Supplementary Materials for:

Mild, green copper/4-dimethylaminopyridine catalysed aerobic oxidation of alcohols mediated by nitroxyl radicals in water

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Experimental Details

General Considerations. 4-dimethylaminopyridine (DMAP), 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO), 9-azabicylco[3.3.3]nonane N-oxyl (ABNO), and other reagents and solvents were purchased from Sigma-Aldrich in the US and used as received. All reactions were performed at ambient conditions. ^{1}H NMR spectra were recorded on a Bruker Avance III 400 NMR spectrometer. Solution electronic absorption were measured on a Shimadzu UV-1800 UV-Vis spectrophotometer and FT-IR spectra were obtained on a Nicolet Avatar 370 DTGS instrument with solid samples using a Golden Gate ATR accessory. GC-MS analysis was carried out on a Shimadzu GCMS-QP2010S gas chromatograph mass spectrometer.

General procedure for Cu^I/DMAP catalyzed aerobic oxidation. Under typical conditions, the reactions were performed in flasks fitted with water circulated condensors which are open to the air. 1.0 mmol of alcohol substrate, DMAP (0.10 mmol, 10 mol%), CuCl (0.050 mmol, 5 mol%) and TEMPO or ABNO (0.050 mmol, 5 mol%) were placed in the flask, to which 5 cm^3 of deionized water was sequentially added. The reaction was allowed to stir rigorously upon exposure to the air at room temperature for indicated times, after which ethyl acetate was then added for the extraction (2 × 8 cm^3) (Fig. S1). The combined organic phase was isolated and solvent was removed by a rotary evaporator under reduced pressure. A little amount of the crude products were diluted with dichloromethane and analyzed by GC-MS. The products were passed through a silica gel filter and washed with ethyl acetate. In a few cases in Table 1 when GC

conversions were less than 95%, column chromatography (eluent: hexane/ethyl acetate) was applied to purify the products. Isolated products were characterized by ^{1}H NMR and GC-MS with spectra matching those reported previously[1] or authentic samples.

Synthesis of 1. DMAP (61.0 mg, 0.500 mmol) and 2,2,6,6-tetramethylpiperidinyl-1-oxyl (31.2 mg, 0.200 mmol) were dissolved in CH_2Cl_2/CH_3OH (9.0 cm^3, v/v, 2:1), to which a solution of $CuCl_2 \cdot 2H_2O$ (84.4 mg, 0.500 mmol) in CH_3OH (4.0 cm^3) was added, followed by benzylic alcohol (108 mg, 1.00 mmol) under stirring at room temperature. The resulting light-brown solution was allowed to stir for 10 min, then filtered to remove the grey-green precipitate. Slow evaporation of the filtrate over 2 days upon exposure to the air resulted in the formation of yellow-brown blocks, which was suitable for single-crystal X-ray structural analysis. The bulk product was collected by decanting the solvent and washed with MeOH and dried in vacuo. Yield: 35.7 mg (28.2%). UV-Vis λ_{max}/nm (2.0×10^{-5} mol dm^{-3}, CH_2Cl_2) 275 ($\varepsilon/10^3$ dm^3 mol^{-1} cm^{-1} 55.6), 372 (8.5), 446sh (6.85), 615 (0.450). FT-IR (solid, cm^{-1}): 1697s, 1614s, 1536s, 1442m, 1390s, 1346w, 1309w, 1228s, 1118w, 1072s, 1020s, 948m, 808s, 763w, 747m, 687m, 649w. Elemental analysis calcd. (%) for $C_{28}H_{40}Cl_6Cu_4N_8O \cdot 0.5CH_2Cl_2$: C 33.76, H 4.08, N 11.05; found C 34.05, H 4.19, N 10.76% (Note: partial loss of co-crystallized solvent molecules from large void spaces as observed in the crystals is possible before it was submitted for microanalysis).

X-ray Structure Determination

A suitable crystal of **1** was mounted on a Cryoloop with Paratone-N oil and data was collected at 100 K with a Bruker APEX II CCD using Mo Kα radiation. Data were corrected for absorption with SADABS and structure solved by direct methods. All non-hydrogen atoms were refined anisotropically by full-matrix least squares on F^2. All non-hydrogen atoms were refined ansiotropopically by full matrix least squares on F^2 and all hydrogen atoms were placed in calculated positions with appropriate riding parameters. Diffused electron density was treated using Platon program SQUEEZE;[2] void volume of 884 Å^3 with electron count 243e was found, and this was treated as 6 dichloromethane solvent molecules and unit card was adjusted to account for changes in chemical formula, molecular mass, density and F000 value. Investigation of data as the triclinic *P*-1 yielded similar results with large void volume and indications of missing symmetry. Thus, centrosymmetric space group C2/c was chosen for presentation. Bruker suite of single crystal X-ray programs were used for data collection, structural solutions, refinements, ORTEP structure,[2] and the Fig. 1b and molecular packing figures were drawn with the program Mercury v. 2.4.[4,5] CCDC 1007017 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)

1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

Crystal data for 1: $C_{28}H_{40}Cl_6Cu_4N_8O \cdot 0.75(CH_2Cl_2)$, M = 1035.23, yellow-brown block, monoclinic, space group $C2/c$, a = 22.6652(13), b = 22.2630(13), c = 19.2193(11) Å, β = 92.319(3), U = 9690.0(10) Å^3, Z = 8, D_c = 1.419 Mg m^{-3}, μ(Mo-Kα) = 2.176 mm^{-1}, T =100(2) K. Total 9917 reflections, 9572 unique. Refinement of 7403 reflections (432 parameters) with $I > 2\sigma(I)$ converged at final R_1 = 0.0286 (R_1 all data = 0.0426), wR_2 = 0.0668 (wR_2 all data = 0.0707), GOF = 1.054.

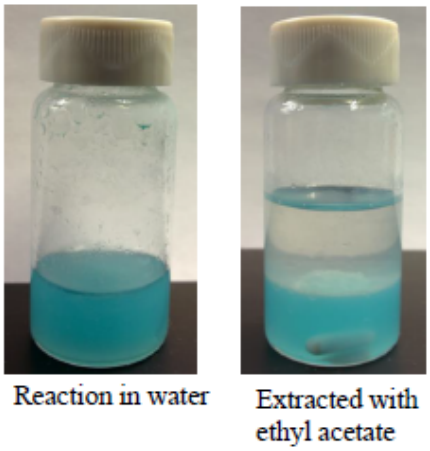

Fig. S1. The photographs of the reaction mixtures in water (left) and after extraction with ethyl acetate (right).

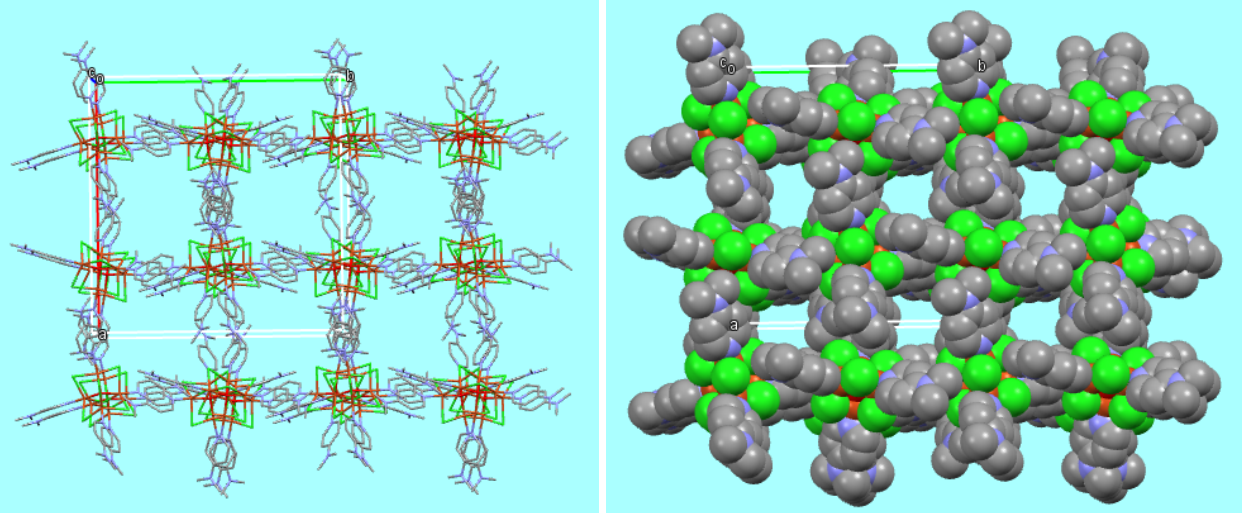

Fig. S2. The crystal packing in **1** showing porous void channels existing in the 3-dimensional supramolecular framework formed by weak intermolecular C-H...Cl hydrogen bonds and π–stacking as viewed along the crystallographic *c* axis.

Table S1 The screening for various copper salt catalysed aerobic oxidation of benzylic alcohol in water.[a]

Entry	Copper salts	Conv. [%][b]
1[c]	CuCl	89
2	CuCl	>99
3	CuBr	90
4	CuI	>99
5	$CuCl_2$	79
6	$Cu(OAc)_2$	80
7	$Cu(NO_3)_2$	66

[a] Condition: 1.0 mmol of the substrate, 0.10 mmol (5 mol%) of copper salts and 0.10 mmol (10 mol%) of DMAP, and 0.050 mmol (5 mol%) of TEMPO in 5 mL water, 1 atm. air, room temperature, 5 h. [b] Conversions based on GC-MS analysis. [c] reaction run for 3 hrs.

Spectroscopic data:

^{1}H NMR and GC-MS data for isolated products:

benzaldehyde (colorless oil, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.90-7.88 (m, 2H), 7.66-7.62 (m, 1H), 7.56-7.52 (m, 2H). GC-MS (m/z): 106 (calc. 106)

4-methylbenzaldehyde (white solid, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 2.45 (s, 3H, H^{CH3}). GC-MS (m/z): 120 (calc. 120).

4-methoxybenzaldehyde (colorless oil, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.90 (s, 3H, H^{OCH3}). GC-MS (m/z): 136 (calc. 136).

2-methylbenzaldehyde (white solid, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 7.80 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.48 (td, *J* = 7.5, 1.6 Hz, 1H), 7.36 (td, *J* = 7.6, 1.4 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.23 – 7.11 (m, 1H), 2.67 (s, 3H). GC-MS (m/z): 120 (calc. 120).

2-methoxybenzaldehyde (white solid, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.48 (s, 1H), 7.83 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.3, 1.8 Hz, 1H), 7.03 (d, *J* = 15.0 Hz, 1H), 7.04-6.94 (overlapping, m, 1H), 3.94 (s, $3H^{OCH3}$). GC-MS (m/z): 136 (calc. 136).

3,4-dimethoxybenzaldehyde (white solid, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.42 (s, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 3.98 (s, 3H, H^{OCH3}), 3.95 (s, 3H, H^{OCH3}). GC-MS (m/z): 166 (calc. 166).

4-nitrobenzaldehyde (pale-yellow solid, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.41 (d, *J* = 8.6 Hz, 2H), 8.09 (d, *J* = 8.7 Hz, 2H). GC-MS (m/z): 151 (calc. 151).

4-chlorobenzaldehyde (white solid, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H). GC-MS (m/z): 140 (calc. 140).

4-bromobenzaldehyde (pale-yellow solid, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H). GC-MS (m/z): 184 (calc. 184).

4-iodobenzaldehyde (pale-yellow solid, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H). GC-MS (m/z): 232 (calc. 232).

2-chlorobenzaldehyde (white solid, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.52 (s, 1H), 7.96 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.43 (t, *J* = 7.4 Hz, 1H). GC-MS (m/z): 140 (calc. 140).

4-(2-furyl)benzaldehyde (white solid, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.96 – 7.84 (m, 2H), 7.83 – 7.74 (m, 2H), 7.48 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.41 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.15 (dd, *J* = 5.1, 3.6 Hz, 1H). GC-MS (m/z): 188 (calc. 188).

2-formylfuran (colorless oil, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.70-7.69 (m, 1H), 7.26-7.25 (m, 1H), 6.61 (dd, *J* = 3.6, 1.7 Hz, 1H). GC-MS (m/z): 96 (calc. 96).

2-formylthiophene (pale-yellow oil, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (d, *J* = 1.1 Hz, 1H), 7.82 (d, *J* = 3.6 Hz, 1H), 7.80 (d, *J* = 4.8 Hz, 1H), 7.25 (dd, *J* = 4.8, 3.6 Hz, 1H). GC-MS (m/z): 112 (calc. 112).

3-pyridinecarboxaldehyde (white solid, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 9.09 (d, *J* = 2.1 Hz, 1H), 8.86 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.19 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.50 (dd, *J* = 7.8, 4.8 Hz, 1H). GC-MS (m/z): 107 (calc. 107).

cinnamyl aldehyde (pale-yellow oil, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (d, 1H, *J* = 7.2 Hz), 7.59-7.55 (m, 2H), 7.48 (d, 1H, *J* = 16.0 Hz), 7.44-7.42 (m, 3H), 6.73 (dd, 1H, *J* = 16.0, 7.6 Hz).

acetophenone (pale-yellow oil, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 2.59 (s, 3H, C*H*$_3$).

phenyl isopropyl ketone (colorless oil, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 3.55 (m, 1H), 1.20 (d, *J* = 6.7 Hz, 6H, C*H*$_3$).

3'-methoxyacetophenone (pale-yellow oil, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.6 Hz, 1H), 7.48-7.42 (m, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.08 (dd, *J* = 8.3, 2.7 Hz, 1H), 3.83 (s, 3H, OC*H*$_3$), 2.57 (s, 3H, C*H*$_3$).

3,4-dihydro-1(2*H*)-naphthalenone (white solid, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 2.94 (t, *J* = 6.0 Hz, 2H, C*H*$_2$), 2.63 (t, *J* = 6.5 Hz, 2H, C*H*$_2$), 2.16 – 2.05 (m, 2H, C*H*$_2$).

2-acetonaphenone (white solid, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.02 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.88-7.84 (m, 2H), 7.63-7.49 (m, 2H), 2.71 (s, 3H, C*H*$_3$).

benzophenone (white solid, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 4H), 7.58 (t, *J* = 7.4 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 4H).

