Supporting Information for

Pd(II)-Catalyzed One-Pot, Three-Step route for the Synthesis of Unsymmetrical Acridines

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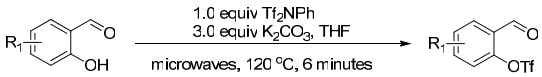
1. General Information: NMR spectra were recorded with a 400 MHz spectrometer for ^{1}H NMR, 100 MHz for ^{13}C NMR. Chemical shifts δ are given in ppm relative to the residual proton signals of the deuterated solvent $CDCl_3$ for ^{1}H and ^{13}C NMR. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). High resolution mass spectra were recorded on a 3000 mass spectrometer. For column chromatography silica gel (200-300 mesh) was used as the stationary phase. All regents and solvents were purchased from commercial sources and purified commonly before used. Microwave reaction was performed using Beijing XiangHu Science and Technology Development Co., Ltd. XH-200A.

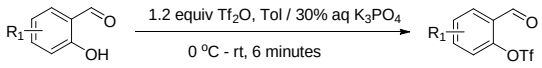
2. Synthesis of starting materials

Staring materials **1a, 1e, 1f, 1g, 1j** were synthesized according to the corresponding reference. [1]



Phenol (2.0 mmol), *N*-phenyl-bis(trifluoromethane-sulfonimide) (2.0 mmol, 710 mg), K_2CO_3 (6.0 mmol, 830 mg) and THF (3.0 mL) were mixed in a septum capped tube (a Smith process vial). The reaction mixture was heated to 120 ^oC for 6 minutes in a microwave synthesizer. After cooling, the reaction mixture was extracted with H_2O/EtOAc, the organic phase was combined, dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography with EtOAc/petroleum (5-50%) as the eluant.

Staring materials **1d, 1h, 1i, 1k, 1l** were synthesized according to the corresponding reference. [2]



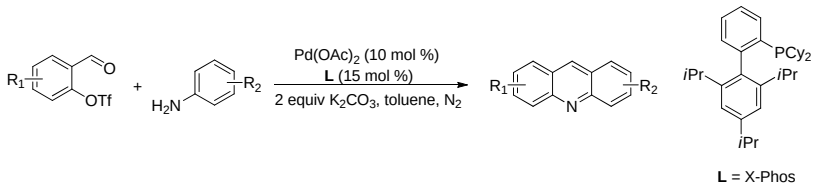
To a cooled (0 ^oC) biphasic mixture of toluene (10.0 mL), 30% (w/v) aqueous K_3PO_4 (10 mL), and phenol (5.0 mmol). Tf_2O (6.0 mmol) was added dropwise at a rate to maintain the reaction temperature less than 10 ^oC. The reaction was allowed to warm to ambient temperature and stirred for 30 minutes. The mixture was diluted with water then extracted with ethyl acetate. The extracts were combined, washed with brine, and then dried over anhydrous Na_2SO_4. The crude material was purified by column chromatography on silica gel (eluting with petroleum ether/ethyl acetate mixtures) to give the corresponding triflate product.

3. Reference:

[1] Bengtson, A.; Hallberg, A.; Larhed, M. *Org. Lett.* **2002**, *4*, 1231-1233.

[2] Frantz, D. E.; Weaver, D. G.; Carey, J. P.; Kress, M. H.; Dolling, U. H. *Org. Lett.* **2002**, 4, 4717-4718.

4. General procedure

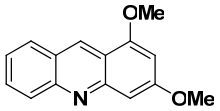


In an oven-dried Schlenk tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with anilines (0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), X-Phos (14.3 mg, 0.03 mmol), K_2CO_3 (55.2 mg, 0.4 mmol). The vessel was evacuated and backfilled with nitrogen (this process was repeated a total of 3 times) and toluene (1.5 mL) was added via syringe. After addition of the solvent, the solution was heated to 105 ^{o}C for 15 minutes.

A second oven-dried test tube, which was equipped with a magnetic stir bar, was charged with 2-formylphenyl triflate (0.24 mmol) and toluene (0.5 mL), stirred until well blended. Then the mixture was added via syringe into the first Schlenk tube. The solution was heated to 105 ^{o}C until 2-formylphenyl triflate had been completely consumed as judged by TLC detection. The reaction mixture was then cooled to room temperature, diluted with brine (3.0 mL) and extracted with ethyl acetate (3×3.0 mL). The organic layers were collected and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude material was purified by column chromatography on silica gel (eluting with petroleum ether/ethyl acetate mixtures) to give the desired products.

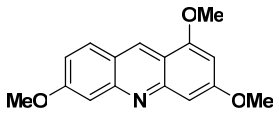
5. Characterization of compounds

1,3-Dimethoxyacridine (3a)



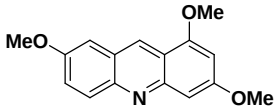
Yellow solid. M.p. 102-104 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:8. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.06 (s, 1H), 6.42 (s, 1H), 4.01 (s, 3H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 156.2, 151.0, 149.3, 131.4, 130.5, 128.8, 128.4, 124.9, 124.5, 117.4, 98.0, 97.5, 55.9, 55.7; HRMS: calcd for $C_{15}H_{14}NO_2$ [M+H$^+$] 240.1019, found 240.1027.

1,3,6-Trimethoxyacridine (3d)



Yellow solid. M.p. 63-65 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:6. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.37 (d, *J* = 2.4 Hz, 1H), 7.12 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.01 (d, *J* = 1.6 Hz, 1H), 6.40 (d, *J* = 2.4 Hz, 1H), 4.01 (s, 3H), 3.98 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 161.8, 156.5, 151.0, 131.1, 129.9, 120.8, 119.4, 115.7, 104.7, 97.7, 96.7, 55.8, 55.7, 55.5; HRMS: calcd for $C_{16}H_{16}NO_3$ [M+H$^+$] 270.1125, found 270.1126.

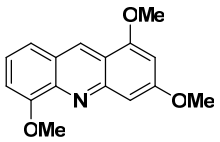
1,3,7-Trimethoxyacridine (3e)



Brown solid. M.p. 159-161 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/ petroleum ether = 1:8. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.10 (d, *J* = 9.6 Hz, 1H), 7.46 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.19 (d, *J* = 2.8 Hz, 1H), 7.13 (d, *J* = 1.6 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 4.04 (s, 3H), 3.99 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 156.2, 155.8, 149.3, 146.2, 129.9, 129.3, 125.5, 125.1, 117.5, 104.3, 98.0, 97.6, 55.8, 55.7, 55.5; HRMS: calcd for $C_{16}H_{16}NO_3$

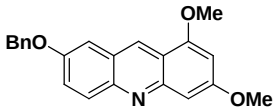
[M+H$^+$] 270.1125, found 270.1126.

1,3,5-Trimethoxyacridine (3f)



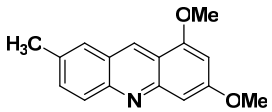
Yellow solid. M.p. 119-121 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/ petroleum ether = 1:10. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 1.6 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.46 (d, *J* = 2.0 Hz, 1H), 4.14 (s, 3H), 4.03 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 155.9, 154.6, 150.1, 142.1, 131.2, 125.8, 124.2, 120.6, 117.6, 107.0, 99.2, 97.9, 56.1, 55.9, 55.8; HRMS: calcd for $C_{16}H_{15}NO_3Na$ [M+Na$^+$] 292.0944, found 292.0941.

7-(Benzyloxy)-1,3-dimethoxyacridine (3g)



Yellow solid. M.p. 132-134 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:12. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.51-7.49 (m, 3H), 7.43-7.39 (m, 2H), 7.37-7.32 (m, 1H), 7.22 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.07 (d, *J* = 1.6 Hz, 1H), 6.42 (d, *J* = 2.0 Hz, 1H), 5.20 (s, 2H) , 4.03 (s, 3H) , 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 161.6, 156.6, 136.1, 132.5, 130.2, 129.2, 128.7, 128.3, 127.9, 124.0, 120.7, 120.0, 115.7, 104.7, 97.0, 96.6, 70.4, 56.0, 55.9, 29.7; HRMS: calcd for $C_{22}H_{19}NO_3Na$ [M+Na$^+$] 368.1257, found 368.1255.

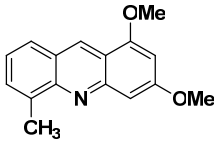
1,3-Dimethoxy-7-methylacridine (3h)



Yellow solid. M.p. 133-135 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:10. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.02 (d, *J* = 8.8 Hz, 1H), 7.70 (s, 1H),

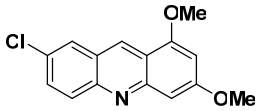
7.57 (d, J = 7.6 Hz, 1H), 7.05 (d, J = 2.0 Hz,1H), 6.39 (d, J = 2.0 Hz, 1H), 4.00 (s, 3H), 3.96 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 156.2, 150.0, 147.7, 134.2, 133.6, 130.8, 127.6, 127.0, 124.8, 117.4, 97.5, 55.9, 55.7, 21.7; HRMS: calcd for $C_{16}H_{16}NO_2$ [M+H$^+$] 254.1176, found 254.1176.

1,3-Dimethoxy-5-methylacridine (3i)



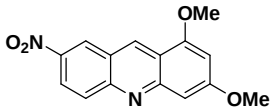
Yellow solid. M.p. 131-133 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:8. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 6.4 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.13 (s, 1H), 6.44 (s, 1H), 4.04 (s, 3H), 4.01 (s, 3H), 2.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 136.0, 131.4, 131.4, 130.0, 126.9, 124.8, 124.3, 117.1, 98.6, 97.5, 55.9, 55.8, 18.5; HRMS: calcd for $C_{16}H_{15}NO_2Na$ [M+Na$^+$] 276.0995, found 276.0989.

7-Chloro-1,3-dimethoxyacridine (3j)



Brown solid. M.p. 119-121 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:16. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 2.0 Hz, 1H), 7.70 (dd, J = 9.2, 2.0 Hz, 1H), 7.15 (s, 1H), 6.48 (d, J = 1.6 Hz, 1H), 4.05 (s, 3H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 131.9, 127.0, 124.9, 117.9, 98.4, 95.4, 56.1, 56.0; HRMS: calcd for $C_{15}H_{13}ClNO_2$ [M+H$^+$] 274.0629, found 274.0633.

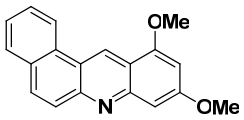
1,3-Dimethoxy-7-nitroacridine (3k)



Brown solid. M.p. 175-177 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:18. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.98 (s, 1H), 8.48 (dd, J = 9.6, 2.4 Hz,

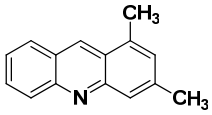
1H), 8.17 (d, J = 9.2 Hz, 1H), 7.09 (s, 1H), 6.52 (s, 1H), 4.08 (s, 3H), 4.03 (s, 3H); HRMS: calcd for $C_{15}H_{13}N_2O_4$ [M+H$^+$] 285.0870, found 285.0869.

9,11-Dimethoxybenzo[a]acridine (3l)



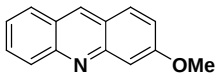
Brown solid. M.p. 153-155 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:11. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.75 (d, J = 8.0 Hz, 1H), 8.06-7.98 (m, 2H), 7.89 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 7.63 (t, J = 7.2 Hz, 1H), 7.24 (s, 1H), 6.53 (d,J = 1.6 Hz, 1H), 4.08 (s, 3H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 156.3, 152.0, 133.4, 130.8, 130.3, 128.9, 127.7, 127.2, 122.7, 121.6, 116.4, 98.2, 56.0, 55.9; HRMS: calcd for $C_{19}H_{16}NO_2$ [M+H$^+$] 290.1176, found 290.1172.

1,3-Dimethylacridine (3m)



Brown solid. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:20. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89(s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.92 (s, 1H), 7.81-7.77 (m, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.23 (s, 1H), 2.80 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 128.9, 128.5, 125.9, 125.4, 124.9, 118.9, 22.3, 18.9. HRMS: calcd for $C_{15}H_{14}N$ [M+H$^+$] 208.1121, found 208.1125.

