

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

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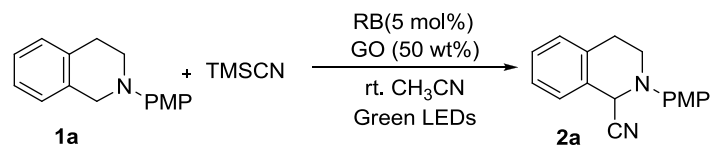
Supporting Information

General procedures and methods	S2
Experimental procedure for α -Cyanations	S3
Experimental procedure for α -Trifluoromethylation	S5
UV/Vis absorption of RB and GO	S6
Fluorescence spectra study of RB and GO	S6
Control experiments for singlet oxygen sensitization	S7
Copies of NMR spectra	S9

General procedures and methods

^1H 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 CH₃CN followed by adding TMSCN (31.3 μ l, 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, ¹H NMR (500 MHz, CDCl₃, 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, ¹H NMR (500 MHz, CDCl₃, 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⁺)

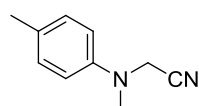
2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2c**)** ^[3]

yellow solid, ¹H NMR (500 MHz, CDCl₃, 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]

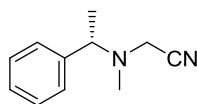
white solid, ¹H NMR (500 MHz, CDCl₃, ppm) δ 7.38 – 7.21 (m, 5H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 5.46 (s, 1H), 3.80 – 3.65 (m, 1H), 3.53 – 3.39 (m, 1H), 3.25 – 3.11 (m, 1H), 3.06 – 2.89 (m, 1H), 2.32 (s, 3H). LRMS (ESI) *m/z* 249.1 (*M* + H⁺)

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



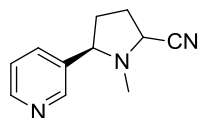
yellow oil, ¹H NMR (500 MHz, CDCl₃, ppm) δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.14 (s, 2H), 2.97 (s, 3H), 2.29 (s, 3H). LRMS (ESI) *m/z* 169.0 (*M* + *H*⁺)

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



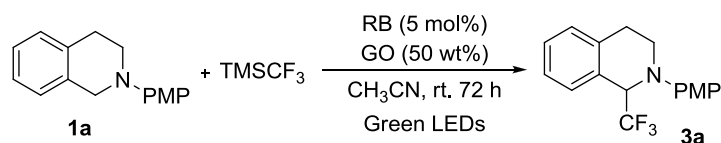
pale yellow oil, con. = 0.05M, O₂ balloon was required, [α]_D²⁹ = -133.6 (*c* 0.75, CHCl₃) ¹H NMR (500 MHz, CDCl₃, ppm) δ 7.33 – 7.26 (m, 5H), 3.51 (q, *J* = 6.6 Hz, 1H), 3.46 (dd, *J* = 81.0, 17.2 Hz, 2H), 2.40 (s, 3H), 1.39 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃, ppm) δ 143.7, 129.0, 127.9, 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 C₁₁H₁₁N₂ 174.1157

5'-cyanonicotine (2h)



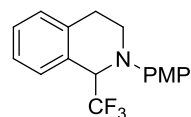
pale yellow oil, con. = 0.05M, O₂ balloon was required, dr = 3:2. ¹H NMR (500 MHz, CDCl₃, ppm) mixture of the two diastereoisomers: δ 8.65 – 8.45 (m, 2H), 7.75 (d, *J* = 7.9 Hz, 0.3H, minor isomer), 7.65 (d, *J* = 7.8 Hz, 0.6H, major isomer), 7.34 – 7.26 (m, 1H), 4.15 (d, *J* = 7.4 Hz, 0.5H), 3.58 (t, *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). ¹³C NMR (75 MHz, CDCl₃, 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 C₁₁H₁₄N₃ 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_3CN followed by adding TMSCF_3 (73.4 μl , 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, ^1H 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 ($\text{M} + \text{H}^+$), HRMS (ESI) m/z 308.1246 ($\text{M} + \text{H}^+$), calc. for $\text{C}_{17}\text{H}_{17}\text{F}_3\text{NO}$ 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 μ l) to 1 μ M 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.

