

Two Asymmetric Syntheses of AMG 221, an Inhibitor of 11 β - Hydroxysteroid Dehydrogenase Type 1

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Supporting Information

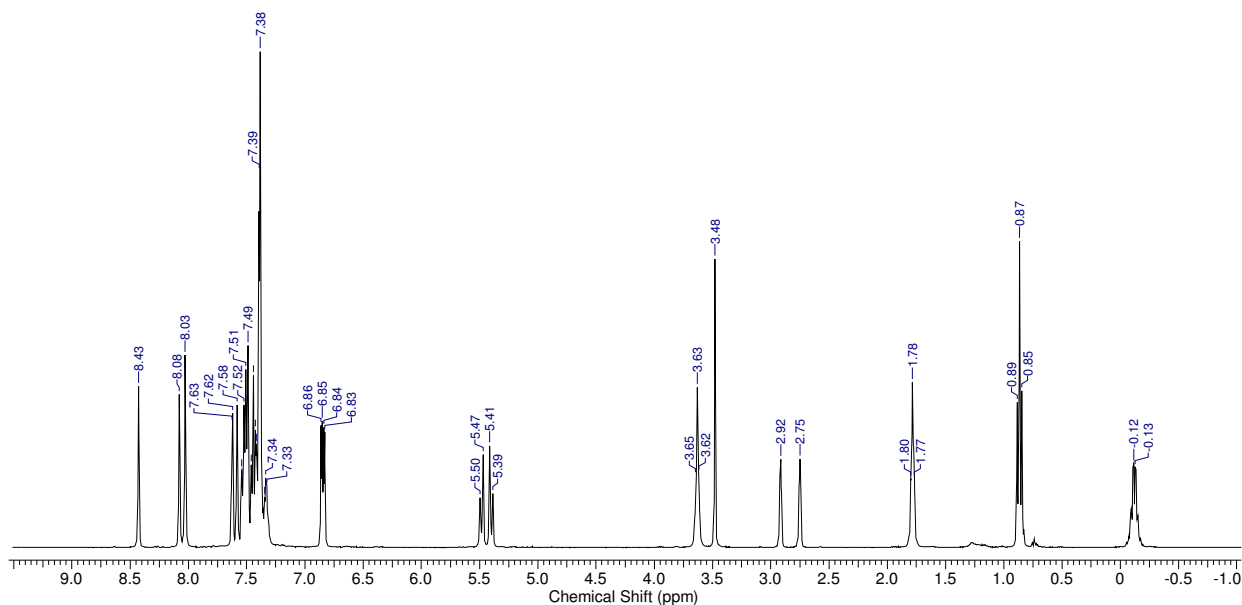
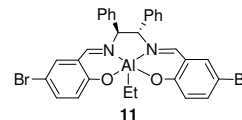
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COSY, HSQC, HMBC and ¹ H- ¹⁵ N HMBC Spectra for racemic compound 17	14

¹H NMR for compound **11**:



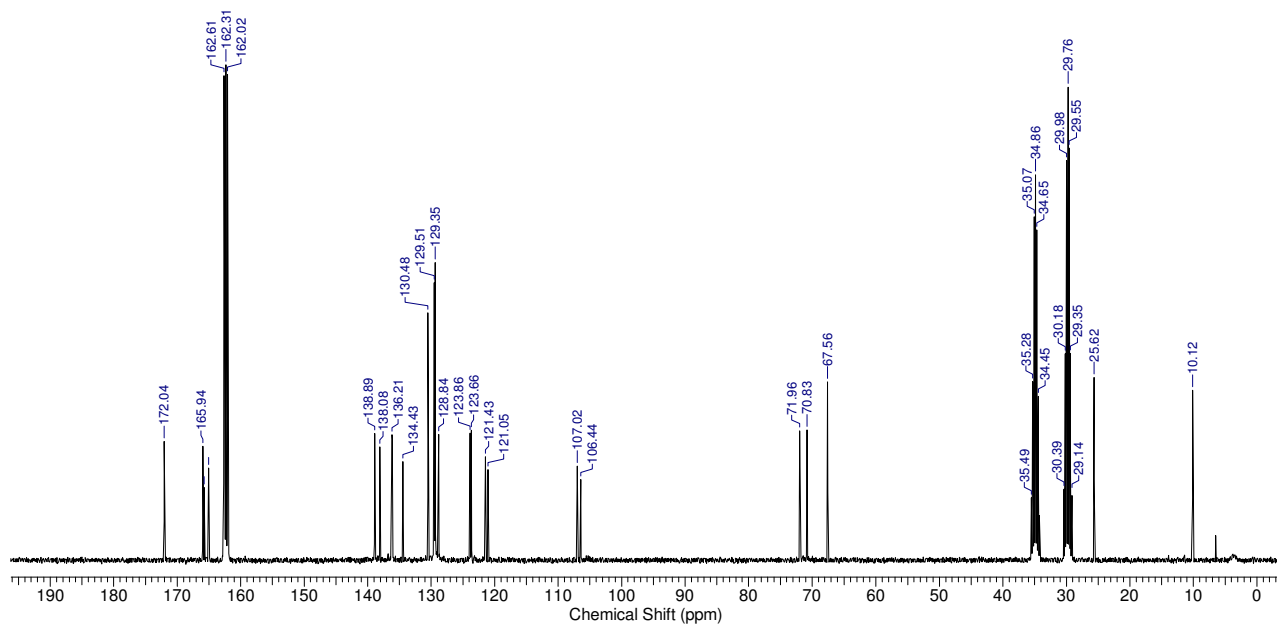
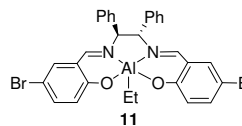
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Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	600.3422	Sweep Width (Hz)	6409.86
Temperature (degree C)	27.000		



¹³C NMR for compound **11**:



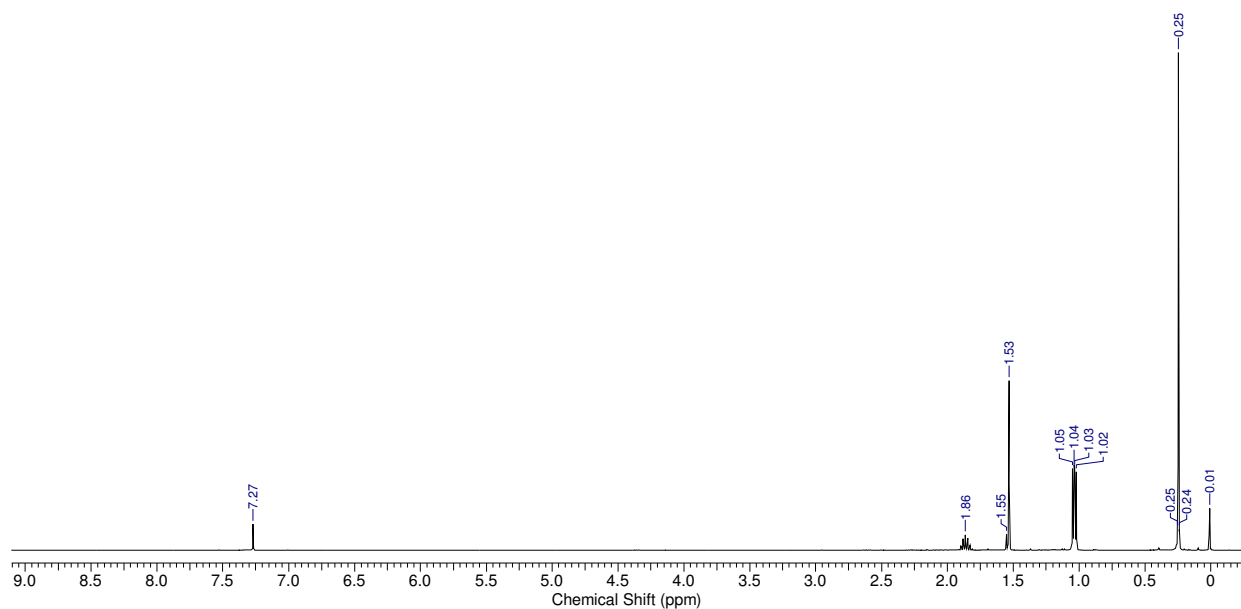
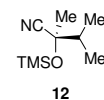
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Points Count	32768	SW(cyclical) (Hz)	28408.22
Solvent	DMF	Spectrum Offset (Hz)	12084.8838
Sweep Width (Hz)	28407.36	Temperature (degree C)	27.000



¹H NMR for compound **12**:



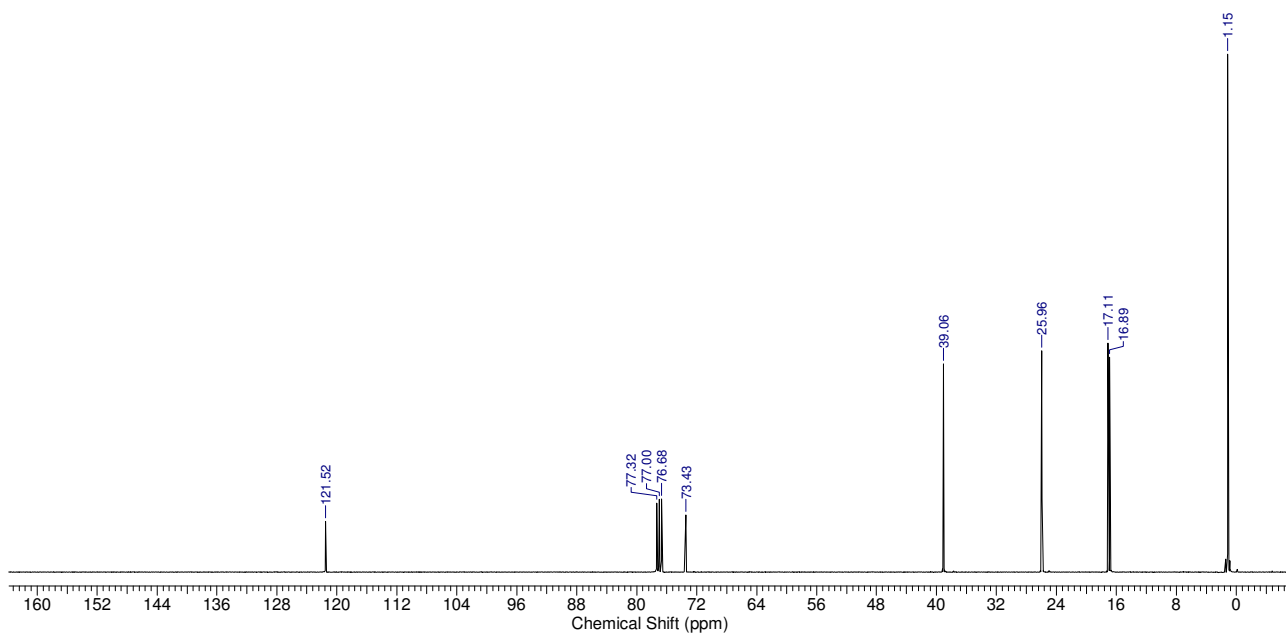
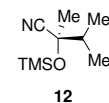
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Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
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Temperature (degree C)	27.000		



¹³C NMR for compound **12**:



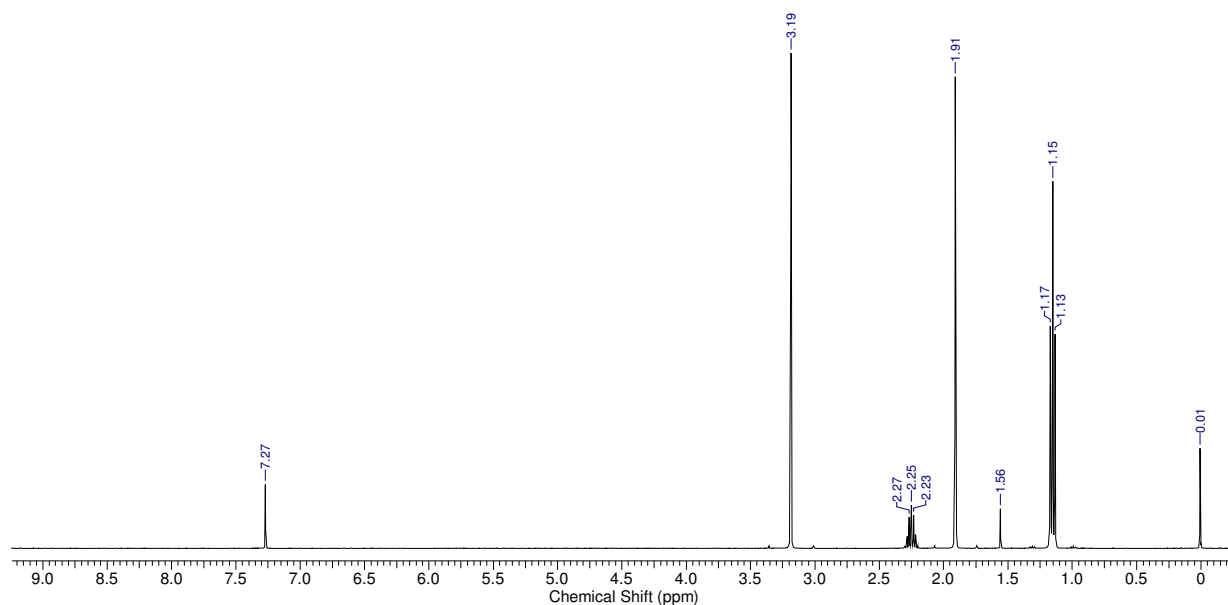
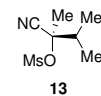
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Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28409.09
Solvent	CHLOROFORM-d		
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Temperature (degree C)	26.900		



¹H NMR for compound **13**:



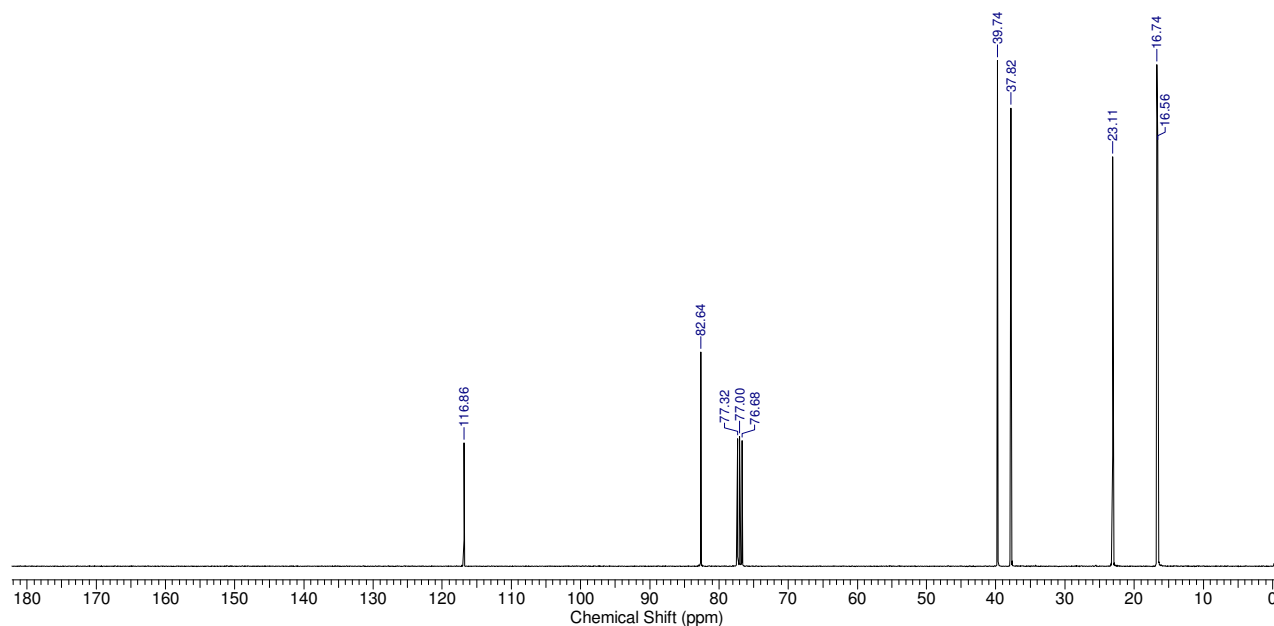
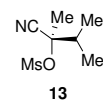
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Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
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Temperature (degree C)	27.000		



¹³C NMR for compound **13**:



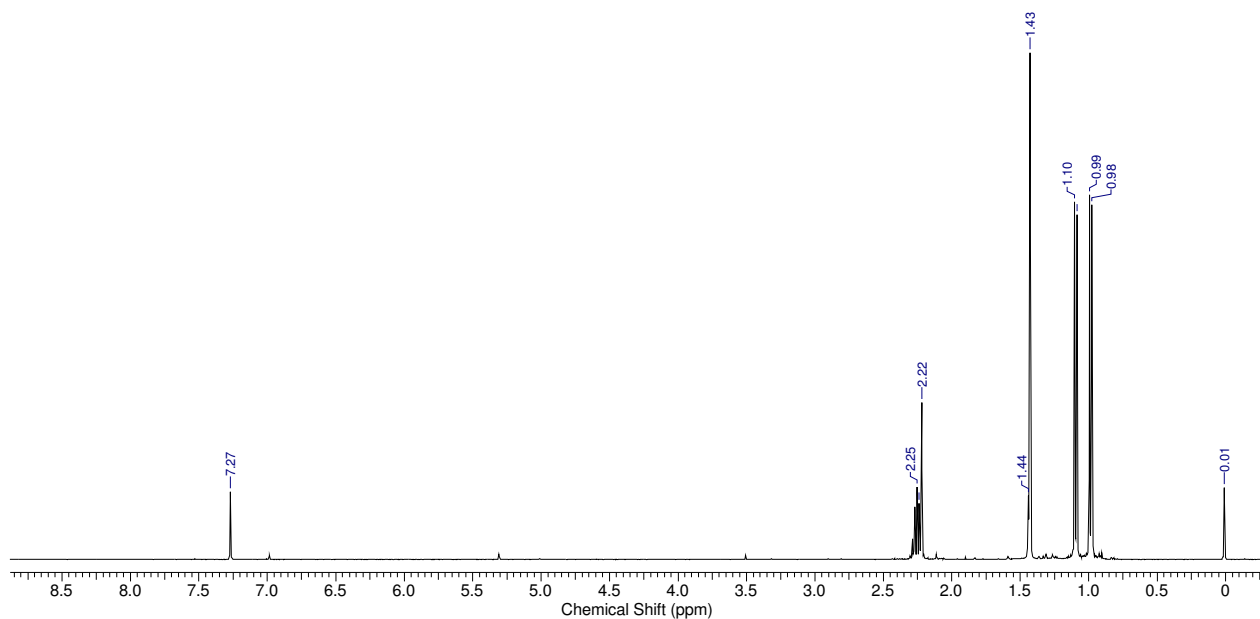
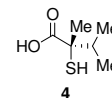
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Points Count	32768	SW(cyclical) (Hz)	28409.09
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Temperature (degree C)	26.900		



¹H NMR for compound 4:



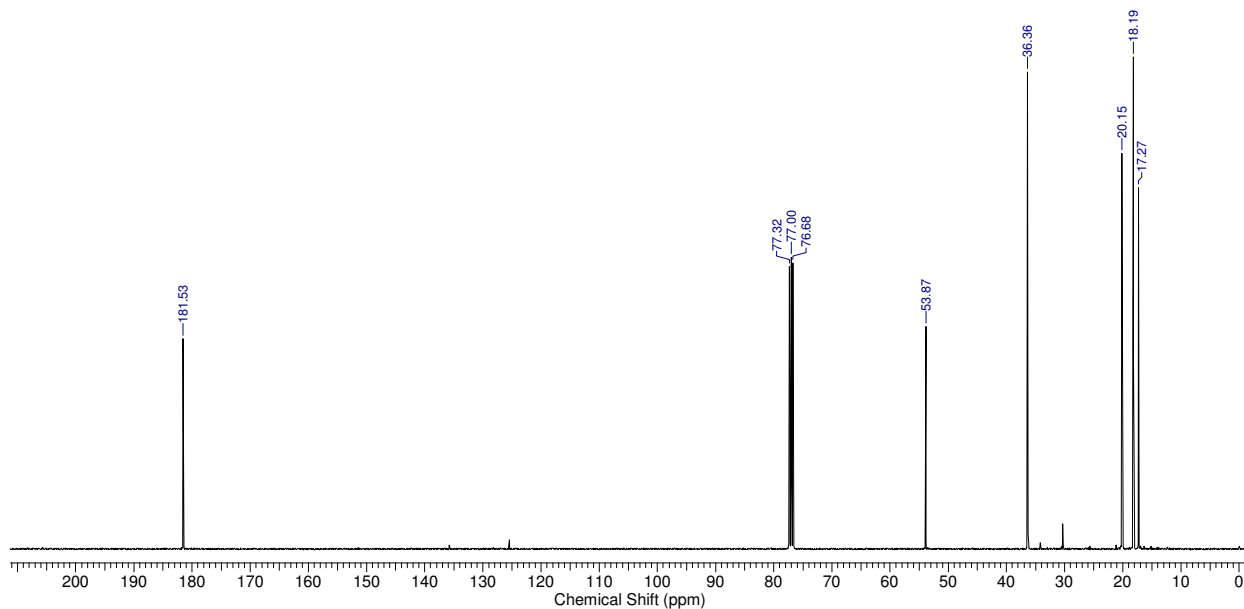
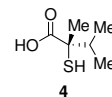
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Frequency (MHz)	400.23	Nucleus	1H
Number of Transients	16	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2400.1829	Sweep Width (Hz)	6410.06
Temperature (degree C)	27.000		



¹³C NMR for compound 4:



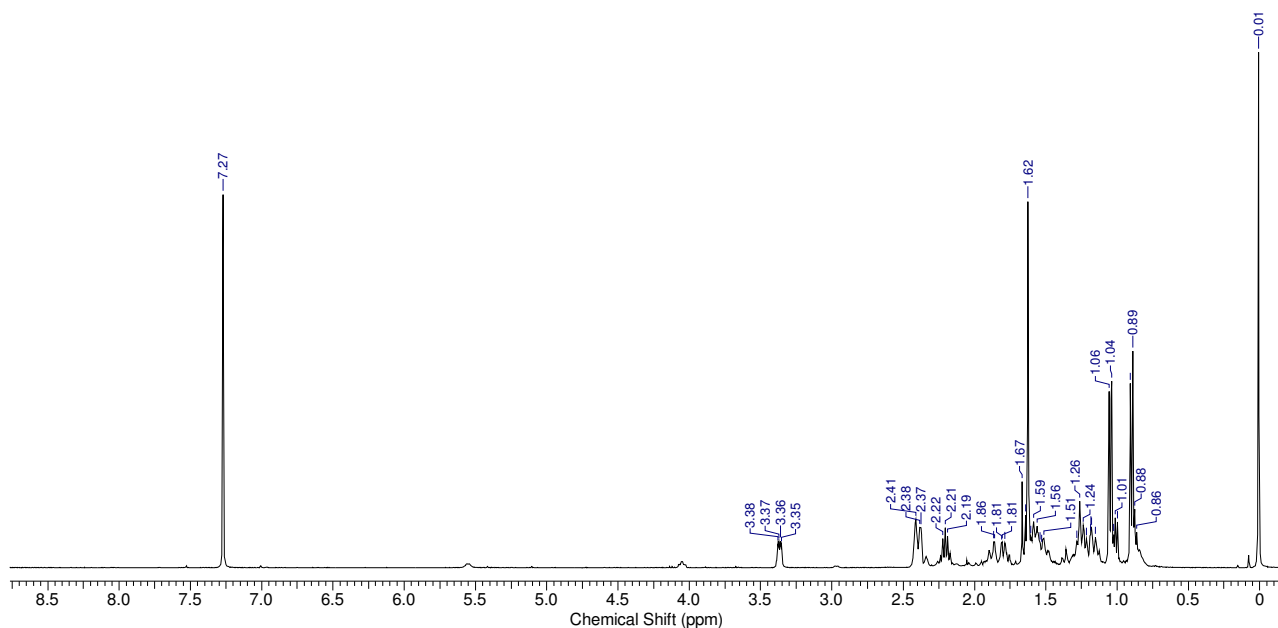
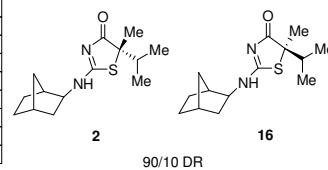
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Solvent	CHLOROFORM-d		
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Temperature (degree C)	26.900		



^1H NMR for compound **2/16** mixture (90/10 DR, displacement route):



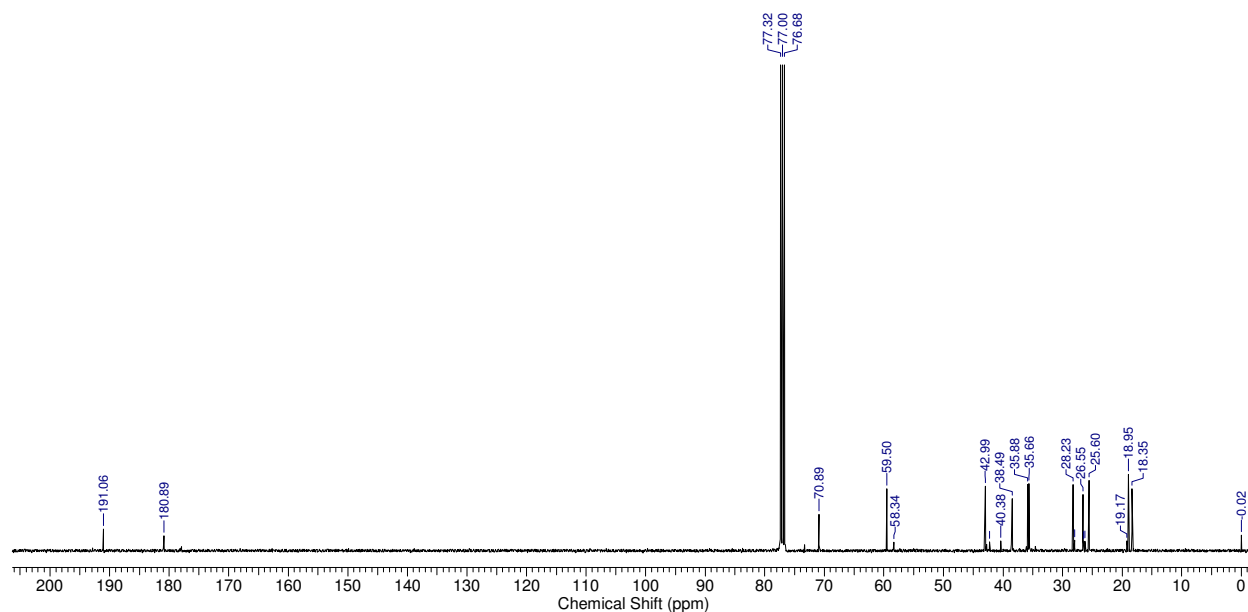
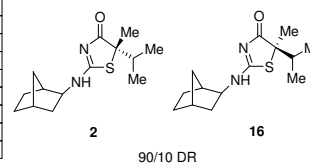
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Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2395.5435	Sweep Width (Hz)	6410.06
Temperature (degree C)	25.000		



^{13}C NMR for compound **2/16** mixture (90/10 DR, displacement route):



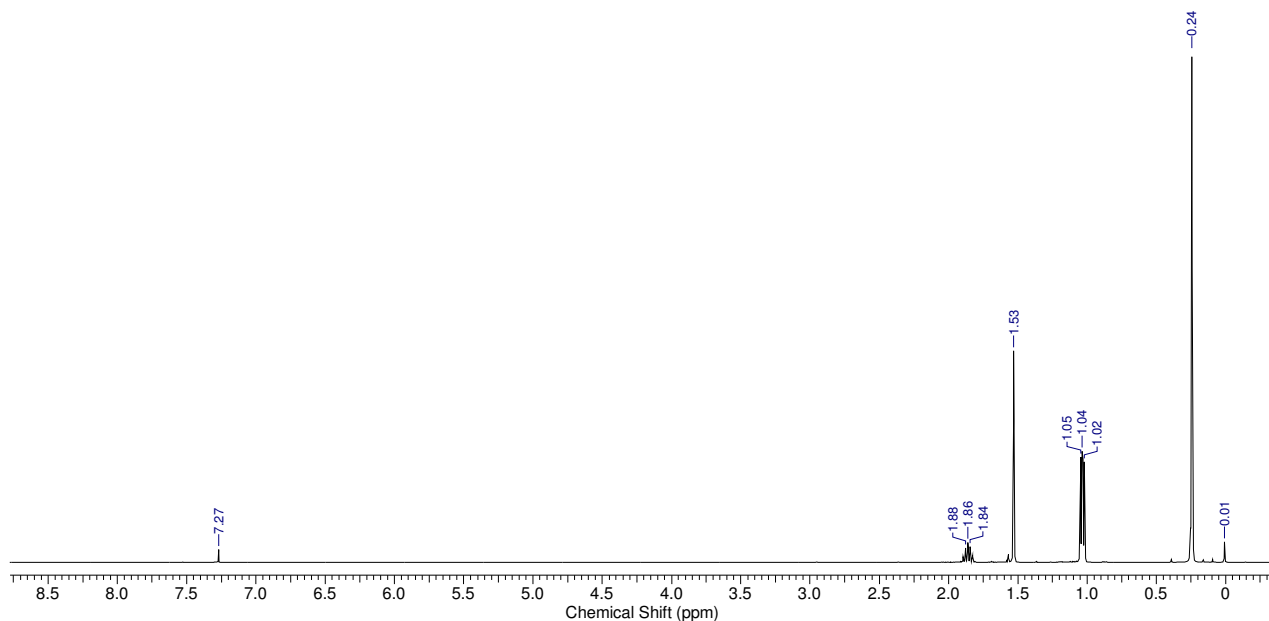
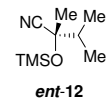
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Points Count	32768	SW(cyclical) (Hz)	28409.09
Solvent	CHLOROFORM-d		
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Temperature (degree C)	24.900		



¹H NMR for compound *ent-12*:



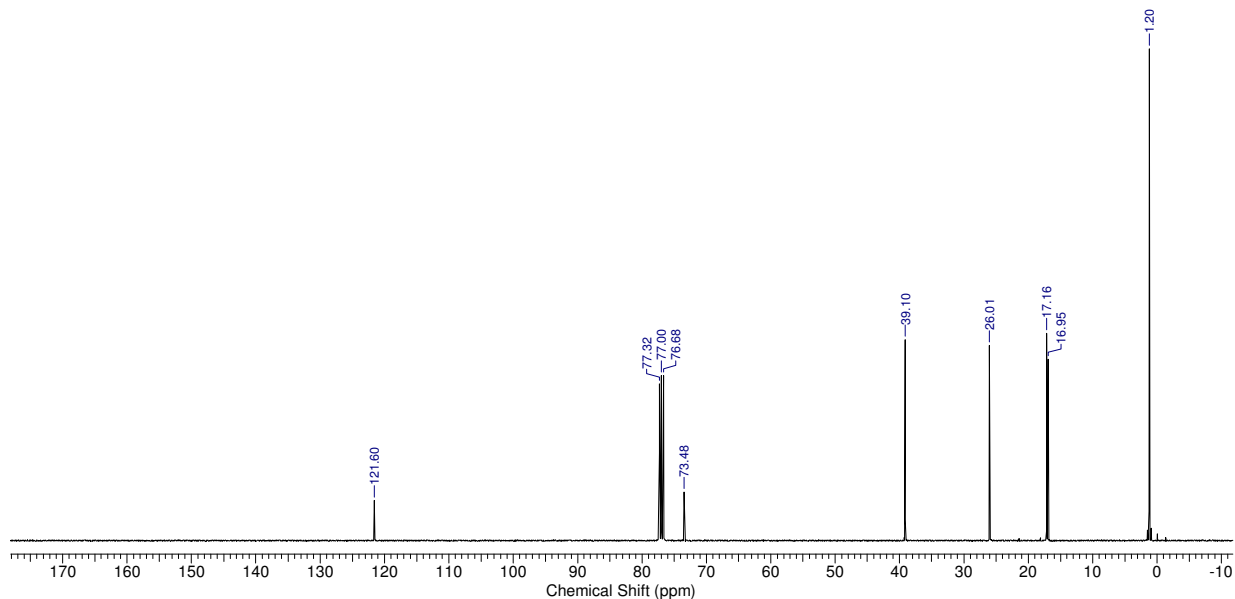
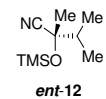
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Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
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Temperature (degree C)	27.000		



¹³C NMR for compound *ent-12*:



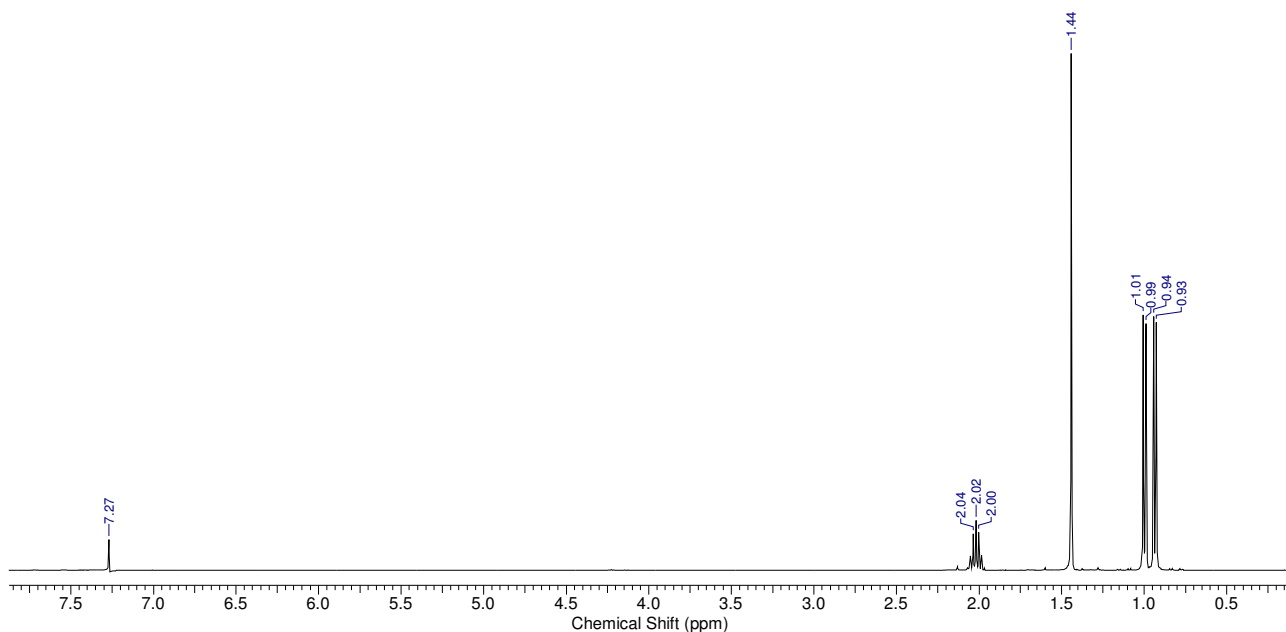
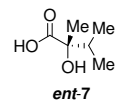
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Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28409.09
Solvent	CHLOROFORM-d		
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Temperature (degree C)	27.000		



^1H NMR for compound *ent-7*:



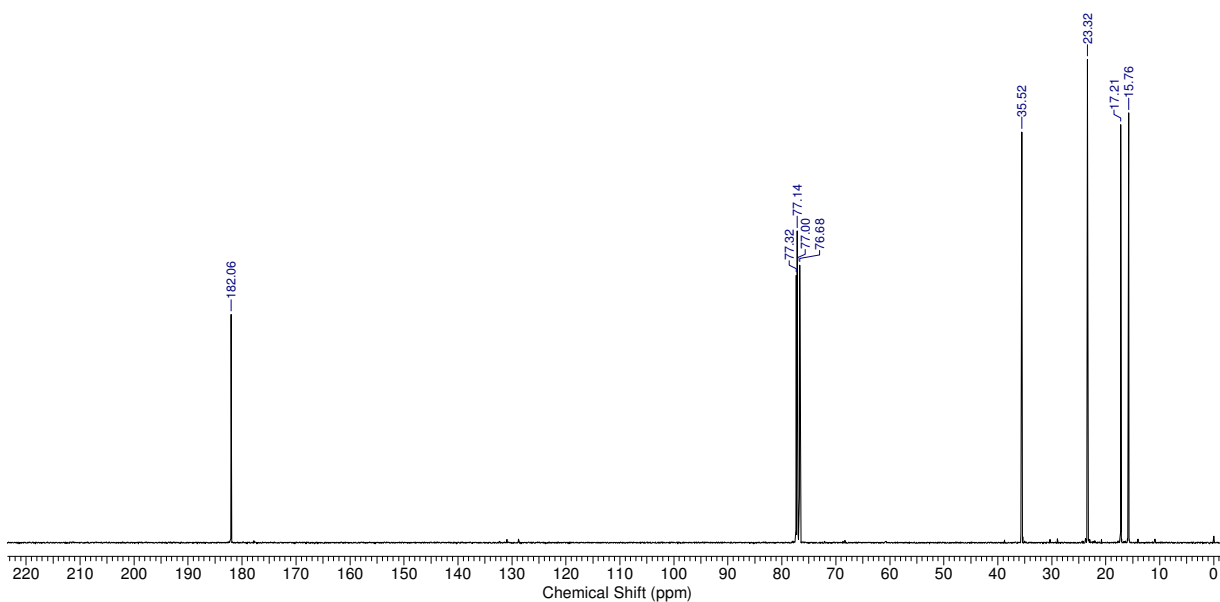
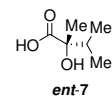
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Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
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Temperature (degree C)	27.000		



^{13}C NMR for compound *ent-7*:



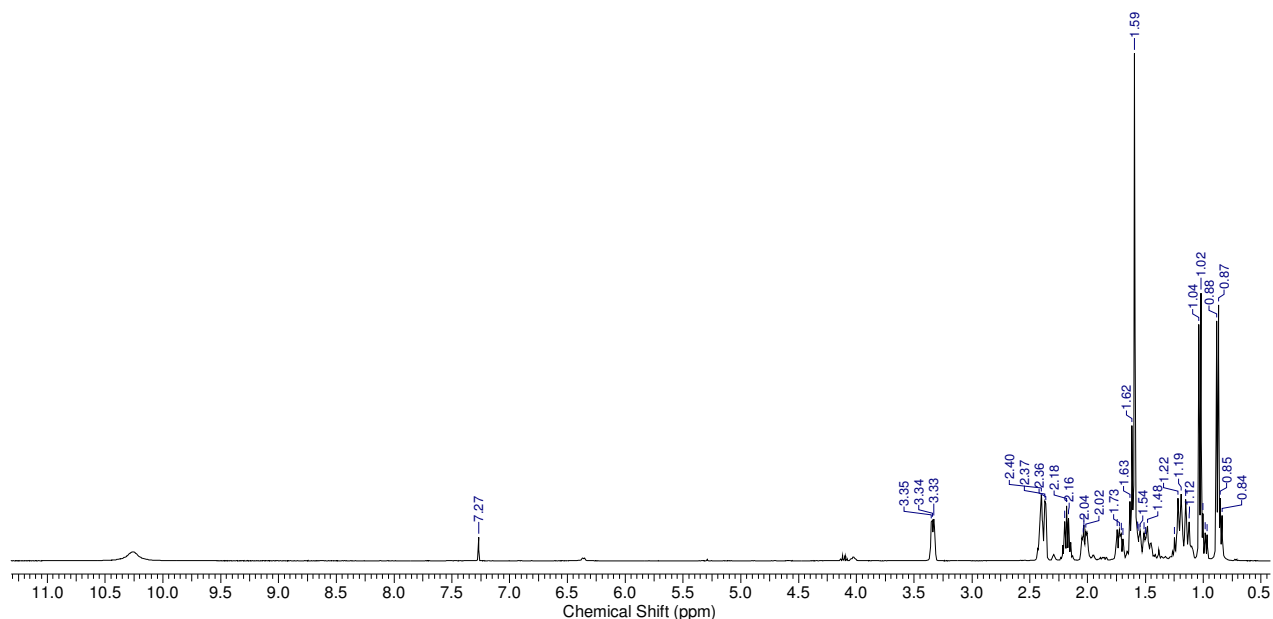
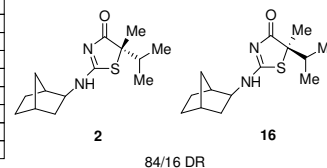
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Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28409.09
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	12076.6963	Sweep Width (Hz)	28408.22
Temperature (degree C)	27.000		



^1H NMR for compound **2/16** mixture (84/16 DR, cyclization route):



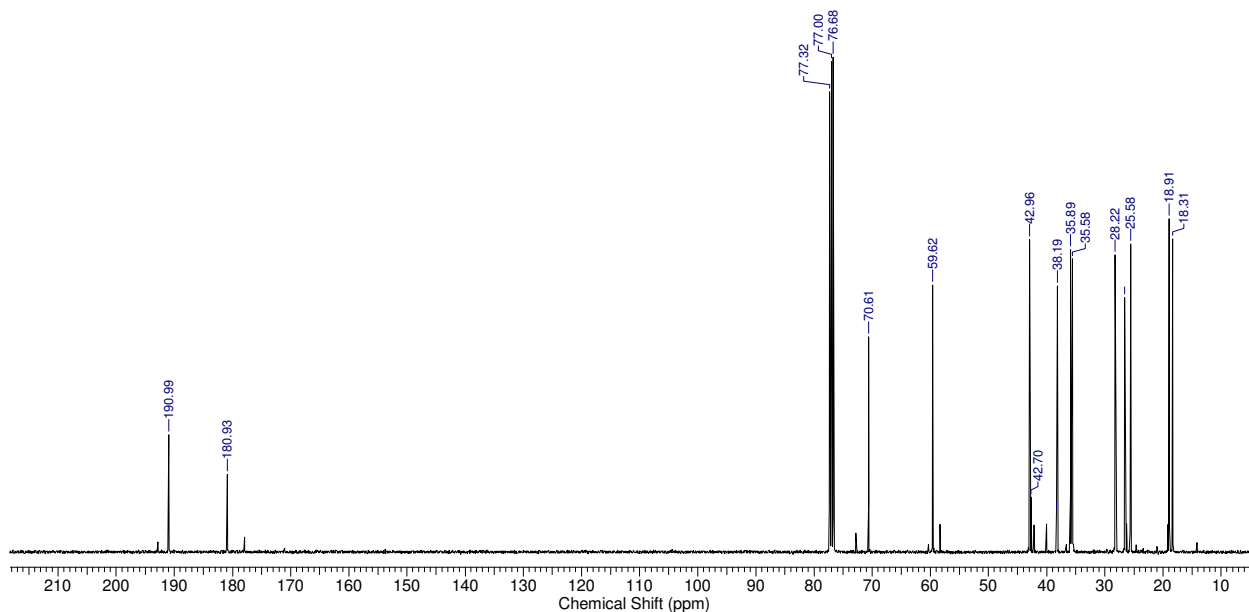
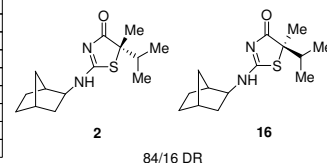
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Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	6410.26
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2399.9873	Sweep Width (Hz)	6410.06
Temperature (degree C)	27.000		



^{13}C NMR for compound **2/16** mixture (84/16 DR, cyclization route):



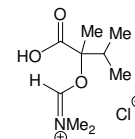
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Number of Transients	4096	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28409.09
Solvent	CHLOROFORM-d		
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Temperature (degree C)	26.900		



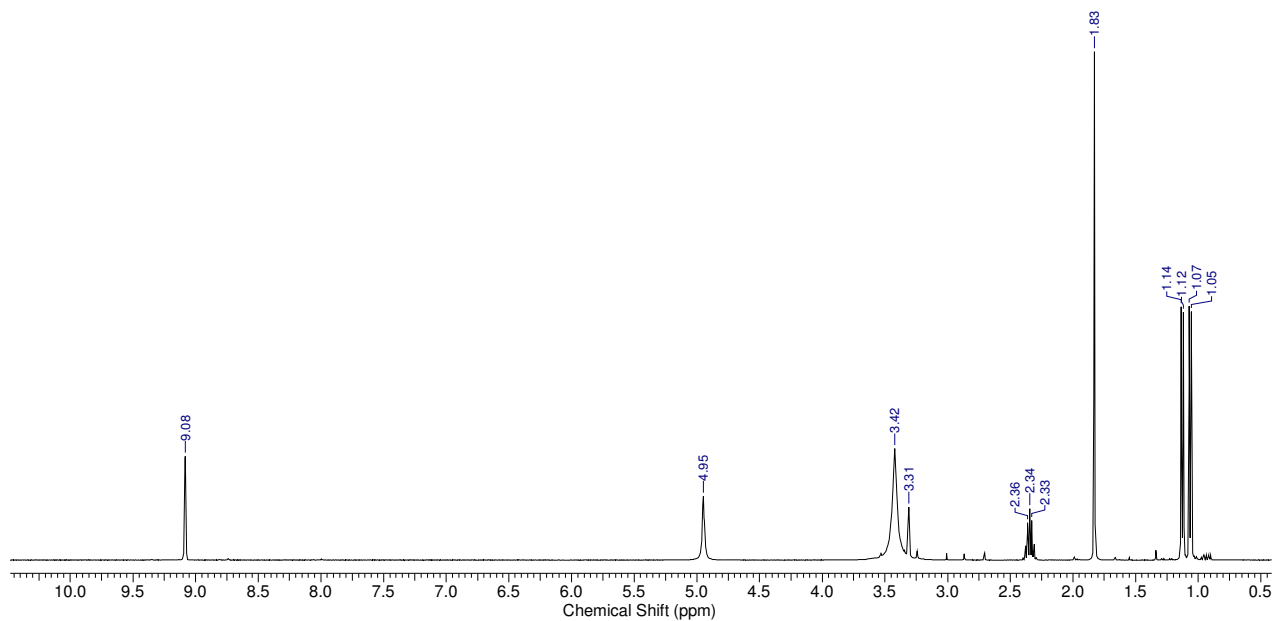
¹H NMR for racemic compound **17**:



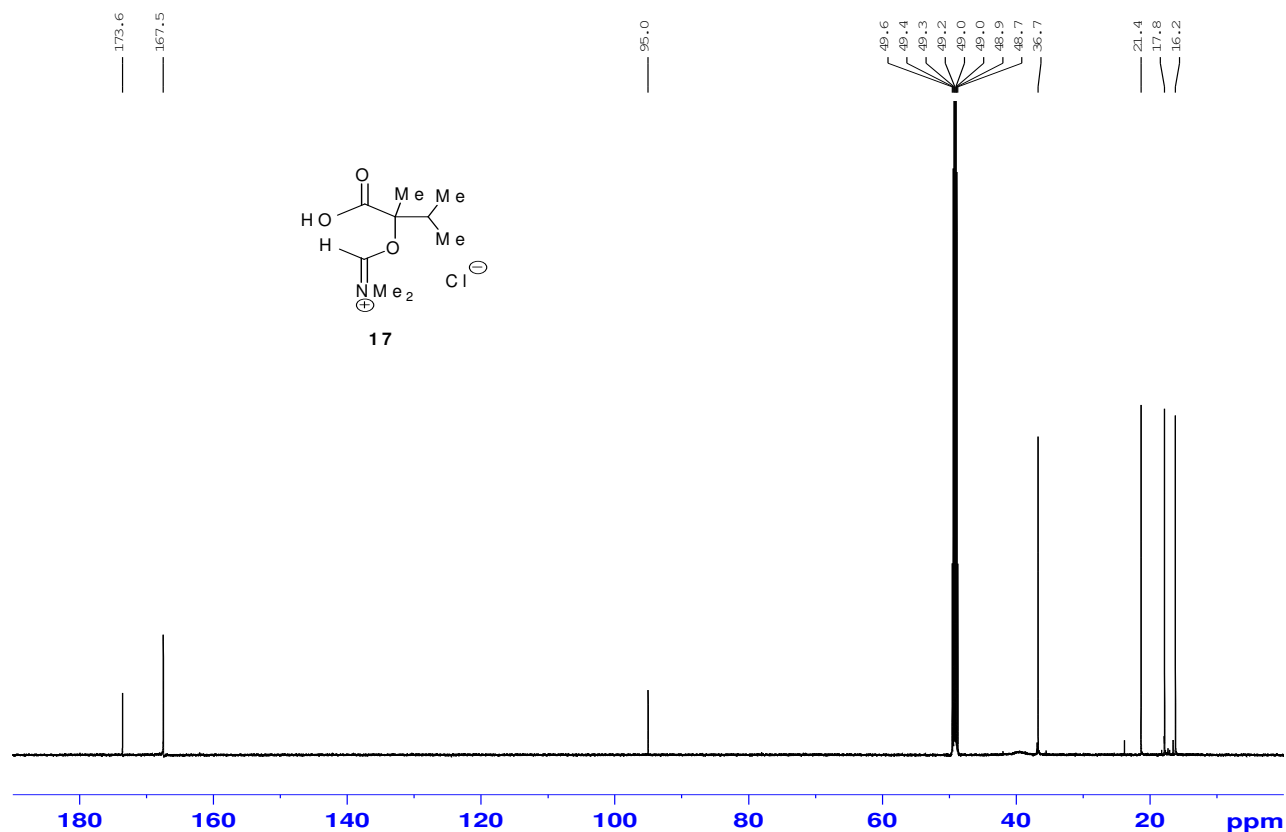
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Number of Transients	16	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	6410.26
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17



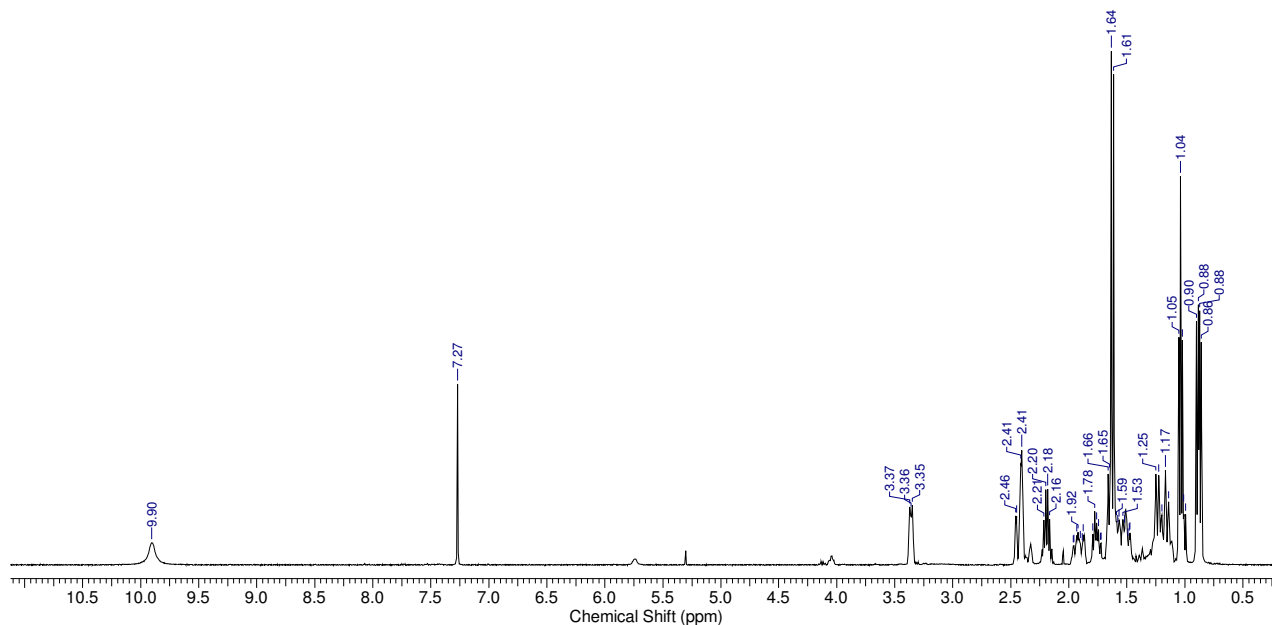
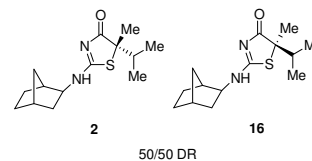
¹³C NMR for racemic compound **17**:



^1H NMR for compound **2/16** mixture (50/50 DR):



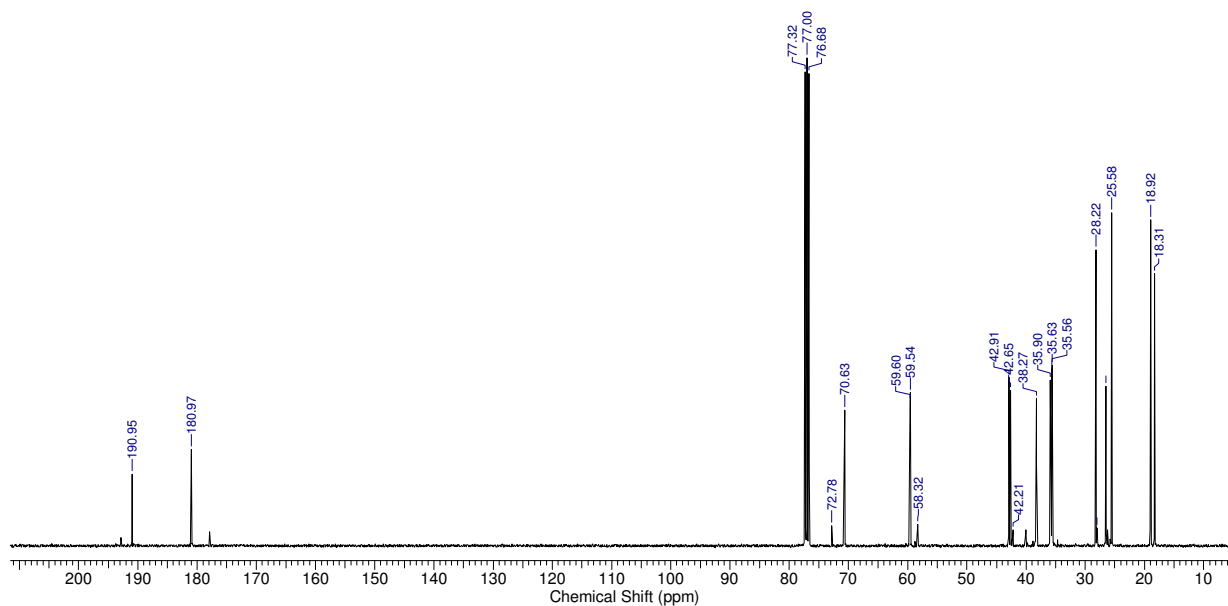
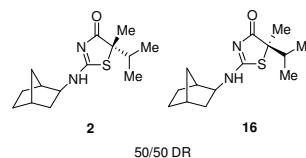
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Date	27 Oct 2008 23:30:09		
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Frequency (MHz)	400.23	Nucleus	^1H
Number of Transients	16	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	6410.06
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2400.0027	Sweep Width (Hz)	6409.86
Temperature (degree C)	27.000		



^{13}C NMR for compound **2/16** mixture (50/50 DR):



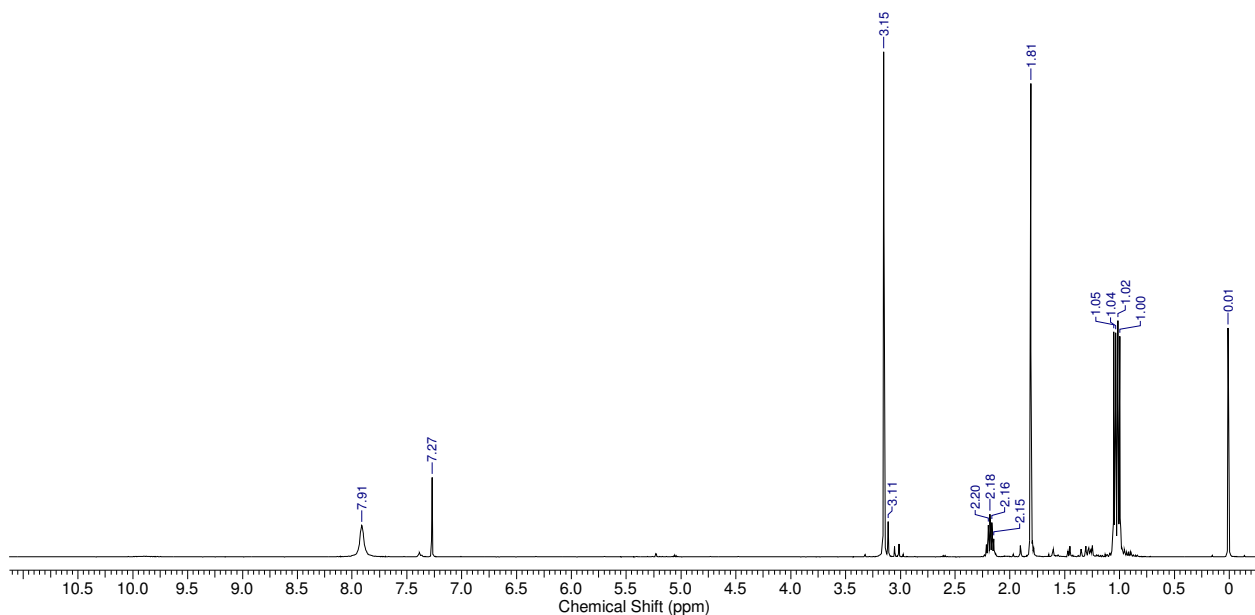
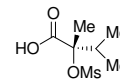
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File Name	\scone\NMR-Archive\JCAMP\SCAILLE\221 PAPER\50-50 2-16 MIXTURE C.DX		
Frequency (MHz)	100.65	Nucleus	^{13}C
Number of Transients	4096	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28408.22
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	12073.9639	Sweep Width (Hz)	28407.36
Temperature (degree C)	27.000		



^1H NMR for (*S*)-2,3-dimethyl-2-(methylsulfonyloxy)butanoic acid (synthesis of **18**):



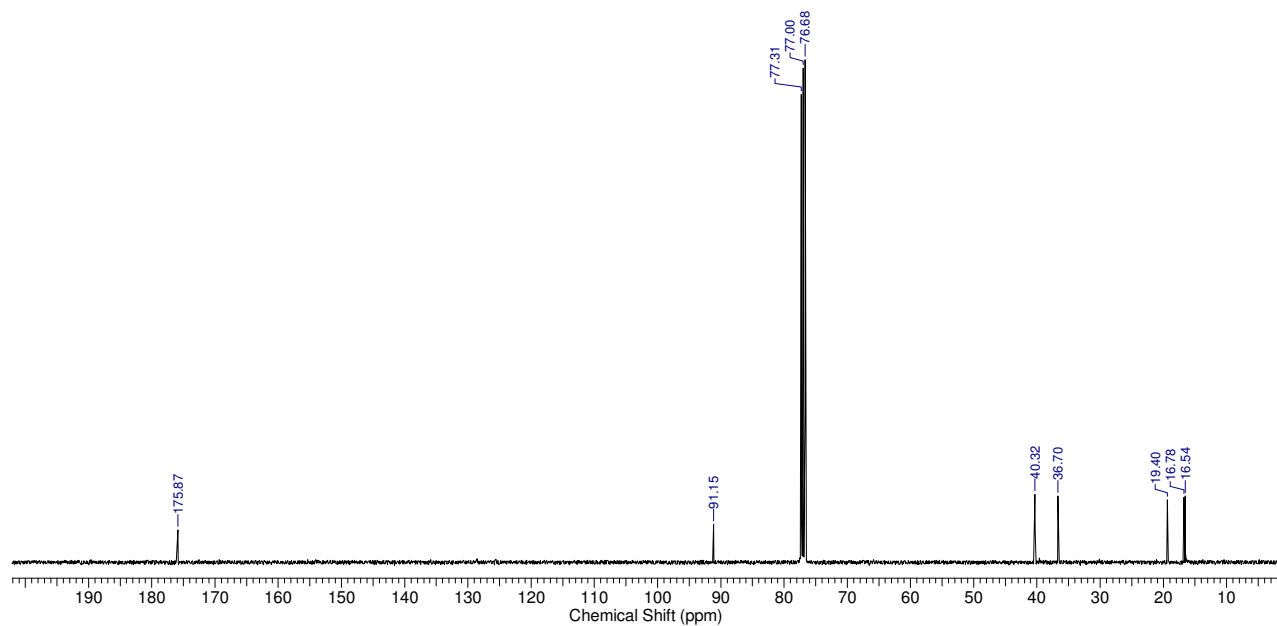
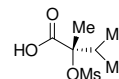
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Number of Transients	16	Origin	Bruker BioSpin GmbH
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Points Count	16384	SW(cyclical) (Hz)	8223.18
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2467.2554	Sweep Width (Hz)	8222.68
Temperature (degree C)	25.000		



^{13}C NMR for (*S*)-2,3-dimethyl-2-(methylsulfonyloxy)butanoic acid (synthesis of **18**):



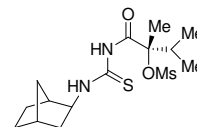
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Date	18 Sep 2008 03:25:22		
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Frequency (MHz)	100.63	Nucleus	^{13}C
Number of Transients	2048	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28408.22
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	12073.4746	Sweep Width (Hz)	28407.36
Temperature (degree C)	25.000		



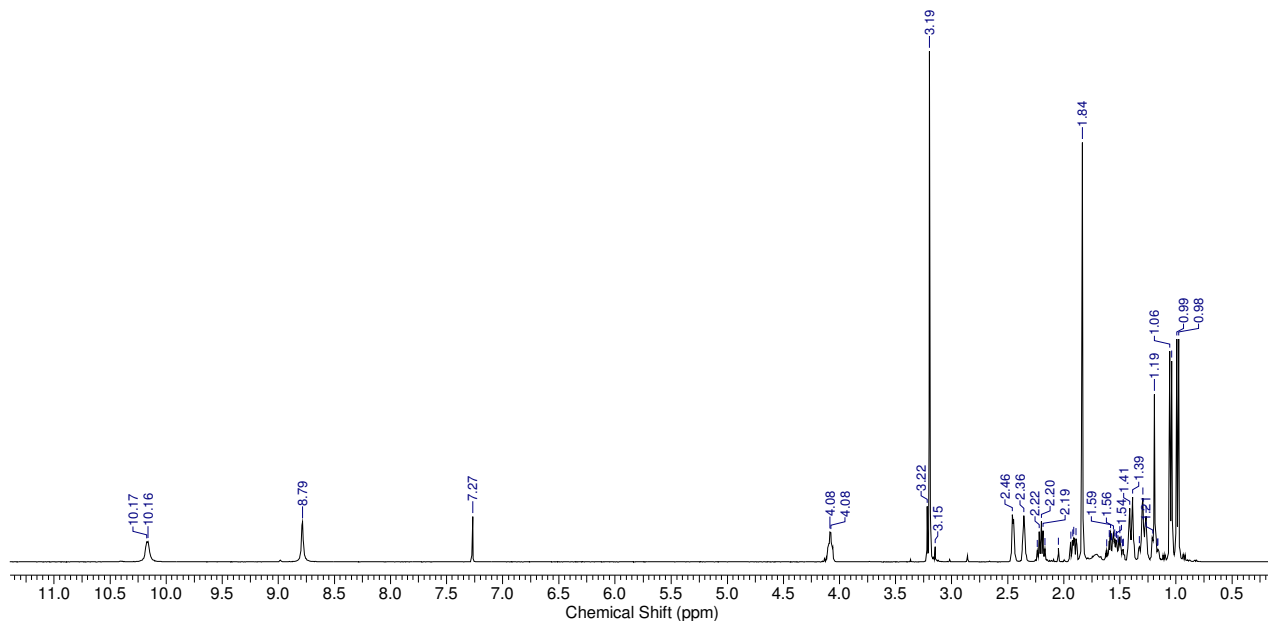
¹H NMR for compound **18**:



Acquisition Time (sec)	1.9925	Comment	scui
Date	18 Sep 2008 01:27:39		
File Name	\\scone\NMR-Archive\JCAMP\SCAILLE\221 PAPER\CPD 18-H.DX		
Frequency (MHz)	400.16	Nucleus	1H
Number of Transients	16	Origin	Bruker BioSpin GmbH
Original Points Count	16384	Owner	smallmolecules
Points Count	16384	SW(cyclical) (Hz)	8223.18
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	2467.2554	Sweep Width (Hz)	8222.68
Temperature (degree C)	25.000		



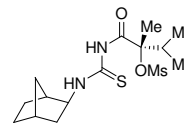
18



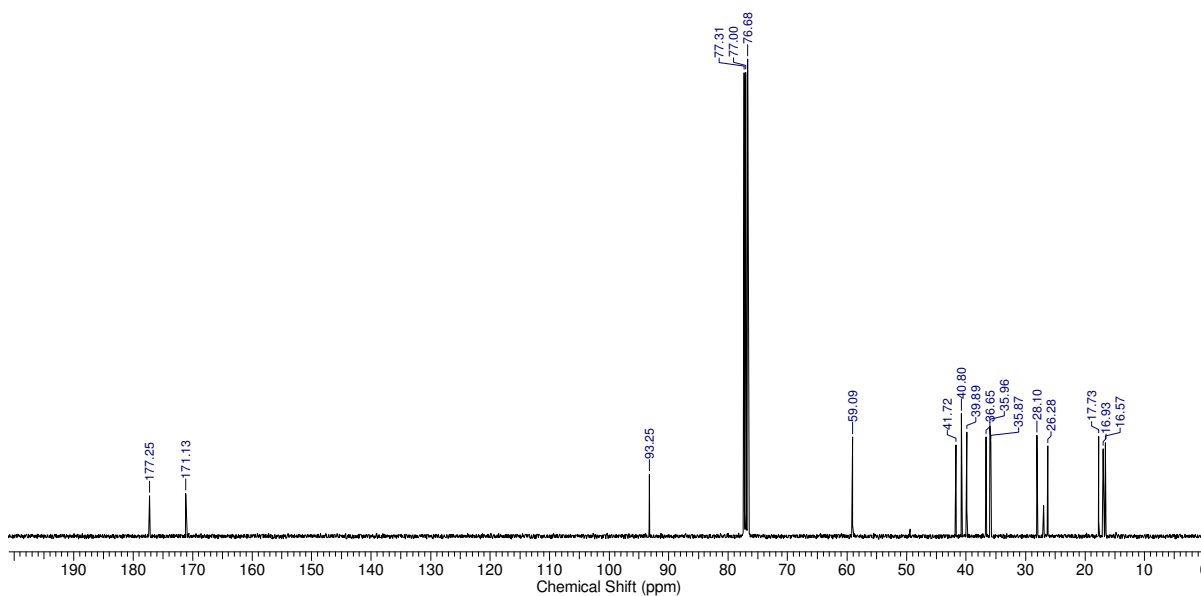
¹³C NMR for compound **18**:



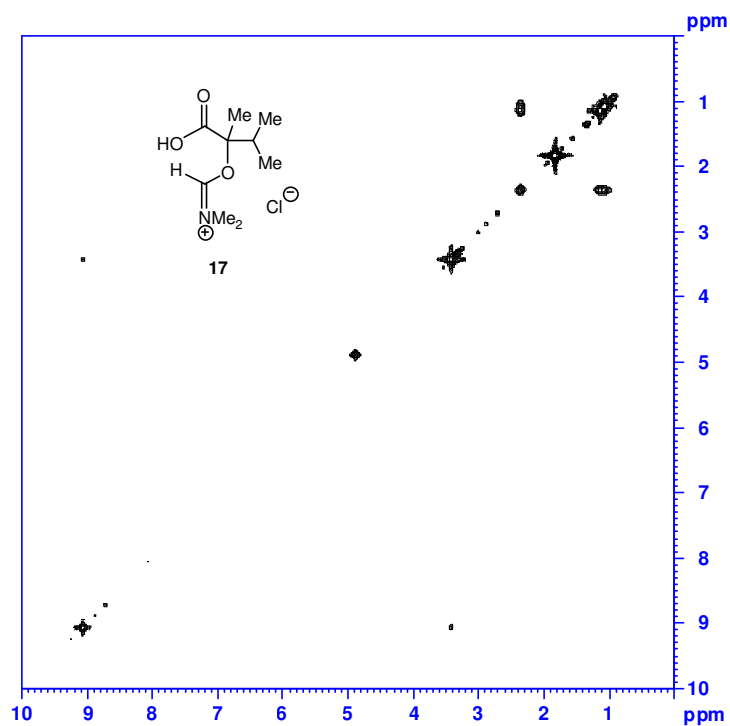
Acquisition Time (sec)	1.1535	Comment	scui
Date	18 Sep 2008 06:12:53		
File Name	\\scone\NMR-Archive\JCAMP\SCAILLE\221 PAPER\CPD 18-C.DX		
Frequency (MHz)	100.63	Nucleus	13C
Number of Transients	2048	Origin	Bruker BioSpin GmbH
Original Points Count	32768	Owner	smallmolecules
Points Count	32768	SW(cyclical) (Hz)	28408.22
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	12071.7412	Sweep Width (Hz)	28407.36
Temperature (degree C)	25.000		



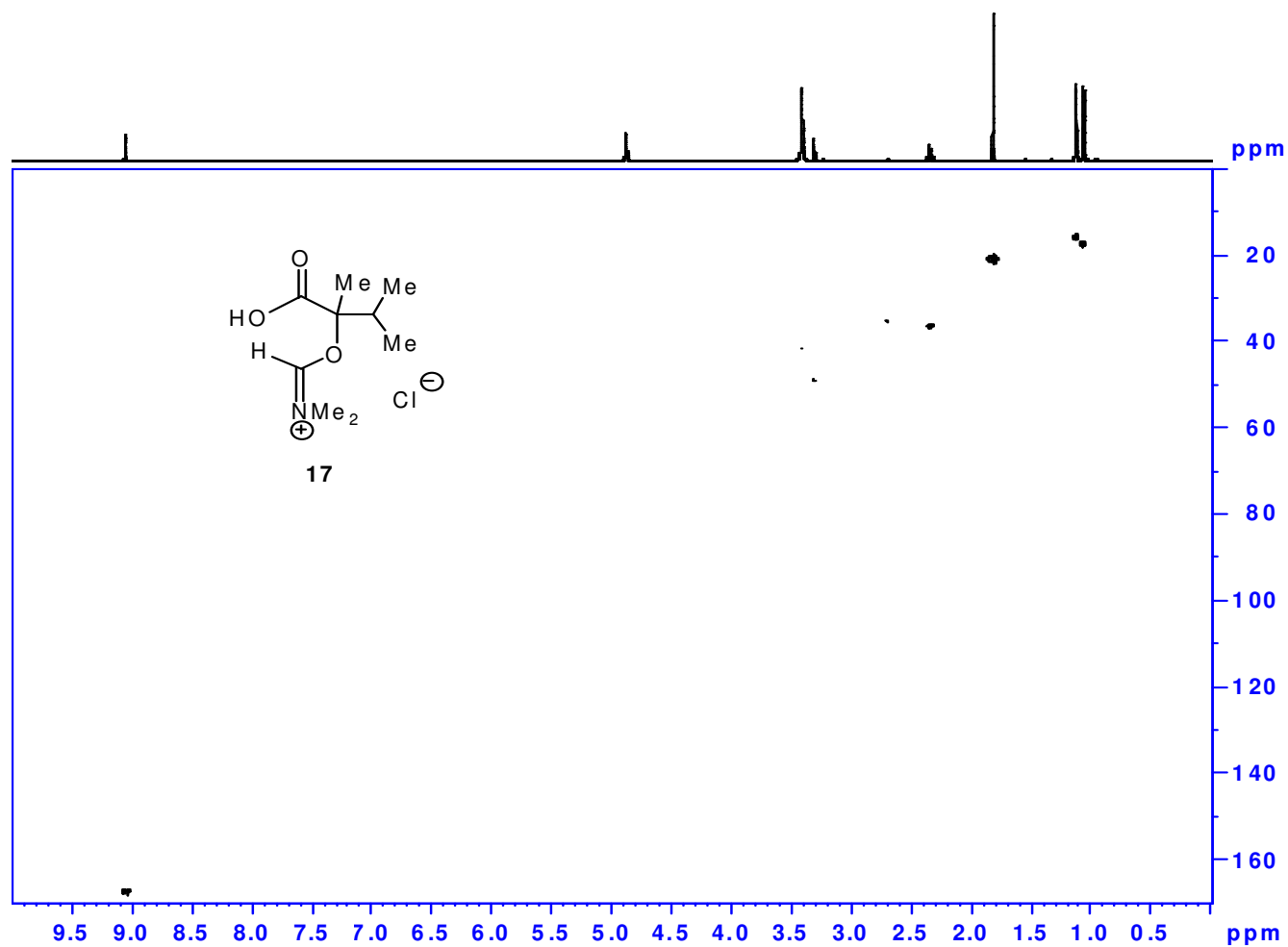
18



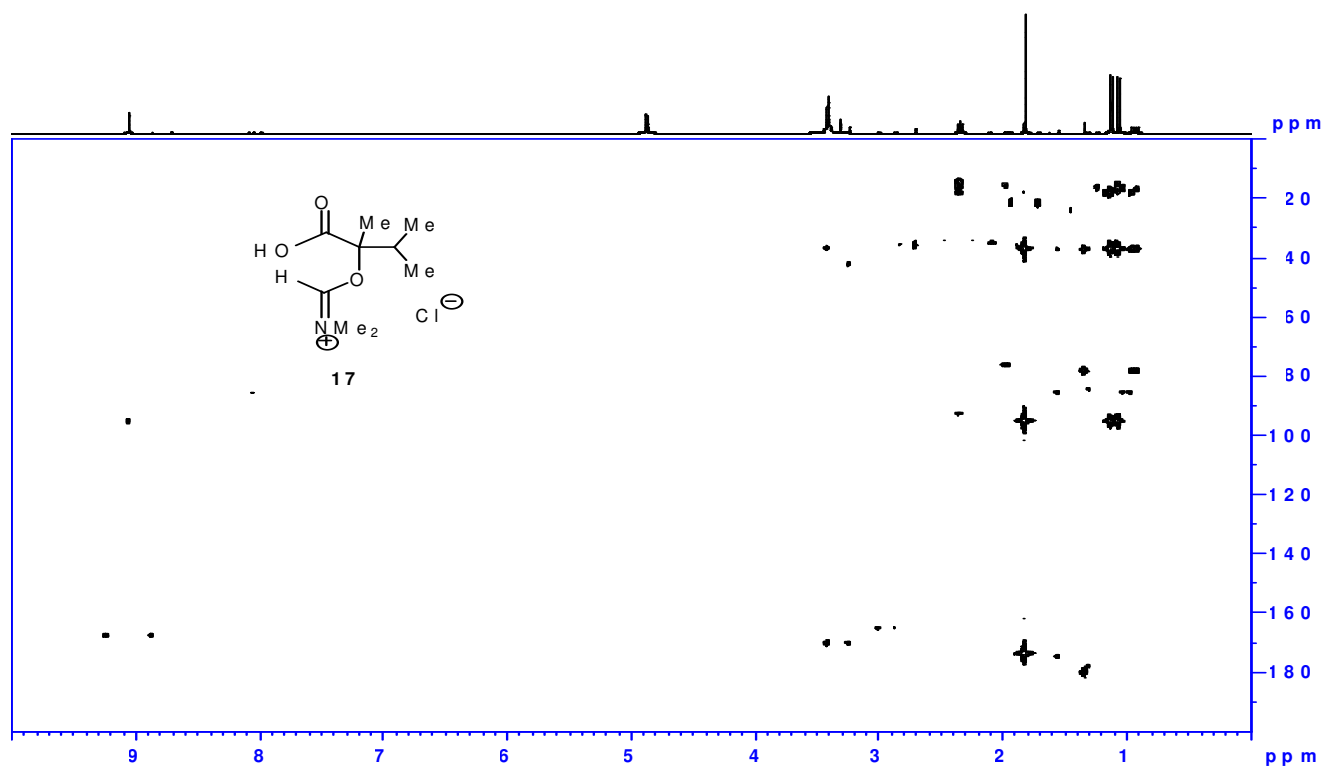
COSY for racemic compound **17**:



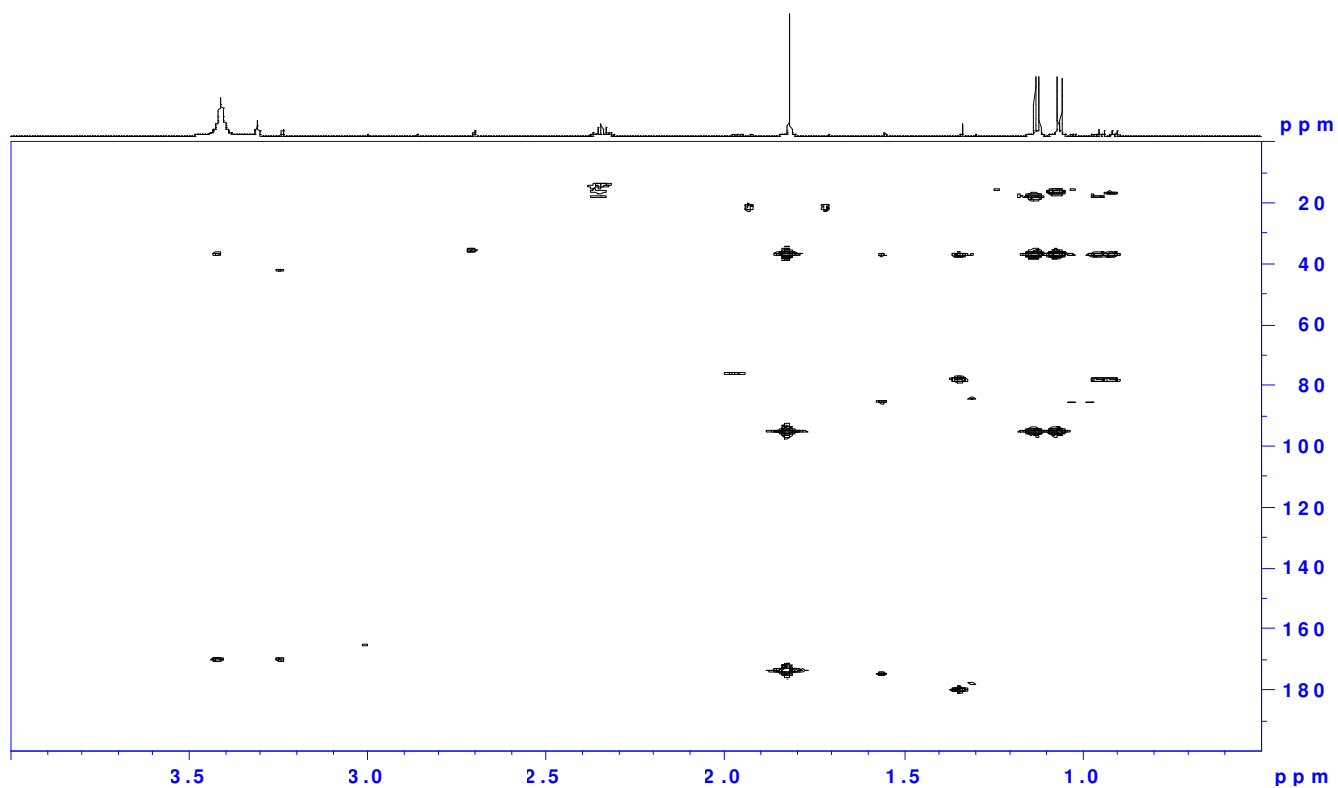
HSQC for racemic compound **17**:



HMBC for racemic compound **17**:



HMBC for racemic compound **17** (expansion):



^1H - ^{15}N HMBC for racemic compound **17**:

