Electronic Supplementary Material (ESI) for Green Chemistry
This journal is © The Royal Society of Chemistry 2011

Graphene Oxide and Rose Bengal: Oxidative C-H Functionalization of Tertiary Amines using Visible Light

*Yuanhang Pan, Shuai Wang, Choon Wee Kee, Emilie Dubuisson, Yuanyong Yang, Kian Ping Loh, and Choon-Hong Tan**

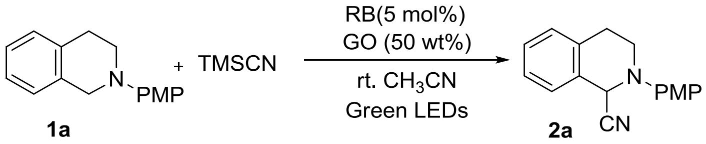
Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore, 117543.
chmtanch@nus.edu.sg

Supporting Information

General procedures and methods

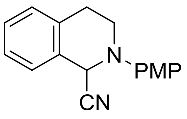
^{1}H and ^{13}C NMR spectra were recorded on a Bruker ACF300 (300MHz), Bruker DPX300 (300MHz) DRX500 (500MHz) or AMX500 (500MHz) spectrometer. Chemical shifts are reported in parts per million (ppm). The residual solvent peak was used as an internal reference. Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode and a Finnigan/MAT 95XL-T mass spectrometer in FAB mode. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. UV-Vis spectroscopic data was collected using the UV-2450 Shimadzu UV-Vis Spectrometer with water as the solvent and a path length of 1 cm. Analytical thin layer chromatography (TLC) was performed with Merck pre-coated TLC plates, silica gel 60F-254, layer thickness 0.25 mm. Flash chromatography separations were performed on Merck 60 (0.040 - 0.063mm) mesh silica gel. Reagents and solvents were commercial grade and were used as supplied without further purification, unless otherwise stated. Graphene Oxide (GO) was prepared according to the reported method.[1] Characterization of GO was reported in ref 1. Irradiation with green light was performed using 0.5-5W LEDs. LEDs were bought from LED POWER SUPPLY, CE-IKEA, TYPE: SLT5-12V.

Representative procedure for α-Cyanation between *N*-aryl-tetrahydroisoquinoline 1a and TMSCN catalyzed by the combination of Rose Bengal and GO



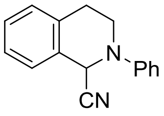
1a (23.9 mg, 0.1 mmol, 1.0 equiv.) and GO (12.0 mg, 50 wt%) were added to a solution of RB (5.0 mg, 0.005 mmol, 5 mol%) in 1.0 ml CH_3CN followed by adding TMSCN (31.3 ul, 0.25 mmol, 2.5 equiv.) slowly. The reaction mixture was stirred under green LEDs irradiation at room temperature. After 30 hours, the solvent was removed in vacuo and the crude product was directly loaded onto a short silica gel column. Flash chromatography was performed using gradient elution with hexane/EA mixtures (40/1 - 10/1 ratio). After removing solvent, product **2a** (25.5 mg) was obtained as pale yellow solid in 97% yield.

2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2a) [2]



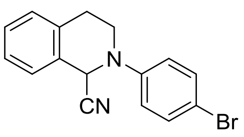
pale yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.34 – 7.15 (m, 4H), 7.06 (d, *J* = 8.9 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.33 (s, 1H), 3.77 (d, *J* = 0.5 Hz, 3H), 3.61 – 3.49 (m, 1H), 3.48 – 3.31 (m, 1H), 3.24 – 3.06 (m, 1H), 2.91 (d, *J* = 16.4 Hz, 1H). LRMS (ESI) m/z 265.1 (M + H$^+$).

2-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2b) [2]



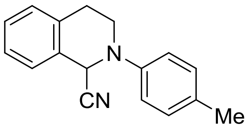
white solid, ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.45 – 7.24 (m, 5H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.05 (t, *J* = 7.3 Hz, 1H), 5.54 (s, 1H), 3.90 – 3.75 (m, 1H), 3.62 – 3.45 (m, 1H), 3.29 – 3.12 (m, 1H), 3.10 – 2.93 (m, 1H). LRMS (ESI) m/z 235.1 (M + H$^+$)

2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2c) [3]



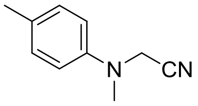
yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.55 – 7.42 (m, 2H), 7.40 – 7.21 (m, 4H), 7.03 – 6.89 (m, 2H), 5.46 (s, 1H), 3.80 – 3.66 (m, 1H), 3.56 – 3.41 (m, 1H), 3.23 – 3.10 (m, 1H), 3.07 – 2.92 (m, 1H). LRMS (ESI) m/z 313.0 (M + H$^+$)