References

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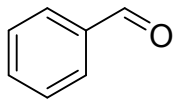
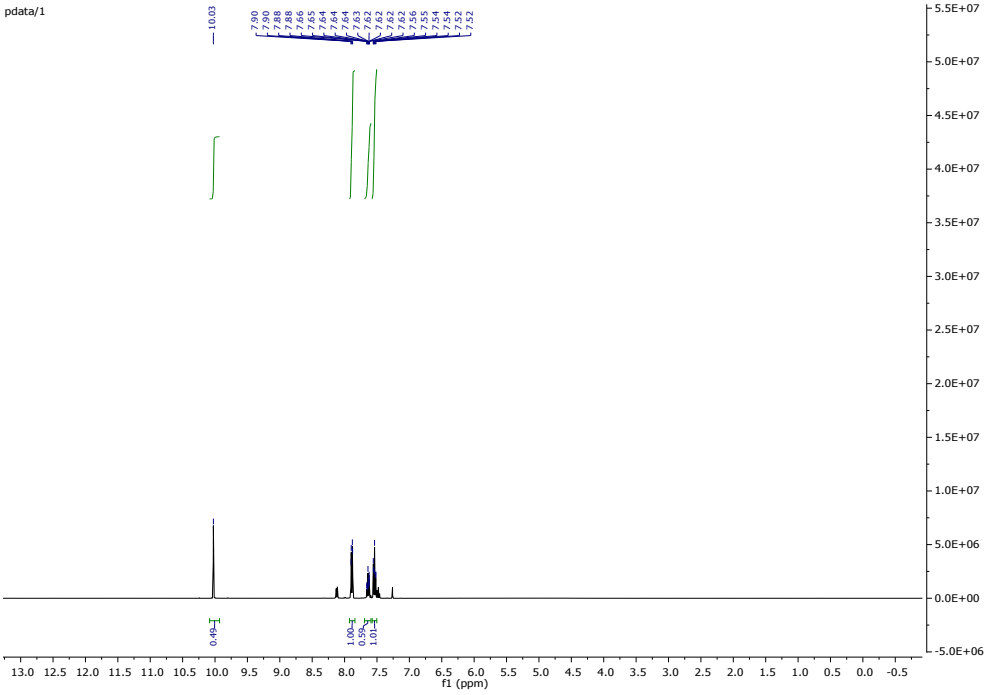
Appendix.

Copies of NMR and GC-MS data:

1. benzaldehyde (^{1}H NMR, $CDCl_3$)





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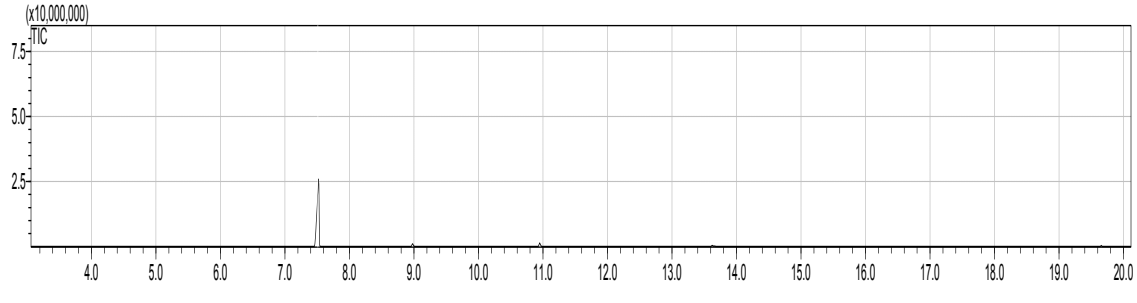
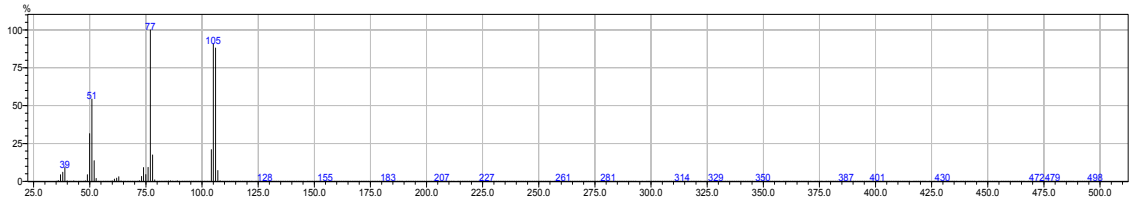
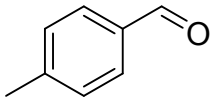
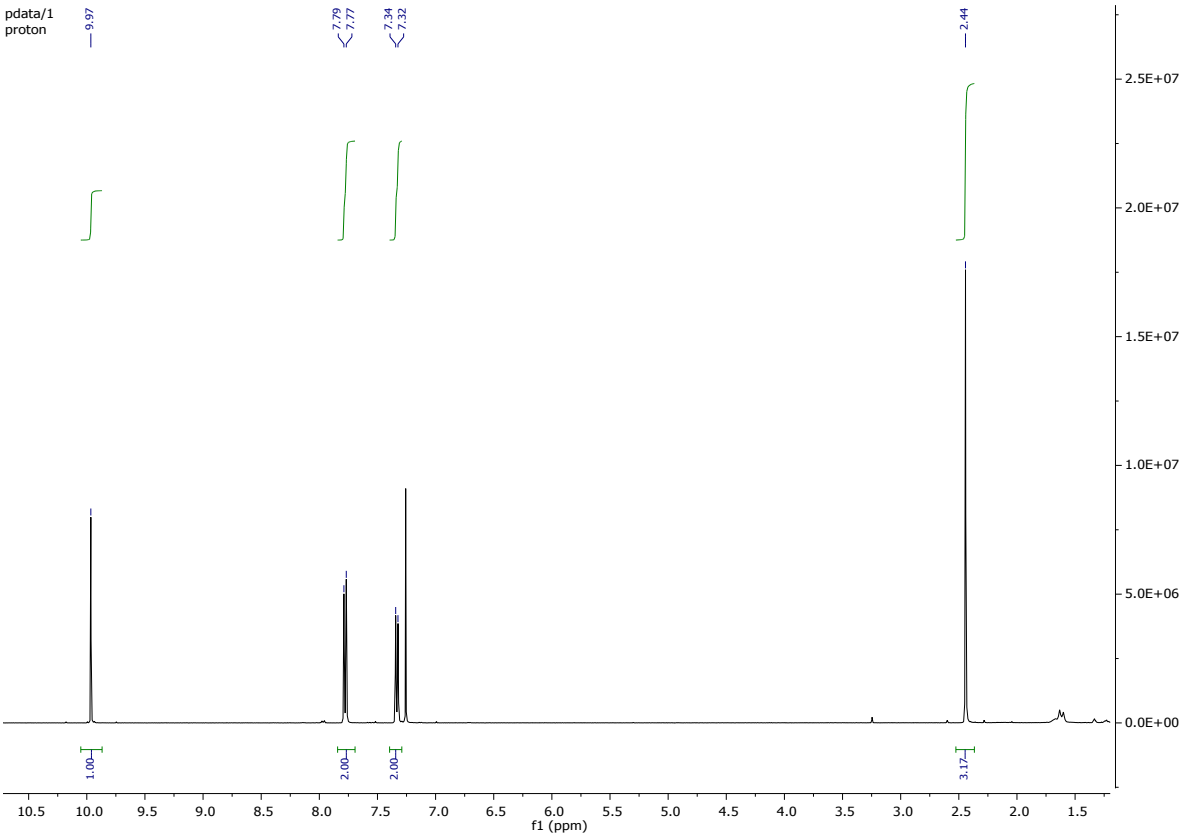




2. 4-methylbenzaldehyde (^{1}H NMR, $CDCl_3$)





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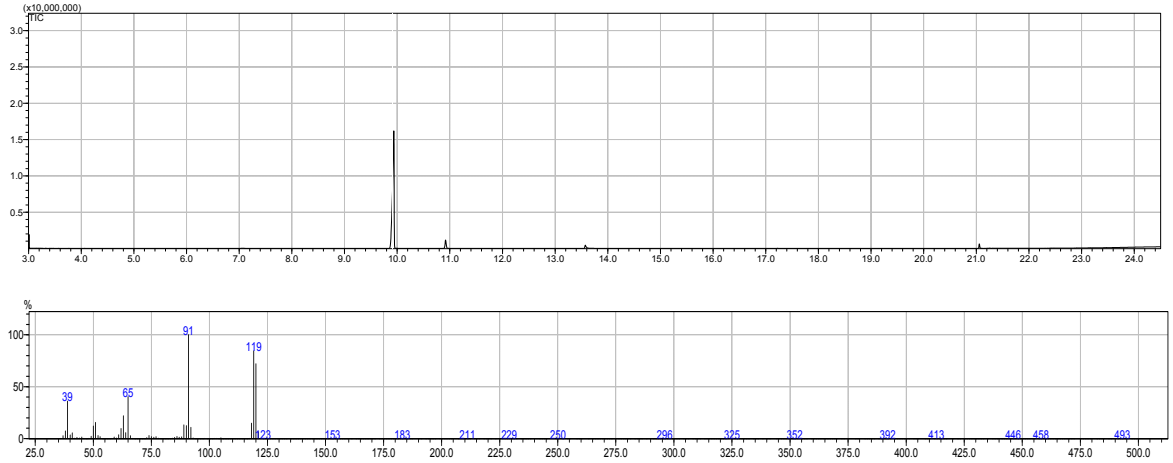
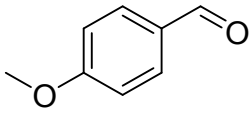
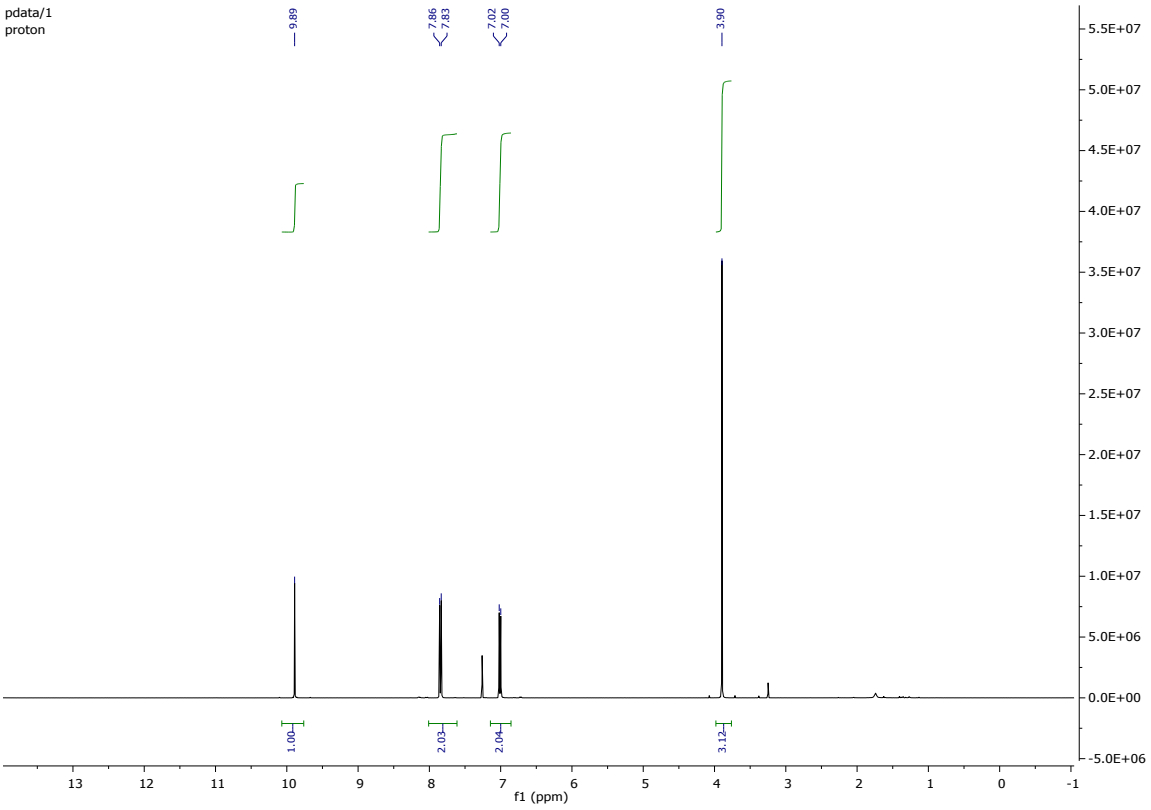


3. 4-methoxybenzaldehyde (^{1}H NMR, $CDCl_3$)





