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SUPPORTING INFORMATION

DOI: 10.1002/ejoc.201300157
Title: Concise Chemoenzymatic Three-Step Total Synthesis of Isosolenopsin through Medium Engineering
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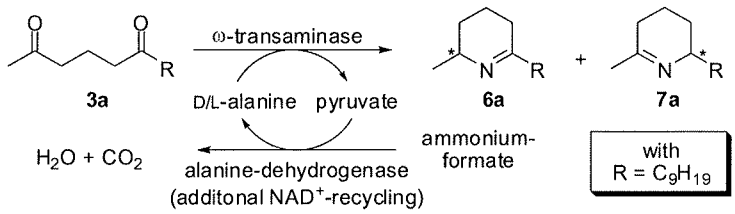
General Information:

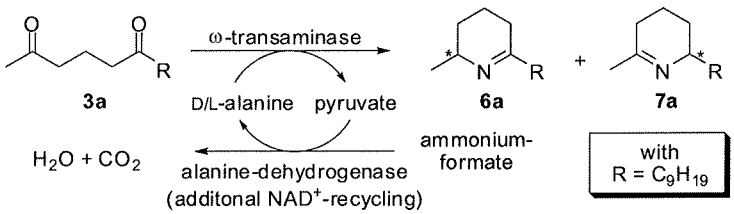
Unless stated otherwise, reagents and organic solvents were obtained from commercial suppliers and used as received. Toluene, methanol and acetonitrile used for anhydrous reactions were dried over appropriate molecular sieves (4Å for toluene, 3Å for MeOH and MeCN) for at least 48 hours. THF used for anhydrous reactions was distilled from potassium/benzophenone directly prior to use. For anhydrous reactions, flasks were oven-dried at 120 °C over night and flushed with dry nitrogen just before use. The reactions were carried out with standard *Schlenk* techniques under N_2 atmosphere.

Initial Enzyme Testing (Selected Results)



		50 mM **3a**, 5 vol % toluene			25 mM **3a**, 10 vol % toluene		
entry	enzyme	**3a** [%]	**6a** [%]	**7a** [%]	**3a** [%]	**6a** [%]	**7a** [%]
1	*Chromobacterium violaceum*	> 99	< 1	–	99.5	0.5	–
2	*Bacillus megaterium*	98.9	1.1	–	99.6	0.4	–
3	*Paracoccus denitrificans*	> 99	< 1	–	99.4	0.6	–
4	*Vibrio fluvialis*	98.5	1.5	–	98.4	1.6	–
5	*Arthrobacter* sp.	80.2	19.8	–	83.6	16.4	–
6	*Aspergillus terreus*	> 99	< 1	–	98.8	1.2	–
7	*Hyphomonas neptunium*	71.5	29.5	–	75.6	24.5	–

Table S1. Results of the enzyme testing. Conditions: 25 (6 mg/mL) respective 50 mM (12 mg/mL) diketone **3a** in the presence of various vol% of tolune, 1 mM PLP, 1 mM NAD^+, 150 mM ammonium formate, 250 mM D- respective L-alanine, 11 U FDH, 12 U AlaDH. Reactions were run at 30 °C for 24 hours in an Eppendorf orbital shaker at 600 rpm with the tubes in horizontal position. Conversions were determined by achiral GC analysis.

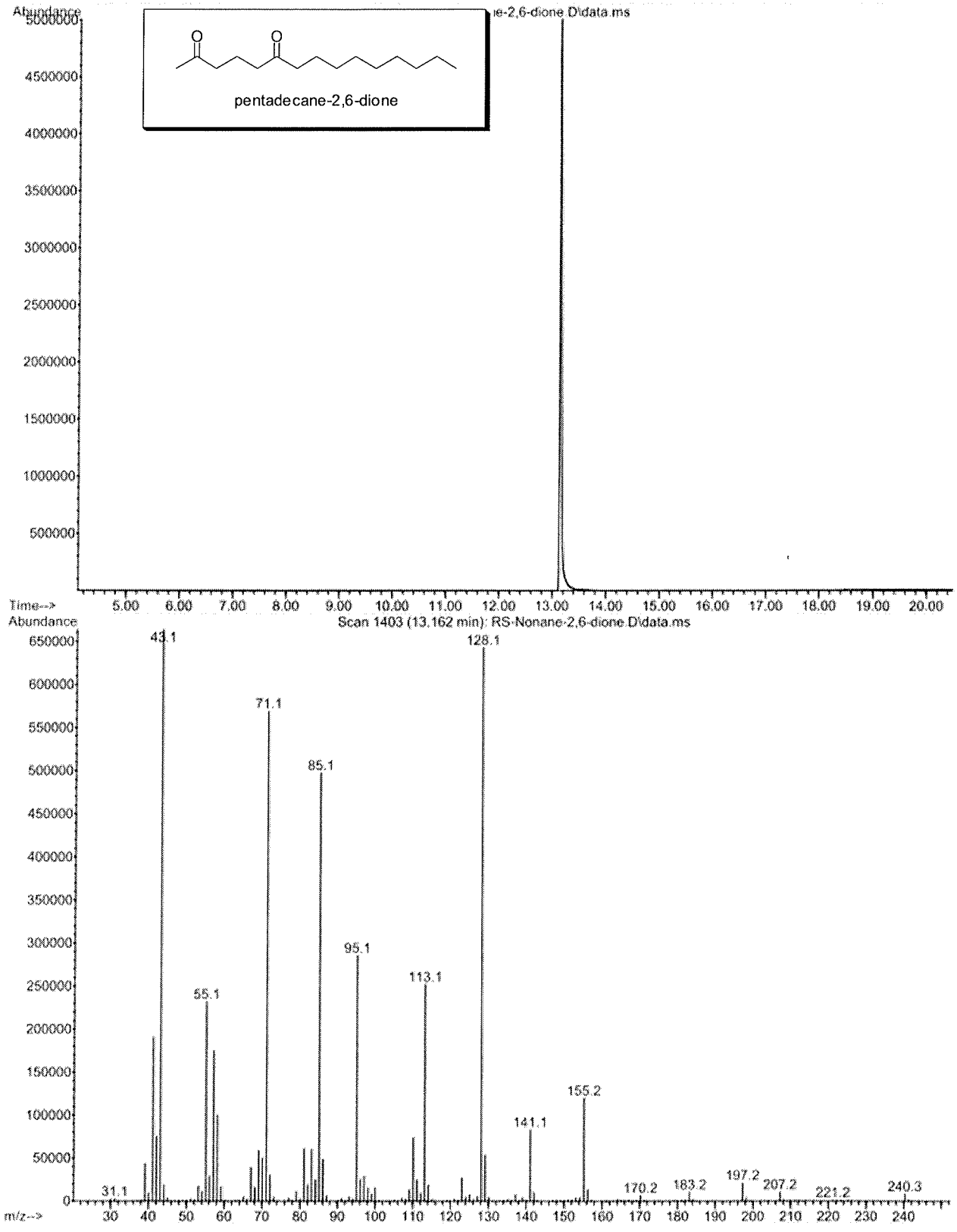


		10 vol% THF			10 vol% MeCN			10 vol% DME			10 vol% Heptane		
entry	enzyme	**3a** [%]	**6a** [%]	**7a** [%]	**3a** [%]	**6a** [%]	**7a** [%]	**3a** [%]	**6a** [%]	**7a** [%]	**3a** [%]	**6a** [%]	**7a** [%]
1	*Chromobacterium violaceum*	> 99	–	–	> 99	–	–	99.3	0.7	–	98	2.0	–
2	*Bacillus megaterium*	> 99	–	–	99.1	0.9	–	99.6	0.4	–	94.7	5.3	–
3	*Paracoccus denitrificans*	> 99	–	–	> 99	–	–	99.6	0.4	–	98	2.0	–
4	*Vibrio fluvialis*	> 99	–	–	99.6	0.4	–	98.9	1.1	–	96.4	3.6	–
5	*Arthrobacter* sp.	96.9	3.1	–	98.5	1.5	–	74.5	25.5	–	59.6	40.4	–
6	*Aspergillus terreus*	> 99	–	–	98.9	1.1	–	98.4	1.6	–	98.2	1.8	–
7	*Hyphomonas neptunium*	> 99	–	–	87.9	12.1	–	61.6	38.4	–	66.1	33.9	–

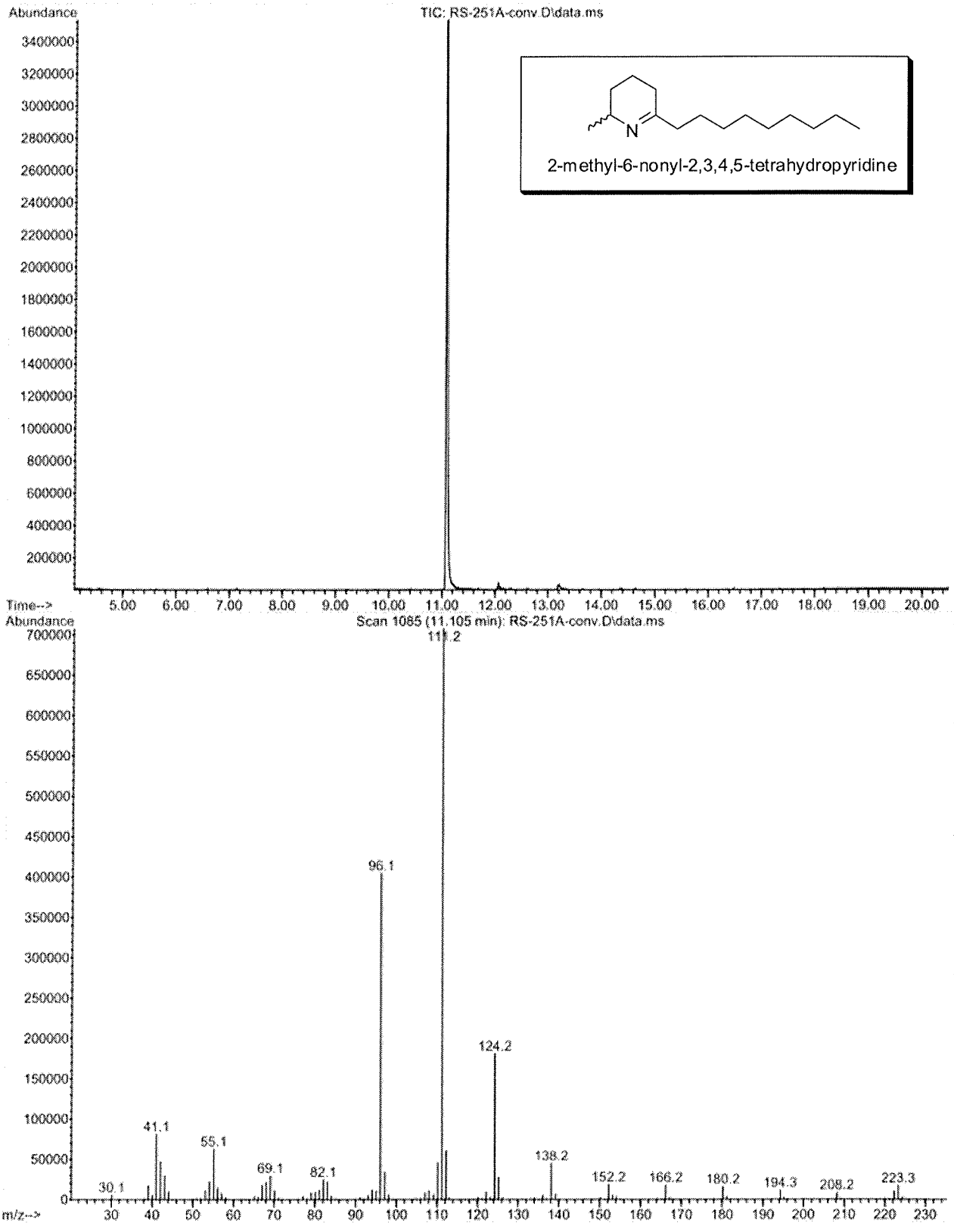
Table S2. Results of the enzyme testing. Conditions: 25 mM (6 mg/mL) diketone **3a** in the presence of various organic solvents (10 vol%), 1 mM PLP, 1 mM NAD^+, 150 mM ammonium formate, 250 mM D- respective L-alanine, 11 U FDH, 12 U AlaDH. Reactions were run at 30 °C for 24 hours in an Eppendorf orbital shaker at 600 rpm with the tubes in horizontal position. Conversions were determined via achiral GC analysis.

GC-MS Spectra

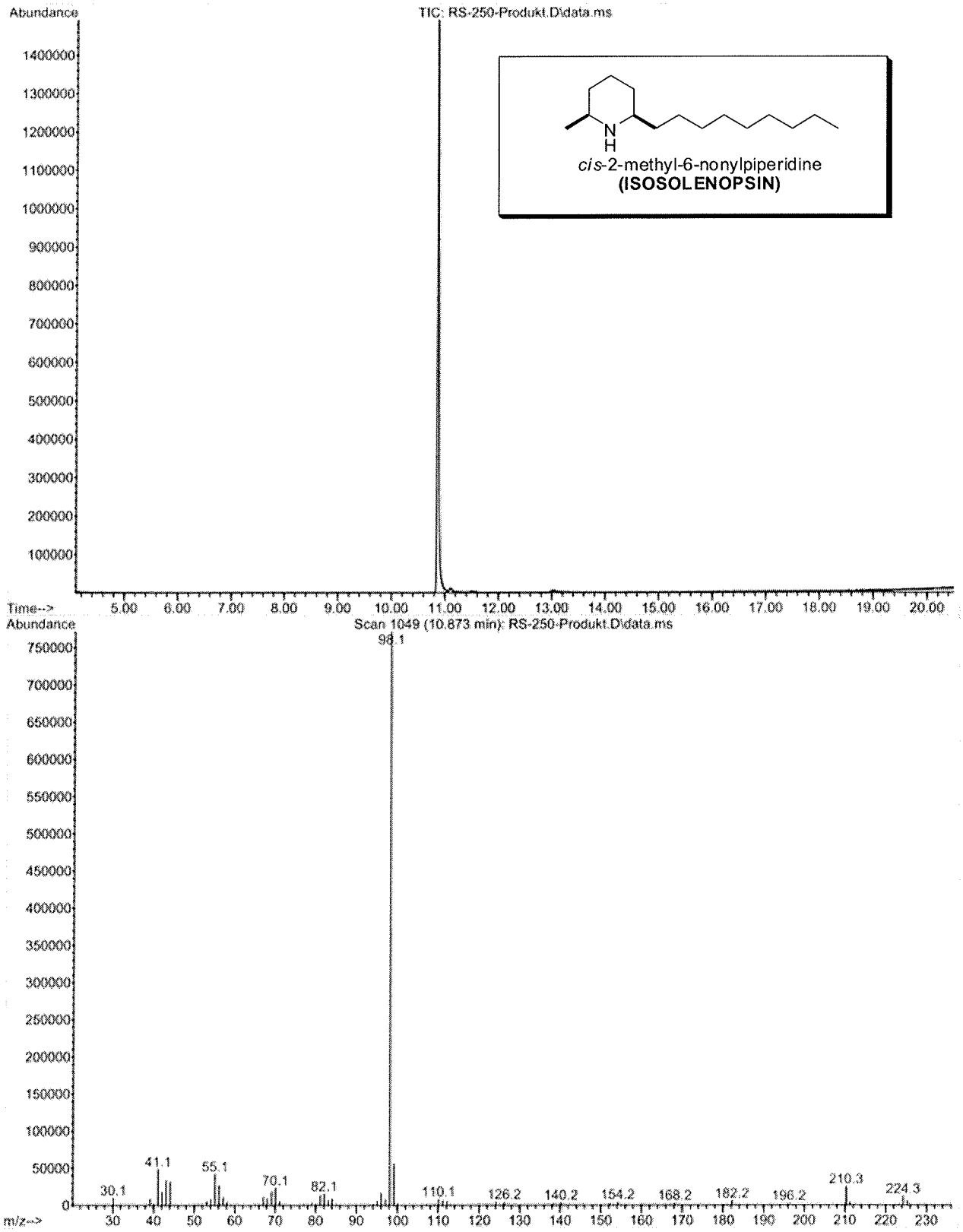
GS-MS spectrum of Nonane-2,6-dione (3a)



GC-MS spectrum of piperideine 6a

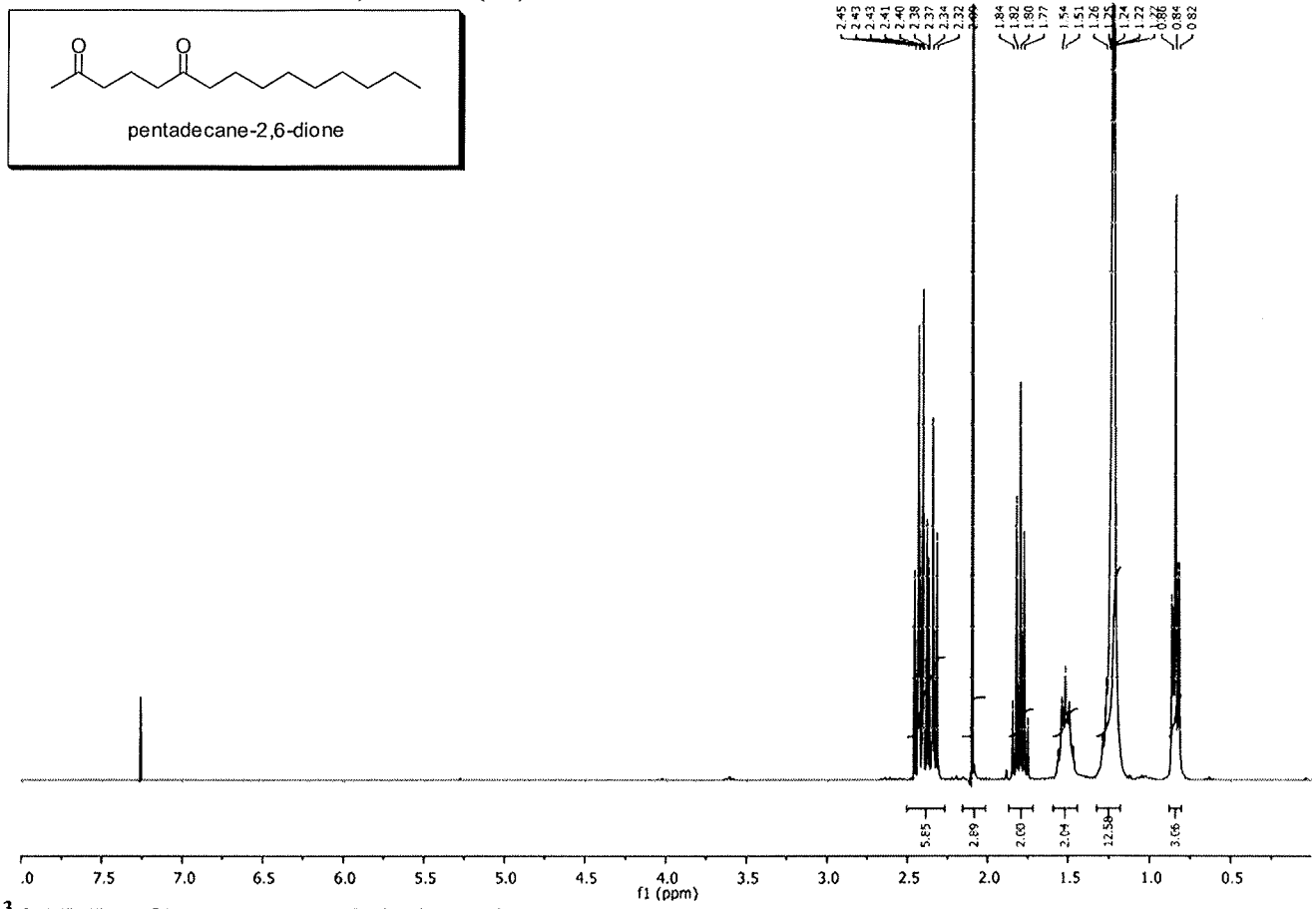


GC-MS spectrum of 2-Methyl-6-nonylpiperidine (Isosolenopsin [1a])

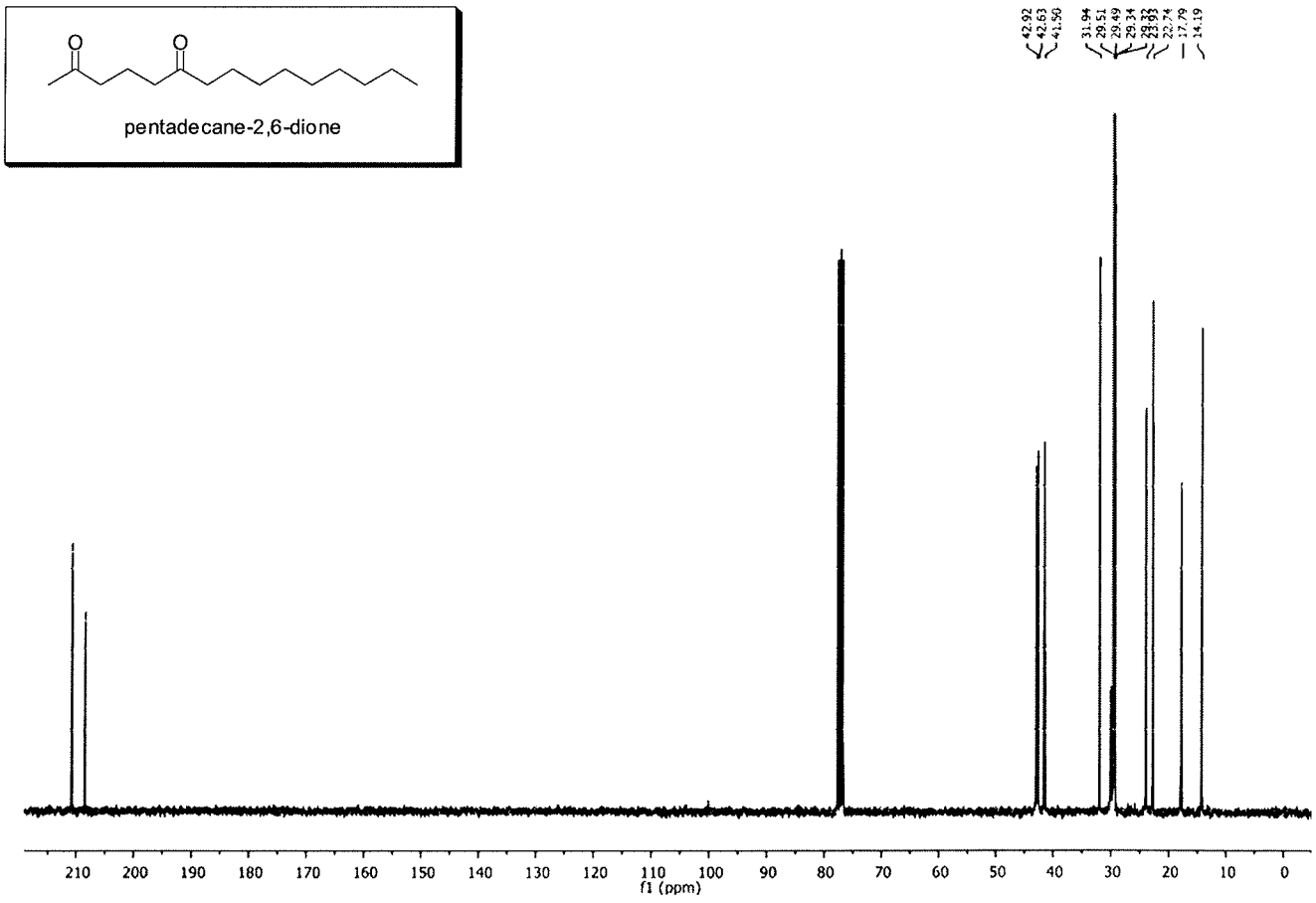


2 NMR Spectra

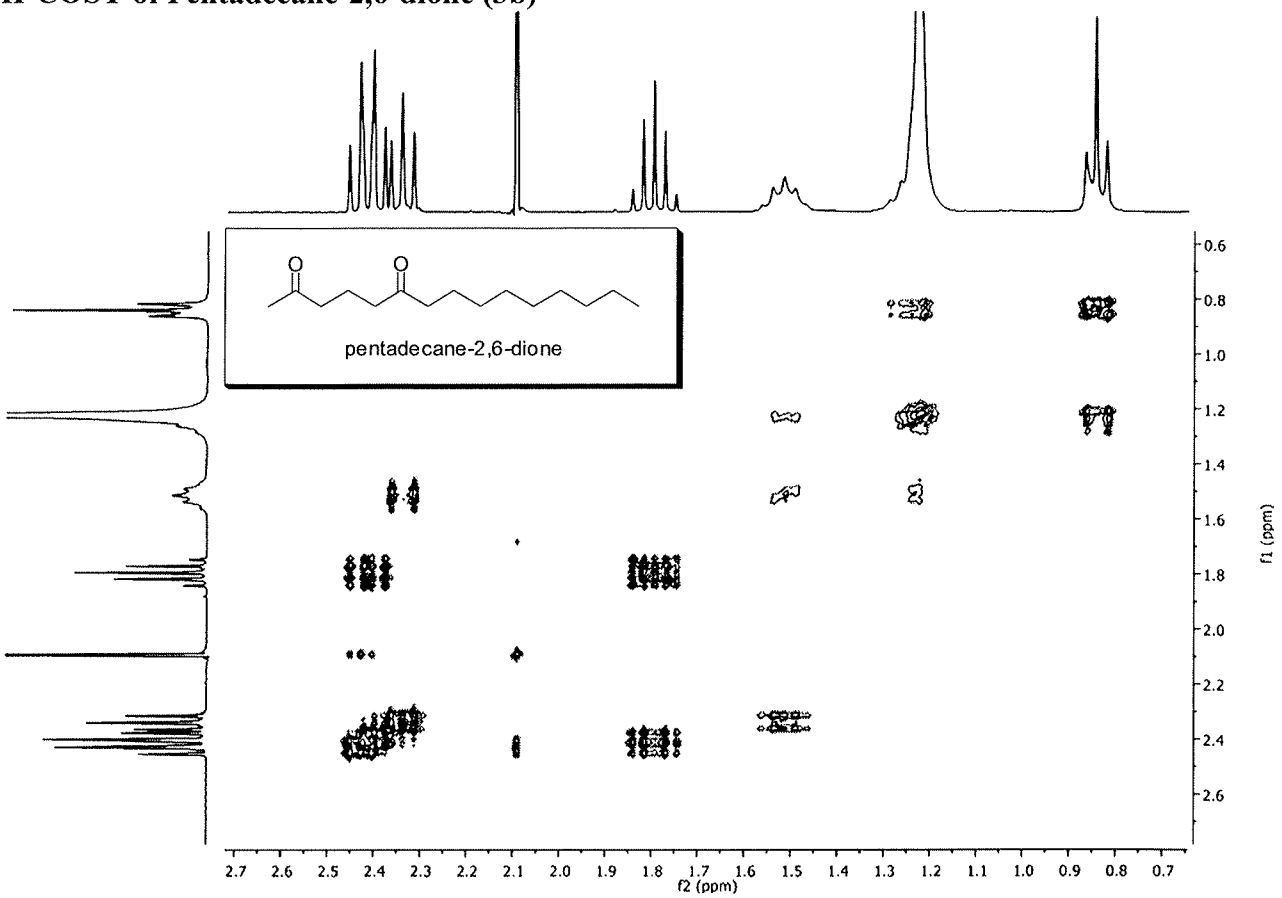
^{1}H-NMR of Pentadecene-2,6-dione (3b)



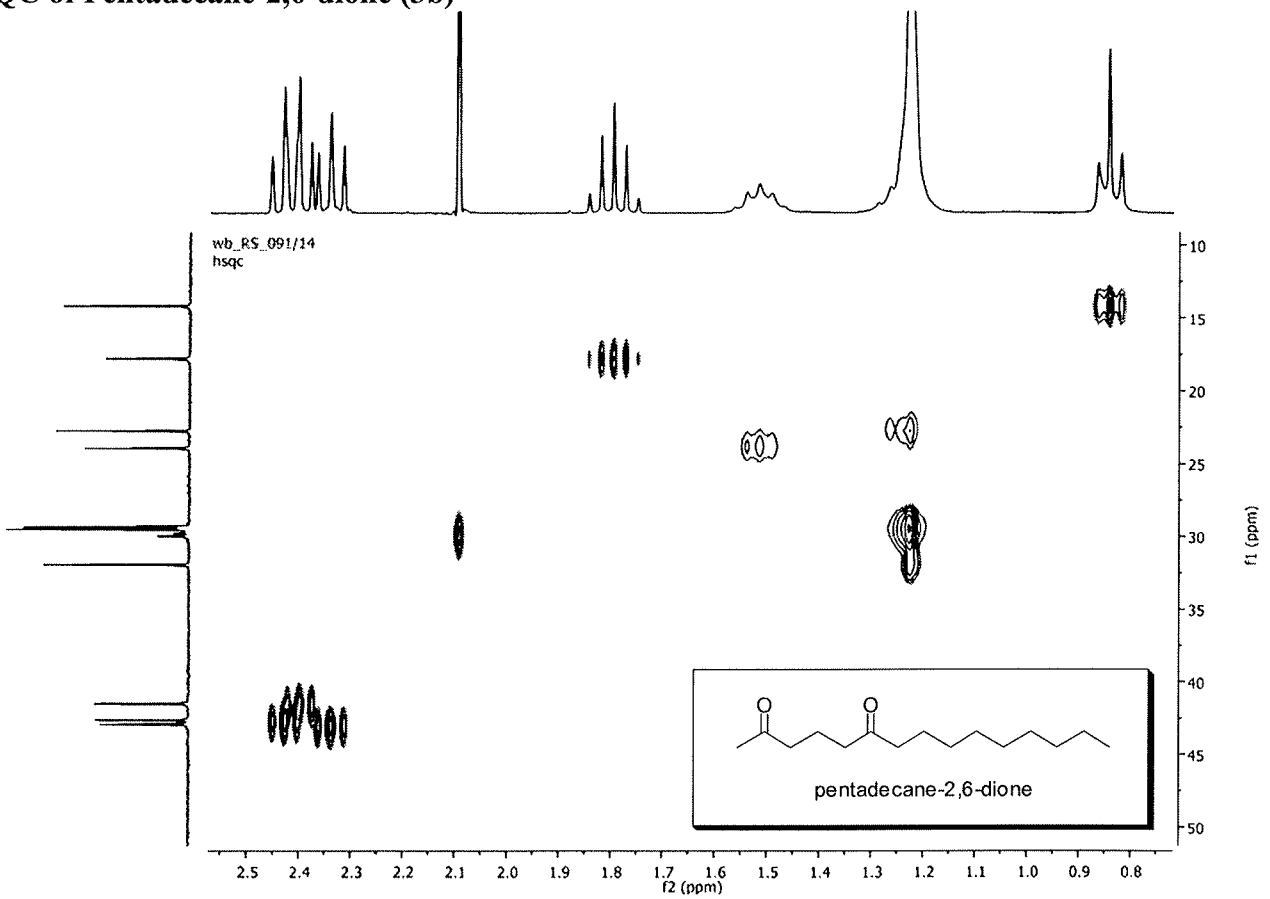
^{13}C-NMR of Pentadecane-2,6-dione (3b)



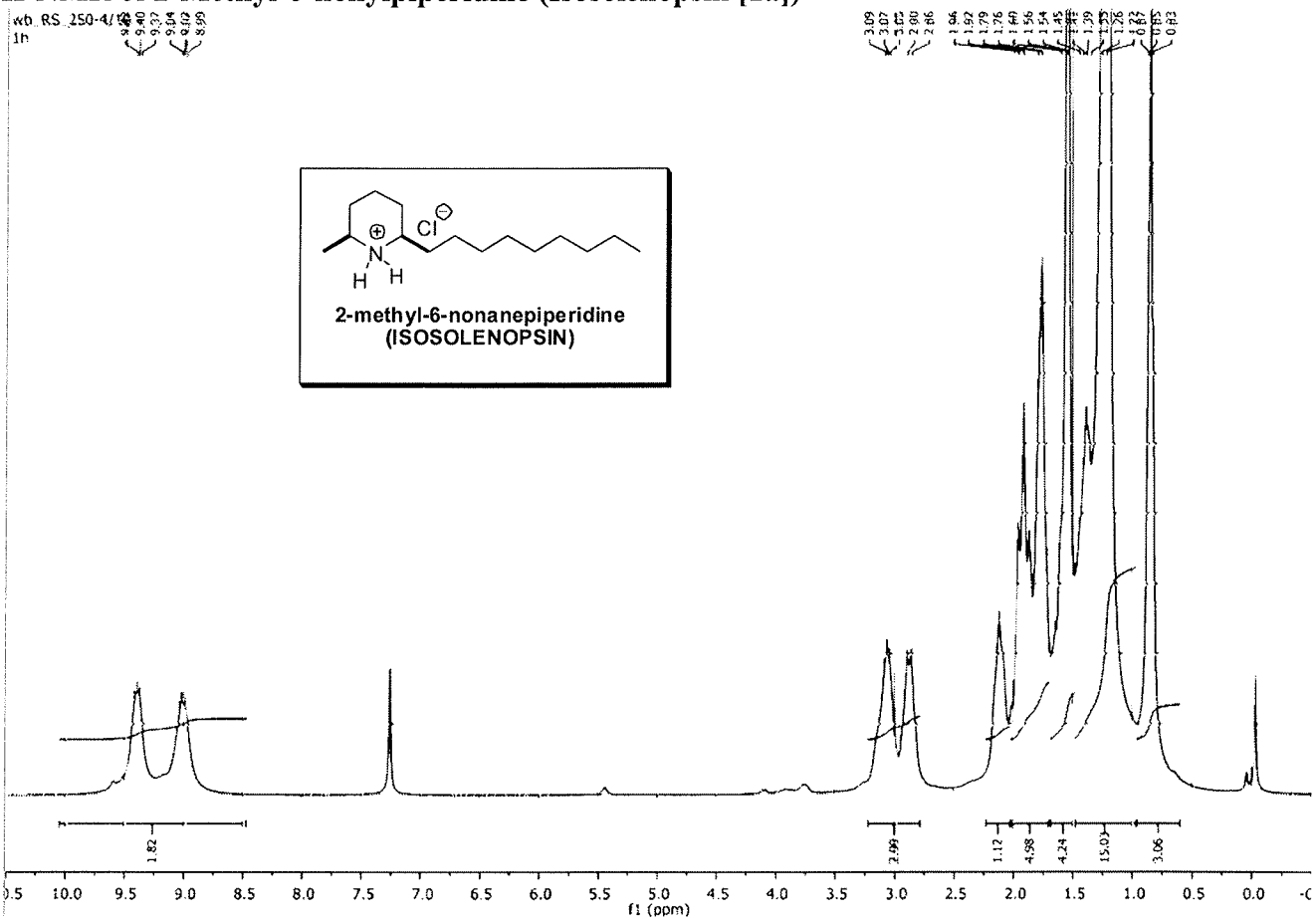
H,H-COSY of Pentadecane-2,6-dione (3b)



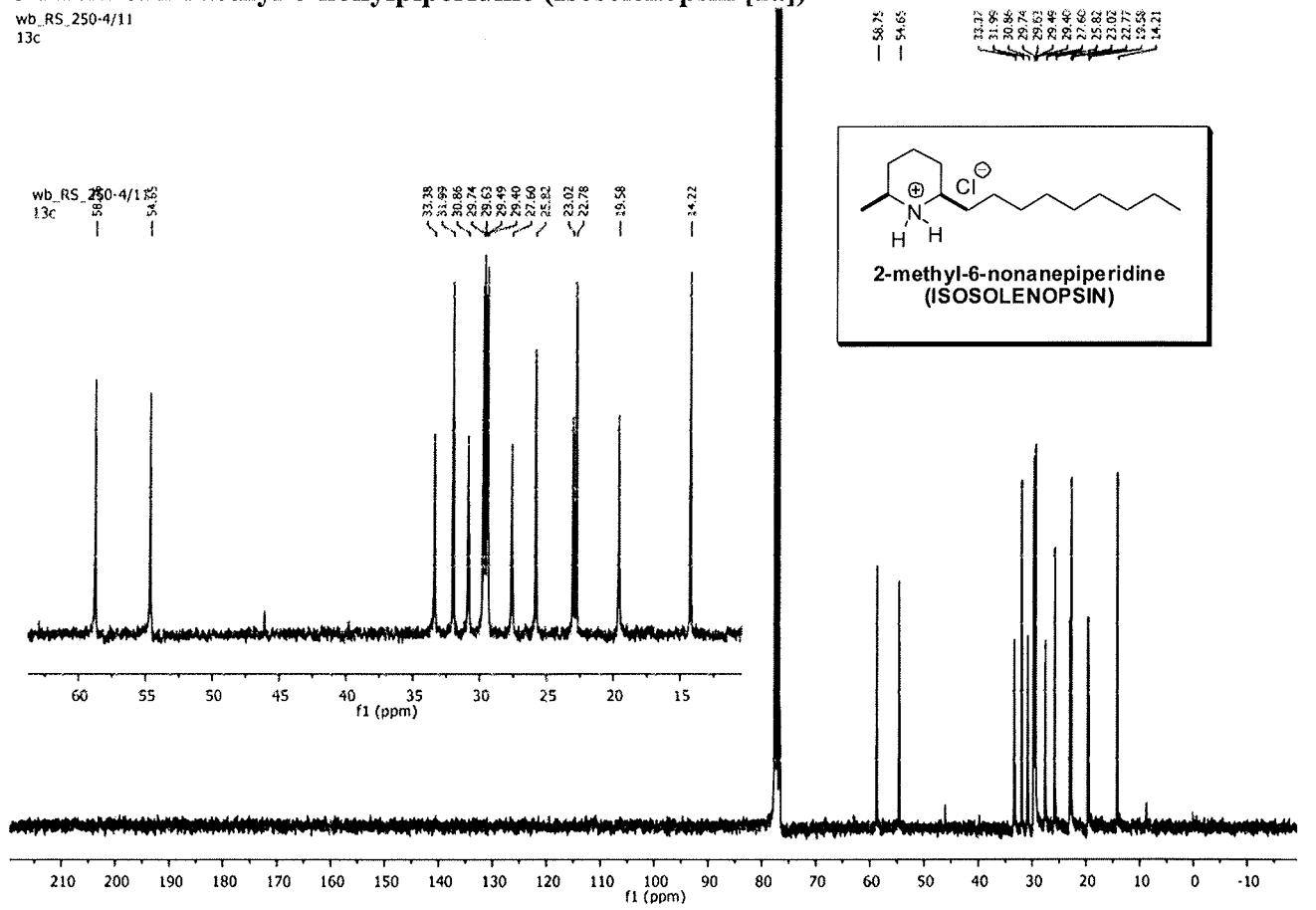
HSQC of Pentadecane-2,6-dione (3b)



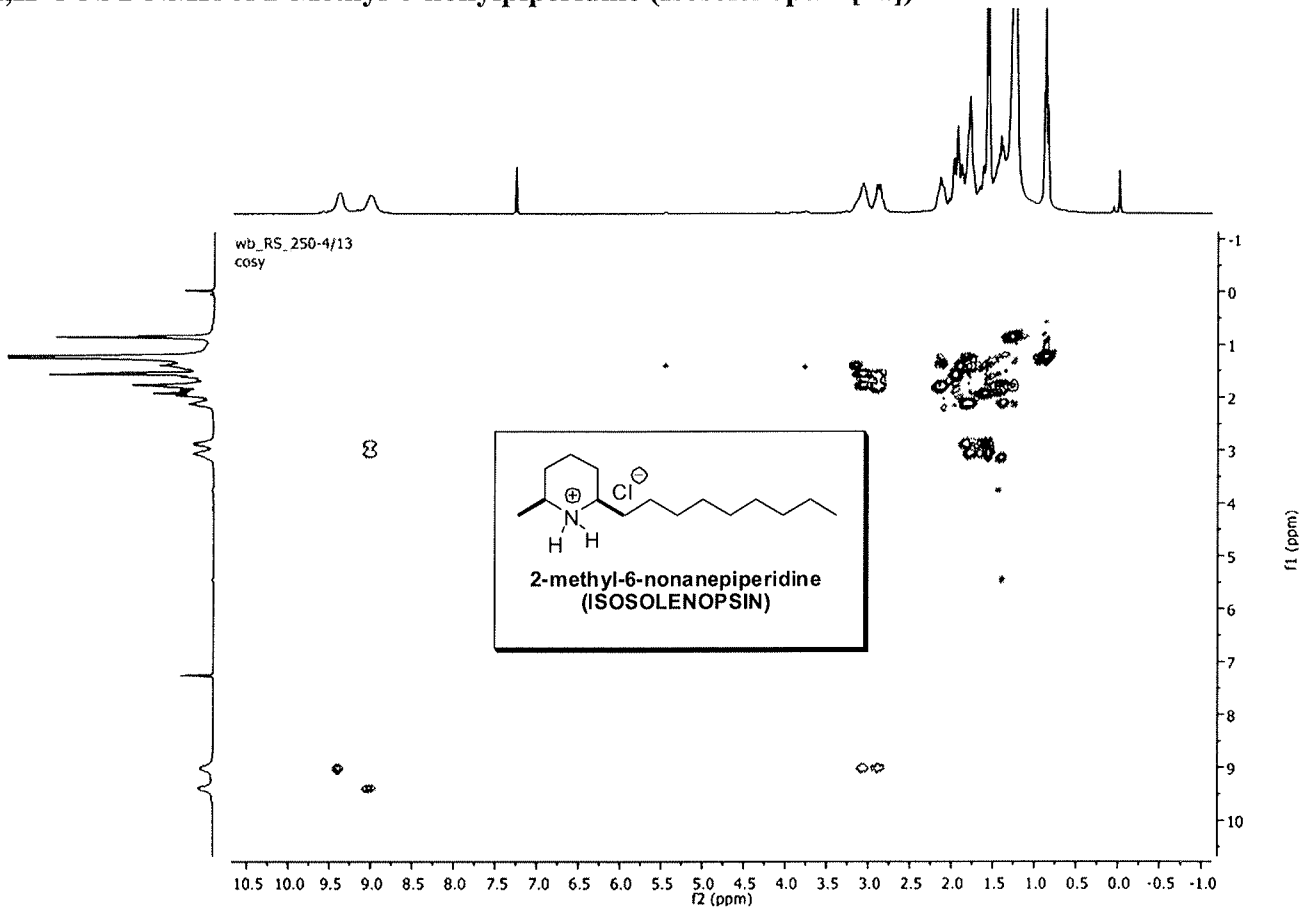
^{1}H-NMR of 2-Methyl-6-nonylpiperidine (Isosolenopsin [1a])



^{13}C-NMR of 2-Methyl-6-nonylpiperidine (Isosolenopsin [1a])



H,H-COSY NMR of 2-Methyl-6-nonylpiperidine (Isosolenopsin [1a])



HSQC NMR of 2-Methyl-6-nonylpiperidine (Isosolenopsin [1a])