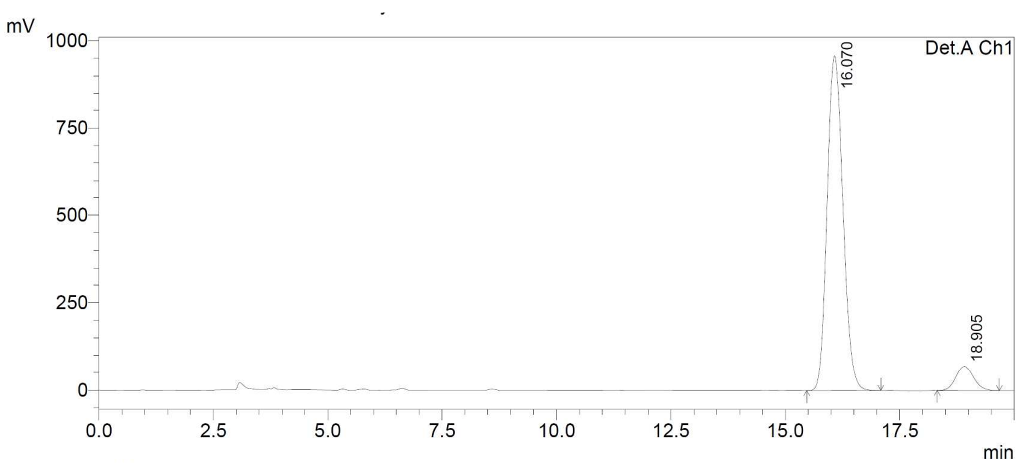
5s



PeakTable

Detector A Ch1 210nm

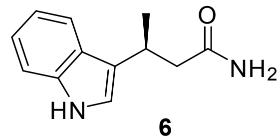
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.044	5843277	253502	50.224	54.140
2	18.847	5791134	214732	49.776	45.860
Total		11634411	468234	100.000	100.000



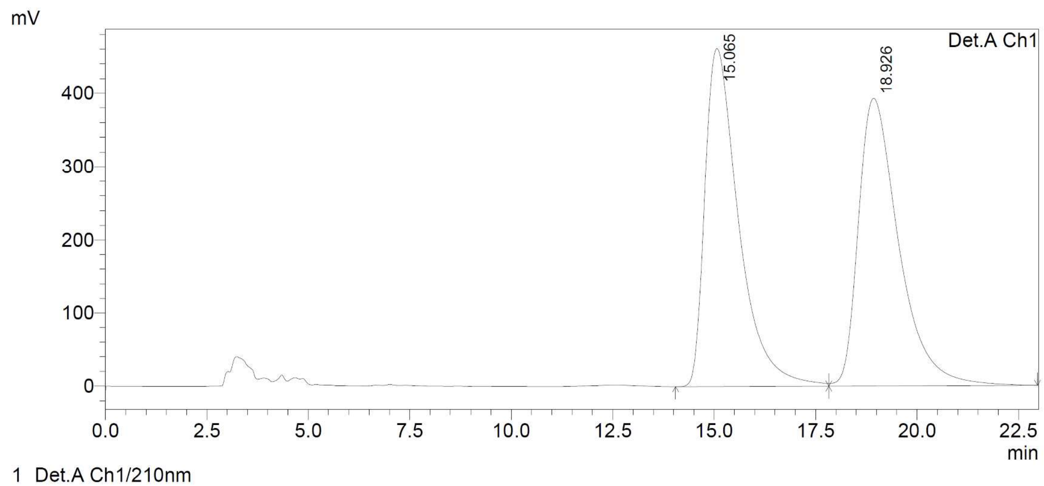
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.070	23058097	958083	92.446	93.170
2	18.905	1884176	70236	7.554	6.830
Total		24942273	1028319	100.000	100.000



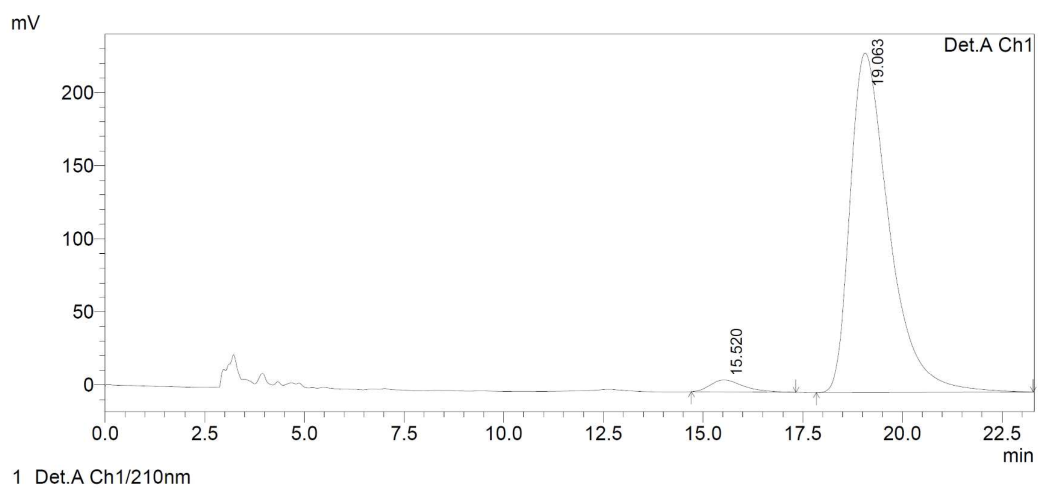
6



PeakTable

Detector A Ch1 210nm

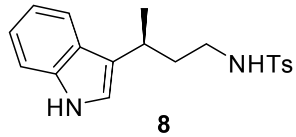
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.065	26759928	461530	49.596	54.038
2	18.926	27195757	392560	50.404	45.962
Total		53955684	854090	100.000	100.000