2-*p*-tolyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2d) [3]



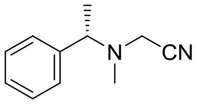
white solid, ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.38 – 7.21 (m, 5H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 5.46 (s, 1H), 3.80 – 3.65 (m, 1H), 3.53 – 3.39 (m, 1H), 3.25 – 3.11 (m, 1H), 3.06 – 2.89 (m, 1H), 2.32 (s, 3H). LRMS (ESI) m/z 249.1 (M + H$^+$)

2-(methyl(*p*-tolyl)amino)acetonitrile (2e)[2]



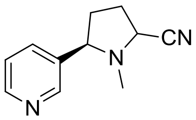
yellow oil, ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.14 (s, 2H), 2.97 (s, 3H), 2.29 (s, 3H). LRMS (ESI) m/z 169.0 ($M + H^+$)

(*S*)-2-(methyl(1-phenylethyl)amino)acetonitrile (2g) [4]



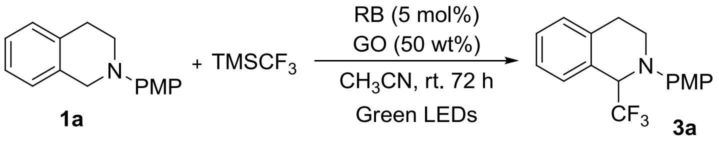
pale yellow oil, con. = 0.05M, O_2 balloon was required, $[\alpha]^{29}_{D}$ = -133.6 (*c* 0.75, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 7.33 – 7.26 (m, 5H), 3.51 (q, *J* = 6.6 Hz, 1H), 3.46 (dd, *J* = 81.0, 17.2 Hz, 2H), 2.40 (s, 3H), 1.39 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 143.7, 129.0, 127.9, 127.4, 115.2, 63.1, 44.0, 40.6, 21.6. LRMS (EI) m/z 174.1 (M^+), HRMS (EI) m/z 174.1158 (M^+), calc. for $C_{11}H_{11}N_2$ 174.1157

5’-cyanonicotine (2h)



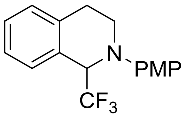
pale yellow oil, con. = 0.05M, O_2 balloon was required, dr = 3:2. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) mixture of the two diastereoisomers: δ 8.65 – 8.45 (m, 2H), 7.75 (d, *J* = 7.9 Hz, 0.3H, minor isomer), 7.65 (d, *J* = 7.8 Hz, 0.6H, major isomer), 7.34 – 7.26 (m, 1H), 4.15 (d, *J* = 7.4 Hz, 0.5H), 3.58 (t, *J* = 8.1 Hz, 0.7H), 3.42 – 3.36 (m, 0.7H), 2.52 – 2.41 (m, 0.8H), 2.41 – 2.32 (m, 0.8H), 2.32 (s, 1H), 2.29 (s, 2H), 2.28 – 2.21 (m, 0.6H), 2.21 – 2.14 (m, 0.8H), 1.90 – 1.74 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) mixture of the two diastereoisomers: δ major isomer: 149.5, 149.3, 137.7, 135.1, 123.9, 117.6, 65.3, 56.9, 36.7, 33.4, 28.6; minor isomer: 149.4, 149.3, 137.2, 134.9, 124.1, 120.2, 68.2, 56.0, 39.1, 34.4, 28.8. LRMS (ESI) m/z 188.1 ($M + H^+$), HRMS (ESI) m/z 188.1182 ($M + H^+$), calc. for $C_{11}H_{14}N_3$ 188.1182

Procedure for α-Trifluoromethylation between *N*-aryl-tetrahydroisoquinoline 1a and TMSCF$_3$ catalyzed by the combination of Rose Bengal and GO



1a (23.9 mg, 0.1 mmol, 1.0 equiv.) and GO (12.0 mg, 50 wt%) were added to a solution of RB (5.0 mg, 0.005 mmol, 5 mol%) in 1.0 ml CH$_3$CN followed by adding TMSCF$_3$ (73.4 ul, 0.5 mmol, 5.0 equiv.) slowly. The reaction mixture was stirred under green LEDs irradiation at room temperature. After 72 hours, the solvent was removed in vacuo and the crude product was directly loaded onto a short silica gel column. Flash chromatography was performed using gradient elution with hexane/EA mixtures (40/1 - 20/1 ratio). After removing solvent, product **3a** (23.1 mg) was obtained as yellow oil in 75% yield.

