Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information

Sodium periodate/TEMPO as selective and efficient system for amine oxidation

P. Galletti,* G. Martelli, G. Prandini, C. Colucci, and D. Giacomini*

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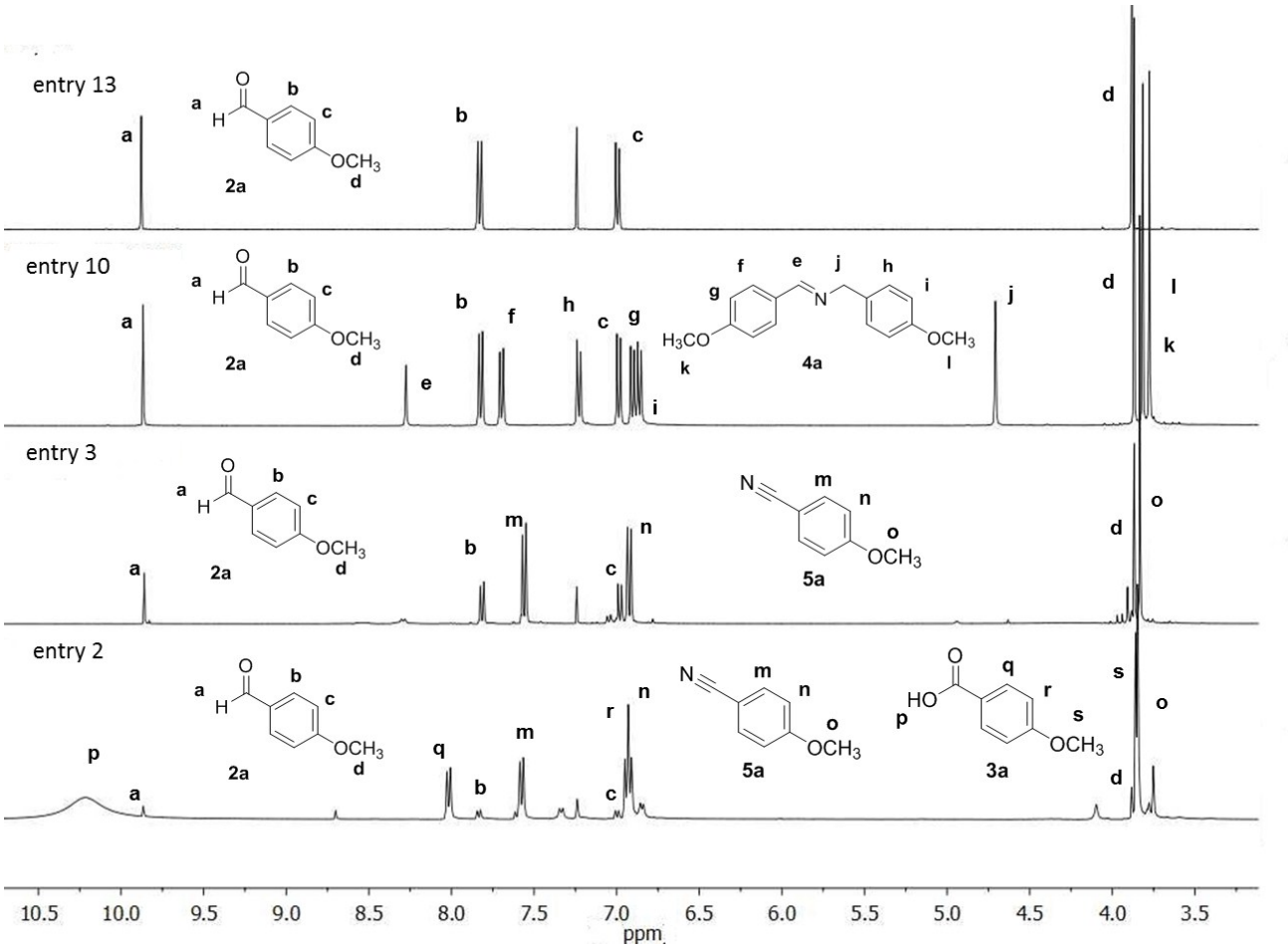


Figure 1S. ^{1}H NMR spectra (400 MHz, $CDCl_3$) of products distribution in crude reaction mixtures in different reaction conditions (Table 1 entry 2, 3, 10 and 13)

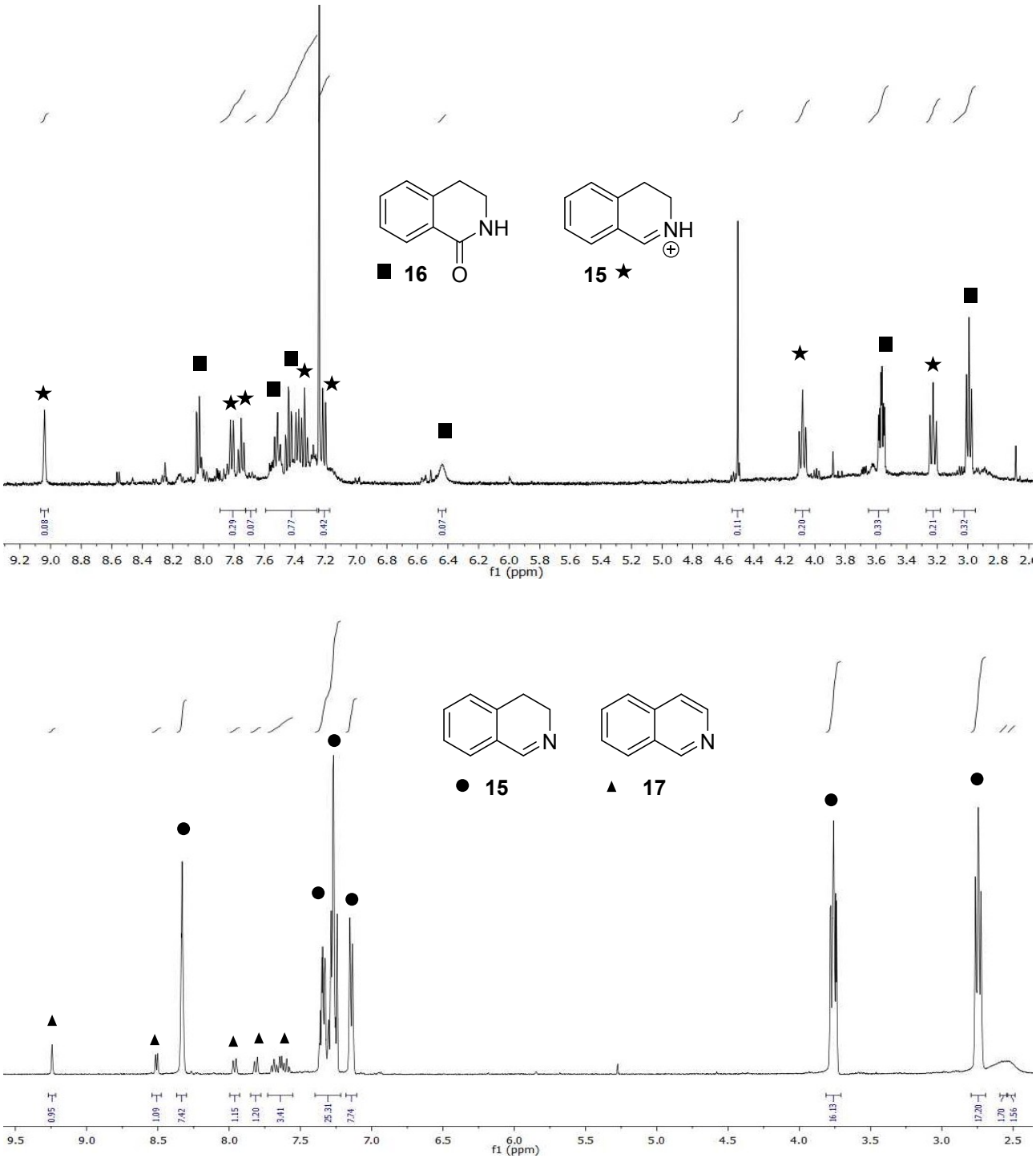
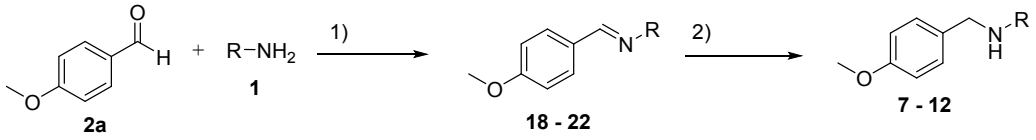
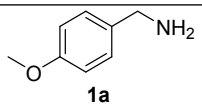
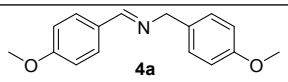
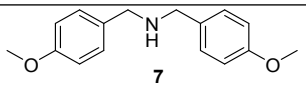
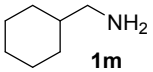
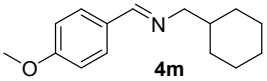
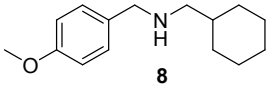
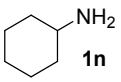
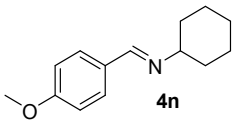
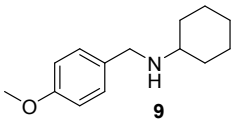
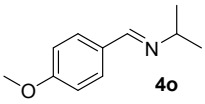
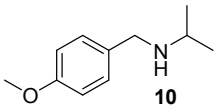
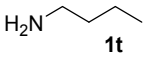
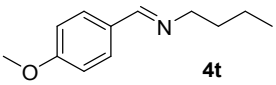
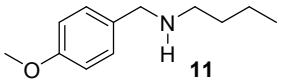
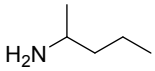
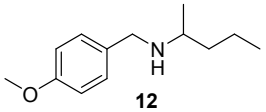


Figure 2S. ^{1}H NMR (400 MHz, $CDCl_3$) of products distribution in crude reaction mixture of entry 6, table 5 (acid and basic work-up respectively)

Table 1S. Secondary amines preparation



Entry	Amine	Imine	Yield imine (%)	Secondary amine	Yield secondary amine (%)
1[a]	 1a	 4a	99	 7	90
2[a]	 1m	 4m	97	 8	83
3[a]	 1n	 4n	83	 9	86
4[a]	 1o	 4o	99	 10	92
5[a]	 1t	 4t	96	 11	83
6[b]	 1j			 12	89

[a] Reaction conditions: 1) aldehyde (1 equiv.), amine (from 1 to 2 equiv.), $MgSO_4$ (4 equiv.), CH_2Cl_2 (10mL), r.t., 24h; 2) imine (1 equiv.), $NaBH_4$ (2 equiv.), CH_3OH (5mL), r.t., 24h

[b] Reaction conditions: aldehyde (1 equiv.), amine (1.5 equiv.), $NaBH(OAc)_3$ (2 equiv.), AcOH (1.5 equiv.), CH_2Cl_2 (10mL), r.t., 24h

General procedure for synthesis of imines **4a**, **4m**, **4n**, **4o** and **4t** *(GP5):*

In a 50 mL two-necked flask under nitrogen atmosphere, *p*-anisaldehyde **2a** and the desired amine (**1a**, **1m**, **1n**, **1o**, or **1t**) were diluted in anhydrous CH_2Cl_2 (10 mL); $MgSO_4$ was added and the solution was stirred overnight. After completion (TLC monitoring, 24h), the mixture was filtered on celite under vacuum and the solvent evaporated under reduced pressure. The desired imines **4a**, **4m**, **4n**, **4o** and **4t** were obtained as yellow oils without further purification.

N-(4-methoxybenzyl)-1-(4-methoxyphenyl)methanimine (**4a**)

Following GP5, *p*-anisaldehyde **2a** (248 µL, 2 mmol, 1 equiv), *p*-methoxybenzylamine **1a** (266 µL, 2 mmol, 1 equiv) and $MgSO_4$ (963 mg, 8 mmol, 4 equiv) yielded imine **4a** (506 mg, 99% yield).

N-(cyclohexylmethyl)-1-(4-methoxyphenyl)methanimine (**4m**)

Following GP5, *p*-anisaldehyde **2a** (248 µL, 2 mmol, 1 equiv), cyclohexylmethylamine **1m** (265 µL, 2 mmol, 1 equiv) and $MgSO_4$ (963 mg, 8 mmol, 4 equiv) yielded imine **4m** (447 mg, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.14 (s, 1H), 7.66 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 3H), 3.41 (d, *J* = 6.4 Hz, 2H), 1.79 – 1.65 (m, 6H), 1.31 – 1.11 (m, 3H), 1.02 – 0.93 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 161.4, 160.1, 131.9, 129.5, 113.9, 68.6, 55.3, 39.0, 31.5, 26.6, 26.1; IR (film, cm^{-1}): 2923, 2849, 1698, 1649, 1606, 1579, 1253, 1165; HPLC-MS (ESI^+): R_t = 1.73 min; m/z = 232 $[M+H]^+$.

N-cyclohexyl-1-(4-methoxyphenyl)methanimine (**4n**)
Following GP5, *p*-anisaldehyde **2a** (248 µL, 2 mmol, 1 equiv), cyclohexylamine **1n** (299 µL, 2.6 mmol, 1 equiv) and $MgSO_4$ (1.20 g, 10 mmol, 5 equiv) yielded imine **4n** (362 mg, 83% yield).

N-isopropyl-1-(4-methoxyphenyl)methanimine (**4o**)
Following GP5, *p*-anisaldehyde **2a** (310 µL, 2.5 mmol, 1 equiv), isopropylamine **1o** (677 µL, 7.5 mmol, 2 equiv) and $MgSO_4$ (1.81 g, 15 mmol, 6 equiv) yielded imine **4o** (437 mg, 99% yield).

N-butyl-1-(4-methoxyphenyl)methanimine (**4t**)
Following GP5, *p*-anisaldehyde **2a** (248 µL, 2 mmol, 1 equiv), butylamine **4t** (300µL, 3 mmol, 1.5 equiv) and $MgSO_4$ (1.69 g, 14 mmol, 7 equiv) yielded imine **4t** (369 mg, 96% yield).

*General procedure for synthesis of secondary amines **7**-**11** (GP6):*
In a 25 mL two-necked flask under nitrogen atmosphere, imines **4a**, **4m**, **4n**, **4o** or **4t** (1 equiv.) were diluted in anhydrous CH_3OH (5 mL) and $NaBH_4$ (2 equiv.) was added; the solution was stirred overnight. After completion (TLC monitoring, 24 h), the mixture was quenched with water and HCl 6M until pH 2 and left 30 minutes under stirring. The organic solvent was then evaporated under reduced pressure and the mixture was basified until pH 11 with NaOH 5M. The precipitate was filtered out under vacuum, the aqueous phase was extracted with EtOAc (3 x 10 mL). The collected organic layers were dried on anhydrous Na_2SO_4, filtered and concentrated to afford the corresponding amines **7**-**11** as yellow oils without further purification. Spectroscopic data of amines **7**-**11** were consistent with those reported in the literature and in the NMR spectroscopy database (SDBS).

bis(4-methoxybenzyl)amine (**7**)
Following GP6, imine **4a** (510 mg, 2 mmol) yielded the secondary amine **7** (463 mg, 90% yield).

1-cyclohexyl-N-(4-methoxybenzyl)methanamine (**8**)
Following GP6, imine **4m** (447 mg, 1.9 mmol) yielded the secondary amine **8** (366 mg, 83% yield).

N-(4-methoxybenzyl)cyclohexanamine (**9**)
Following GP6, imine **4n** (359 mg, 1.65 mmol) yielded the secondary amine **9** (315 mg, 87% yield).

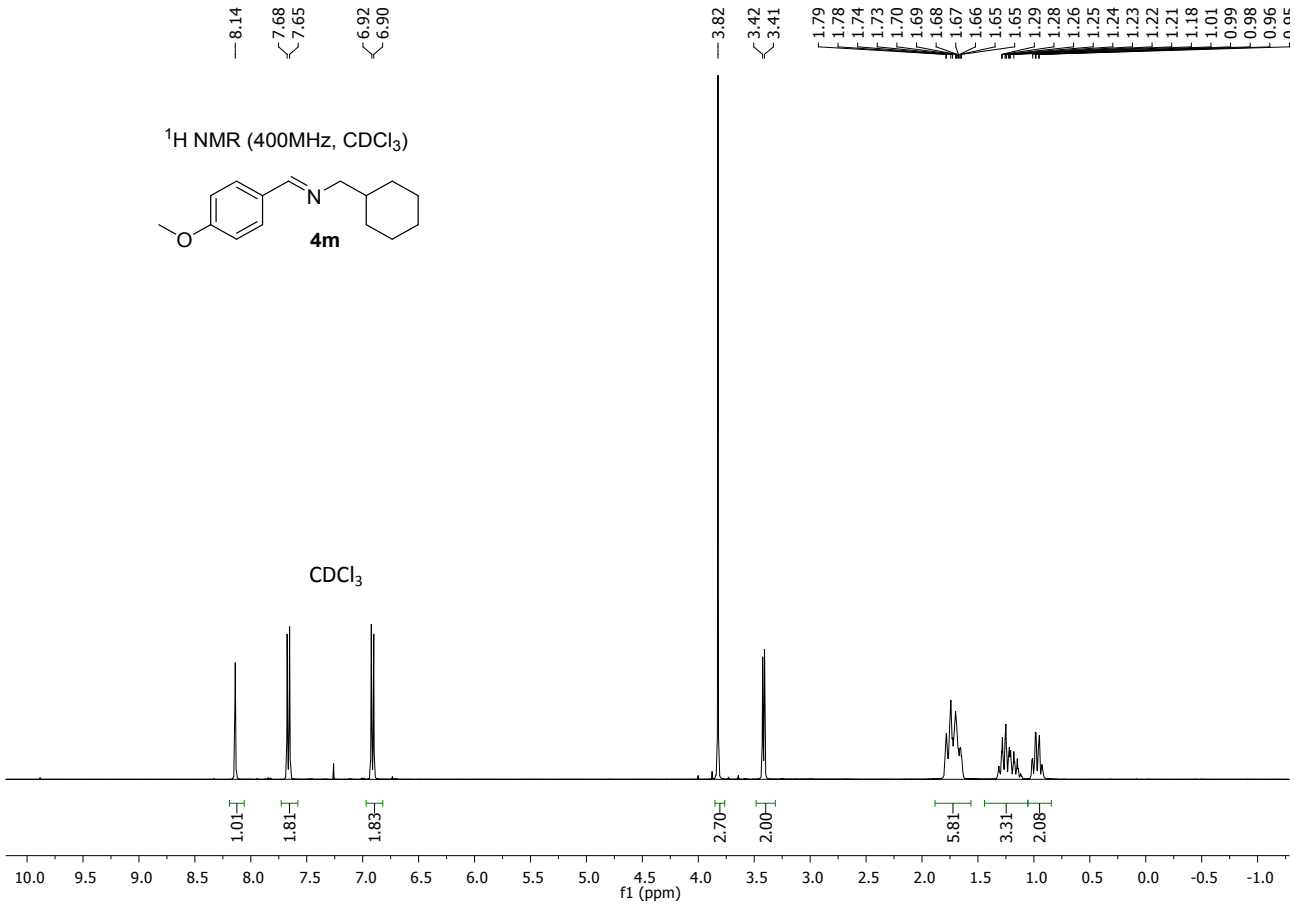
N-(4-methoxybenzyl)propan-2-amine (**10**)
Following GP6, imine **4o** (437 mg, 2.5 mmol) yielded the secondary amine **10** (408 mg, 92% yield).

N-(4-methoxybenzyl)butan-1-amine (**11**)
Following GP6, imine **4t** (365 mg, 1.9 mmol) yielded the secondary amine **11** (307 mg, 83% yield).

N-(4-methoxybenzyl)pentan-2-amine (**12**)

In a 25 mL two-necked flask under nitrogen atmosphere, 2-aminopentane **1j** (366 µL, 3 mmol, 1.5 equiv.) and acetic acid (172 µL, 3 mmol, 1.5 equiv.) were added to a solution of *p*-anisaldehyde **2a** (248 µL, 2 mmol, 1 equiv.) in anhydrous CH_2Cl_2 (5 mL). The mixture was left 15 minutes under stirring, then $NaBH(OAc)_3$ (874 mg, 4 mmol, 2 equiv.) was added at 0°C and the solution was diluted with 2 mL of anhydrous CH_2Cl_2 and stirred overnight. After completion (TLC monitoring, 24 h), the mixture was quenched with HCl 6M and left 30 minutes under stirring. The mixture was then diluted with water and basified until pH 11 with NaOH 5M. The aqueous phase was extracted with CH_2Cl_2 (1 x 10 mL) and Et_2O (2 x 10 mL), the collected organic layers were dried on anhydrous Na_2SO_4, filtered and concentrated to afford the target amine **12** as a yellow oil without further purification (370 mg, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.23 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H), 3.76 (d, J_{AB} = 12.7 Hz, 1H), 3.67 (d, J_{AB} = 12.7 Hz, 1H), 2.69 – 2.65 (m, 1H), 1.47 – 1.31 (m, 4H), 1.07 (d, *J* = 6.2 Hz, 3H), 0.90 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 158.5, 133.0, 129.2, 113.7, 55.2, 52.1, 50.7, 39.3, 20.2, 19.1, 14.2; IR (film, cm^{-1}): 2958, 2930, 2870, 1612, 1512, 1463, 1299, 1246, 1038; HPLC-MS (ESI^+): R_t = 2.0 min; m/z = 208 $[M+H]^+$.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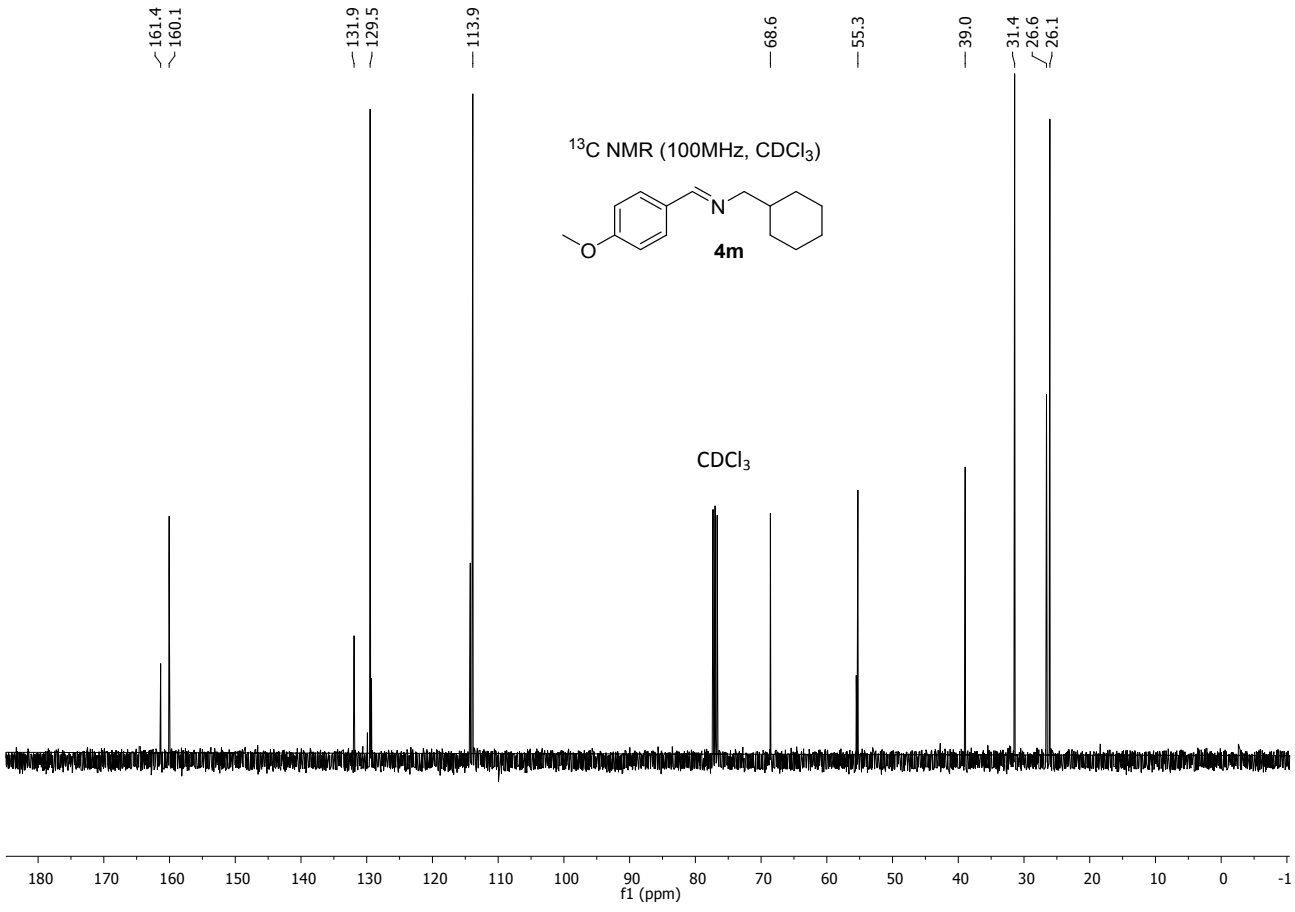
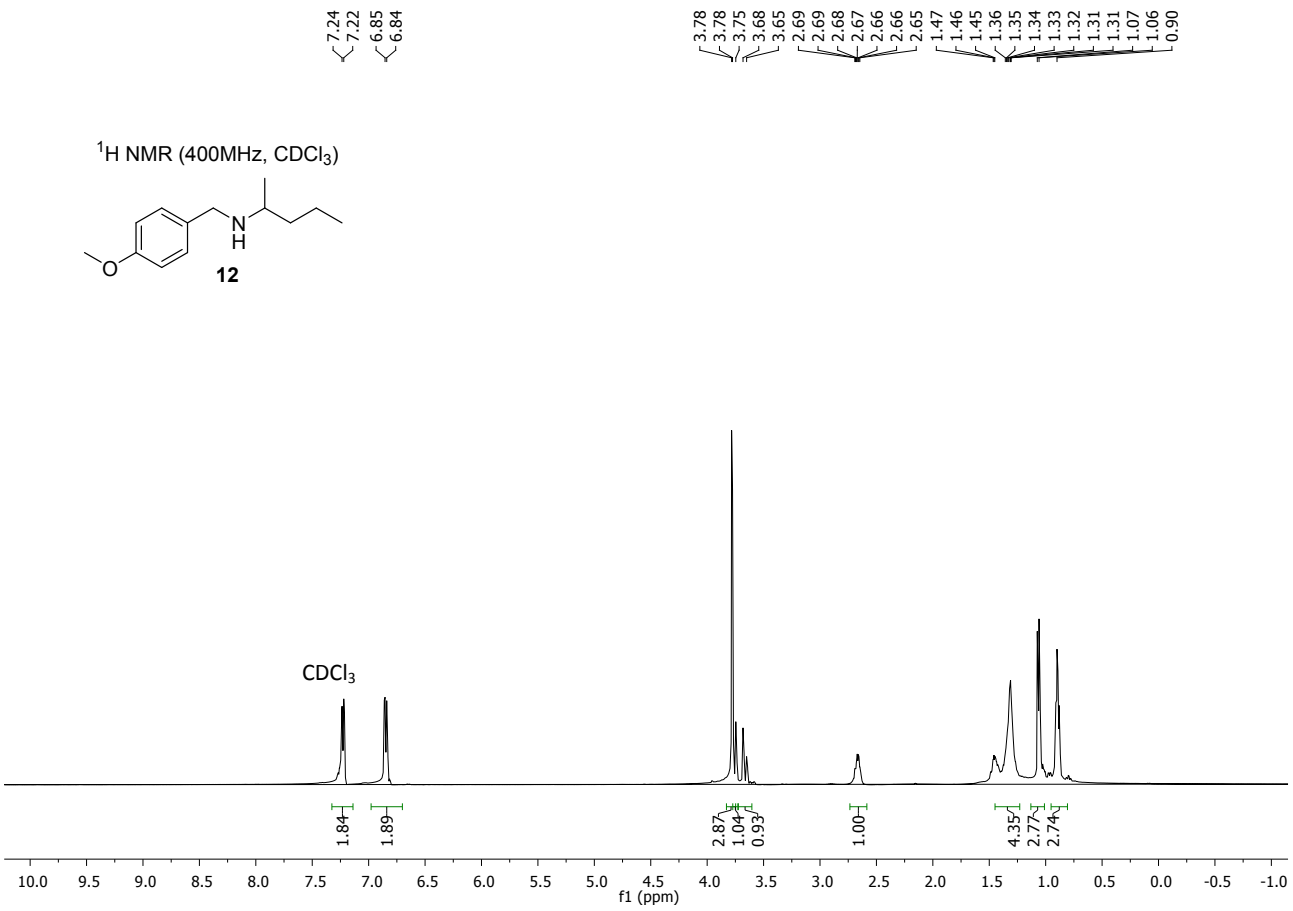
7.68
7.65
6.92
6.90
3.82
3.42
3.41
1.79
1.78
1.74
1.73
1.70
1.69
1.68
1.67
1.66
1.65
1.29
1.28
1.26
1.25
1.24
1.23
1.22
1.21
1.18
1.01
0.99
0.98
0.96
^{1}H NMR (400MHz, $CDCl_3$)
N
O
4m
$CDCl_3$
1.01
1.81
1.83
2.70
2.00
5.81
3.31
2.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


161.4
160.1
131.9
129.5
113.9
68.6
55.3
39.0
31.4
26.6
26.1
^{13}C NMR (100MHz, $CDCl_3$)
N
O
4m
$CDCl_3$
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)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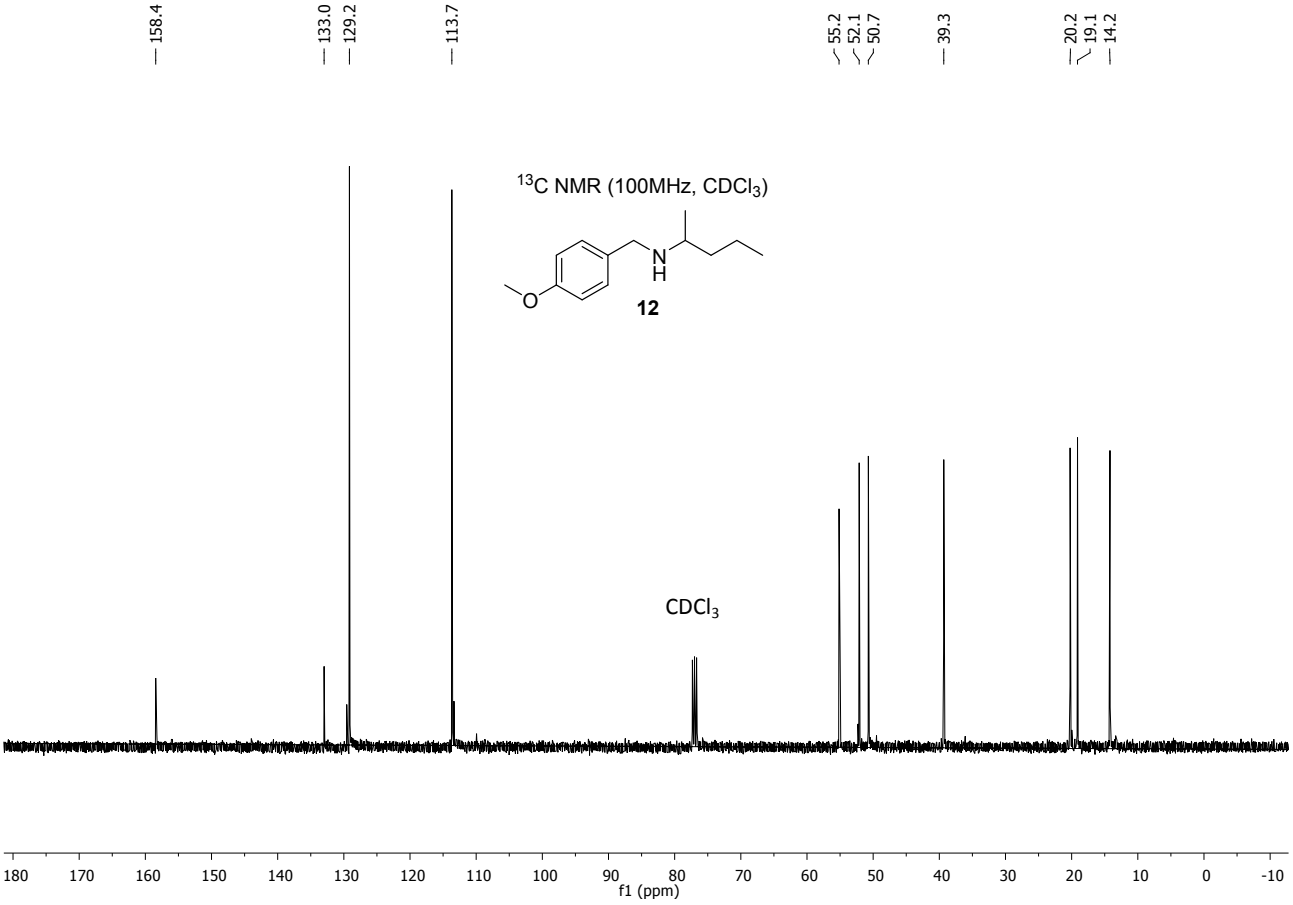
1.47
1.46
1.45
1.36
1.35
1.34
1.33
1.32
1.31
1.31
1.07
1.06
0.90
^{1}H NMR (400MHz, $CDCl_3$)
N
H
O
12
$CDCl_3$
1.84
1.89
2.87
1.04
0.93
1.00
4.35
2.77
2.74
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


158.4
133.0
129.2
113.7
55.2
52.1
50.7
39.3
20.2
19.1
14.2
^{13}C NMR (100MHz, $CDCl_3$)
N
H
O
12
$CDCl_3$
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)