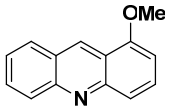
3-Methoxyacridine (3n)



Brown solid. M.p. 44-46 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:10. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 9.2 Hz, 1H), 7.78-7.73 (m, 1H), 7.50-7.45 (m, 2H), 7.21 (dd, J = 9.2, 2.4 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 150.8, 149.1, 135.8, 130.4, 129.4, 128.7, 128.3, 125.5, 124.8, 122.9, 121.3, 105.1, 55.6; HRMS: calcd for $C_{14}H_{12}NO$ [M+H$^+$] 210.0913,

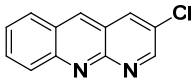
found 210.0907.

1-Methoxyacridine (3n')



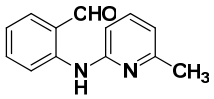
Brown solid. M.p. 106-108 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:10. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.82-7.76 (m, 2H), 7.69-7.65 (m, 1H), 7.54-7.51 (m, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 149.7, 149.1, 131.6, 130.5, 130.4, 129.1, 128.8, 126.0, 125.4, 121.5, 120.4, 101.7, 55.8; HRMS: calcd for $C_{14}H_{12}NO$ [M+H$^+$] 210.0913, found 210.0918.

3-Chlorobenzo[b][1,8]naphthyridine (3o)



Yellow solid. M.p. 141-143 ^{o}C. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:9. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.48-7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 148.2, 145.9, 135.6, 135.3, 127.5, 127.4, 127.2, 126.0, 124.2, 121.2, 116.2; HRMS: calcd for $C_{12}H_8ClN_2$ [M+H$^+$], 215.0370, found 215.0374.

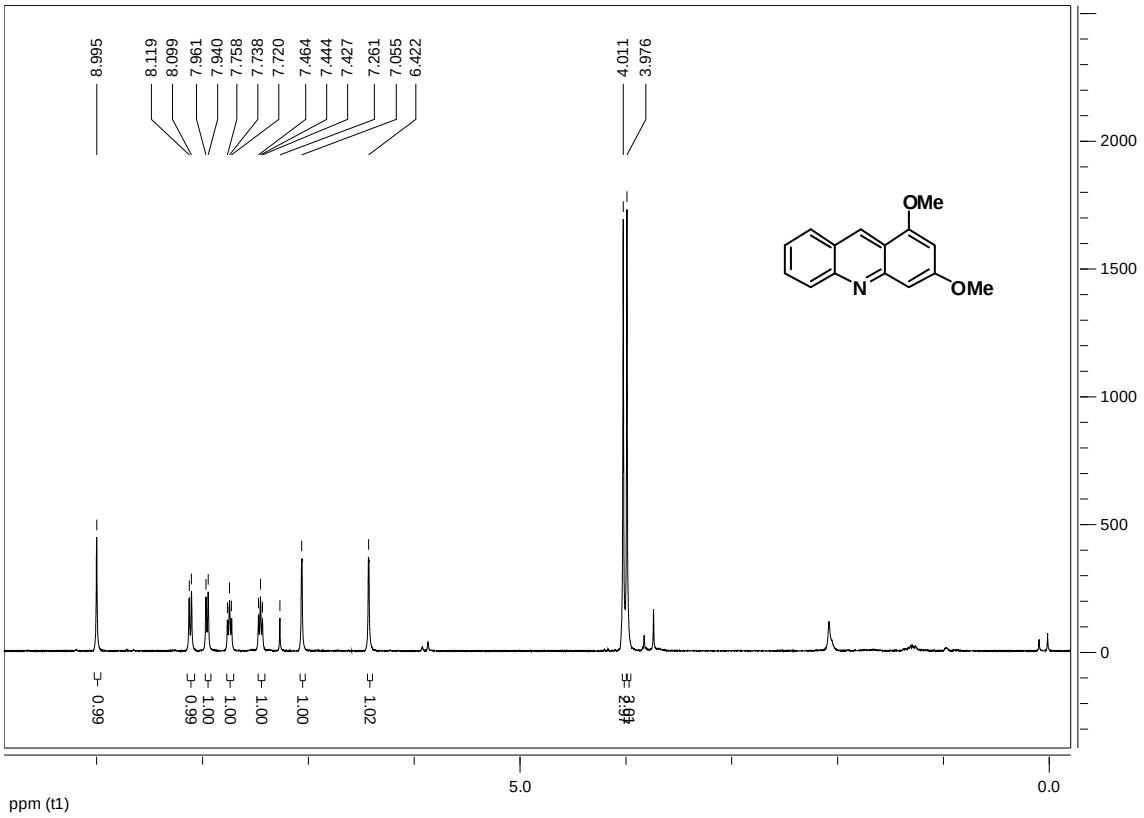
2-((6-Methyl-2,3-dihydropyridin-2-yl)amino)benzaldehyde (4p)



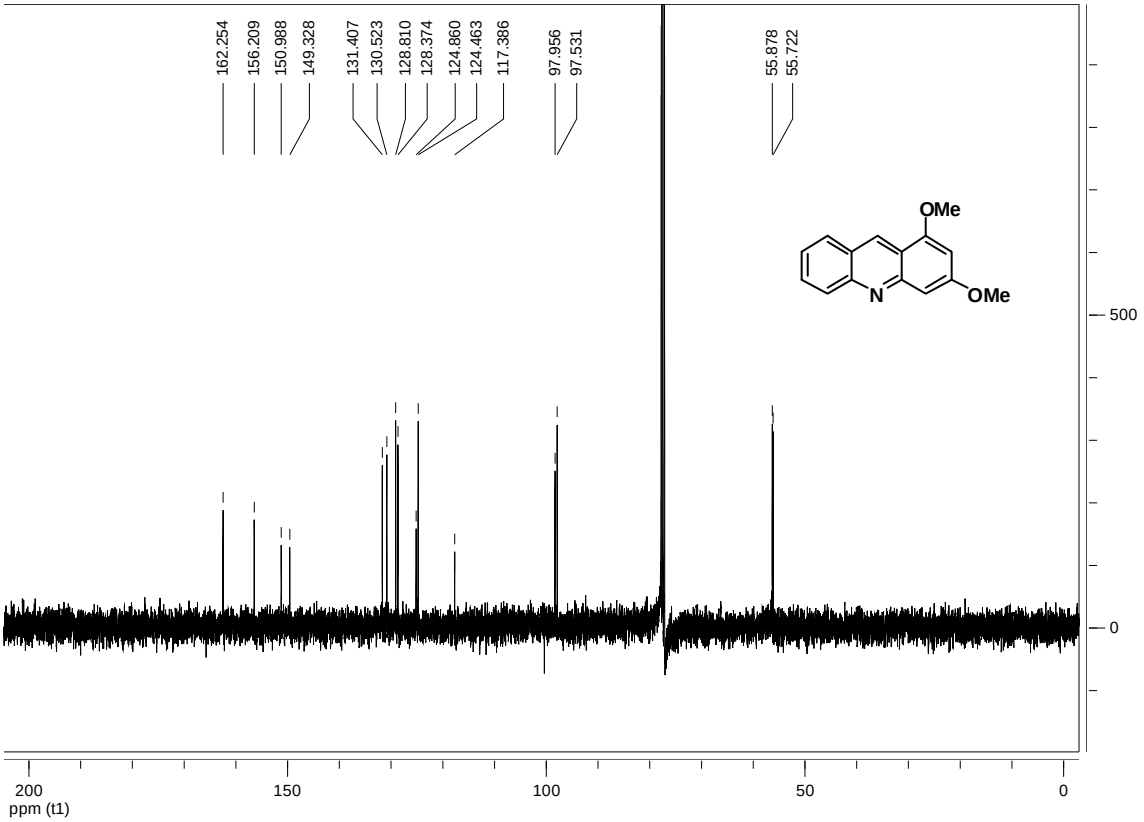
Light yellow oil. Column material: 20 g silica gel. Solvent: ethyl acetate/petroleum ether = 1:12. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (s, 1H), 9.91 (s, 1H), 8.87 (d, *J* = 8.8 Hz, 1H), 7.60 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.56-7.52 (m, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.01-6.96 (m, 1H), 6.73 (t, *J* = 7.2 Hz, 2H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 137.9, 136.5, 136.4, 135.9, 120.2, 119.0, 117.3, 115.9, 110.1, 24.4. HRMS: calcd for $C_{13}H_{13}N_2O$ [M+H$^+$], 215.1178, found 215.1173.