2-(4-methoxyphenyl)-1-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinoline (3a)



yellow oil, ^{1}H NMR (500 MHz, CDCl$_3$, ppm) δ 7.42 – 7.28 (m, 2H), 7.27 – 7.18 (m, 2H), 6.94 (d, *J* = 9.1 Hz, 2H), 6.91 – 6.80 (m, 2H), 5.02 (q, *J* = 7.9 Hz, 1H), 3.77 (s, 3H), 3.74 (dd, *J* = 12.4, 6.4 Hz, 1H), 3.43 (dt, *J* = 12.1, 6.0 Hz, 1H), 2.98 (t, *J* = 6.1 Hz, 2H); ^{19}F NMR (282 MHz, CDCl$_3$, ppm) δ 4.93 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, CDCl$_3$, ppm) δ 153.9, 144.3, 137.2, 129.0, 128.9, 128.7, 126.5, 126.3 (q, *J* = 286.6 Hz), 117.9, 114.9, 62.1 (q, *J* = 29.4 Hz), 55.9, 44.9, 27.4. LRMS (ESI) m/z 308.1 (M + H$^+$), HRMS (ESI) m/z 308.1246 (M + H$^+$), calc. for $C_{17}H_{17}F_3NO$ 308.1257

UV/Vis absorption of RB and GO

UV/Vis absorption spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-800 ul) to 1 uM RB in H_2O (3 ml). The spectra revealed that the molecular absorption peak of RB was not affected by GO addition, so we cannot conclude the presence of any charge or energy transfer arising from π-π interaction.

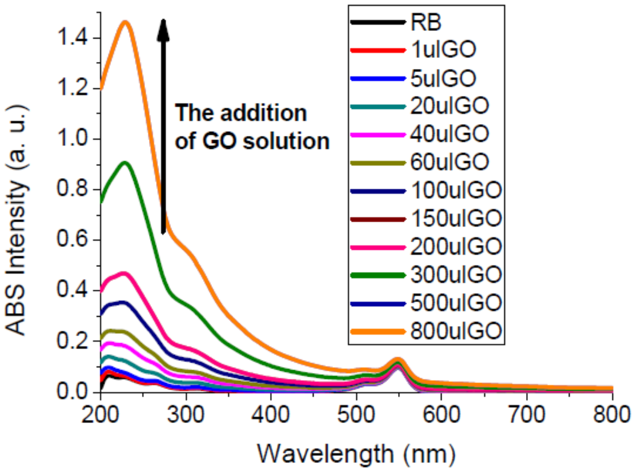


Figure S1. UV/Vis absorption spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-800 ul) to 1 uM RB in H_2O (3 ml)

Fluorescence spectra study of RB and GO

PL spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-1000 ul) to 1 uM RB in H_2O (3 ml). The intensity of PL only slowly decreased with the addition of GO, which is possible only due to the dilution. No significant quenching was observed, which means that there is no strong π-π interaction between RB and GO.

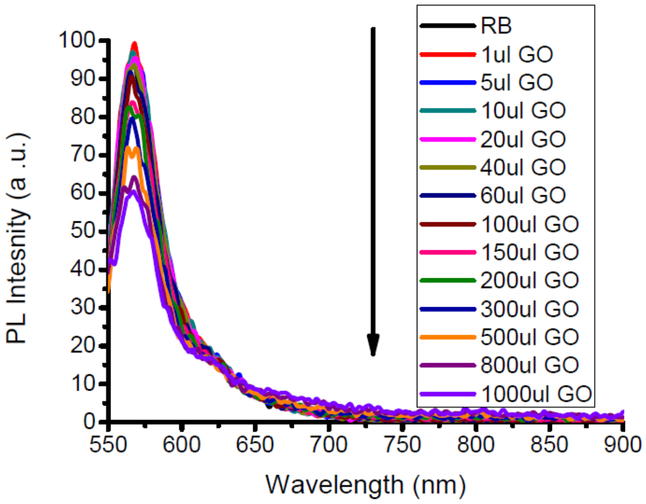


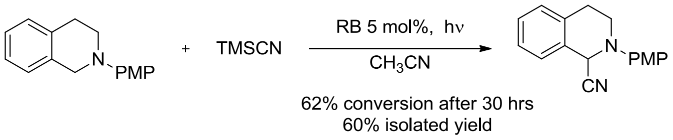
Figure S2. Fluoresence spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-1000 ul) to 1 uM RB in H_2O (3 ml)