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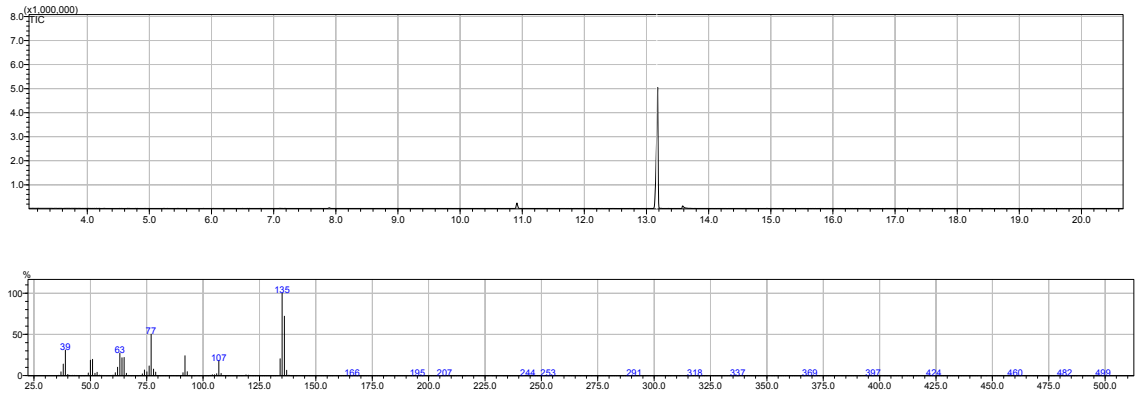
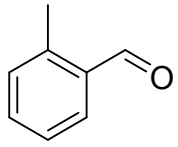
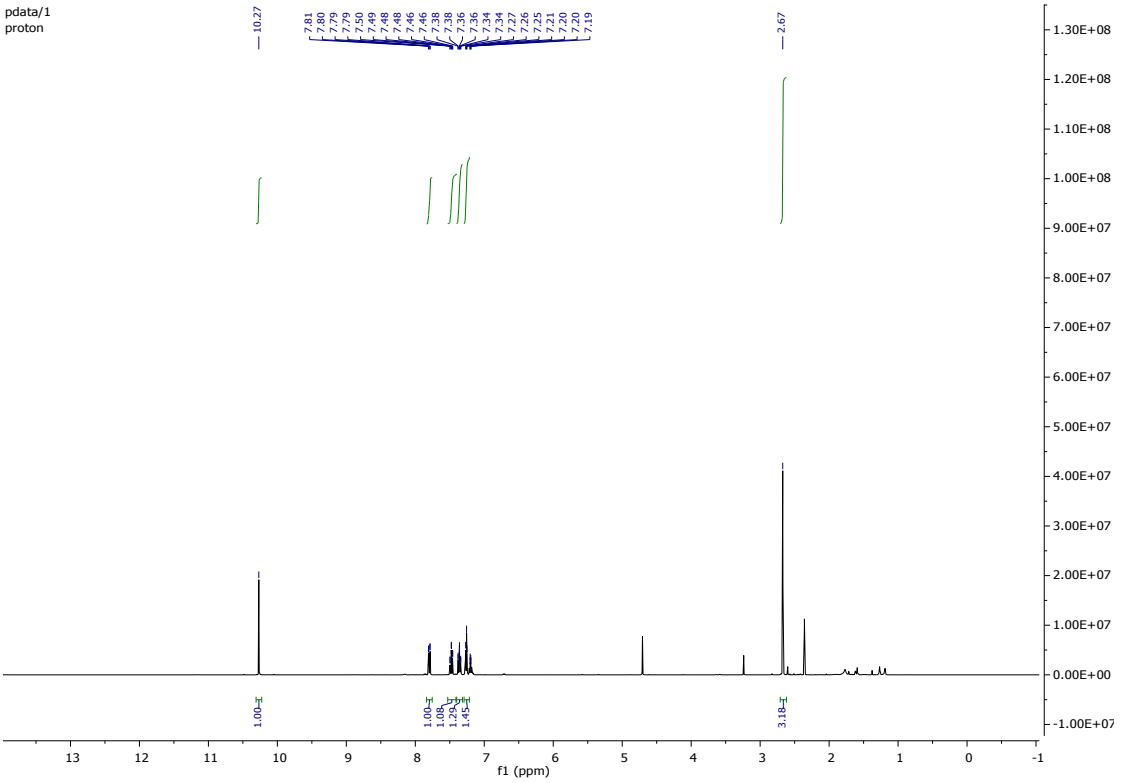


4. 2-methylbenzaldehyde (^{1}H NMR, $CDCl_3$)





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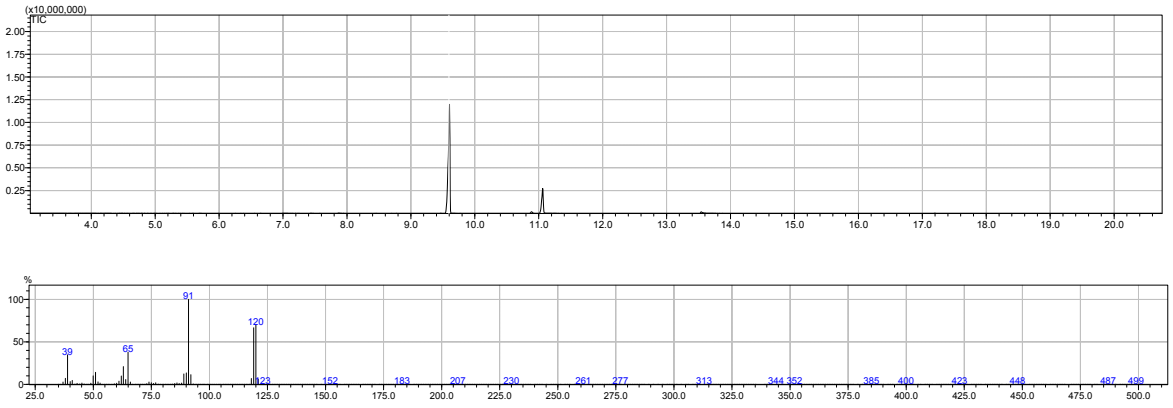
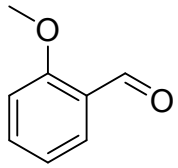
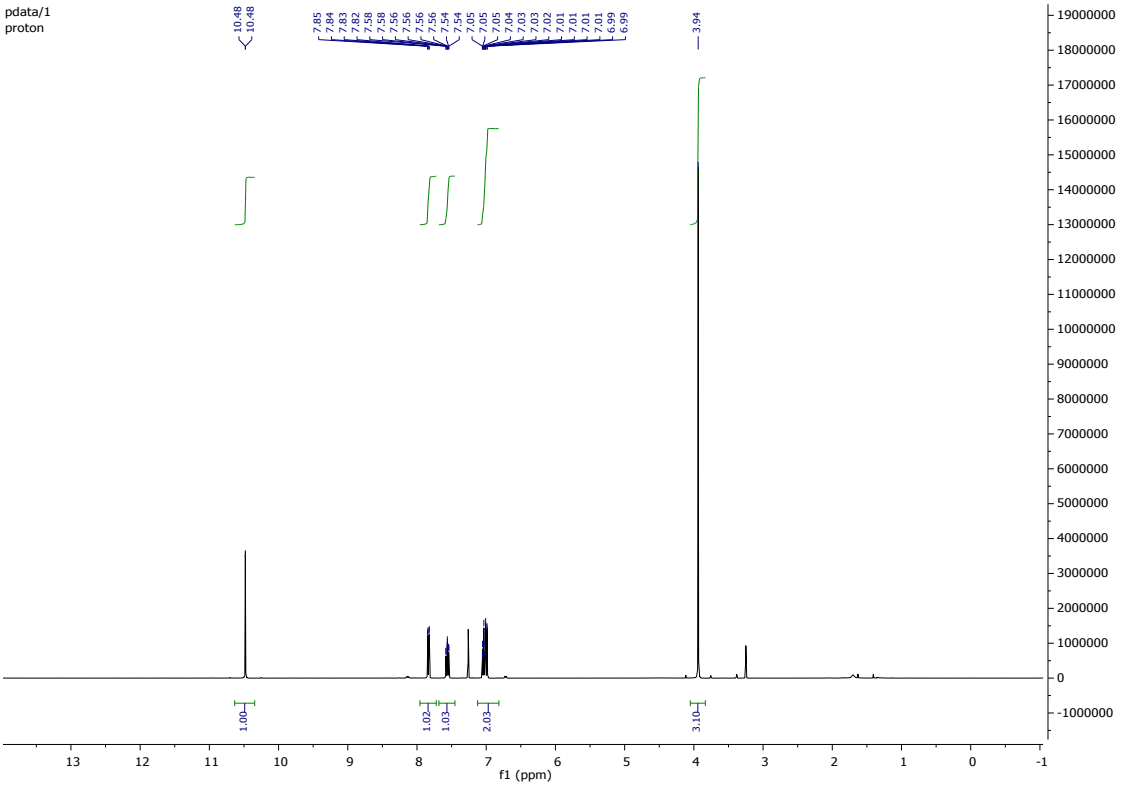


5. 2-methoxybenzaldehyde (^{1}H NMR, $CDCl_3$)





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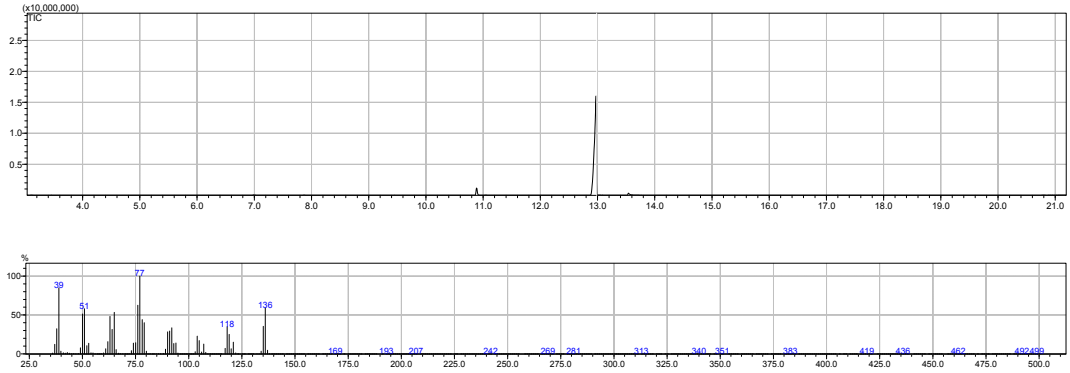
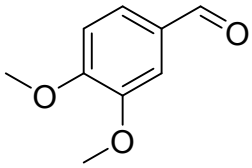
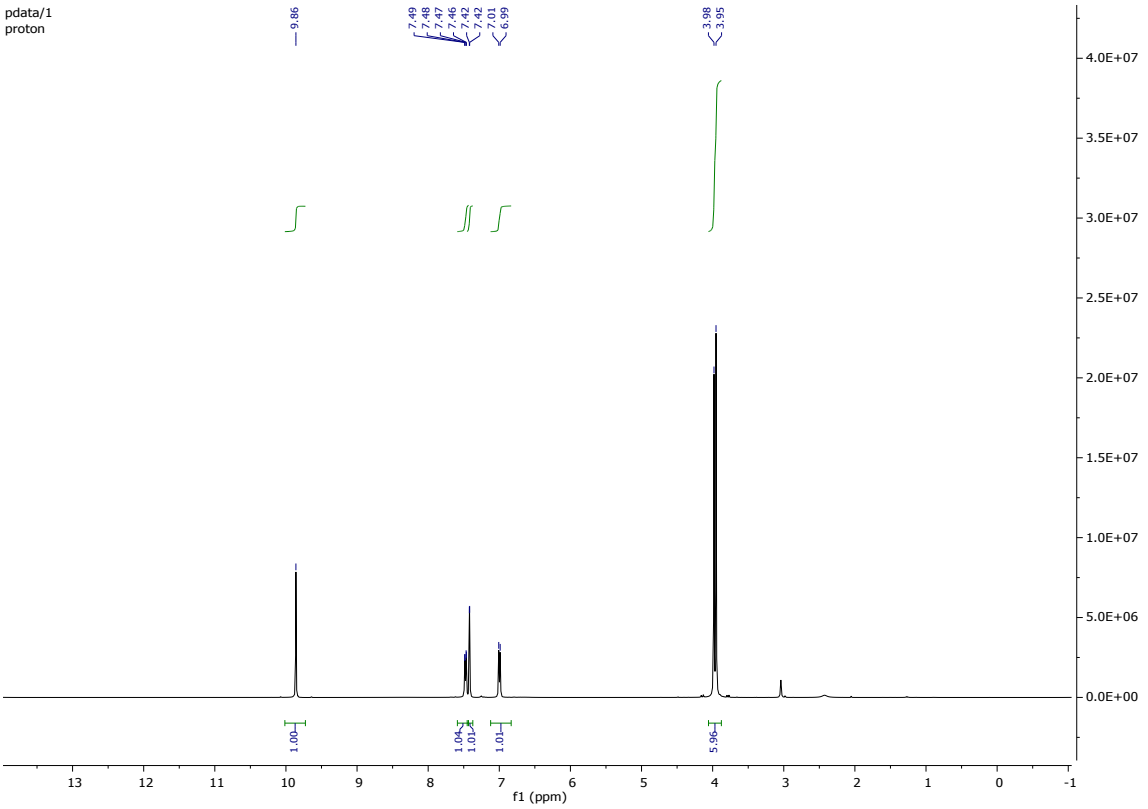


6. 3,4-dimethoxybenzaldehyde (^{1}H NMR, $CDCl_3$)





