Highly enantioslelctive yttrium(III)-catalyzed Friedel-Crafts alkylation of β-trichloro(trifluoro)methyl aryl enones with indoles

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1. General remarks

Reactions were carried out using commercial available reagents in over-dried apparatus. CH_2Cl_2 was dried over powdered CaH_2 and distilled under nitrogen just before use. Enantiomeric excesses (*ee*) were determined by HPLC analysis using the corresponding commercial chiral column as stated in the experimental procedures at 23 ^{o}C with UV detector at 210 nm and 254 nm. Optical rotations were reported as follows: $[\alpha]^{T}_{D}$ (c g/100 mL, in solvent). ^{1}H NMR spectra were recorded on commercial instruments (400 MHz or 600 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration and assignment. ^{13}C NMR spectra were collected on commercial instruments (100 MHz or 150 Hz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). HRMS was recorded on a commercial apparatus (ESI Source).

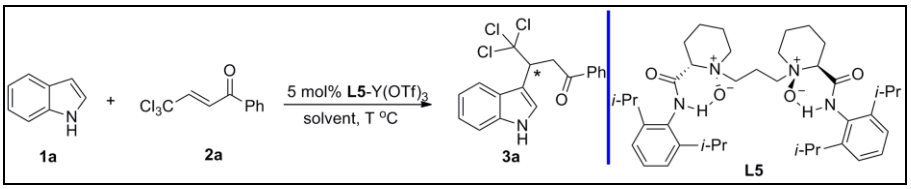
All indoles **1** and other reagents were commercially available and used as purchased without further purification.

The *N*,*N*'-dioxide ligands **L1-L8** were known compounds and synthesized by the same procedure in

the literature.[1] The β-trichloro(trifluoro)methyl aryl enones were prepared according to literature.[2]

All of racemic samples **3**, **5** were prepared using 1 mol% $Sc(OTf)_3$ in CH_2Cl_2 at 35 °C.

2. Extra Optimizations



Entry[a]	Solvent	T (°C)	t (h)	Yield[b] (%)	ee[c] (%)
1	$CHCl_3$	35	36	41	94 (*S*)
2	CH_2ClCH_2Cl	35	36	35	86 (*S*)
3	THF	35	26	NR[d]	-
4	toluene	35	45	27	66 (*S*)
5	CH_2Cl_2	25	40	trace	-
6[e]	CH_2Cl_2	35	45	98	92 (*S*)
7[f]	CH_2Cl_2	35	50	55	93 (*S*)

[a] Unless otherwise noted, reactions were carried out with 5 mol% **L5**-$Y(OTf)_3$ (1:1), **1a** (0.12 mmol) and **2a** (0.10 mmol) in solvent (0.25 mL) at T °C. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] NR = No Reaction. [e] Reaction was conducted with 10 mol% **L5**-$Y(OTf)_3$ in 0.15 mL CH_2Cl_2. [f] Reaction was conducted with 2.5 mol% **L5**-$Y(OTf)_3$ in 0.15 mL CH_2Cl_2.

3. General procedure for the catalytic asymmetric Friedel-Crafts reaction

*For β-trichloromethyl aryl enones **2:*** a solution of *N,N'*-dioxide **L5** (3.3 mg, 0.005 mmol), yttrium triflate (2.7 mg, 0.005 mmol), and *β*-trichloromethyl aryl enones **2** (0.10 mmol) in CH_2Cl_2 (0.10 mL) was stirred in a dry reaction tube under N_2 atmosphere at 35 °C for 0.5 h, then indole **1** (50 μL, 2.4 M in CH_2Cl_2) was added. The sealed tube was stirred at 35 °C for the corresponding time. And then the reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford the desired product **3**.

*For β-trifluoromethyl aryl enones **4:*** a solution of *N,N'*-dioxide **L5** (3.3 mg, 0.005 mmol), yttrium triflate (2.7 mg, 0.005 mmol), and *β*-trifluoromethyl aryl enones **4** (0.10 mmol) in CH_2Cl_2 (0.20 mL) was stirred in a dry reaction tube under N_2 atmosphere at 35 °C for 0.5 h, then indole **1** (50 μL, 2.4 M in CH_2Cl_2) was added. The sealed tube was stirred at 35 °C for the corresponding time. And then the

1. (*a*) Z. P. Yu, X. H. Liu, Z. H. Dong, M. S. Xie and X. M. Feng, *Angew. Chem., Int. Ed.*, 2008, **47**, 1308; (b) X. Zhang, D. H. Chen, X. H. Liu and X. M. Feng, *J. Org. Chem.*, 2007, **72**, 5227; (*c*) W. Li, J. Wang, X. L. Hu, K. Shen, W. T. Wang, Y. Y. Chu, L. L. Lin, X. H. Liu and X. M. Feng, *J. Am. Chem. Soc.*, 2010, **132**, 8532; (*d*) D. H. Chen, Z. L. Chen, X. Xiao, Z. G. Yang, L. L. Lin, X. H. Liu and X. M. Feng, *Chem. Eur. J.*, 2009, **15**, 6807; (e) Y. L. Liu, D. J. Shang, X. Zhou, X. H. Liu and X. M. Feng, *Chem. Eur. J.*, 2009, **15**, 2055; (f) W. T. ang, X. H. Liu, W. D. Cao, J. Wang, L. L. Lin and X. M. Feng, *Chem. Eur. J.*, 2010, **16**, 1664; (*g*) K. Shen, X. H. Liu, K. Zheng, W. Li, X. L. Hu, L. L. Lin and X. M. Feng, *Chem. Eur. J.*, 2010, **16**, 3736; (*h*) Y. H. Hui, J. Jiang, W. T. Wang, W. L. Chen, Y. F. Cai, L. L. Lin, X. H. Liu and X. M. Feng, *Angew. Chem., Int. Ed.*, 2010, **49**, 4290.
2 (*a*) G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and C. Vila, *Chem. Eur. J.*, 2010, **16**, 9117; (*b*) A. Guirado, B. Martiz, R. Andreu, D. Bautista and J. Gálvez, *Tetrahedron* 2007, **63**, 1175; (*c*) A. Guirado, B. Martiz and R. Andreu, *Tetrahedron Lett.*, 2004, **45**, 8523.

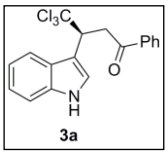
reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford the desired product **5**.

For the catalytic asymmetric Friedel-Crafts reaction on 1.0 mmol-scale: a solution of *N,N'*-dioxide **L5** (33.0 mg, 0.05 mmol), yttrium triflate (26.8 mg, 0.05 mmol), and *β*-trichloro(trifluoro)methyl aryl enones **2** or **4** (1.0 mmol) in CH_2Cl_2 (0.50 mL) was stirred in a dry reaction tube under N_2 atmosphere at 35 ^oC for 0.5 h, then indole **1** (1.2 mmol in 0.2 mL CH_2Cl_2) was added. The sealed tube was stirred at 35 ^oC for the corresponding time. And then the reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford the desired product **3a** or **5a**.

Product 3a: 64 h, 310 mg, 85% yield, 93% *ee*.

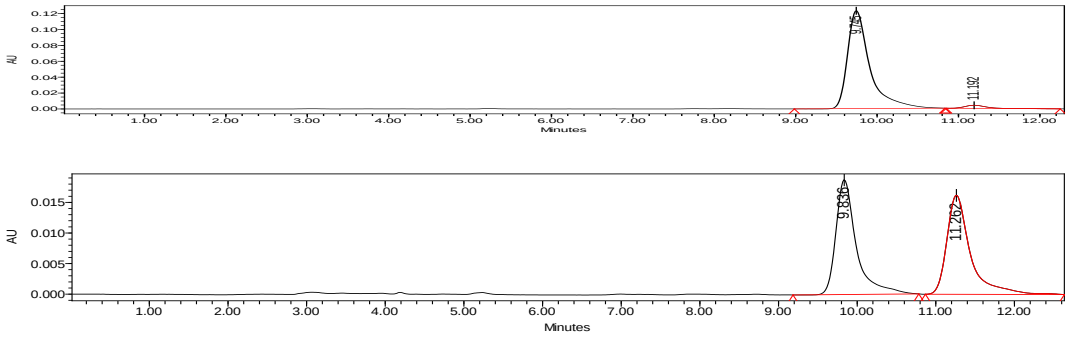
Product 5a: 24 h, 215 mg, 99% yield, 94% *ee*.

4. Characterization of the new products

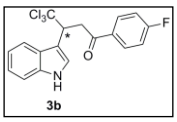


3a

(*S*)-4,4,4-trichloro-3-(1H-indol-3-yl)-1-phenylbutan-1-one (3a): 52 h, 32.7 mg, white solid, 89% yield; $[\alpha]^{18}_D$ = -69.1 (c = 0.56, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.745 min, t_r (minor) = 11.192 min, 94% *ee*; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 8.00 – 7.90 (m, 2H), 7.90 – 7.82 (m, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.24 – 7.12 (m, 2H), 5.03 (dd, *J* = 9.1, 3.3 Hz, 1H), 4.01 (qd, *J* = 17.2, 6.2 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.03, 135.48, 134.40, 132.32, 127.63, 127.06, 126.84, 122.57, 121.32, 119.12, 118.63, 112.08, 110.17, 103.66, 51.89, 41.90 ppm; EI-HRMS: Calcd for $C_{18}H_{14}Cl_3NO$ $[M+Na]^+$ 388.0033, Found 388.0038.



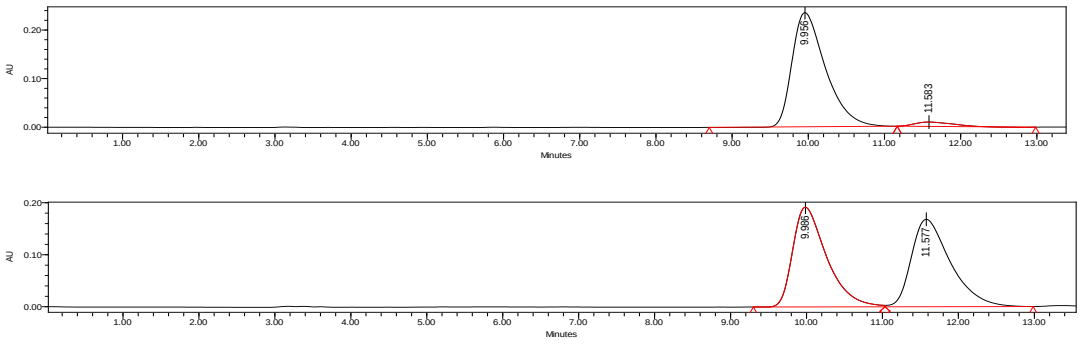
	Retention Time	Area	% Area
1	11.192	70218	2.91
2	9.745	2345595	97.09



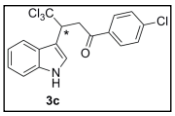
3b

4,4,4-trichloro-1-(4-fluorophenyl)-3-(1H-indol-3-yl)butan-1-one (3b): 52 h, 33.5 mg, white solid, 87% yield; $[\alpha]^{18}_D$ = -124.9 (c = 0.654, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.956 min, t_r (minor) = 11.583 min, 91% *ee*; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.02 – 7.91 (m, 2H), 7.89 – 7.81 (m, 1H), 7.36 – 7.24 (m, 2H), 7.23 – 7.15 (m, 2H), 7.10 (t, *J* = 8.6 Hz, 2H), 5.01 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.97 (qd, *J* = 17.2, 6.2 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.48, 166.08, 163.54, 134.41, 131.93, 131.90, 129.79, 129.70, 126.80, 122.57, 121.39, 119.18, 118.59, 114.88, 114.66, 112.00, 110.23, 103.57, 51.93, 41.82 ppm; EI-HRMS:

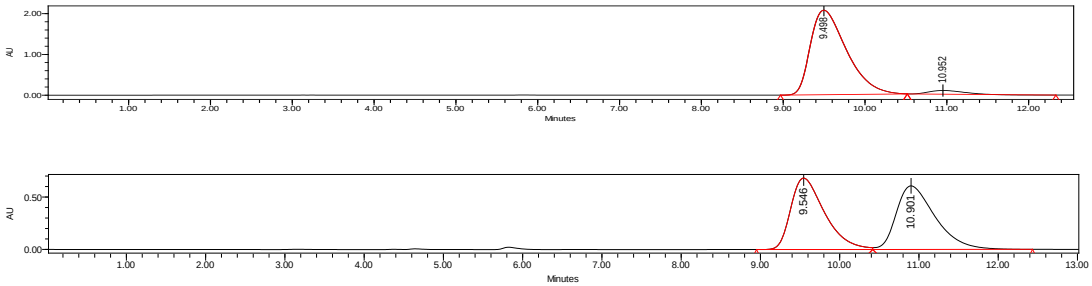
Calcd for $C_{18}H_{13}Cl_3FNO$ $[M+Na]^+$ 405.9939, Found 405.9956.



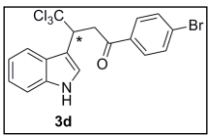
	Retention Time	Area	% Area
1	9.956	7198625	95.61
2	11.583	330644	4.39



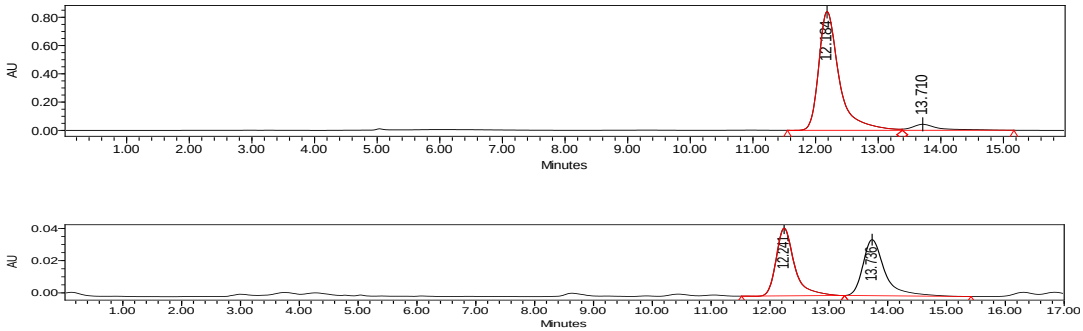
4,4,4-trichloro-1-(4-chlorophenyl)-3-(1H-indol-3-yl)butan-1-one (3c): 52 h, 37.9 mg, white solid, 95% yield; $[\alpha]^{18}_D$ = -94.3 (c = 0.582, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.498 min, t_r (minor) = 10.952 min, 92% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.96 – 7.75 (m, 3H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.35 – 7.24 (m, 2H), 7.23 – 7.09 (m, 2H), 4.99 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.96 (ddd, *J* = 26.4, 17.2, 6.2 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.87, 138.80, 134.40, 133.79, 128.49, 127.95, 126.79, 122.55, 121.42, 119.20, 118.58, 111.97, 110.23, 103.51, 51.91, 41.87 ppm; EI-HRMS: Calcd for $C_{18}H_{13}C_{l4}NO$ $[M+Na]^+$ 421.9643, Found 421.9647.



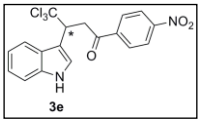
	Retention Time	Area	% Area
1	9.498	63620008	95.80
2	10.952	2789515	4.20



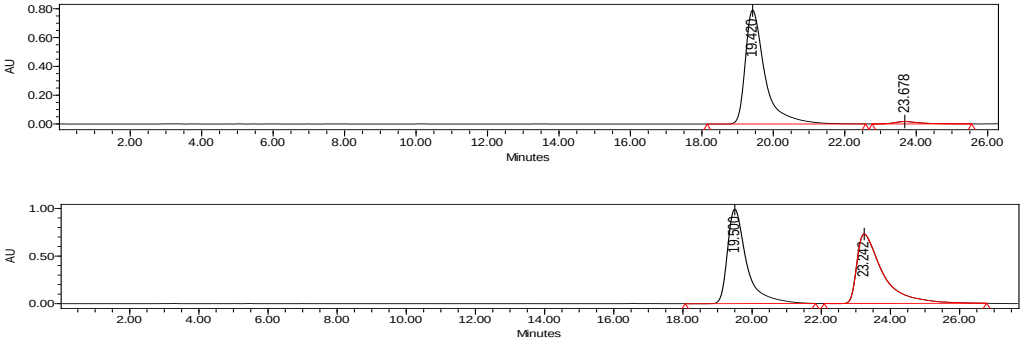
1-(4-bromophenyl)-4,4,4-trichloro-3-(1H-indol-3-yl)butan-1-one (3d): 46 h, 34.4 mg, white solid, 77% yield; $[\alpha]^{18}_D$ = -89.9 (c = 0.68, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 12.184 min, t_r (minor) = 13.710 min, 88% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.87 (dd, *J* = 8.2, 4.3 Hz, 1H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.34 (dt, *J* = 7.4, 3.1 Hz, 2H), 7.25 – 7.15 (m, 2H), 5.01 (dd, *J* = 9.1, 3.3 Hz, 1H), 3.97 (qd, *J* = 17.2, 6.2 Hz, 2H) ppm; ^{13}C NMR (101 MHz, CDCl3) δ 195.08, 135.46, 135.24, 131.99, 129.63, 128.57, 127.84, 123.60, 122.45, 120.23, 119.62, 112.99, 111.27, 104.55, 52.93, 42.90 ppm; EI-HRMS: Calcd for $C_{18}H_{13}BrCl_3NO$ $[M+Na]^+$ 465.9138, Found 465.9154.



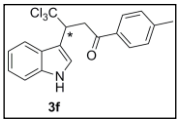
	Retention Time	Area	% Area
1	12.184	19097597	93.89
2	13.710	1351736	6.11



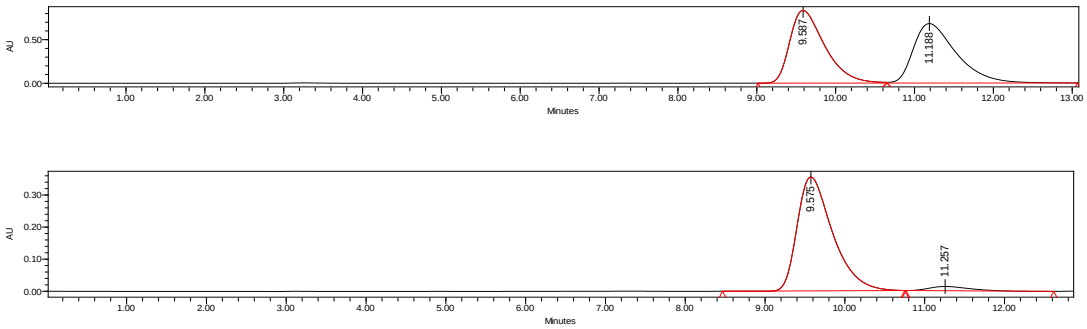
4,4,4-trichloro-3-(1H-indol-3-yl)-1-(4-nitrophenyl)butan-1-one (3e): 26 h, 38.2 mg, yellow solid, 93% yield; $[\alpha]^{18}_{D}$ = -107.1 (c = 0.75, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 19.420 min, t_r (minor) = 23.678 min, 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.7 Hz, 3H), 8.01 (d, *J* = 8.8 Hz, 2H), 7.89 – 7.73 (m, 1H), 7.41 – 7.27 (m, 2H), 7.19 (p, *J* = 6.6 Hz, 2H), 4.97 (dd, *J* = 9.2, 3.2 Hz, 1H), 4.01 (ddd, *J* = 26.6, 17.4, 6.3 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.69, 149.30, 139.84, 134.37, 128.06, 126.65, 122.83, 122.54, 121.55, 119.29, 118.43, 111.69, 110.27, 103.16, 51.87, 42.50 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_3N_2O_3$ $[M+Na]^+$ 432.9884, Found 432.9886.



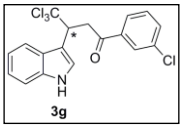
	Retention Time	Area	% Area
1	19.420	30132421	97.62
2	23.678	735785	2.38



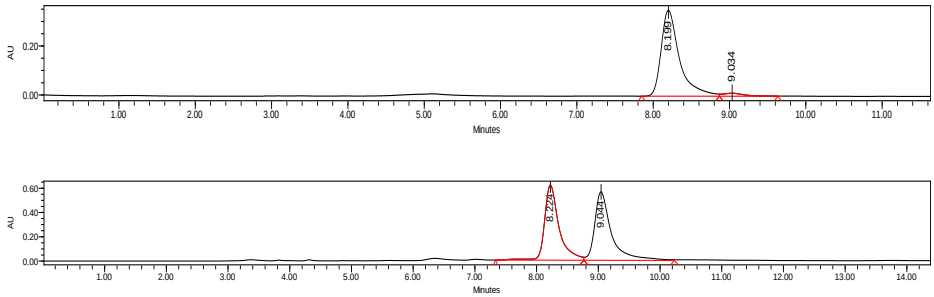
4,4,4-trichloro-3-(1H-indol-3-yl)-1-(p-tolyl)butan-1-one (3f): 52 h, 26.9 mg, white solid, 71% yield; $[\alpha]^{18}_{D}$ = -131.5 (c = 0.518, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.575 min, t_r (minor) = 11.257 min, 90% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.91 – 7.75 (m, 3H), 7.30 (dt, J = 8.4, 3.3 Hz, 2H), 7.25 – 7.11 (m, 4H), 5.01 (dd, J = 9.1, 3.4 Hz, 1H), 3.97 (qd, J = 17.2, 6.2 Hz, 2H), 2.40 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.62, 143.19, 134.42, 133.04, 128.30, 127.20, 126.88, 122.58, 121.29, 119.09, 118.68, 112.16, 110.16, 103.74, 51.93, 41.73, 20.62 ppm; EI-HRMS: Calcd for $C_{19}H_{16}Cl_3NO$ $[M+Na]^+$ 402.0190, Found 402.0191.



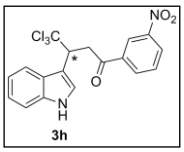
	Retention Time	Area	% Area
1	9.575	11111548	94.91
2	11.257	596128	5.09



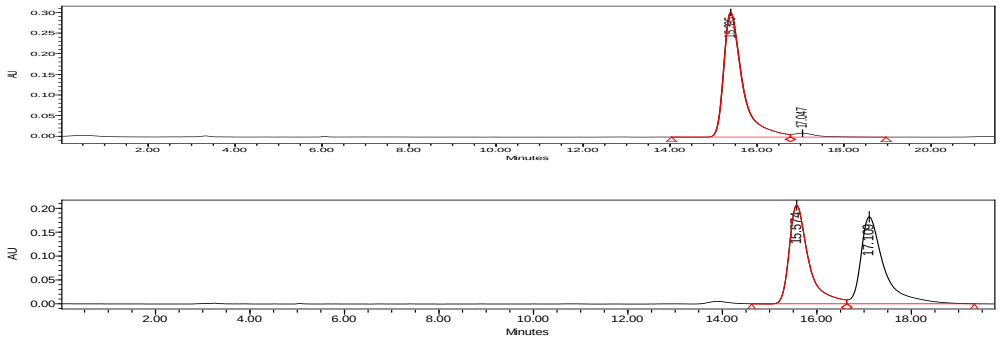
4,4,4-trichloro-1-(3-chlorophenyl)-3-(1H-indol-3-yl)butan-1-one (3g): 45 h, 38.7 mg, white solid, 97% yield; $[\alpha]^{18}_{D}$ = -70.7 (c = 0.532, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 8.199 min, t_r (minor) = 9.034 min, 92% *ee*; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.94 – 7.85 (m, 2H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.34 (dd, *J* = 10.0, 3.3 Hz, 2H), 7.22 (p, *J* = 6.2 Hz, 2H), 5.01 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.98 (ddd, *J* = 26.6, 17.3, 6.2 Hz, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.83, 138.03, 135.44, 135.00, 133.29, 130.03, 128.23, 127.84, 126.19, 123.55, 122.49, 120.27, 119.63, 113.03, 111.26, 104.48, 52.84, 43.11 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_4NO$ $[M+Na]^+$ 421.9643, Found 421.9640.



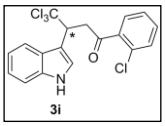
	Retention Time	Area	% Area
1	8.199	5866017	96.10
2	9.034	238255	3.90



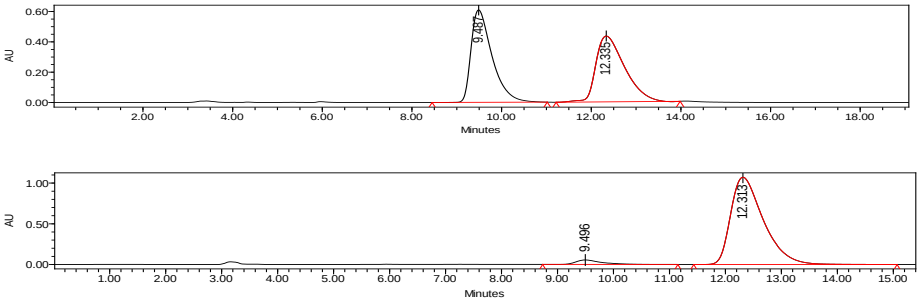
4,4,4-trichloro-3-(1H-indol-3-yl)-1-(3-nitrophenyl)butan-1-one (3h): 46 h, 39.7 mg, yellow solid, 97% yield; $[\alpha]^{16}_{D}$ = -92.6 (c = 0.794, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 15.395 min, t_r (minor) = 17.047 min, 93% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (t, *J* = 1.8 Hz, 1H), 8.48 – 8.17 (m, 3H), 7.93 – 7.81 (m, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.43 – 7.30 (m, 2H), 7.26 – 7.16 (m, 2H), 5.03 (dd, *J* = 8.9, 3.5 Hz, 1H), 4.06 (qd, *J* = 17.4, 6.2 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.05, 147.28, 136.61, 134.36, 132.63, 128.95, 126.69, 126.55, 122.56, 121.91, 121.50, 119.26, 118.41, 111.74, 110.28, 103.19, 51.82, 42.26 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_3N_2O_3$ $[M+Na]^+$ 432.9884, Found 432.9879.



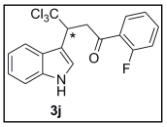
	Retention Time	Area	% Area
1	15.395	9089421	96.62
2	17.047	318174	3.38



4,4,4-trichloro-1-(2-chlorophenyl)-3-(1H-indol-3-yl)butan-1-one (3i): 45 h, 38.5 mg, white solid, 96% yield; $[\alpha]^{18}_{D}$ = -3.9 (c = 0.76, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.496 min, t_r (minor) = 12.313 min, 91% *ee*; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.33 (dt, *J* = 15.8, 7.9 Hz, 3H), 7.27 (t, *J* = 4.9 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (dd, *J* = 14.5, 7.4 Hz, 2H), 7.02 (d, *J* = 7.7 Hz, 1H), 4.83 (dd, *J* = 10.0, 3.5 Hz, 1H), 4.12 (dd, *J* = 16.8, 3.5 Hz, 1H), 3.87 (dd, *J* = 16.8, 10.1 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.86, 138.70, 135.39, 131.90, 130.62, 130.36, 129.01, 127.84, 126.87, 124.23, 122.38, 120.15, 119.39, 112.17, 111.22, 104.15, 53.31, 47.13 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_4NO$ $[M+Na]^+$ 421.9643, Found 421.9639.

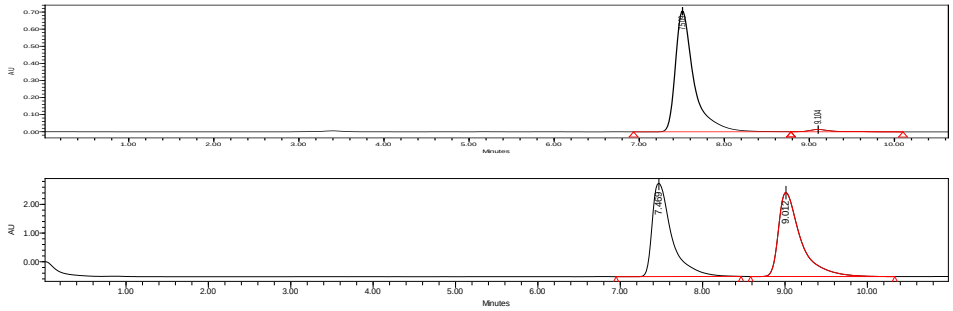


	Retention Time	Area	% Area
1	9.496	1734330	4.35
2	12.313	43256303	95.65

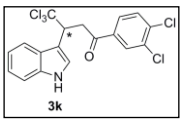


4,4,4-trichloro-1-(2-fluorophenyl)-3-(1H-indol-3-yl)butan-1-one (3j): 45 h, 36.9 mg, white solid, 96% yield; $[\alpha]^{18}_{D}$ = -71.3 (c = 0.72, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 7.509 min, t_r (minor) = 9.104 min, 96% *ee*; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.84 (d, *J* = 7.3 Hz, 1H), 7.64 (dd, *J* = 10.7, 4.4 Hz, 1H), 7.56 – 7.46 (m, 1H), 7.37 – 7.28 (m, 2H), 7.24 – 7.05 (m, 4H), 5.01 (dd, *J* = 9.4, 2.5 Hz, 1H), 4.10 (dt, *J* = 17.9, 2.4 Hz, 1H), 3.97 (ddd, *J* = 17.9, 9.5, 2.0 Hz, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 194.70, 194.68, 162.60, 160.92, 135.40, 134.85, 134.79, 130.72, 127.97, 125.33, 125.25, 124.57, 124.55, 123.82, 122.35, 120.14, 119.59, 116.73, 116.58, 113.08, 111.21, 104.49, 53.49, 52.60, 47.84, 47.78 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_3FNO$

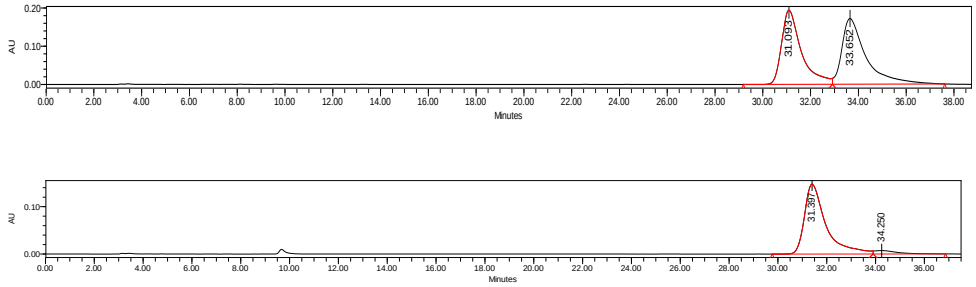
$[M+Na]^+$ 405.9939, Found 405.9946.



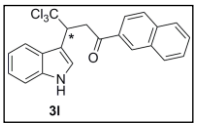
	Retention Time	Area	% Area
1	7.509	10687665	97.78
2	9.104	242593	2.22



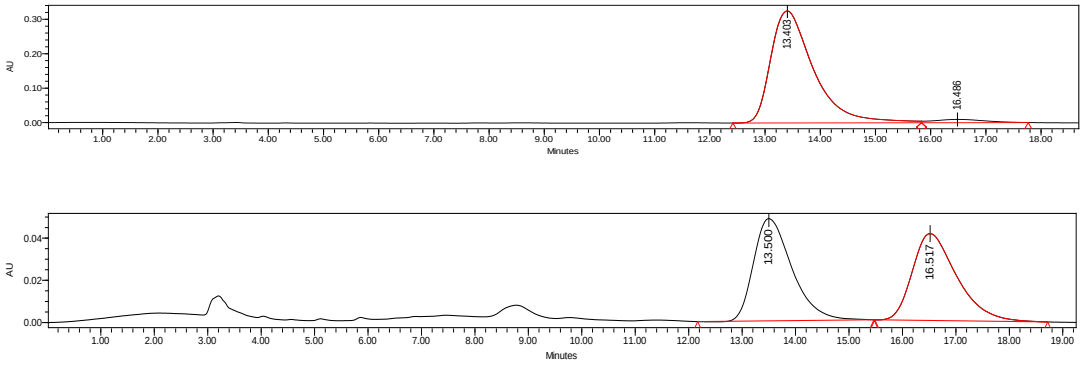
4,4,4-trichloro-1-(3,4-dichlorophenyl)-3-(1H-indol-3-yl)butan-1-one (3k): 45 h, 43.1 mg, white solid, 99% yield; $[\alpha]^{18}_D$ = -87.0 (c = 0.88, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 5/95, 1.0 mL/min, 254 nm), t_r (major) = 31.397 min, t_r (minor) = 34.250 min, 90% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.95 (d, *J* = 2.0 Hz, 1H), 7.90 – 7.78 (m, 1H), 7.71 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.52 – 7.43 (m, 1H), 7.37 – 7.26 (m, 2H), 7.23 – 7.10 (m, 2H), 4.96 (dd, *J* = 9.1, 3.3 Hz, 1H), 3.92 (qd, *J* = 17.3, 6.2 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.91, 137.98, 136.05, 135.45, 133.40, 130.80, 130.11, 127.79, 127.12, 123.52, 122.57, 120.33, 119.59, 112.96, 111.29, 104.38, 52.92, 43.01 ppm; EI-HRMS: Calcd for $C_{18}H_{12}Cl_5NO$ $[M+Na]^+$ 455.9254, Found 455.9246.



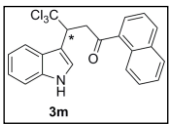
	Retention Time	Area	% Area
1	31.397	8931620	94.84
2	34.250	485739	5.16



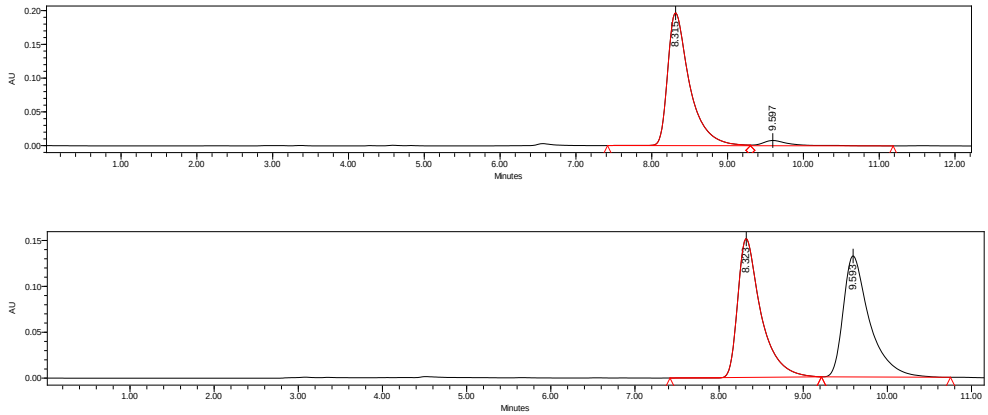
4,4,4-trichloro-3-(1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3l): 74 h, white solid, 39.5 mg, 95% yield; $[\alpha]^{20}_D$ = -167.5 (c = 0.79, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 13.403 min, t_r (minor) = 16.486 min, 94% *ee*; ^{1}H NMR (400 MHz, DMSO) δ 11.18 (s, 1H), 8.77 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 8.00 – 7.83 (m, 3H), 7.79 – 7.70 (m, 1H), 7.69 – 7.55 (m, 3H), 7.31 (d, *J* = 7.1 Hz, 1H), 7.06 (p, *J* = 7.7 Hz, 2H), 4.96 – 4.82 (m, 1H), 4.40 (dd, *J* = 17.3, 9.9 Hz, 1H), 3.95 (dd, *J* = 17.3, 2.4 Hz, 1H) ppm; ^{13}C NMR (101 MHz, DMSO) δ 195.59, 134.90, 134.52, 132.90, 131.55, 129.75, 129.09, 128.21, 127.70, 127.31, 127.03, 126.37, 124.65, 122.85, 120.53, 118.49, 118.45, 110.89, 110.65, 104.68, 52.25, 41.47 ppm; EI-HRMS: Calcd for $C_{22}H_{16}Cl_3NO$ $[M+Na]^+$ 438.0190, Found 438.0196.



