Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is © The Royal Society of Chemistry 2013

Supporting Information

One-pot synthesis of 4-methylisoquinolines via sequential Pd-catalyzed Heck reaction and intramolecular cyclization

Yulin Tian[a,b], Jianguo Qi[b], Chenbin Sun[b], Dali Yin[a,b], Xiaojian Wang*[a,b], Qiong Xiao[b]

[a] *State Key Laboratory of Bioactive Substances and Functions of Natural Medicines, Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100050, PR China. E -mail: wangxiaojian@imm.ac.cn; Fax: +86 10 63165248 ; Tel: +86 10 63165248*
[b] *Department of Medicinal Chemistry , Beijing Key Laboratory of Active Substances Discovery and Drugability Evaluation, Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences , Beijing 100050, PR China*

Contents

This journal is © The Royal Society of Chemistry 2013

General Information

Equipment Melting points were determined on Yanaco MP-J3 microscope melting point apparatus. NMR spectra were recorded on Mercury-400 spectrometer. Chemical shifts are referenced to the residual solvent peak and reported in ppm (δ scale) and all coupling constant (*J*) values are given in Hz. The following multiplicity abbreviations are used: (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, and (br) broad. ESI-HRMS data were measured on Thermo Exactive Orbitrap plus spectrometer. Flash column chromatography was performed on Biotage Isolera one.

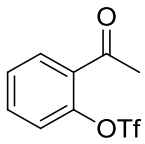
Solvents and chemicals All the solvents and chemicals were obtained from commercial sources and used without further purification.

This journal is © The Royal Society of Chemistry 2013

Experimental Procedures and Characterization Data:
2-acetyl/benzoylphenyl triflates

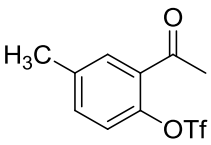
General procedure for the synthesis of 2-acetyl/benzoylphenyl triflates (1a-k, 5l-p)[1]:

To a solution of 2-acetyl/benzoylphenol (10.0 mmol) in pyridine (10 mL) was added Tf_2O (12.0 mmol) dropwise at 0 °C. The reaction mixture was then allowed to stir at room temperature for 12 h. Then the mixture was diluted by EtOAc (20 mL) and washed with 1M solution of $CuSO_4$ (10mL×4) and brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography over silica gel (eluting with PE/EA=100/1) to provide the desired product.



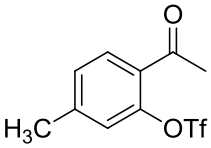
1a

2-acetylphenyl triflate 1a.[2] Yield:98%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.61 (td, *J* = 8.2, 1.8 Hz, 1H), 7.49 (td, *J* = 7.6, 1.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 2.64 (s, 3H); ESI-HRMS m/z calcd for $C_9H_8O_4F_3S$ $[M+H]^+$ 269.0090, found 269.0083.



1b

2-acetyl-4-methylphenyl triflate 1b.[3] Yield:96%.White solid. m.p. 30-32 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 2.62 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.86, 144.74, 138.92, 134.12, 131.80, 131.20, 122.46 (d, *J* = 1 Hz), 118.64 (q, *J* = 319 Hz), 29.47, 20.86; ESI-HRMS m/z calcd for $C_{10}H_{10}O_4F_3S$ $[M+H]^+$ 283.0246, found 283.0248.

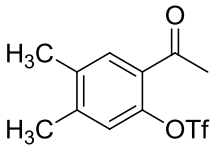


1c

2-acetyl-5-methylphenyl triflate 1c. Yield:98%. Yellow solid. m.p. 48-50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.13 (s, 1H), 2.61 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.22, 146.90, 145.50, 130.92, 129.19, 129.04, 123.21 (d, *J* = 1 Hz), 118.64 (q, *J* = 319 Hz), 29.24, 21.41; ESI-HRMS m/z calcd for $C_{10}H_{10}O_4FS$ $[M+H]^+$ 283.0246, found

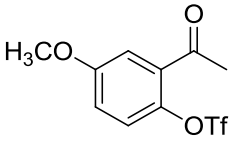
This journal is © The Royal Society of Chemistry 2013

283.0245.



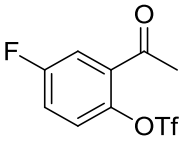
1d

2-acetyl-4, 5-dimethylphenyl triflate 1d. Yield:95%. Light yellow solid. m.p. 34-36 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.08 (s, 1H), 2.60 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.39, 144.86, 143.85, 137.46, 131.82, 129.03, 123.44 (d, J = 1 Hz), 118.65 (q, J = 319 Hz) 29.25, 20.00, 19.21; ESI-HRMS m/z calcd for $C_{11}H_{12}O_4F_3S$ $[M+H]^+$ 297.0403, found 297.0405.



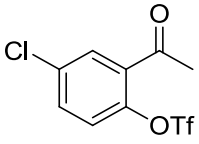
1e

2-acetyl-4-methoxylphenyl triflate 1e. Yield:95%. Brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.06 (dd, J = 9.1, 3.1 Hz, 1H), 3.87 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.52, 158.88, 139.98, 132.96, 123.77 (d, J = 1 Hz), 118.61 (q, J = 319 Hz), 118.16, 115.73, 55.90, 29.33; ESI-HRMS m/z calcd for $C_{10}H_{10}O_5F_3S$ $[M+H]^+$ 299.0196, found 299.0197.



1f

2-acetyl-4-fluorophenyl triflate 1f. Yield:92%. White solid. m.p. 33-35 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, J = 8.0, 2.7 Hz, 1H), 7.35 (dd, J = 9.0, 4.4 Hz, 1H), 7.32 – 7.25 (m, 1H), 2.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.26 (d, J = 1.2 Hz), 162.39, 159.88, 142.43 (d, J = 3.4 Hz), 133.83 (d, J = 6.4 Hz), 124.68 (dd, J = 8.4, 0.8 Hz), 118.98 (dd, J = 277.3, 23.7 Hz), 118.59 (q, J = 319 Hz), 29.41; ESI-HRMS m/z calcd for $C_9H_7O_4F_4S$ $[M+H]^+$ 286.9996, found 286.9998.

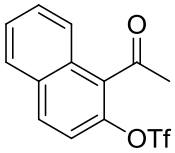


1g

2-acetyl-4-chlorophenyl triflate 1g.[4] Yield:94%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J

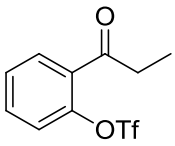
This journal is © The Royal Society of Chemistry 2013

= 2.6 Hz, 1H), 7.56 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 2.63 (s, 3H); ESI-HRMS m/z calcd for $C_9H_7O_4ClF_3S$ $[M+H]^+$ 302.9700, found 302.9699.



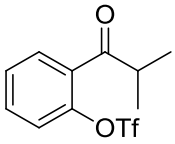
1h

1-acetylnaphthalen-2-yl triflate 1h. Yield:92%. White solid. m.p. 35-37 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.1 Hz, 1H), 7.92 (dd, *J* = 6.3, 3.0 Hz, 1H), 7.81 (dd, *J* = 6.7, 2.7 Hz, 1H), 7.66 – 7.55 (m, 2H), 7.45 (d, *J* = 9.1 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.69, 142.37, 132.47, 132.00, 131.74, 129.66, 128.65, 128.58, 127.58, 124.93, 119.04, 118.53 (q, J = 318 Hz), 32.77; ESI-HRMS m/z calcd for $C_{13}H_{10}O_4F_3S$ $[M+H]^+$ 319.0246, found 319.0249.



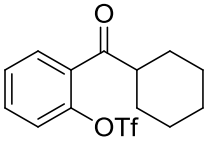
1i

2-propionylphenyl triflate 1i. [2a] Yield:95%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.48 (td, *J* = 7.6, 1.0 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 2.97 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H); ESI-HRMS m/z calcd for $C_{10}H_{10}O_4F_3S$ $[M+H]^+$ 283.0246, found 283.0241.



1j

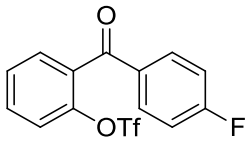
2-isobutyrylphenyl triflate 1j. [2a] Yield:90%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.58 (td, *J* = 8.0, 1.6 Hz, 1H), 7.48 (td, *J* = 7.6, 0.7 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 3.41 – 3.34 (m, 1H), 1.20 (d, *J* = 6.9 Hz, 6H); ESI-HRMS m/z calcd for $C_{11}H_{12}O_4F_3S$ $[M+H]^+$ 297.0403, found 297.0398.



1k

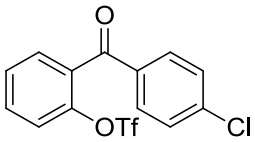
2-(cyclohexanecarbonyl)phenyl triflate 1k. Yield:92%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.70 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.62 – 7.52 (m, 1H), 7.47 (td, *J* = 7.6, 1.0 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 3.07 (tt, *J* = 11.3, 3.3 Hz, 1H), 1.89 (d, *J* = 13.1 Hz, 2H), 1.85 – 1.77 (m, 2H), 1.75 – 1.65 (m, 1H), 1.53 – 1.40 (m, 2H), 1.39 – 1.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.97, 146.63, 132.87, 132.38, 130.11, 128.44, 122.58 (d, J = 0.8 Hz), 118.59 (q, *J* = 319 Hz), 48.89, 28.72, 25.79, 25.65; ESI-HRMS m/z calcd for $C_{14}H_{16}O_4F_3S$ $[M+H]^+$ 337.0716, found 337.0711.



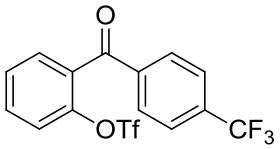
5l

2-(4-fluorobenzoyl)phenyl triflate 5l. Yield:94%. Brown oil. ^{1}H NMR (400 MHz, Acetone) δ 7.97 – 7.88 (m, 2H), 7.84 (ddd, *J* = 8.3, 7.3, 2.0 Hz, 1H), 7.77 – 7.59 (m, 3H), 7.40 – 7.30 (m, 2H); ^{13}C NMR (100 MHz, Acetone) δ 191.35, 154.00, 150.88, 146.78, 137.04, 133.93, 132.20, 131.68, 131.48, 128.94, 123.73, 122.80, 118.52 (q, *J* = 318 Hz); ESI-HRMS m/z calcd for $C_{14}H_9O_4F_4S$ $[M+H]^+$ 349.0152, found 349.0148.



5m

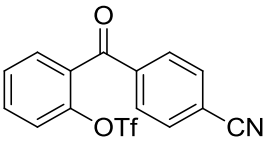
2-(4-chlorobenzoyl)phenyl triflate 5m. Yield:94%. Yellow solid. m.p. 35-37 °C. ^{1}H NMR (400 MHz, Acetone) δ 7.89 – 7.82 (m, 3H), 7.74 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.72 – 7.66 (m, 1H), 7.66 – 7.59 (m, 3H); ^{13}C NMR (100 MHz, Acetone) δ 191.05, 146.72, 139.65, 135.21, 133.45, 131.91, 131.64, 131.36, 128.96, 128.75, 122.64 (d, *J* = 0.6 Hz), 118.50 (q, *J* = 318 Hz); ESI-HRMS m/z calcd for $C_{14}H_9O_4ClF_3S$ $[M+H]^+$ 364.9857, found 364.9853.



5n

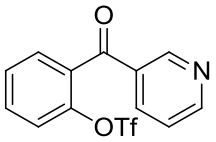
2-(4-(trifluoromethyl)benzoyl)phenyl triflate 5n. Yield:91%. White solid. m.p. 62-64 °C. ^{1}H NMR (400 MHz, Acetone) δ 8.04 (d, *J* = 8.2 Hz, 2H), 7.97 – 7.92 (m, 2H), 7.89 (td, *J* = 8.3, 1.8 Hz, 1H), 7.79 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.72 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.68 (dd, *J* = 11.0, 4.6 Hz, 1H); ^{13}C NMR (100 MHz, Acetone) δ 191.48, 146.84, 139.84, 133.90, 131.70, 131.53, 130.59, 129.57, 128.86, 125.73 (q, *J* = 3.8 Hz), 123.89 (q, *J* = 270 Hz), 122.78 (d, *J* = 0.6 Hz), 118.51 (q, *J* = 318 Hz); ESI-HRMS m/z calcd for $C_{15}H_9O_4F_6S$ $[M+H]^+$ 399.0120, found 399.0118.

This journal is © The Royal Society of Chemistry 2013



5o

2-(4-cyanobenzoyl)phenyl triflate 5o. Yield:95%. Yellow solid. m.p. 79-81 °C. ^{1}H NMR (400 MHz, Acetone) δ 8.06 – 7.95 (m, 4H), 7.93 – 7.85 (m, 1H), 7.78 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.71 (td, *J* = 7.6, 1.0 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, Acetone) δ 191.36, 146.83, 139.85, 134.04, 132.63, 131.73, 130.46, 128.90, 128.15, 122.81 (d, J = 0.6 Hz), 118.50 (q, J = 318 Hz), 117.65, 116.65; ESI-HRMS m/z calcd for $C_{15}H_9O_4NF_3S$ $[M+H]^+$ 356.0199, found 356.0199.



5p

2-nicotinoylphenyl triflate 5p. Yield:90%. Brown oil. ^{1}H NMR (400 MHz, Acetone) δ 8.95 (d, *J* = 1.6 Hz, 1H), 8.87 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.22 – 8.15 (m, 1H), 7.89 (ddd, *J* = 8.3, 7.5, 1.8 Hz, 1H), 7.81 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.72 (td, *J* = 7.6, 1.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.61 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, Acetone) δ 190.68, 167.30, 164.78, 146.67, 133.28, 132.97, 132.87, 131.25, 128.73, 122.58 (d, *J* = 0.6 Hz), 118.59 (q, *J* = 318 Hz), 115.88, 115.66; ESI-HRMS m/z calcd for $C_{13}H_9O_4NF_3S$ $[M+H]^+$ 332.0199, found 332.0195.

This journal is © The Royal Society of Chemistry 2013

Experimental Procedures and Characterization Data:

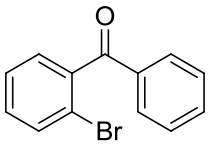
2-benzoylphenyl halide

General procedure for the synthesis of 2-benzoylphenyl halide Method A:(5a-g)[5]:

The substituted 2-bromobenzoic acid (10.0 mmol), thionyl chloride (15 mL) and one drop of N, N-dimethylformamide were heated under reflux for 2 h. The excess thionyl chloride was removed from the cooled reaction mixture and the remaining acid chloride was dissolved in benzene (20 mL). Aluminium chloride (11.0 mmol) was added portion-wise over 10 min to this solution and the resulting suspension was refluxed for 1 h. The reaction mixture was poured slowly into 2N HCl (20 mL) and ice. The organic layer was separated and the aqueous layer extracted with EtOAc (5 mL×3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography over silica gel (eluting with PE/EA=100/1) to provide the desired product.

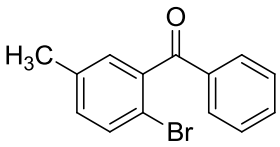
General procedure for the synthesis of 2-benzoylphenyl halide Method B:(5h-k)[6]:

A solution of 2-iodobenzoic acid (10.0 mmol) and $SOCl_2$ (25.0 mmol) in CH_2Cl_2 (20 mL) was stirred overnight. The excess $SOCl_2$ was removed and the remaining acid chloride was dissolved in anhydrous CH_2Cl_2 (20 mL), then substituted benzene (12.0 mmol) was added. After the mixture was cooled to 0 ^oC, $AlCl_3$ (11.0 mmol) was added portion-wise over 10 min. The reaction mixture was allowed to stir at room temperature for 6 h, then poured slowly into 2N HCl (20 mL) and ice. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (5 mL×3). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography over silica gel (eluting with PE/EA=100/1) to provide the desired product.



5a

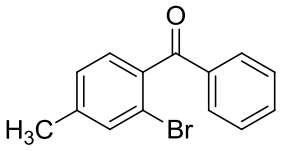
2-benzoyl-1-bromobenzene 5a.[7] Yield:85%. Yellow oil. ^1H NMR (400 MHz, Acetone) δ 7.81 – 7.73 (m, 3H), 7.70 (ddd, *J* = 8.7, 2.5, 1.3 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.50 (td, *J* = 7.7, 1.9 Hz, 1H), 7.45 (dd, *J* = 7.3, 1.8 Hz, 1H); ESI-HRMS m/z calcd for $C_{13}H_{10}OBr$ $[M+H]^+$ 260.9910, found 260.9910.



5b

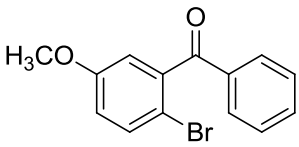
2-benzoyl-4-methyl-1-bromobenzene 5b.[8] Yield:87%. Yellow solid. m.p. 30-32 ^oC. ^1H NMR (400 MHz, Acetone) δ 7.81 – 7.74 (m, 2H), 7.72 – 7.64 (m, 1H), 7.63 – 7.50 (m, 3H), 7.31 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.25 (d, *J* = 1.5 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, Acetone) δ 195.08, 140.76, 137.85, 136.27, 133.73, 132.74, 132.13, 129.83, 129.38, 128.81, 115.39, 19.98; ESI-HRMS m/z

calcd for $C_{14}H_{12}OBr$ $[M+H]^+$ 275.0066, found 275.0071.



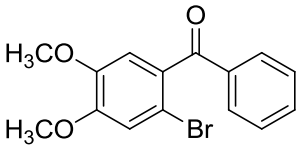
5c

2-benzoyl-5-methyl-1-bromobenzene 5c.[7a] Yield:82%. White solid. m.p. 28-30 °C. ^{1}H NMR (400 MHz, Acetone) δ 7.82 – 7.73 (m, 2H), 7.70 – 7.64 (m, 1H), 7.59 – 7.49 (m, 3H), 7.37 – 7.29 (m, 2H), 2.43 (s, 3H); ESI-HRMS m/z calcd for $C_{14}H_{12}OBr$ $[M+H]^+$ 275.0066, found 275.0067.



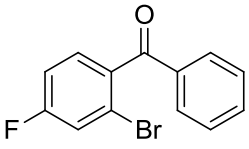
5d

2-benzoyl-4-methoxyl-1-bromobenzene 5d.[7a] Yield: 78%. Yellow oil. ^{1}H NMR (400 MHz, Acetone) δ 7.82 – 7.77 (m, 2H), 7.73 – 7.65 (m, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.07 (dd, *J* = 8.8, 3.0 Hz, 1H), 7.02 (d, *J* = 3.0 Hz, 1H), 3.86 (s, 3H); ESI-HRMS m/z calcd for $C_{14}H_{12}O_2Br$ $[M+H]^+$ 291.0015, found 291.0019.



5e

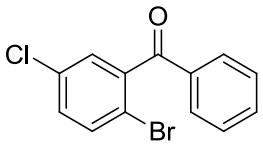
2-benzoyl-4, 5-dimethoxyl-1-bromobenzene 5e.[9] Yield: 80%. Light yellow solid. m.p. 60-62 °C. ^{1}H NMR (400 MHz, Acetone) δ 7.81 – 7.76 (m, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.22 (s, 1H), 7.03 (s, 1H), 3.94 (s, 3H), 3.84 (s, 3H); ESI-HRMS m/z calcd for $C_{15}H_{14}O_3Br$ $[M+H]^+$ 321.0121, found 321.0123.



5f

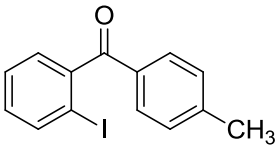
2-benzoyl-5-fluoro-1-bromobenzene 5f. [10] Yield: 88%. Yellow oil. ^{1}H NMR (400 MHz, Acetone) δ 7.83 – 7.76 (m, 1H), 7.69 (q, *J* = 7.0 Hz, 1H), 7.64 – 7.50 (m, 3H), 7.42 – 7.25 (m, 2H), 7.11 (dd, *J* = 15.8, 7.9 Hz, 1H); ESI-HRMS m/z calcd for $C_{13}H_9OBrF$ $[M+H]^+$ 278.9815, found 278.9818.

This journal is © The Royal Society of Chemistry 2013



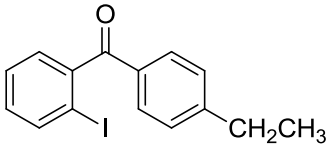
5g

2-benzoyl-4-chloro-1-bromobenzene 5g. [11] Yield: 85%. Yellow solid. m.p. 88-90 °C. ^{1}H NMR (400 MHz, Acetone) δ 7.82 (d, *J* = 1.1 Hz, 1H), 7.80 (t, *J* = 1.6 Hz, 1H), 7.79 – 7.74 (m, 1H), 7.72 (ddd, *J* = 8.7, 2.5, 1.2 Hz, 1H), 7.59 (d, *J* = 1.5 Hz, 1H), 7.57 (s, 1H), 7.55 (t, *J* = 2.1 Hz, 1H), 7.53 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, Acetone) δ 193.54, 142.55, 135.64, 134.65, 134.14, 133.46, 131.32, 129.90, 128.97, 128.60, 116.99; ESI-HRMS m/z calcd for $C_{13}H_9OBrCl$ $[M+H]^+$ 294.9520, found 294.9526.



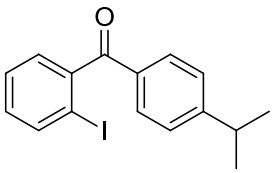
5h

2-(4-methylbenzoyl)-1-iodobenzene 5h. [12] Yield: 86%. Light yellow solid. m.p. 42-44 °C. ^{1}H NMR (400 MHz, Acetone) δ 8.00 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.57 (td, *J* = 7.5, 1.1 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 3H), 7.33 – 7.27 (m, 1H), 2.43 (s, 3H); ESI-HRMS m/z calcd for $C_{14}H_{12}OI$ $[M+H]^+$ 322.9927, found 322.9932.



5i

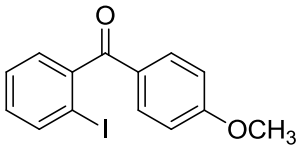
2-(4-ethylbenzoyl)-1-iodobenzene 5i. Yield: 82%. Yellow oil. ^{1}H NMR (400 MHz, Acetone) δ 8.00 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.57 (tt, *J* = 6.0, 3.0 Hz, 1H), 7.42 – 7.35 (m, 3H), 7.30 (td, *J* = 7.8, 1.7 Hz, 1H), 2.77 – 2.71 (m, 2H), 1.25 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, Acetone) δ 196.01, 150.85, 145.04, 139.54, 133.46, 131.12, 130.40, 128.36, 128.21, 128.10, 91.73, 28.73, 14.84; ESI-HRMS m/z calcd for $C_{15}H_{14}OI$ $[M+H]^+$ 337.0084, found 337.0085.



5j

2-(4-isopropylbenzoyl)-1-iodobenzene 5j. Yield: 80%. Brown oil. ^{1}H NMR (400 MHz, Acetone) δ 8.00 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.57 (td, *J* = 7.5, 1.1 Hz, 1H), 7.43 (d, *J* = 8.2 Hz,

2H), 7.36 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.34 – 7.26 (m, 1H), 3.02 (hept, *J* = 6.9 Hz, 1H), 1.27 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, Acetone) δ 195.97, 155.31, 145.01, 139.66, 133.66, 131.25, 130.61, 128.35, 128.18, 127.05, 92.07, 34.26, 30.10; ESI-HRMS m/z calcd for $C_{16}H_{16}OI$ $[M+H]^+$ 351.0240, found 351.0239.



5k

2-(4-methoxylbenzoyl)-1-iodobenzene 5j. [13] Yield: 77%. White solid. m.p. 78-80 °C. ^{1}H NMR (400 MHz, Acetone) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.9 Hz, 2H), 7.55 (td, *J* = 7.5, 0.7 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.27 (td, *J* = 7.8, 1.6 Hz, 1H), 7.05 (d, *J* = 8.9 Hz, 2H), 3.90 (s, 3H); ESI-HRMS m/z calcd for $C_{14}H_{12}O_2I$ $[M+H]^+$ 338.9877, found 338.9879.

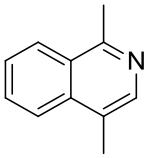
This journal is © The Royal Society of Chemistry 2013

Experimental Procedures and Characterization Data:

4-methylisoquinolines

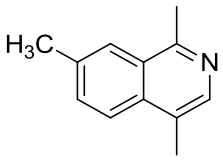
General procedure for the synthesis of 4-methylisoquinolines:

To a solution of the 2-acetyl/benzoylphenyl triflates/halide (1.0 mmol) in ethylene glycol (10 mL) was sequentially added N-Boc allylamine (1.2 mmol), $Pd(OA)_2$ (0.05 mmol), dppp (0.1 mmol) and NaOAc (2.0 mmol). The reaction mixture was heated at 120 ^oC under argon for 12 h, then cooled to room temperature. Water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (10mL×3). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash column chromatography over silica gel (eluting with CH_2Cl_2/EA=100/1 to 20/1) to provide the desired product.



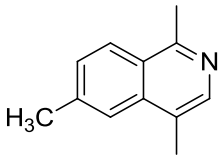
4a

1,4-dimethylisoquinoline 4a Yield: 62%. Brown oil. ^1H NMR (400 MHz, CD_3OD) δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.98 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 2.77 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 156.50, 139.52, 135.30, 130.16, 126.85, 126.70, 126.37, 125.81, 123.33, 20.15, 14.43; ESI-HRMS m/z calcd for $C_{11}H_{12}N$ $[M+H]^+$ 158.0964, found 158.0965.



4b

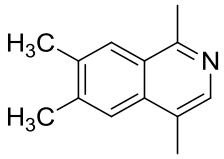
1,4,7-trimethylisoquinoline 4b Yield: 65%. Brown oil. ^1H NMR (400 MHz, CD_3OD) δ 7.79 (s, 1H), 7.67 (s, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 2.61 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.73, 138.72, 136.98, 133.50, 132.15, 126.86, 126.21, 124.66, 123.18, 20.49, 20.11, 14.41; ESI-HRMS m/z calcd for $C_{12}H_{14}N$ $[M+H]^+$ 172.1121, found 172.1122.



4c

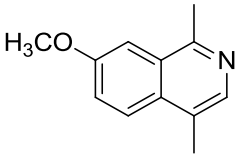
1,4,6-trimethylisoquinoline 4c Yield: 65%. Brown oil. ^1H NMR (400 MHz, CD_3OD) δ 8.04 (d, *J* = 8.6 Hz, 1H), 7.98 (s, 1H), 7.74 (s, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 2.78 (s, 3H), 2.51 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 156.19, 140.97, 139.51, 135.70, 128.95, 125.97, 125.78, 125.11, 122.41, 20.74, 20.01, 14.47; ESI-HRMS m/z calcd for $C_{12}H_{14}N$ $[M+H]^+$ 172.1121, found 172.1122.

This journal is © The Royal Society of Chemistry 2013



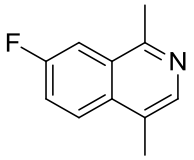
4d

1,4,6,7-tetramethylisoquinoline 4d Yield: 70%. Brown solid. m.p. 39-42 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 7.88 (s, 1H), 7.82 (s, 1H), 7.64 (s, 1H), 2.73 (s, 3H), 2.44 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.29, 140.66, 138.63, 136.80, 134.16, 125.62, 125.59, 125.12, 122.81, 19.99, 19.25, 18.98, 14.44; ESI-HRMS m/z calcd for $C_{13}H_{16}N$ $[M+H]^+$ 186.1277, found 186.1281.



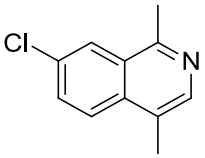
4e

7-methoxy-1,4-dimethylisoquinoline 4e Yield: 72%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 7.89 (s, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.37 – 7.29 (m, 2H), 3.88 (s, 3H), 2.75 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.34, 154.89, 137.70, 130.70, 128.05, 126.36, 125.06, 122.52, 103.70, 54.54, 20.21, 14.42; ESI-HRMS m/z calcd for $C_{12}H_{14}ON$ $[M+H]^+$ 188.1070, found 188.1071.



4f

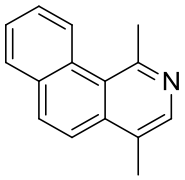
7-fluoro-1,4-dimethylisoquinoline 4f Yield: 63%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.05 (dd, *J* = 8.6, 4.5 Hz, 2H), 7.80 (dd, *J* = 10.1, 2.4 Hz, 1H), 7.56 (td, *J* = 8.5, 1.9 Hz, 1H), 2.78 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 162.03, 159.57, 156.16, 156.10, 139.33, 139.30, 132.53, 127.87, 127.78, 126.70, 126.61, 126.52, 126.50, 120.30, 120.05, 109.42, 109.21, 20.22, 14.46; ESI-HRMS m/z calcd for $C_{11}H_{11}NF$ $[M+H]^+$ 176.0870, found 176.0874.



4g

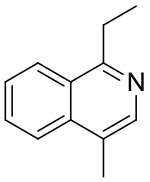
7-chloro-1,4-dimethylisoquinoline 4g Yield: 60%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (s, 1H), 8.04 (s, 1H), 7.93 (d, *J* = 8.9 Hz, 1H), 7.67 (d, *J* = 9.0 Hz, 1H), 2.77 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.96, 140.19, 133.76, 132.58, 130.82, 127.51, 126.49, 125.64, 124.81, 20.17, 14.33; ESI-HRMS m/z calcd for $C_{11}H_{11}NCl$ $[M+H]^+$ 192.0575, found 192.0578.

This journal is © The Royal Society of Chemistry 2013



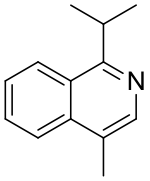
4h

1,4-dimethylbenzo[h]isoquinoline 4h Yield: 65%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.82 (d, *J* = 8.5 Hz, 1H), 8.26 (s, 1H), 8.00 (d, *J* = 9.0 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.87 (d, *J* = 9.1 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 3.19 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 154.42, 141.89, 136.72, 133.16, 131.82, 130.04, 128.82, 126.86, 126.77, 126.58, 126.53, 124.52, 121.06, 28.19, 15.09; ESI-HRMS m/z calcd for $C_{15}H_{14}N$ $[M+H]^+$ 208.1121, found 208.1124.



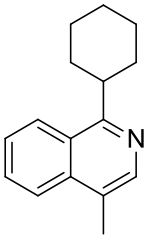
4i

1-ethyl-4-methylisoquinoline 4i Yield: 64%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.05 (d, *J* = 8.4 Hz, 1H), 7.99 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.65 – 7.58 (m, 1H), 7.55 – 7.47 (m, 1H), 3.11 (q, *J* = 7.6 Hz, 2H), 2.40 (s, 3H), 1.25 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, MeOD) δ 164.65, 140.06, 135.80, 129.80, 126.71, 125.79, 125.53, 124.95, 123.58, 30.18, 21.14, 14.52; ESI-HRMS m/z calcd for $C_{12}H_{14}N$ $[M+H]^+$ 172.1121, found 172.1117.



4j

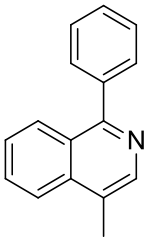
1-isopropyl-4-methylisoquinoline 4j Yield: 63%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.18 (d, *J* = 8.5 Hz, 1H), 8.07 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.67 – 7.59 (m, 1H), 7.56 – 7.46 (m, 1H), 3.91 – 3.81 (m, 1H), 2.44 (s, 3H), 1.27 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, MeOD) δ 161.44, 139.76, 135.70, 130.01, 126.81, 126.23, 125.77, 125.47, 123.49, 27.42, 14.46, 13.19; ESI-HRMS m/z calcd for $C_{13}H_{16}N$ $[M+H]^+$ 186.1277, found 186.1275.



4k

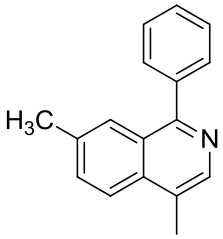
1-cyclohexyl-4-methylisoquinoline 4k Yield: 66%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.12 (d,

J = 8.5 Hz, 1H), 8.00 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.63 – 7.54 (m, 1H), 7.52 – 7.41 (m, 1H), 3.49 – 3.35 (m, 1H), 2.39 (s, 3H), 1.73 (d, *J* = 11.1 Hz, 4H), 1.67 – 1.51 (m, 2H), 1.49 – 1.33 (m, 2H), 1.26 – 1.15 (m, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 165.35, 141.51, 137.27, 131.22, 128.13, 127.12, 127.03, 126.32, 125.04, 42.32, 33.69, 27.81, 27.35, 15.95; ESI-HRMS m/z calcd for $C_{16}H_{20}N$ $[M+H]^+$ 226.1590, found 226.1587.



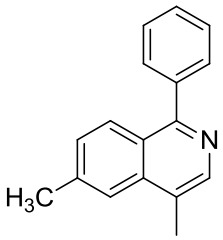
6a

4-methyl-1-phenylisoquinoline 6a Yield: 65%. Brown solid. m.p. 58-60 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.17 (s, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.68 – 7.60 (m, 1H), 7.41 – 7.39 (m, 6H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.17, 140.26, 138.88, 136.21, 130.35, 129.54, 128.45, 128.05, 127.67, 127.51, 127.06, 126.08, 123.31, 14.66; ESI-HRMS m/z calcd for $C_{16}H_{14}N$ $[M+H]^+$ 220.1121, found 220.1122.



6b

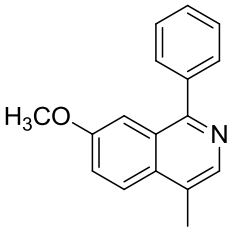
4,7-dimethyl-1-phenylisoquinoline 6b Yield: 70%. Brown solid. m.p. 85-88 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (s, 1H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.61 (s, 1H), 7.50 (d, *J* = 8.6 Hz, 1H), 7.42 (s, 5H), 2.49 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.50, 139.54, 139.04, 137.07, 134.49, 132.41, 129.50, 128.35, 128.03, 127.37, 126.34, 126.30, 123.22, 20.47, 14.62; ESI-HRMS m/z calcd for $C_{17}H_{16}N$ $[M+H]^+$ 234.1277, found 234.1280.



6c

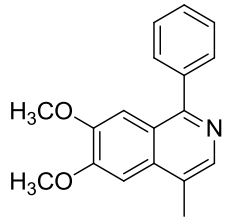
4,6-dimethyl-1-phenylisoquinoline 6c Yield: 70%. Brown solid. m.p. 75-78 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.11 (s, 1H), 7.71 (d, *J* = 9.1 Hz, 2H), 7.40 (s, 5H), 7.24 (d, *J* = 8.7 Hz, 1H), 2.47 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.80, 141.09, 140.30, 138.97, 136.47, 129.51, 129.13, 128.37, 128.00, 127.52, 126.91, 124.39, 122.28, 20.78, 14.70; ESI-HRMS m/z calcd for $C_{17}H_{16}N$ $[M+H]^+$ 234.1277, found 234.1279.

This journal is © The Royal Society of Chemistry 2013



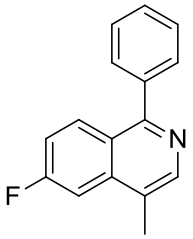
6d

7-methoxy-4-methyl-1-phenylisoquinoline 6d Yield: 71%. Brown solid. m.p. 91-93 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.10 (s, 1H), 7.91 (d, *J* = 9.2 Hz, 1H), 7.54 – 7.41 (m, 5H), 7.38 – 7.31 (m, 1H), 7.19 (d, *J* = 2.4 Hz, 1H), 3.66 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.44, 157.65, 139.18, 138.66, 131.72, 129.33, 128.38, 128.16, 127.51, 127.46, 125.08, 122.79, 105.30, 54.33, 14.61; ESI-HRMS m/z calcd for $C_{17}H_{16}ON$ $[M+H]^+$ 250.1226, found 250.1228.



6e

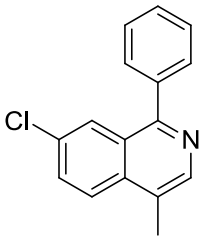
6,7-dimethoxy-4-methyl-1-phenylisoquinoline 6e Yield: 75%. Brown solid. m.p. 150-152 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (s, 1H), 7.55 – 7.41 (m, 5H), 7.19 (d, *J* = 8.2 Hz, 2H), 3.95 (s, 3H), 3.69 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 156.58, 153.18, 150.13, 139.34, 139.29, 133.21, 129.32, 128.31, 128.15, 126.35, 122.00, 105.68, 101.76, 55.07, 54.68, 14.85; ESI-HRMS m/z calcd for $C_{18}H_{18}O_2N$ $[M+H]^+$ 280.1332, found 280.1335.



6f

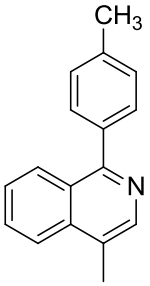
6-fluoro-4-methyl-1-phenylisoquinoline 6f Yield: 65%. Brown solid. m.p. 106-109 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.28 (s, 1H), 8.02 (dd, *J* = 9.3, 5.7 Hz, 1H), 7.70 (dd, *J* = 10.3, 2.4 Hz, 1H), 7.55 – 7.47 (m, 5H), 7.36 (td, *J* = 9.1, 2.5 Hz, 1H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 164.60, 162.09, 159.11, 141.18, 138.67, 138.24, 138.14, 131.43, 131.33, 129.48, 128.62, 128.13, 127.36, 127.31, 123.42, 117.22, 116.97, 107.19, 106.98, 14.64; ESI-HRMS m/z calcd for $C_{16}H_{13}NF$ $[M+H]^+$ 238.1027, found 238.1028.

This journal is © The Royal Society of Chemistry 2013



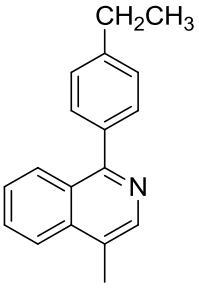
6g

6-chloro-4-methyl-1-phenylisoquinoline 6g Yield: 64%. Brown solid. m.p. 80-82 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 (s, 1H), 8.03 (d, *J* = 8.9 Hz, 1H), 7.83 (s, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.49 (s, 5H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 158.33, 140.95, 138.27, 134.53, 132.78, 130.93, 129.42, 128.73, 128.22, 127.58, 126.75, 126.17, 125.64, 14.56; ESI-HRMS m/z calcd for $C_{16}H_{13}NCl$ $[M+H]^+$ 254.0731, found 254.0734.



6h

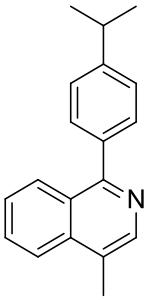
4-methyl-1-(p-tolyl)isoquinoline 6h Yield: 70%. Brown solid. m.p. 51-54 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.20 (s, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.70 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.48 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 2.56 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.29, 140.22, 138.56, 136.25, 136.00, 130.31, 129.49, 128.65, 127.79, 127.28, 126.97, 126.17, 123.28, 19.97, 14.63; ESI-HRMS m/z calcd for $C_{17}H_{16}N$ $[M+H]^+$ 234.1277, found 234.1280.



6i

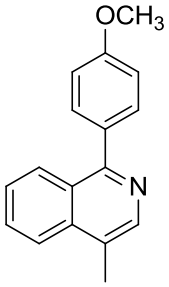
1-(4-ethylphenyl)-4-methylisoquinoline 6i Yield: 71%. Brown solid. m.p. 38-40 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.19 (s, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.69 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.47 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 2.69 – 2.63 (m, 2H), 2.55 (s, 3H), 1.23 – 1.19 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.32, 144.98, 140.23, 136.27, 136.25, 130.31, 129.60, 127.81, 127.50, 127.28, 126.98, 126.18, 123.28, 28.30, 14.74, 14.64; ESI-HRMS m/z calcd for $C_{18}H_{18}N$ $[M+H]^+$ 248.1435, found 248.1435.

This journal is © The Royal Society of Chemistry 2013



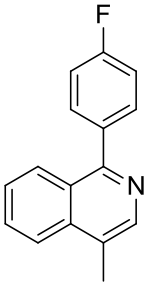
6j

1-(4-isopropylphenyl)-4-methylisoquinoline 6j Yield: 70%. Brown oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.21 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 2.93 (hept, *J* = 6.7 Hz, 1H), 2.58 (s, 3H), 1.24 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, CD_3OD) δ 159.29, 149.53, 140.25, 136.42, 136.24, 130.30, 129.62, 127.83, 127.27, 126.98, 126.17, 126.07, 123.28, 33.89, 23.03, 14.65; ESI-HRMS m/z calcd for $C_{19}H_{20}N$ $[M+H]^+$ 262.1590, found 262.1595.



6k

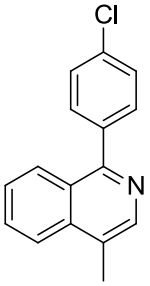
1-(4-methoxyphenyl)-4-methylisoquinoline 6k Yield: 75%. Brown solid. m.p. 100-102 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.18 (s, 1H), 7.95 (dd, *J* = 12.6, 8.6 Hz, 2H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 160.33, 159.00, 140.21, 136.30, 131.14, 130.91, 130.27, 127.82, 127.05, 126.94, 126.20, 123.28, 113.45, 54.46, 14.62; ESI-HRMS m/z calcd for $C_{17}H_{16}ON$ $[M+H]^+$ 250.1226, found 250.1228.



6l

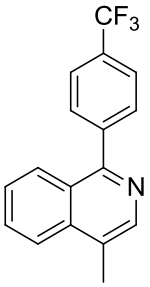
1-(4-fluorophenyl)-4-methylisoquinoline 6l Yield: 67%. Brown solid. m.p. 140-142 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.24 (s, 1H), 8.03 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.53 (dd, *J* = 8.4, 5.6 Hz, 3H), 7.21 (t, *J* = 8.7 Hz, 2H), 2.59 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 164.38, 161.92, 158.12, 140.31, 136.28, 135.14, 135.11, 131.63, 131.55, 130.45, 127.73, 127.47, 127.23, 126.10, 123.42, 115.02, 114.80, 14.62; ESI-HRMS m/z calcd for $C_{16}H_{13}NF$ $[M+H]^+$ 238.1027, found 238.1028.

This journal is © The Royal Society of Chemistry 2013



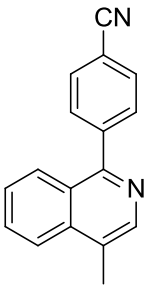
6m

1-(4-chlorophenyl)-4-methylisoquinoline 6m Yield: 65%. Brown solid. m.p. 97-99 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.25 (s, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.75 (t, *J* = 7.7 Hz, 1H), 7.56 – 7.46 (m, 5H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 157.83, 140.40, 137.49, 136.24, 134.58, 131.12, 130.46, 128.23, 127.89, 127.30, 127.29, 125.94, 123.43, 14.65; ESI-HRMS m/z calcd for $C_{16}H_{13}NCl$ $[M+H]^+$ 254.0731, found 254.0734.