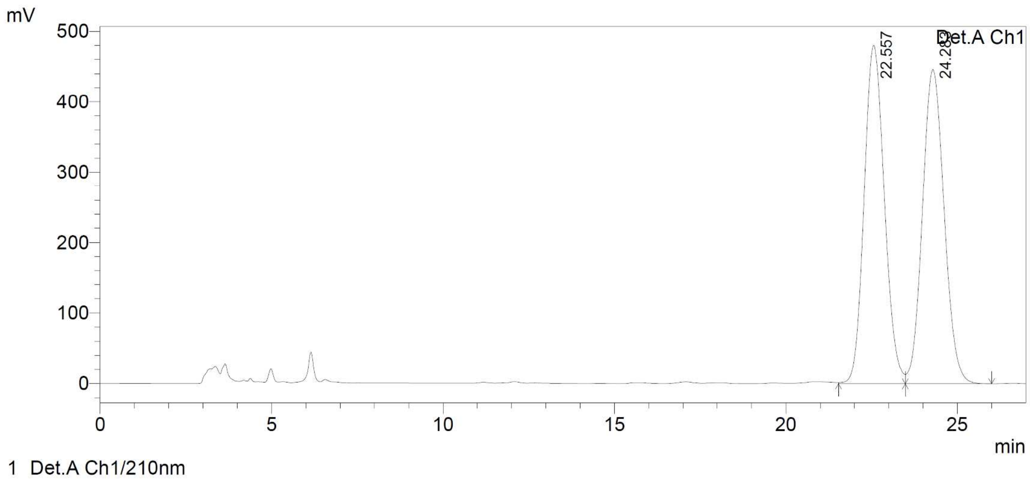
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.520	464061	8050	2.843	3.351
2	19.063	15859167	232144	97.157	96.649
Total		16323228	240193	100.000	100.000



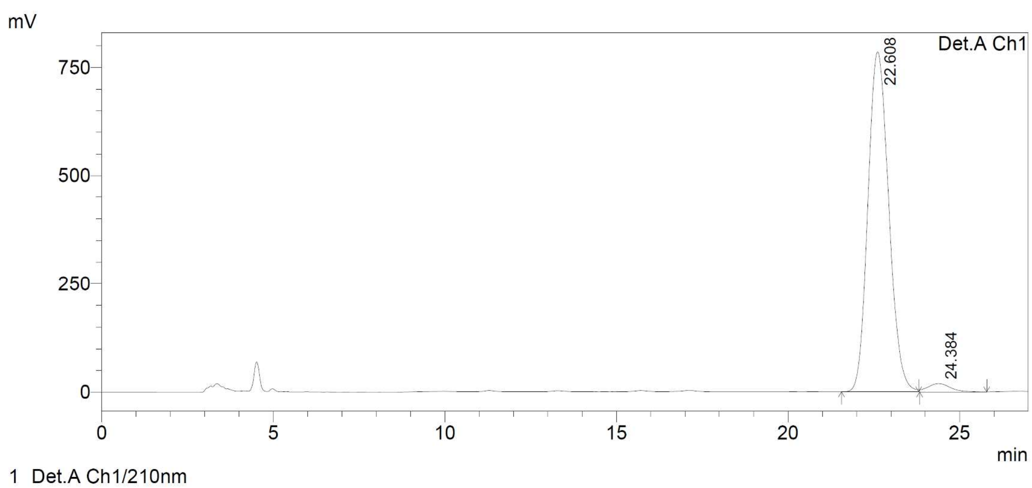
8



PeakTable

Detector A Ch1 210nm

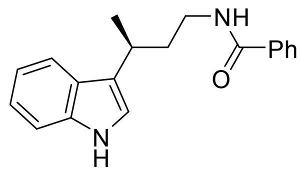
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.557	19799494	480524	50.143	51.841
2	24.283	19686311	446399	49.857	48.159
Total		39485805	926923	100.000	100.000



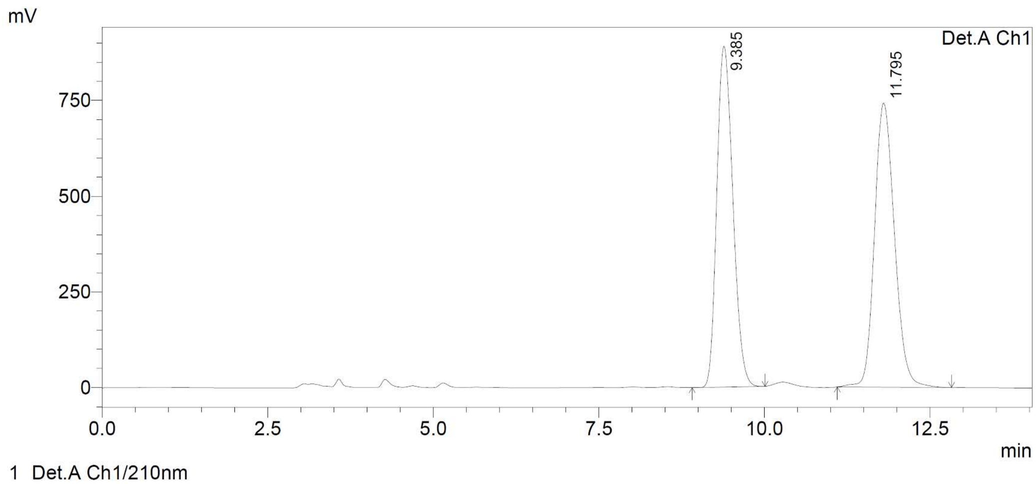
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.608	33126386	785323	97.389	97.597
2	24.384	888219	19332	2.611	2.403
Total		34014605	804656	100.000	100.000



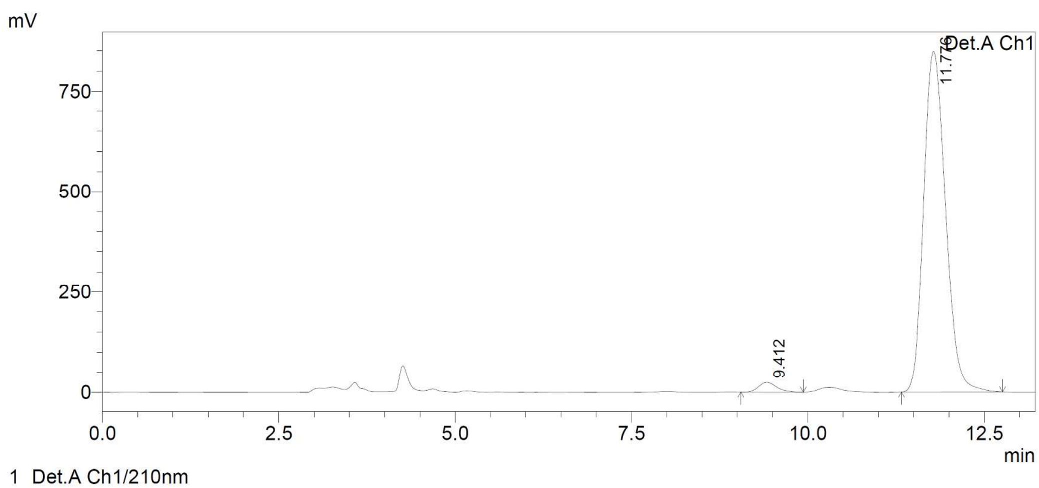
9



PeakTable

Detector A Ch1 210nm

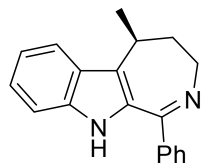
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.385	15027141	889676	49.128	54.561
2	11.795	15560535	740947	50.872	45.439
Total		30587675	1630623	100.000	100.000