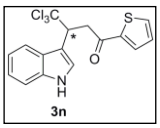
	Retention Time	Area	% Area
1	13.403	17495005	96.90
2	16.486	596734	3.10



4,4,4-trichloro-3-(1H-indol-3-yl)-1-(naphthalen-1-yl)butan-1-one (3m): 74 h, 27.0 mg, white solid, 65% yield; $[\alpha]^{20}_{D}$ = -6.5 (c = 0.54, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AD-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 8.315 min, t_r (minor) = 9.597 min, 91% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.92 (t, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.52 – 7.37 (m, 2H), 7.28 (td, *J* = 8.3, 3.4 Hz, 3H), 7.21 – 7.03 (m, 2H), 4.98 (dd, *J* = 9.6, 3.7 Hz, 1H), 4.13 (dd, *J* = 16.4, 3.7 Hz, 1H), 3.93 (dd, *J* = 16.4, 9.6 Hz, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.48, 134.98, 134.36, 132.71, 131.52, 128.74, 127.11, 126.74, 126.63, 125.76, 125.39, 124.25, 123.15, 122.91, 121.33, 119.11, 118.50, 111.64, 110.04, 103.35, 52.51, 45.27 ppm; EI-HRMS: Calcd for $C_{22}H_{16}Cl_3NO$ $[M+Na]^+$ 438.0190, Found 438.0197.

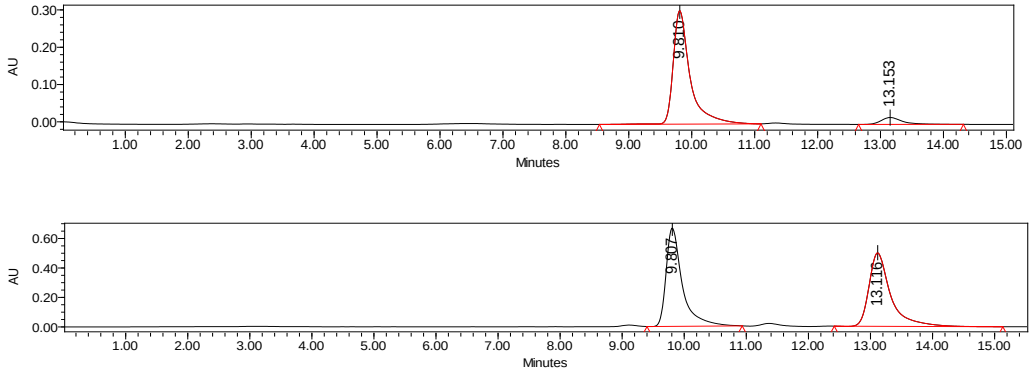


	Retention Time	Area	% Area
1	8.315	3948819	95.47
2	9.597	187407	4.53

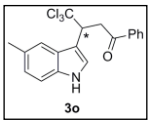


4,4,4-trichloro-3-(1H-indol-3-yl)-1-(thiophen-2-yl)butan-1-one (3n): 46 h, 31.1 mg, white solid, 84% yield; $[\alpha]^{18}_{D}$ = -45.5 (c = 0.20, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.810 min, t_r (minor) = 13.153 min, 85% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.91 – 7.81 (m, 1H), 7.81 – 7.74 (m, 1H), 7.65 – 7.53 (m, 1H), 7.43 – 7.28 (m, 2H), 7.23 – 7.13

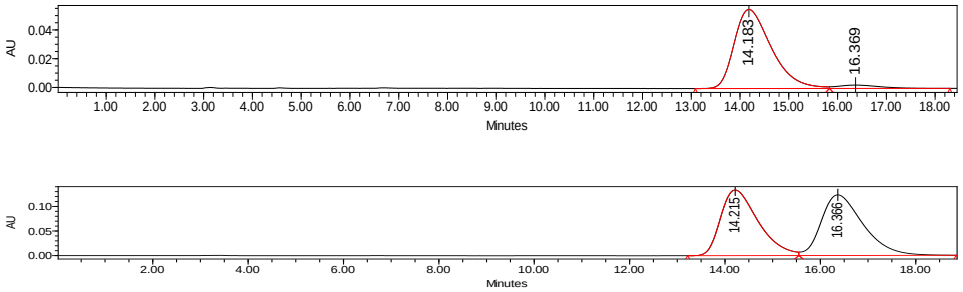
(m, 2H), 7.11 (dd, *J* = 4.7, 4.1 Hz, 1H), 4.97 (dd, *J* = 9.3, 3.4 Hz, 1H), 3.91 (ddd, *J* = 26.0, 16.7, 6.4 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 187.67, 142.64, 134.43, 132.88, 130.94, 127.02, 126.77, 122.60, 121.35, 119.14, 118.66, 111.85, 110.10, 103.42, 52.03, 42.38 ppm; EI-HRMS: Calcd for $C_{16}H_{12}Cl_3NOS$ $[M+Na]^+$ 393.9597, Found 393.9601.



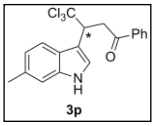
	Retention Time	Area	% Area
1	9.810	5762341	92.58
2	13.153	462068	7.42



4,4,4-trichloro-3-(5-methyl-1H-indol-3-yl)-1-phenylbutan-1-one (3o): 44 h, 35.5 mg, white solid, 94% yield; $[\alpha]^{18}_D$ = -87.5 (c = 0.65, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 10/90, 1.0 mL/min, 254 nm), t_r (major) = 14.183 min, t_r (minor) = 16.369 min, 90% *ee*; ^{1}H NMR (400 MHz, DMSO) δ 11.05 (s, 1H), 7.96 (d, *J* = 7.4 Hz, 2H), 7.66 – 7.42 (m, 5H), 7.21 (d, *J* = 8.2 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 4.82 (d, *J* = 9.7 Hz, 1H), 4.20 (dd, *J* = 17.4, 9.8 Hz, 1H), 3.83 (dd, *J* = 17.3, 2.3 Hz, 1H), 2.40 (s, 3H) ppm; ^{13}C NMR (101 MHz, DMSO) δ 195.64, 135.59, 133.23, 132.89, 128.15, 127.60, 127.54, 126.92, 124.44, 122.19, 117.85, 110.60, 110.18, 104.69, 52.01, 41.66, 20.80 ppm; EI-HRMS: Calcd for $C_{19}H_{16}Cl_3NO$ $[M+Na]^+$ 402.0190, Found 402.0190.

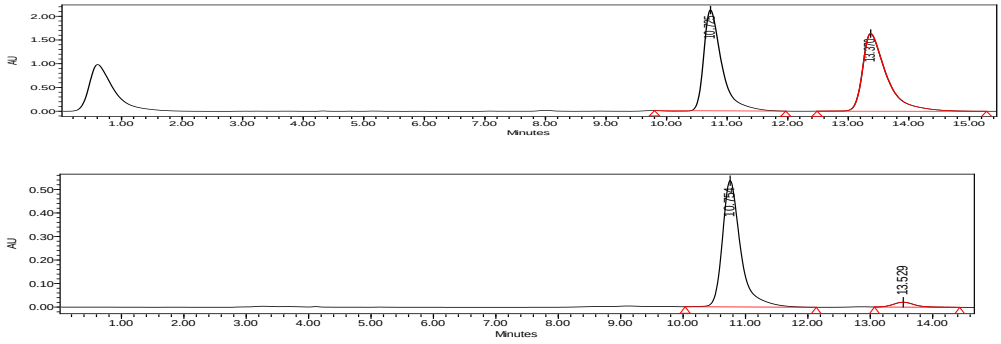


	Retention Time	Area	% Area
1	14.183	2905495	95.28
2	16.369	144046	4.72

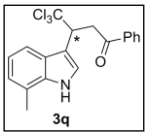


4,4,4-trichloro-3-(6-methyl-1H-indol-3-yl)-1-phenylbutan-1-one (3p): 45 h, 36.1 mg, white solid, 95% yield; $[\alpha]^{18}_D$ = -65.5 (c = 0.682, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 10.754 min, t_r (minor) = 13.529 min, 90% *ee*; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.95 (d, *J* = 7.9 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H),

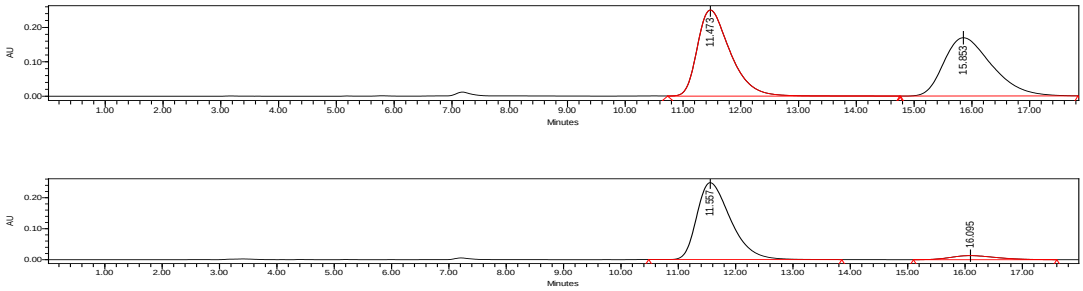
7.23 (d, *J* = 2.3 Hz, 1H), 7.11 (s, 1H), 7.05 (d, *J* = 8.2 Hz, 1H), 5.01 (dd, *J* = 9.2, 3.0 Hz, 1H), 4.01 (ddd, *J* = 26.5, 17.2, 6.2 Hz, 2H), 2.46 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.13, 136.57, 135.91, 133.37, 132.19, 128.69, 128.15, 125.76, 123.06, 121.98, 119.32, 112.94, 111.21, 104.79, 53.07, 42.92, 21.68 ppm; EI-HRMS: Calcd for $C_{19}H_{16}Cl_3NO$ $[M+Na]^+$ 402.0190, Found 402.0201.



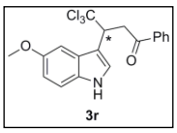
	Retention Time	Area	% Area
1	10.754	10909738	95.32
2	13.529	535693	4.68



4,4,4-trichloro-3-(7-methyl-1H-indol-3-yl)-1-phenylbutan-1-one (3q): 45 h, 35.8 mg, white solid, 94% yield; $[\alpha]^{16}_D$ = -56.6 (c = 0.70, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 11.557 min, t_r (minor) = 16.095 min, 86% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.91 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.60 – 7.48 (m, 1H), 7.42 (dd, *J* = 10.5, 4.7 Hz, 2H), 7.32 (d, *J* = 2.6 Hz, 1H), 7.16 – 7.05 (m, 1H), 6.98 (d, *J* = 7.1 Hz, 1H), 4.99 (dd, *J* = 9.1, 3.4 Hz, 1H), 3.99 (qd, *J* = 17.2, 6.2 Hz, 2H), 2.41 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.00, 136.57, 135.08, 133.33, 128.66, 128.14, 127.44, 123.33, 122.96, 120.40, 120.29, 117.51, 113.69, 104.74, 53.14, 42.93, 16.49 ppm; EI-HRMS: Calcd for $C_{19}H_{16}Cl_3NO$ $[M+Na]^+$ 402.0190, Found 402.0191.

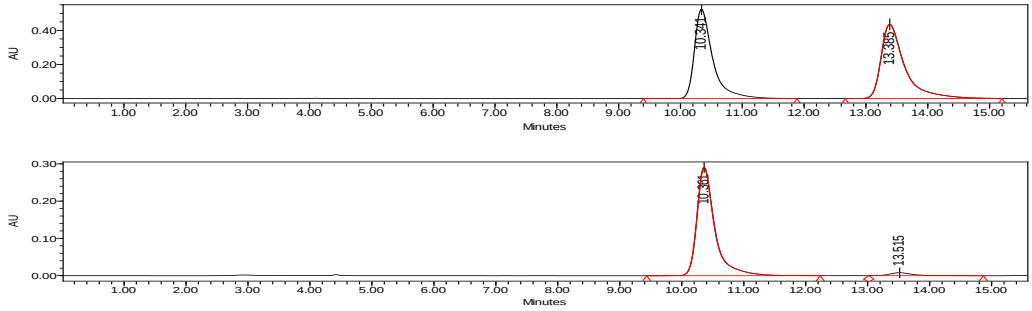


	Retention Time	Area	% Area
1	11.557	10138182	93.23
2	16.095	736315	6.77

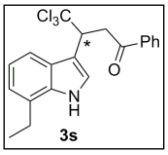


4,4,4-trichloro-3-(5-methoxy-1H-indol-3-yl)-1-phenylbutan-1-one (3r): 45 h, 39.2 mg, white solid, 99% yield; $[\alpha]^{16}_D$ = -94.0 (c = 0.78, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 10.361 min, t_r (minor) = 13.515 min, 93% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.91 (d, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H),

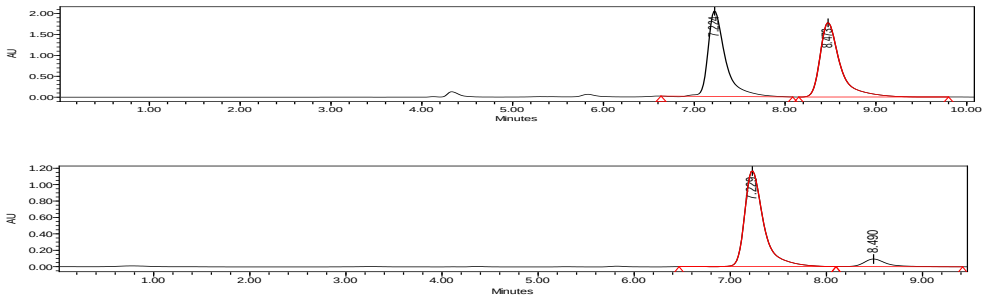
7.26 (dd, *J* = 10.6, 2.4 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.3 Hz, 1H), 4.95 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.96 (ddd, *J* = 24.3, 16.1, 5.2 Hz, 2H), 3.89 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.11, 154.48, 136.60, 133.35, 130.56, 128.68, 128.51, 128.12, 124.08, 112.99, 112.79, 111.88, 104.82, 101.35, 55.92, 52.92, 42.98 ppm; EI-HRMS: Calcd for $C_{19}H_{16}Cl_3NO_2$ $[M+Na]^+$ 418.0139, Found 418.0140.



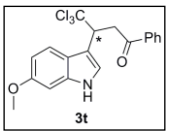
	Retention Time	Area	% Area
1	10.361	5828843	96.53
2	13.515	209525	3.47



4,4,4-trichloro-3-(7-ethyl-1H-indol-3-yl)-1-phenylbutan-1-one (3s): 45 h, 38.5 mg, oil, 98% yield; $[\alpha]^{16}_D$ = -53.0 (c = 0.76, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 7.229 min, t_r (minor) = 8.490 min, 83% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.01 – 7.86 (m, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.59 – 7.49 (m, 1H), 7.42 (dd, *J* = 10.5, 4.8 Hz, 2H), 7.30 (d, *J* = 2.6 Hz, 1H), 7.19 – 7.07 (m, 1H), 7.02 (d, *J* = 7.1 Hz, 1H), 5.00 (dd, *J* = 9.0, 3.4 Hz, 1H), 3.99 (qd, *J* = 17.3, 6.2 Hz, 2H), 2.77 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.05, 136.57, 134.42, 133.34, 128.67, 128.15, 127.61, 126.41, 123.27, 120.81, 120.43, 117.49, 113.63, 104.78, 53.10, 42.98, 23.76, 13.60. ppm; EI-HRMS: Calcd for $C_{20}H_{18}Cl_3NO$ $[M+Na]^+$ 416.0346, Found 416.0358.

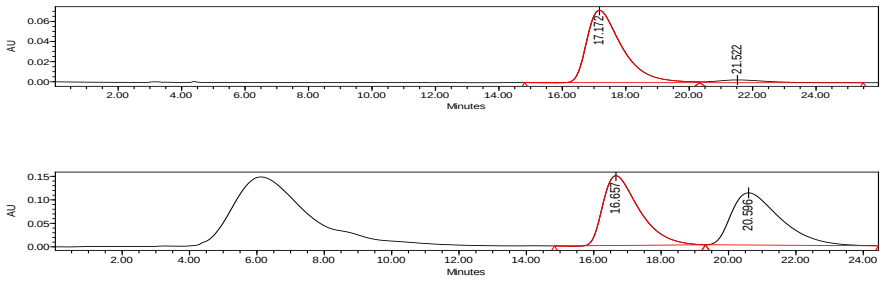


	Retention Time	Area	% Area
1	7.229	16317597	91.56
2	8.490	1601472	8.44

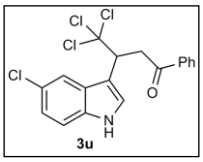


4,4,4-trichloro-3-(6-methoxy-1H-indol-3-yl)-1-phenylbutan-1-one (3t): 48 h, 31.0 mg, white solid, 78% yield; $[\alpha]^{20}_D$ = -72.0 (c = 0.364, CH_2Cl_2); the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 17.172 min, t_r (minor) = 21.522 min, 90% *ee*; ^{1}H NMR (400

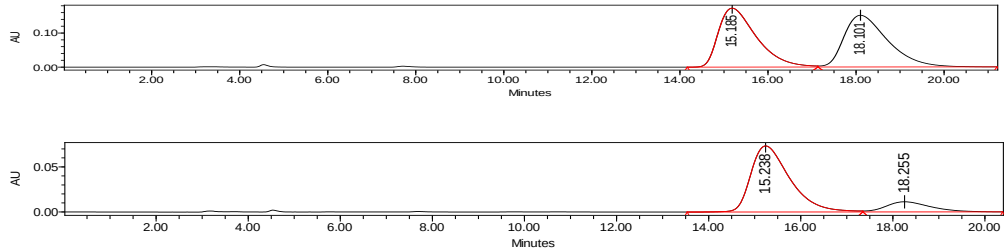
MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.93 (d, *J* = 7.4 Hz, 2H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.17 (d, *J* = 2.3 Hz, 1H), 6.85 (dd, *J* = 8.7, 2.1 Hz, 1H), 6.77 (d, *J* = 1.9 Hz, 1H), 4.94 (dd, *J* = 9.1, 3.3 Hz, 1H), 3.97 (qd, *J* = 17.2, 6.2 Hz, 2H), 3.80 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.09, 155.53, 135.50, 135.14, 132.31, 127.63, 127.08, 121.34, 121.20, 119.24, 112.04, 109.21, 103.63, 93.49, 54.57, 52.02, 41.88 ppm; EI-HRMS: Calcd for $C_{19}H_{16}Cl_3NO_2$ $[M+Na]^+$ 418.0139, Found 418.0157.



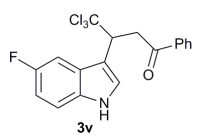
	Retention Time	Area	% Area
1	17.172	5571182	95.00
2	21.522	292985	5.00



4,4,4-trichloro-3-(5-chloro-1H-indol-3-yl)-1-phenylbutan-1-one (3u): 44 h, 68% yield; the ee was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 10/90, 1.0 mL/min, 254 nm), t_r (major) = 15.238 min, t_r (minor) = 18.255 min, 72% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 7.81 (s, 1H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 2.5 Hz, 1H), 7.15 (dt, *J* = 8.6, 5.0 Hz, 2H), 4.91 (dd, *J* = 9.5, 2.9 Hz, 1H), 3.97 (ddd, *J* = 26.8, 17.3, 6.3 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.90, 135.39, 132.79, 132.45, 128.04, 127.70, 127.06, 125.06, 123.78, 121.83, 118.16, 111.97, 111.19, 103.29, 51.84, 41.80 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_4NO$ $[M+Na]^+$ 421.9643, Found 421.9637.

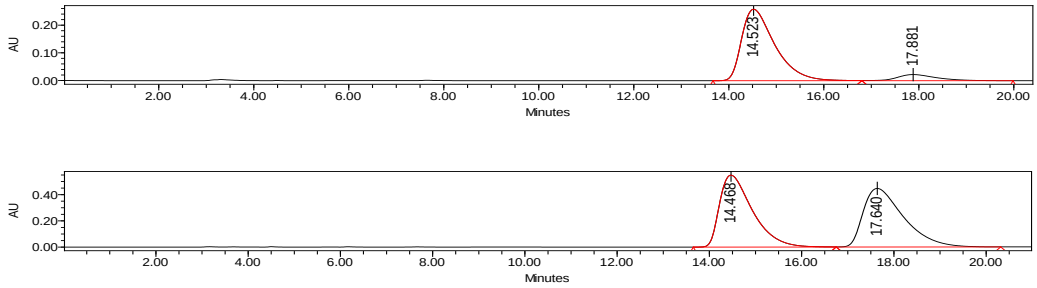


	Retention Time	% Area
1	15.238	86.02
2	18.255	13.98

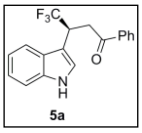


4,4,4-trichloro-3-(5-fluoro-1H-indol-3-yl)-1-phenylbutan-1-one (3v): 45 h, 40% yield; the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 10/90, 1.0 mL/min, 254 nm), t_r (major) = 14.523 min, t_r (minor) = 17.881 min, 82% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.93 (d, *J* = 7.7 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.53 – 7.40 (m, 3H), 7.34 (d, *J* = 2.5 Hz, 1H), 7.20 (dd, *J* = 8.8, 4.4 Hz, 1H), 6.93 (td, *J* = 9.0, 2.3 Hz, 1H), 4.90 (dd, *J* = 9.4, 3.0 Hz, 1H), 3.98 (ddd, *J* = 26.7, 17.3, 6.2 Hz,

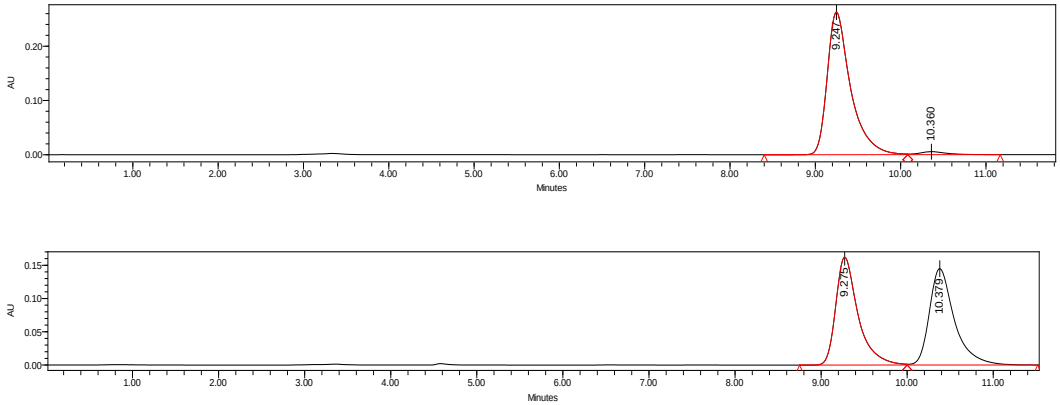
2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.94, 158.33, 156.00, 135.41, 132.42, 130.93, 127.68, 127.44, 127.35, 127.06, 124.25, 112.33, 112.28, 110.90, 110.80, 110.07, 109.81, 103.82, 103.58, 103.43, 52.01, 41.71 ppm; EI-HRMS: Calcd for $C_{18}H_{13}Cl_3FNO$ $[M+Na]^+$ 405.9939, Found 405.9937.



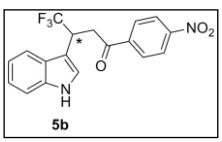
	Retention Time	% Area
1	14.523	90.81
2	17.881	9.19



(*S*)-4,4,4-trifluoro-3-(1H-indol-3-yl)-1-phenylbutan-1-one (5a): 20 h, 29.5 mg, white solid, 93% yield; $[\alpha]^{20}_D$ = -61.0 (c = 0.59, $CHCl_3$); known compound, $[\alpha]^{25}_D$ = +57.5 (c = 0.74, $CHCl_3$, 99% ee for *R*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 9.247 min, t_r (minor) = 10.360 min, 94% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.98 – 7.85 (m, 2H), 7.76 (d, *J* = 7.4 Hz, 1H), 7.59 – 7.50 (m, 1H), 7.47 – 7.38 (m, 2H), 7.31 (dt, *J* = 7.5, 2.9 Hz, 1H), 7.22 – 7.08 (m, 3H), 4.62 (m, 1H), 3.70 (qd, *J* = 17.5, 6.5 Hz, 2H) ppm.

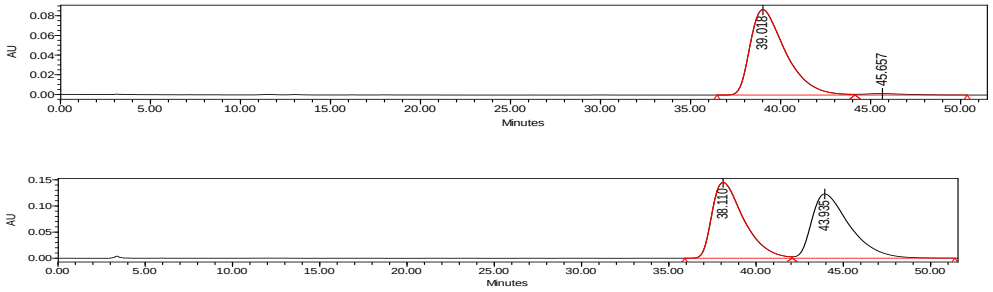


	Retention Time	Area	% Area
1	9.247	4992079	97.21
2	10.360	122352	2.79

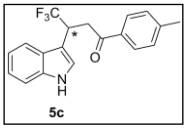


4,4,4-trifluoro-3-(1H-indol-3-yl)-1-(4-nitrophenyl)butan-1-one (5b): 17 h, 36.0 mg, oil, 99% yield; $[\alpha]^{20}_D$ = -74. 2 (c = 0.72, $CHCl_3$); known compound, $[\alpha]^{25}_D$ = +42.9 (c = 0.64, $CHCl_3$, 64% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the *ee* was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 10/90, 1.0 mL/min, 254 nm), t_r (major) = 39.018 min, t_r (minor) = 45.657 min, 96% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 –

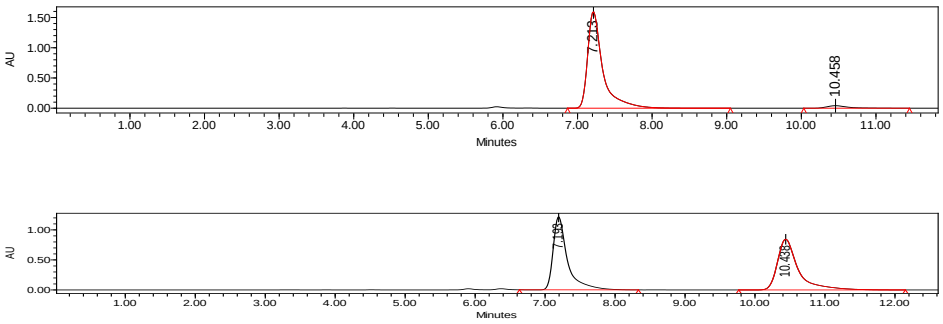
8.08 (m, 3H), 8.06 – 7.97 (m, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.33 (dd, *J* = 7.0, 1.4 Hz, 1H), 7.24 – 7.12 (m, 3H), 4.69 – 4.48 (m, 1H), 3.72 (qd, *J* = 17.6, 6.5 Hz, 2H) ppm.



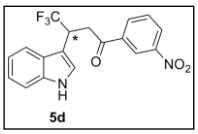
	Retention Time	Area	% Area
1	39.018	11857665	98.07
2	45.657	233140	1.93



4,4,4-trifluoro-3-(1H-indol-3-yl)-1-(p-tolyl)butan-1-one (5c): 27 h, 31.5 mg, white solid, 95% yield; $[\alpha]^{20}_{D}$ = -68. 1 (c = 0.63, $CHCl_3$); known compound, $[\alpha]^{25}_{D}$ = +58.5 (c = 0.77, $CHCl_3$, 97% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 20/80, 1.0 mL/min, 254 nm), t_r (major) = 7.213 min, t_r (minor) = 10.458 min, 93% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.76 (d, *J* = 7.4 Hz, 1H), 7.32 (dd, *J* = 6.7, 1.7 Hz, 1H), 7.26 – 7.07 (m, 5H), 4.83 – 4.35 (m, 1H), 3.67 (qd, *J* = 17.4, 6.5 Hz, 2H), 2.38 (s, 3H) ppm.

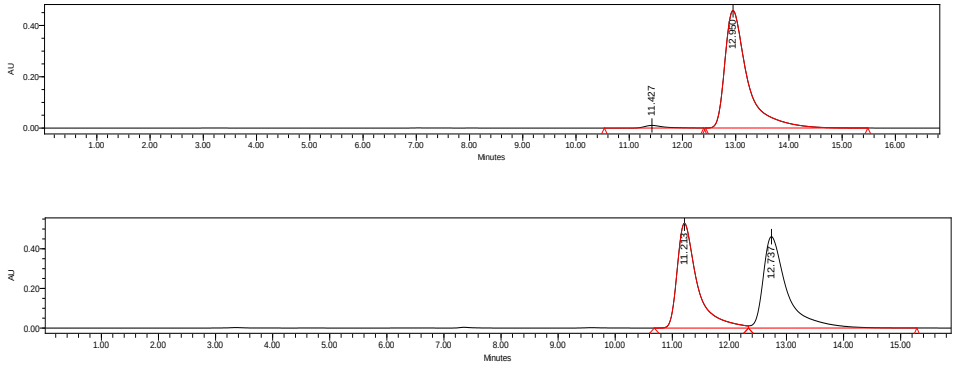


	Retention Time	Area	% Area
1	10.458	778835	3.35
2	7.213	22502233	96.65

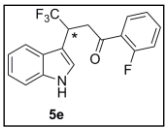


4,4,4-trifluoro-3-(1H-indol-3-yl)-1-(3-nitrophenyl)butan-1-one (5d): 17 h, 35.9 mg, oil, 99% yield; $[\alpha]^{20}_{D}$ = -77.3 (c = 0.718, $CHCl_3$); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 20/80, 1.0 mL/min, 254 nm), t_r (major) = 12.950 min, t_r (minor) = 11.427 min, 93% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (t, *J* = 1.9 Hz, 1H), 8.38 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 8.27 – 8.11 (m, 2H), 7.75 (d, *J* = 7.4 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.34 (dd, *J* = 6.7, 1.8 Hz, 1H), 7.24 – 7.08 (m, 3H), 4.61 (pd, *J* = 9.5, 4.6 Hz, 1H), 3.74 (qd, *J* = 17.6, 6.5 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.85, 148.39, 137.56, 136.05, 133.59, 130.02, 128.58, 127.70, 126.37, 123.51, 122.95, 122.68, 120.34, 119.12, 111.47, 109.40, 38.88, 37.02, 36.73 ppm; EI-HRMS: Calcd for $C_{18}H_{13}F_3N_2O_3$ $[M+Na]^+$ 385.0770,

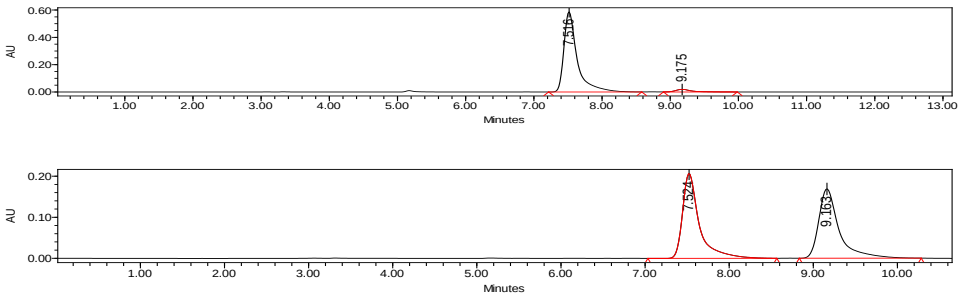
Found 385.0786.



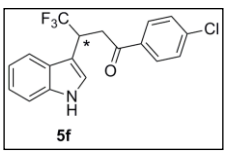
	Retention Time	Area	% Area
1	11.427	265285	1.92
2	12.950	13515970	98.08



4,4,4-trifluoro-1-(2-fluorophenyl)-3-(1H-indol-3-yl)butan-1-one (5e): 26 h, 32.3 mg, white solid, 96% yield; $[\alpha]^{21}_{D}$ = -65.0 (c = 0.646, $CHCl_3$); the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 7.516 min, t_r (minor) = 9.175 min, 92% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.73 (ddd, *J* = 7.6, 4.7, 1.9 Hz, 2H), 7.54 – 7.42 (m, 1H), 7.32 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.23 – 7.02 (m, 5H), 4.78 – 4.44 (m, 1H), 3.74 – 3.69 (m, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.24, 194.20, 163.19, 160.66, 136.05, 135.04, 134.95, 130.77, 130.75, 128.71, 126.67, 125.93, 125.13, 125.00, 124.62, 124.58, 123.49, 122.48, 120.14, 119.26, 116.83, 116.59, 111.33, 109.84, 43.34, 43.26, 36.66, 36.37 ppm; EI-HRMS: Calcd for $C_{18}H_{13}F_4NO$ $[M+Na]^+$ 358.0825, Found 358.0832.