6n

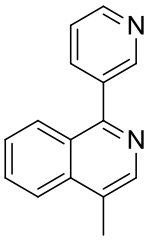
4-methyl-1-(4-(trifluoromethyl)phenyl)isoquinoline 6n Yield: 63%. Brown solid. m.p. 123-126 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.29 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.82 – 7.74 (m, 3H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.56 (dd, *J* = 8.1, 7.2 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 157.58, 142.80, 140.54, 136.26, 130.59, 130.28, 128.36, 127.51, 127.13, 125.92, 125.06, 125.02, 124.99, 124.95, 123.54, 14.66; ESI-HRMS m/z calcd for $C_{17}H_{13}NF_3$ $[M+H]^+$ 288.0995, found 288.0998.



6o

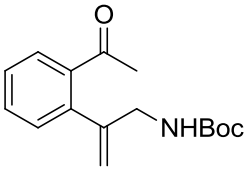
4-(4-methylisoquinolin-1-yl)benzonitrile 6o Yield: 62%. Brown solid. m.p. 139-141 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.31 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.91 – 7.81 (m, 3H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 1H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 157.13, 143.56, 140.68, 136.28, 132.00, 130.64, 130.58, 128.59, 127.60, 126.94, 125.77, 123.61, 118.09, 112.24, 14.68; ESI-HRMS m/z calcd for $C_{17}H_{13}N_2$ $[M+H]^+$ 245.1073, found 245.1077.

This journal is © The Royal Society of Chemistry 2013



6p

4-methyl-1-(pyridin-3-yl)isoquinoline 6p. Yield: 62%. Brown solid. m.p. 76-79 ^{o}C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.73 (s, 1H), 8.65 (d, *J* = 4.4 Hz, 1H), 8.35 (s, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.08 – 8.01 (m, 1H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.67 – 7.53 (m, 2H), 2.65 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 155.40, 149.44, 148.83, 140.87, 138.07, 136.22, 135.38, 130.90, 130.62, 128.47, 127.66, 126.76, 126.08, 123.63, 14.69; ESI-HRMS m/z calcd for $C_{15}H_{13}N_2$ $[M+H]^+$ 221.1073, found 221.1076.



3a

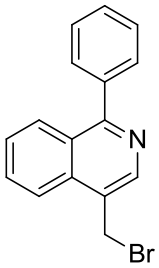
Tert-butyl (2-(2-acetylphenyl)allyl)carbamate 3a. Yield: 85%. Brown oil. ^{1}H NMR (400 MHz, Acetone) δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.48 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.41 (td, *J* = 7.5, 1.2 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 6.22 (s, 1H), 5.25 (d, *J* = 1.5 Hz, 1H), 4.90 (d, *J* = 1.3 Hz, 1H), 4.01 (d, *J* = 6.1 Hz, 2H), 2.51 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, Acetone) δ 202.09, 155.69, 147.95, 139.87, 139.75, 130.55, 129.51, 128.06, 127.47, 113.71, 76.81, 45.60, 29.19, 27.69; ESI-HRMS m/z calcd for $C_{16}H_{21}O_3NNa$ $[M+Na]^+$ 298.1414, found 298.1417.

This journal is © The Royal Society of Chemistry 2013

Experimental Procedures and Characterization Data:

Isoquinolines derivatives

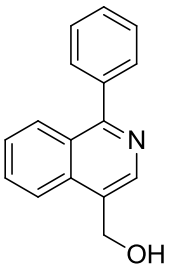
General procedure for the synthesis of 1-phenyl-4-(bromomethyl)isoquinoline (7)[14]:



7

A solution of **6a** (220 mg, 1 mmol), NBS (196 mg, 1.1 mmol) and AIBN (17 mg, 0.1 mmol) in benzene (10 mL) was reflux under argon for 1h. After cooled to room temperature, the solvent was removed *in vacuo*. The residue was dissolved in EtOAc (15 mL), washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography over silica gel (eluting with CH_2Cl_2/EA=100:1) to provide the desired product (253 mg, 85% yield) as yellow solid. m.p. 225-227 °C. ^{1}H NMR (400 MHz, Acetone) δ 8.75 (s, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 7.97 – 7.89 (m, 1H), 7.74 – 7.67 (m, 3H), 7.62 – 7.52 (m, 3H), 5.22 (s, 2H); ^{13}C NMR (100 MHz, Acetone) δ161.68, 142.88, 139.55, 134.57, 130.48, 130.03, 128.68, 128.19, 127.95, 127.63, 126.78, 126.40, 123.67, 28.78; ESI-HRMS m/z calcd for $C_{16}H_{13}NBr$ $[M+H]^+$ 298.0226, found 298.0236.

General procedure for the synthesis of 1-phenyl-4-(hydroxymethyl)isoquinoline (8):

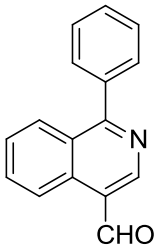


8

A solution of **7** (230 mg, 0.77 mmol), CH_3COOH (70 mg, 1.2 mmol) and Et_3N (155 mg, 1.5 mmol) in CH_3CN (10 mL) was heated at 60 °C for 30 min. Then solvent was removed *in vacuo* and the residue was dissolved in MeOH (10 mL) followed by NaOH (616 mg, 15.4 mmol) added. The mixture was reflux for 1 h, then cooled to room temperature. After MeOH was removed *in vacuo*, the residue was dissolved in CH_2Cl_2 (10 mL), washed with saturated aqueous NH_4Cl solution and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude residue was purified by flash column chromatography over silica gel (eluting with CH_2Cl_2/MeOH=100:1 to 30:1)) to provide the desired product (127 mg, 70%) as yellow solid. m.p. 105-108 °C. ^{1}H NMR (400 MHz, Acetone) δ 8.60 (s, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.83 – 7.79 (m, 1H), 7.71 – 7.66 (m, 2H), 7.66 – 7.60 (m, 1H), 7.60 – 7.49 (m, 3H), 5.14 (s, 2H); ^{13}C NMR (100 MHz, Acetone) δ160.25, 140.89, 139.96, 135.14, 129.99, 129.92, 129.63, 128.35, 128.11, 127.49, 126.95, 126.08, 123.89, 60.10;

ESI-HRMS m/z calcd for $C_{16}H_{14}ON$ $[M+H]^+$ 236.1070, found 236.1072.

General procedure for the synthesis of 1-phenylisoquinoline-4-carbaldehyde (9):



9

To a solution of **8** (100 mg, 0.43 mmol) in CH_2Cl_2 (5 mL) was added MnO_2 (740 mg, 8.5 mmol). The mixture was stirred at room temperature for 6 h, then filtered through diatomite and the filtrate was concentrated *in vacuo* to afford **9** (90 mg, 90%) as white solid. m.p. 149-151 ^oC. ^1H NMR (400 MHz, Acetone) δ 10.49 (s, 1H), 9.31 (d, *J* = 8.6 Hz, 1H), 9.12 (s, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.06 – 7.92 (m, 1H), 7.82 – 7.73 (m, 3H), 7.65 – 7.58 (m, 3H); ^{13}C NMR (100 MHz, Acetone) δ193.04, 166.02, 152.19, 139.15, 133.41, 132.84, 130.18, 129.38, 128.31, 128.23, 128.18, 126.12, 124.29, 123.69; ESI-HRMS m/z calcd for $C_{16}H_{12}ON$ $[M+H]^+$ 234.0913, found 234.0915.

Reference

1 W. M. Seganish and P. DeShong, *J. Org. Chem.*, 2004, **69**, 1137.

2 (a) J. W. Coe, K. E. Bianco, B. P. Boscoe, P. R. Brooks, E. D. Cox and M. G. Vetelino, *J. Org. Chem.*, 2003, **68**, 9964; (b) W. M. Seganish and P. DeShong, *J. Org. Chem.*, 2004, **69**, 1137 ; (c) C. P. Park, A. Nagle, C. H. Yoon, C. Chen and K. W. Jung, *J. Org. Chem.*, 2009, **74**, 6231.

3 P. G. Ciattini, G. Mastropietro, E. Morera and G. Ortar, *Tetrahedron Lett.*, 1993, **34**, 3763.

4 J. J. Crawford, P. W. Kenny, J. Bowyer, C. R. Cook, J. E. Finlayson, C. Heyes, A. J. Highton, J. A. Hudson, A. Jestel, S. Krapp, S. Martin, P. A. Macfaul, B. P. McDermott, T. M. McGuire, A. D. Morley, J. J. Morris, K. M. Page, L. R. Ribeiro, H. Sawney, S. Steinbacher, C. Smith and A. G. Dossetter, *J. Med. Chem.*, 2012, **55**, 8827.

5 C. D. Gabbutt, B. M. Heron and A. C. Instone, *Tetrahedron,* 2006, **62**, 737.

6 H. A. Reisch, V. Enkelmann and U. Scherf, *J. Org. Chem.*, 1999, **64**, 655.

7 (a) K. Inamoto, M. Katsuno, T. Yoshino, Y. Arai, K. Hiroya and T. Sakamoto, *Tetrahedron*, 2007, **63**, 2695; (b) M. Li, C. Wang and H. Ge, *Org. Lett.*, 2011, **13**, 2062; (c) A. Yu, L. Shen, X. Cui, D. Peng and Y. Wu, *Tetrahedron*, 2012, **68**, 2283.

8 B. F. S. E. De Sousa, A. E. Siegrist, *Helv. Chim. Acta*, 1978, **61**, 2904.

9 (a) W. Zhao, X. Feng, S. Ban, W. Lin and Q. Li, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 4132; (b) J. N. Moorthy and S. Samanta, *J. Org. Chem.*, 2007, **72**, 9786.

10 Bui-Khac-Diep, *C.R. Acad. Sci., Ser. IIc: Chim.*, 1966, **263**, 145.

11 K. Kobayashi, W. Miyatani, N. Matsumoto, *Helv. Chim. Acta*, 2013, **96**, 239.

12 C. CopCret, T. Sugihara, G. Wu, I. Shimoyama and E.-i. Negishi, *J. Am. Chem. Soc.*, 1995, **117**, 3422.

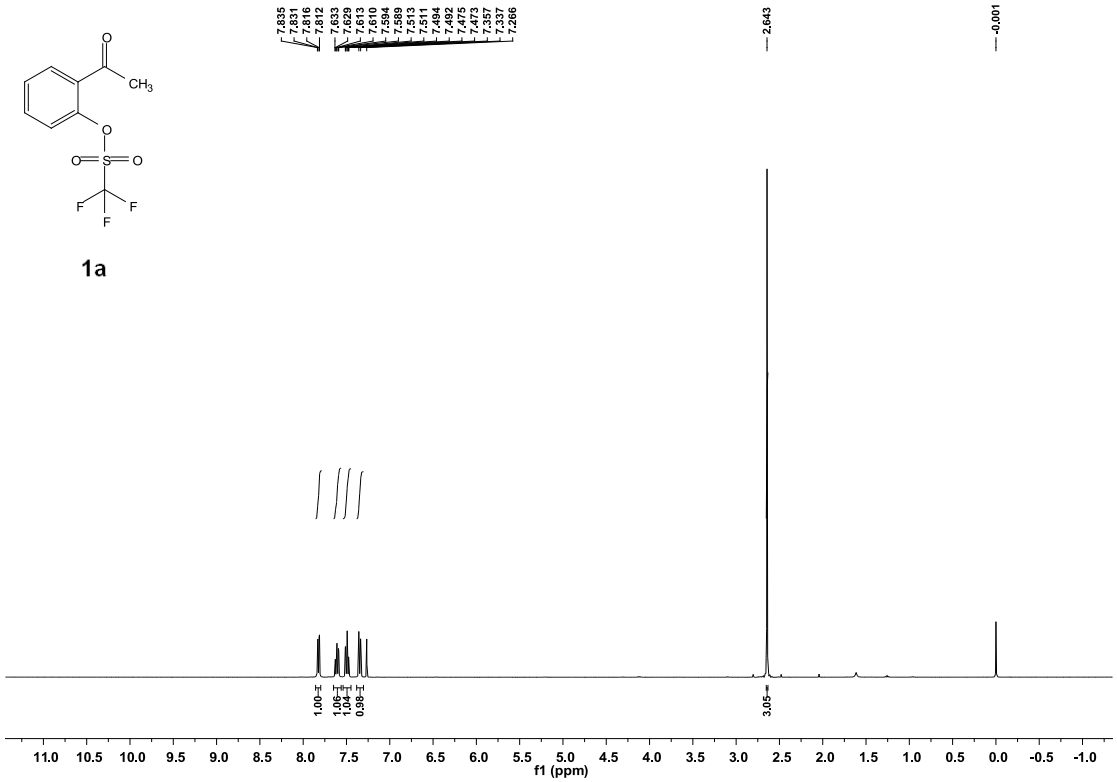
13 Y. Gan, D. H. Blank, J. E. Ney and T. A. Spencer, *J. Org. Chem.*, 2006, **71**, 5864.

14 J. D. Kendall, G. W. Rewcastle, R. Frederick, C. Mawson, W. A. Denny, E. S. Marshall, B. C. Baguley, C. Chaussade, S. P. Jackson and P. R. Shepherd, *Bioorg. Med. Chem.*, 2007, **15**, 7677.

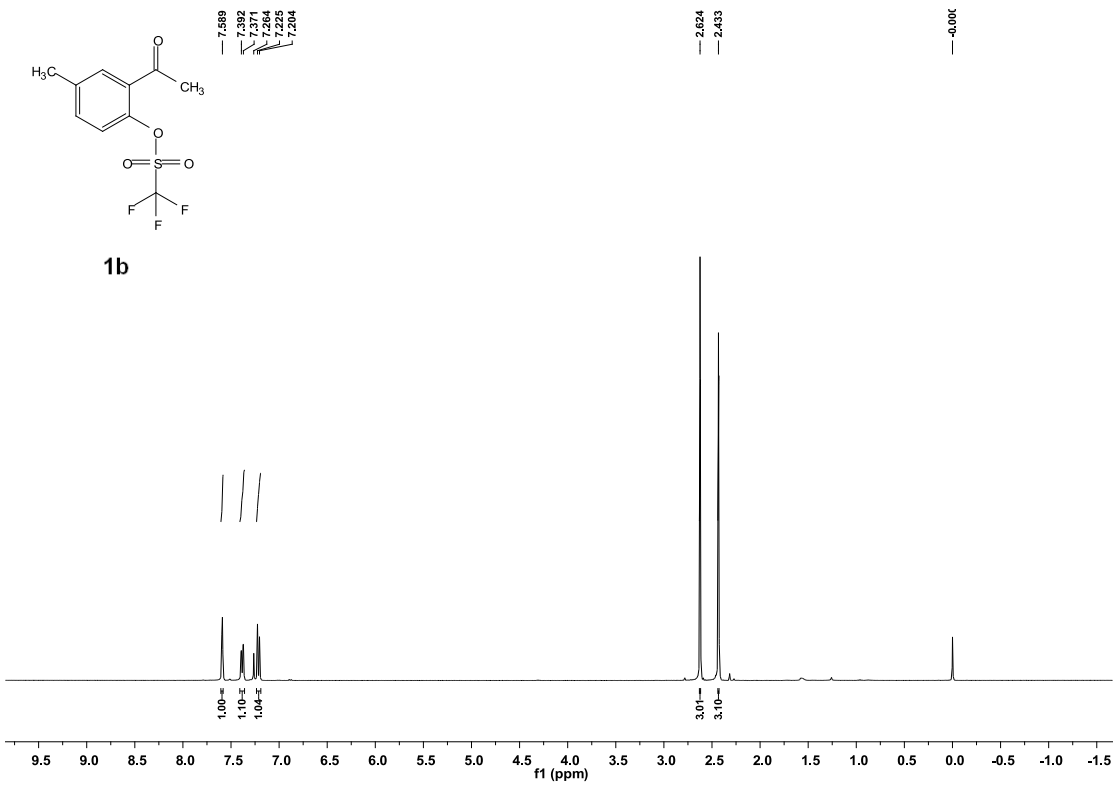
This journal is © The Royal Society of Chemistry 2013

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

This journal is © The Royal Society of Chemistry 2013

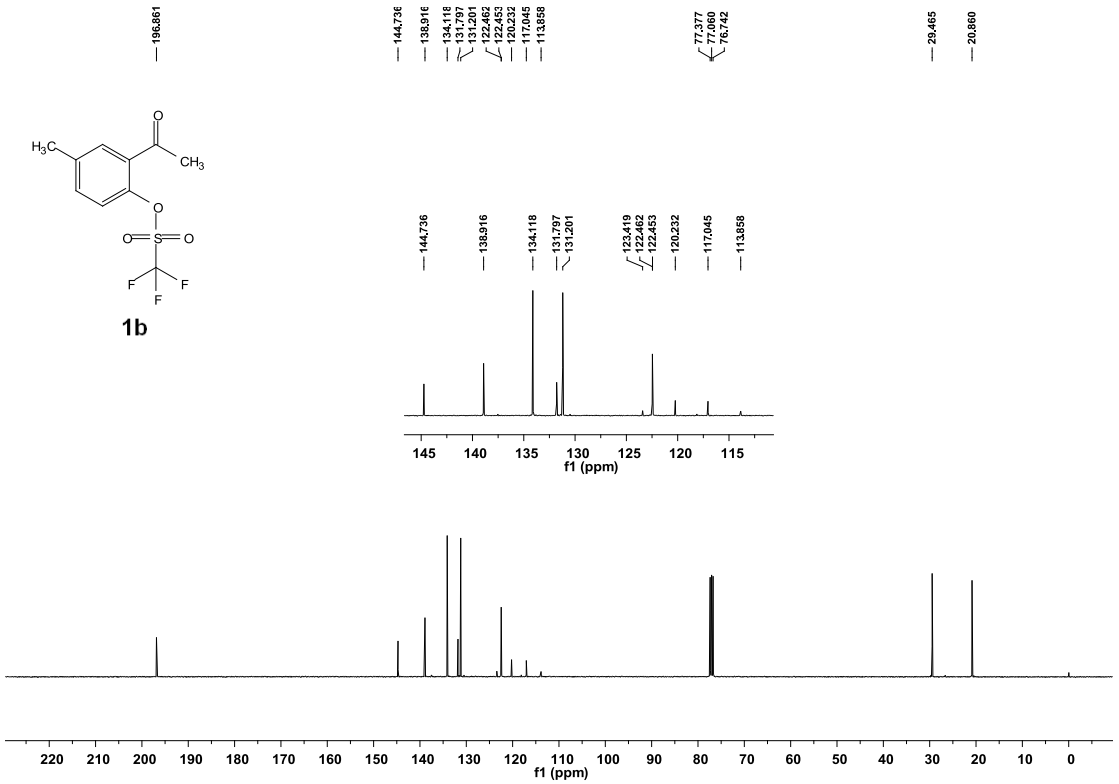


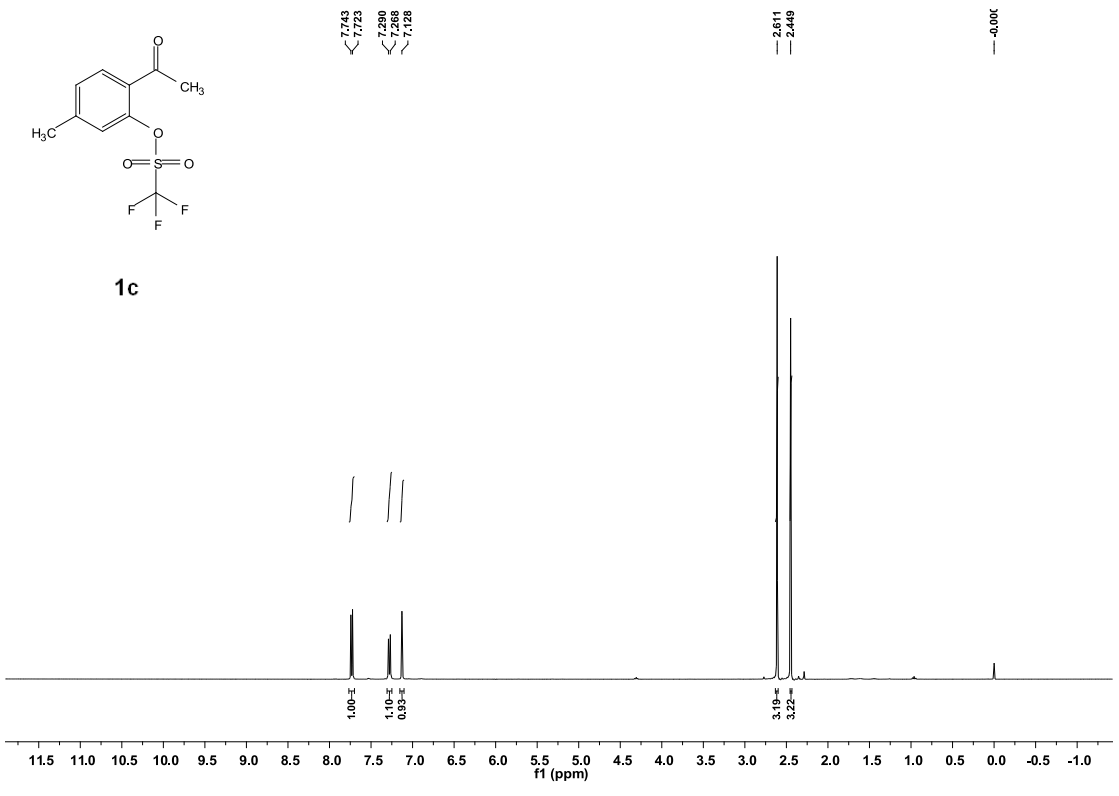
1a



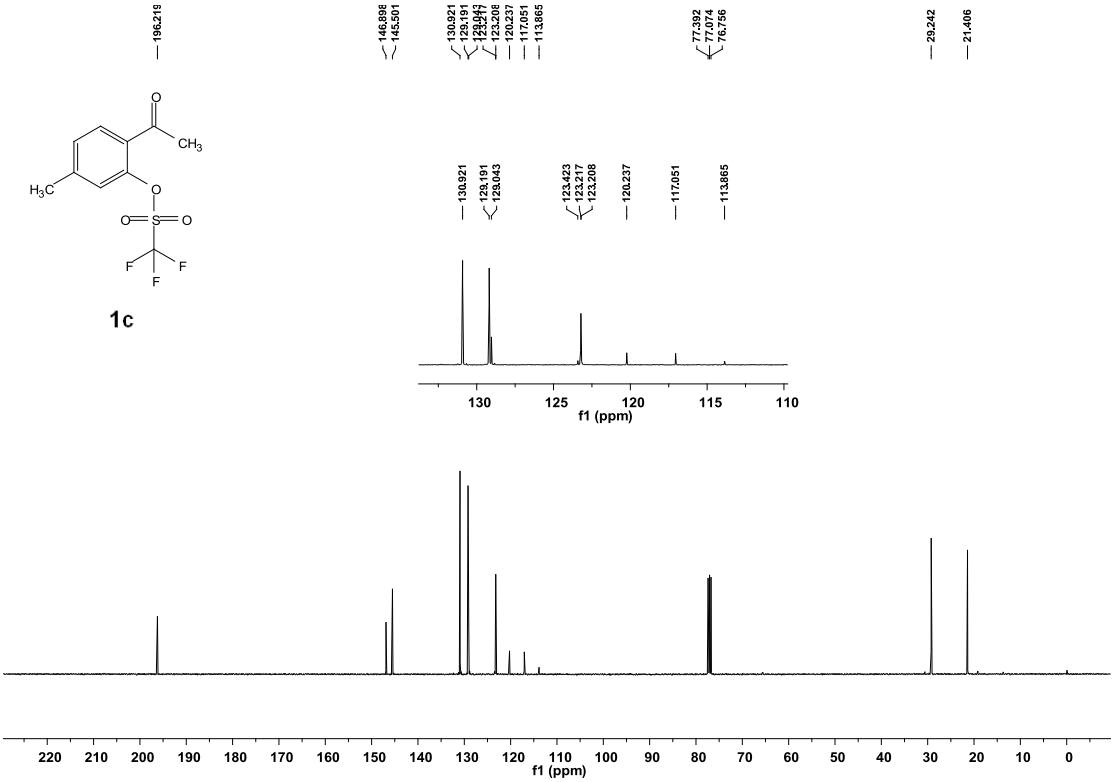
1b

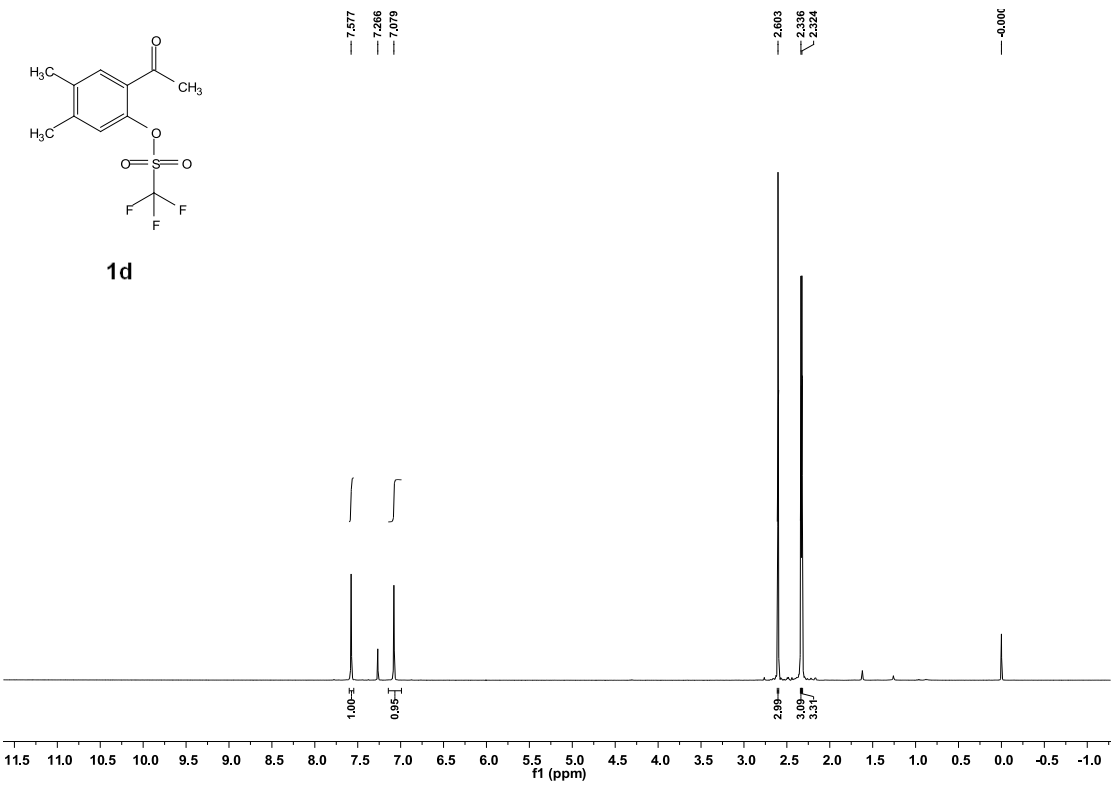
This journal is © The Royal Society of Chemistry 2013

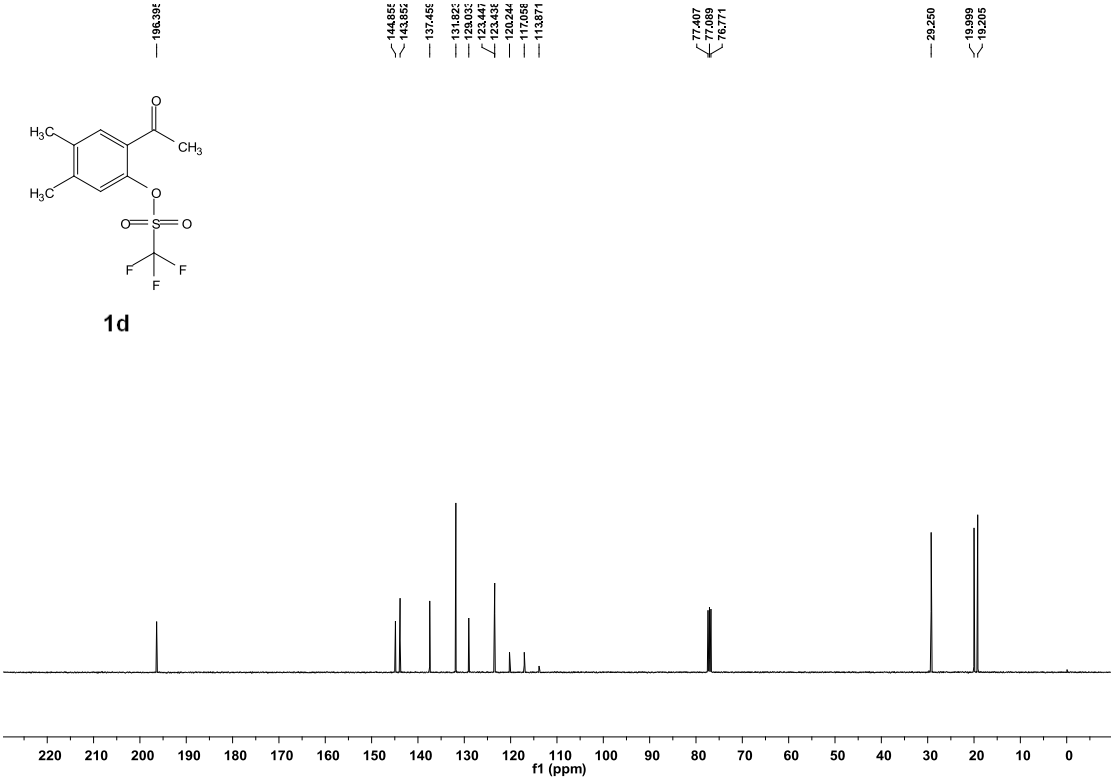




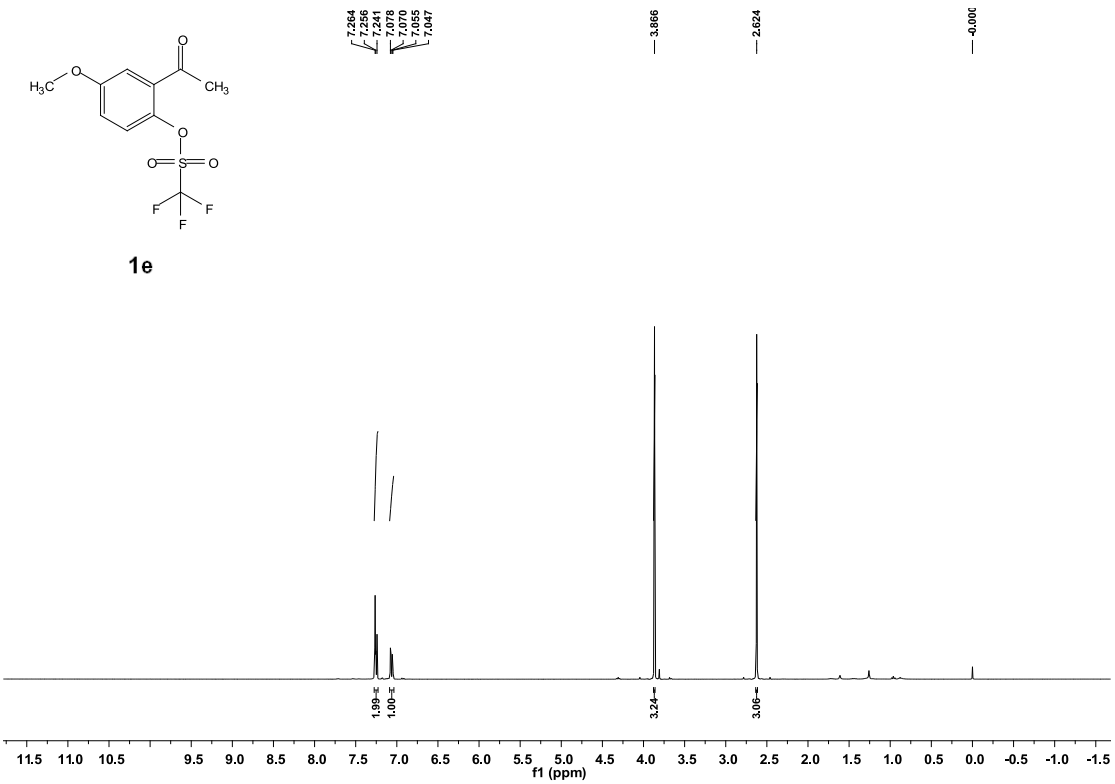
This journal is © The Royal Society of Chemistry 2013



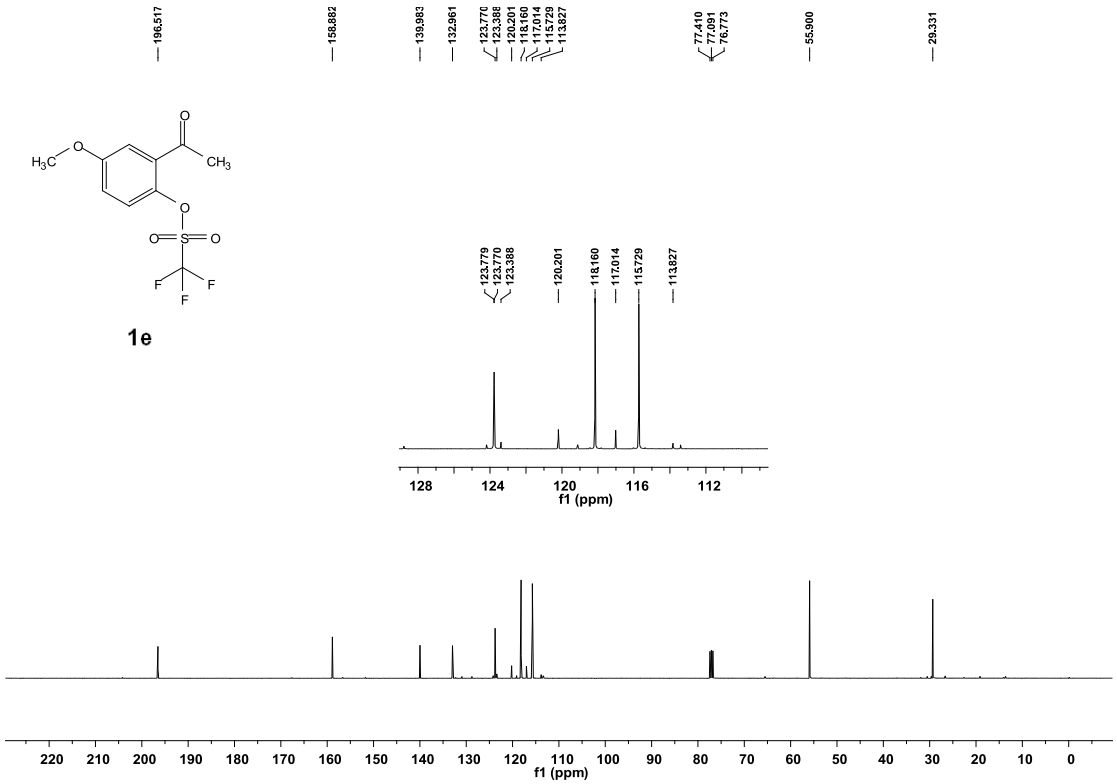


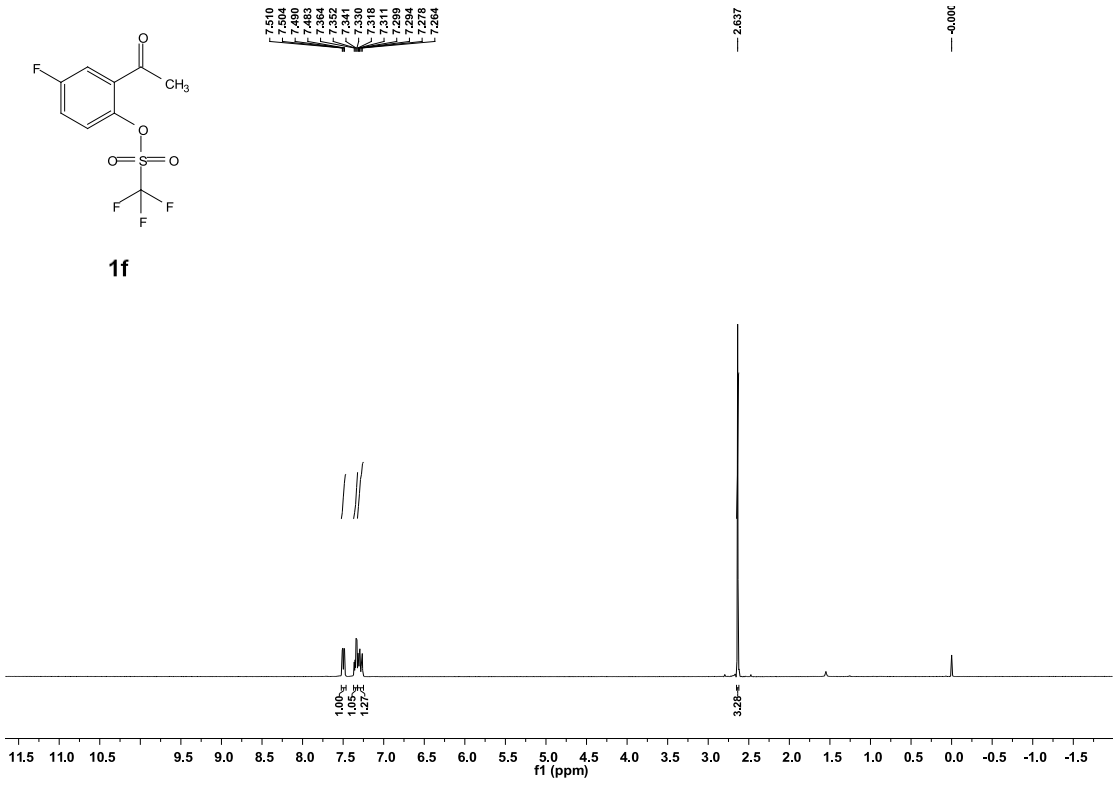

196.394
144.855
143.852
137.456
131.822
129.033
123.447
123.438
120.244
117.058
113.871
77.407
77.089
76.771
29.250
19.999
19.205
H3C
CH3
H3C
O
O
S
O
O
F
F
F
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1d

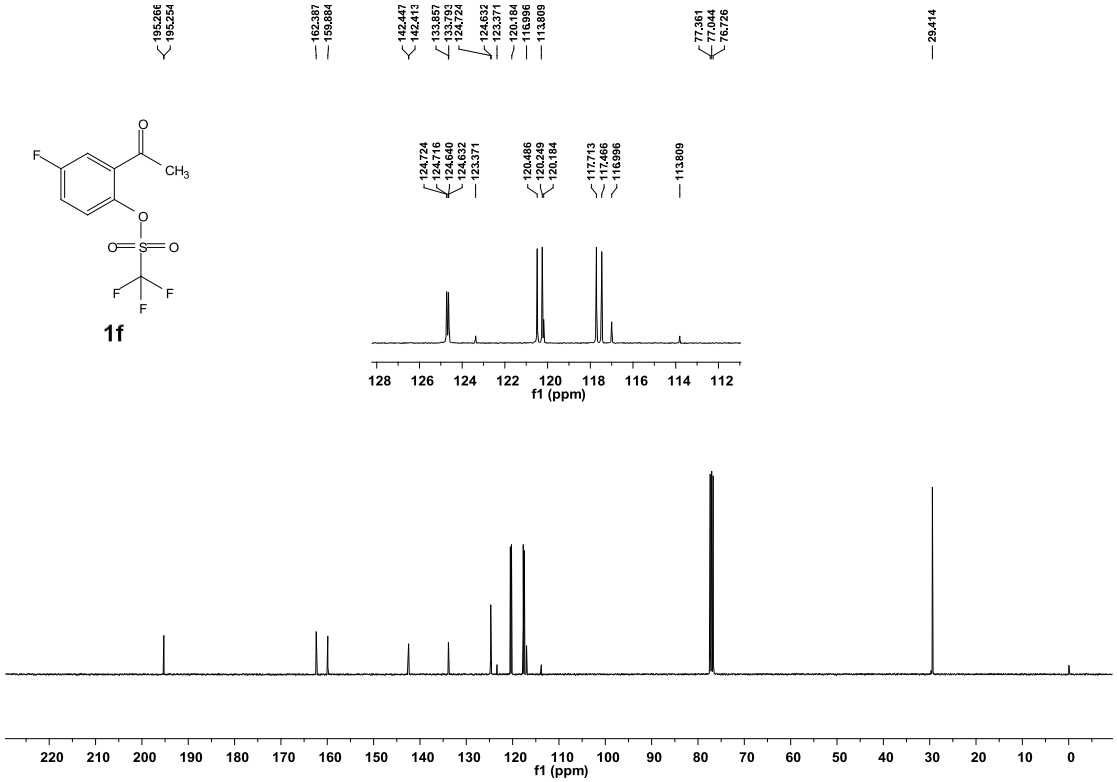

7.264
7.256
7.241
7.078
7.070
7.055
7.047
3.866
2.624
-0.000
H3C
O
CH3
O
O
S
O
O
F
F
F
1.99
1.00
3.24
3.06
11.5 11.0 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