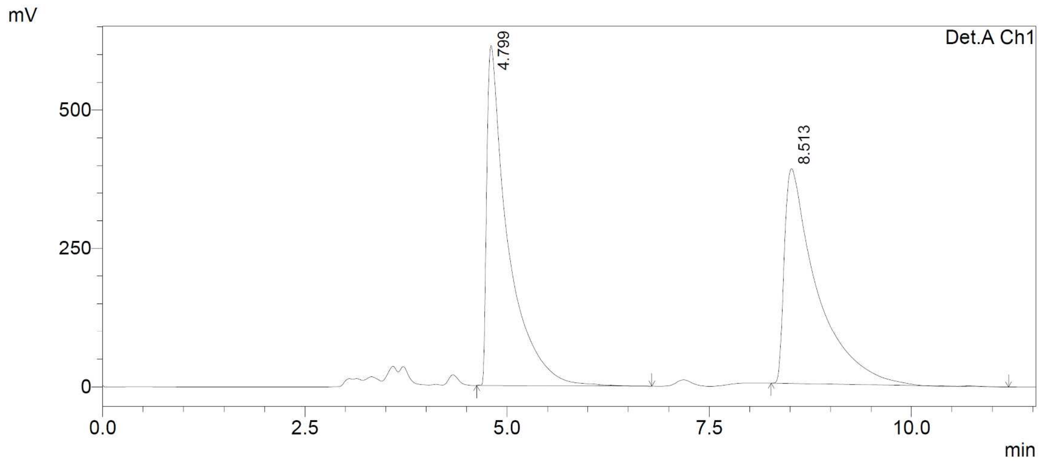
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.412	430401	24426	2.298	2.799
2	11.776	18295850	848152	97.702	97.201
Total		18726251	872577	100.000	100.000



10

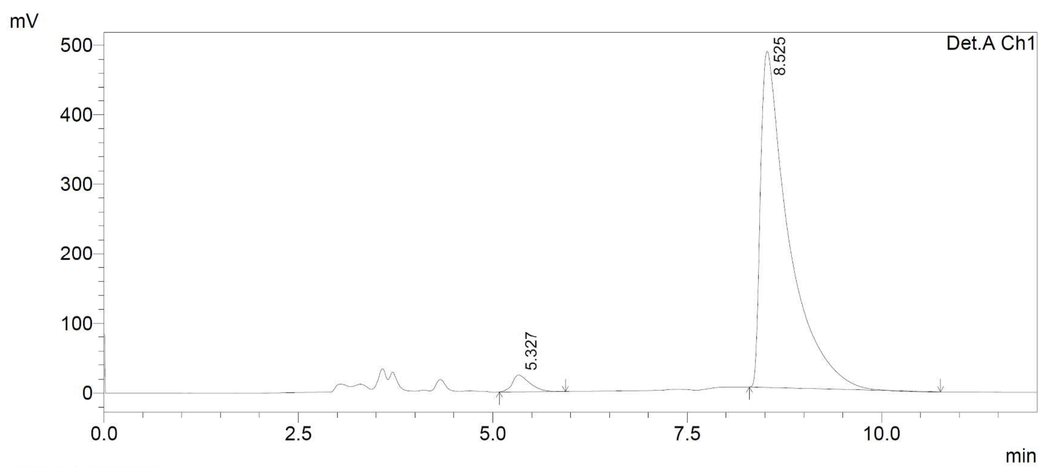


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.799	11119621	613586	50.642	61.284
2	8.513	10837512	387632	49.358	38.716
Total		21957133	1001218	100.000	100.000



1 Det.A Ch1/210nm

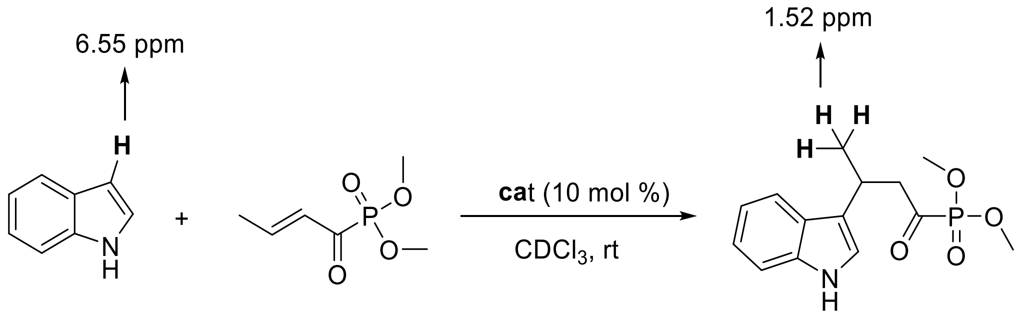
PeakTable

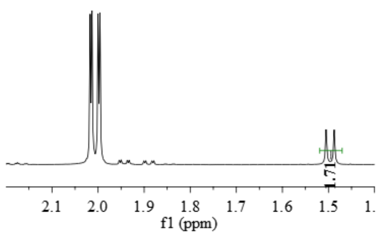
Detector A Ch1 210nm

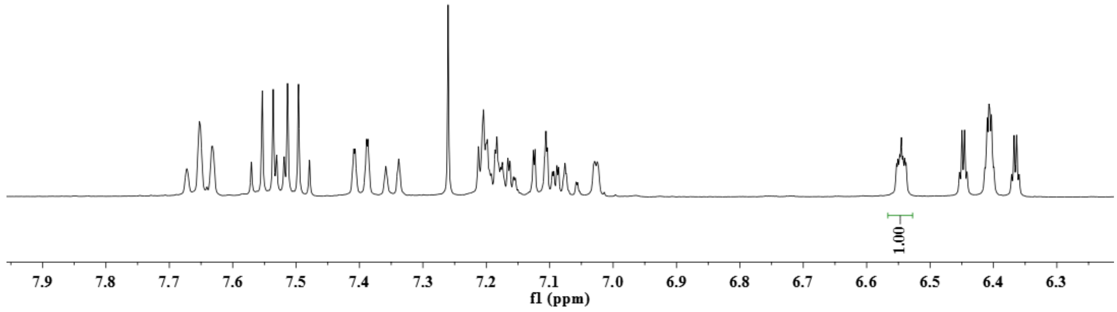
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.327	375530	24001	2.988	4.730
2	8.525	12190936	483468	97.012	95.270
Total		12566466	507469	100.000	100.000