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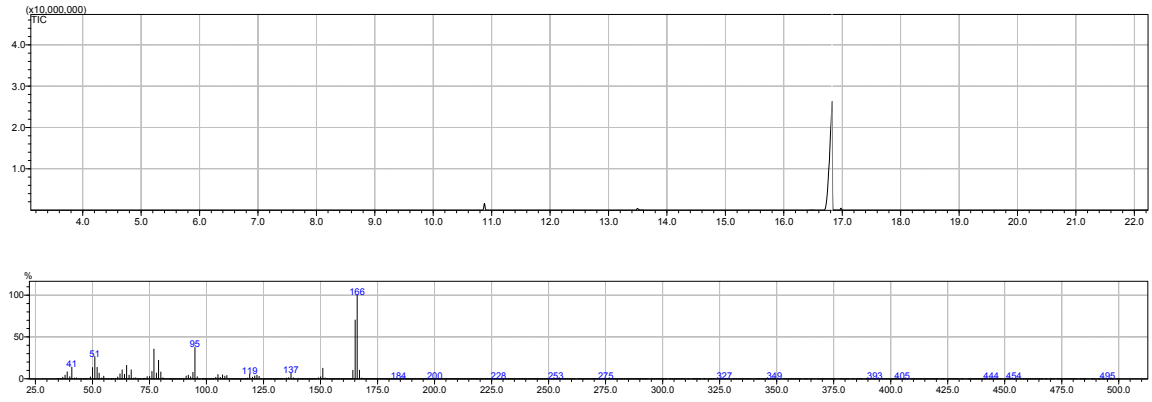
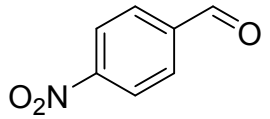
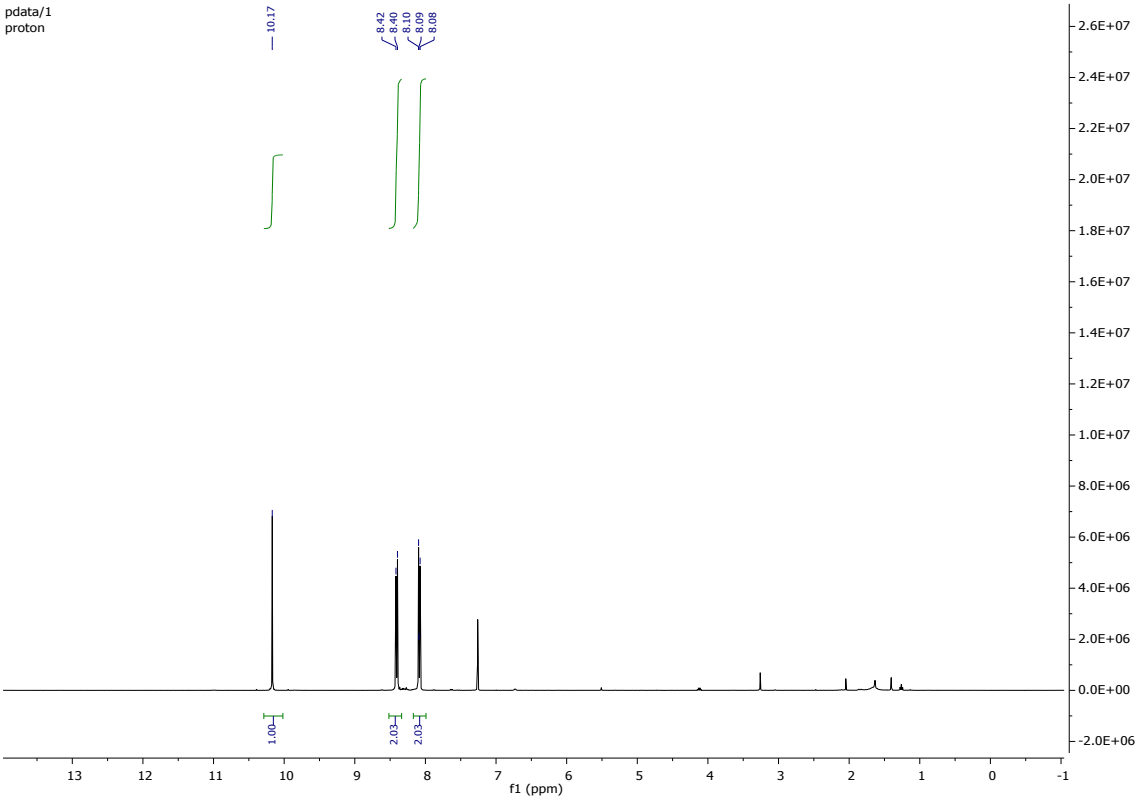
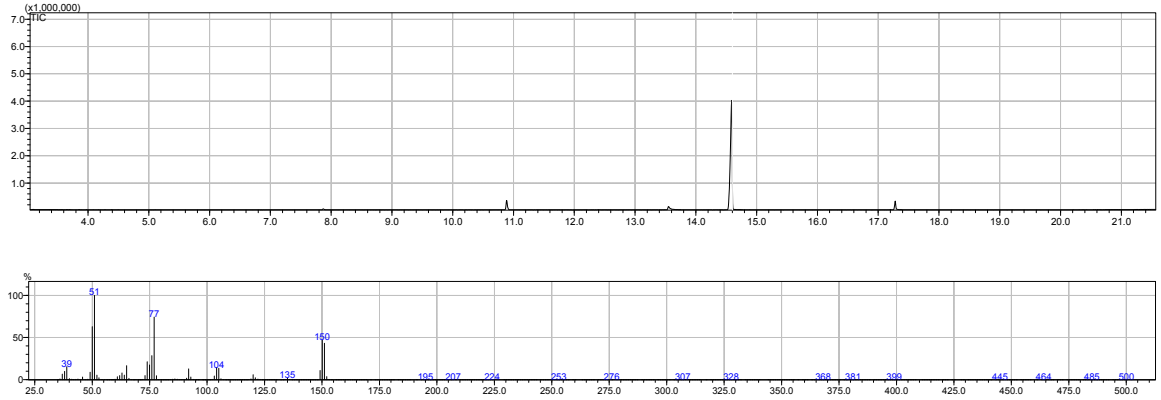


7. 4-nitrobenzaldehyde (^{1}H NMR, $CDCl_3$)

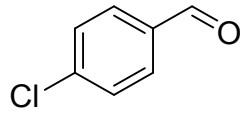


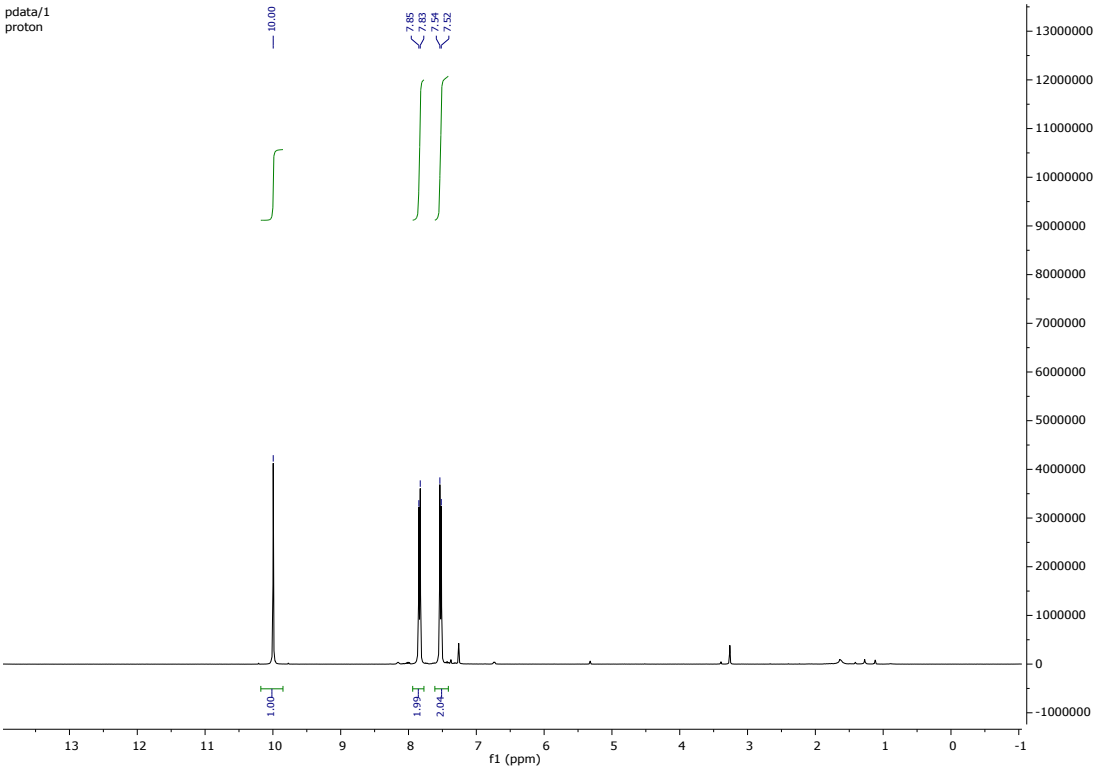


GC-MS:



8. 4-chlorobenzaldehyde (^{1}H NMR, $CDCl_3$)





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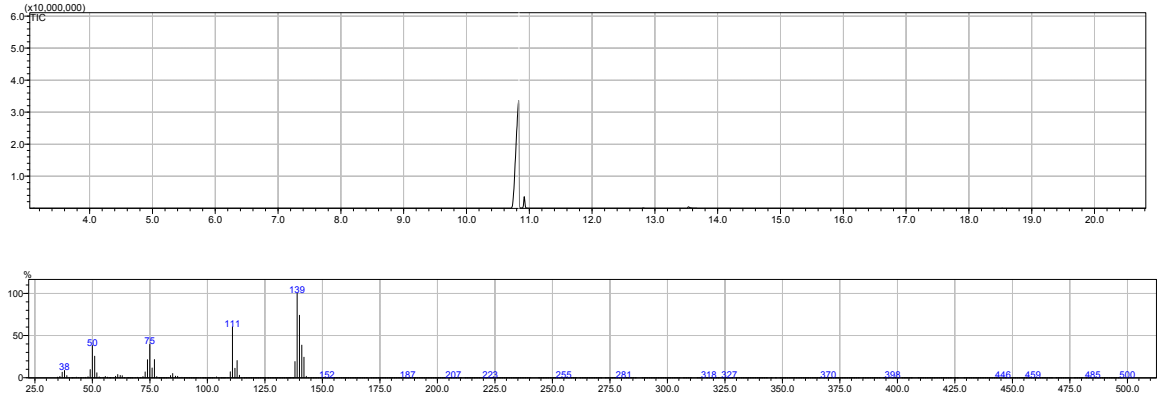
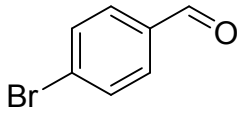
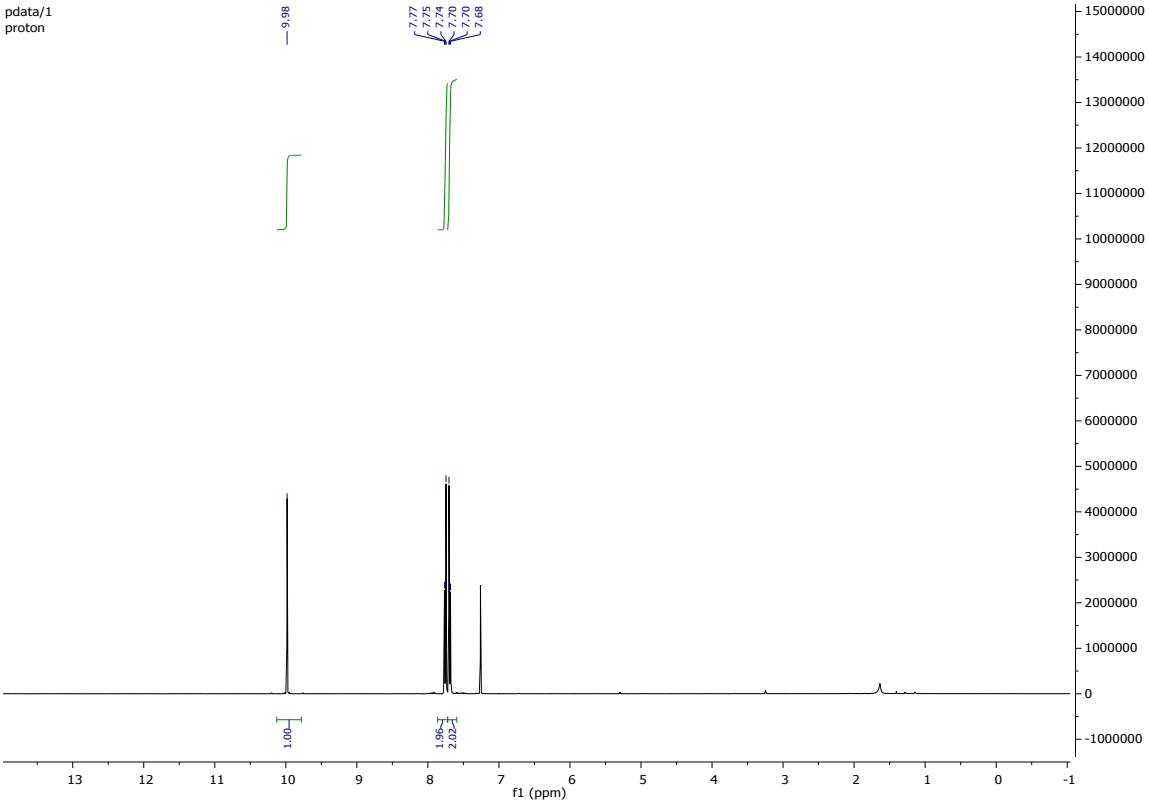


9. 4-bromobenzaldehyde (^{1}H NMR, $CDCl_3$)





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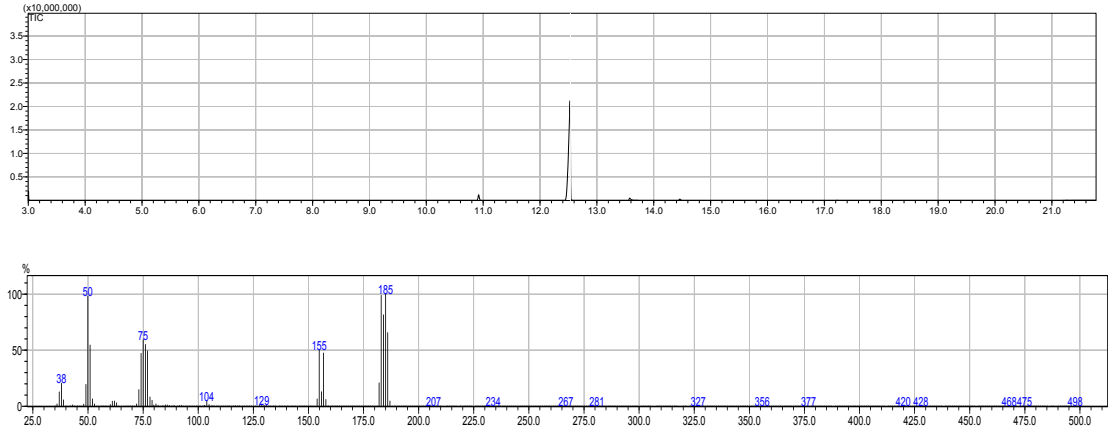
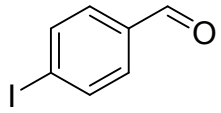
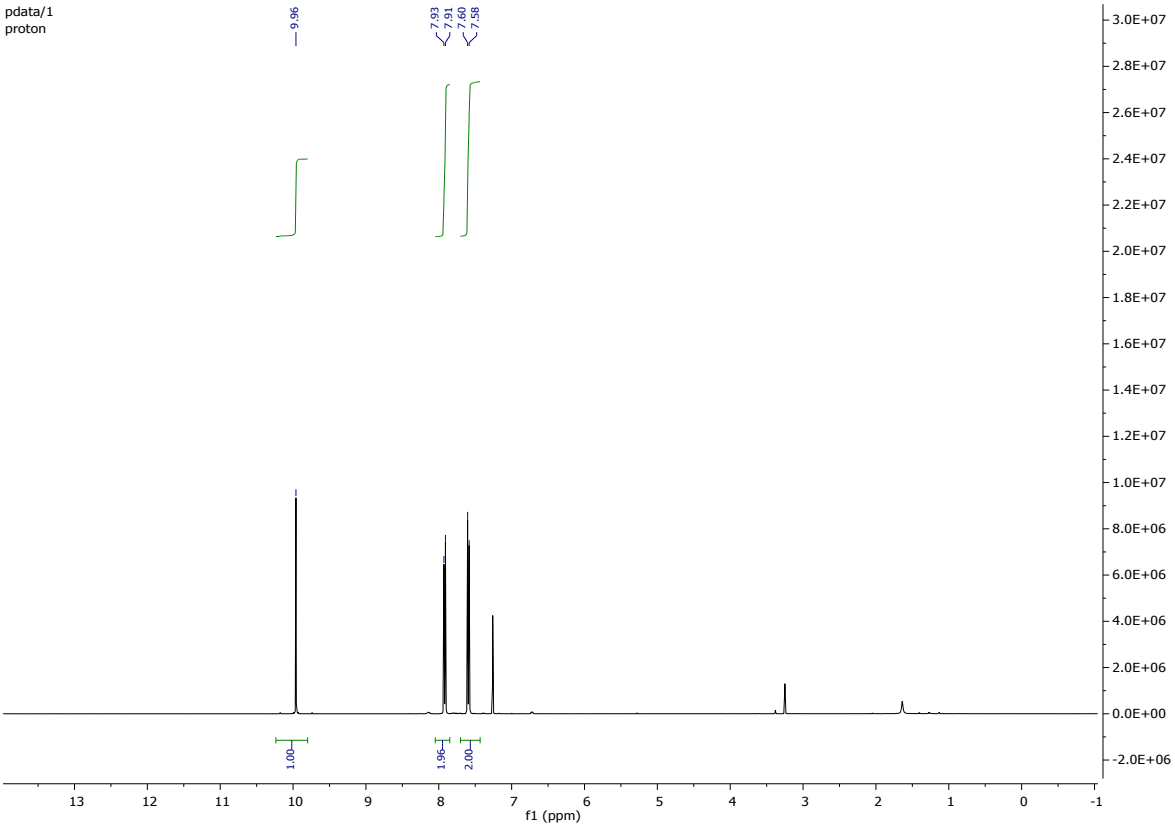
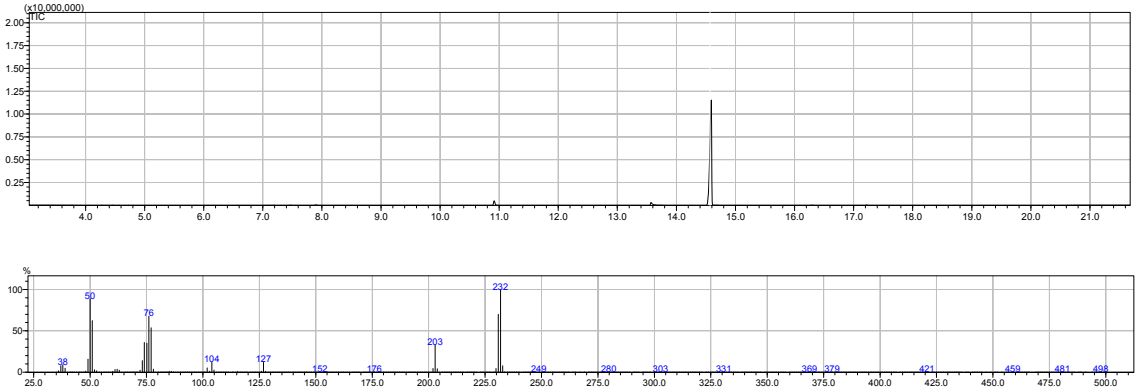