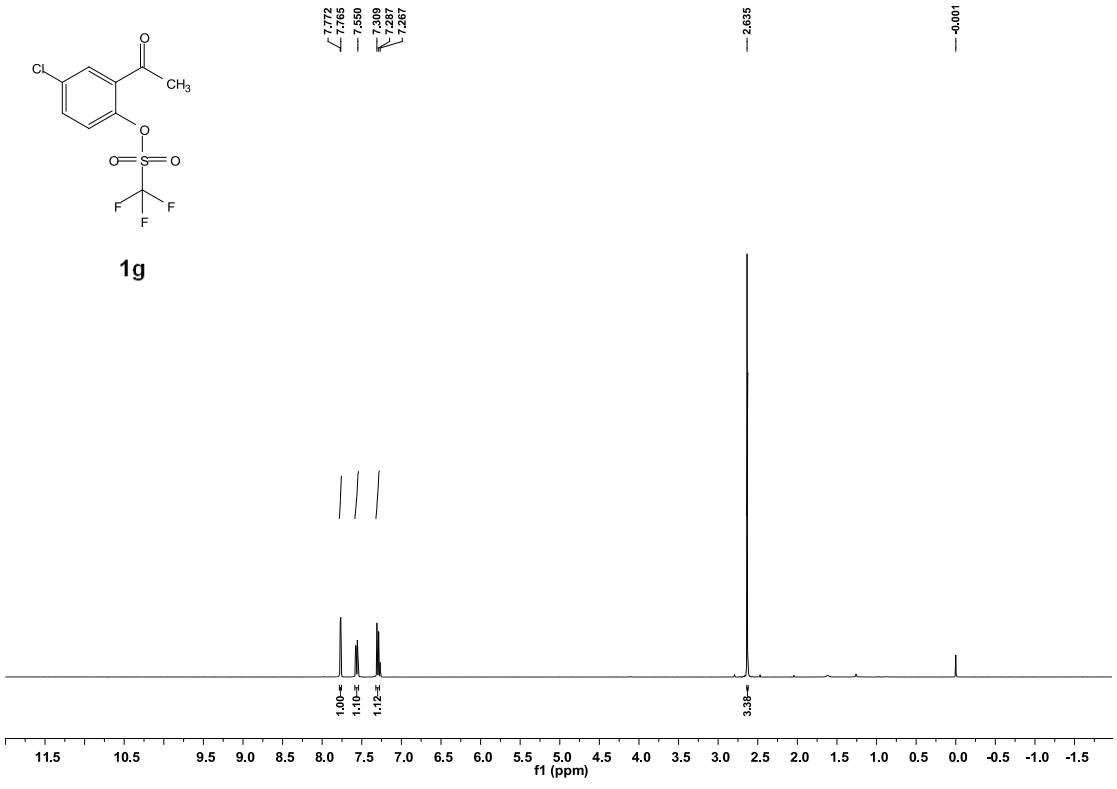
1e

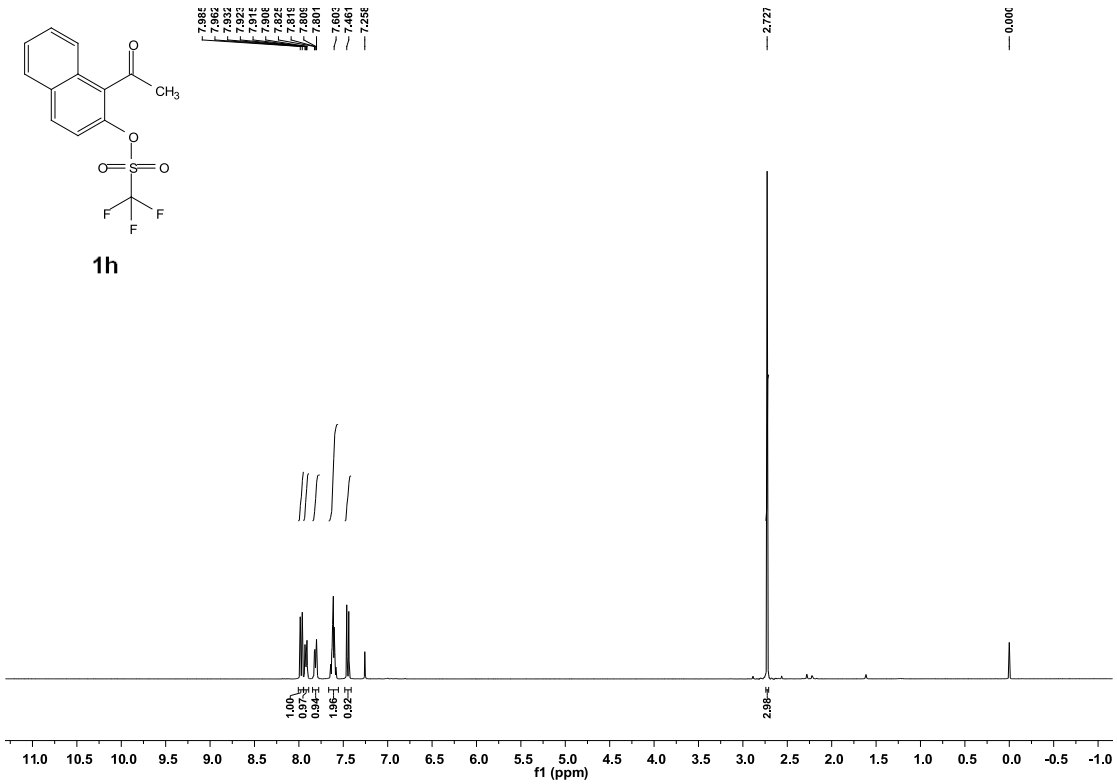

196.517
158.882
139.983
132.961
123.770
123.388
120.201
118.160
117.014
115.729
113.827
77.410
77.091
76.773
55.900
29.331
H3C
O
CH3
O
O
S
O
F
F
F
1e
123.779
123.770
123.388
120.201
118.160
117.014
115.729
113.827
128
124
120
116
112
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

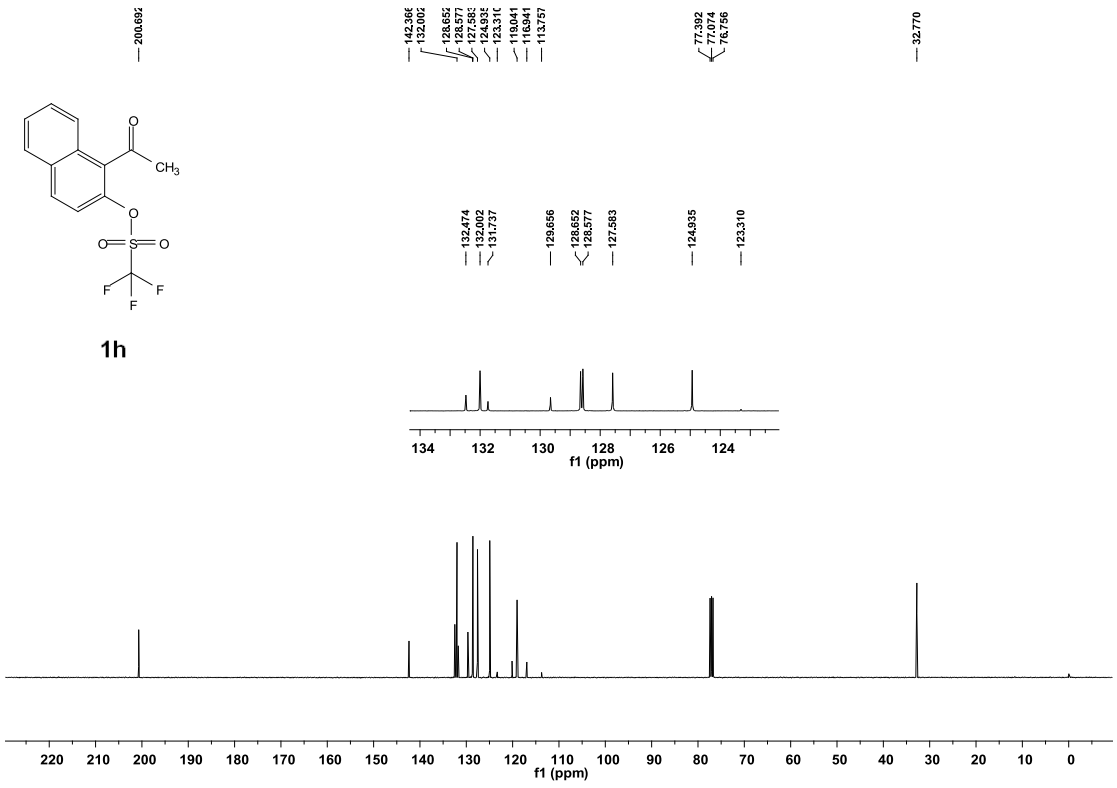

7.510
7.504
7.490
7.483
7.364
7.352
7.341
7.330
7.318
7.311
7.299
7.294
7.278
7.264
2.637
-0.000
F
O
CH3
O
O
S
O
F
F
F
1f
1.00
1.05
1.27
3.28
11.5
11.0
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)

This journal is © The Royal Society of Chemistry 2013

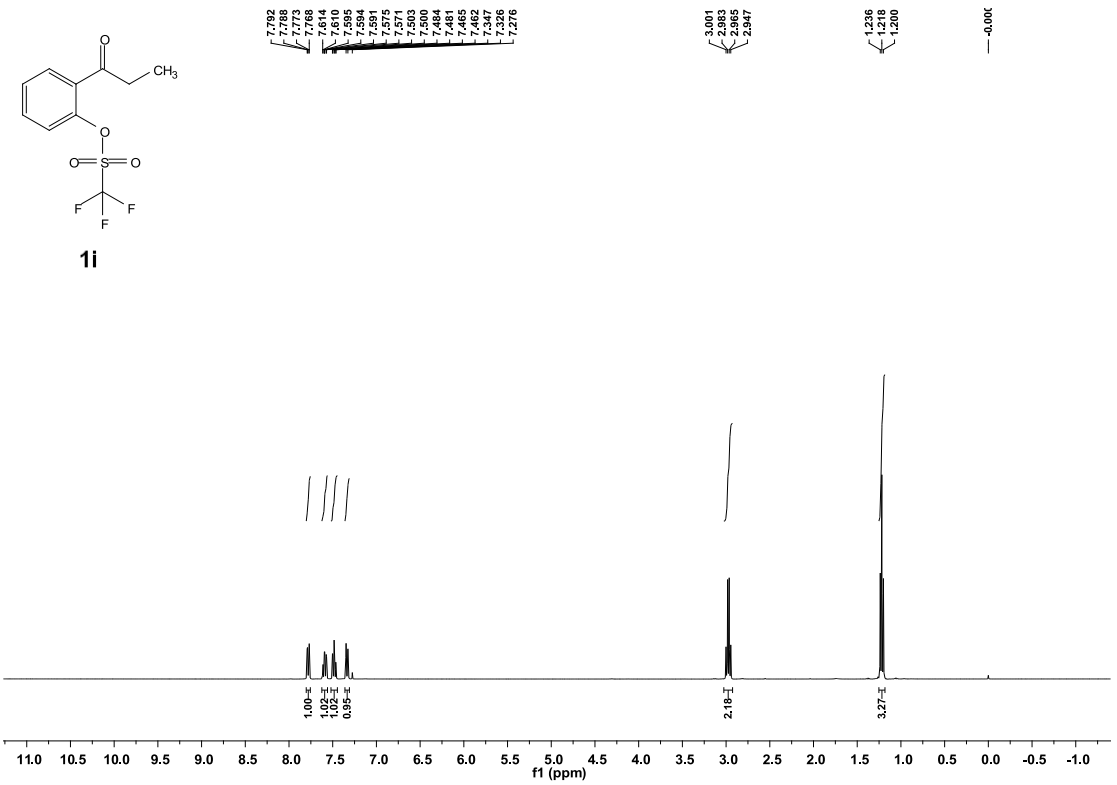




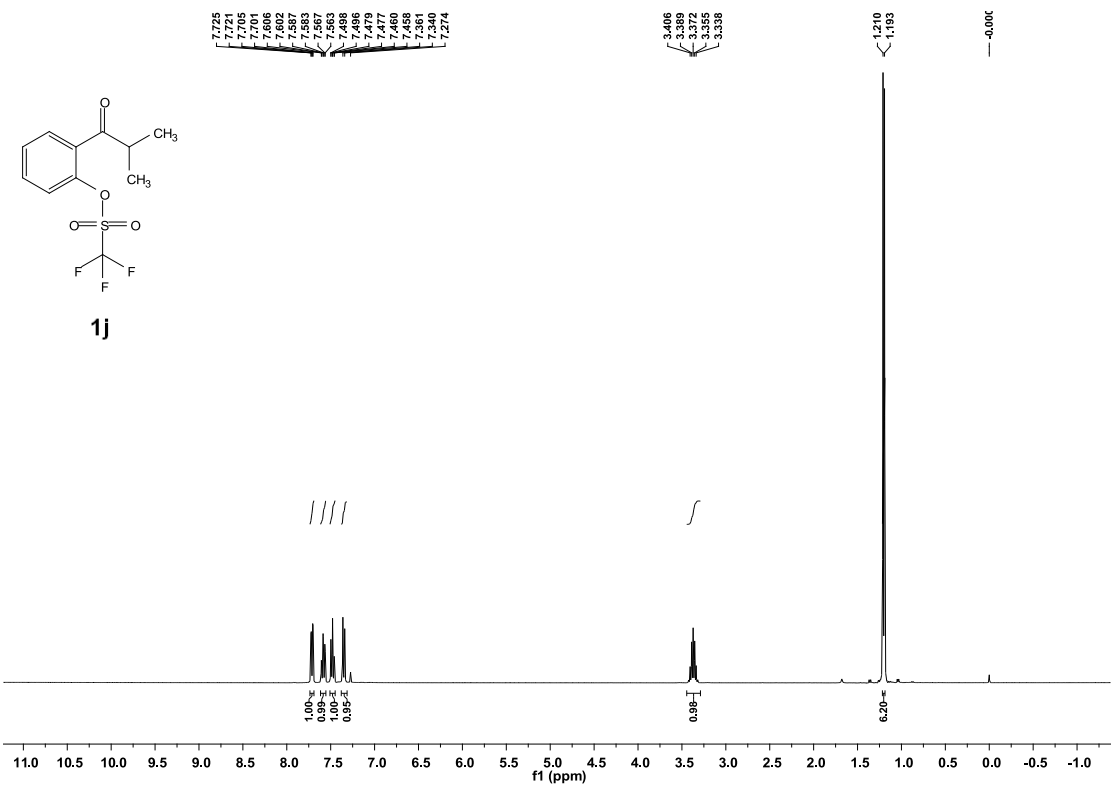

1h
f1 (ppm)


1h
f1 (ppm)
f1 (ppm)

This journal is © The Royal Society of Chemistry 2013

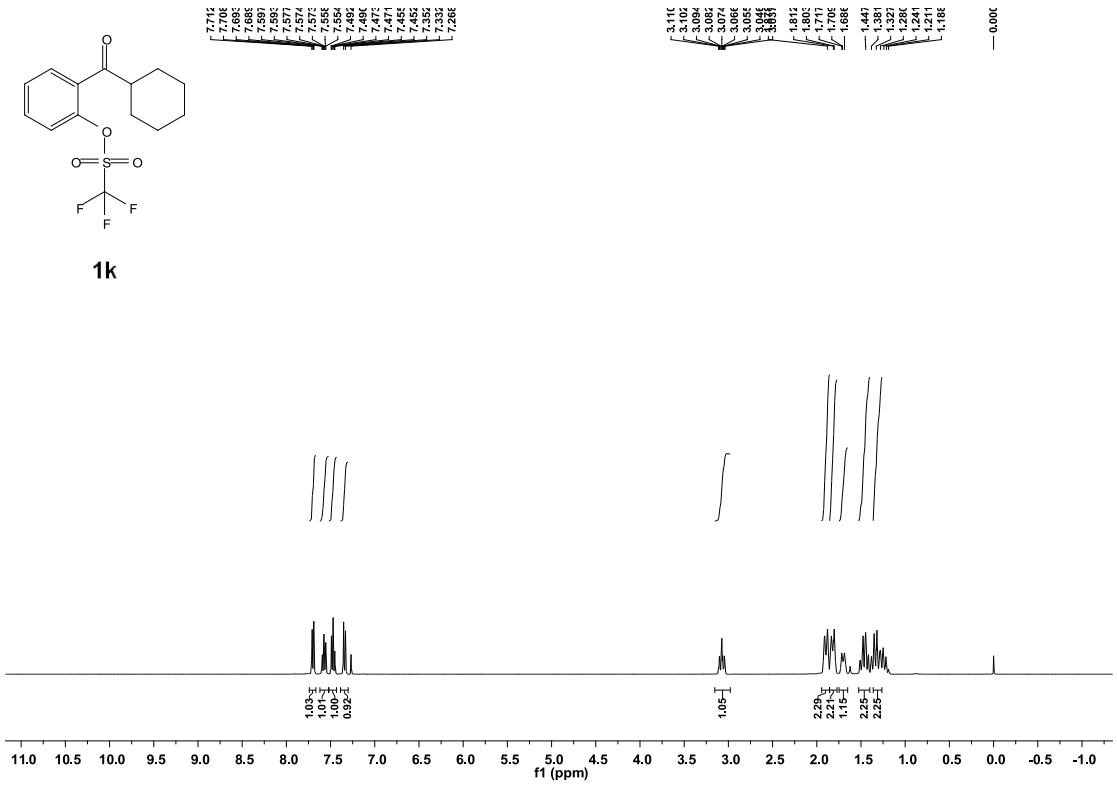


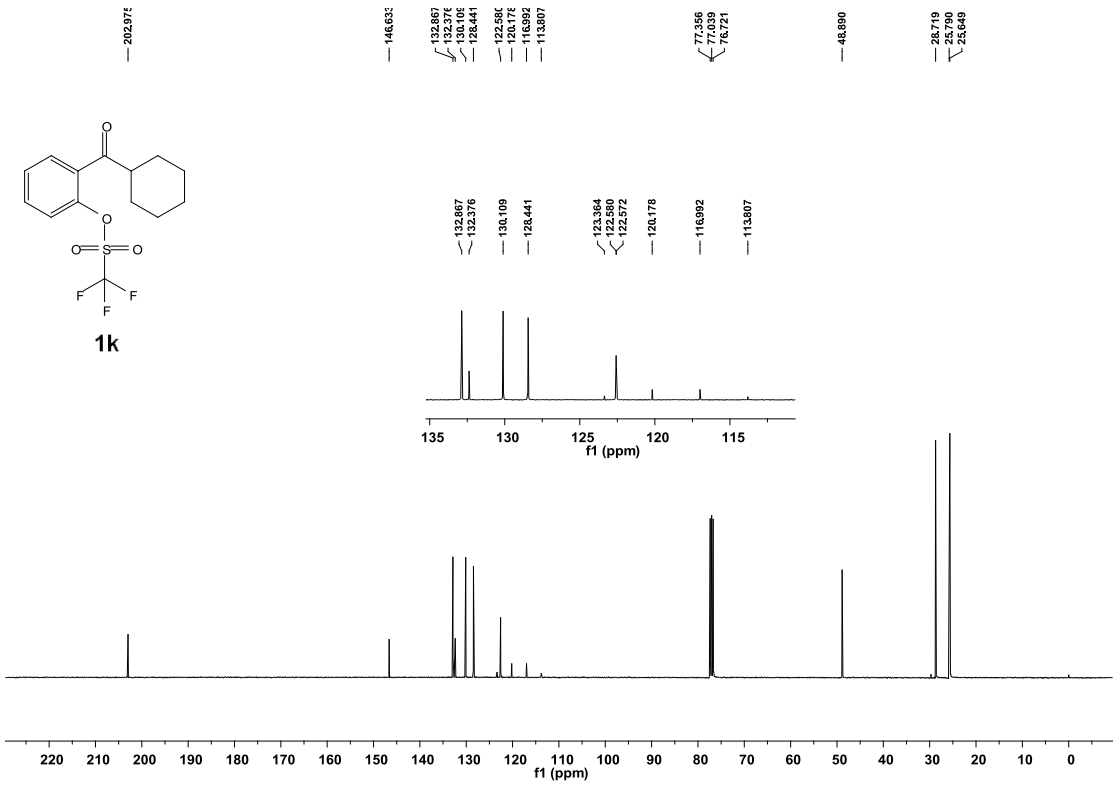
1i



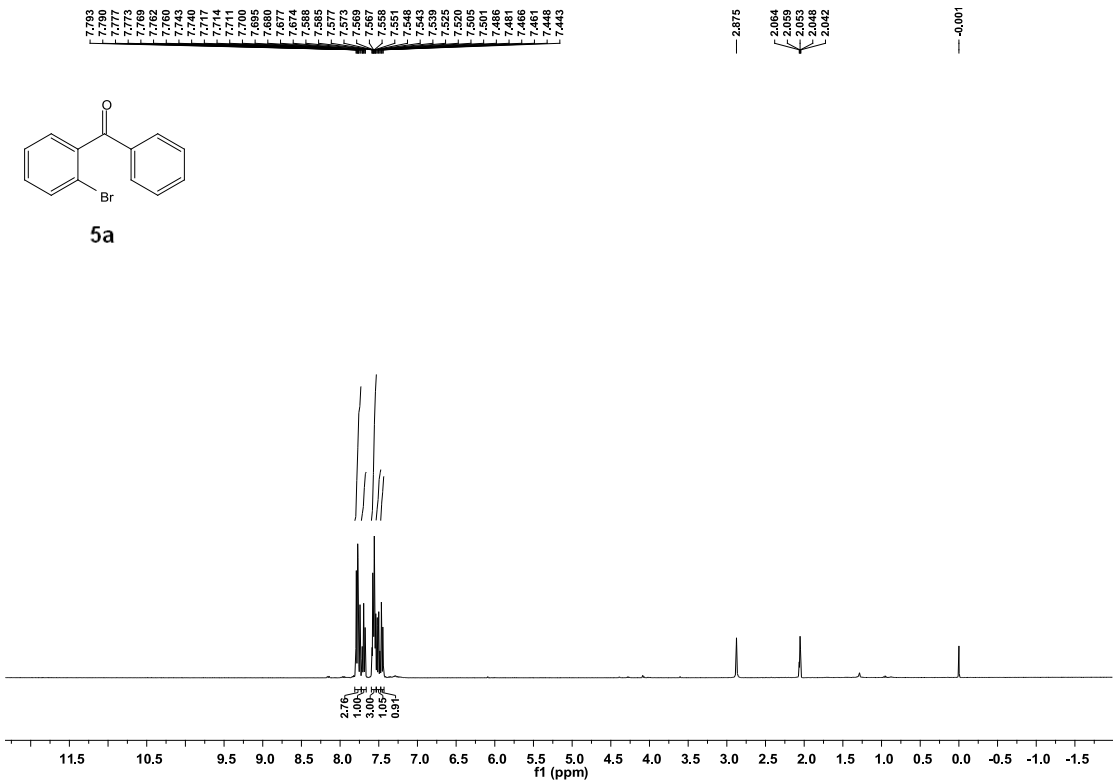
1j

This journal is © The Royal Society of Chemistry 2013

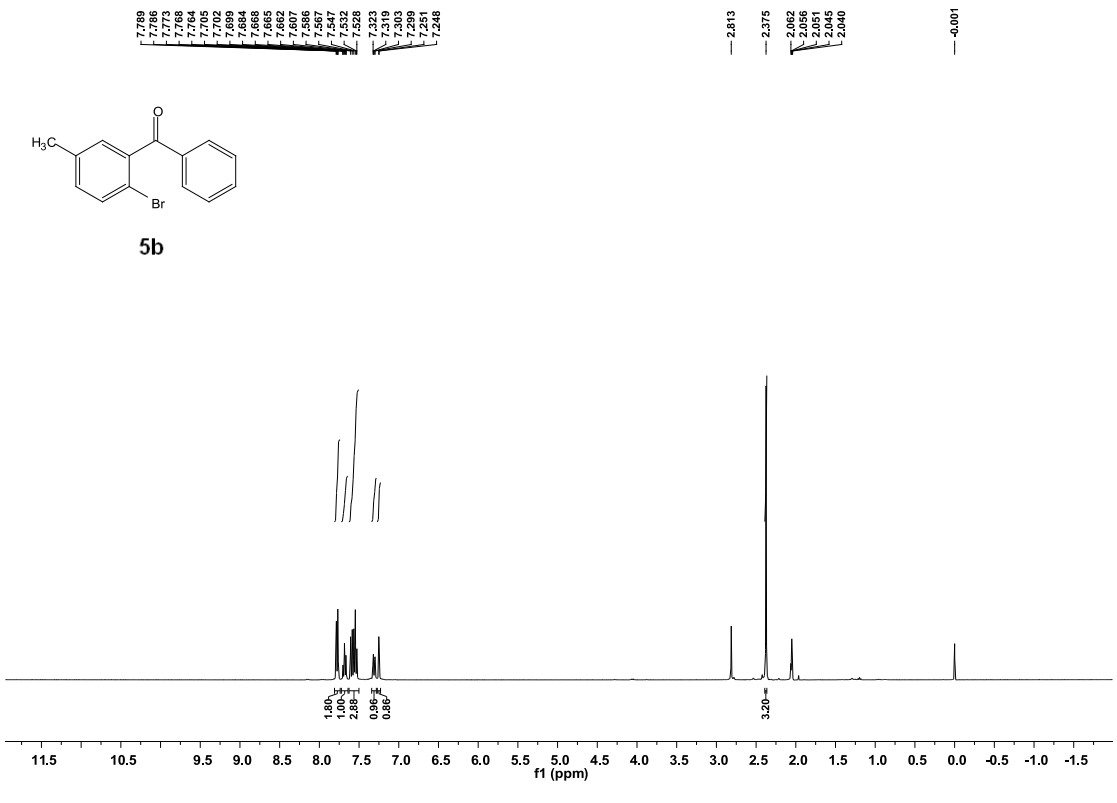




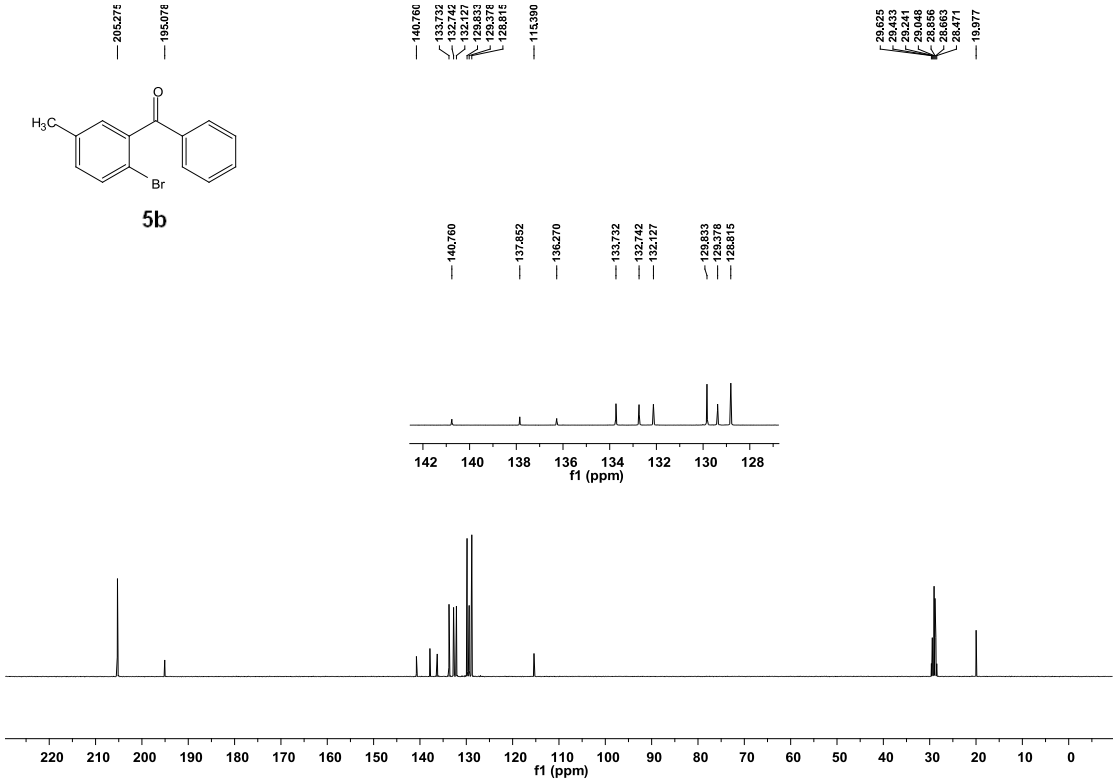
This journal is © The Royal Society of Chemistry 2013

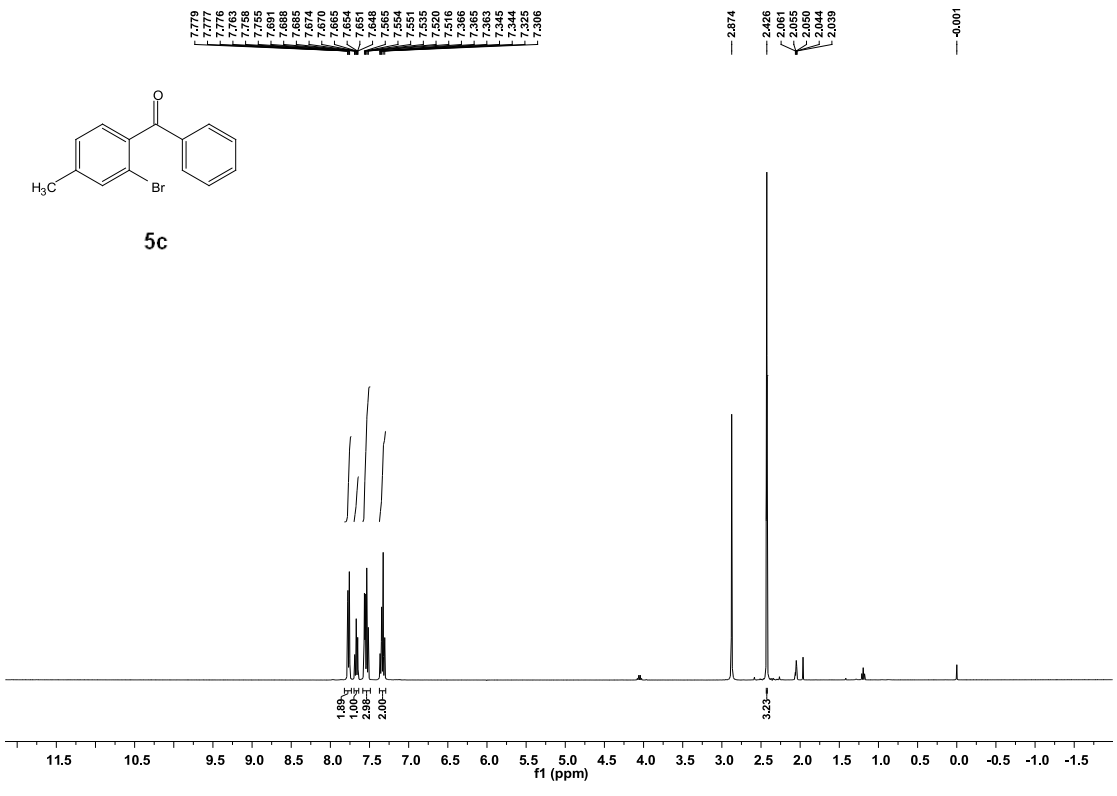


5a

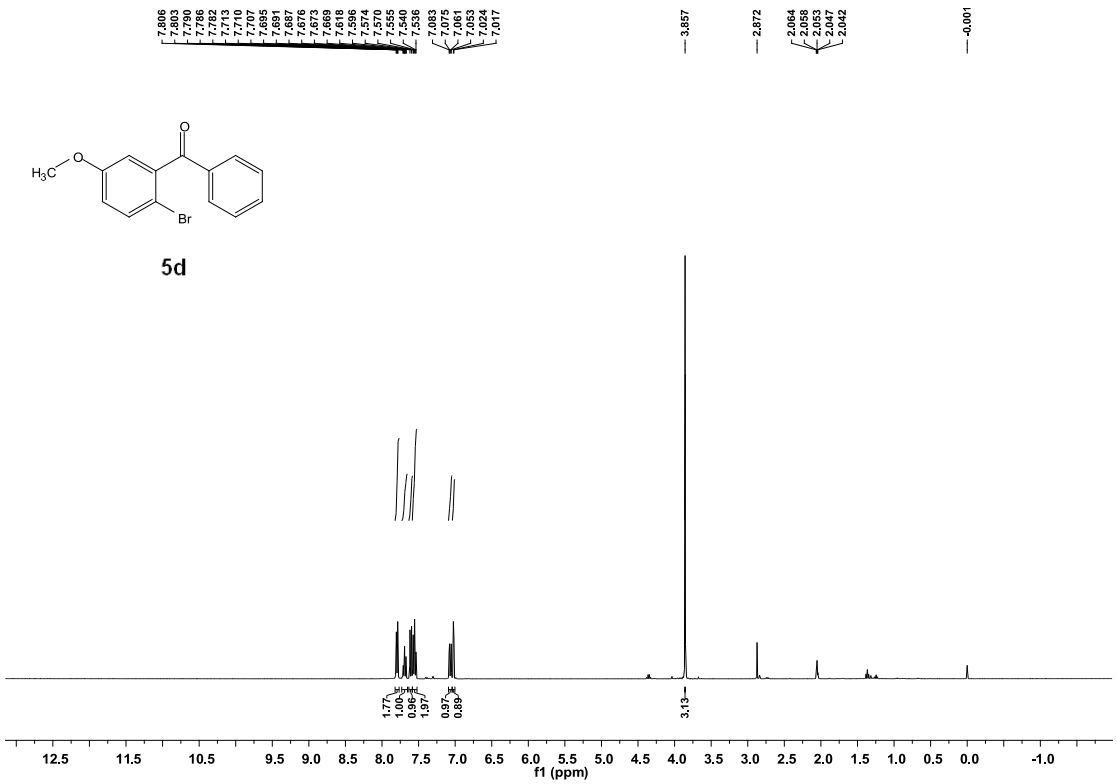


5b

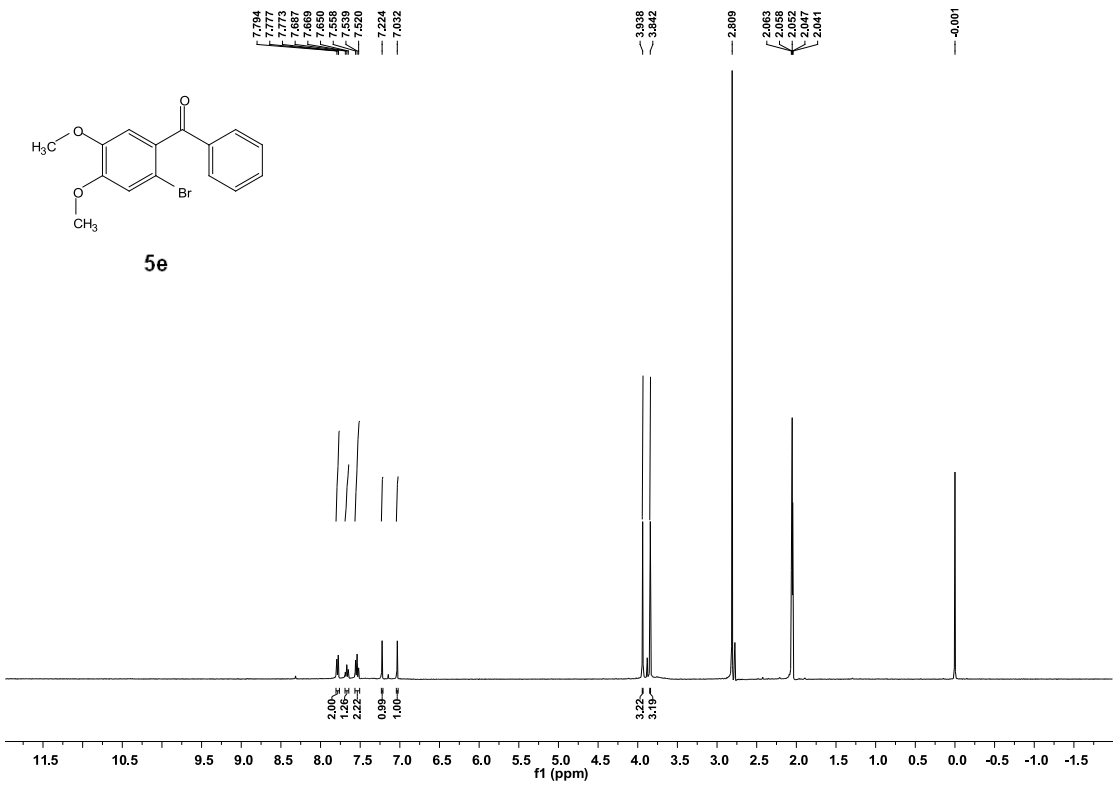

205.275
195.078
140.760
133.732
132.742
132.127
129.833
129.378
128.815
115.390
29.625
29.433
29.241
29.048
28.856
28.663
28.471
19.977
O
H3C
Br
5b
140.760
137.852
136.270
133.732
132.742
132.127
129.833
129.378
128.815
142 140 138 136 134 132 130 128
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.779
7.777
7.776
7.763
7.758
7.755
7.691
7.688
7.685
7.674
7.670
7.665
7.654
7.651
7.648
7.565
7.554
7.551
7.535
7.520
7.516
7.366
7.365
7.363
7.345
7.344
7.325
7.306
2.874
2.426
2.061
2.055
2.050
2.044
2.039
-0.001
O
H3C
Br
5c
1.89
1.00
2.98
2.00
3.23
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

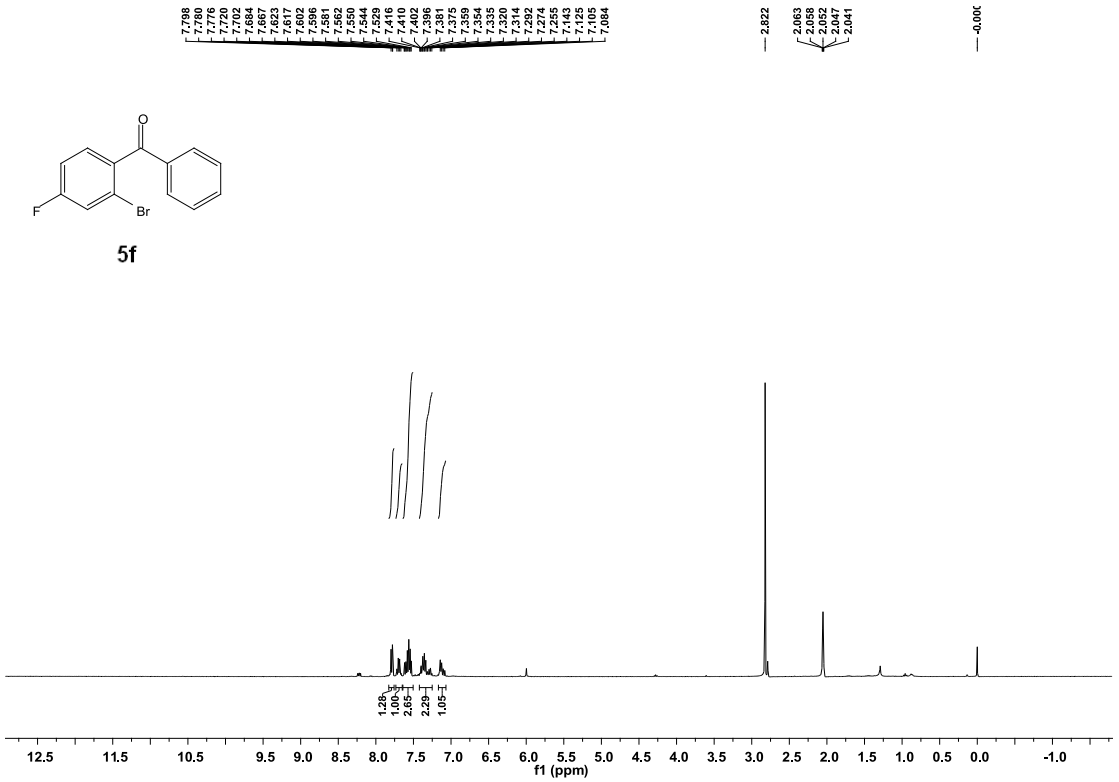
This journal is © The Royal Society of Chemistry 2013



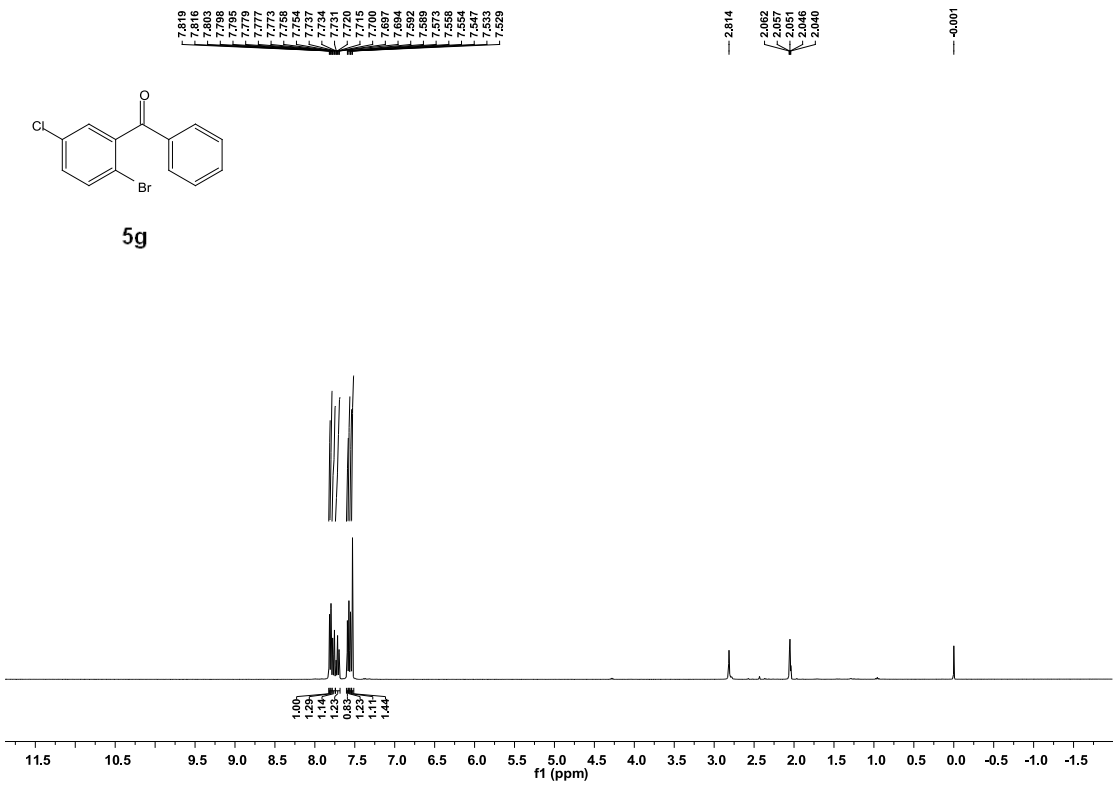
5d



5e

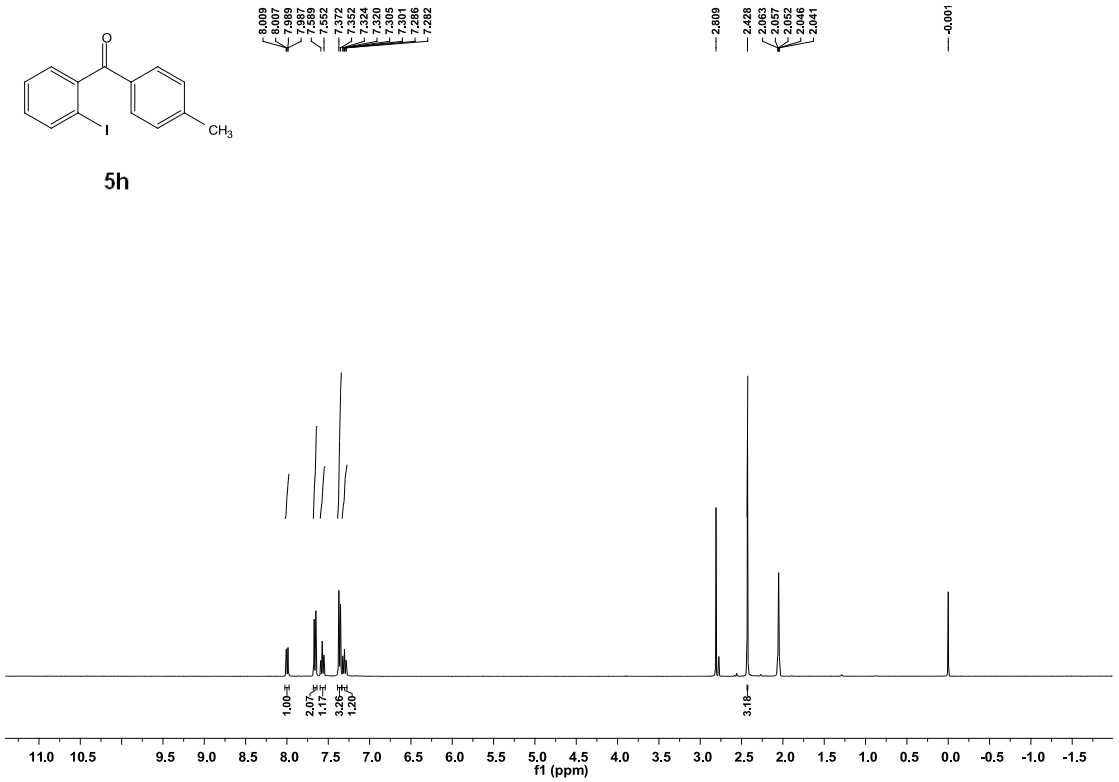

7.798
7.780
7.776
7.720
7.703
7.684
7.667
7.623
7.617
7.602
7.596
7.581
7.562
7.550
7.544
7.538
7.416
7.410
7.402
7.396
7.381
7.375
7.359
7.354
7.335
7.330
7.314
7.292
7.274
7.255
7.143
7.125
7.105
7.084
2.822
2.063
2.058
2.052
2.047
2.041
-0.000
O
F
Br
1.28
1.05
2.65
2.29
1.05
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-1.0
f1 (ppm)