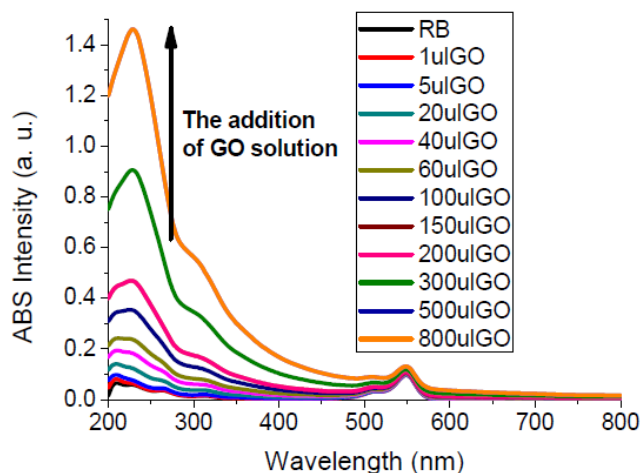


Figure S1. UV/Vis absorption spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-800 μ l) to 1 μ M RB in H_2O (3 ml)

Fluorescence spectra study of RB and GO

PL spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-1000 μ l) to 1 μ M 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.

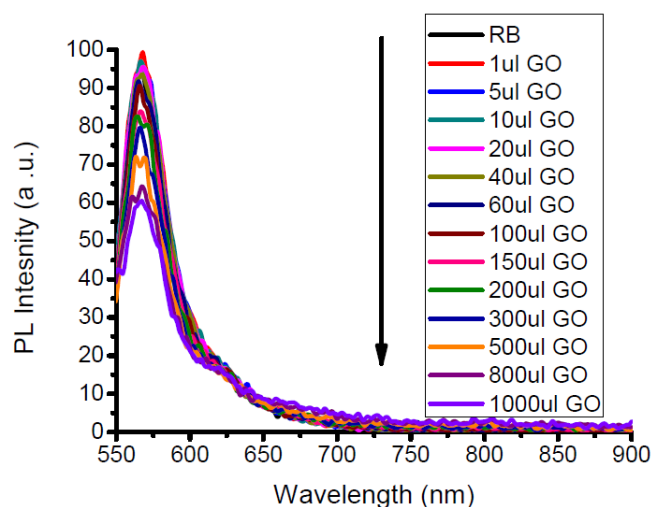


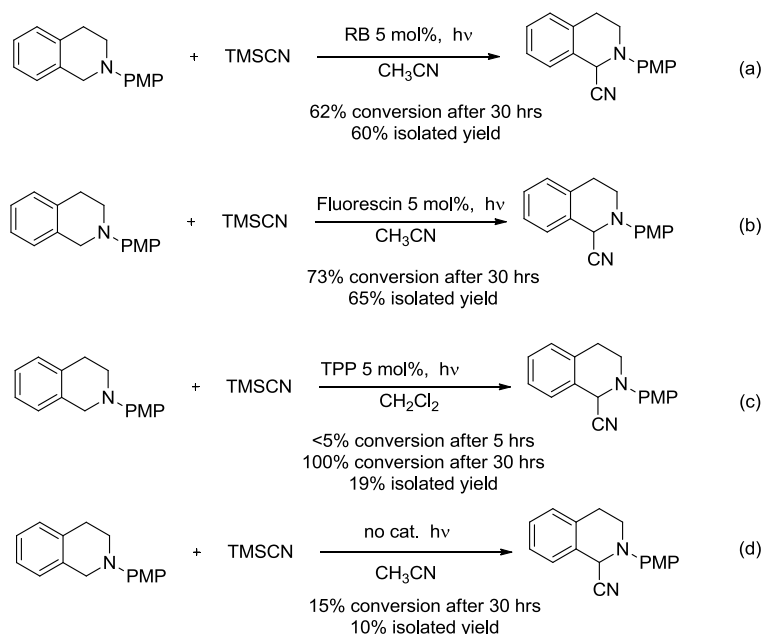
Figure S2. Fluorescence spectra recorded during addition of 0.25 mg/ml GO aqueous solution (0-1000 μ l) to 1 μ M RB in H_2O (3 ml)

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 sensitizer triplet energy $E_T > 95 \text{ kJ/mol}$. 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.