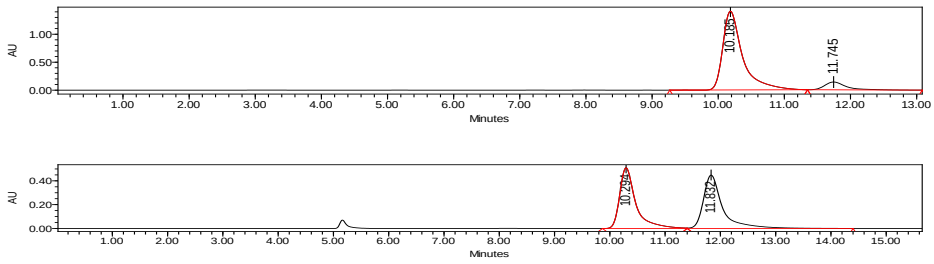


	Retention Time	Area	% Area
1	7.516	7979929	96.14
2	9.175	320095	3.86

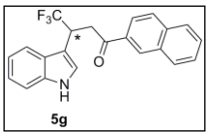


1-(4-chlorophenyl)-4,4,4-trifluoro-3-(1H-indol-3-yl)butan-1-one (5f): 26 h, 33.6 mg, white solid, 96% yield; $[\alpha]^{21}_{D}$ = -61.8 (c = 0.568, $CHCl_3$); known compound, $[\alpha]^{25}_{D}$ = +70.4 (c = 0.57, $CHCl_3$, 93% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the *ee* was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 15/85, 1.0 mL/min, 254 nm), t_r (major) = 10.185 min, t_r (minor) = 11.745 min, 80% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.32

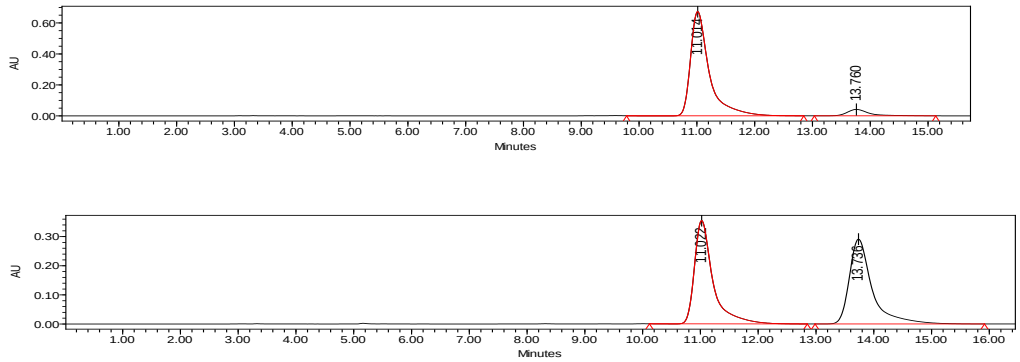
(d, *J* = 7.2 Hz, 1H), 7.23 – 7.10 (m, 3H), 4.86 – 4.36 (m, 1H), 3.65 (qd, *J* = 17.5, 6.5 Hz, 2H) ppm.



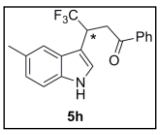
	Retention Time	Area	% Area
1	10.185	29663132	90.24
2	11.745	3464257	9.76



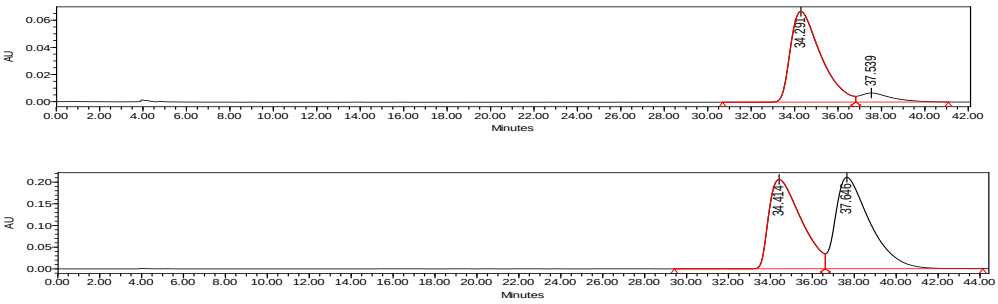
4,4,4-trifluoro-3-(1H-indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (5g): 30 h, 32.2 mg, white solid, 88% yield; $[\alpha]^{21}_{D}$ = -147.8 (c = 0.644, $CHCl_3$); known compound, $[\alpha]^{25}_{D}$ = +139.6 (c = 0.75, $CHCl_3$, 92% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the ee was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 20/80, 1.0 mL/min, 254 nm), t_r (major) = 11.014 min, t_r (minor) = 13.760 min, 86% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.14 (s, 1H), 8.00 – 7.88 (m, 2H), 7.82 (dd, *J* = 15.1, 5.5 Hz, 3H), 7.68 – 7.45 (m, 2H), 7.37 – 7.27 (m, 1H), 7.23 – 7.13 (m, 3H), 4.76 – 4.59 (m, 1H), 3.83 (ddd, *J* = 21.7, 17.3, 6.5 Hz, 2H) ppm.



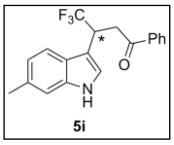
	Retention Time	Area	% Area
1	11.014	15125924	93.30
2	13.760	1086419	6.70



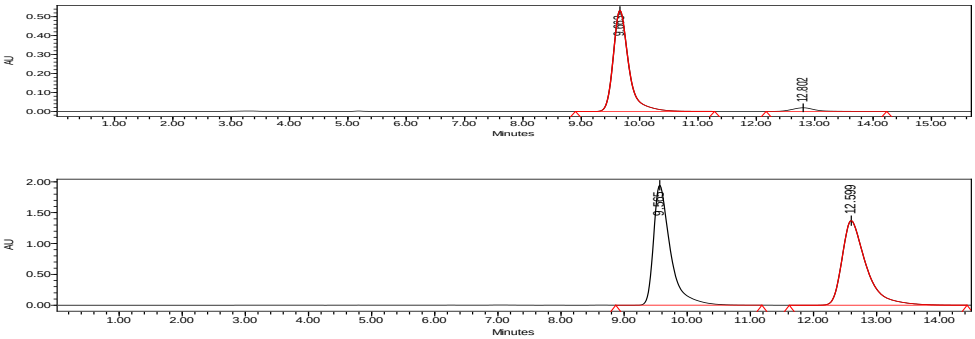
4,4,4-trifluoro-3-(5-methyl-1H-indol-3-yl)-1-phenylbutan-1-one (5h): 24 h, 33.1 mg, white solid, 99% yield; $[\alpha]^{20}_{D}$ = -65.9 (c = 0.662, $CHCl_3$); known compound, $[\alpha]^{25}_{D}$ = +66.3 (c = 0.63, $CHCl_3$, 94% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the ee was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 5/95, 1.0 mL/min, 254 nm), t_r (major) = 34.291 min, t_r (minor) = 37.539 min, 81% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.97 – 7.83 (m, 2H), 7.55 (dd, *J* = 14.9, 7.5 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.30 – 7.22 (m, 1H), 7.15 (d, *J* = 2.5 Hz, 1H), 7.03 (d, *J* = 8.3 Hz, 1H), 4.60 (ddd, *J* = 9.6, 8.0, 5.2 Hz, 1H), 3.98 – 3.50 (m, 2H), 2.47 (s, 3H) ppm.



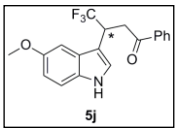
	Retention Time	Area	% Area
1	34.291	6494592	90.63
2	37.539	671527	9.37



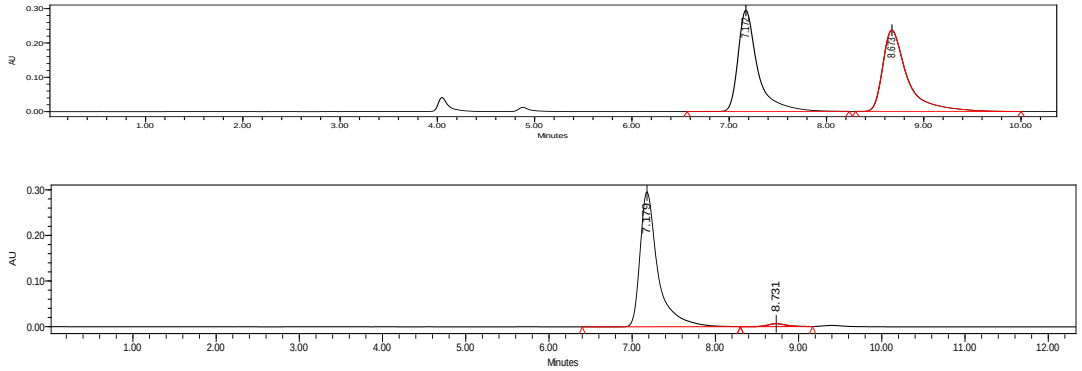
4,4,4-trifluoro-3-(6-methyl-1H-indol-3-yl)-1-phenylbutan-1-one (5i): 24 h, 30.1 mg, white solid, 87% yield; $[\alpha]^{14}_{D}$ = -54.7 (c = 0.602, $CHCl_3$); known compound, $[\alpha]^{25}_{D}$ = +43.3 (c = 0.91, $CHCl_3$, 90% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the ee was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 20/80, 1.0 mL/min, 254 nm), t_r (major) = 9.663 min, t_r (minor) = 12.802 min, 90% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.95 – 7.85 (m, 2H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.16 – 7.03 (m, 2H), 7.00 (d, *J* = 8.2 Hz, 1H), 4.58 (pd, *J* = 9.7, 4.6 Hz, 1H), 3.86 – 3.53 (m, 2H), 2.43 (s, 3H) ppm.



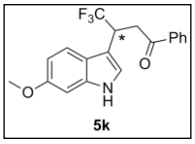
	Retention Time	Area	% Area
1	12.802	506988	4.91
2	9.663	9823876	95.09



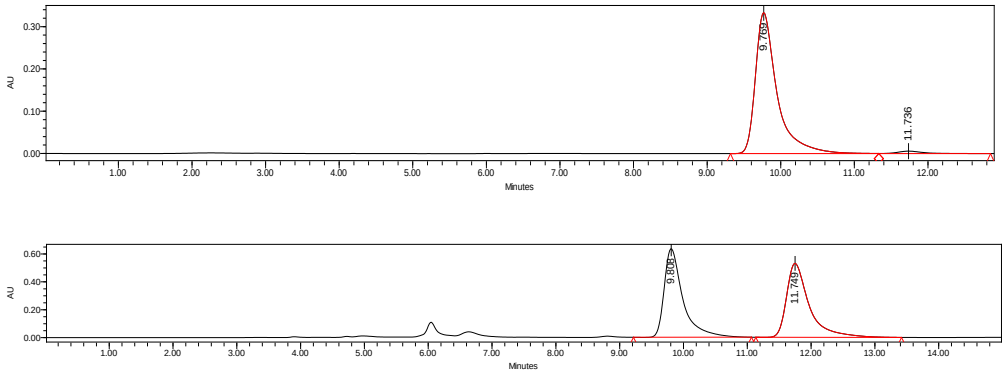
4,4,4-trifluoro-3-(5-methoxy-1H-indol-3-yl)-1-phenylbutan-1-one (5j): 24 h, 34.5 mg, white solid, 99% yield; $[\alpha]^{20}_{D}$ = -92.9 (c = 0.69, $CHCl_3$); known compound, $[\alpha]^{25}_{D}$ = +72.1 (c = 0.75, $CHCl_3$, 85% *ee*); see ref.: G. Blay, I. Fernández, M. C. Muńoz, J. R. Pedro and Vila C., *Chem. Eur. J.*, 2010, **16**, 9117; the ee was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 20/80, 1.0 mL/min, 254 nm), t_r (major) = 7.179 min, t_r (minor) = 8.731 min, 96% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.99 – 7.84 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.23 – 7.07 (m, 3H), 6.86 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.67 – 4.45 (m, 1H), 3.87 (s, 3H), 3.79 – 3.58 (m, 2H) ppm.



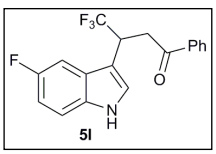
	Retention Time	Area	% Area
2	8.731	94977	2.12
1	7.179	4388691	97.88



4,4,4-trifluoro-3-(6-methoxy-1H-indol-3-yl)-1-phenylbutan-1-one (5k): 24 h, 34.3 mg, white solid, 99% yield; $[\alpha]^{20}_{D}$ = -43.9 (c = 0.686, $CHCl_3$); the ee was determined by HPLC analysis using a chiral IA column (*i*-PrOH/hexane = 20/80, 1.0 mL/min, 254 nm), t_r (major) = 9.769 min, t_r (minor) = 11.736 min, 96% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.95 – 7.87 (m, 2H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.06 (d, *J* = 2.4 Hz, 1H), 6.92 – 6.72 (m, 2H), 4.56 (pd, *J* = 9.6, 4.5 Hz, 1H), 3.81 (s, 3H), 3.77 – 3.58 (m, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.81, 156.74, 136.90, 136.45, 133.45, 128.70, 128.08, 122.19, 120.92, 119.93, 110.27, 94.69, 55.66, 38.35, 37.04, 36.75 ppm; EI-HRMS: Calcd for $C_{19}H_{16}F_3NO_2$ $[M+Na]^+$ 370.1025, Found 370.1038.

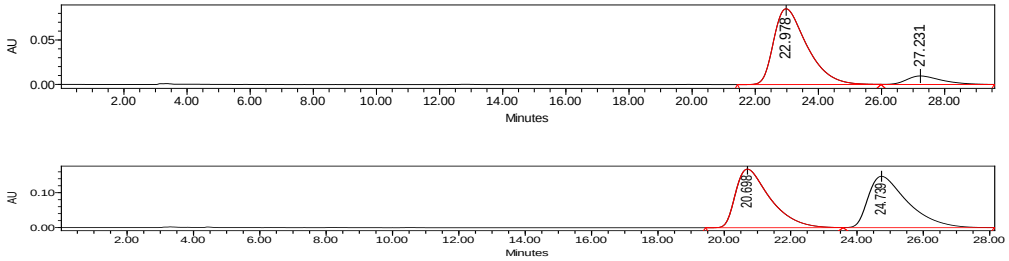


	Retention Time	Area	% Area
1	9.769	6792411	97.99
2	11.736	139581	2.01



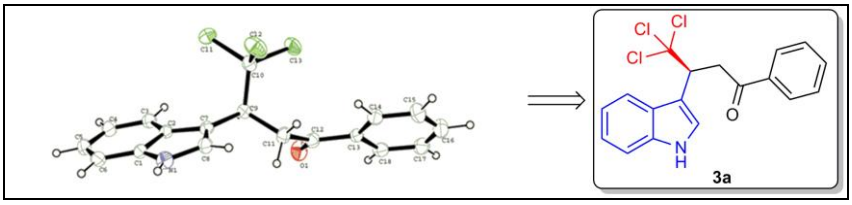
4,4,4-trifluoro-3-(5-fluoro-1H-indol-3-yl)-1-phenylbutan-1-one (5l): 28 h, 60% yield; the ee was determined by HPLC analysis using a chiral AS-H column (*i*-PrOH/hexane = 5/95, 1.0 mL/min, 254 nm), t_r (major) = 22.978 min, t_r (minor) = 27.271 min, 79% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.93 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.49 – 7.37 (m, 3H), 7.24 – 7.15 (m, 2H), 6.94 (td, *J* = 9.0, 2.3 Hz, 1H), 4.54 (pd, *J* = 9.5, 4.4 Hz, 1H), 3.70 (qd, *J* = 17.5, 6.6 Hz, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.76, 158.23, 155.89, 135.26, 132.56, 131.57, 127.72, 127.67, 127.03, 125.95, 125.86,

124.89, 124.18, 111.09, 110.99, 110.11, 109.84, 108.90, 103.40, 103.16, 37.10, 35.97, 35.69, 28.67 ppm; EI-HRMS: Calcd for $C_{18}H_{13}F_4NO$ $[M+Na]^+$ 358.0825, Found 358.0823.



	Retention Time	% Area
1	22.978	89.45
2	27.271	10.55

5. Determination of absolute configuration and the X-ray structure of 3a

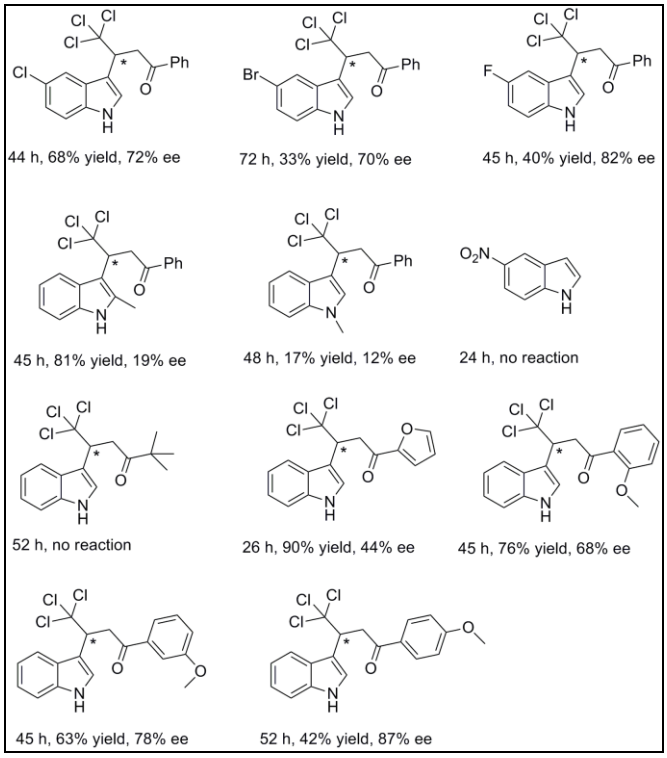


Single crystals of $C_{18}H_{14}Cl_3NO$ 3a was recrystallized from EtOH, the absolute configuration of C9 is *S*. The thermal ellipsoids' level is 30 % for the above crystal structure. CCDC 807085 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.

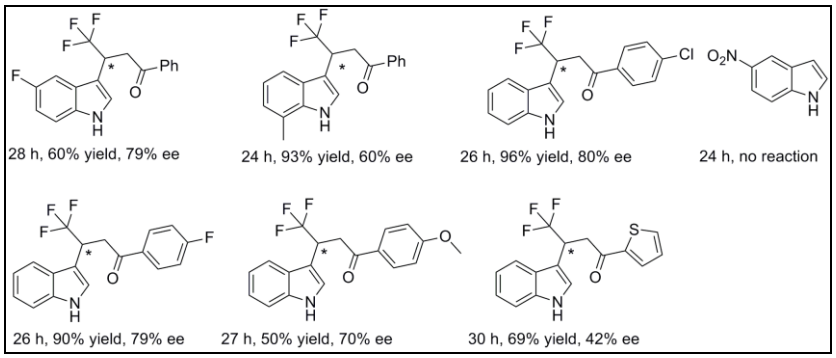
Crystal Data. $C_{18}H_{14}Cl_3NO$, M =366.65, Orthorhombic, a = 19.6727(8) Å, b = 14.1660(7) Å, c = 5.9443(2) Å, U = 1656.56(13) $Å^3$, T = 293(2), space group $P2_12_12$ (no. 18), Z = 4, μ(Mo Kα) = 0.556, 5029 reflections measured, 3111 unique (Rint = 0.0220) which were used in all calculations. The final *w*R(F_2) was 0.0752 (all data).

6. Results for sub-optimal substrates

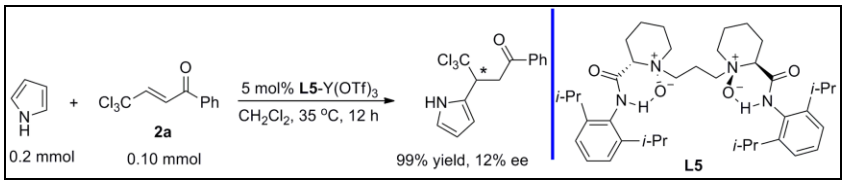
*For β-trichloromethyl aryl enones **2:*** a solution of *N,N'*-dioxide **L5** (3.3 mg, 0.005 mmol), yttrium triflate (2.7 mg, 0.005 mmol), and β-trichloromethyl aryl enones **2** (0.10 mmol) in CH_2Cl_2 (0.10 mL) was stirred in a dry reaction tube under N_2 atmosphere at 35 °C for 0.5 h, then indole **1** (50 μL, 2.4 M in CH_2Cl_2) was added. The sealed tube was stirred at 35 °C for the corresponding time. And then the reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford the desired product **3**.

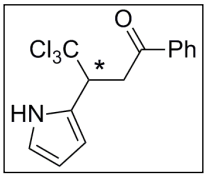


*For β-trifluoromethyl aryl enones **4**:* a solution of *N,N'*-dioxide **L5** (3.3 mg, 0.005 mmol), yttrium triflate (2.7 mg, 0.005 mmol), and β-trifluoromethyl aryl enones **4** (0.10 mmol) in CH_2Cl_2 (0.20 mL) was stirred in a dry reaction tube under N_2 atmosphere at 35 °C for 0.5 h, then indole **1** (50 μL, 2.4 M in CH_2Cl_2) was added. The sealed tube was stirred at 35 °C for the corresponding time. And then the reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to afford the desired product **5**.



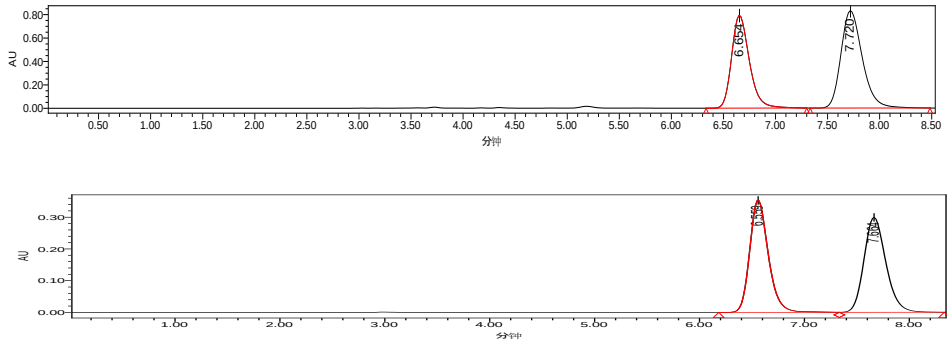
Under the optimal conditions, pyrrole was also investigated and the results were collected as follows:





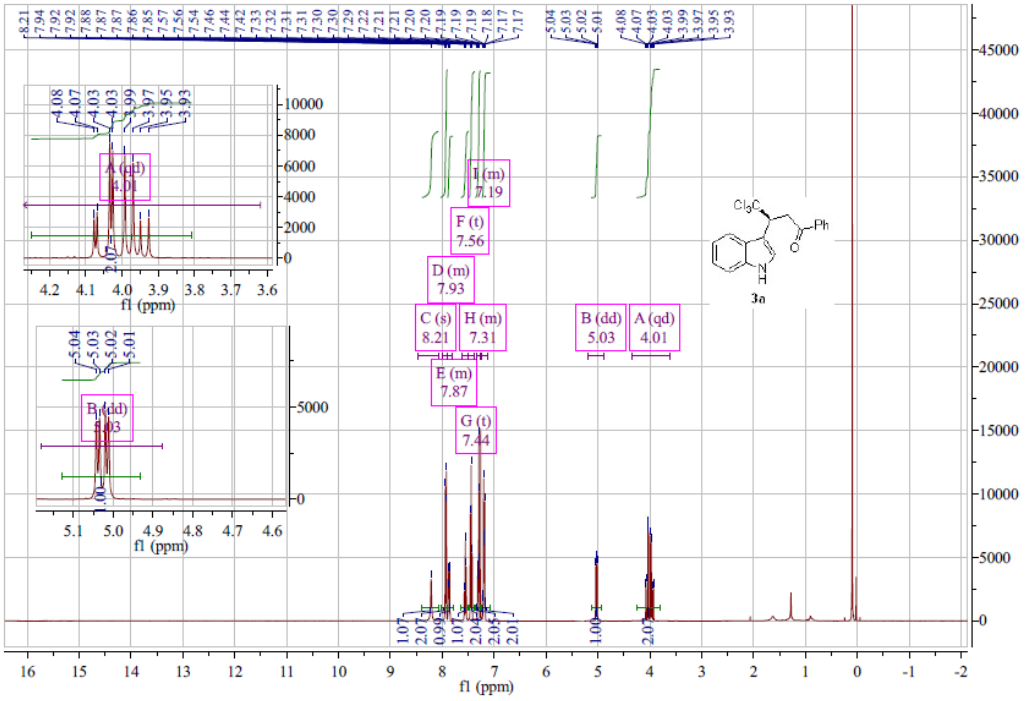
12 h, 99% yield, the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, 1.0 mL/min, 254 nm), t_r (major) = 7.720 min, t_r (minor) = 6.654 min, 12% *ee*; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.98 (d, *J* = 7.7 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 6.77 (s, 1H), 6.30 (s, 1H), 6.16 (d, *J* = 2.4 Hz, 1H), 4.66 (d, *J* = 8.2 Hz, 1H), 3.99 – 3.84 (m, 2H)

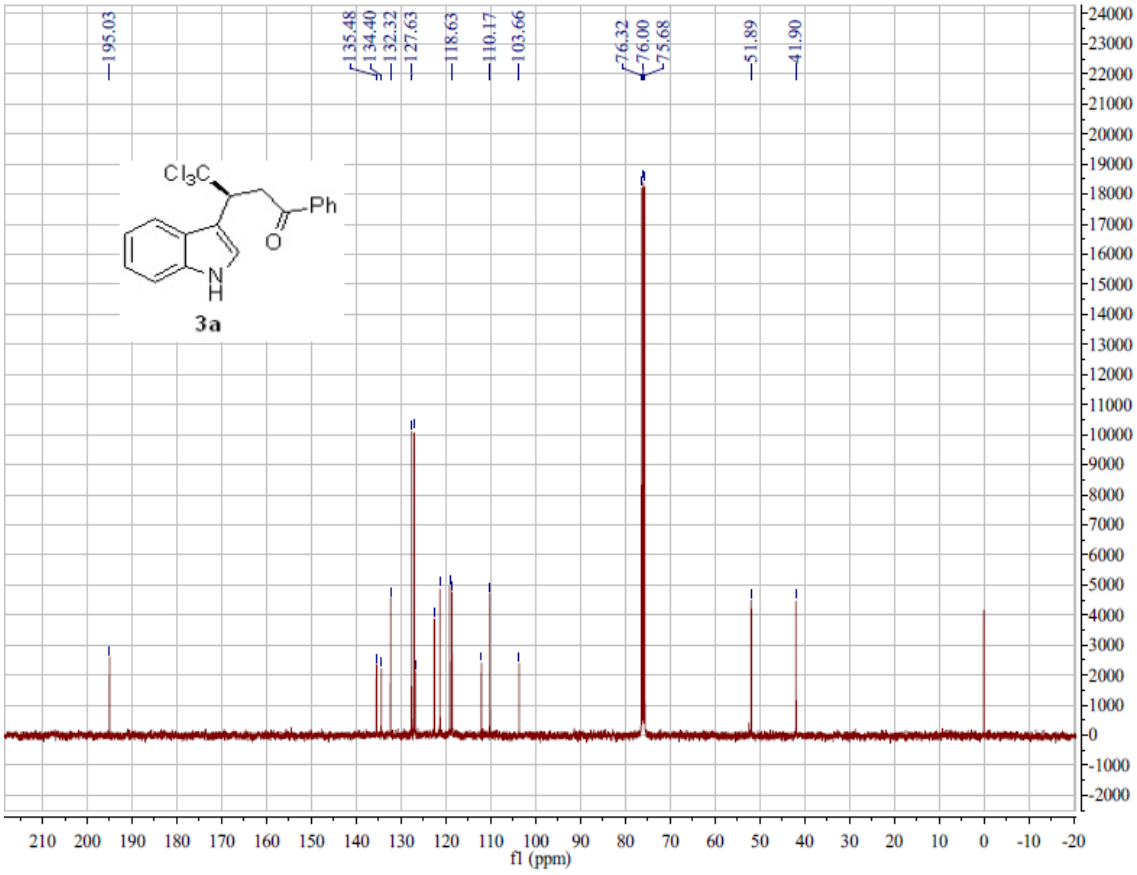
ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 196.10, 136.31, 133.64, 128.76, 128.16, 127.41, 118.00, 108.54, 108.11, 103.15, 55.04, 42.29 ppm; EI-HRMS: Calcd for $C_{14}H_{12}Cl_3NO$ $[M+H]^+$ 316.0057, Found 316.0053.

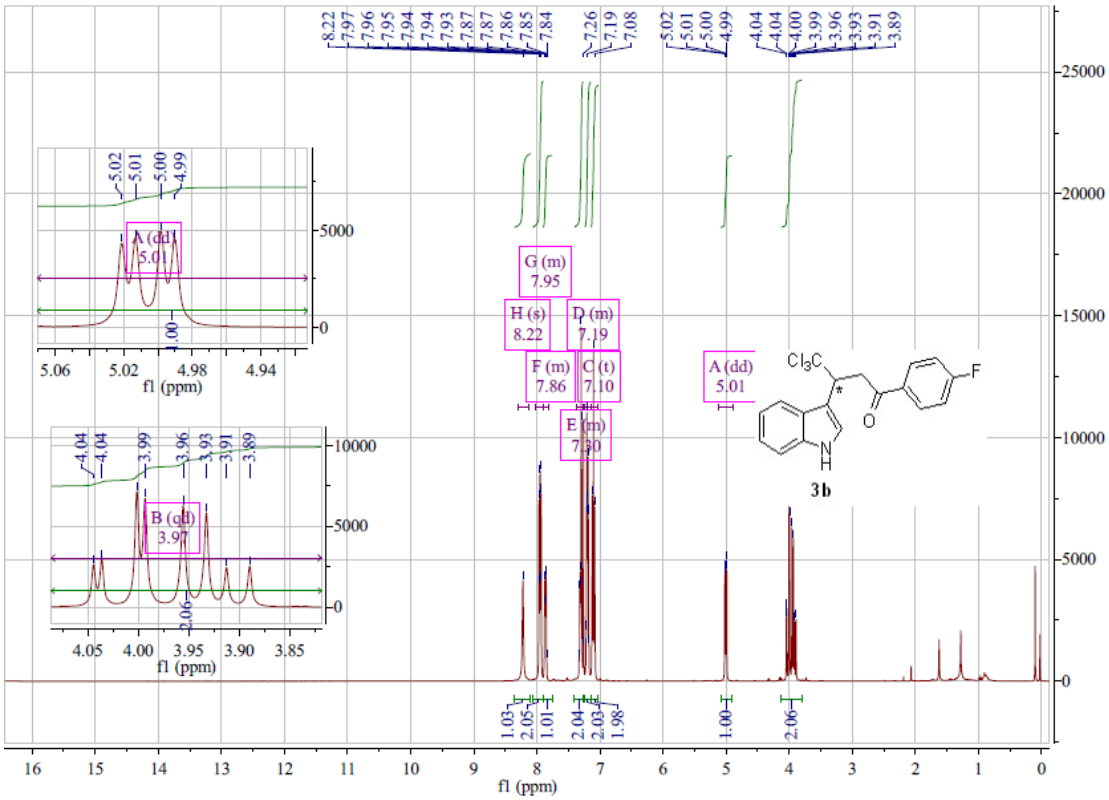


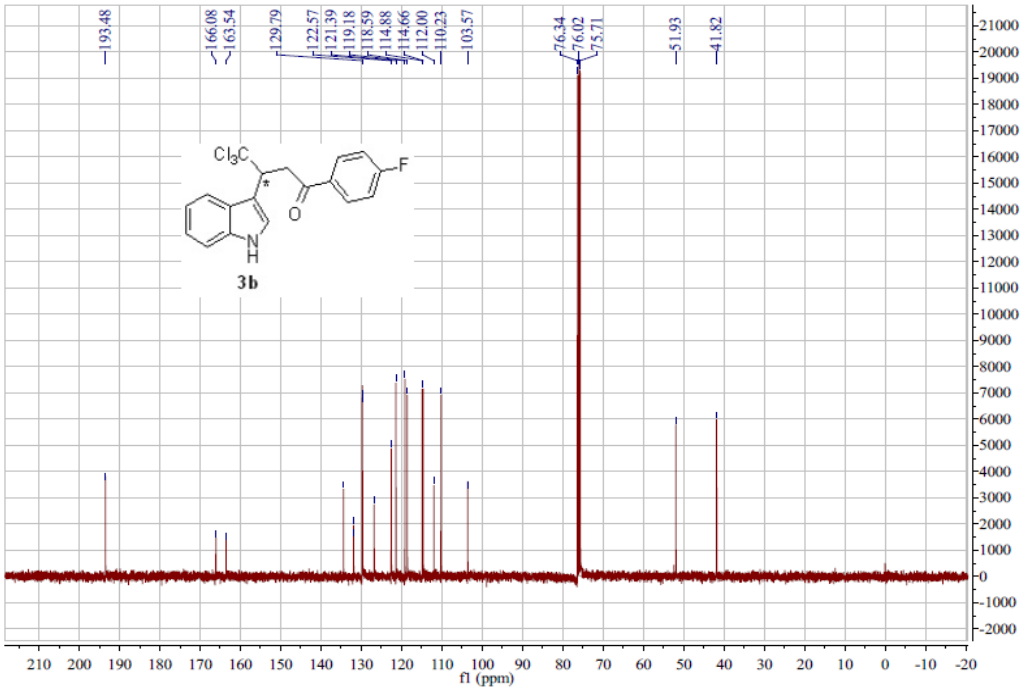
	Retention Time	% Area
1	6.654	44.21
2	7.720	55.79

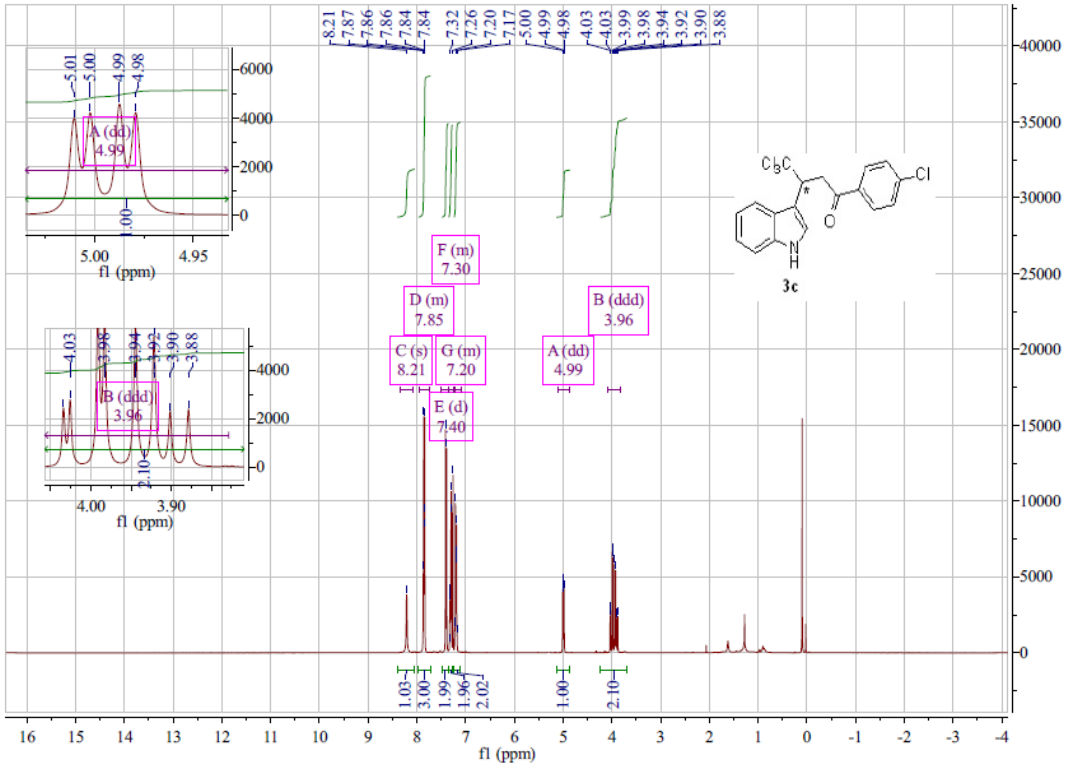
7 Copy of ^{1}H NMR and ^{13}C NMR spectra for products