Control experiments for singlet oxygen sensitization

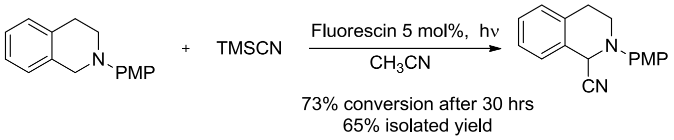
Singlet oxygen is generated by triplet-triplet energy transfer from the photosensitizer triplet state, the process is feasible if the sensitizier triplet energy ET > 95kJ/mol. Upon absorption of photon, the excited dyes are initially in a singlet state, therefore there is a need to undergo intersystem crossing to a triplet state before photosensitizing of dioxygen via the spin-allowed triplet-triplet energy transfer is possible. However the transition from a singlet potential energy surface to a triplet one is forbidden, but can be facilitated by spin-orbit coupling which requires the presence of heavy atom as in the case of RB or vibronic spin-orbit coupling as in TPP.[5] The lack of heavy atom and vibronic spin-orbit coupling in Fluorescein result in its low triplet quantum yield of 0.02 [6], and thus its inability to photosensitize triplet oxygen via triplet-triplet energy transfer.

Controlled experiments were conducted using Fluorescein and TPP as sensitizer in the same reaction. Fluorescein showed similar result with RB [Eq. (a) and (b)]. Although TPP gave full conversion after 30 hrs; isolated yield was only 19% which was similar to the background reaction [Eq. (c) and (d)]. Based on these, singlet oxygen is not crucial for this reaction.

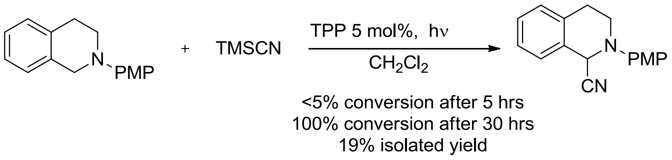
An insightful reviewer also suggested in the presence of very high concentration of solid surface, the rate of physical quenching of singlet oxygen will be very high. Its lifetime in acetonitrile is also not high. Therefore, the reaction may occur predominantly on electron-transfer process rather than singlet oxygen process.



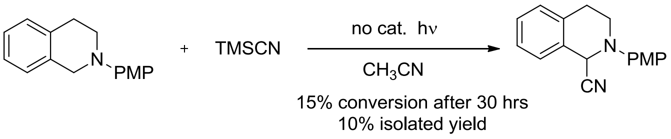
(a)



(b)



(c)



(d)

References

[1] S. Wang, P. K. Ang, Z. Wang, A. L. L. Tang, J. T. L. Thong, K. P. Loh, *Nano Lett.* **2010**, *10*, 92-98.

[2] W. Han, A. R. Ofial, *Chem. Commun.*, **2009**, 5024–5026

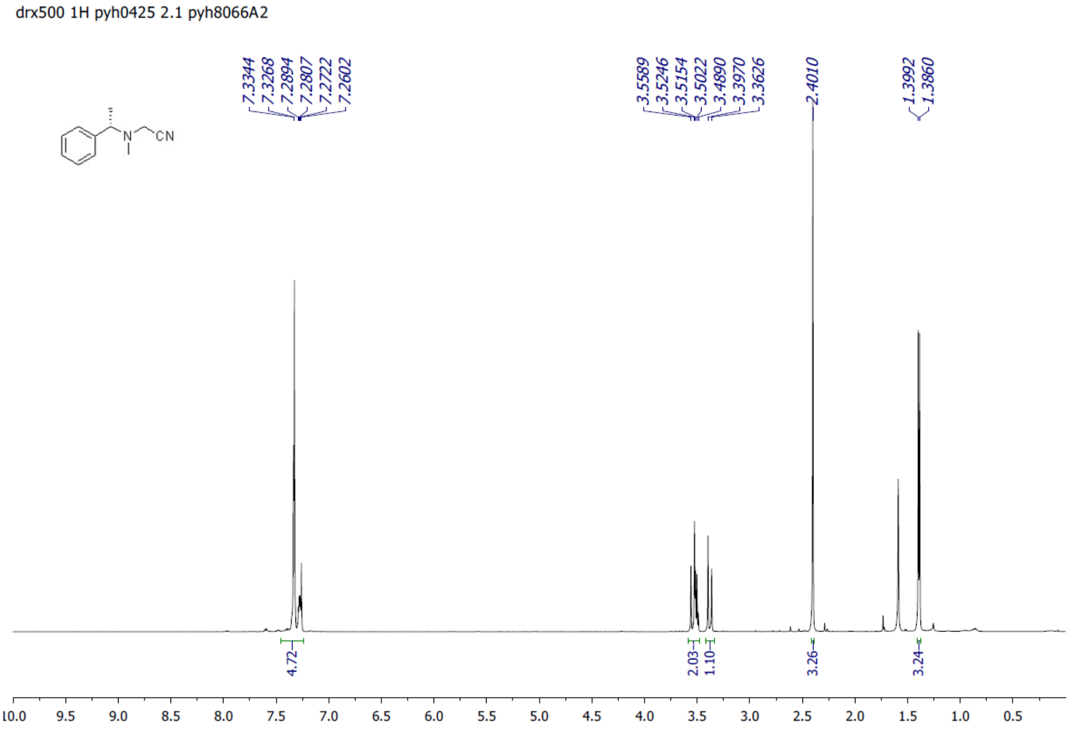
[3] X.-Z., Shu, X.-F. Xia, Y.-F., Yang, K.-G., Ji, X.-Y. Liu, Y.-M., Liang , *J. Org. Chem.* **2009**, *74*, 7464–7469.