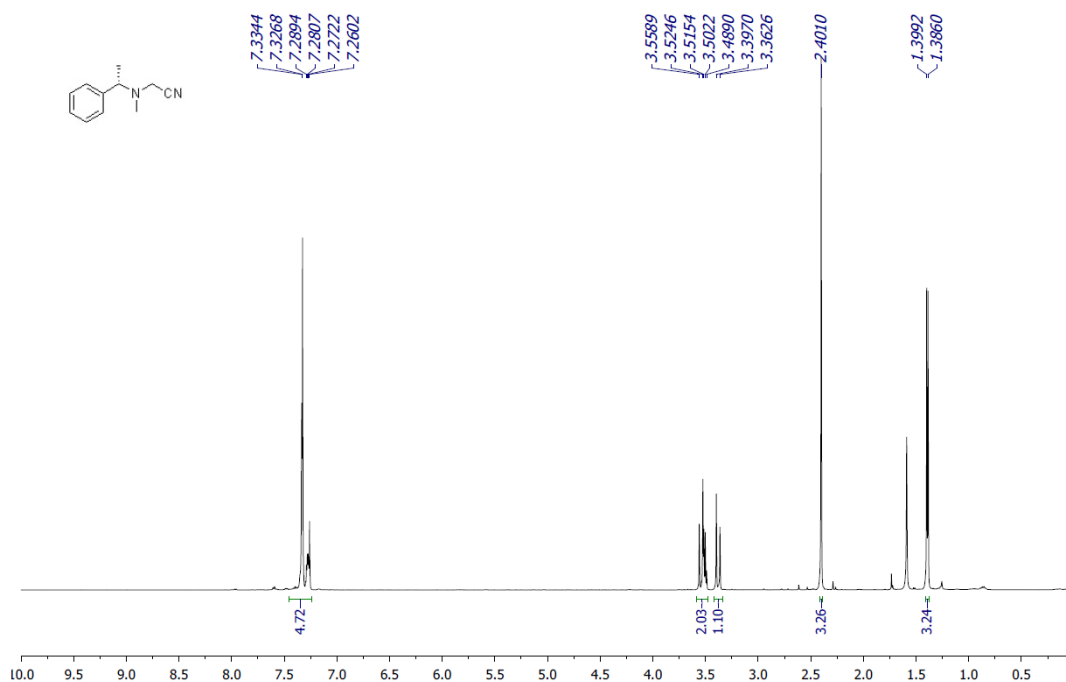


References

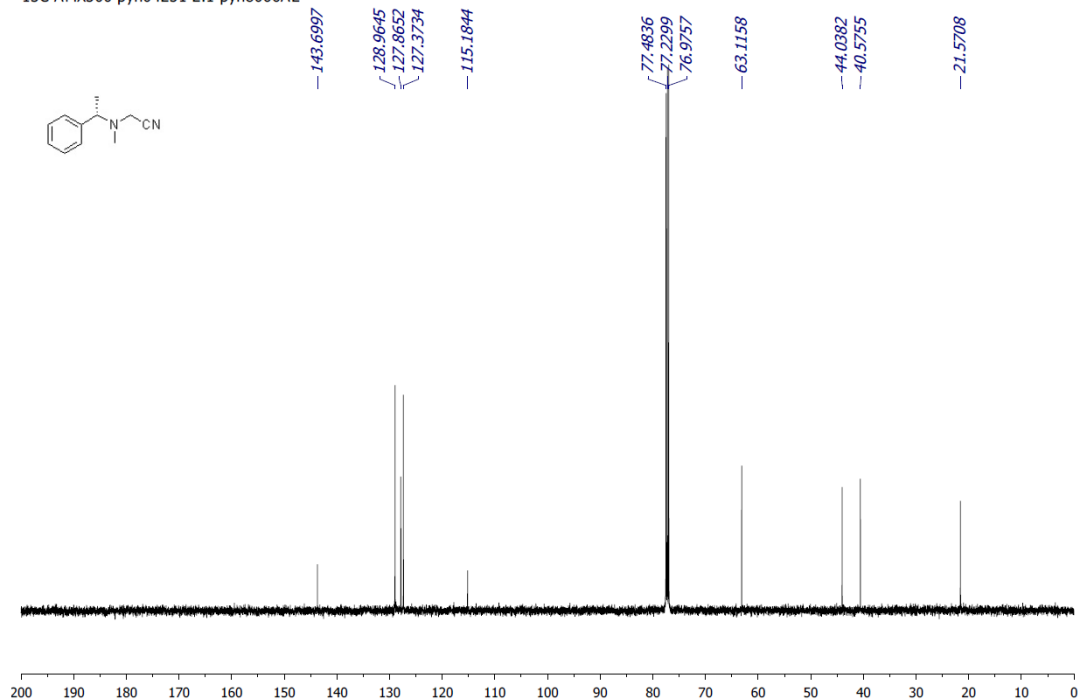
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NMR Spectra of New Compounds