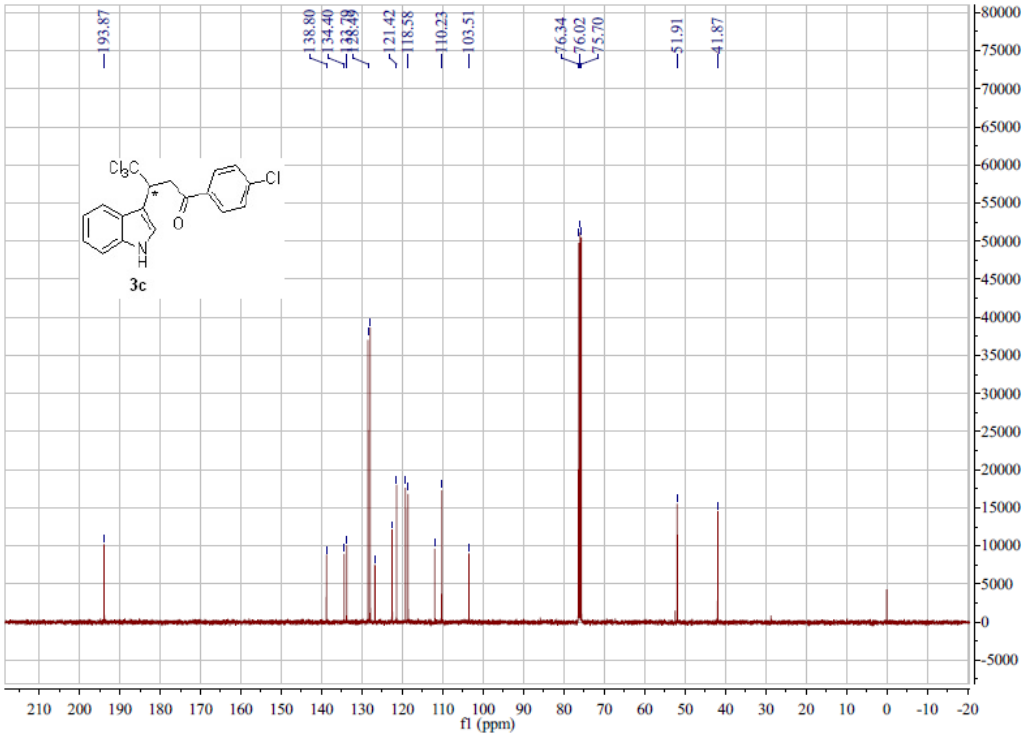


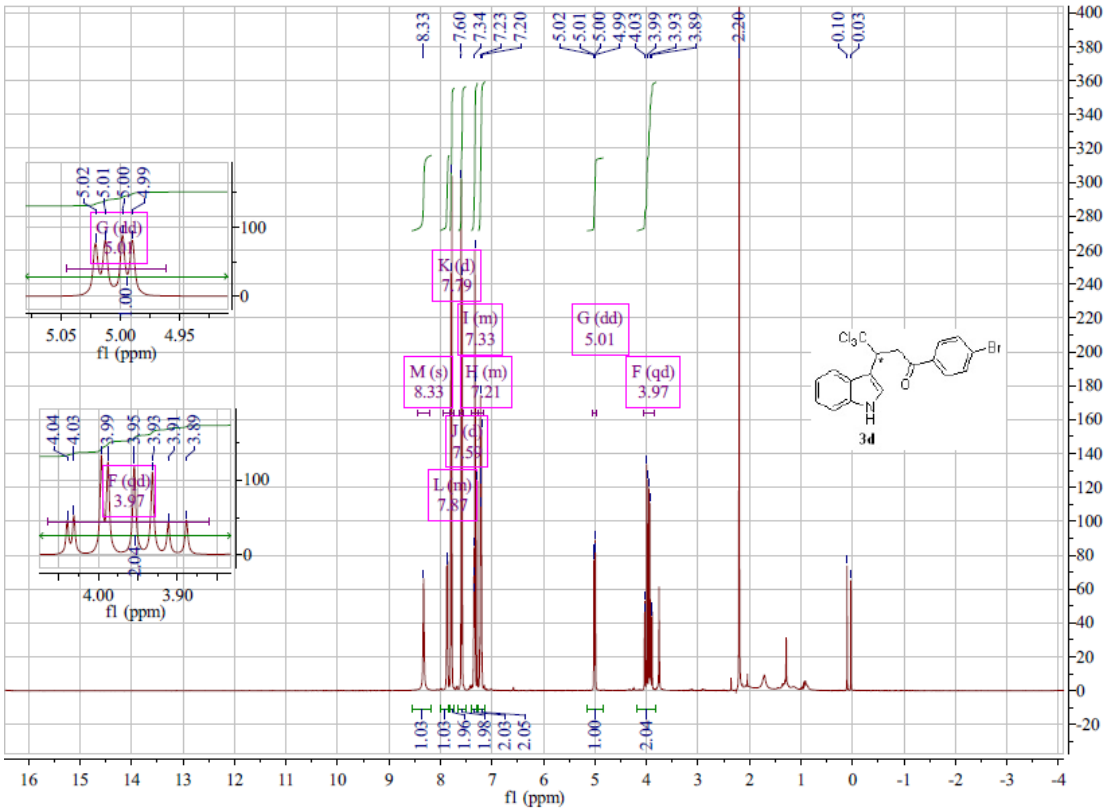

195.03
135.48
134.40
132.32
127.63
118.63
110.17
103.66
76.32
76.00
75.68
51.89
41.90
Cl3C
Ph
O
N
H
3a
fl (ppm)

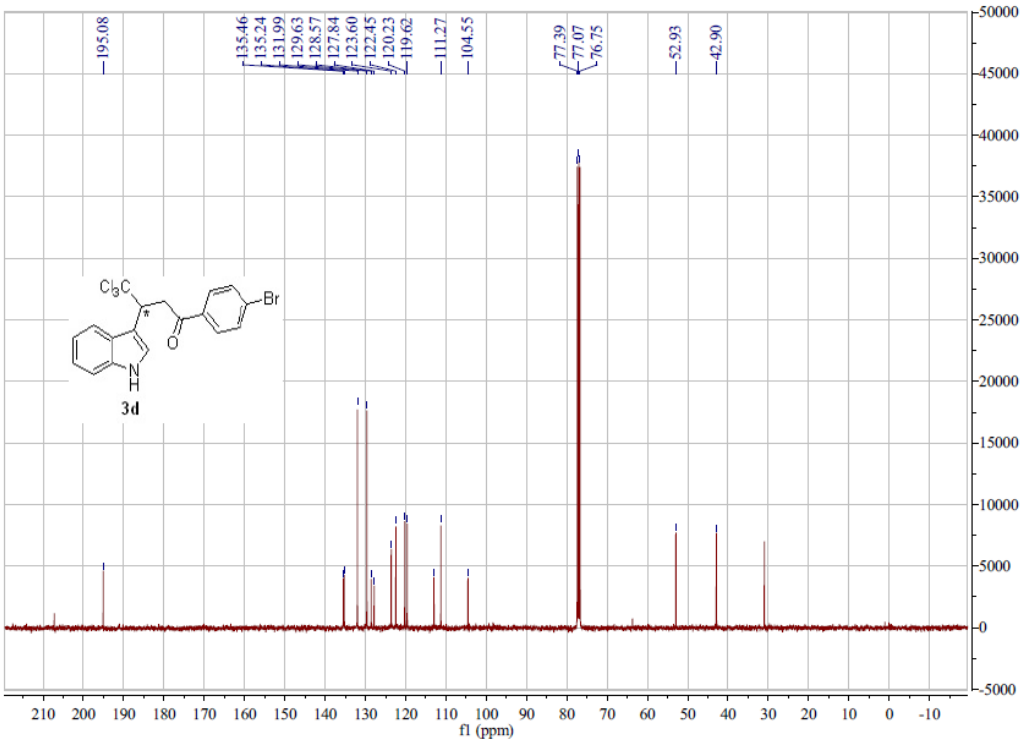

8.22
7.97
7.96
7.95
7.94
7.94
7.93
7.87
7.87
7.86
7.85
7.84
7.26
7.19
7.08
5.02
5.01
5.00
4.99
4.04
4.04
4.00
3.99
3.96
3.93
3.91
3.89
A (dd) 5.01
G (m) 7.95
H (s) 8.22
D (m) 7.19
F (m) 7.86
C (t) 7.10
E (m) 7.30
B (qd) 3.97
A (dd) 5.01
Cl3C
F
O
N
H
3b
fl (ppm)

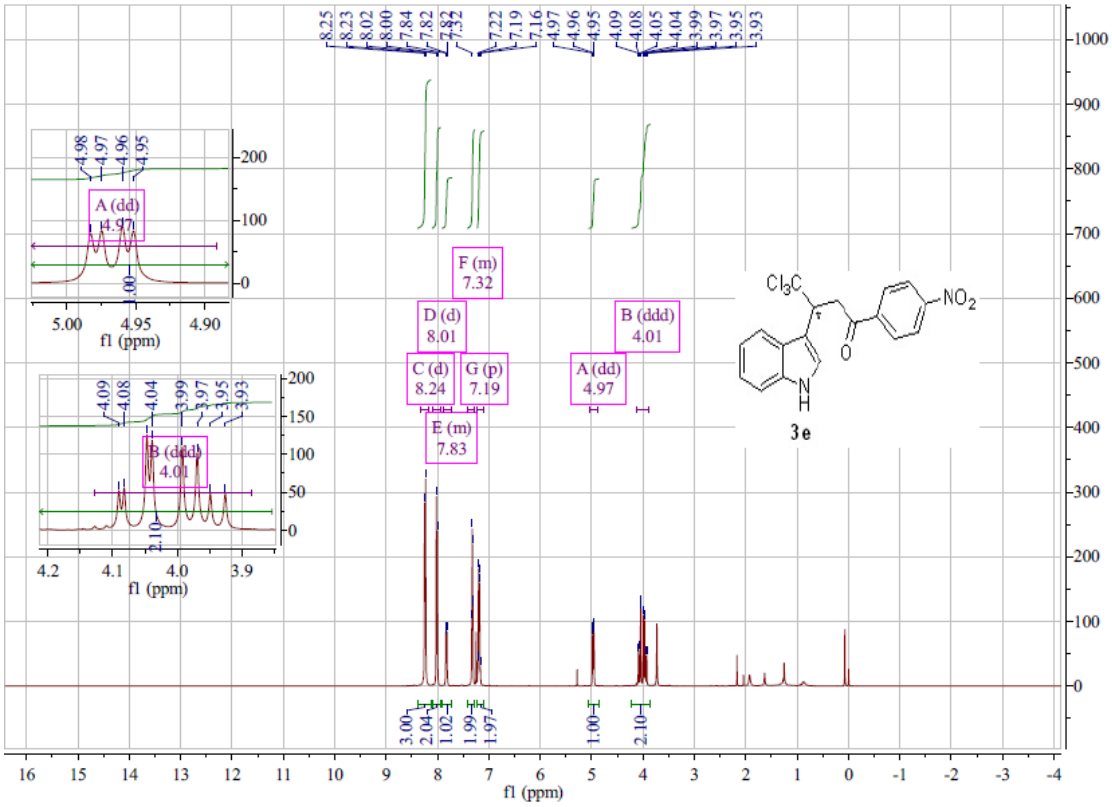

193.48
166.08
163.54
129.79
122.57
121.39
119.18
118.59
114.88
114.66
112.00
110.23
103.57
76.34
76.02
75.71
51.93
41.82
3b
f1 (ppm)

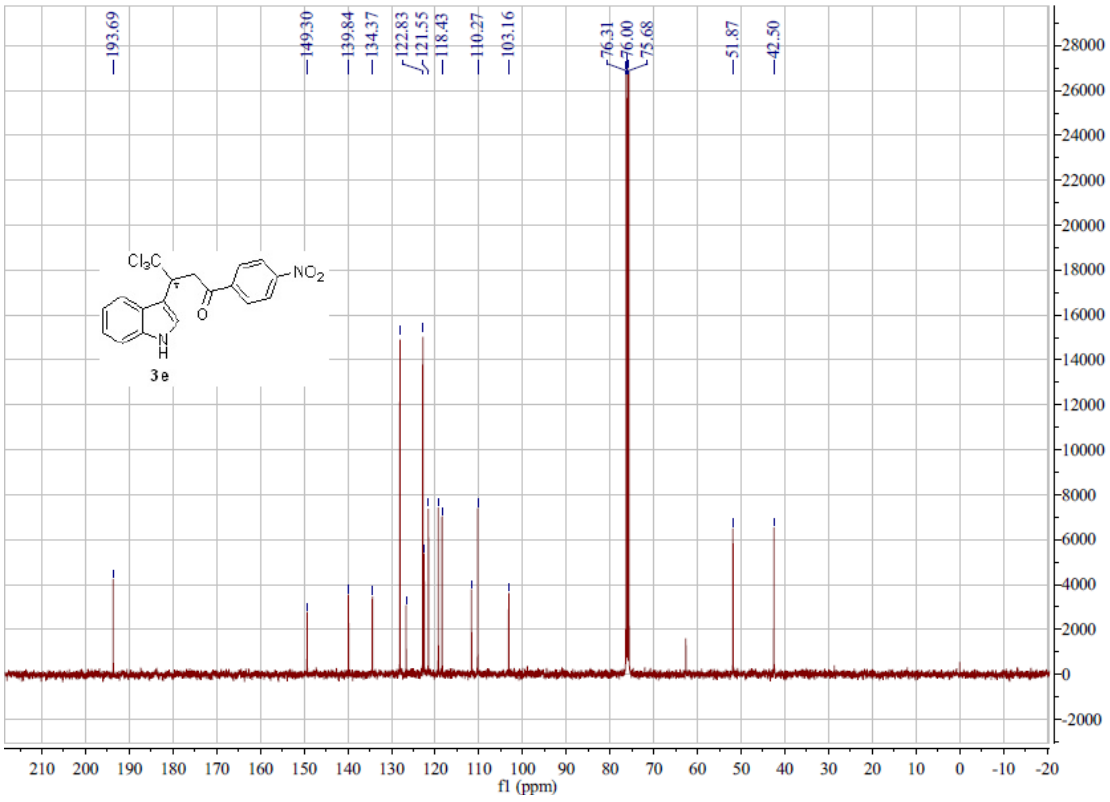

8.21
7.87
7.86
7.86
7.84
7.84
7.32
7.26
7.20
7.17
5.00
4.99
4.98
4.03
4.03
3.99
3.98
3.94
3.92
3.90
3.88
A (dd) 4.99
B (ddd) 3.96
C (s) 8.21
D (m) 7.85
E (d) 7.40
F (m) 7.30
G (m) 7.20
3c
f1 (ppm)

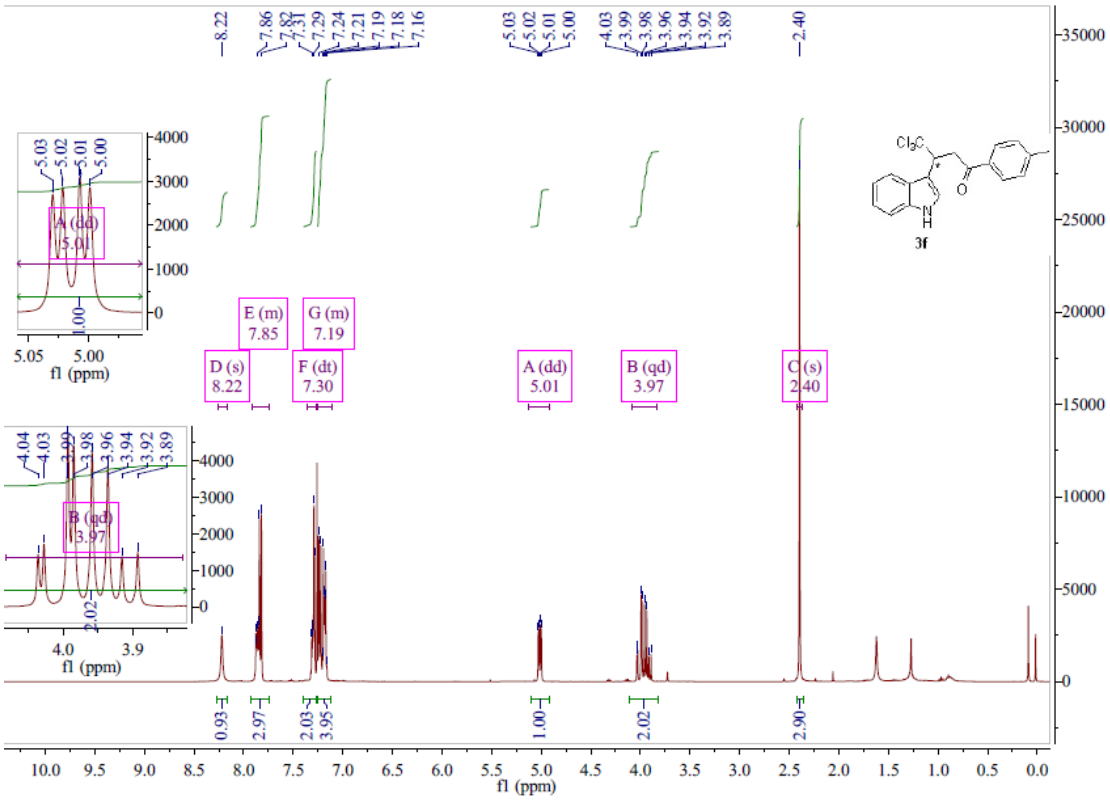

193.87
138.80
134.40
121.42
118.58
110.23
103.51
76.34
76.02
75.70
51.91
41.87
3c
f1 (ppm)

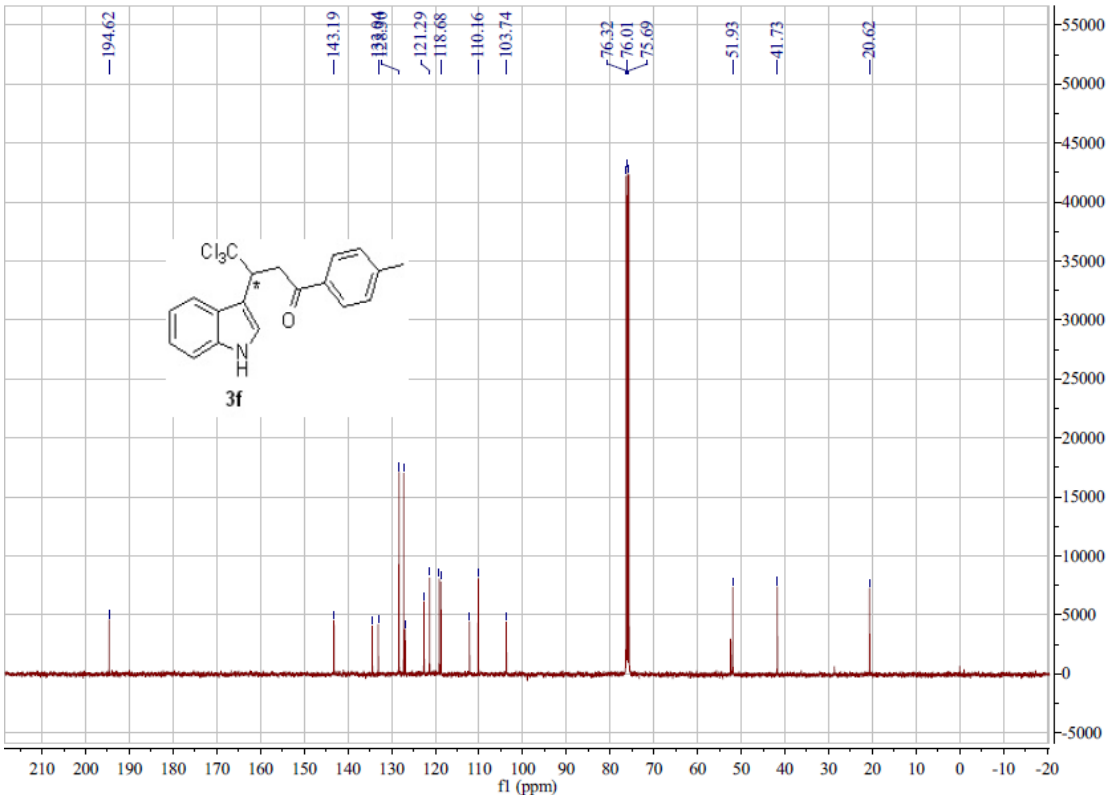

8.33
7.60
7.34
7.23
7.20
5.02
5.01
5.00
4.99
4.03
3.99
3.93
3.89
2.20
0.10
0.03
K (d) 7.79
I (m) 7.33
G (dd) 5.01
M (s) 8.33
H (m) 7.21
F (qd) 3.97
J (d) 7.59
L (m) 7.87
3d
f1 (ppm)

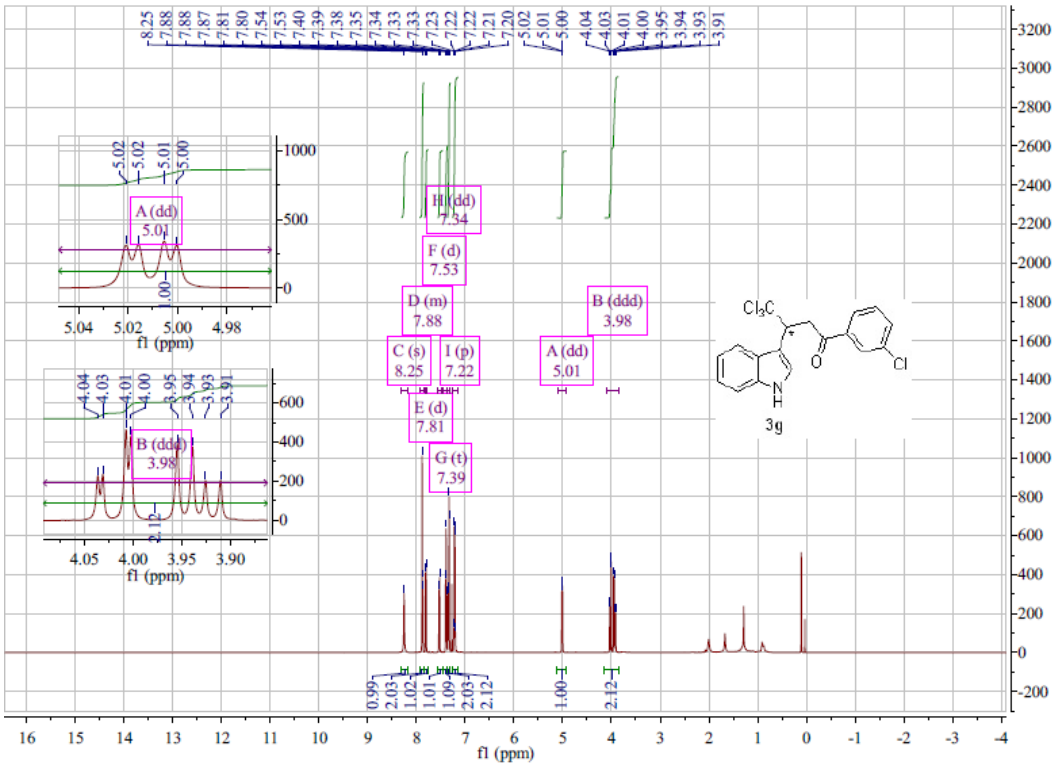

195.08
135.46
135.24
131.99
129.63
128.57
127.84
123.60
122.45
120.23
119.62
111.27
104.55
77.39
77.07
76.75
52.93
42.90
Cl3C
Br
O
N
H
3d
fl (ppm)

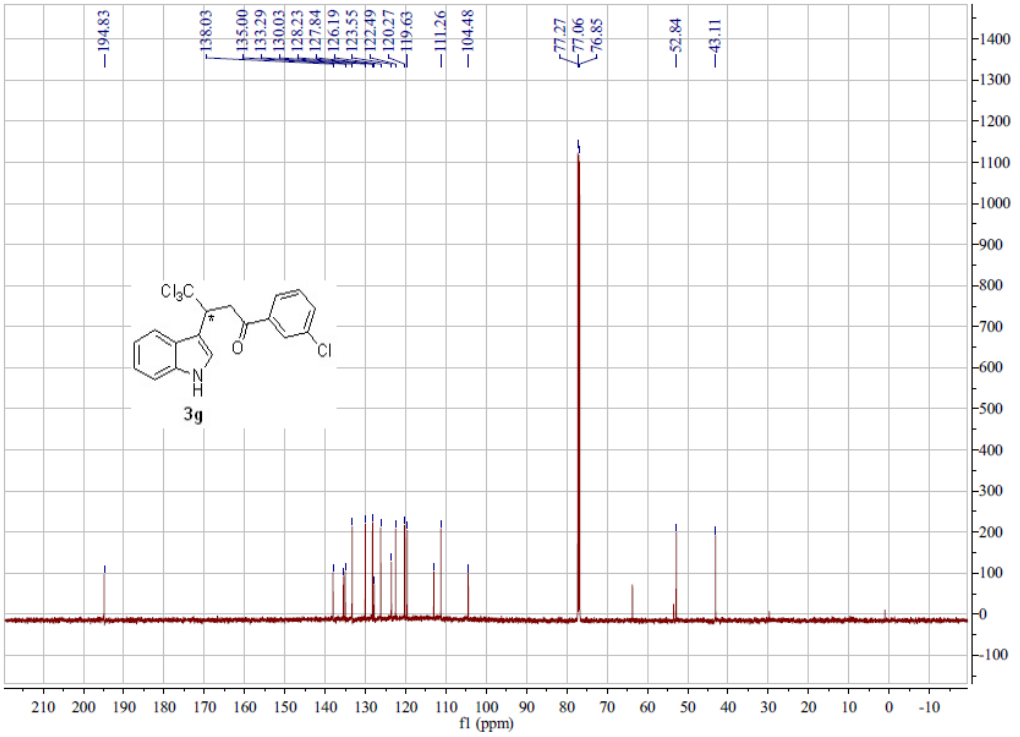

8.25
8.23
8.02
8.00
7.84
7.82
7.32
7.22
7.19
7.16
4.97
4.96
4.95
4.09
4.08
4.05
4.04
3.99
3.97
3.95
3.93
A (dd)
4.97
B (ddd)
4.01
C (d)
8.24
D (d)
8,01
E (m)
7.83
F (m)
7.32
G (p)
7.19
Cl3C
NO2
O
N
H
3e
fl (ppm)

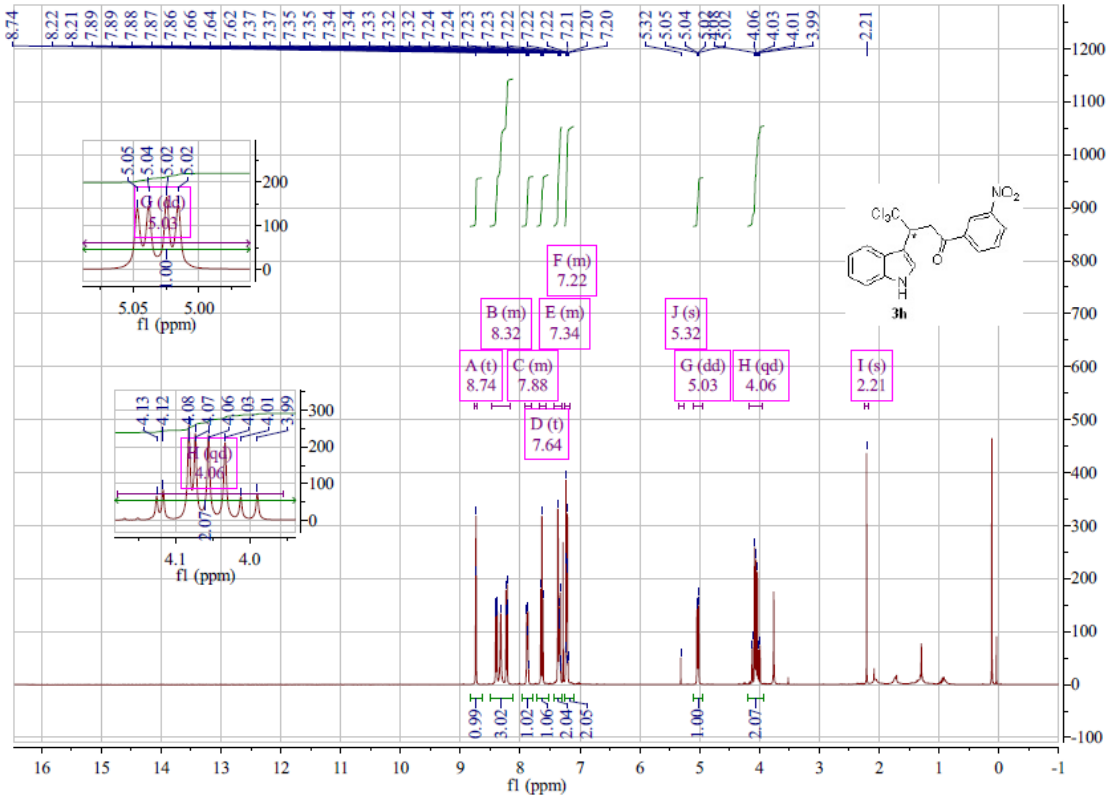

193.69
149.30
139.84
134.37
122.83
121.55
118.43
110.27
103.16
76.31
76.00
75.68
51.87
42.50
3e
f1 (ppm)

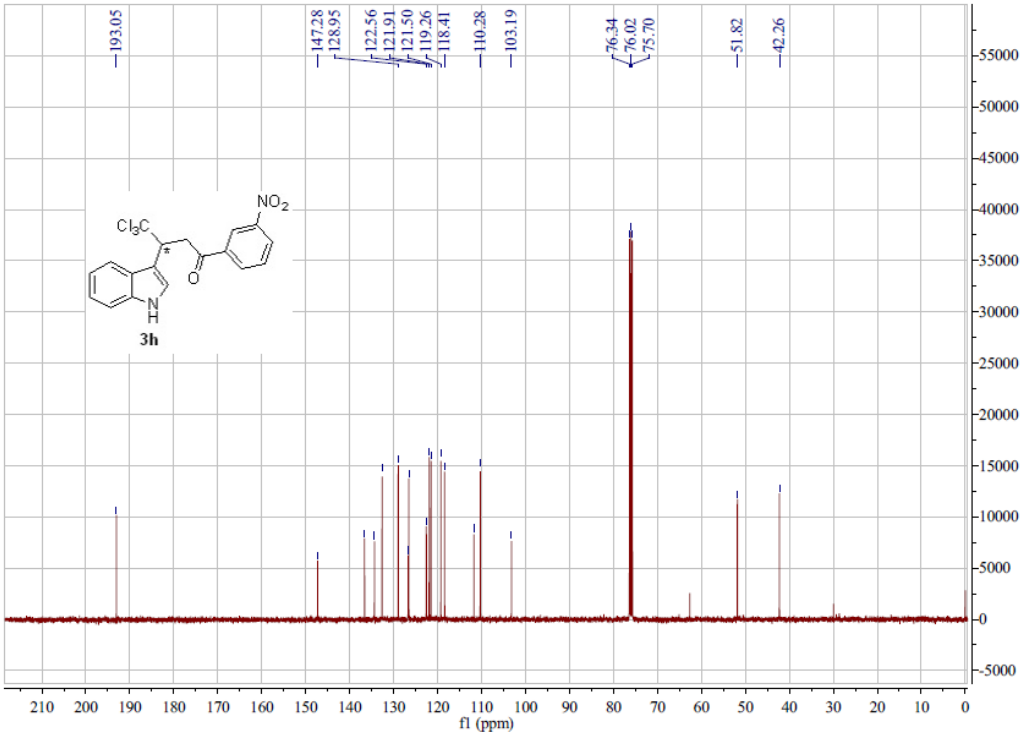

8.22
7.86
7.82
7.31
7.29
7.24
7.21
7.19
7.18
7.16
5.03
5.02
5.01
5.00
4.03
3.99
3.98
3.96
3.94
3.92
3.89
2.40
A (dd) 5.01
E (m) 7.85
G (m) 7.19
D (s) 8.22
F (dt) 7.30
A (dd) 5.01
B (qd) 3.97
C (s) 2.40
3f
f1 (ppm)

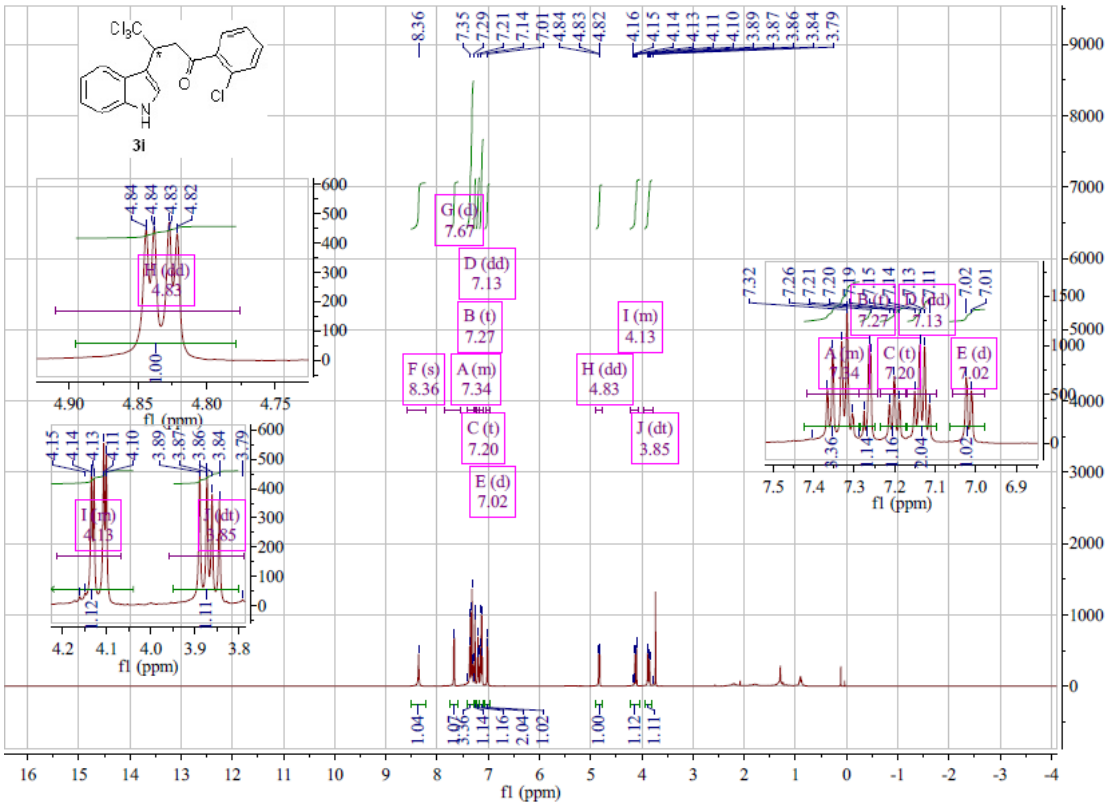

194.62
143.19
138.96
138.04
121.29
118.68
110.16
103.74
76.32
76.01
75.69
51.93
41.73
20.62
Cl3C
O
N
H
3f
f1 (ppm)

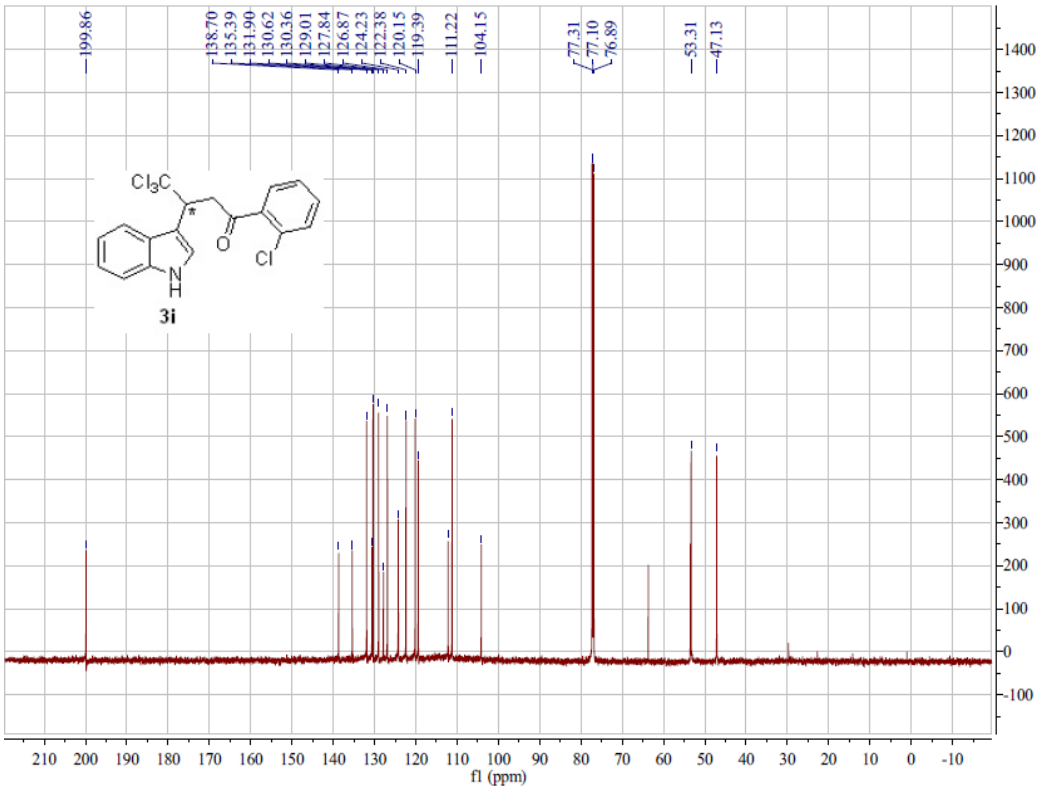

A (dd)
5.01
H (dd)
7.54
F (d)
7.53
D (m)
7.88
C (s)
8.25
I (p)
7.22
E (d)
7.81
G (t)
7.39
B (ddd)
3.98
Cl3C
O
Cl
N
H
3g
f1 (ppm)

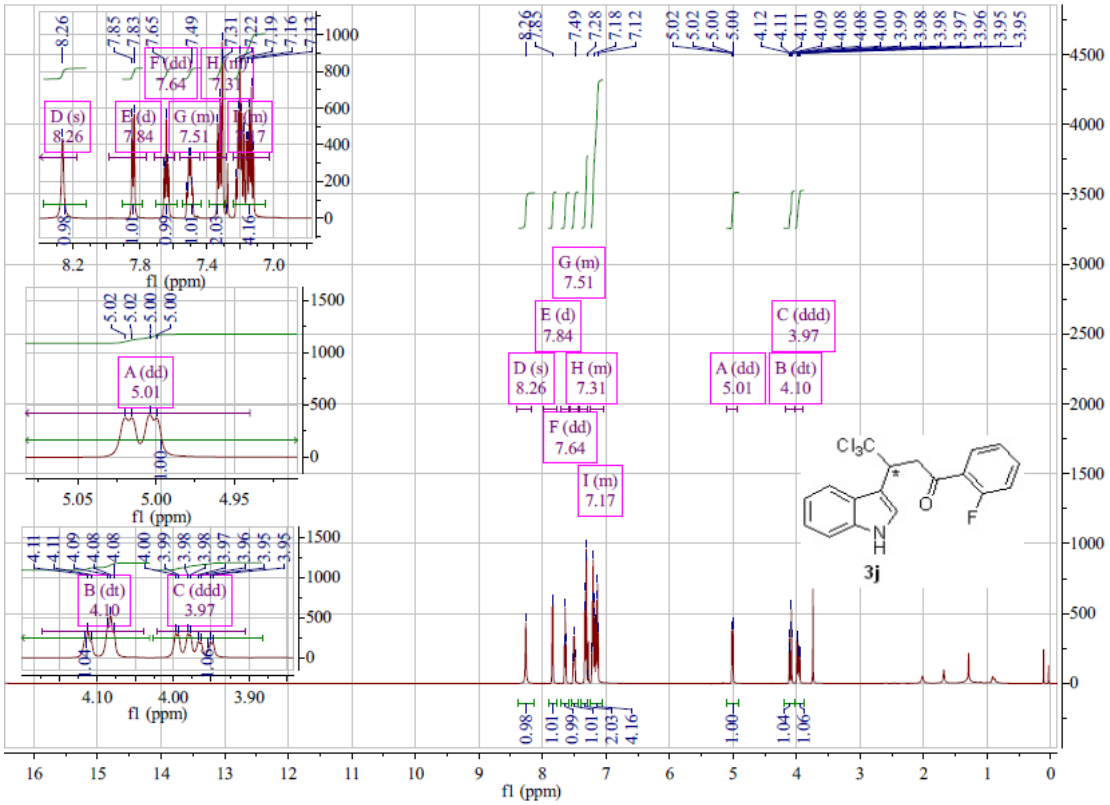

194.83
138.03
135.00
133.29
130.03
128.23
127.84
126.19
123.55
122.49
120.27
119.63
111.26
104.48
77.27
77.06
76.85
52.84
43.11
3g
f1 (ppm)

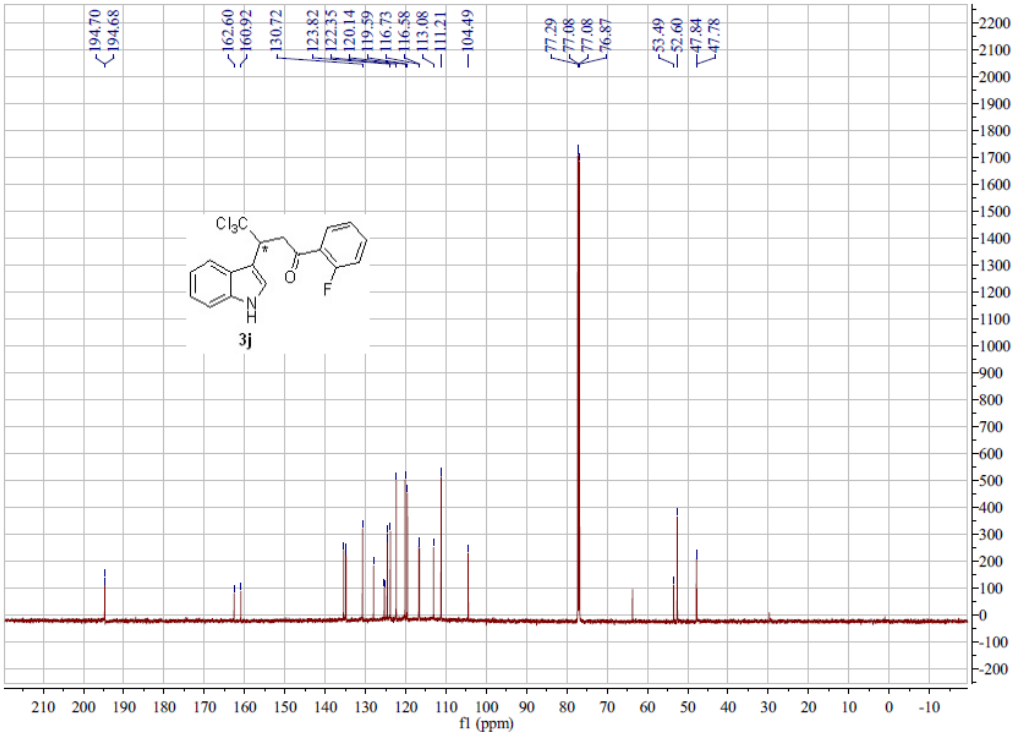

G (dd)
5.03
f1 (ppm)
H (qd)
4.06
f1 (ppm)
F (m)
7.22
B (m)
8.32
E (m)
7.34
J (s)
5.32
A (t)
8.74
C (m)
7.88
G (dd)
5.03
H (qd)
4.06
I (s)
2.21
D (t)
7.64
3h
f1 (ppm)

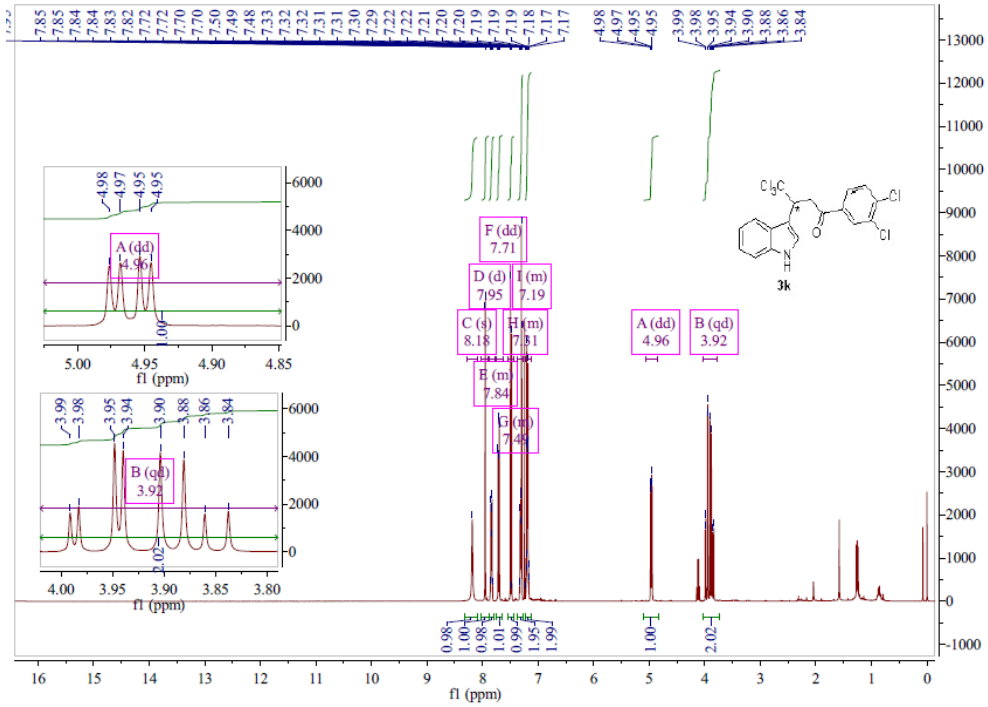

193.05
147.28
128.95
122.56
121.91
121.50
119.26
118.41
110.28
103.19
76.34
76.02
75.70
51.82
42.26
NO2
Cl3C
O
N
H
3h
fl (ppm)

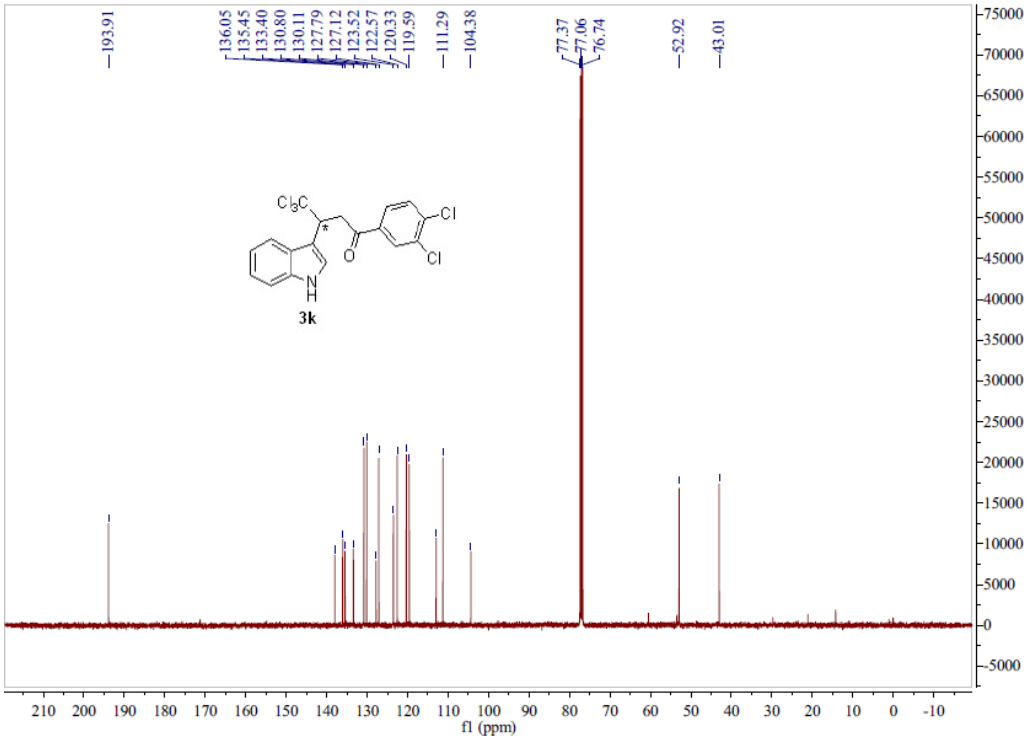

Cl3C
O
Cl
N
H
3i
8.36
7.35
7.29
7.21
7.14
7.01
4.84
4.83
4.82
4.16
4.15
4.14
4.13
4.11
4.10
3.89
3.87
3.86
3.84
3.79
G (d) 7.67
D (dd) 7.13
B (t) 7.27
F (s) 8.36
A (m) 7.34
C (t) 7.20
E (d) 7.02
I (m) 4.13
H (dd) 4.83
J (dt) 3.85
fl (ppm)

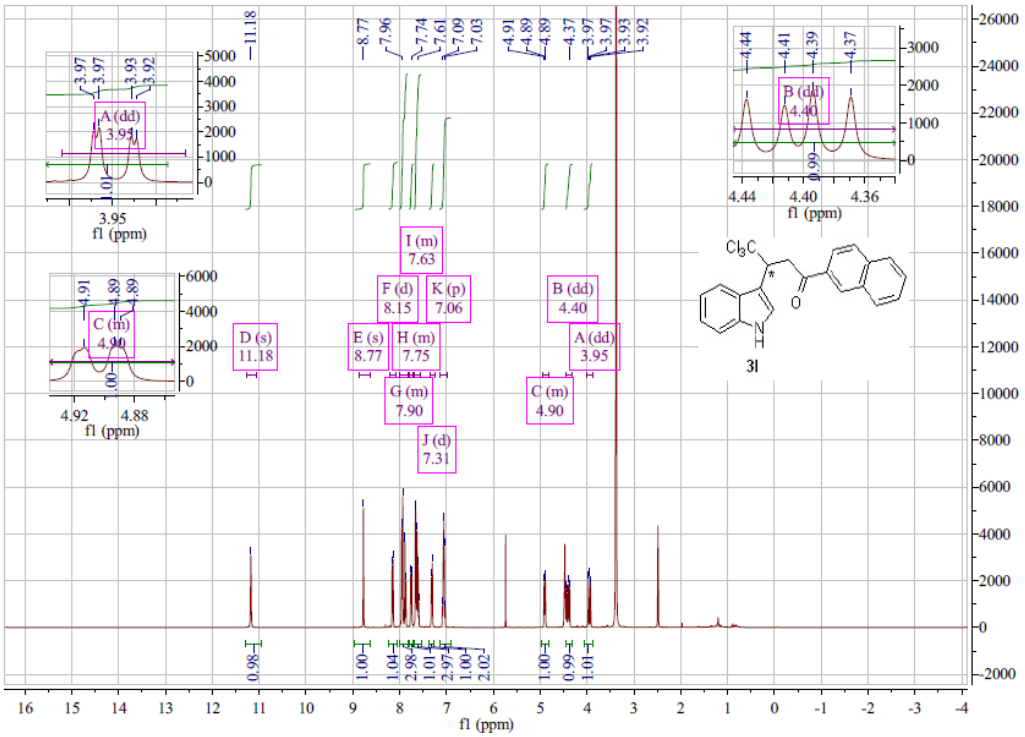

199.86
138.70
135.39
131.90
130.62
130.36
129.01
127.84
126.87
124.23
122.38
120.15
119.39
111.22
104.15
77.31
77.10
76.89
53.31
47.13
Cl3C
O
Cl
N
H
3i
fl (ppm)

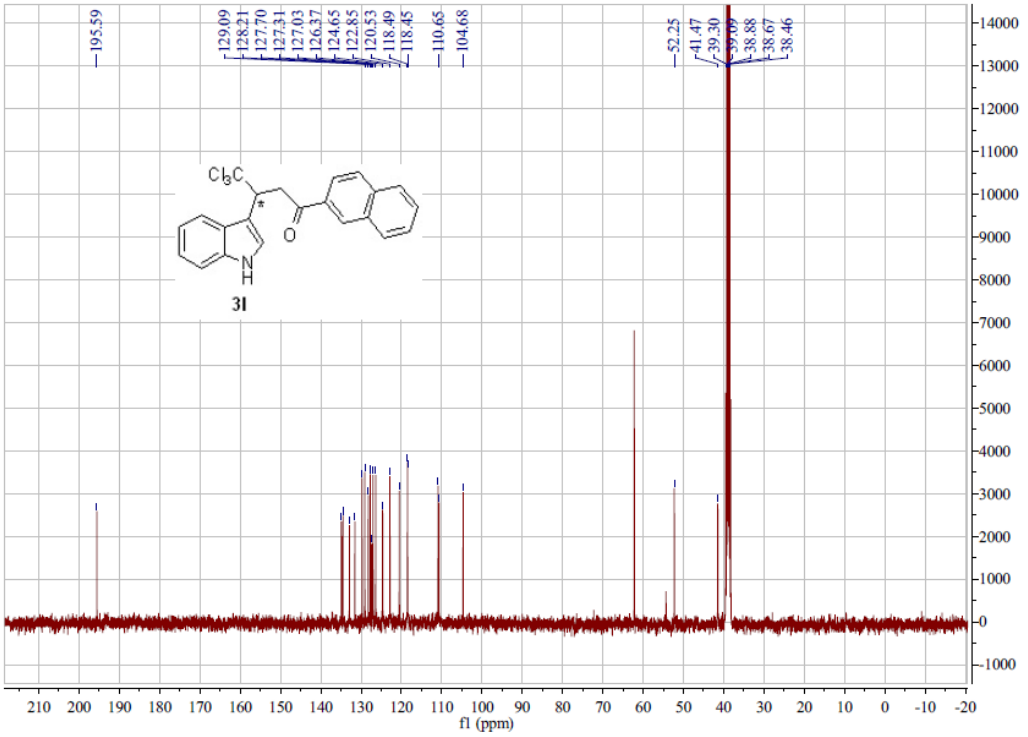

D (s) 8.26
E (d) 7.84
F (dd) 7.64
G (m) 7.51
H (m) 7.31
I (m) 7.17
A (dd) 5.01
B (dt) 4.10
C (ddd) 3.97
Cl3C
O
F
N
H
3j
fl (ppm)

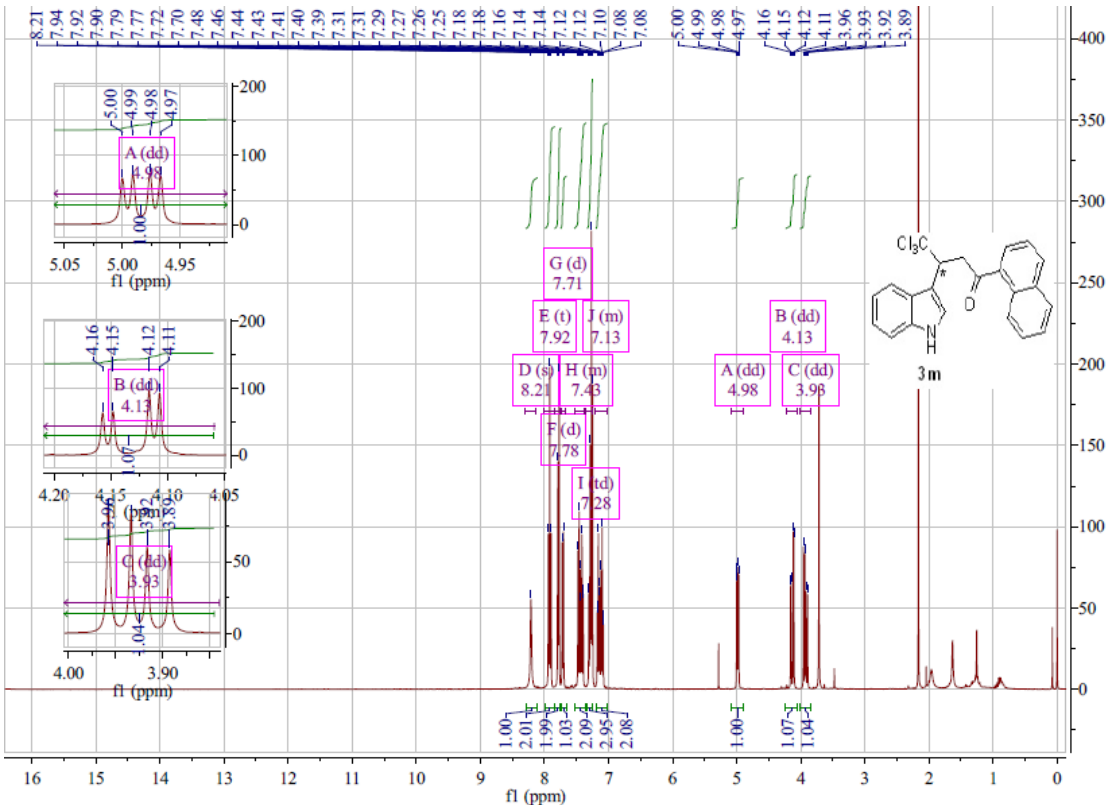

194.70
194.68
162.60
160.92
130.72
123.82
122.35
120.14
119.59
116.73
116.58
113.08
111.21
104.49
77.29
77.08
77.08
76.87
53.49
52.60
47.84
47.78
Cl3C
O
F
N
H
3j
f1 (ppm)

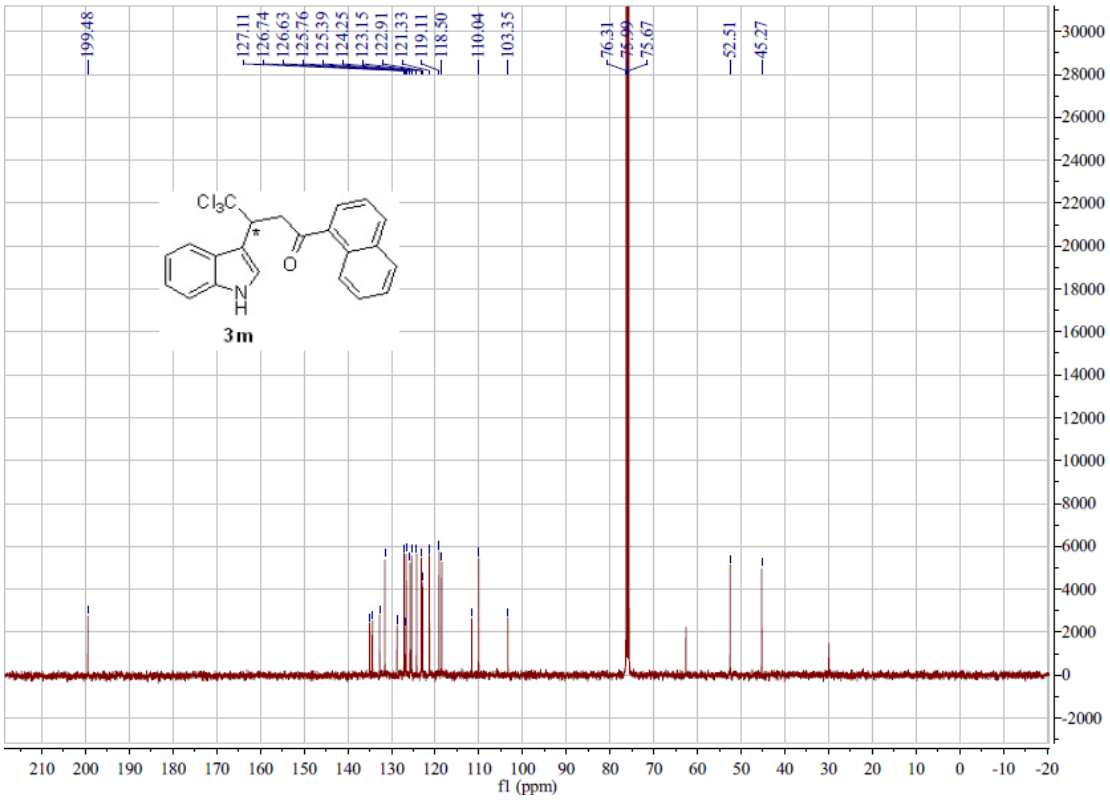

A (dd)
4.96
B (qd)
3.92
C (s)
8.18
D (d)
7.95
E (m)
7.84
F (dd)
7.71
G (m)
7.48
H (m)
7.51
I (m)
7.19
Cl3C
Cl
Cl
O
N
H
3k
f1 (ppm)

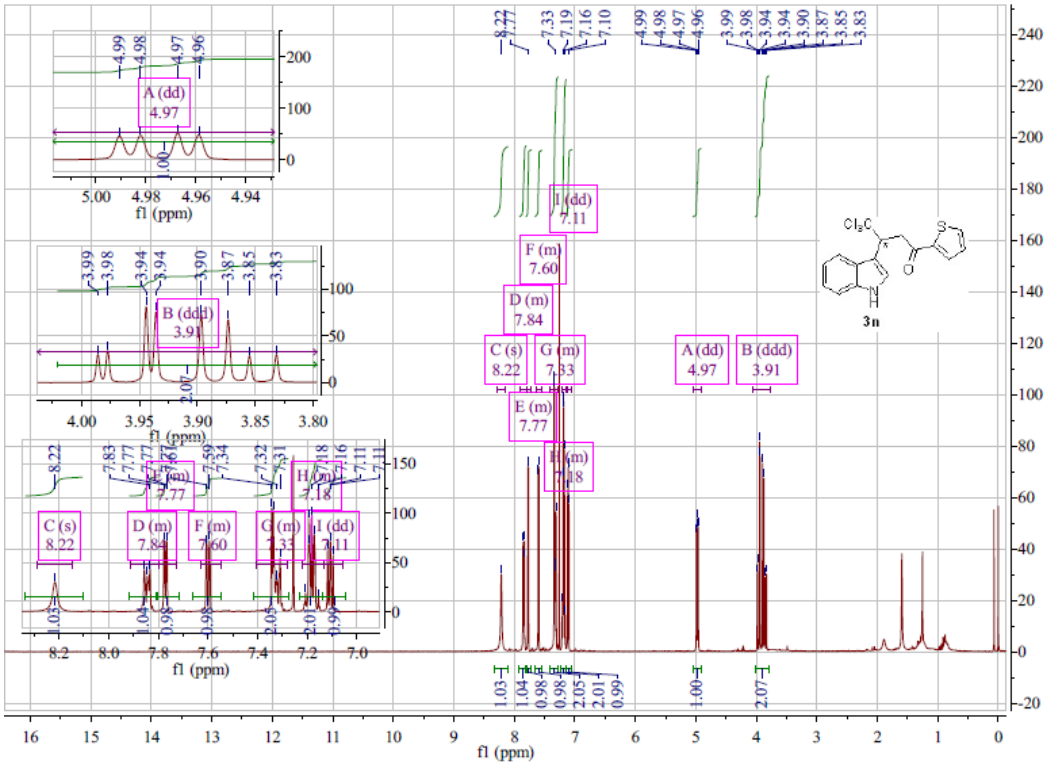

193.91
136.05
135.45
133.40
130.80
130.11
127.79
127.12
123.52
122.57
120.33
119.59
111.29
104.38
77.37
77.06
76.74
52.92
43.01
3k
fl (ppm)

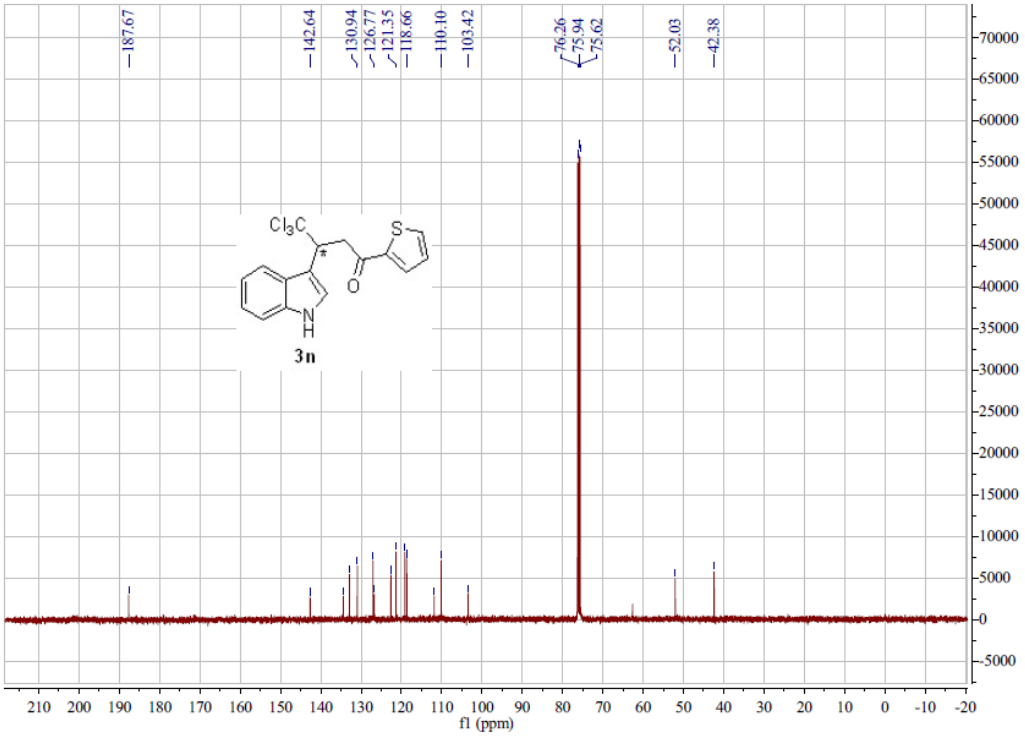

11.18
8.77
7.96
7.74
7.61
7.09
7.03
4.91
4.89
4.89
4.37
3.97
3.97
3.93
3.92
A (dd) 3.95
B (dd) 4.40
C (m) 4.90
D (s) 11.18
E (s) 8.77
F (d) 8.15
G (m) 7.90
H (m) 7.75
I (m) 7.63
J (d) 7.31
K (p) 7.06
3l
fl (ppm)

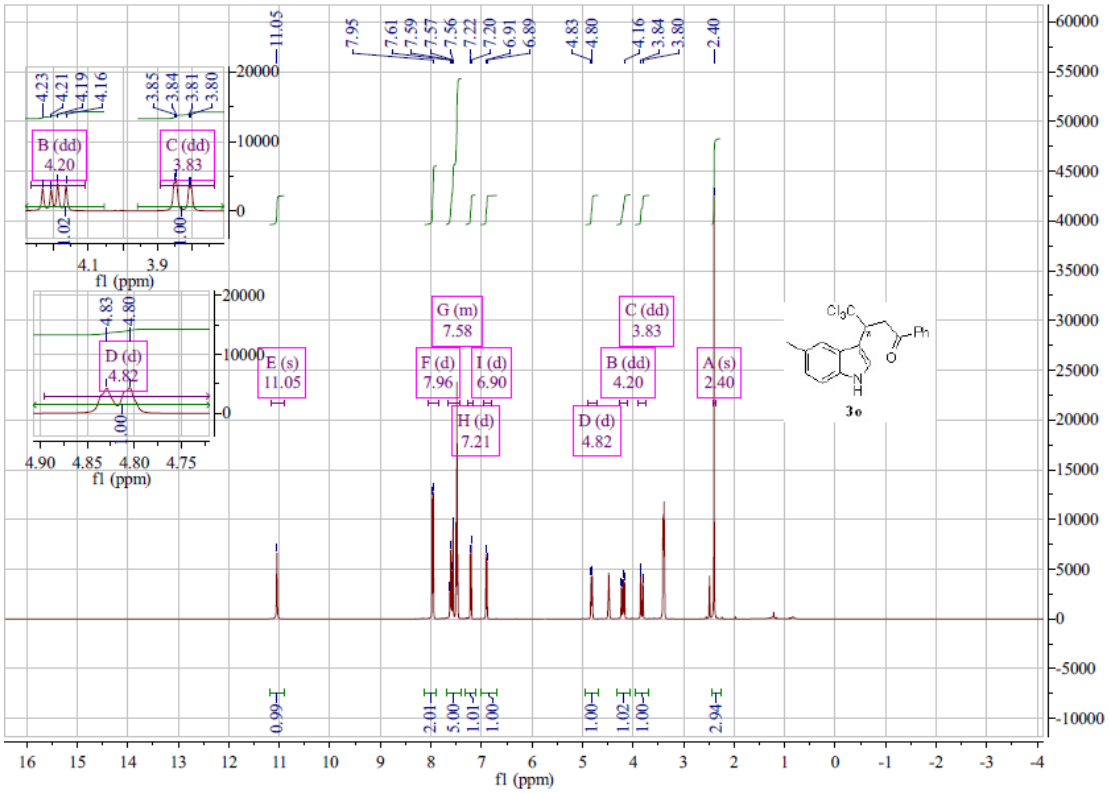

195.59
129.09
128.21
127.70
127.31
127.03
126.37
124.65
122.85
120.53
118.49
118.45
110.65
104.68
52.25
41.47
39.30
39.09
38.88
38.67
38.46
3l
fl (ppm)

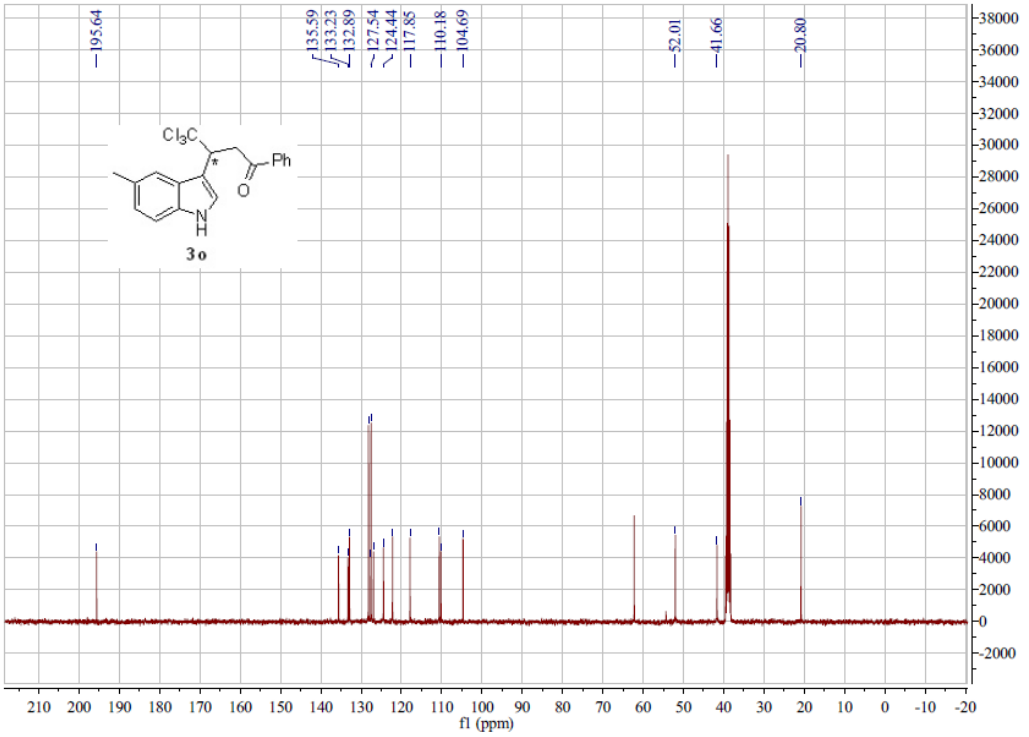

A (dd) 4.98
B (dd) 4.13
C (dd) 3.93
G (d) 7.71
E (t) 7.92
J (m) 7.13
D (s) 8.21
H (m) 7.43
F (d) 7.78
I (td) 7.28
3m
fl (ppm)

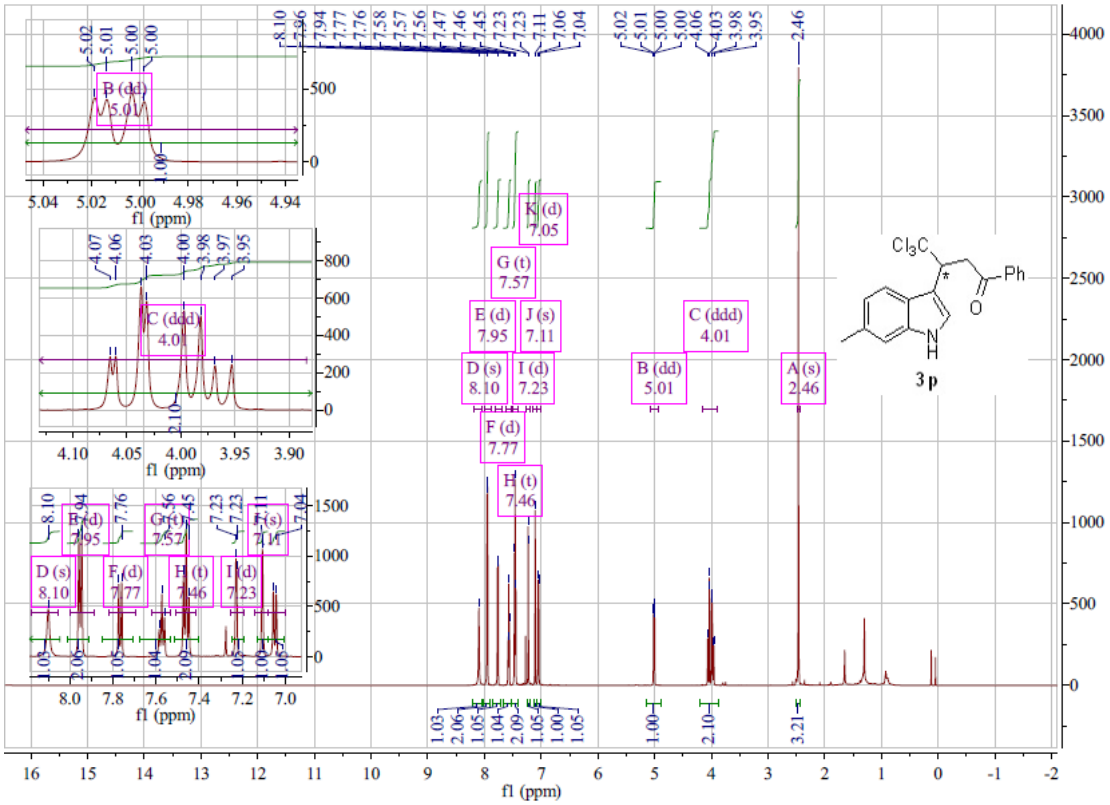

199.48
127.11
126.74
126.63
125.76
125.39
124.25
123.15
122.91
121.33
119.11
118.50
110.04
103.35
76.31
75.99
75.67
52.51
45.27
3m
fl (ppm)

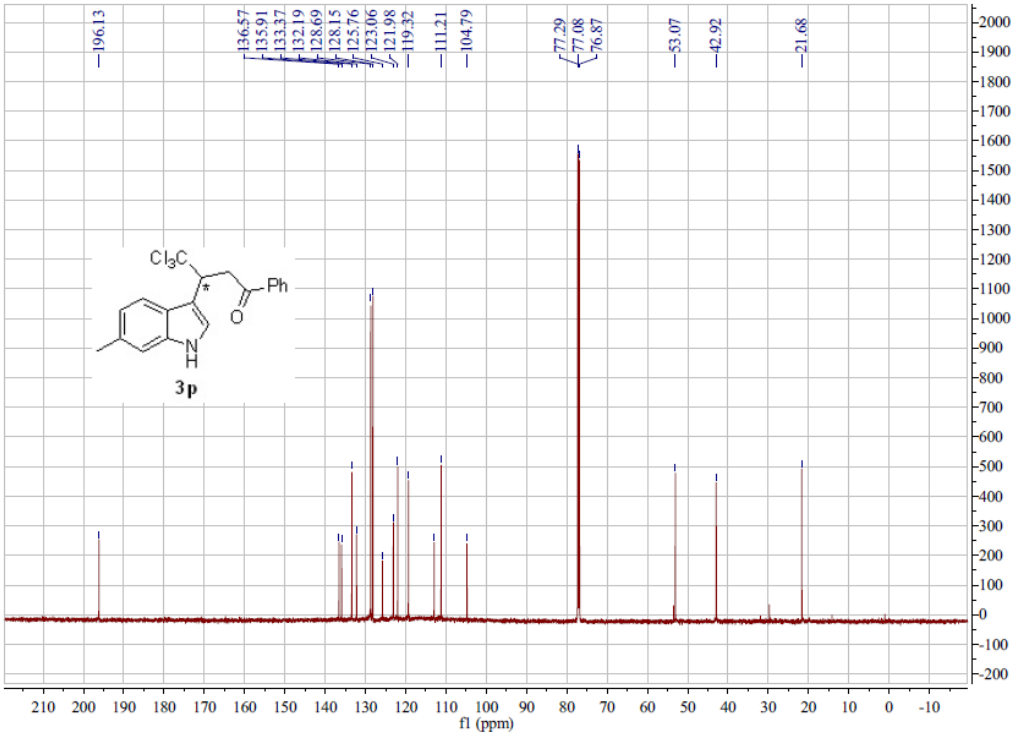

A (dd) 4.97
B (ddd) 3.91
C (s) 8.22
D (m) 7.84
E (m) 7.77
F (m) 7.60
G (m) 7.33
H (m) 7.18
I (dd) 7.11
3n
fl (ppm)

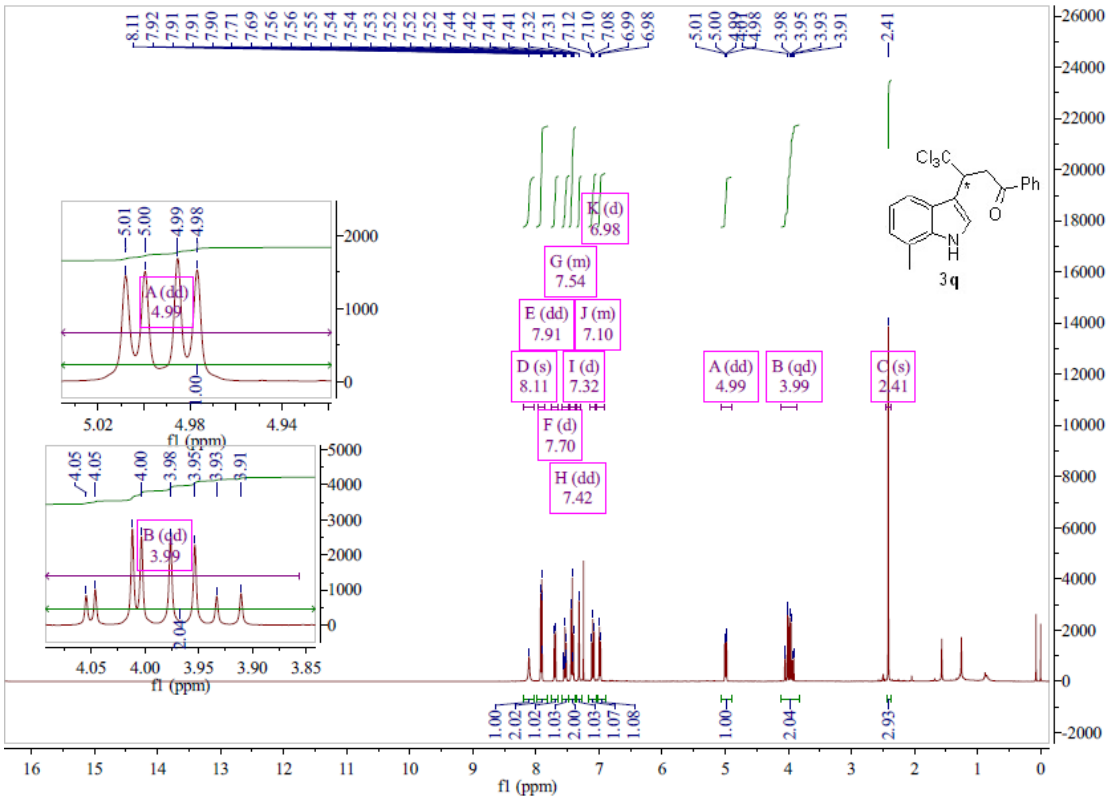

187.67
142.64
130.94
126.77
121.35
118.66
110.10
103.42
76.26
75.94
75.62
52.03
42.38
3n
f1 (ppm)

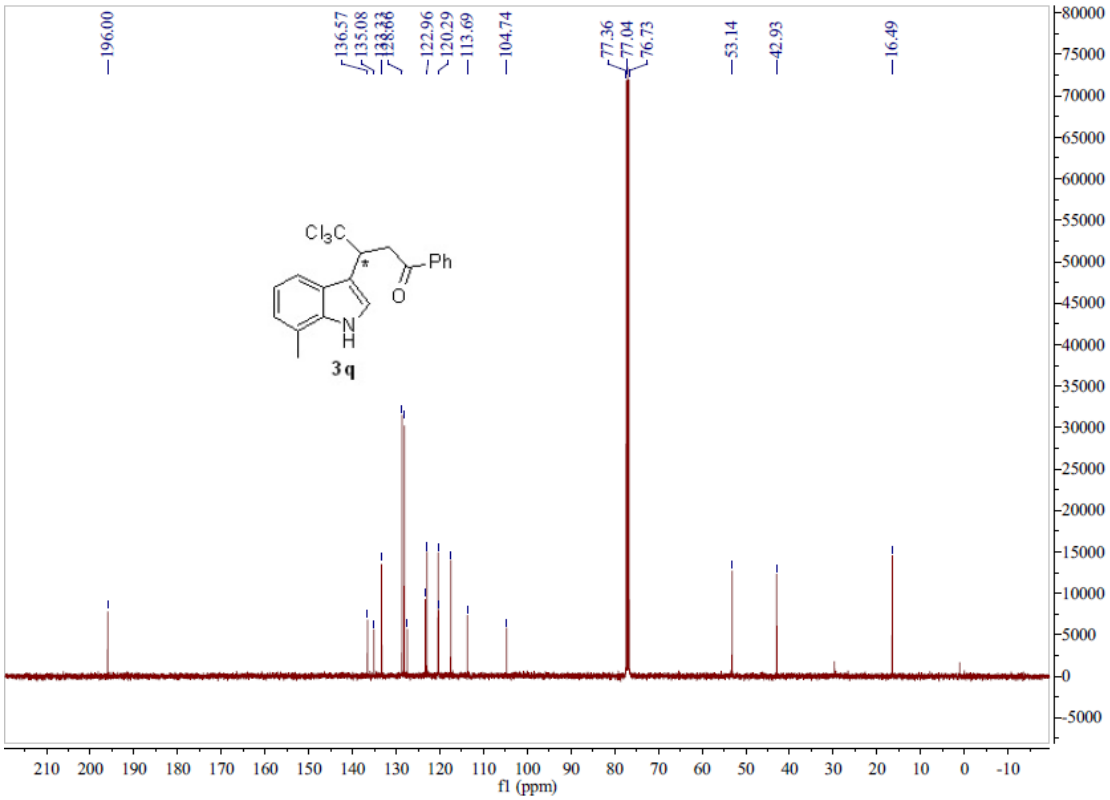

11.05
7.95
7.61
7.59
7.57
7.56
7.22
7.20
6.91
6.89
4.83
4.80
4.16
3.84
3.80
2.40
B (dd) 4.20
C (dd) 3.83
D (d) 4.82
E (s) 11.05
F (d) 7.96
G (m) 7.58
H (d) 7.21
I (d) 6.90
A (s) 2.40
3o
f1 (ppm)

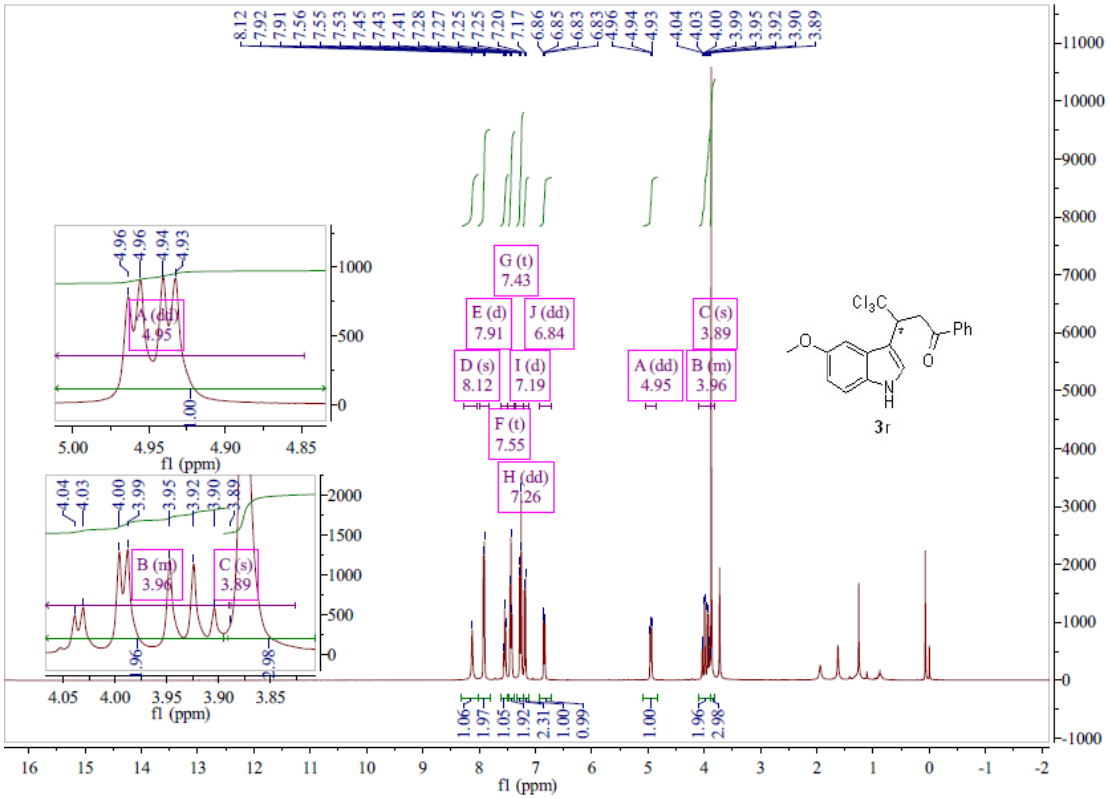

195.64
135.59
133.23
132.89
127.54
124.44
117.85
110.18
104.69
52.01
41.66
20.80
Cl3C
Ph
O
N
H
3o
f1 (ppm)

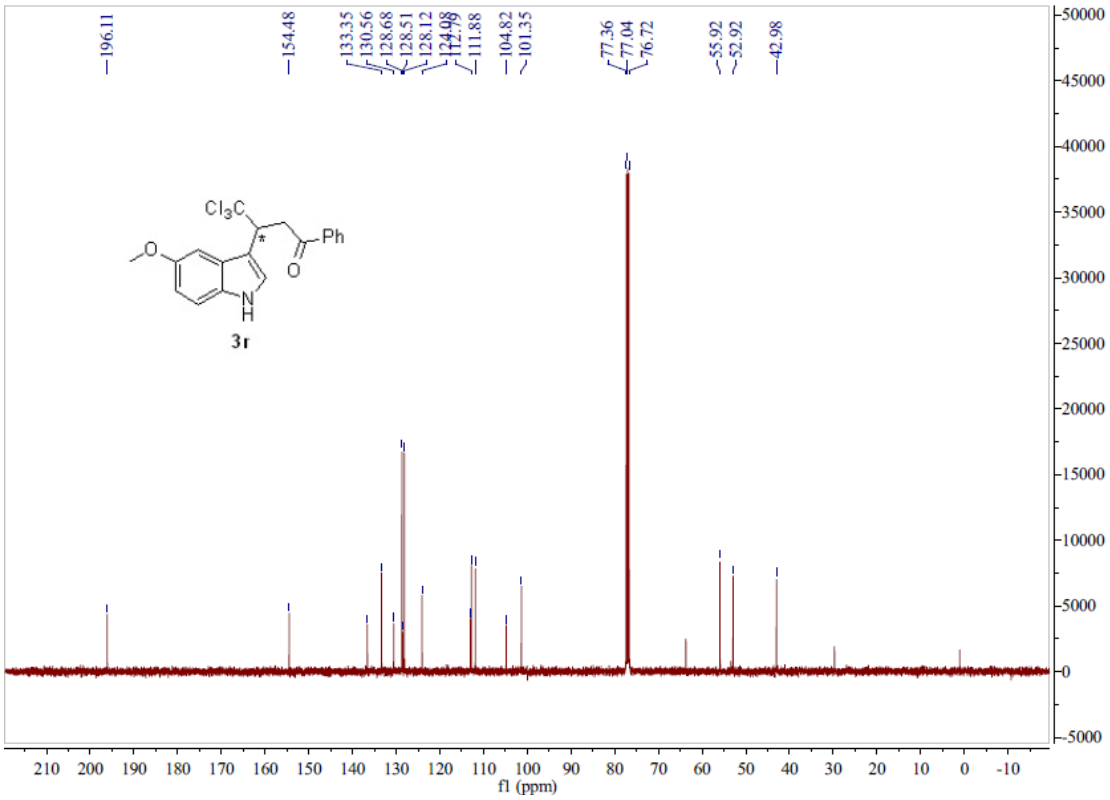

B (dd) 5.01
C (ddd) 4.01
D (s) 8.10
E (d) 7.95
F (d) 7.77
G (t) 7.57
H (t) 7.46
I (d) 7.23
J (s) 7.11
K (d) 7.05
A (s) 2.46
Cl3C
Ph
O
N
H
3p
f1 (ppm)

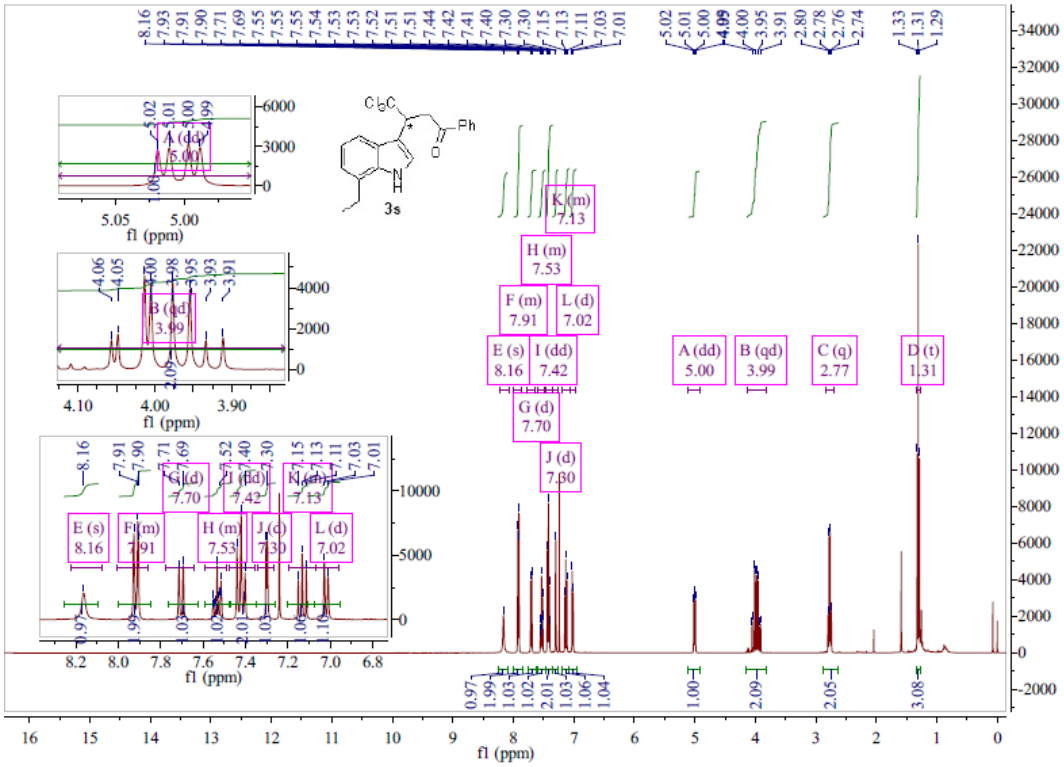

196.13
136.57
135.91
133.37
132.19
128.69
128.15
125.76
123.06
121.98
119.32
111.21
104.79
77.29
77.08
76.87
53.07
42.92
21.68
Cl3C
Ph
O
N
H
3p
f1 (ppm)

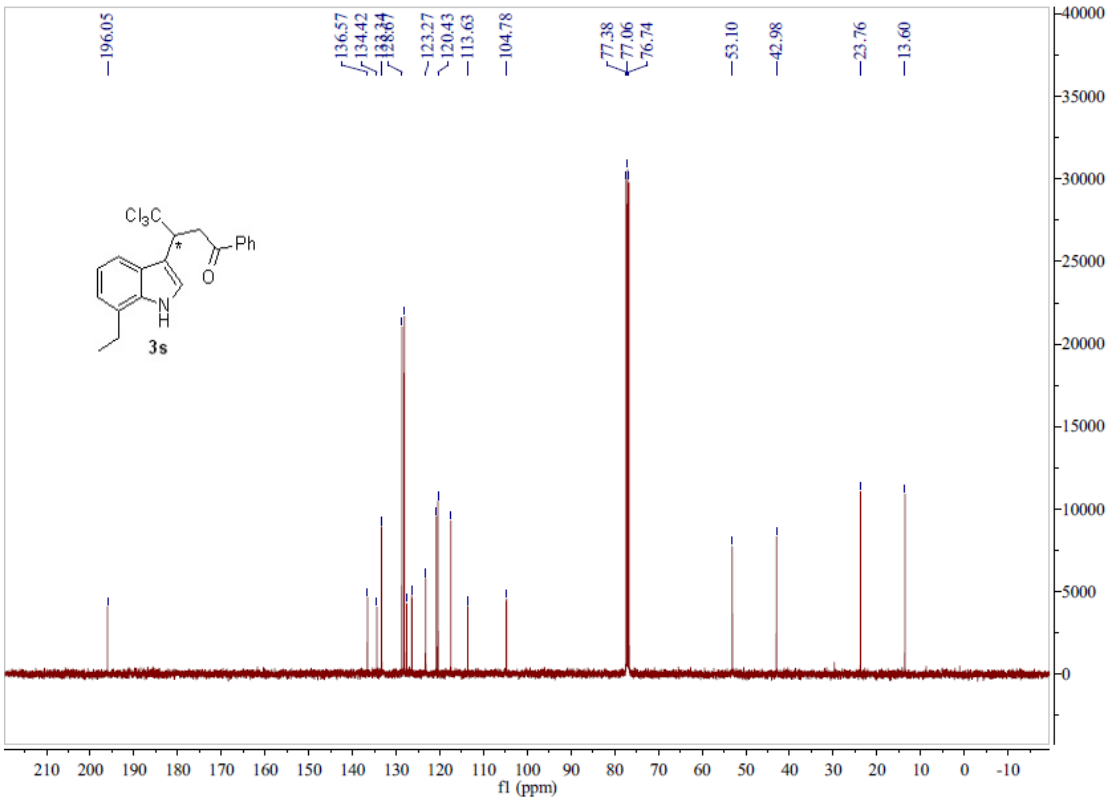

A (dd) 4.99
B (dd) 3.99
K (d) 6.98
G (m) 7.54
E (dd) 7.91
J (m) 7.10
D (s) 8.11
I (d) 7.32
F (d) 7.70
H (dd) 7.42
A (dd) 4.99
B (qd) 3.99
C (s) 2.41
Cl3C
Ph
O
N
H
3q
f1 (ppm)

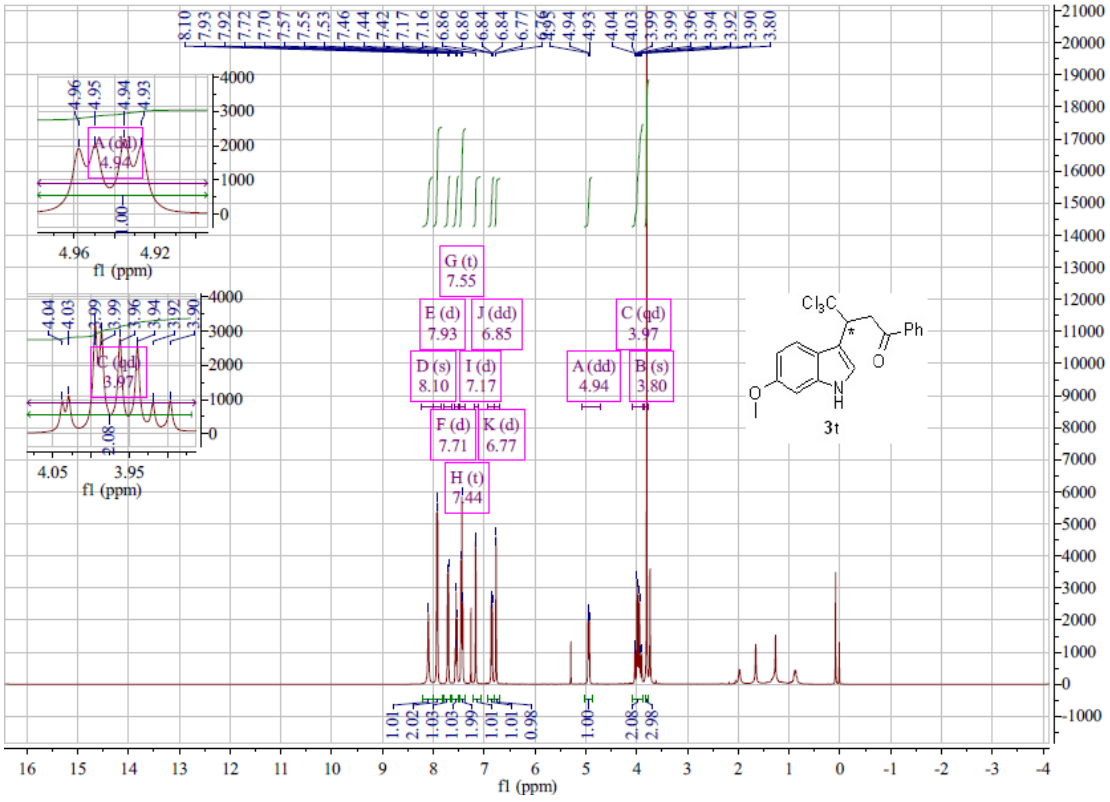

196.00
136.57
135.08
128.86
122.96
120.29
113.69
104.74
77.36
77.04
76.73
53.14
42.93
16.49
Cl3C
Ph
O
N
H
3q
fl (ppm)

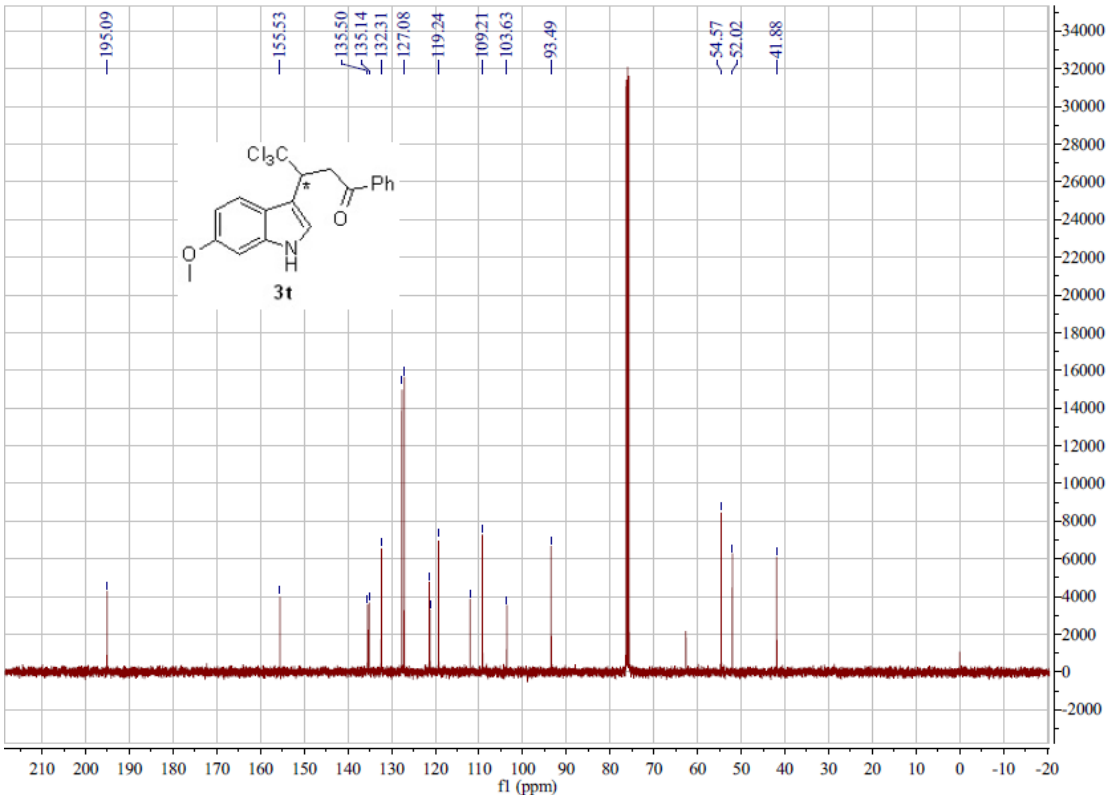

8.12
7.92
7.91
7.56
7.55
7.53
7.45
7.43
7.41
7.28
7.27
7.25
7.20
7.17
6.86
6.85
6.83
6.83
4.96
4.94
4.93
4.04
4.03
4.00
3.99
3.95
3.92
3.90
3.89
A (dd) 4.95
G (t) 7.43
E (d) 7.91
J (dd) 6.84
C (s) 3.89
D (s) 8.12
I (d) 7.19
A (dd) 4.95
B (m) 3.96
F (t) 7.55
H (dd) 7.26
B (m) 3.96
C (s) 3.89
Cl3C
Ph
O
N
H
3r
fl (ppm)

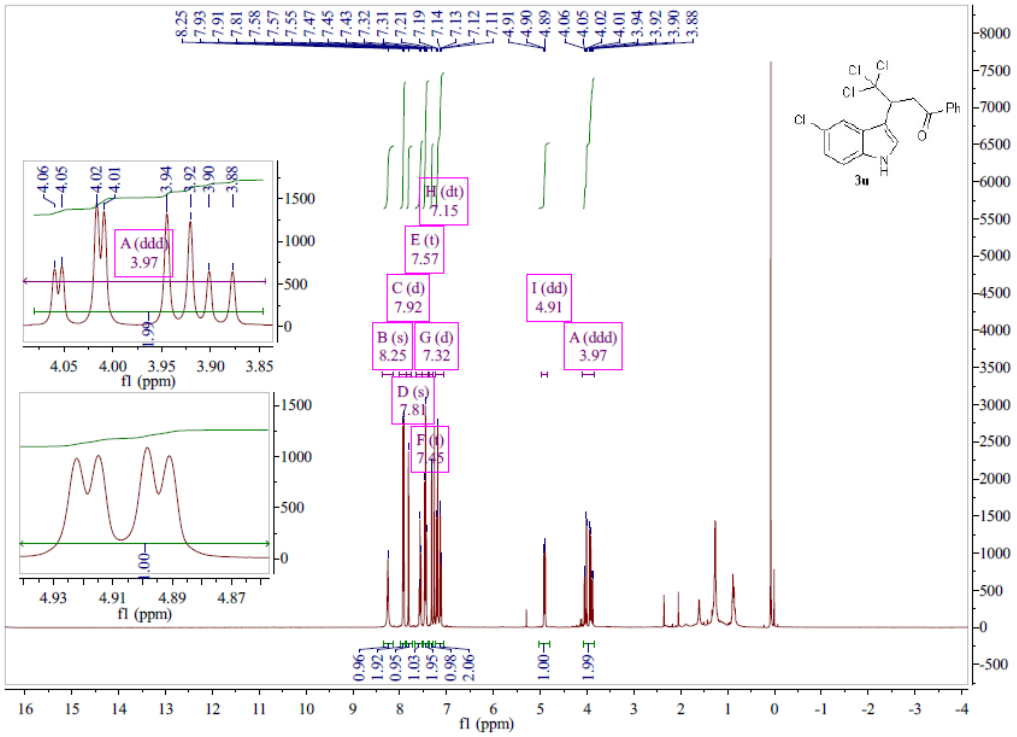

196.11
154.48
133.35
130.56
128.68
128.51
128.12
124.08
122.78
111.88
104.82
101.35
77.36
77.04
76.72
55.92
52.92
42.98
Cl3C
Ph
O
N
H
3r
fl (ppm)

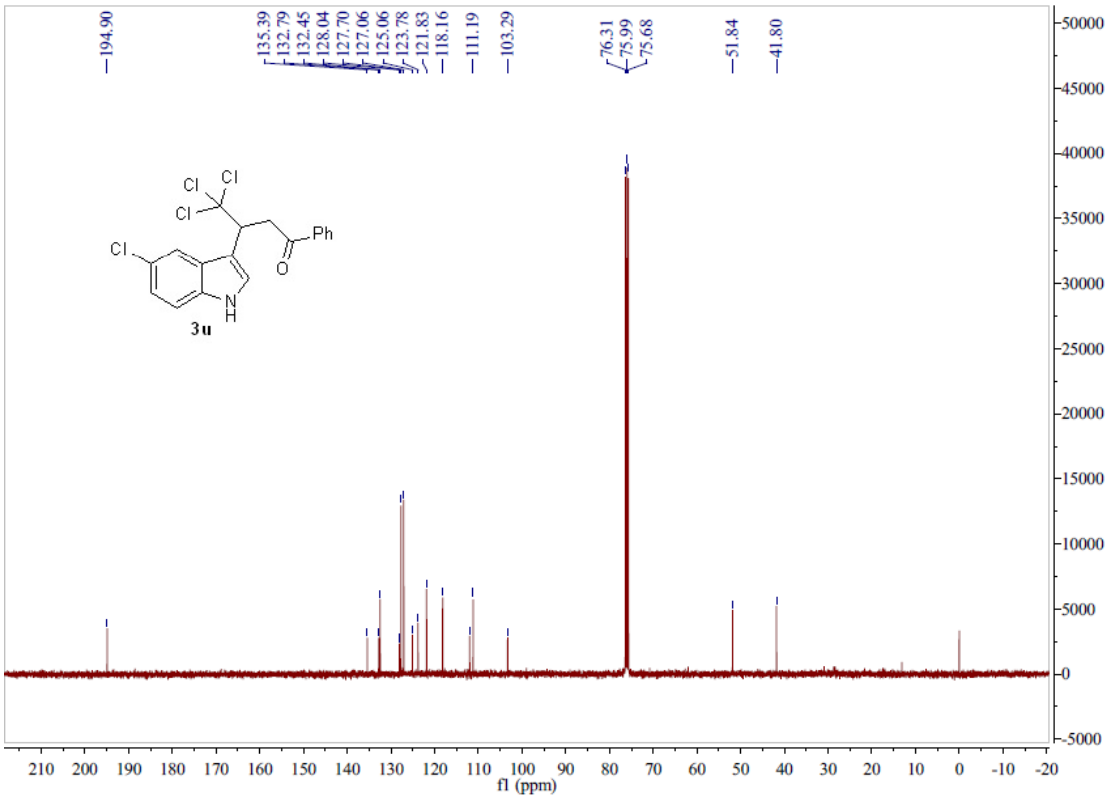

3s
A (dd) 5.00
B (qd) 3.99
C (q) 2.77
D (t) 1.31
E (s) 8.16
F (m) 7.91
G (d) 7.70
H (m) 7.53
I (dd) 7.42
J (d) 7.30
K (m) 7.13
L (d) 7.02
fl (ppm)

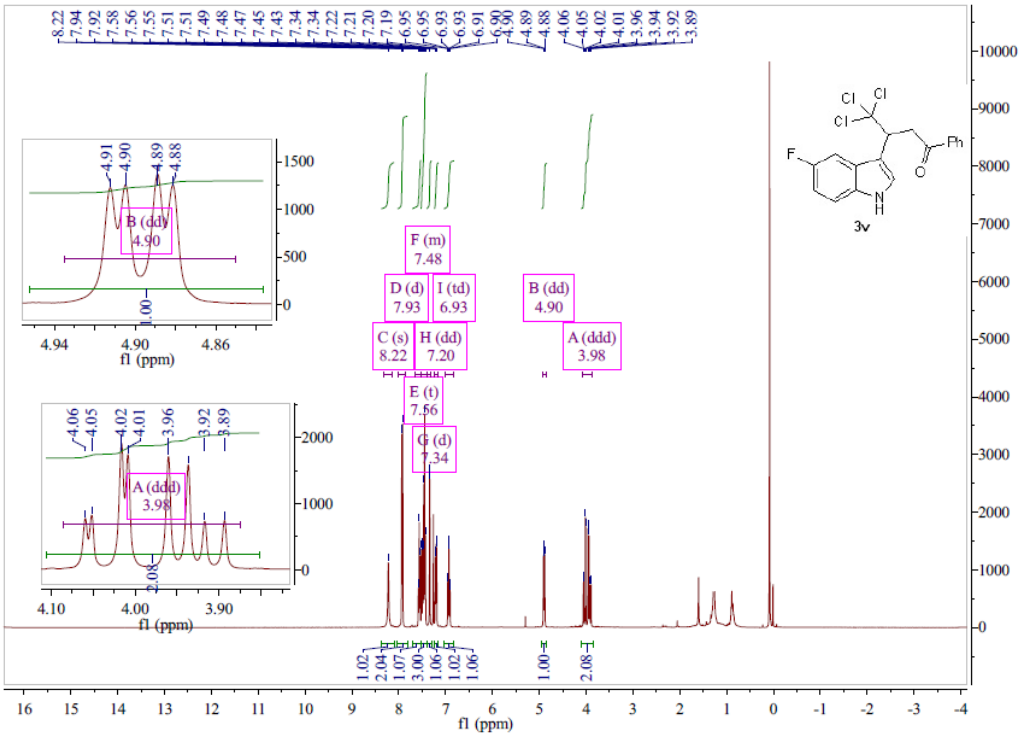

196.05
136.57
134.42
128.87
123.27
120.43
113.63
104.78
77.38
77.06
76.74
53.10
42.98
23.76
13.60
Cl3C
Ph
O
N
H
3s
f1 (ppm)

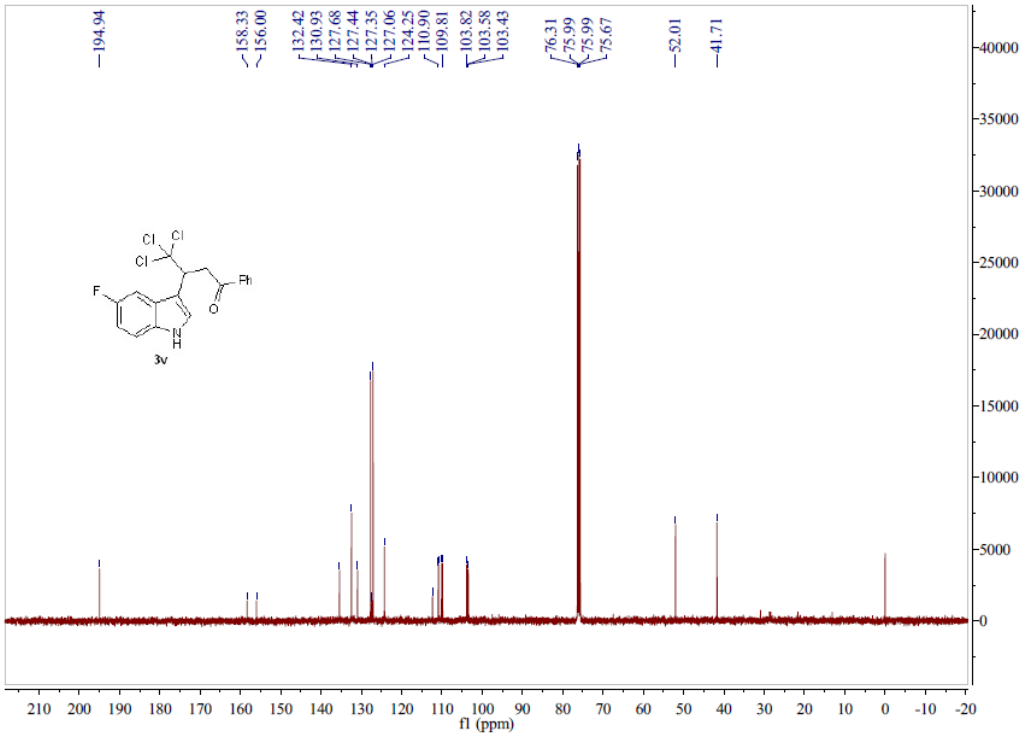

A (dd) 4.94
C (qd) 3.97
G (t) 7.55
E (d) 7.93
J (dd) 6.85
D (s) 8.10
I (d) 7.17
F (d) 7.71
K (d) 6.77
H (t) 7.44
A (dd) 4.94
B (s) 3.80
C (qd) 3.97
Cl3C
Ph
O
N
H
3t
f1 (ppm)


195.09
155.53
135.50
135.14
132.31
127.08
119.24
109.21
103.63
93.49
54.57
52.02
41.88
3t
fl (ppm)


A (ddd) 3.97
H (dt) 7.15
E (t) 7.57
C (d) 7.92
B (s) 8.25
G (d) 7.32
D (s) 7.81
F (t) 7.45
I (dd) 4.91
A (ddd) 3.97
3u
fl (ppm)


194.90
135.39
132.79
132.45
128.04
127.70
127.06
125.06
123.78
121.83
118.16
111.19
103.29
76.31
75.99
75.68
51.84
41.80
Cl
Cl
Cl
Ph
O
N
H
3u
f1 (ppm)


B (dd) 4.90
F (m) 7.48
D (d) 7.93
I (td) 6.93
B (dd) 4.90
C (s) 8.22
H (dd) 7.20
A (ddd) 3.98
E (t) 7.56
G (d) 7.34
A (ddd) 3.98
F
Cl
Cl
Cl
Ph
O
N
H
3v
f1 (ppm)


194.94
158.33
156.00
132.42
130.93
127.68
127.44
127.35
127.06
124.25
110.90
109.81
103.82
103.58
103.43
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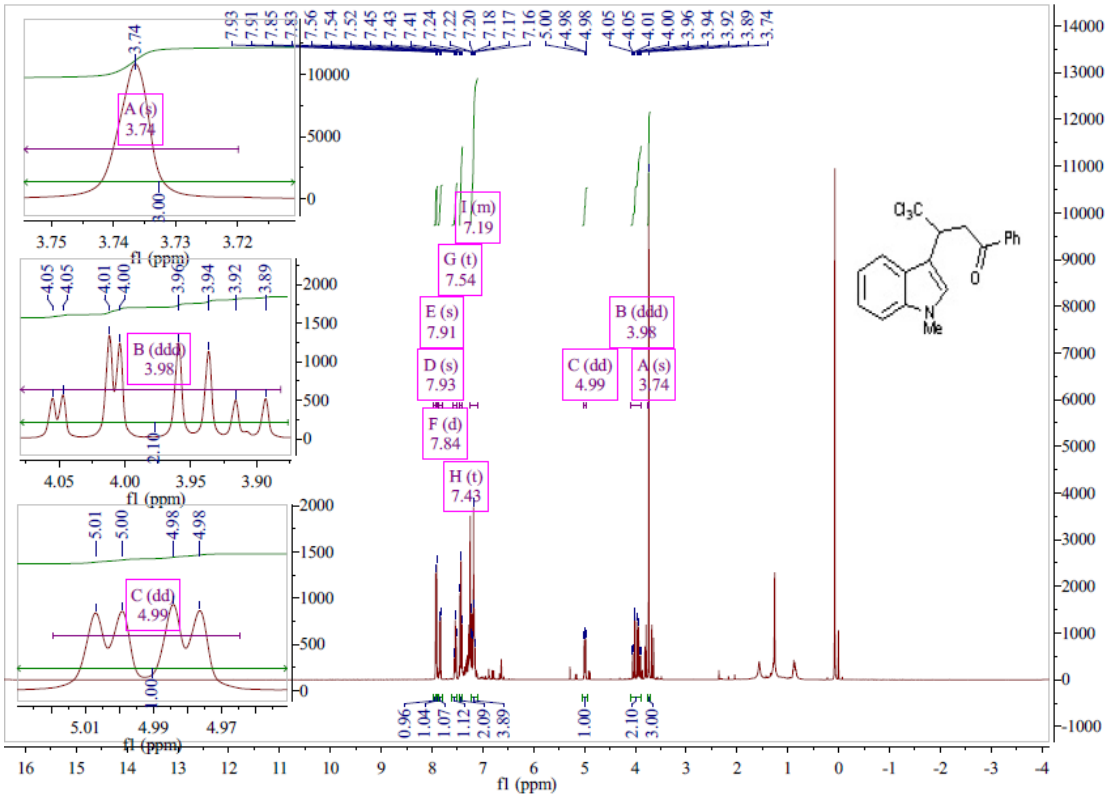
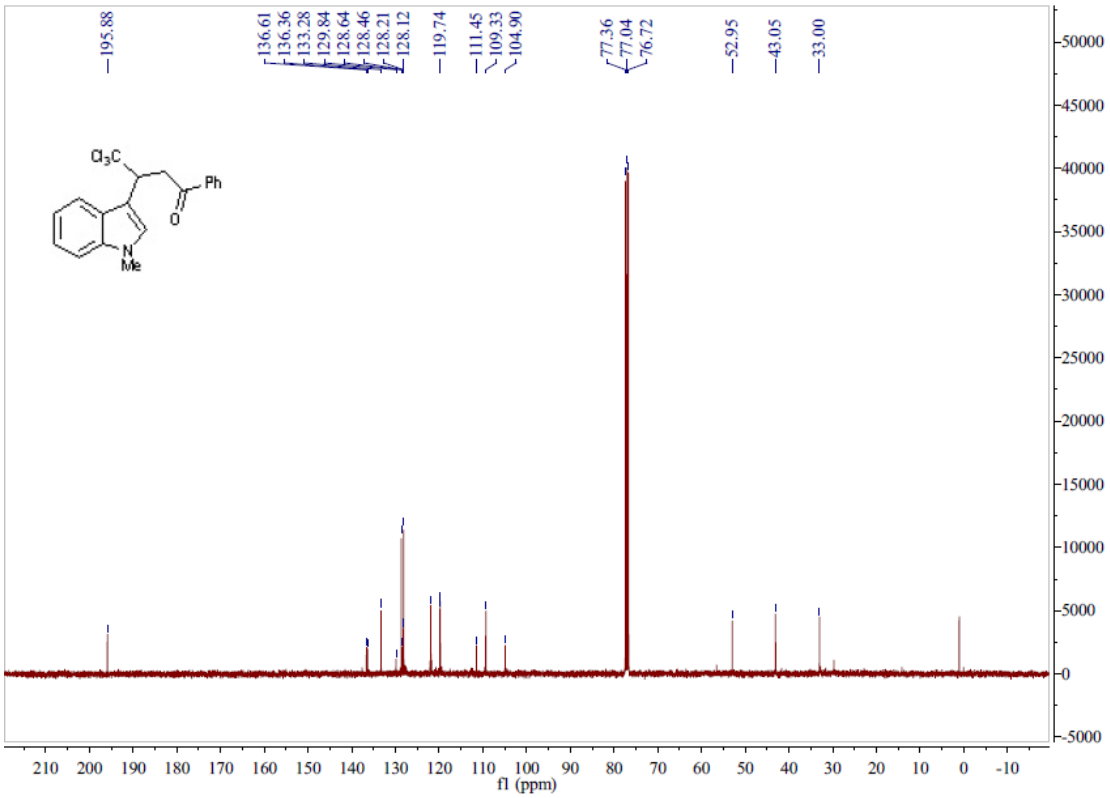
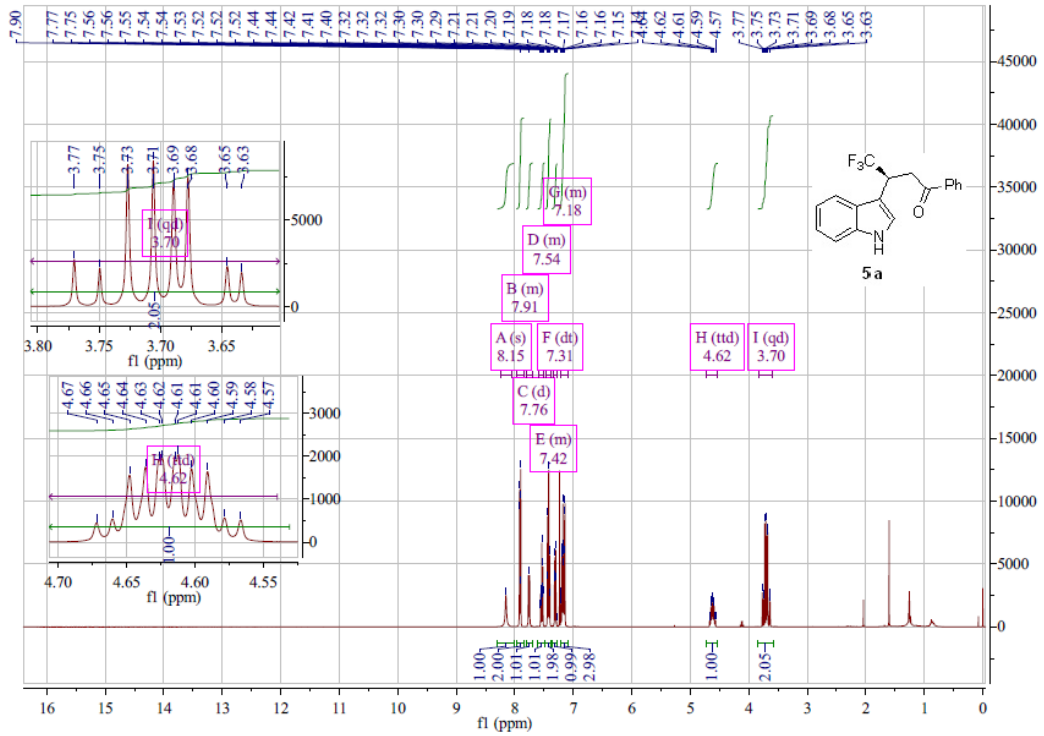
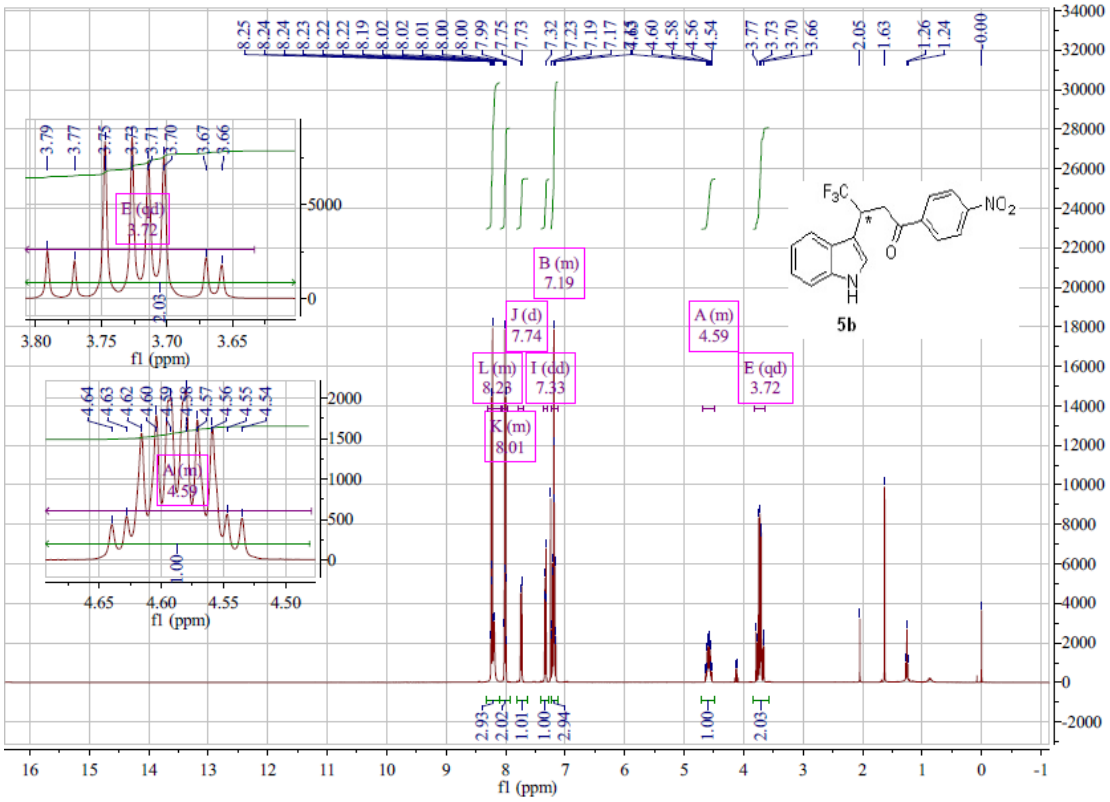
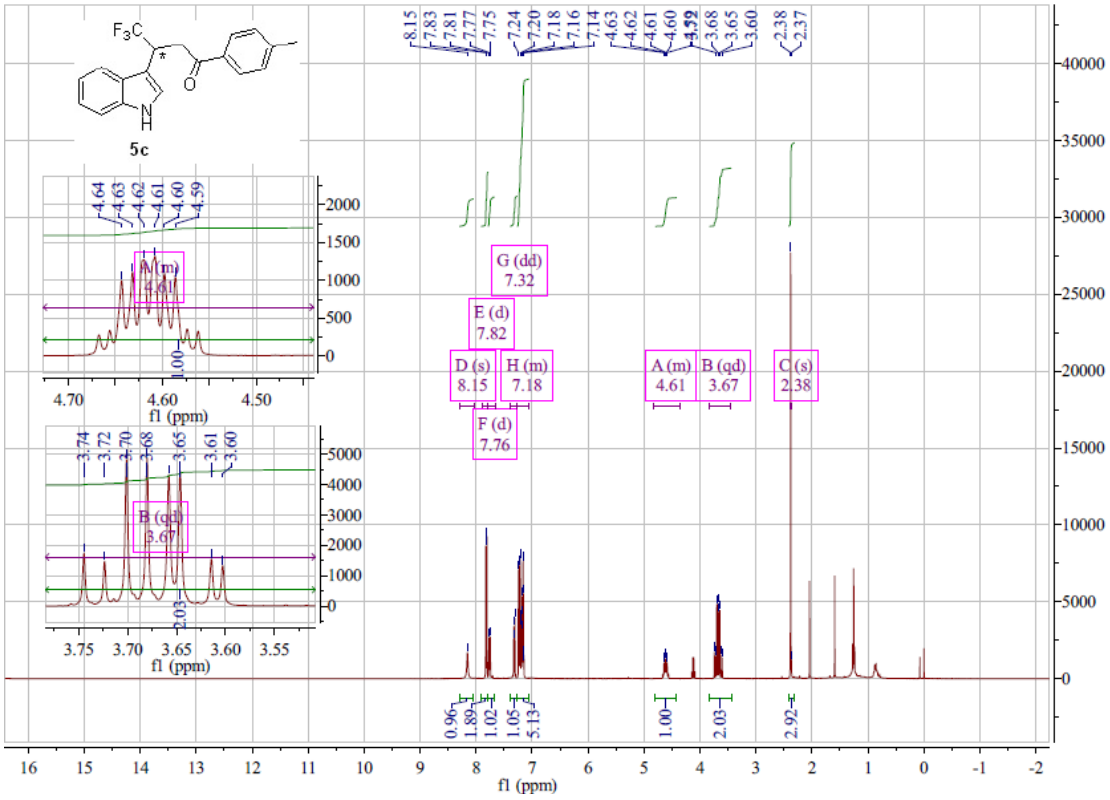
75.99
75.99
75.67
52.01
41.71
3v
f1 (ppm)

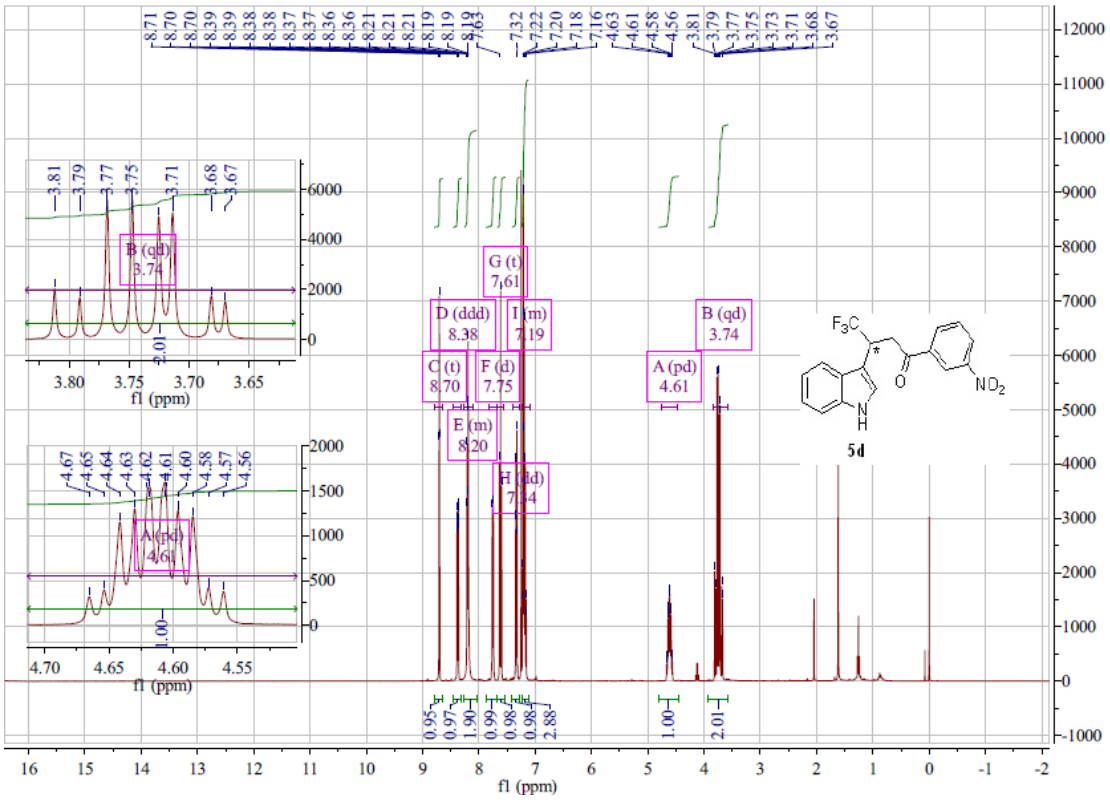

A (s) 3.74
I (m) 7.19
G (t) 7.54
E (s) 7.91
D (s) 7.93
F (d) 7.84
H (t) 7.43
B (ddd) 3.98
C (dd) 4.99
A (s) 3.74
Me
f1 (ppm)

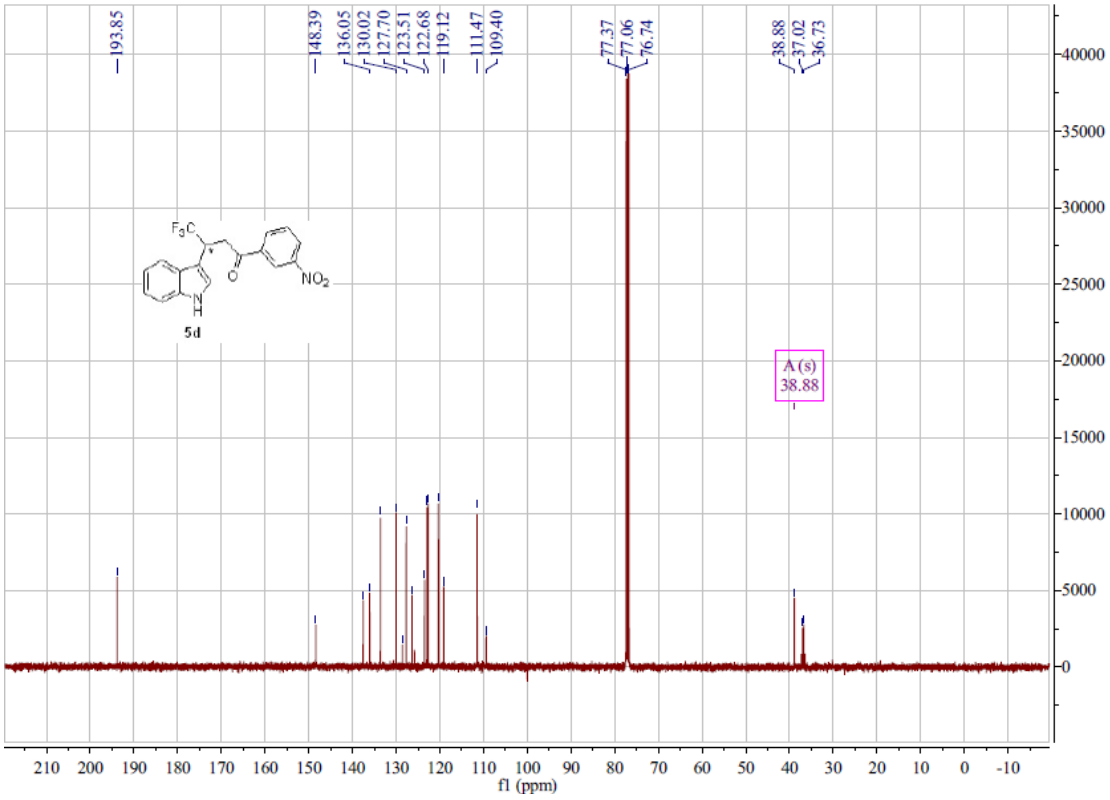

195.88
136.61
136.36
133.28
129.84
128.64
128.46
128.21
128.12
119.74
111.45
109.33
104.90
77.36
77.04
76.72
52.95
43.05
33.00
Cl3C
Ph
O
N
Me
f1 (ppm)

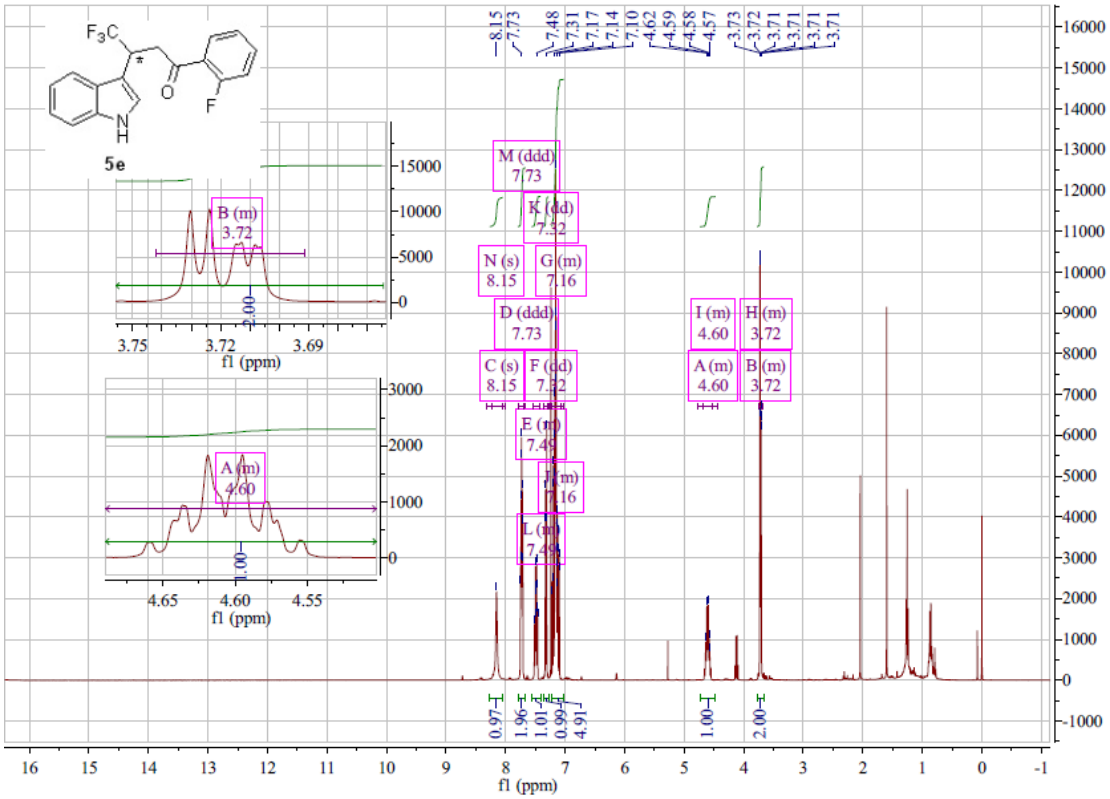

G (m) 7.18
D (m) 7.54
B (m) 7.91
A (s) 8.15
F (dt) 7.31
C (d) 7.76
E (m) 7,42
H (ttd) 4.62
I (qd) 3.70
F3C
Ph
O
N
H
5a
f1 (ppm)

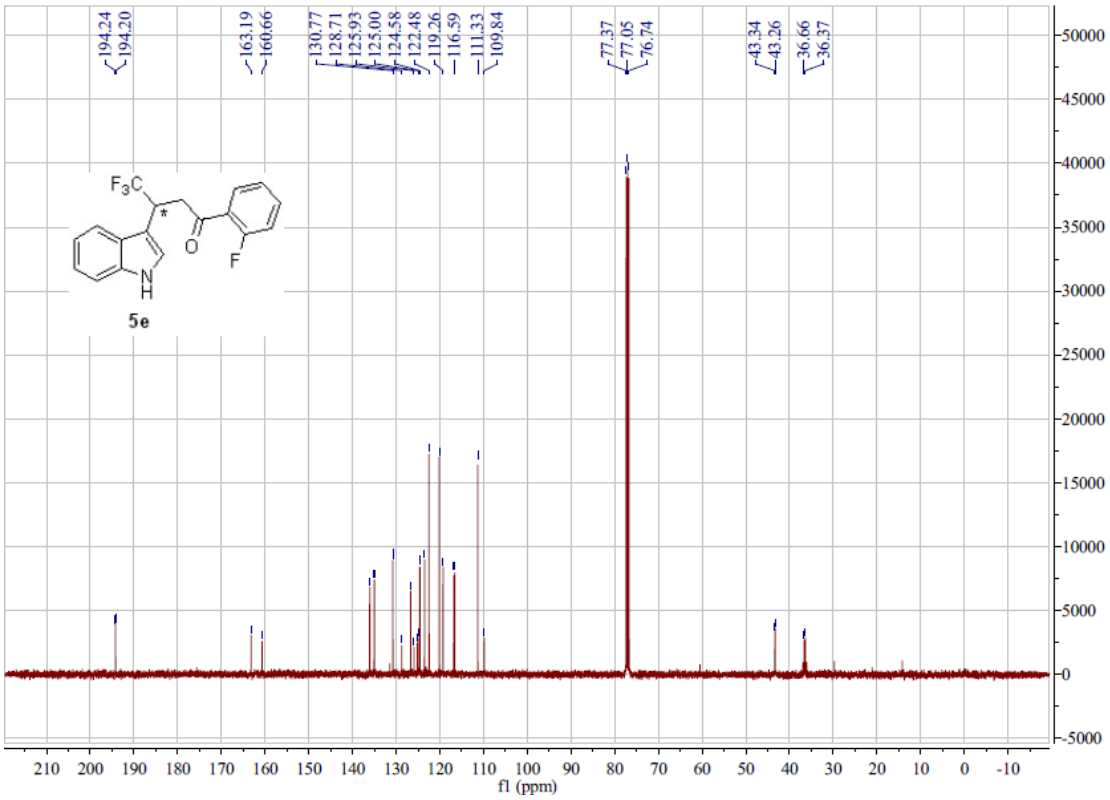

5b
E (qd) 3.72
B (m) 7.19
J (d) 7.74
L (m) 8.23
I (dd) 7.33
K (m) 8.01
A (m) 4.59
E (qd) 3.72
f1 (ppm)

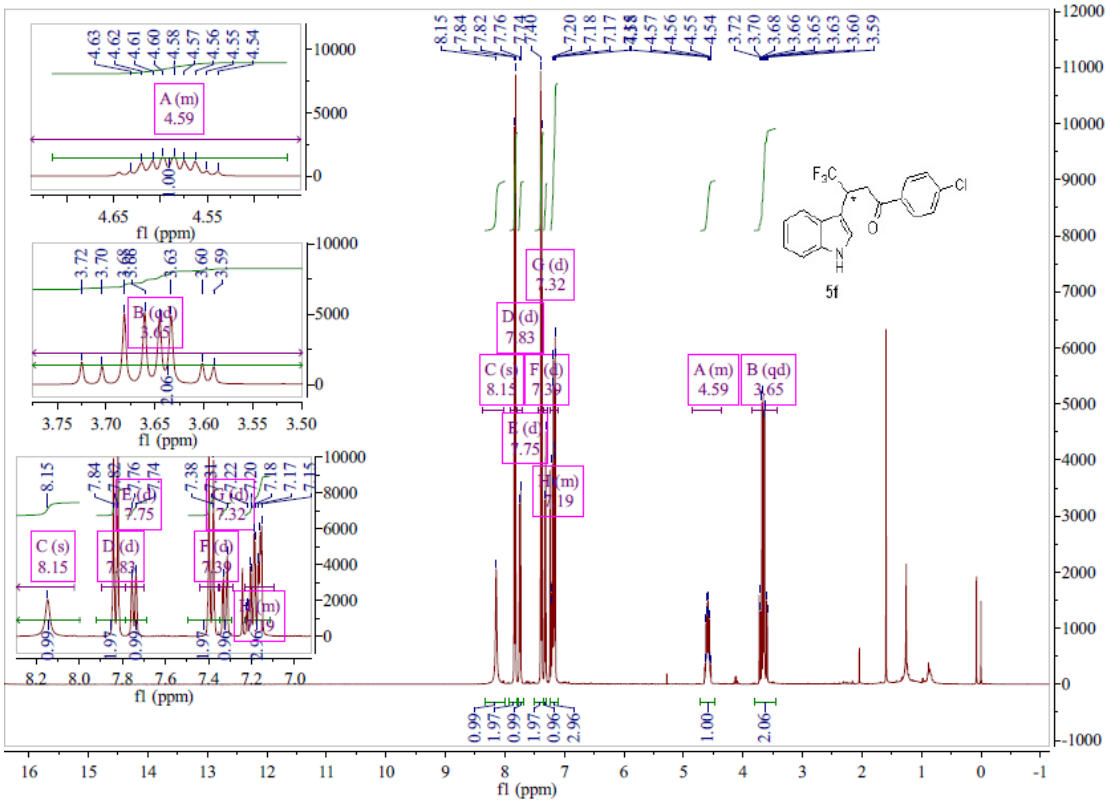

5c
A (m) 4.61
G (dd) 7.32
E (d) 7.82
D (s) 8.15
H (m) 7.18
F (d) 7.76
A (m) 4.61
B (qd) 3.67
C (s) 2.38
f1 (ppm)

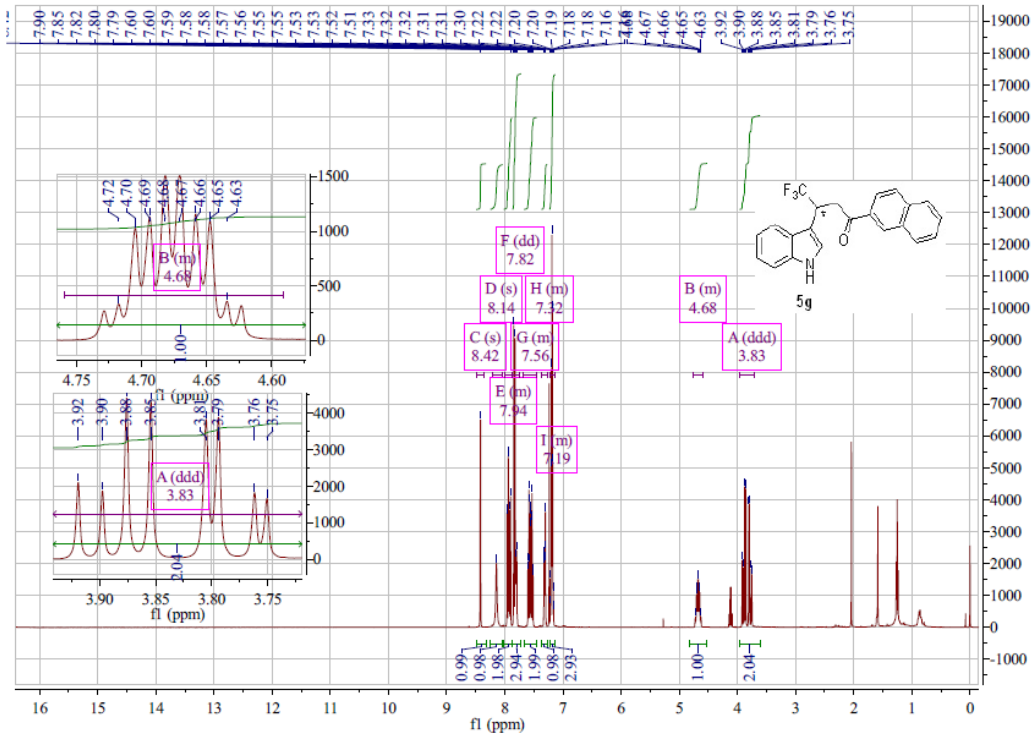

B (qd)
3.74
G (t)
7.61
D (ddd)
8.38
I (m)
7.19
C (t)
8.70
F (d)
7.75
E (m)
8.20
H (dd)
7.14
A (pd)
4.61
B (qd)
3.74
5d
fl (ppm)

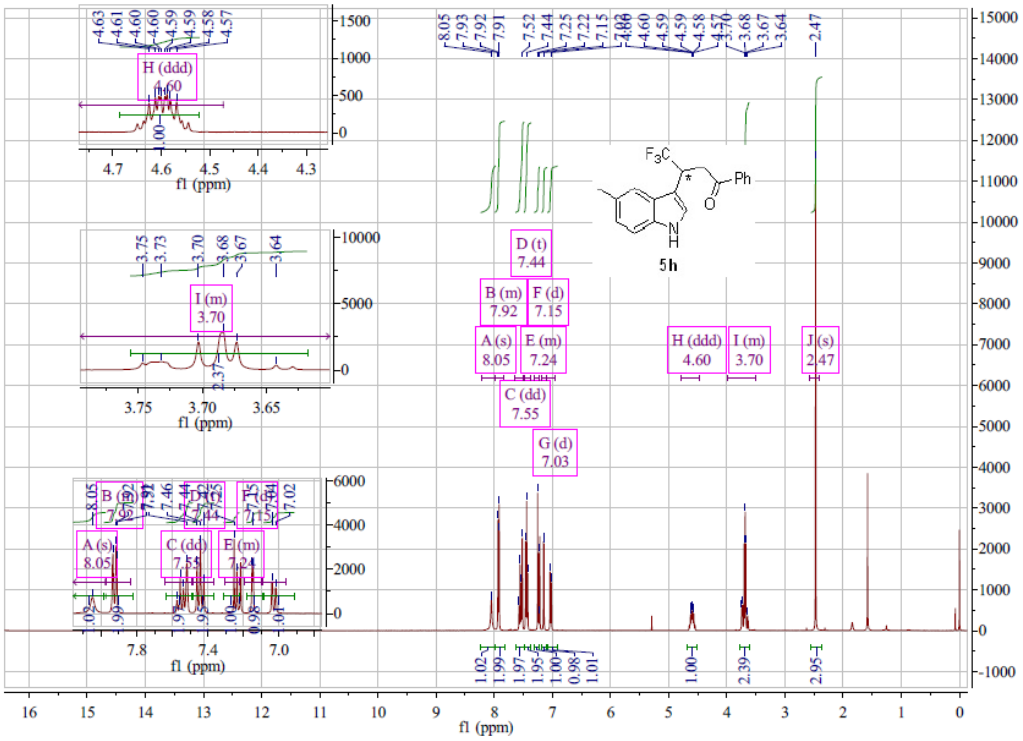

A (s)
38.88
5d
fl (ppm)

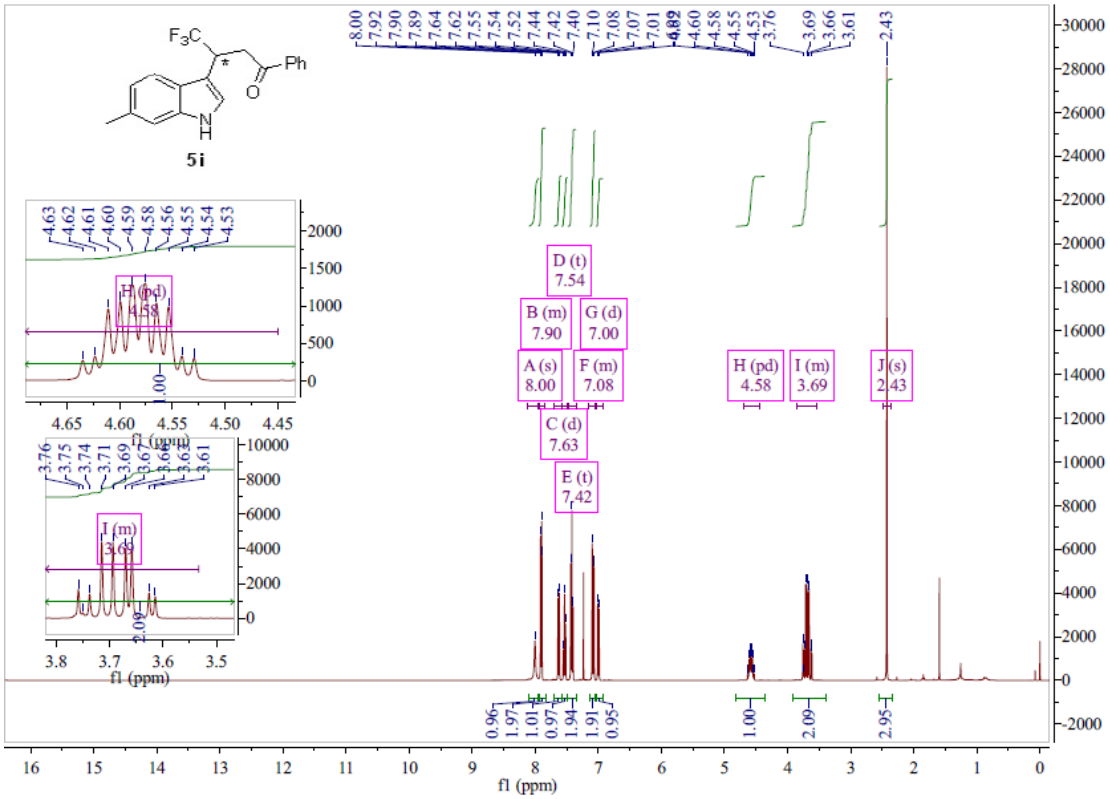

5e
M (ddd) 7.73
K (dd) 7.52
N (s) 8.15
G (m) 7.16
D (ddd) 7.73
I (m) 4.60
H (m) 3.72
C (s) 8.15
F (dd) 7.52
A (m) 4.60
B (m) 3.72
E (m) 7.49
L (m) 7.49
B (m) 3.72
A (m) 4.60
f1 (ppm)

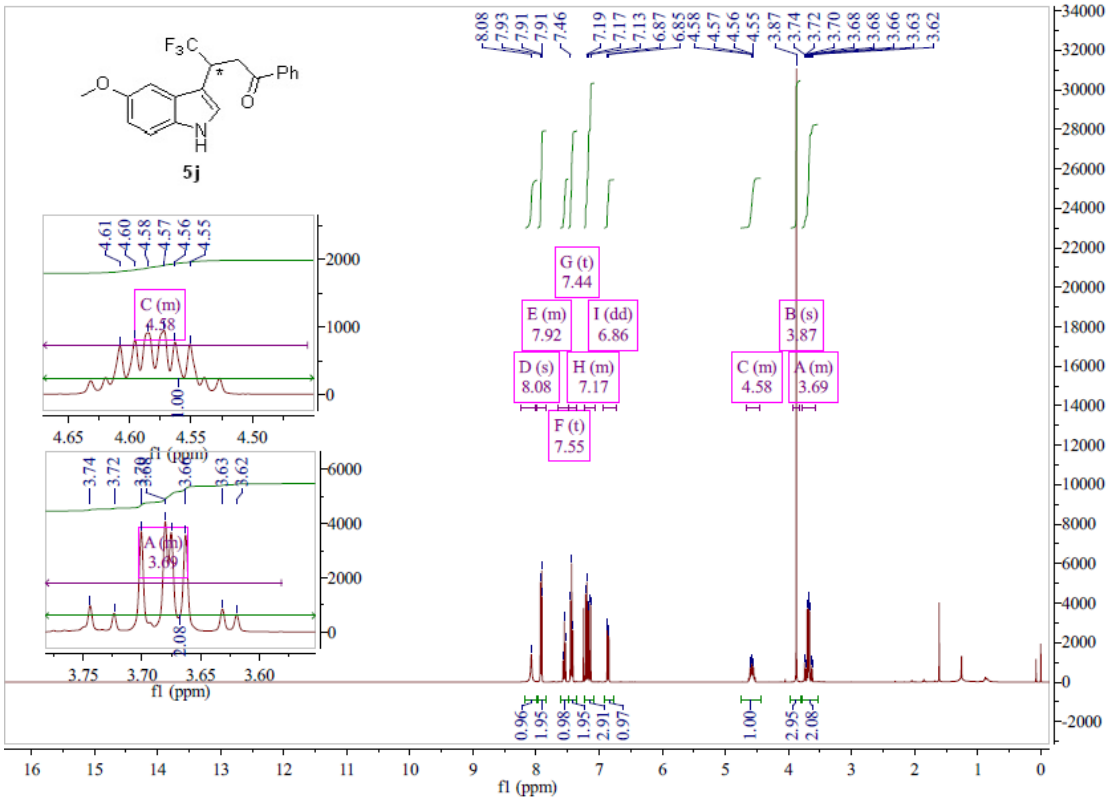

5e
f1 (ppm)

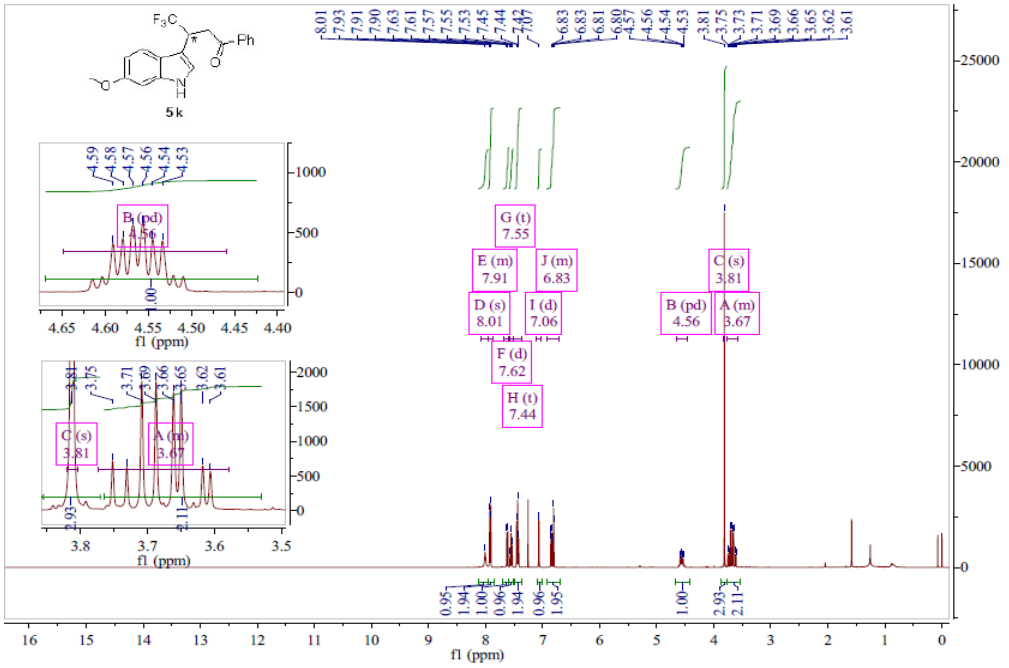

A (m) 4.59
B (qd) 3.65
C (s) 8.15
D (d) 7.83
E (d) 7.75
F (d) 7.39
G (d) 7.32
H (m) 7.19
5f

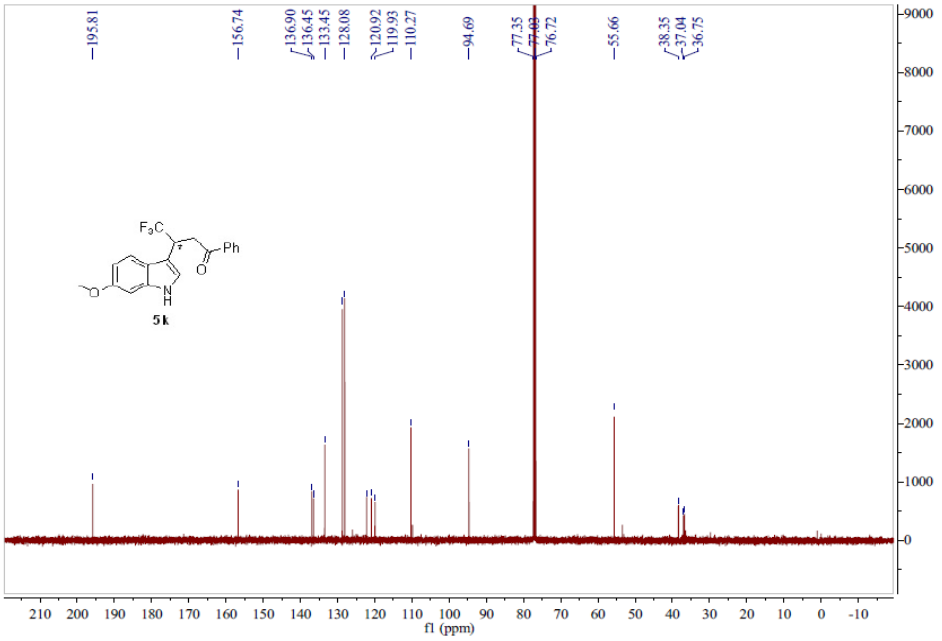

B (m) 4.68
A (ddd) 3.83
C (s) 8.42
D (s) 8.14
E (m) 7.94
F (dd) 7.82
G (m) 7.56
H (m) 7.32
I (m) 7.19
5g

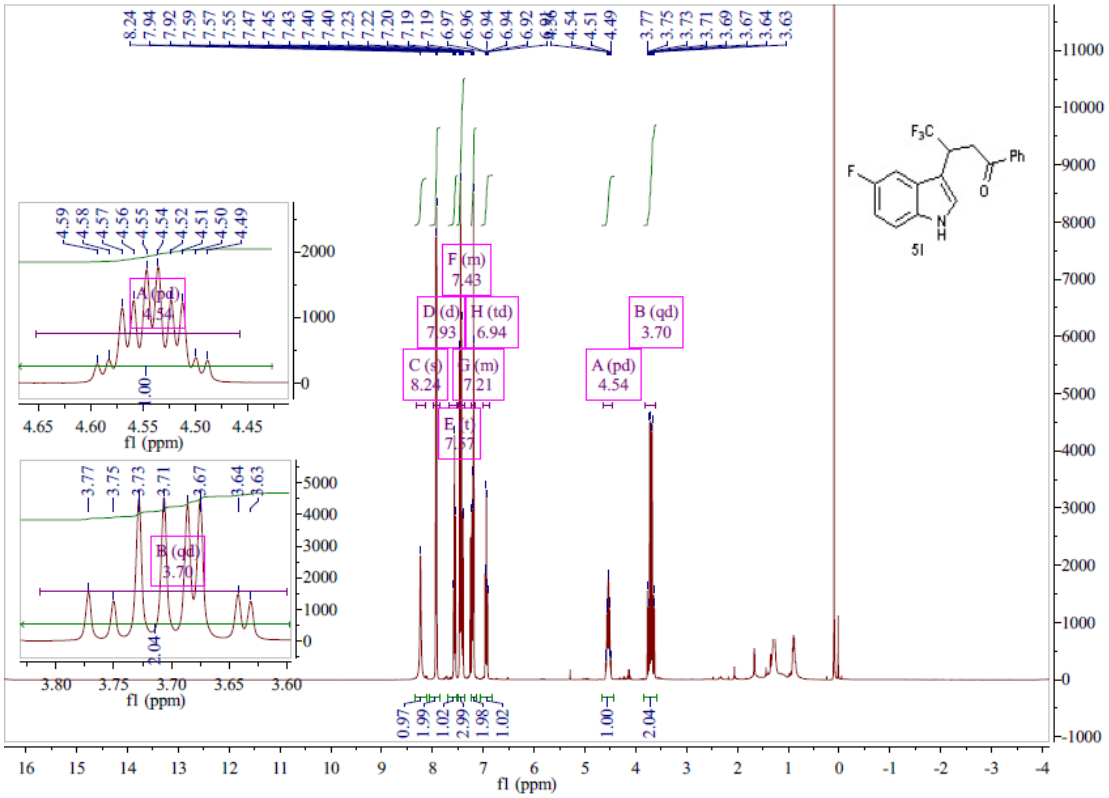

H (ddd) 4.60
I (m) 3.70
D (t) 7.44
B (m) 7.92
F (d) 7.15
A (s) 8.05
E (m) 7.24
H (ddd) 4.60
I (m) 3.70
J (s) 2.47
C (dd) 7.55
G (d) 7.03
5h
f1 (ppm)

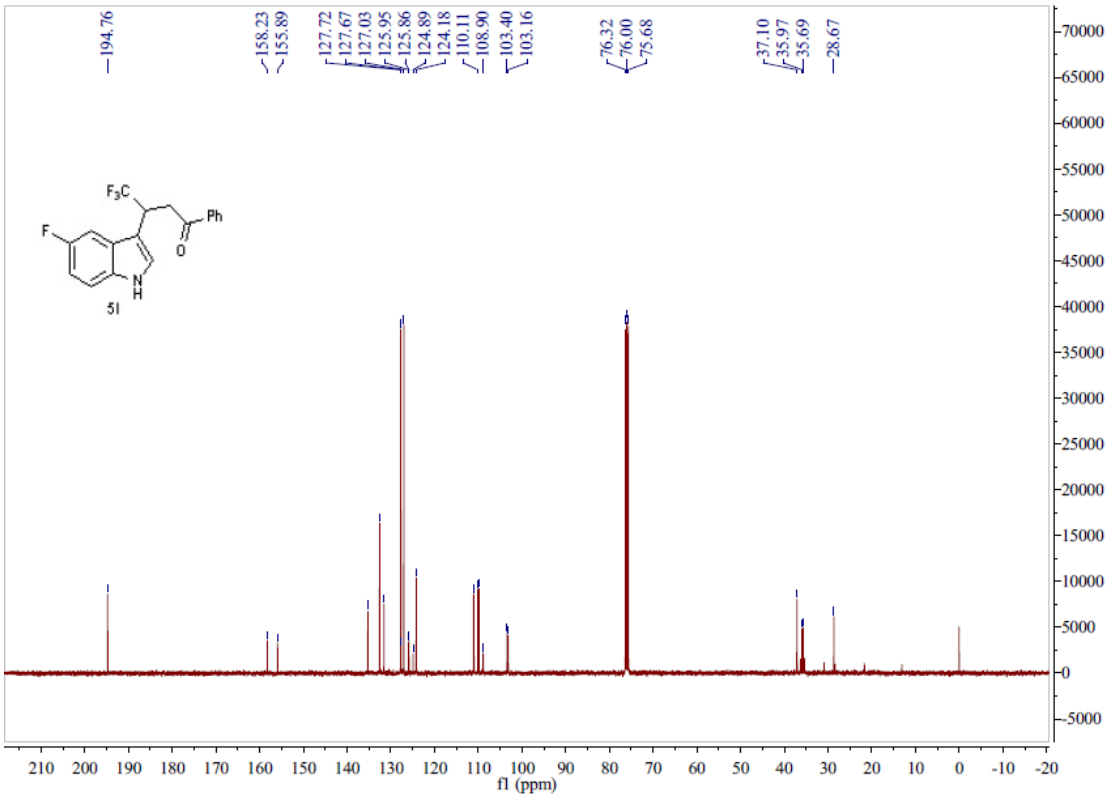

5i
H (pd) 4.58
I (m) 3.69
D (t) 7.54
B (m) 7.90
G (d) 7.00
A (s) 8.00
F (m) 7.08
H (pd) 4.58
I (m) 3.69
J (s) 2.43
C (d) 7.63
E (t) 7.42
f1 (ppm)

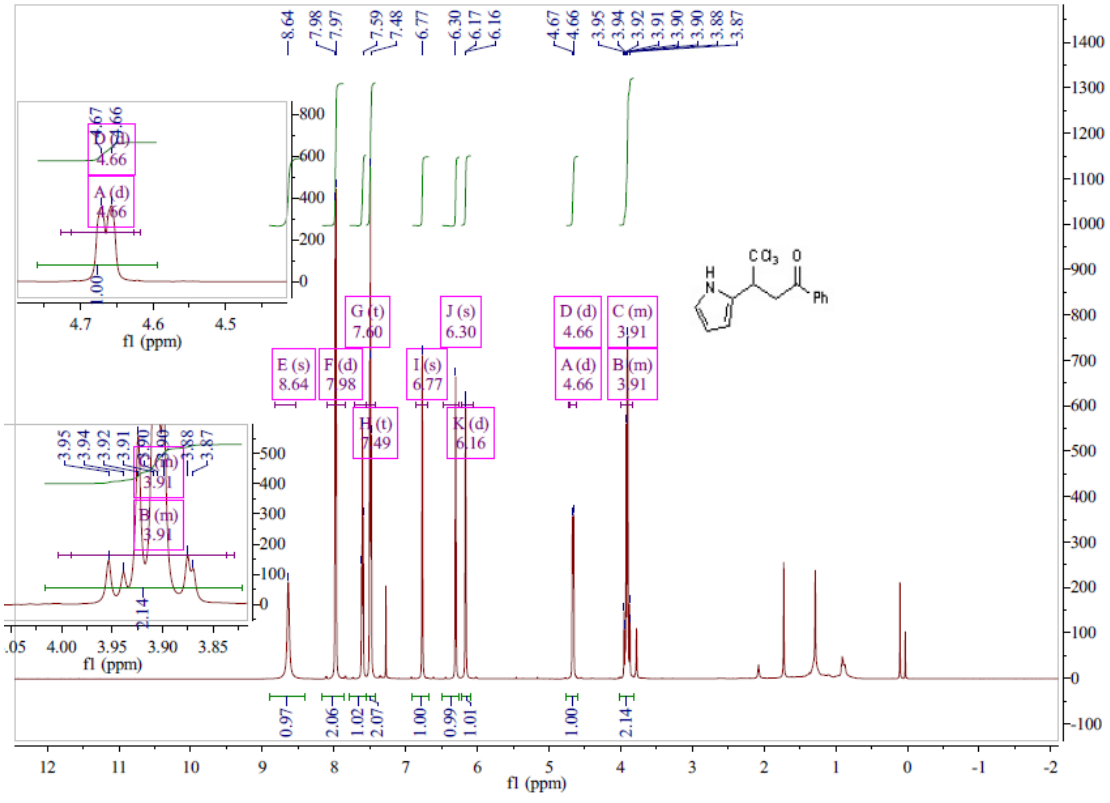

5j
G (t) 7.44
E (m) 7.92
I (dd) 6.86
B (s) 3.87
D (s) 8.08
H (m) 7.17
C (m) 4.58
A (m) 3.69
F (t) 7.55
C (m) 4.58
A (m) 3.69
f1 (ppm)

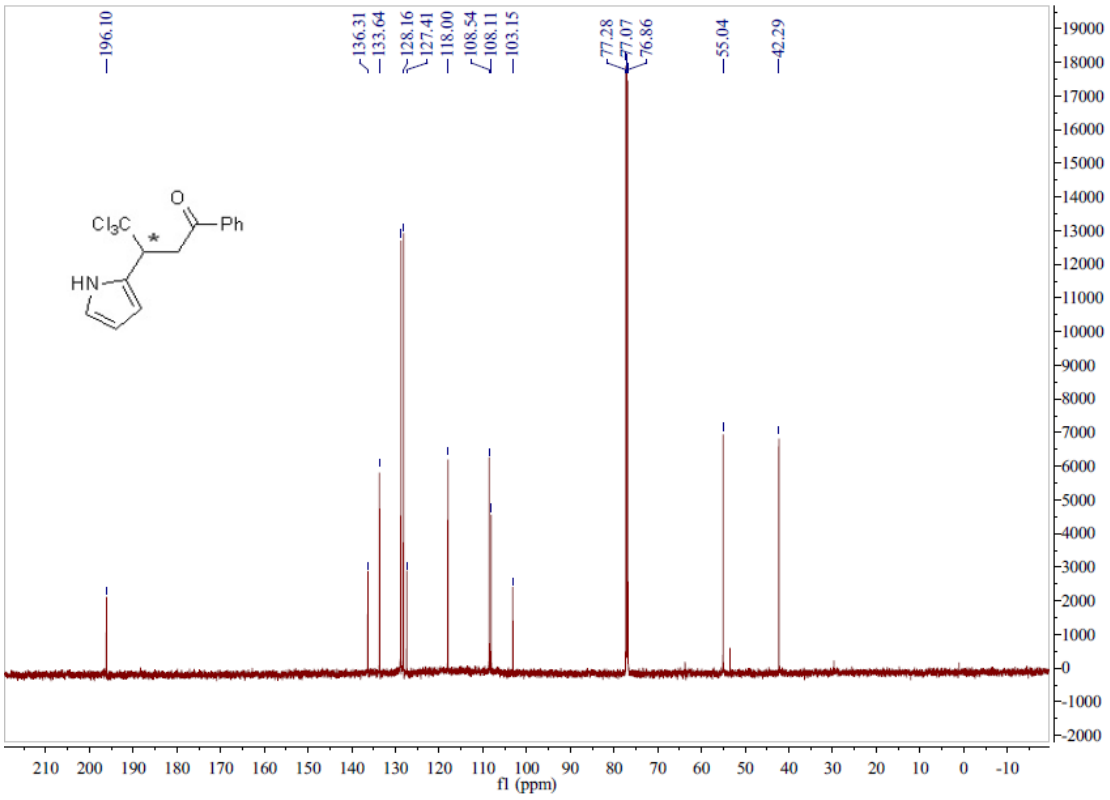

5k
B (pd) 4.56
G (t) 7.55
E (m) 7.91
J (m) 6.83
C (s) 3.81
D (s) 8.01
I (d) 7.06
B (pd) 4.56
A (m) 3.67
F (d) 7.62
H (t) 7.44
C (s) 3.81
A (m) 3.67
f1 (ppm)


195.81
156.74
136.90
136.45
133.45
128.08
120.92
119.93
110.27
94.69
77.35
77.03
76.72
55.66
38.35
37.04
36.75
F3C
Ph
O
N
H
5k
fl (ppm)


F3C
Ph
F
O
N
H
5l
F (m) 7.43
D (d) 7.93
H (td) 6.94
B (qd) 3.70
C (s) 8.24
G (m) 7.21
A (pd) 4.54
E (t) 7.57
A (pd) 4.54
B (qd) 3.70
fl (ppm)


194.76
158.23
155.89
127.72
127.67
127.03
125.95
125.86
124.89
124.18
110.11
108.90
103.40
103.16
76.32
76.00
75.68
37.10
35.97
35.69
28.67
F3C
Ph
F
O
N
H
5l
fl (ppm)


8.64
7.98
7.97
7.59
7.48
6.77
6.30
6.17
6.16
4.67
4.66
3.95
3.94
3.92
3.91
3.90
3.88
3.87
A (d) 4.66
D (d) 4.66
C (m) 3.91
B (m) 3.91
E (s) 8.64
F (d) 7.98
G (t) 7.60
H (t) 7.49
I (s) 6.77
J (s) 6.30
K (d) 6.16
CCl3
O
H
N
Ph
0.97
2.06
1.02
2.07
1.00
0.99
1.01
1.00
2.14
fl (ppm)


196.10
136.31
133.64
128.16
127.41
118.00
108.54
108.11
103.15
77.28
77.07
76.86
55.04
42.29
O
Cl3C
Ph
HN
fl (ppm)