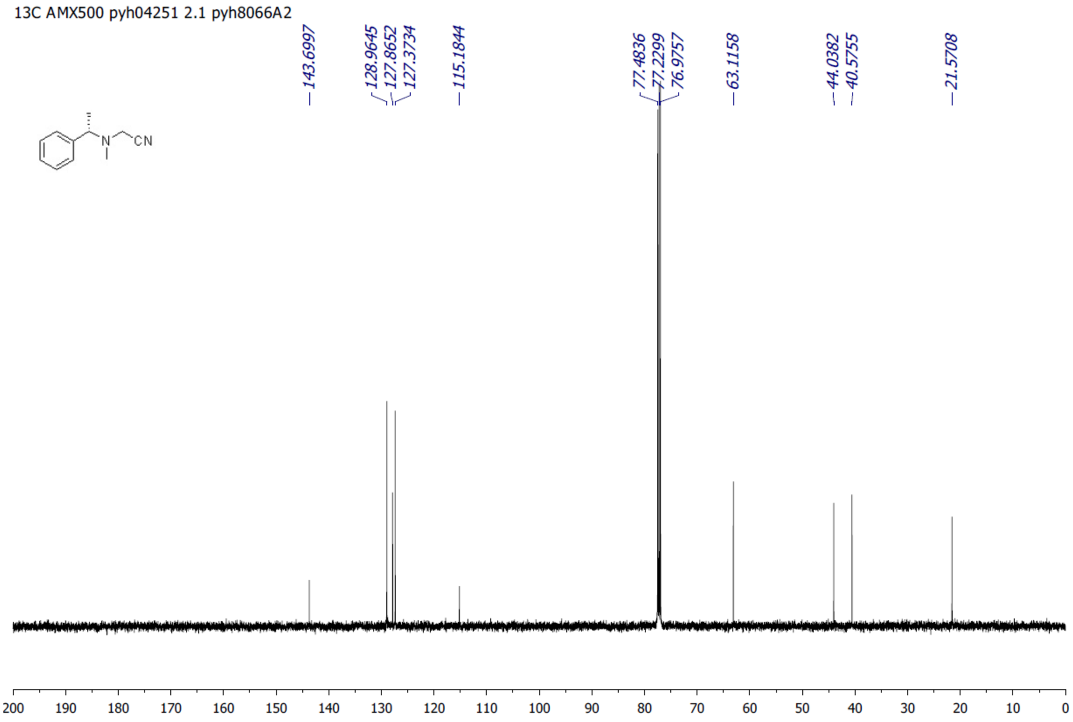
[4] O. G. Nabiev, Z. O. Nabizade, R. G. Kostyanovsky, *Mendeleev Commun.*, **2009**, *19*, 281–283