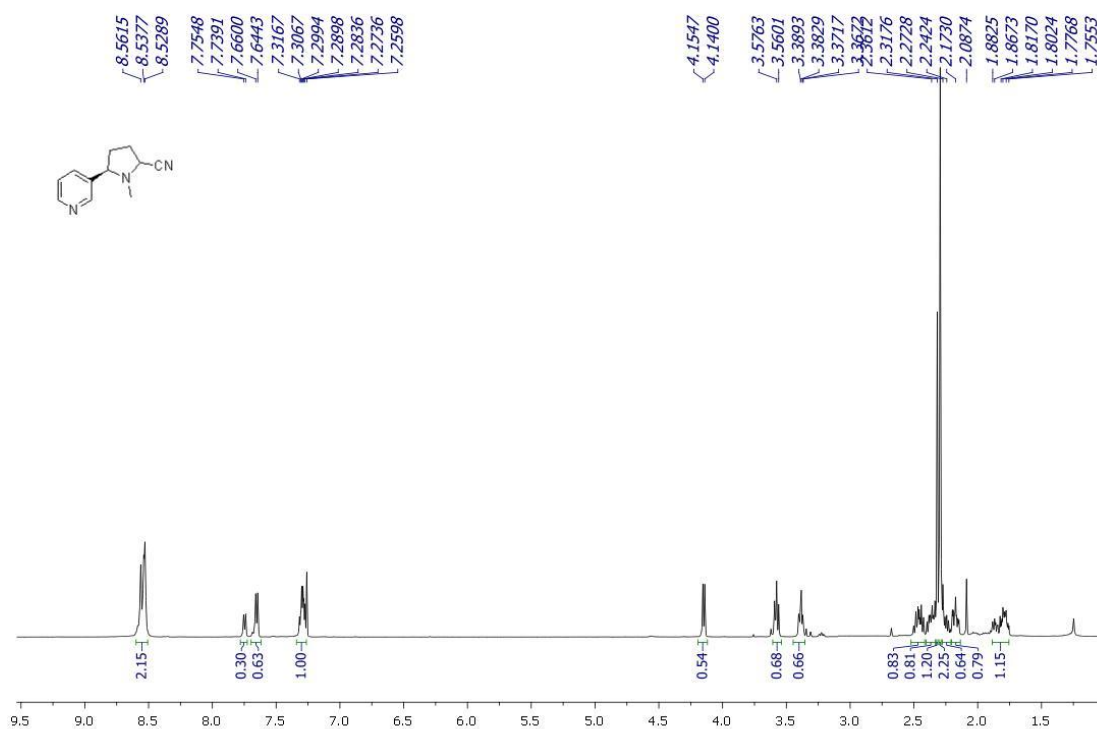
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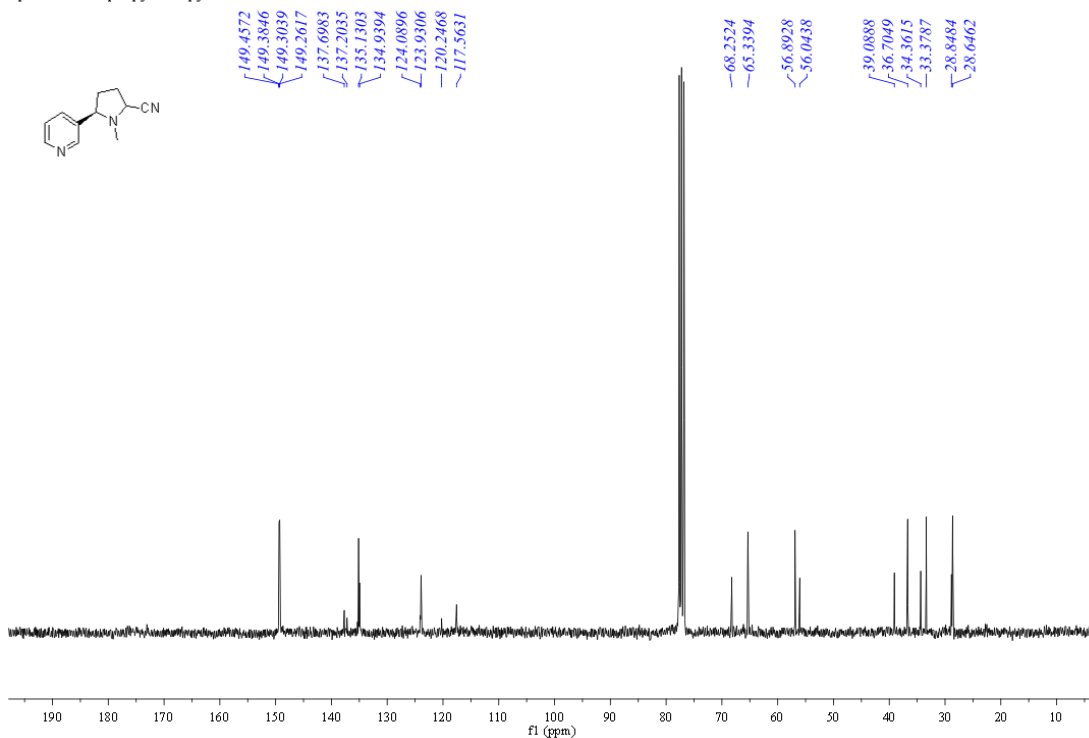
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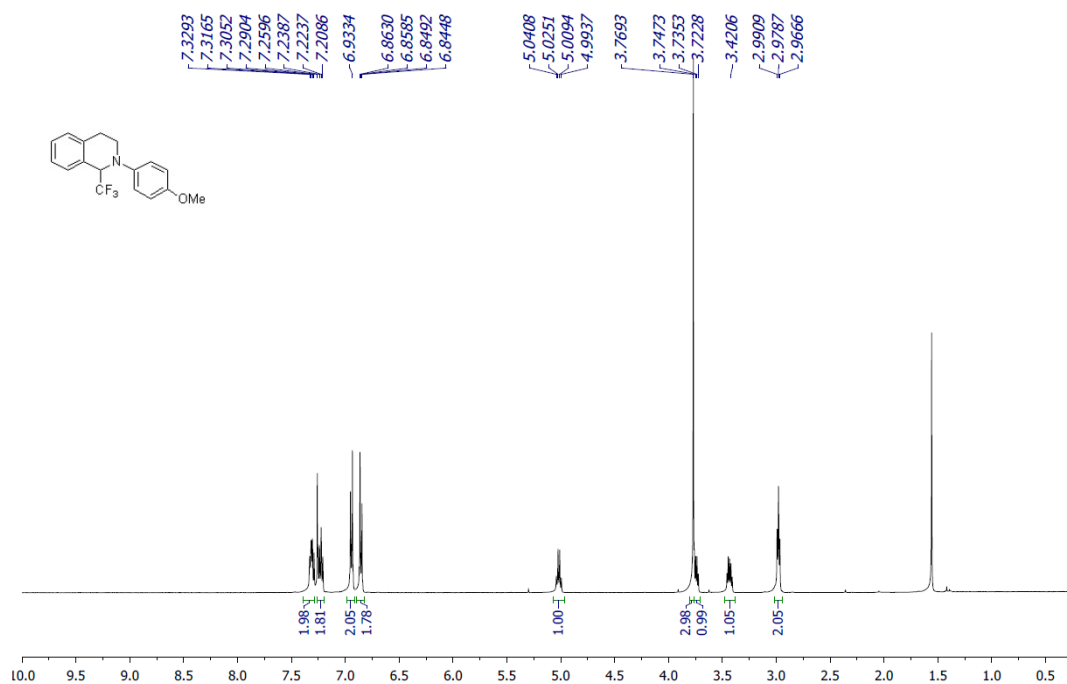
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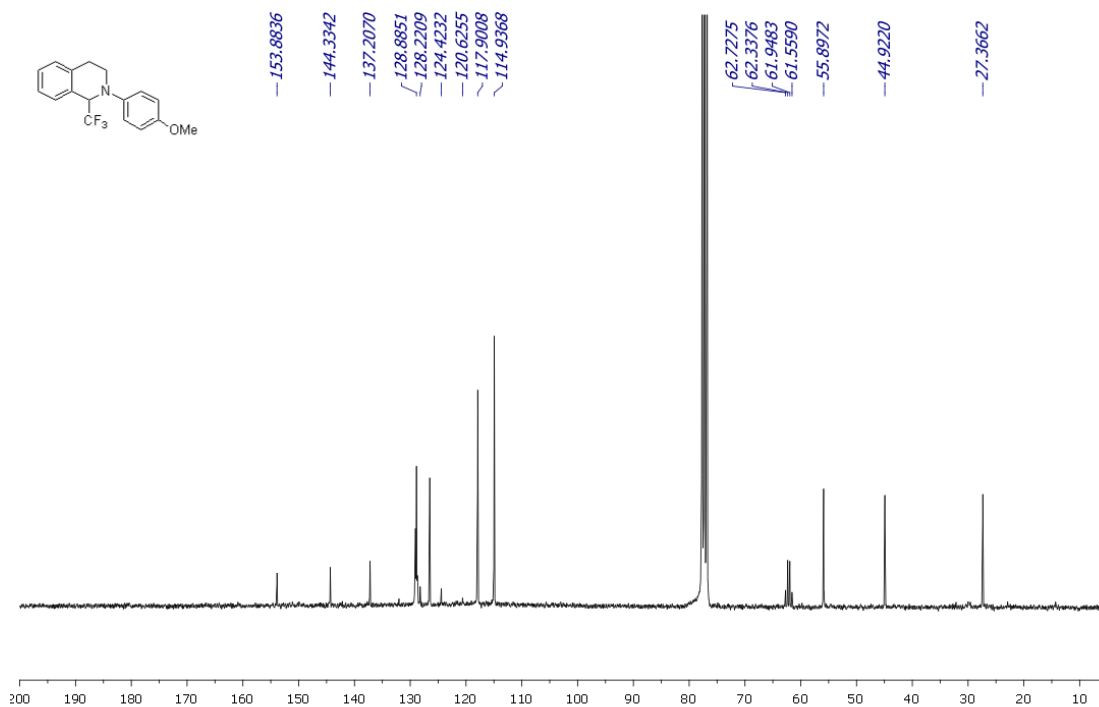
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drx500 1H pyh0303 2.1 pyh8014A2



dpX300 13C ma04pyh1.1 pyh8014A2



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