10. 4-iodobenzaldehyde (^{1}H NMR, $CDCl_3$)

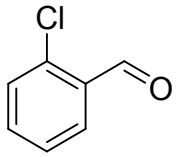


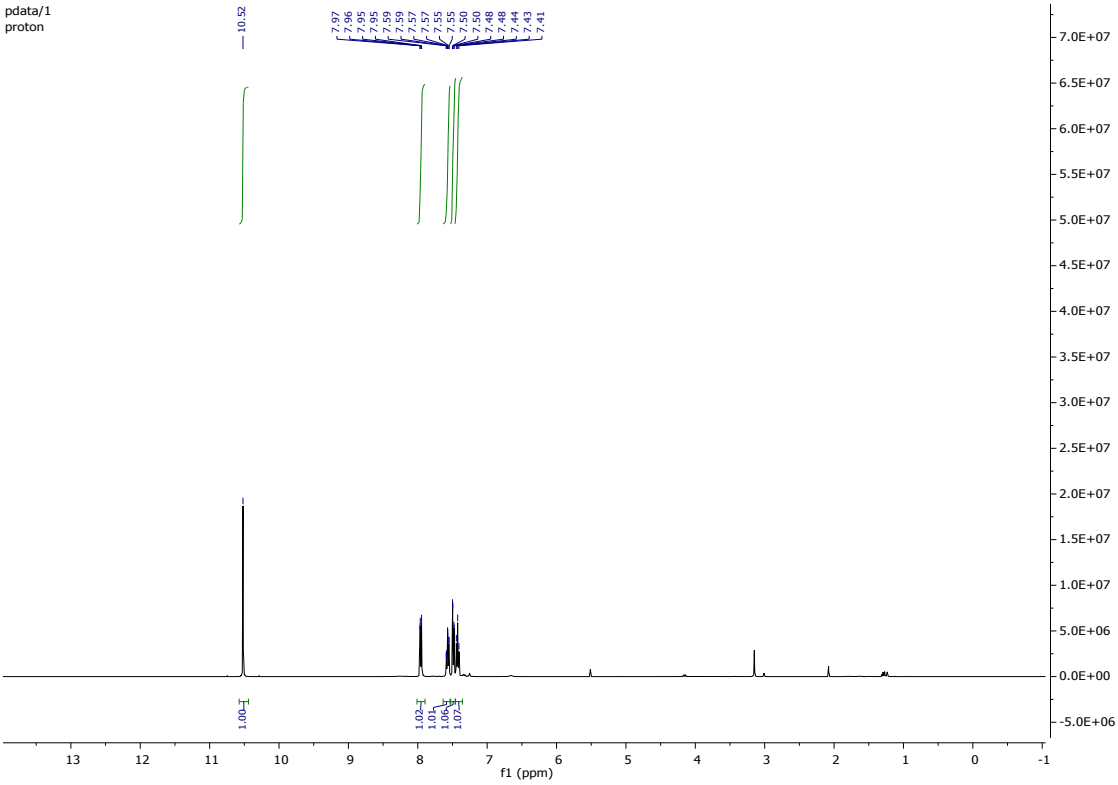


GC-MS:

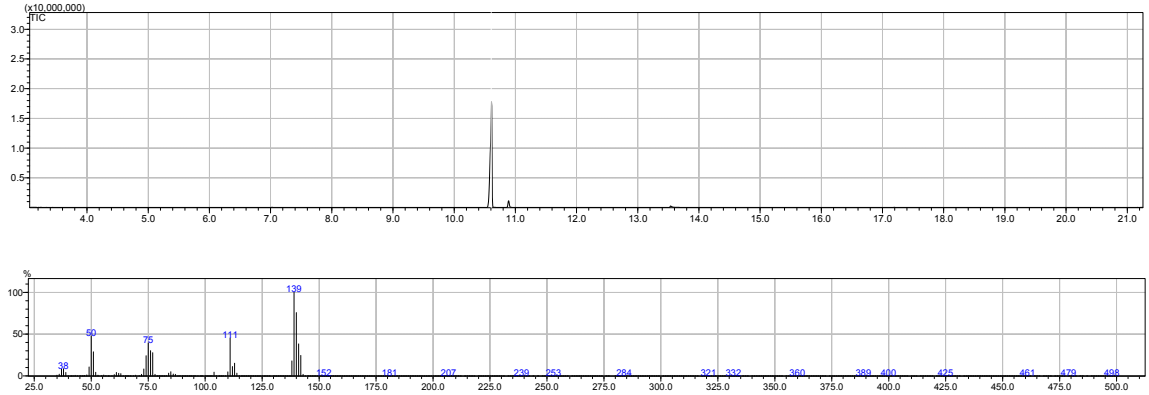


11. 2-chlorobenzaldehyde (^{1}H NMR, $CDCl_3$)

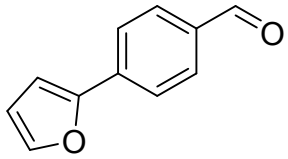


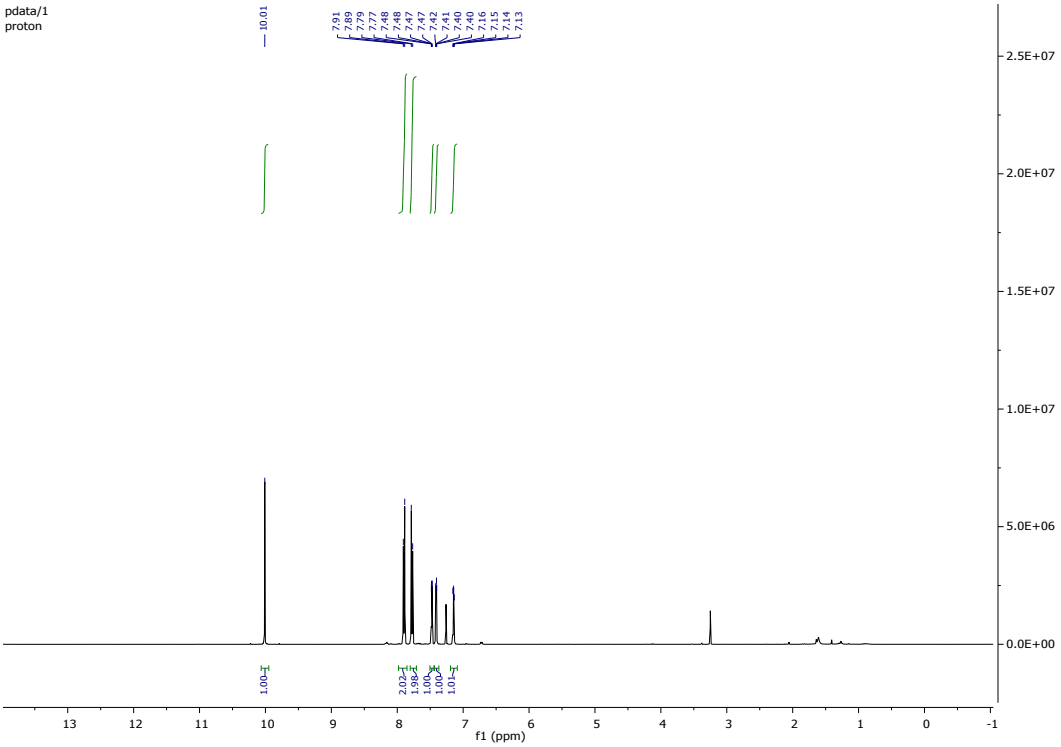


GC-MS:



12. 4-(2-furyl)benzaldehyde (^{1}H NMR, $CDCl_3$)





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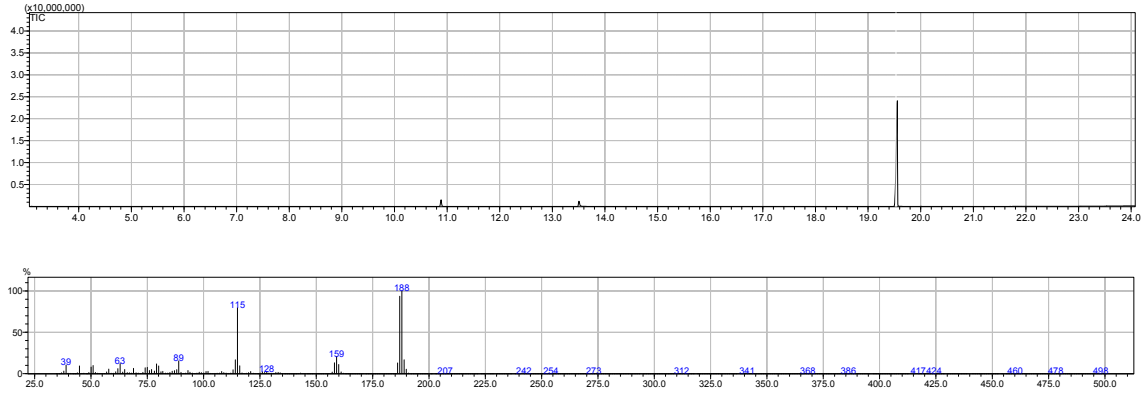
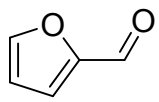
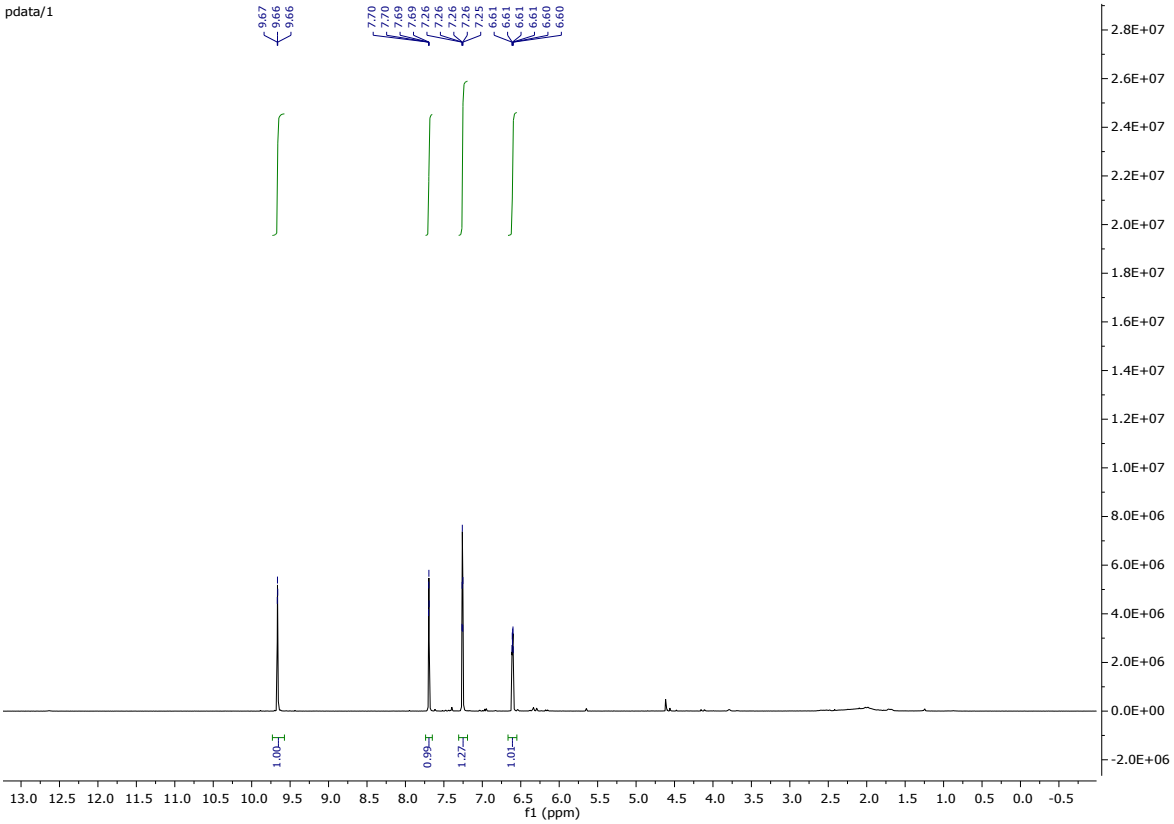