6. Copies of ^{1}H and ^{13}C NMR spectra

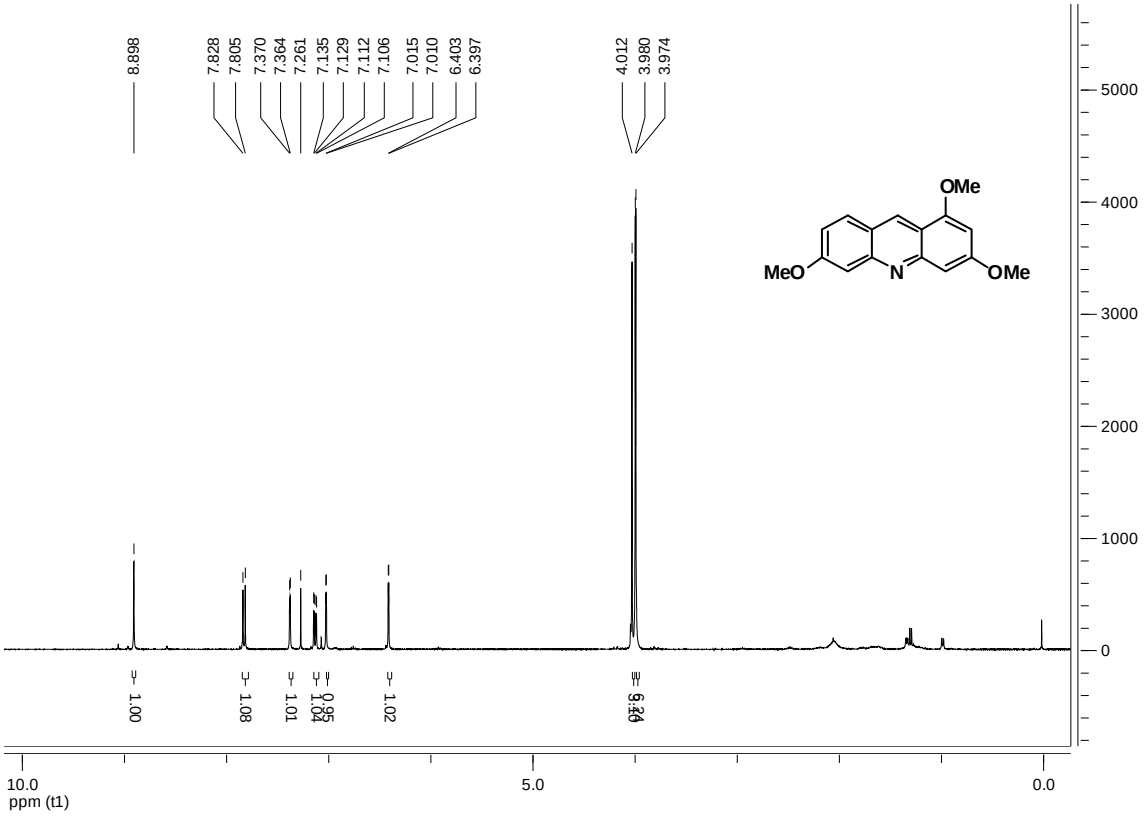
^{1}H NMR of 3a



^{13}C NMR of 3a



^{1}H NMR of 3d



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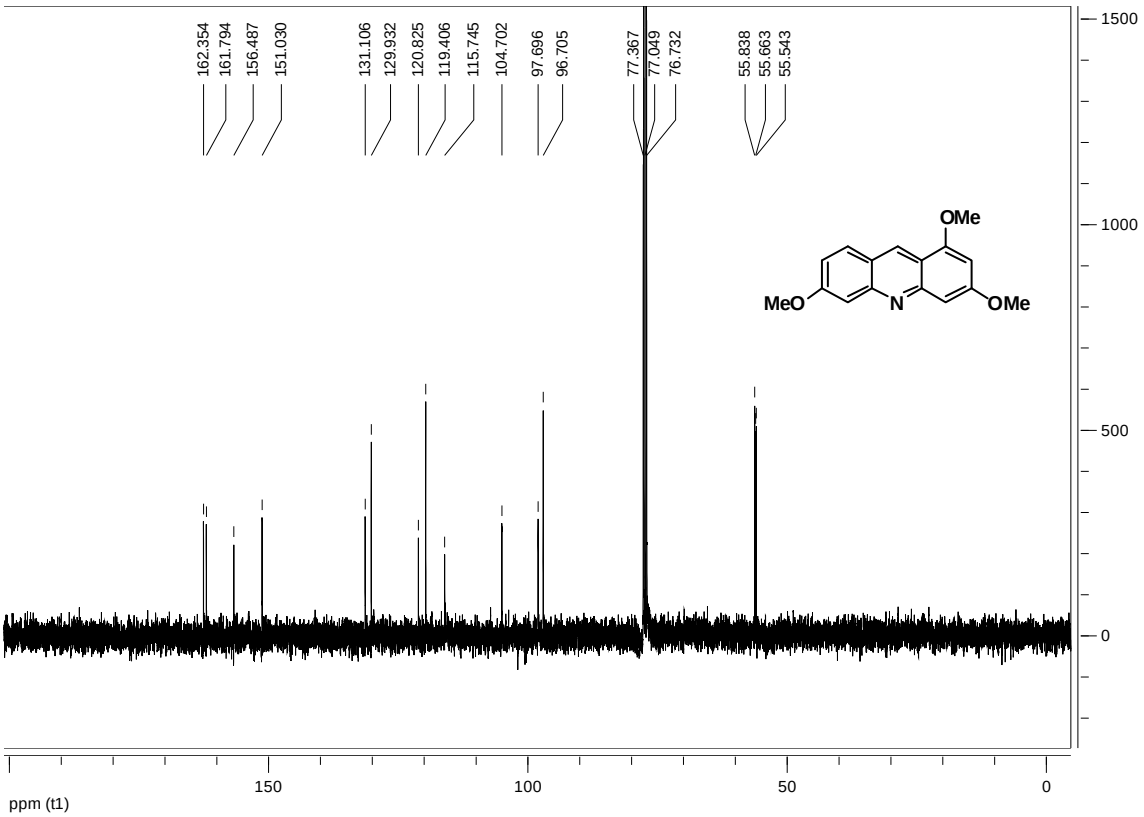
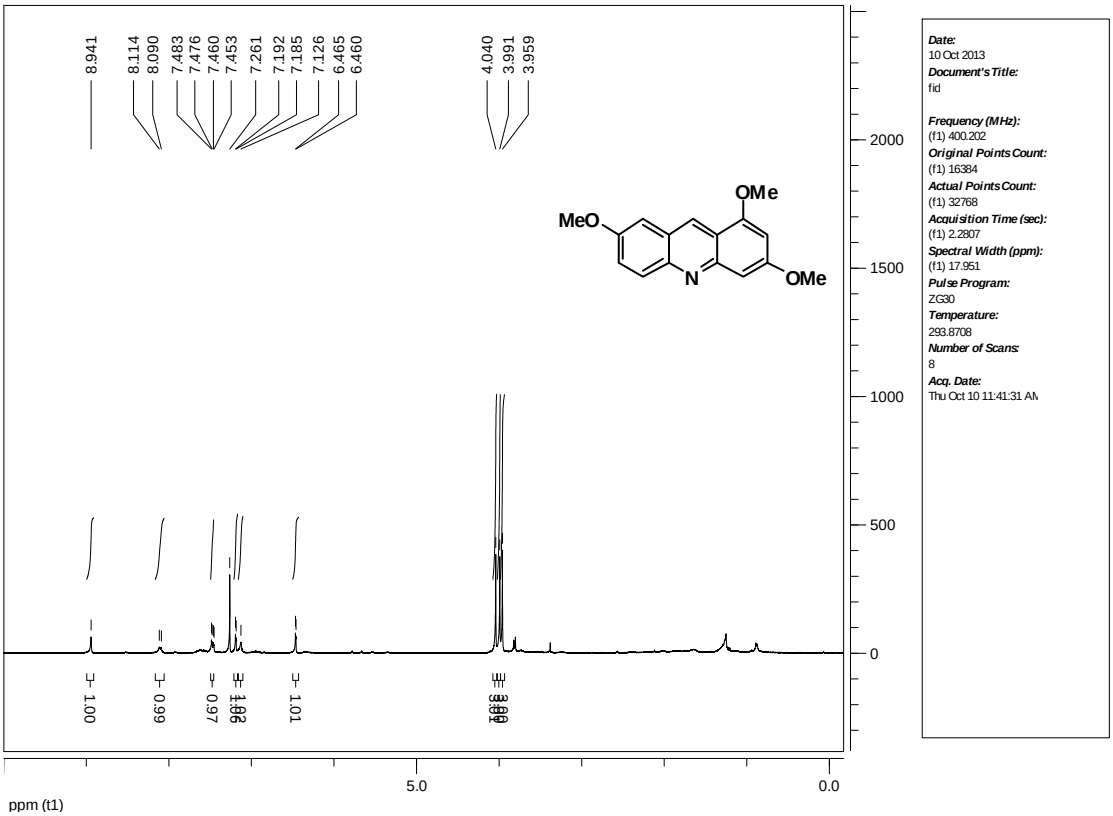


^{1}H NMR of 3e



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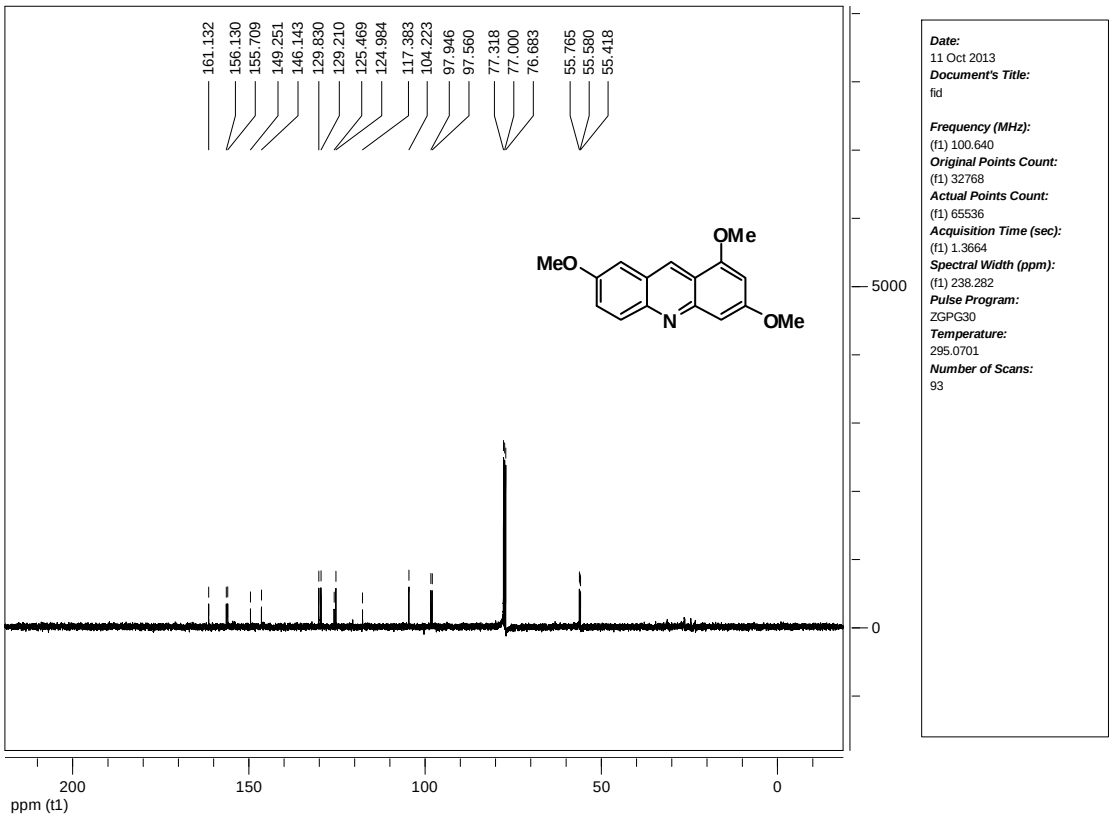
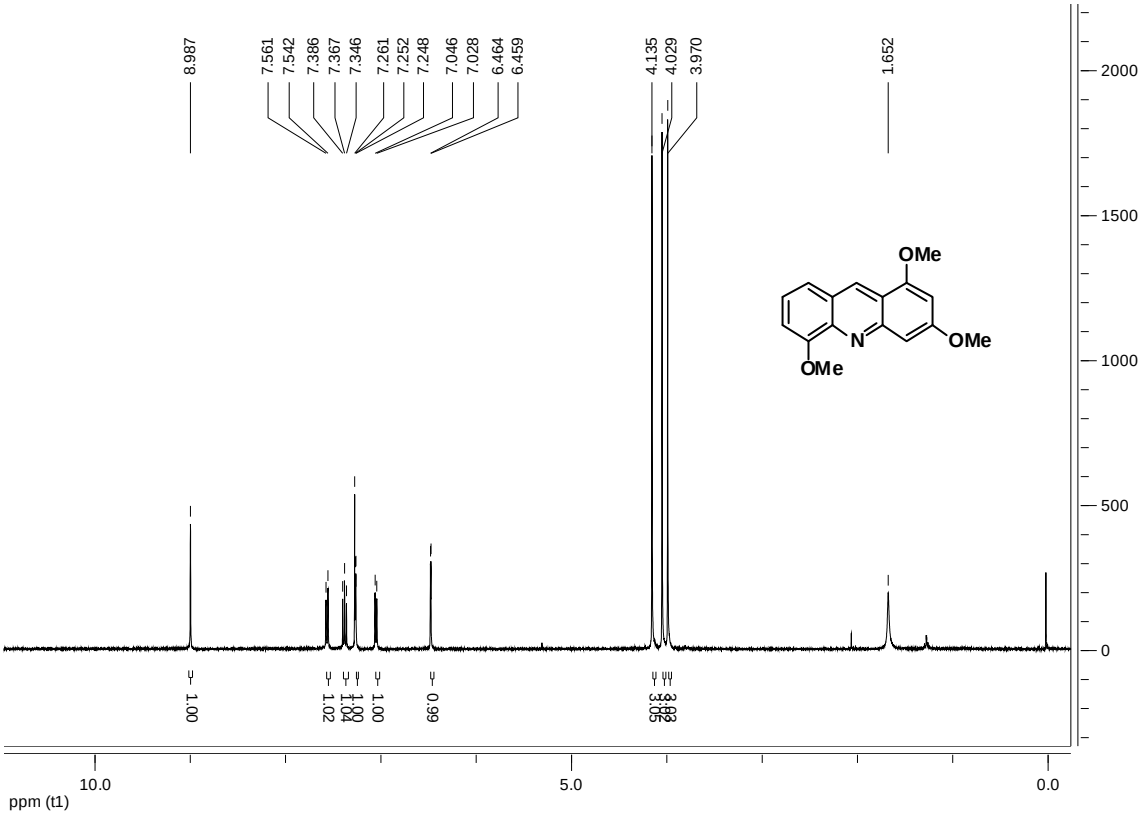
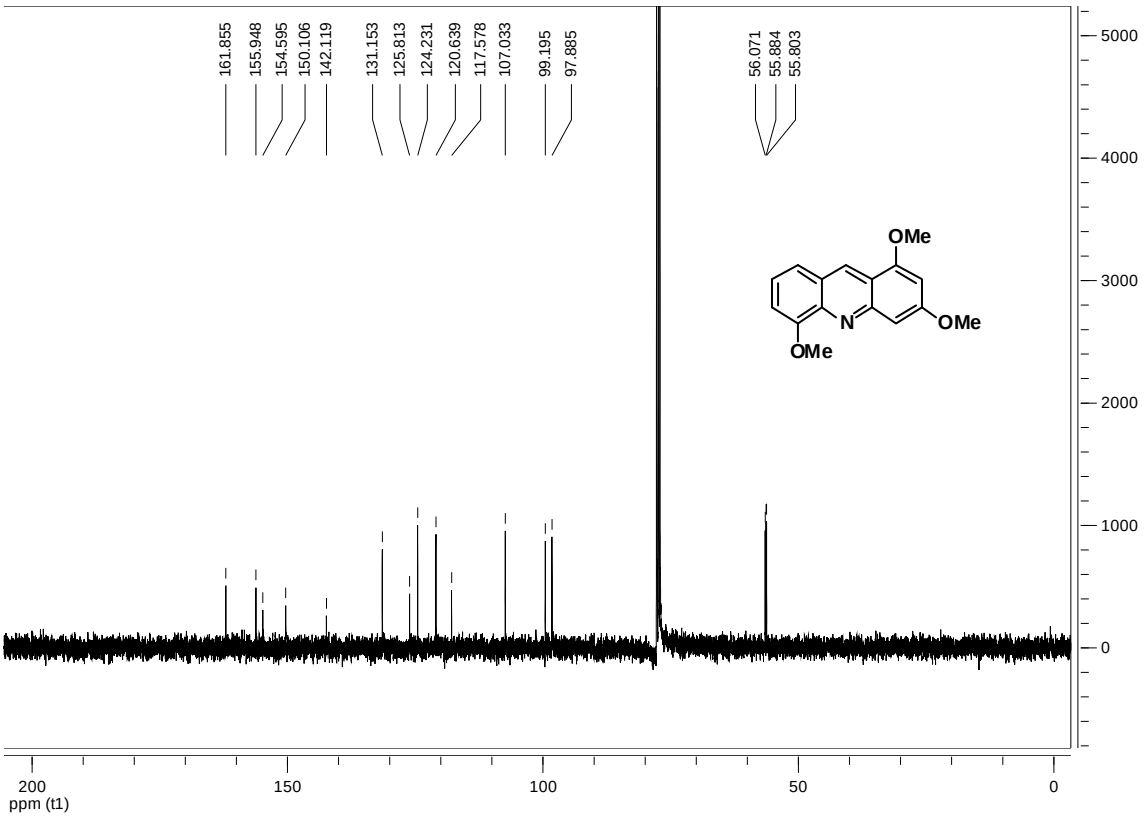