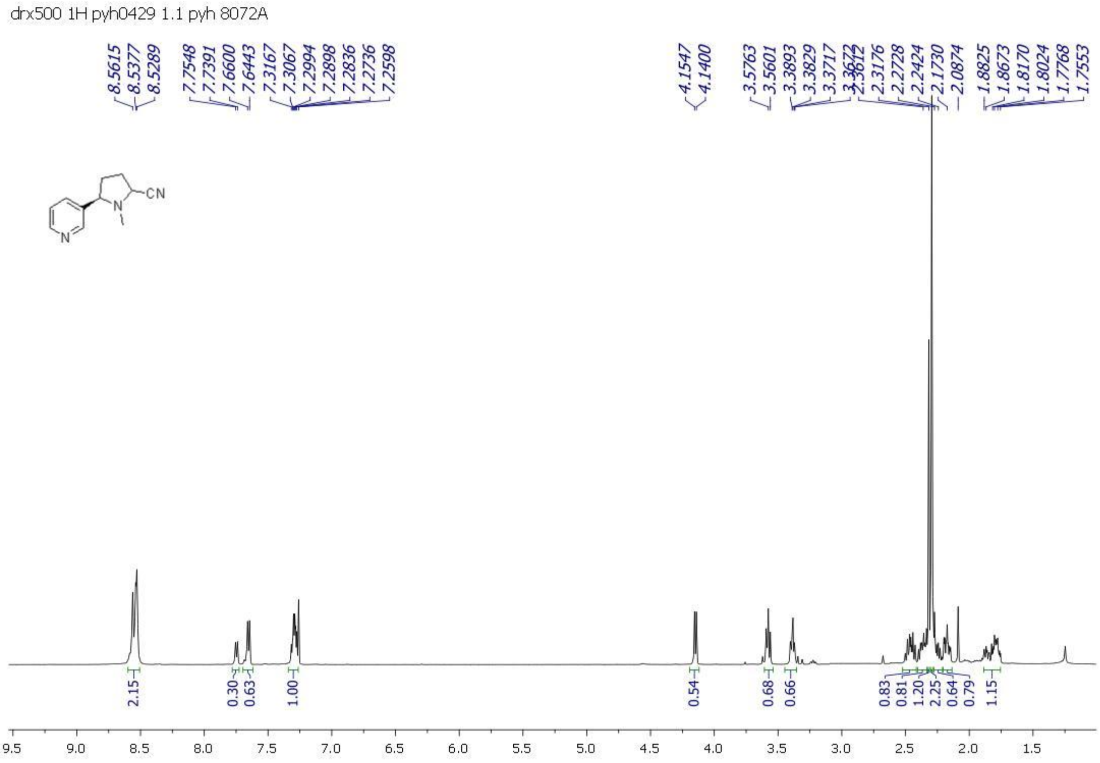
[5] S. Perun, J. Tatchen, C. M. Marian, *ChemPhysChem*, **2008**, *9*, 282-292.

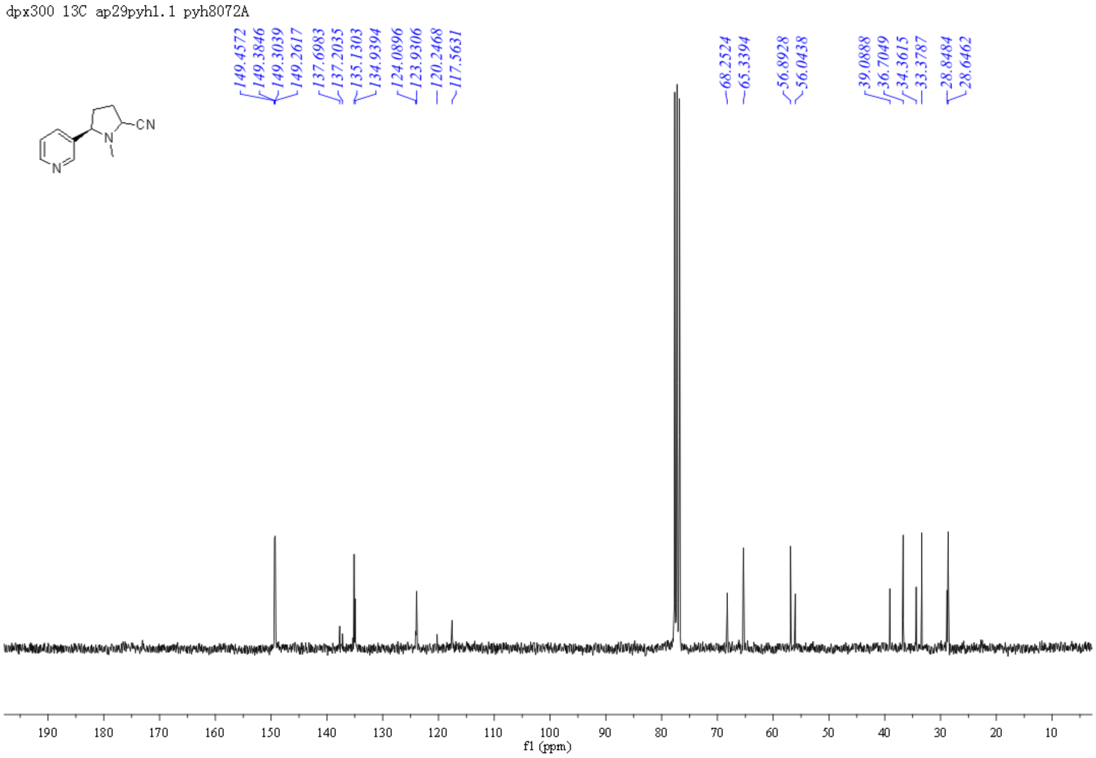
[6] M. Montalti, S. L. Murov, *Handbook of photochemistry*, 3rd edn., CRC/Taylor & Francis, Boca Raton, **2006**.

