Electronic Supplementary Material (ESI) for ChemComm.

Biomimetic synthesis of 2-substituted *N*-heterocycle alkaloids by one-pot hydrolysis, transamination and decarboxylative Mannich reaction

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ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

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Chemicals and enzymes

All commercially available reagents and solvents were used without further purification. Diamine dihydrochlorides and ketoesters were purchased from Sigma-Aldrich, Alfa Aesar or Fluorochem.

Lipases used in the screening (listed in the following table) were obtained commercially from Sigma-Aldrich, Amano or Novozymes, and used as supplied.

Lipase	**Source**	**Notes**	**Supplier**
PPL	porcine pancreas	Type II, 100-500 U/mg protein	Sigma-Aldrich
PSL	*Burkholderia cepacia*	>30,000 U/g	Amano
CALB	*Candida antarctica*	Novozym® 435, 10,000 PLU/g (immobilised on acrylic resin)	Novozymes
F-AP15	*Rhizopus oryzae*	≥150,000 U/g	Sigma-Aldrich
TLL	*Thermomyces lanuginosus*	≥100,000 U/g	Sigma-Aldrich

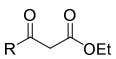
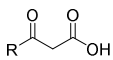
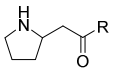
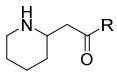
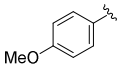
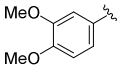
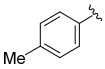
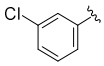
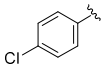
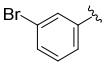
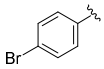
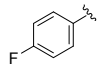
The diamine transaminase YgjG from *E. coli* K12 was produced in *E. coli* BL21(DE3) according to a previously published procedure (Slabu et al. *ChemCatChem* 2016, **8**, 1038-1042) as follows. A fresh colony of *E. coli* BL21(DE3) harbouring the plasmid pET28b-YgjG was used to inoculate LB medium (8 mL) containing kanamycin (50 µg mL^{-1}). This starter culture was grown overnight at 37°C and 220 rpm, and used to inoculate LB medium (800 mL) containing kanamycin (50 µg mL^{-1}). The culture was grown at 37°C and 220 rpm until OD600 reached 0.6-0.8, then the temperature was lowered to 18°C and expression was induced by addition of IPTG (0.2 mM final concentration). Expression was continued for 16 h at 18°C and 220 rpm. Cells were harvested by centrifugation (4°C, 3,250 *g*, 20 min) and stored at –20°C until needed. For the preparation of the crude lysate, cells were resuspended (1 g of wet cell paste in 10 mL) in lysis buffer (50 mM Tris-HCl, 1 mM PLP, pH 8.0) and lysed in an ice bath by ultrasonication in a Soniprep 150 (20 s on, 20 s off, 20 cycles). After centrifugation (4°C, 16,000 g, 20 min) the clarified lysate was used directly for the biotransformations.

Analytical methods

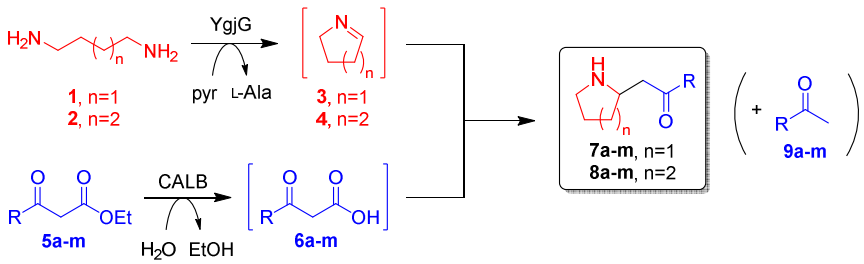
^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance 400 instrument (400 MHz for ^{1}H and 100 MHz for ^{13}C) in $CDCl_3$, using residual protic solvent as internal standard. Chemical shifts (δ) are reported in parts per million (ppm) relative to the residual protic solvent signal ($CHCl_3$ in $CDCl_3$, ^{1}H= 7.26; ^{13}C= 77.0).

HRMS analyses were performed using an Agilent 1200 series LC system, coupled to an Agilent 6520 QTOF mass spectrometer, ESI positive mode. The sample (2 µL) was flow-injected into 0.3 mL min^{-1} MeCN/H_2O 1:1 + formic acid 0.1% *v/v*. The data was analysed using Agilent MassHunter software.

Reverse-phase HPLC analyses were performed on an Agilent 1200 series LC system equipped with a non-chiral Zorbax Extend C18 column (50 mm × 4.6 mm × 3.5 µm, Agilent), according to the following method: flow rate 1.0 mL min^{-1}; temperature: 40°C; detection wavelength 250 nm; mobile phase aq. NH_4OH 0.1 M pH 10.0 / MeOH; gradient elution 90:10 (0-1 min), 90:10-10:90 (1-18 min), 10:90 (18-21 min), 10:90-90:10 (21-23 min), 90:10 (23-30 min). Retention times are listed in the following table.

		Retention times [min]				
	R	 **5a-i**	 **6a-i**	 **7a-i**	 **8a-i**	 **9a-i**
a		12.4	3.0	11.4	13.2	9.8
b		12.5	4.6	11.8	13.4	10.7
c		11.3	4.7	10.2	11.9	9.4
d		14.0	5.7	13.9	15.2	12.2
e		15.1	8.4	14.9	16.1	12.8
f		15.1	7.5	14.9	16.0	12.9
g		15.6	9.0	15.4	16.5	13.4
h		15.5	9.3	15.4	16.5	13.5
i		12.5	4.4	11.9	13.6	9.9

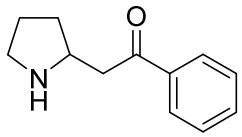
General procedure for the synthesis of alkaloids 7-8 on preparative scale



The diamine dihydrochloride salt (30 mM), sodium pyruvate (40 mM) and PLP (1 mM) were dissolved in 30 mL Tris-HCl buffer (50 mM, pH 9.0). The suitable ketoester (25 mM) was dissolved in 5 mL MeOH (10% *v/v*) and added to the mixture and adjusted to pH 9.0. Lipase Novozyme 435 (5 mg/mL) and clarified cell lysate containing transaminase YgjG (15 mL, from 1.5 g of wet cell pellet) were added and the reaction was incubated at 37°C, 250 rpm for 18 h. The reaction mixture was filtered through Celite and the aminoketone products were isolated *via* acid-base work up. The solution was acidified to pH 2.0 with aqueous HCl (1 M), washed with Et_2O (2 × 10 mL), then re-adjusted to pH 10.0 with aqueous NaOH (1 M) and the basified mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined CH_2Cl_2 phase was dried on $MgSO_4$ and concentrated under reduced pressure to afford alkaloids as oils or solids.

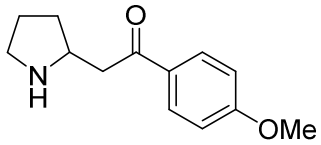
Characterisation of compounds 7a-c, 8a-c, 7j-m, 8k-m and 11

1-phenyl-2-(pyrrolidin-2-yl)ethan-1-one (7a)



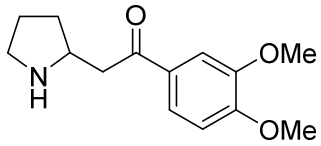
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7a** was obtained as a yellow oil, 149 mg, 64% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 2H), 7.50 – 7.45 (m, 1H), 7.37 (dd, *J* = 8.2, 6.9 Hz, 2H), 3.59 – 3.47 (m, 1H), 3.20 – 3.06 (m, 2H), 3.01 – 2.93 (m, 1H), 2.92 – 2.81 (m, 1H), 2.05 – 1.85 (m, 1H), 1.84 – 1.62 (m, 2H), 1.45 – 1.28 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 199.6, 136.1, 133.1, 128.6, 128.1, 54.5, 46.2, 45.2, 31.3, 24.7. **HRMS** calcd. for $C_{12}H_{16}NO^+$ 190.1232 $[M+H]^+$, found 190.1213.

1-(4-methoxyphenyl)-2-(pyrrolidin-2-yl)ethan-1-one (7b)



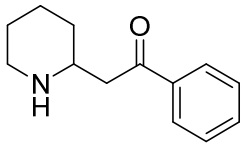
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7b** was obtained as a yellow solid, 220 mg, 81% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 – 7.90 (m, 2H), 7.00 – 6.88 (m, 2H), 3.88 (s, 3H), 3.63 – 3.50 (m, 1H), 3.18 – 3.08 (m, 2H), 3.09 – 3.01 (m, 1H), 2.93 (ddd, *J* = 10.0, 8.2, 6.8 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.90 – 1.71 (m, 2H), 1.48 – 1.37 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.2, 163.5, 130.4, 130.2, 113.7, 55.5, 54.7, 46.2, 44.7, 31.3, 24.6. **HRMS** calcd. for $C_{13}H_{18}NO_2^+$ 220.1338 $[M+H]^+$, found 220.1323.

1-(3,4-dimethoxyphenyl)-2-(pyrrolidin-2-yl)ethan-1-one (7c, ruspolinone)



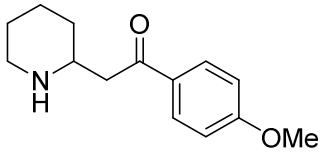
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7c** was obtained as a yellow solid, 221 mg, 71% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.55 (d, *J* = 2.0 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 3.97 (s, 3H), 3.96 (s, 3H), 3.65 – 3.55 (m, 1H), 3.16 (dd, *J* = 7.1, 4.0 Hz, 2H), 3.12 – 3.03 (m, 1H), 3.10 – 2.91 (m, 1H), 2.09 – 1.98 (m, 1H), 1.91 – 1.78 (m, 2H), 1.51 – 1.40 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.8, 153.6, 149.0, 129.2, 123.2, 110.0, 110.0, 56.1, 56.0, 55.9, 44.9, 40.6, 30.7, 23.7. **HRMS** calcd. for $C_{14}H_{20}NO_3^+$ 250.1443 $[M+H]^+$, found 250.1429.

1-phenyl-2-(piperidin-2-yl)ethan-1-one (8a, norsedaminone)



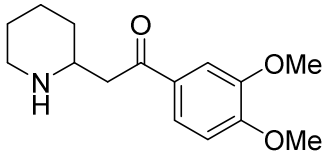
Following the general procedure for the α,ω-DTA/lipase cascade, compound **16** was obtained as a yellow solid, 154 mg, 60% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 – 7.93 (m, 2H), 7.62 – 7.54 (m, 1H), 7.53 – 7.44 (m, 2H), 3.21 – 3.10 (m, 1H), 3.10 – 3.03 (m, 3H), 2.74 (td, *J* = 11.7, 2.8 Hz, 1H), 1.92 – 1.77 (m, 1H), 1.74 – 1.57 (m, 2H), 1.55 – 1.25 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.0, 137.5, 133.6, 129.1, 128.5, 53.3, 47.4, 46.1, 33.2, 26.5, 25.2. **HRMS** calcd. for $C_{13}H_{18}NO^+$ 204.1388 $[M+H]^+$, found 204.1385

1-(4-methoxyphenyl)-2-(piperidin-2-yl)ethan-1-one (8b)



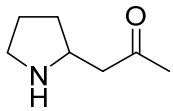
Following the general procedure for the α,ω-DTA/lipase cascade, compound **8b** was obtained as a yellow solid, 213 mg, 73% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 7.86 (m, 2H), 7.02 – 6.87 (m, 2H), 3.88 (s, 3H), 3.17 – 3.02 (m, 1H), 3.02 – 2.96 (m, 3H), 2.78 – 2.68 (m, 1H), 1.87 – 1.78 (m, 1H), 1.69 – 1.57 (m, 2H), 1.53 – 1.26 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.1, 163.5, 130.3, 130.2, 113.7, 55.5, 53.4, 46.9, 45.3, 32.8, 26.0, 24.8. **HRMS** calcd. for $C_{14}H_{20}NO_2^+$ 234.3190 $[M+H]^+$, found 234.1505.

1-(3,4-dimethoxyphenyl)-2-(piperidin-2-yl)ethan-1-one (8c)



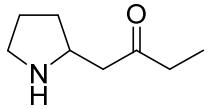
Following the general procedure for the α,ω-DTA/lipase cascade, compound **8c** was obtained as a yellow solid, 226 mg, 69% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.44 (d, J = 2.0 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.12 – 2.85 (m, 4H), 2.64 (td, *J* = 11.7, 2.8 Hz, 1H), 1.79 – 1.66 (m, 1H), 1.64 – 1.50 (m, 2H), 1.47 – 1.11 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.1, 153.4, 149.0, 130.3, 123.3, 122.9, 109.9, 56.1, 56.0, 46.9, 45.1, 32.7, 26.2, 26.0, 24.7. **HRMS** calcd. for $C_{15}H_{22}NO_3^+$ 264.1600 $[M+H]^+$, found 264.1611.

1-(pyrrolidin-2-yl)propan-2-one (7j, norhygrine)



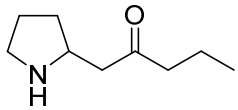
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7j** was obtained as a yellow oil, 65 mg, 50% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.46 – 3.35 (m, 1H), 2.99 (dd, *J* = 7.7, 5.3 Hz, 1H), 2.91 (dd, *J* = 8.2, 6.9 Hz, 1H), 2.69 – 2.56 (m, 2H), 2.18 (s, 3H), 1.96 – 1.86 (m, 1H), 1.88 – 1.67 (m, 2H), 1.39 – 1.21 (m, 1H). **^{13}C NMR** (100 MHz, chloroform-*d*) δ 208.5, 54.1, 50.0, 46.2, 31.1, 30.5, 24.6. **HRMS** calcd. for $C_7H_{14}NO^+$ 128.1075 $[M+H]^+$, found 128.1079.

1-(pyrrolidin-2-yl)butan-2-one (7k)



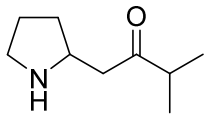
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7k** was obtained as pale a yellow oil, 89 mg, 50% yield.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.36 (dq, *J* = 8.5, 6.7 Hz, 1H), 2.94 (ddd, *J* = 10.2, 7.7, 5.4 Hz, 1H), 2.83 (ddd, *J* = 10.3, 8.2, 6.8 Hz, 1H), 2.59 – 2.52 (m, 2H), 2.38 (q, *J* = 7.3 Hz, 2H), 1.92 – 1.81 (m, 1H), 1.80 – 1.57 (m, 2H), 1.32 – 1.14 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.8, 54.3, 48.2, 46.0, 36.4, 31.1, 24.6, 7.7. **HRMS** calcd. for $C_8H_{16}NO^+$ 142.1232 $[M+H]^+$, found 142.1223.

1-(pyrrolidin-2-yl)pentan-2-one (7l)



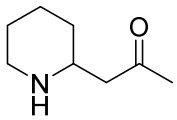
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7l** was obtained as a yellow oil, 153 mg, 78% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.37 – 3.27 (m, 1H), 2.96 – 2.87 (m, 1H), 2.86 – 2.75 (m, 1H), 2.54 (dd, *J* = 6.5, 1.7 Hz, 2H), 2.33 (t, *J* = 7.4 Hz, 2H), 1.91 – 1.78 (m, 1H), 1.78 – 1.59 (m, 2H), 1.53 (q, *J* = 7.4 Hz, 2H), 1.26 – 1.17 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.6, 54.2, 48.9, 46.1, 45.2, 31.1, 24.6, 17.1, 13.7. **HRMS** calcd. for $C_9H_{18}NO^+$ 156.1388 $[M+H]^+$, found 156.1380.

3-methyl-1-(pyrrolidin-2-yl)butan-2-one (7m)



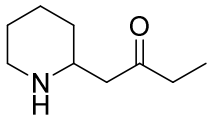
Following the general procedure for the α,ω-DTA/lipase cascade, compound **7m** was obtained as a yellow oil, 89 mg, 54% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.37 – 3.25 (m, 1H), 2.98 – 2.88 (m, 1H), 2.85 – 2.77 (m, 1H), 2.65 – 2.54 (m, 2H), 2.52 (sept., *J* = 6.9 Hz, 1H), 1.90 – 1.81 (m, 1H), 1.78 – 1.59 (m, 2H), 1.29 – 1.16 (m, 1H), 1.03 (dd, *J* = 6.9, 1.1 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 213.0, 54.7, 45.2, 44.2, 40.9, 30.8, 24.1, 18.2, 18.0. **HRMS** calcd. for $C_9H_{18}NO^+$ 156.1388 $[M+H]^+$, found 156.1376.

1-(piperidin-2-yl)propan-2-one (8j, pelletierine)



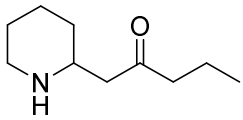
Following the general procedure for the α,ω-DTA/lipase cascade, the formation of compound **8j** was confirmed by HPLC and HRMS, but it has not been possible to isolate it in sufficient purity for characterisation. **HRMS** calcd. for $C_8H_{16}NO^+$ 142.1232 $[M+H]^+$, found 142.1223.

1-(piperidin-2-yl)butan-2-one (8k)



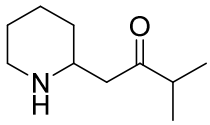
Following the general procedure for the α,ω-DTA/lipase cascade, compound **8k** was obtained as a pale yellow oil, 107 mg, 55% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.08 – 2.90 (m, 2H), 2.72 – 2.61 (m, 1H), 2.51 – 2.45 (m, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 1.85 – 1.69 (m, 1H), 1.64 – 1.51 (m, 2H), 1.44 – 1.31 (m, 2H), 1.23 – 1.09 (m, 1H), 1.06 (t, *J* = 7.3 Hz, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.4, 51.9, 48.3, 46.0, 36.1, 31.6, 25.1, 23.9, 7.1. **HRMS** calcd. for $C_9H_{18}NO^+$ 156.1388 $[M+H]^+$, found 156.1380.

1-(piperidin-2-yl)pentan-2-one (8l)



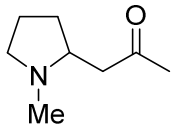
Following the general procedure for the α,ω-DTA/lipase cascade, compound **8l** was obtained as a yellow oil, 124 mg, 59% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.99 – 2.83 (m, 2H), 2.64 – 2.53 (m, 1H), 2.44 – 2.38 (m, 2H), 2.30 (t, *J* = 7.4 Hz, 2H), 1.74 – 1.66 (m, 1H), 1.57 – 1.43 (m, 2H), 1.52 (q, *J* = 7.4 Hz, 2H) 1.40 – 1.23 (m, 2H), 1.15 – 1.05 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.6, 52.4, 49.3, 46.6, 45.4, 32.1, 25.6, 24.5, 17.2, 13.7. **HRMS** calcd. for $C_{10}H_{20}NO^+$ 170.1545 $[M+H]^+$, found 170.1543.

3-methyl-1-(piperidin-2-yl)butan-2-one (8m)



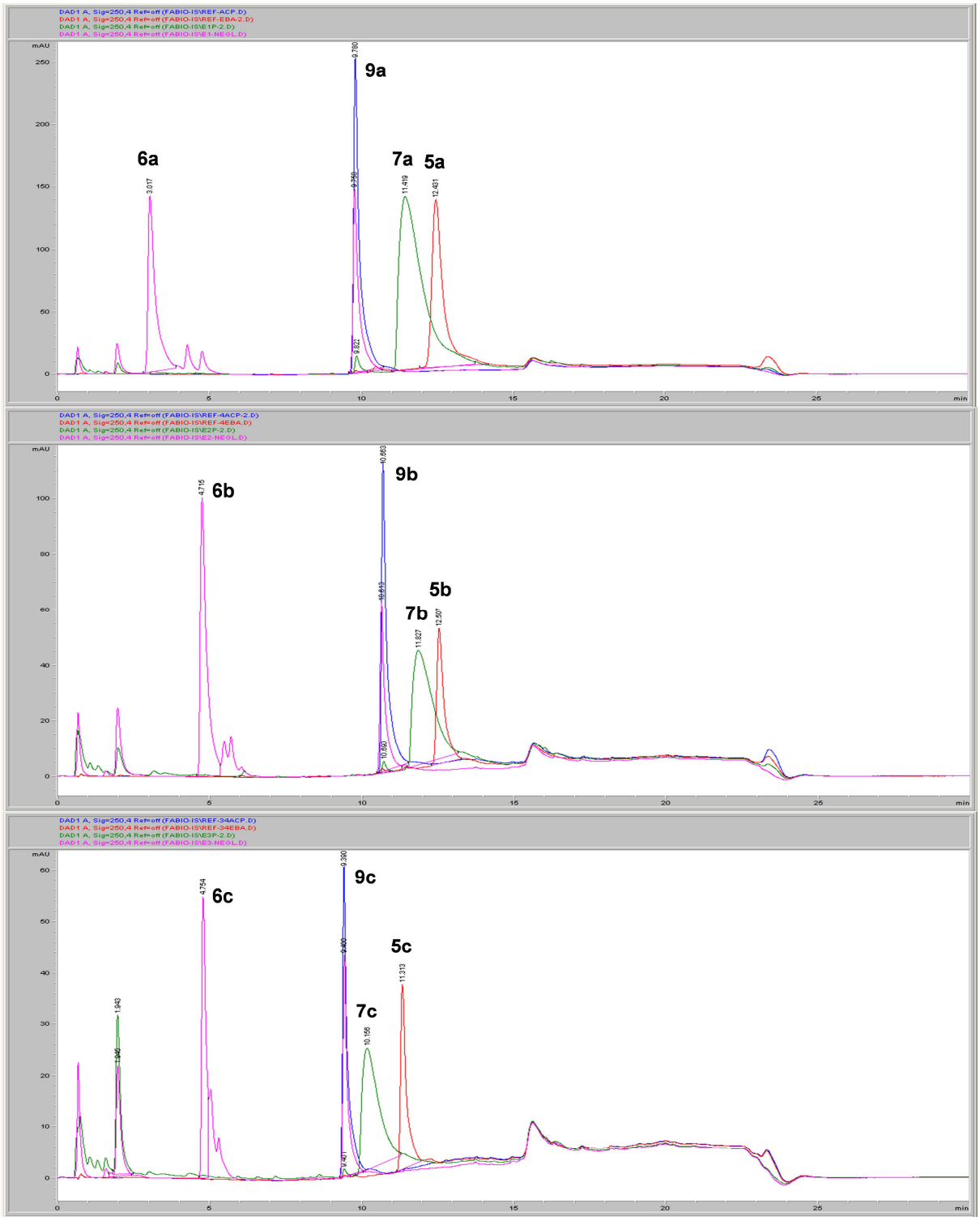
Following the general procedure for the α,ω-DTA/lipase cascade, compound **8m** was obtained as a yellow oil, 142 mg, 67% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.01 – 2.87 (m, 2H), 2.69 – 2.58 (m, 1H), 2.53 (sept., *J* = 7.0 Hz, 1H), 2.52 – 2.45 (m, 2H), 1.77 – 1.69 (m, 1H), 1.59 – 1.47 (m, 2H), 1.44 – 1.26 (m, 3H), 1.05 (d, *J* = 7.0 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 214.3, 52.4, 47.0, 46.6, 41.2, 32.2, 25.7, 24.5, 18.1, 18.1. **HRMS** calcd. for $C_{10}H_{20}NO^+$ 170.1545 $[M+H]^+$, found 170.1539.

1-(1-methylpyrrolidin-2-yl)propan-2-one (11, hygrine)

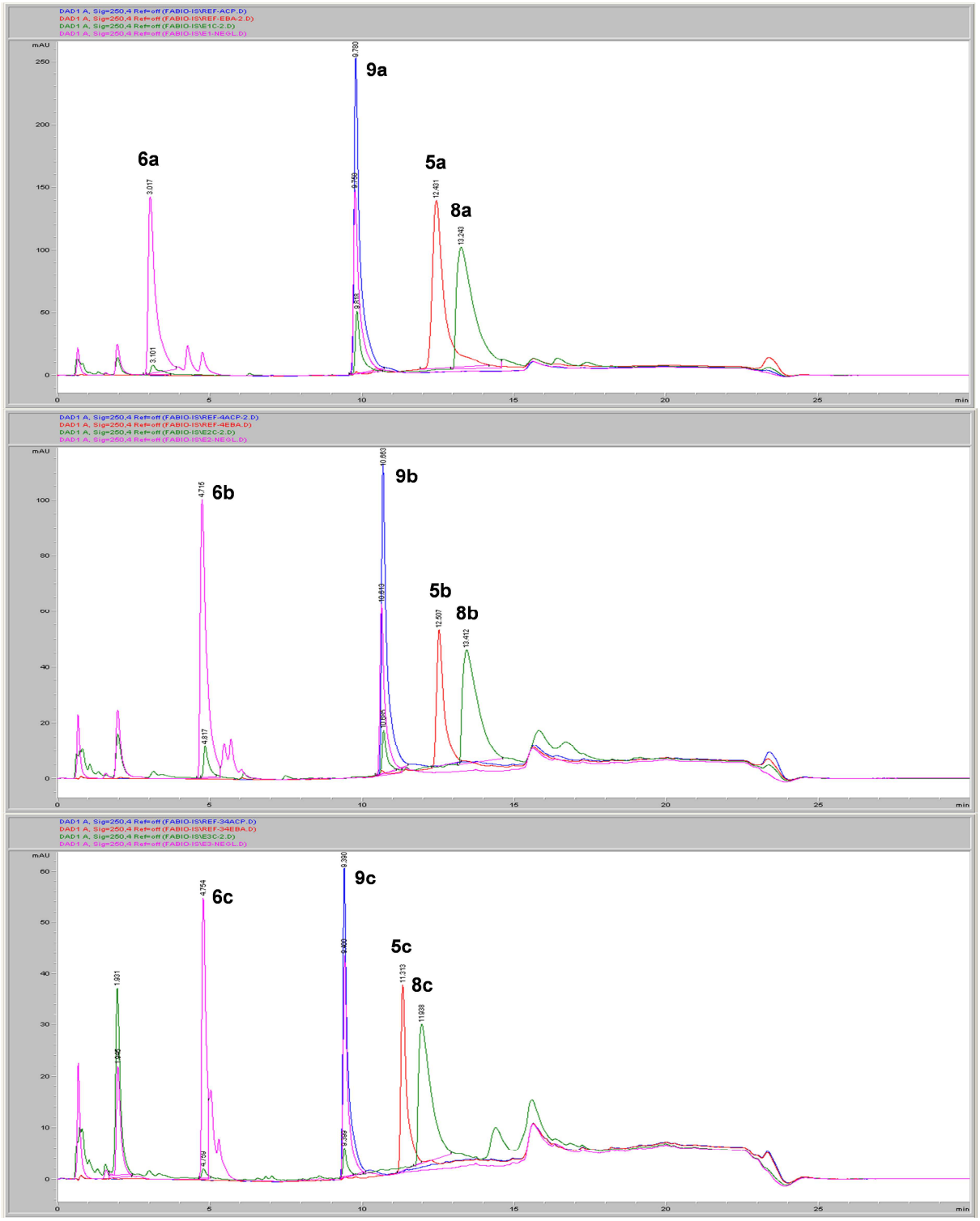


Following the general procedure for the α,ω-DTA/lipase cascade, compound **11** was obtained as a pale yellow oil, 102 mg, 75% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.98 (ddd, *J* = 9.7, 7.5, 2.6 Hz, 1H), 2.74 (dd, *J* = 16.1, 3.8 Hz, 1H), 2.47 (ddd, *J* = 8.3, 7.8, 3.9 Hz, 1H), 2.36 (dd, *J* = 16.1, 8.9, 1H), 2.24 (s, 3H), 2.11 (s, 3H), 2.07 – 1.97 (m, 1H), 1.77 – 1.57 (m, 2H), 1.41 – 1.28 (m, 1H). **^{13}C NMR** (100 MHz, chloroform-*d*) δ 206.6, 62.8, 56.2, 46.1, 40.2, 30.9, 30.4, 21.8. **HRMS** calcd. for $C_8H_{15}NO^+$ 142.1232 $[M+H]^+$, found 142.1227.

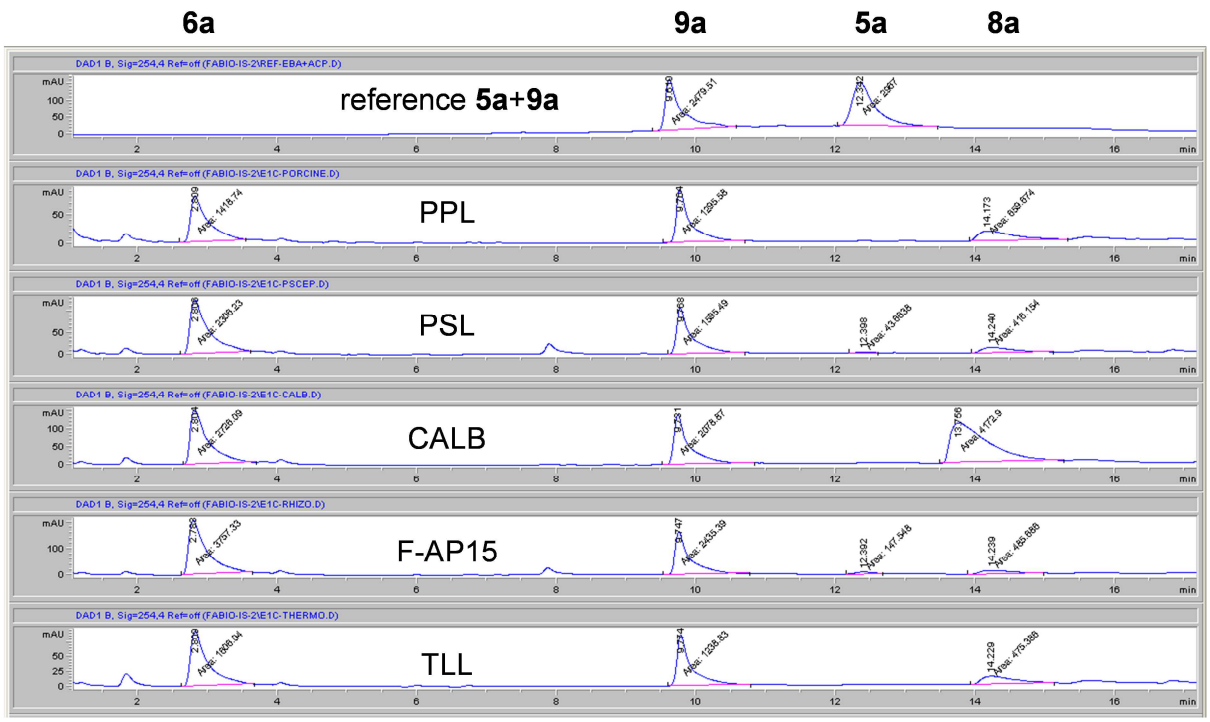
Representative HPLC traces



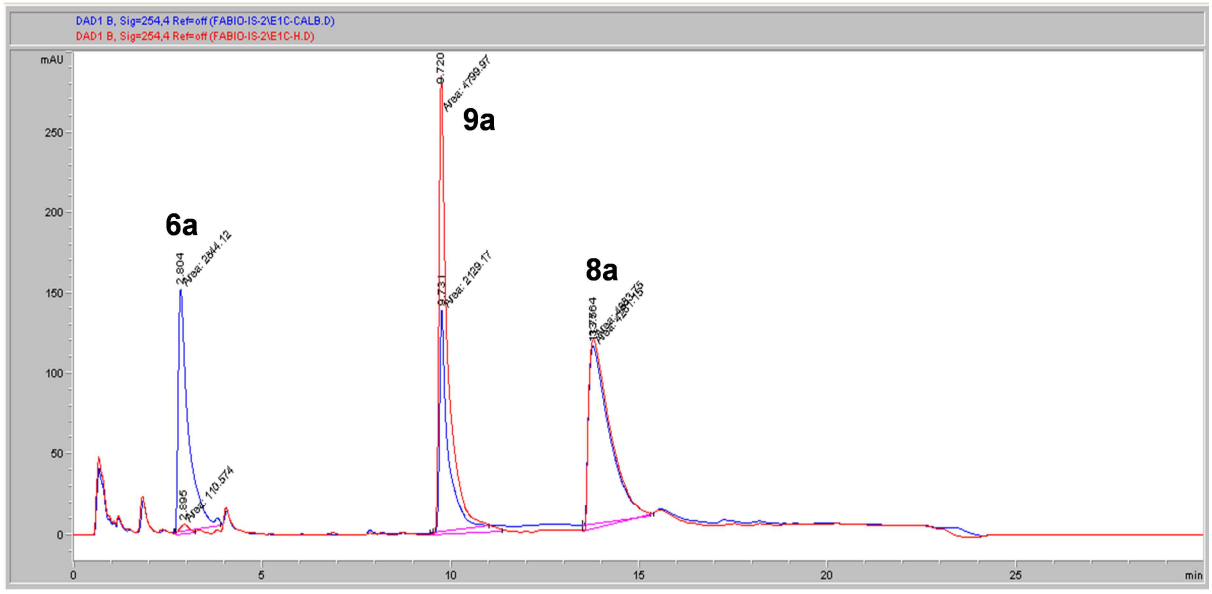
Representative traces for the one-pot α,ω-DTA/lipase cascade synthesis of **7a-c** from **1** and **5a-c**.
Blue trace: reference ketone **9a-c**.
Red trace: reference ketoester **5a-c**.
Green trace: representative biotransformation mixtures containing **7a-c**.
Pink trace: negative control without transaminase (showing hydrolysis and decarboxylation only).



Representative traces for the one-pot lipase/α,ω-DTA cascade synthesis of **8a-c** from **2** and **5a-c**.
Blue trace: reference ketone **9a-c**.
Red trace: reference ketoester **5a-c**.
Green trace: representative biotransformation mixtures containing **8a-c**.
Pink trace: negative control without transaminase (showing hydrolysis and decarboxylation only).



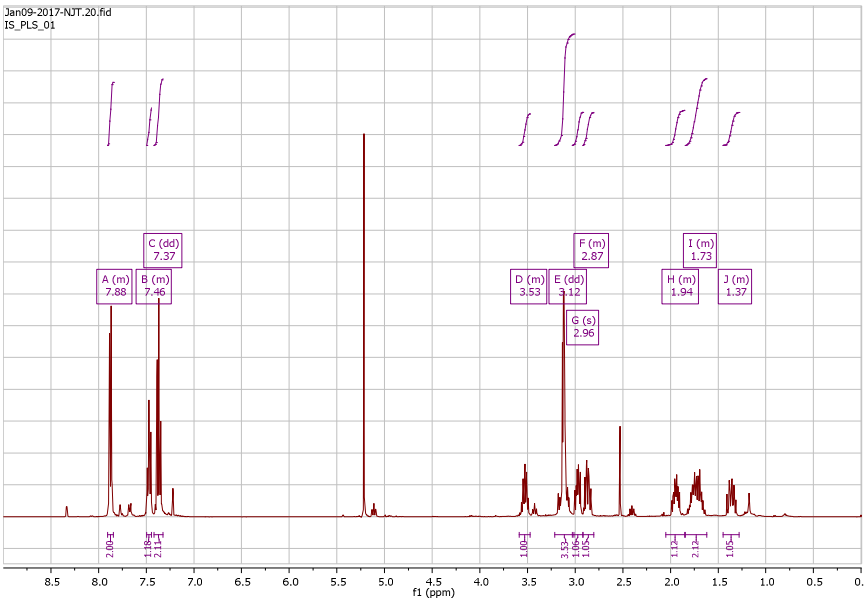
Screening of different lipases for the one-pot synthesis of **8a** from **2**+**5a**

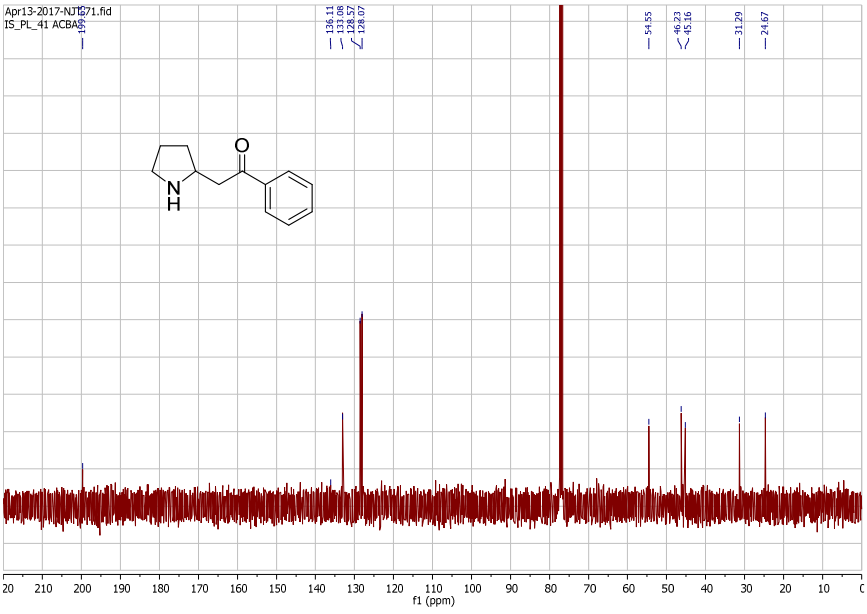


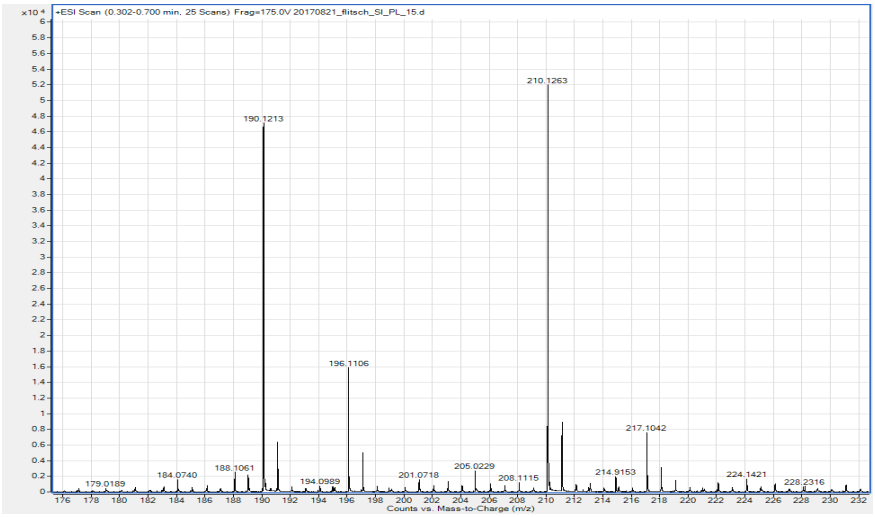
Representative trace showing the conversion of ketoacid **6a** to ketone **9a** upon heating, without appreciable decomposition of alkaloid **8a**.
Red trace: biotransformation mixture (from **2**+**5a**).
Blue trace: same mixture after heating for 1 h at 80°C, showing complete decarboxylation of **6a**.

Copies of the NMR and HRMS spectra

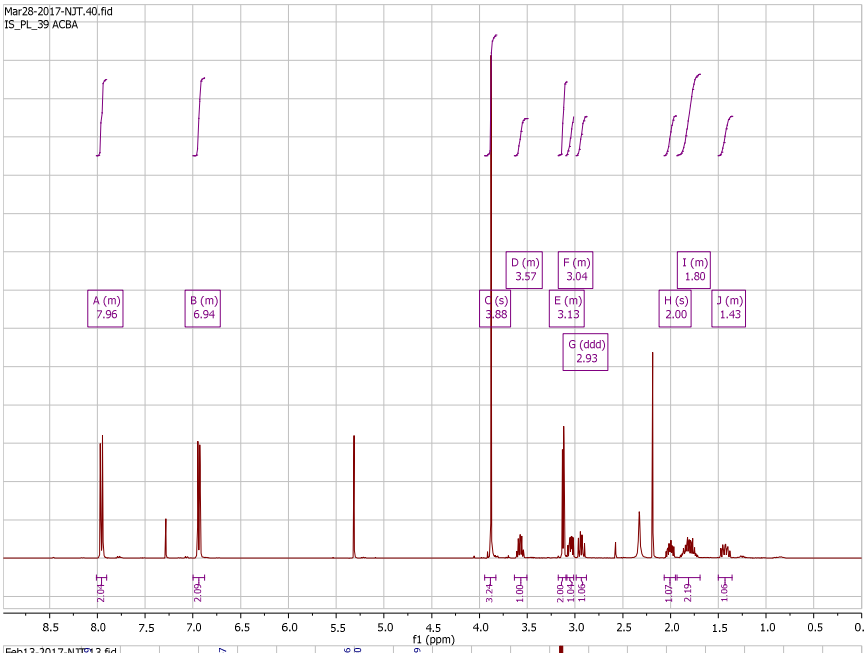
1-phenyl-2-(pyrrolidin-2-yl)ethan-1-one (7a)

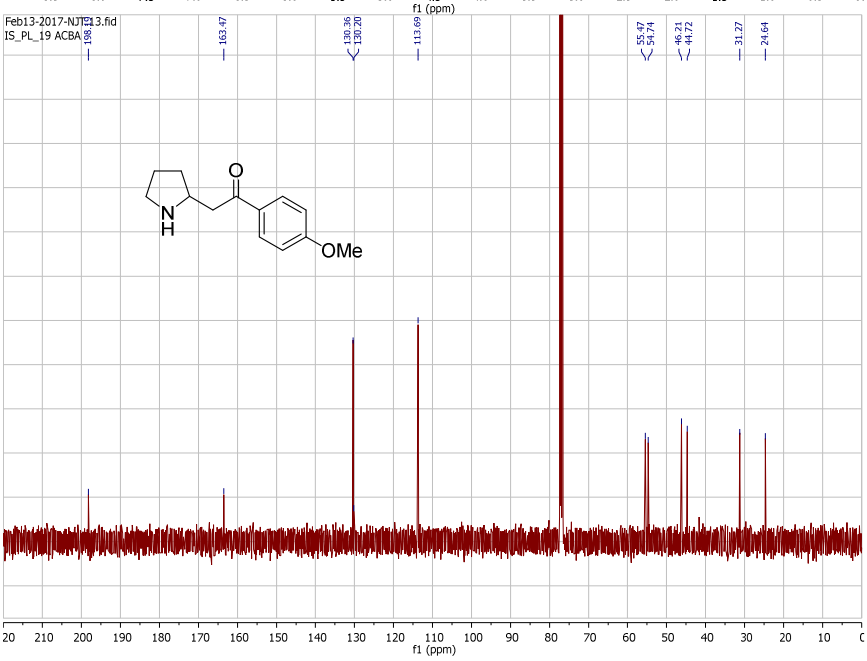


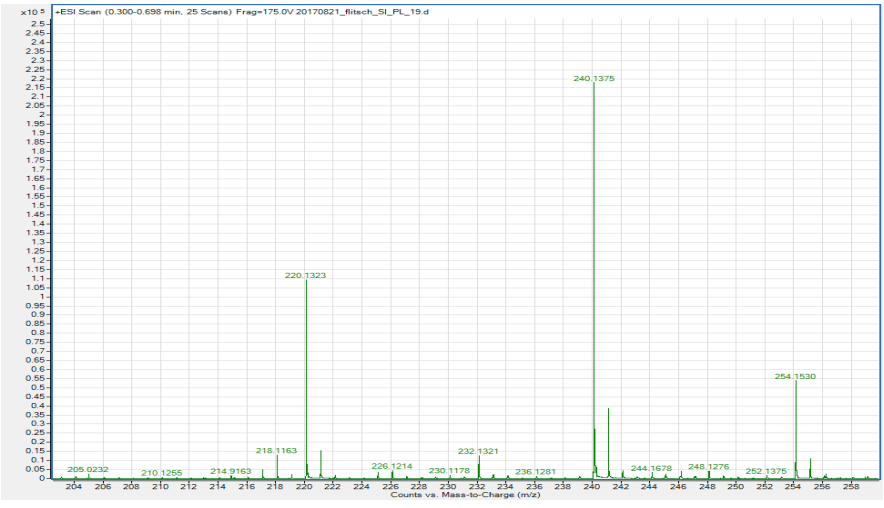




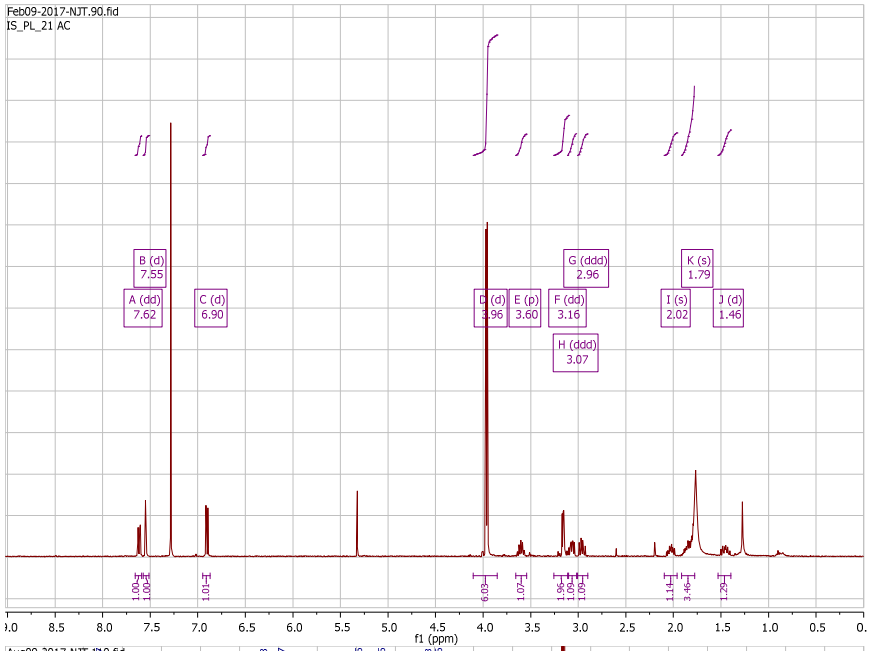
1-(4-methoxyphenyl)-2-(pyrrolidin-2-yl)ethan-1-one (7b)

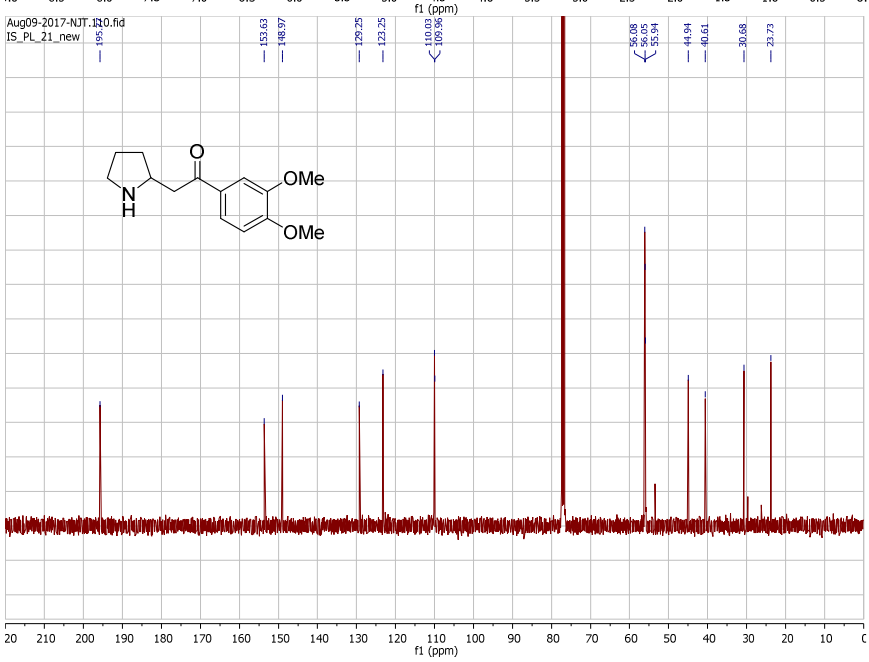


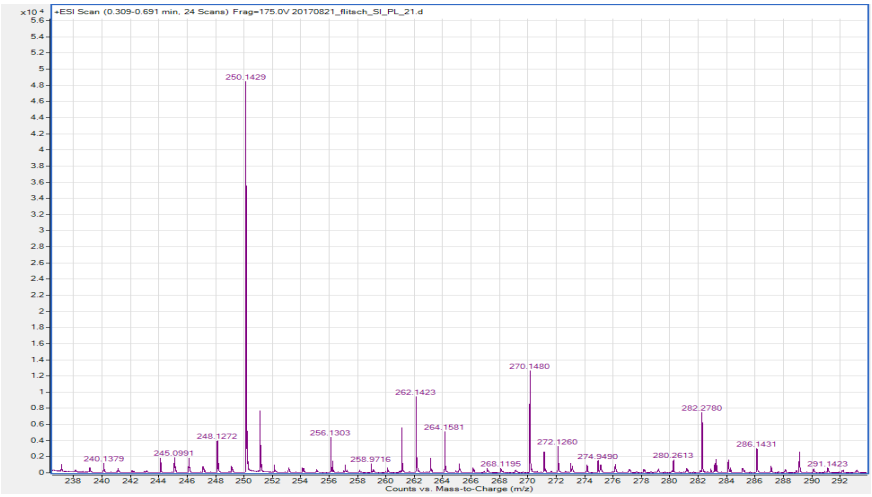




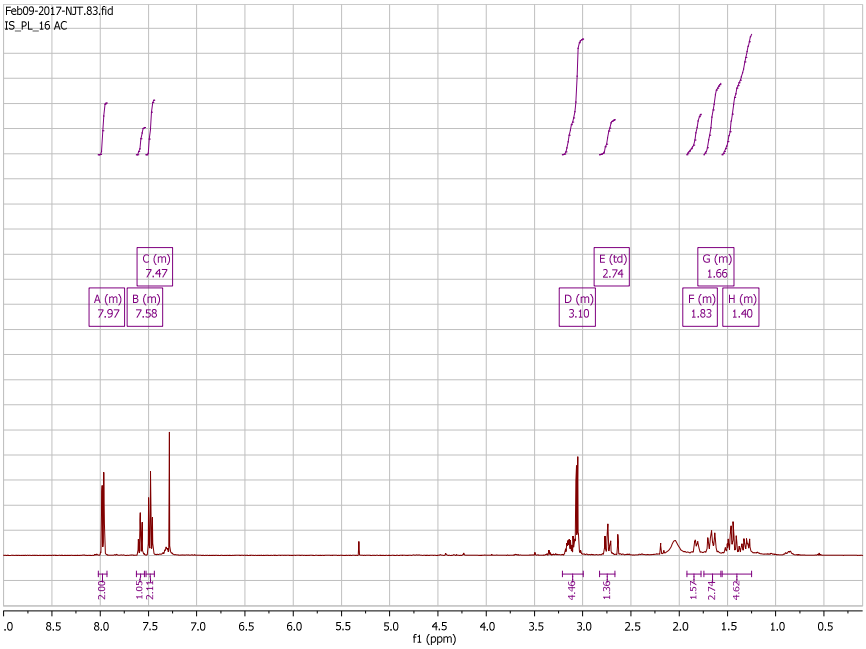
1-(3,4-dimethoxyphenyl)-2-(pyrrolidin-2-yl)ethan-1-one (7c, ruspolinone)

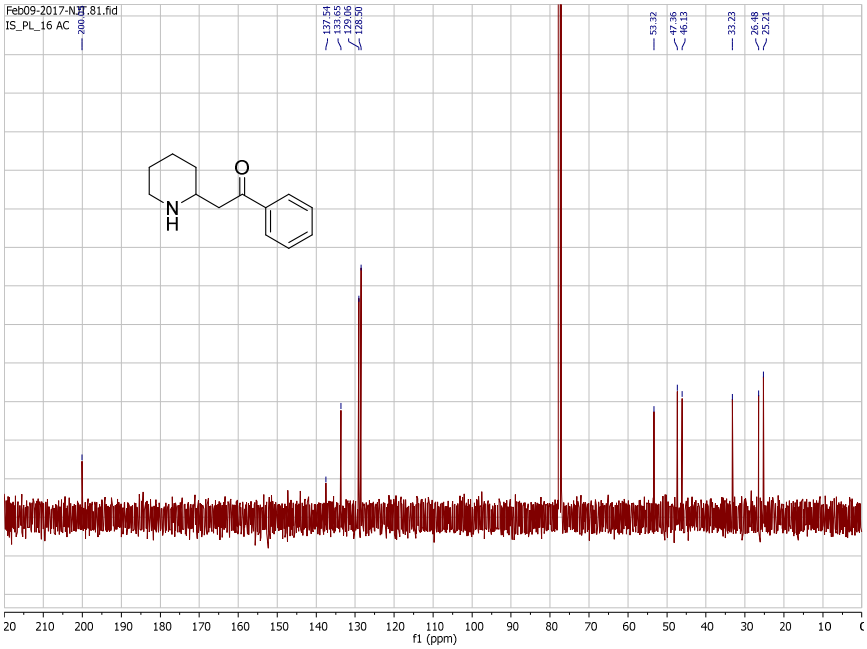


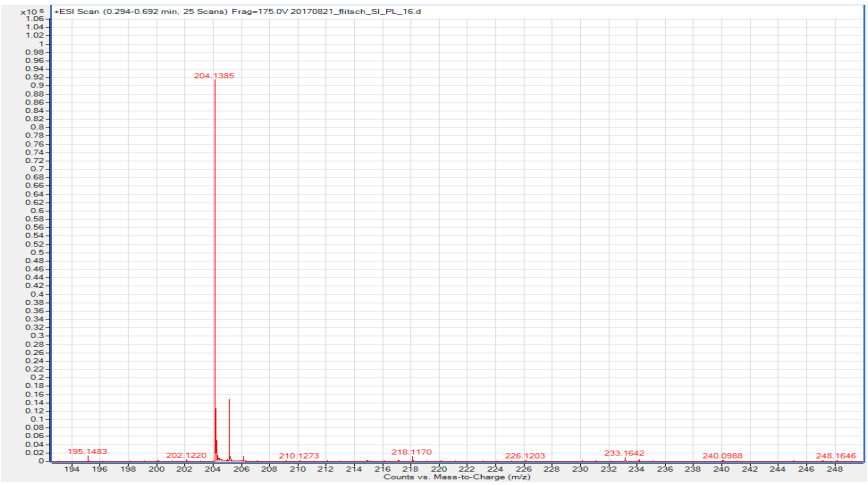




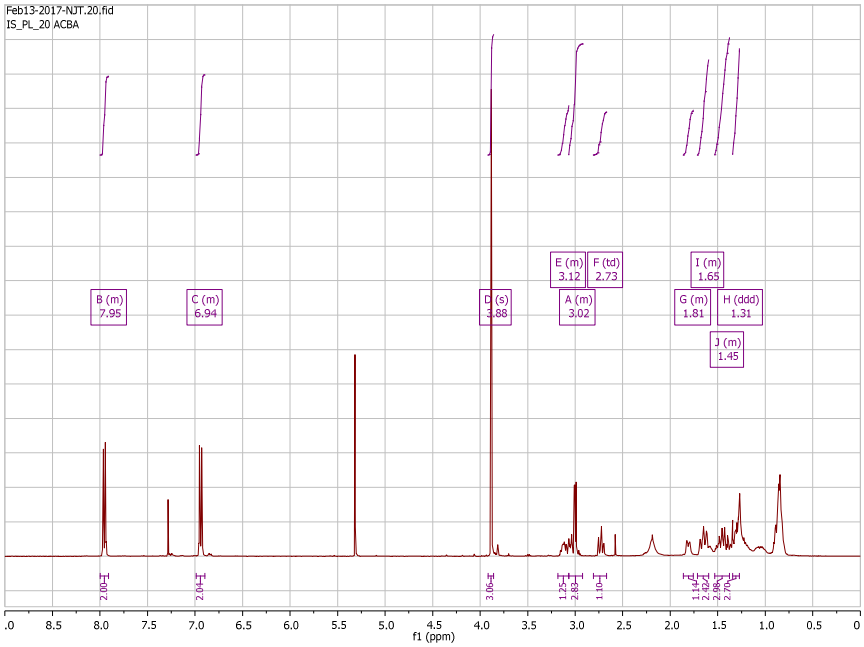
1-phenyl-2-(piperidin-2-yl)ethan-1-one (8a, norsedaminone)

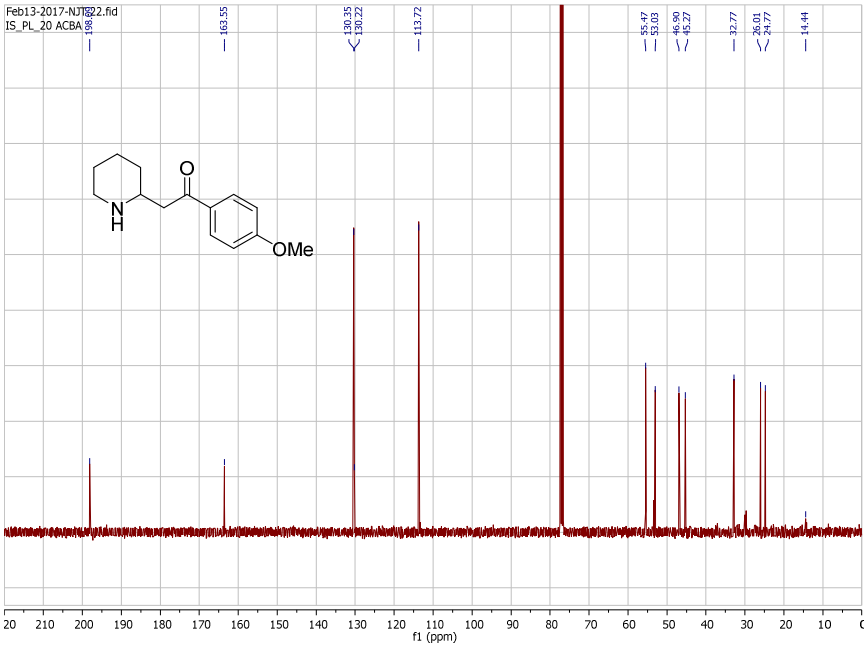


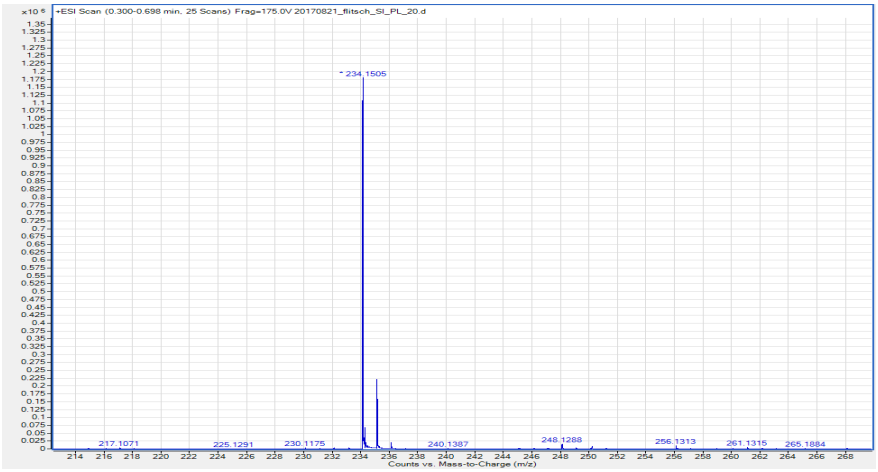




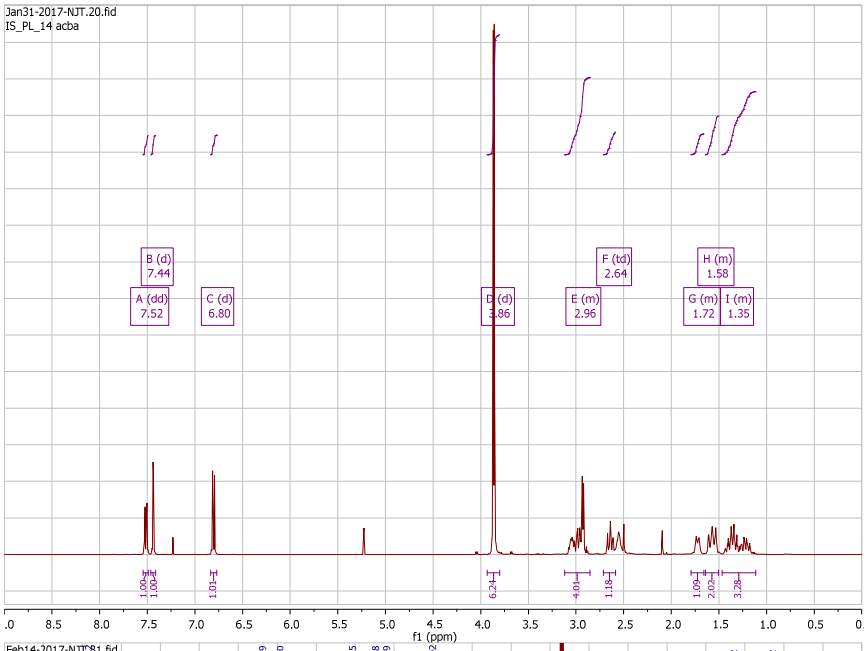
1-(4-methoxyphenyl)-2-(piperidin-2-yl)ethan-1-one (8b)

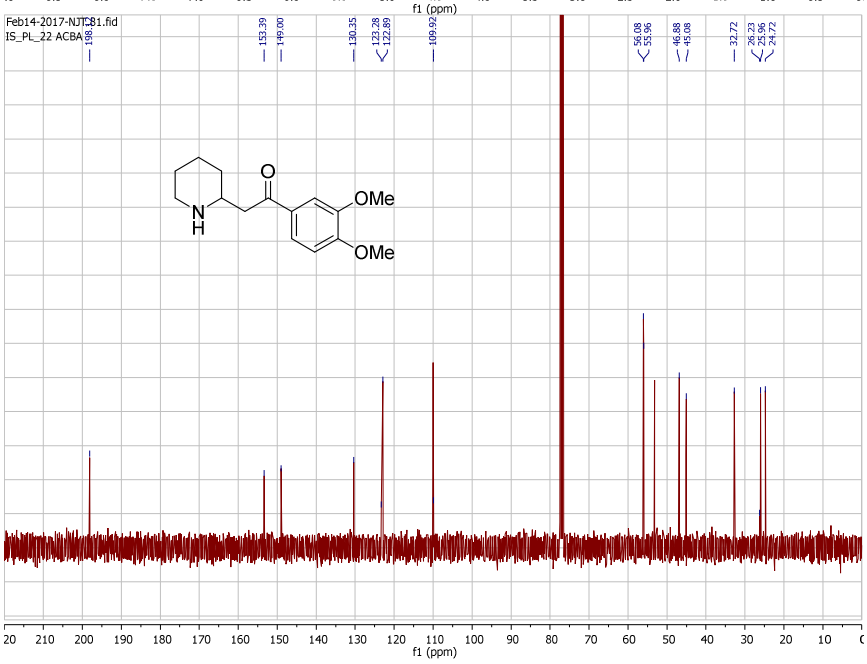


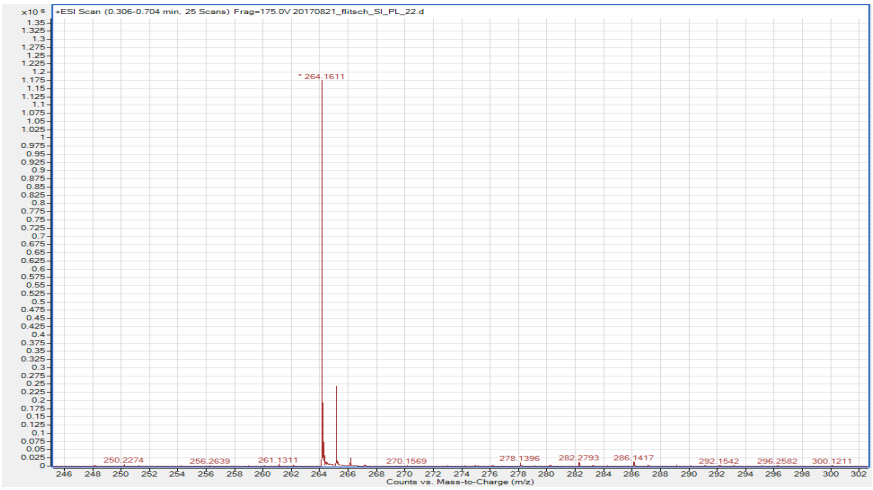




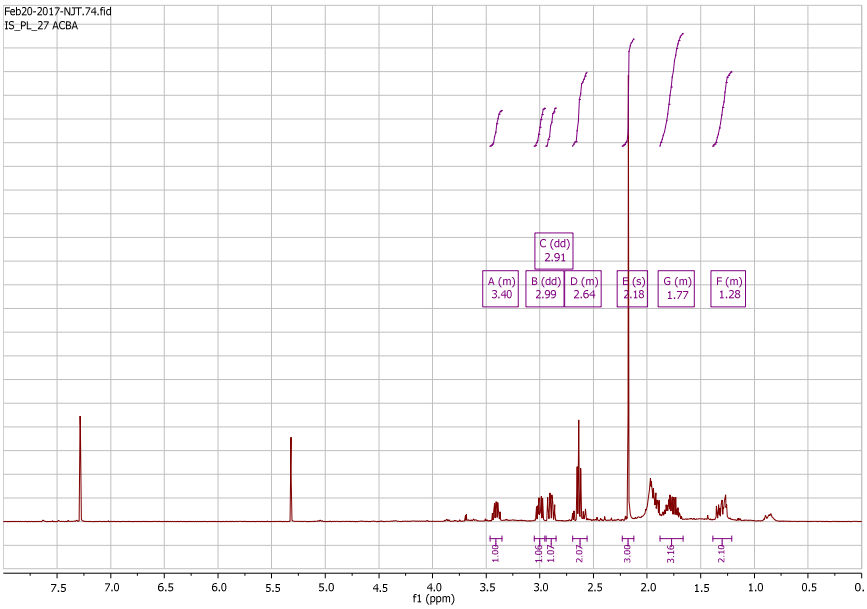
1-(3,4-dimethoxyphenyl)-2-(piperidin-2-yl)ethan-1-one (8c)

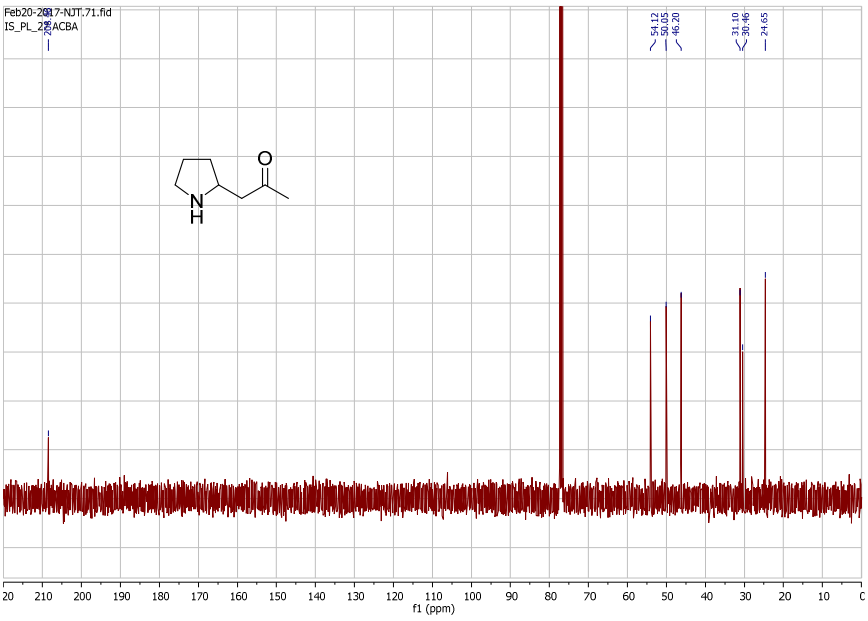


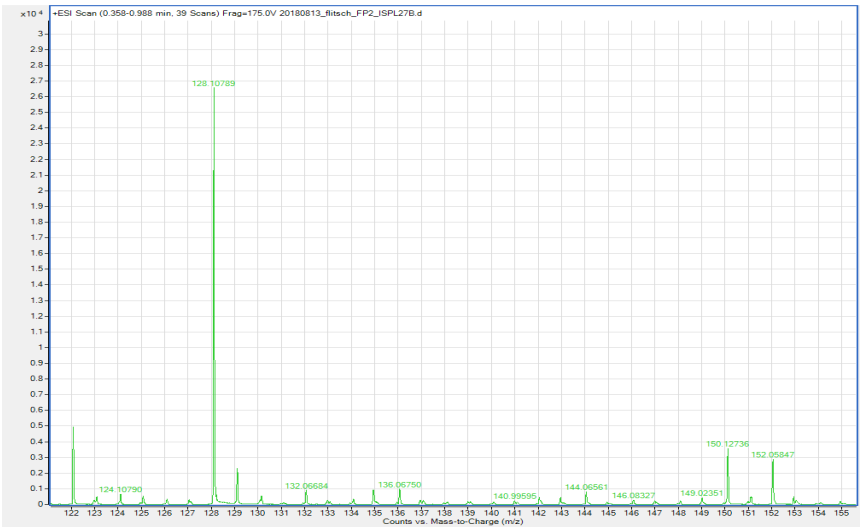




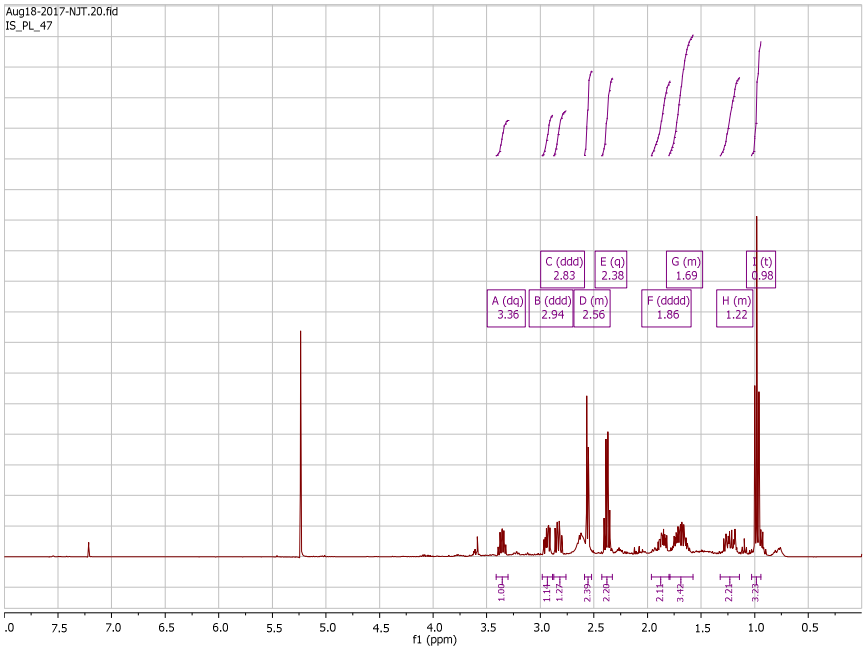
1-(pyrrolidin-2-yl)propan-2-one (7j, norhygrine)

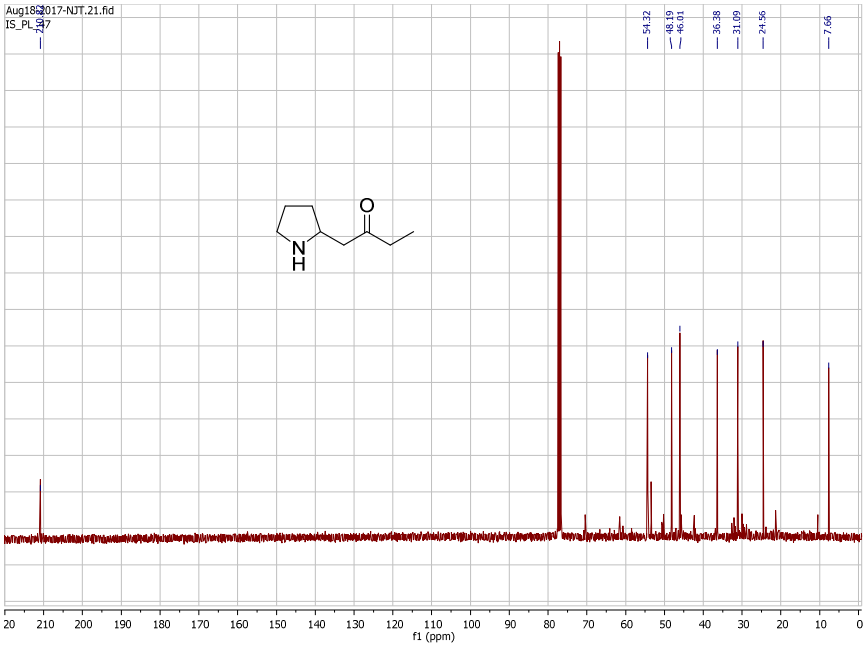


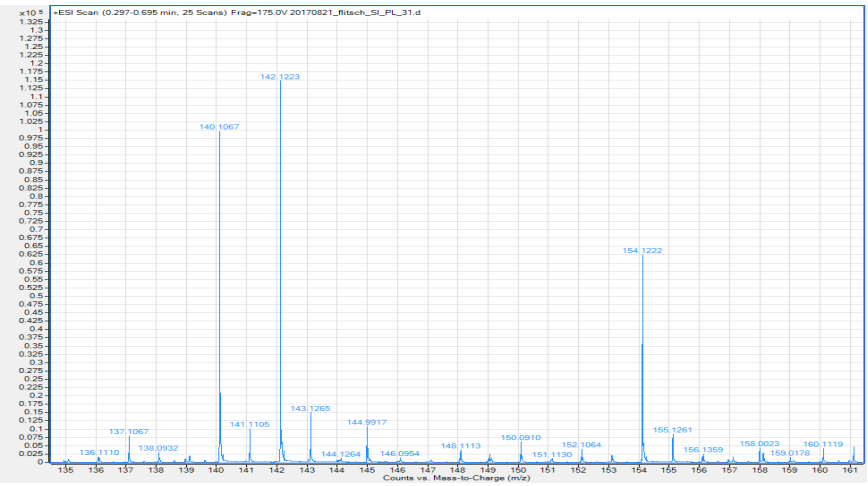




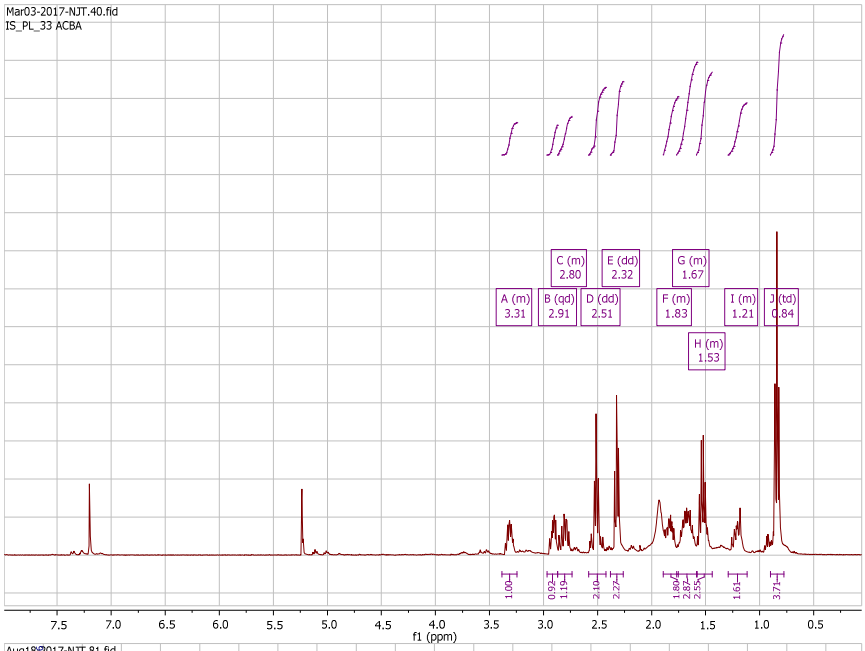
1-(pyrrolidin-2-yl)butan-2-one (7k)

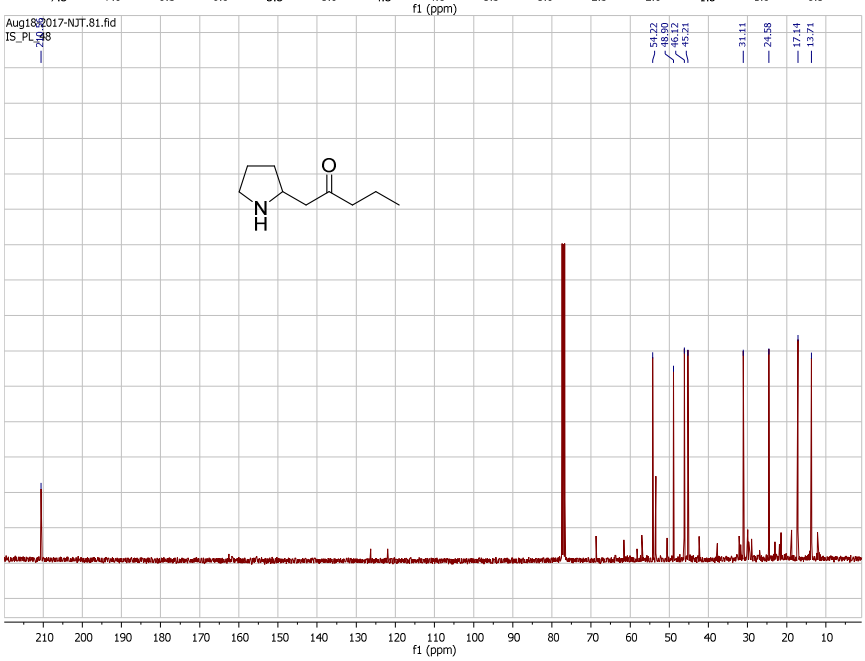


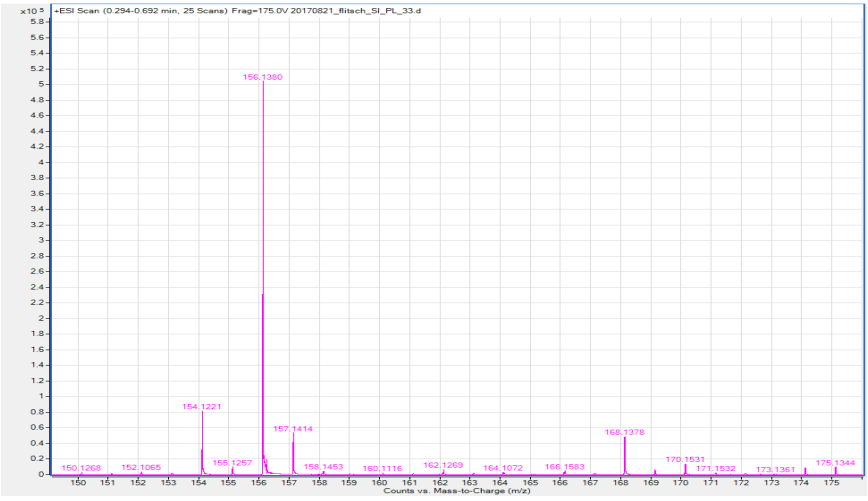




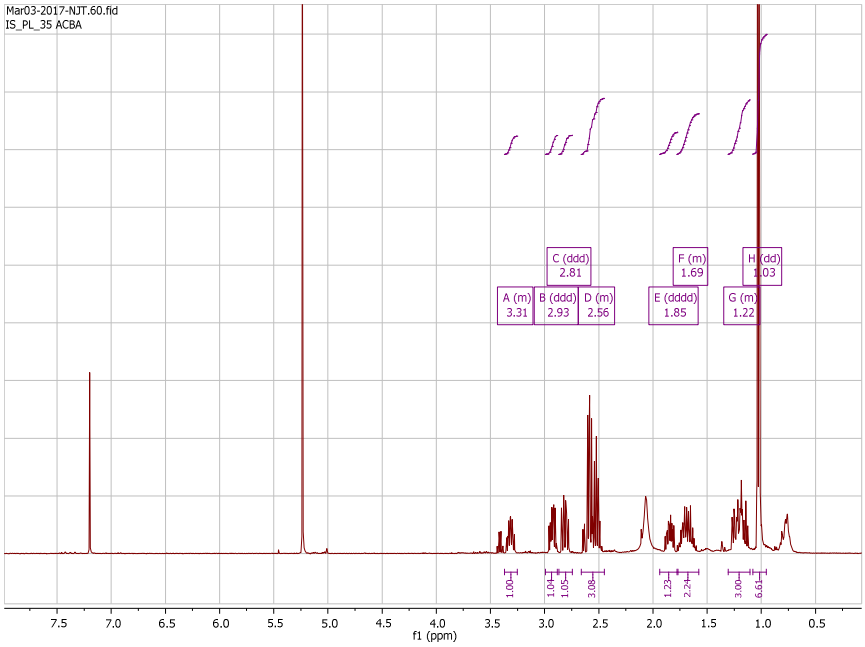
1-(pyrrolidin-2-yl)pentan-2-one (7l)

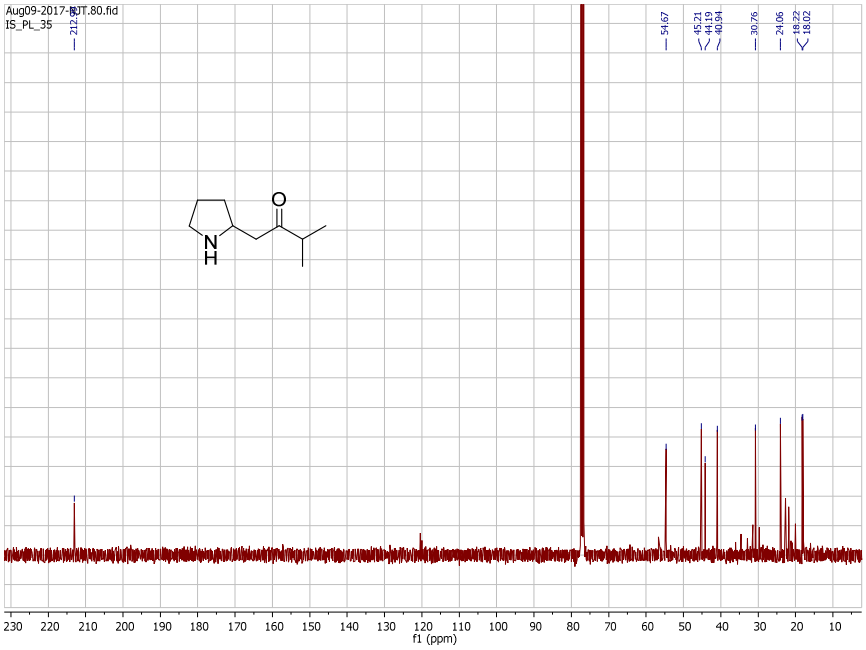


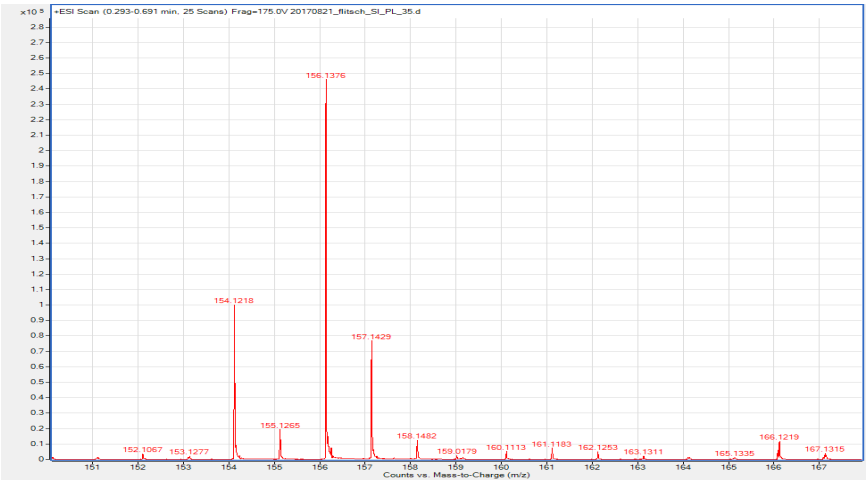




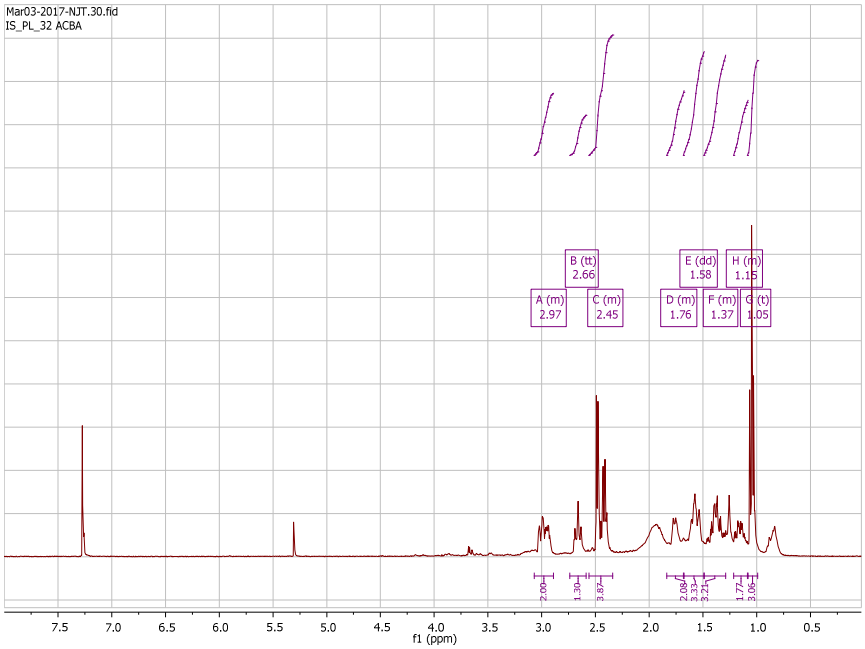
3-methyl-1-(pyrrolidin-2-yl)butan-2-one (7m)

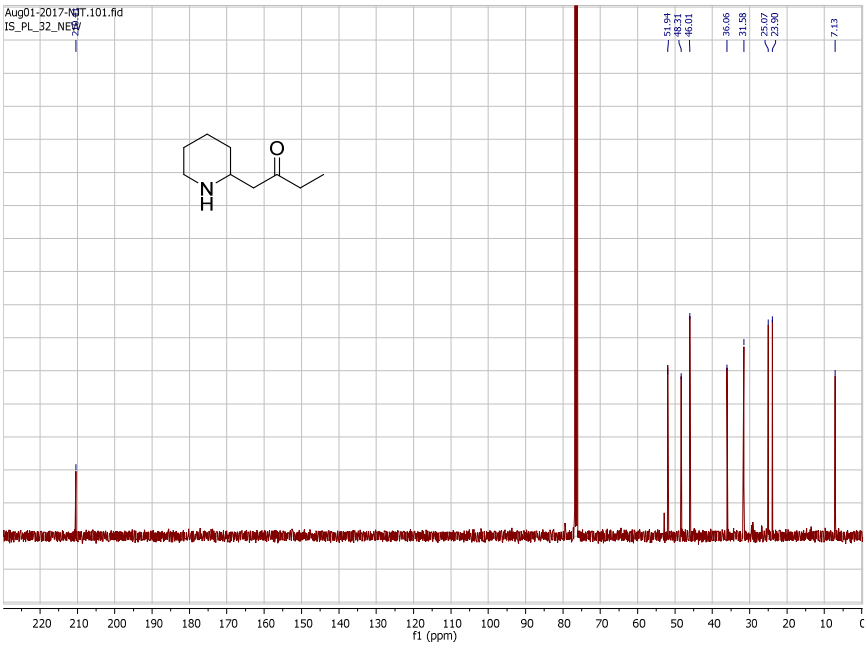


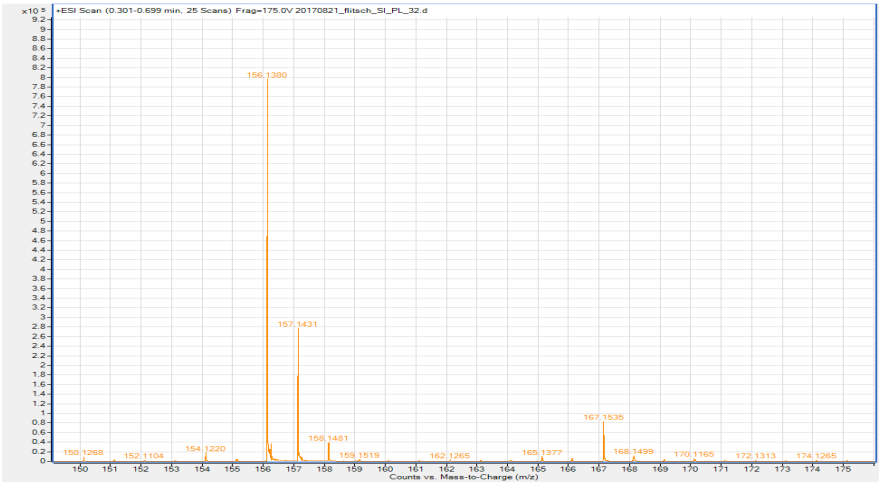




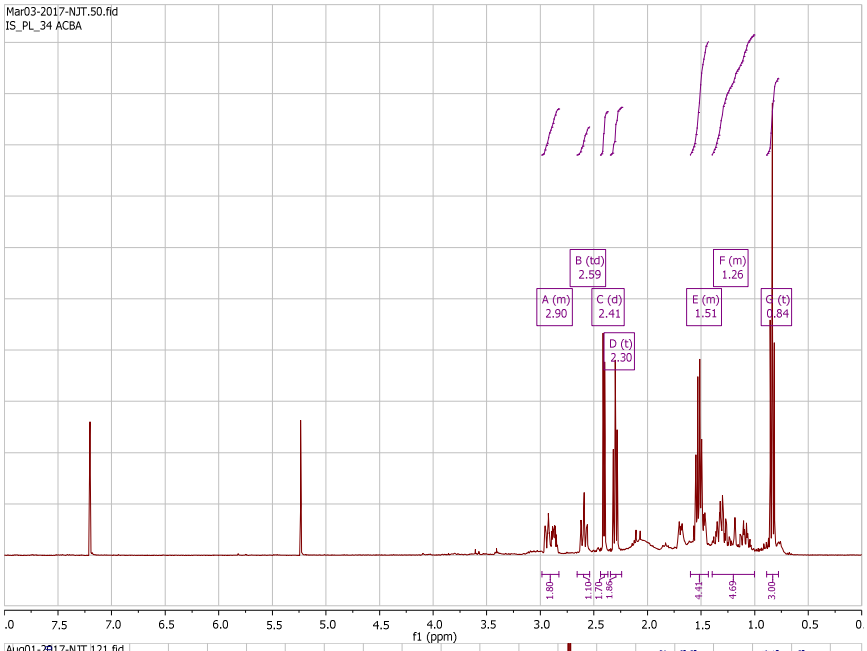
1-(piperidin-2-yl)butan-2-one (8k)

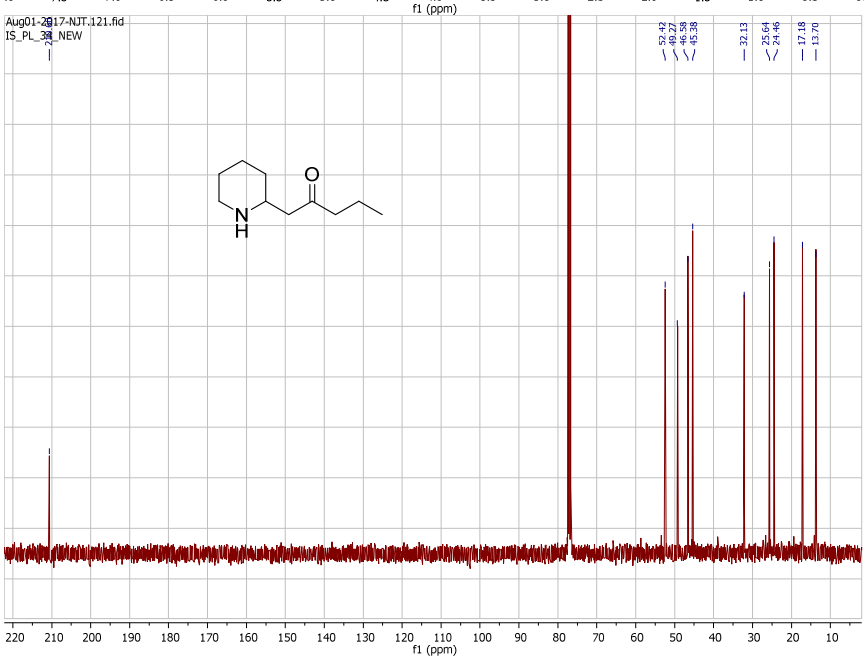


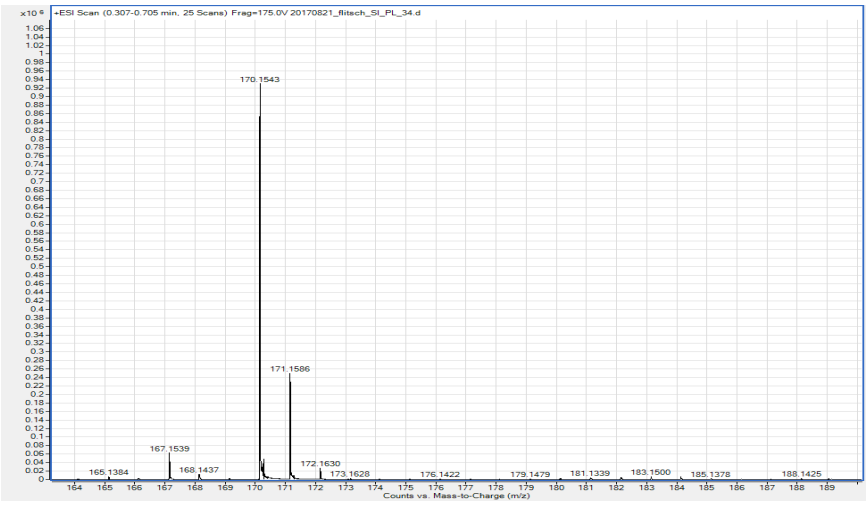




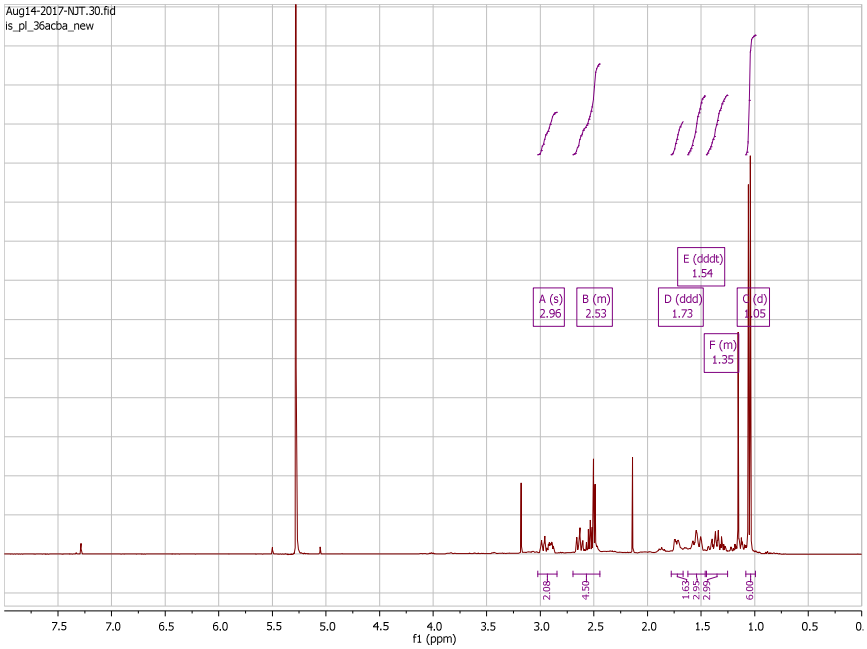
1-(piperidin-2-yl)pentan-2-one (8l)

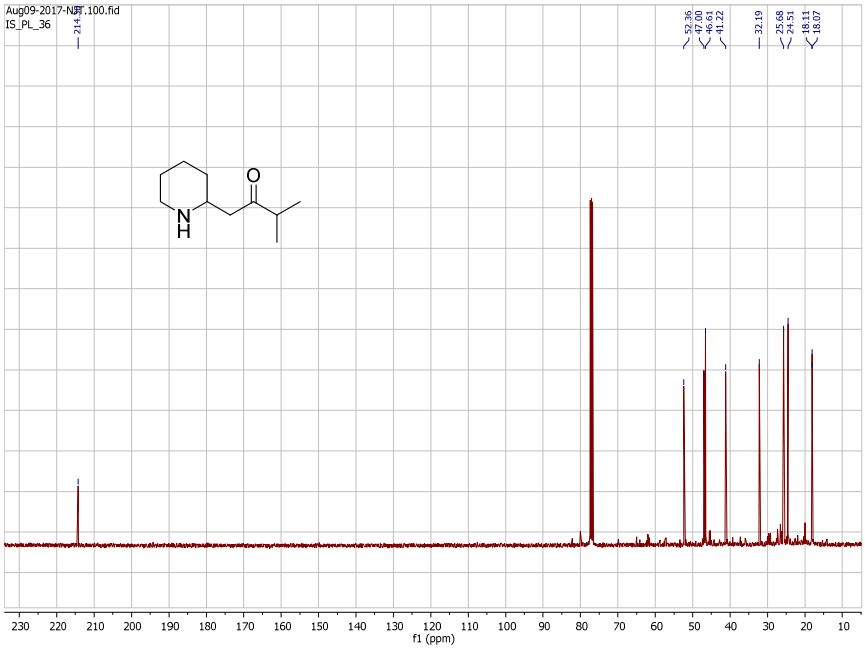


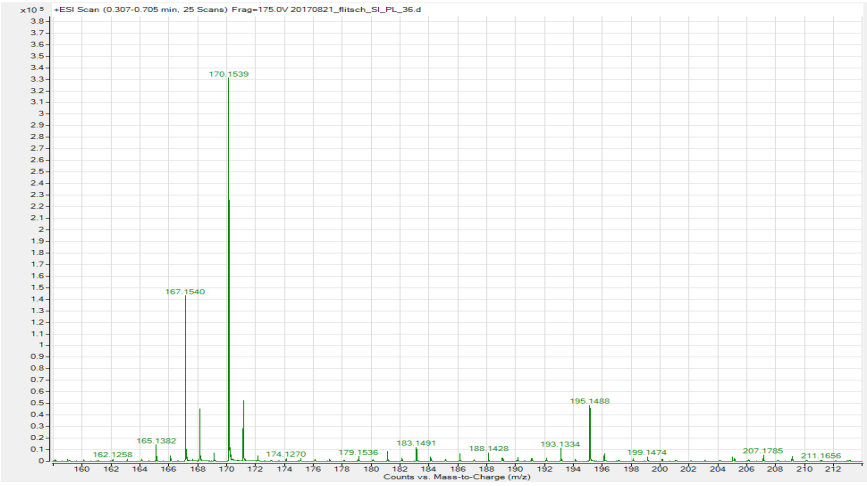




3-methyl-1-(piperidin-2-yl)butan-2-one (8m)







1-(1-methylpyrrolidin-2-yl)propan-2-one (11, hygrine)