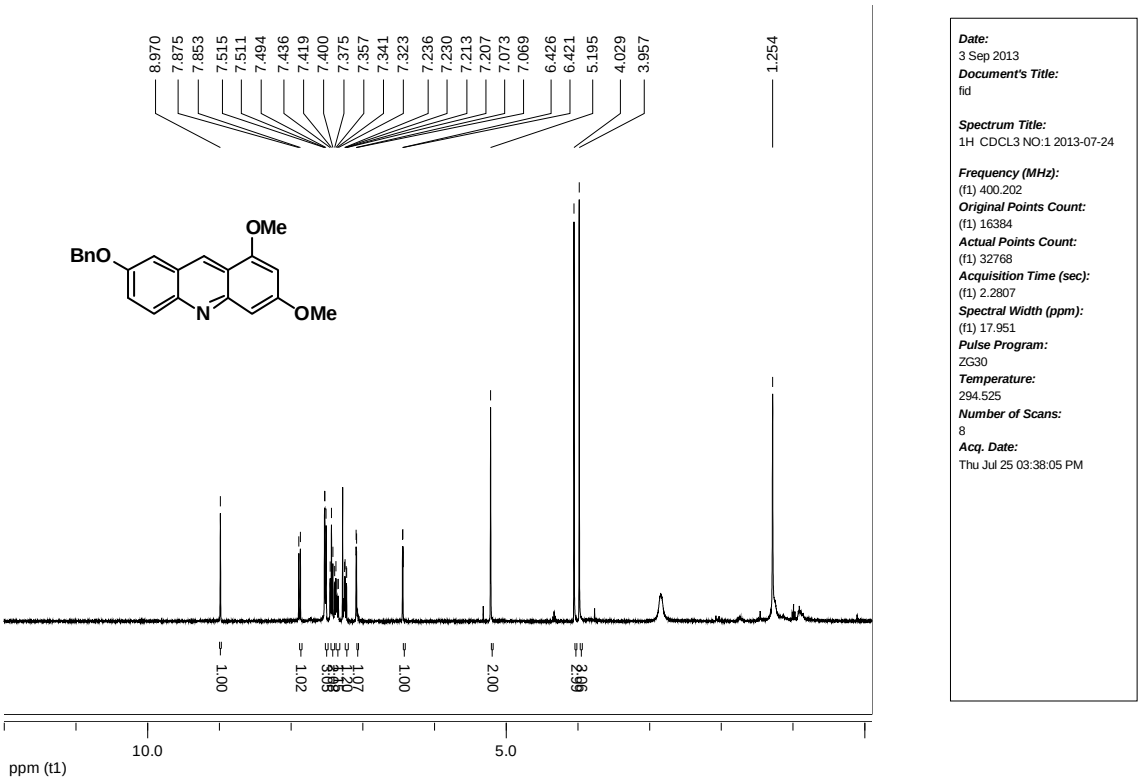
^{1}H NMR of 3f



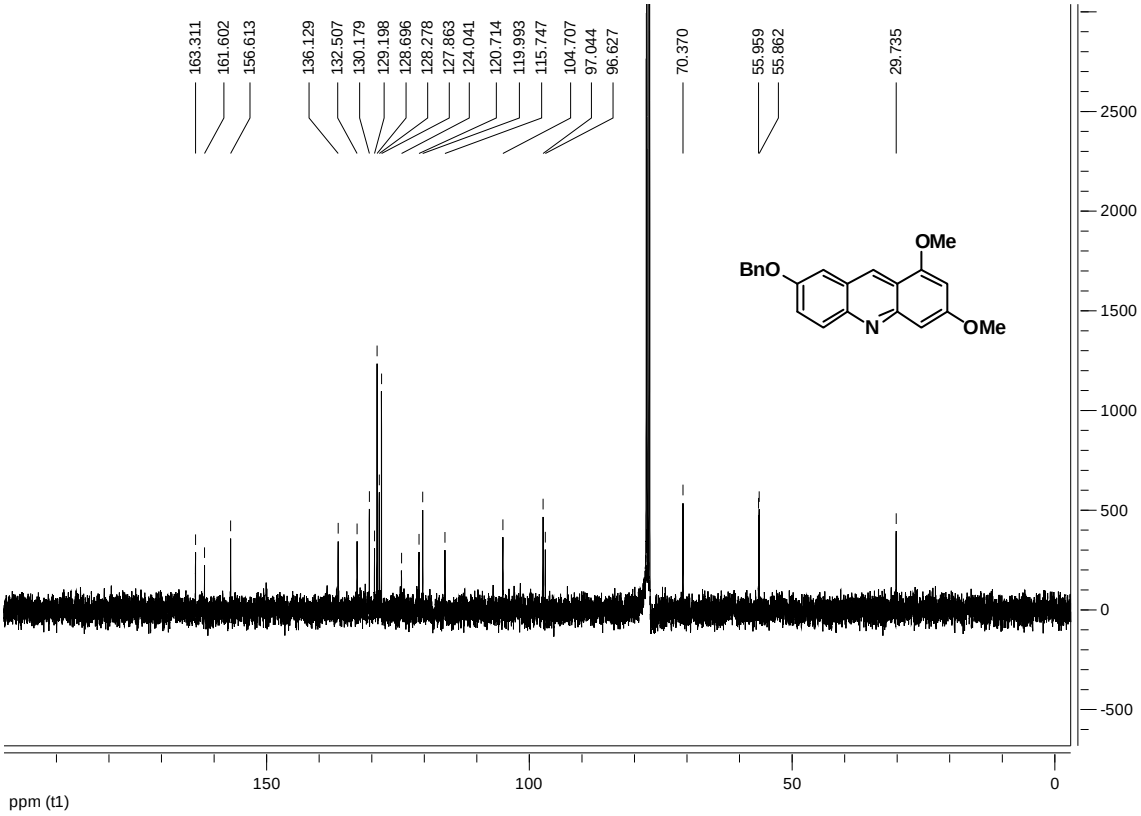
^{13}C NMR of 3f



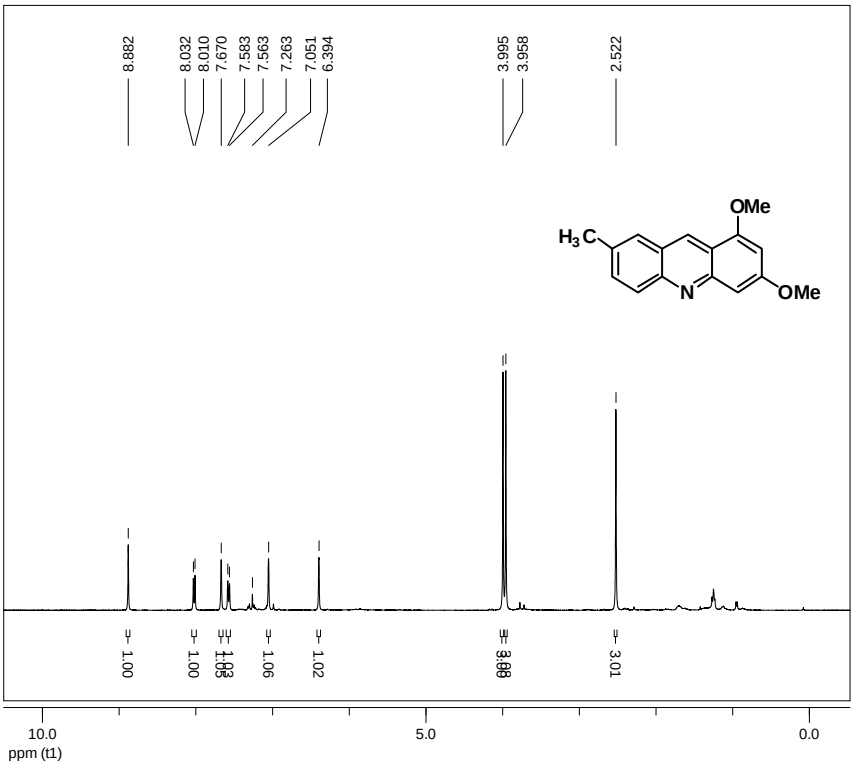
^{1}H NMR of 3g



^{13}C NMR of 3g



^{1}H NMR of 3h



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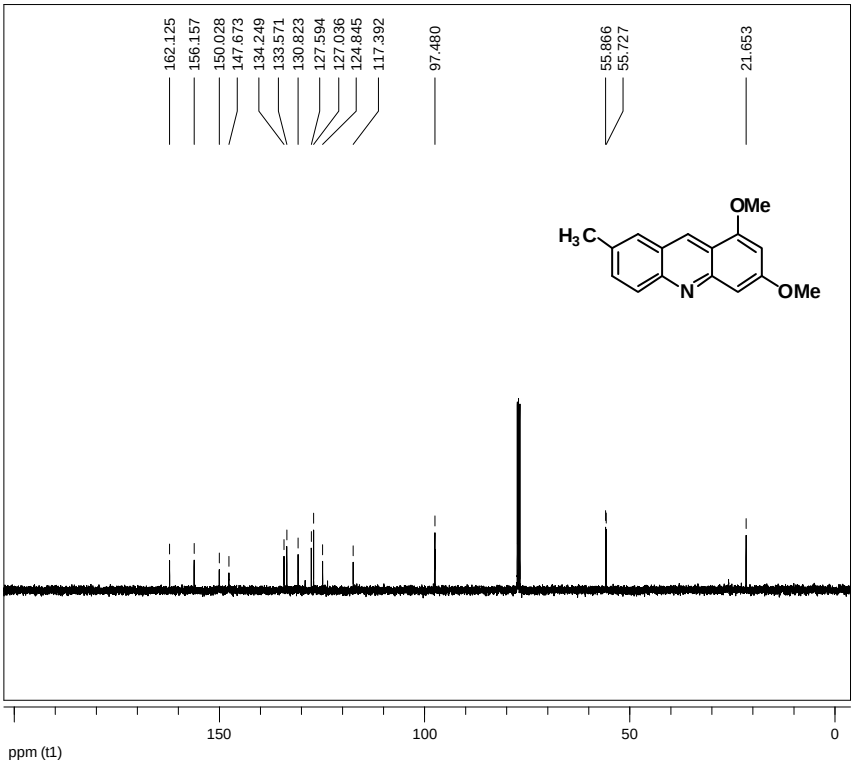
^{13}C NMR of 3h