5f

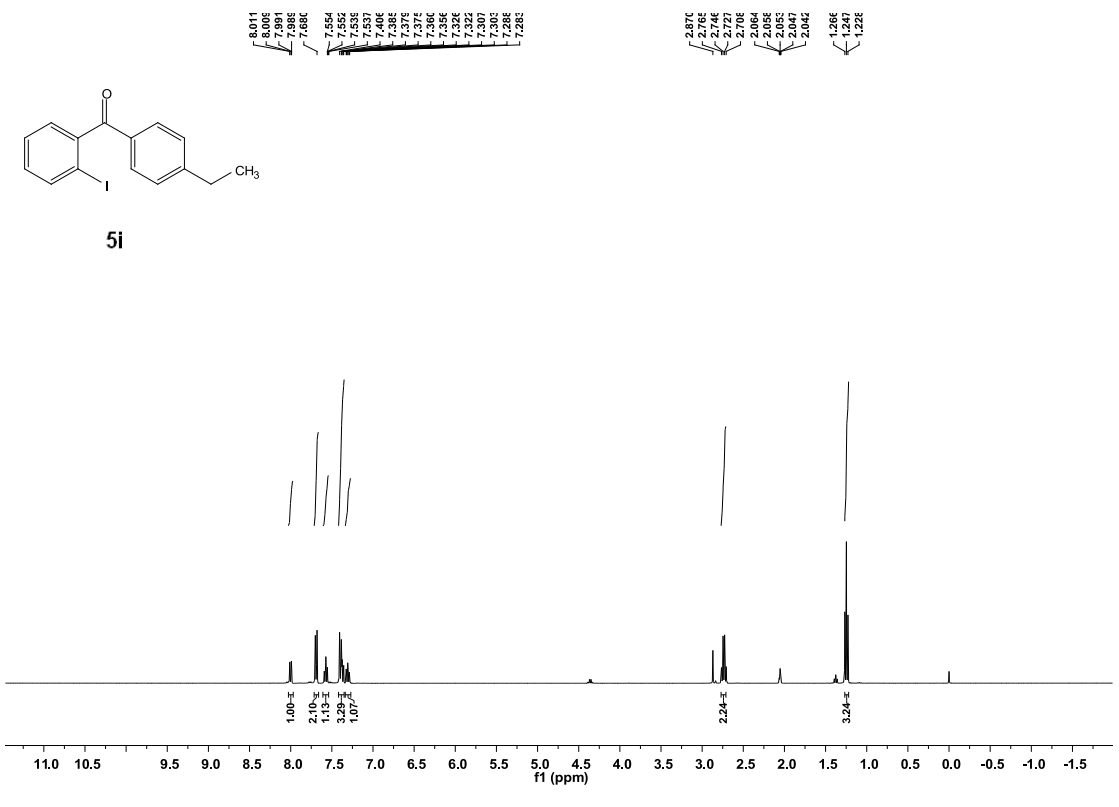

7.819
7.816
7.803
7.798
7.795
7.779
7.777
7.773
7.758
7.754
7.737
7.734
7.731
7.720
7.715
7.700
7.697
7.694
7.592
7.589
7.573
7.558
7.555
7.544
7.541
7.533
7.529
2.814
2.062
2.057
2.051
2.046
2.040
-0.001
O
Cl
Br
1.00
1.29
1.14
1.33
0.83
1.23
1.11
1.44
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)

5g

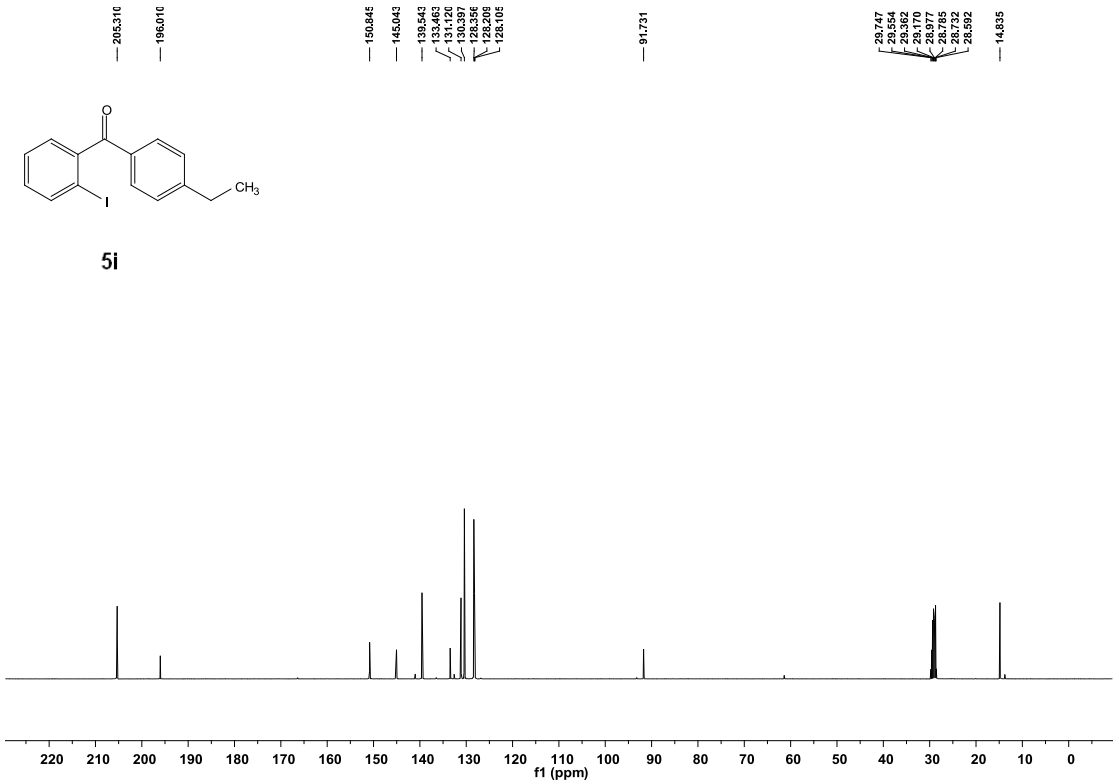
This journal is © The Royal Society of Chemistry 2013



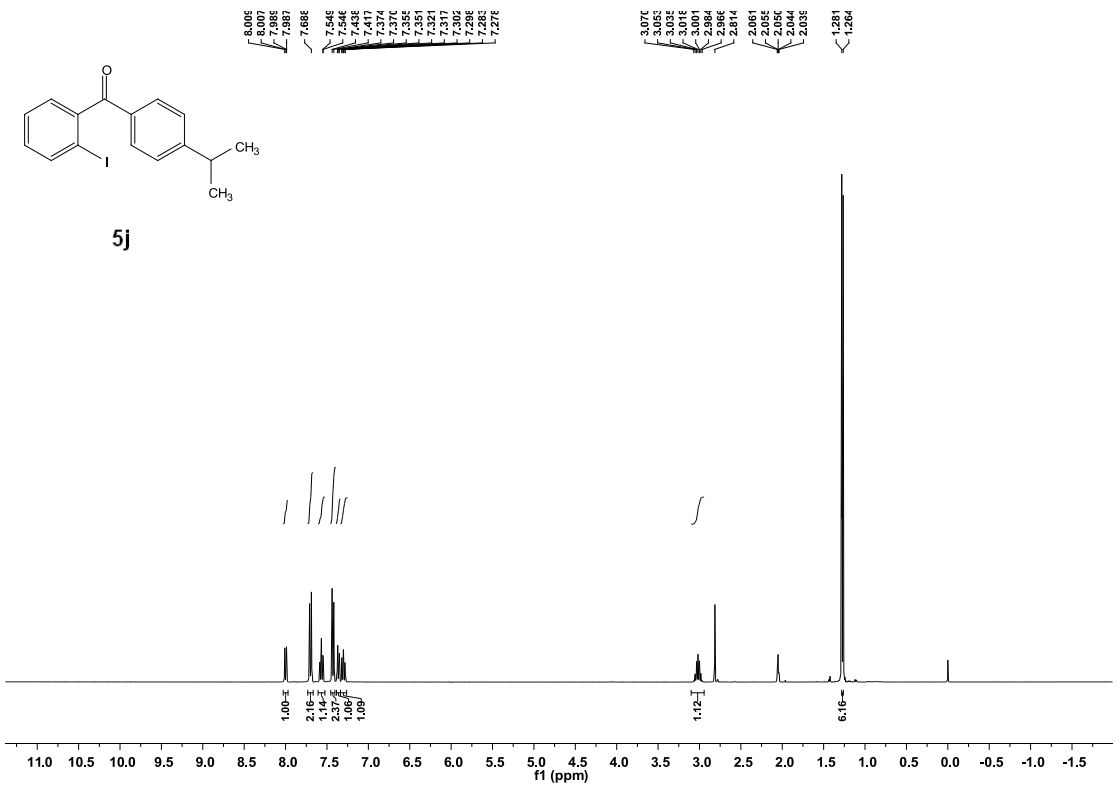
5h



5i

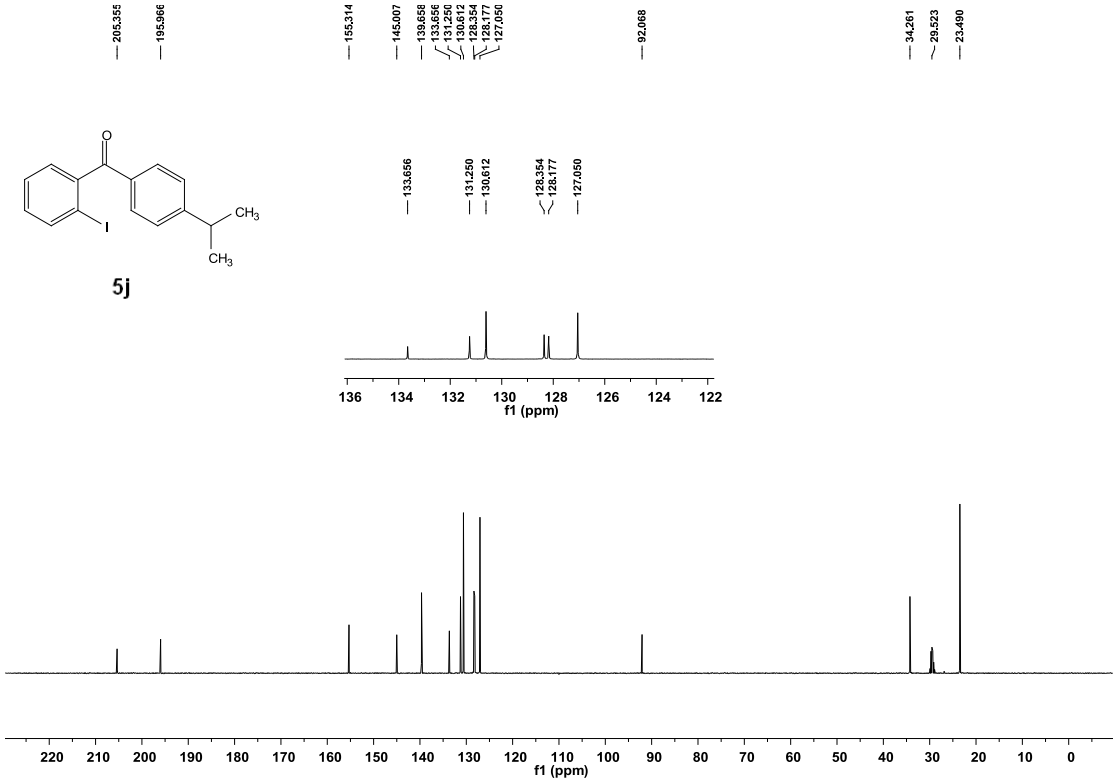

205.310
196.010
150.845
145.043
139.543
133.463
131.126
130.297
128.356
128.208
128.105
91.731
29.747
29.554
29.362
29.170
28.977
28.785
28.732
28.592
14.835
O
I
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

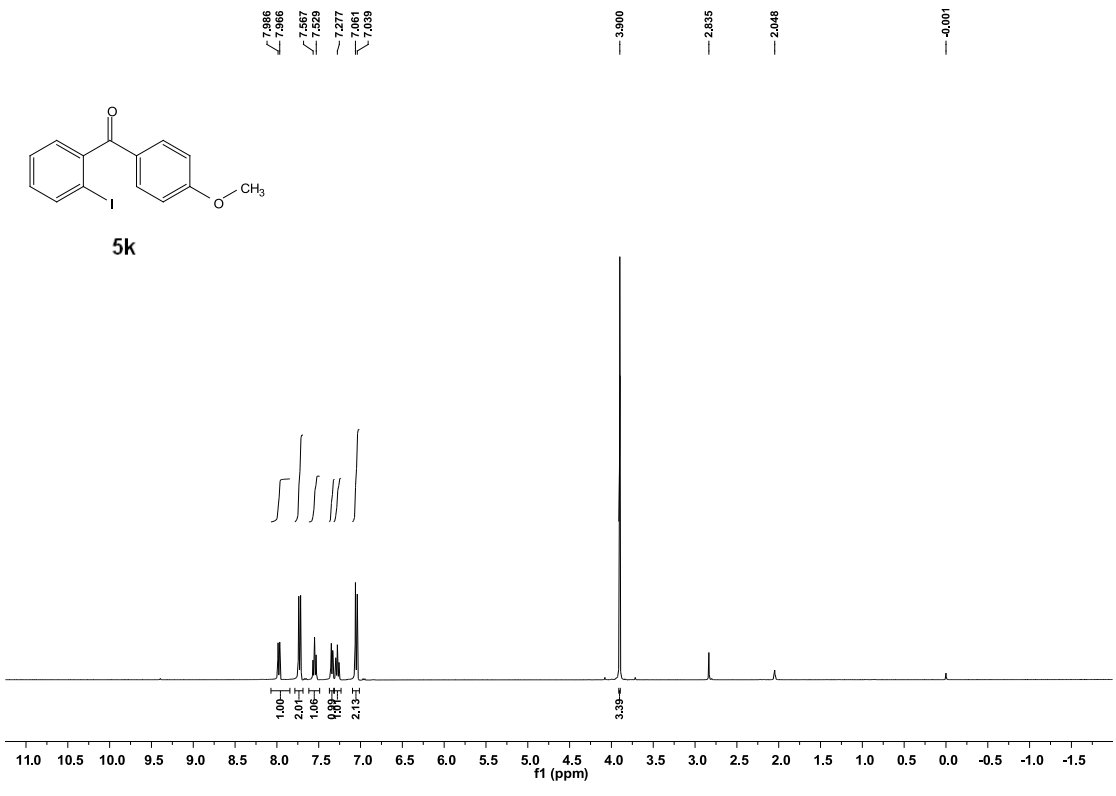
5i


8.005
8.007
7.985
7.987
7.688
7.548
7.546
7.438
7.417
7.374
7.370
7.358
7.351
7.321
7.317
7.302
7.298
7.283
7.278
3.074
3.052
3.031
3.016
3.001
2.984
2.966
2.814
2.061
2.055
2.050
2.044
2.039
1.281
1.264
O
I
CH3
CH3
1.00
2.16
1.14
2.37
1.09
1.12
6.16
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

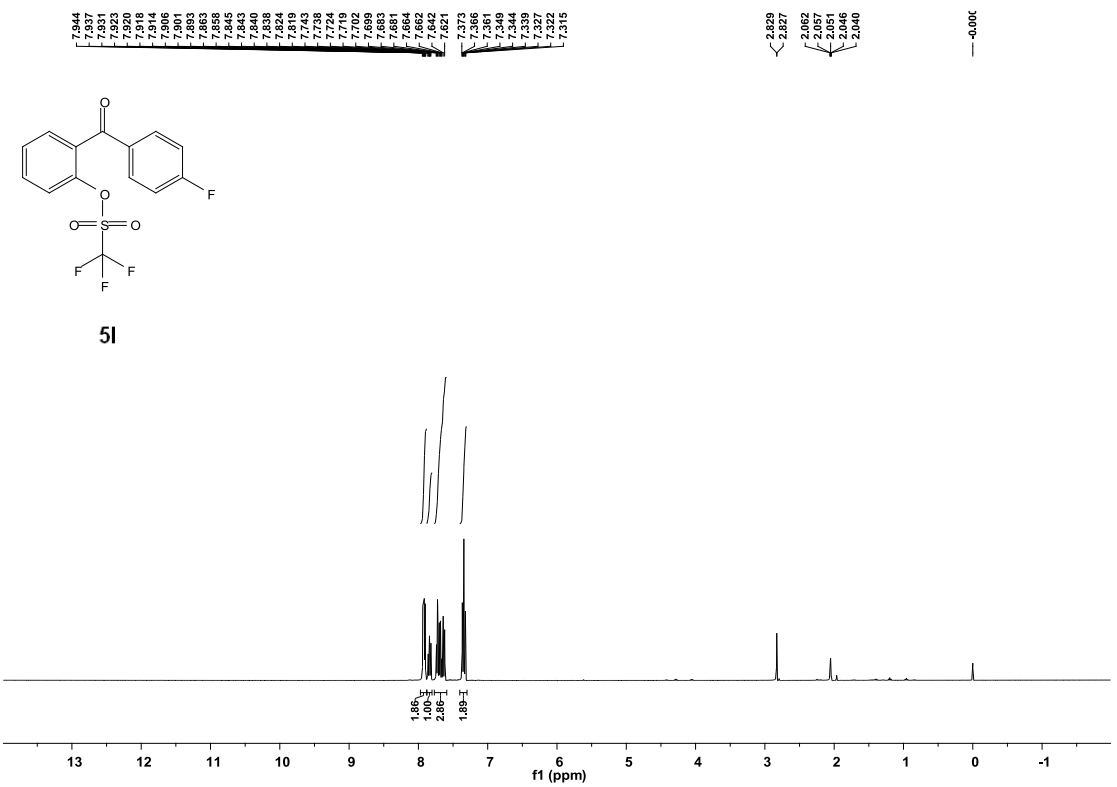
5j

This journal is © The Royal Society of Chemistry 2013

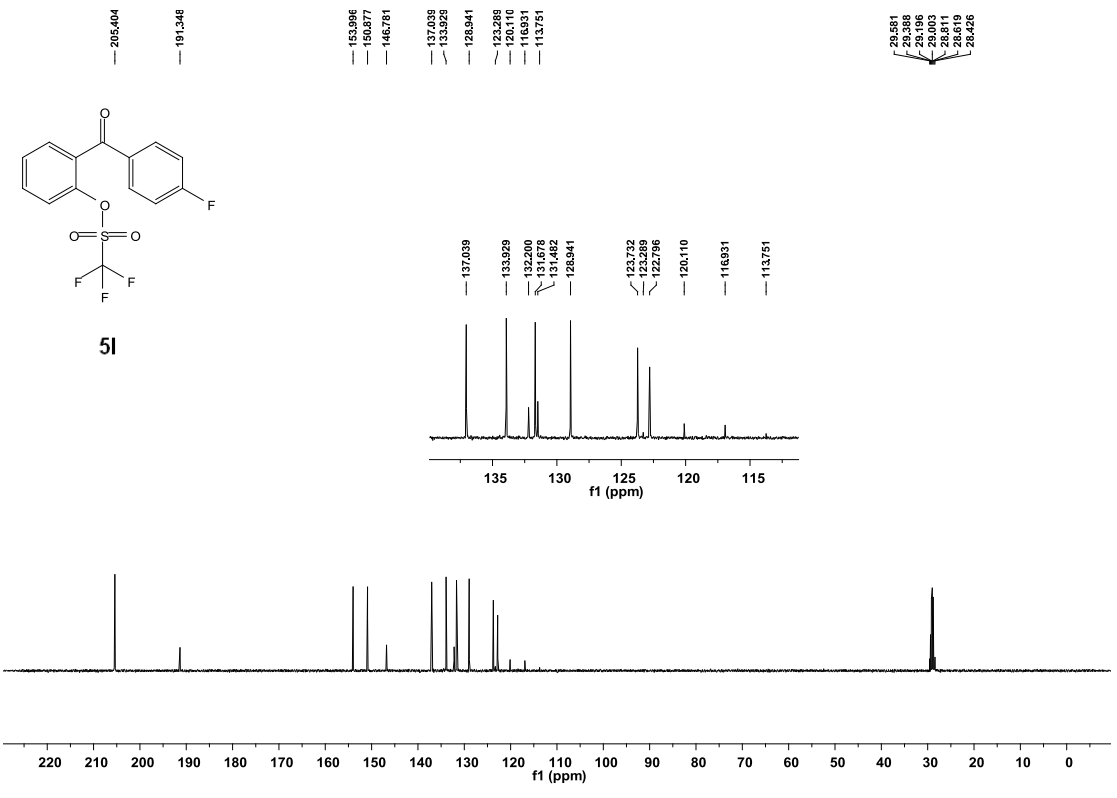




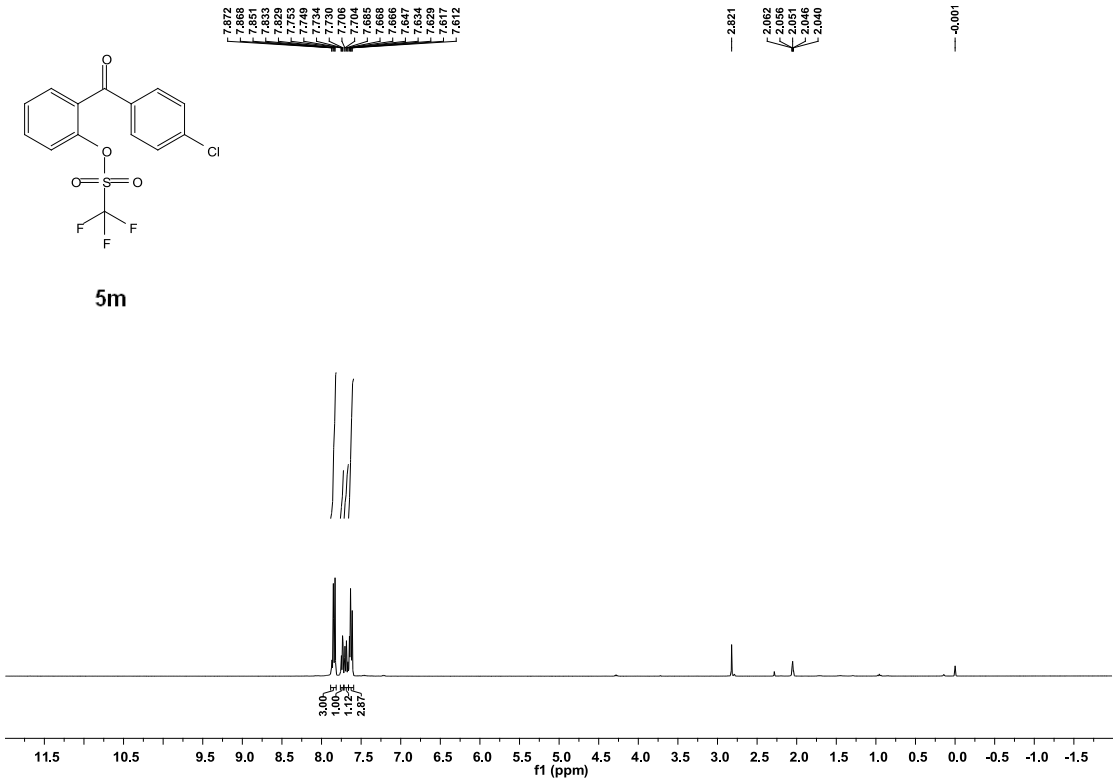
This journal is © The Royal Society of Chemistry 2013

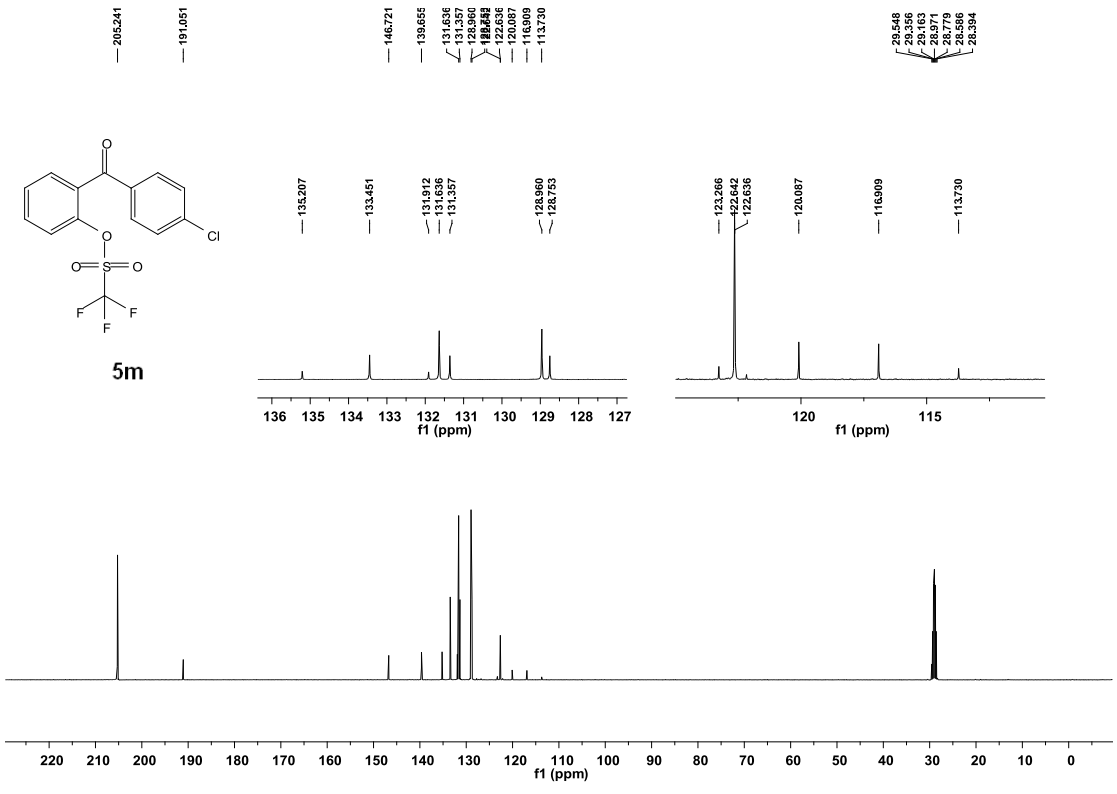


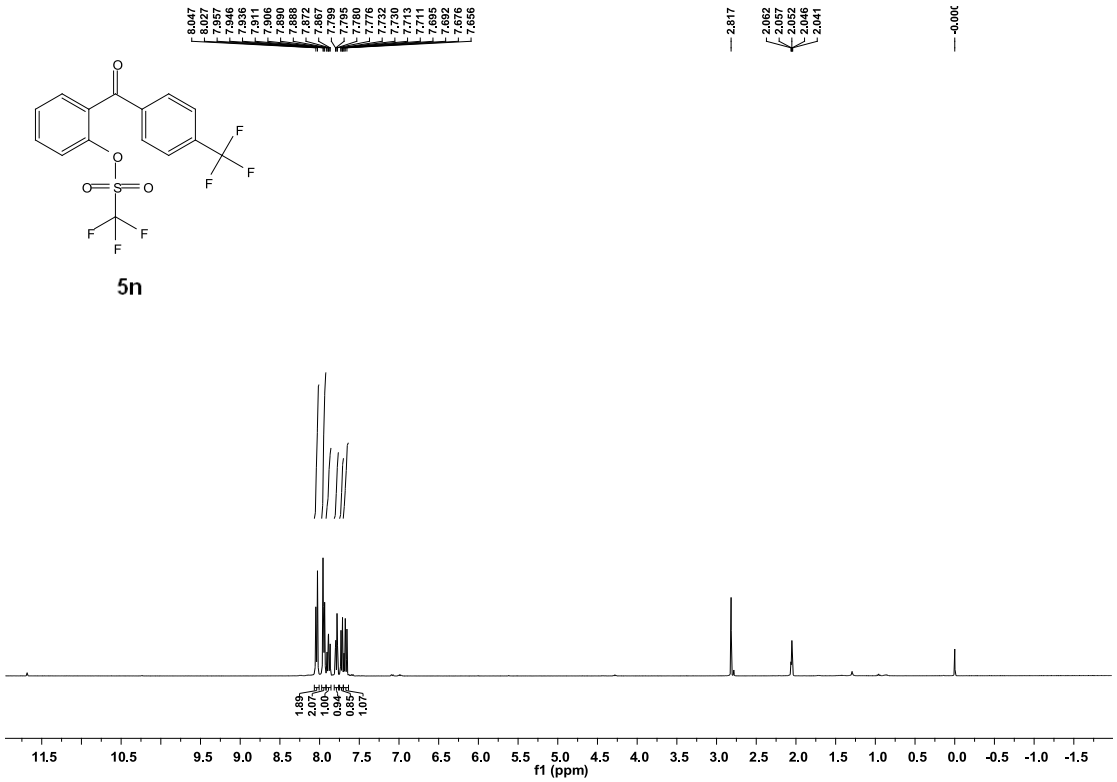
5l



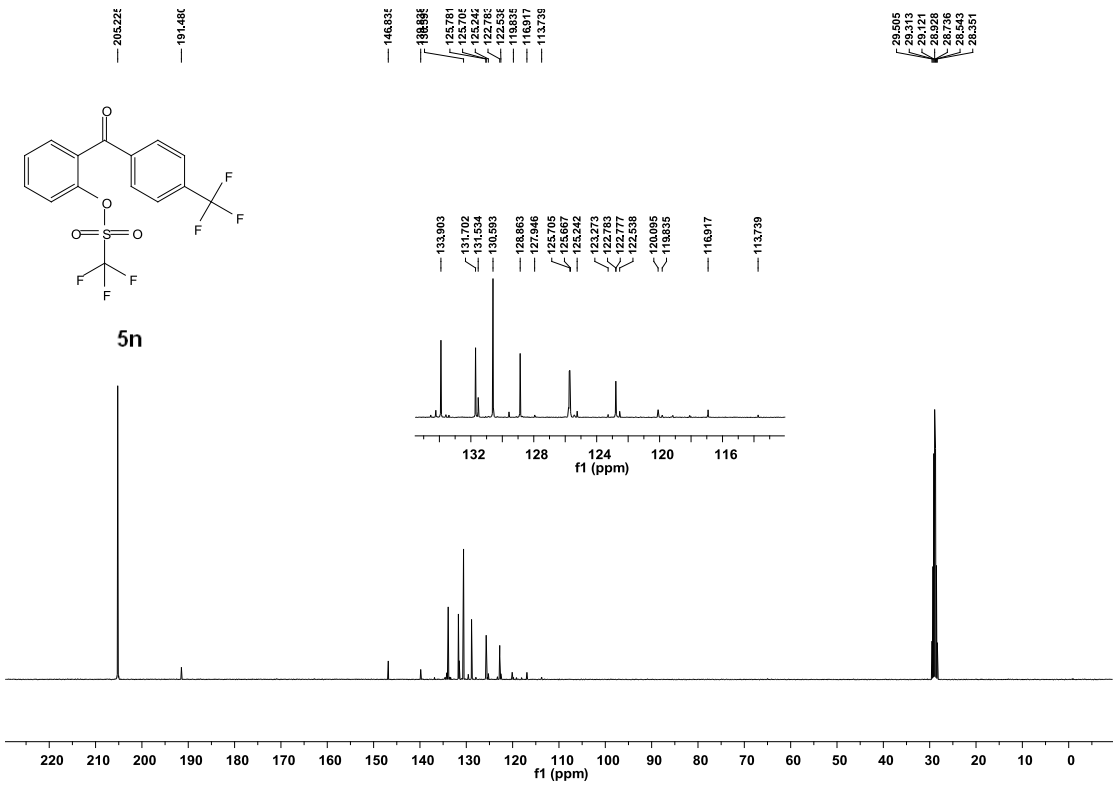
5l


7.872
7.868
7.851
7.833
7.829
7.753
7.749
7.734
7.730
7.706
7.704
7.685
7.668
7.666
7.647
7.634
7.629
7.617
7.612
2.821
2.062
2.056
2.051
2.046
2.040
-0.001
Cl
O
S
F
5m
3.00
1.05
1.17
2.87
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)


205.241
191.051
146.721
139.655
131.636
131.357
128.960
122.636
120.087
116.909
113.730
29.548
29.355
29.163
28.971
28.779
28.586
28.394
Cl
O
S
F
5m
135.207
133.451
131.912
131.636
131.357
128.960
128.753
123.266
122.642
122.636
120.087
116.909
113.730
136
135
134
133
132
131
130
129
128
127
120
115
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

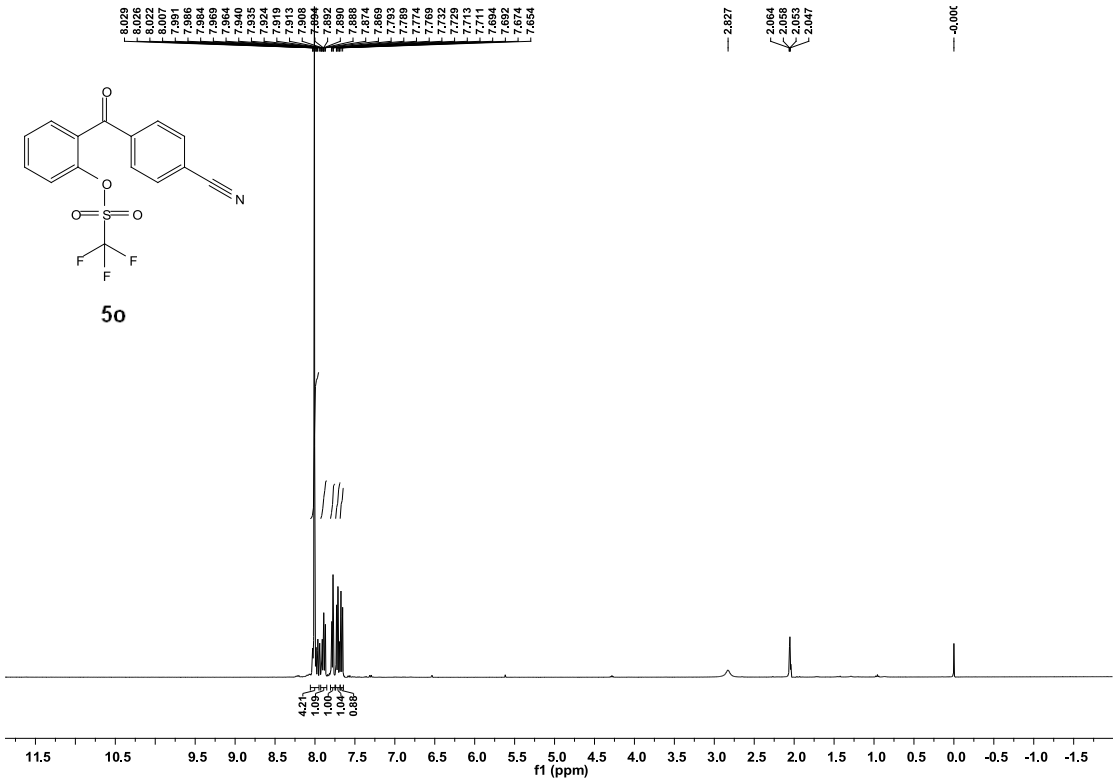

8.047
8.027
7.957
7.946
7.936
7.911
7.906
7.890
7.888
7.872
7.867
7.799
7.795
7.780
7.776
7.732
7.730
7.713
7.711
7.695
7.692
7.676
7.656
2.817
2.062
2.057
2.052
2.046
2.041
1.89
2.07
1.00
0.94
0.85
1.07
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)

5n

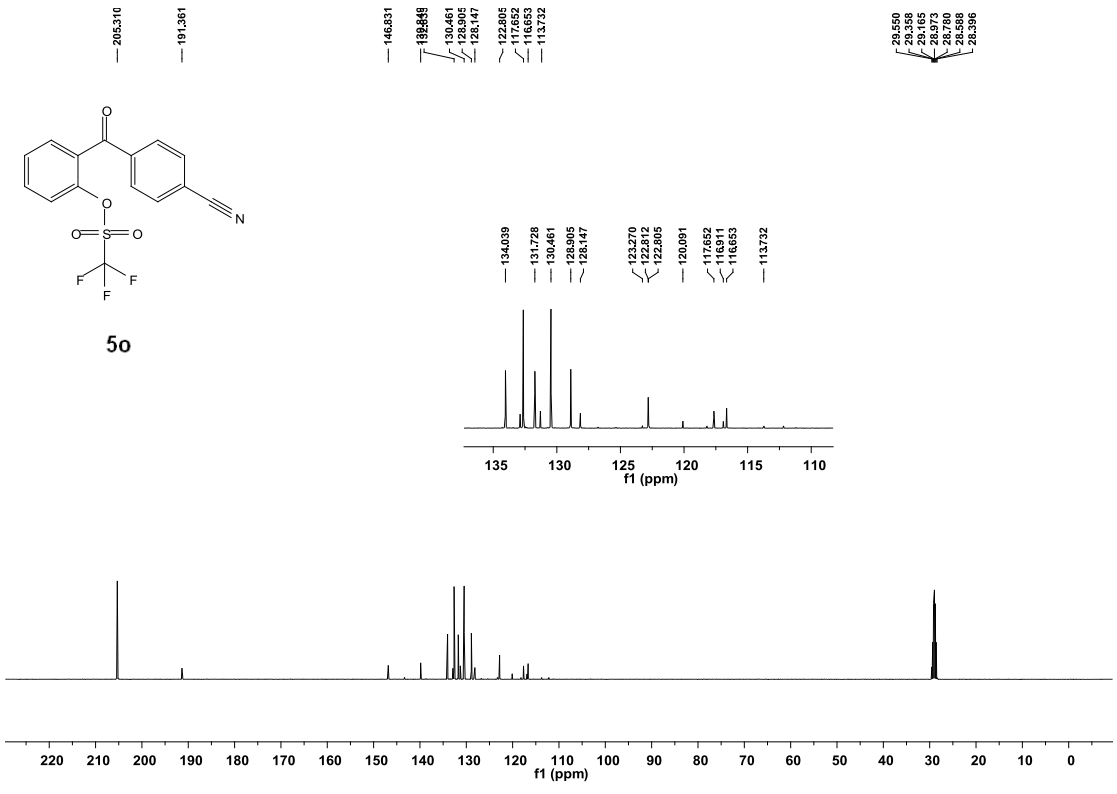

205.225
191.480
146.835
133.903
131.702
131.534
130.593
128.863
127.946
125.705
125.667
125.242
123.273
122.783
122.777
122.538
120.095
119.835
116.917
113.739
29.505
29.313
29.121
28.928
28.736
28.543
28.351
132
128
124
120
116
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

