Supporting Information

Indoles Synthesized from Amines via Copper Catalysis

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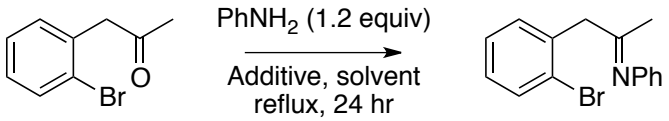
General Considerations

All reactions were carried out in flame- or oven-dried glassware. THF, toluene, benzene, ether, DMF, dioxane, and CH_2Cl_2 were purged with argon and dried over activated alumina columns. Flash chromatography was performed on 60Å silica gel (Sorbent Technologies). Analytical thin layer chromatography was performed on EMD silica gel/TLC plates with fluorescent indicator 254 nm. The ^{1}H, and ^{13}C NMR spectra were recorded on a JEOL ECA-500 or ECX-400P spectrometer using residual solvent peak as an internal reference ($CDCl_3$: 7.25 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR. IR spectra were obtained using a ThermoNicolet Avatar 370 FT-IR instrument. GCMS analyses were performed on a Shimadzu GCMS-QP2010S chromatographer equipped with a Shimadzu column (SHRXI-5MS, 0.25 mm x 0.25 u x 30 M). HRMS analyses were performed under contract by UT Austin's mass spectrometric facility via positive mode ESI method and US10252005 instrument. Commercially available compounds were purchased from

Aldrich Chemical Co., Acros Organics, Alfa Aesar, Strem Chemicals, JT Baker, or TCI America and were used without further purification. CuI and powdered K_3PO_4 were stored and handled in an inert atmosphere.

Reaction Optimization



entry	additive	solvent	SM : imine[a]
1[b]	$MgSO_4$	PhMe	3 : 97
2 [b]	4 Å mol. sieves	PhMe	1 : 99
3	$MgSO_4$	PhMe	70 : 30
4	3 Å mol. sieves	PhMe	20 : 80
5	p-TsOH (0.1 equiv)	PhMe (-H_2O)[c]	4 : 96
6	p-TsOH (0.1 equiv)	PhH (-H_2O)[c]	1 : 99

[a] Determined by GCMS. [b] 2-bromophenylacetaldehyde. [c] Dean-Stark

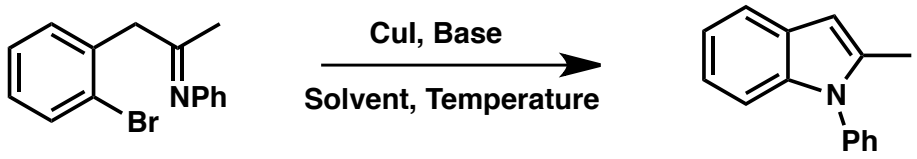
Figure 1. Optimization table for imine formation

All optimization reactions were performed on a 0.33 mmol scale.

General procedure for imine formation from ketones (entry 6): A flame dried two-neck round-bottom flask that was affixed to a Dean-Stark apparatus was charged with 2-bromophenylacetone (**SI-1**) (50 μL, 0.33 mmol) under an argon atmosphere. Anhydrous toluene (3.3 mL) was added. *p*-Toluenesulfonic acid (6.25 mg, 0.033 mmol) and aniline (35 μL, 0.39 mmol) were then added. The reaction mixture was stirred at reflux until GCMS analysis revealed consumption of the ketone (16 hours). The reaction mixture was concentrated (either by reduced pressure or distillation of solvent into the Dean-Stark trap), and the crude imine was then immediately used for the following cyclization.

General procedure for imine formation from aldehydes (entries 1 & 2): A flame dried round-bottom flask containing desiccant was charged with 2-bromophenylacetaldehyde (**SI-2**) (50 μL, 0.33 mmol) under an argon atmosphere. Anhydrous toluene (3.3 mL) was added. Aniline (35 μL, 0.39 mmol) was then added. The reaction mixture was stirred at room temperature until GCMS analysis revealed consumption of the aldehyde. The mixture was then filtered anhydrously through a short plug of flame-dried Celite® via cannula transfer to a receiving flask.

Toluene was used to rinse the donating flask. The mixture containing the crude imine was then concentrated *in vacuo* and immediately used for the following cyclization.



Entry	Catalyst %	Base	Ligand	Solvent	Temp. °C	Time (hr)	Indole:Furan:SM
1	20	K_3PO_4	--	DMF	90	16	65:35:0
2	10	K_3PO_4	--	DMF	90	16	62:37:0
3	5	K_3PO_4	--	DMF	90	16	64:37:0
4	10	K_3PO_4[b]	--	DMF	90	16	80%[a] 99:1:0
5	10	Cs_2CO_3	--	DMF	90	16	68:32:0
6	10	NaOtBu	--	DMF	90	16	81:9:10
7	10	K_3PO_4[b]	--	PhMe	90	16	NR
8	10	Cs_2CO_3	--	PhMe	90	16	NR
9	10	NaOtBu	--	PhMe	90	16	NR
10	10	K_3PO_4[b]	EN	PhMe	90	16	NR
11	10	K_3PO_4[b]	TMEDA	PhMe	90	16	10:0:90
12	10	K_3PO_4[b]	EN	Dioxane	90	16	3:26:71
13	10	K_3PO_4[b]	TMEDA	Dioxane	90	16	NR
14	10	K_3PO_4[b]	EN	DMF	90	16	12:0:88
15	10	K_3PO_4[b]	TMEDA	DMF	90	16	36:0:64

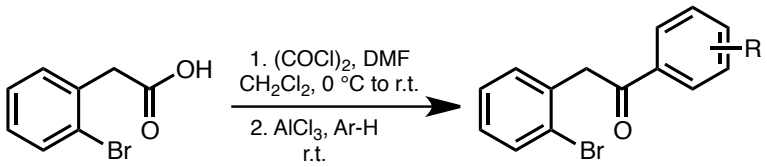
[a]Isolated yields.[b]Flame dried.

Figure 2. Improving indole formation

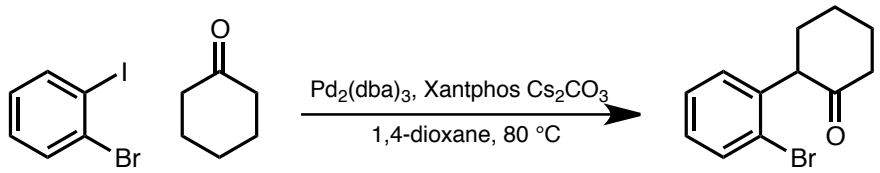
General procedure (entry 4): To the round-bottom flask containing the crude imine, solvent (2 mL), CuI (6.3 mg, 0.033 mmol), and base (0.66 mmol) were added under a stream of argon. The reaction mixture was then vigorously stirred at 110 °C. After 24 hours, TLC and GC analysis showed no trace of the imine. After cooling, the reaction mixture was diluted in 25% ethyl acetate in hexanes and filtered through a short plug of Celite®. Water was added to the filtrate, and the mixture was then extracted 3 times with 25% ethyl acetate in hexanes. The organic phases were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to yield crude product. The residue was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes.

Syntheses of the Starting Materials

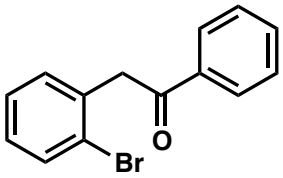
Synthesis of α-Aryl Ketones



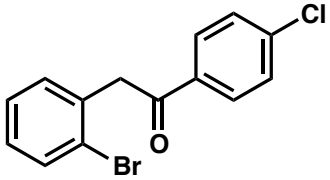
General Procedure A: A flame-dried round-bottom flask was charged with 2-bromophenylacetic acid (200 mg, 0.932 mmol) under an argon atmosphere. Anhydrous CH_2Cl_2 (2 mL) was added, and the flask was cooled to 0 ˚C in an ice bath. DMF (8 μL, 0.093 mmol) and oxalyl chloride (96 μL, 1.116 mmol) were then added drop wise to the stirring solution. The reaction mixture was then stirred for six hours while cooling to room temperature. The reaction was concentrated, and the crude acid chloride was dissolved in anhydrous benzene. A flame-dried round bottom flask was charged with $AlCl_3$ (161.6 mg, 1.21 mmol). Anhydrous benzene was added. To the vigorously stirring mixture of $AlCl_3$ in benzene, the crude acid chloride was added drop wise and allowed to stir at room temperature for 18 hours. The crude mixture was then added to a stirring mixture of HCl/ice for 30 minutes. The organic phase was separated, and the aqueous phase was extracted (2x) with 15 mL of CH_2Cl_2. The organic phases were combined, washed with 10% NaOH, brine, dried over anhydrous $MgSO_4$, and concentrated. The crude product was purified by column chromatography on silica gel.



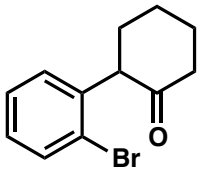
General Procedure B: A flame-dried round-bottom flask was charged with Cs_2CO_3 (9.13 g, 28.0 mmol), $Pd_2(dba)_3$ (58 mg, 0.064 mmol), and Xantphos (88 mg, 0.153 mmol). The flask was purged and back-filled with argon three times before anhydrous 1,4-dioxane (12.7 mL) was added. 1-bromo-2-iodobenzene (1.63 mL, 12.74 mmol) and cyclohexanone (2.66 mL, 25.48 mmol) were then added to the mixture, which was allowed to stir vigorously at 80 °C for 24 hours. After cooling, the reaction mixture was diluted by ether and filtered through a small plug of Celite®. Water was added to the filtrate, and the mixture was extracted (3 times) with ether. The organic extracts were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography on silica gel.



2-(2-bromophenyl)-1-phenylethanone (SI-3) was synthesized from 2-bromophenylacetic acid (200 mg, 0.932 mmol) and benzene following general procedure A. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as the eluent. The product was obtained as white solid (191.5 mg, 75% yield). ^1H and ^{13}C NMR were in accord with the data reported in literature.[1]

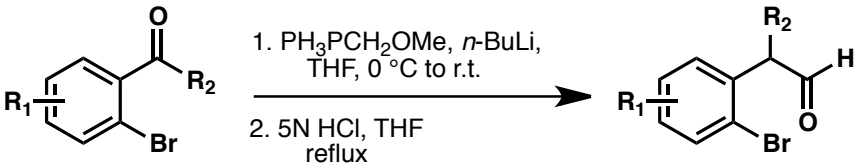


2-(2-bromophenyl)-1-(4-chlorophenyl)ethanone (SI-4) was synthesized from 2-bromophenylacetic acid (400 mg, 1.864 mmol) and chlorobenzene following general procedure A. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 as the eluent. The product was obtained as a white solid (373.6 mg, 65% yield). ^1H and ^{13}C NMR were in accord with the data reported in literature.[2]

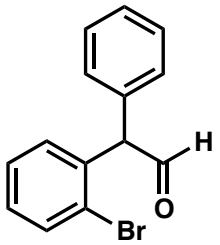


2-(2-bromophenyl)cyclohexanone (SI-5) was synthesized from cyclohexanone (2.66 mL, 25.48 mmol) and 1-bromo-2-iodobenzene (1.63 mL, 12.74 mmol) following general procedure B. The crude product was purified by column chromatography on silica gel using 10% EtOAc in hexanes as the eluent. The product was obtained as a white solid (810.2 mg, 25% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[3]

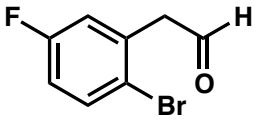
Synthesis of α-Aryl Aldehydes



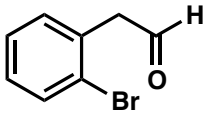
General Procedure C: A flame-dried round-bottom flask was charged with (methoxymethyl)triphenylphosphonium chloride (3.94 g, 11.49 mmol) under an argon atmosphere. Anhydrous THF (25 mL) was added, and the flask was cooled to 0 ˚C. *n*-BuLi (4.6 mL, 2.5M in hexanes) was then added drop wise to the vigorously stirred mixture, which was allowed to stir for 30 minutes at 0 ˚C. The benzylic carbonyl compound (9.58 mmol) was then added dropwise to the ylide solution. The reaction was allowed to stir for 24 hours at room temperature or until TLC analysis revealed consumption of the ketone or aldehyde. The mixture was quenched with saturated NH_4Cl and diluted with ether. The mixture was extracted 3 times with ether, and the organic extracts were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was then diluted in pentane and passed through a short plug of silica to remove the phosphine oxide. The mixture was concentrated, and the crude enol ether was dissolved in THF (25 mL). HCl (5N, 10 mL) was added to the reaction mixture, which was then refluxed until TLC analysis revealed complete hydrolysis of the enol ether (~2-6 hours). After cooling, the reaction mixture was diluted with ether and neutralized with saturated $NaHCO_3$. The mixture was then extracted 3 times with ether. The organic extracts were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo.* The crude product was purified by column chromatography on silica gel.



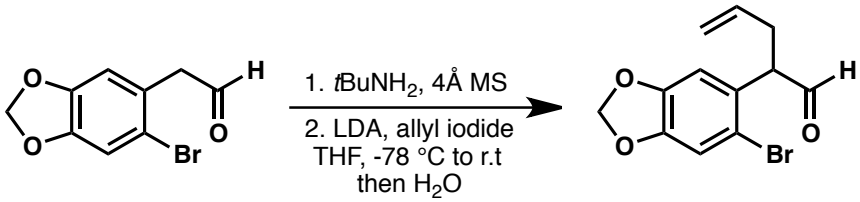
2-(2-bromophenyl)-2-phenylacetaldehyde (SI-6) was synthesized from 2-bromobenzophenone (1.75 mL, 9.58 mmol) following general procedure C. The crude product was purified by column chromatography on silica gel using 5% EtOAc in hexanes as the eluent. The product was obtained as a yellow oil (952.3 mg, 36% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[4]



2-(2-bromo-5-fluorophenyl)acetaldehyde (SI-7) was synthesized from 2-bromo-5-fluorobenzaldehyde (971.4 mg, 4.785 mmol) following general procedure C. The crude product was purified by column chromatography on silica gel using 25% EtOAc in hexanes as the eluent. The product was obtained as a white solid (404.6 mg, 39% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[5]



2-(2-bromophenyl)acetaldehyde (SI-2) was synthesized from 2-bromobenzaldehyde (1.6 mL, 13.71 mmol) following general procedure C. The crude product was purified by vacuum distillation (0.30 mmHg, 65 °C). The product was obtained as a colorless oil (1.80 g, 66% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[6]



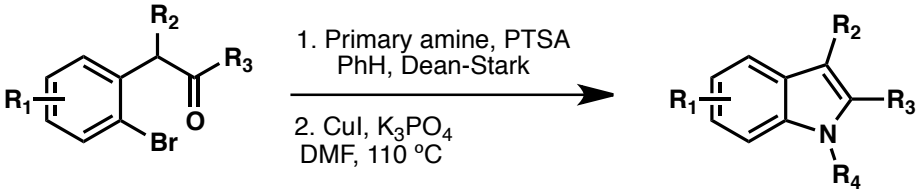
2-(6-bromobenzo[*d*][1,3]dioxol-5-yl)pent-4-enal (SI-9) was synthesized from **2-(6-bromobenzo[*d*][1,3]dioxol-5-yl)acetaldehyde (SI-8)**, which was made from 2-bromopiperonal (5.0 g, 21.83 mmol) following general procedure C. **(SI-8)** was purified by column

chromatography on silica gel using a 10-15% gradient of EtOAc in hexanes as the eluent. The product was obtained as a white solid (3.0 g, 57% yield).

A flame-dried round-bottom flask was charged with **(SI-8)** (3.0 g, 12.34 mmol) and 4Å powdered molecular sieves under an argon atmosphere. *tert*-butylamine (25 mL) was added and the mixture was allowed to stir vigorously at room temperature for 24 hours. The mixture was then filtered anhydrously through a short plug of flame-dried Celite® via cannula transfer to a receiving flask. Benzene was used to rinse the donating flask. The mixture containing the crude imine was then concentrated *in vacuo* and dissolved in anhydrous THF.

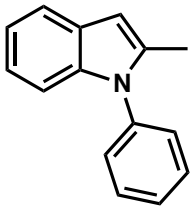
To a flame-dried round-bottom flask, iPr_2NH (2.25 mL, 16.04 mmol) and anhydrous THF (60 mL) were added and cooled to -78 °C via dry ice/acetone bath. *n*-BuLi (5.92 mL, 14.81 mmol) was then added drop wise to the stirring solution to form LDA. After 30 minutes, the crude imine was added via cannula transfer to the stirring solution of LDA. After a period of 30 minutes, allyl iodide (1.24 mL, 13.57 mmol) was added via syringe to the reaction mixture, which was then allowed to cool to room temperature over 2 hours. The solvent was removed *in vacuo* and water was added to the reaction mixture to be stirred over a period of 24 hours. CH_2Cl_2 was added to the flask, and the mixture was extracted 3 times with CH_2Cl_2. The organic extracts were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The crude product was purified by column chromatography on silica gel using a 10-20% gradient of EtOAc in hexanes. The product **(SI-9)** was obtained as a tan-colored oil (1.27 g, 36% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.60 (s, 1H), 7.01 (s, 1H), 6.52 (s, 1H), 5.93 (s, 2H), 5.71-5.63 (m, 1H), 5.00-4.97 (d, *J* = 17 Hz, 1H), 4.96-4.94 (d, *J* = 10 Hz, 1H), 4.11 (t, *J* = 7.2 Hz, 1H), 2.77-2.72 (m, 1H), 2.40-2.35 (m, 1H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 199.4, 148.0, 147.9, 134.5, 128.4, 117.5, 116.1, 113.2, 109.2, 102.1, 56.9, 33.4. **IR (neat, cm^{-1}):** 1725, 1503, 1478, 1251, 1236, 1121, 1037, 928, 862, 832. **HRMS**-ESI m/z: [M+], calculated for $C_{12}H_{11}BrO_3$, 281.9892; found 281.9890. **R_f**: 0.64 in 25% EtOAc/hexanes.

Synthesis of *N*-Substituted Indoles

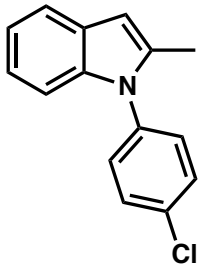


General Procedure D: A flame dried two-neck round-bottom flask that was affixed to a Dean-Stark apparatus was charged with the carbonyl compound (1.0 eq) under an argon atmosphere. Anhydrous benzene (0.1 M) was added. *p*-Toluenesulfonic acid (PTSA, 0.1 eq) and the primary amine (1.2 eq) were then added. The reaction mixture was stirred at reflux until GCMS analysis revealed consumption of the carbonyl compound (~16-24 hours). The reaction mixture was concentrated (either by reduced pressure or distillation of solvent into the Dean-Stark trap), and the crude imine was then immediately used for the following cyclization. To the same flask containing the crude imine, *N,N*-dimethylformamide (0.2 M), CuI (10 mol%), and K_3PO_4 (2.0 eq) were added under a stream of argon. The reaction mixture was then vigorously stirred at 110 °C until TLC analysis showed no trace of the initial carbonyl compound. After cooling, the reaction mixture was diluted in 25% ethyl acetate in hexanes and filtered through a plug of Celite®. Water was added to the filtrate, and the mixture was then extracted 3 times with 25% ethyl acetate in hexanes. The organic phases were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to yield crude product. The residue was purified by column chromatography on neutralized silica gel.

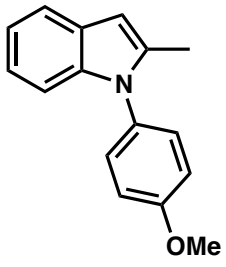
General Procedure E: A flame dried round-bottom flask containing 4Å molecular sieves was charged with the carbonyl compound (1.0 eq) under an argon atmosphere. Anhydrous benzene was added (0.1M), followed by the addition of the amine (1.5 eq). The reaction mixture was stirred vigorously at room temperature until GC analysis revealed consumption of the starting material. The mixture was then filtered anhydrously through a short plug of flame-dried Celite® via cannula transfer to a receiving flask. Benzene was used to rinse the donating flask. The mixture containing the crude imine was then concentrated *in vacuo*. To the same flask containing the crude imine, *N,N*-dimethylformamide (0.2 M), CuI (10 mol%), and K_3PO_4 (2.0 eq) were added under a stream of argon. The reaction mixture was then vigorously stirred at 110 °C until TLC analysis showed no trace of the initial carbonyl compound. After cooling, the reaction mixture was diluted in 25% ethyl acetate in hexanes and filtered through a plug of Celite®. Water was added to the filtrate, and the mixture was then extracted 3 times with 25% ethyl acetate in hexanes. The organic phases were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to yield crude product. The residue was purified by column chromatography on neutralized silica gel.



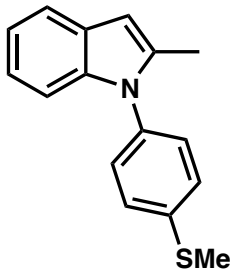
1-phenyl-2-methyl-1H-indole (Table 3, Entry 1) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and aniline (65 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a yellow oil (77 mg, 80% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 86 mg (88% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[7]



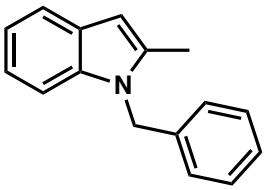
1-(4-chlorophenyl)-2-methyl-1H-indole (Table 3, Entry 2) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 4-chloroaniline (90 mg, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-2% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (86 mg, 76% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 94 mg (83% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.3 Hz, 1H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.11-7.04 (m, 3H), 6.38 (s, 1H), 2.26 (s, 3H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 138.1, 136.8, 136.6, 133.5, 129.8, 129.3, 128.4, 121.4, 120.4, 119.8, 109.9, 101.9, 13.4. **IR (neat, cm^{-1}):** 1492, 1459, 1388, 1323, 1088, 1012, 824, 789, 748, 739. **HRMS**-ESI m/z: [M+H], calculated for $C_{15}H_{13}NCl$, 242.0737; found 242.0731. **R_f**: 0.64 in 25% EtOAc/hexanes.



1-(4-methoxyphenyl)-2-methyl-1H-indole (Table 3, Entry 3) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 4-methoxyaniline (87 mg, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-5% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (97 mg, 87% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 89 mg (80% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[8]

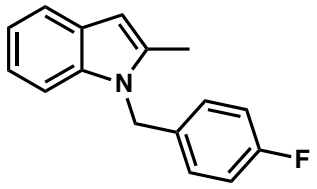


2-methyl-1-(4-methylthiophenyl)-1H-indole (Table 3, Entry 4) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 4-methylthioaniline (88 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-5% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (106 mg, 89% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 98 mg (83% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.16-7.10 (m, 3H), 6.43 (s, 1H), 2.59 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 138.4, 138.3, 137.2, 135.0, 128.5, 128.3, 127.2, 121.2, 120.2, 119.7, 110.1, 101.4, 15.9, 13.5. **IR (neat, cm^{-1}):** 1494, 1458, 1435, 1388, 1320, 1094, 815, 783, 745, 651. **HRMS**-ESI m/z: [M+H], calculated for $C_{16}H_{16}NS$, 254.1003; found 254.1002. **R_f**: 0.72 in 25% EtOAc/hexanes.

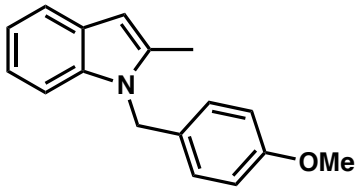


1-benzyl-2-methyl-1H-indole (Table 3, Entry 5) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 4-chloroaniline (90 mg, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a yellow solid (81 mg, 77%

yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 85 mg (82% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[9]

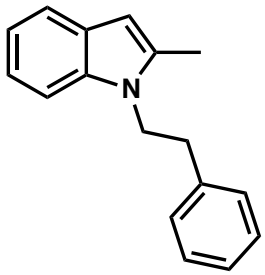


1-(4-fluorobenzyl)-2-methyl-1H-indole (Table 3, Entry 6) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 4-fluorobenzylamine (81 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (98 mg, 87% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 98 mg (87% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (d, J = 6.3 Hz, 1H), 7.25 (d, J = 6.9 Hz, 1H), 7.21-7.17 (m, 2H), 7.03-6.97 (m, 4H), 6.43 (s, 1H), 5.29 (s, 2H), 2.43 (s, 3H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 163.1, 161.2, 137.2, 136.7, 133.8, 128.4, 127.8, 127.7, 121.0, 120.0, 119.8, 115.9, 115.7, 109.3, 45.9, 12.9. **IR (neat, cm^{-1}):** 1507, 1463, 1220, 1155, 848, 829, 783, 760, 748, 738. **HRMS**-ESI m/z: [M+H], calculated for $C_{17}H_{15}NF$, 240.1189; found 240.1180. **R_f**: 0.64 in 25% EtOAc/hexanes.

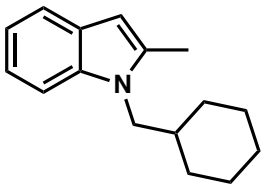


1-(4-methoxybenzyl)-2-methyl-1H-indole (Table 3, Entry 7) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 4-methoxybenzylamine (92 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (89 mg, 76% yield). Two similar experiments each starting with 100 mg (0.470 mmol) of the ketone gave 74 mg (63% yield) and 98 mg (83% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, J = 6.3 Hz, 1H), 7.18 (d, J = 7.5 Hz, 1H), 7.09-7.03 (m, 2H), 6.87 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 8.6 Hz, 2H), 6.29 (s, 1H), 5.19 (s, 2H), 3.70 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 158.8, 137.2, 136.8, 130.0, 128.2, 127.3, 120.8, 119.8, 119.5,

114.2, 109.3, 100.4, 55.3, 46.0, 12.9. **IR (neat, cm^{-1}):** 1510, 1455, 1237, 1174, 1031, 815, 771, 762, 751, 744. **HRMS**-ESI m/z: [M+], calculated for $C_{17}H_{17}NO$, 251.1310; found 251.1313. **R_f**: 0.57 in 25% EtOAc/hexanes.

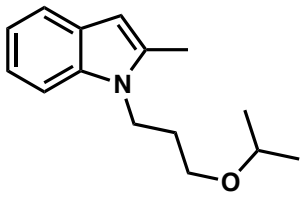


1-phenethyl-2-methyl-1H-indole (Table 3, Entry 8) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and phenethylamine (89 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a colorless oil (81 mg, 74% yield). Two similar experiments each starting with 100 mg (0.470 mmol) of the ketone gave 81 mg (74% yield) and 76 mg (69% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.31-7.24 (m, 3H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 6.9 Hz, 2H), 6.23 (s, 1H), 4.28 (t, *J* = 7.5 Hz, 2H), 3.04 (t, *J* = 7.5 Hz, 2H) 2.16 (s, 3H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 138.8, 136.7, 136.4, 129.0, 128.7, 128.4, 126.8, 120.6, 120.0, 119.8, 119.5, 109.1, 100.0, 99.9, 45.1, 36.5, 12.6. **IR (neat, cm^{-1}):** 1465, 1456, 1400, 1354, 1339, 1311, 771, 747, 736, 699. **HRMS**-ESI m/z: [M+H], calculated for $C_{17}H_{18}N$, 236.1439; found 236.1436. **R_f**: 0.63 in 25% EtOAc/hexanes.

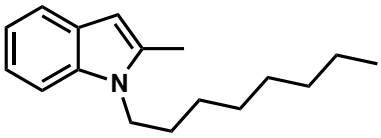


1-cyclohexylmethyl-2-methyl-1H-indole (Table 3, Entry 9) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and cyclohexanemethylamine (92 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (68 mg, 63% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 92 mg (86% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 10.0

Hz, 1H), 7.31 (d, J = 10.0 Hz, 1H), 7.18 (t, J = 7.1 Hz, 1H), 7.11 (t, J = 7.2 Hz, 1H), 6.29 (s, 1H), 3.92 (d, J = 7.5 Hz, 2H), 2.47 (s, 3H) 1.95-1.87 (m, 1H), 1.76-1.68 (m, 5H), 1.27-1.20 (m, 3H), 1.11-1.05 (m, 2H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 137.2, 137.0, 128.1, 120.3, 119.7, 119.2, 109.6, 99.9, 49.8, 39.0, 31.4, 26.5, 26.0, 13.3. **IR (neat, cm^{-1}):** 2932, 2917, 1468, 1450, 1401, 1356, 1342, 787, 749, 729. **HRMS**-ESI m/z: [M+H], calculated for $C_{16}H_{22}N$, 228.1752; found 228.1746. **R_f**: 0.66 in 25% EtOAc/hexanes.

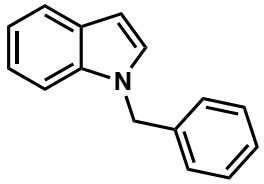


1-(3-isopropoxypropyl)-2-methyl-1H-indole (Table 3, Entry 10) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and 3-isopropoxypropylamine (98 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-2% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (77 mg, 71% yield). Two similar experiments each starting with 100 mg (0.470 mmol) of the ketone gave 74 mg (68% yield) and 83 mg (76% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.5 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 7.4 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 6.31 (s, 1H), 4.26 (t, J = 6.6 Hz, 2H), 3.60 (sept, J = 6.0 Hz 1H) 3.40 (t, J = 5.7 Hz, 2H), 2.51 (s, 3H), 2.06 (quin, J = 6.3 Hz, 2H), 1.25 (d, J = 5.7 Hz, 6H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 136.9, 136.8, 128.2, 120.4, 119.7, 119.3, 109.3, 100.0, 71.6, 64.6, 40.1, 30.7, 22.3, 12.8. **IR (neat, cm^{-1}):** 2976, 1461, 1400, 1336, 1312, 1143, 1129, 1090, 771, 747, 734. **HRMS**-ESI m/z: [M+H], calculated for $C_{15}H_{22}NO$, 232.1701; found 232.1699. **R_f**: 0.56 in 25% EtOAc/hexanes.

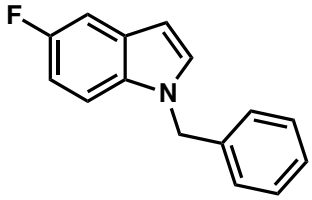


1-octyl-2-methyl-1H-indole (Table 3, Entry 11) was synthesized from 2-bromophenylacetone (100 mg, 0.470 mmol) and octylamine (117 μL, 0.705 mmol) following general procedure D. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a clear, yellow oil (90 mg,

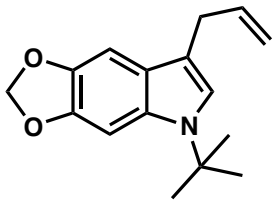
79% yield). A similar experiment starting with 100 mg (0.470 mmol) of the ketone gave 90 mg (79% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 6.9 Hz, 1H), 6.32 (s, 1H), 4.11 (t, *J* = 7.5 Hz, 2H), 2.50 (s, 1H), 1.82 (quin, *J* = 7.4 Hz), 1.41-1.36 (m, 10H), 0.98 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 136.8, 136.5, 128.2, 120.5, 119.8, 119.3, 109.2, 99.9, 43.4, 32.0, 30.4, 29.6, 29.4, 27.3, 22.8, 14.3, 13.0. **IR (neat, cm^{-1}):** 2954, 2926, 2855, 1462, 1401, 1355, 1311, 770, 731, 746. **HRMS**-ESI m/z: [M+H], calculated for $C_{17}H_{26}N$, 244.2065; found 244.2062. **R_f**: 0.69 in 25% EtOAc/hexanes.



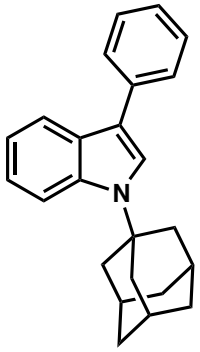
1-benzyl-1H-indole (Table 4, Entry 1) was synthesized from 2-bromophenylacetaldehyde **(SI-2)** (100 mg, 0.502 mmol) and benzylamine (82 μL, 0.754 mmol) following general procedure E. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a clear, yellow oil (45 mg, 43% yield). A similar experiment starting with 100 mg (0.502 mmol) of the aldehyde gave 39 mg (37% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[10]



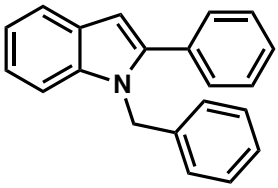
1-benzyl-5-fluoro-1H-indole (Table 4, Entry 2) was synthesized from **2-bromo-5-fluorophenylacetaldehyde (SI-7)** (400 mg, 1.84 mmol) and benzylamine (302 μL, 2.76 mmol) following general procedure D. PTSA was omitted. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a yellow oil (260 mg, 63% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[9]



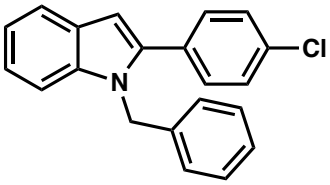
7-allyl-5-*tert*-butyl-5*H*-[1,3]dioxolo[4,5-*f*]indole (Table 4, Entry 3) was synthesized from **2-(6-bromobenzo[*d*][1,3]dioxol-5-yl)pent-4-enal (SI-9)** (100 mg, 0.353 mmol) following general procedure E. *t*-Butylamine (0.1M) was used as the solvent for the imine-forming step. The crude product was purified by column chromatography on neutralized silica gel using hexanes as the eluent. The product was obtained as a light brown solid (52 mg, 57% yield). A similar experiment starting with 100 mg (0.353 mmol) of the aldehyde gave 55 mg (61% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.11 (s, 1H), 6.98 (s, 1H), 6.93 (s, 1H), 6.08-6.00 (m, 1H), 5.91 (s, 1H), 5.17 (d, *J* = 18.0 Hz, 1H), 5.07 (d, *J* = 10.0 Hz, 1H), 3.43 (d, *J* = 6.3 Hz), 1.66 (s, 9H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 144.1, 141.8, 137.6, 130.2, 123.6, 121.7, 115.1, 111.7, 100.6, 97.9, 94.4, 55.5, 30.2, 29.8. **IR (neat, cm^{-1}):** 3089, 2979, 1639, 1466, 1279, 1243, 1222, 1196, 1065, 1034, 949, 907, 837. **HRMS**-ESI m/z: [M+H], calculated for $C_{16}H_{20}NO_2$, 258.1494; found 258.1485. **R_f**: 0.75 in 25% EtOAc/hexanes.



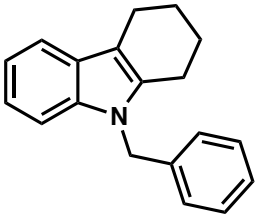
1-(adamantan-1-yl)-3-phenyl-1H-indole (Table 4, Entry 4) was synthesized from **2-(2-bromophenyl)-2-phenylacetaldehyde (SI-6)** (100 mg, 0.363 mmol) and adamantylamine (82 mg, 0.545 mmol) following general procedure D. PTSA was omitted. The crude product was purified by column chromatography on neutralized silica gel using a 0-0.5% gradient of ethyl acetate in hexanes. The product was obtained as a cream colored solid (111 mg, 94% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[11]



1-benzyl-2-phenyl-1H-indole (Table 4, Entry 5) was synthesized from **2-(2-bromophenyl)-1-phenylethanone (SI-3)** (100 mg, 0.363 mmol) and benzylamine (60 μL, 0.545 mmol) following general procedure D. Toluene was used in lieu of benzene. The crude product was purified by column chromatography on neutralized silica gel using a 0-1% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (60 mg, 58% yield). A similar experiment starting with 100 mg (0.363 mmol) of the ketone gave 81 mg (79% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[12]



1-benzyl-2-(4-chlorophenyl)-1H-indole (Table 4, Entry 6) was synthesized from **2-(2-bromophenyl)-1-(4-chlorophenyl)ethanone (SI-4)** (100 mg, 0.323 mmol) and benzylamine (52 μL, 0.485 mmol) following general procedure D. Toluene was used in lieu of benzene. The crude product was purified by column chromatography on neutralized silica gel using a 0-0.5% gradient of ethyl acetate in hexanes. The product was obtained as a white solid (60 mg, 58% yield). A similar experiment starting with 100 mg (0.353 mmol) of the ketone gave 65 mg (63% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (t, *J* = 3.5 Hz, 1H), 7.38 (s, 4H), 7.32-7.19 (m, 6H), 7.04 (d, *J* = 6.9, 2H), 6.69 (s, 1H), 5.36 (s, 2H). **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ 140.6, 138.3, 138.1, 134.4, 131.3, 130.5, 129.0, 128.9, 128.3, 127.4, 126.0, 122.4, 120.8, 120.5, 110.7, 102.8, 47.8. **IR (neat, cm^{-1}):** 1459, 1346, 1088, 1015, 839, 784, 751, 737, 729, 717. **HRMS**-ESI m/z: [M+H], calculated for $C_{21}H_{17}ClN$, 318.10440; found 318.10426. **R_f**: 0.69 in 25% EtOAc/hexanes.



9-benzyl-2,3,4,9-tetrahydro-1H-carbazole (Table 4, Entry 7) was synthesized from **2-(2-bromophenyl)cyclohexanone (SI-5)** (100 mg, 0.395 mmol) and benzylamine (65 μL, 0.594 mmol) following general procedure D. Toluene was used in lieu of benzene. The crude product was purified by column chromatography on neutralized silica gel using hexanes as the eluent. The product was obtained as a yellow solid (93 mg, 90% yield). ^{1}H and ^{13}C NMR were in accord with the data reported in literature.[13]

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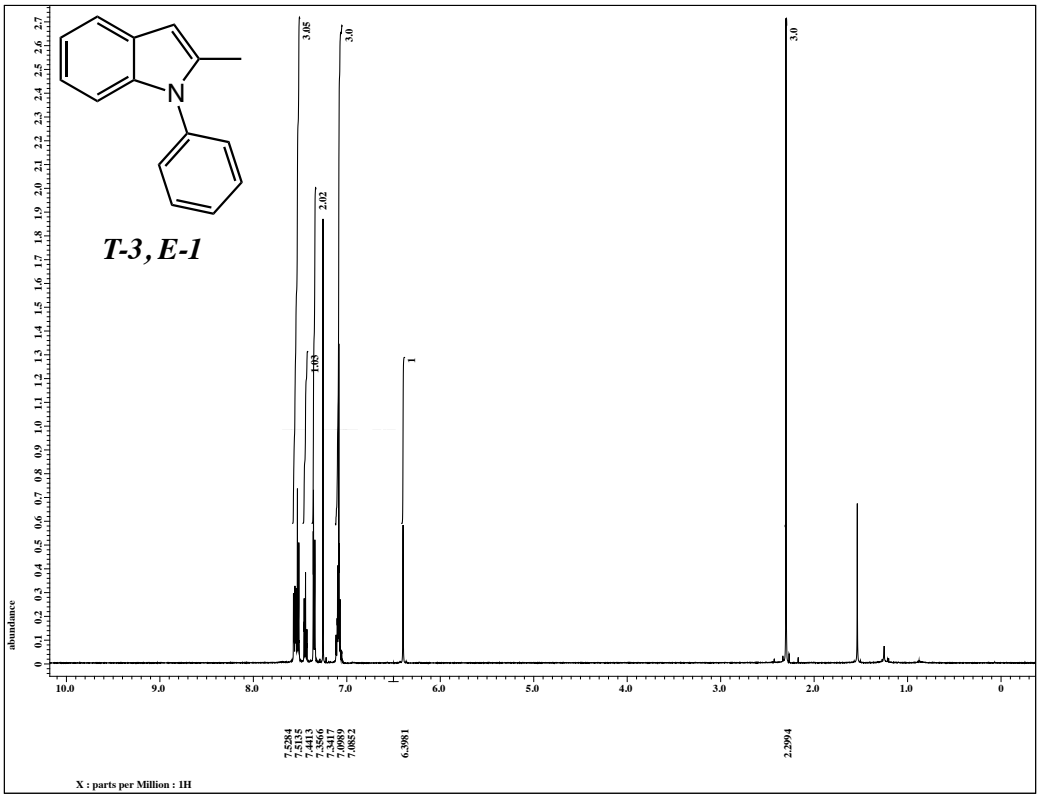
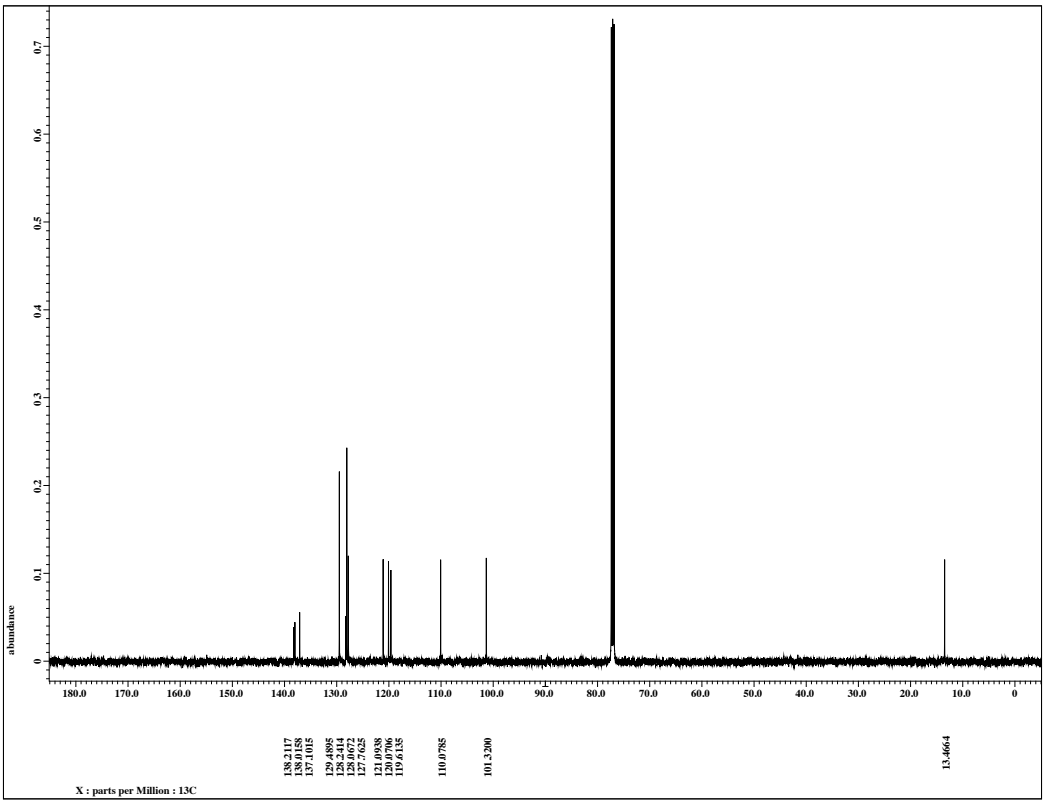
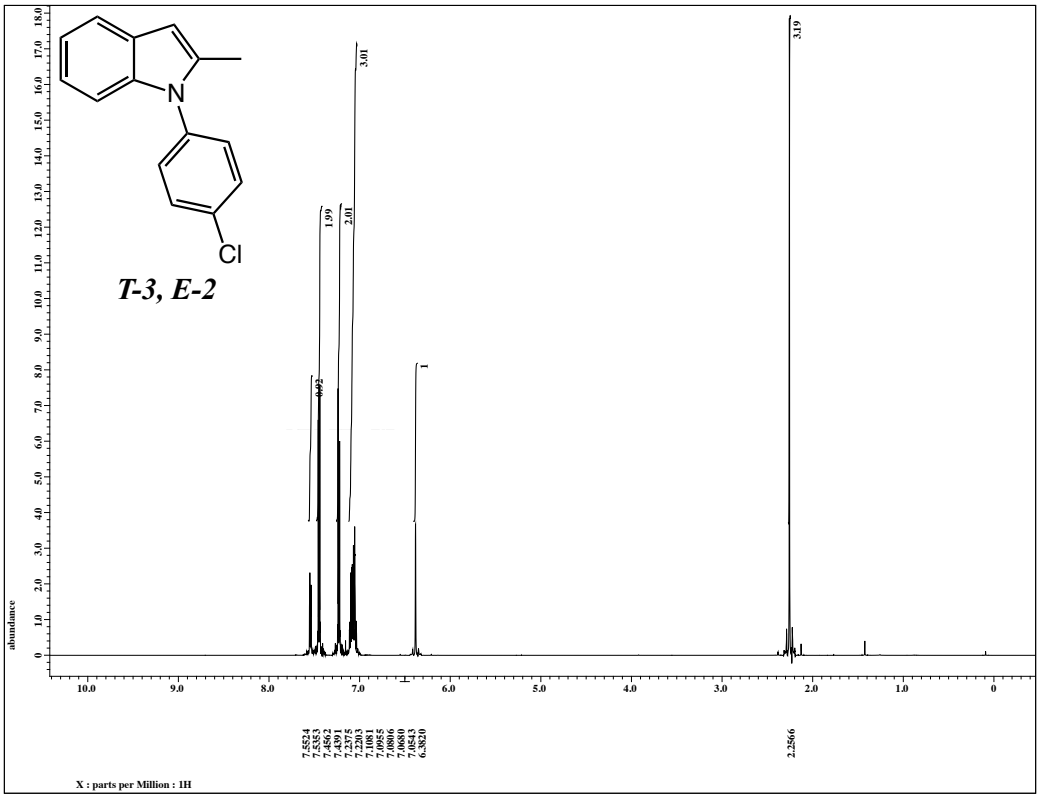
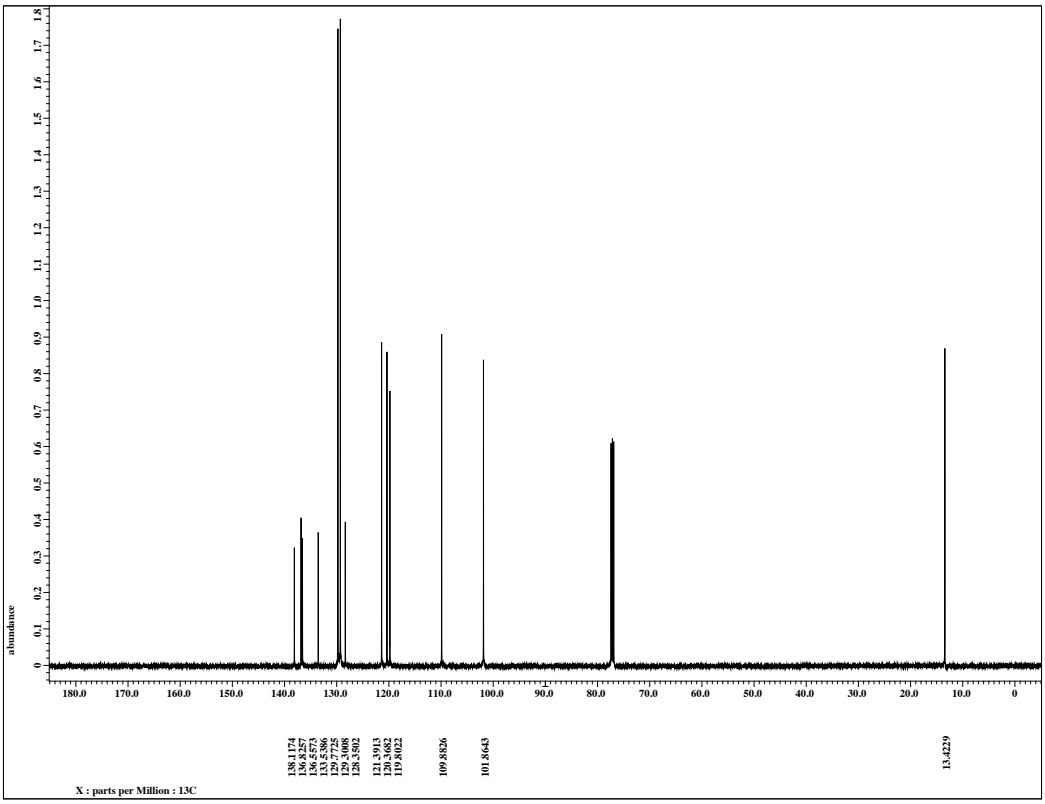
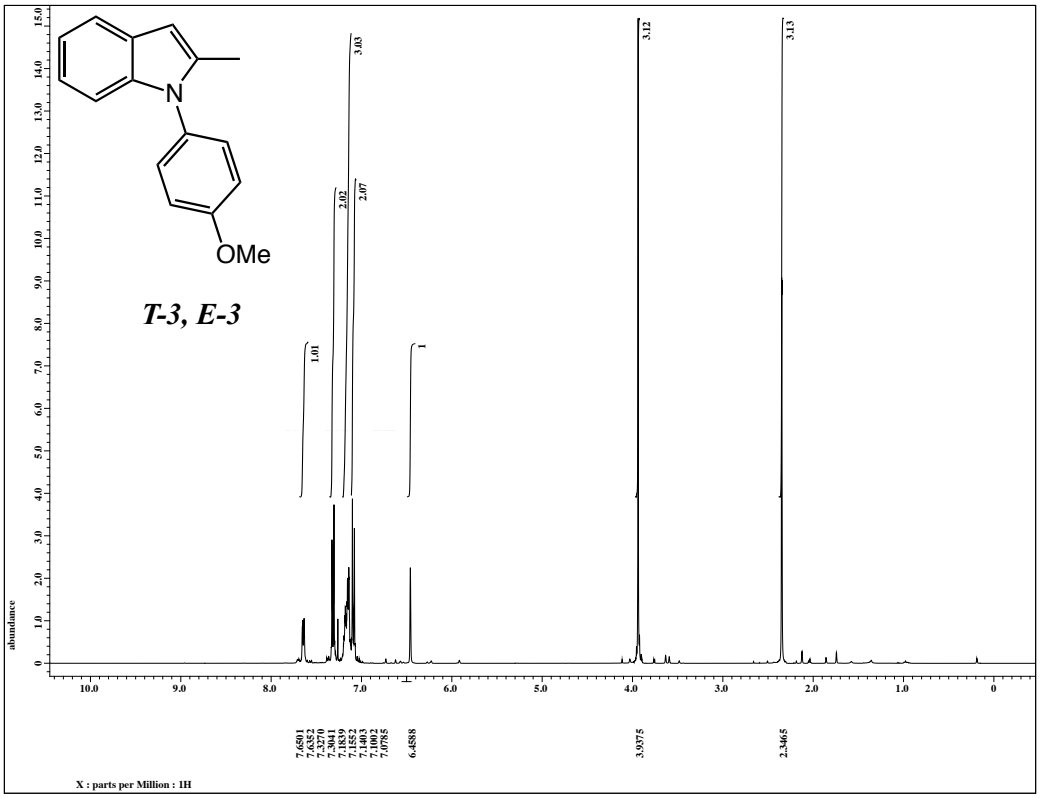
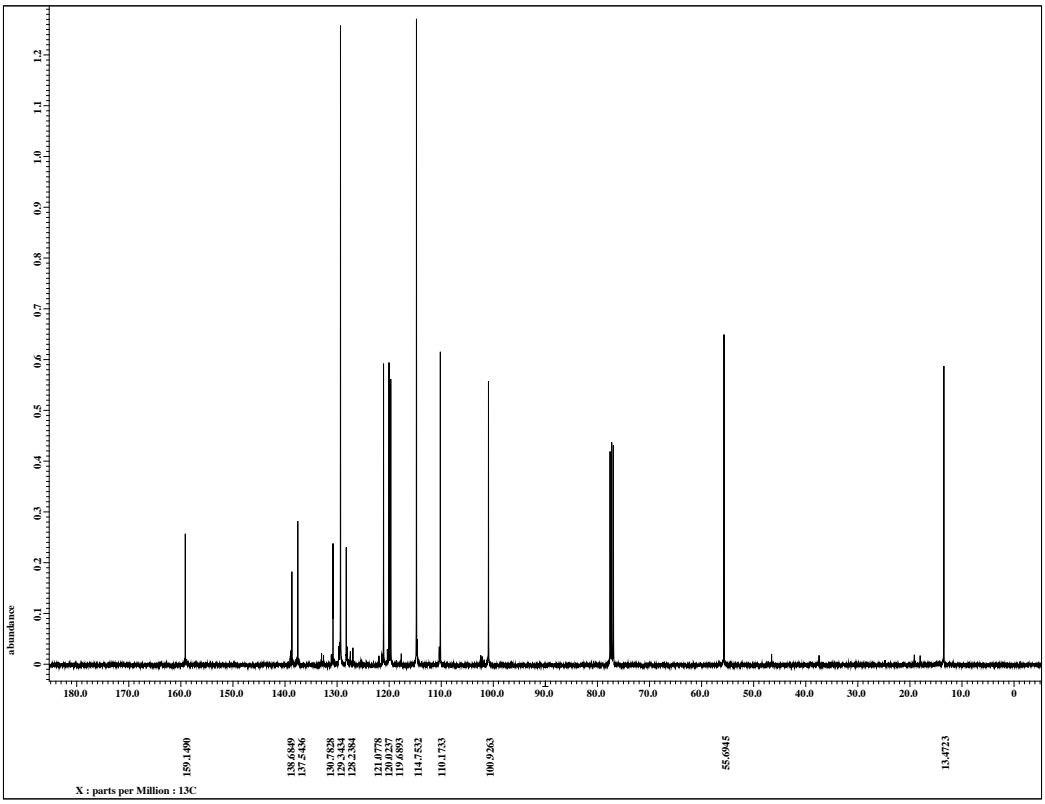

T-3, E-1
3.05
3.0
2.02
1.03
1
3.0
abundance
7.5284
7.5135
7.4143
7.3566
7.3417
7.0999
7.0852
6.3981
2.2994
X : parts per Million : 1H

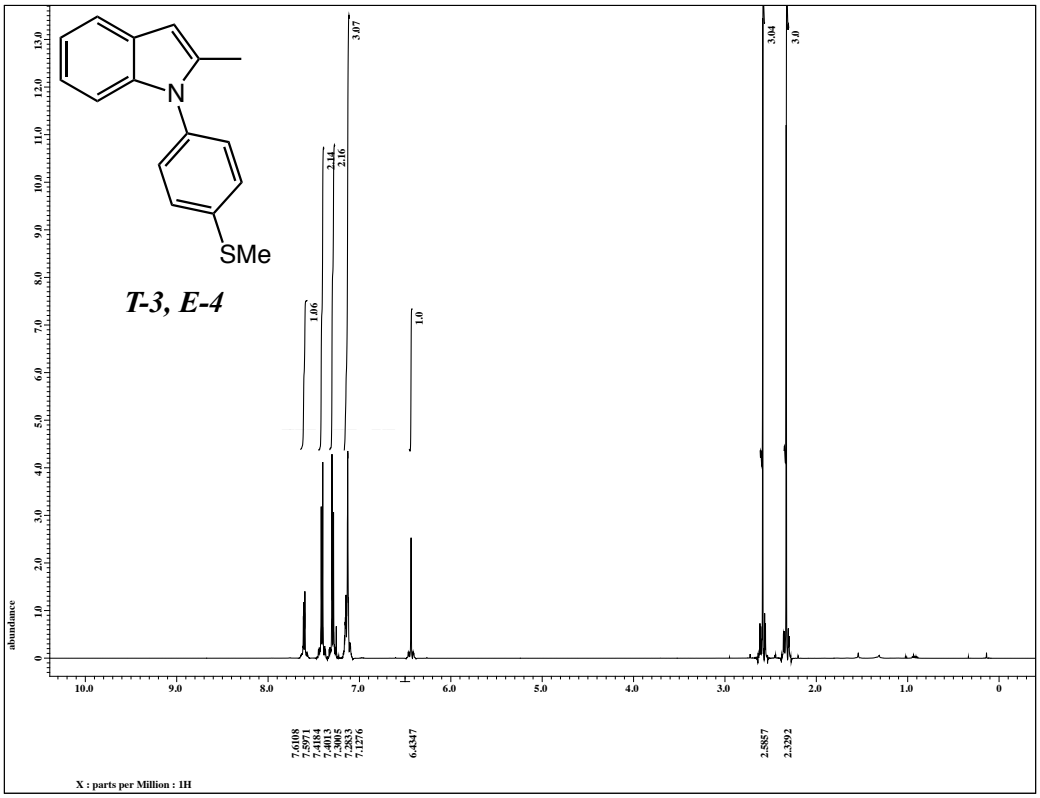

abundance
138.2117
130.1038
127.1018
129.4095
129.2214
128.0672
127.7625
121.0938
120.0706
119.6135
110.0788
101.3200
13.4664
X : parts per Million : 13C

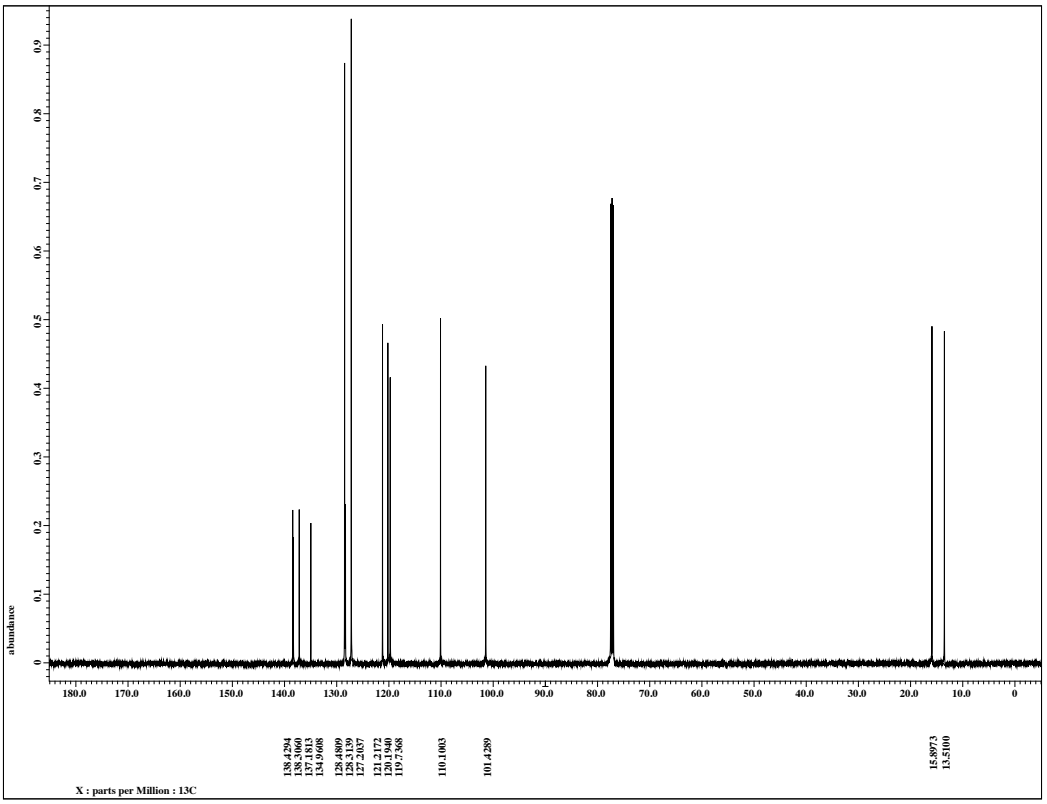

N
Cl
T-3, E-2
abundance
1.99
2.01
3.01
3.19
1
7.5524
7.5353
7.4862
7.4691
7.2375
7.2203
7.1081
7.0965
7.0896
7.0680
7.0543
6.8820
2.2566
X : parts per Million : 1H

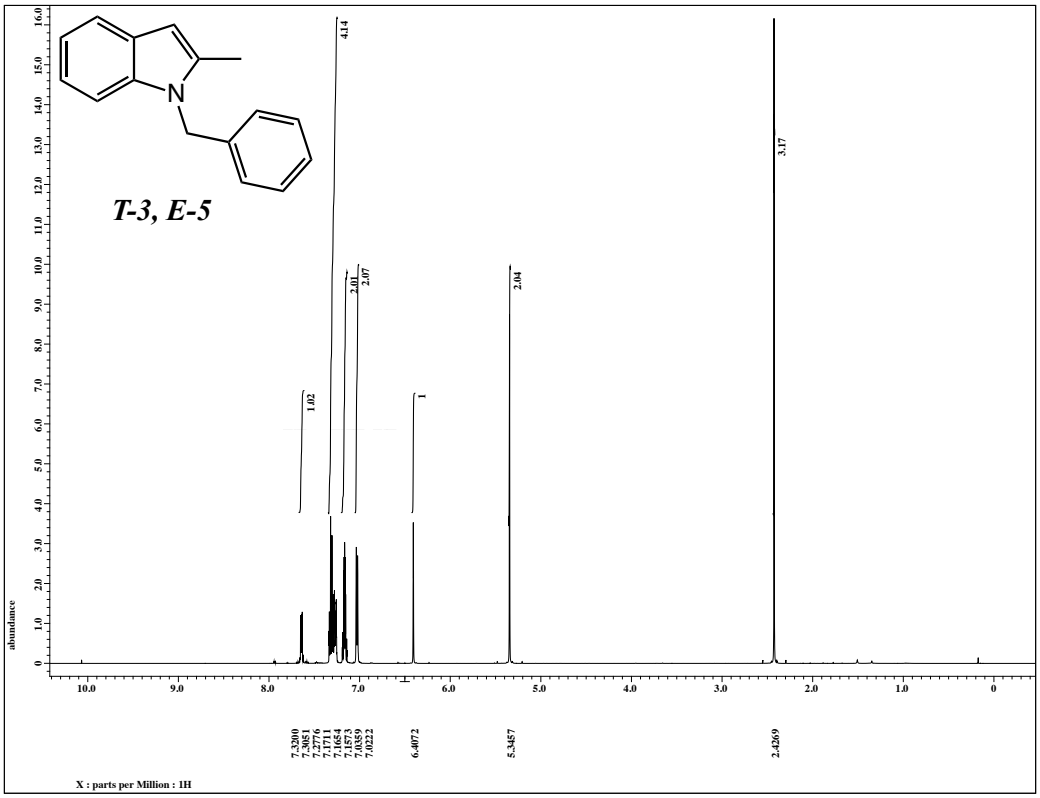

abundance
138.1174
136.8257
130.4573
129.7725
129.3008
128.3802
121.3913
120.3682
119.8022
109.8826
101.8643
13.4229
X : parts per Million : 13C

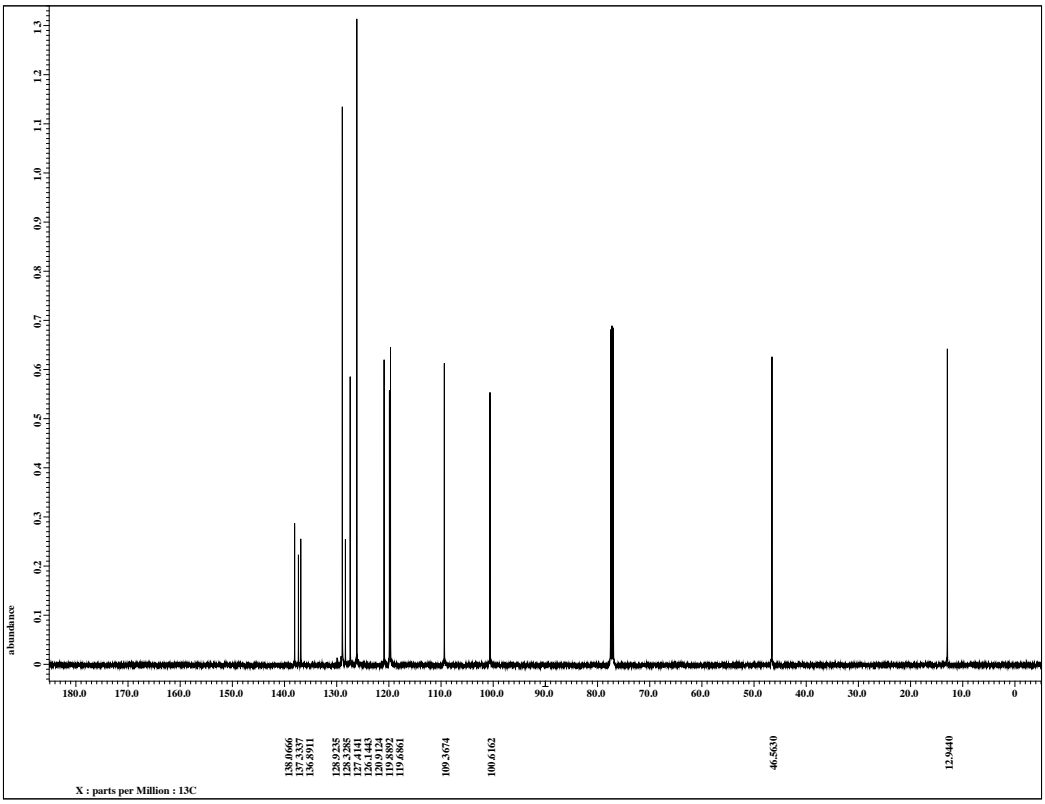

N
OMe
T-3, E-3
abundance
1.01
2.02
3.03
2.07
1
3.12
3.13
7.6501
7.6352
7.3710
7.3041
7.1839
7.1352
7.1045
7.1002
7.0785
6.4588
3.9375
2.3465
X : parts per Million : 1H

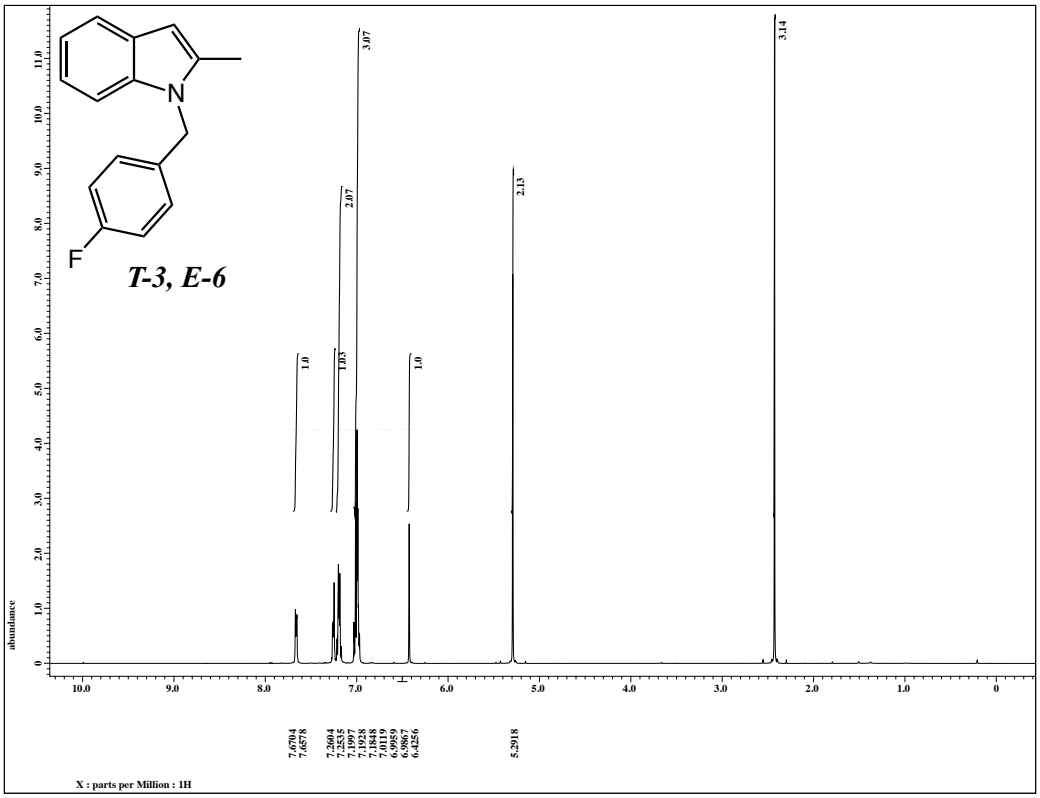

abundance
159.1490
138.6849
137.5436
130.7828
129.2434
128.2484
121.0778
120.0237
119.6893
114.7532
110.1733
100.9263
55.6945
13.4723
X : parts per Million : 13C

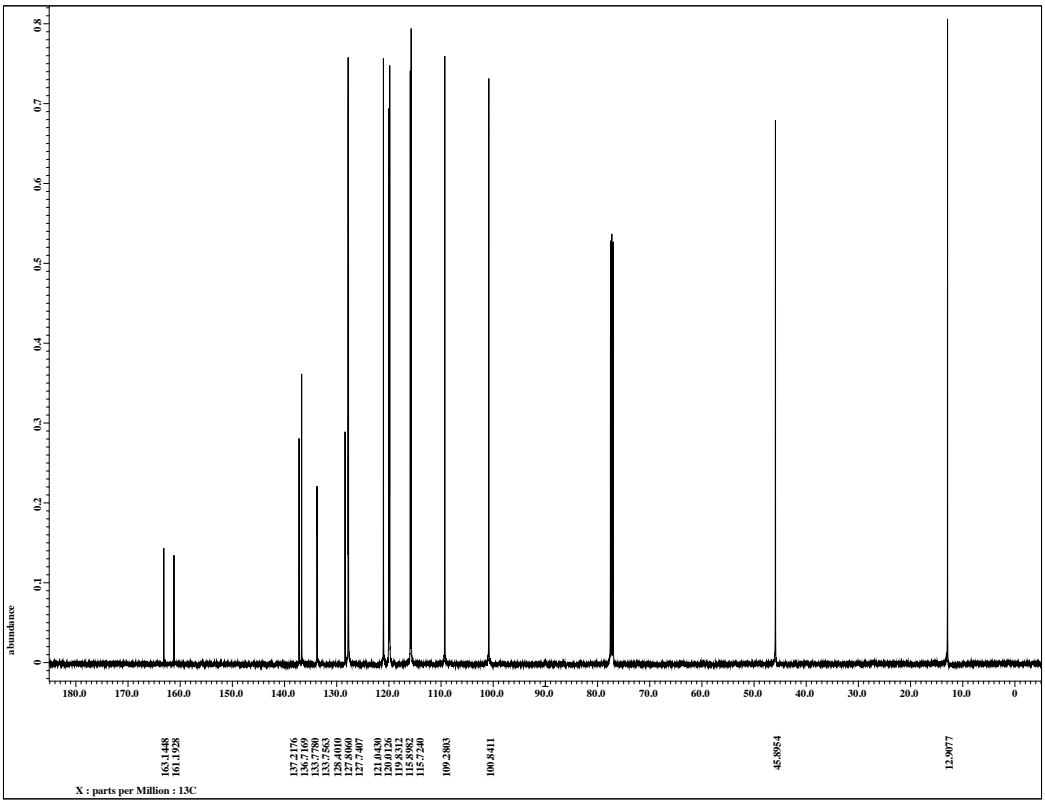

N
SMe
T-3, E-4
abundance
X : parts per Million : 1H

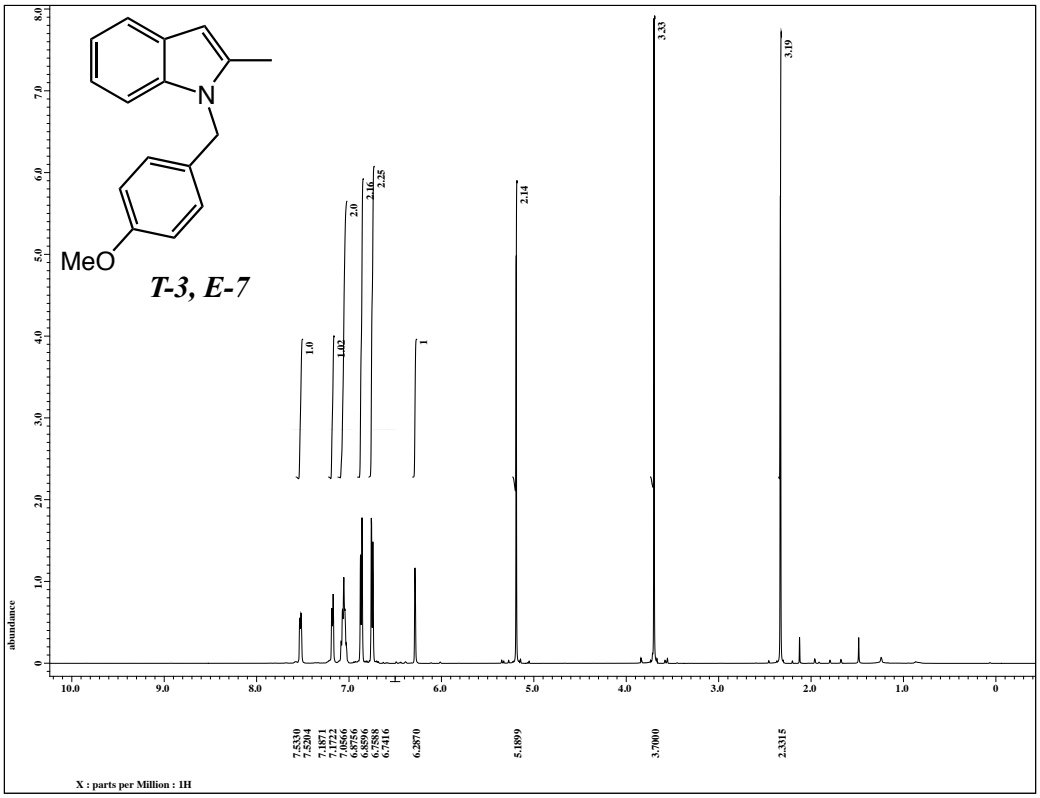

abundance
X : parts per Million : 13C

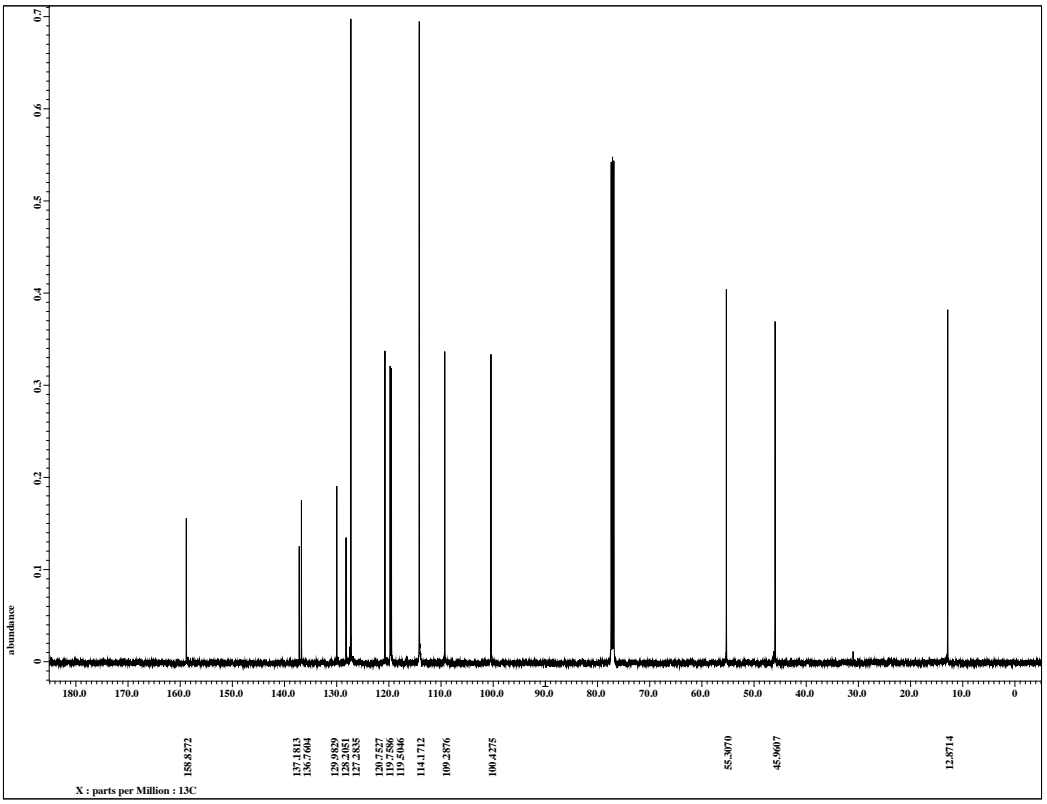

T-3, E-5
abundance
4.14
3.17
2.07
2.01
2.04
1.02
1
7.3200
7.3051
7.2776
7.1711
7.1654
7.1575
7.0359
7.0222
6.4072
5.3457
2.4269
X : parts per Million : 1H

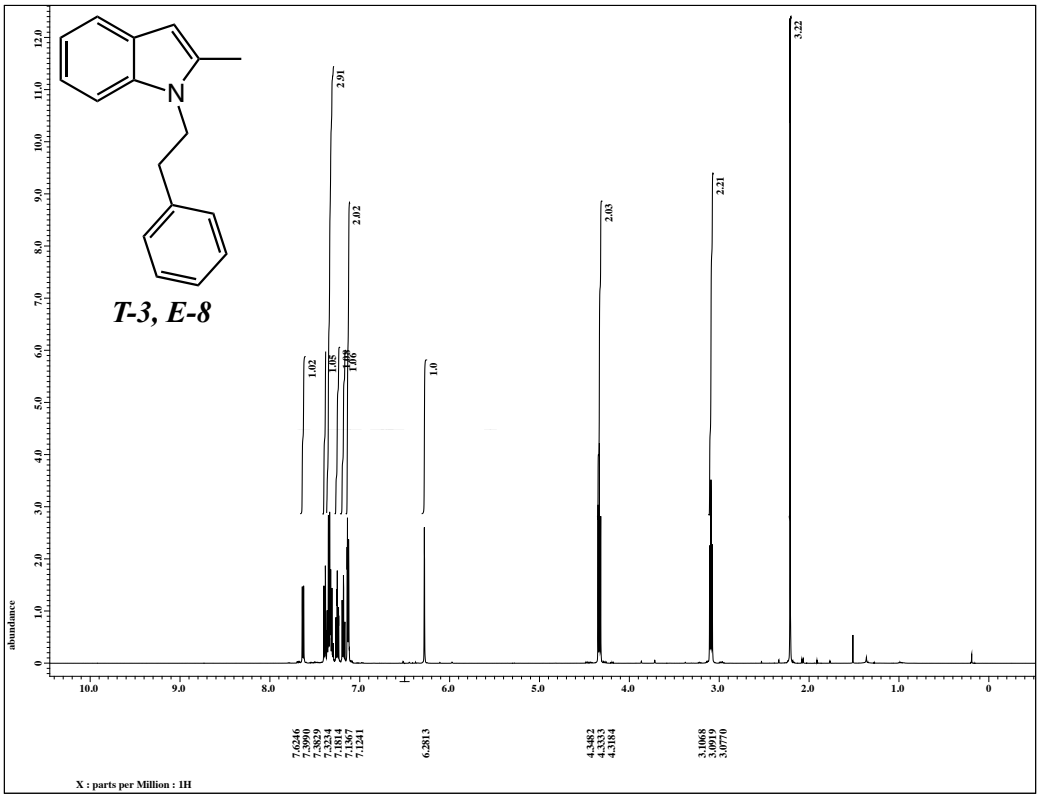

abundance
138.0666
137.2337
136.8711
128.9235
128.3285
127.4141
126.1143
120.9124
119.8892
119.6861
109.3674
100.6162
46.5630
12.9440
X : parts per Million : 13C


T-3, E-6
abundance
1.0
1.03
2.07
3.07
1.0
2.13
3.14
7.6704
7.6578
7.2604
7.2535
7.1997
7.1928
7.1848
7.0119
6.9969
6.9867
6.4256
5.2918
X : parts per Million : 1H


abundance
163.1448
161.1928
137.2176
136.7169
133.7780
133.7756
128.4010
127.8060
127.7407
121.0430
120.0126
119.8312
115.9582
115.7240
109.2803
100.8411
45.8954
12.9077
X : parts per Million : 13C


MeO
T-3, E-7
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C


T-3, E-8
abundance
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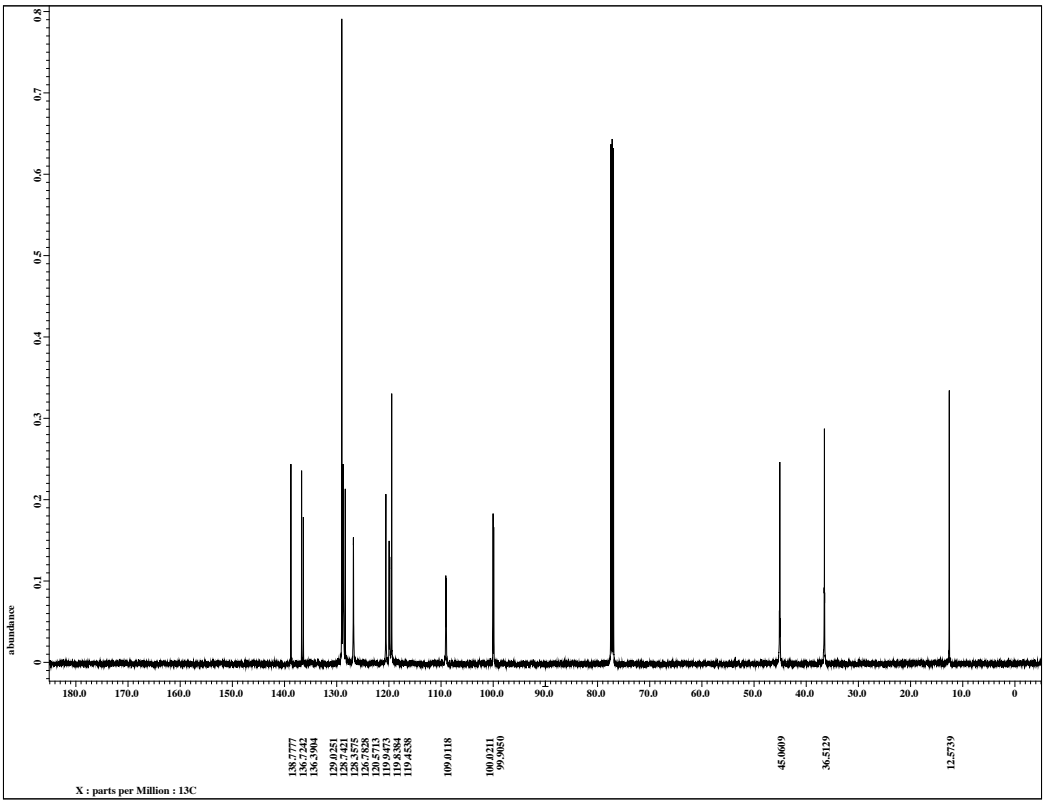
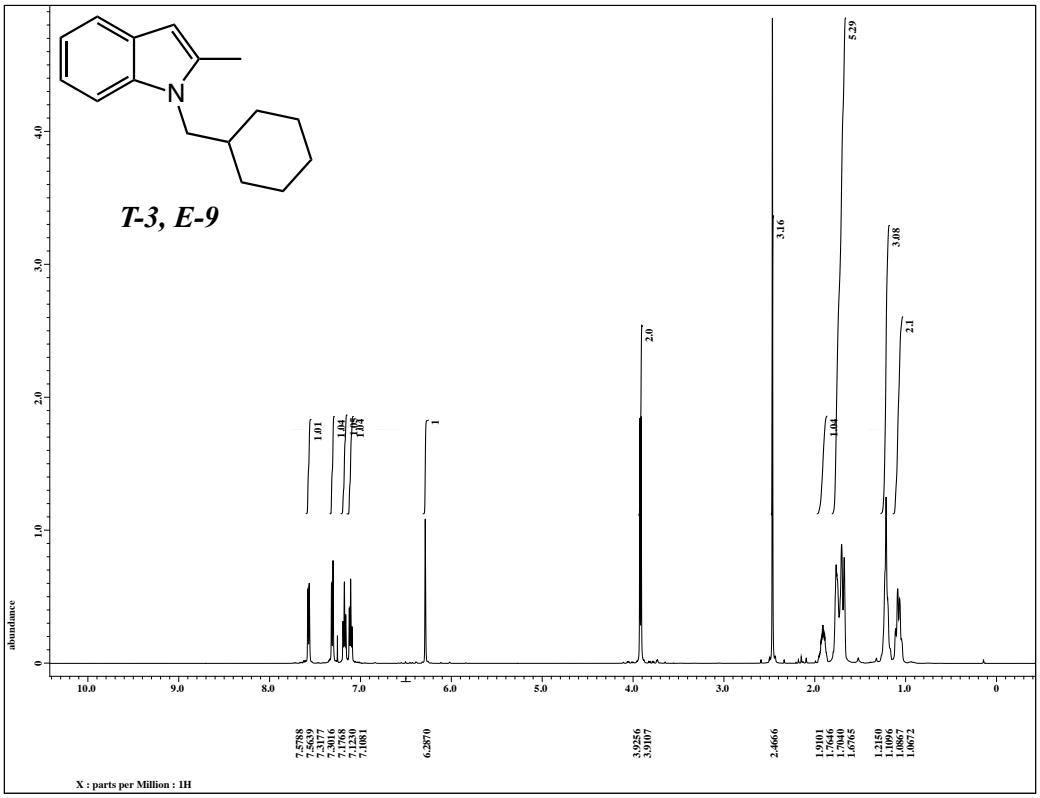
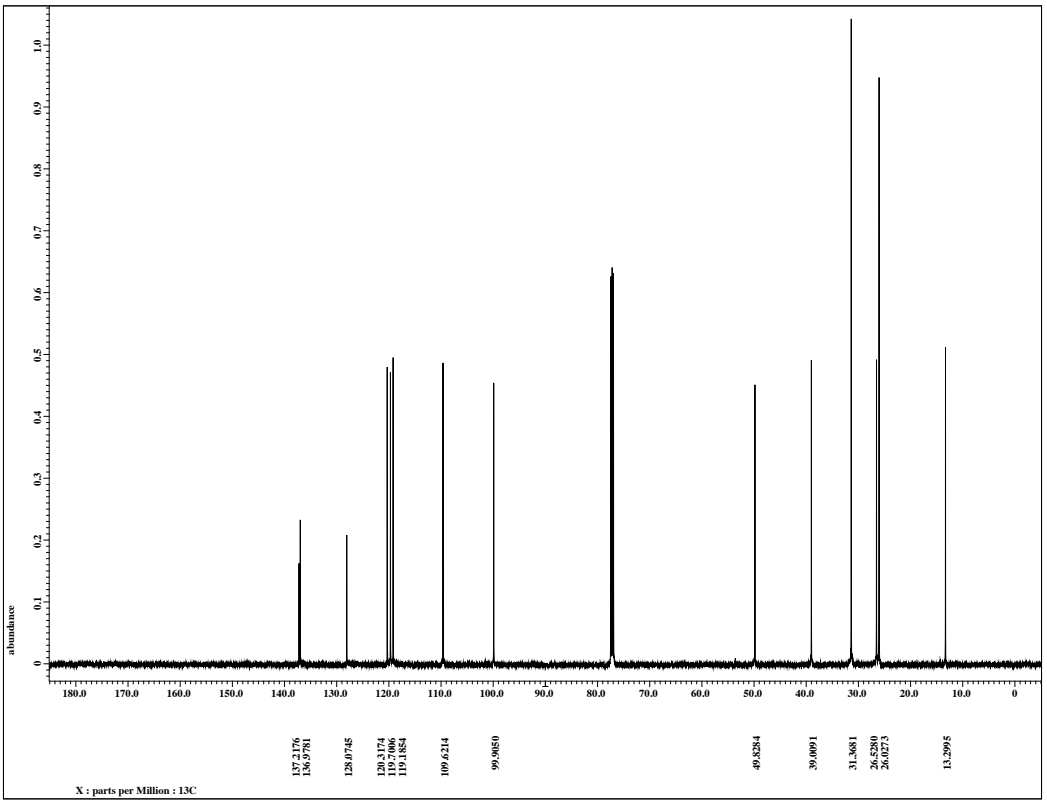
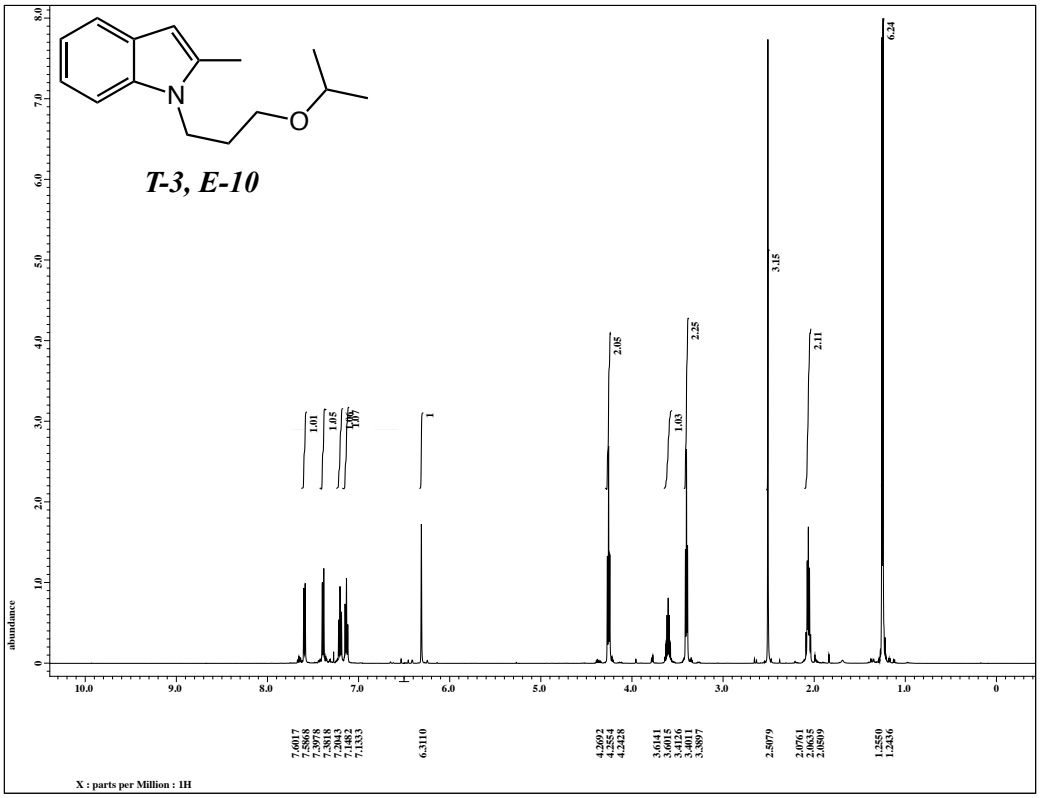
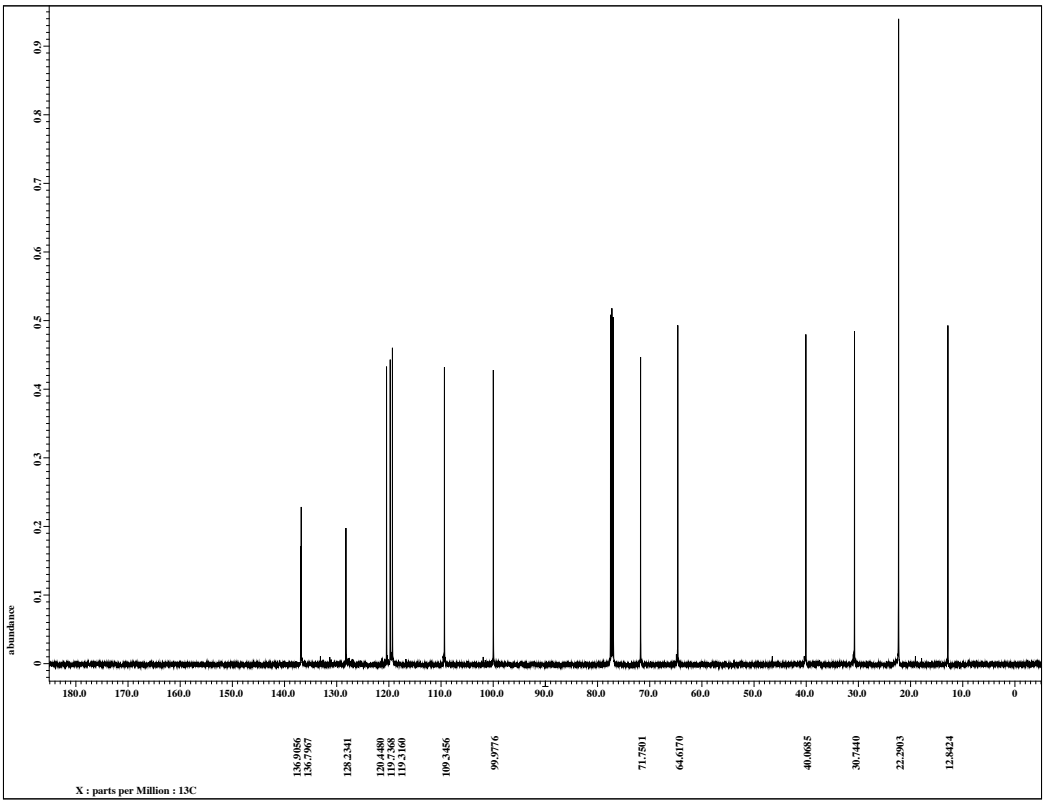
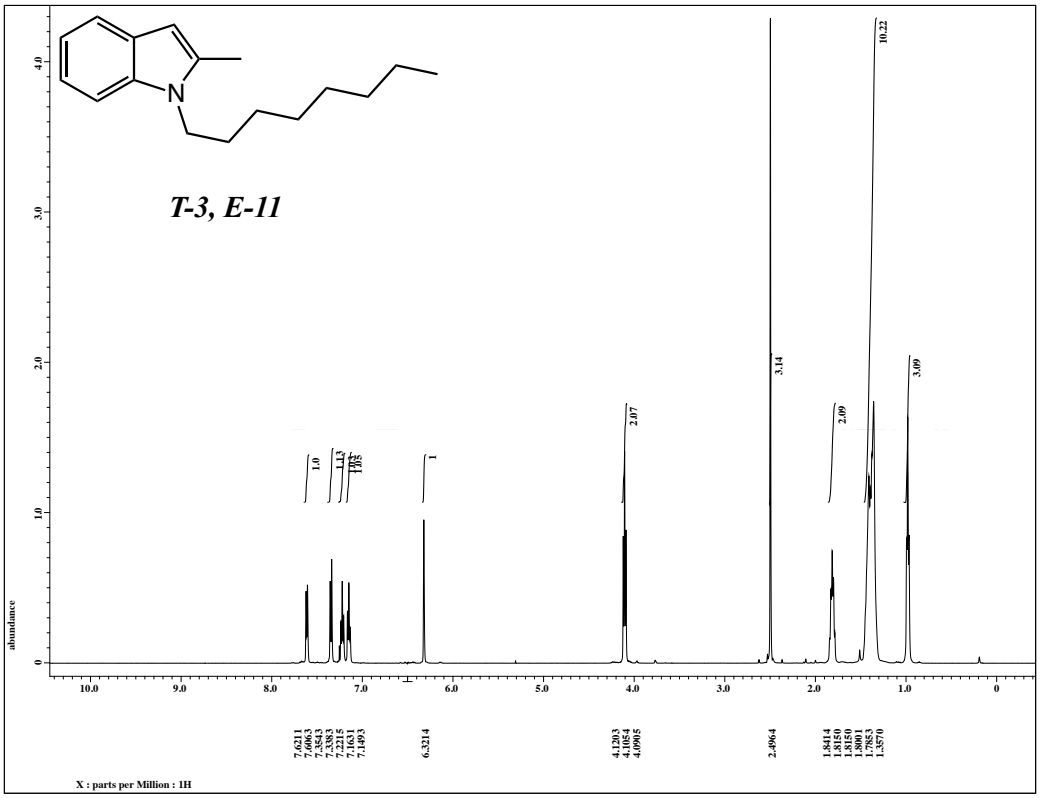

abundance
X : parts per Million : 13C

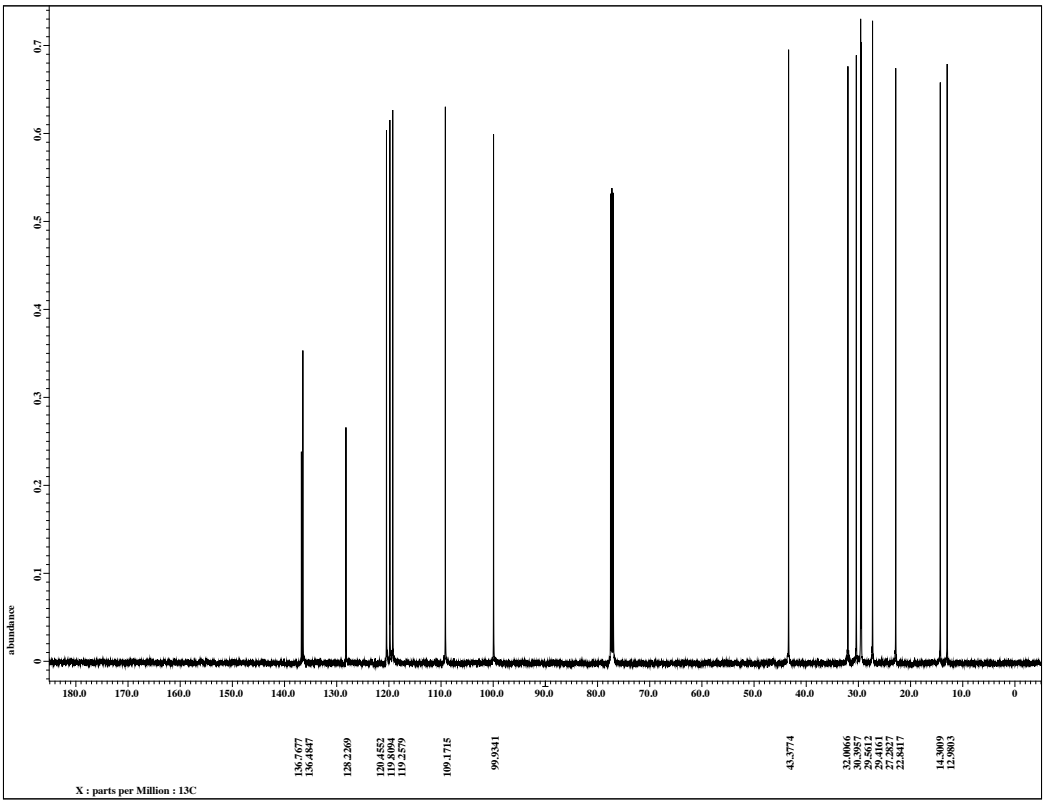

T-3, E-9
abundance
X : parts per Million : 1H

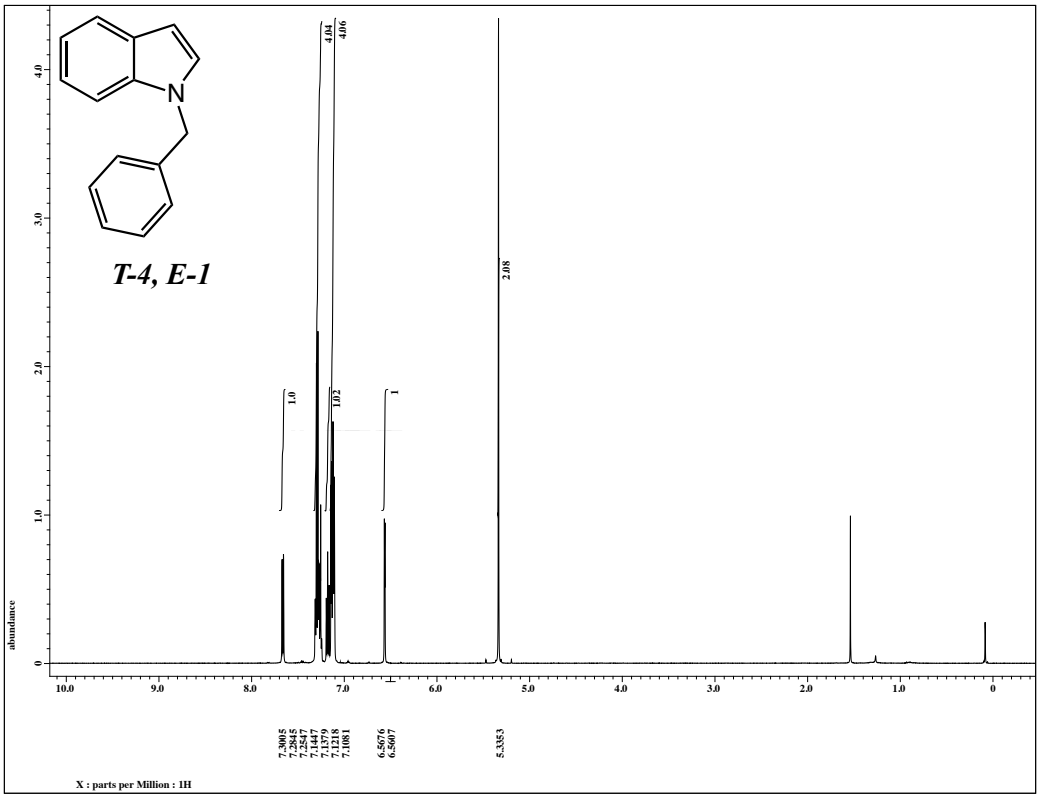

abundance
X : parts per Million : 13C

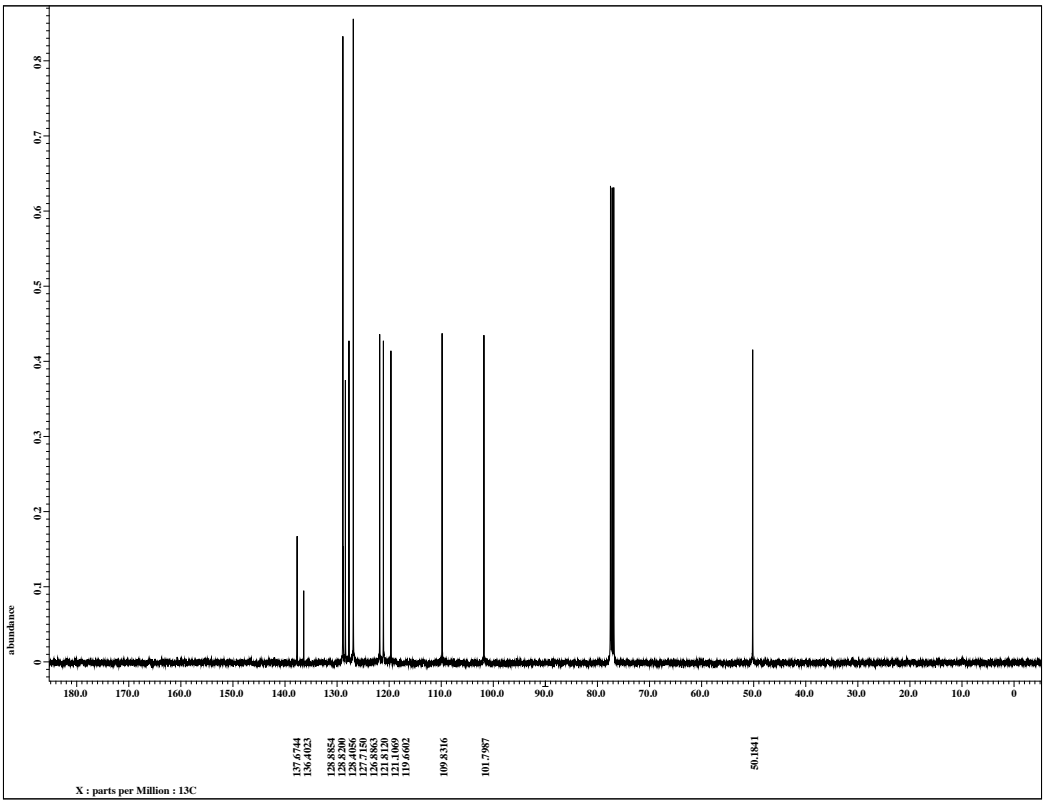

T-3, E-10
abundance
X : parts per Million : 1H

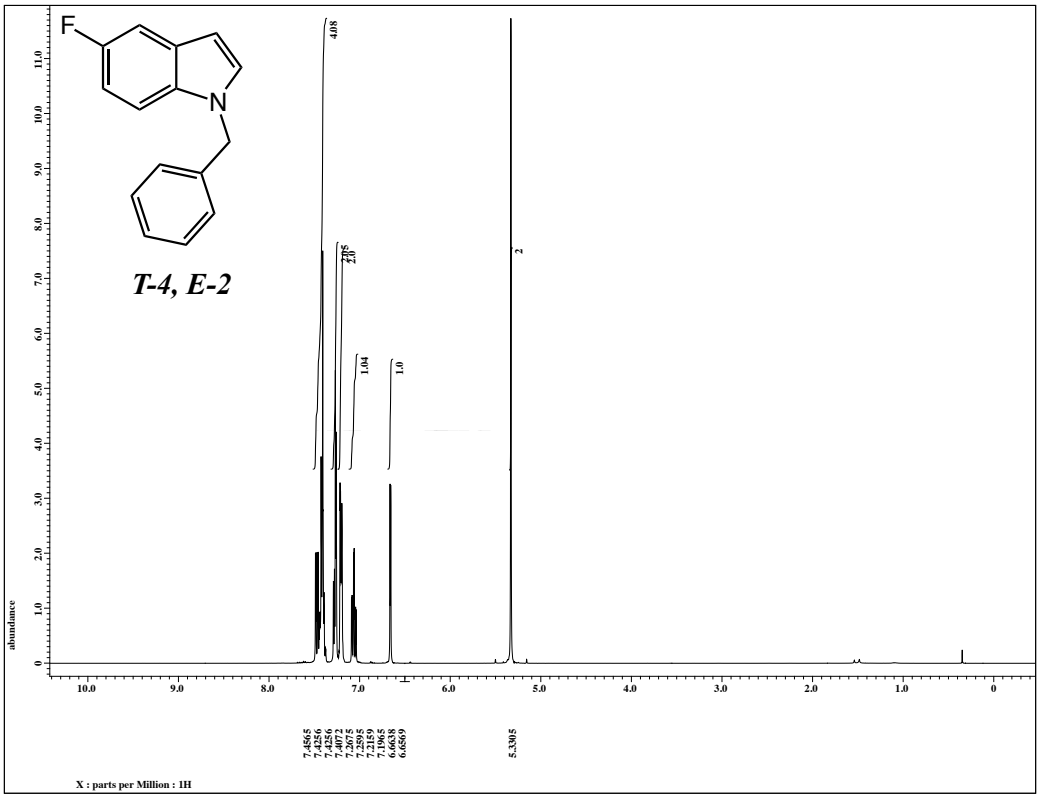

abundance
X : parts per Million : 13C

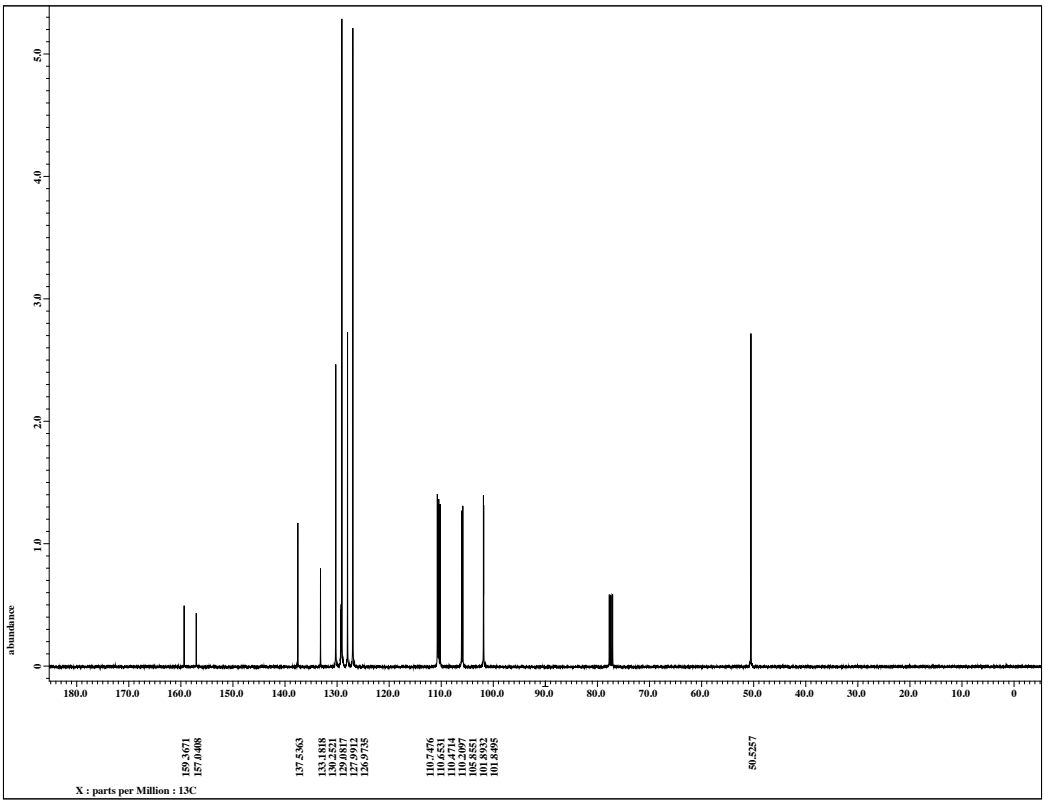

T-3, E-11
abundance
X : parts per Million : 1H

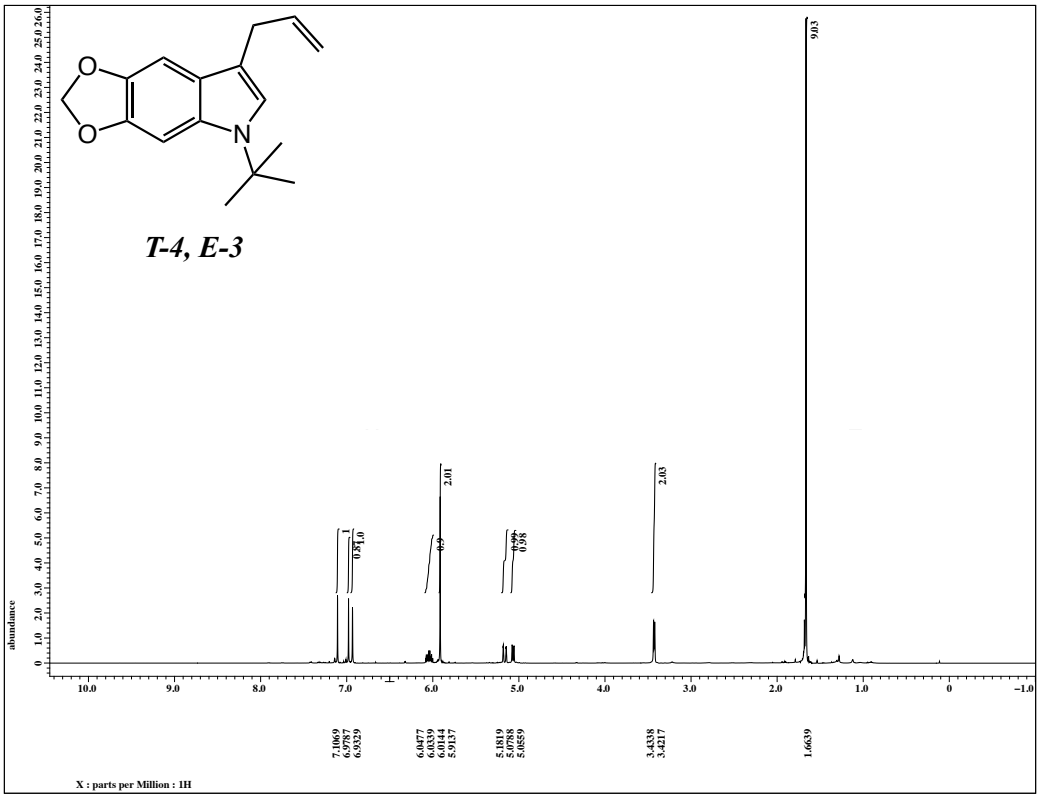

abundance
X : parts per Million : 13C

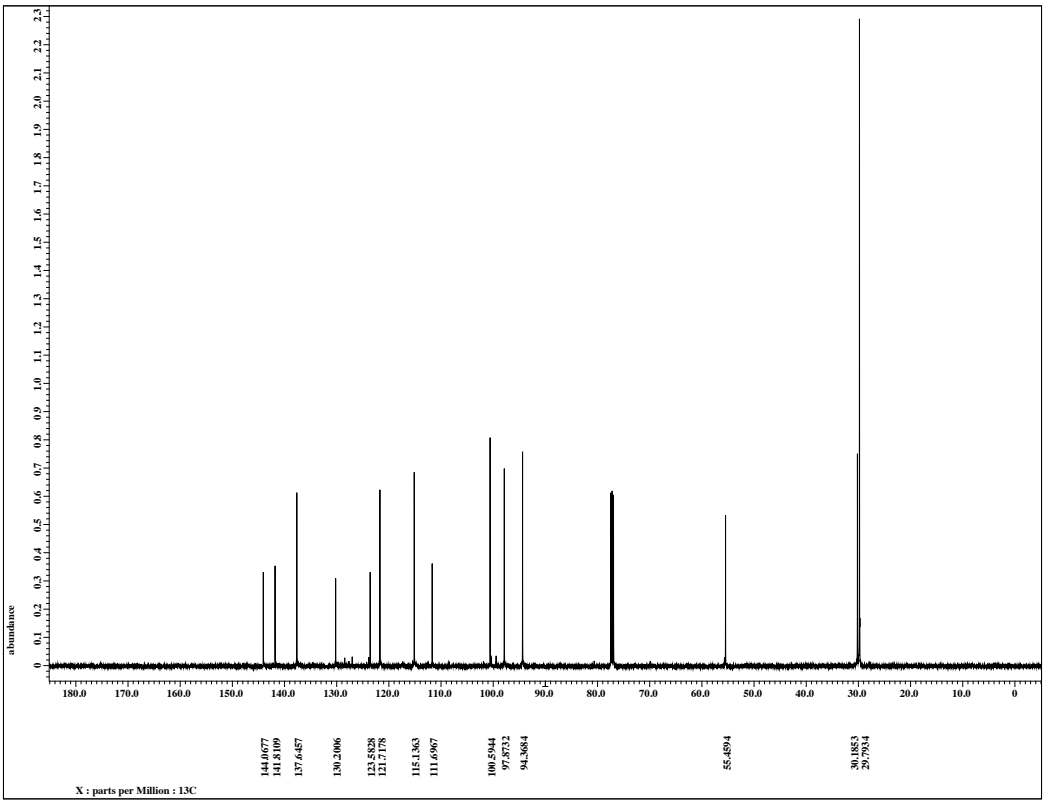

T-4, E-1
4.04
4.06
2.08
1.0
1.02
1
abundance
7.3005
7.2845
7.2547
7.1447
7.1379
7.1158
7.1081
6.5676
6.5607
5.3353
X : parts per Million : 1H

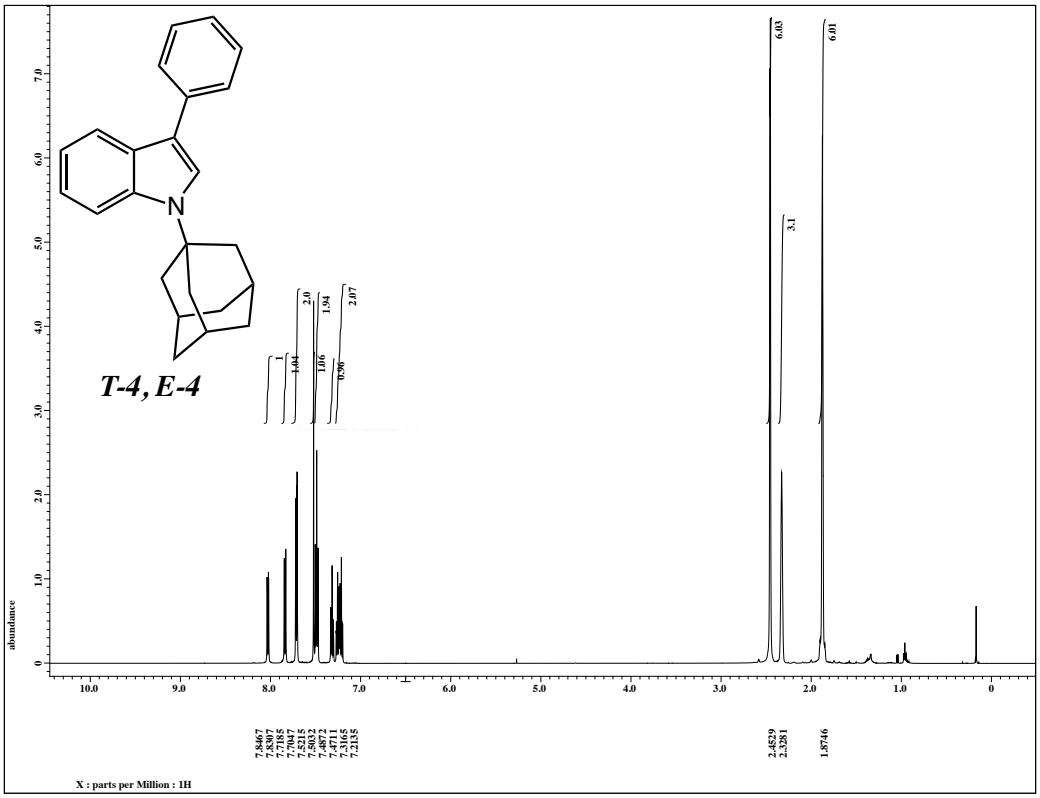

abundance
137.6744
136.4023
128.8584
128.8300
128.4456
127.7150
126.8863
121.8120
121.1460
119.6602
109.8316
101.7987
50.1841
X : parts per Million : 13C

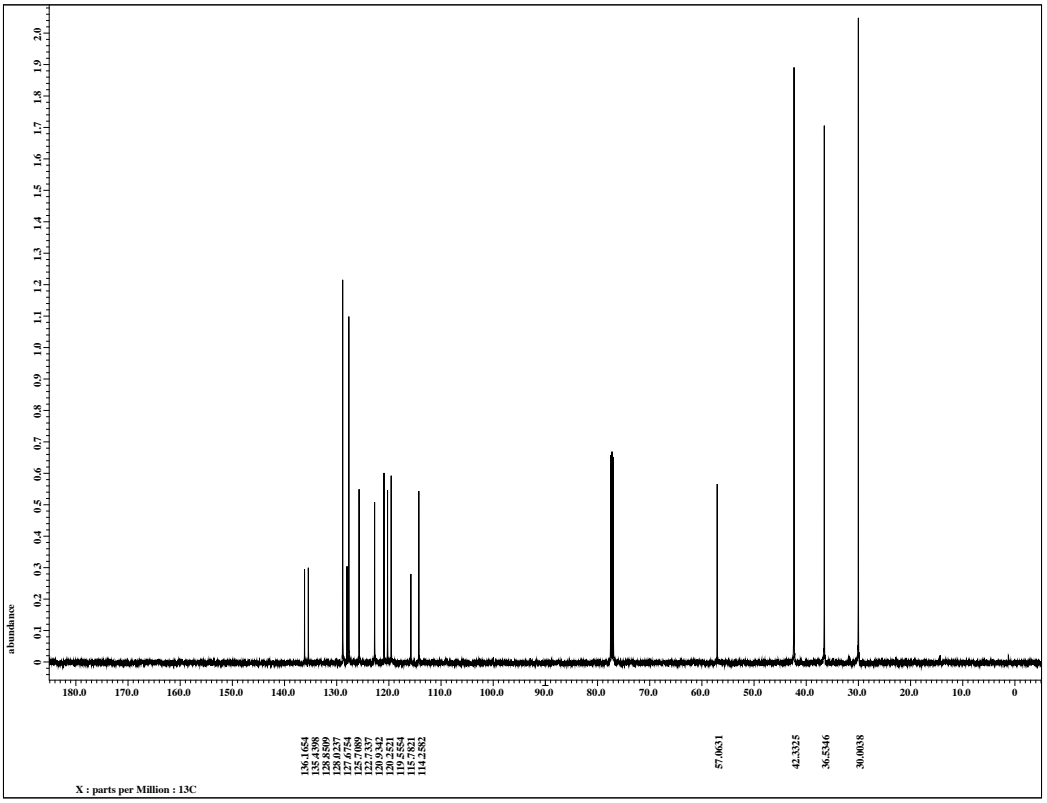

F
N
T-4, E-2
4.08
2.15
2.0
1.04
1.0
2
abundance
7.4565
7.4256
7.4256
7.4077
7.3925
7.2595
7.2159
7.1945
6.6648
6.6569
5.3305
X : parts per Million : 1H

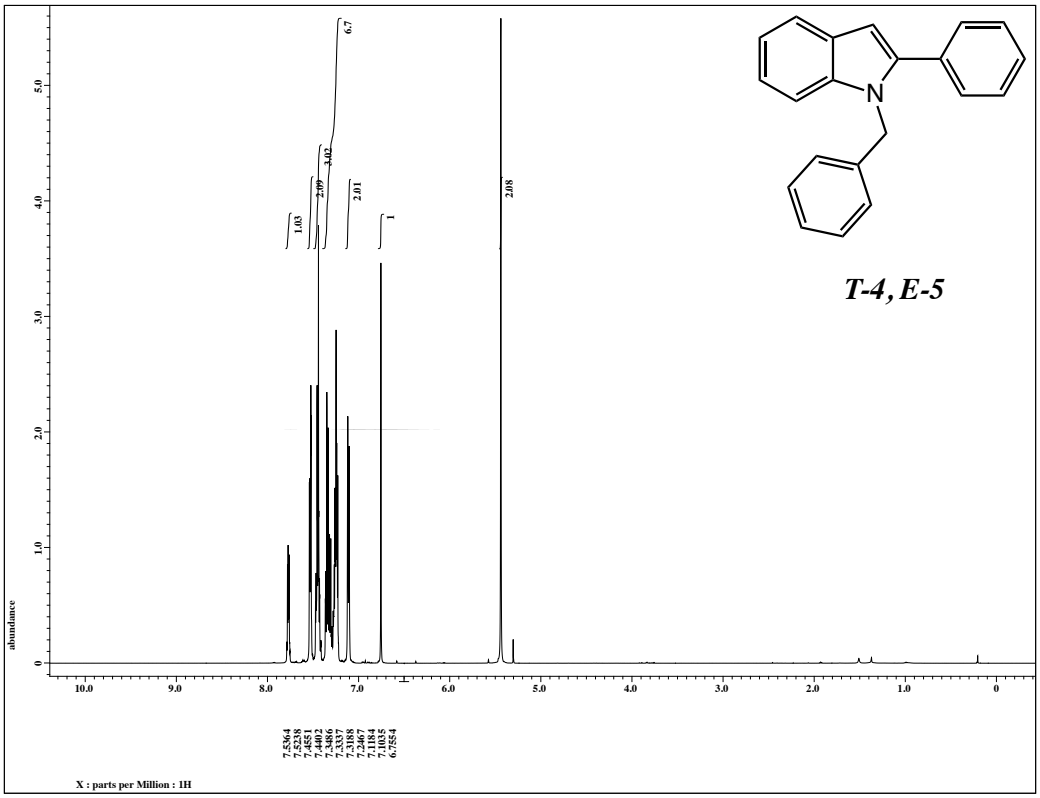

abundance
189.3671
157.0408
137.5363
133.1818
130.2521
129.0817
127.0932
126.9735
110.7476
110.6531
110.4714
110.2097
105.8551
101.8932
101.8495
50.5257
X : parts per Million : 13C


O
O
N
T-4, E-3
abundance
9.03
2.01
2.03
1
0.81
1.0
0.99
0.98
7.1069
6.9787
6.9329
6.0477
6.0339
6.0144
5.9137
5.1819
5.0788
5.0859
3.4338
3.4217
1.6639
X : parts per Million : 1H

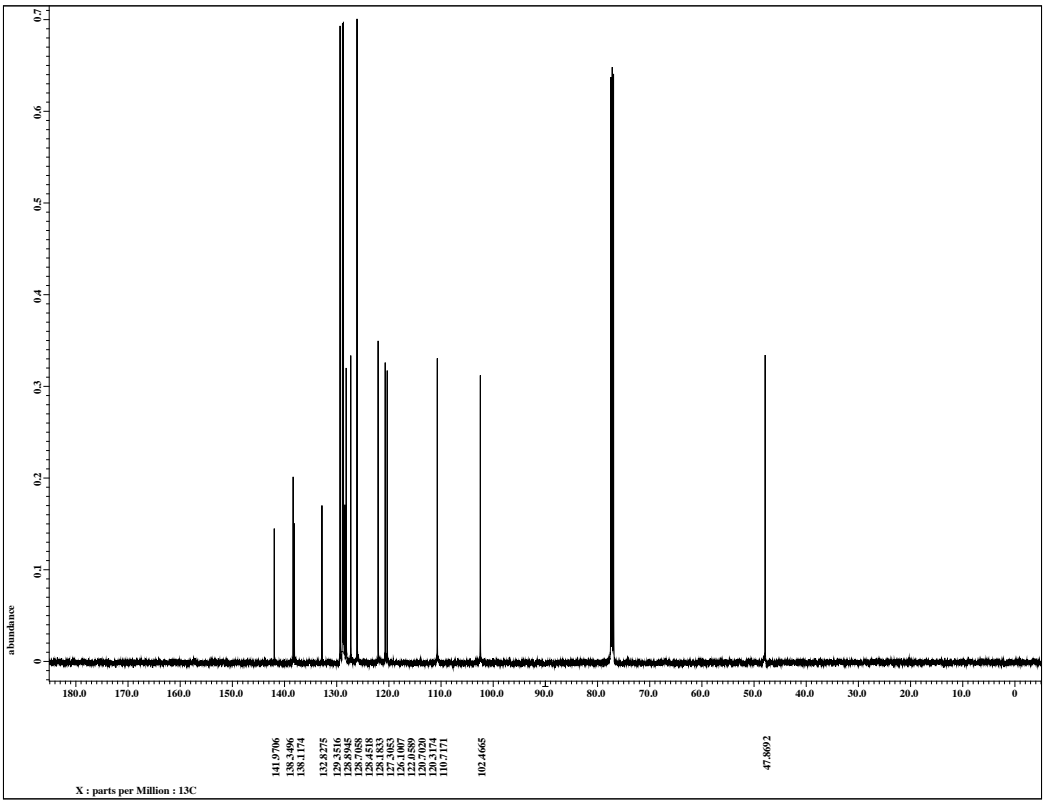

abundance
144.0677
141.8109
137.6487
130.2006
123.5828
121.7178
115.1363
111.6967
100.5944
97.8733
94.3684
55.4894
30.1853
29.7934
X : parts per Million : 13C

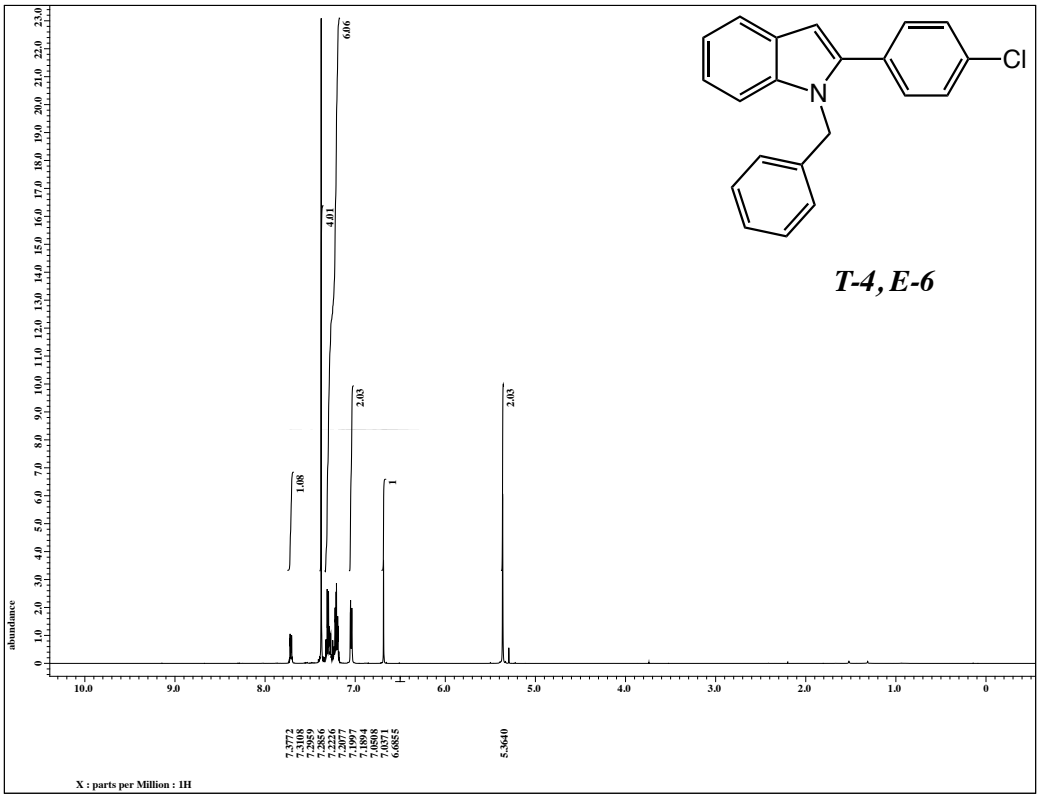

T-4, E-4
abundance
X : parts per Million : 1H

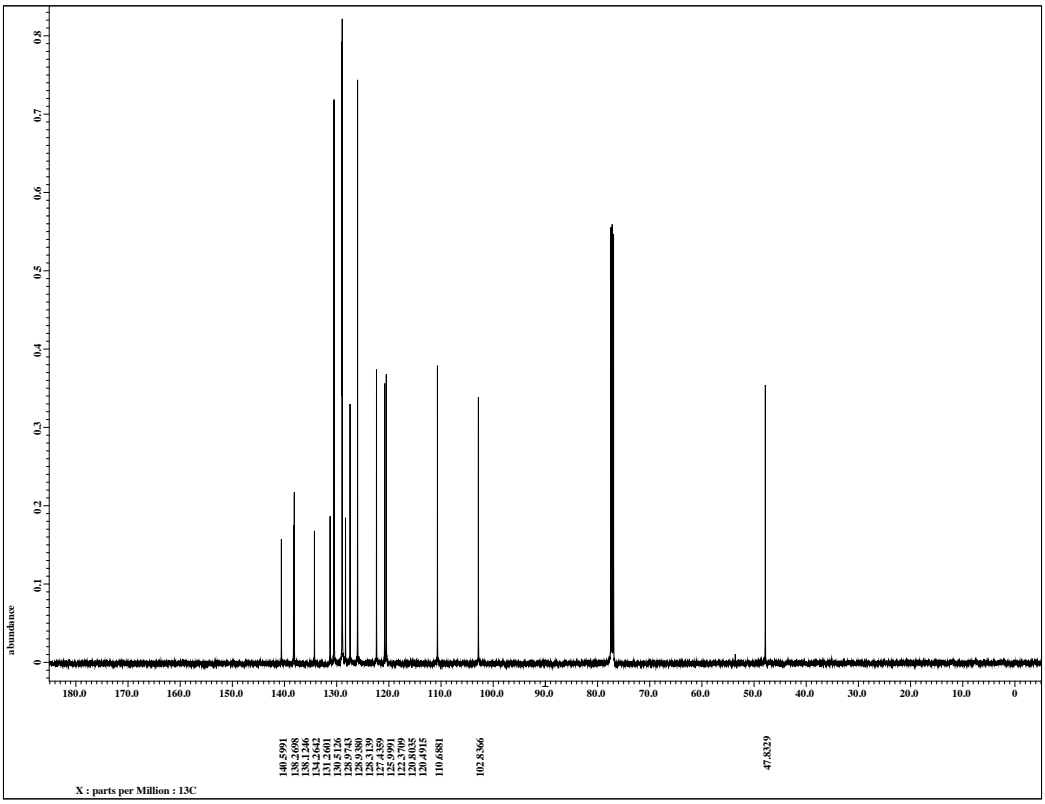

abundance
X : parts per Million : 13C

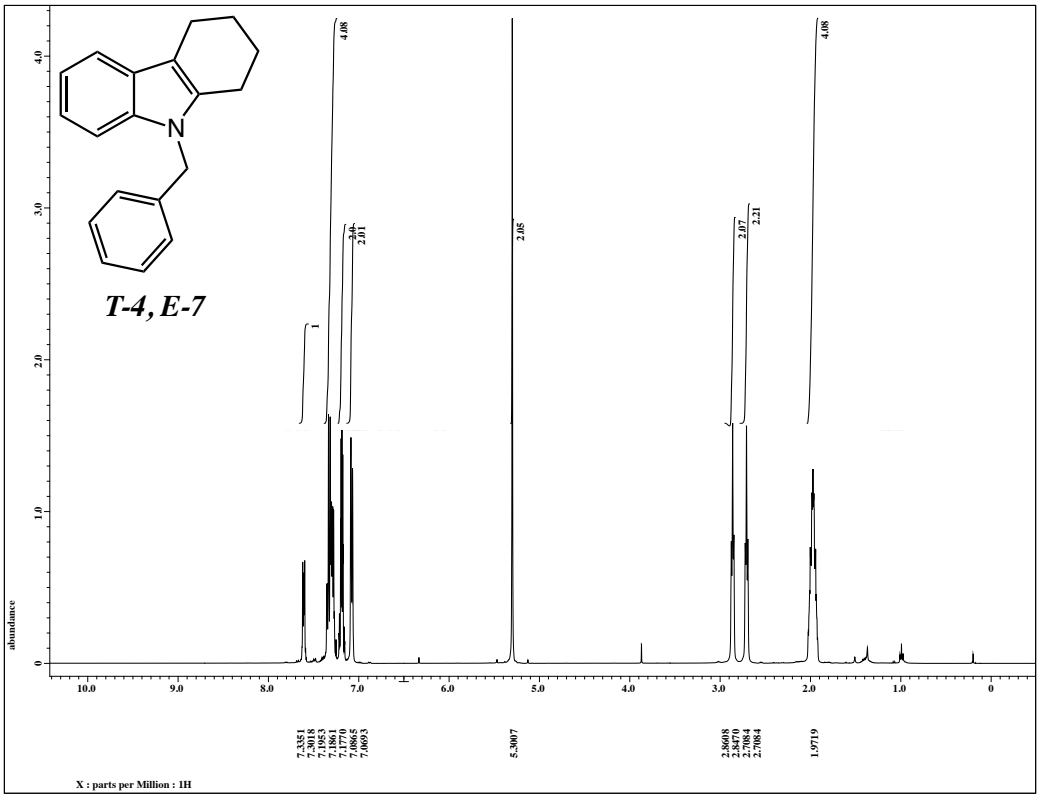

6.7
3.02
2.09
2.01
1.03
1
2.08
abundance
X : parts per Million : 1H

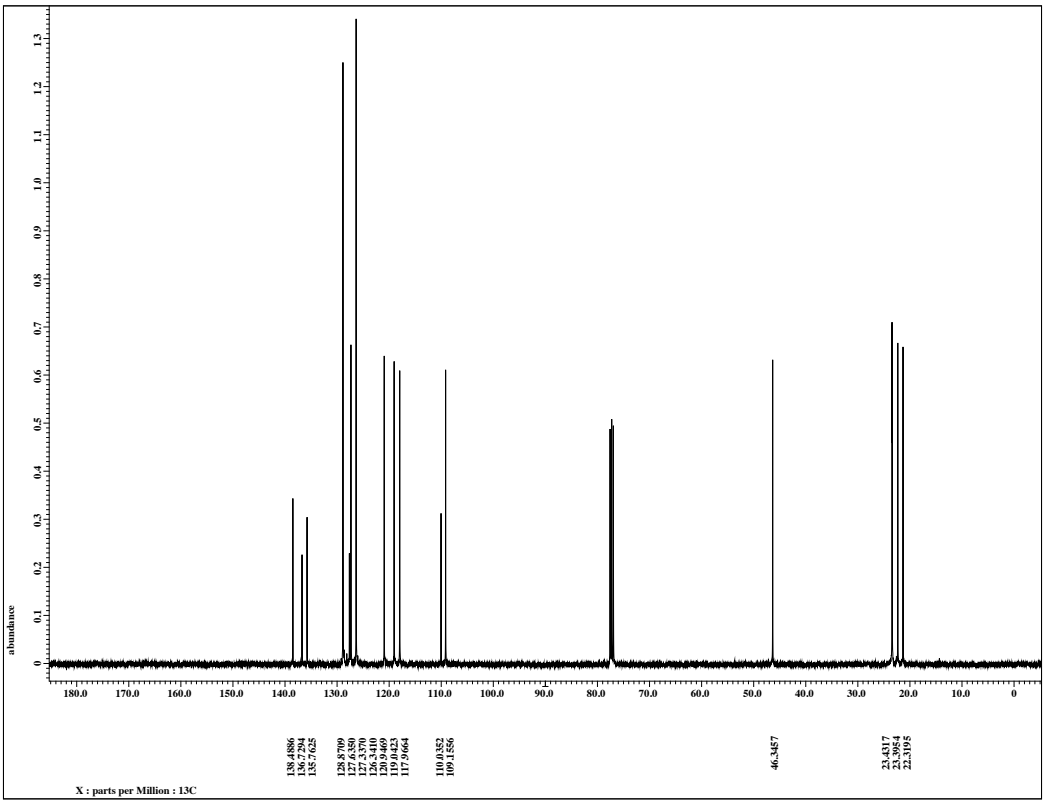
T-4, E-5

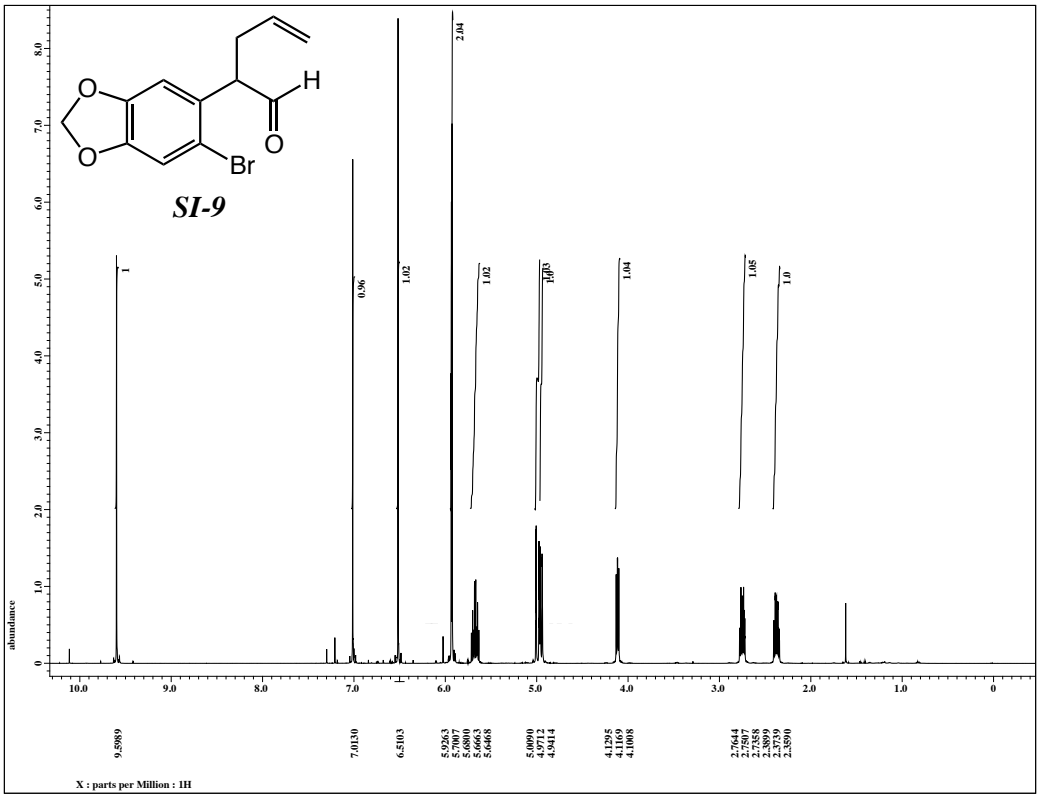

abundance
X : parts per Million : 13C

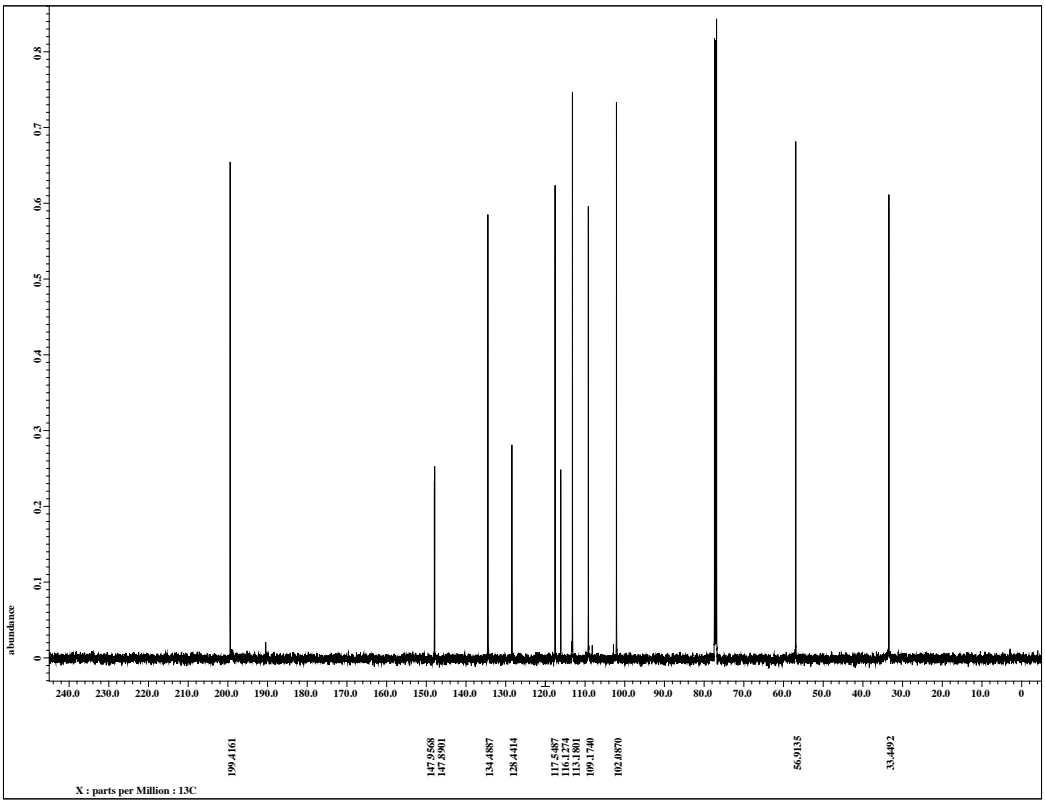

Cl
N
T-4, E-6
6.06
4.01
2.03
2.03
1.08
1
abundance
7.3772
7.3108
7.2989
7.2856
7.2236
7.2077
7.1997
7.1894
7.0508
7.0371
6.6885
5.3640
X : parts per Million : 1H


abundance
140.5991
138.2698
138.1246
134.2642
131.4101
131.3555
128.9743
128.9380
125.3139
122.4198
125.9991
122.3709
120.8038
120.4495
110.6881
102.8366
47.8329
X : parts per Million : 13C


T-4, E-7
4.08
2.05
2.01
2.07
2.21
1
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C


O
O
O
H
Br
SI-9
abundance
X : parts per Million : 1H
9.5989
7.0130
6.5103
5.9263
5.7007
5.6800
5.6643
5.6468
5.0990
4.9712
4.9414
4.1295
4.1169
4.1008
2.7644
2.7507
2.7358
2.3899
2.3739
2.3590


abundance
X : parts per Million : 13C
199.4161
147.9568
147.8901
134.4887
128.4414
117.5487
116.1274
115.1301
109.1740
102.0870
56.9135
33.4492