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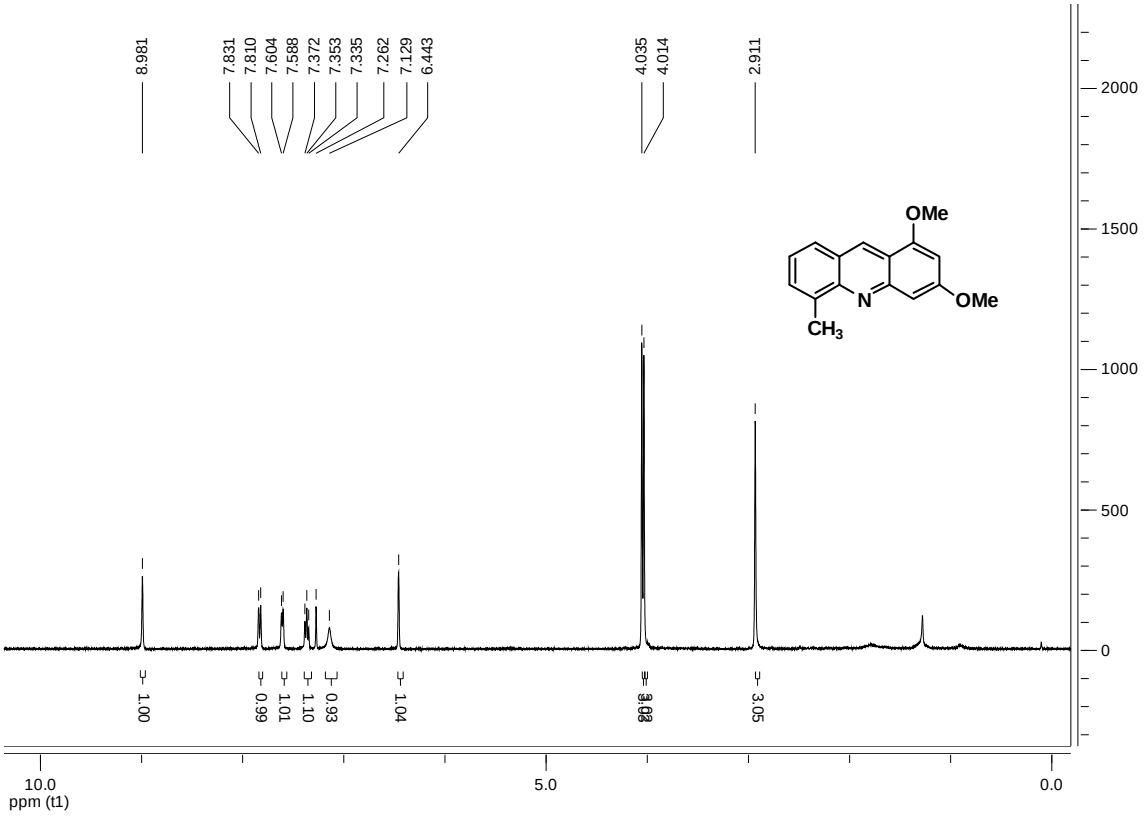
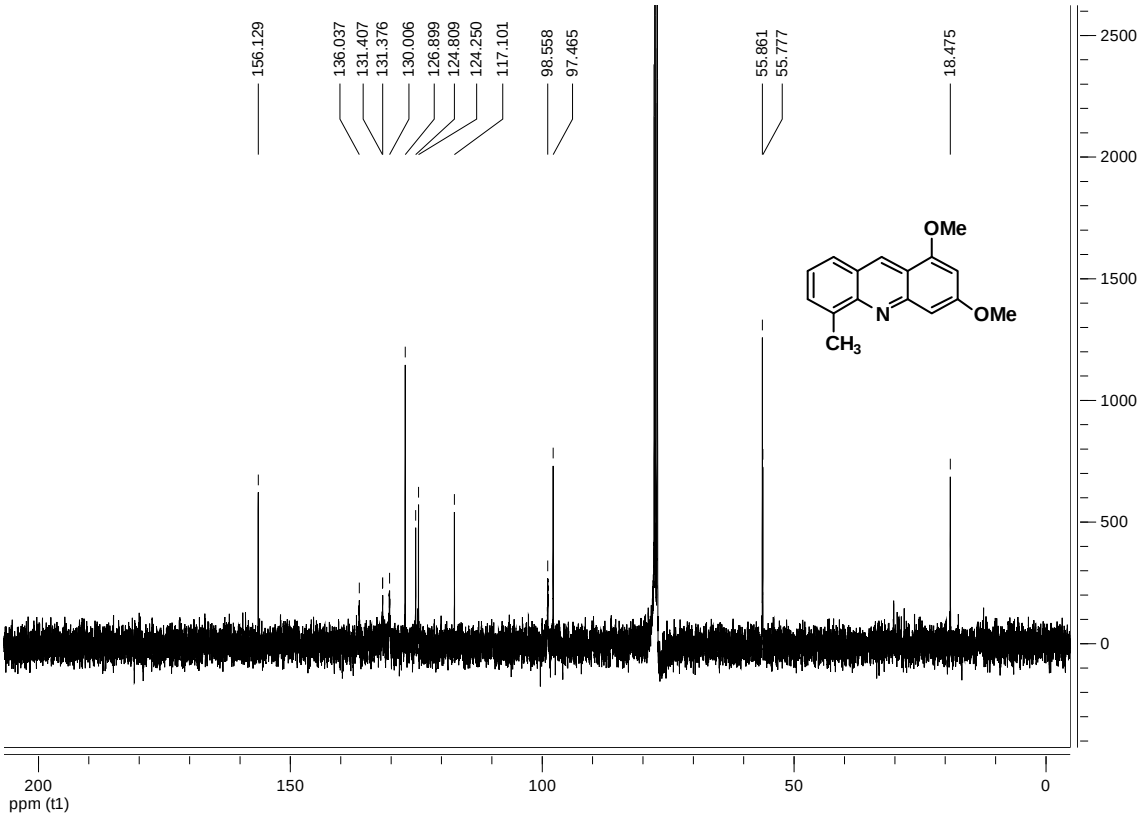
^{1}H NMR of 3i



^{13}C NMR of 3i



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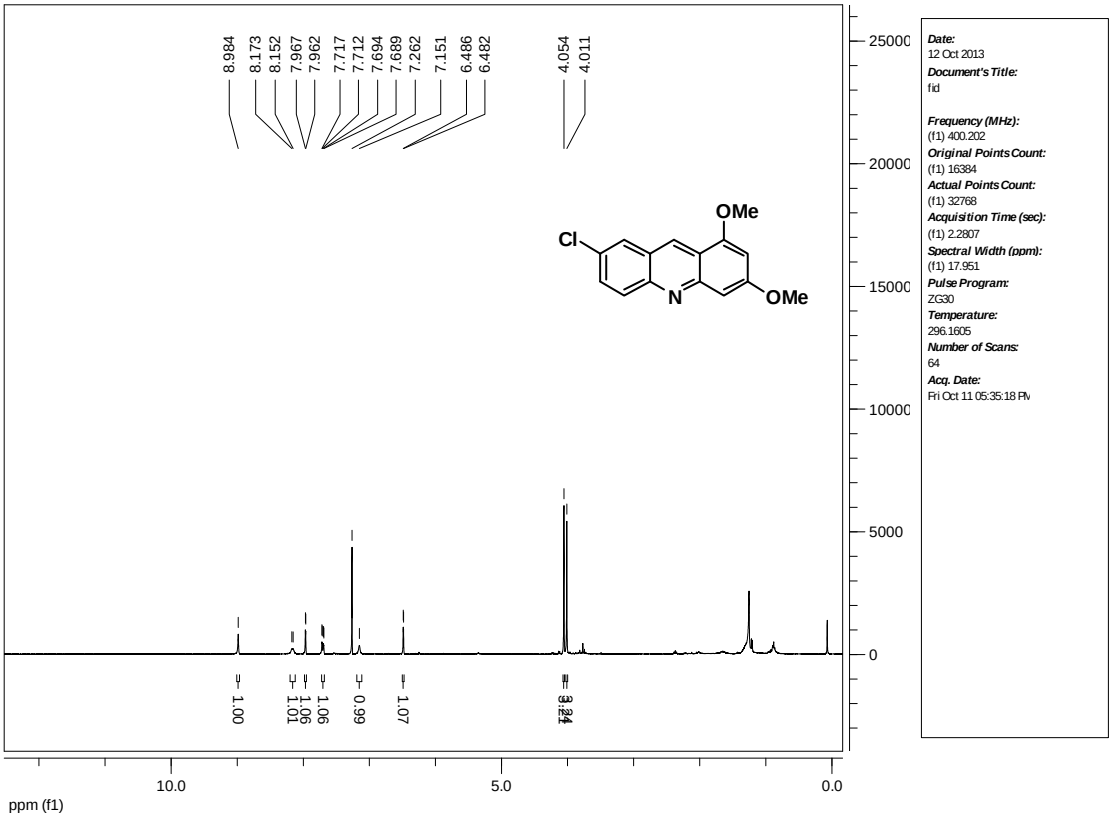
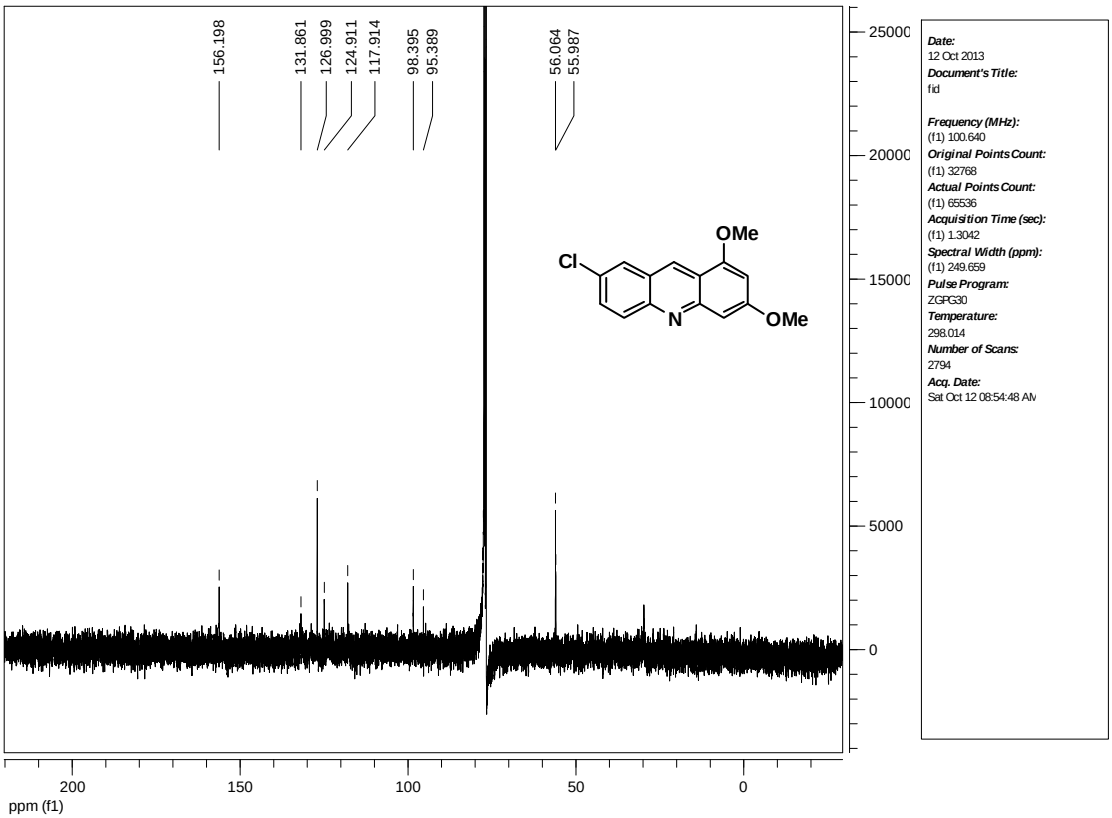


^{13}C NMR of 3j



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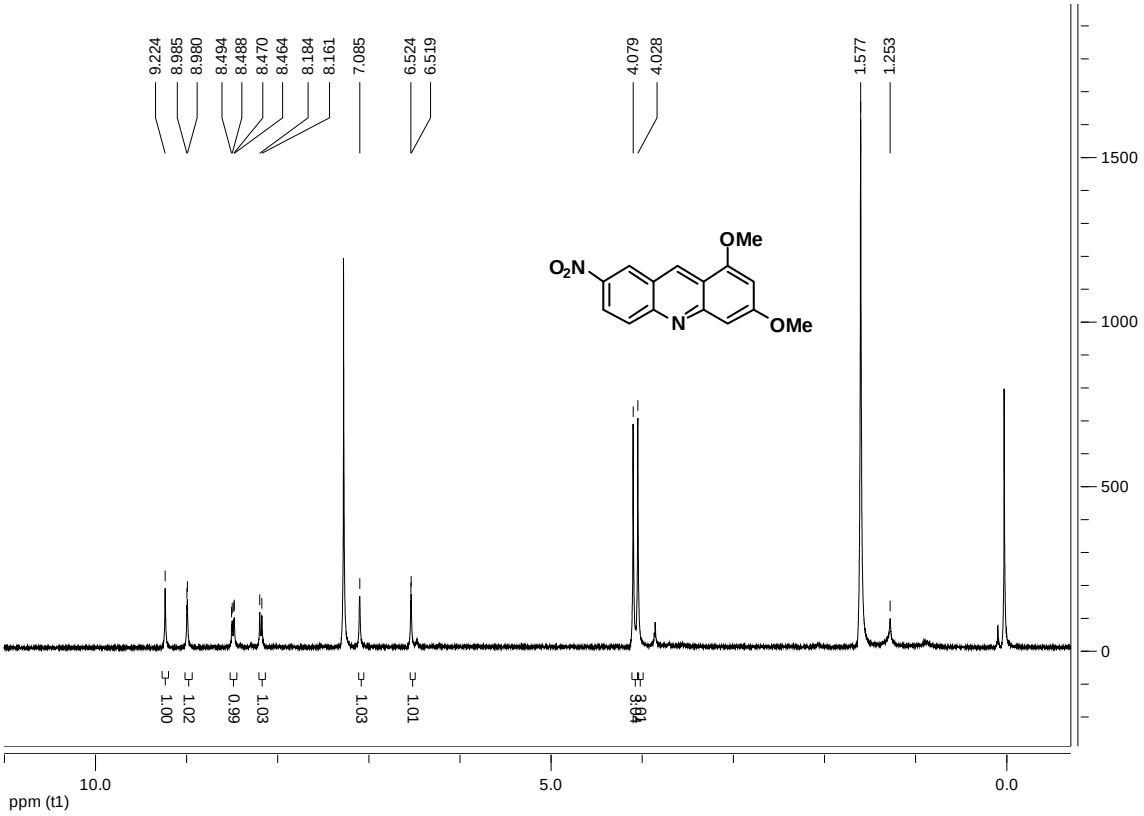

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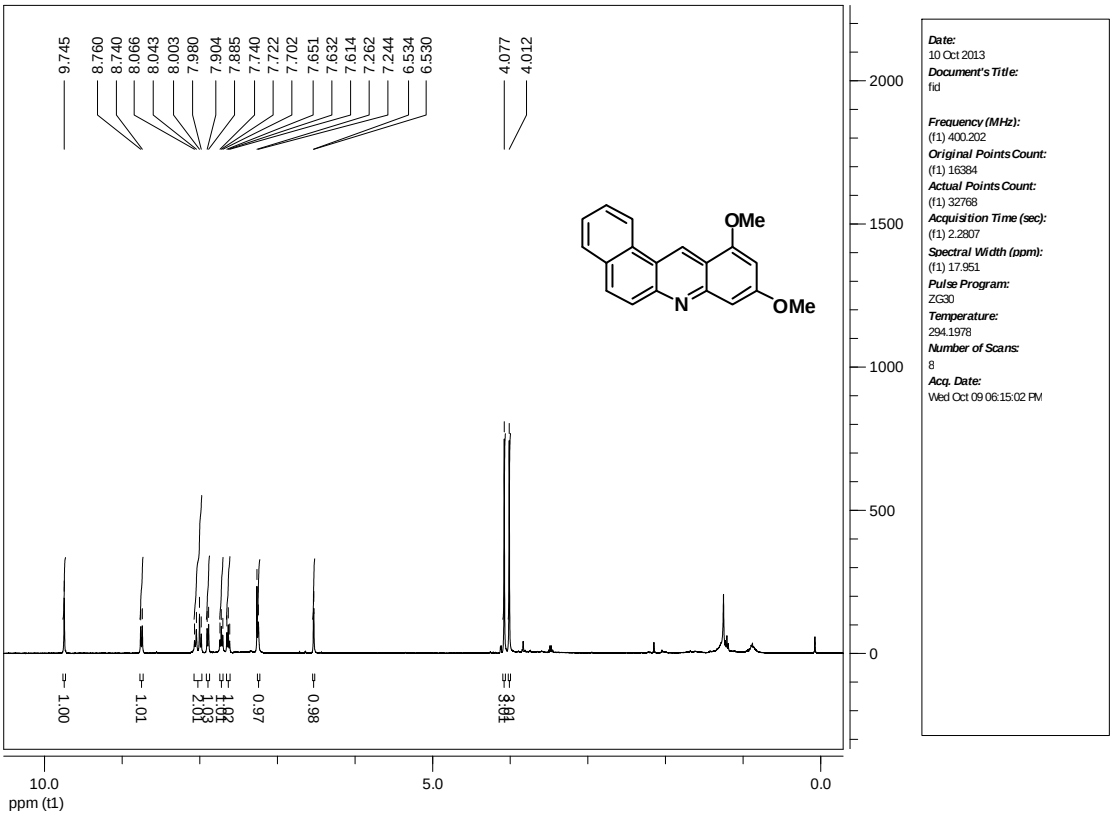

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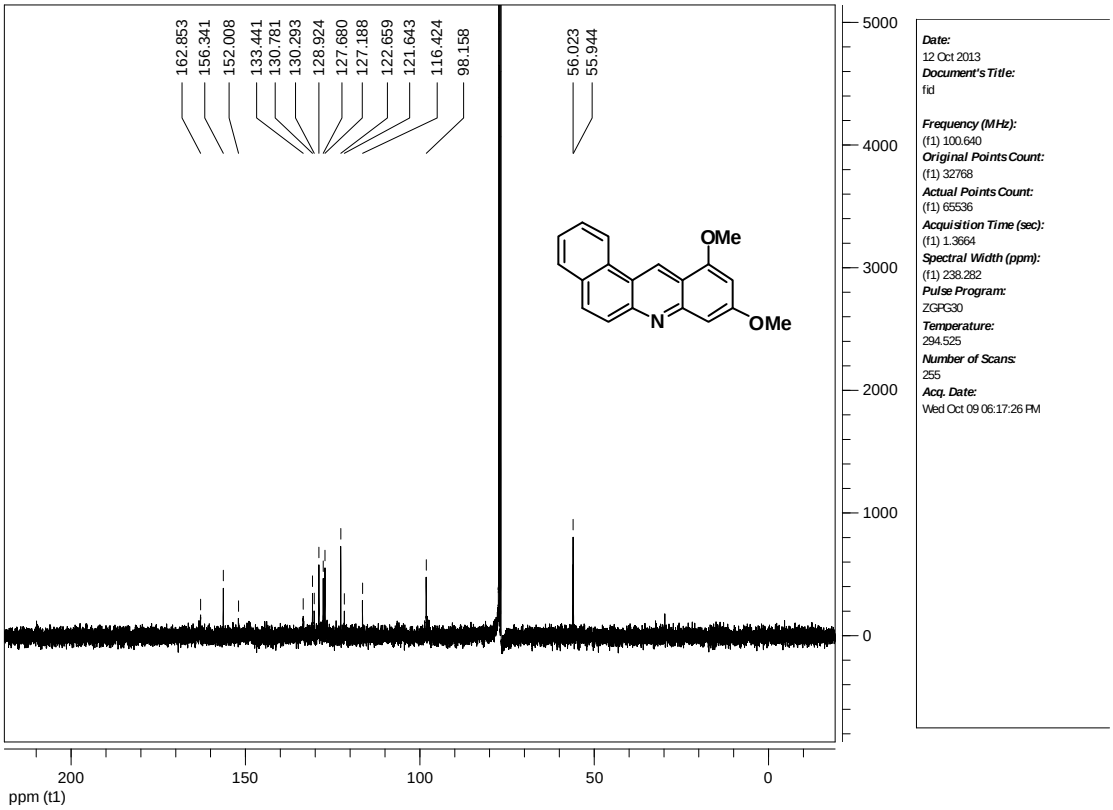

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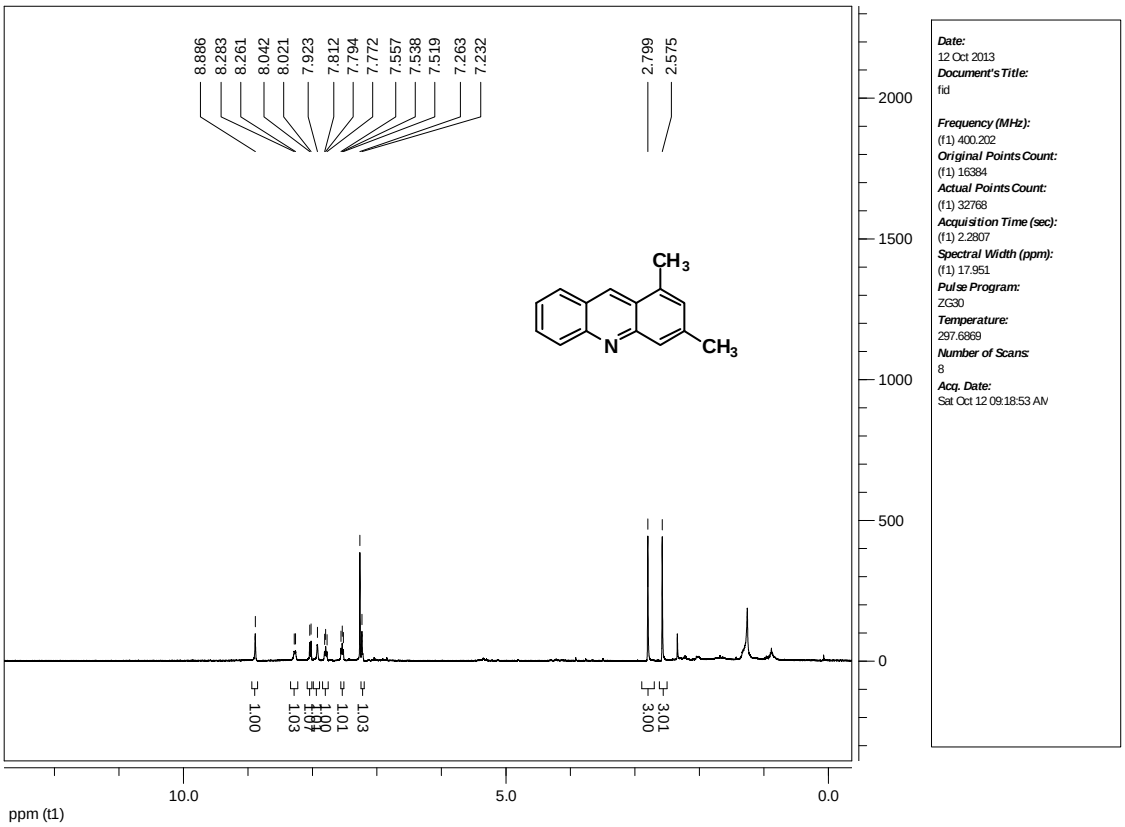

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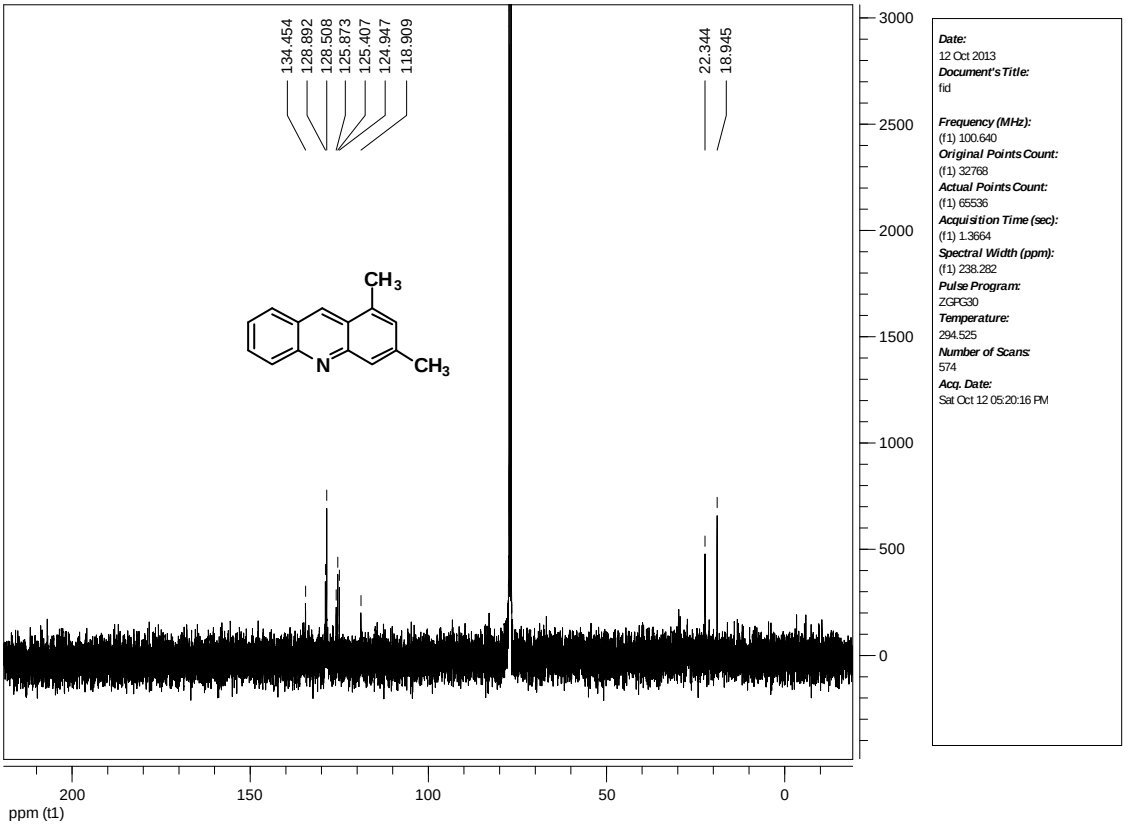
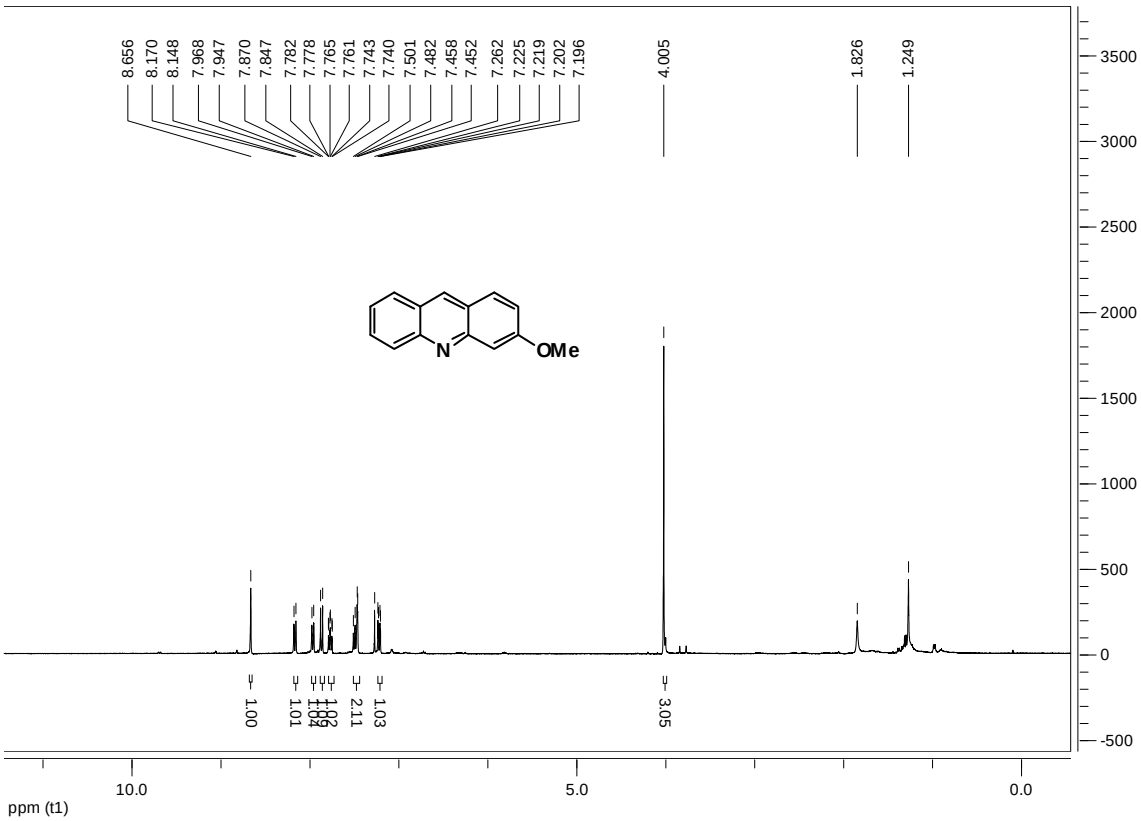


^{1}H NMR of 3n



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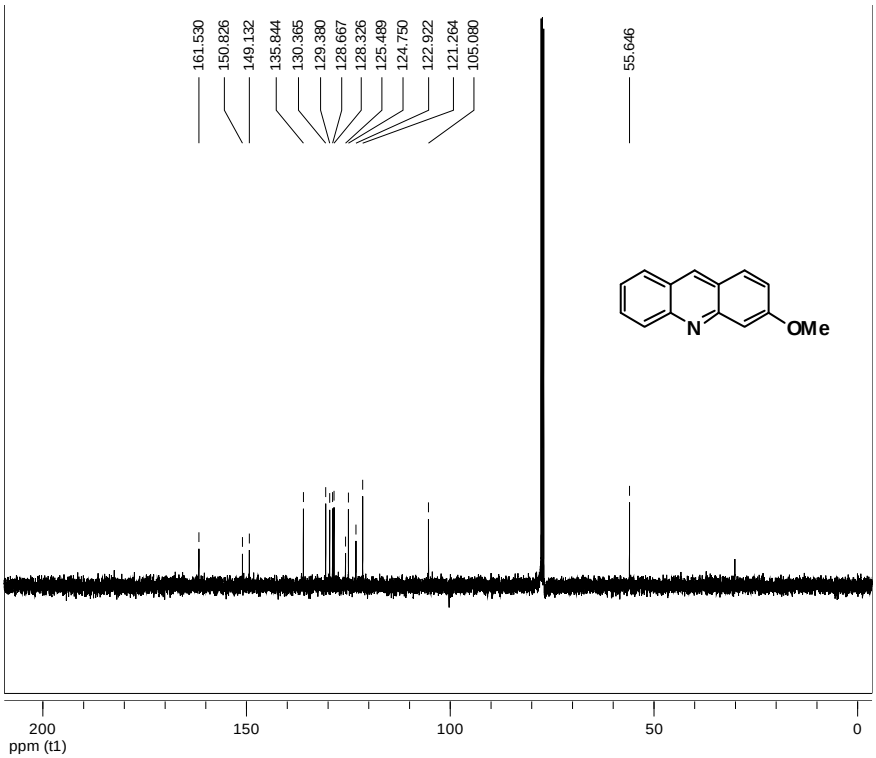

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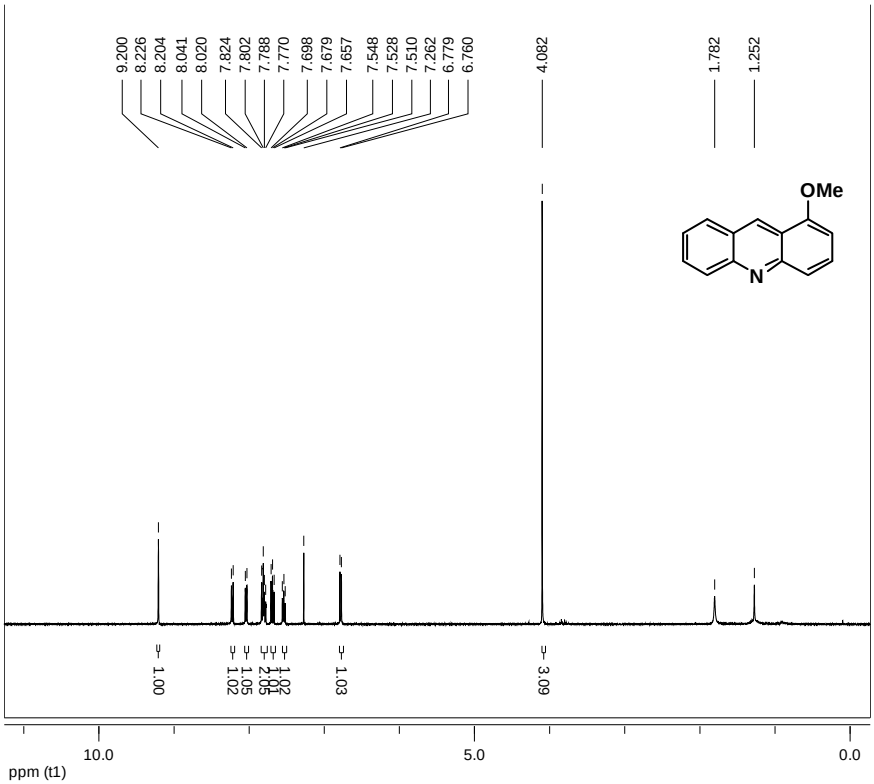

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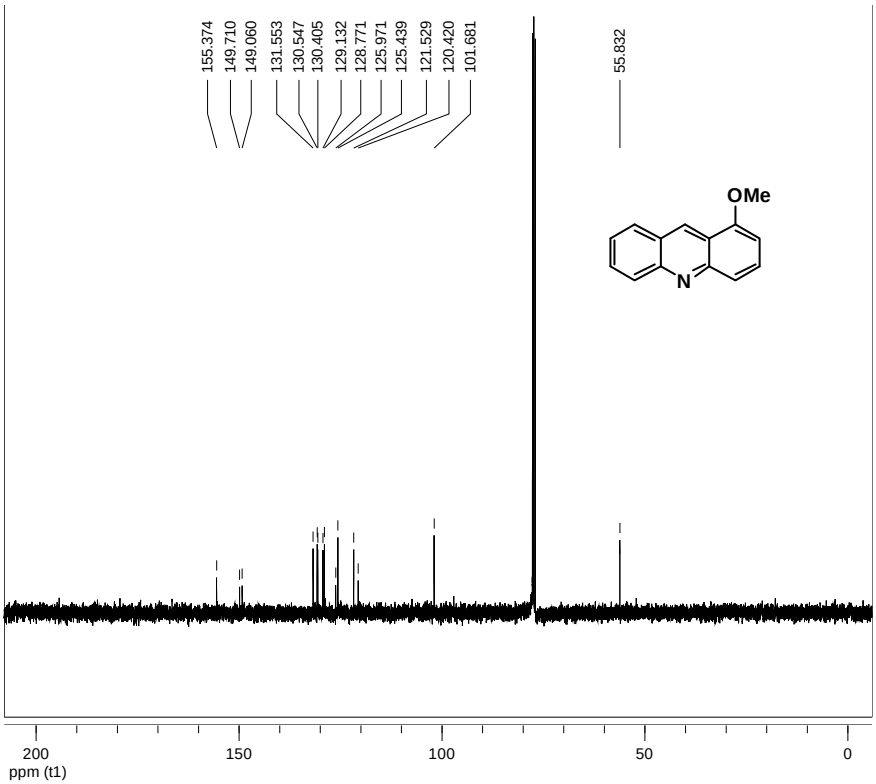
^{13}C NMR of 3n'



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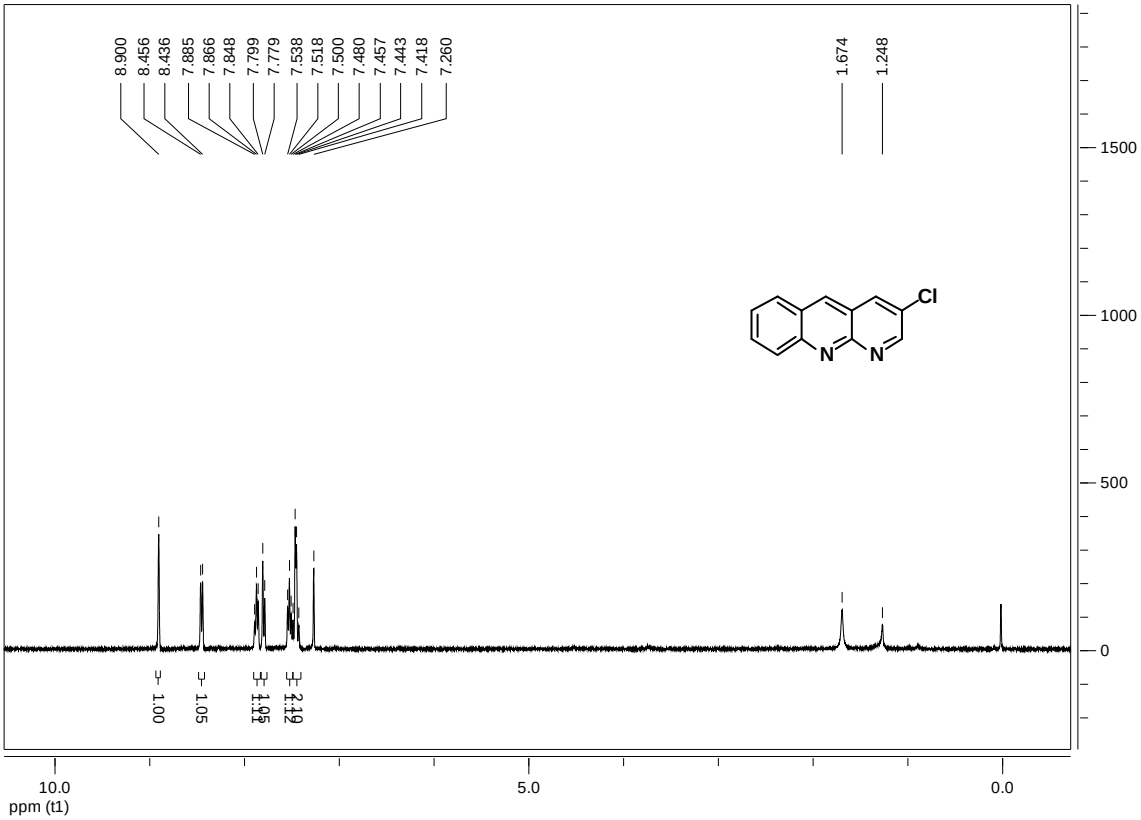
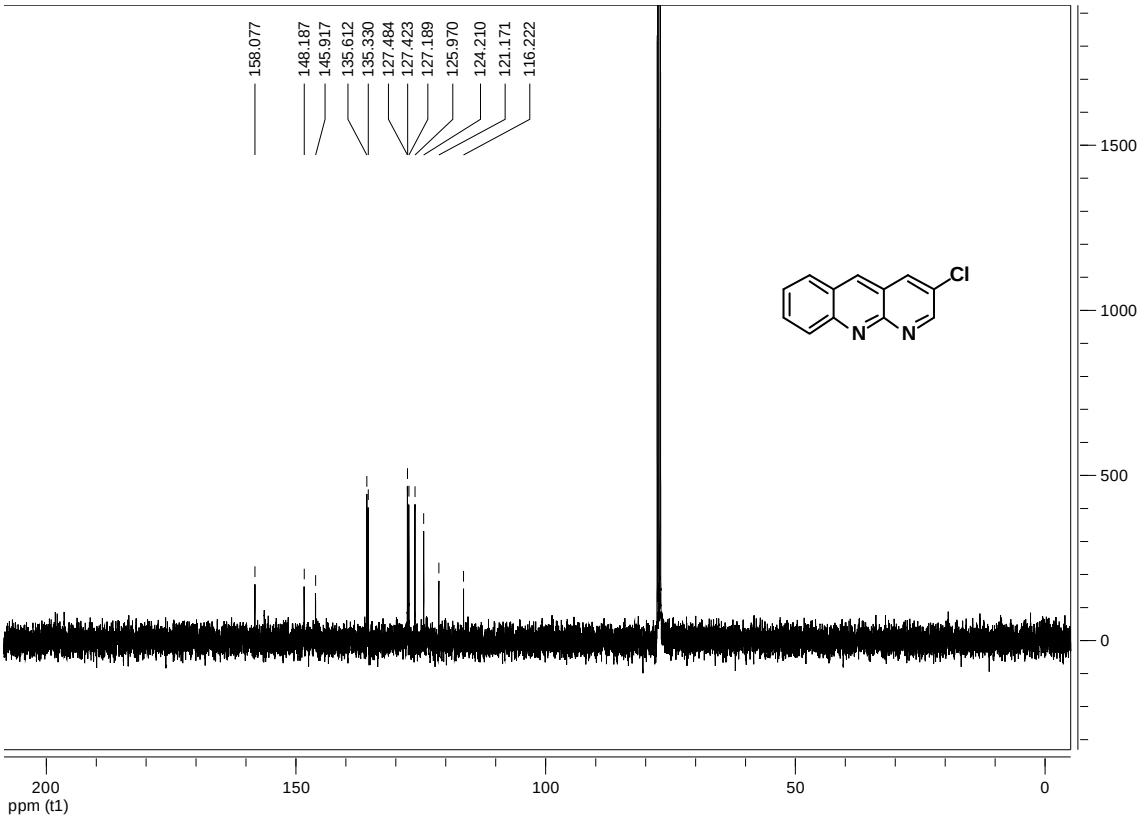
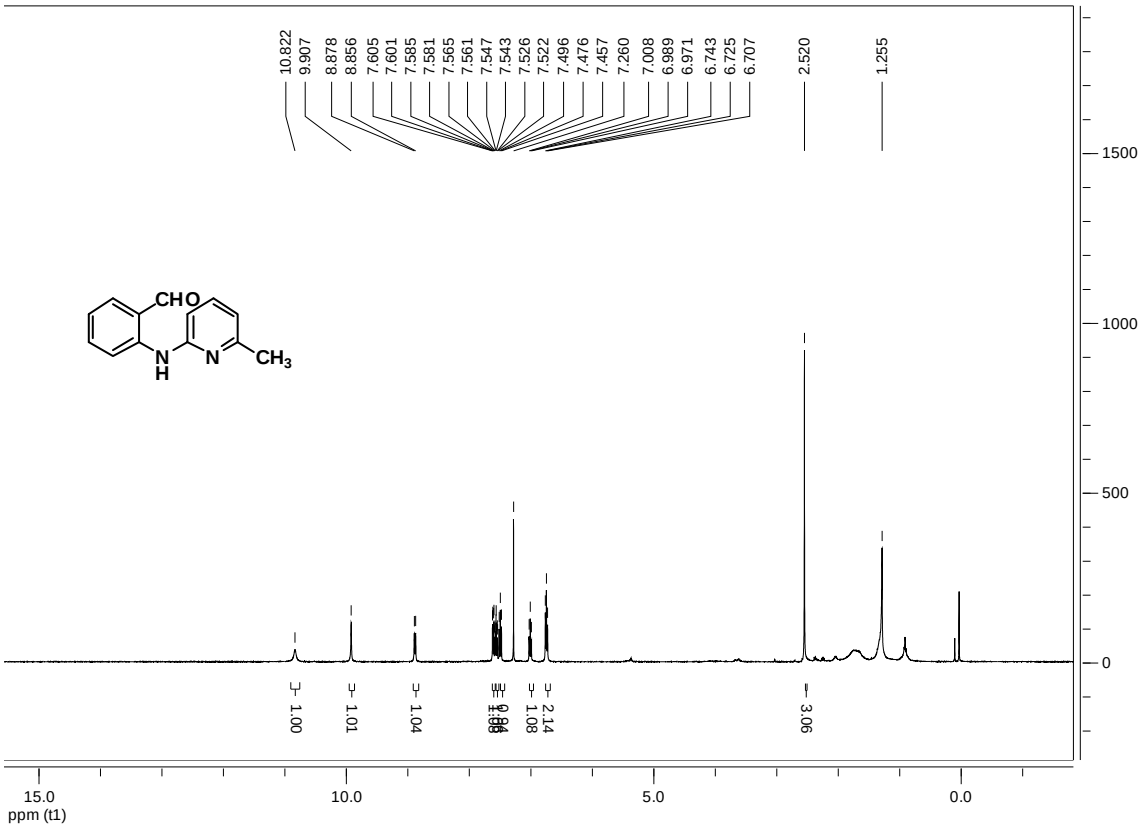
^{1}H NMR of 3o



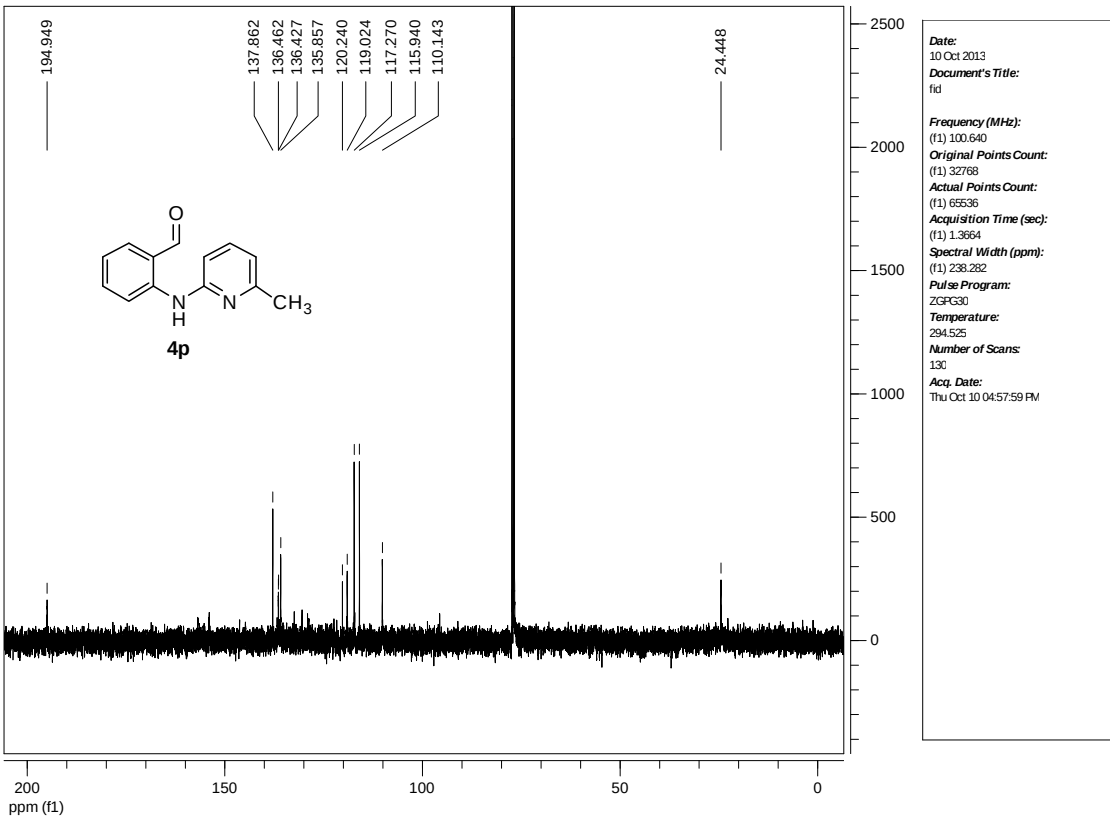
^{13}C NMR of 3o



^{1}H NMR of 4p



^{13}C NMR of 4p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