ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Synthesis and Applications of Secondary Amine Derivatives of (+)-Dehydroabietylamine as Chiral Molecular Recognition

Tiina Laaksonen, Sami Heikkinen and Kristiina Wähälä*

Department of Chemistry, University of Helsinki, A.I. Virtasen aukio 1, P.O. Box 55, FI-00014 University of Helsinki, Finland

*Corresponding author
e-Mail: kristiina.wahala@helsinki.fi

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1 NMR MEASUREMENT AND PROCESSING PARAMETERS

Compound characterisation
All NMR experiments were performed using Varian UNITY INOVA 500 and Varian Mercury Plus 300 instruments at 27 °C. ^{1}H NMR spectra were recorded with 6-16 transients, 8000-6712.5 Hz spectral width, and 1.9 s acquisition time at 500 MHz. ^{13}C NMR spectra were recorded with 1876-532 transients, 31446-20000 Hz spectral width and 1-1.9 s acquisition time at 125 or 75 MHz. All 2D HSQC spectra were recorded using Varian UNITY INOVA 500 with 4 transients, 128 increments, 8000-6712.5 Hz spectral width in ^{1}H-dimension, 25133 Hz spectral width in ^{13}C-dimension, 1.0 s relaxation delay, and 1.3 s acquisition time.

Resolution experiments
All NMR measurements were recorded using Varian UNITY INOVA 500 at 27 °C. ^{1}H NMR spectra were recorded with 16 transients, 8000 Hz spectral width, 5.0 s relaxation delay and 1.9 s acquisition time at 500 MHz. ^{19}F NMR spectra were recorded with 16-32 transients, 19047 Hz spectral width, 5.0 s relaxation delay and 1.0 s acquisition time at 470 MHz. HMBC spectra were recorded using Varian UNITY INOVA 500 with 4-6 transients, 400 increments, 1.0 s relaxation delay and 0.128 s acquisition time. The spectral widths were 4247.2-8000 Hz and 30165.9-25133.5 Hz in ^{1}H- and ^{13}C-dimensions, respectively.

DOSY Experiment (see 3.1.1)
For DOSY experiment, Bipolar Pulse Pair Simulated Echo (BPPSTE)[1] pulse sequence was used. To measure DOSY dataset, 25 different diffusion gradient amplitudes were used (range 0.5-20.0 G/cm). Gradient pulse shape was rectangular. Diffusion gradient duration was 1.0 ms, eddy current recovery delay was 0.2 ms, and diffusion time was 250.0 ms. The DOSY dataset was measured using 16 steady state scans, 4 transients, and 2.0 s relaxation delay. Spectral width in ^{1}H-dimension was 6982.63 Hz and the number of acquired complex data points was 7000. The data was apodized by Gaussian weighting function and zero-filled up to 16384 complex points prior to Fourier transformation. Finally, two-dimensional DOSY spectra was calculated using DOSY-macro (a monoexponential fit) incorporated in Varian VNMR 6.1C spectrometer operating software.

1 M. D. Pelta, H. Barjat, G. A. Morris, A. L. Davis, S. J. Hammond, *Magn. Reson. Chem.*, **1998**, *36*, 10, 706-714

Dynamic NMR studies (see 3.1.1)
All NMR measuremnets were recorded using Varian UNITY INOVA 500. ^{1}H NMR spectra were recorded with 16-64 transients, 8000 Hz spectral width, and 1.9 s acquisition time at temperature range -65 to +50 °C.

2 CHIRAL RECOGNITION STUDIES

Solutions of **7** and **8** (22.0 mM in $CDCl_3$) were prepared. Compound **1-6 ab** (1.0 eq or 2.0 eq) were dissolved in 0.5 mL (1.0 eq) of prepared solution of guest and both ^1H and ^{19}F NMR spectra were recorded.

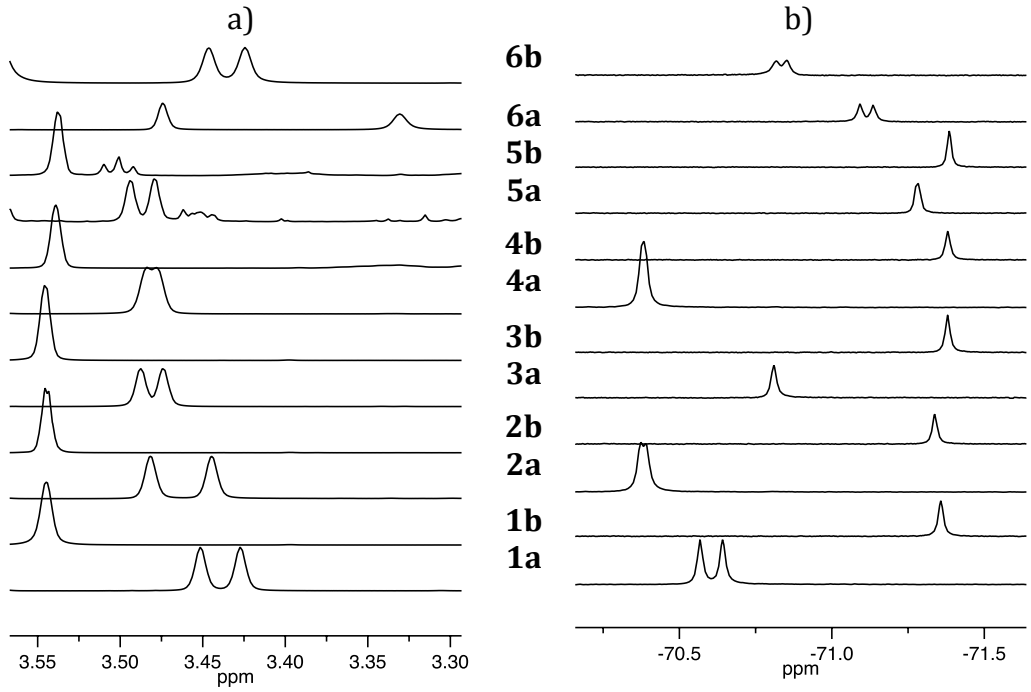


Figure 1. Chiral recognition of enantiomers of **7**. Host:guest molar ratio 1:1 a) ^1H NMR (OCH_3 peak) and b) ^{19}F NMR (CF_3 peak)

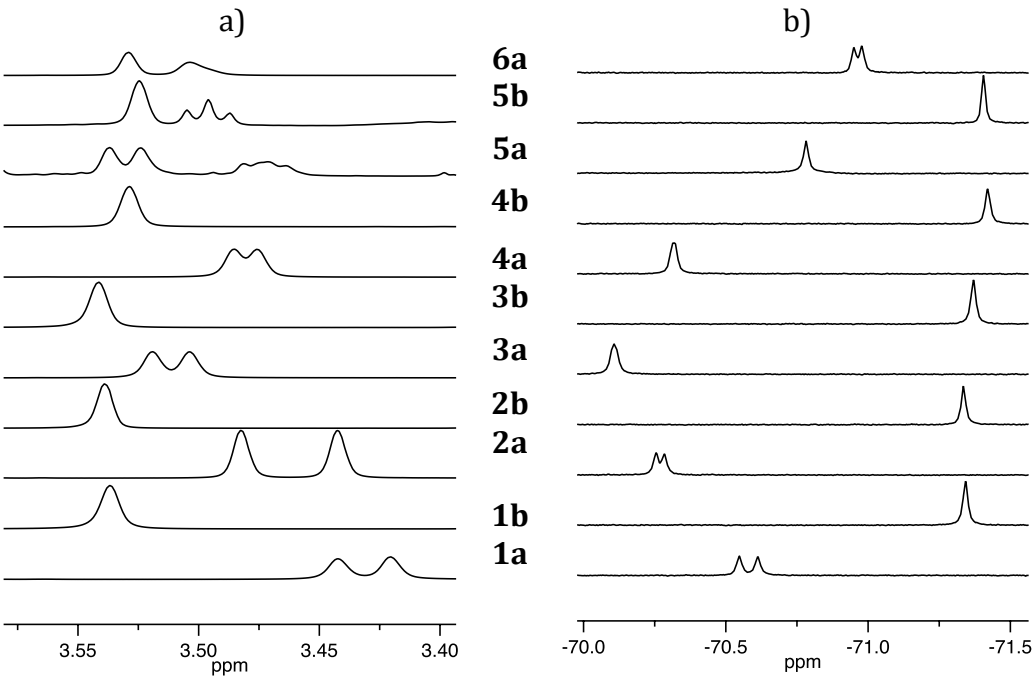


Figure 2 Chiral recognition of enantiomers of **7**. Host:guest molar ratio 2:1 a) ^1H NMR (OCH_3 peak) and b) ^{19}F NMR (CF_3 peak)

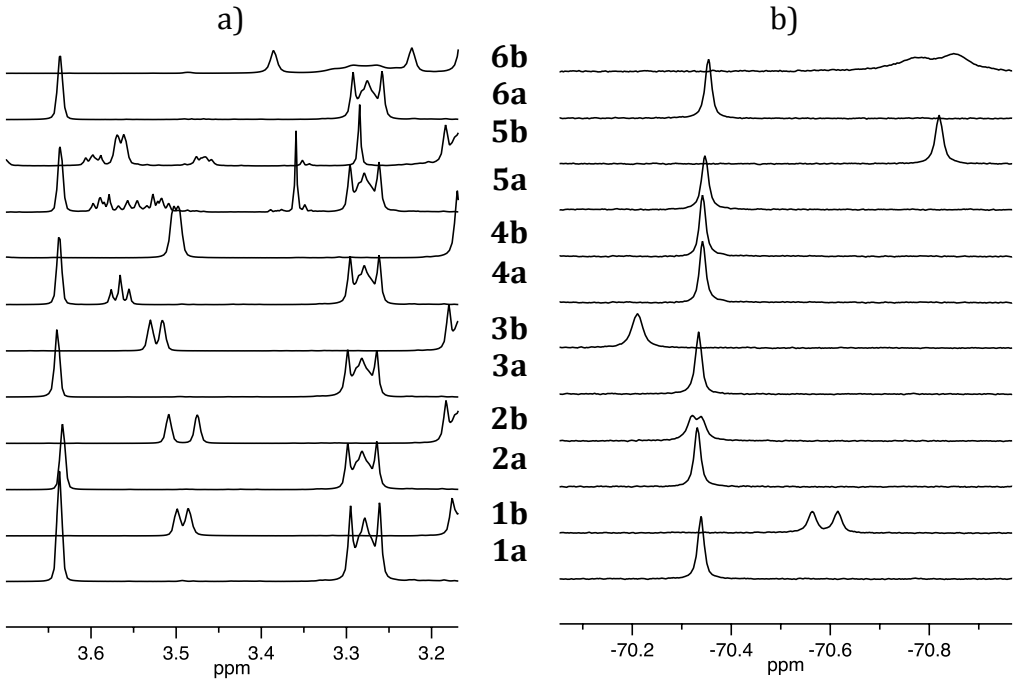


Figure 3. Chiral recognition of enantiomers of **8**. Host:guest molar ratio 1:1 a) ^{1}H NMR (OCH_3 peak) and b) ^{19}F NMR (CF_3 peak)

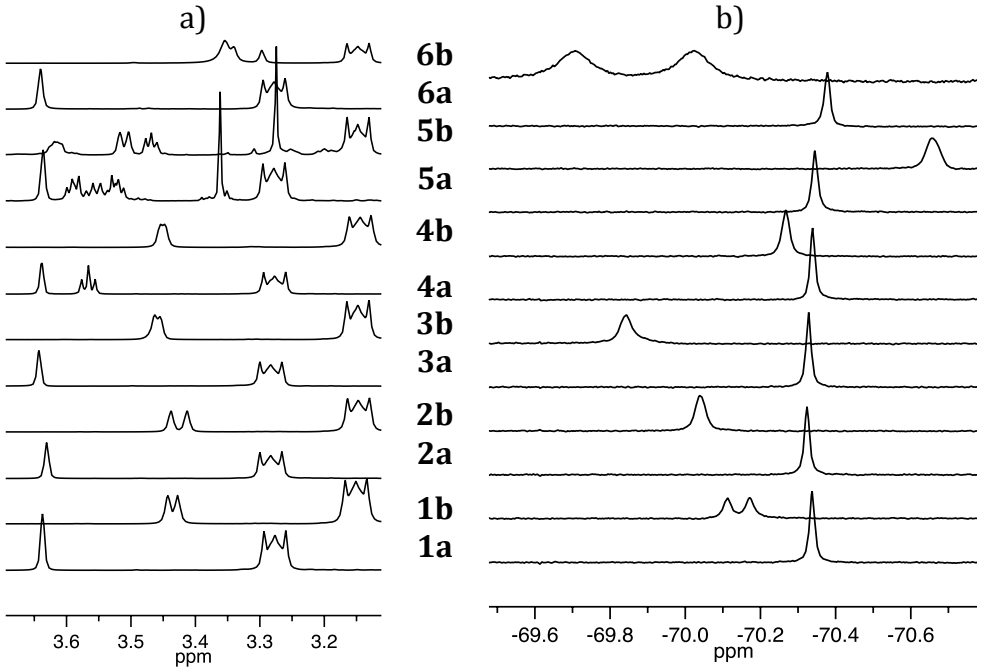


Figure 4. Chiral recognition of enantiomers of **8**. Host:guest molar ratio 2:1 a) ^{1}H NMR (OCH_3 peak) and b) ^{19}F NMR (CF_3 peak)

HMBC spectra from sample containing **6a** and **7**, as well as from sample containing **6b** and **8** were recorded. From spectra was noticed that **6a** and **6b** are able to resolve the chiral carbon of the used model compound (Fig 5).

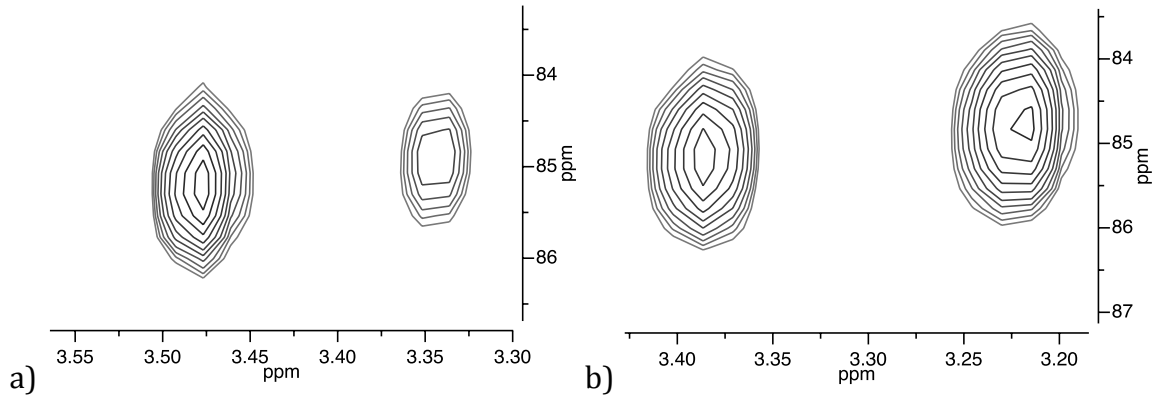


Figure 5. Separation of chiral carbon of *S* and *R* enantiomers (in HMBC spectra) of a) **7** with **6a** (Δδ 0.28 ppm, 35.3 Hz) and b) **8** with **6b** (Δδ 0.42 ppm, 52.5 Hz) in guest:host ratio 1:1.

3 TITRATION

3.1 Titration of 7 with 6a

Titration solutions containing the guest, **7** (2.0 mM) and host, **6a** (46.6 mM) were prepared. In NMR tube 0.5 mL of guest solution was measured and titrated by 1.0-5.0 μL doses of host solution. Both ^{1}H and ^{19}F NMR spectra were recorded. Concentration of guest is assumed to remain constant during the titration.

Table 1. Experimental data from titration of **7** with **6a**

		^{1}H NMR				^{19}F NMR			
c of **6a** (mM)	V of **6a** (mL)	δ of *S* (ppm)	δ of *R* (ppm)	$\Delta\delta_S$ of *S* (ppm)	$\Delta\delta_R$ of *R* (ppm)	δ of *S* (ppm)	δ of *R* (ppm)	$\Delta\delta_S$ of *S* (ppm)	$\Delta\delta_R$ of *R* (ppm)
0	0	3.5335	3.5335	0	0	-71.053	-71.053	0	0
0.093013972	0.001	3.495	3.521	0.0385	0.0125	-71.074	-71.074	0.021	0.021
0.231840796	0.0025	3.443	3.502	0.0905	0.0315	-71.09	-71.09	0.037	0.037
0.461386139	0.005	3.362	3.473	0.1715	0.0605	-71.124	-71.124	0.071	0.071
0.688669951	0.0075	3.289	3.446	0.2445	0.0875	-71.135	-71.172	0.082	0.119
0.91372549	0.01	3.23	3.423	0.3035	0.1105	-71.148	-71.221	0.095	0.168
1.003131115	0.011	3.219	3.419	0.3145	0.1145	-71.147	-71.231	0.094	0.178
1.0921875	0.012	3.225	3.424	0.3085	0.1095	-71.143	-71.231	0.09	0.178
1.180896686	0.013	3.241	3.433	0.2925	0.1005	-71.137	-71.219	0.084	0.166
1.357281553	0.015	3.279	3.453	0.2545	0.0805	-71.123	-71.196	0.07	0.143
1.792307692	0.02	3.378	3.491	0.1555	0.0425	-71.095	-71.147	0.042	0.094
2.219047619	0.025	3.442	3.513	0.0915	0.0205	-71.074	-71.117	0.021	0.064
2.637735849	0.03	3.477	3.523	0.0565	0.0105	-71.061	-71.101	0.008	0.048
3.048598131	0.035	3.497	3.528	0.0365	0.0055	-71.055	-71.093	0.002	0.04
3.451851852	0.04	3.509	3.532	0.0245	0.0015	-71.05	-71.086	-0.003	0.033
3.847706422	0.045	3.518	3.533	0.0155	0.0005	-71.045	-71.083	-0.008	0.03
4.236363636	0.05	3.524	3.534	0.0095	-0.0005	-71.043	-71.08	-0.01	0.027
4.618018018	0.055	3.535	3.535	-0.0015	-0.0015	-71.043	-71.077	-0.01	0.024
4.992857143	0.06	3.535	3.535	-0.0015	-0.0015	-71.04	-71.075	-0.013	0.022

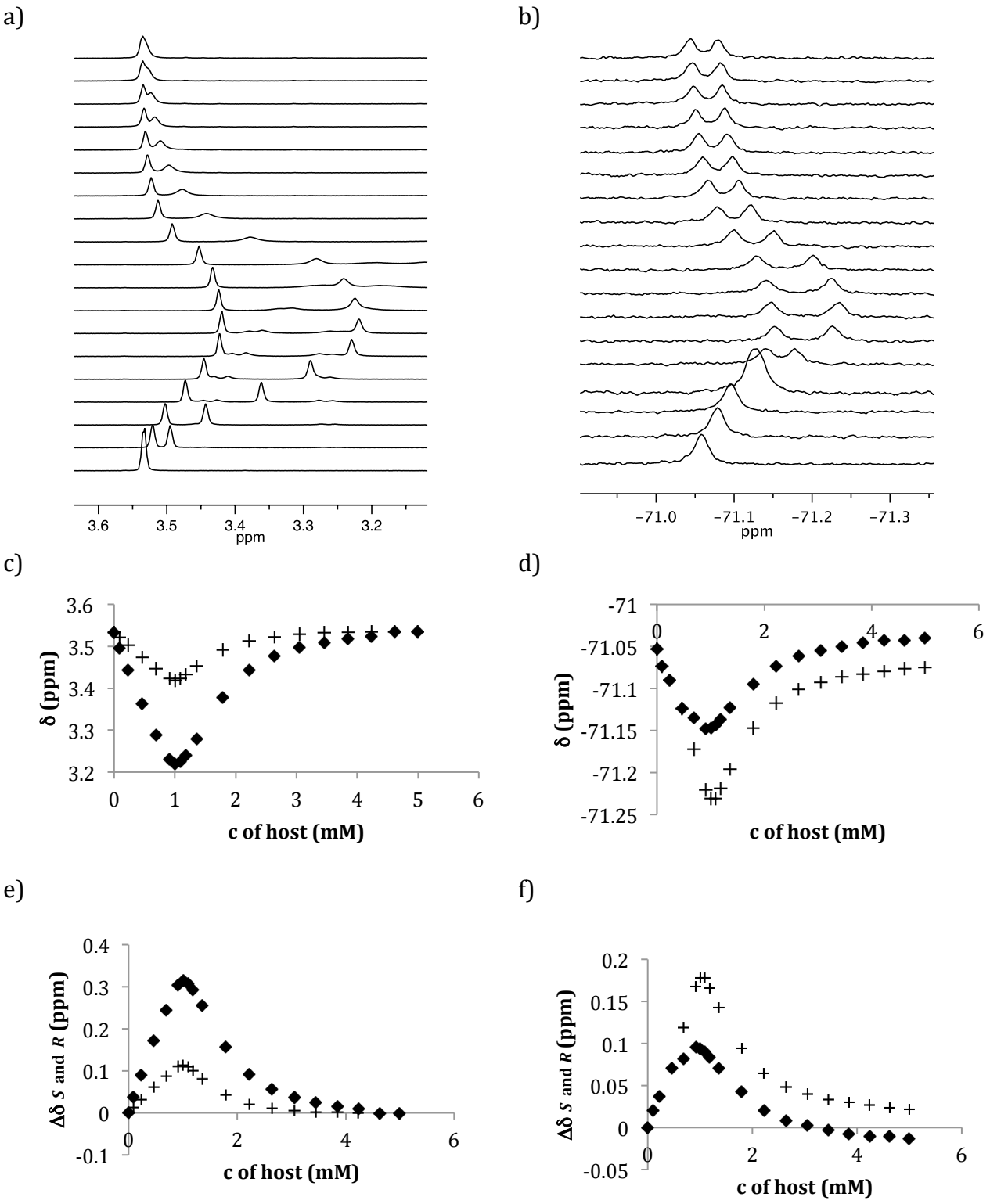


Figure 6. Spectra from titration of **7** with **6a** a) ^{1}H NMR and b) ^{19}F NMR. The change of chemical shifts of *S* and *R* enantiomers of **7** as a function of the concentration of **6a** c) ^{1}H NMR and d) ^{19}F NMR . The chemical shift change of the *S* and *R* enantiomers ($\Delta\delta_S$ and $\Delta\delta_R$) of **7**, as a function of the concentration of **6a** e)^{1}H NMR and f) ^{19}F NMR. (+ *R* enantiomer and ◆ *S* enantiomer)

To study the complexation Job's plot was calculated from the titration results (Fig 7). At the point where the molar ratio is 0.5:1 Job's plot indicated complexation 0.5:1 (both *S* and *R* enantiomer has the maximum at point at 0.333 at the Job's plot).

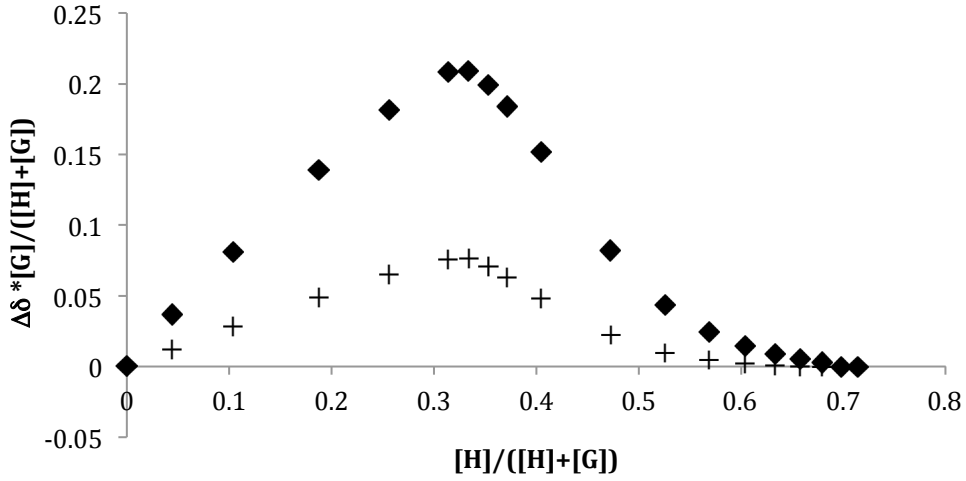


Figure 7. Job's plot from titration results (based on results from ^{1}H NMR) (+ *R* enantiomer and ◆ *S* enantiomer).

*3.1.1 The effect of increasing concentration of **6a***

During the titration (as well as while performing chiral recognition studies) the methoxy peak signal from *S* enantiomer of **7** was noted to broaden. This was presumed to originate from strong binding of *S* enantiomer to host **6a** leading to intermediate exchange between free and bound forms.

To observe the free and bound forms of *S* enantiomer dynamic NMR study was performed (Fig 8). Sample (in CD_2Cl_2) containing only *S*-**7** (0.5 mL, 2.0 M, 1.0 eq) and host **6a** (0.22 μL, 46.6 M, 1.0 eq) was cooled down to -65 °C. To maximise the temperature range CD_2Cl_2 (min -95 °C) was used as solvent instead of $CDCl_3$ (-63 °C). Also the effect of increasing temperature to the peak width was studied. Sample containing **7** (0.5 mL, 2.0 M, 1.0 eq) and host **6a** (0.22 μL, 46.6 M, 1.0 eq) in $CDCl_3$ was heated up to +50 °C.

At temperature -65 °C the separation of the free and bound forms of *S* enantiomer is clearly detected (Fig. 8 a)). Temperature has notable effect on the shape of peak of *S* enantiomer (Fig 8 b)). The line width increases while temperature decreases (i.e. decreased exchange rate between free and bound form) and oppositely decreases at higher temperature (i.e. increased exchange rate between free and bound form). The line width of *R* enantiomer remains virtually unaffected throughout the studied temperature range. The result thus indicates higher affinity of *S* enantiomer with the host compared to *R* enantiomer.

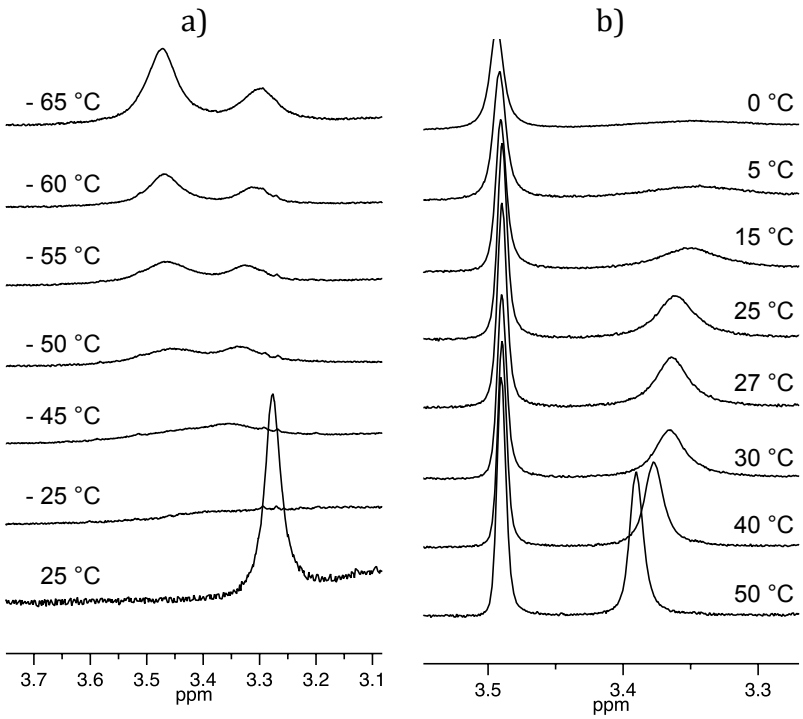


Figure 8. a) Dynamic NMR experinment in CD_2Cl_2 with enantiopure *S*-**7** (-65 °C to +25 °C) and b) dynamic NMR experinment in $CDCl_3$ with **7** (0 °C to 50 °C)

Stronger binding also increases apparent molar weight of *S* enantiomer compare to *R* enantiomer. This was observed in DOSY experiment (Fig 9) where *S* enantiomer displays smaller diffusion coefficient.

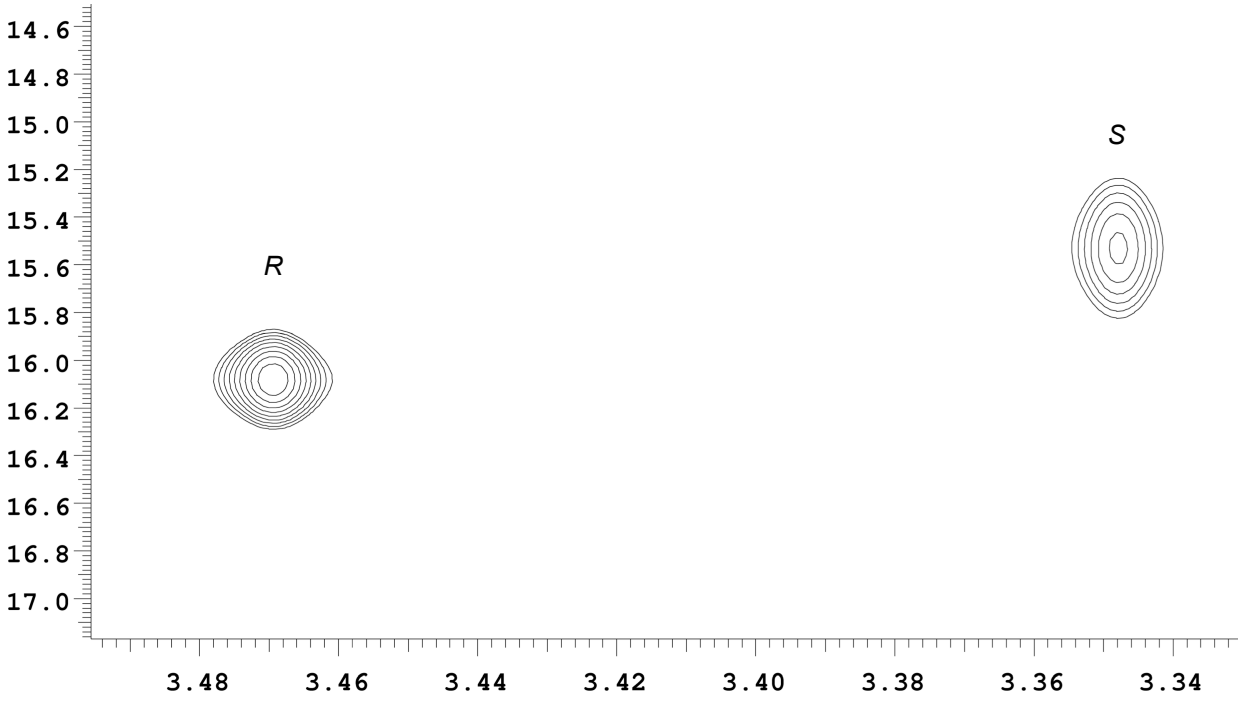


Figure 9. DOSY experiment of sample containing **7** and **6a** in 1:1 composition ($D_S = 15.5\times10^{-10}$ m^2/s and $D_R = 16.1\times10^{-10}$ m^2/s).

To find if the complex formation occur in the same manner with pure enantiomer, *S*-**7** was titrated with **6a** (Fig. 10). As in the case of racemic **7** the maximum separation was obtained at point where the host guest ratio was 1:2. When the concentration of host was increased the chemical shift change decreased as in the case of **7**. Also the peak width was observed to increase when the 1:2 host:guest ratio was reached.

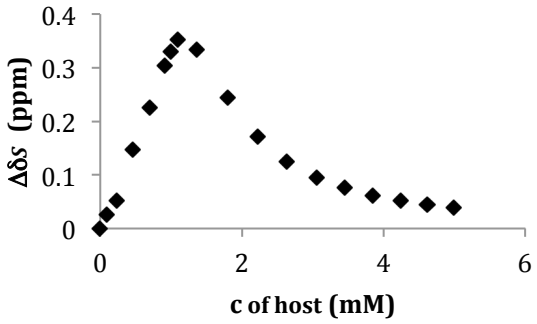


Figure 10. Chemical shift change of *S*-**7** in the function of concentration.

The chemical shift of *S*-enantiomer in racemic mixture (0.315 ppm) was smaller than in titration containing only *S*-enantiomer (0.352 ppm). This might be caused by formation of complex *SHR* in racemic mixture instead of *SHS* as with pure *S*-**7**. It is also possible that some amount of *SHS* (as well as *RHR*) is formed with *SHR* when racemic **7** is titrated. Based on these asumptions the complexation pattern could be presumed to go in the manner illustrated in the Figure 11.

Host guest ratio 1:2			Host guest ratio 1:1		
H + *R* + *S*	→	*R*:H:*S* or *S*:H:*S* or *R*:H:*R*	*R*:H:*S* or *S*:H:*S* or *R*:H:*R* + H	→	H:*S* + H:*R* or 2 H:*S* or 2 H:*R*

Figure 11. Possible complexation pattern formation in the titration of **7** with **6a**.

3.2 Titration of 8 with 6b

Due to solubility problems of **6b** to $CDCl_3$, titration was performed in opposite manner compared to **6a**. Titration solutions containing the **6b**, host (2.0 mM) and guest **8** (46.6 mM) were prepared. In NMR tube 0.5 mL of host solution (1.0 eq) was measured and titrated by 2.5-5.0 μL doses of guest solution. Both ^1H and ^{19}F NMR spectra were recorded. Concentration of host (**6b**) is presumed to remain constant during titration.

Table 2. Experimental data from titration of **8** with **6b**

		^1H NMR[a]				^{19}F NMR[b]			
c of **8** (mM)	V of **8** (mL)	δ of *S* (ppm)	δ of *R* (ppm)	$\Delta\delta_S$ of *S* (ppm)	$\Delta\delta_R$ of *R* (ppm)	δ of *S* (ppm)	δ of *R* (ppm)	$\Delta\delta_S$ of *S* (ppm)	$\Delta\delta_R$ of *R* (ppm)
0	0	0	0	0	0	0	0	0	0
0.231840796	0.0025	3.328	3.407	0.303	0.224	-70.585	-70.636	-0.029	0.022
0.461386139	0.005	3.325	3.406	0.306	0.225	-70.614	-70.676	0	0.062
0.91372549	0.01	3.329	3.406	0.302	0.225	-70.745	-70.797	0.131	0.183
1.357281553	0.015	3.241	3.408	0.39	0.223	-71.007	-71.007	0.393	0.393
1.575845411	0.0175	3.223	3.41	0.408	0.221	-71.069	-71.108	0.455	0.494
1.792307692	0.02	3.213	3.412	0.418	0.219	-71.109	-71.18	0.495	0.566
2.006698565	0.0225	3.213	3.417	0.418	0.214	-71.133	-71.219	0.519	0.605
2.219047619	0.025	3.221	3.425	0.41	0.206	-71.143	-71.236	0.529	0.622
2.429383886	0.0275	3.242	3.443	0.389	0.188	-71.127	-71.206	0.513	0.592
2.637735849	0.03	3.273	3.462	0.358	0.169	-71.105	-71.166	0.491	0.552
3.048598131	0.035	3.323	3.493	0.308	0.138	-71.061	-71.095	0.447	0.481
3.451851852	0.04	3.364	3.516	0.267	0.115	-71.024	-71.024	0.41	0.41
3.847706422	0.045	3.395	3.532	0.236	0.099	-70.986	-70.986	0.372	0.372
4.236363636	0.05	3.421	3.543	0.21	0.088	-70.951	-70.951	0.337	0.337
4.618018018	0.055	3.441	3.553	0.19	0.078	-70.922	-70.922	0.308	0.308
4.992857143	0.06	3.458	3.561	0.173	0.07	-70.896	-70.896	0.282	0.282
5.722807018	0.07	3.485	3.571	0.146	0.06	-70.854	-70.854	0.24	0.24
6.427586207	0.08	3.505	3.579	0.126	0.052	-70.823	-70.823	0.209	0.209
7.108474576	0.09	3.521	3.586	0.11	0.045	-70.796	-70.796	0.182	0.182

[a] The peak of OCH_3 in ^1H NMR is at 3.631 ppm and [b] the peak of CF_3 in ^{19}F NMR is at -70.614 ppm when the concentration of **8** is 2.0 mM (no host added).

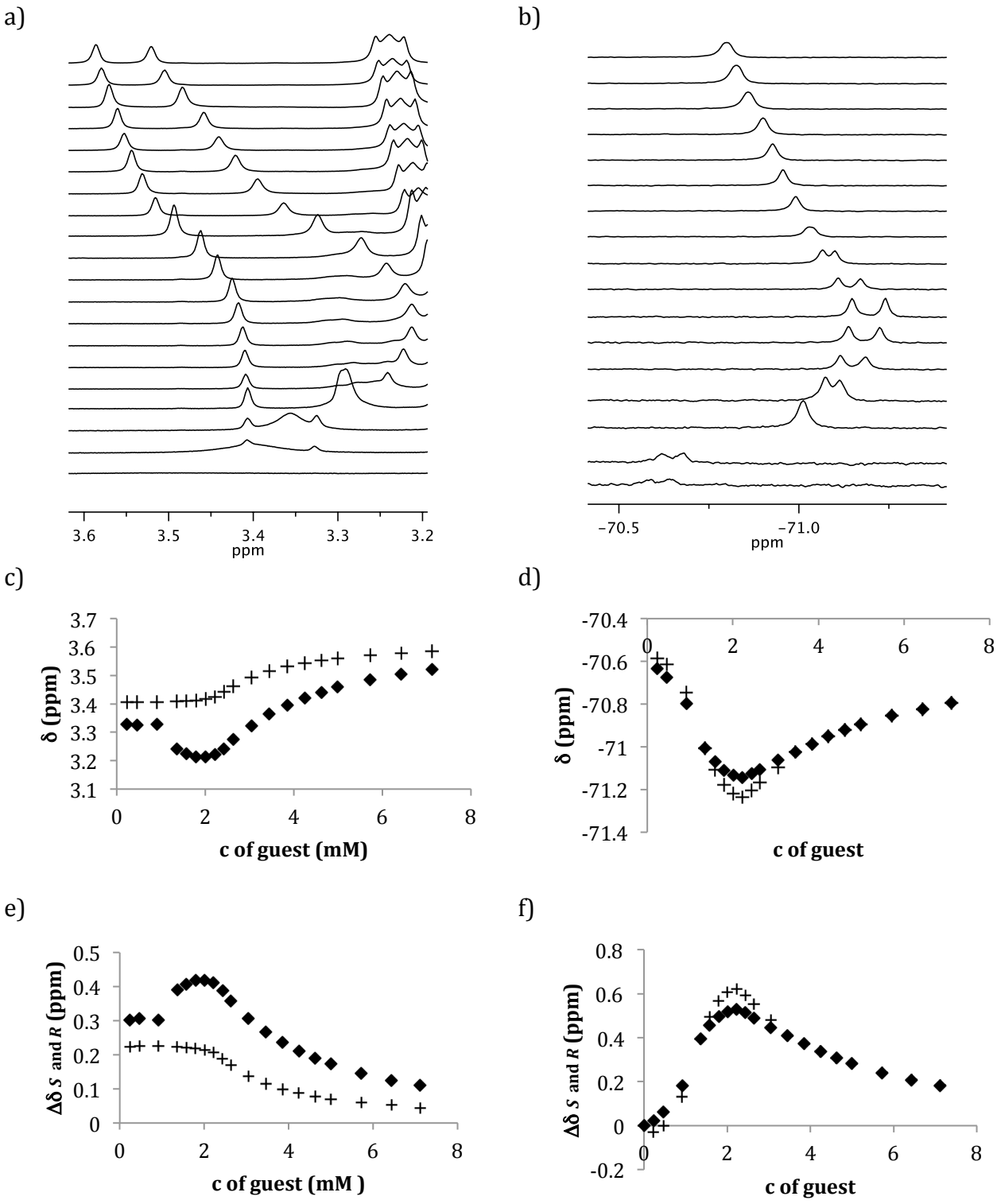


Figure 12. Spectra from titration of **8** with **6b** a) ^{1}H NMR and b) ^{19}F NMR. The change of chemical shifts of *S* and *R* enantiomers of **8** c) ^{1}H NMR and d) ^{19}F NMR . The chemical shift change of the *S* and *R* enantiomers ($\Delta\delta_S$ and $\Delta\delta_R$) of **8** e)^{1}H NMR and f) ^{19}F NMR. (+ *R* enantiomer and ◆ *S* enantiomer)

To study the complexation Job's plot was calculated from the titration results (Fig. 12). At the point where the molar ratio is 1:1 Job's plot indicated complexation1:1 (both *S* and *R* enantiomer has the maximum at point at 0.5).

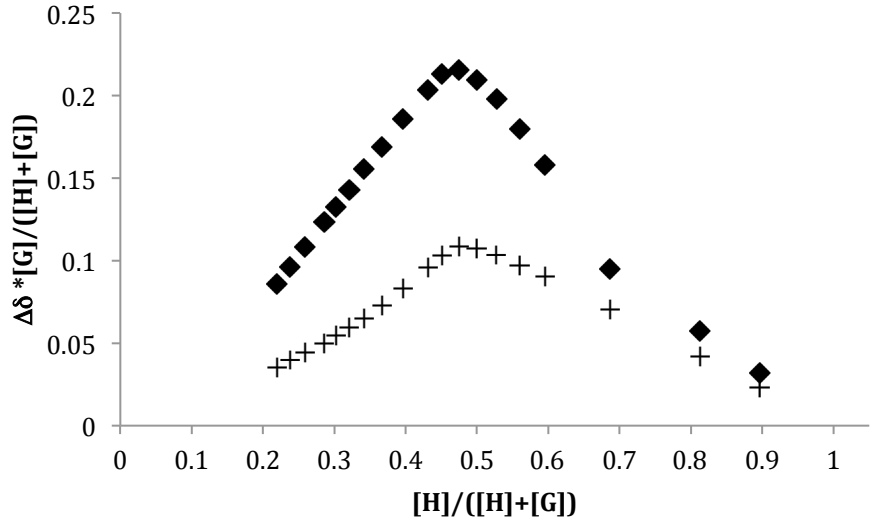


Figure 13. Job's plot from titration results (based on results from ^{1}H NMR) (+ *R* enantiomer and ◆ *S* enantiomer).

3.2.1 Dependence of concentration on Δδ

During the titration of **6b** (2.0 mM) the chemical shift difference between *R* and *S* enantiomers (Δδ) in ^{19}F NMR spectra was not as high as in enatiomeric separation experiments (22.0 mM). To investigate if the concentration had an effect on Δδ, a sample containing host:guest in ration 2:1 (22.0 mM) was diluted by $CDCl_3$ (Fig. 14). Results indicate that the concentration has distinct effect on the Δδ at ^{19}F NMR (change of Δδ: 0.08 ppm, 37.6 Hz), however, in the case of ^{1}H NMR slight increase in Δδ values was detected (change of Δδ: 0.006 ppm, 3.0 Hz).

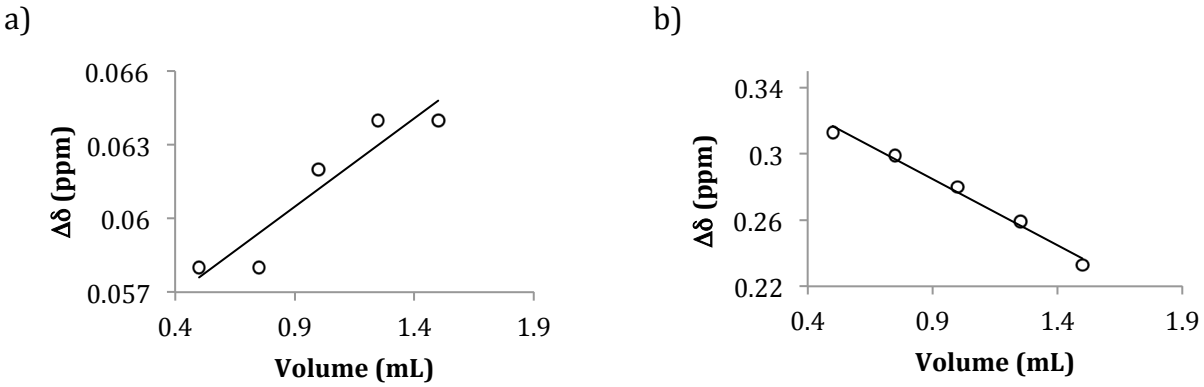


Figure 14. The effect of increased solvent volume ($CDCl_3$) on Δδ in a) ^{1}H NMR and b) ^{19}F NMR.

4 ENANTIOMERIC EXCESS STUDIES

4.1 Enantiomeric excess measurements of 7 with 6a

In ee% determination studies solutions of racemic **7** and *S*-**7** were prepared (2.0 mM). Mixtures of enantiomerically enriched samples were prepared in NMR tube (0.5 mL, 2.0 mM, 1.0 eq) and added **6a** (46.6 mM, 22.5 μL, 1.0 eq) and recorded spectra. Due to overlapping of peaks of host and guest, 1.0 eq (22.5 μL 46.6 mM) of **6a** was added instead of 0.5.

Table 3. ee% determined from ^{1}H NMR spectra

S (mL)	*R*/*S* (mL)	Expected *S*/*R*	Measured *S*/*R*	Area *S*	Area *R*	Expected ee% (*S*)	Measured ee% (*S*)
0	0.5	1	0.965717071	2488.509	2576.851	50	49.12797906
0.1	0.4	1.5	1.474179057	23892.418	16207.27	60	59.58255336
0.2	0.3	2.333	2.31684909	25898.506	11178.331	70	69.85090449
0.25	0.25	3	2.915923268	28472.871	9764.616	75	74.46323813
0.3	0.2	4	3.401767245	28246.343	8303.432	80	77.28185194

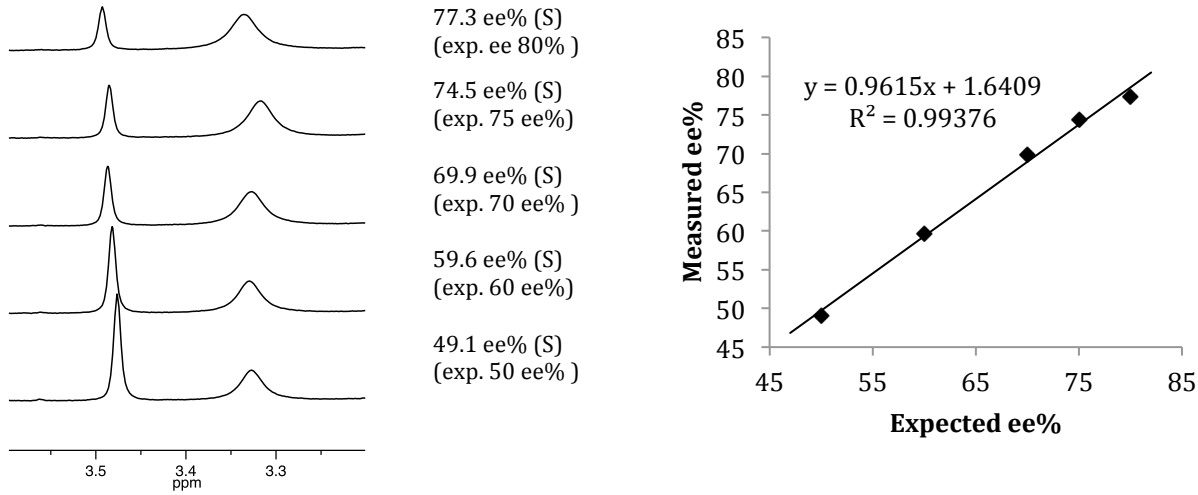


Figure 15. Results from ee% determination (^{1}H NMR).

4.2 Enantiomeric excess measurements of 8 with 6b

Due to solubility problems of **6b** ee% measurements were performed in opposite manner compared to **6a**. Solutions of racemic **8** and *S*-**8** were prepared (46.6 mM) as well as solution containing the host (2.0 mM). To NMR tube containing the host (0.5 mL, 2.0 mM, 1.0 eq) was added different portions of solutions containing racemic **8** and *S*-**8** (46.6 mM) to yield total 60.0 μL (2.8 eq) of guest. (Higher equivalent rate was chosen to ease the calculation of *S*:*R* ratio and addition of analyte.)

Table 4. ee% determined from ^{1}H NMR spectra

S (μL)	*R*/*S* (μL)	Expected *S*/*R*	Measured *S*/*R*	Area *S*	Area *R*	Expected ee% (*S*)	Measured ee% (*S*)
0.0	60.0	1	0.982591241	10594.285	10781.986	50	49.56095944
10.0	50.0	1.4	1.445427826	13368.496	9248.816	58	59.10735988
20.0	40.0	2	1.976496042	15224.866	7702.958	67	66.40344936
30.0	30.0	3	3.020116878	16154.578	5348.991	75	75.12510133
25.0	35.0	3.8	3.705853512	16159.793	4360.613	79	78.74986976

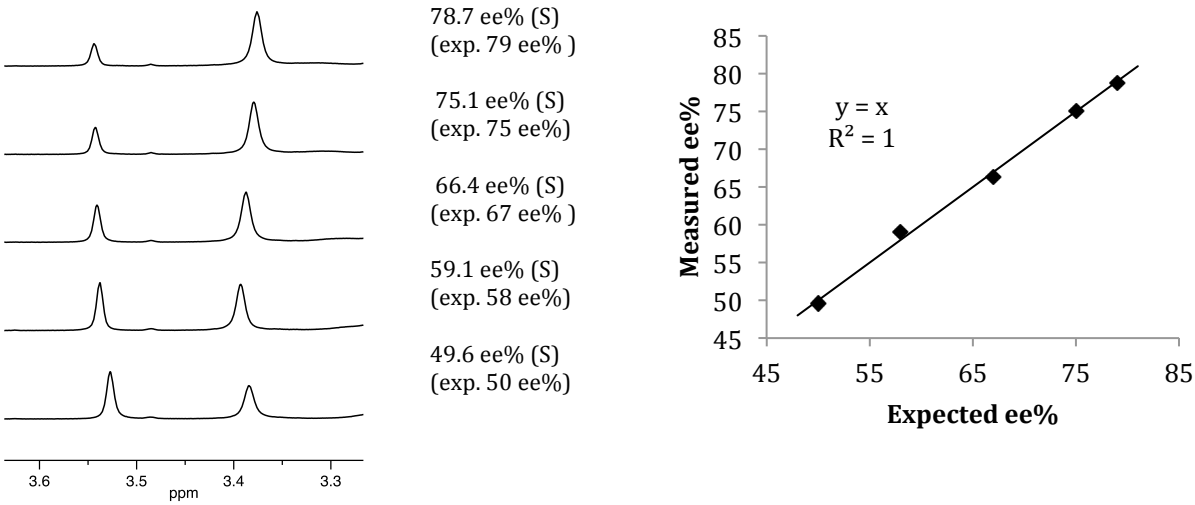


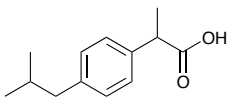
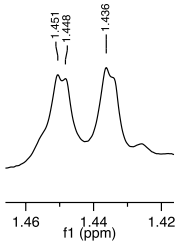
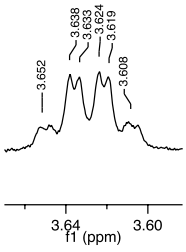
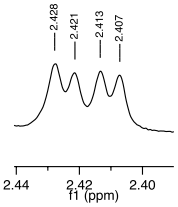
Figure 16. Results from ee% determination (^{1}H NMR).

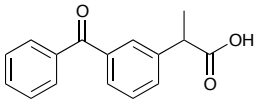
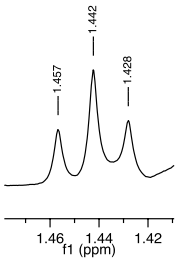
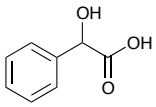
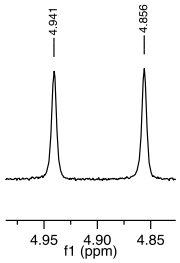
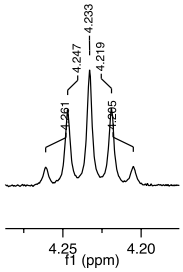
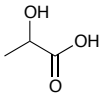
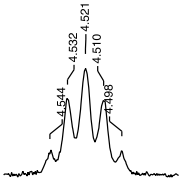
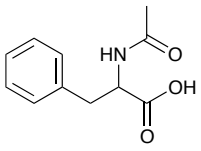
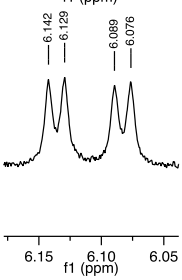
5 SEPARATION OF CARBOXYLIC ACIDS

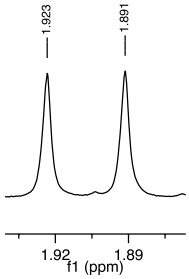
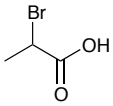
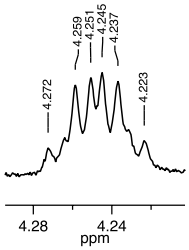
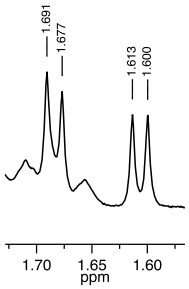
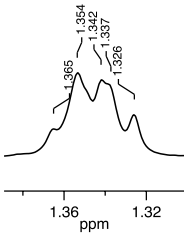
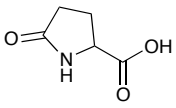
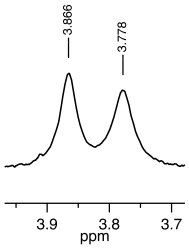
5.1 Separation of carboxylic acids with 6a

In chiral recognition ability determination study of racemic carboxylic acids, solutions of different racemic carboxylic acids were prepared (2.0 mM). Experiment was performed by adding 11.0 μL of solution containing host (46.6 mM, 0.5 eq) to NMR tube containing 0.5 mL of guest (2.0 mM, 1.0 eq) and recorded spectra.

Table 5. Determination of the chemical shift difference between enantiomers (Δδ) of five racemic carboxylic acids in the presence of **6a**, using ^{1}H NMR (500 MHz) in $CDCl_3$ at 27 °C.

No.	Racemic carboxylic acid	Actual multiplet		Spectra (if split is detected)	Δδ (ppm)
9a		Me	d		0.002
		H	q		0.0052
		CH_2	d		0.0062

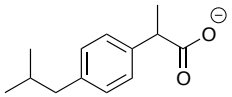
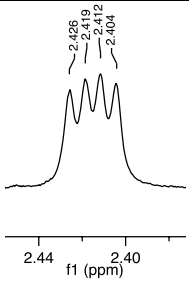
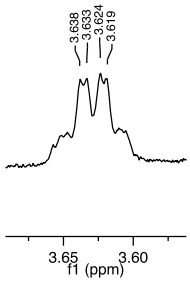
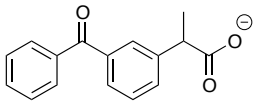
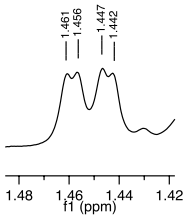
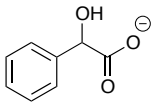
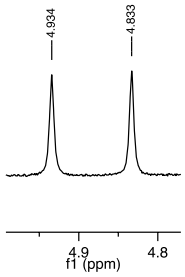
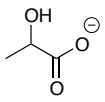
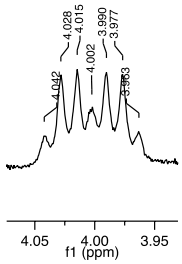
10a		Me	d		0.014
		H	q	nd	nd
11a		H	s		0.084
		H	q		0.014
12a		Me	d		0.0062
		H	q		0.01
13a		NH	d		0.052

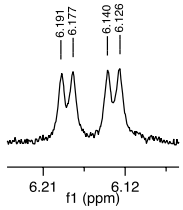
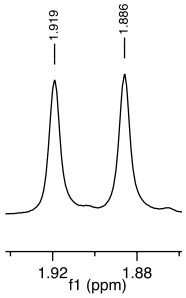
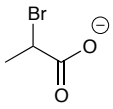
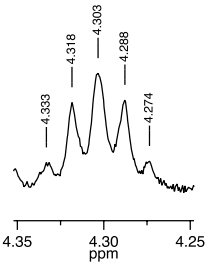
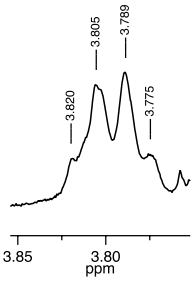
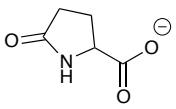
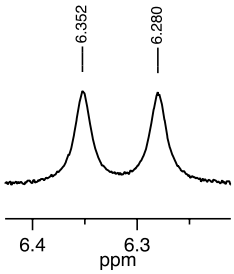
		Me	s		0.033
14a		H	q		0.014
		Me	d		0.077
		H	t		0.016
15a					
		NH	br. s		0.088

5.2 Separation of carboxylic acids with 6b

In chiral recognition ability determination study of racemic carboxylic acids, solutions of different $[Bu_4N]^+$ salts of carboxylic acids were prepared (46.6 mM). Experiment was performed by adding 22.5 μL of solution containing guest to NMR tube containing 0.5 mL of host (2.0 mM, 1.0 eq) and recorded spectra.

Table 6. Determination of the chemical shift difference between enantiomers (Δδ) of five racemic carboxylic acid $[Bu_4N]^+$ salts in the presence of **6**, using ^1H NMR (500 MHz) in $CDCl_3$ at 27 °C.

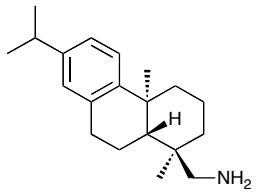
No.	$[Bu_4N]^+$ salt of racemic carboxylic acid	Actual multiplet		Spectra	Δδ (ppm)
9b		Me	d		0.0099
		H	q		0.0053
		CH_2	d	-	-[a]
10b		Me	d		0.01
		H	q	nd	nd
11b		H	s		0.10
12b		H	q		0.038
		Me	d	-	-[a]
13b		H	q	nd	nd

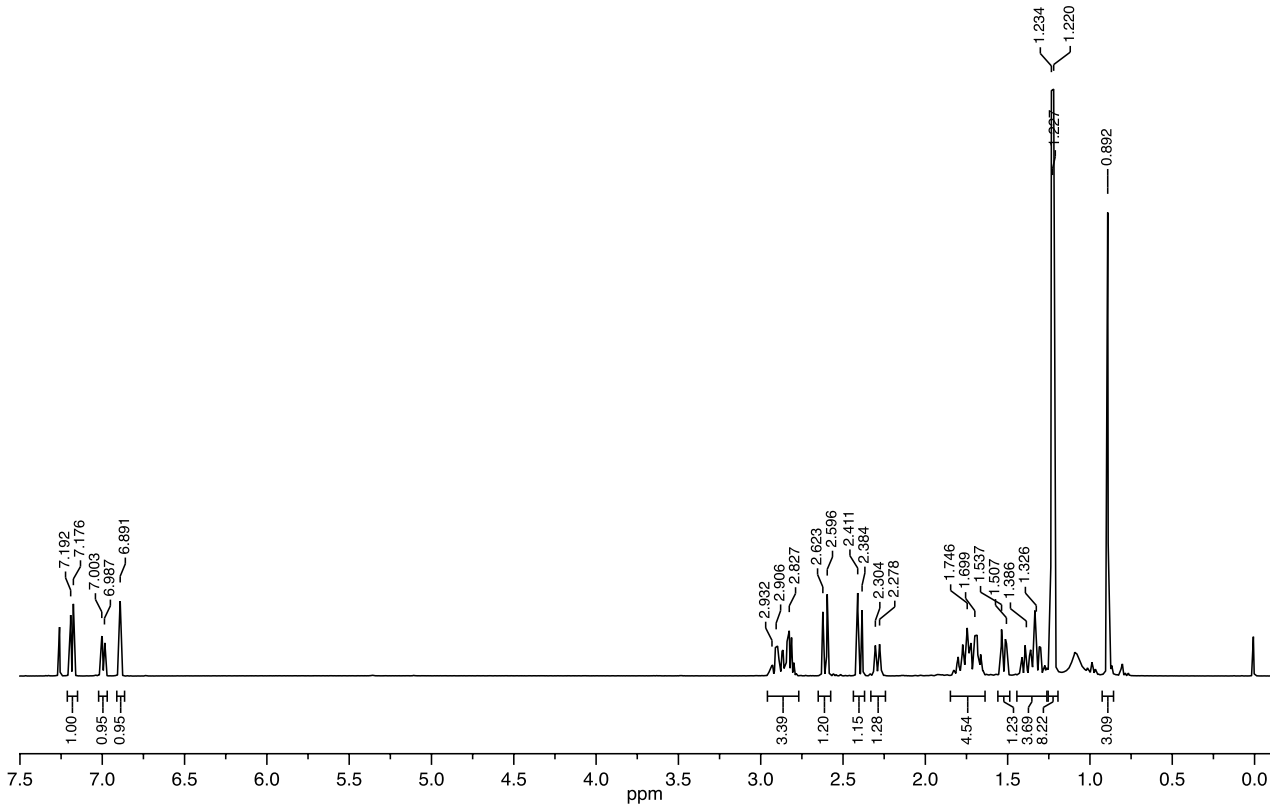
		NH	d		0.051
		Me	s		0.033
14a		H	q		0.016
		Me	d	-	-[a]
		H	t		0.017
15a					
		NH	br. s		0.072

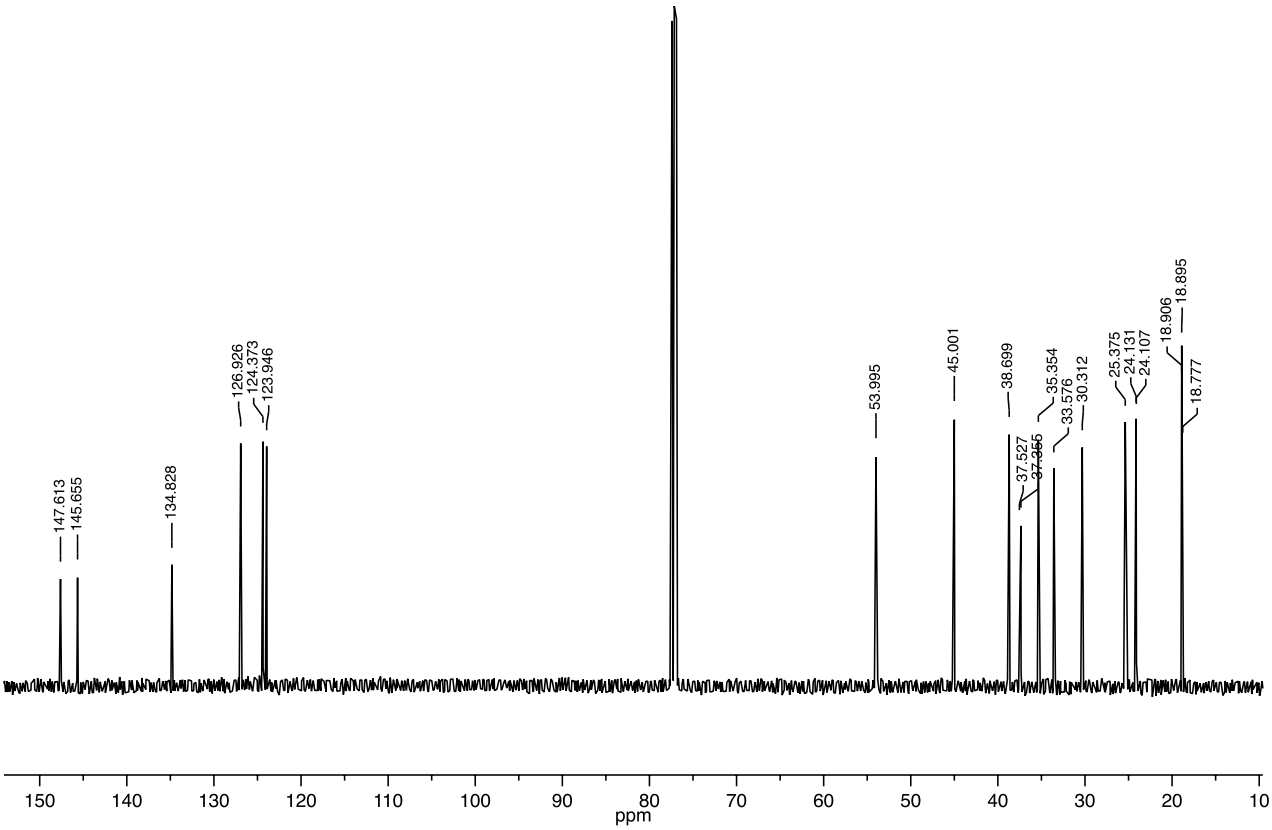
[a] Peaks overlapped, nd (resolution not detected)

6 NMR SPECTRA OF SYNTHESISED CSAS

1H, 13C and HSQC spectra of compound 1a



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38.699
37.527
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30.312
25.375
24.131
24.107
18.906
18.895
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150
140
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120
110
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90
80
70
60
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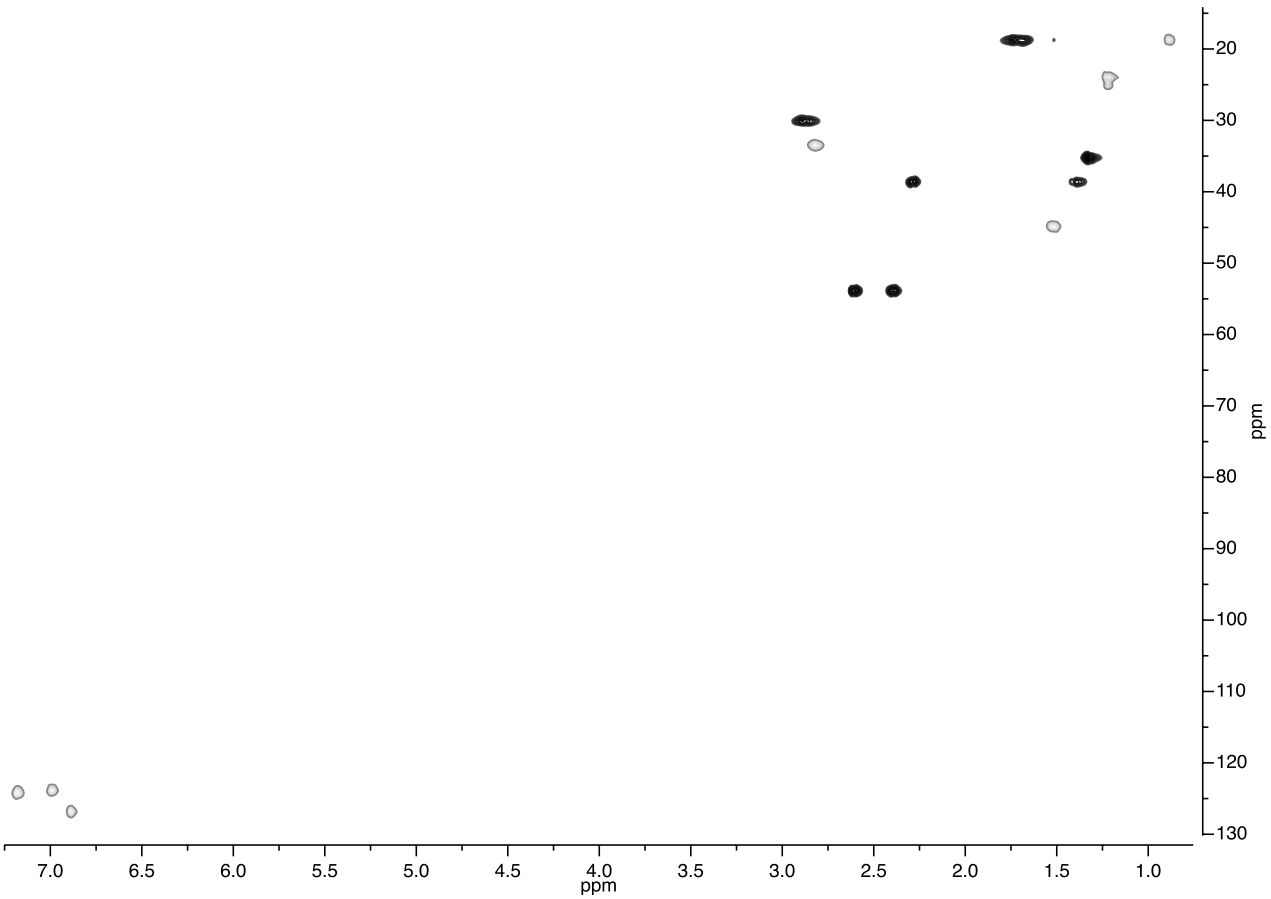
40
30
20
10
ppm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120
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6.0
5.5
5.0
4.5
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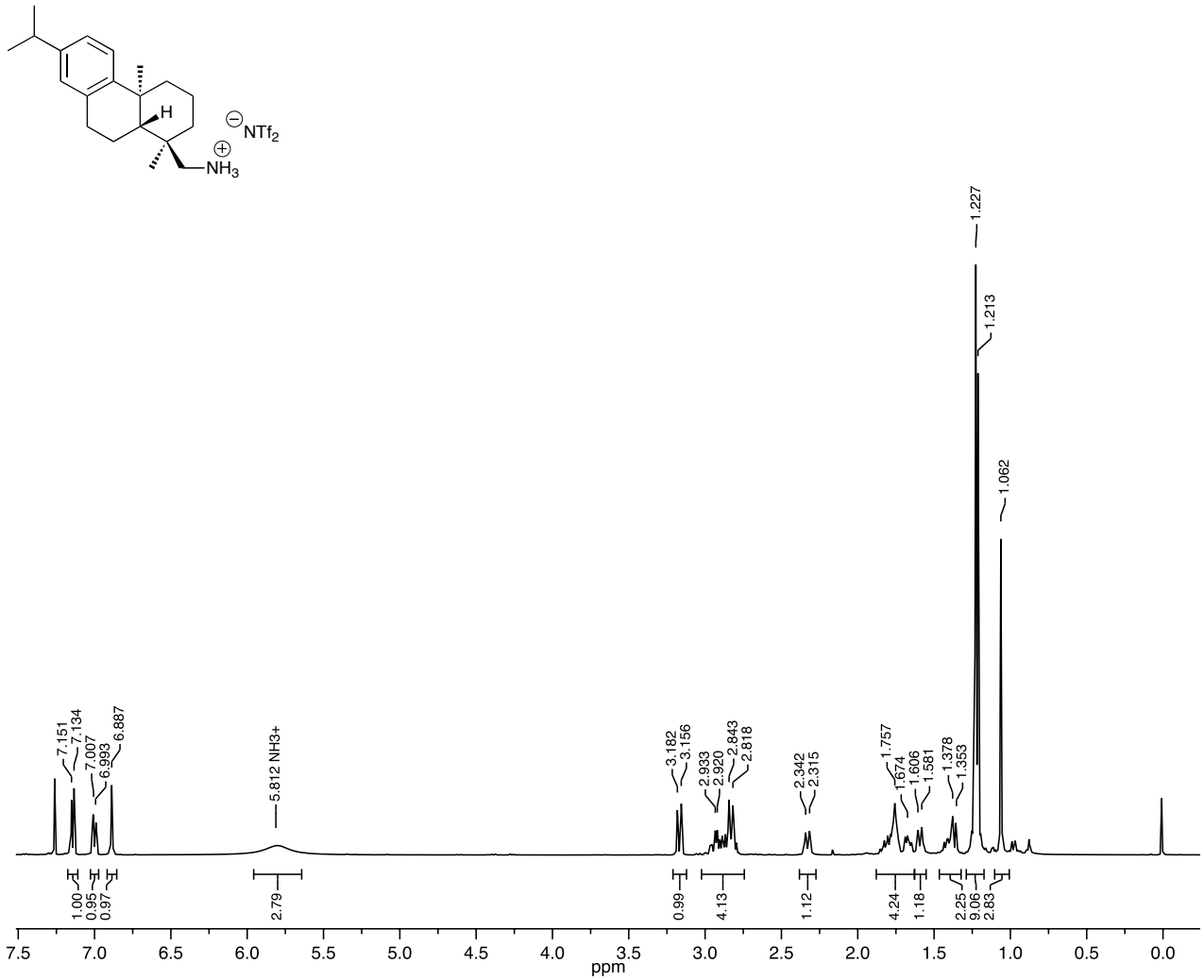
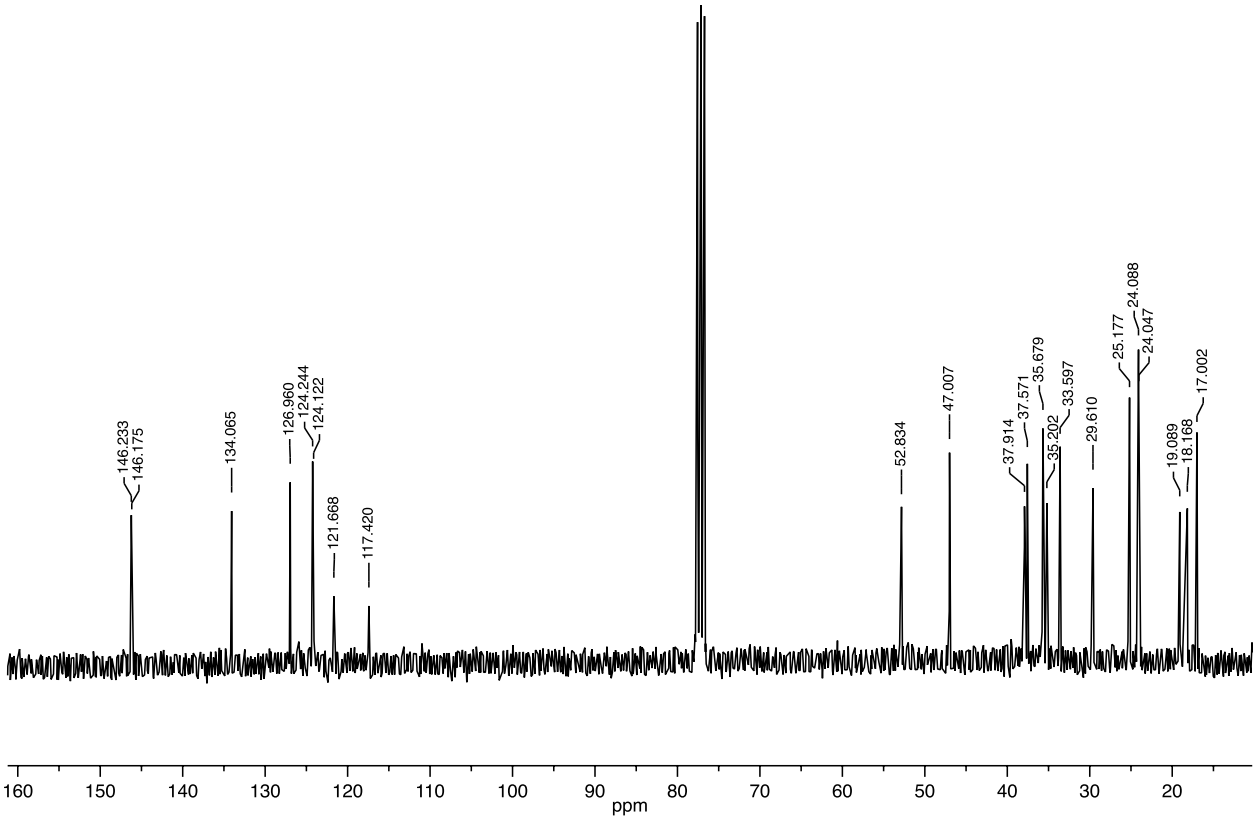
3.5
3.0
2.5
2.0
1.5
1.0
ppm

1H, 13C and HSQC spectra of compound 1b

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124.122
121.668
117.420
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47.007
37.914
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35.202
33.597
29.610
25.177
24.088
24.047
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40
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20
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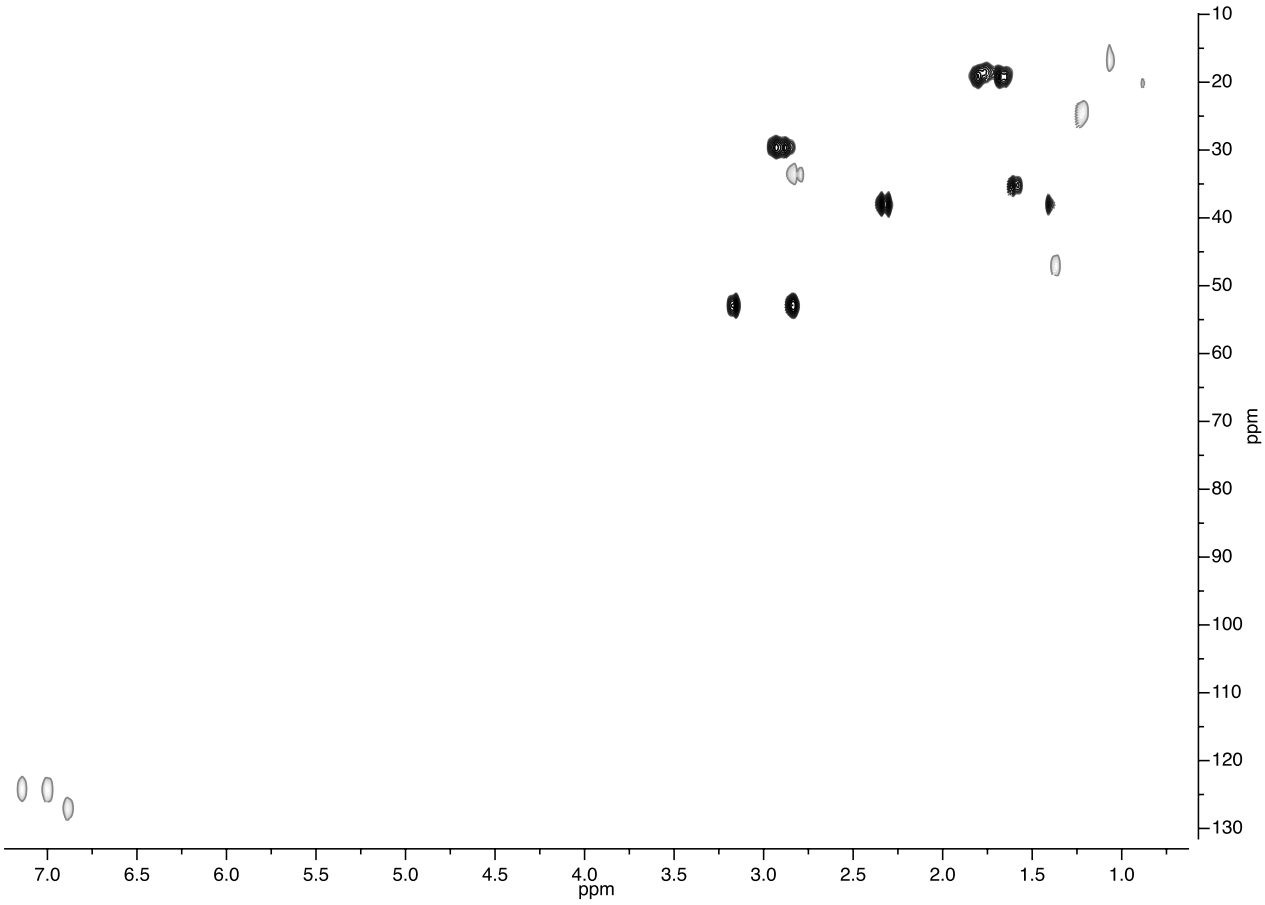
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60
70
80
90
100
110
120
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ppm
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6.0
5.5
5.0
4.5
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3.5
3.0
2.5
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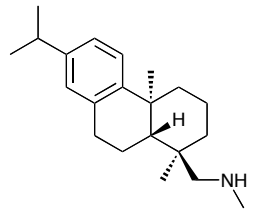
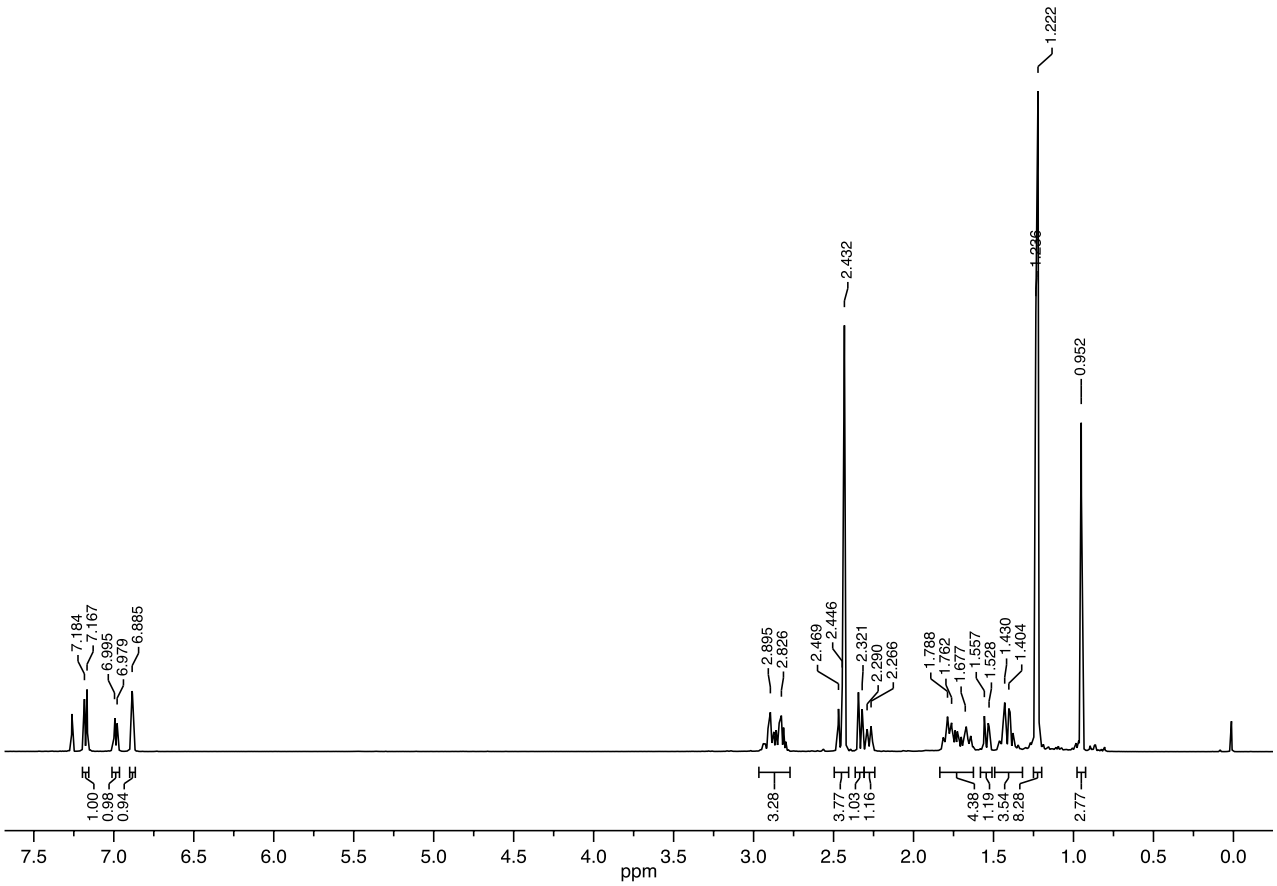
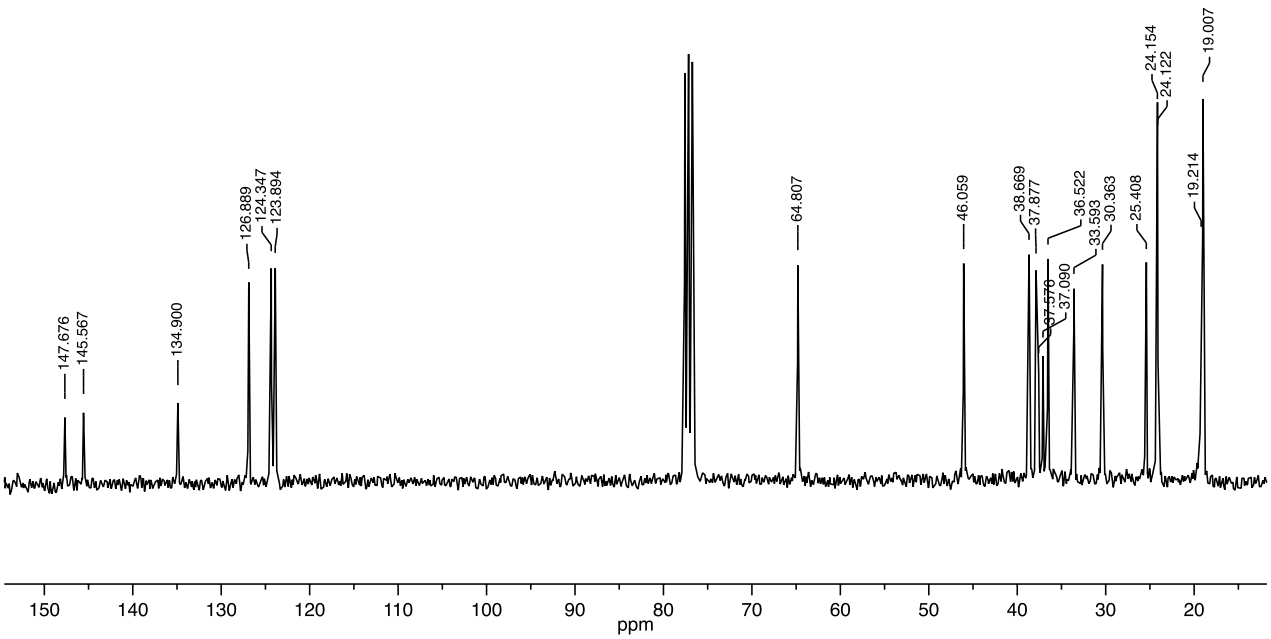
1.5
1.0
ppm

1H, 13C and HSQC spectra of compound 2a



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46.059
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30.363
25.408
24.154
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80
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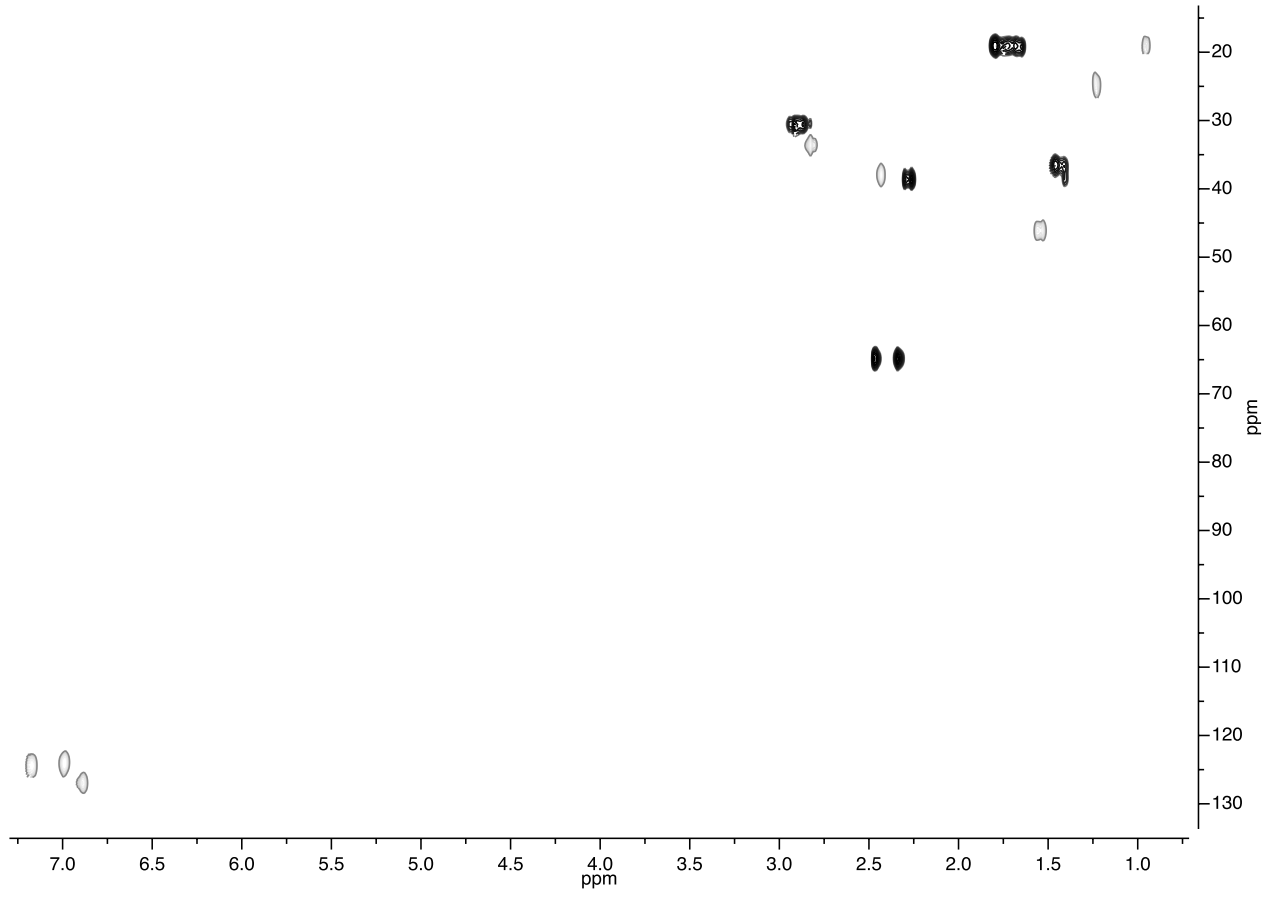
30
20
ppm


20
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80
90
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120
130
ppm
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6.0
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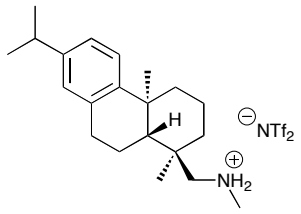
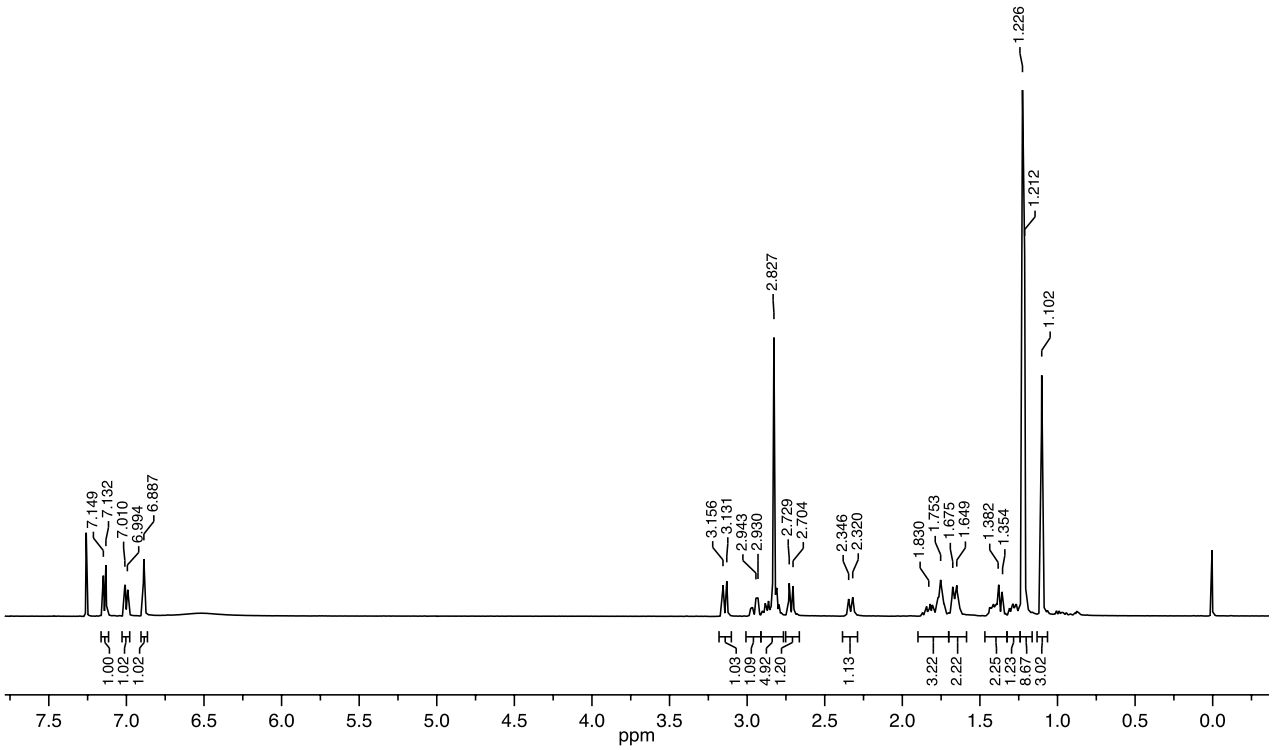
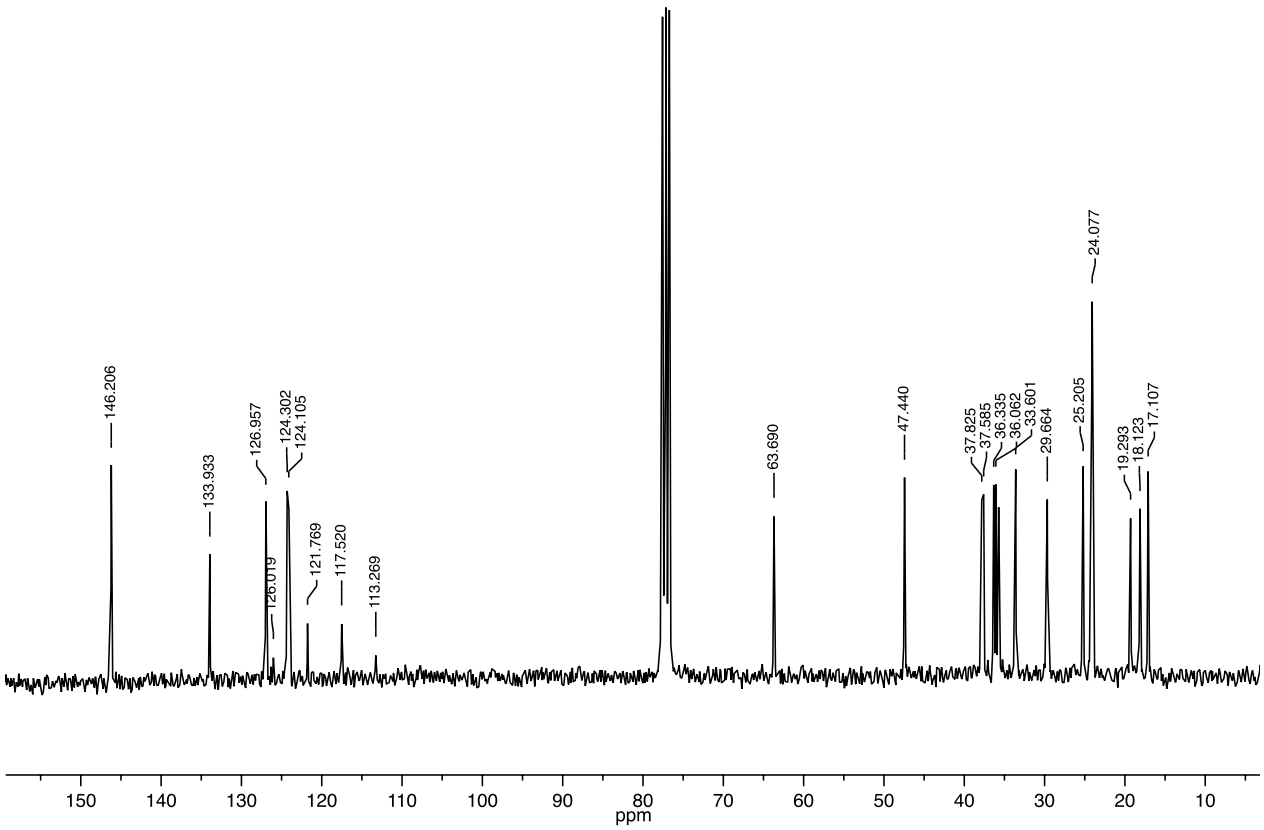
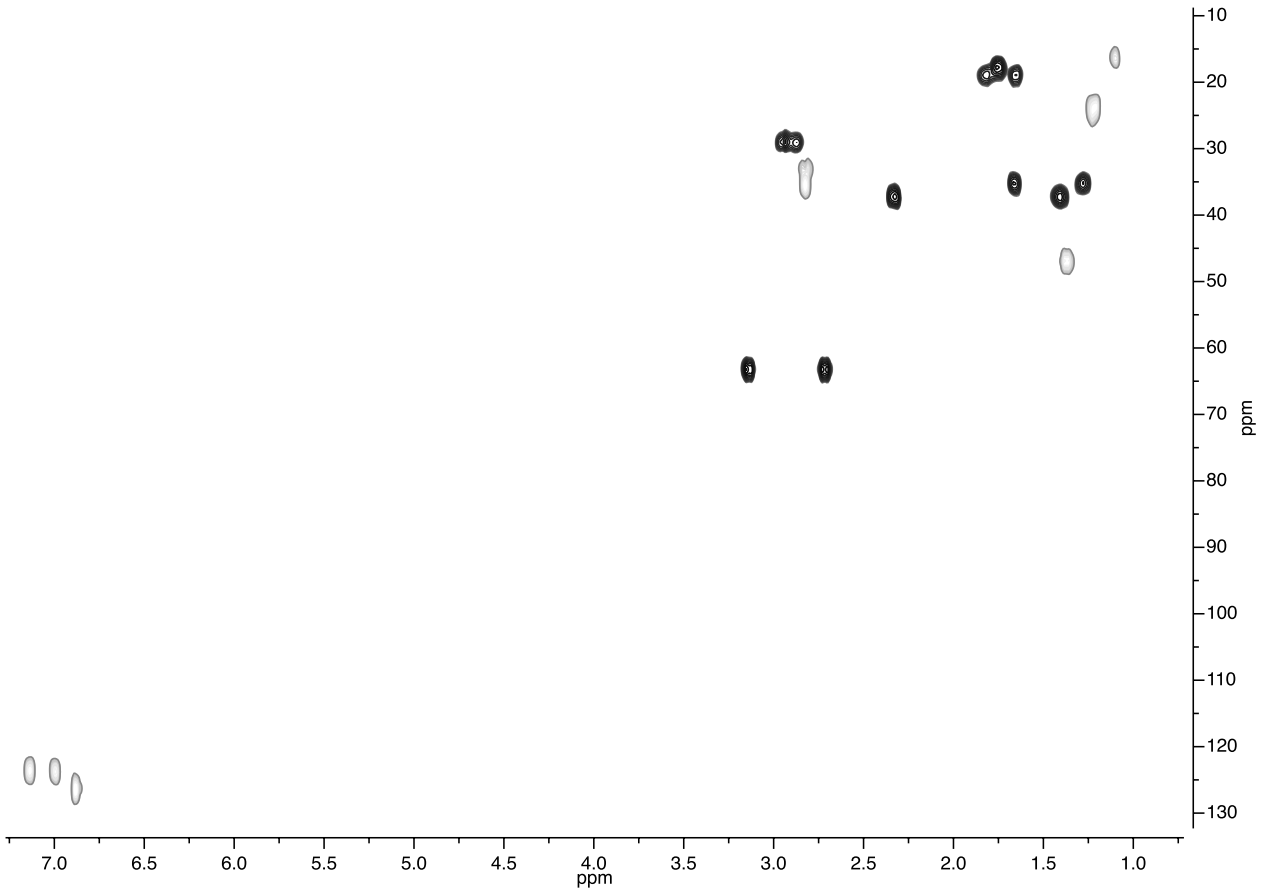
2.5
2.0
1.5
1.0
ppm

1H, 13C and HSQC spectra of compound 2b

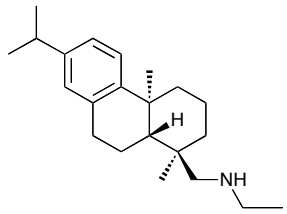


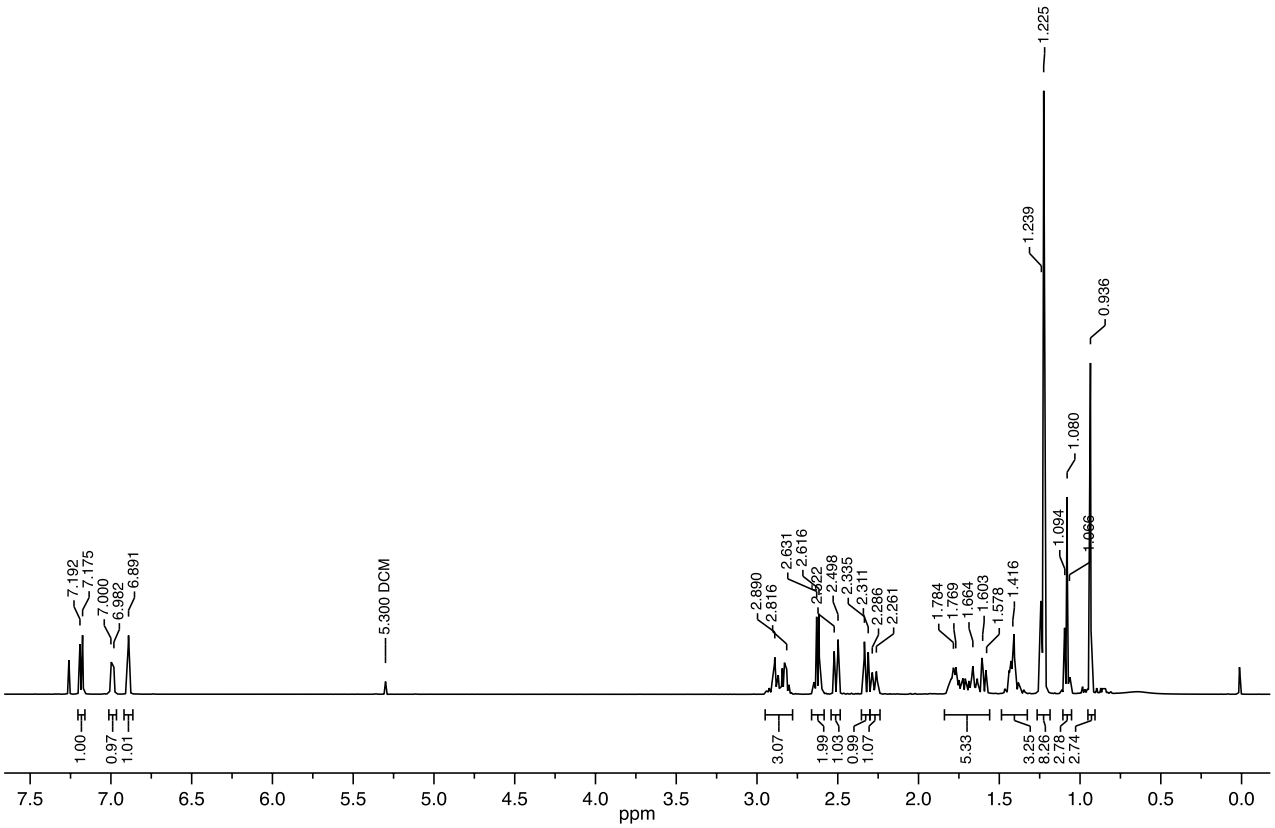


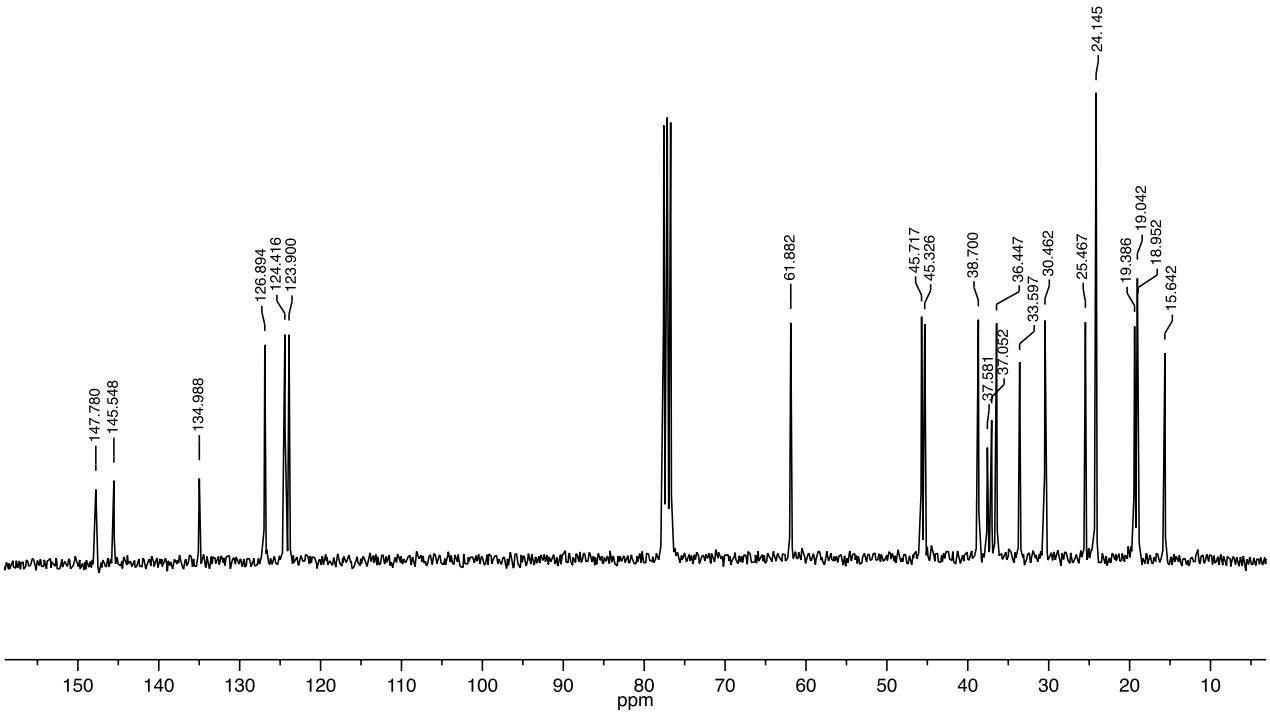

146.206
133.933
126.957
126.019
124.302
124.105
121.769
117.520
113.269
63.690
47.440
37.825
37.585
36.335
36.062
33.601
29.664
25.205
24.077
19.293
18.123
17.107
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

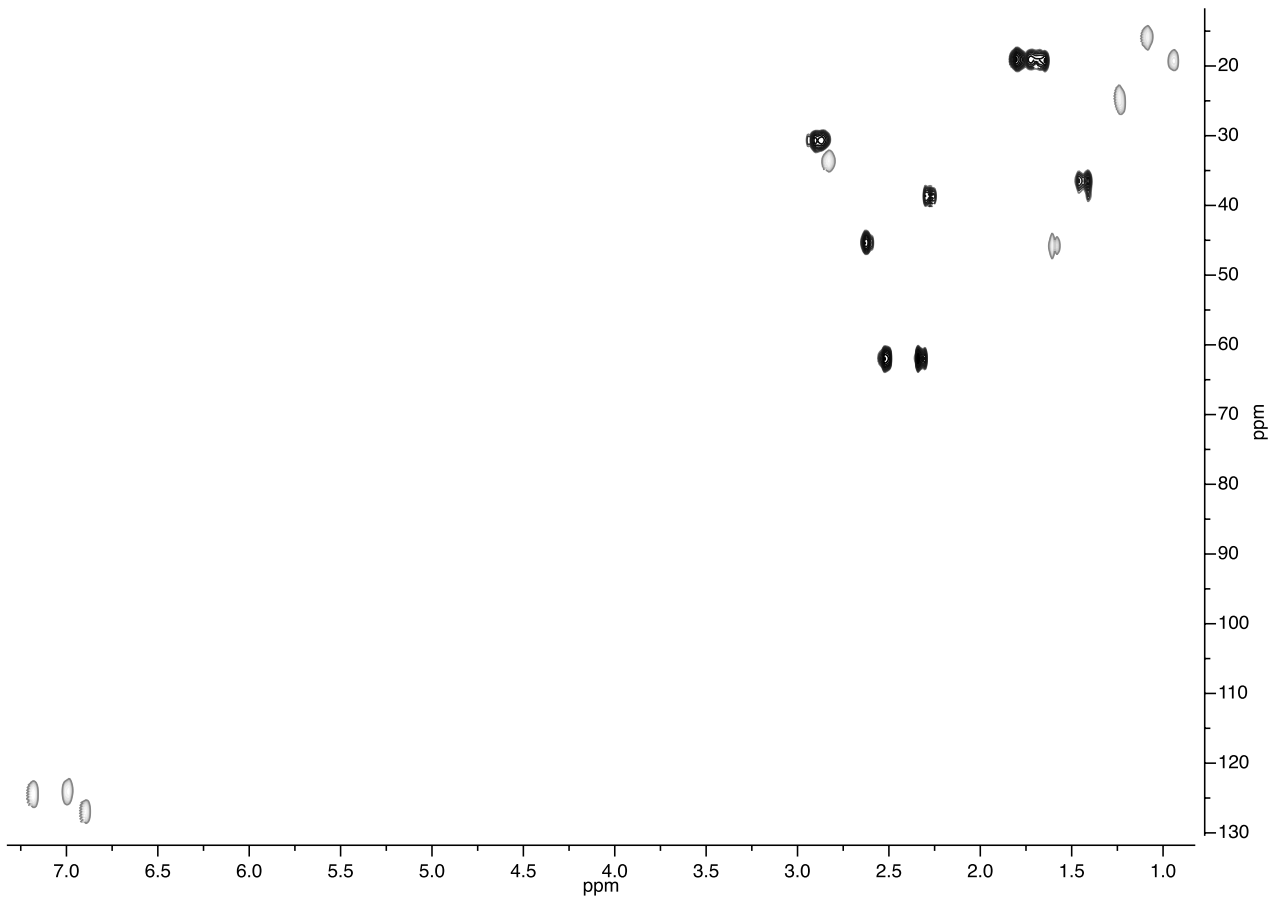

10 20 30 40 50 60 70 80 90 100 110 120 130
ppm
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm

1H, 13C and HSQC spectra of compound 3a

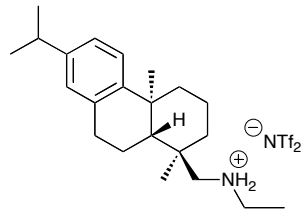


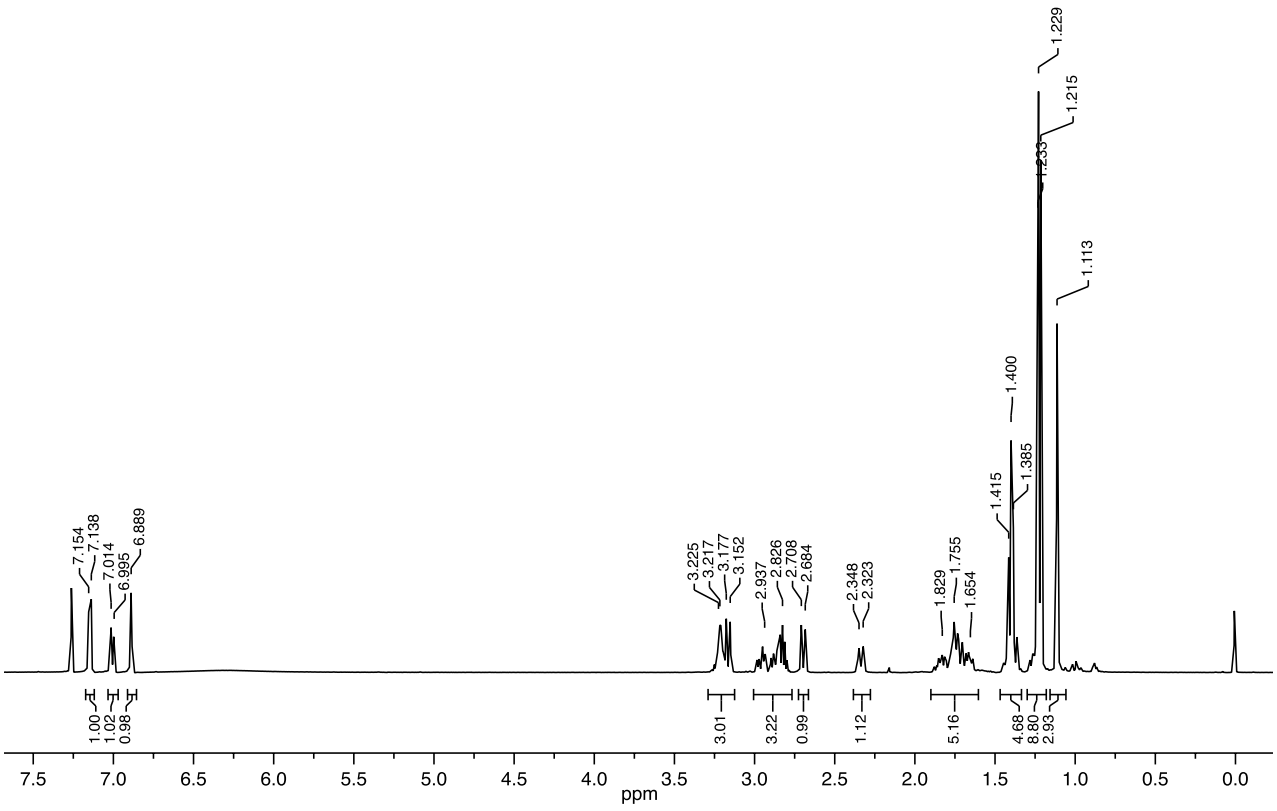


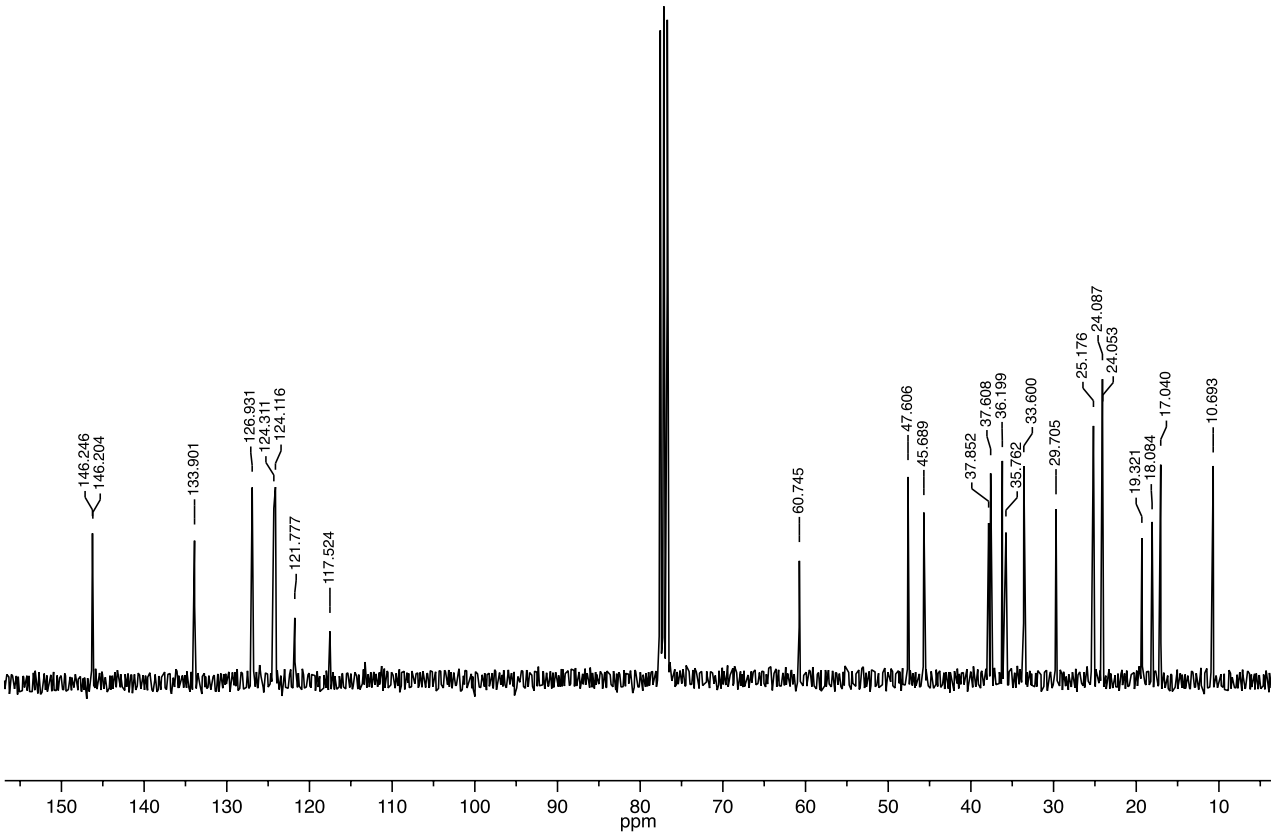

147.780
145.548
134.988
126.894
124.416
123.900
61.882
45.717
45.326
38.700
37.581
37.052
36.447
33.597
30.462
25.467
24.145
19.386
19.042
18.952
15.642
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

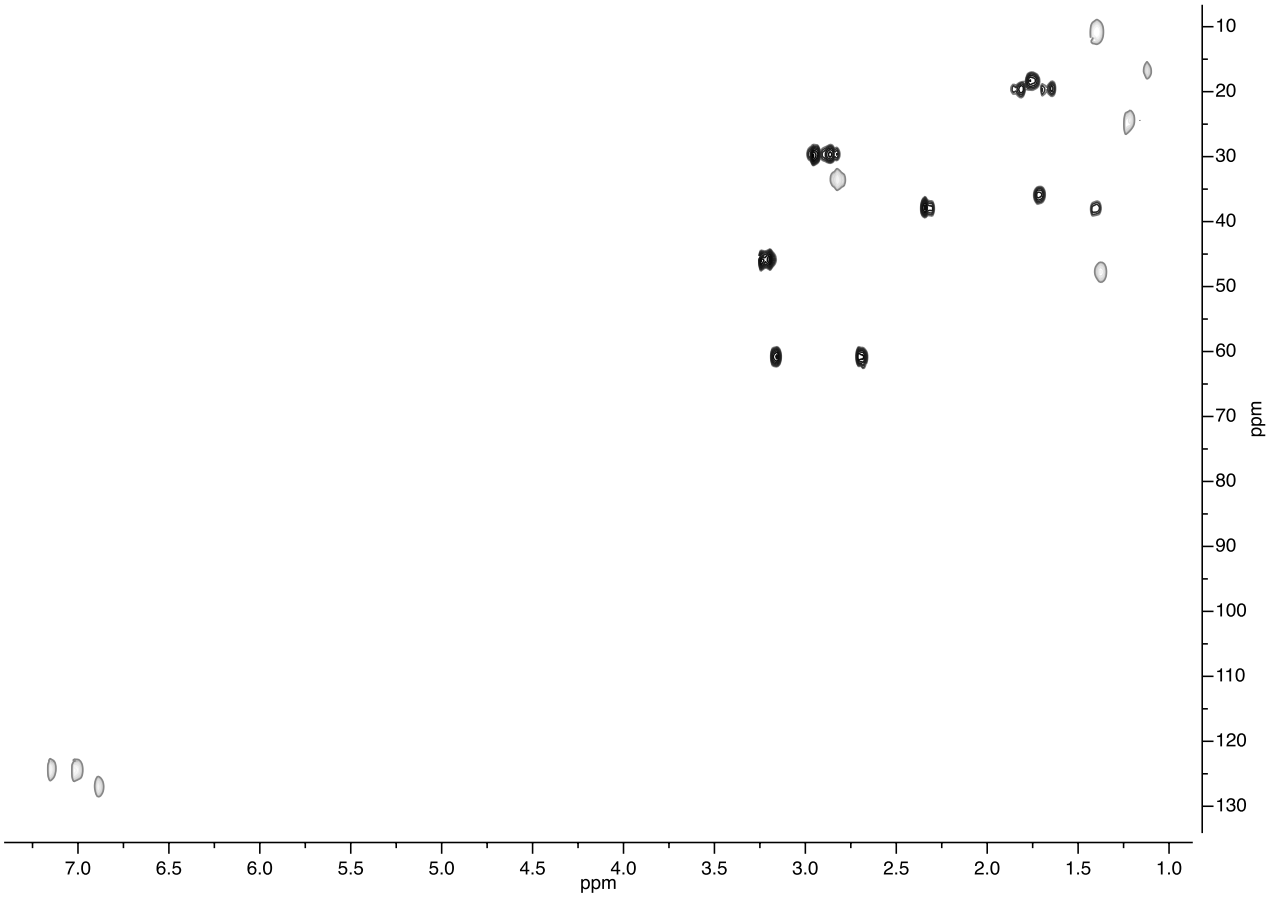

20
30
40
50
60
70
80
90
100
110
120
130
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

1H, 13C and HSQC spectra of compound 3b

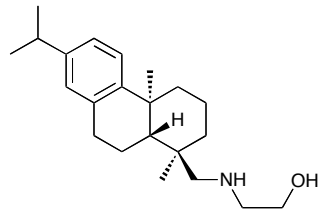


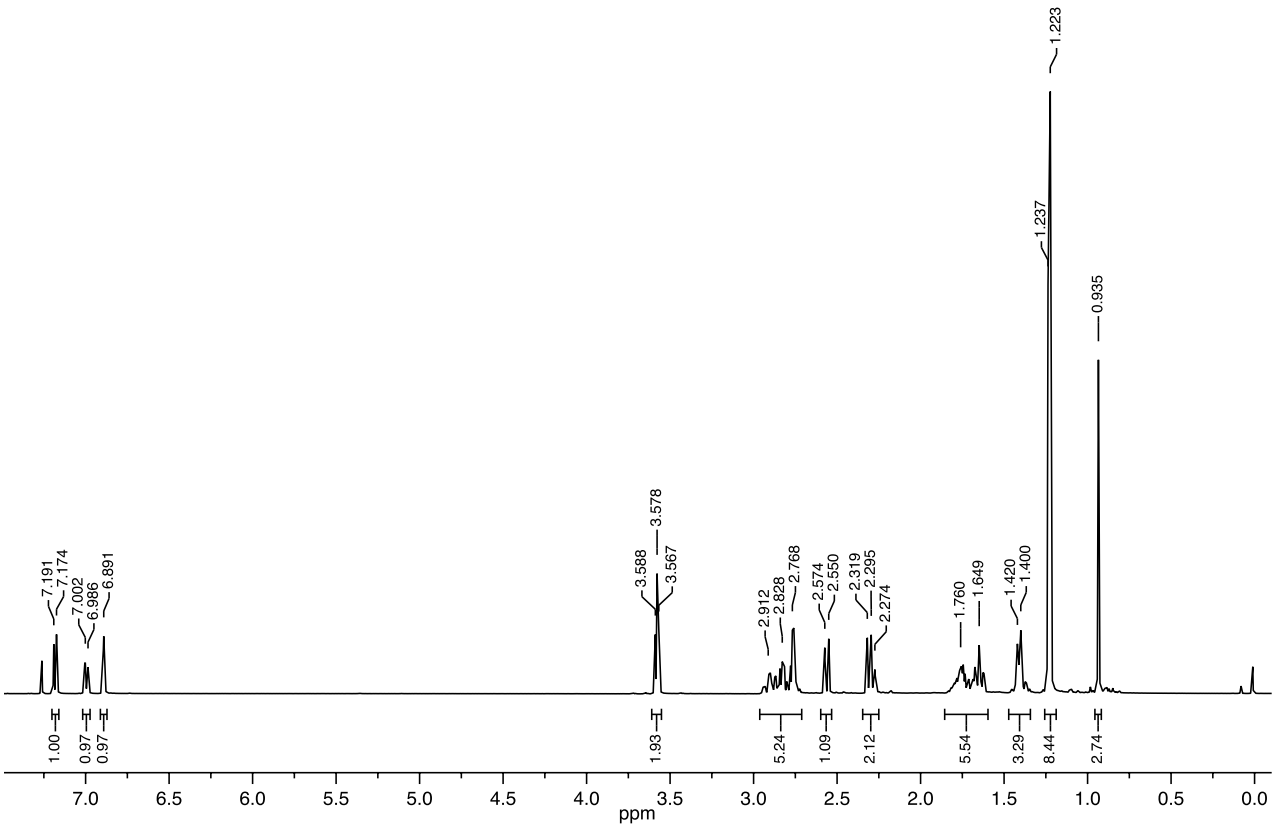


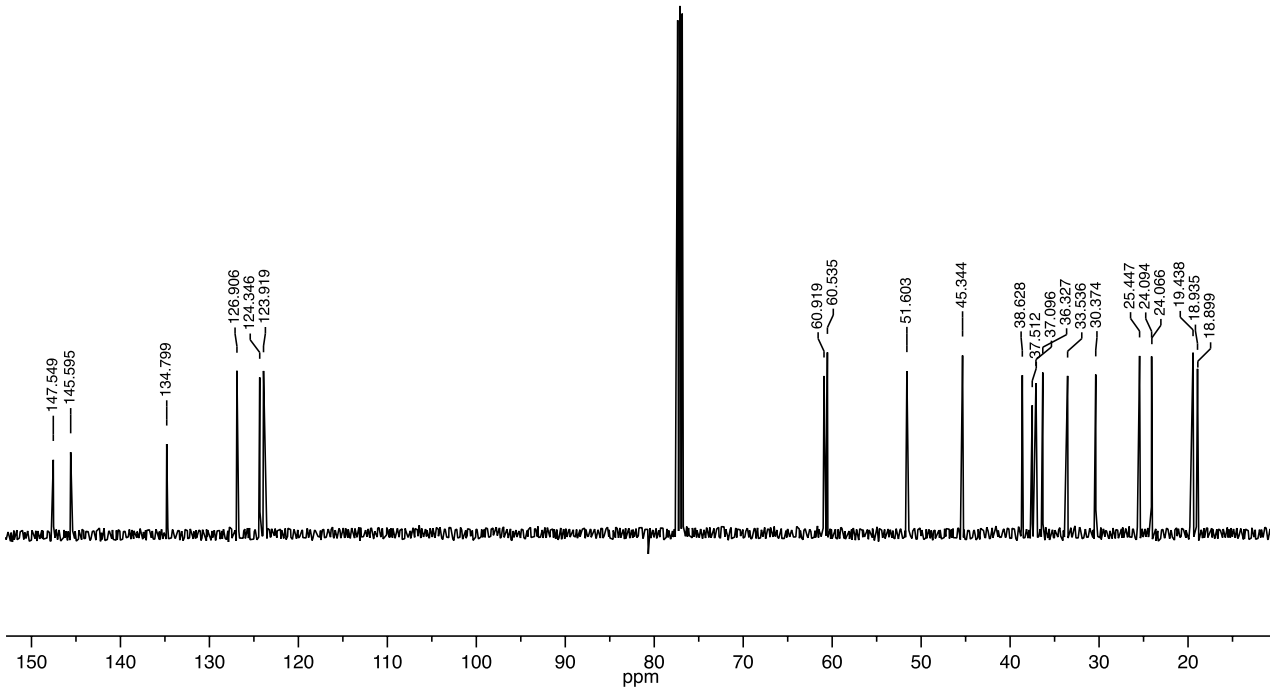

146.246
146.204
133.901
126.931
124.311
124.116
121.777
117.524
60.745
47.606
45.689
37.852
37.608
36.199
35.762
33.600
29.705
25.176
24.087
24.053
19.321
18.084
17.040
10.693
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

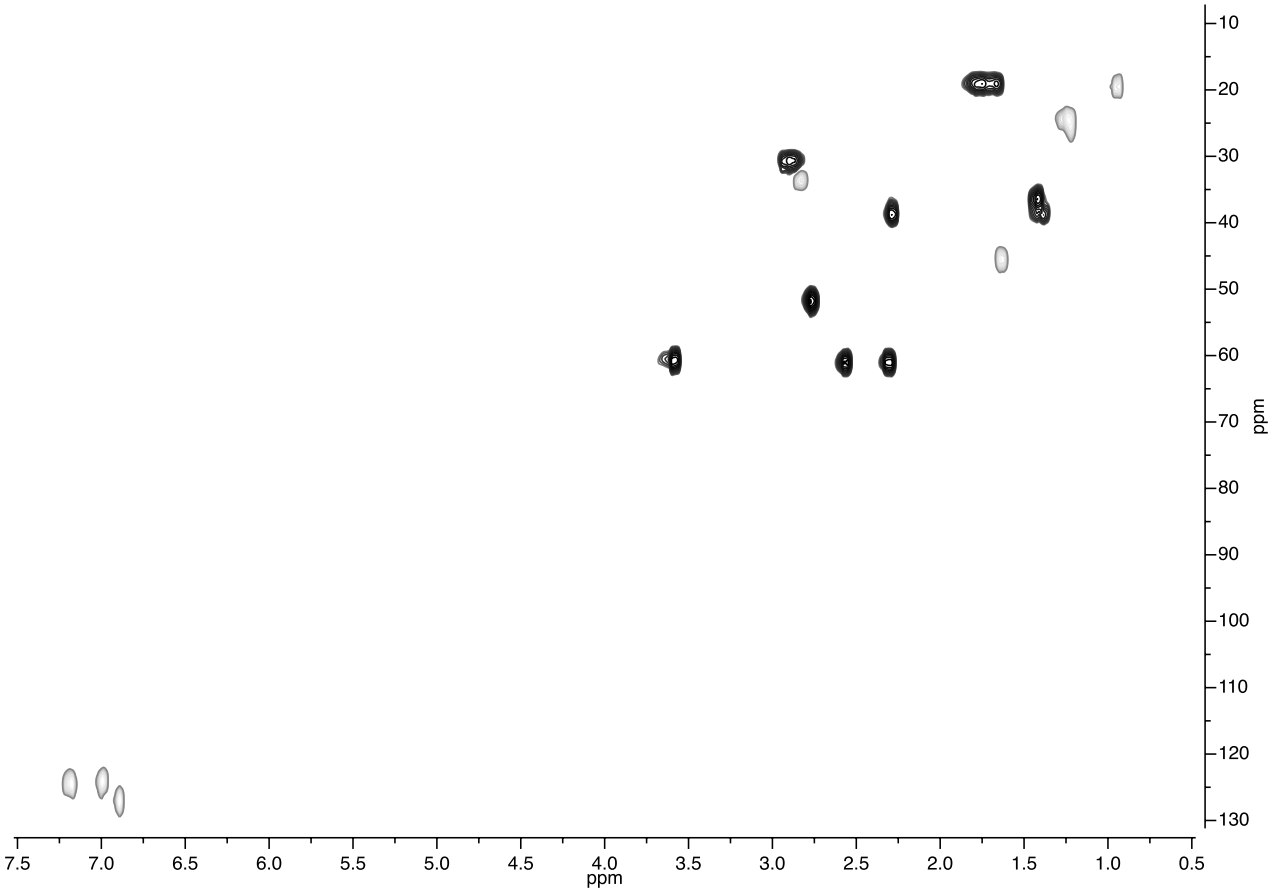

10 20 30 40 50 60 70 80 90 100 110 120 130
ppm
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm

1H, 13C and HSQC spectra of compound 4a

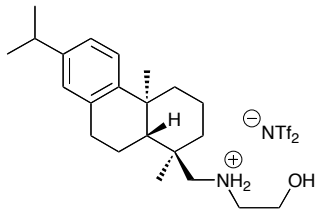


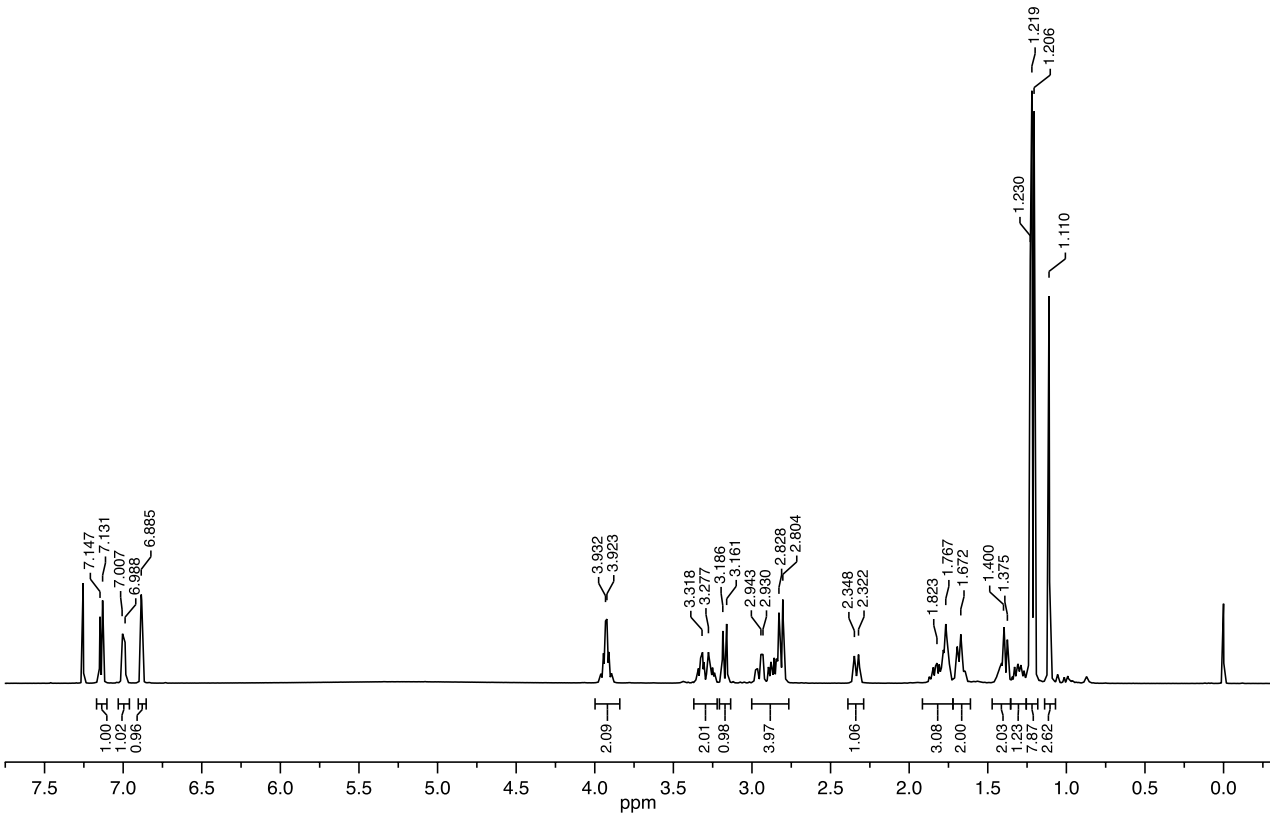


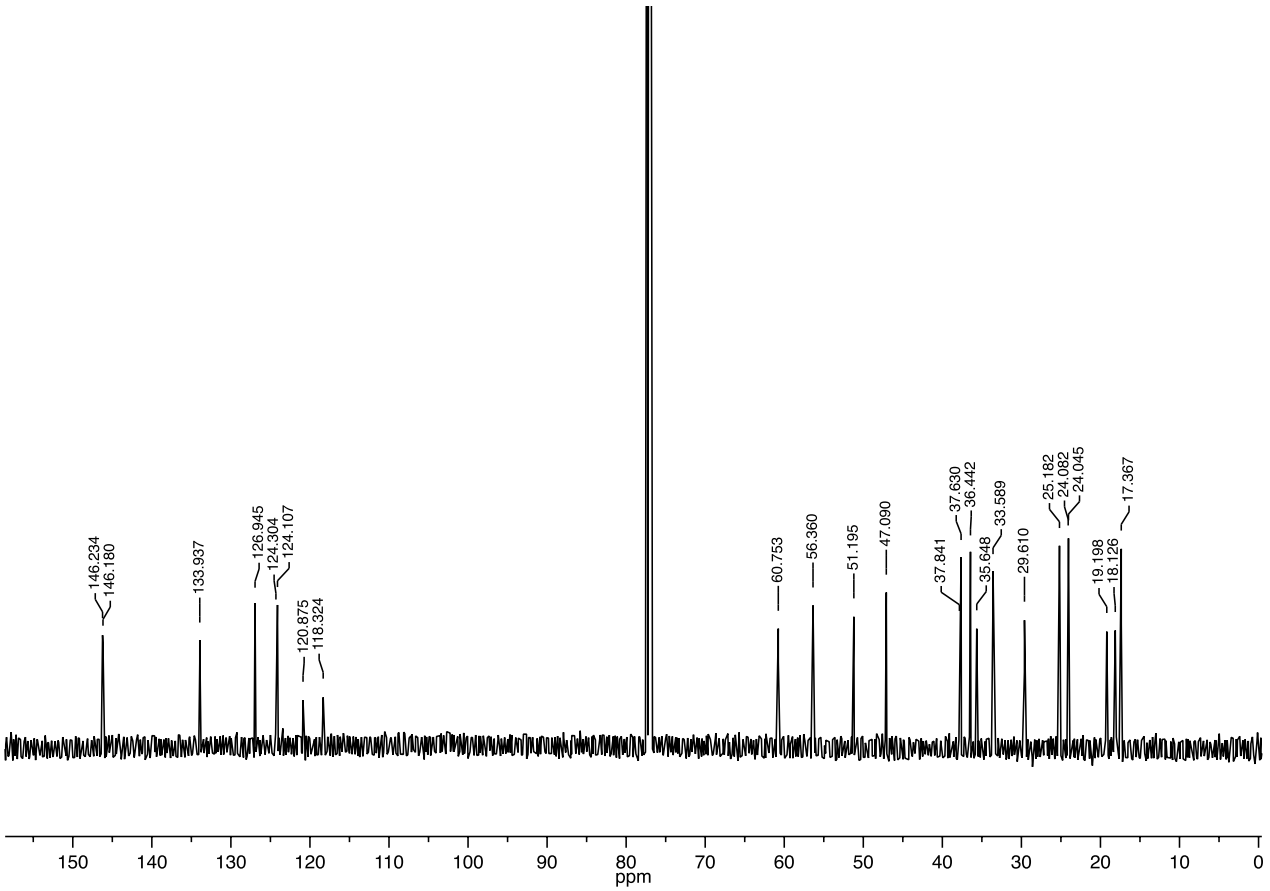

147.549
145.595
134.799
126.906
124.346
123.919
60.919
60.535
51.603
45.344
38.628
37.512
37.096
36.327
33.536
30.374
25.447
24.094
24.066
19.438
18.935
18.899
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

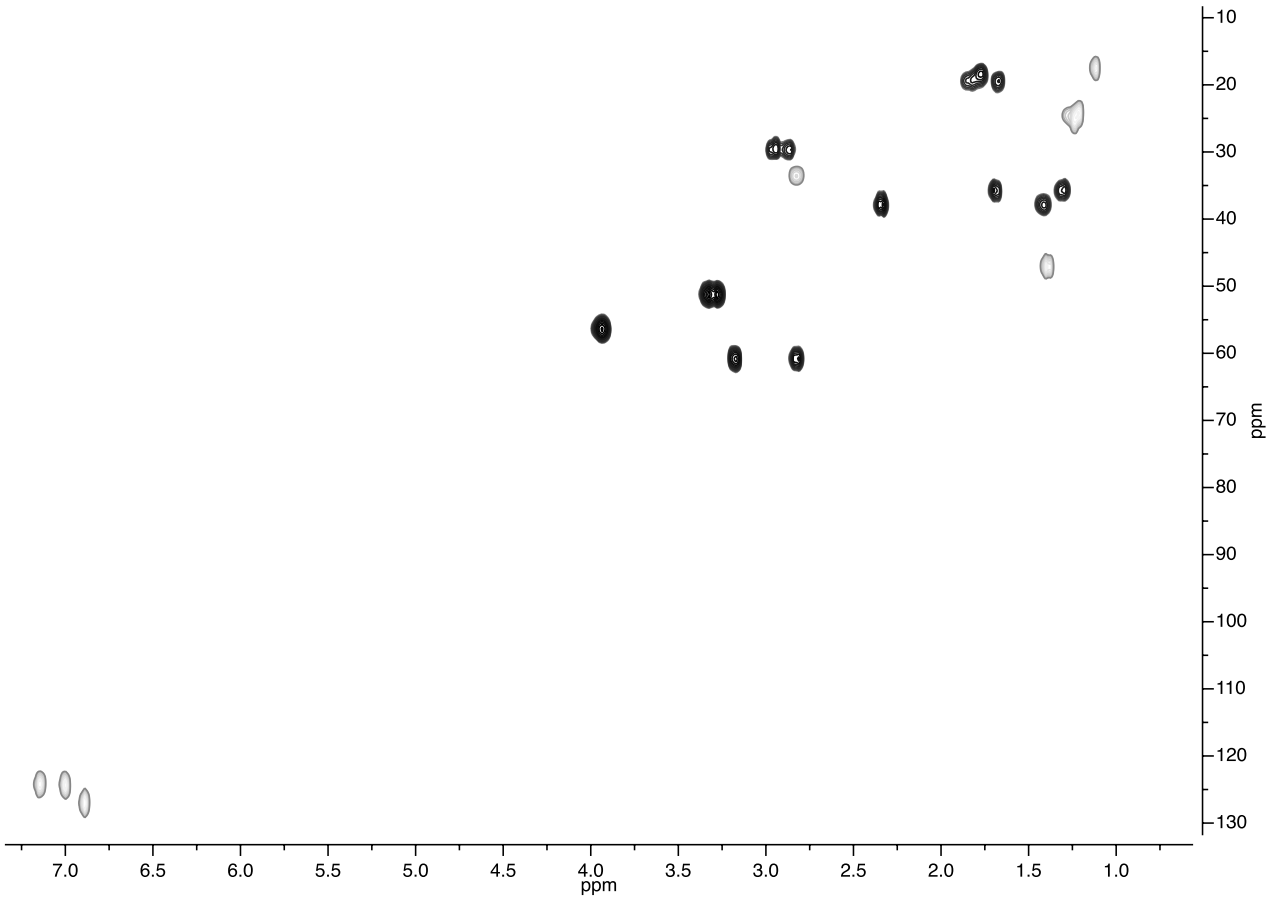

10
20
30
40
50
60
70
80
90
100
110
120
130
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

1H, 13C and HSQC spectra of compound 4b

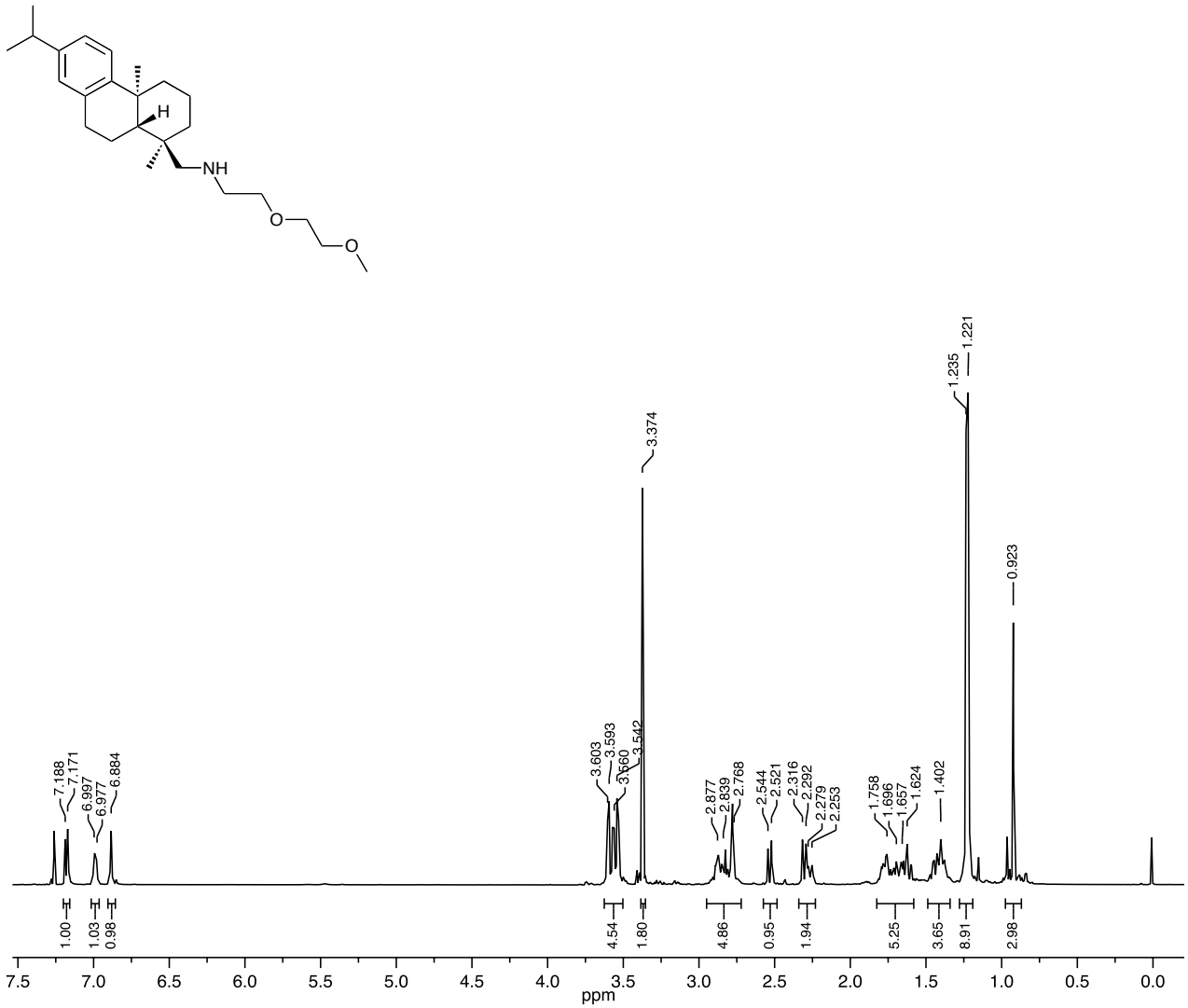


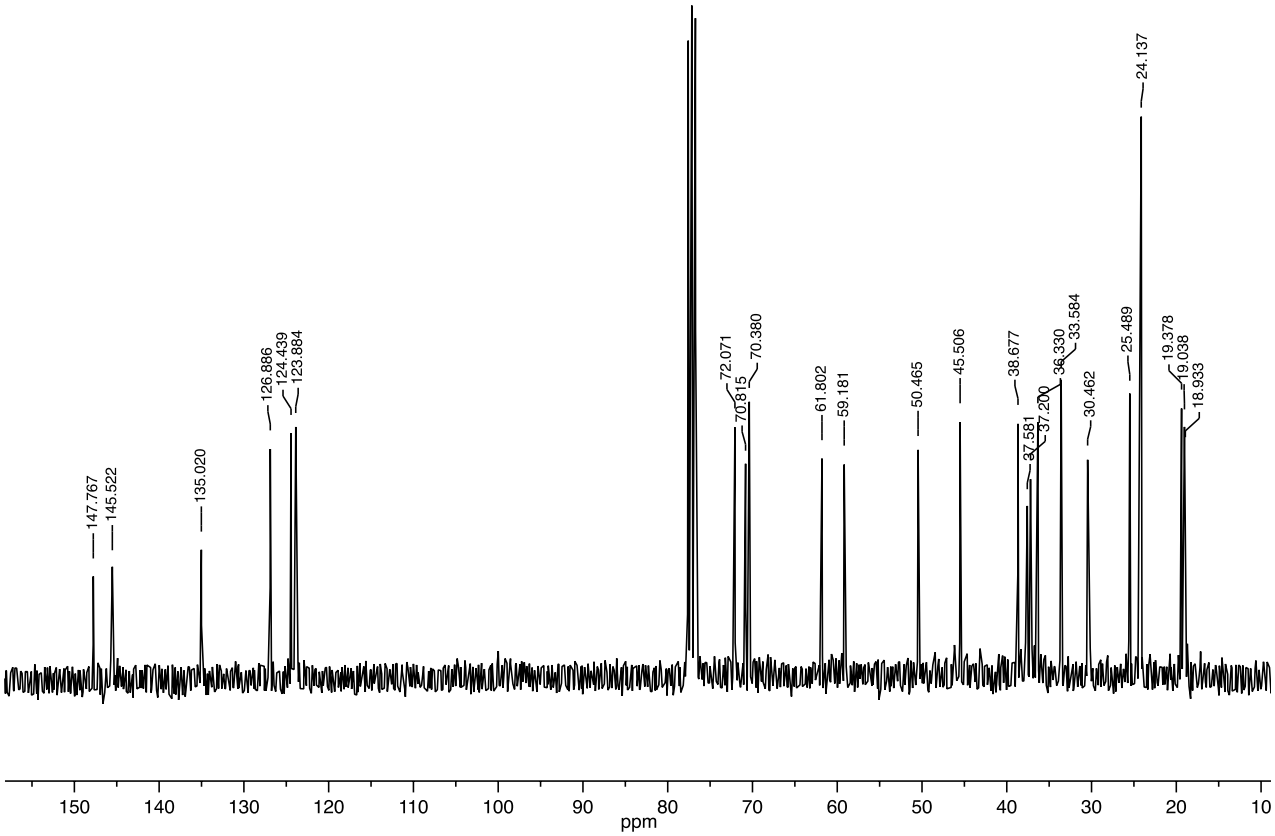


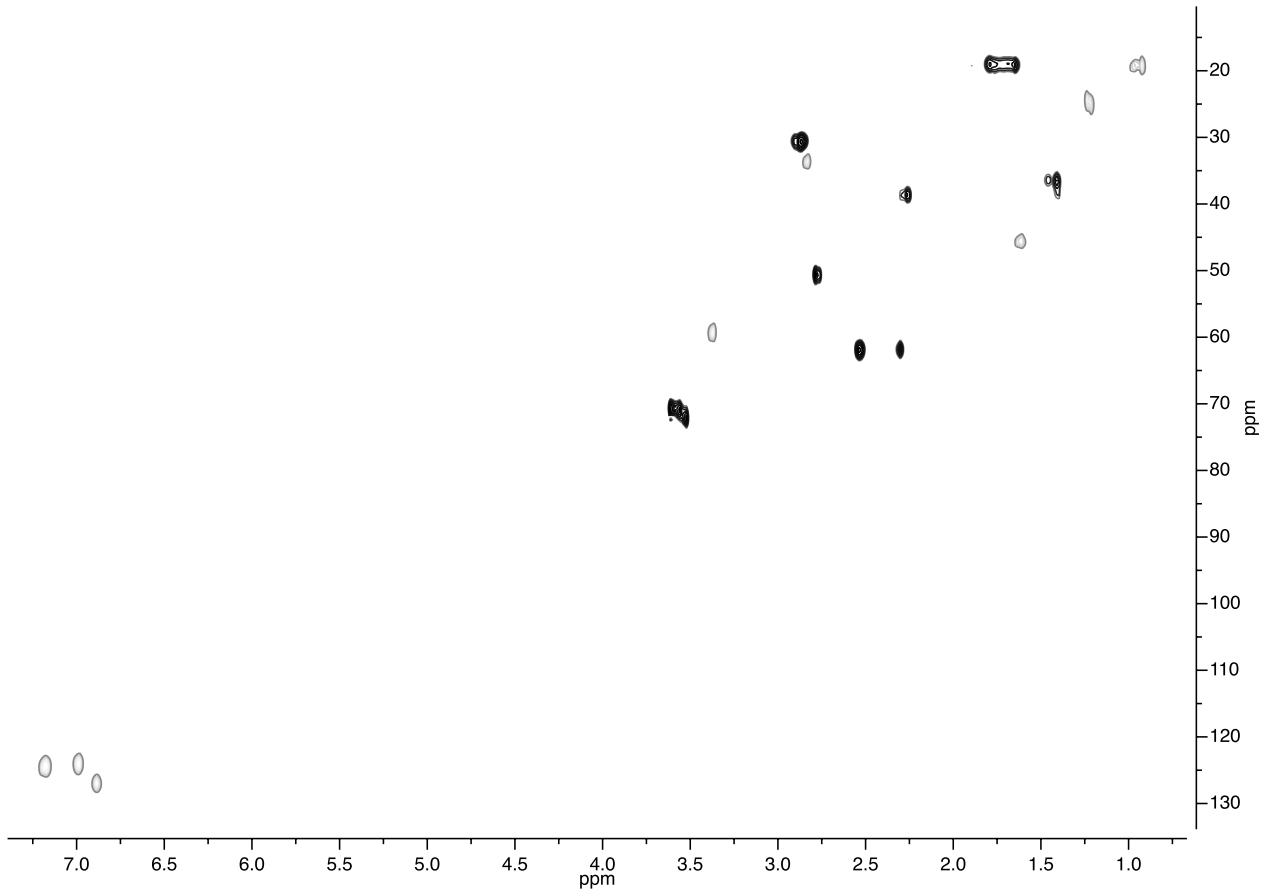

146.234
146.180
133.937
126.945
124.304
124.107
120.875
118.324
60.753
56.360
51.195
47.090
37.841
37.630
36.442
35.648
33.589
29.610
25.182
24.082
24.045
19.198
18.126
17.367
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm


10 20 30 40 50 60 70 80 90 100 110 120 130
ppm
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
ppm

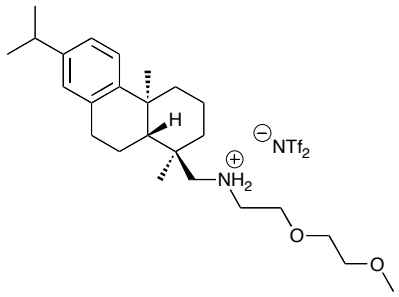
1H, 13C and HSQC spectra of compound 5a

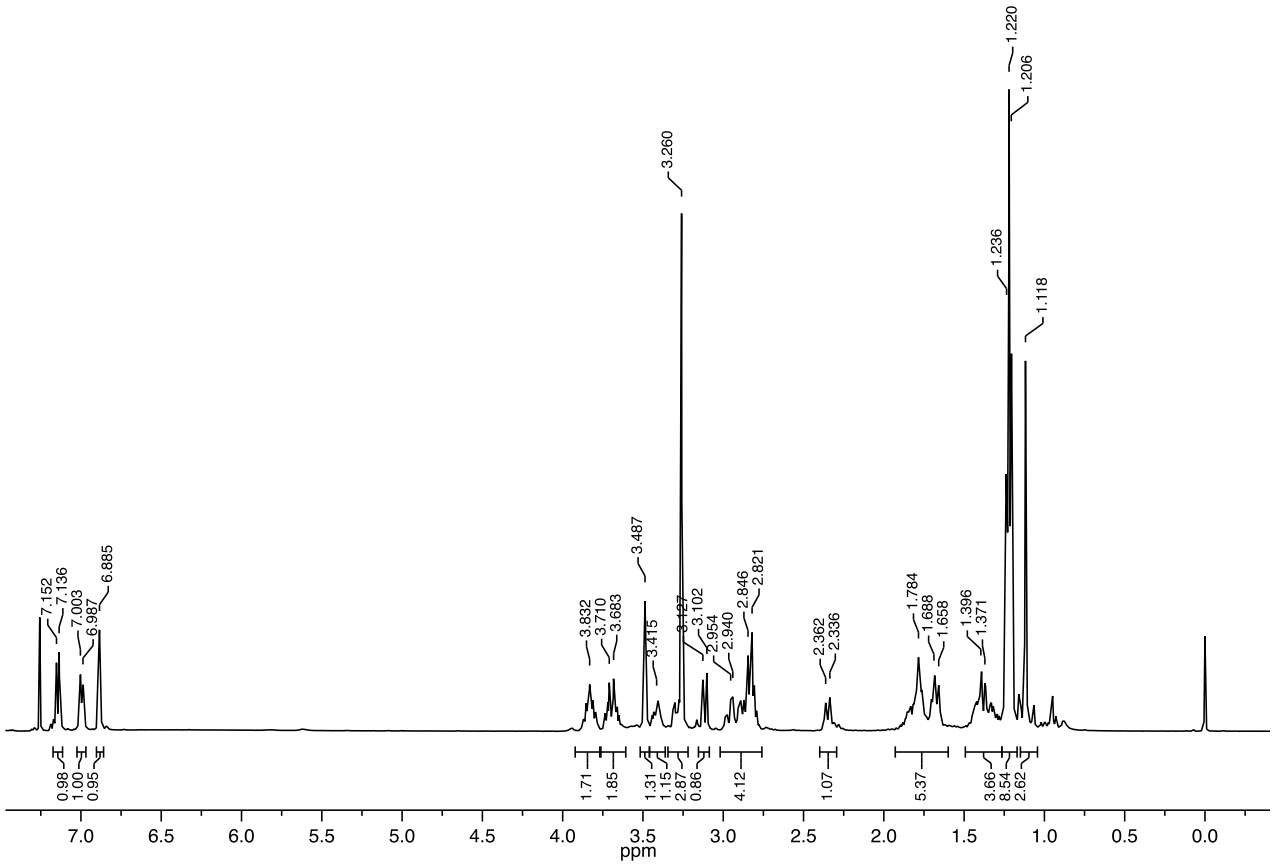


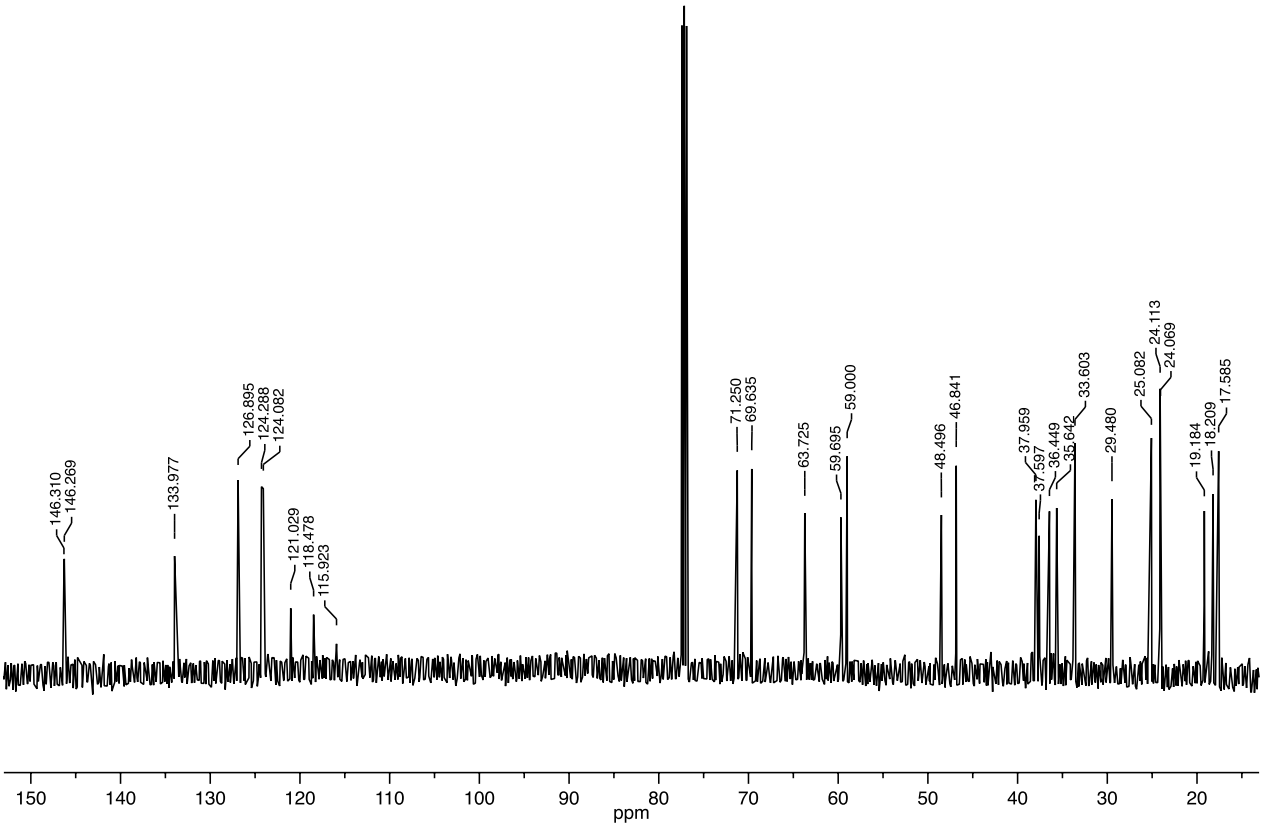

147.767
145.522
135.020
126.886
124.439
123.884
72.071
70.815
70.380
61.802
59.181
50.465
45.506
38.677
37.581
37.200
36.330
33.584
30.462
25.489
24.137
19.378
19.038
18.933
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

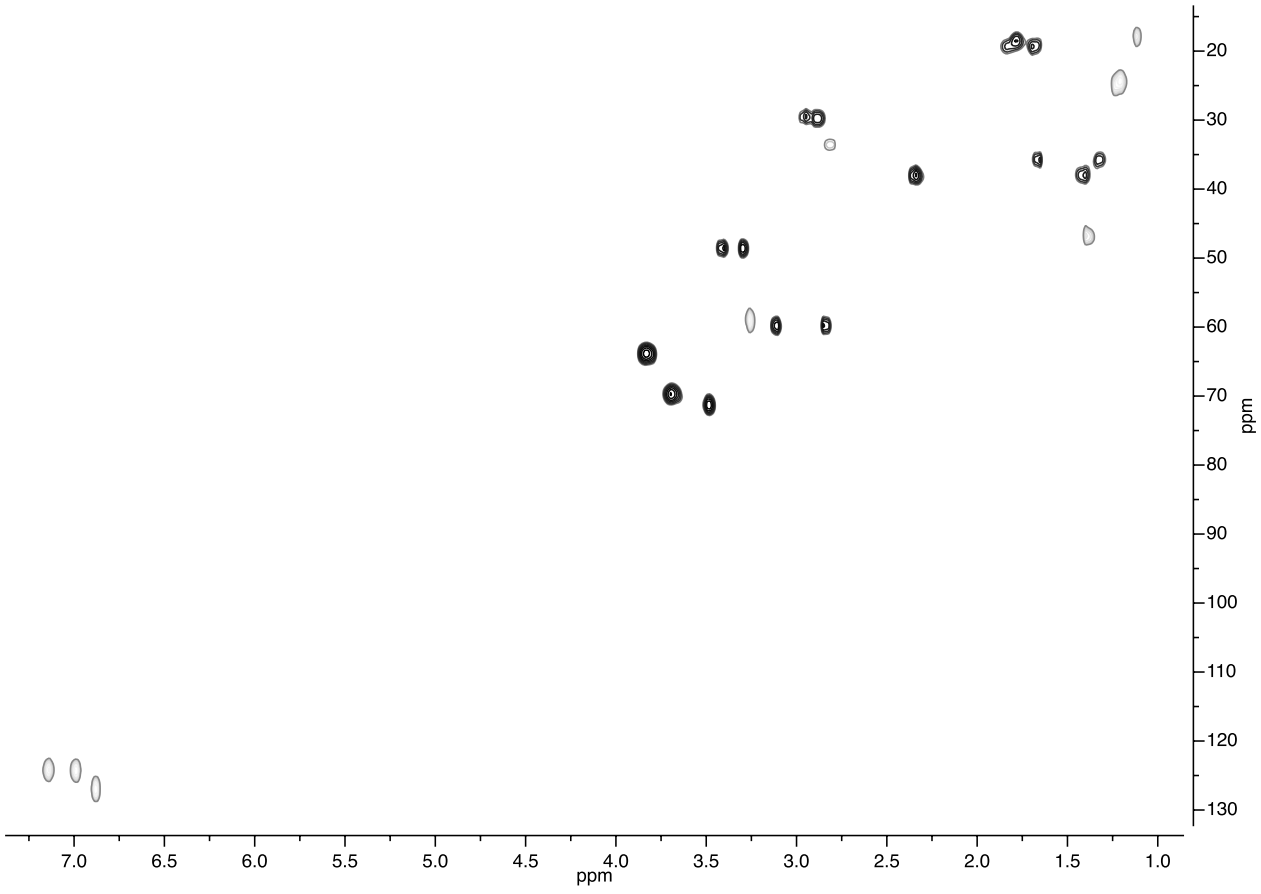

20
30
40
50
60
70
80
90
100
110
120
130
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

1H, 13C and HSQC spectra of compound 5b

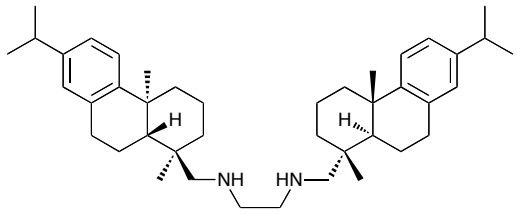


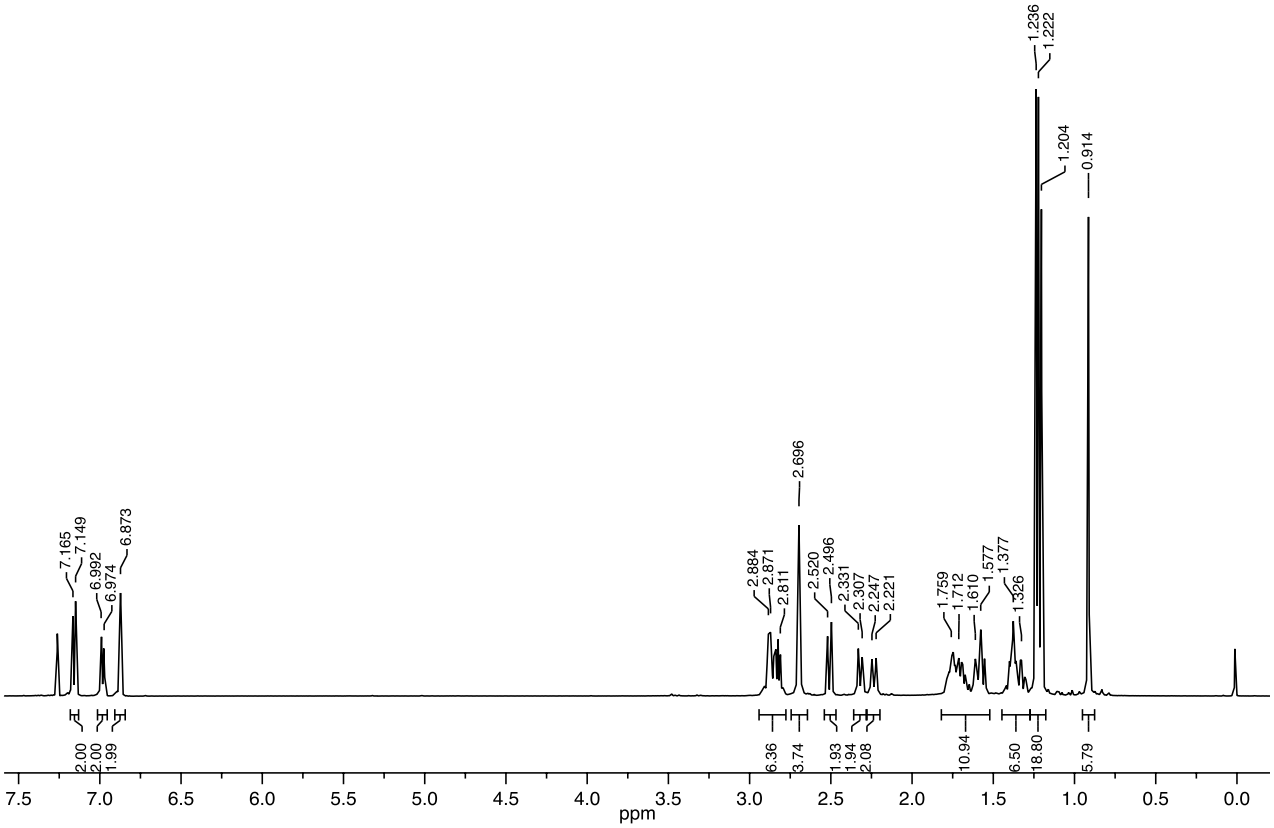


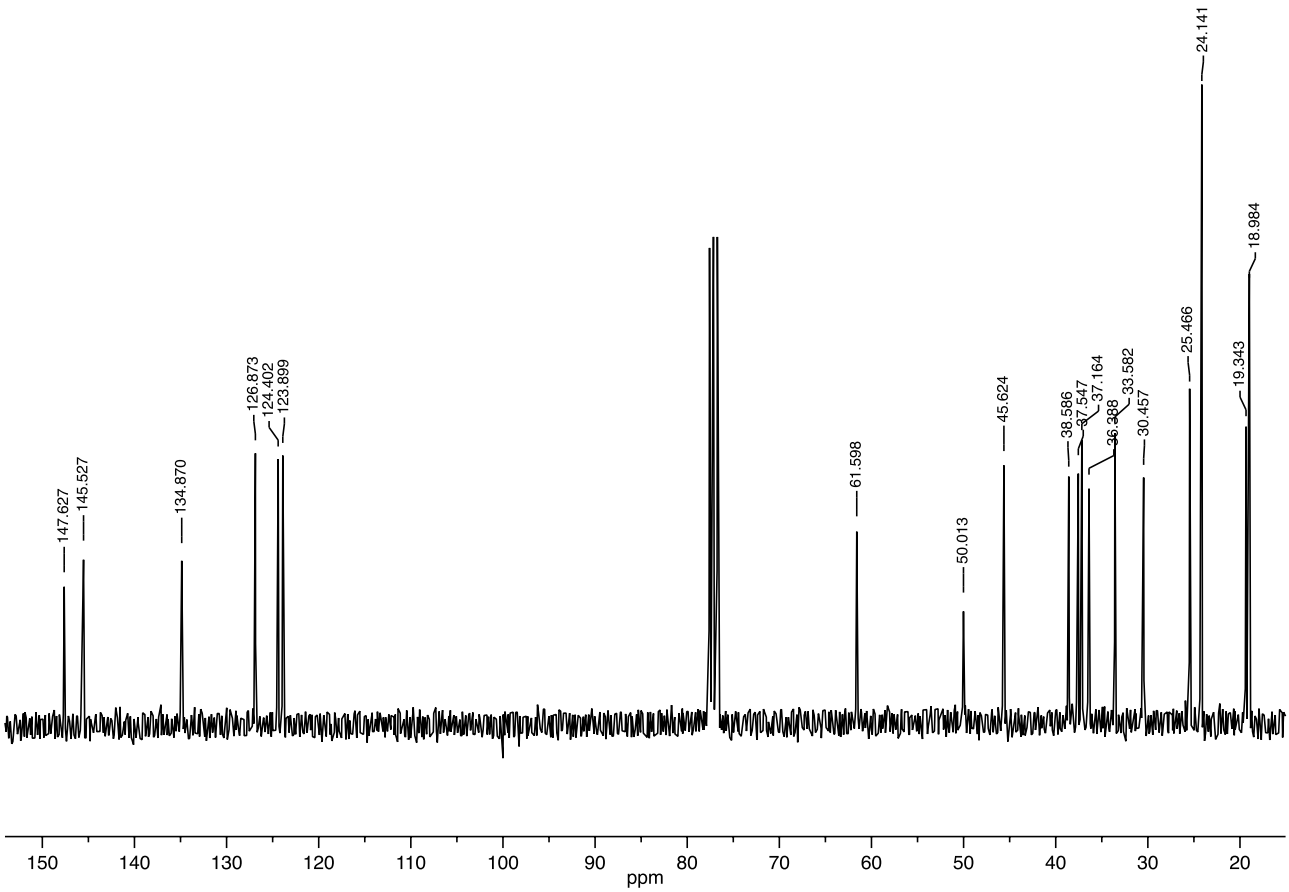

146.310
146.269
133.977
126.895
124.288
124.082
121.029
118.478
115.923
71.250
69.635
63.725
59.695
59.000
48.496
46.841
37.959
37.597
36.449
35.642
33.603
29.480
25.082
24.113
24.069
19.184
18.209
17.585
150 140 130 120 110 100 90 80 70 60 50 40 30 20
ppm

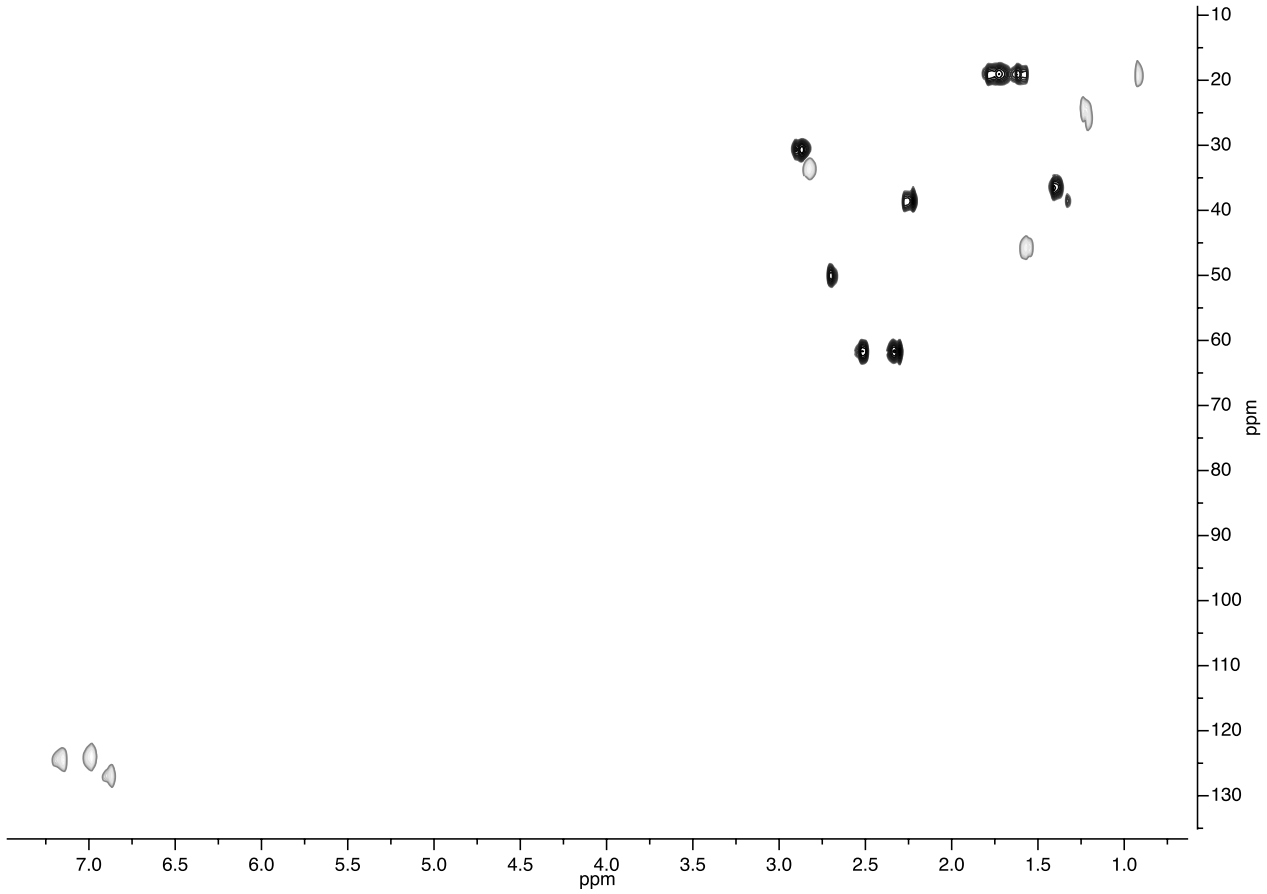

20 30 40 50 60 70 80 90 100 110 120 130
ppm
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
ppm

1H, 13C and HSQC spectra of compound 6a

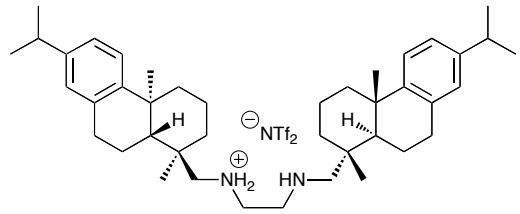


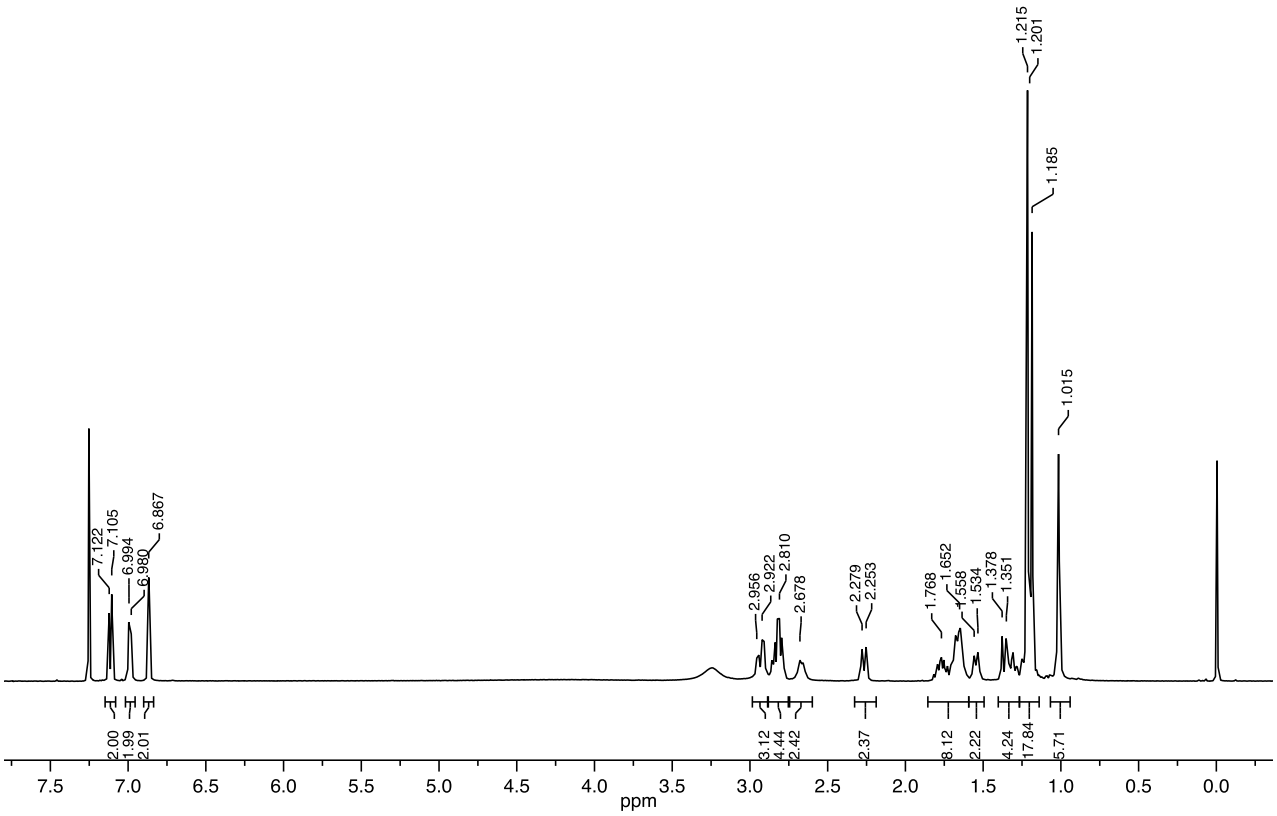


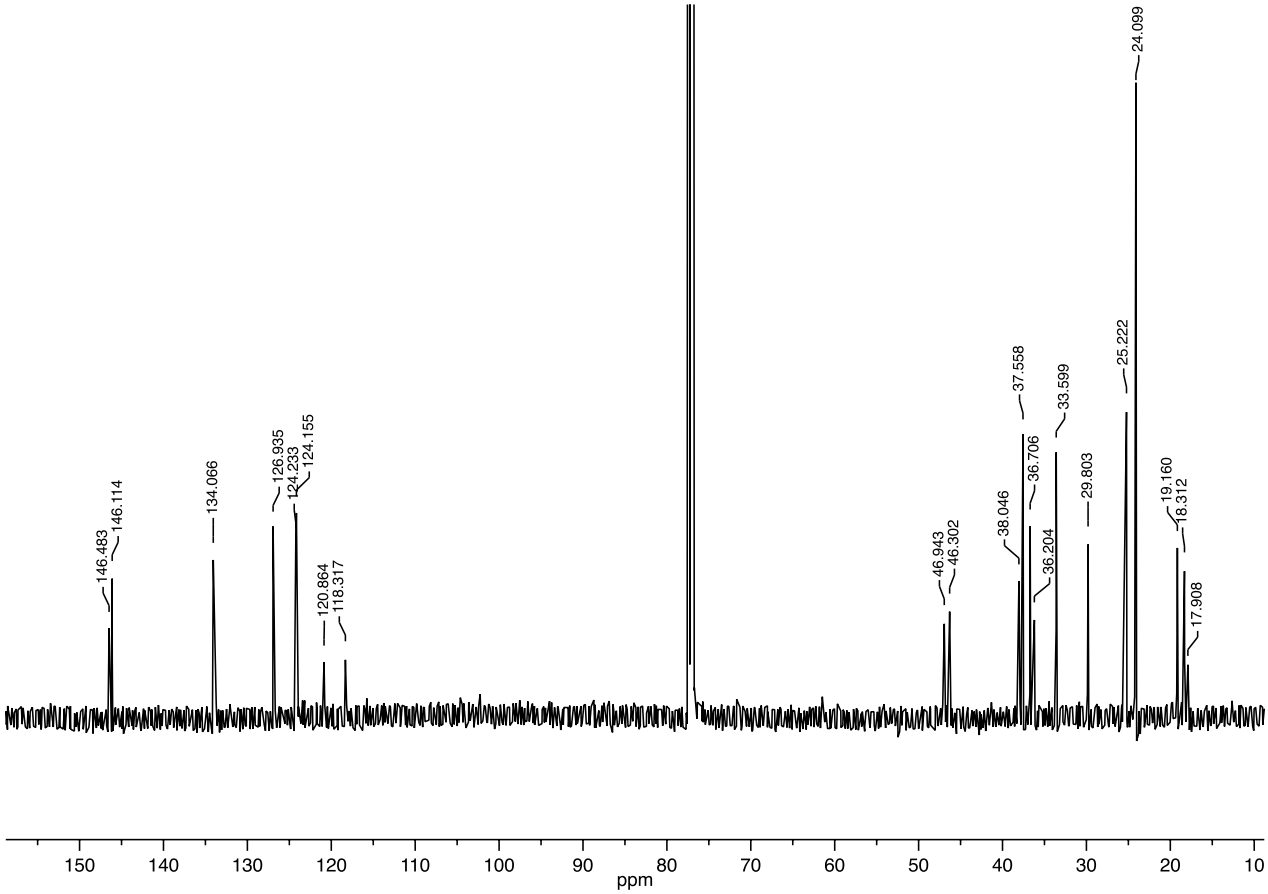

147.627
145.527
134.870
126.873
124.402
123.899
61.598
50.013
45.624
38.586
37.547
37.164
36.388
33.582
30.457
25.466
24.141
19.343
18.984
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

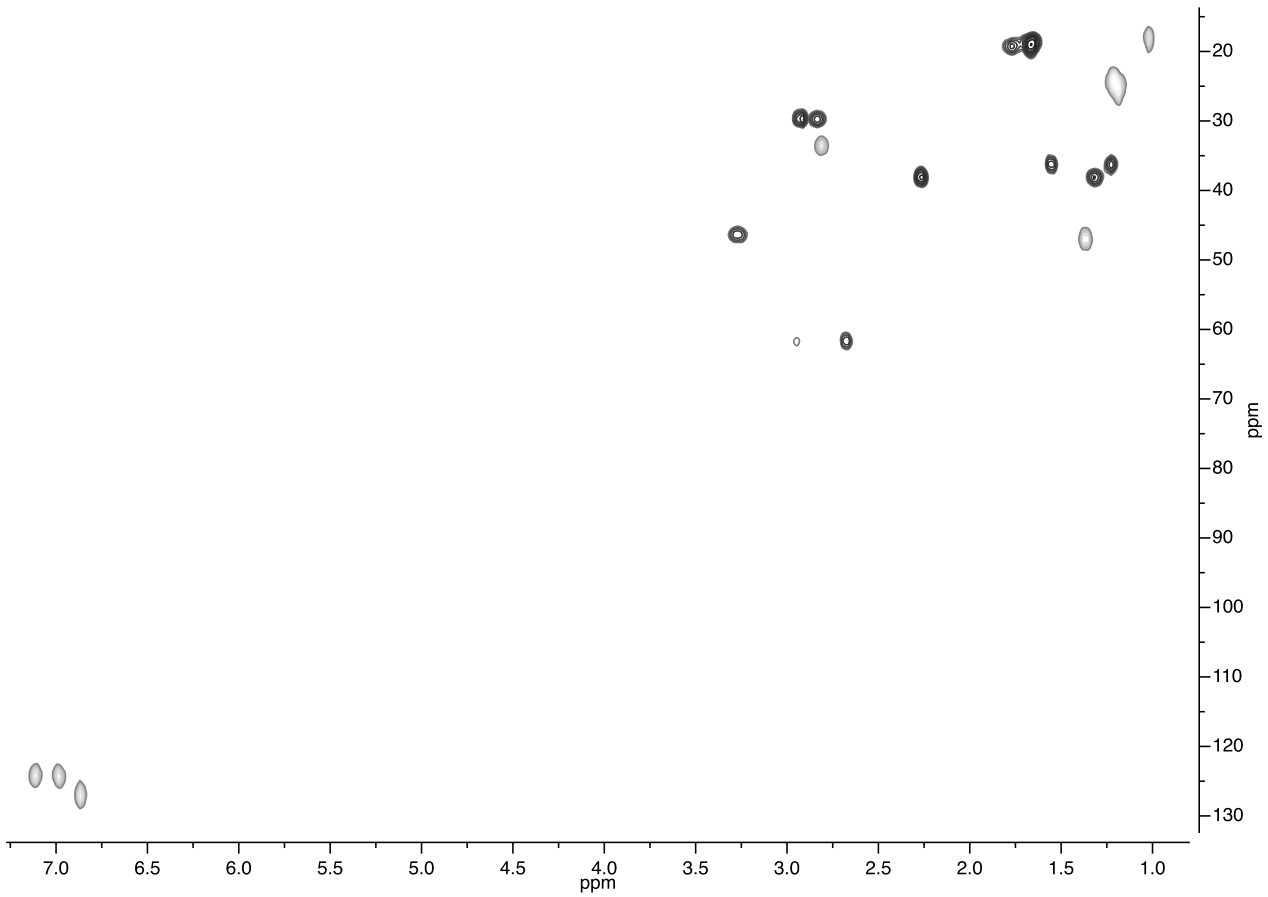

10
20
30
40
50
60
70
80
90
100
110
120
130
ppm
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

1H, 13C and HSQC spectra of compound 6b






146.483
146.114
134.066
126.935
124.233
124.155
120.864
118.317
46.943
46.302
38.046
37.558
36.706
36.204
33.599
29.803
25.222
24.099
19.160
18.312
17.908
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


20
30
40
50
60
70
80
90
100
110
120
130
ppm
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
ppm