5n

This journal is © The Royal Society of Chemistry 2013

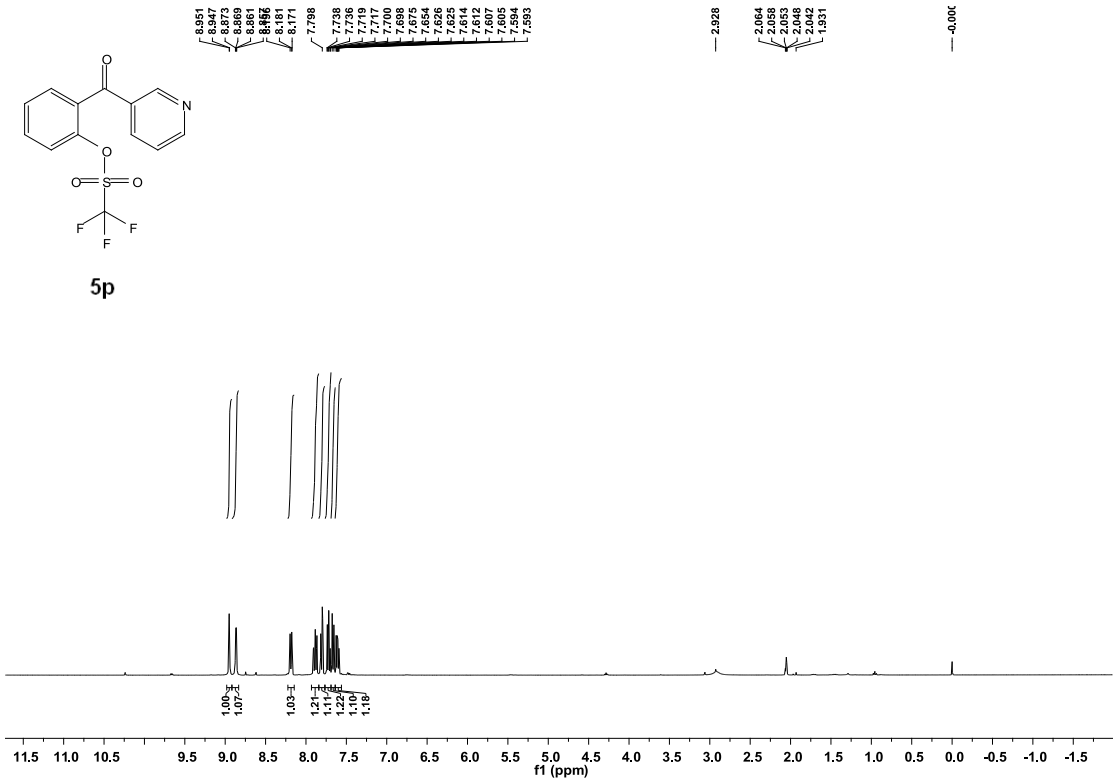


5o

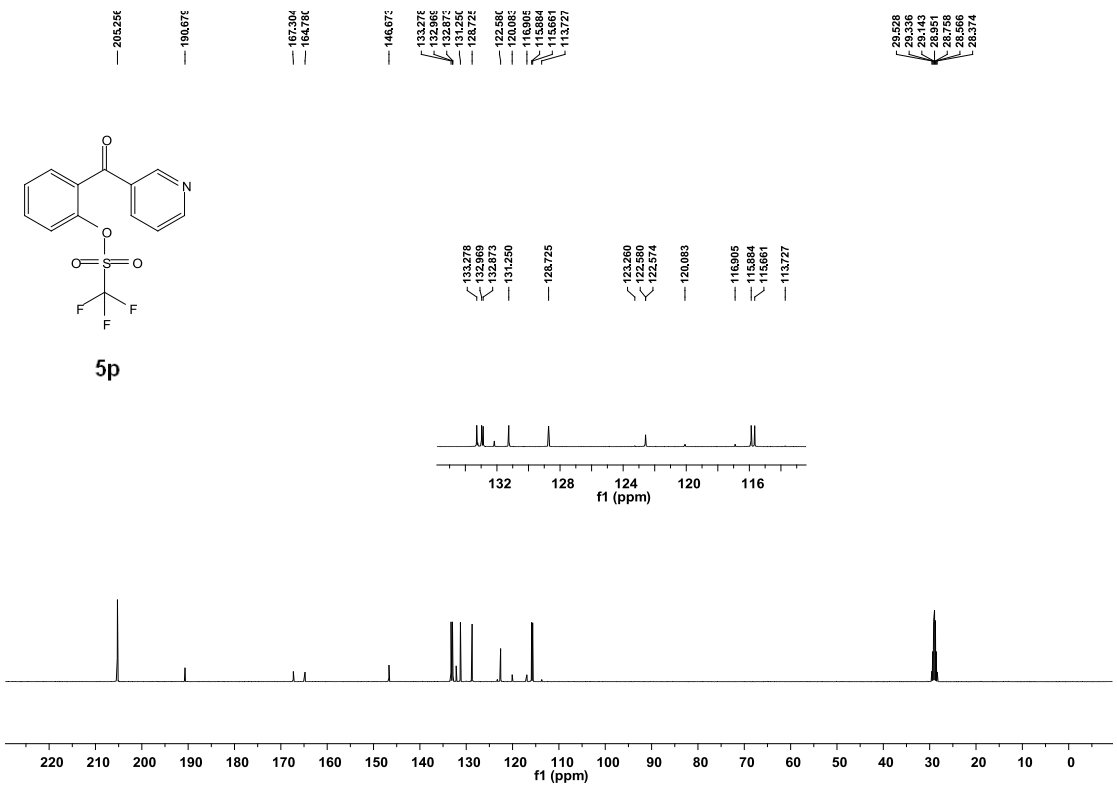


5o

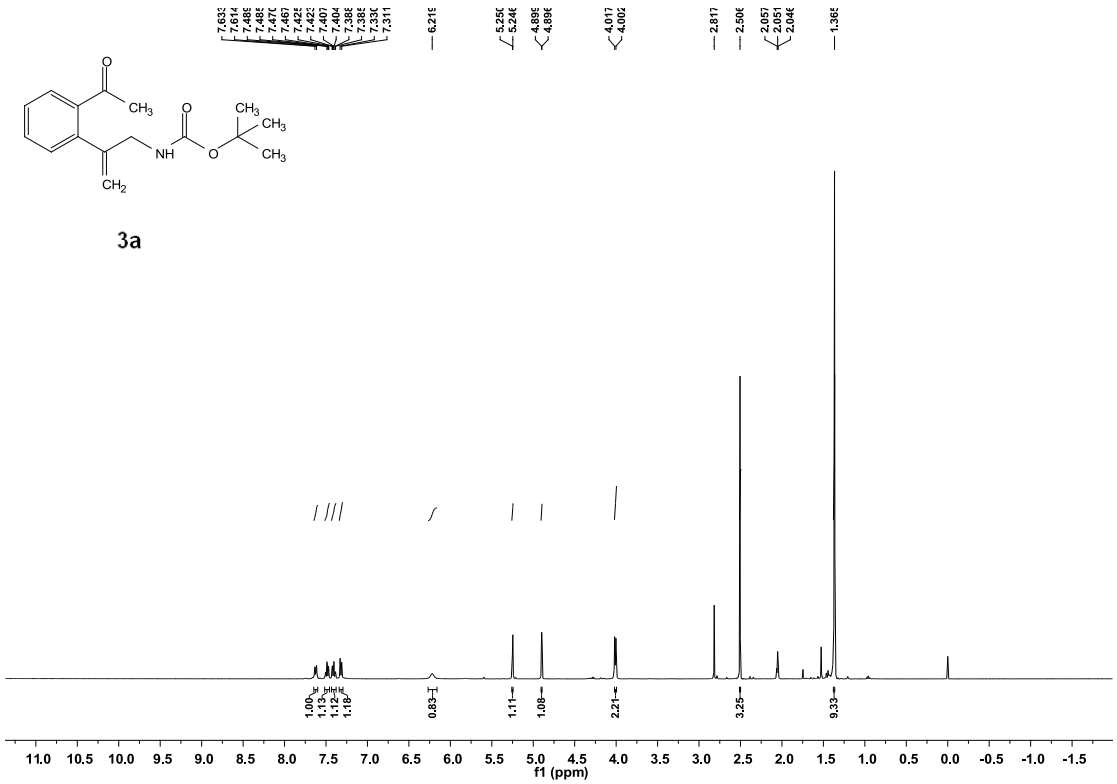
This journal is © The Royal Society of Chemistry 2013

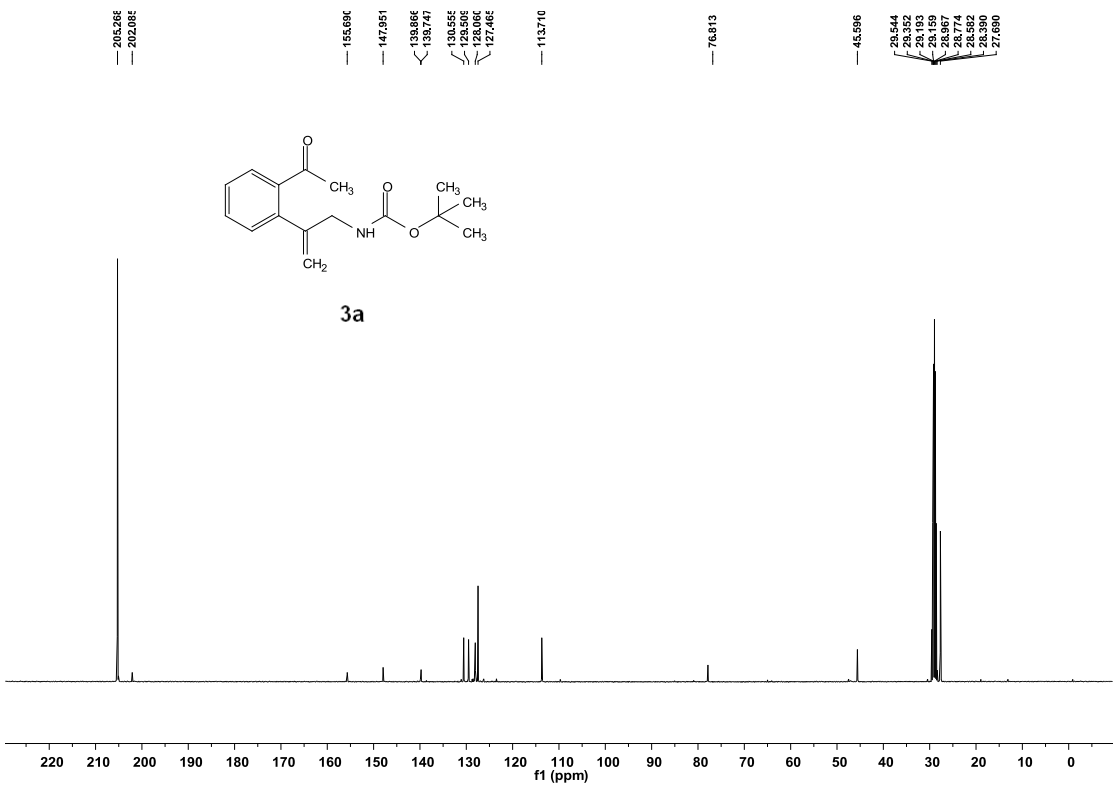


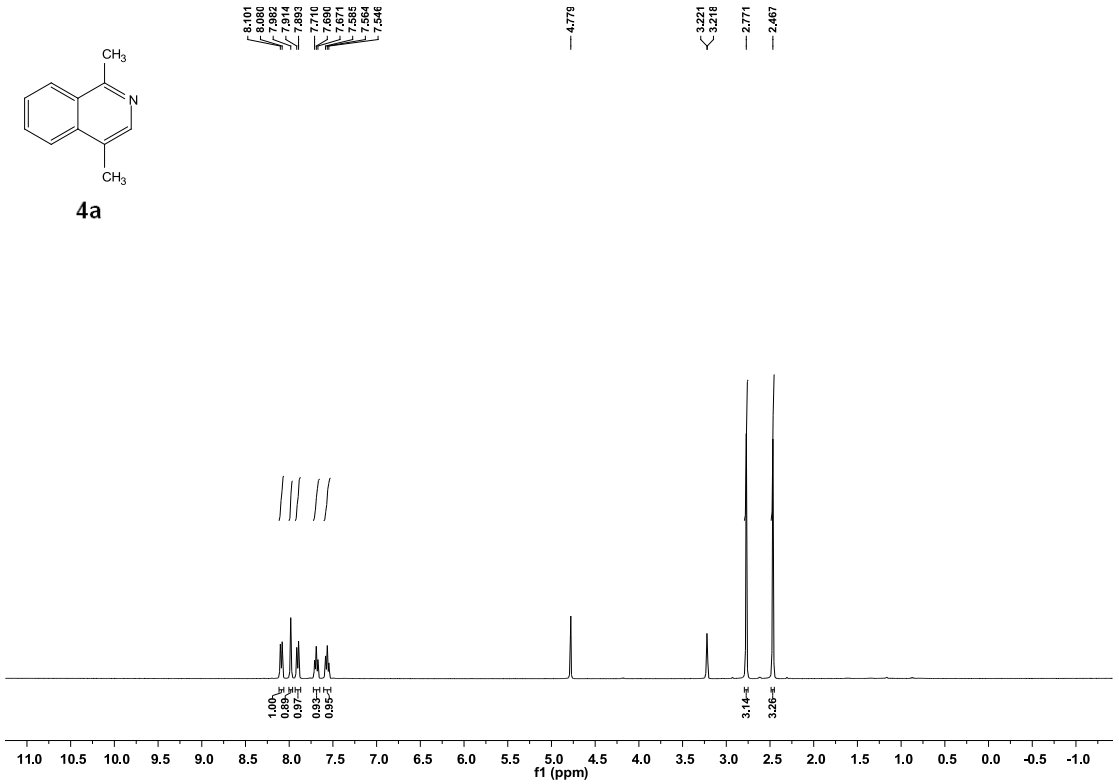
5p



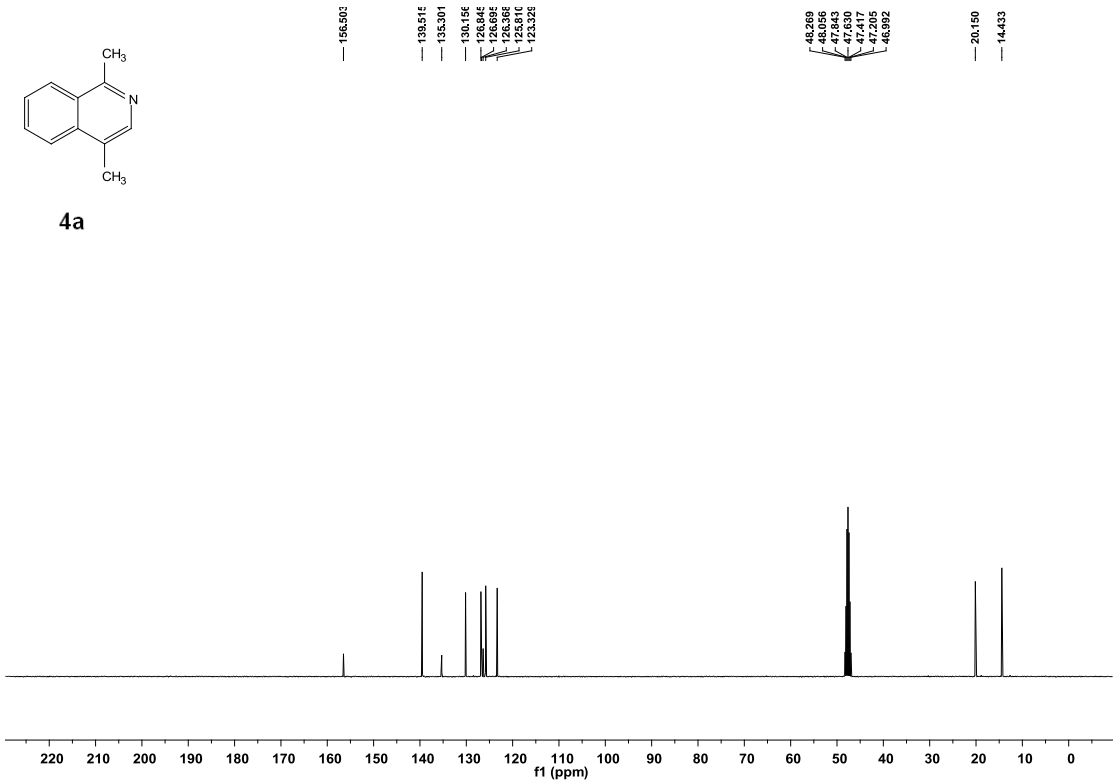
5p


3a
f1 (ppm)

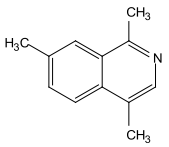

3a
f1 (ppm)


8.101
8.080
7.982
7.914
7.893
7.710
7.690
7.671
7.585
7.564
7.546
4.779
3.221
3.216
2.771
2.467
CH3
N
CH3
1.00
0.89
0.97
0.93
0.95
3.14
3.26
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

4a

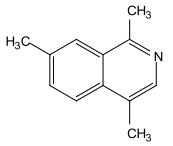

156.503
139.515
135.301
130.156
126.845
126.695
126.368
125.810
123.328
48.269
48.056
47.843
47.630
47.417
47.205
46.992
20.150
14.433
CH3
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4a


CH3
H3C
N
CH3

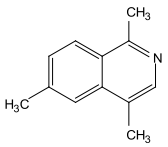
4b

7.788
7.666
7.614
7.592
7.383
7.362
4.779
3.186
3.184
2.610
2.358
2.306
1.00
1.06
1.04
1.05
3.04
3.21
3.29
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)


CH3
H3C
N
CH3

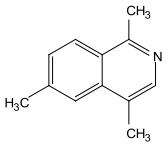
4b

155.734
138.719
136.978
132.148
126.864
126.213
124.660
123.182
48.262
48.048
47.836
47.623
47.410
47.197
46.984
20.485
20.113
14.406
138.719
136.978
133.501
132.148
126.864
126.213
124.660
123.182
140 135 130 125 120
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


CH3
N
H3C
CH3

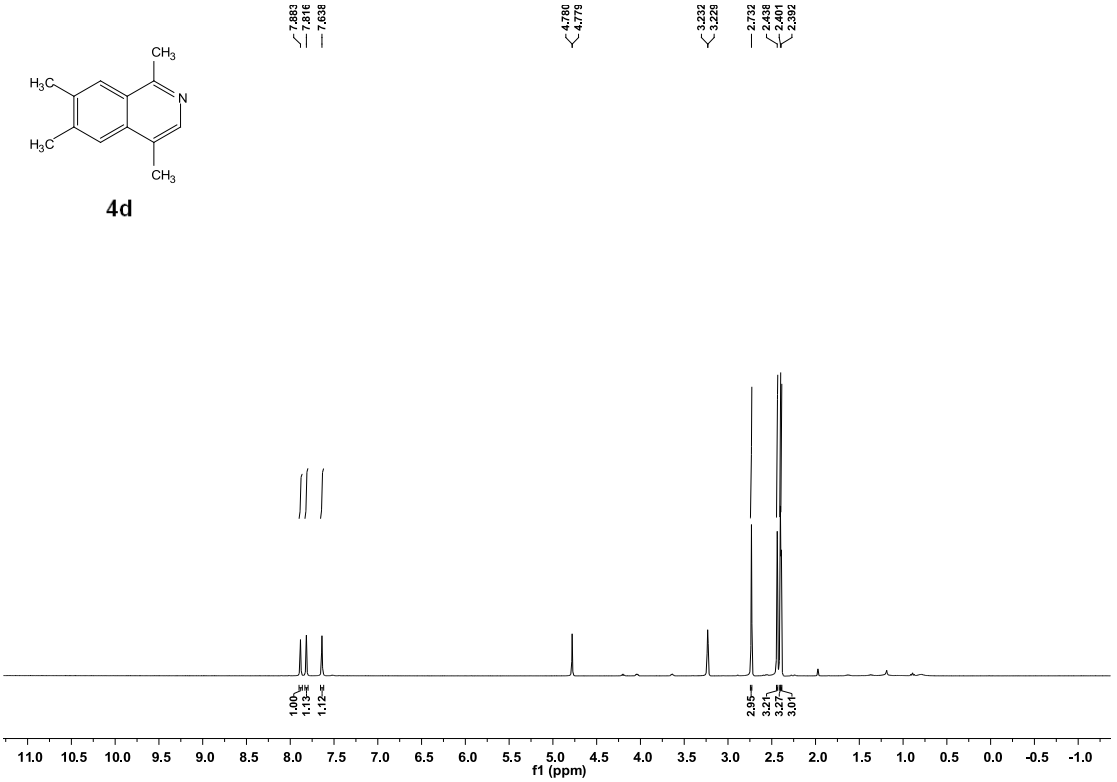
4c

8.052
8.031
7.979
7.737
7.469
7.448
4.779
3.236
2.784
2.512
2.491
1.00
0.94
0.93
0.94
3.12
2.91
3.01
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

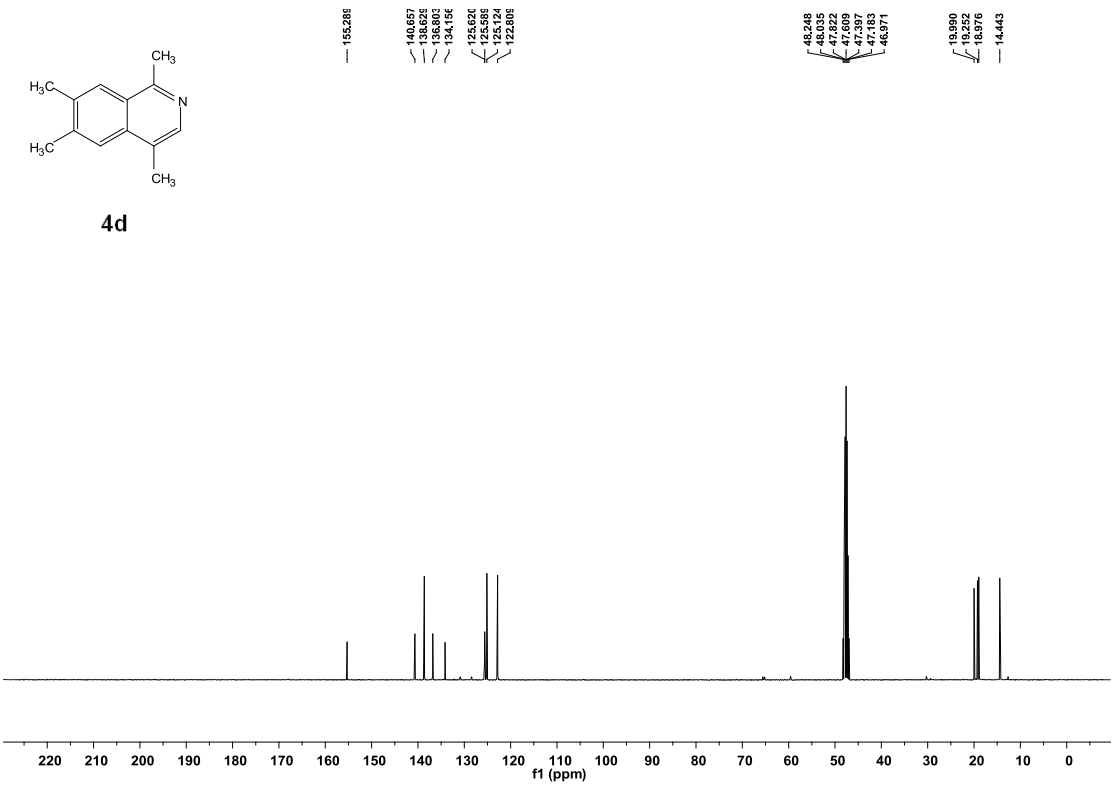

CH3
N
H3C
CH3

4c

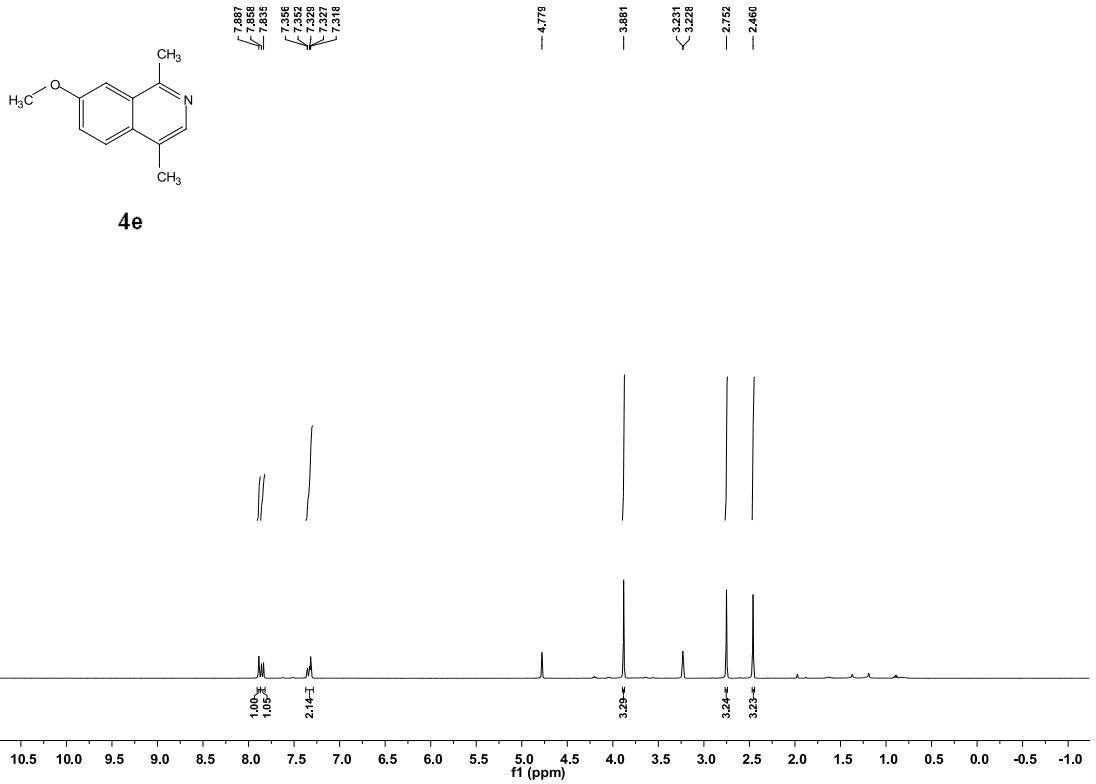
156.194
140.972
139.507
135.704
128.946
125.967
125.775
125.111
122.414
48.242
48.029
47.816
47.603
47.390
47.178
46.965
20.737
20.009
14.475
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.883
7.816
7.638
4.786
4.779
3.232
3.229
2.732
2.438
2.401
2.392
1.00
1.13
1.12
2.95
3.21
3.27
3.01
f1 (ppm)

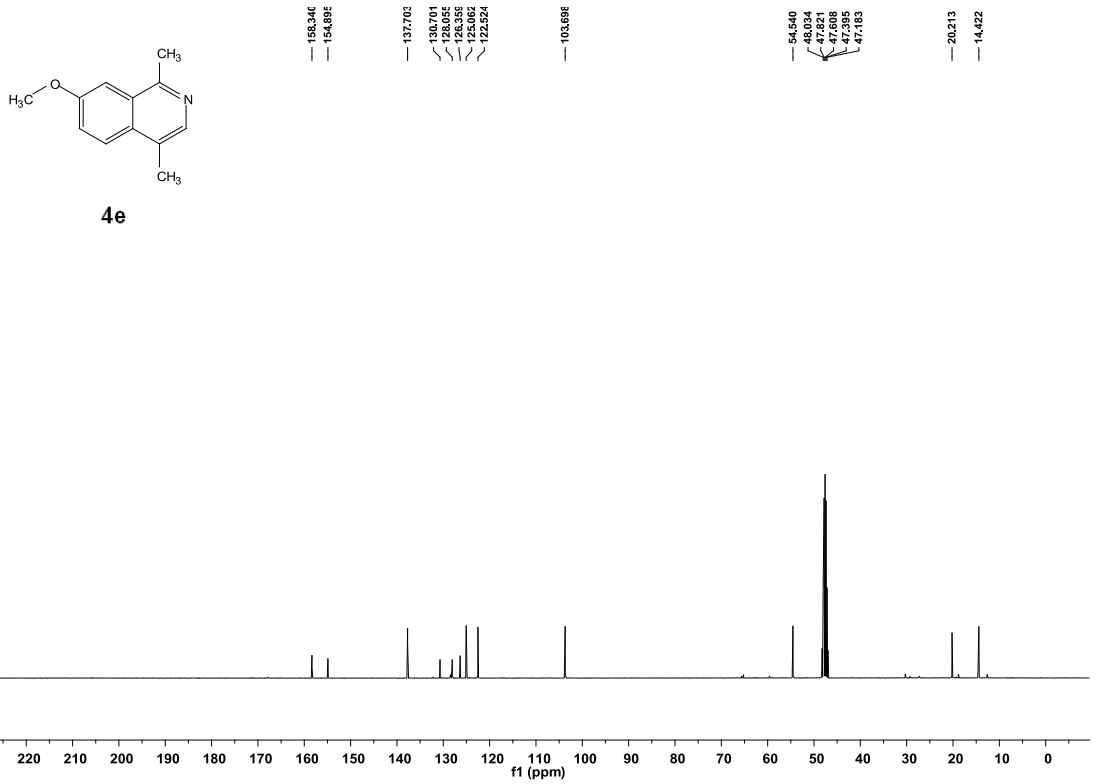
4d


155.286
140.657
138.625
136.803
134.156
125.620
125.585
125.124
122.809
48.248
48.035
47.822
47.609
47.397
47.183
46.971
19.990
18.252
16.976
14.443
f1 (ppm)

4d

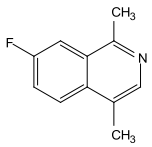

7.887
7.858
7.835
7.356
7.352
7.329
7.327
7.318
4.779
3.881
3.231
3.228
2.752
2.460
CH3
H3C
O
N
CH3
1.00
1.05
2.14
3.29
3.24
3.23
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

4e

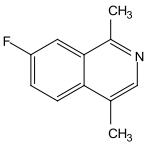

158.340
154.895
137.703
130.701
128.055
126.359
125.062
122.524
103.698
54.540
48.034
47.821
47.608
47.395
47.183
20.213
14.422
CH3
H3C
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4e

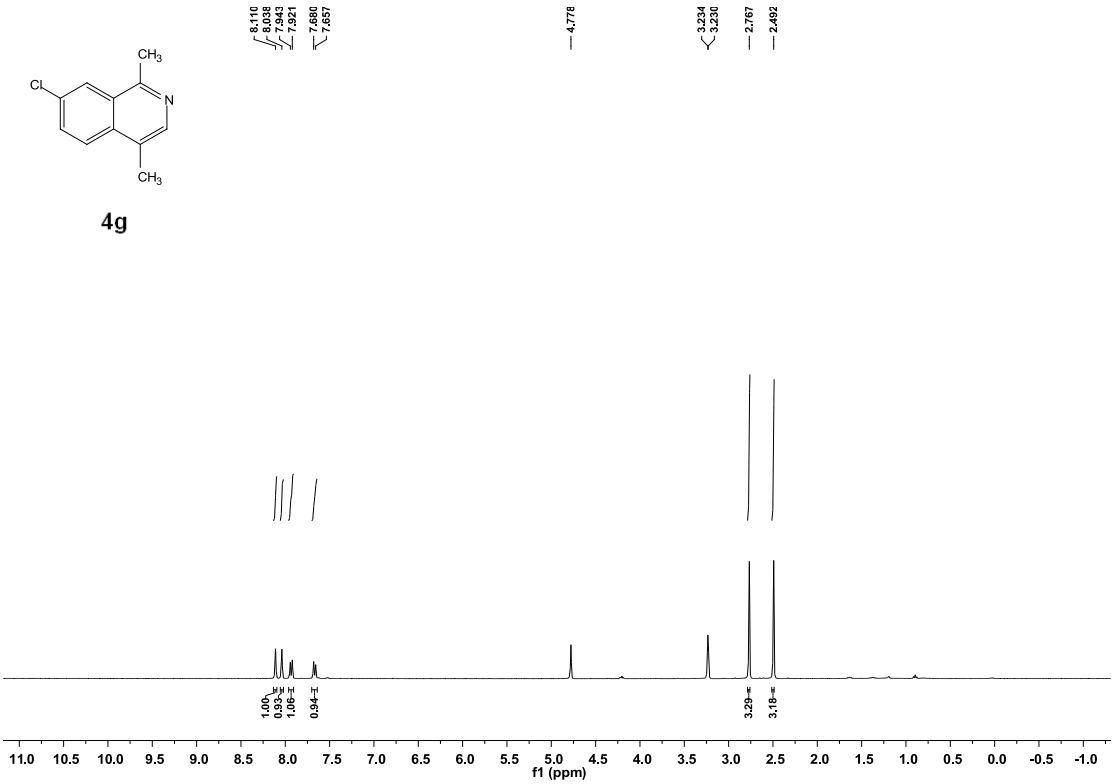
This journal is © The Royal Society of Chemistry 2013



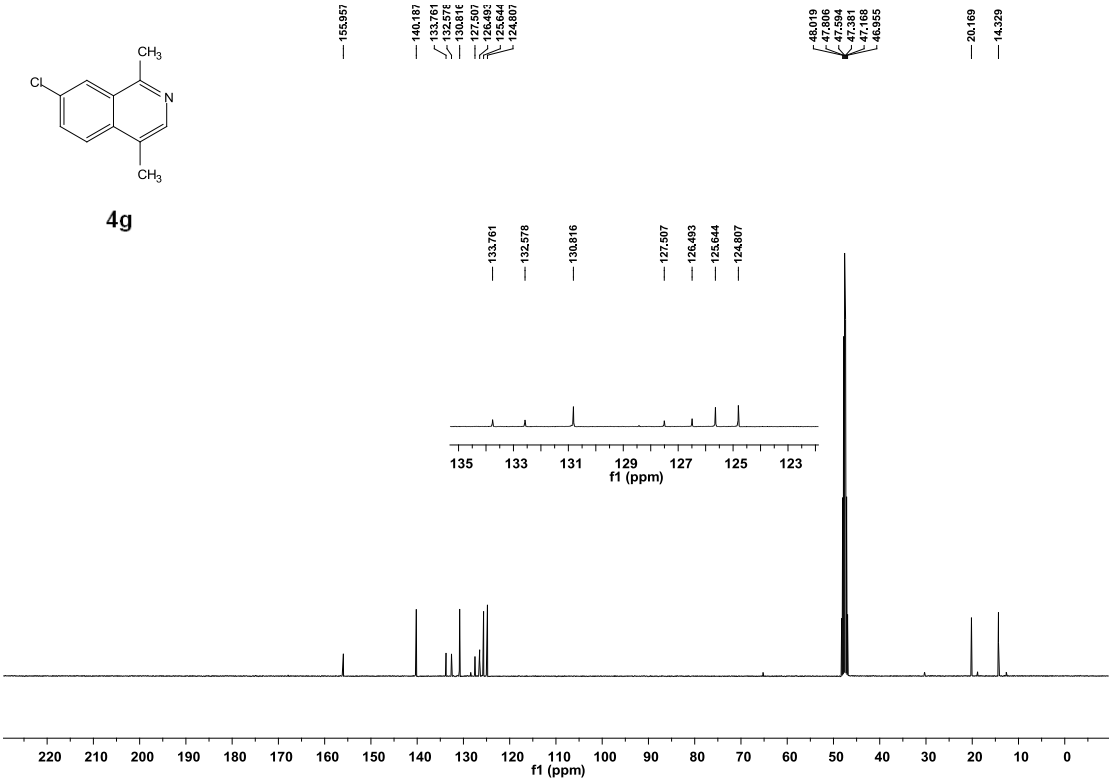
4f



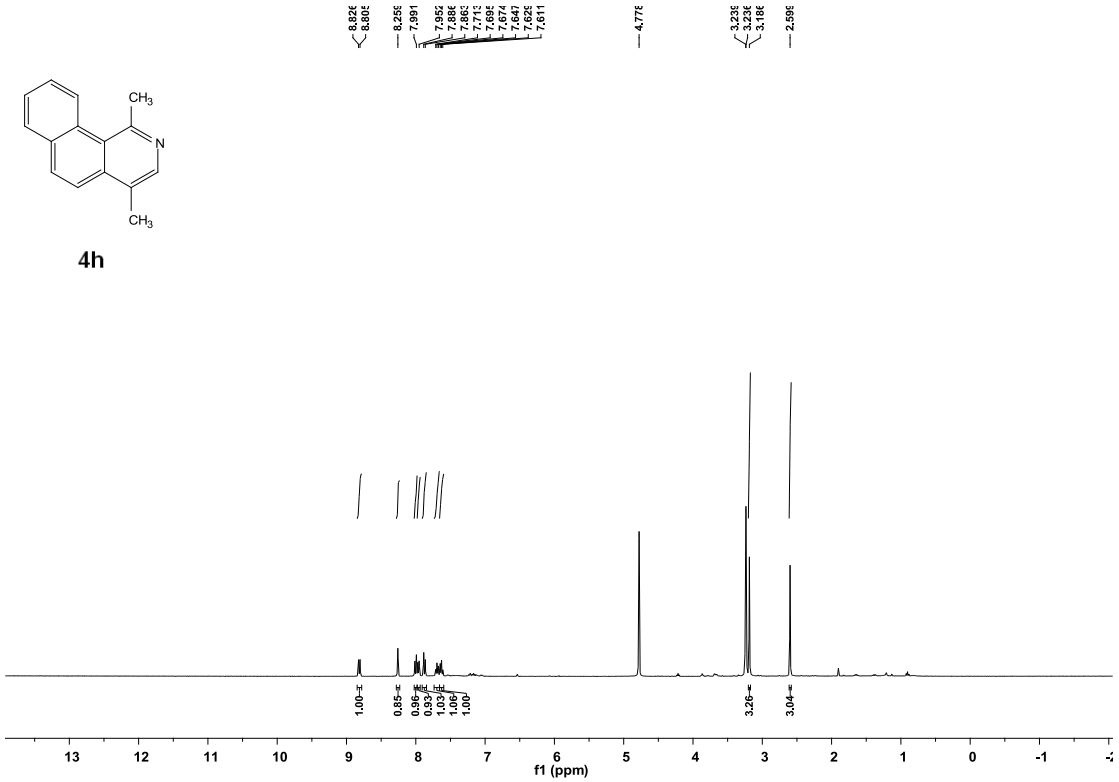
4f


8.110
8.038
7.943
7.921
7.680
7.657
4.778
3.234
3.230
2.767
2.492
CH3
Cl
N
CH3
1.00
0.93
1.05
0.94
3.29
3.18
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

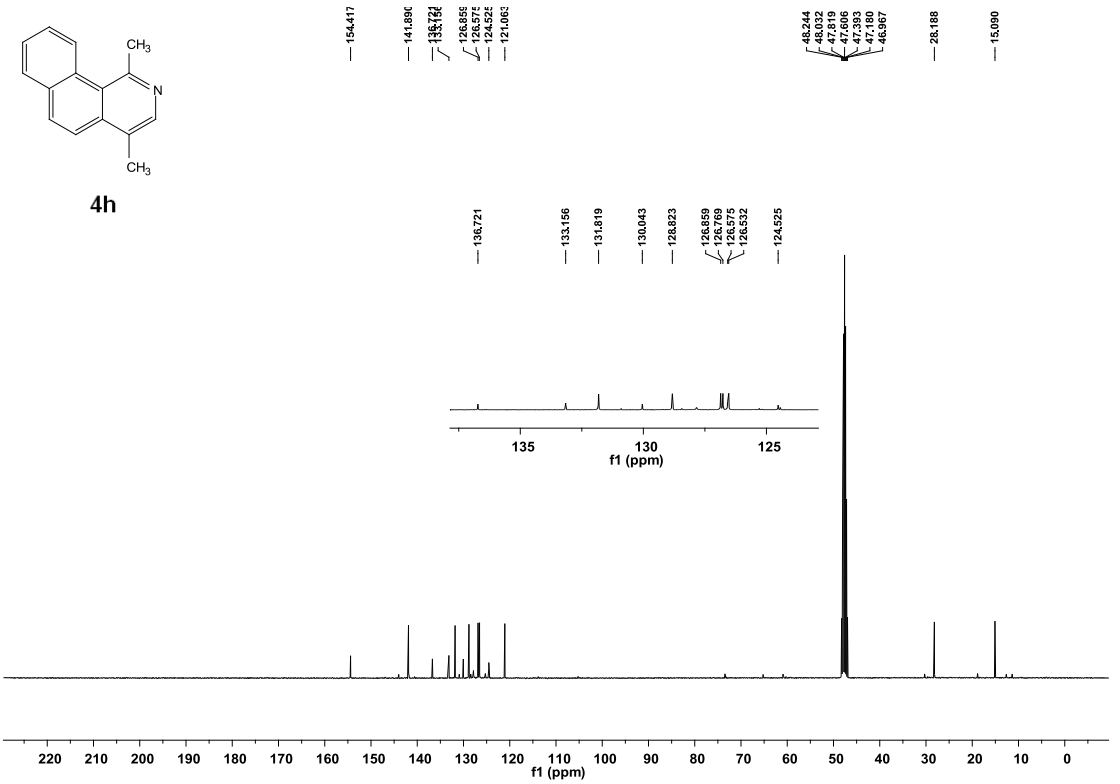
4g


155.957
140.187
133.761
132.578
130.816
127.507
126.493
125.644
124.807
48.019
47.806
47.594
47.381
47.168
46.955
20.169
14.329
CH3
Cl
N
CH3
133.761
132.578
130.816
127.507
126.493
125.644
124.807
135 133 131 129 127 125 123
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

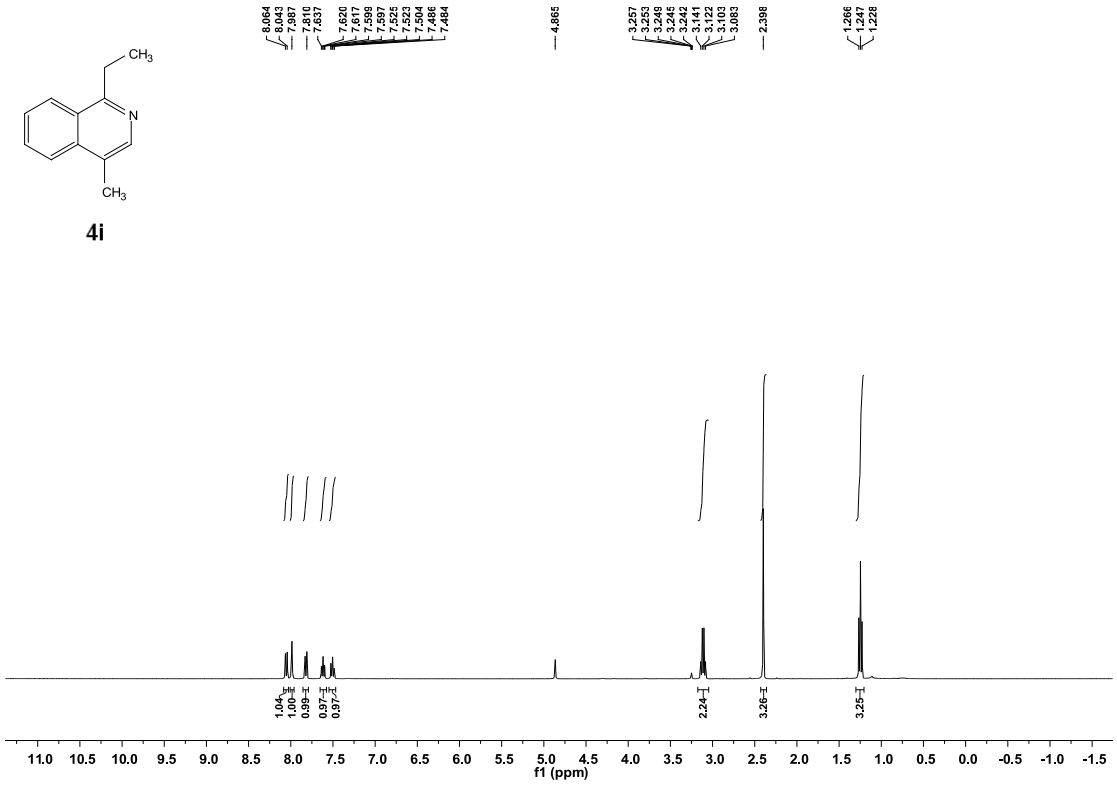
4g



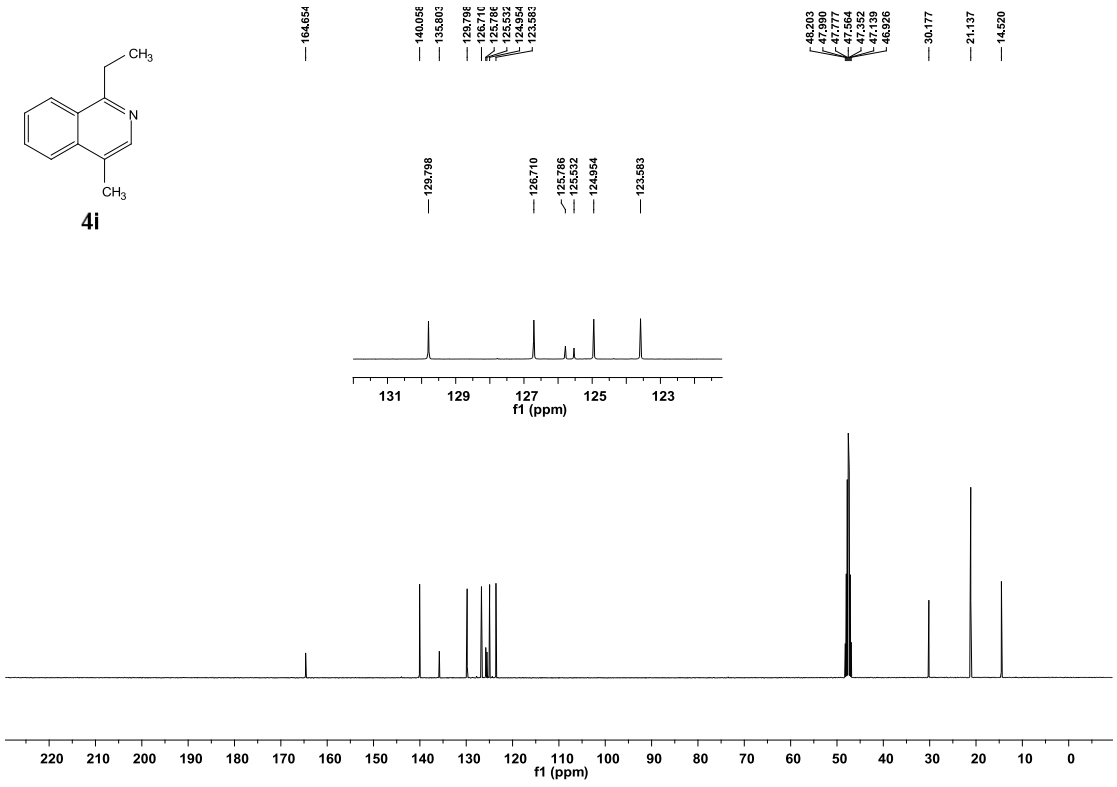
4h



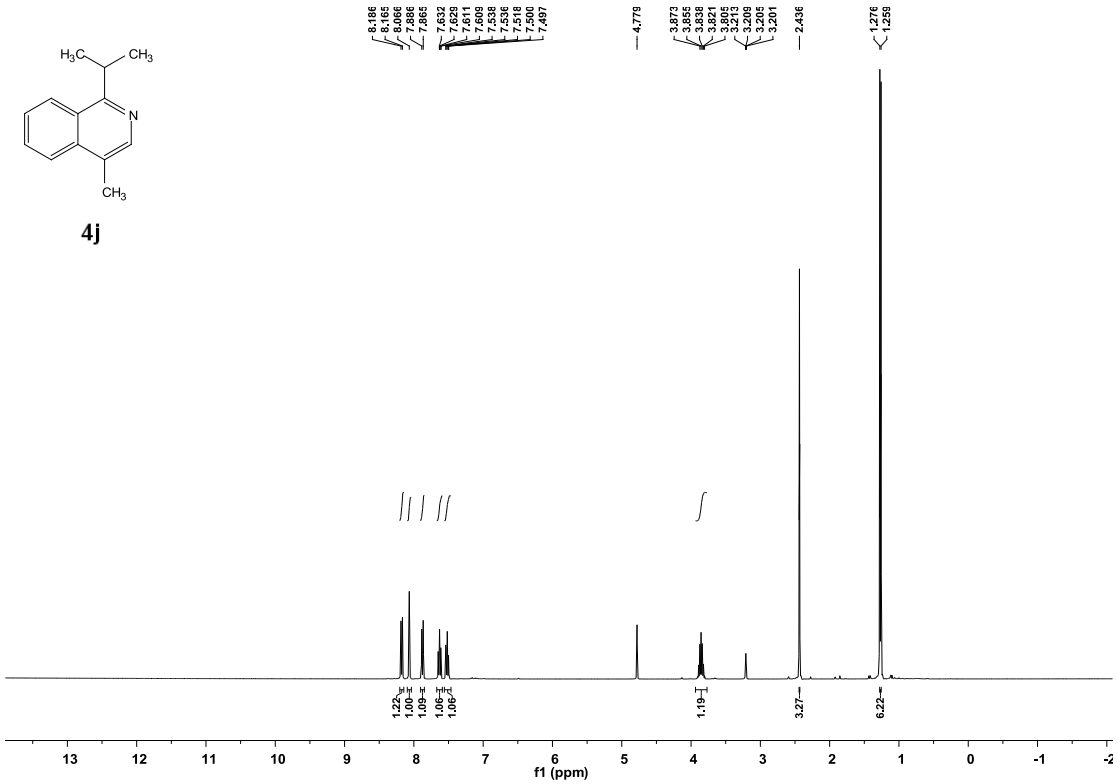
4h


8.064
8.045
7.997
7.810
7.637
7.620
7.617
7.599
7.597
7.525
7.523
7.504
7.486
7.484
4.865
3.257
3.253
3.248
3.245
3.244
3.141
3.122
3.103
3.083
2.398
1.266
1.247
1.228
CH3
N
CH3
1.04
1.00
0.99
0.97
0.97
2.24
3.26
3.25
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

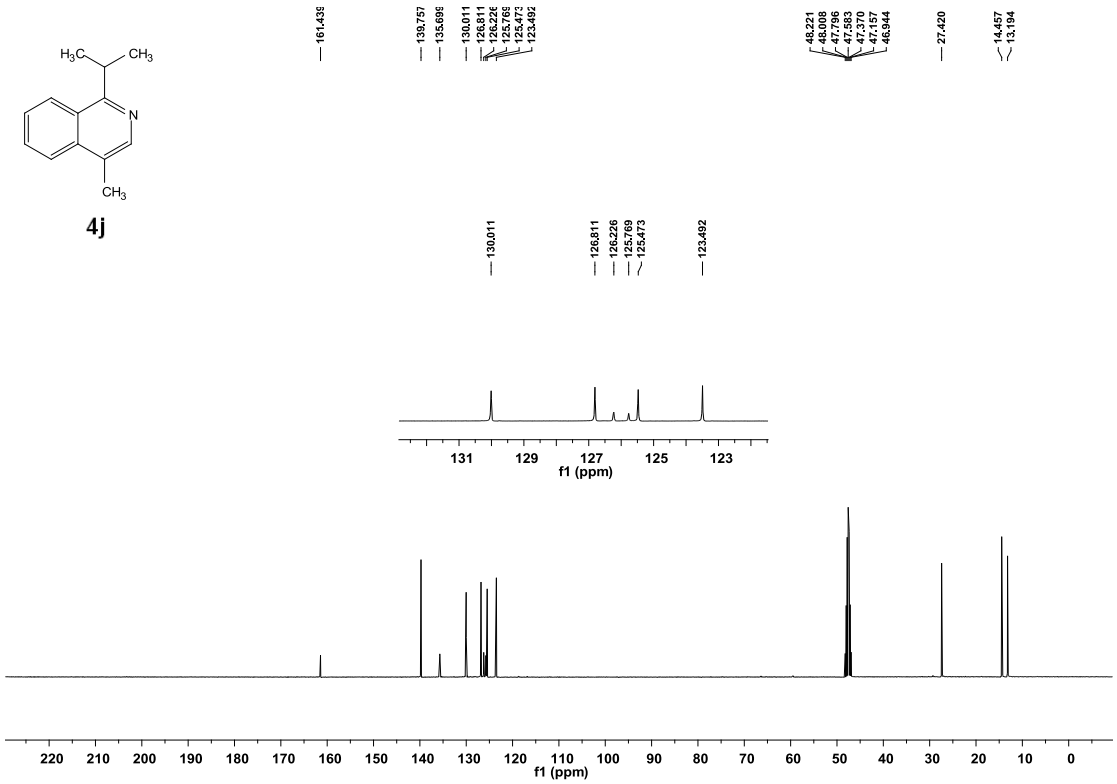
4i


164.654
140.058
135.803
129.798
126.710
125.786
125.532
124.954
123.583
48.203
47.990
47.777
47.564
47.352
47.139
46.926
30.177
21.137
14.520
CH3
N
CH3
129.798
126.710
125.786
125.532
124.954
123.583
131 129 127 125 123
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

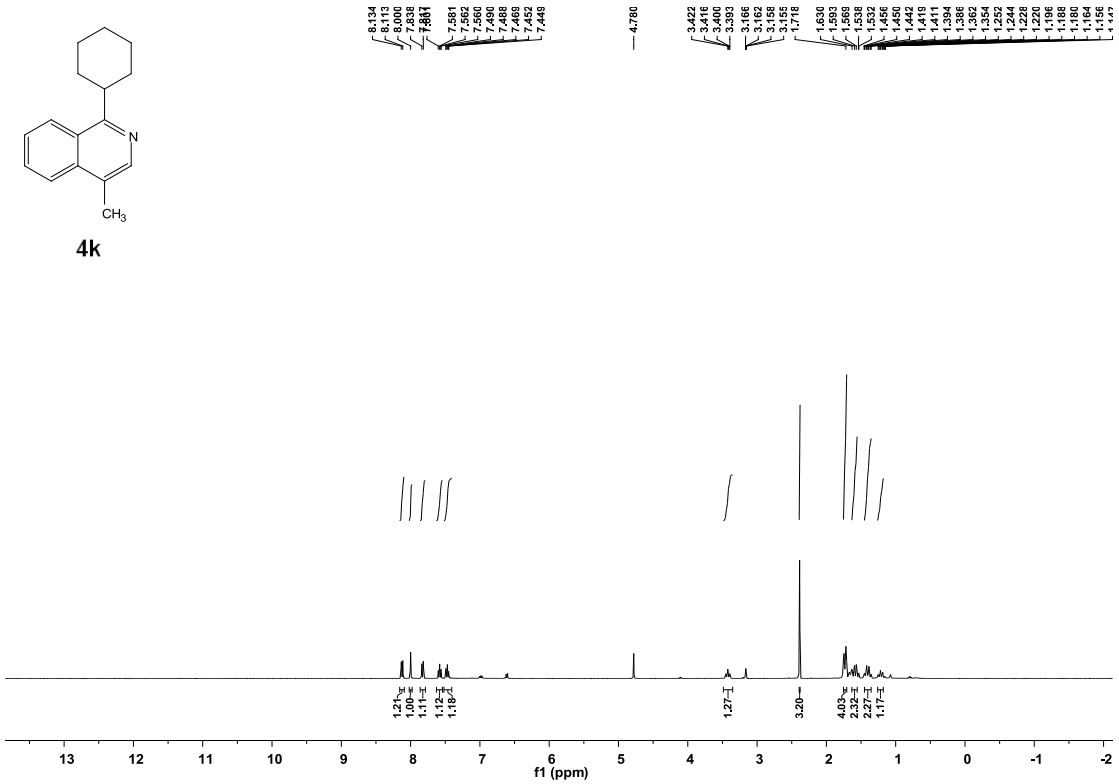
4i

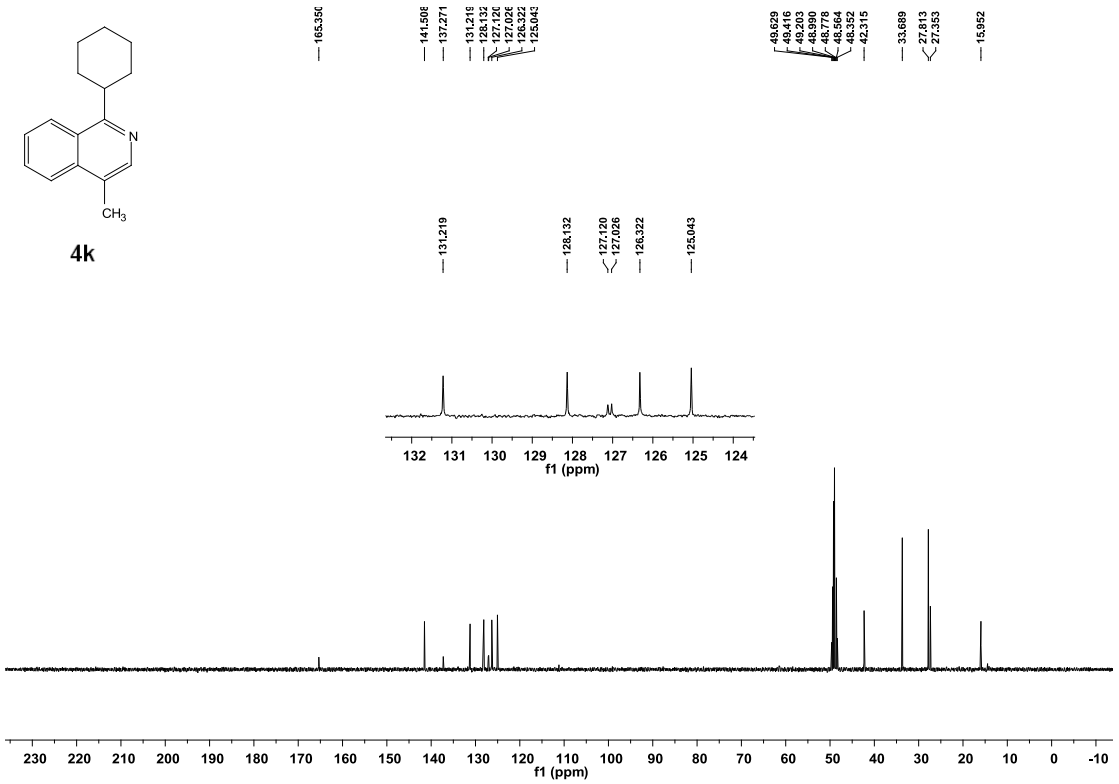

8.186
8.165
8.066
7.886
7.865
7.632
7.629
7.611
7.609
7.538
7.536
7.516
7.500
7.497
4.779
3.873
3.855
3.838
3.821
3.805
3.213
3.209
3.205
3.201
2.436
1.276
1.259
1.22
1.09
1.09
1.06
1.06
1.19
3.27
6.22
f1 (ppm)

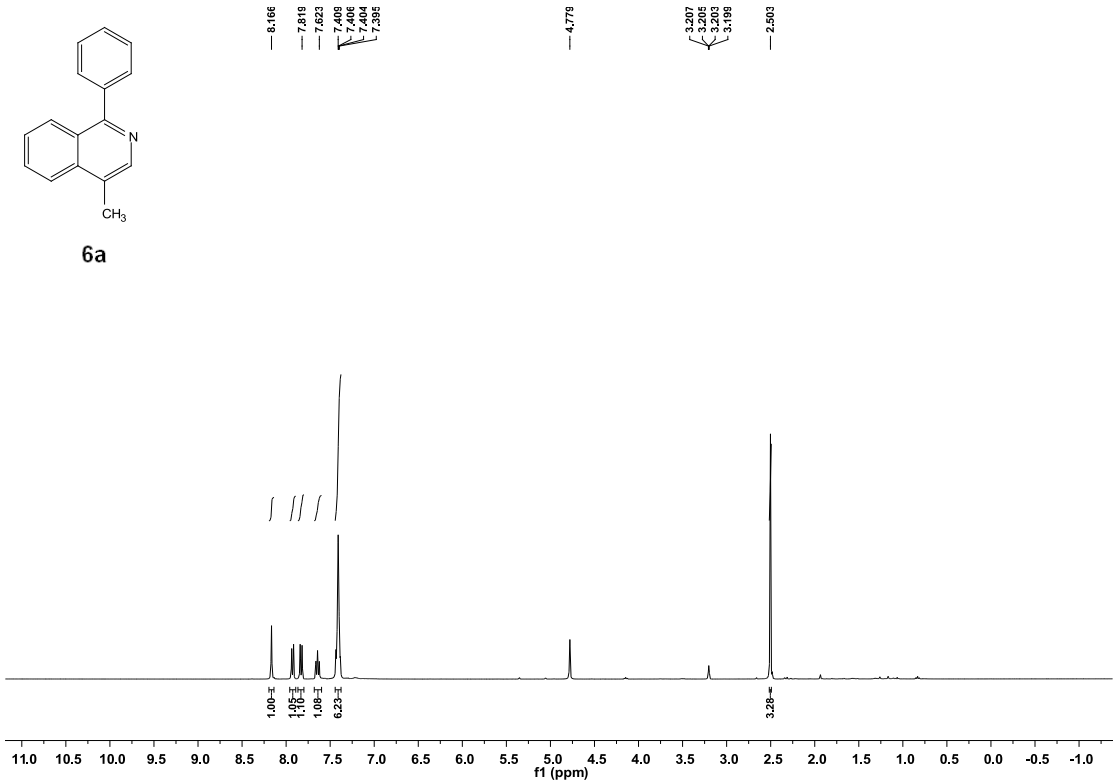
4j


161.435
139.757
135.695
130.011
126.811
126.226
125.769
125.473
123.492
48.221
48.008
47.796
47.583
47.370
47.157
46.944
27.420
14.457
13.194
130.011
126.811
126.226
125.769
125.473
123.492
f1 (ppm)
f1 (ppm)

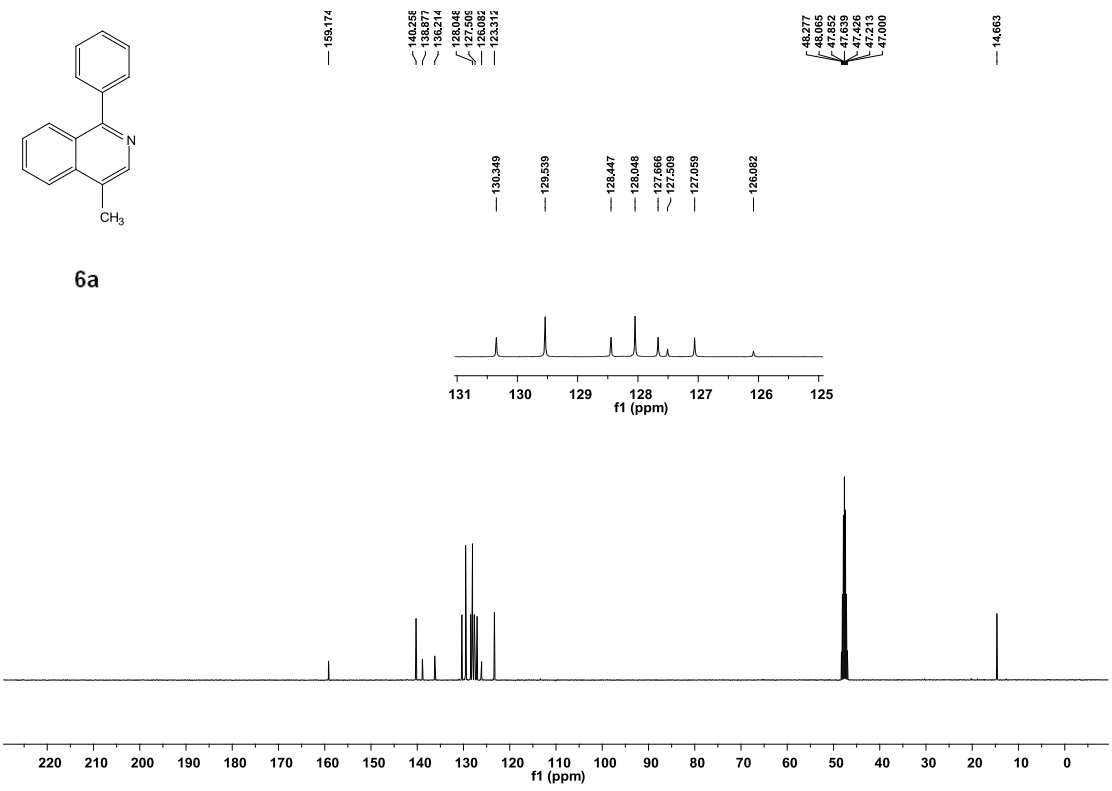
4j


N
CH3
4k
f1 (ppm)

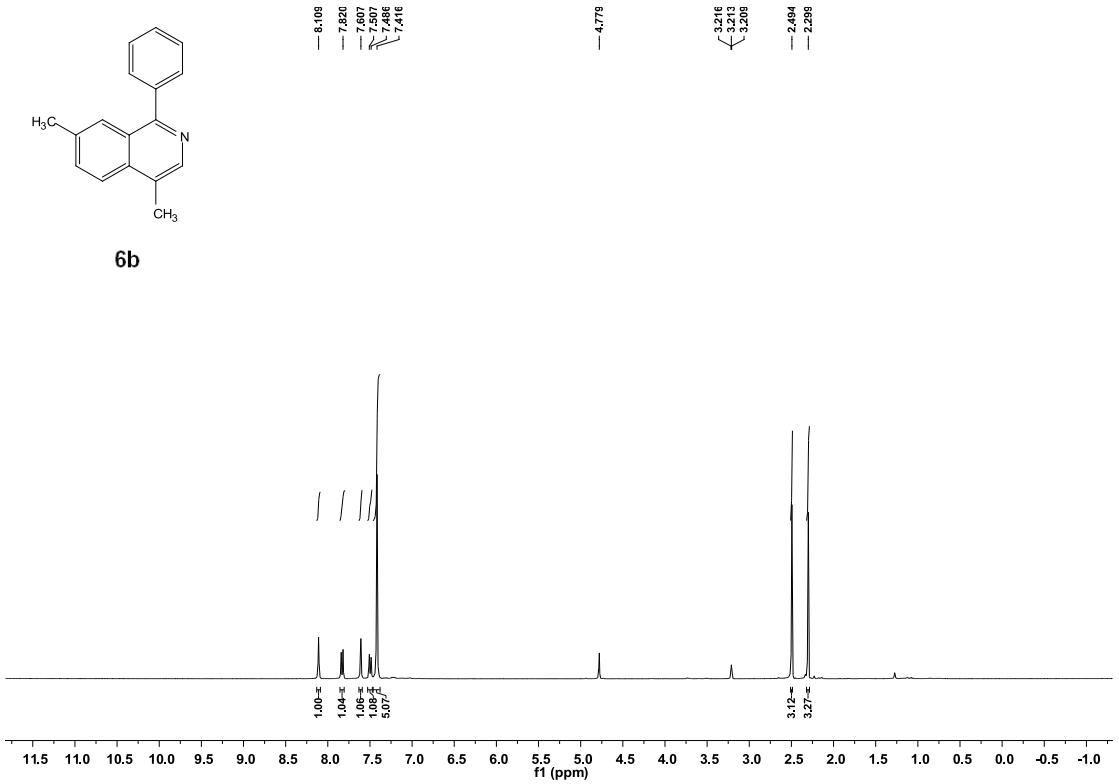

N
CH3
4k
f1 (ppm)
f1 (ppm)


8.166
7.819
7.623
7.409
7.406
7.404
7.396
4.779
3.207
3.205
3.203
3.199
2.503
N
CH3
1.00
1.05
1.10
1.08
6.23
3.28
f1 (ppm)

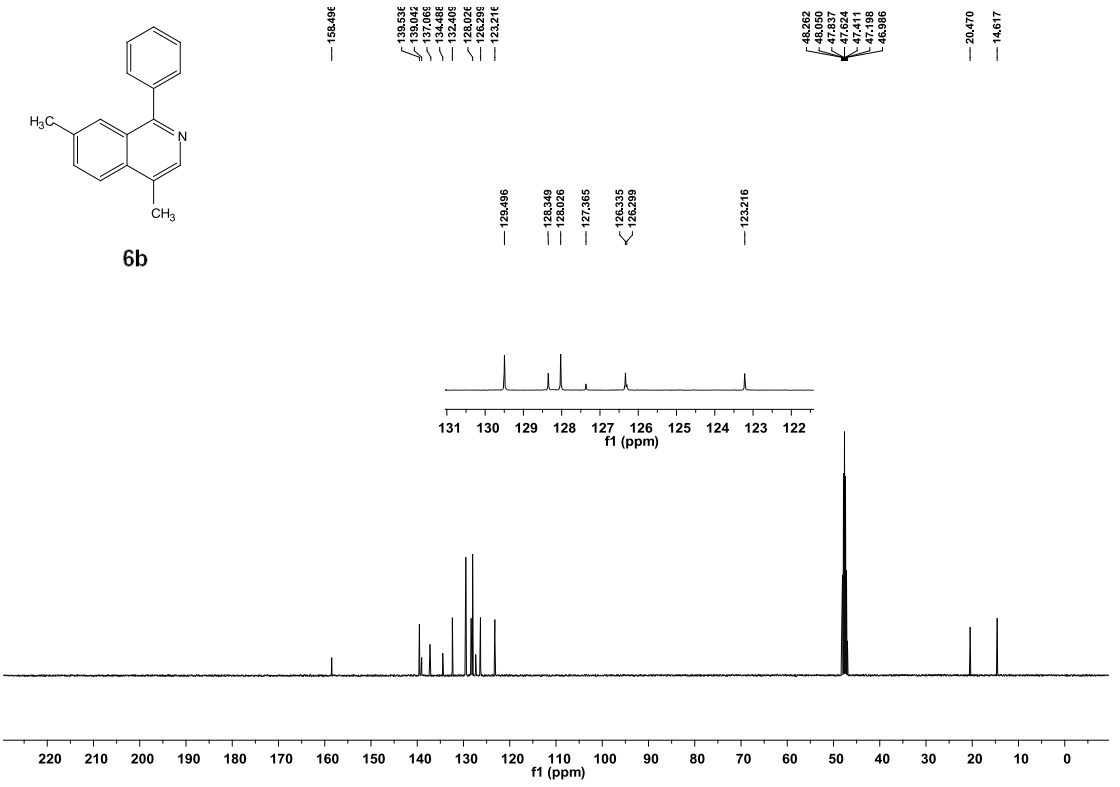
6a


159.174
140.258
138.877
136.214
128.048
127.505
126.082
123.312
48.277
48.065
47.852
47.639
47.426
47.213
47.000
14.663
130.349
129.539
128.447
128.048
127.666
127.509
127.059
126.082
N
CH3
f1 (ppm)

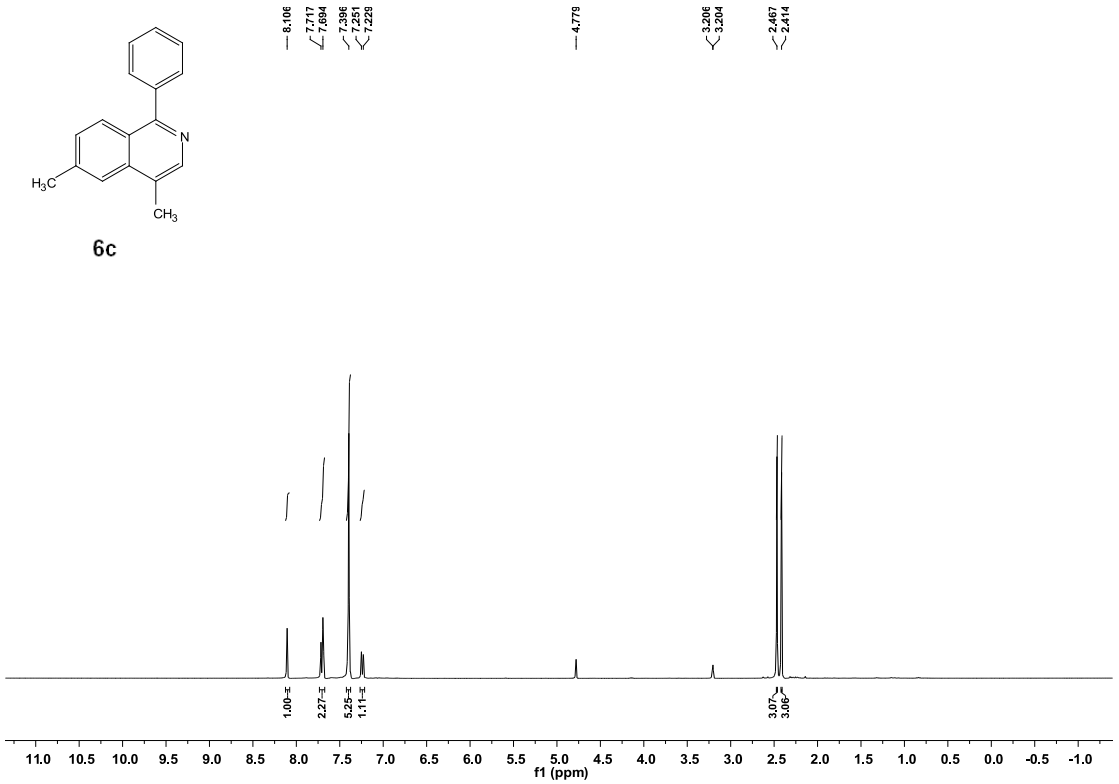
6a


8.109
7.820
7.607
7.507
7.486
7.416
4.779
3.216
3.213
3.209
2.494
2.299
H3C
N
CH3
1.00
1.04
1.06
1.08
5.07
3.12
3.27
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

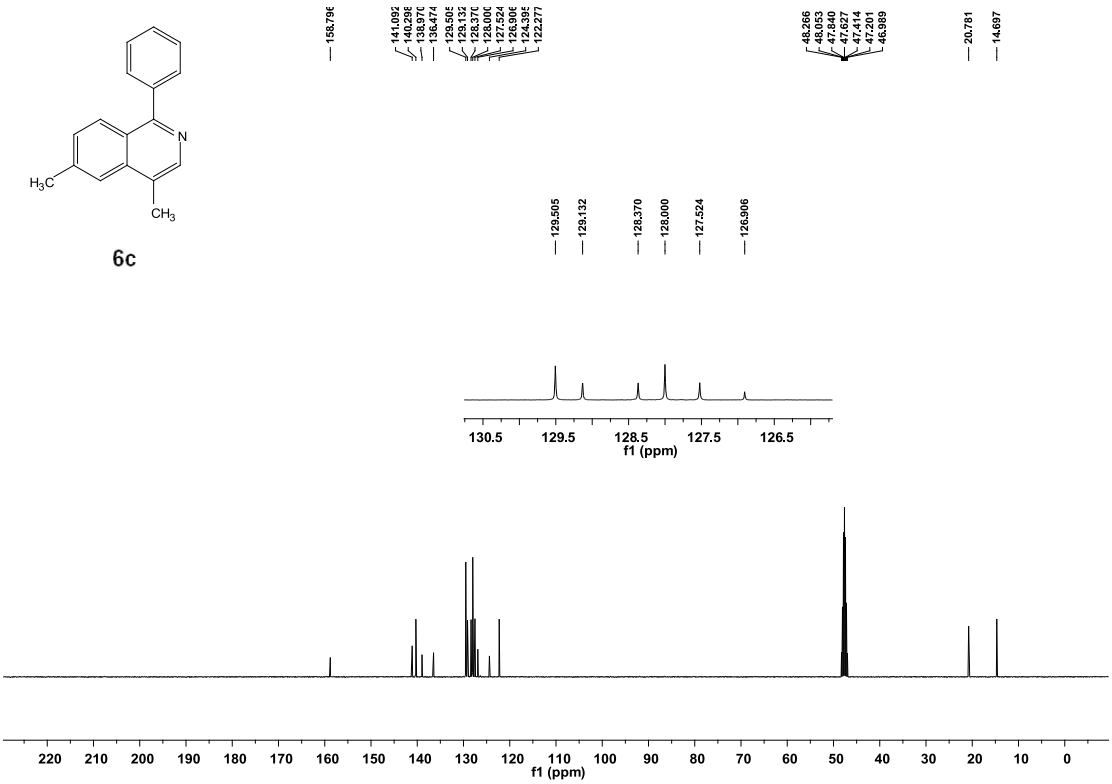
6b


158.496
139.536
139.042
137.065
134.488
132.405
128.026
126.299
123.216
48.262
48.050
47.837
47.624
47.411
47.198
46.986
20.470
14.617
129.496
128.349
128.026
127.365
126.335
126.299
123.216
H3C
N
CH3
131 130 129 128 127 126 125 124 123 122
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

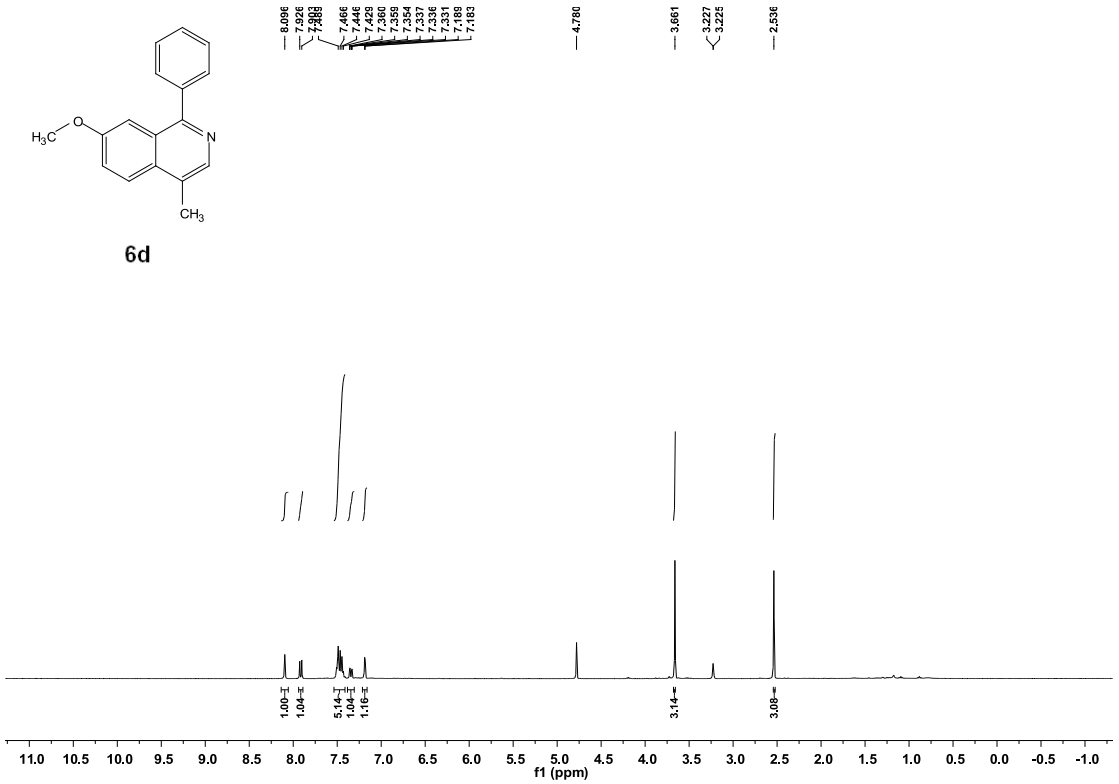
6b


8.106
7.717
7.694
7.396
7.251
7.228
4.779
3.206
3.204
2.467
2.414
N
H3C
CH3
1.00
2.27
5.25
1.14
3.07
3.06
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

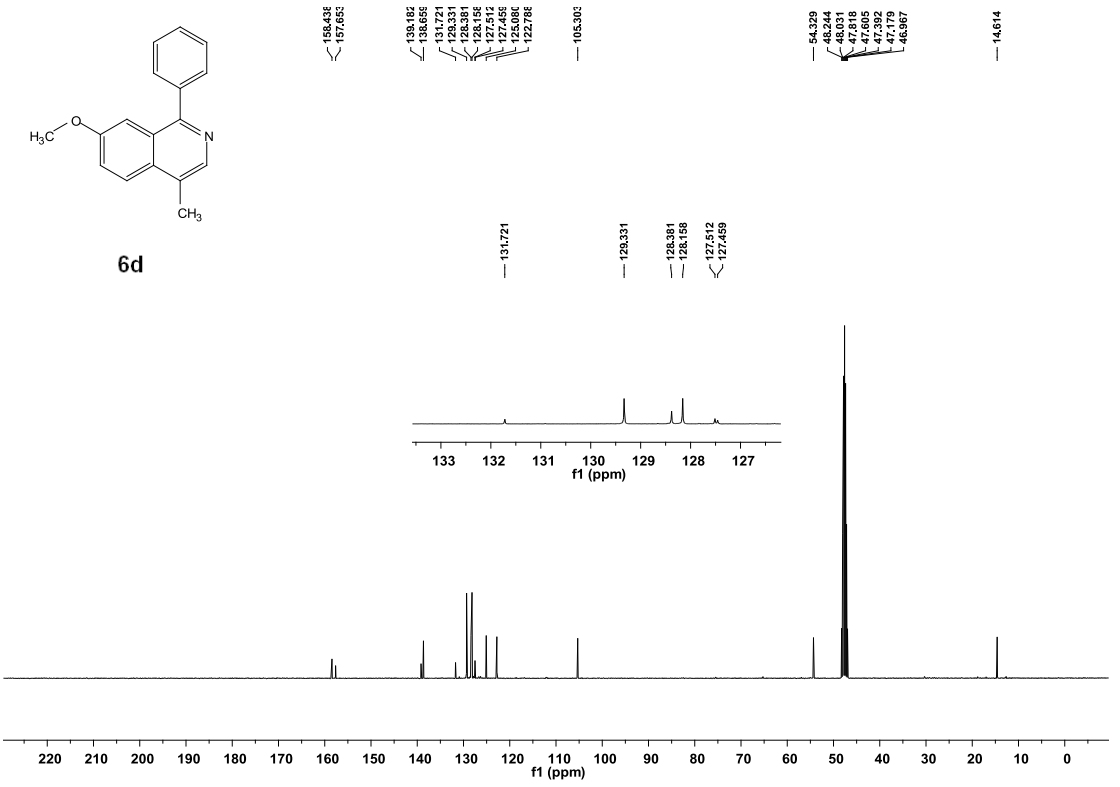
6c


158.796
141.095
140.298
138.977
136.474
128.505
128.132
128.371
128.000
127.524
126.906
124.395
122.277
48.266
48.053
47.840
47.627
47.414
47.201
46.989
20.781
14.697
N
H3C
CH3
129.505
129.132
128.370
128.000
127.524
126.906
130.5 129.5 128.5 127.5 126.5
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

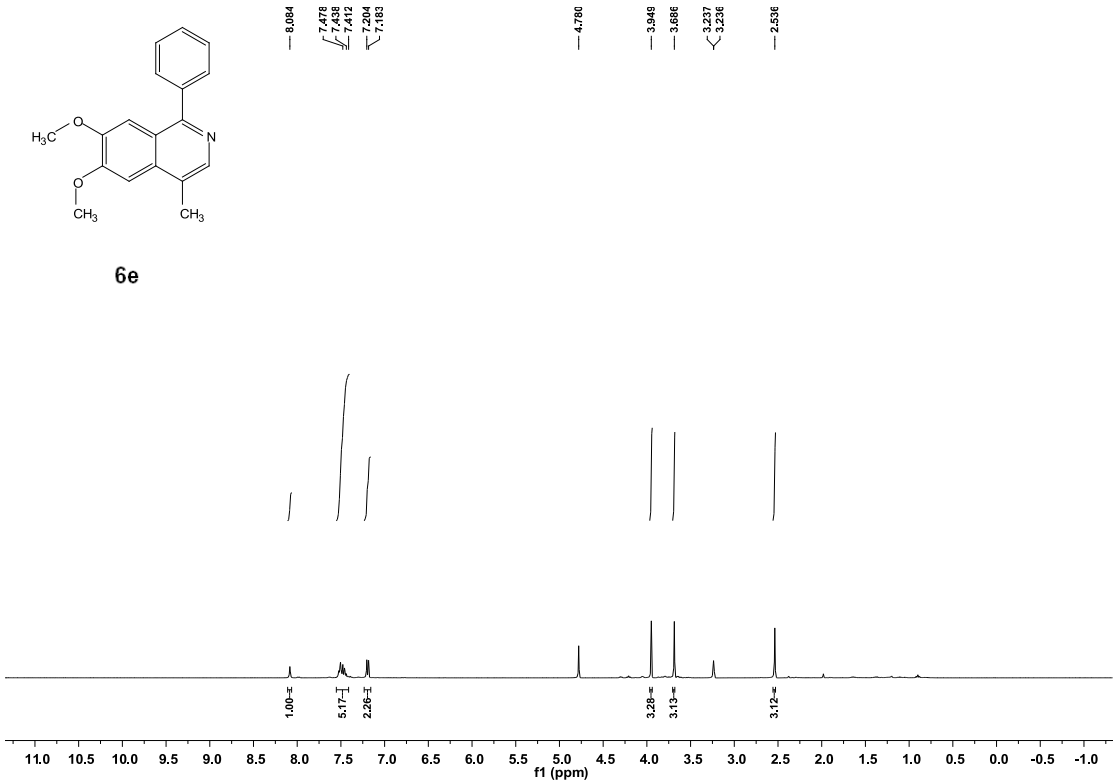
6c


8.096
7.926
7.466
7.446
7.429
7.360
7.358
7.354
7.337
7.336
7.331
7.189
7.183
4.780
3.661
3.227
3.225
2.536
O
H_3C
N
CH_3
1.00
1.04
5.14
1.04
1.16
3.14
3.08
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