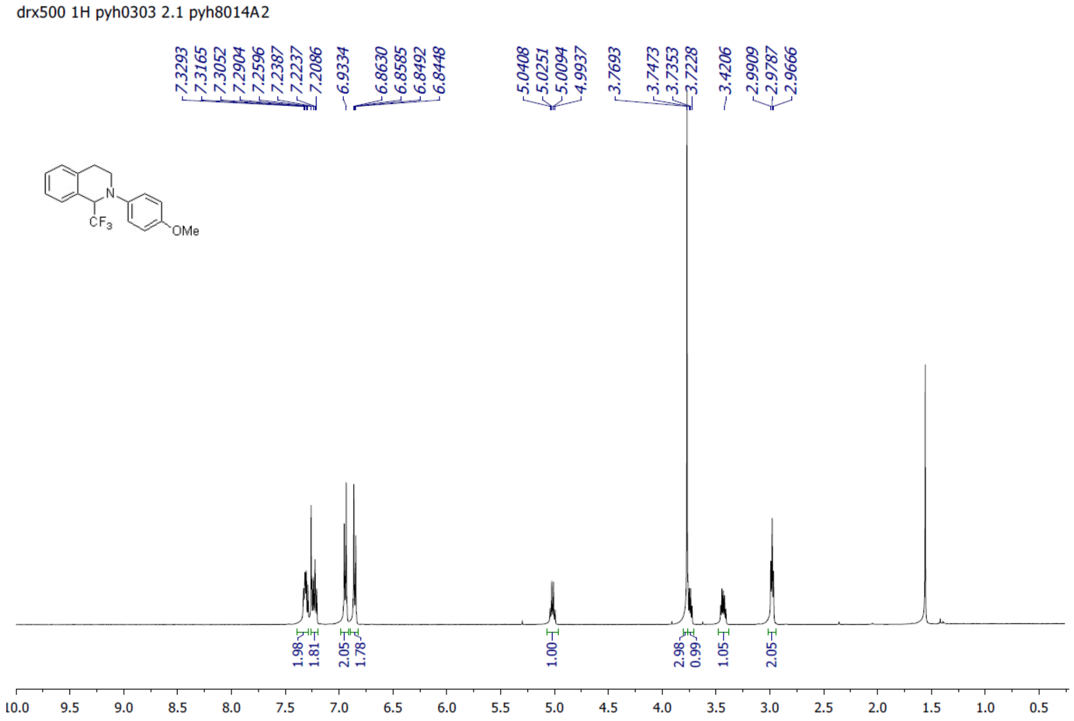
NMR Spectra of New Compounds

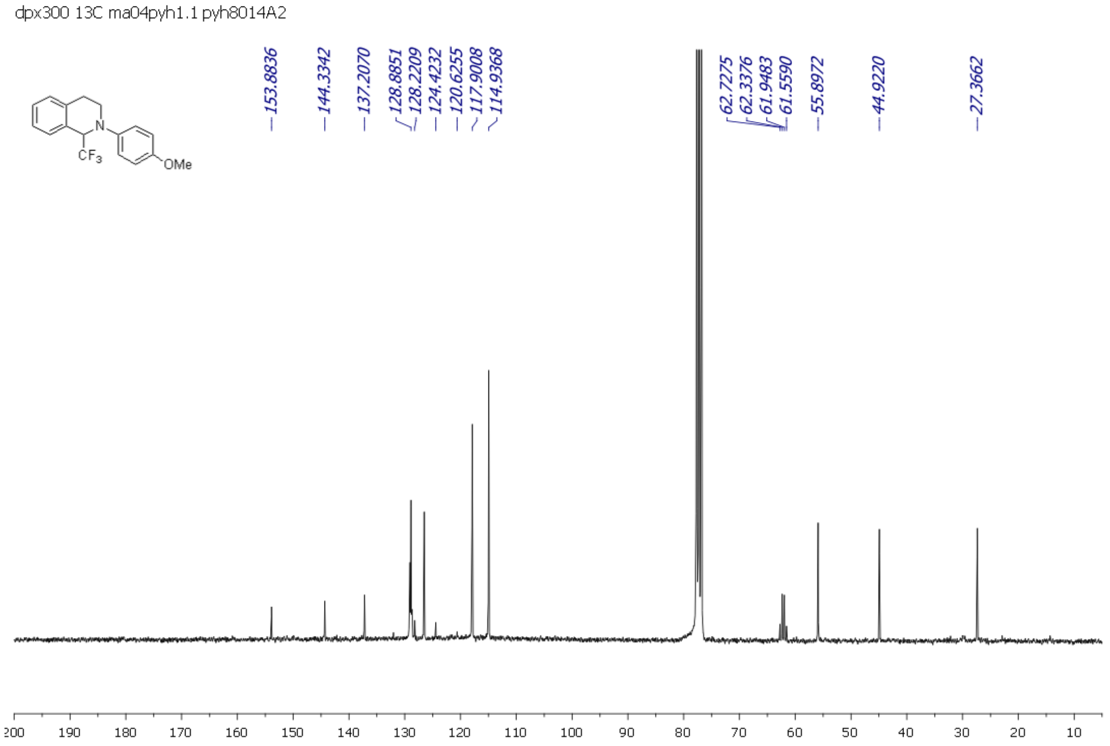


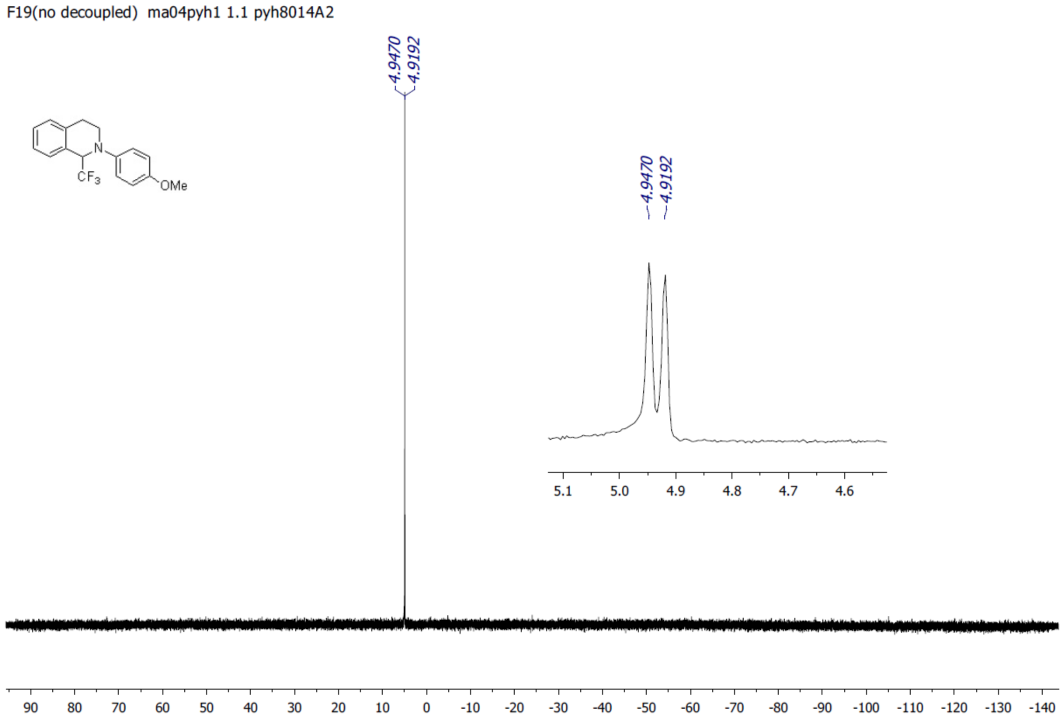



drx500 1H pyh0429 1.1 pyh 8072A
8.5615
8.5377
8.5289
7.7548
7.7391
7.6600
7.6443
7.3167
7.3067
7.2994
7.2898
7.2836
7.2736
7.2598
4.1547
4.1400
3.5763
3.5601
3.3893
3.3829
3.3717
3.3673
3.3612
2.3176
2.2728
2.2424
2.1730
2.0874
1.8825
1.8673
1.8170
1.8024
1.7768
1.7553
CN
N
N
2.15
0.30
0.63
1.00
0.54
0.68
0.66
0.83
0.81
1.20
2.25
0.64
0.79
1.15
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


dpx300 13C ap29pyh1.1 pyh8072A
149.4572
149.3846
149.3039
149.2617
137.6983
137.2035
135.1303
134.9394
124.0896
123.9306
120.2468
117.5631
68.2524
65.3394
56.8928
56.0438
39.0888
36.7049
34.3615
33.3787
28.8484
28.6462
CN
N
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


drx500 1H pyh0303 2.1 pyh8014A2
7.3293
7.3165
7.3052
7.2904
7.2596
7.2387
7.2237
7.2086
6.9334
6.8630
6.8585
6.8492
6.8448
5.0408
5.0251
5.0094
4.9937
3.7693
3.7473
3.7353
3.7228
3.4206
2.9909
2.9787
2.9666
N
CF3
OMe
1.98
1.81
2.05
1.78
1.00
2.98
0.99
1.05
2.05
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


dpx300 13C ma04pyh1.1 pyh8014A2
153.8836
144.3342
137.2070
128.8851
128.2209
124.4232
120.6255
117.9008
114.9368
62.7275
62.3376
61.9483
61.5590
55.8972
44.9220
27.3662
N
CF3
OMe
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


F19(no decoupled) ma04pyh1 1.1 pyh8014A2