8. Experimental procedure for the kinetic study by ^{1}H NMR

A dry, screw-capped reaction vial containing a magnetic stir bar was charged with acyl phosphonate **4a** (0.2 mmol, 2 equiv), catalyst **2b** or **2i** (0.01 mmol, 0.1 equiv). After 10 min of stirring, indole **3a** (0.1 mmol, 1 equiv) was added. After 10 min, the solution was transferred to a NMR tube. The reaction progress was monitored by a Bruker AV400 spectrometer in situ. For each reaction, both the signal of hydrogen of indole at 6.55 ppm and the appearance of new signal at 1.52 ppm (doublet) were recorded. The conversion was determined by calculating the ratio of the integral of **3a** and **5a'**.

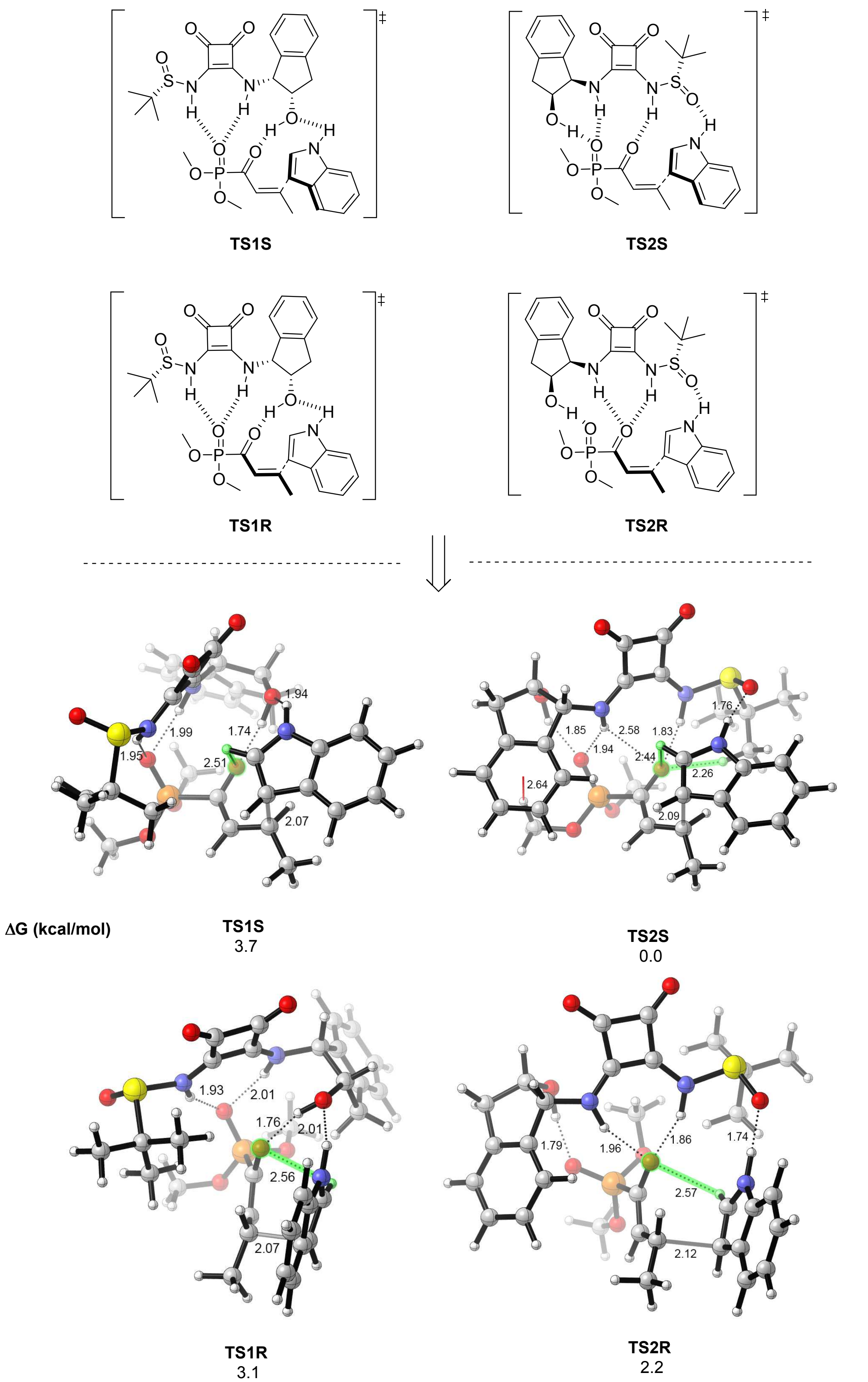






9. Computational details

The transition states structures were optimized using the functional M06-2X[5] and the 6-311G(d) basis set as implemented in Gaussian 09.[6] The IEF-PCM solvation model was used to account for the effects of the chloroform environment.[7] The transition structures were confirmed by frequency calculations at the same level. The single-point energy calculations were performed at the M06-2X/def2TZVPP[8]-IEF-PCM(chloroform) level with the previously optimized structures. AIM analysis[9] were conducted by using Multiwfn.[10] The estimated energies of hydrogen bonding interactions in transition states were calculated using the formula (E=1/2V(r)) reported by Espinosa et al.[11] The C−H···O hydrogen bonding in **TS2S** was confirmed by electron density and its Laplacian (See Table S2), which are within the range of criteria for hydrogen bonding (0.002-0.04 au for the electron density and 0.02-0.15 au for its Laplacian).[12] All energetics reported throughout the text are in kcal/mol and the bond lengths are in angstroms (Å). Structures were generated using CYLview.[13]



Optimized Transition States calculated with M06-2X/def2-TZVPP-IEF-PCM (Chloroform)//M06-2X/6-311G(d)-IEF-PCM (Chloroform)

Table S2. Topological Parameters (in Hartree) at the Bond Critical Points of Hydrogen bonding interactions and Estimated Hydrogen bonding energy (kcal/mol) in the Transition-State Structures.

TS1S	Bond length	ρ(r)	$\nabla^2\rho(r)$	G(r)	H(r)	V(r)	E
N−H···O=P	1.95	0.0249	0.0919	0.0222	0.0008	-0.0213	-6.7
N−H···O=P	1.99	0.0225	0.0843	0.0199	0.0011	-0.0188	-5.9
O−H···O=C	1.74	0.0371	0.1166	0.0341	-0.0049	-0.0390	-12.2
N−H···O=C	1.94	0.0250	0.1038	0.0242	0.0018	-0.0224	-7.0
TS1R	Bond length	ρ(r)	$\nabla^2\rho(r)$	G(r)	H(r)	V(r)	E
N−H···O=P	1.93	0.0256	0.0923	0.0227	0.0004	-0.0223	-7.0
N−H···O=P	2.01	0.0224	0.0831	0.0196	0.0011	-0.0185	-5.8
O−H···O=C	1.76	0.0352	0.1130	0.0322	-0.0039	-0.0361	-11.3
N−H···O=C	2.01	0.0220	0.0893	0.0203	0.0020	-0.0183	-5.7
TS2S	Bond length	ρ(r)	$\nabla^2\rho(r)$	G(r)	H(r)	V(r)	E
N−H···O=S	1.76	0.0392	0.1069	0.0328	-0.0060	-0.0388	-12.2
C−H···O=C	**2.26**	**0.0140**	**0.0542**	**0.0115**	**0.0021**	**-0.0094**	**-3.0**
N−H···O=C	1.83	0.0296	0.1107	0.0282	-0.0005	-0.0287	-9.0
N−H···O=P	1.94	0.0261	0.0950	0.0234	0.0004	-0.0230	-7.2
O−H···O=P	1.85	0.0285	0.1049	0.0268	-0.0005	-0.0273	-8.6
N−H···O=C	2.58	0.0080	0.0307	0.0062	0.0015	-0.0048	-1.5
TS2R	Bond length	ρ(r)	$\nabla^2\rho(r)$	G(r)	H(r)	V(r)	E
N−H···O=S	1.74	0.0397	0.1135	0.0343	-0.0059	-0.0402	-12.6
N−H···O=C	1.86	0.0275	0.1070	0.0264	0.0003	-0.0261	-8.2
N−H···O=C	1.96	0.0248	0.0889	0.0218	0.0004	-0.0214	-6.7
O−H···O=P	1.79	0.0336	0.1046	0.0298	-0.0036	-0.0334	-10.5

M06-2X/6-311G(d)-IEF-PCM (chloroform) calculated Cartesian coordinates, energies and free energies (in Hartrees), and imaginary frequencies of the transition states structures.

TS1S

M06-2X/6-311G(d)−IEFPCM(chloroform) Energy = -2709.412876

M06-2X/6-311G(d)−IEFPCM(chloroform) Free Energy = -2708.824934

M06-2X/def2-TZVPP−IEFPCM(chloroform) Energy = -2709.772429

Imaginary Frequencies = -393.03

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.218228	0.885947	2.215661
2	6	0	-1.034321	0.254979	3.261875
3	7	0	-0.361321	2.006948	1.453565
4	1	0	0.437542	2.254339	0.863080
5	8	0	-2.065847	0.510866	3.832624
6	6	0	4.942504	-0.708796	1.325800
7	1	0	4.863151	0.004598	2.139694
8	6	0	6.087281	-0.763068	0.536937
9	1	0	6.914942	-0.092468	0.737361
10	6	0	6.175171	-1.680715	-0.511816
11	1	0	7.073116	-1.715356	-1.118949
12	6	0	5.122521	-2.549555	-0.785668
13	1	0	5.193737	-3.254876	-1.607554
14	6	0	3.973060	-2.489675	-0.002614
15	6	0	3.894585	-1.580126	1.047726
16	6	0	2.555094	-1.640877	1.733197
17	1	0	2.644809	-1.792872	2.810612
18	6	0	1.850590	-2.886989	1.081653
19	1	0	1.875362	-3.695921	1.812656
20	6	0	2.690399	-3.260625	-0.162731
21	1	0	2.850388	-4.337945	-0.237150
22	1	0	2.167310	-2.945248	-1.072105
23	6	0	0.721171	-0.140372	2.206208
24	6	0	-0.004002	-0.877769	3.273132
25	7	0	1.835809	-0.390159	1.532027
26	1	0	2.055001	0.197339	0.729687
27	8	0	0.492845	-2.671220	0.781433
28	1	0	0.448761	-2.100221	-0.008130
29	8	0	0.160098	-1.920489	3.850616
30	6	0	-1.744412	4.011012	0.349895
31	6	0	-2.367469	2.950513	-0.547528
32	1	0	-1.651366	2.169688	-0.807693
33	1	0	-2.709417	3.419050	-1.474644

34	1	0	-3.231777	2.483037	-0.066067
35	6	0	-0.449436	4.581929	-0.210086
36	1	0	0.018329	5.250993	0.513653
37	1	0	-0.672767	5.149818	-1.117550
38	1	0	0.262424	3.800345	-0.479493
39	6	0	-2.740207	5.129776	0.658071
40	1	0	-3.659779	4.737134	1.099423
41	1	0	-3.001482	5.640545	-0.271343
42	1	0	-2.309445	5.862581	1.342115
43	16	0	-1.413017	3.245756	2.007333
44	8	0	-0.619173	4.265918	2.758448
45	6	0	-1.958152	-0.909006	-2.619859
46	1	0	-1.549170	-1.877935	-2.340966
47	6	0	-1.030624	0.162261	-2.641490
48	1	0	-1.271444	1.086311	-3.153690
49	6	0	-3.030953	-0.941352	-3.673372
50	1	0	-3.764170	-1.726646	-3.500530
51	1	0	-3.538851	0.021279	-3.759110
52	1	0	-2.544989	-1.144793	-4.632632
53	6	0	0.178532	0.039098	-1.973054
54	8	0	0.586372	-0.943831	-1.298748
55	15	0	1.390495	1.406414	-1.905838
56	8	0	1.747470	1.743139	-0.492843
57	8	0	2.659409	0.975539	-2.770420
58	8	0	0.782877	2.596601	-2.760629
59	6	0	3.570035	-0.023816	-2.272529
60	1	0	3.092054	-1.002057	-2.313988
61	1	0	4.439104	-0.000306	-2.924250
62	1	0	3.867747	0.206855	-1.247799
63	6	0	1.570152	3.772134	-3.029815
64	1	0	0.886958	4.507333	-3.444873
65	1	0	2.011325	4.152957	-2.107756
66	1	0	2.350465	3.529652	-3.749599
67	6	0	-2.092893	-0.907034	0.002731
68	6	0	-3.135732	-0.724560	-0.932471
69	6	0	-3.301209	-2.783174	0.083669
70	6	0	-3.770060	-4.054647	0.395883
71	6	0	-4.960349	-4.446255	-0.196930
72	6	0	-5.655800	-3.591191	-1.065803
73	6	0	-5.169416	-2.330495	-1.377987
74	6	0	-3.963093	-1.918259	-0.805069
75	1	0	-3.233631	-4.701959	1.079143
76	1	0	-5.366937	-5.426337	0.022675
77	1	0	-6.593385	-3.923981	-1.495644

78	1	0	-5.720484	-1.675306	-2.043560
79	1	0	-3.505088	0.249466	-1.218054
80	1	0	-1.273375	-0.243140	0.232704
81	7	0	-2.170102	-2.115858	0.555898
82	1	0	-1.415687	-2.528709	1.104606

TS1R

M06-2X/6-311G(d)−IEFPCM(chloroform) Energy = -2709.412592

M06-2X/6-311G(d)−IEFPCM(chloroform) Free Energy = -2708.825836

M06-2X/def2-TZVPP−IEFPCM(chloroform) Energy = -2709.772254

Imaginary Frequencies = -391.94

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.330912	2.247480	-1.661425
2	6	0	0.234862	2.306424	-3.017210
3	7	0	-0.014047	2.844063	-0.493170
4	1	0	-0.506814	2.569954	0.362474
5	8	0	1.146842	2.894660	-3.550356
6	6	0	-5.363916	-0.259774	-1.189120
7	1	0	-5.529622	0.641668	-1.769965
8	6	0	-6.383844	-0.798714	-0.408166
9	1	0	-7.353723	-0.315487	-0.378097
10	6	0	-6.169596	-1.967149	0.323617
11	1	0	-6.976880	-2.383678	0.915967
12	6	0	-4.929838	-2.601176	0.303115
13	1	0	-4.763471	-3.504248	0.881674
14	6	0	-3.906410	-2.054234	-0.461260
15	6	0	-4.132922	-0.903403	-1.217839
16	6	0	-2.894537	-0.511883	-1.985322
17	1	0	-3.093272	-0.267192	-3.029421
18	6	0	-2.010223	-1.799642	-1.885580
19	1	0	-2.241600	-2.421882	-2.752353
20	6	0	-2.479430	-2.512546	-0.603316
21	1	0	-2.365822	-3.596854	-0.660223
22	1	0	-1.903899	-2.156960	0.259258
23	6	0	-1.282681	1.297219	-2.020728
24	6	0	-0.813661	1.276884	-3.425027

25	7	0	-2.253924	0.649365	-1.377228
26	1	0	-2.352634	0.824828	-0.380320
27	8	0	-0.628023	-1.542241	-1.934298
28	1	0	-0.394954	-0.975468	-1.174919
29	8	0	-1.130470	0.689234	-4.428323
30	6	0	2.625173	2.948480	0.227342
31	6	0	2.811502	1.801744	-0.760162
32	1	0	1.986150	1.087609	-0.696714
33	1	0	3.737081	1.270968	-0.517649
34	1	0	2.892231	2.162922	-1.788972
35	6	0	2.273621	2.458537	1.619959
36	1	0	2.082708	3.294893	2.293812
37	1	0	3.100766	1.863732	2.019496
38	1	0	1.391577	1.816819	1.588610
39	6	0	3.833571	3.882877	0.244040
40	1	0	4.052258	4.269867	-0.754559
41	1	0	4.710527	3.330422	0.590255
42	1	0	3.672195	4.725087	0.919797
43	16	0	1.232286	4.011231	-0.391974
44	8	0	0.849412	4.874372	0.770713
45	6	0	2.350481	-1.254038	1.944638
46	1	0	2.603341	-0.772743	1.000463
47	6	0	1.079192	-0.908768	2.462056
48	1	0	0.863696	-1.007681	3.520014
49	6	0	3.483773	-1.418648	2.919749
50	1	0	4.398169	-1.766659	2.444010
51	1	0	3.692313	-0.437604	3.358688
52	1	0	3.216517	-2.092545	3.735669
53	6	0	0.127022	-0.394413	1.589672
54	8	0	0.230613	-0.328245	0.340619
55	15	0	-1.392467	0.400938	2.248384
56	8	0	-1.785182	1.563542	1.397992
57	8	0	-2.476657	-0.755624	2.330866
58	8	0	-1.174749	0.775299	3.785367
59	6	0	-3.854026	-0.405395	2.591146
60	1	0	-4.291867	0.049541	1.701943
61	1	0	-4.364054	-1.335628	2.819787
62	1	0	-3.913581	0.274125	3.441800
63	6	0	-0.391910	1.933028	4.128734
64	1	0	0.668470	1.704287	4.008322
65	1	0	-0.667740	2.780612	3.500195
66	1	0	-0.609528	2.153333	5.169764
67	6	0	1.303261	-2.925705	0.153540
68	6	0	2.358367	-3.132181	1.068386

69	6	0	3.169687	-2.822698	-1.065561
70	6	0	4.072769	-2.670733	-2.112116
71	6	0	5.410517	-2.898500	-1.825593
72	6	0	5.824011	-3.271025	-0.537872
73	6	0	4.913658	-3.402835	0.500934
74	6	0	3.561638	-3.162655	0.242946
75	1	0	3.743018	-2.394323	-3.106414
76	1	0	6.147818	-2.795132	-2.612841
77	1	0	6.874748	-3.462150	-0.353857
78	1	0	5.245529	-3.703783	1.488252
79	1	0	2.227935	-3.667008	1.997813
80	1	0	0.242356	-2.892653	0.343541
81	7	0	1.779734	-2.704009	-1.067352
82	1	0	1.178674	-2.418008	-1.837362

TS2S

M06-2X/6-311G(d)−IEFPCM(chloroform) Energy = -2709.414894

M06-2X/6-311G(d)−IEFPCM(chloroform) Free Energy = -2708.831170

M06-2X/def2-TZVPP−IEFPCM(chloroform) Energy = -2709.774143

Imaginary Frequencies = -375.39

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.716709	-2.489434	-0.812576
2	6	0	1.005270	-3.383484	-1.943478
3	7	0	1.416913	-2.169217	0.314032
4	1	0	1.118851	-1.333266	0.826889
5	8	0	1.901336	-4.130594	-2.242180
6	6	0	-2.857520	1.447756	-1.273725
7	1	0	-1.781944	1.577384	-1.198226
8	6	0	-3.713600	2.541953	-1.160757
9	1	0	-3.303348	3.531463	-0.990021
10	6	0	-5.093193	2.369866	-1.263304
11	1	0	-5.749226	3.229315	-1.178312
12	6	0	-5.638654	1.100053	-1.453396
13	1	0	-6.714217	0.968824	-1.514907
14	6	0	-4.786198	0.006926	-1.551358
15	6	0	-3.405966	0.190676	-1.477689
16	6	0	-2.703356	-1.131169	-1.686599
17	1	0	-2.447478	-1.242260	-2.744796

18	6	0	-3.806409	-2.173455	-1.342477
19	1	0	-3.648105	-3.100856	-1.895152
20	6	0	-5.105635	-1.454475	-1.765396
21	1	0	-5.320036	-1.644444	-2.822622
22	1	0	-5.955742	-1.809419	-1.180465
23	6	0	-0.512512	-2.095114	-1.322372
24	6	0	-0.329565	-2.930005	-2.541801
25	7	0	-1.470013	-1.255538	-0.926243
26	1	0	-1.537911	-1.029381	0.065618
27	8	0	-3.801223	-2.522604	0.020062
28	1	0	-3.661601	-1.737222	0.573774
29	8	0	-0.962330	-3.127105	-3.544141
30	6	0	3.424685	-2.079586	2.090282
31	6	0	2.393690	-2.672674	3.044865
32	1	0	1.412415	-2.212228	2.924618
33	1	0	2.728534	-2.498642	4.070610
34	1	0	2.289870	-3.752036	2.906539
35	6	0	3.453509	-0.556895	2.112343
36	1	0	4.167038	-0.171402	1.381669
37	1	0	3.777245	-0.233085	3.105001
38	1	0	2.474131	-0.114000	1.920998
39	6	0	4.818132	-2.651219	2.359741
40	1	0	4.818002	-3.743112	2.332069
41	1	0	5.140899	-2.336045	3.354192
42	1	0	5.544808	-2.280251	1.634400
43	16	0	3.051043	-2.667468	0.370831
44	8	0	3.838945	-1.755983	-0.540037
45	6	0	1.074791	2.894855	0.787006
46	1	0	1.881717	2.232635	1.095866
47	6	0	-0.231441	2.489539	1.143622
48	1	0	-1.036600	3.215155	1.171830
49	6	0	1.384104	4.366381	0.845594
50	1	0	2.389851	4.598399	0.503943
51	1	0	0.660840	4.951025	0.273262
52	1	0	1.305385	4.678344	1.891536
53	6	0	-0.496314	1.170889	1.486219
54	8	0	0.289724	0.188839	1.416693
55	15	0	-2.127939	0.704223	2.183786
56	8	0	-2.661862	-0.547545	1.576661
57	8	0	-1.900692	0.574931	3.761152
58	8	0	-3.074844	1.968203	2.077284
59	6	0	-1.129534	-0.521186	4.280058
60	1	0	-0.070223	-0.346399	4.089455
61	1	0	-1.318683	-0.550182	5.349395

62	1	0	-1.444662	-1.457281	3.817985
63	6	0	-4.501477	1.769063	2.017168
64	1	0	-4.933078	2.739578	1.791015
65	1	0	-4.741415	1.058850	1.225945
66	1	0	-4.863457	1.409419	2.980495
67	6	0	1.432973	1.117713	-1.144332
68	6	0	1.384449	2.527350	-1.248686
69	6	0	3.548623	1.776306	-1.402405
70	6	0	4.934955	1.788218	-1.526305
71	6	0	5.527285	3.009787	-1.805291
72	6	0	4.756176	4.173953	-1.956198
73	6	0	3.376879	4.148506	-1.814847
74	6	0	2.756748	2.930312	-1.522345
75	1	0	5.514823	0.878358	-1.423303
76	1	0	6.603465	3.066090	-1.919104
77	1	0	5.251756	5.108735	-2.190793
78	1	0	2.792113	5.053903	-1.934948
79	1	0	0.505522	3.067665	-1.568330
80	1	0	0.617083	0.426057	-0.989091
81	7	0	2.696270	0.696954	-1.177137
82	1	0	3.035526	-0.262490	-1.015009

TS2R

M06-2X/6-311G(d)−IEFPCM(chloroform) Energy = -2709.413803

M06-2X/6-311G(d)−IEFPCM(chloroform) Free Energy = -2708.826507

M06-2X/def2-TZVPP−IEFPCM(chloroform) Energy = -2709.774199

Imaginary Frequencies = -366.93

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.269364	2.601057	-1.202150
2	6	0	0.727029	3.874710	-1.764156
3	7	0	-0.819150	2.217164	-0.486152
4	1	0	-0.856695	1.265172	-0.110416
5	8	0	0.309017	5.007206	-1.789760
6	6	0	2.293566	-2.283866	-1.757845
7	1	0	1.270646	-2.048424	-2.039297
8	6	0	2.659446	-3.593507	-1.449470
9	1	0	1.918428	-4.384141	-1.490431
10	6	0	3.970542	-3.891491	-1.084600

11	1	0	4.240092	-4.913837	-0.842850
12	6	0	4.935780	-2.886773	-1.012186
13	1	0	5.950573	-3.122657	-0.708675
14	6	0	4.570448	-1.581394	-1.307255
15	6	0	3.260689	-1.292862	-1.686410
16	6	0	3.107607	0.190816	-1.916378
17	1	0	3.230466	0.432015	-2.978861
18	6	0	4.312935	0.791535	-1.128828
19	6	0	5.386362	-0.310324	-1.260216
20	1	0	5.950623	-0.182227	-2.190419
21	1	0	6.092849	-0.270487	-0.429393
22	6	0	1.401643	1.907286	-1.613024
23	6	0	1.967843	3.122488	-2.255833
24	7	0	1.802406	0.650445	-1.481673
25	1	0	1.262185	0.052652	-0.860880
26	8	0	3.978806	1.057515	0.209669
27	1	0	3.652100	0.243421	0.636269
28	8	0	2.970116	3.374819	-2.870908
29	6	0	-1.830138	3.603932	1.611550
30	6	0	-0.500994	4.347846	1.692375
31	1	0	0.337974	3.718139	1.393166
32	1	0	-0.332700	4.665663	2.724316
33	1	0	-0.500453	5.239310	1.060262
34	6	0	-1.831936	2.292638	2.383653
35	1	0	-2.798120	1.792265	2.286512
36	1	0	-1.669226	2.501624	3.444192
37	1	0	-1.039654	1.611502	2.060368
38	6	0	-2.993670	4.499522	2.032895
39	1	0	-3.020455	5.422010	1.447432
40	1	0	-2.869337	4.771686	3.083399
41	1	0	-3.949083	3.984646	1.921742
42	16	0	-2.116878	3.265419	-0.184136
43	8	0	-3.345199	2.389002	-0.224803
44	6	0	-1.485729	-2.949761	-0.122446
45	1	0	-1.574256	-2.191713	-0.897533
46	6	0	-0.482754	-2.729146	0.844348
47	1	0	-0.163402	-3.529778	1.500657
48	6	0	-1.788917	-4.358543	-0.543494
49	1	0	-0.935435	-4.717234	-1.128460
50	1	0	-1.900683	-5.021653	0.316240
51	1	0	-2.671827	-4.423824	-1.176112
52	6	0	0.087241	-1.469672	0.962855
53	8	0	-0.230349	-0.437689	0.305551
54	15	0	1.471817	-1.178069	2.127645

55	8	0	2.816049	-1.087699	1.501153
56	8	0	1.075451	0.173010	2.894627
57	8	0	1.297232	-2.299055	3.238450
58	6	0	1.651404	1.416575	2.459811
59	1	0	1.412290	1.600678	1.409417
60	1	0	1.213049	2.188011	3.088698
61	1	0	2.733117	1.399168	2.581444
62	6	0	2.262936	-2.393005	4.301444
63	1	0	3.258746	-2.546315	3.887059
64	1	0	2.238020	-1.483972	4.902705
65	1	0	1.971087	-3.247501	4.904368
66	6	0	-3.070237	-1.084433	0.938465
67	6	0	-3.354674	-2.450933	0.743277
68	6	0	-4.498161	-1.154526	-0.769726
69	6	0	-5.329500	-0.805266	-1.829844
70	6	0	-6.045329	-1.828811	-2.430593
71	6	0	-5.933141	-3.155062	-1.982472
72	6	0	-5.090706	-3.491860	-0.933983
73	6	0	-4.348226	-2.479049	-0.318229
74	1	0	-5.415392	0.222701	-2.161742
75	1	0	-6.708627	-1.600415	-3.256467
76	1	0	-6.519161	-3.927925	-2.466075
77	1	0	-5.019017	-4.518065	-0.590560
78	1	0	-3.243506	-3.196772	1.515984
79	1	0	-2.402304	-0.634517	1.657437
80	7	0	-3.703559	-0.340279	0.032857
81	1	0	-3.585691	0.676730	-0.074803
82	1	0	4.624379	1.741483	-1.563436

----

10. References

1 (a) Evans, D. A.; Johnson, J. S. *J. Am. Chem. Soc.* **1998**, *120*, 4895-4896. (b) Evans, D. A.; Johnson, J. S.; Olhava, E. J. *J. Am. Chem. Soc.* **2000**, *122*, 1635-1649. (c) Evans, D. A.; Scheidt K. A.; Fandrick, K. R.; Lam, H. W.; Wu, J. *J. Am. Chem. Soc.* **2003**, *125*, 10780-10781.

2 Li, J.-C.; Zhou, H.-B.; Chen, Y.-Z. *J. Sichuan Univ. Nat. Sci. Ed.* **1998**, *35*, 144-146.

3 Qian, Y.; Ma, G.-Y.; Lv, A.-F.; Zhu, H.-L.; Zhao, J.; Rawal, V. H. *Chem. Commun*. **2010**, *46*, 3004-3006.

4 Kang, Y. K.; Suh, K. H.; Kim, D. Y. *Synlett* **2011**, 1125-1128.

5 (a) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* 2008, *41*, 157-167. (b) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* 2008, *120*, 215-241.

6 Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

7 (a) Cancès, E.; Mennucci, B.; Tomasi, J. *J. Chem. Phys.* **1997**, *107*, 3032-3041. (b) Tomasi, J.; Mennucci, B.; Cancès, E. *J. Mol. Struct. (Theochem)* **1999**, *464*, 211-226. (c) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999-3093.

8 Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7,* 3297-3305.

9 (a) Bader, R. F. W. *Acc. Chem. Res.* **1985**, *18*, 9-15. (b) Bader, R. F. W. *Chem. Rev.* **1991**, *91*, 893-928. (c) Matta, C. F.; Boyd, R. J. *The Quantum Theory of Atoms in Molecules: From Solid State to DNA and Drug Design*; WileyVCH; Weinheim, 2007. (d) Grabowski, S. J. *Chem. Rev.* **2011**, *111*, 2597-2625.

10 Lu, T.; Chen, F. *J. Comput. Chem.* **2012**, *33*, 580-592.

11 Espinosa, E.; Molins, E.; Lecomte, C. *Chem. Phys. Lett.* **1998**, *285*, 170-173.

12 (a) Koch, U.; Popelier, P. L. A. *J. Phys. Chem.* **1995**, *99*, 9747-9751. (b) Popelier, P. L. A. *J. Phys. Chem. A* **1998**, *102*, 1873-1878. (c) Lipkowski, P.; Grabowski, S. J.; Robinson, T, L,; Leszczynski, J.; *J. Phys. Chem. A* **2004**, *108*, 10865-10872.

13 CYLview, 1.0b; Legault, C. Y. Université de Sherbrooke, 2009. (http://www.cylview.org).