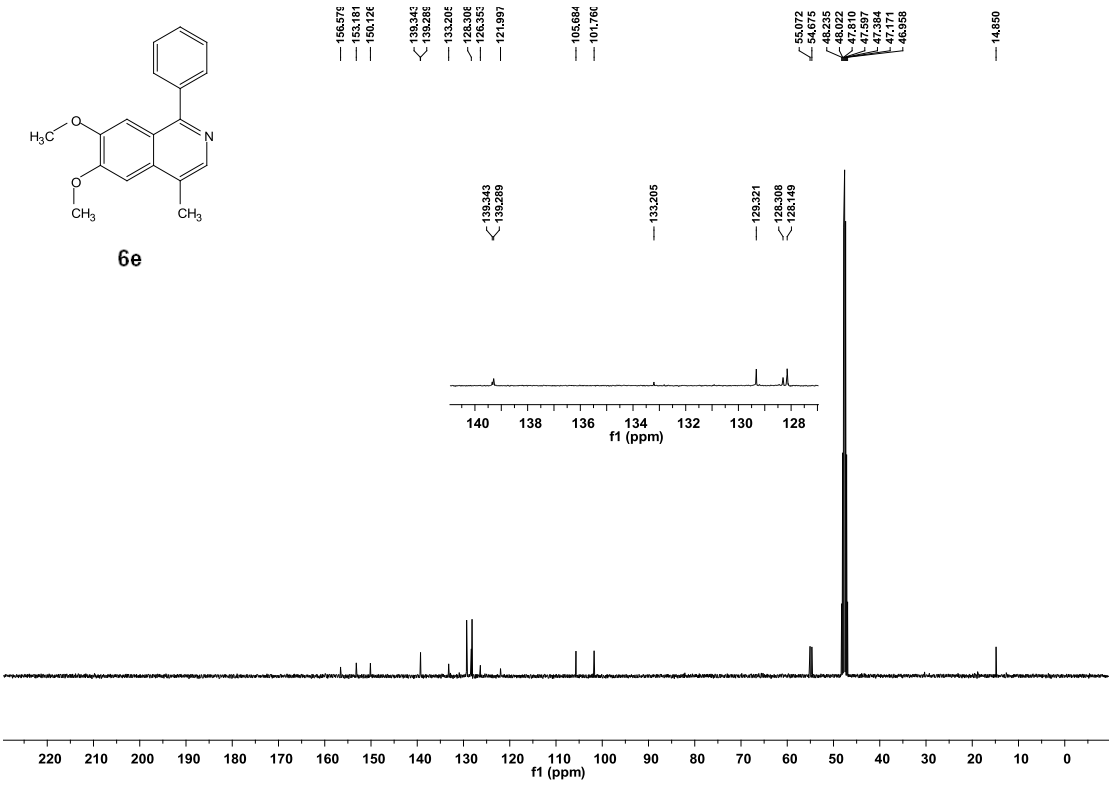
6d


158.438
157.653
139.182
138.659
131.721
129.331
128.381
128.158
127.512
127.459
125.088
122.788
105.303
54.329
48.244
47.831
47.818
47.605
47.392
47.179
46.967
14.614
O
H_3C
N
CH_3
131.721
129.331
128.381
128.158
127.512
127.459
133 132 131 130 129 128 127
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

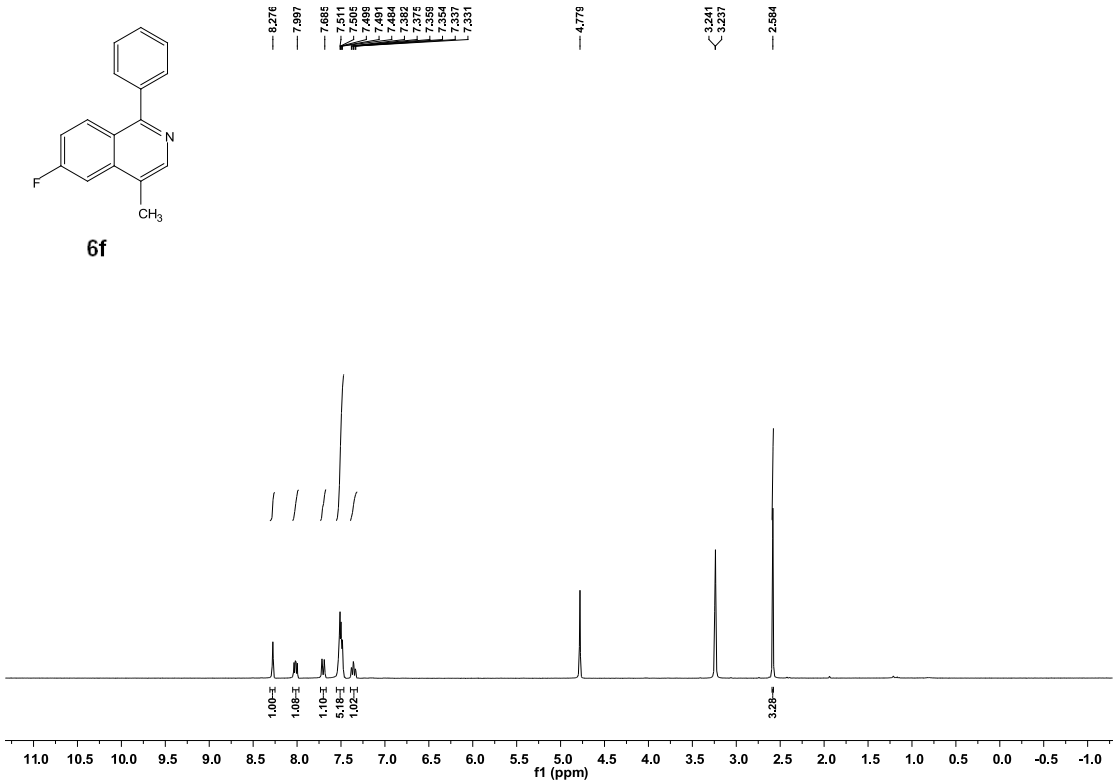
6d


8.084
7.478
7.438
7.412
7.204
7.183
4.780
3.949
3.686
3.237
3.236
2.536
O
H3C
O
CH3
N
CH3
1.00
5.17
2.26
3.28
3.13
3.12
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

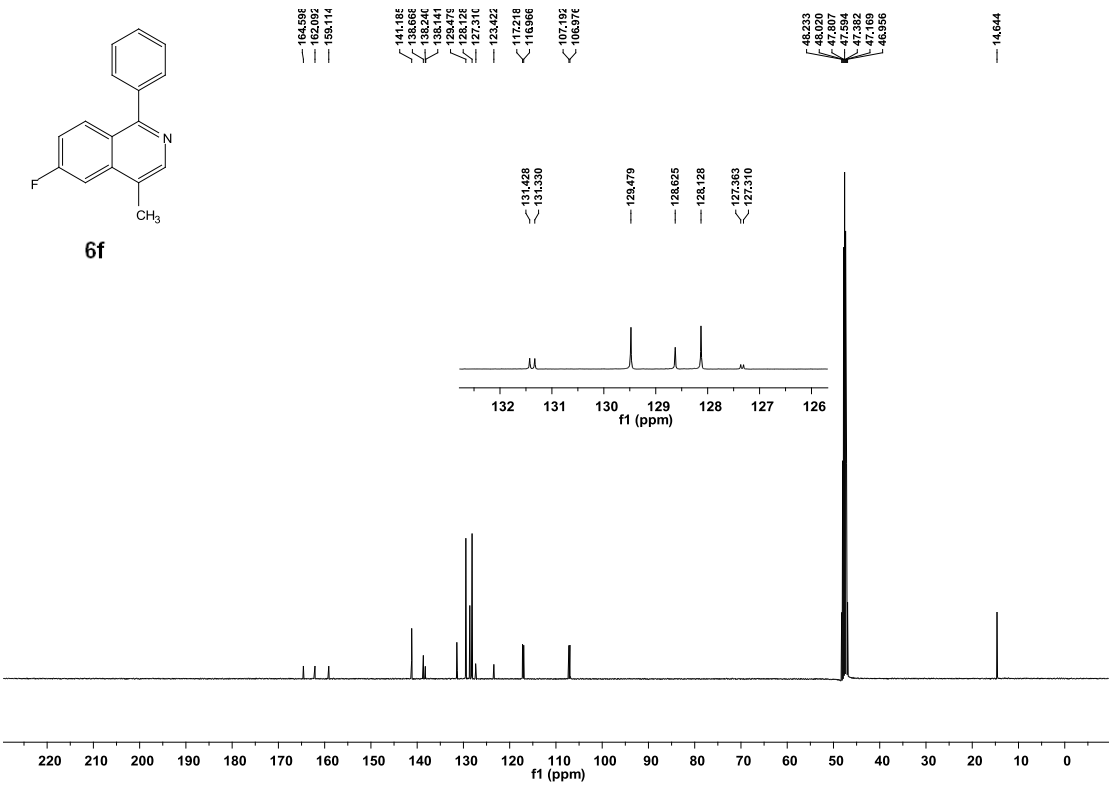
6e


156.575
153.181
150.128
139.343
139.289
133.205
128.308
126.353
121.997
105.684
101.760
55.072
54.675
48.222
47.810
47.597
47.384
47.171
46.958
14.850
O
H3C
O
CH3
N
CH3
139.343
139.289
133.205
129.321
128.308
128.149
140 138 136 134 132 130 128
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

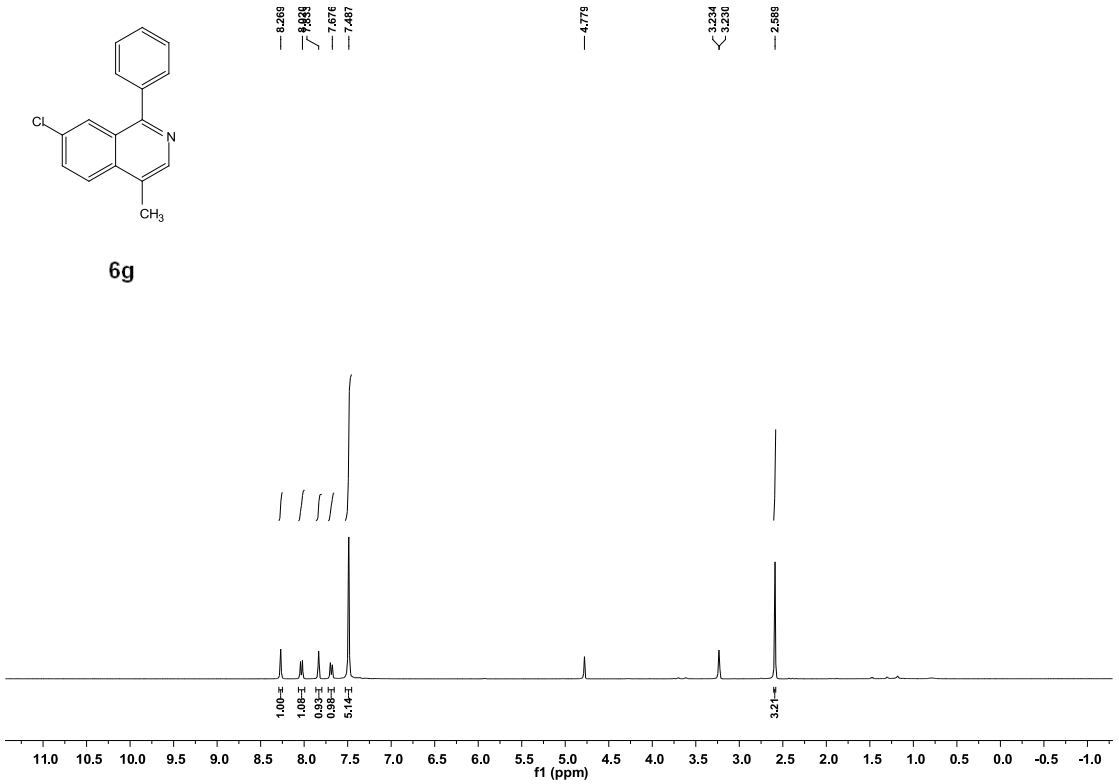
6e


8.276
7.997
7.685
7.511
7.505
7.498
7.491
7.484
7.375
7.359
7.354
7.337
7.331
4.779
3.241
3.237
2.584
N
F
CH3
1.00
1.09
1.10
5.18
1.02
3.28
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

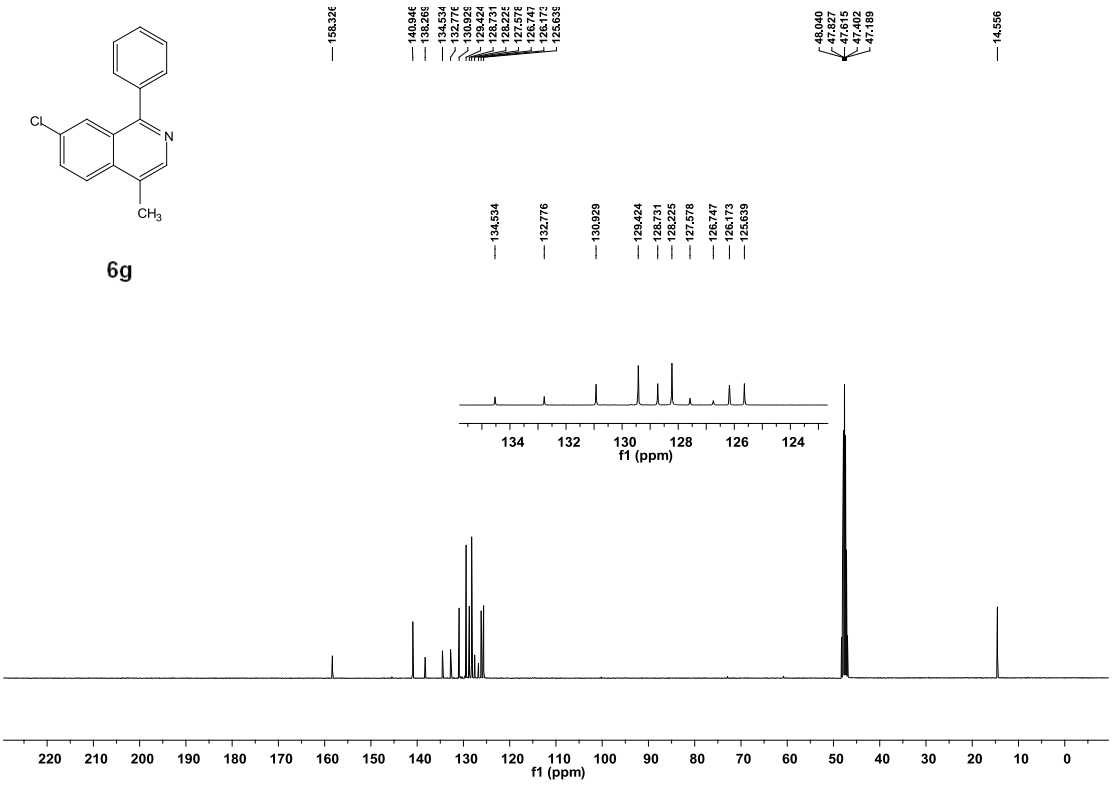
6f


164.598
162.092
159.114
141.185
138.668
138.240
138.141
128.473
128.122
127.310
123.422
117.218
116.966
107.192
106.976
48.233
48.020
47.807
47.594
47.382
47.169
46.956
14.644
131.428
131.330
129.479
128.625
128.128
127.363
127.310
132 131 130 129 128 127 126
f1 (ppm)
N
F
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

6f

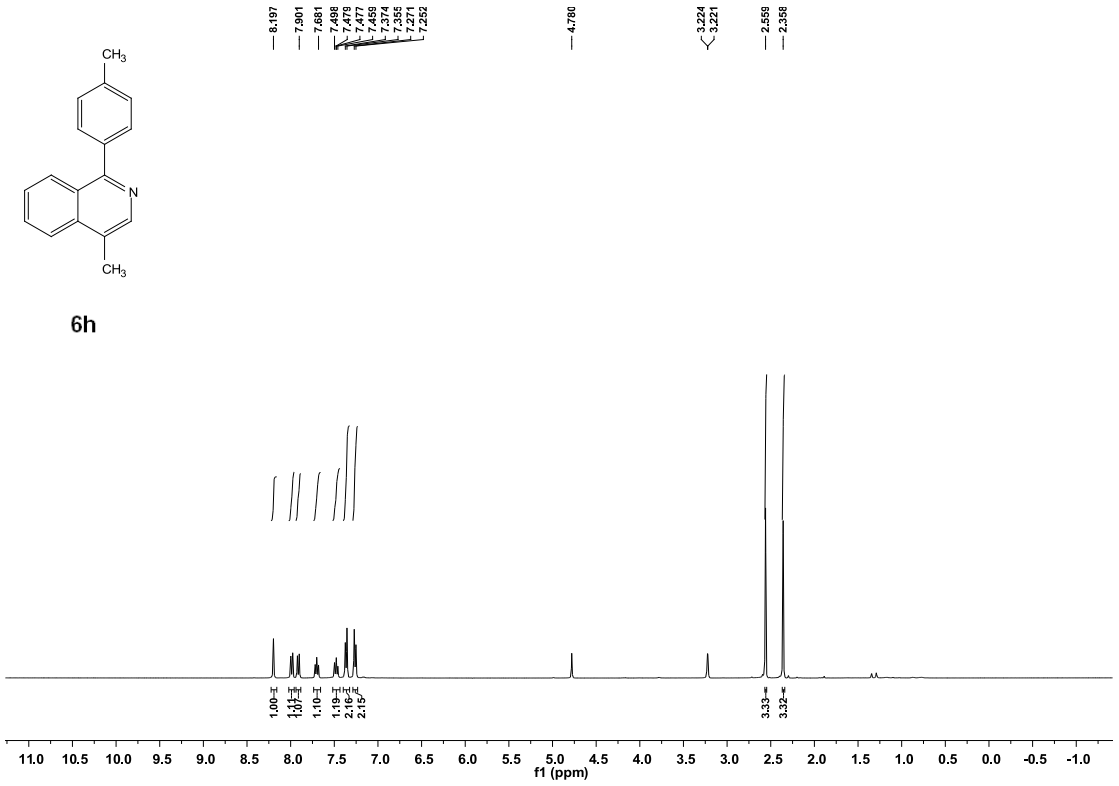

Cl
N
CH3
8.269
7.676
7.487
4.779
3.234
3.230
2.589
1.00
1.08
0.93
0.98
5.14
3.21
f1 (ppm)

6g

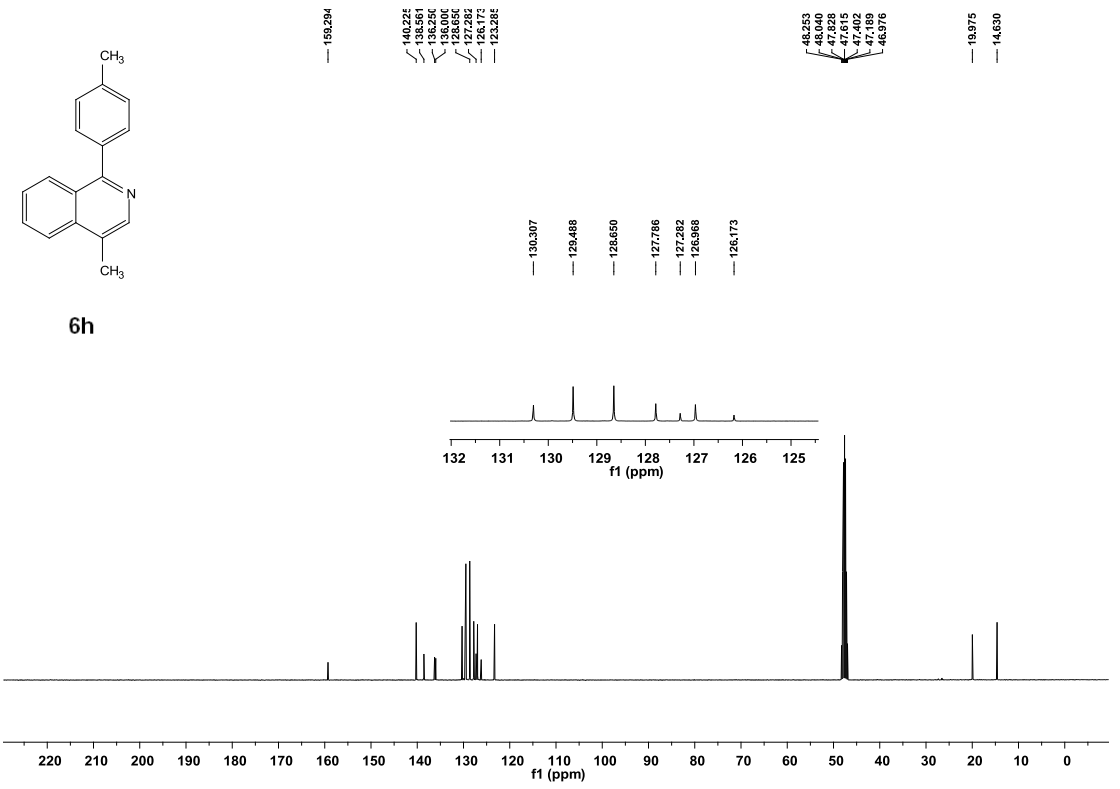

Cl
N
CH3
158.326
140.946
138.268
134.534
132.776
130.929
129.424
128.731
128.225
127.578
126.747
126.173
125.639
48.040
47.827
47.615
47.402
47.189
14.556
f1 (ppm)

6g

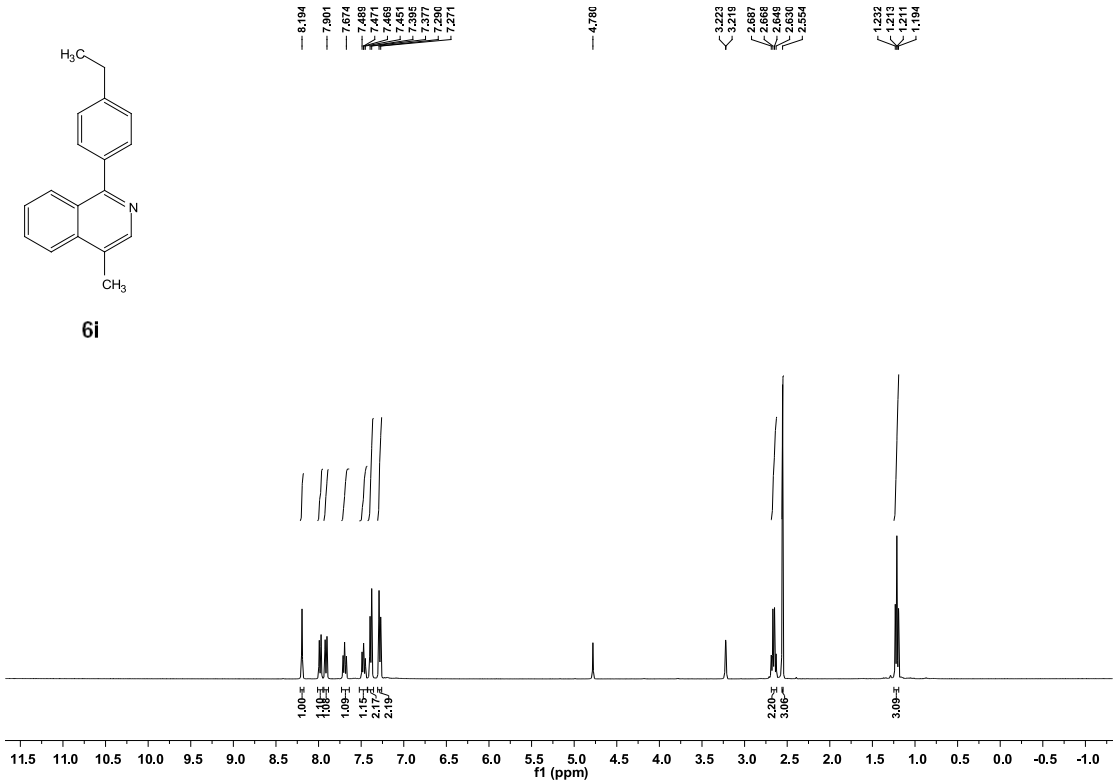
This journal is © The Royal Society of Chemistry 2013



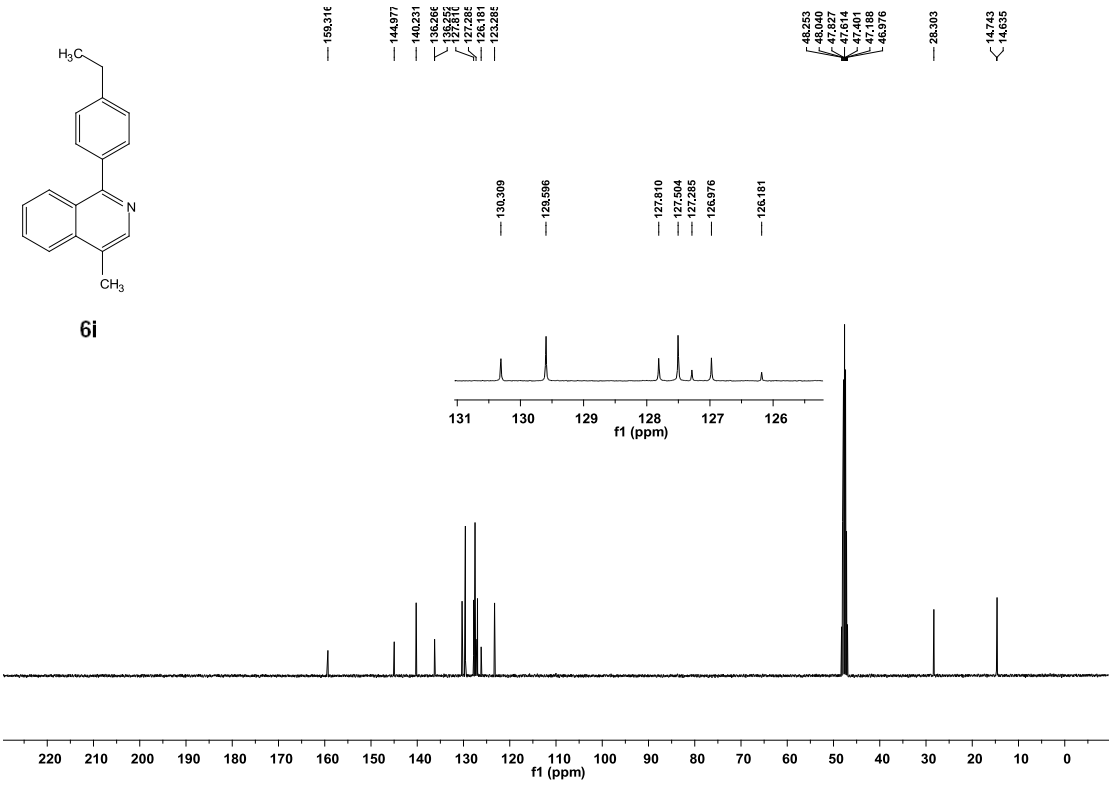
6h



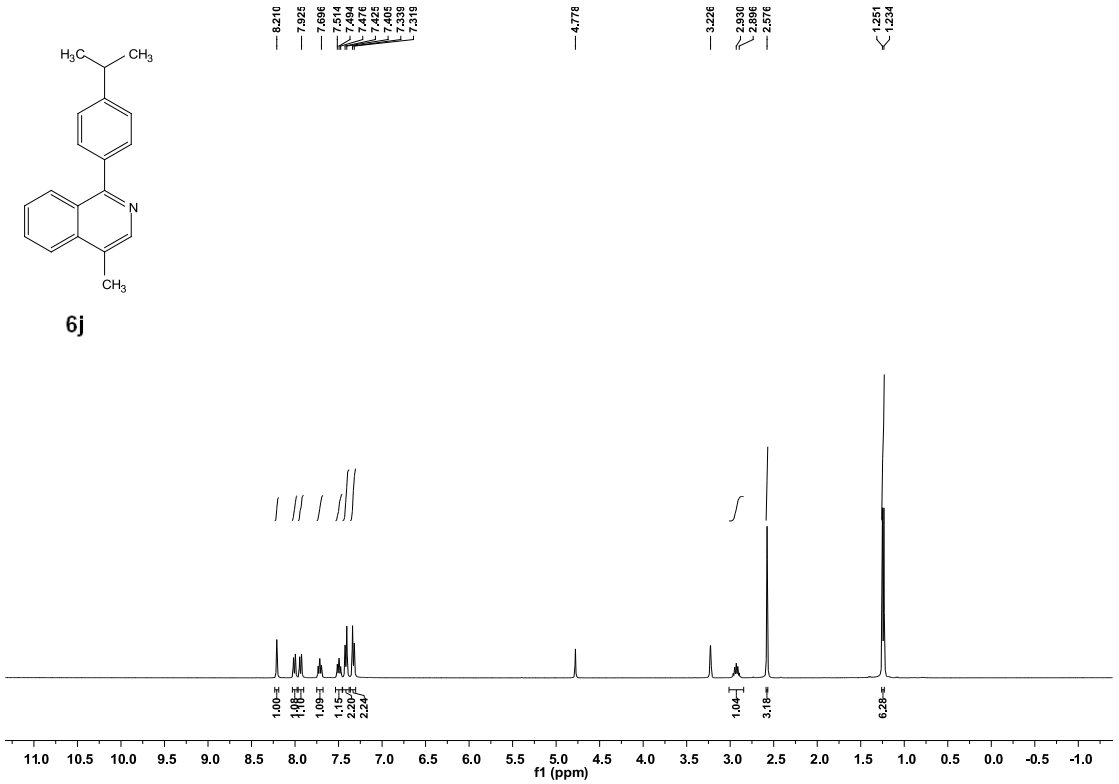
6h


8.194
7.901
7.674
7.489
7.471
7.468
7.451
7.395
7.377
7.290
7.271
4.780
3.223
3.219
2.687
2.668
2.649
2.630
2.554
1.232
1.213
1.211
1.194
H3C
N
CH3
1.00
1.10
1.08
1.09
1.15
2.17
2.19
2.20
3.06
3.09
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

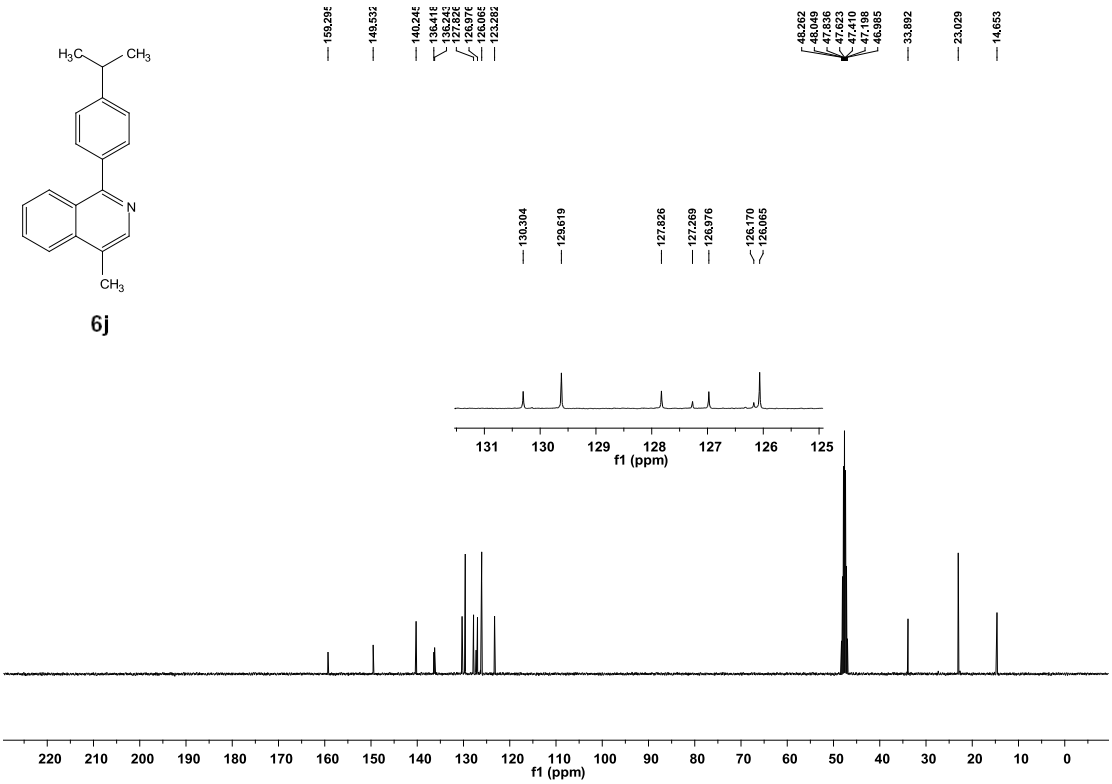
6i


159.316
144.977
140.231
136.266
136.251
127.811
127.285
126.181
123.285
48.253
48.040
47.827
47.614
47.401
47.188
46.976
28.303
14.743
14.635
130.309
129.596
127.810
127.504
127.285
126.976
126.181
H3C
N
CH3
131 130 129 128 127 126
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

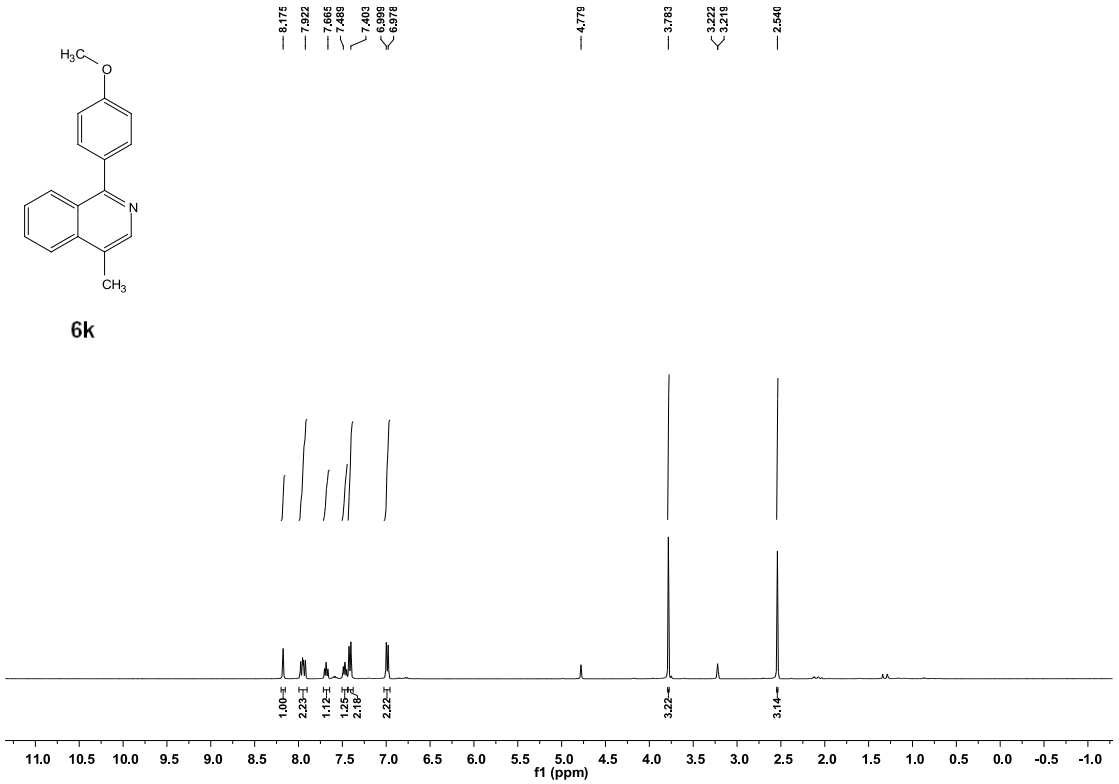
6i


8.210
7.925
7.696
7.514
7.494
7.476
7.425
7.405
7.339
7.319
4.778
3.226
2.930
2.896
2.576
1.251
1.234
1.00
1.08
1.09
1.15
2.20
2.24
1.04
3.18
6.28
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

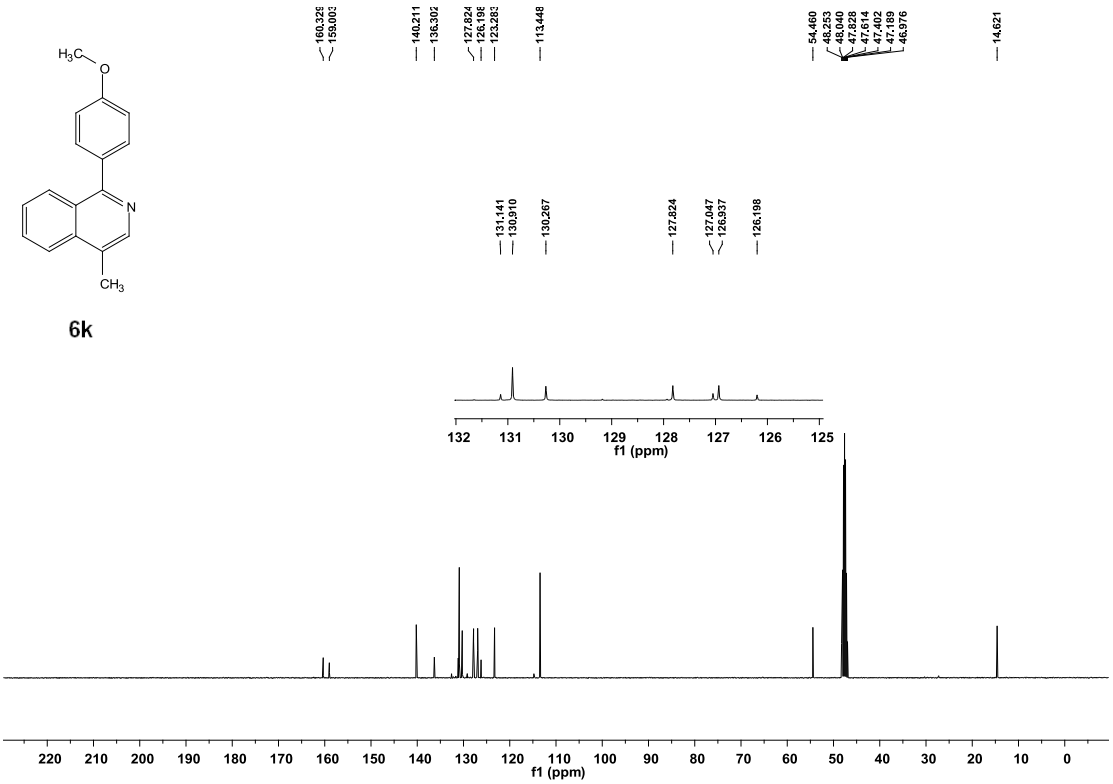
6j


159.295
149.532
140.245
136.418
136.243
127.826
126.976
126.065
123.282
48.262
48.049
47.836
47.623
47.410
47.198
46.985
33.892
23.029
14.653
130.304
128.619
127.826
127.269
126.976
126.170
126.065
131 130 129 128 127 126 125
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

6j

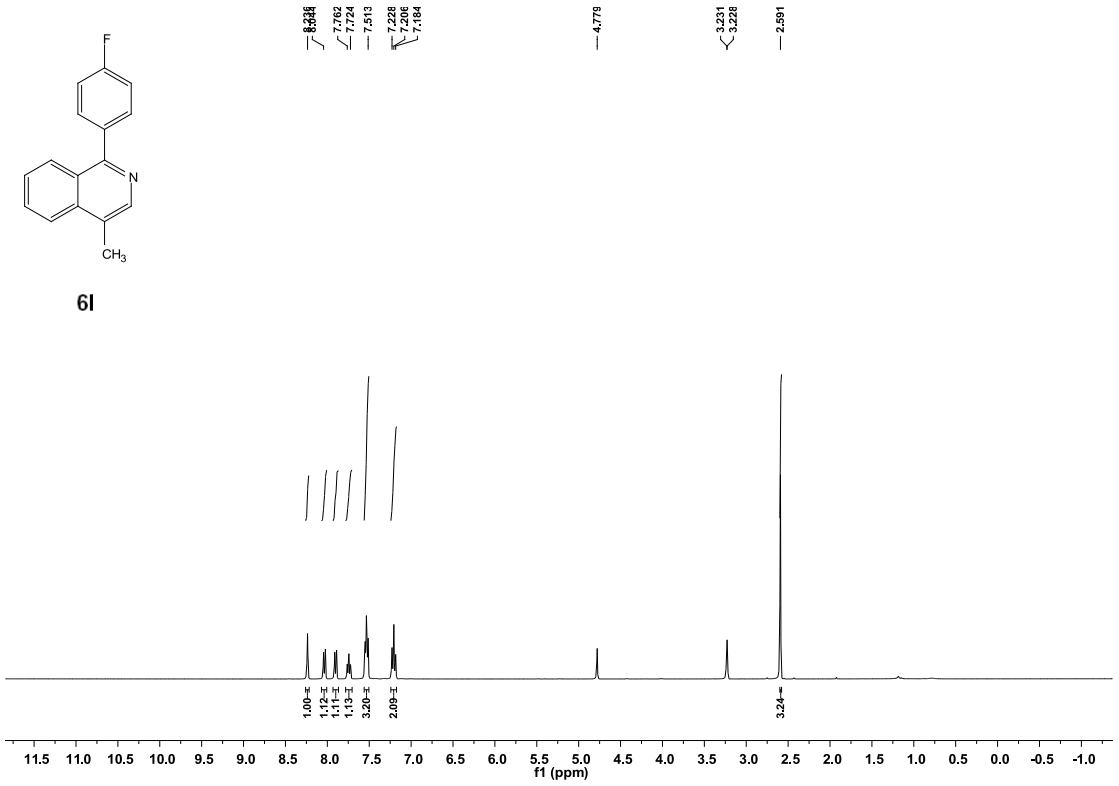

8.175
7.922
7.665
7.489
7.403
6.998
6.978
4.779
3.783
3.222
3.219
2.540
H3C
O
N
CH3
1.00
2.23
1.12
1.25
2.18
2.22
3.22
3.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

6k

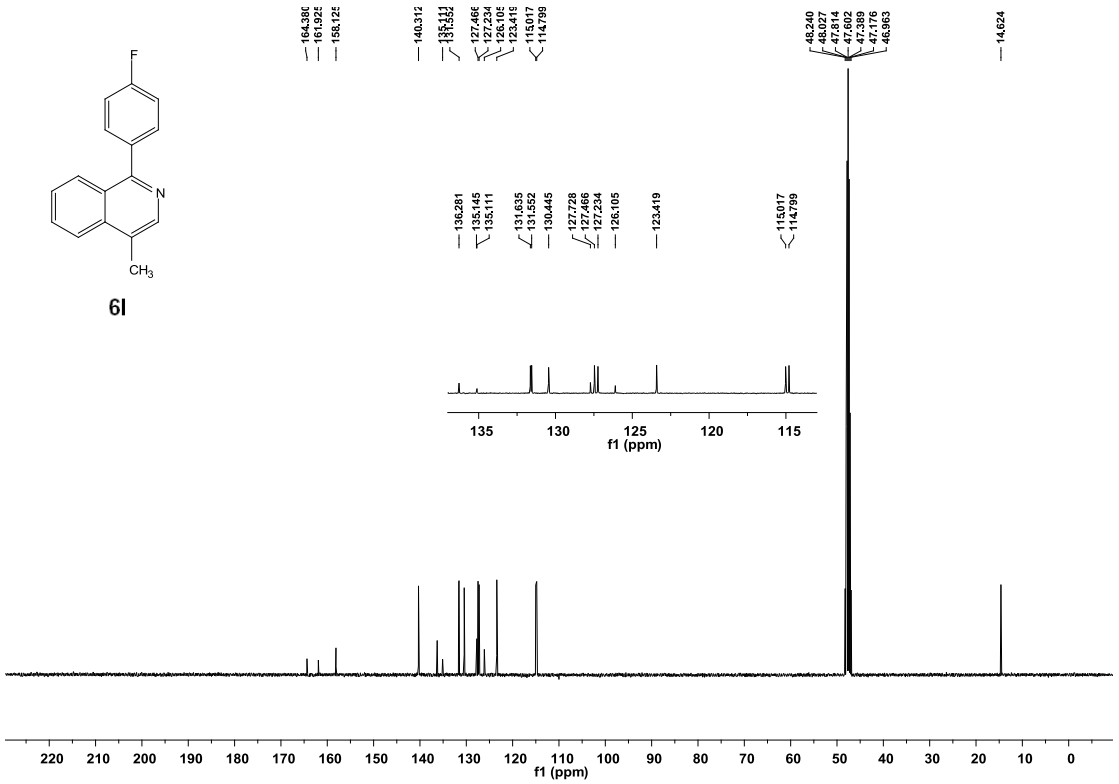

160.325
159.003
140.211
136.302
127.824
126.198
123.283
113.448
54.460
48.253
47.040
47.828
47.614
47.402
47.189
46.976
14.621
131.141
130.910
130.267
127.824
127.047
126.937
126.198
H3C
O
N
CH3
132 131 130 129 128 127 126 125
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

6k

This journal is © The Royal Society of Chemistry 2013

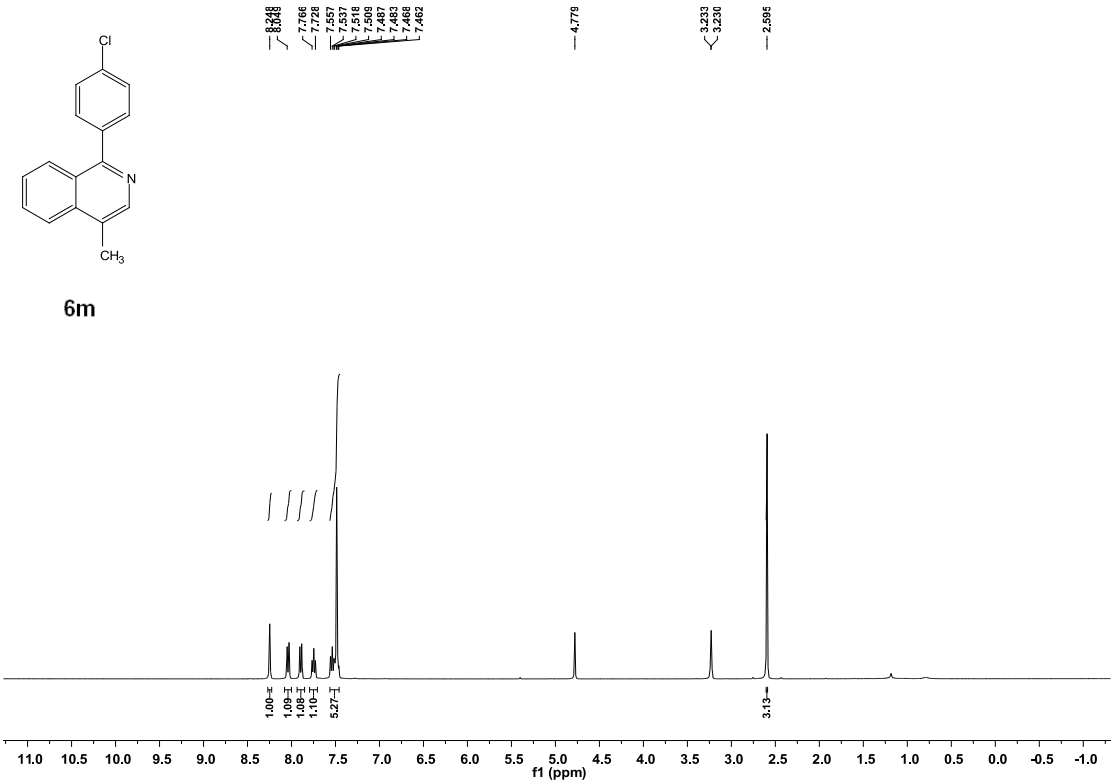


6l

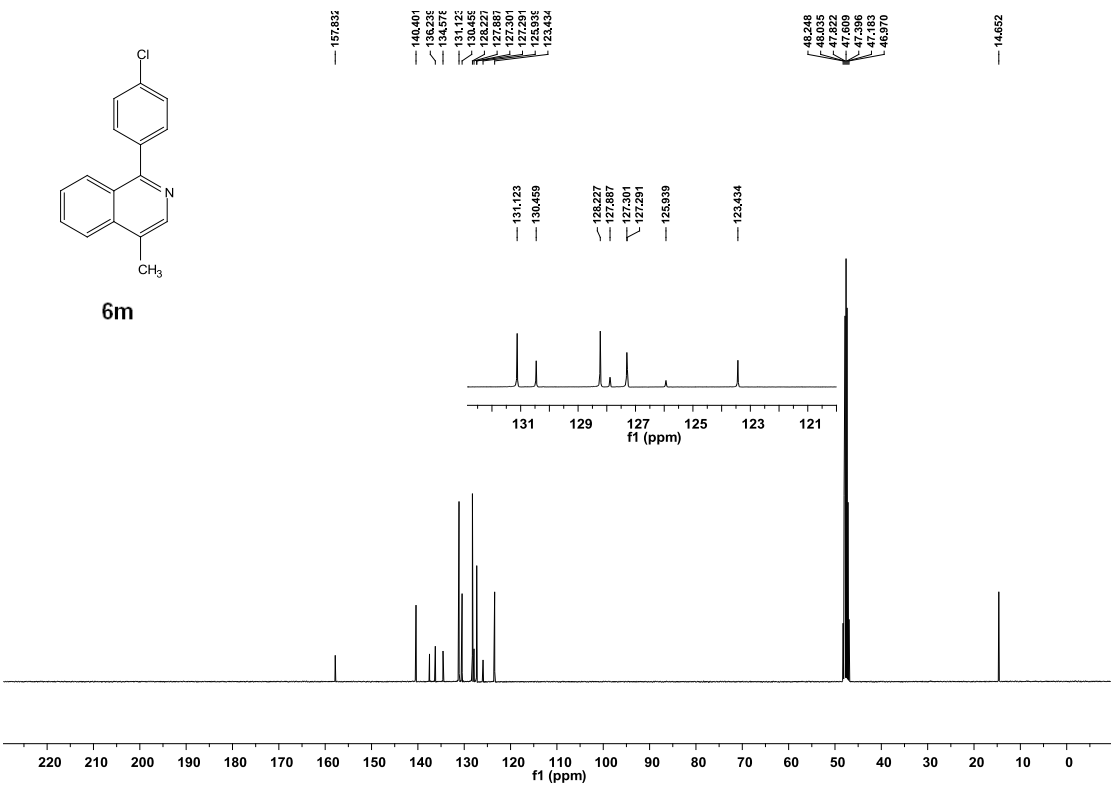


6l

This journal is © The Royal Society of Chemistry 2013

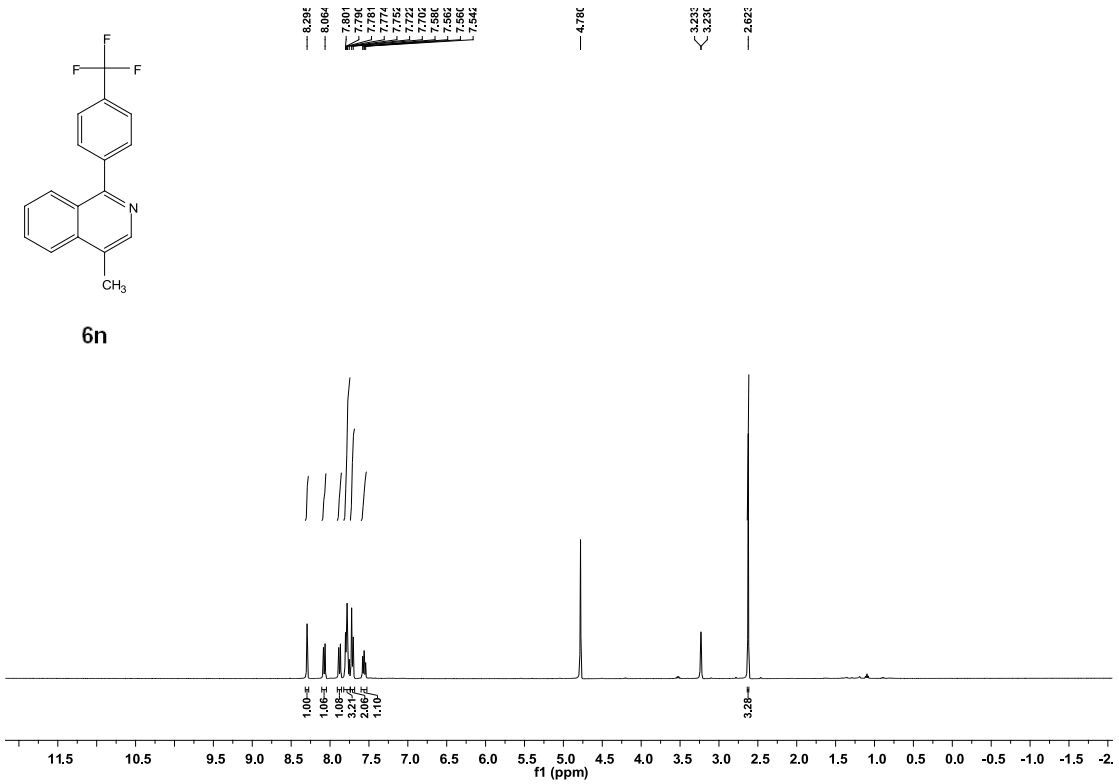


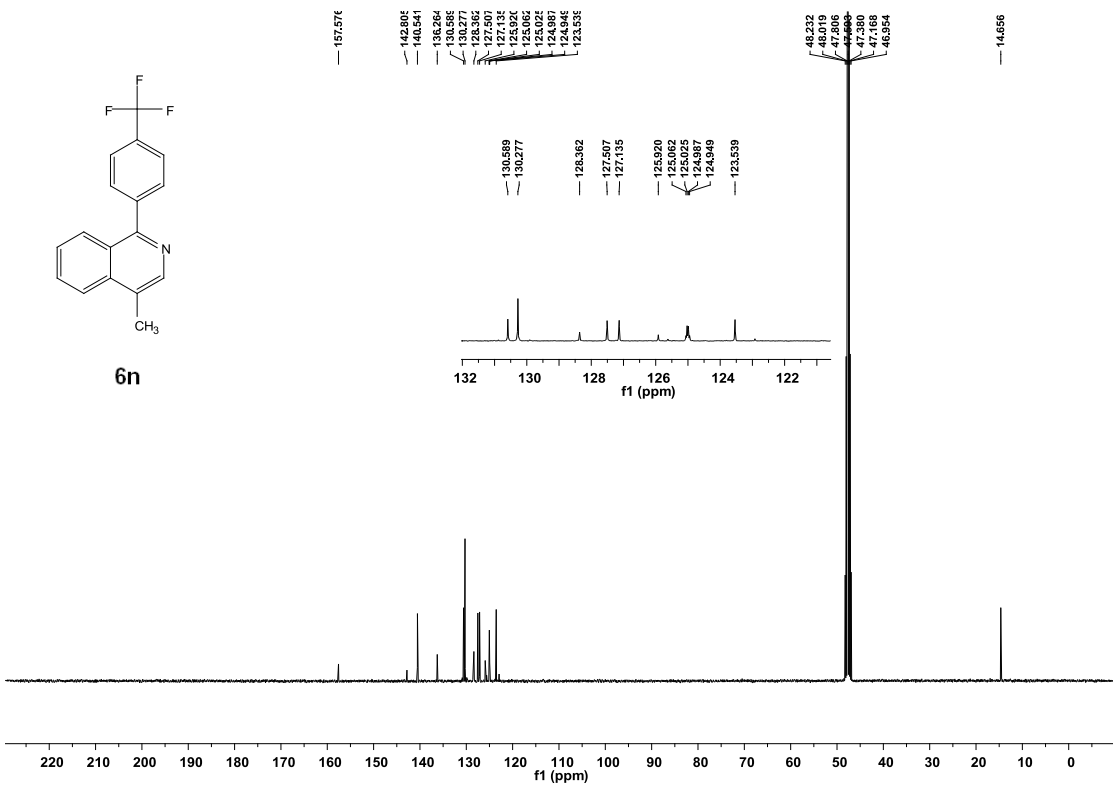
6m

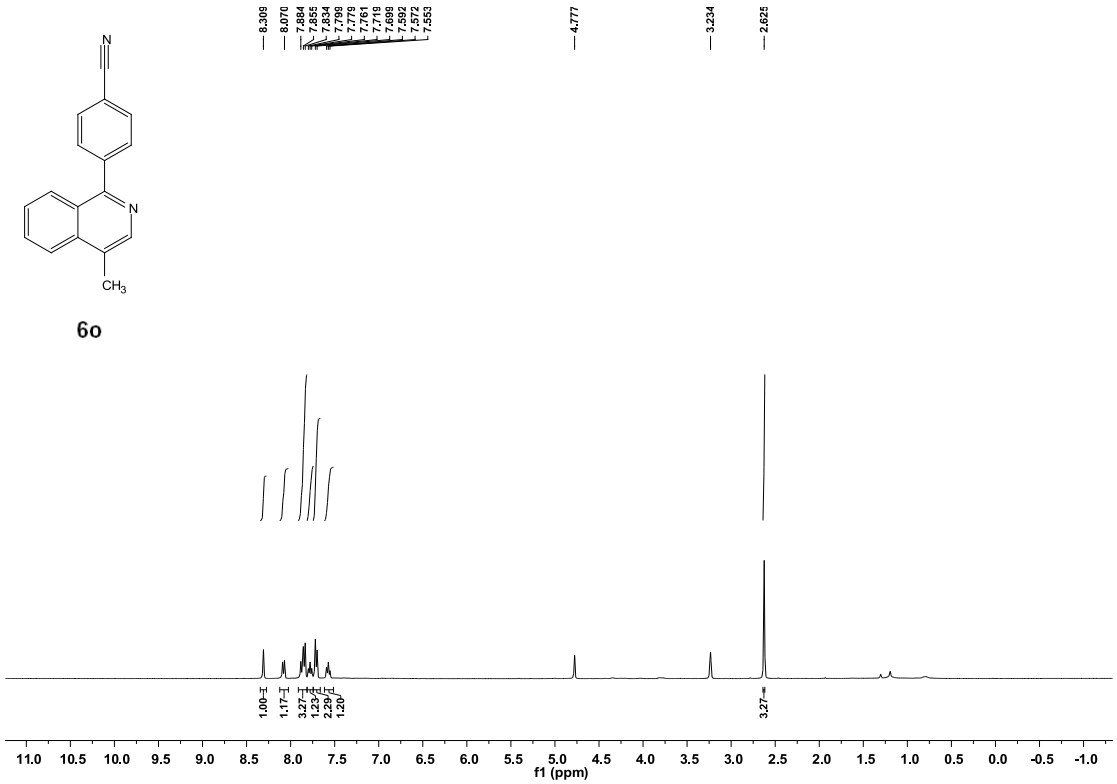


6m

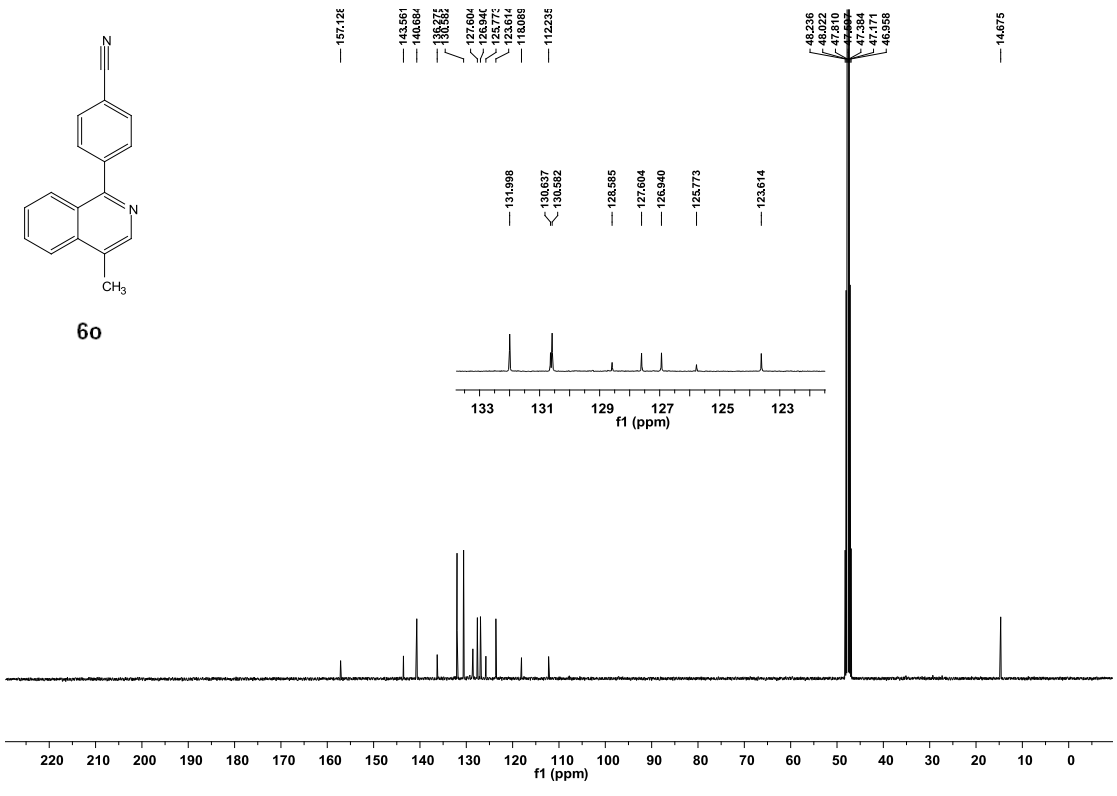
This journal is © The Royal Society of Chemistry 2013





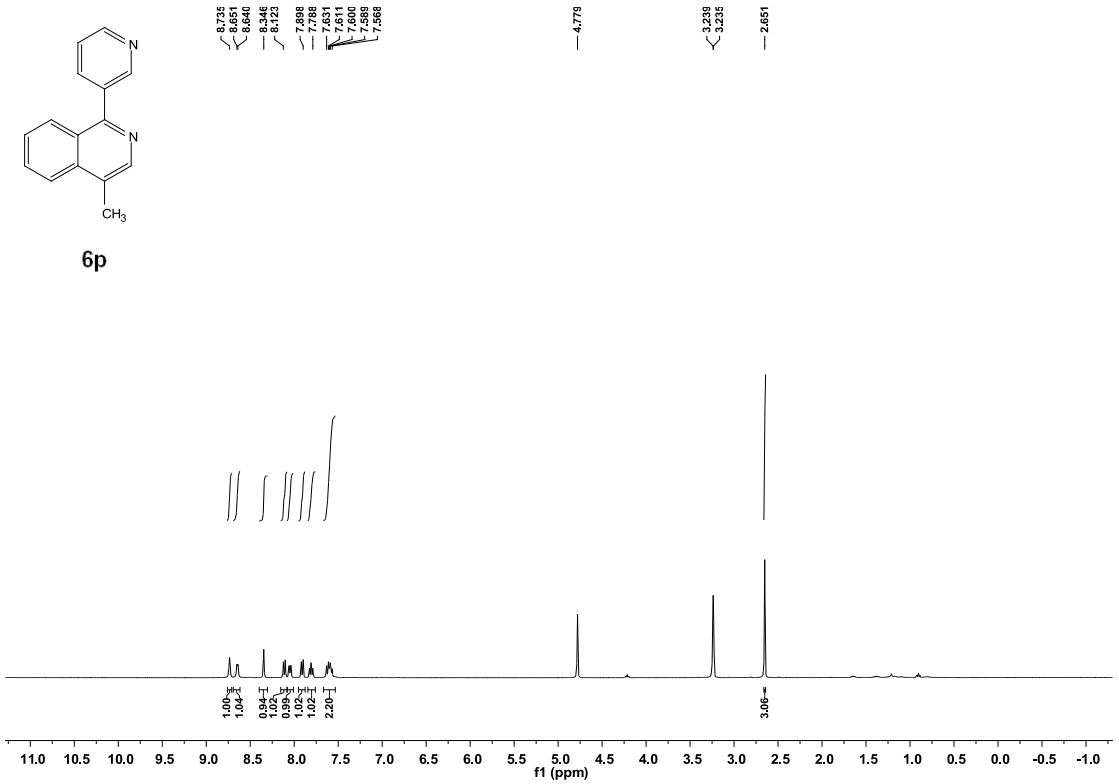

8.309
8.070
7.884
7.855
7.834
7.798
7.779
7.761
7.716
7.698
7.592
7.572
7.553
4.777
3.234
2.625
1.00
1.17
3.27
1.23
2.29
1.20
3.27
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

6o

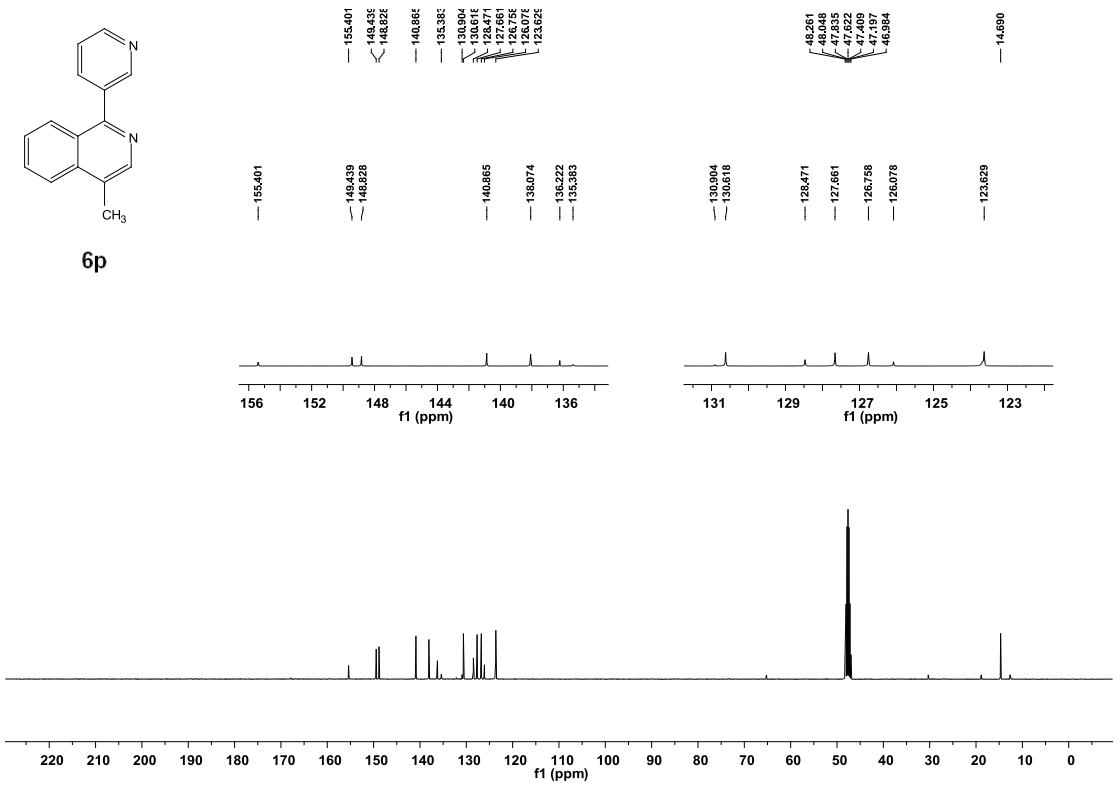

157.128
143.561
140.684
131.998
130.637
130.582
128.585
127.604
126.940
125.773
123.614
118.089
112.235
48.236
48.022
47.810
47.384
47.171
46.958
14.675
133 131 129 127 125 123
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

6o

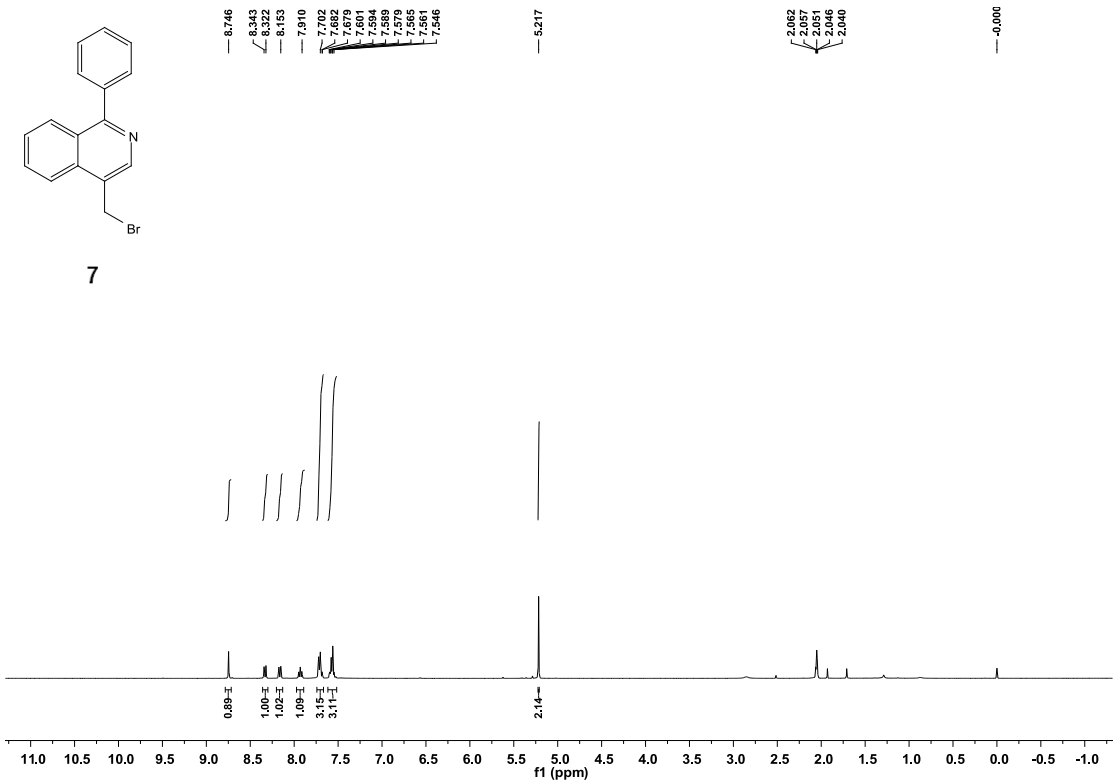
This journal is © The Royal Society of Chemistry 2013



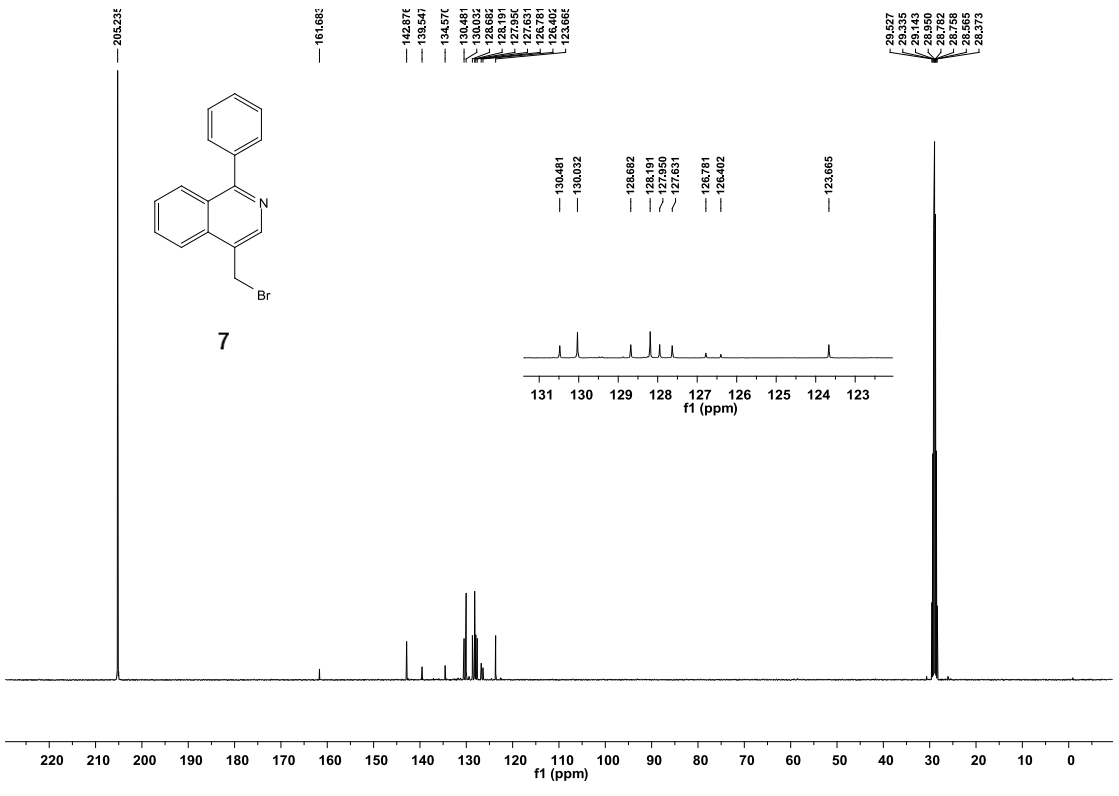
6p



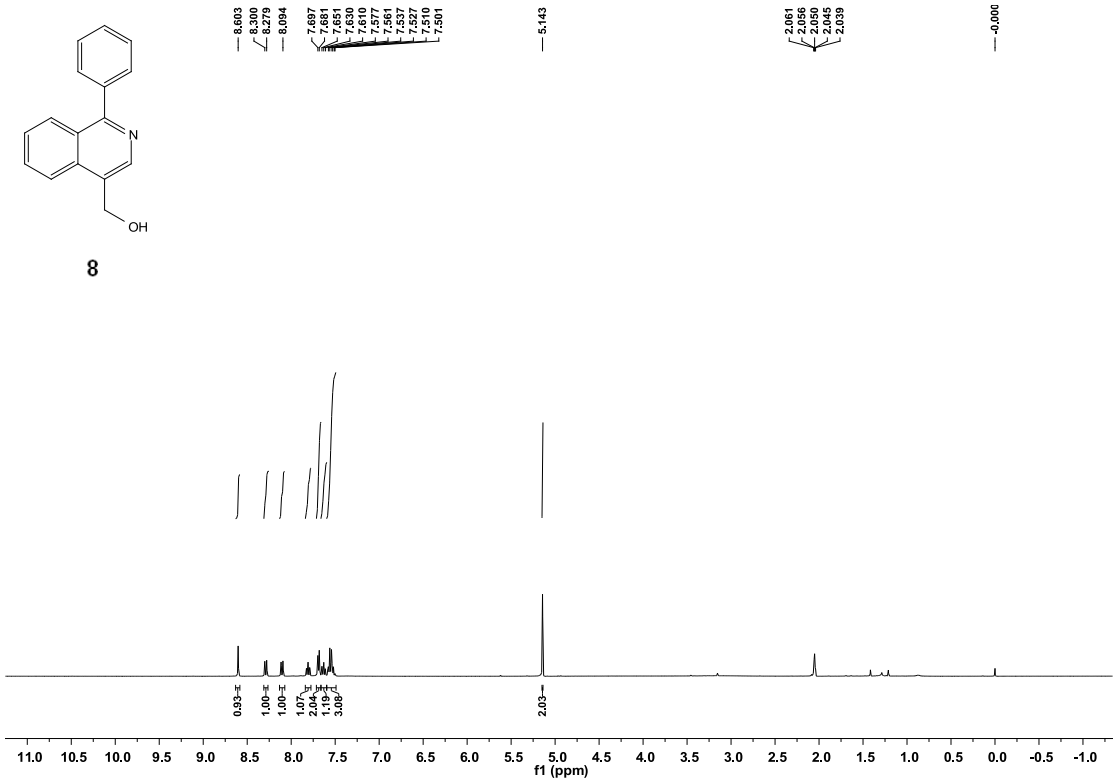
6p

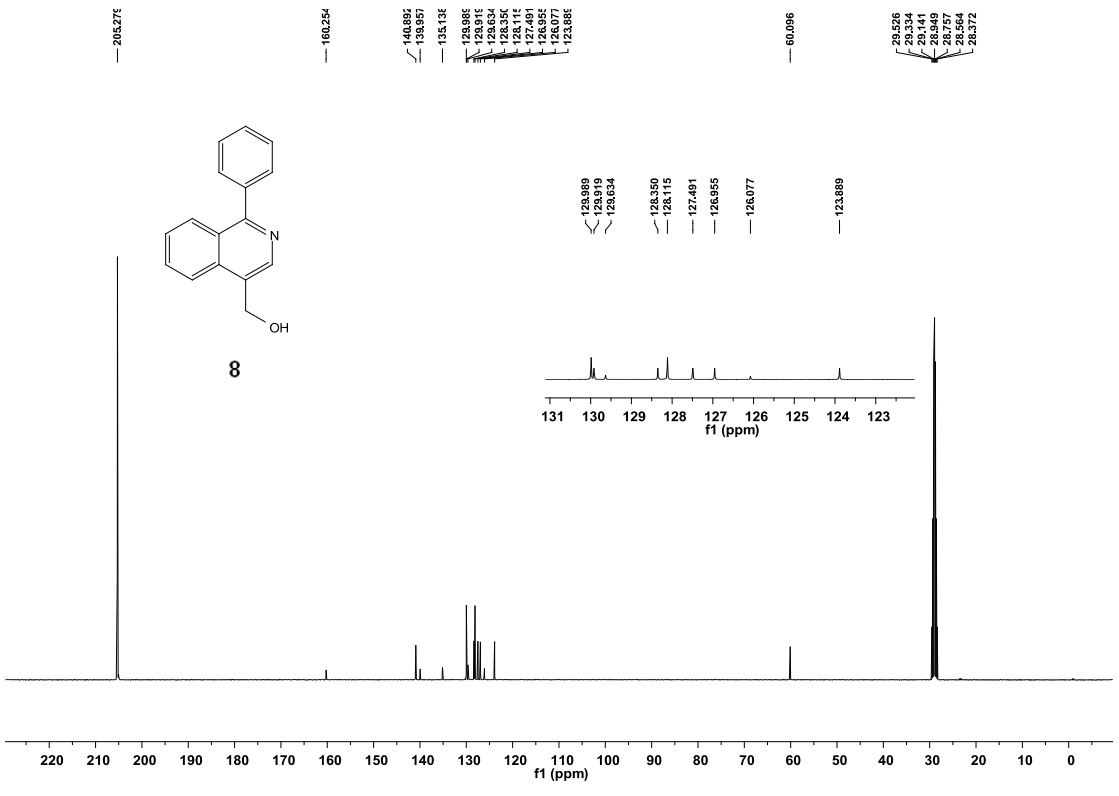

8.746
8.343
8.322
8.153
7.910
7.702
7.693
7.679
7.601
7.594
7.589
7.579
7.565
7.561
7.546
5.217
2.062
2.057
2.051
2.046
2.040
-0.000
N
Br
0.89
1.00
1.02
1.09
3.15
3.11
2.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

7

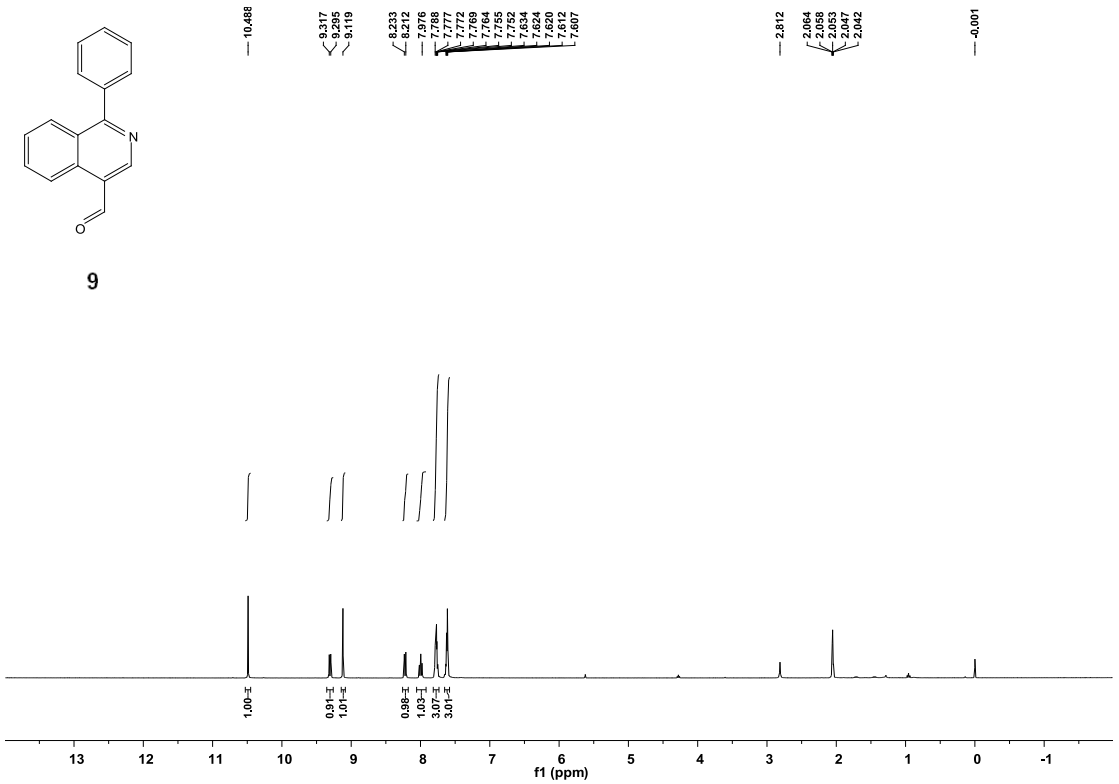

205.23
161.68
142.87
139.54
134.57
130.48
130.03
128.68
128.19
127.95
127.63
126.78
126.40
123.66
29.527
29.335
29.143
28.950
28.782
28.758
28.565
28.373
N
Br
130.481
130.032
128.682
128.191
127.950
127.631
126.781
126.402
123.665
131 130 129 128 127 126 125 124 123
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

7

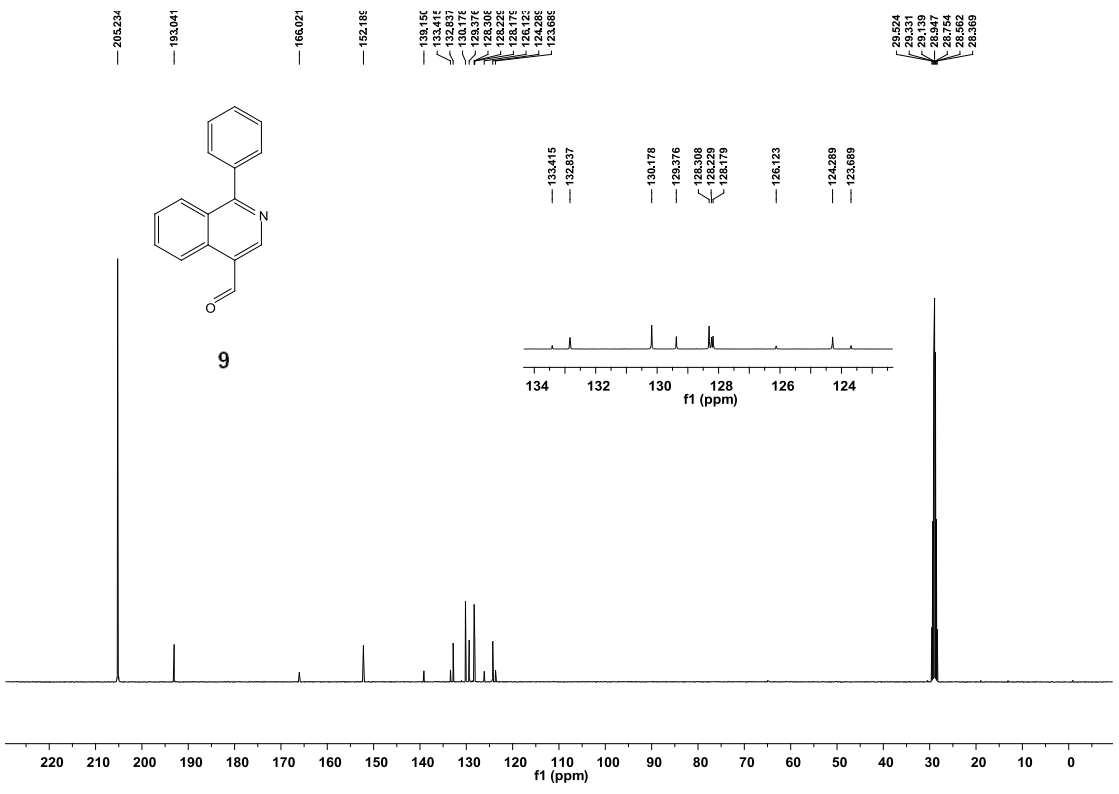

8.603
8.300
8.279
8.094
7.697
7.681
7.651
7.630
7.610
7.577
7.561
7.537
7.527
7.510
7.501
5.143
2.061
2.056
2.050
2.045
2.039
-0.000
N
OH
8
0.93
1.00
1.00
1.07
2.04
1.19
3.08
2.03
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


205.275
160.254
140.895
139.957
135.138
129.989
129.919
129.634
128.350
128.115
127.491
126.955
126.077
123.889
60.096
29.526
29.334
29.141
28.949
28.757
28.564
28.372
N
OH
8
131 130 129 128 127 126 125 124 123
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

This journal is © The Royal Society of Chemistry 2013



9



9