13. 2-formylfuran (^{1}H NMR, $CDCl_3$)





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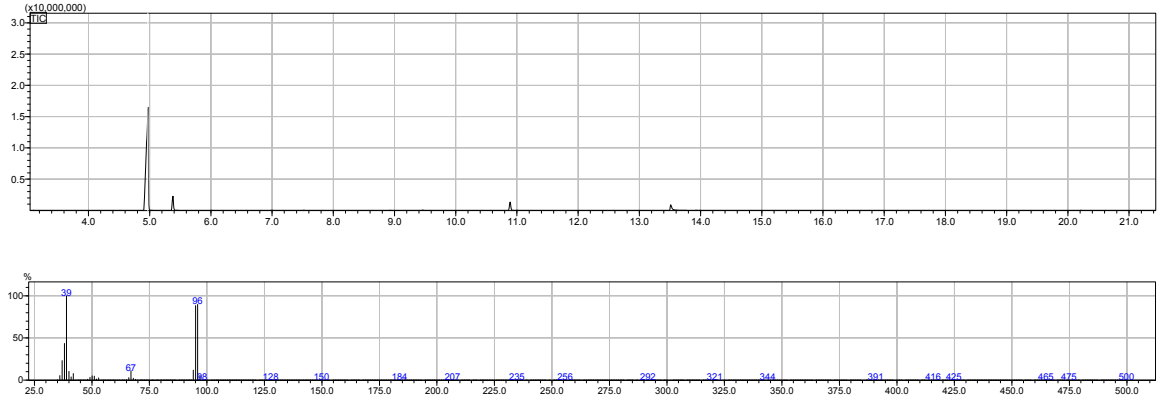
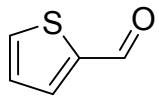
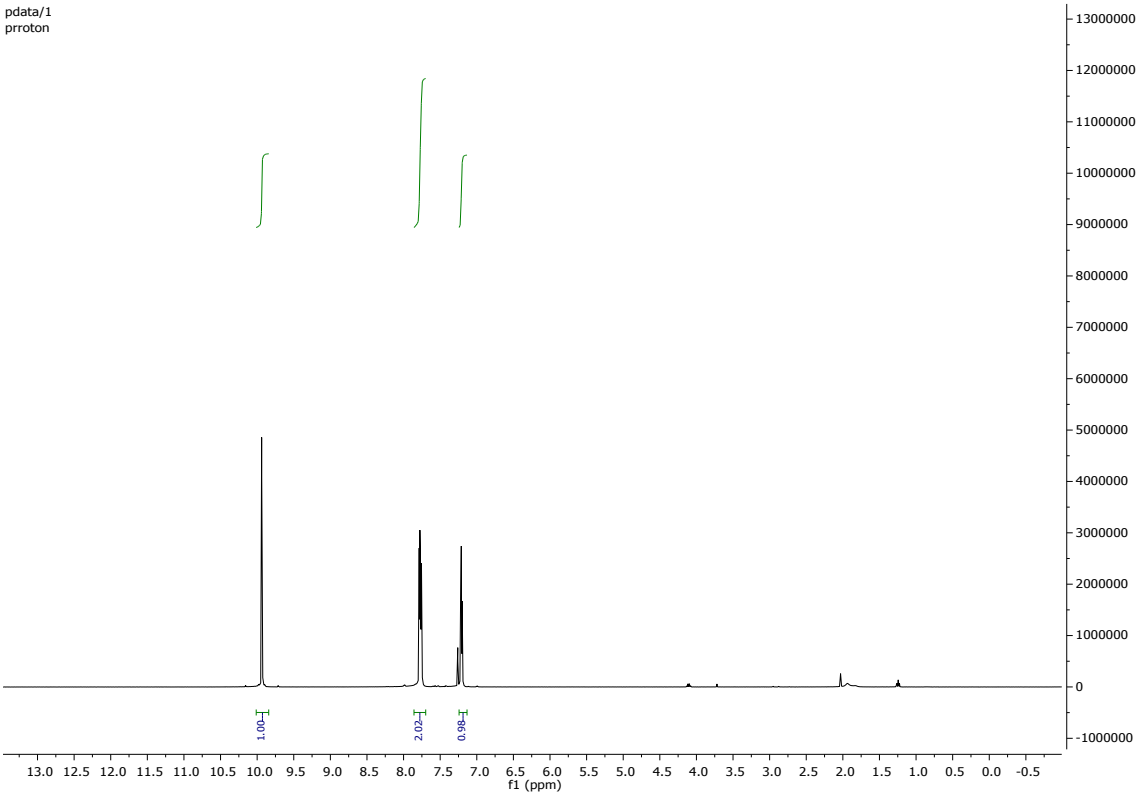


14. 2-formylthiophene (^{1}H NMR, $CDCl_3$)





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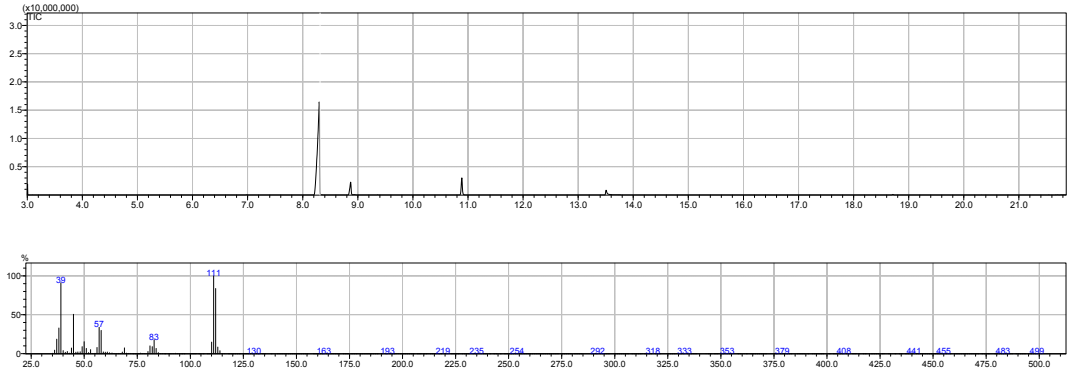
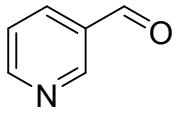
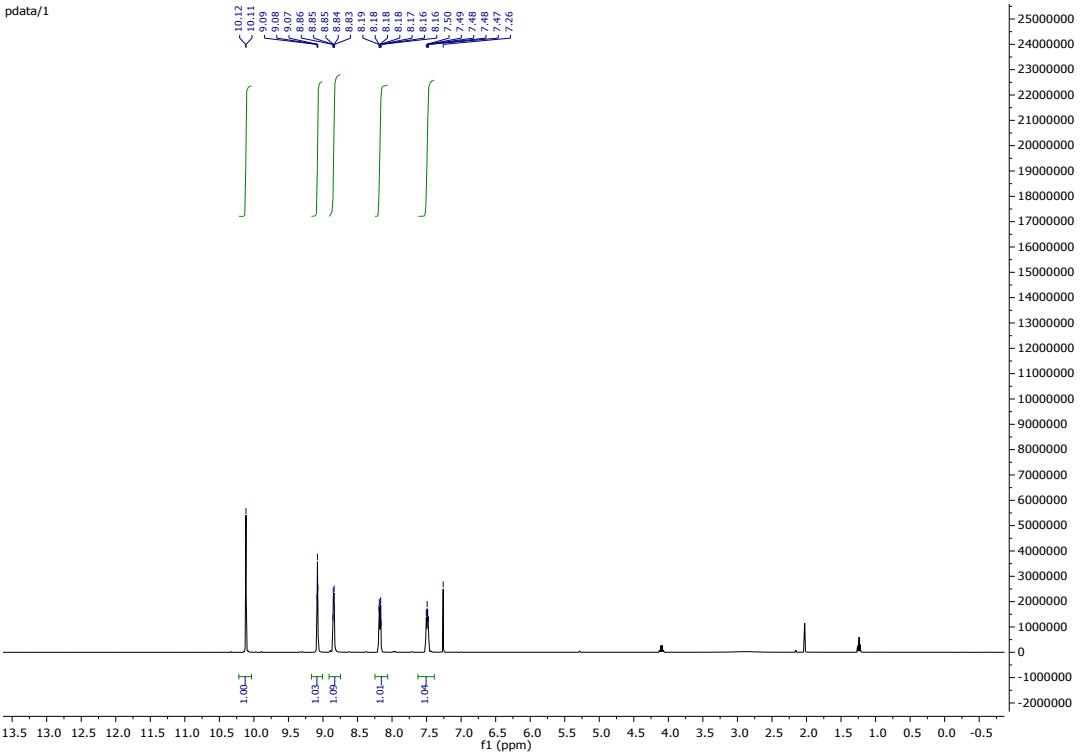


15. 3-pyridinecarboxaldehyde (^{1}H NMR, $CDCl_3$)





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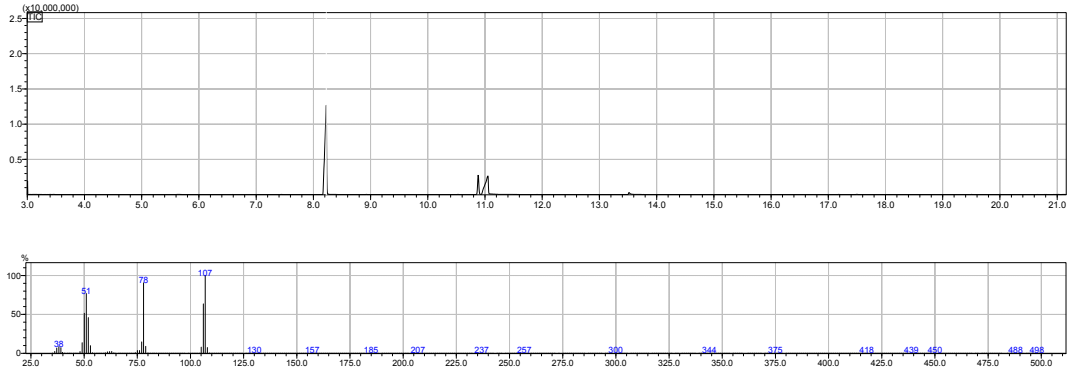
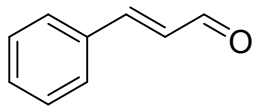
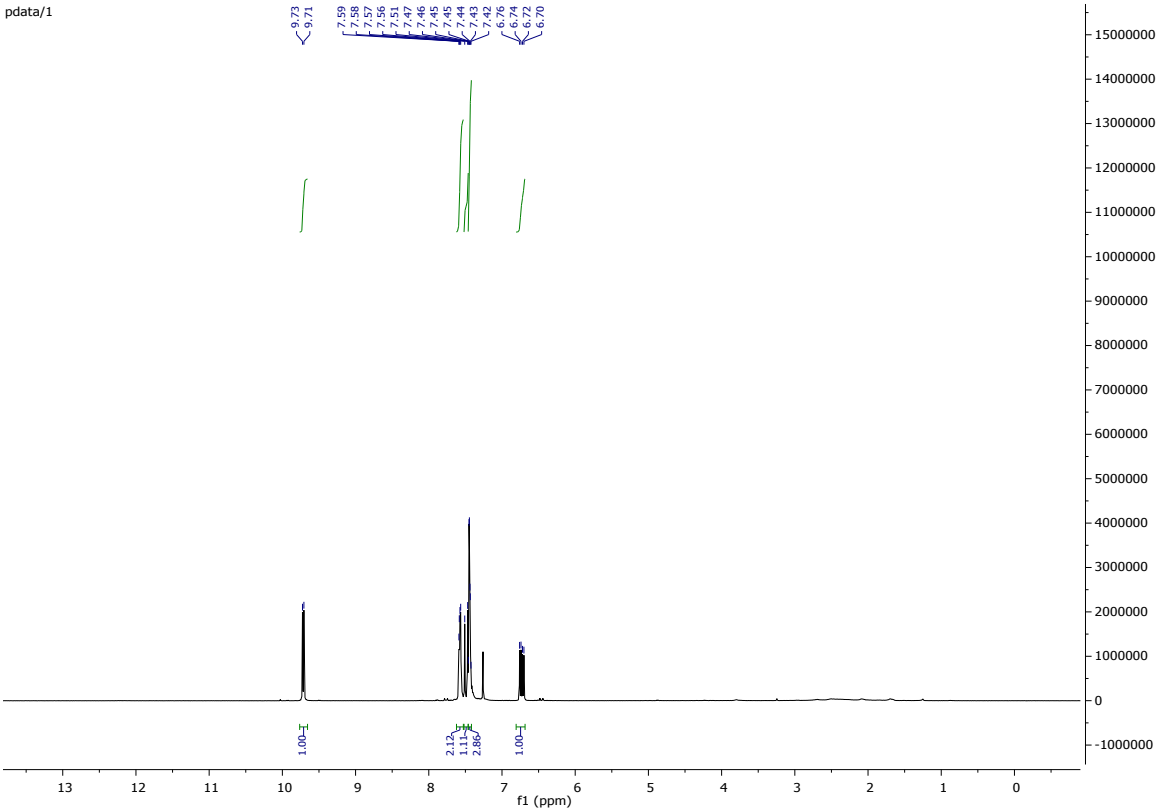


16. cinnamyl aldehyde (^{1}H NMR, $CDCl_3$)





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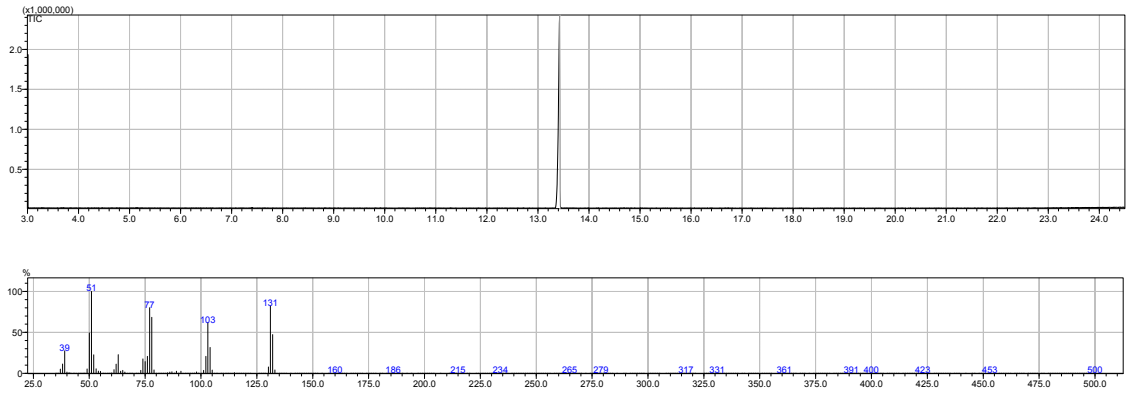
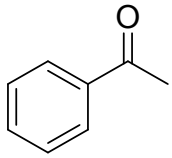
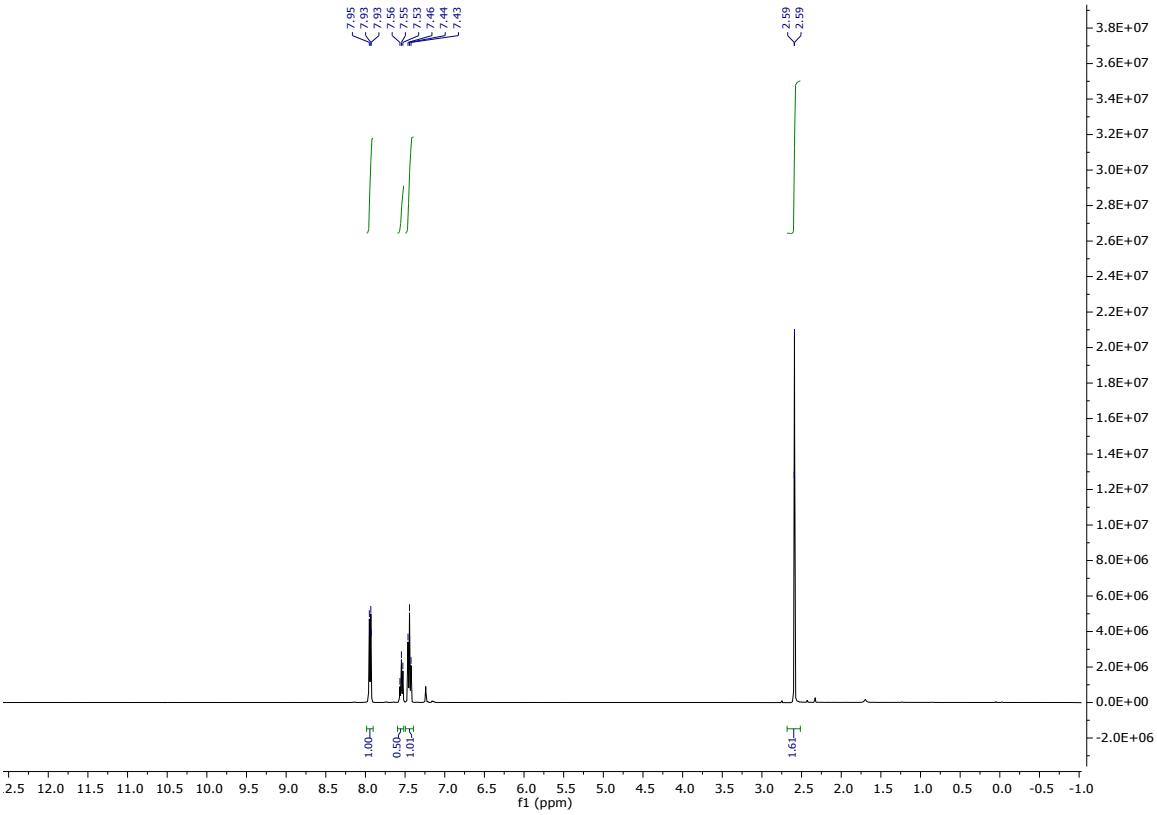
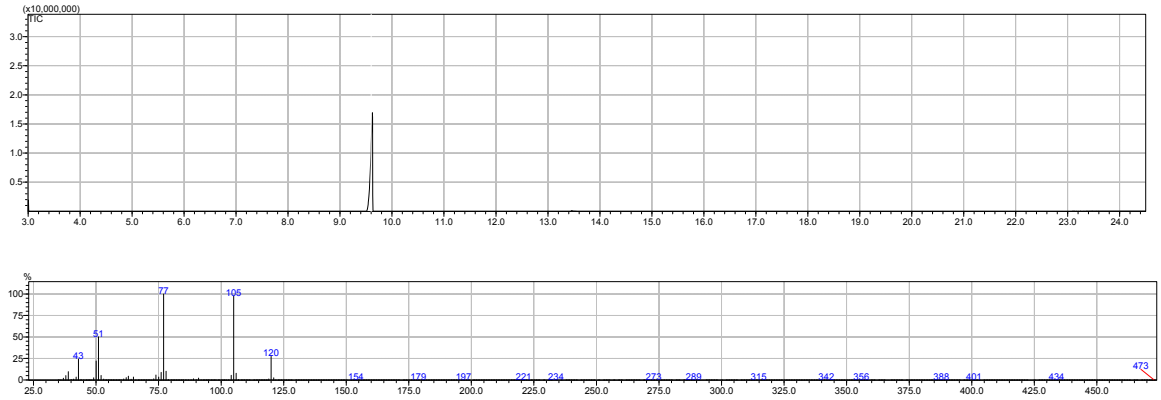


17. acetophenone (^{1}H NMR, $CDCl_3$)

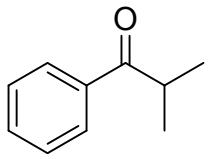


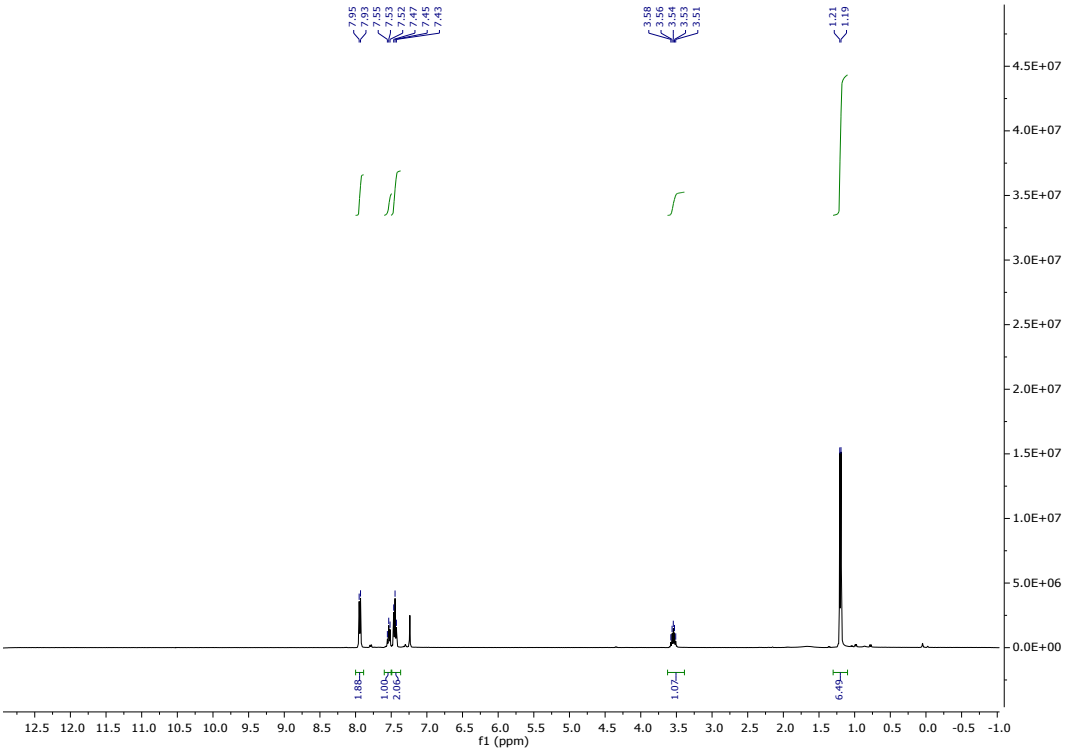


GC-MS:

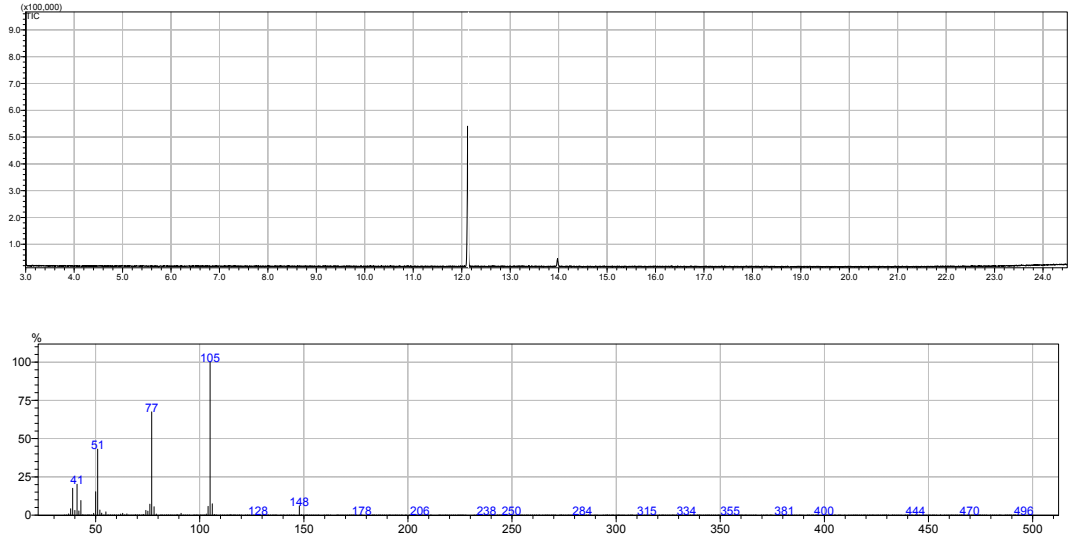


18. phenyl isopropyl ketone (^{1}H NMR, $CDCl_3$)

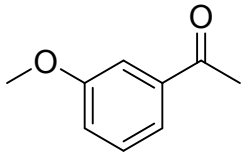


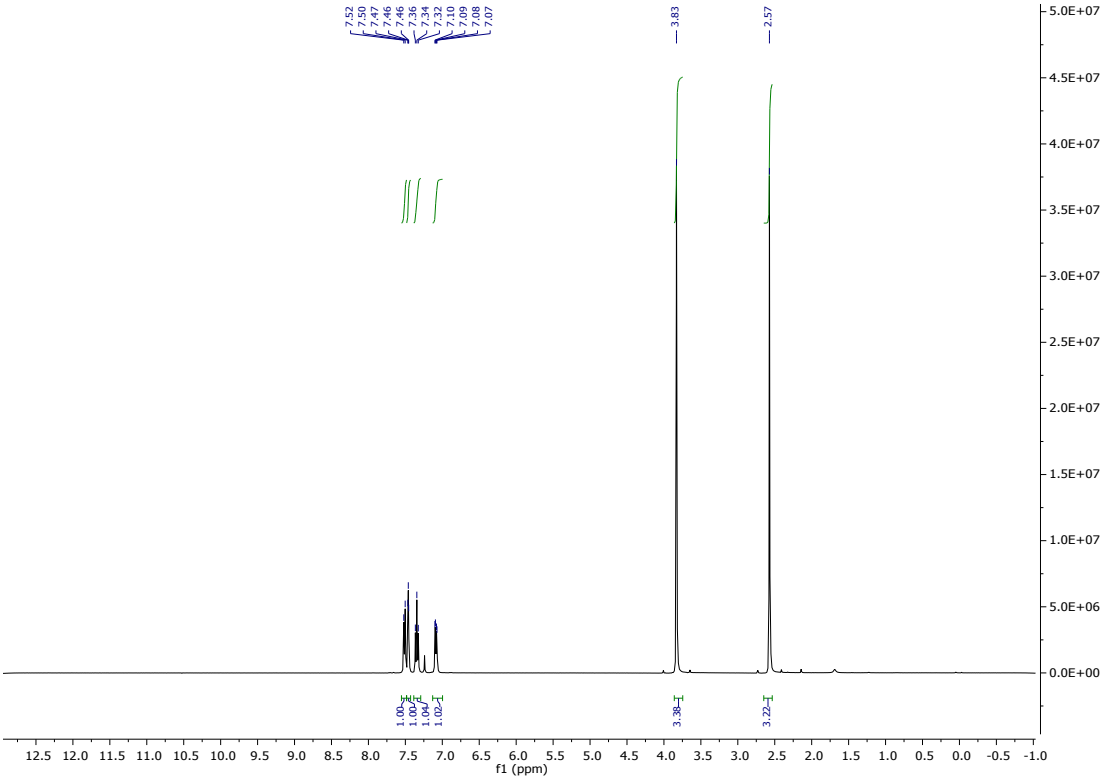

7.95
7.93
7.55
7.53
7.52
7.47
7.45
7.43
3.58
3.56
3.54
3.53
3.51
1.21
1.19
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
1.88
1.00
2.06
1.07
6.49
f1 (ppm)

GC-MS:


(x100,000)
TIC
105
77
51
41
148
128
178
206
238
250
284
315
334
355
381
400
444
470
496

19. 3’-methoxyacetophenone (^{1}H NMR, $CDCl_3$)





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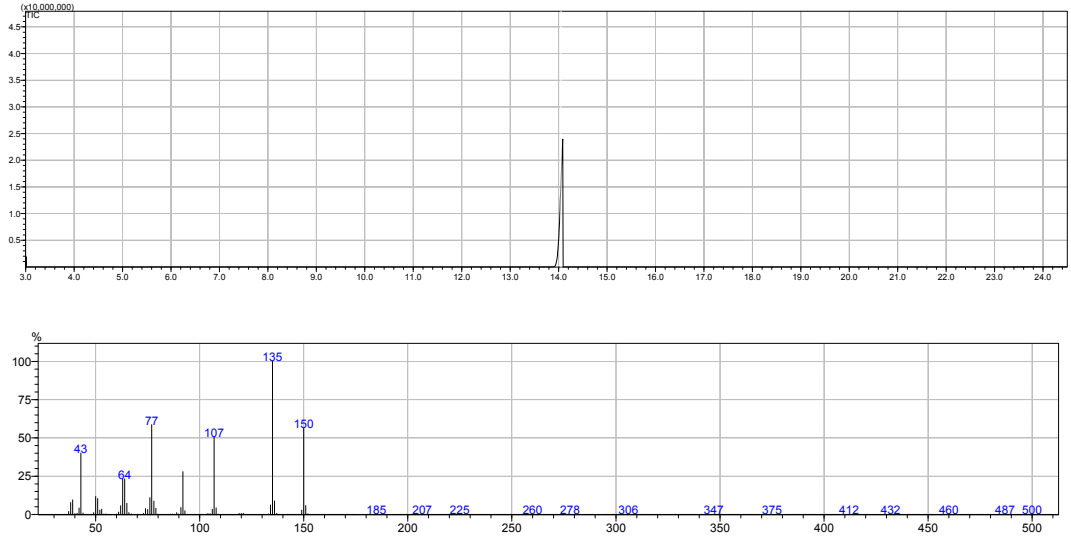
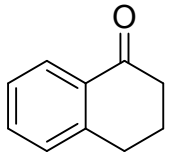
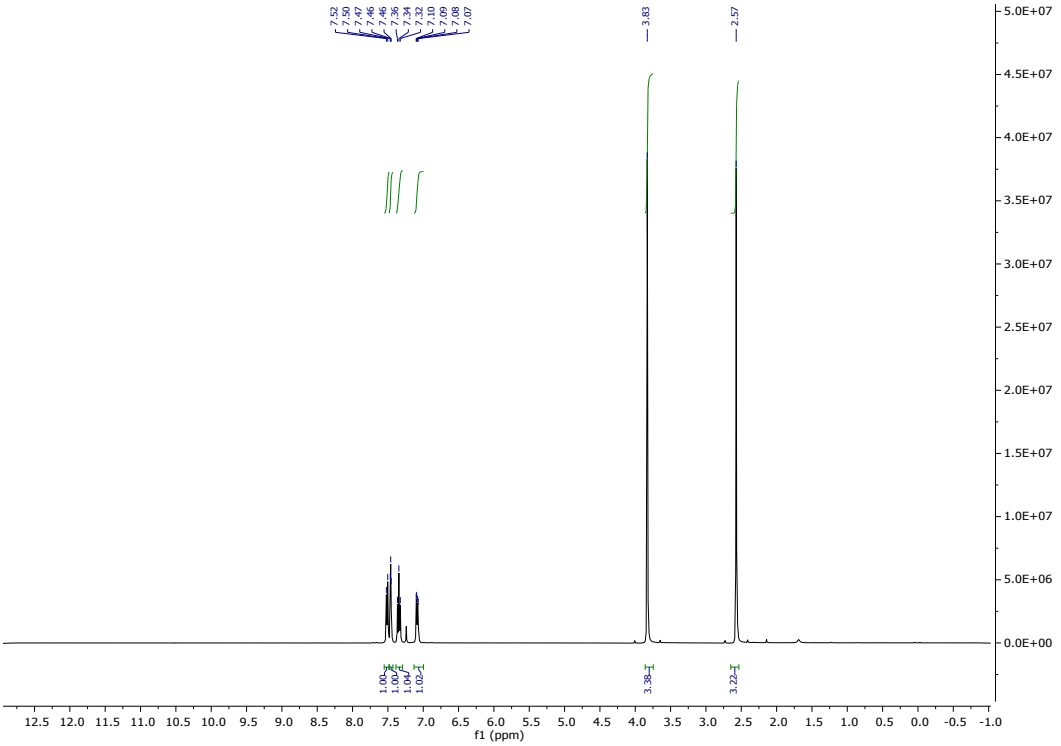


20. 3,4-dihydro-1(2*H*)-naphthalenone (^{1}H NMR, $CDCl_3$)





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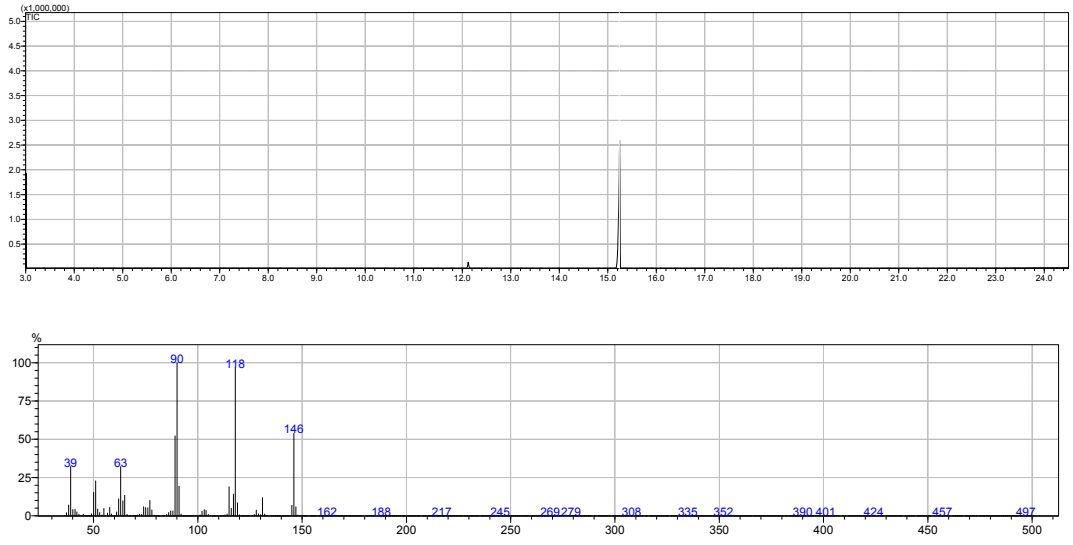
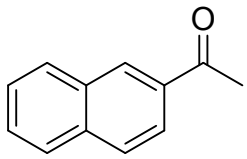
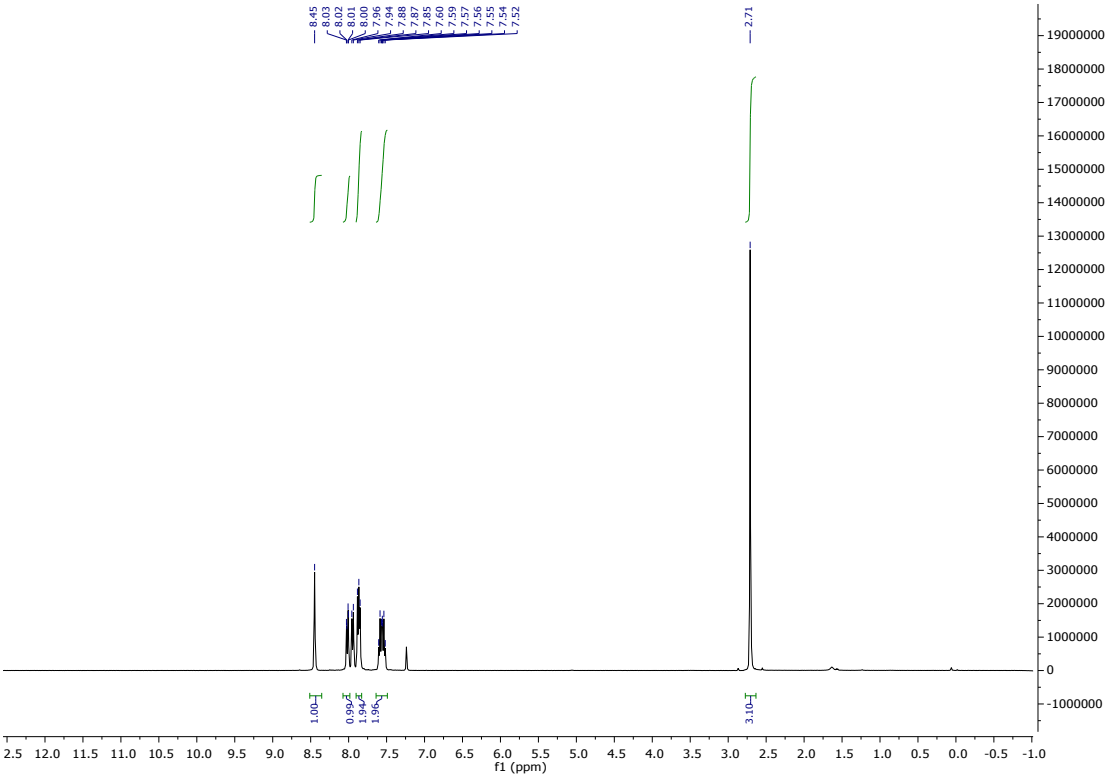


21. 2-acetonaphenone (^{1}H NMR, $CDCl_3$)





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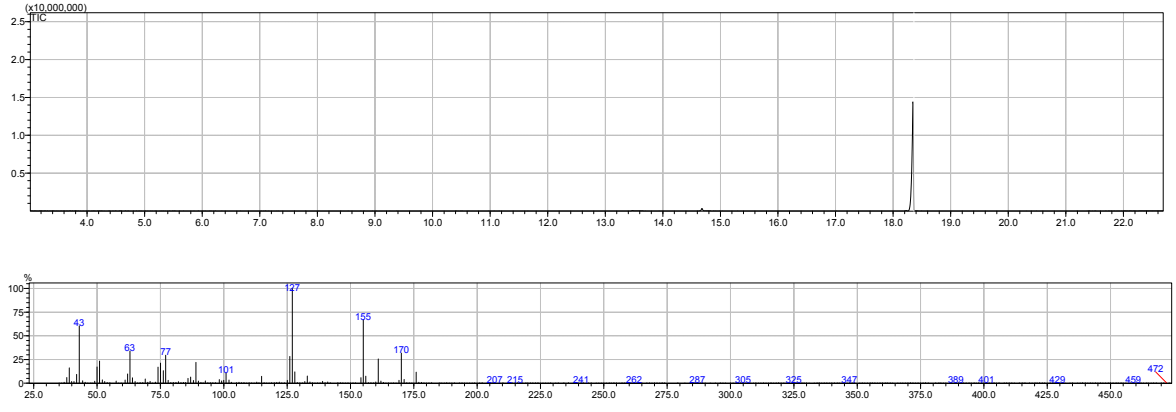
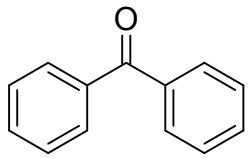
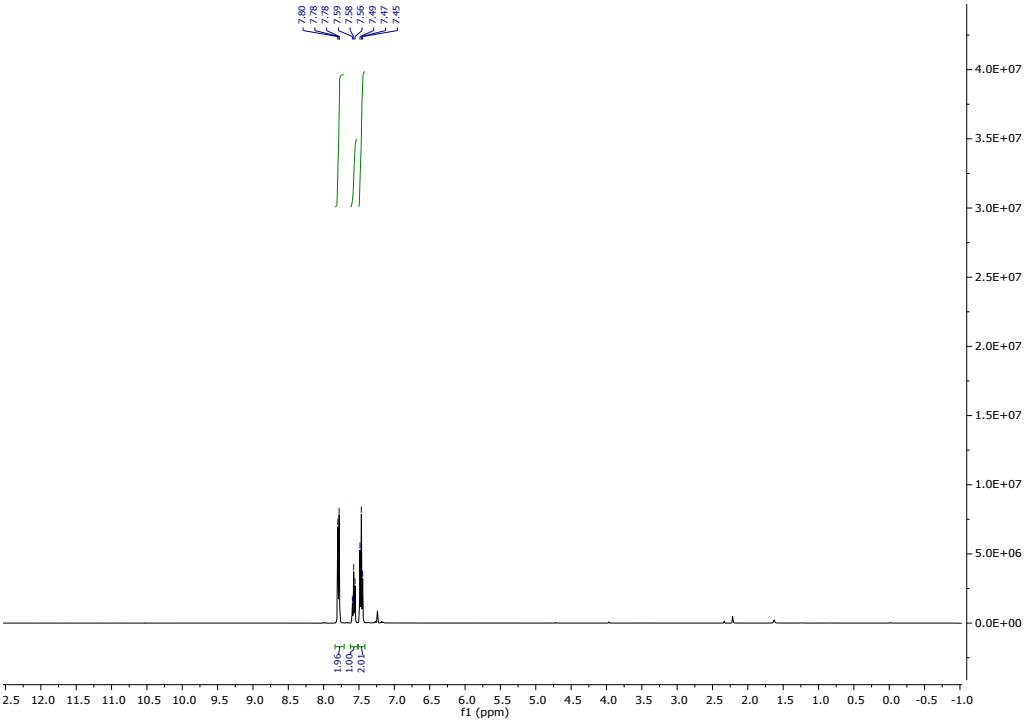
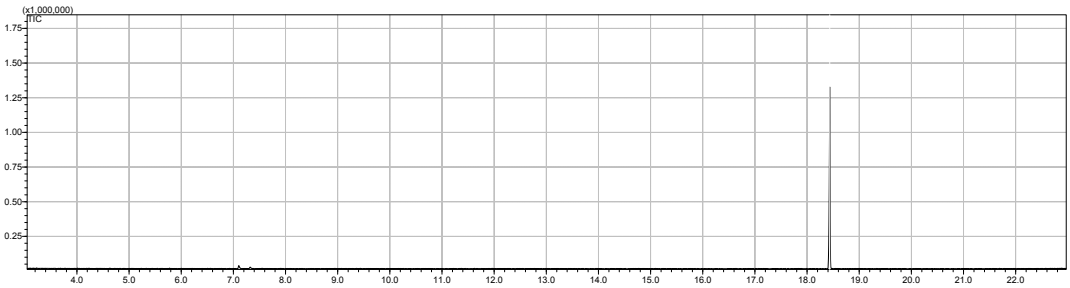


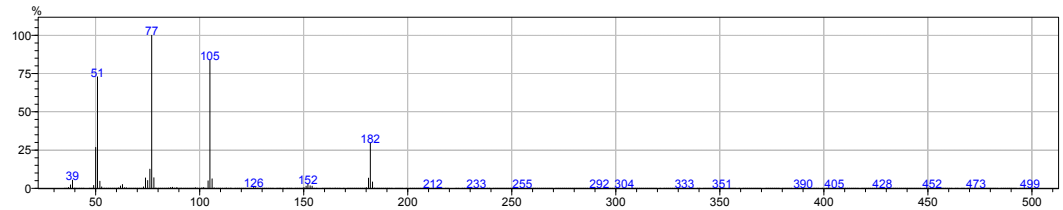
22. benzophenone (^{1}H NMR, $CDCl_3$)



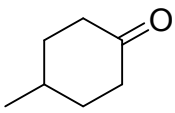


GC-MS:





23. 4-methylcyclohexanone



GC-MS: