

Total Synthesis of (-)-Cryptocaryol A

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Acquisition Time (sec)	3.1654	Comment	Paula PKK8 C6D6 250 MHz mar14pkkH1	Date	14 Mar 2013 18:54:14
File Name	C:\Users\Usuário\Documents\Unicamp\Mestrado\Espectros RMN\250\mar14pkkH1 (PKK8)_001001r			Frequency (MHz)	250.13
Nucleus	1H	Number of Transients	12	Original Points Count	16384
Pulse Sequence	zg30	Solvent	BENZENE-D6	Sweep Width (Hz)	5175.98
				Points Count	32768
				Temperature (degree C)	25.160

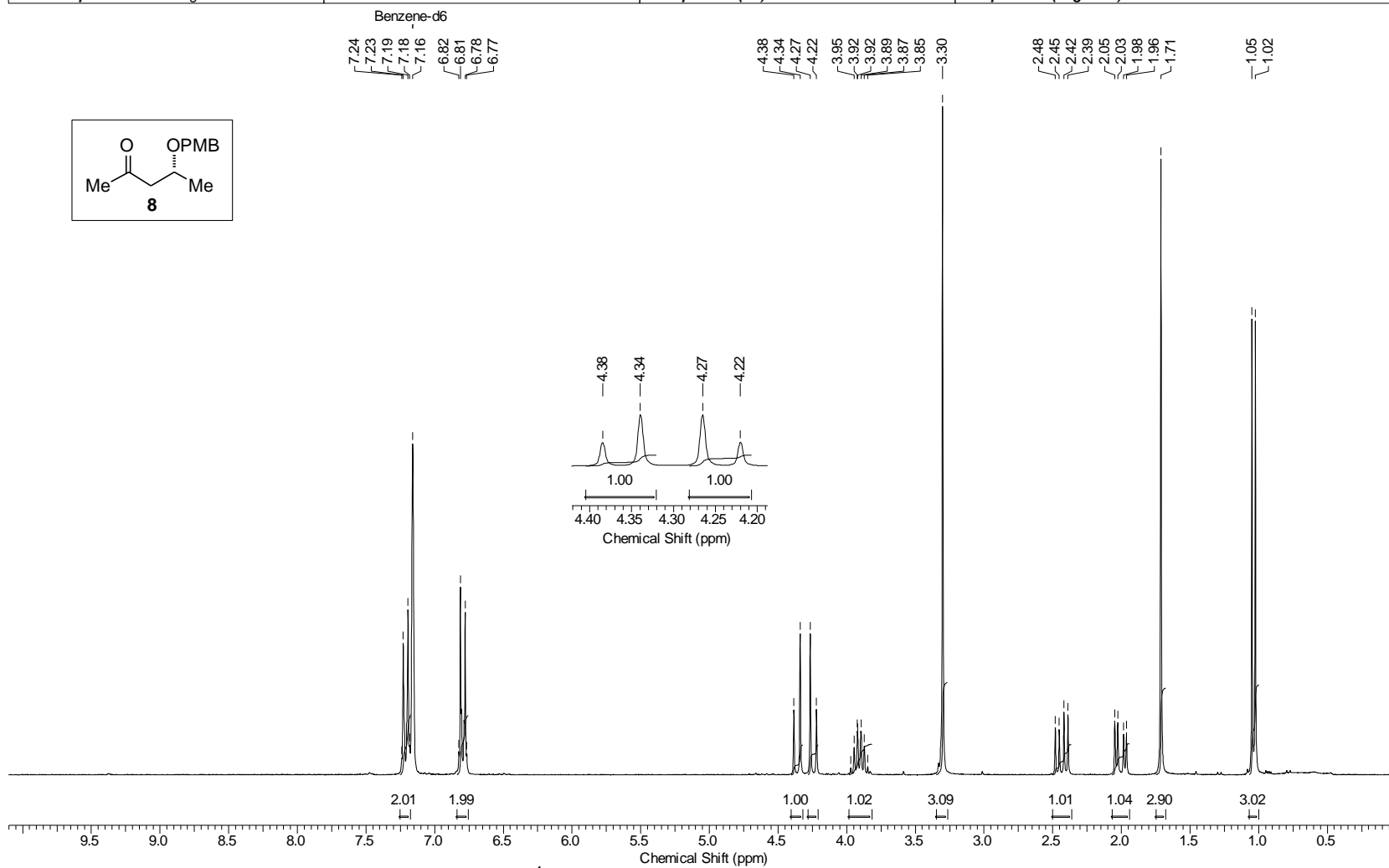


Figure S1. ^1H NMR spectrum of **8** (250 MHz; C_6D_6).

Acquisition Time (sec)	0.5439	Comment	Paula PKK8 C6D6 250 MHz mar14pkkC1 13C	Date	15 Mar 2013 08:30:38
File Name	C:\Users\Usuário\Documents\Unicamp\Mestrado\Espectros RMN\250\mar14pkkC1 (PKK8)_002001r	Number of Transients	15963	Frequency (MHz)	62.90
Nucleus	13C	Original Points Count	8192	Points Count	32768
Pulse Sequence	zpgg30	Solvent	BENZENE-D6	Sweep Width (Hz)	15060.24
		Temperature (degree C)	25.160		

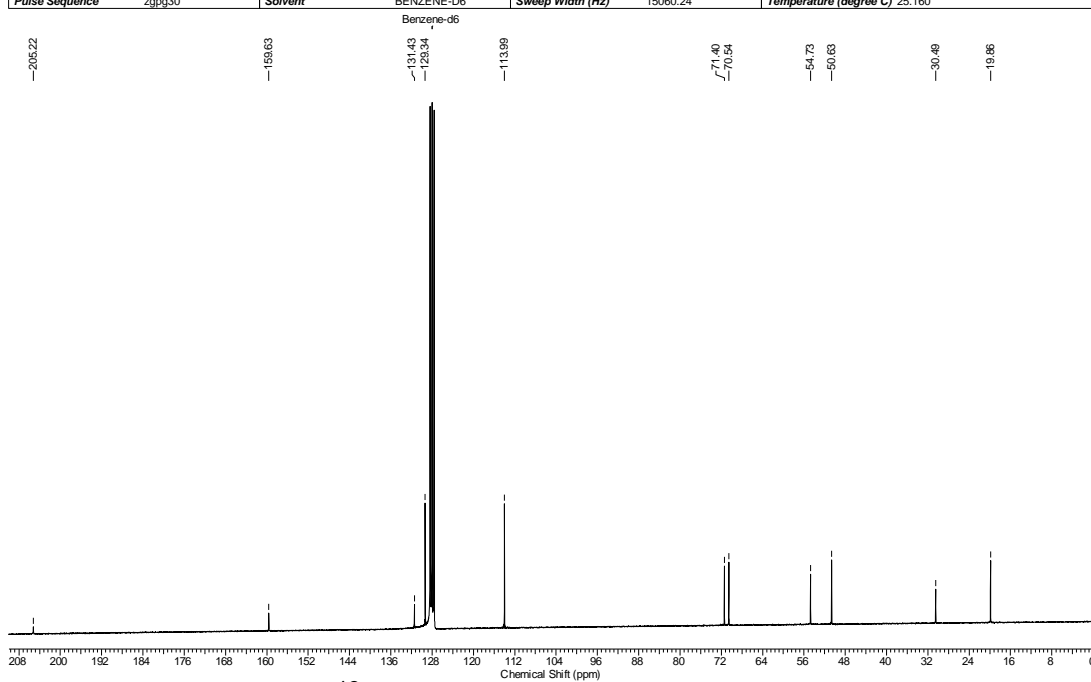


Figure S2. ^{13}C NMR spectrum of **8** (62.5 MHz; C_6D_6).

Acquisition Time (sec)	0.5439	Comment	Paula PKK8 C6D6 250 MHz mar14pkkC1 C13DEPT135	Date	15 Mar 2013 08:31:56
File Name	C:\Users\Usuário\Documents\Unicamp\Mestrado\Espectros RMN\250\mar14pkkC1 (PKK8)_001001r	Number of Transients	3072	Frequency (MHz)	62.90
Nucleus	13C	Original Points Count	8192	Points Count	32768
Pulse Sequence	dept135	Solvent	BENZENE-D6	Sweep Width (Hz)	15060.24
		Temperature (degree C)	25.160		

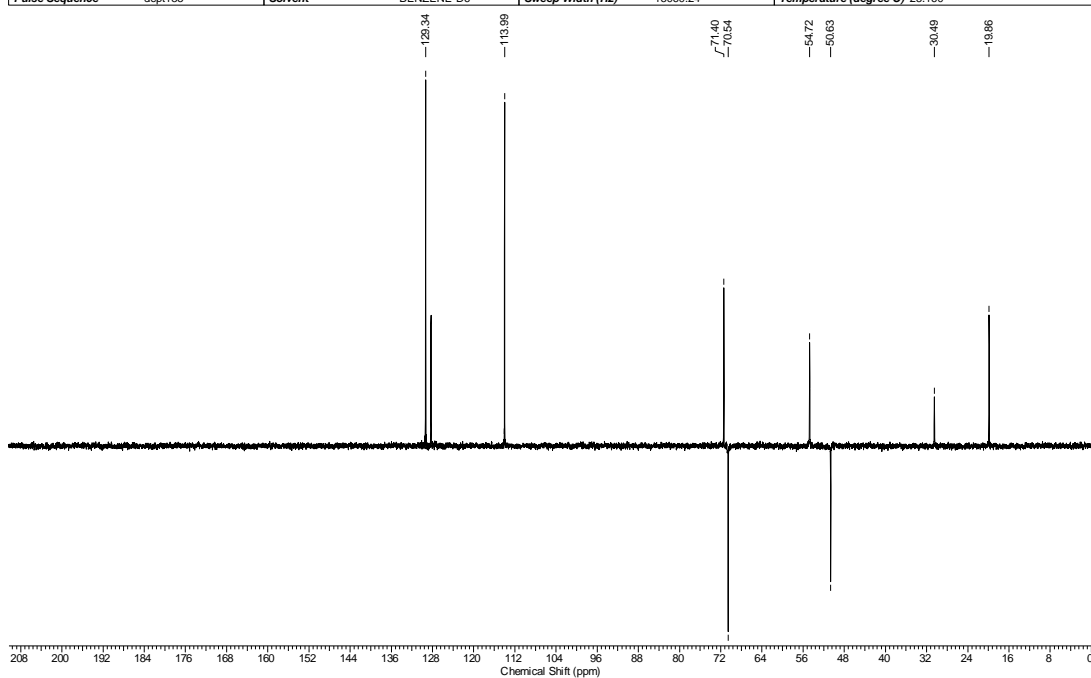


Figure S3. ^{13}C NMR spectrum (DEPT 135) of **8** (62.5 MHz; C_6D_6).

Title	cial do Brasil (GMT-3:00)	Origin	cial do Brasil (GMT-3:00)	File Name	E:\MESTRADO\IV PAULA\PKK8.SP
Date Stamp	mon jul 15 16:25:16 2013 Hora oficial do Brasil (GMT-3:00)	Date	mon jul 15 16:25:16 2013 Hora oficial do Brasil (GMT-3:00)	Spectral Region	IR
Technique	Infrared	Instrument	Spectrum Two	X Axis	Wavenumber (cm-1)
Y Axis	%Transmittance	Spectrum Range	550.0000 - 4000.0000	Points Count	3451
				Data Spacing	1.0000

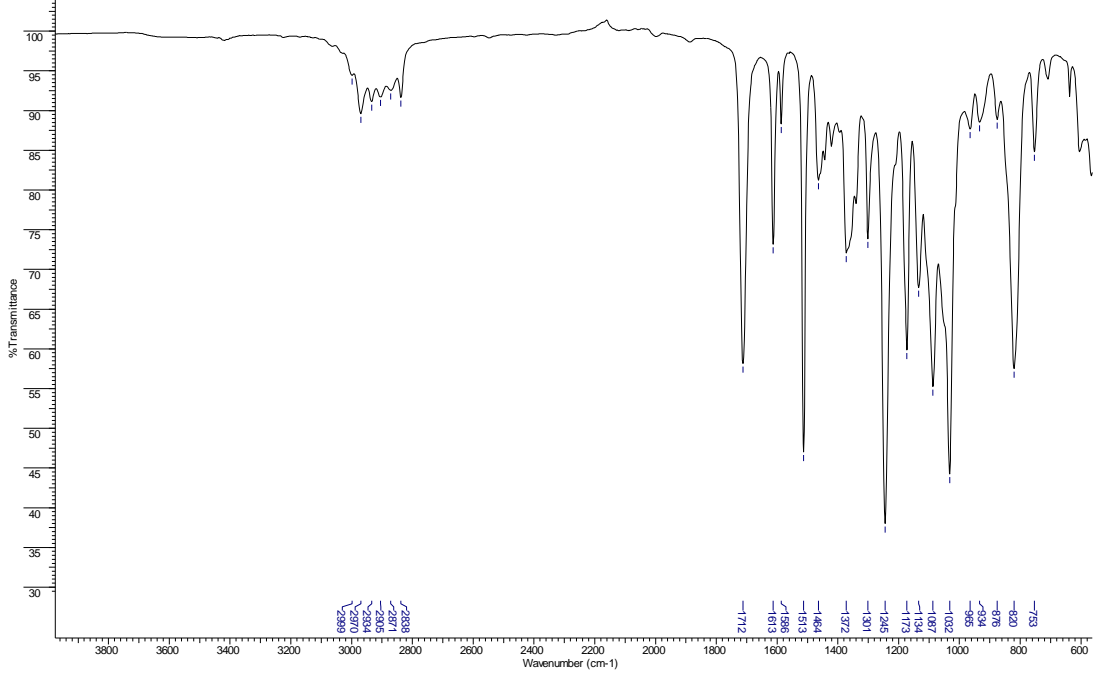


Figure S4. IR spectrum of 8.

Acquisition Time (sec)	1.3282	Date	15 Apr 2013 07:47:14				
File Name	F:\Mestrado\Espectros RMN\600\abr15pkkH1 (PKK12)_001001r			Frequency (MHz)	600.17	Nucleus	1H
Number of Transients	16	Original Points Count	16384	Points Count	65536	Pulse Sequence	zg30
Sweep Width (Hz)	12335.53	Temperature (degree C)	25.153				

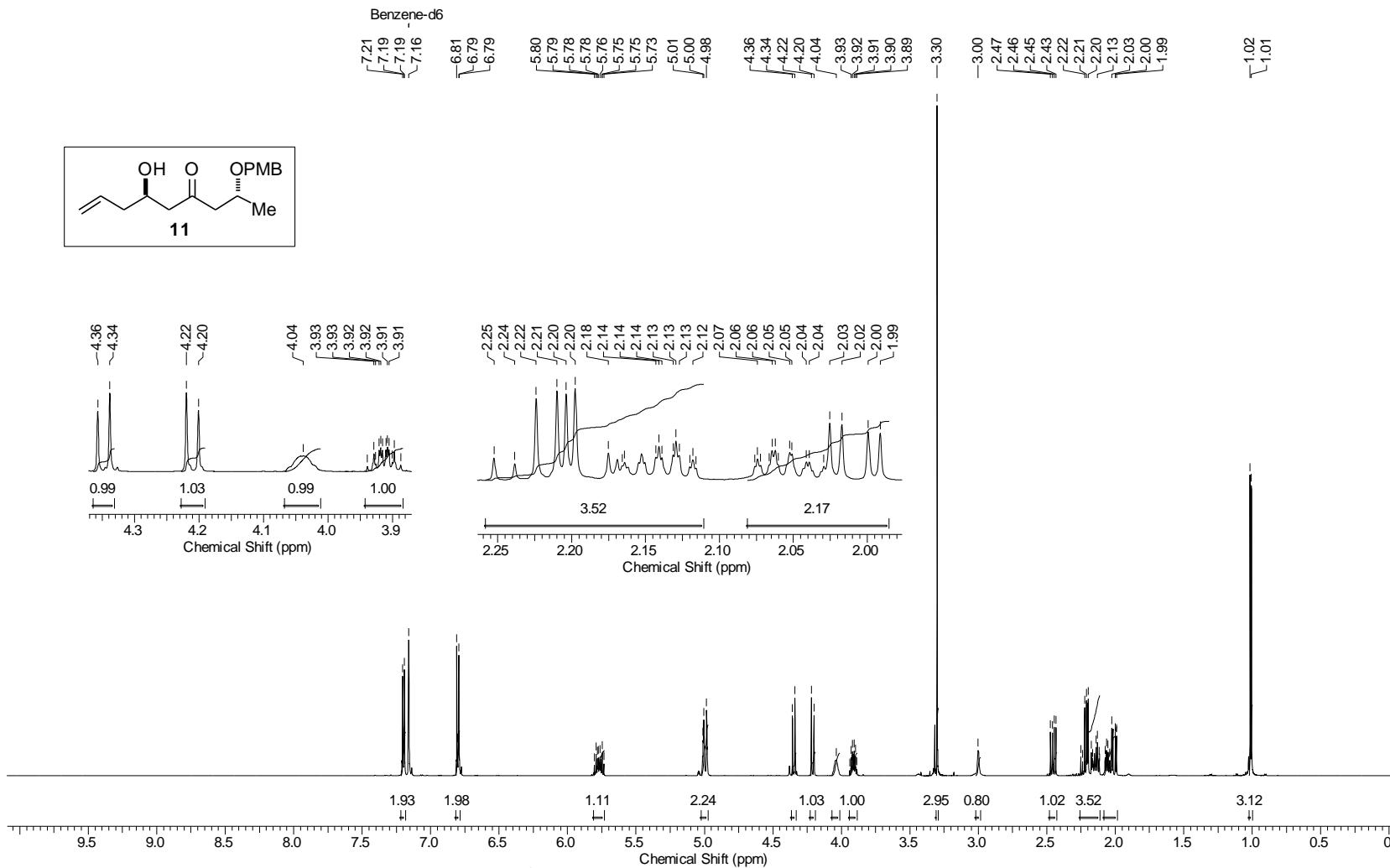


Figure S5. ^1H NMR spectrum of **11** (600 MHz; C_6D_6).

Acquisition Time (sec)	0.5505	Comment	Paula PKK12 c6d6 AV500 MHz abr05pkkH1 - 13C	Date	05 Apr 2013 14:56:24
File Name	F:\Mestrado\Espectros RMN500\abr05pkkH1 (PKK12)_002001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	849	Original Points Count	16384	Points Count	131072
Solvent	BENZENE-D6	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.147

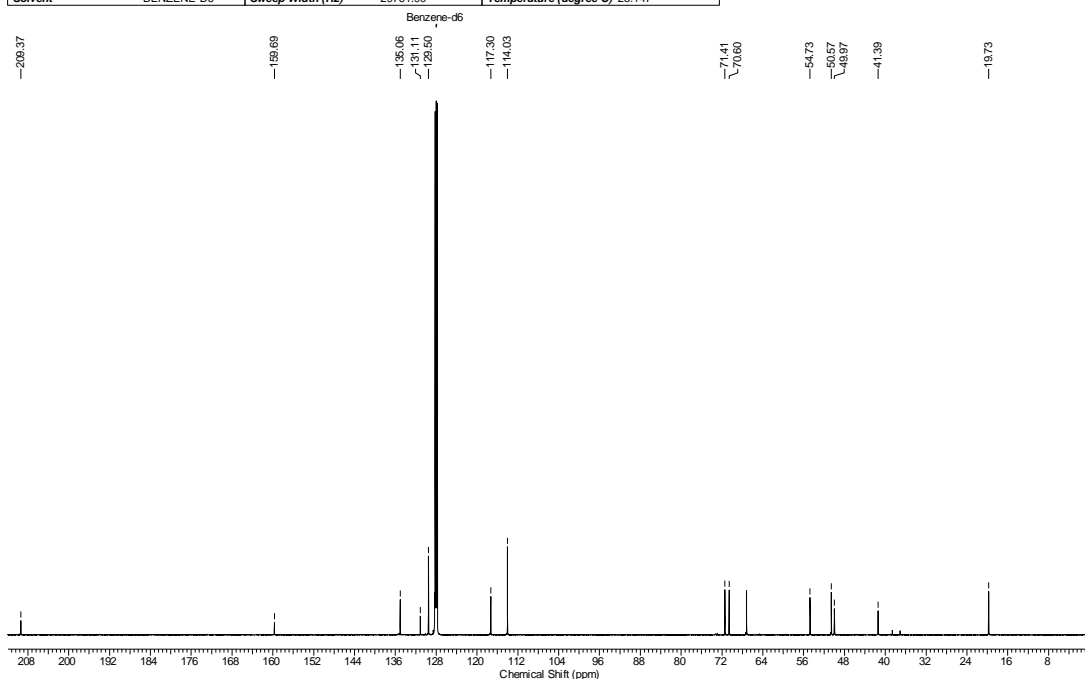


Figure S6. ^{13}C NMR spectrum of **11** (125 MHz; C_6D_6).

Acquisition Time (sec)	0.5505	Comment	Paula PKK12 c6d6 AV500 MHz abr05pkkH1 - dept 135	Date	05 Apr 2013 14:56:18
File Name	F:\Mestrado\Espectros RMN500\abr05pkkH1 (PKK12)_003001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	320	Original Points Count	16384	Points Count	32768
Solvent	BENZENE-D6	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.158

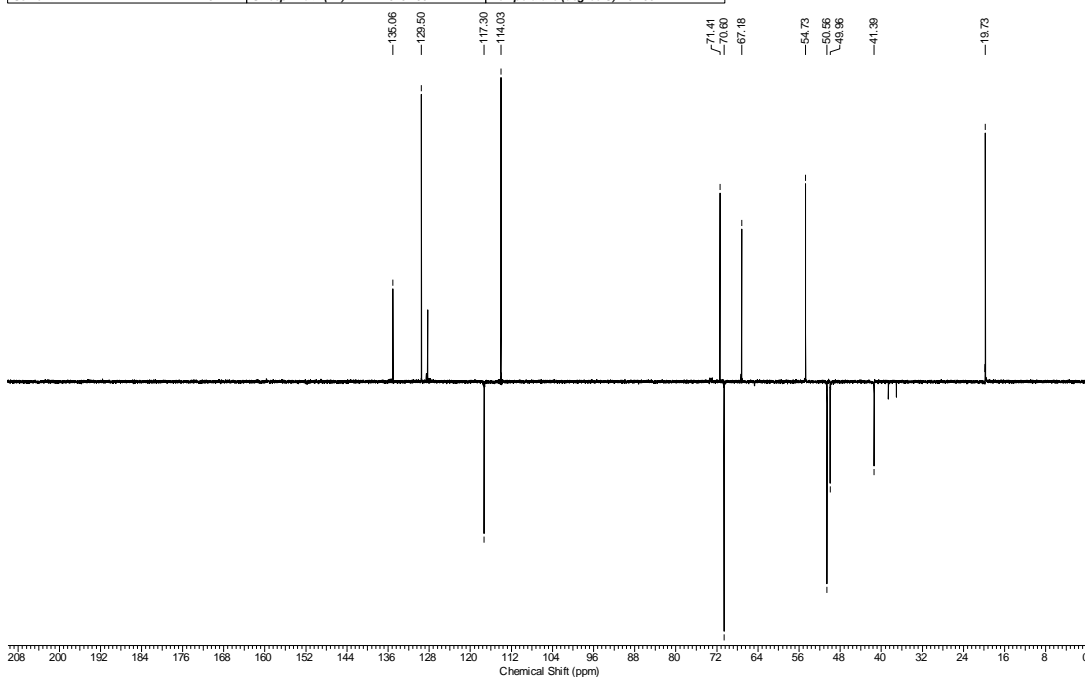
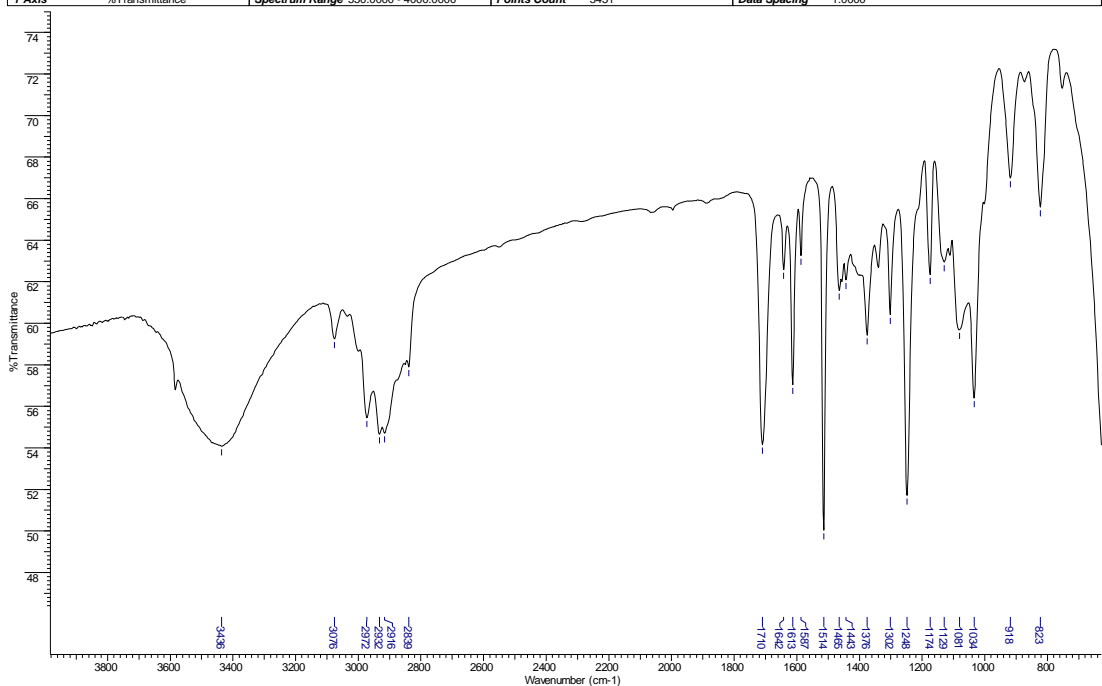


Figure S7. ^{13}C NMR spectrum (DEPT 135) of **11** (125 MHz; C_6D_6).

Title	cial do Brasil (GMT-3:00)	Origin	cial do Brasil (GMT-3:00)	File Name	E:\MESTRADO\IV PAULA\PKK12.SP
Date Stamp	mon jul 15 18:05:35 2013 Hora oficial do Brasil (GMT-3:00)	Date	mon jul 15 18:05:35 2013 Hora oficial do Brasil (GMT-3:00)	Spectral Region	IR
Technique	Infrared	Instrument	Spectrum Two	X Axis	Wavenumber (cm-1)
Y Axis	%Transmittance	Spectrum Range	550.0000 - 4000.0000	Points Count	3451
				Data Spacing	1.0000



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T: FTMS + p ESI Full ms [150.00-1500.00]

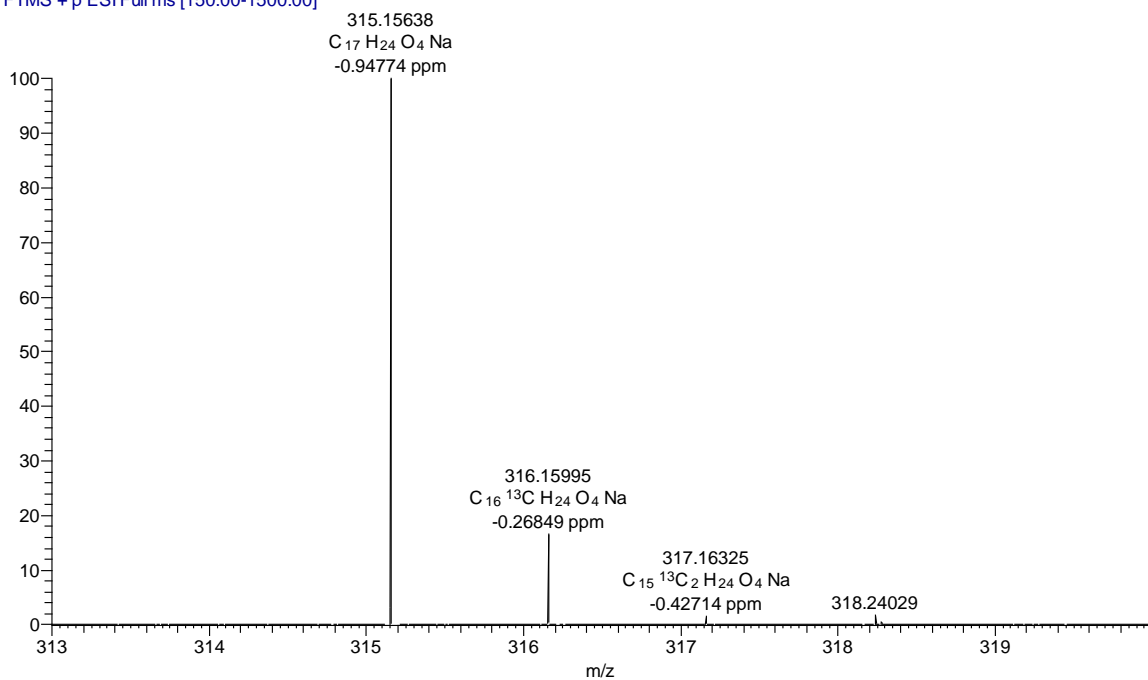


Figure S8. IR and HRMS spectra of 11.

Acquisition Time (sec)	1.6384	Comment	Paula "PKK13" cdc13/Av500MHz abr09pkkH1	Date	17 Dec 2013 13:23:40
File Name	F:\Mestrado\Espectros RMN\500\abr09pkkH1 (PKK13)_001001r	Frequency (MHz)	499.87	Nucleus	1H
Number of Transients	16	Original Points Count	16384	Points Count	65536
Solvent	CHLOROFORM-D	Sweep Width (Hz)	10000.00	Pulse Sequence	zg30
				Temperature (degree C)	25.136

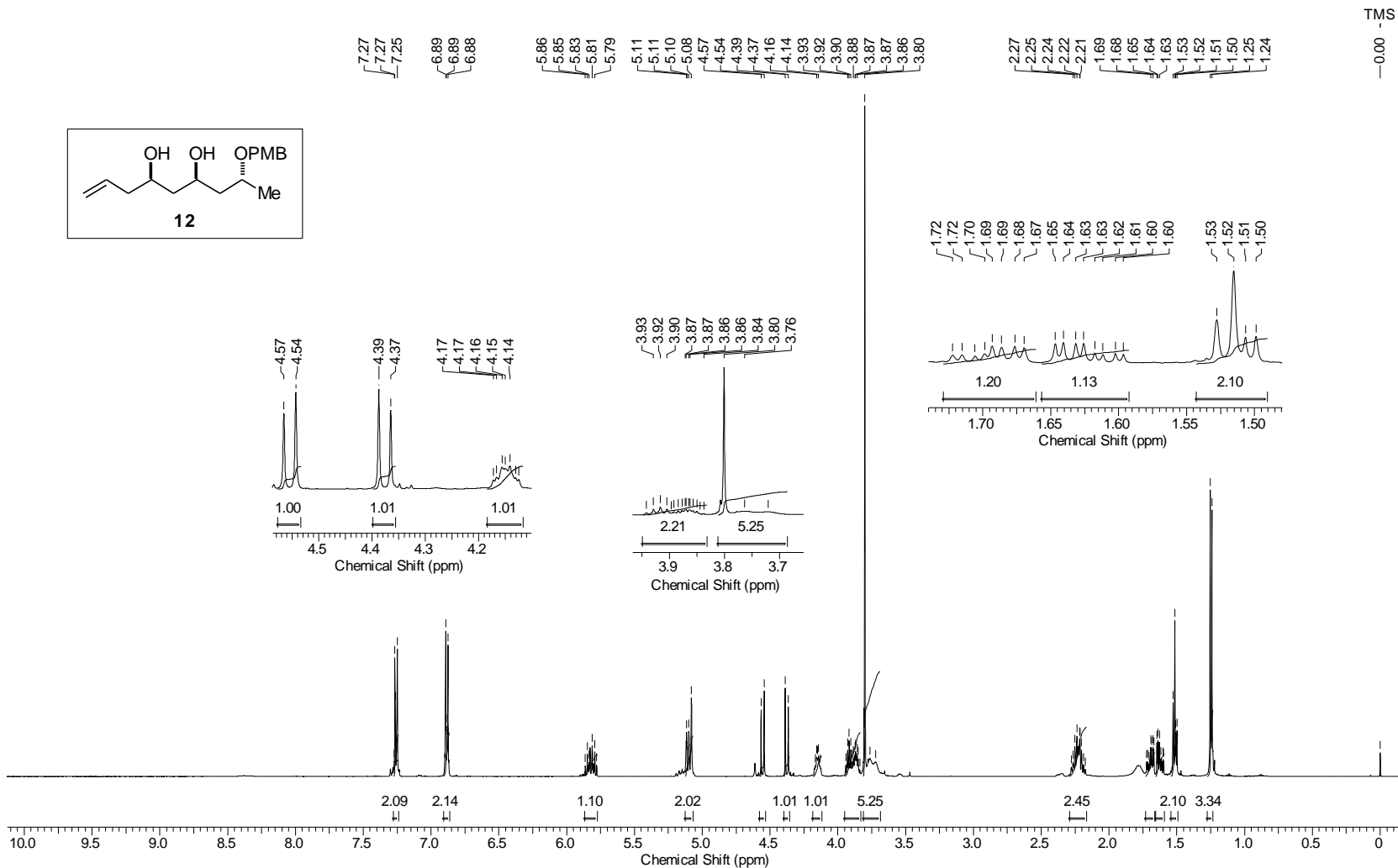


Figure S9. ^1H NMR spectrum of **12** (500 MHz; CDCl_3).

Acquisition Time (sec)	0.5505	Comment	Paula "PKK13" cdcl3/Av500MHz abr09pkkH1 -13C	Date	10 Apr 2013 06:57:32
File Name	C:\Users\Usuário\Documents\Unicamp\Mestrado\Espectros RMN\500\abr09pkkH1 (PKK13)_002001r	Number of Transients	3072	Frequency (MHz)	125.69
Nucleus	13C	Original Points Count	16384	Points Count	32768
Pulse Sequence	zpgg30	Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90
				Temperature (degree C)	25.143

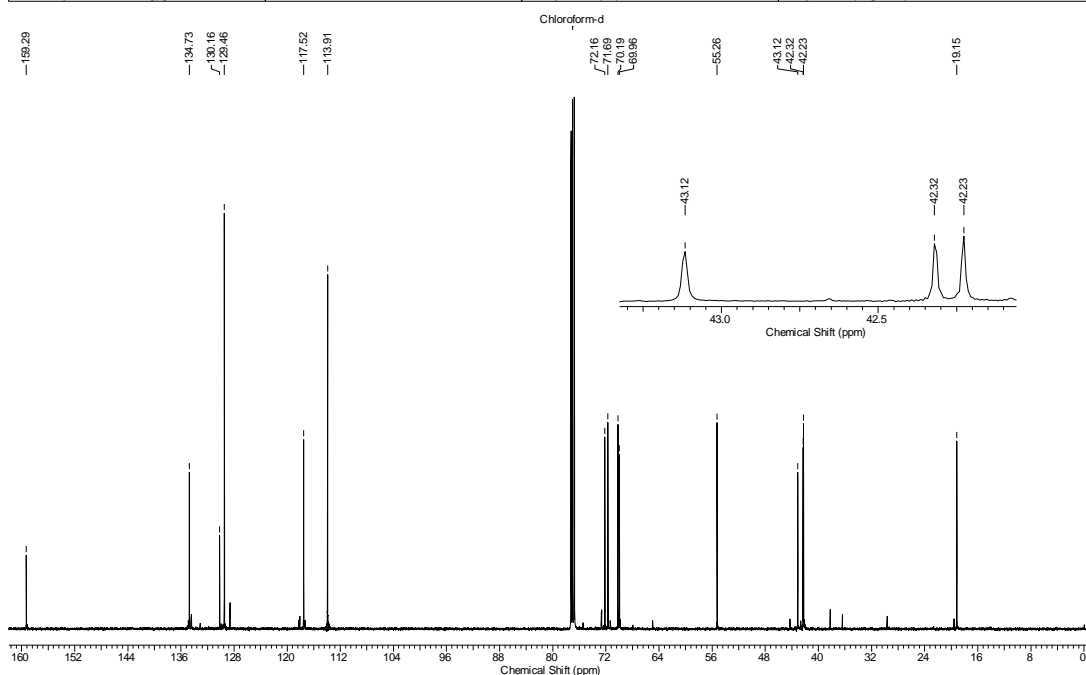


Figure S10. ^{13}C NMR spectrum of **12** (125 MHz; CDCl_3).

Acquisition Time (sec)	0.5505	Comment	Paula "PKK13" cdcl3/Av500MHz abr09pkkH1 -Dept135	Date	10 Apr 2013 12:37:06
File Name	C:\Users\Usuário\Documents\Unicamp\Mestrado\Espectros RMN\500\abr09pkkH1 (PKK13)_003001r	Number of Transients	1024	Frequency (MHz)	125.69
Nucleus	13C	Original Points Count	16384	Points Count	32768
Pulse Sequence	dept135	Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90
				Temperature (degree C)	25.145

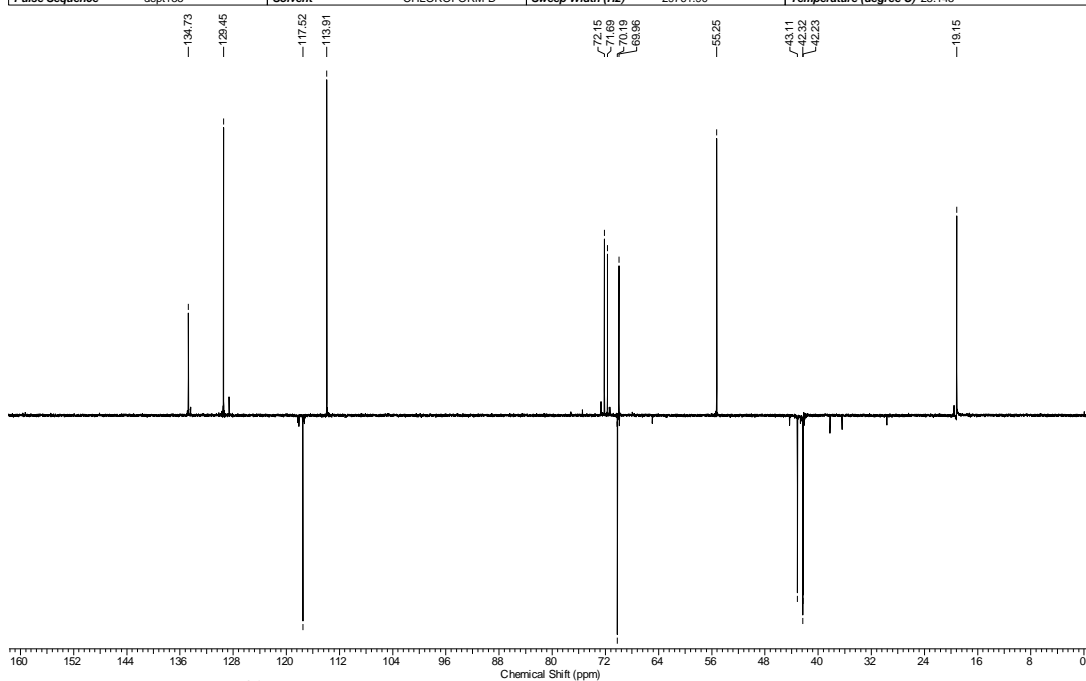
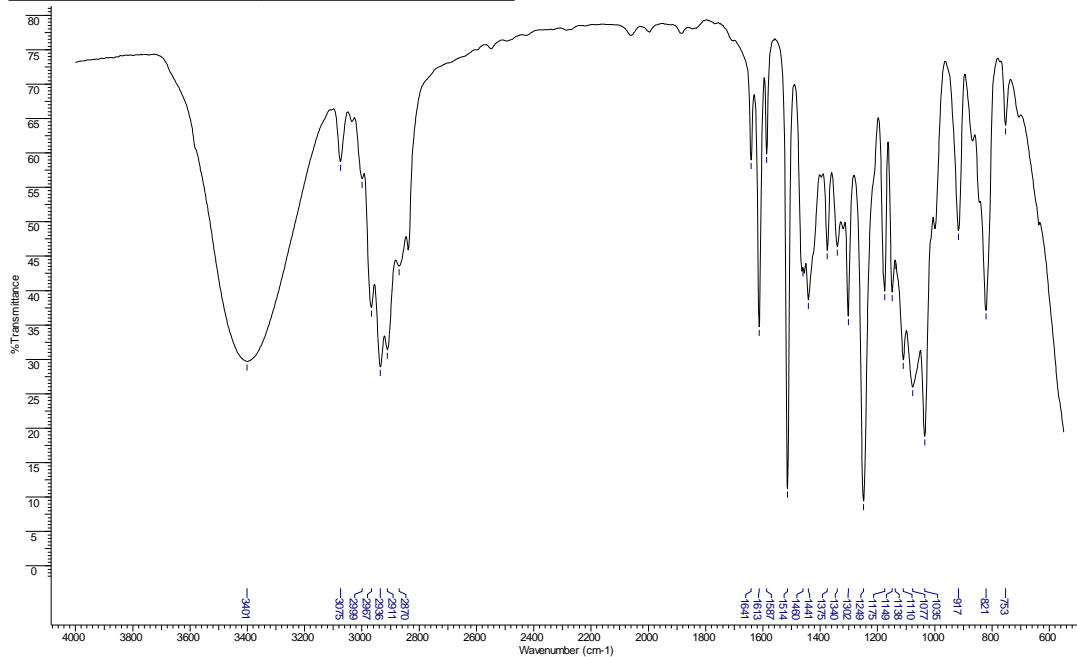


Figure S11. ^{13}C NMR spectrum (DEPT 135) of **12** (125 MHz; CDCl_3).

Title	cial do Brasil (GMT-3:00)	Comment	Amostra 000 por LQOS data segunda-feira, julho 15 2013	Origin	cial do Brasil (GMT-3:00)
File Name	E:\MESTRADO\IV PAULA\PKK13.SP	Date Stamp	mon jul 15 17:41:50 2013 Hora oficial do Brasil (GMT-3:00)	Technique	Infrared
Date	mon jul 15 17:41:50 2013 Hora oficial do Brasil (GMT-3:00)	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Spectral Region	IR	Data Spacing	1.0000	Instrument	Spectrum Two
Points Count	3451			Spectrum Range	550.0000 - 4000.0000



C012 #7 RT: 0.10 AV: 1 NL: 3.09E7
T: FTMS + p ESI Full ms [150.00-1500.00]

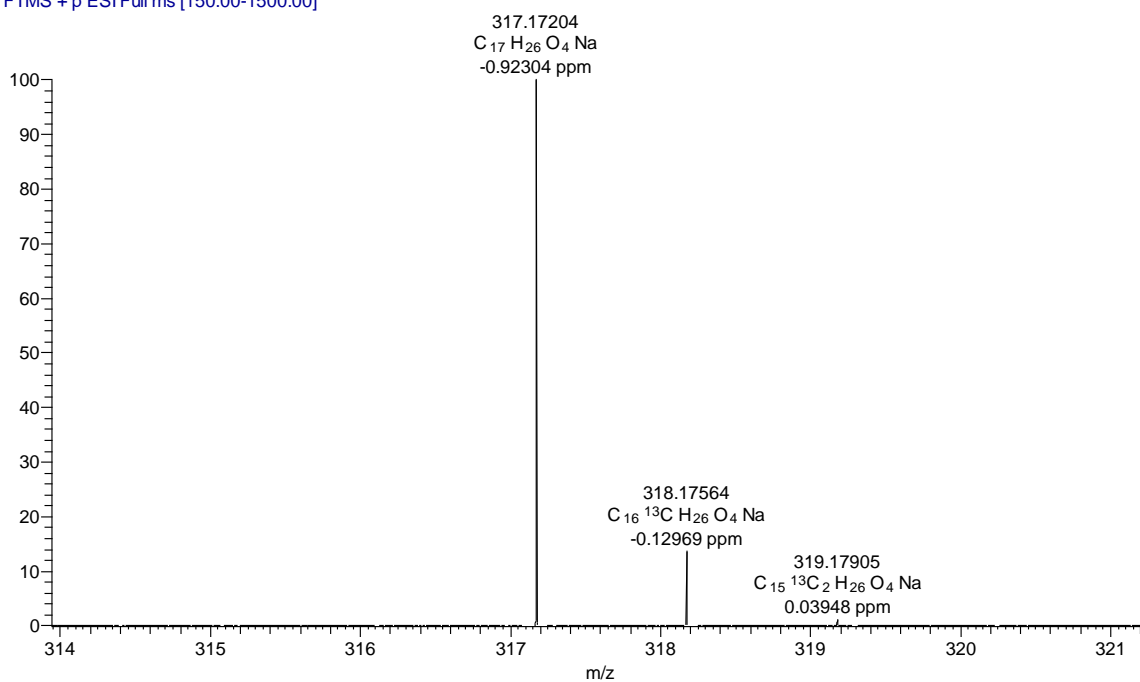
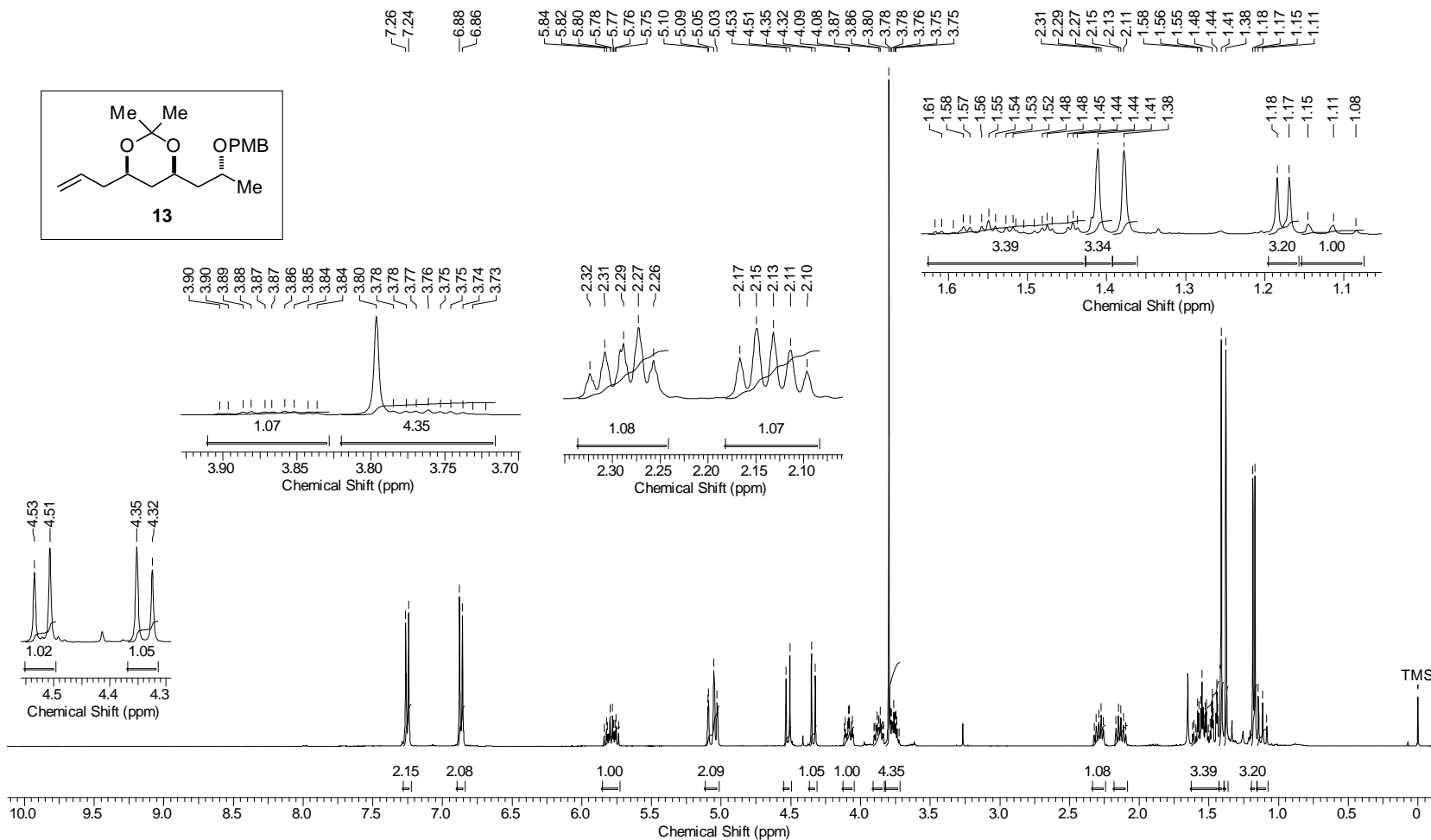


Figure S12. IR and HRMS spectra of 12.

Acquisition Time (sec)	1.9923	Date	30 Apr 2013 16:00:54	Frequency (MHz)	400.18
File Name	F:\Mestrado\Espectros RMN\400\abr30pkkH1 (PKK17)_001001r			Points Count	32768
Nucleus	1H	Number of Transients	16	Original Points Count	16384
Pulse Sequence	zg30	Solvent	CHLOROFORM-D	Sweep Width (Hz)	8223.68
Temperature (degree C)	25.260				



Acquisition Time (sec)	0.6816	Date	30 Apr 2013 16:57:36	Frequency (MHz)	100.63
File Name	F:\Mestrado\Espectros RMN\400\abr30pkkH1 (PKK17)_002001r	Number of Transients	1024	Original Points Count	16384
Nucleus	13C	Pulse Sequence	zpgg30	Solvent	CHLOROFORM-D
Temperature (degree C)	25.160			Points Count	32768
				Sweep Width (Hz)	24038.46

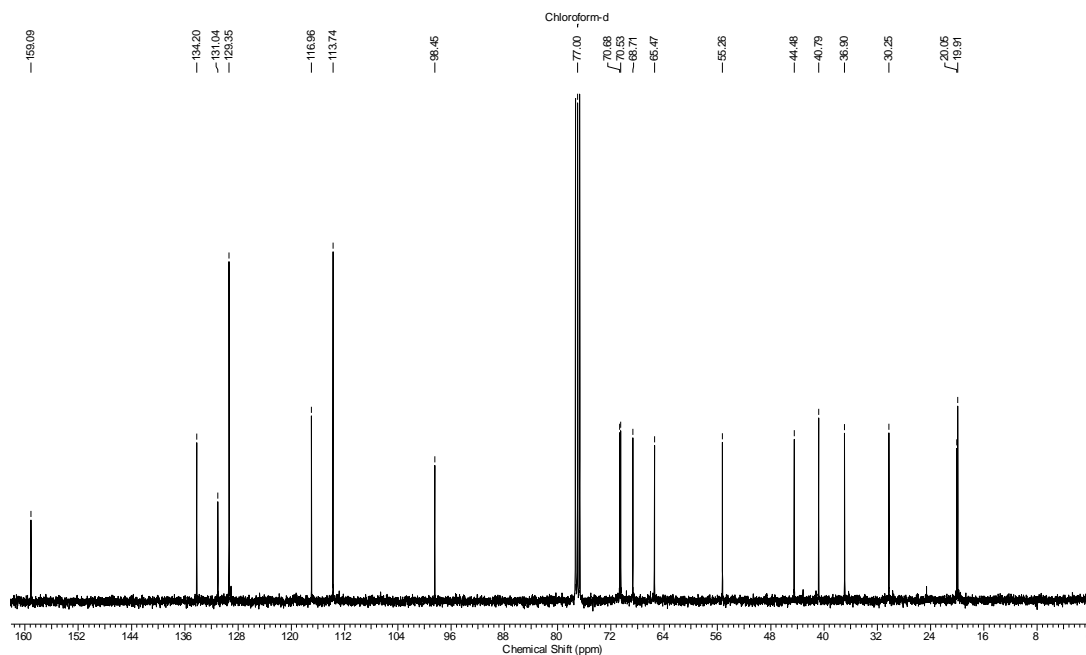


Figure S14. ^{13}C NMR spectrum of **13** (100 MHz; CDCl_3).

Acquisition Time (sec)	0.6816	Date	30 Apr 2013 17:10:52	Frequency (MHz)	100.63
File Name	F:\Mestrado\Espectros RMN\400\abr30pkkH1 (PKK17)_003001r	Number of Transients	473	Original Points Count	16384
Nucleus	13C	Pulse Sequence	dept135	Solvent	CHLOROFORM-D
Temperature (degree C)	25.160			Points Count	32768
				Sweep Width (Hz)	24038.46

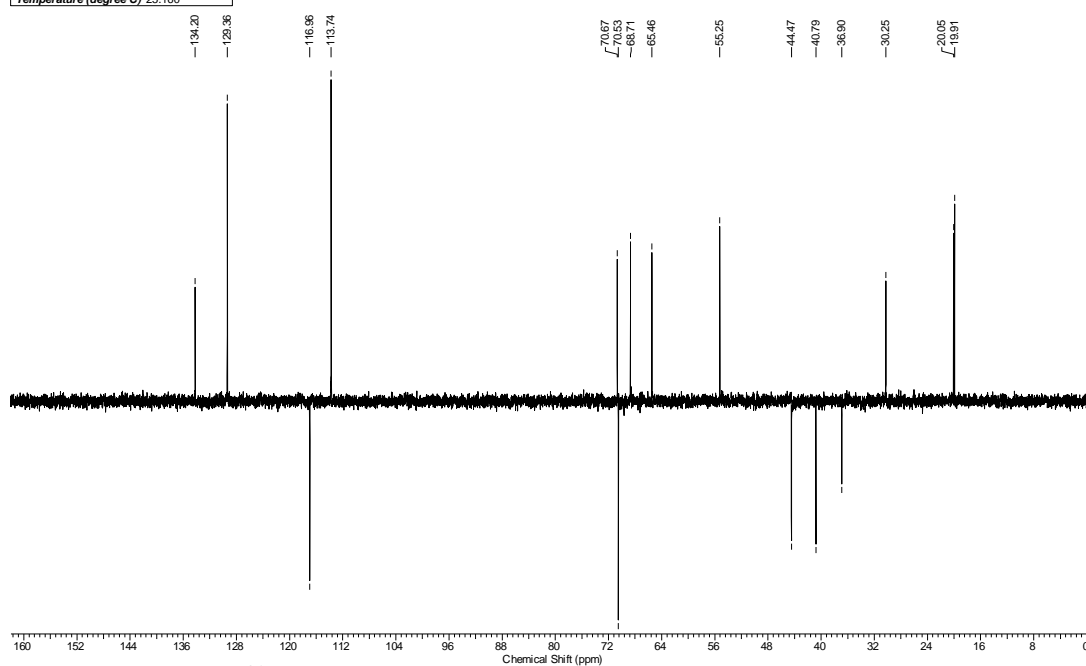
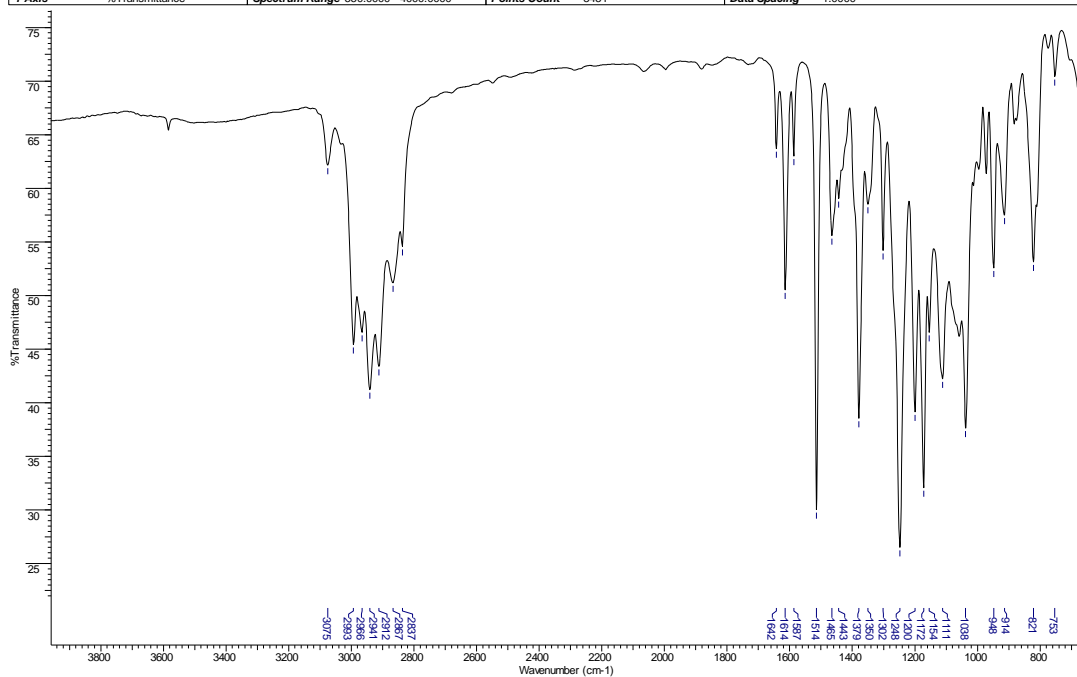


Figure S15. ^{13}C NMR spectrum (DEPT 135) of **13** (100 MHz; CDCl_3).

Title	cial do Brasil (GMT-3:00)	Origin	cial do Brasil (GMT-3:00)	File Name	E:\MESTRADO\IV PAULA\PKK17.SP
Date Stamp	mon jul 15 17:58:48 2013 Hora oficial do Brasil (GMT-3:00)	Instrument	Spectrum Two	Date	mon jul 15 17:58:48 2013 Hora oficial do Brasil (GMT-3:00)
Technique	Infrared	Spectral Range	550.0000 - 4000.0000	Spectral Region	IR
Y Axis	%Transmittance	Points Count	3451	X Axis	Wavenumber (cm-1)
				Data Spacing	1.0000



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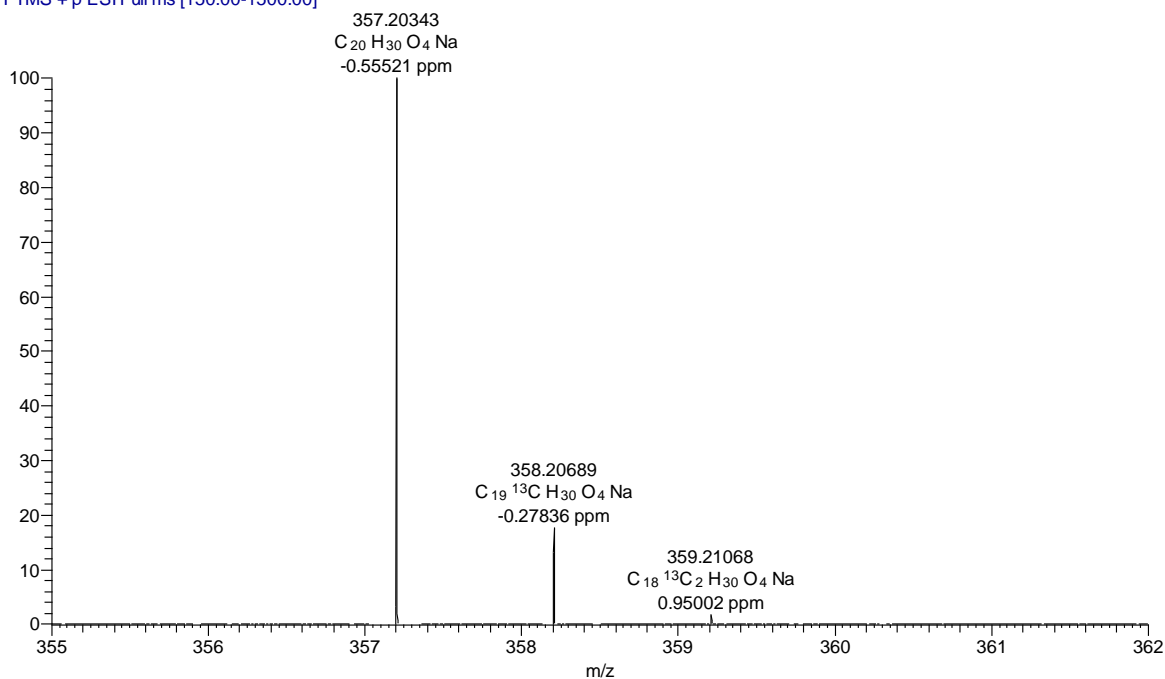


Figure S16. IR and HRMS spectra of **13**.

Acquisition Time (sec)	1.6384	Comment	Paula - PKK 15 - CDCl3 - Avance 500 MHz - abr12pkkH2 - 1H	Date	15 Apr 2013 07:43:16
File Name	F:\Mestrado\Espectros RMN\500\abr12pkkH2 (PKK16)_001001r	Frequency (MHz)	499.87	Nucleus	1H
Number of Transients	16	Original Points Count	16384	Points Count	65536
Solvent	CHLOROFORM-D	Sweep Width (Hz)	10000.00	Temperature (degree C)	25.151
				Pulse Sequence	zg30

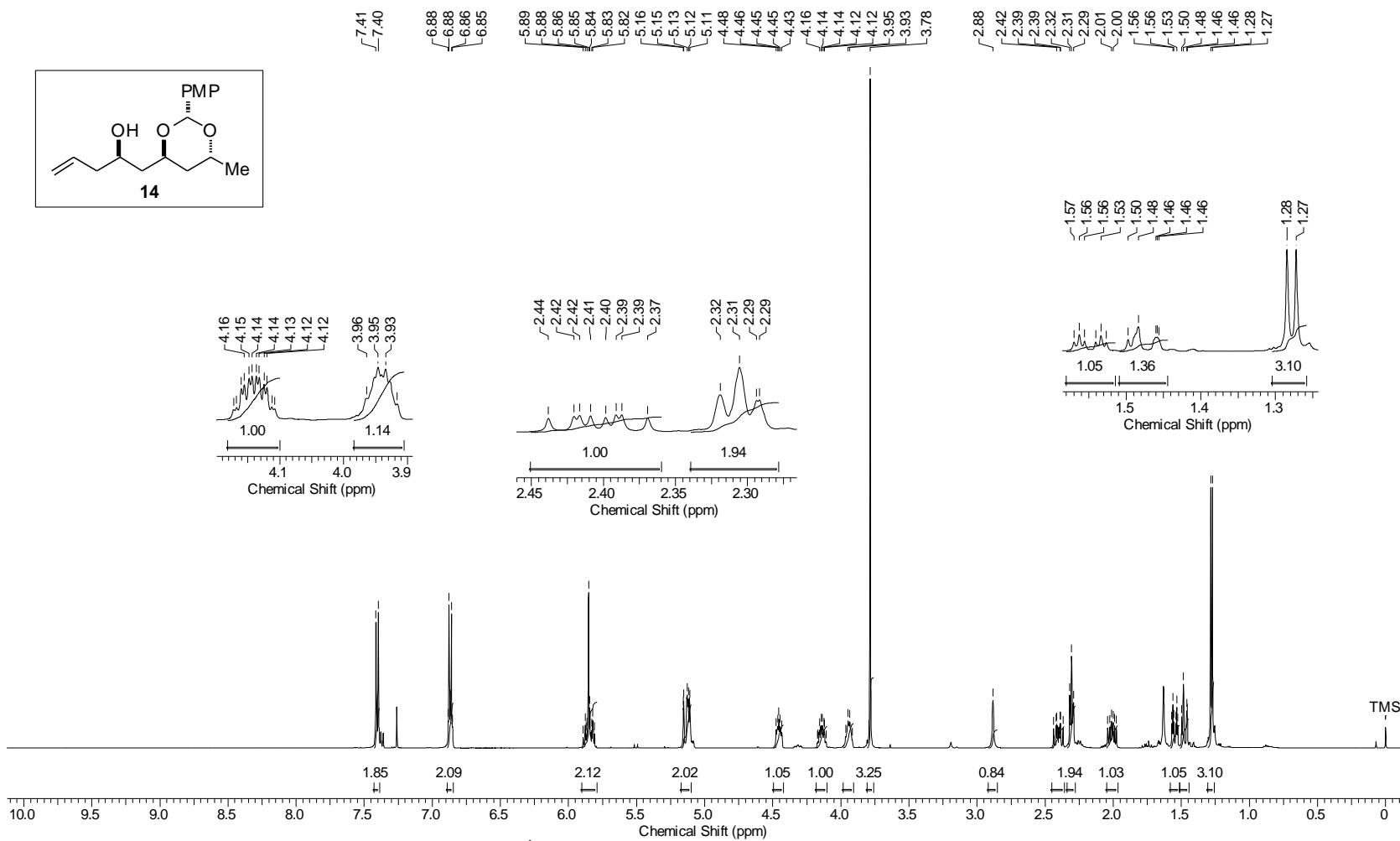


Figure S17. ¹H NMR spectrum of **14** (500 MHz; CDCl₃).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK 15 - CDCl3 - Avance 500 MHz - abr12pkkH2 - 13C	Date	12 Apr 2013 08:43:16		
File Name	F:\Mestrado\Espectros	RMN500\abr12pkkH2 (PKK15)_002001r	Frequency (MHz)	125.69	Nucleus	13C	
Number of Transients	512	Original Points Count	16384	Points Count	32768	Pulse Sequence	zpgq30
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.175		

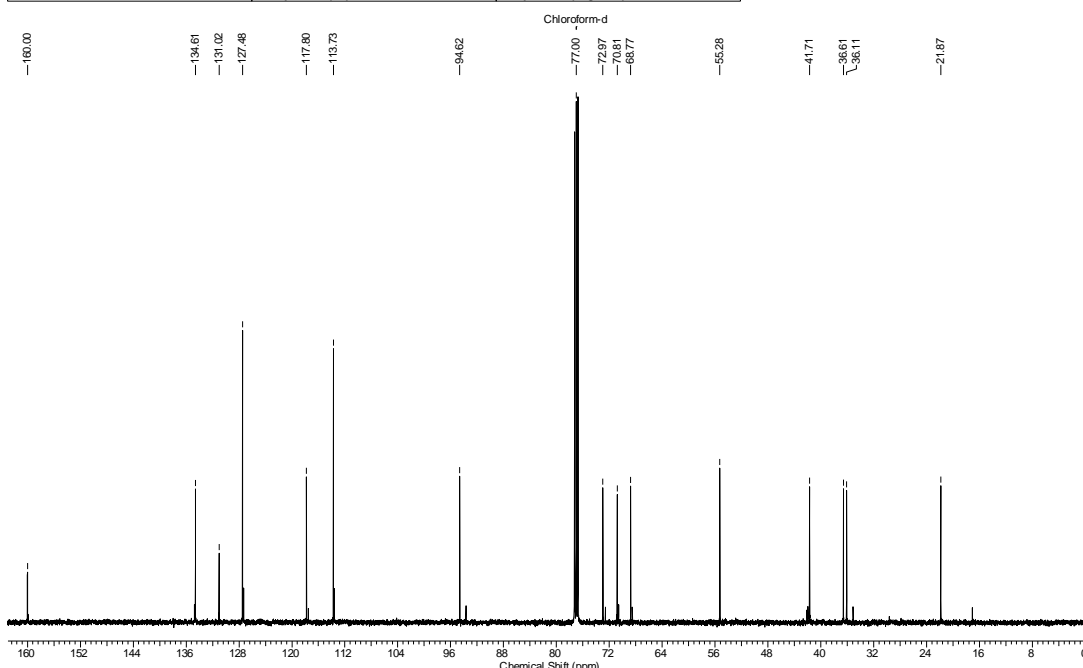


Figure S18. ^{13}C NMR spectrum of **14** (125 MHz; CDCl_3).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK 15 - CDCl3 - Avance 500 MHz - abr12pkkH2 - DEPT 135	Date	12 Apr 2013 09:23:06		
File Name	F:\Mestrado\Espectros	RMN500\abr12pkkH2 (PKK15)_003001r	Frequency (MHz)	125.69	Nucleus	13C	
Number of Transients	256	Original Points Count	16384	Points Count	32768	Pulse Sequence	dept135
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.159		

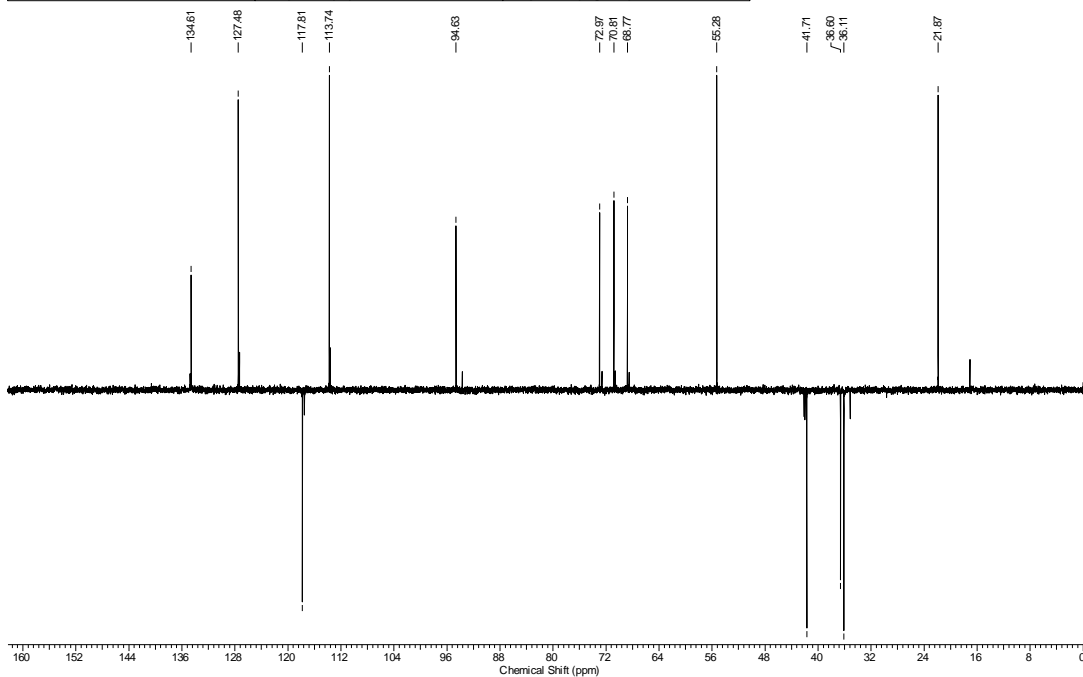


Figure S19. ^{13}C NMR spectrum (DEPT 135) of **14** (125 MHz; CDCl_3).

Paula - PKK 15 - CDC13 - Avance 500 MHz - abr15pkkH1- COSY

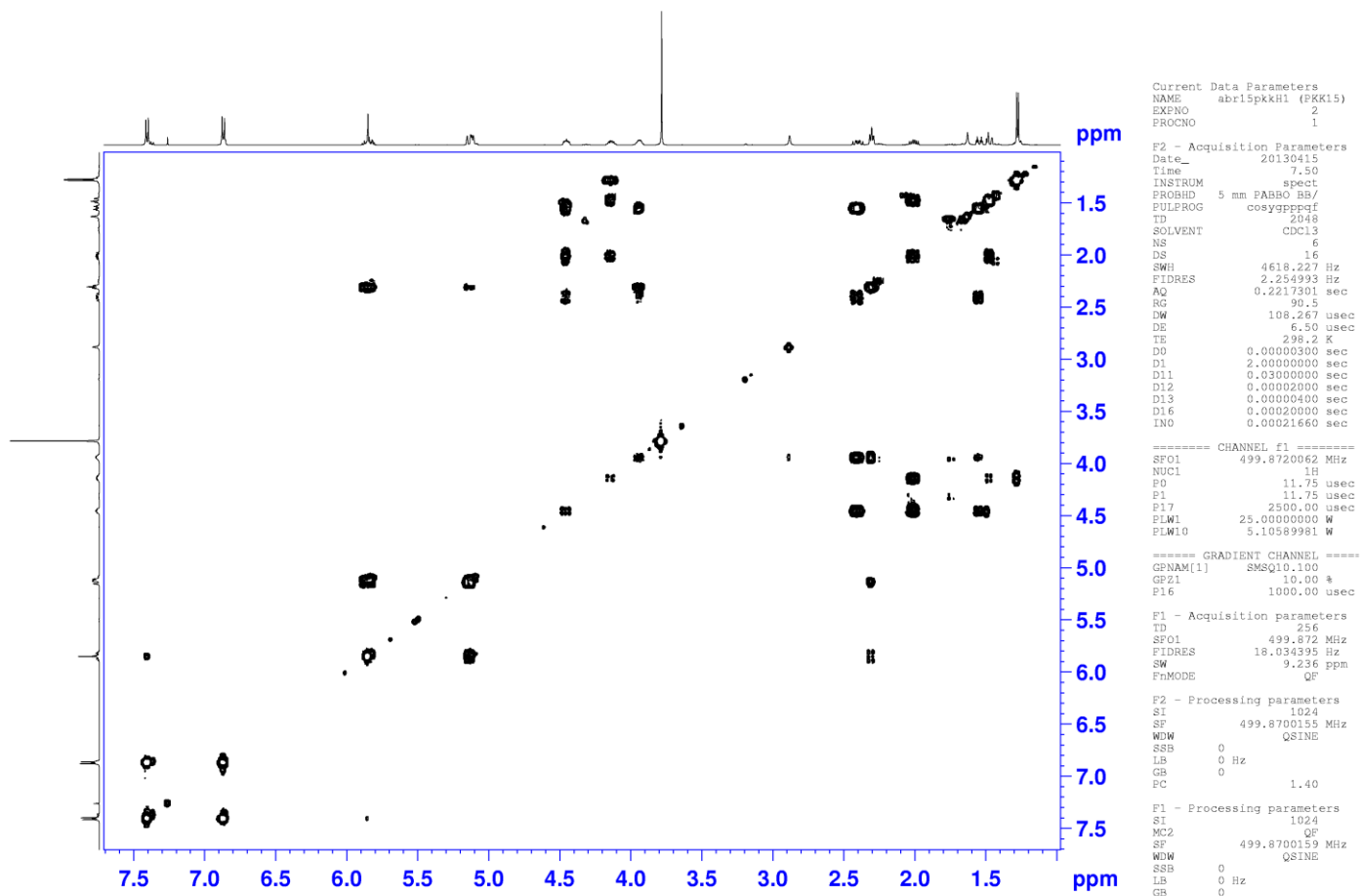


Figure S20. COSY contour map for 14.

Paula - PKK 15 - CDC13 - Avance 500 MHz - abr15pkkH1- HSQC

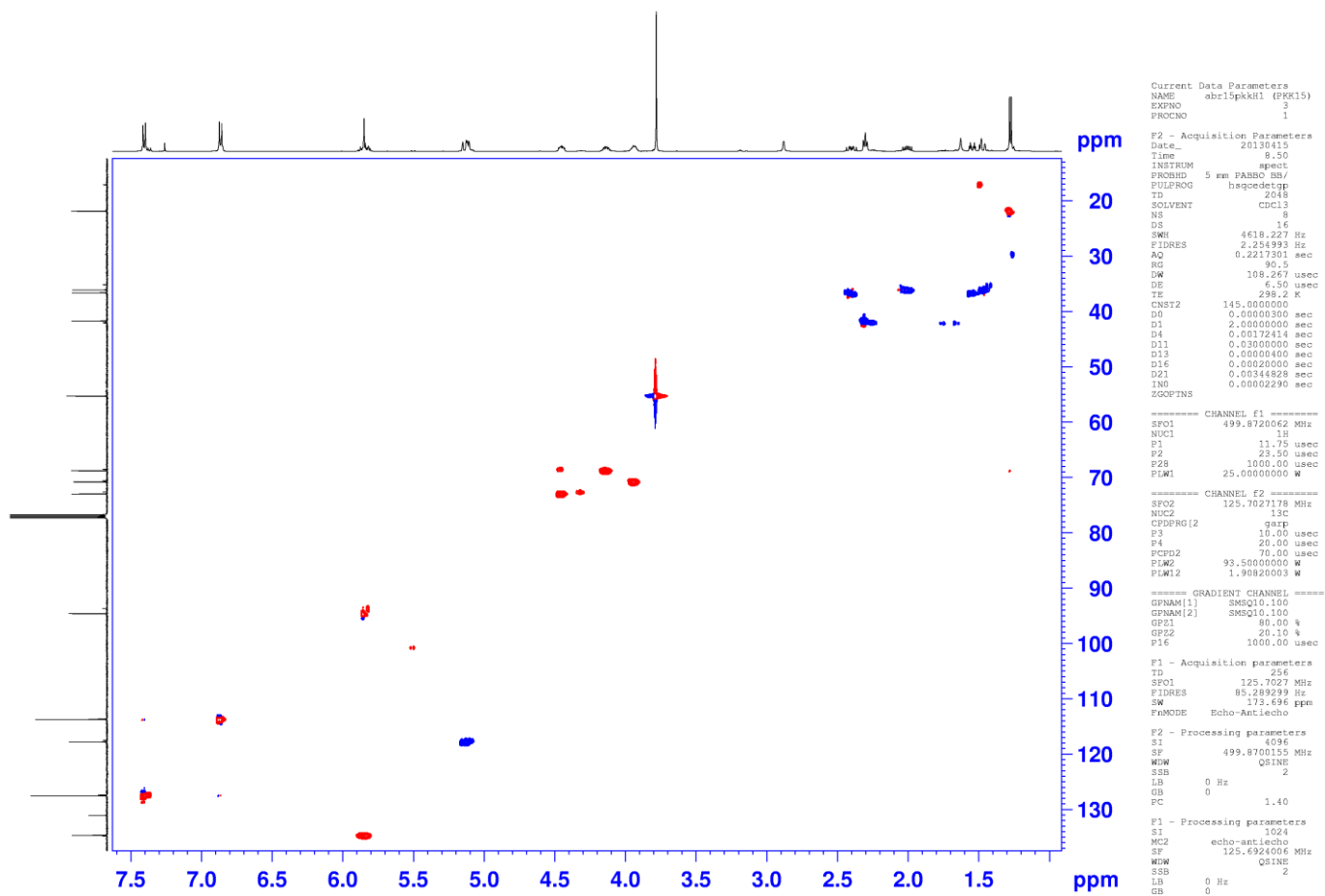


Figure S21. HSQC contour map for 14.

Paula - PKK 15 - CDC13 - Avance 500 MHz - abr15pkkH1- HMBC

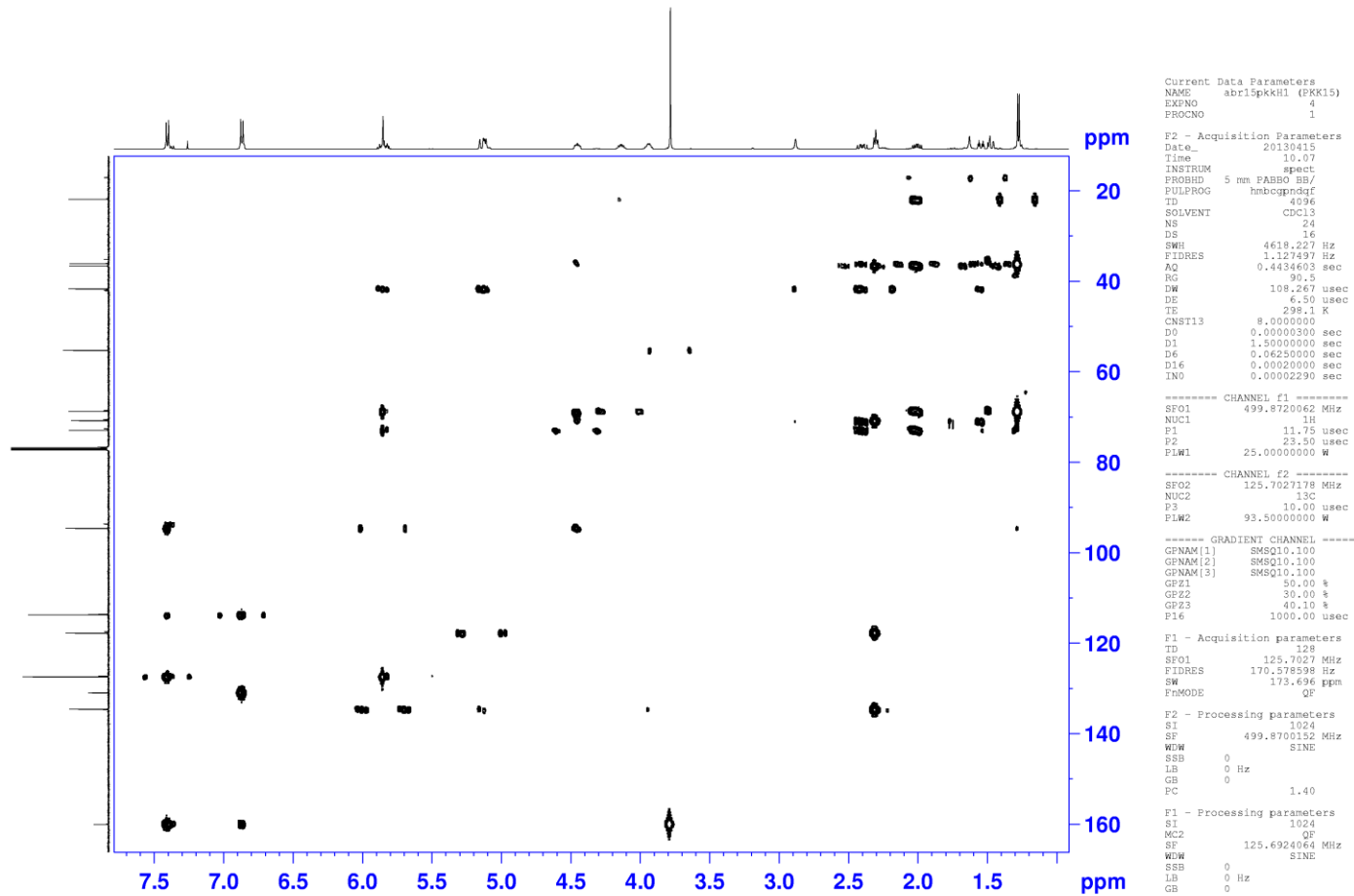
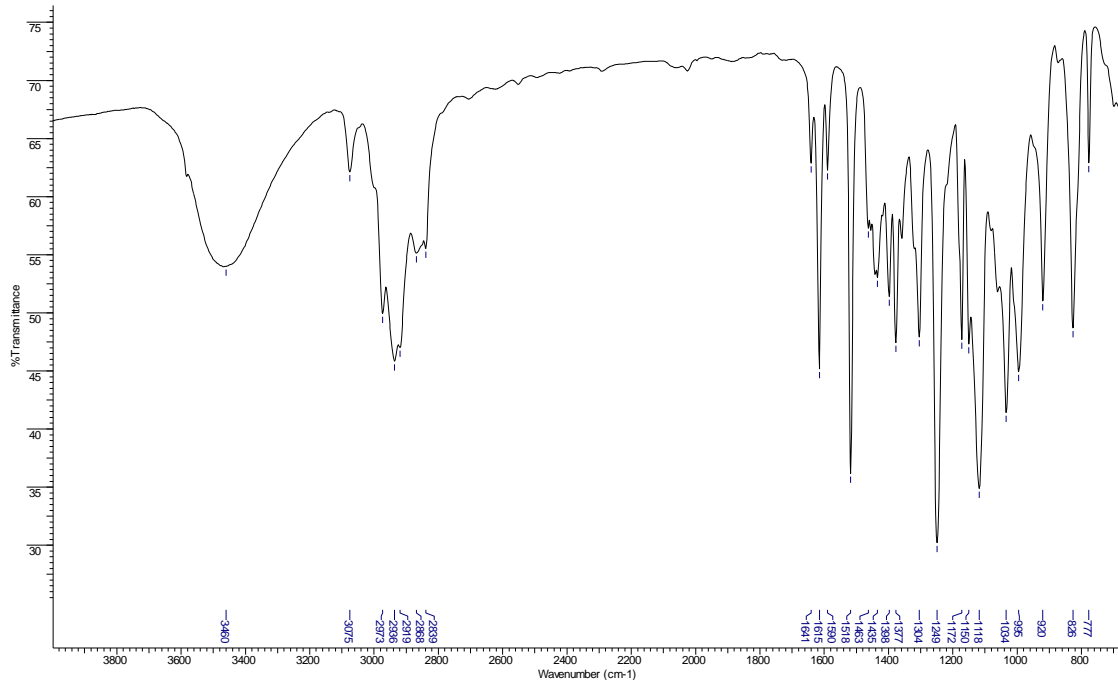


Figure S22. HMBC contour map for 14.

Title	cial do Brasil (GMT-3:00)	Comment	Amostra 003 por LOOS data segunda-feira, julho 15 2013	Origin	cial do Brasil (GMT-3:00)
File Name	E:\MESTRADO\IV PAULA\PKK15.SP	Date Stamp	mon jul 15 17:49:52 2013 Hora oficial do Brasil (GMT-3:00)		
Date	mon jul 15 17:49:52 2013 Hora oficial do Brasil (GMT-3:00)	Technique	Infrared	Instrument	Spectrum Two
Spectral Region	IR	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Points Count	3451	Data Spacing	1.0000	Spectrum Range	550.0000 - 4000.0000



C013 #8 RT: 0.11 AV: 1 NL: 9.09E6
T: FTMS + p ESI Full ms [150.00-1500.00]

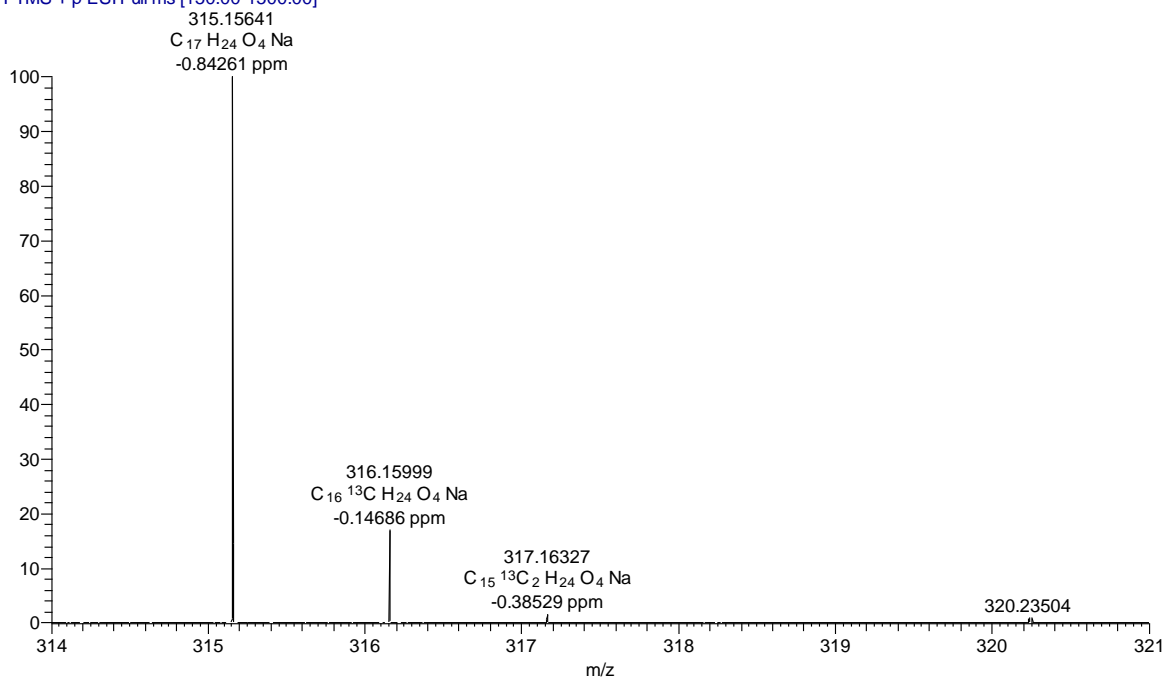


Figure S23. IR and HRMS spectra of 14.

Acquisition Time (sec)	3.1654	Comment	PKK69 250MHz nov27pkkH2	Date	27 Nov 2013 13:45:12
File Name	F:\Mestrado\Espectros RMN\250\nov27pkkH2 (PKK69)_001001r			Frequency (MHz)	250.13
Nucleus	1H	Number of Transients	16	Original Points Count	16384
Pulse Sequence	zg30	Solvent	CHLOROFORM-D	Points Count	32768
Temperature (degree C)	25.160			Sweep Width (Hz)	5175.98

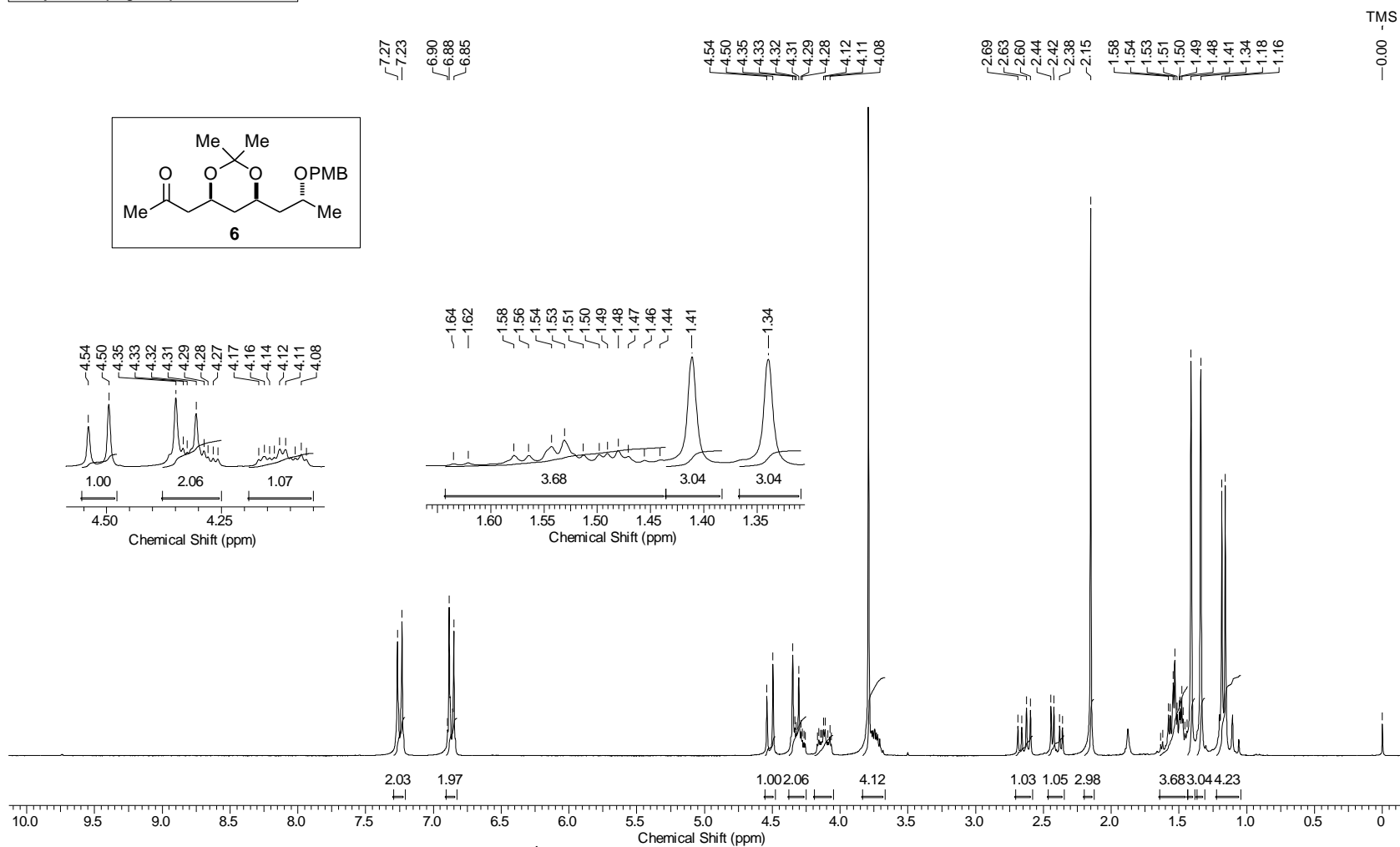


Figure S24. ¹H NMR spectrum of **6** (250 MHz; CDCl₃).

Acquisition Time (sec)	0.5439	Comment	PKK69 250MHz nov24pkkC1	Date	06 Mar 2014 16:43:06
File Name	C:\Users\Usuário\Documents\Unicamp\Mestrado\Espectros RMN1250\nov24pkkC1 (PKK69 C)_001001r	Frequency (MHz)	62.90	Nucleus	13C
Nucleus	13C	Number of Transients	10000	Original Points Count	8192
Pulse Sequence	zpgg30	Solvent	CHLOROFORM-D	Sweep Width (Hz)	15060.24
				Points Count	32768
				Temperature (degree C)	25.160

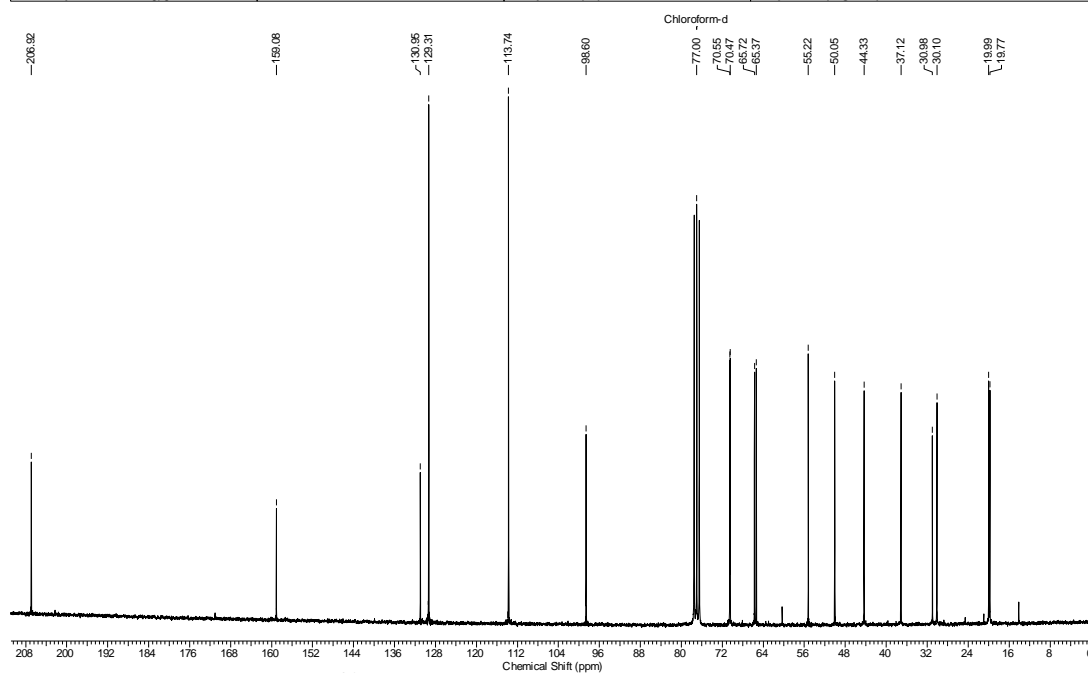


Figure S25. ^{13}C NMR spectrum of **6** (62.5 MHz; CDCl_3).

Acquisition Time (sec)	0.5439	Comment	PKK69 250MHz nov24pkkC1 dept135	Date	25 Nov 2013 07:38:44
File Name	F:\Mestrado\Espectros RMN250\nov24pkkC1 (PKK69)_002001r	Frequency (MHz)	62.90	Nucleus	13C
Number of Transients	5000	Original Points Count	8192	Points Count	32768
Solvent	CHLOROFORM-D	Sweep Width (Hz)	15060.24	Pulse Sequence	dept135
				Temperature (degree C)	25.160

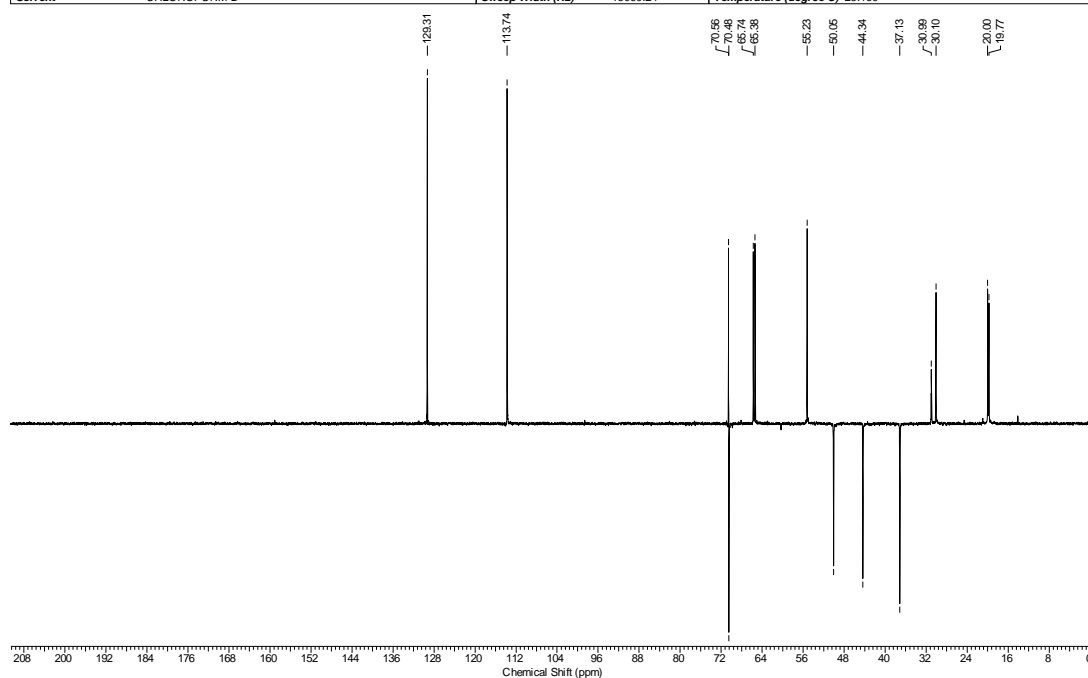
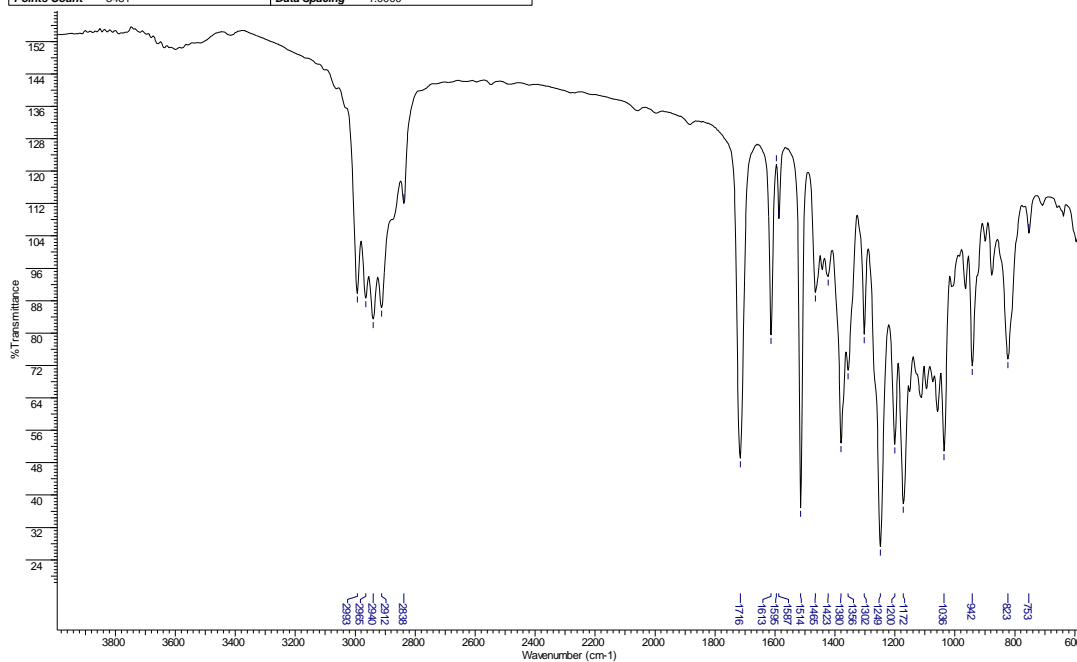


Figure S26. ^{13}C NMR spectrum (DEPT 135) of **6** (62.5 MHz; CDCl_3).

Title	brasileiro de verão (GMT-2:00)	Comment	Amostra 014 por LQOS data sexta-feira, dezembro 20 2013	Origin	brasileiro de verão (GMT-2:00)
File Name	E:\MESTRADO\IV PAULA\PKK69.SP	Date Stamp	fri dec 20 10:43:36 2013 Horário brasileiro de verão (GMT-2:00)	Technique	Infrared
Date	fri dec 20 10:43:36 2013 Horário brasileiro de verão (GMT-2:00)	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Spectral Region	IR	Data Spacing	1.0000	Instrument	Spectrum Two
Points Count	3451			Spectrum Range	550.0000 - 4000.0000



C002 #16 RT: 0.25 AV: 1 NL: 7.32E7
T: FTMS + p ESI Full ms [150.00-1500.00]

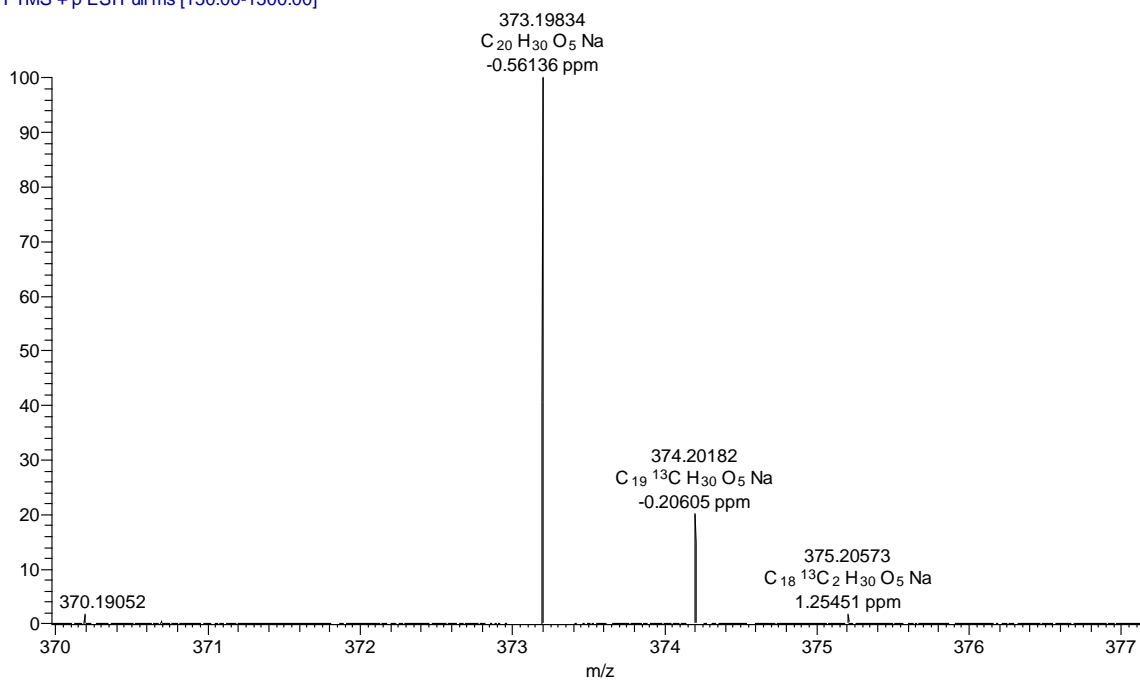


Figure S27. IR and HRMS spectra of 6.

Acquisition Time (sec)	1.6384	Comment	Paula - PKK 72 - C6D6 - Avance 500 MHz - dez02pkkH1 - 1H	Date	03 Dec 2013 07:28:20
File Name	E:\Mestrado\Espectros RMN\500\dez02pkkH1 (PKK72)_001001r	Frequency (MHz)	499.87	Nucleus	1H
Number of Transients	16	Original Points Count	16384	Points Count	65536
Solvent	BENZENE-D6	Sweep Width (Hz)	10000.00	Temperature (degree C)	25.154

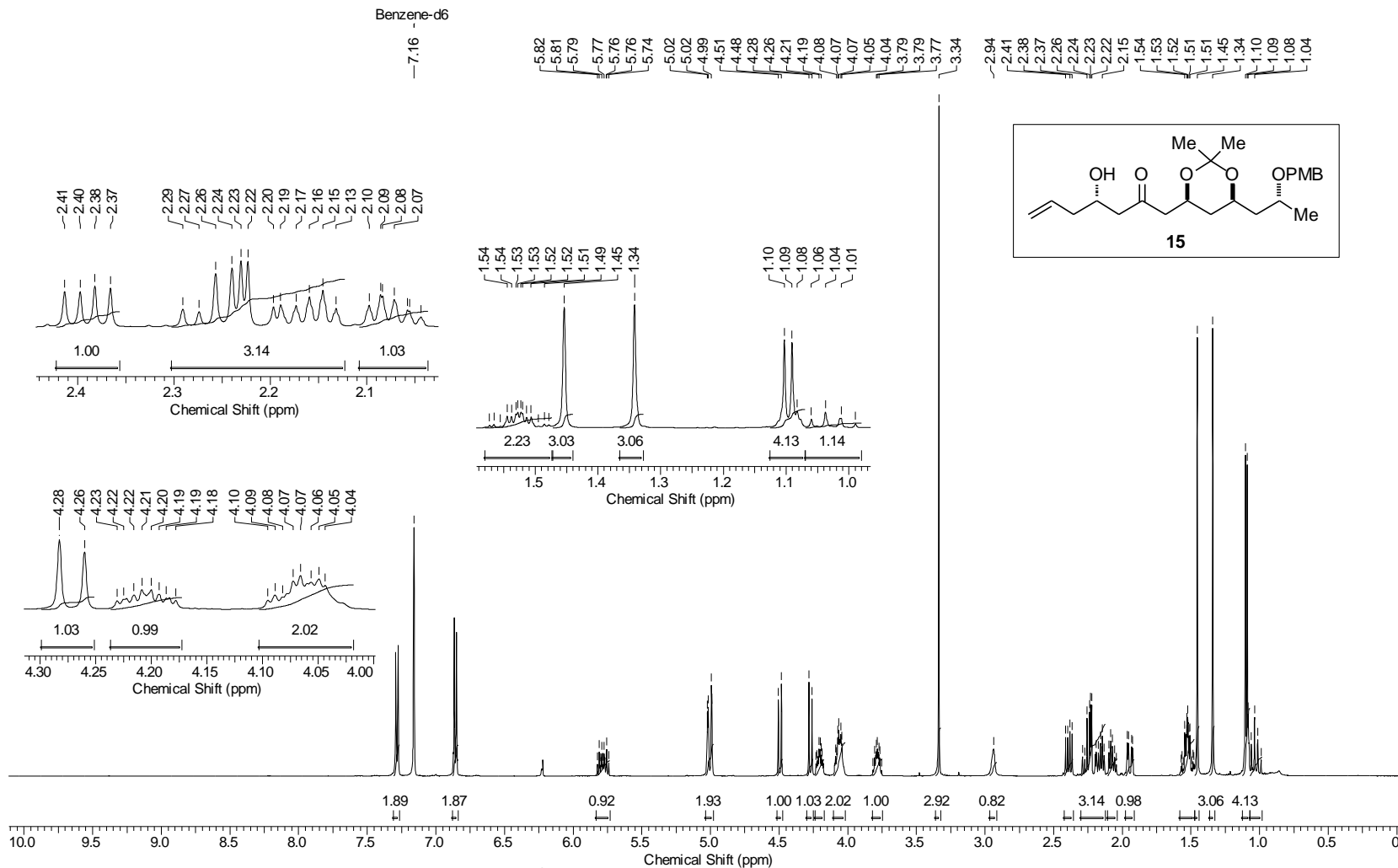


Figure S28. ^1H NMR spectrum of **15** (500 MHz; C_6D_6).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK 72 - C6D6 - Avance 500 MHz - dez02pkkH1 - 13C	Date	03 Dec 2013 07:28:30
File Name	E:\Mestrado\Espectros\RMN500\dez02pkkH1 (PKK72)_002001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	919	Original Points Count	16384	Points Count	32768
Solvent	BENZENE-D6	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.147

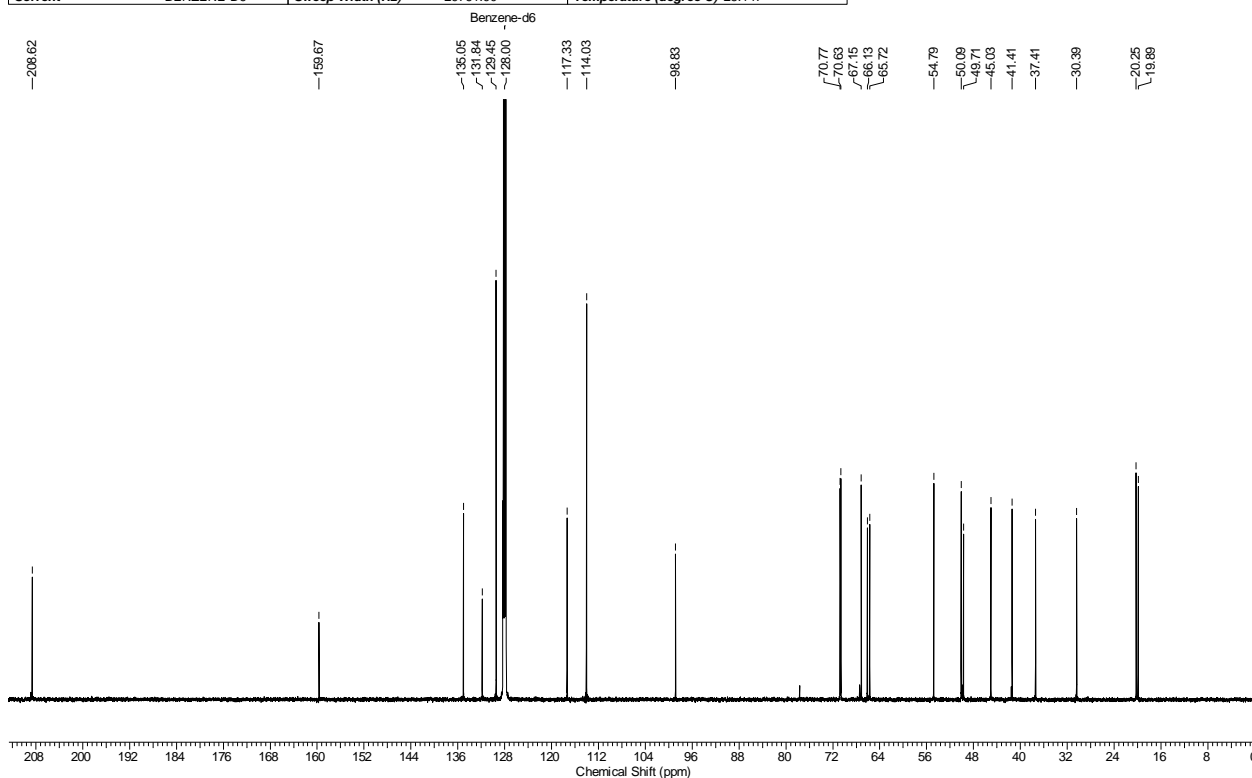


Figure S29. ^{13}C NMR spectrum of **15** (125 MHz; C_6D_6).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK 72 - C6D6 - Avance 500 MHz - dez02pkkH1 - DEP 135	Date	03 Dec 2013 07:28:40
File Name	E:\Mestrado\Espectros\RMN500\dez02pkkH1 (PKK72)_003001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	512	Original Points Count	16384	Points Count	32768
Solvent	BENZENE-D6	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.139

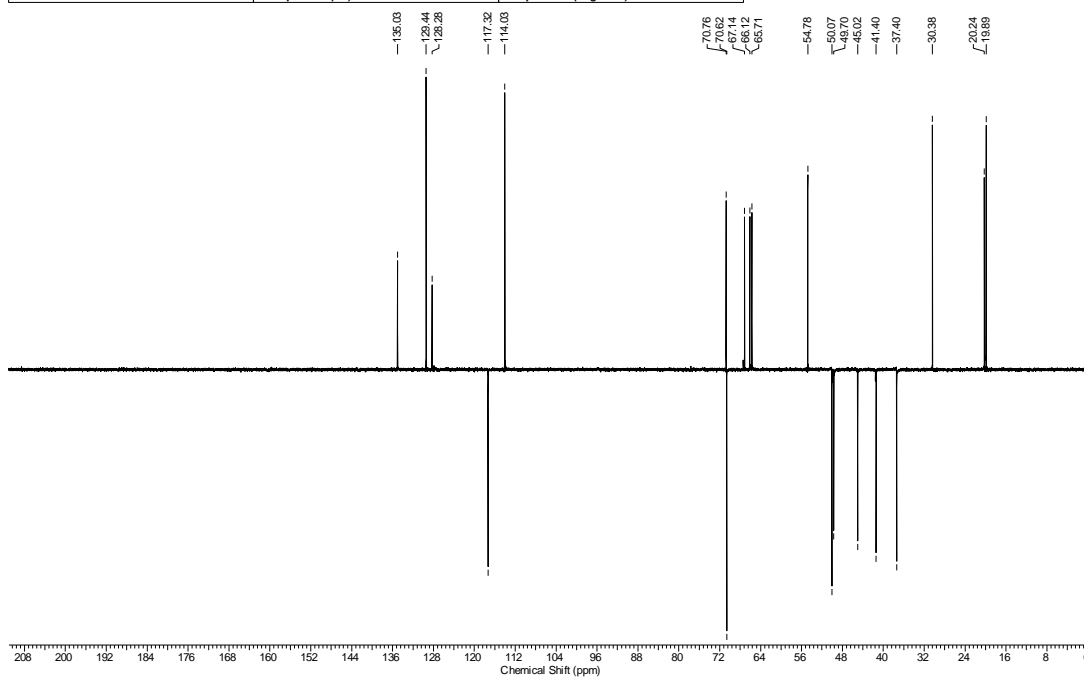
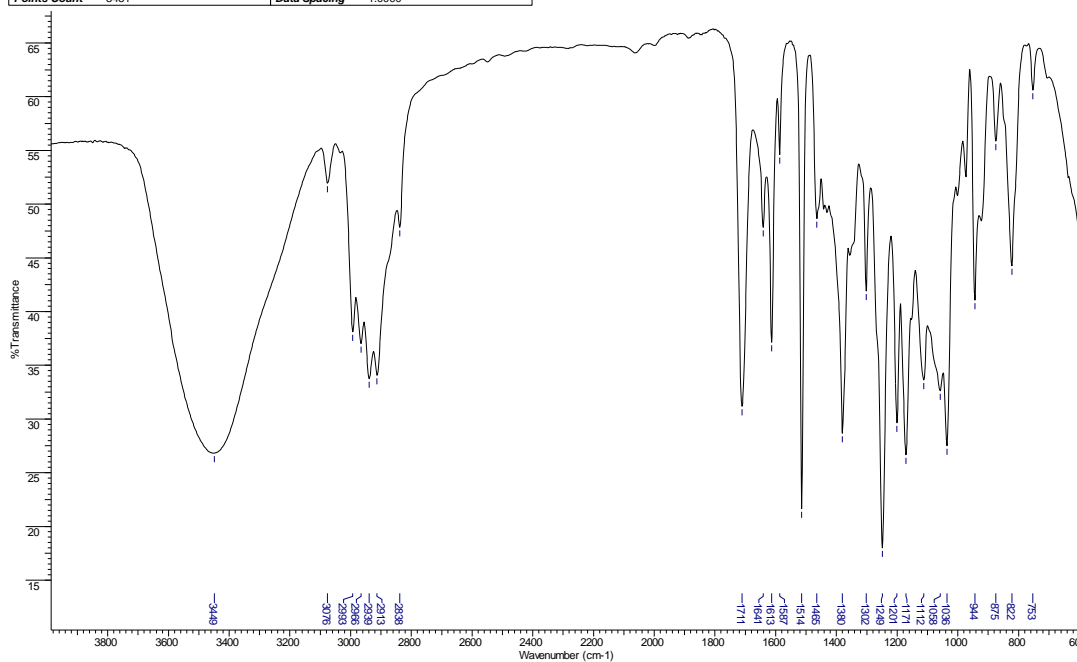


Figure S30. ^{13}C NMR spectrum (DEPT 135) of **15** (125 MHz; C_6D_6).

Title	brasileiro de verão (GMT-2:00)	Comment	Amostra 006 por LQOS data sexta-feira, dezembro 20 2013	Origin	brasileiro de verão (GMT-2:00)
File Name	E:\MESTRADO\IV PAULA\PKK72.SP	Date Stamp	fri dec 20 10:07:40 2013 Horário brasileiro de verão (GMT-2:00)	Instrument	Spectrum Two
Date	fri dec 20 10:07:40 2013 Horário brasileiro de verão (GMT-2:00)	Technique	Infrared	Spectrum Range	550.0000 - 4000.0000
Spectral Region	IR	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Points Count	3451	Data Spacing	1.0000		



C003 #53 RT: 0.80 AV: 1 NL: 9.34E7
T: FTMS + p ESI Full ms [150.00-1500.00]

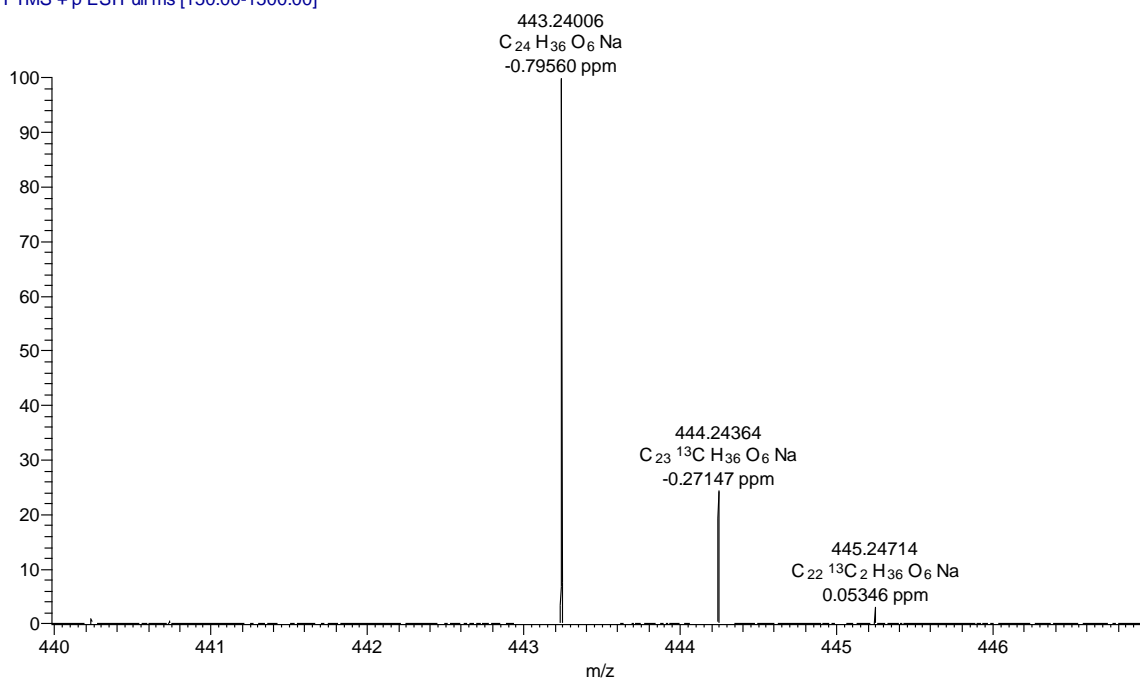


Figure S31. IR and HRMS spectra of 15.

Acquisition Time (sec)	1.6384	Comment	Paula "PKK-74" cdcl3/Av500MHz dez09pkkH1	Date	10 Dec 2013 08:08:14
File Name	E:\Mestrado\Espectros RMN\500\dez09pkkH1 (PKK74)_001001r	Frequency (MHz)	499.87	Nucleus	¹ H
Number of Transients	16	Original Points Count	16384	Points Count	65536
Solvent	CHLOROFORM-D	Sweep Width (Hz)	10000.00	Temperature (degree C)	25.138

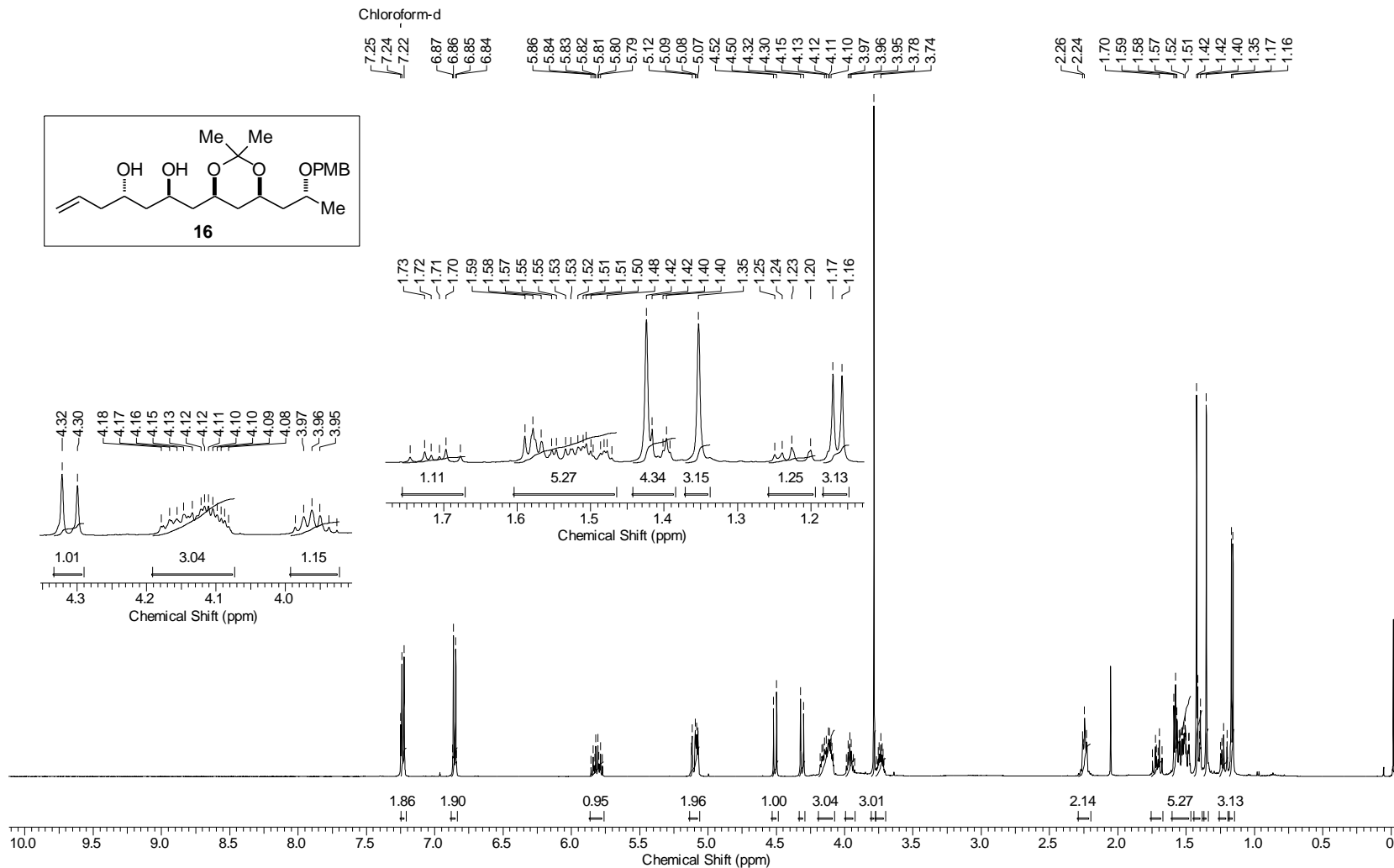


Figure S32. ¹H NMR spectrum of **16** (500 MHz; CDCl₃).

Acquisition Time (sec)	0.4981	Comment	Paula "PKK-98" cdc13/Av500MHz mar18pkkC1	Date	19 Mar 2014 07:39:16
File Name	F:\Mestrado\Espectros RMN500\mar18pkkC1_001001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	2048	Original Points Count	16384	Points Count	32768
Solvent	CHLOROFORM-D	Sweep Width (Hz)	32894.74	Pulse Sequence	zgpg
				Temperature (degree C)	25.145

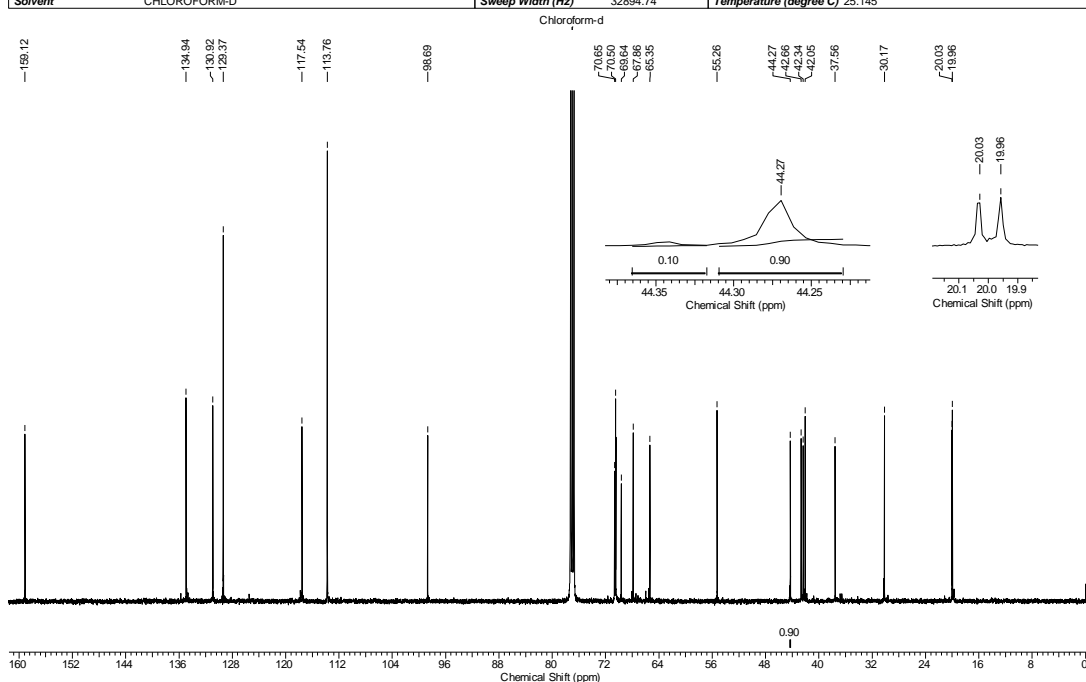


Figure S33. ^{13}C NMR spectrum of **16** (125 MHz; CDCl_3).

Acquisition Time (sec)	0.5505	Comment	Paula "PKK-74" cdc13/Av500MHz dez09pkkH1 - Dept135	Date	10 Dec 2013 08:08:38
File Name	E:\Mestrado\Espectros RMN500\dez09pkkH1 (PKK74)_003001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	1024	Original Points Count	16384	Points Count	32768
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.156
				Pulse Sequence	dept135

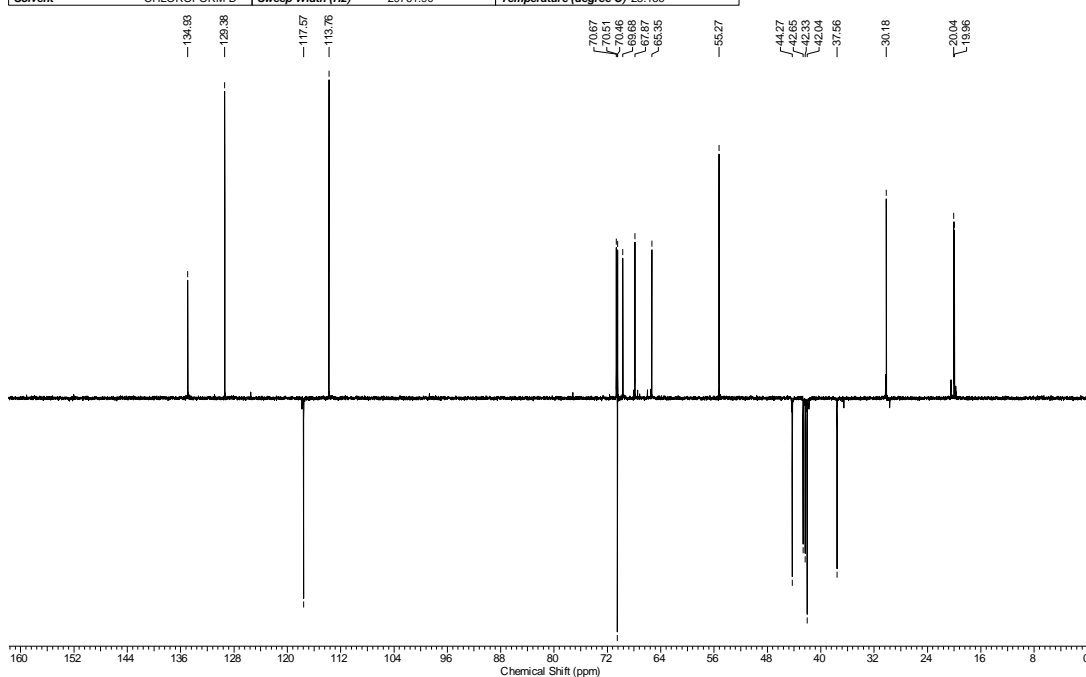
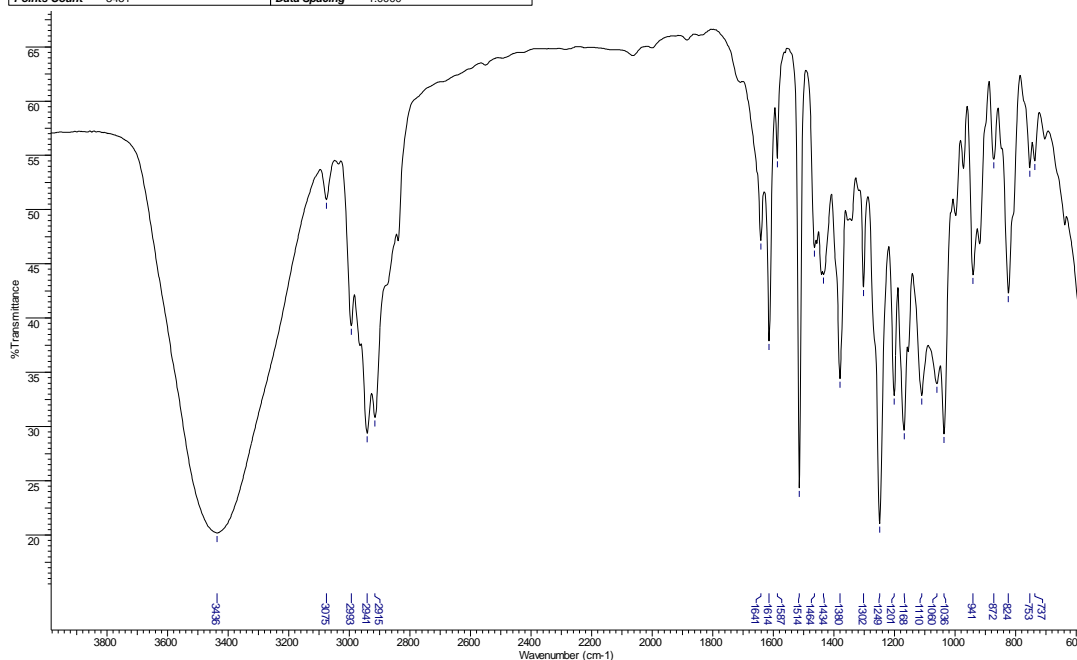


Figure S34. ^{13}C NMR spectrum (DEPT 135) of **16** (125 MHz; CDCl_3).

Title	brasileiro de verão (GMT-2:00)	Comment	Amostra 007 por LQOS data sexta-feira, dezembro 20 2013	Origin	brasileiro de verão (GMT-2:00)
File Name	E:\MESTRADO\IV PAULA\PKK74.SP	Date Stamp	fri dec 20 10:12:05 2013 Horário brasileiro de verão (GMT-2:00)	Instrument	Spectrum Two
Date	fri dec 20 10:12:05 2013 Horário brasileiro de verão (GMT-2:00)	Technique	Infrared	Y Axis	%Transmittance
Spectral Region	IR	X Axis	Wavenumber (cm-1)	Spectrum Range	550.0000 - 4000.0000
Points Count	3451	Data Spacing	1.0000		



C004 #20 RT: 0.30 AV: 1 NL: 1.04E8
T: FTMS + p ESI Full ms [150.00-1500.00]

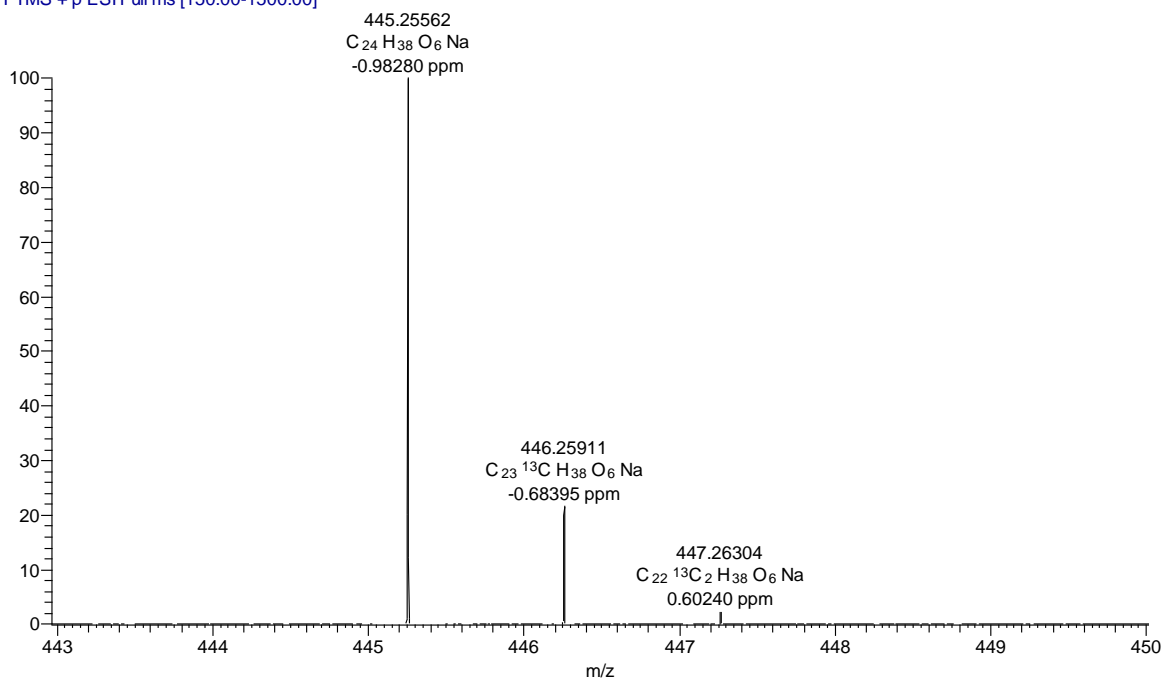
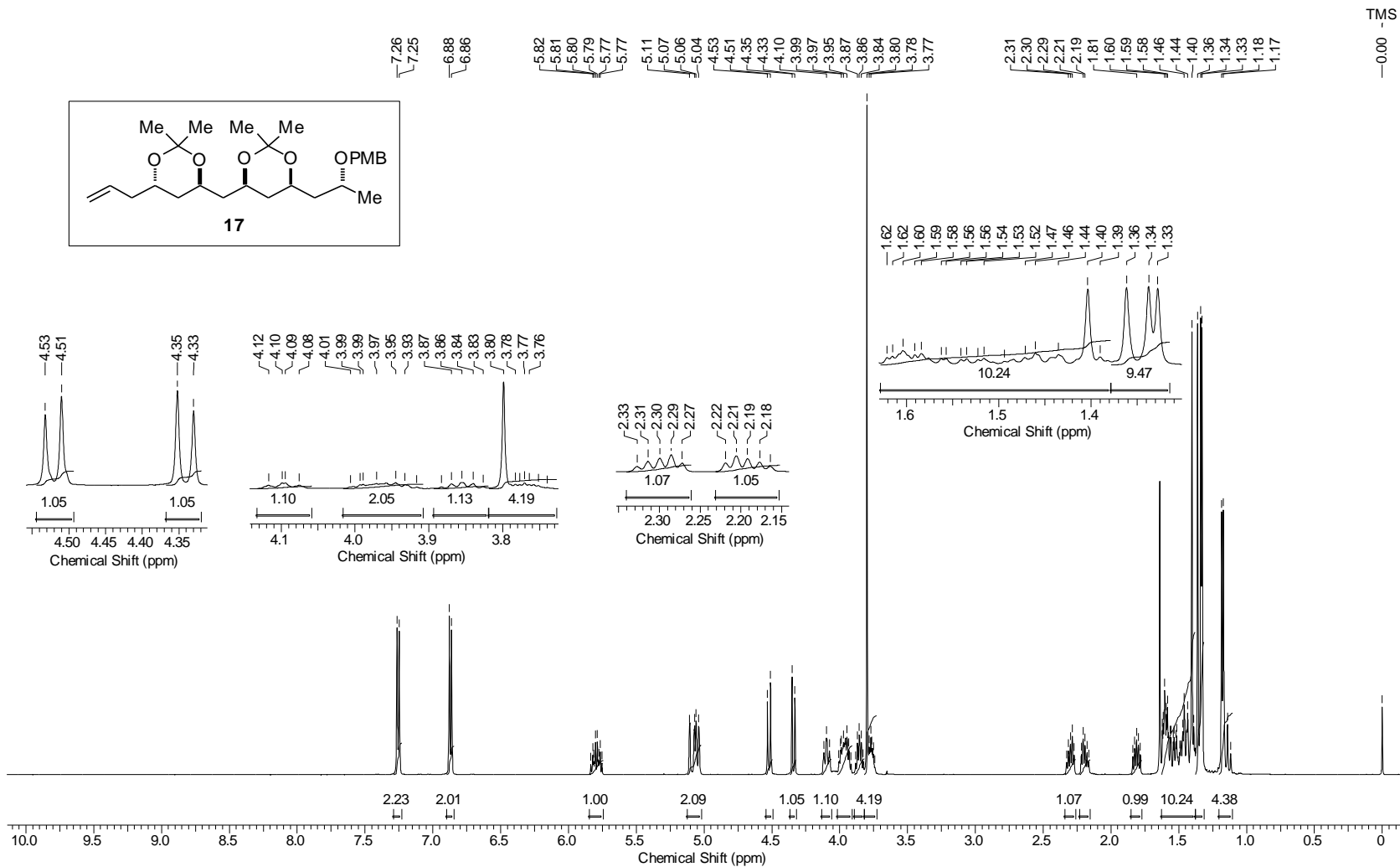


Figure S35. IR and HRMS spectra of 16.

Acquisition Time (sec)	1.6384	Comment	Paula - PKK99 - CDCI3 - Av 500 MHz - mar20pkkH2	Date	20 Mar 2014 10:54:36
File Name	F:\Mestrado\Espectros RMN\500\mar20pkkH2 (PKK99)_001001r	Frequency (MHz)	499.87	Nucleus	1H
Number of Transients	16	Original Points Count	16384	Points Count	65536
Solvent	CHLOROFORM-D	Sweep Width (Hz)	10000.00	Temperature (degree C)	25.151
				Pulse Sequence	zg30



Acquisition Time (sec)	0.5505	Comment	Paula - PKK99 - CDCl ₃ - Av 500 MHz - mar20pkkH2 13C	Date	20 Mar 2014 11:22:54
File Name	F:\Mestrado\Espectros\RMN500\mar20pkkH2 (PKK99)_002001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	512	Original Points Count	16384	Points Count	32768
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.150

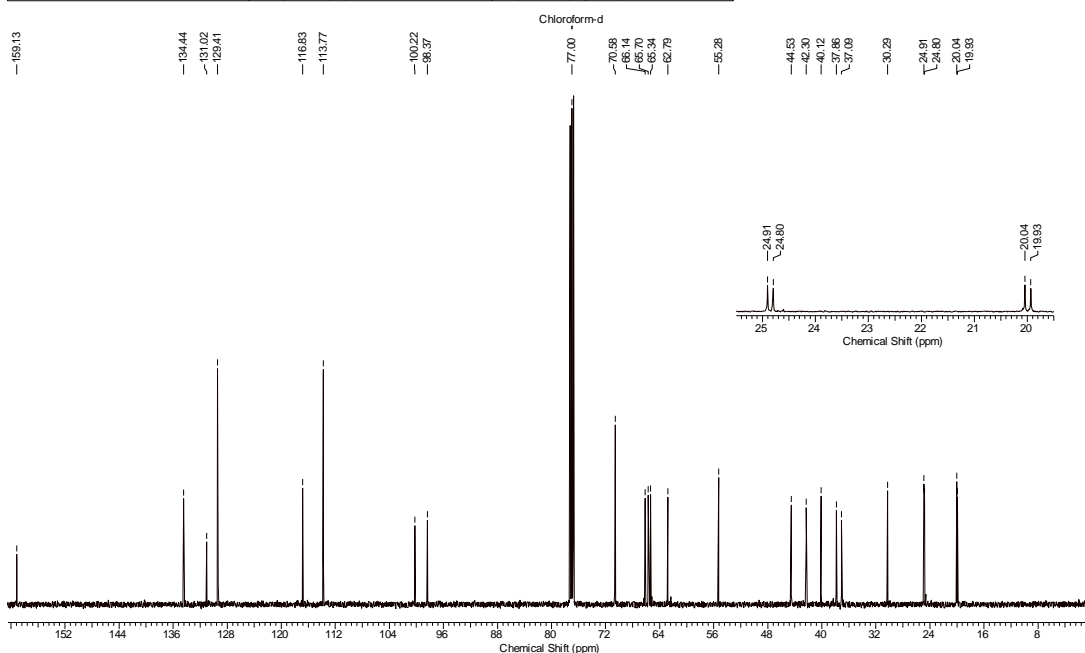


Figure S37. ¹³C NMR spectrum of **17** (125 MHz; CDCl₃).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK99 - CDCl ₃ - Av 500 MHz - mar20pkkH2 DEPT135	Date	20 Mar 2014 11:23:08
File Name	F:\Mestrado\Espectros\RMN500\mar20pkkH2 (PKK99)_003001r	Frequency (MHz)	125.69	Nucleus	13C
Number of Transients	128	Original Points Count	16384	Points Count	32768
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.147

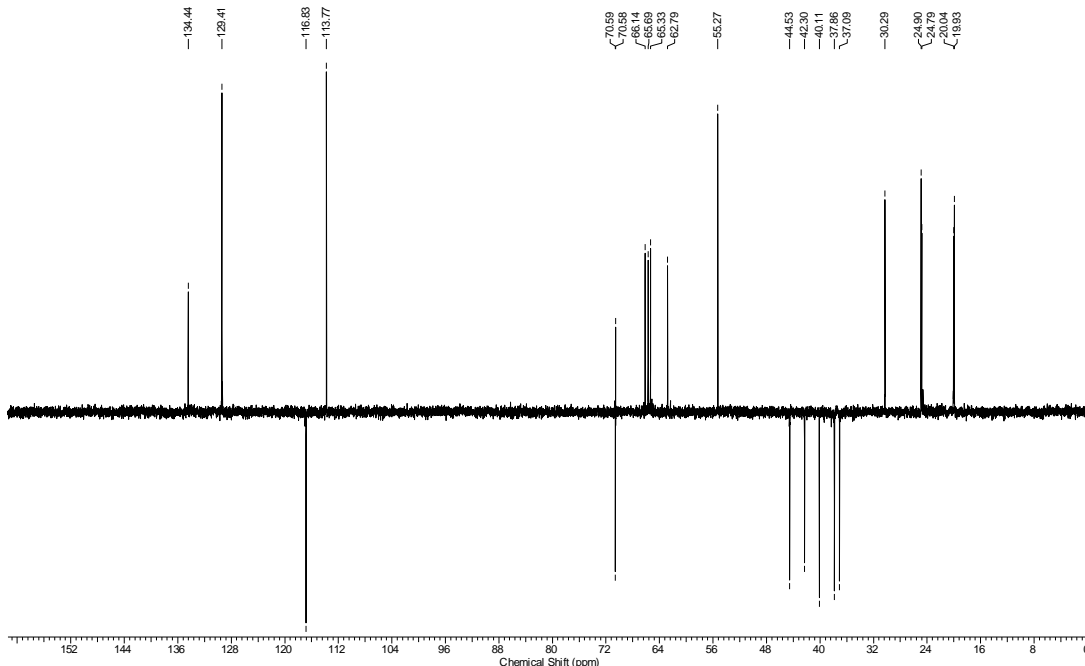
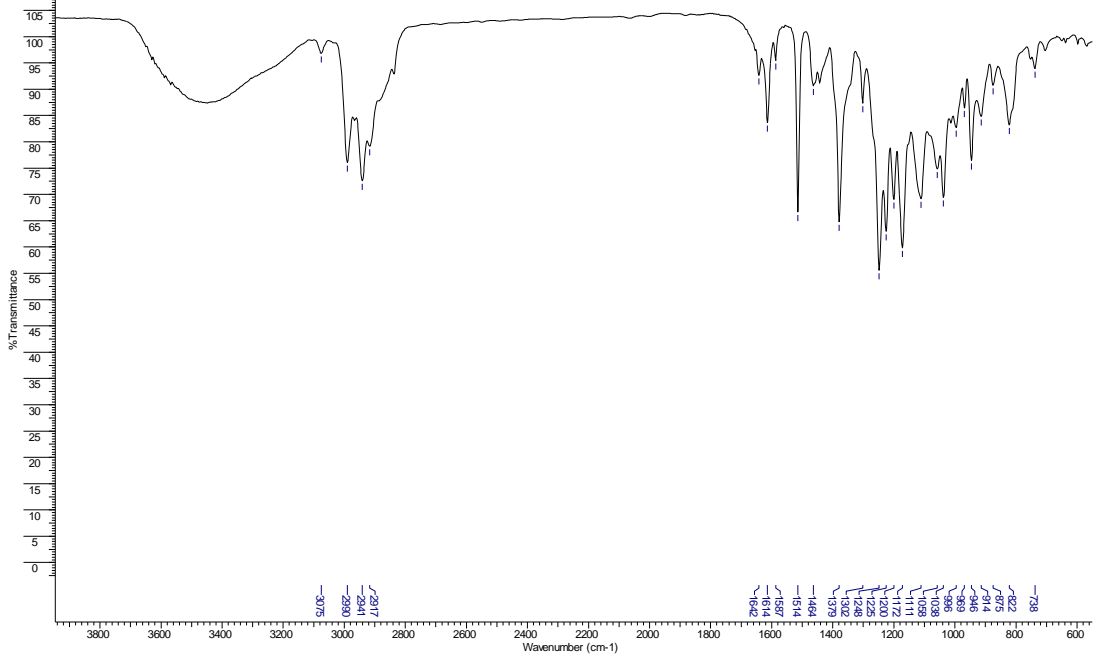


Figure S38. ¹³C NMR spectrum (DEPT 135) of **17** (125 MHz; CDCl₃).

Title	cial do Brasil (GMT-3:00)	Comment	Amostra 003 por LQOS data quarta-feira, abril 16 2014	Origin	cial do Brasil (GMT-3:00)
File Name	E:\MESTRADO\IV PAULA\PKK99_1.SP	Date Stamp	wed apr 16 15:05:17 2014 Hora oficial do Brasil (GMT-3:00)	Technique	Infrared
Date	wed apr 16 15:05:17 2014 Hora oficial do Brasil (GMT-3:00)	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Spectral Region	IR	Data Spacing	1.0000	Instrument	Spectrum Two
Points Count	3451			Spectrum Range	550.0000 - 4000.0000



C005 #16 RT: 0.24 AV: 1 NL: 3.94E7
T: FTMS + p ESI Full ms [150.00-1500.00]

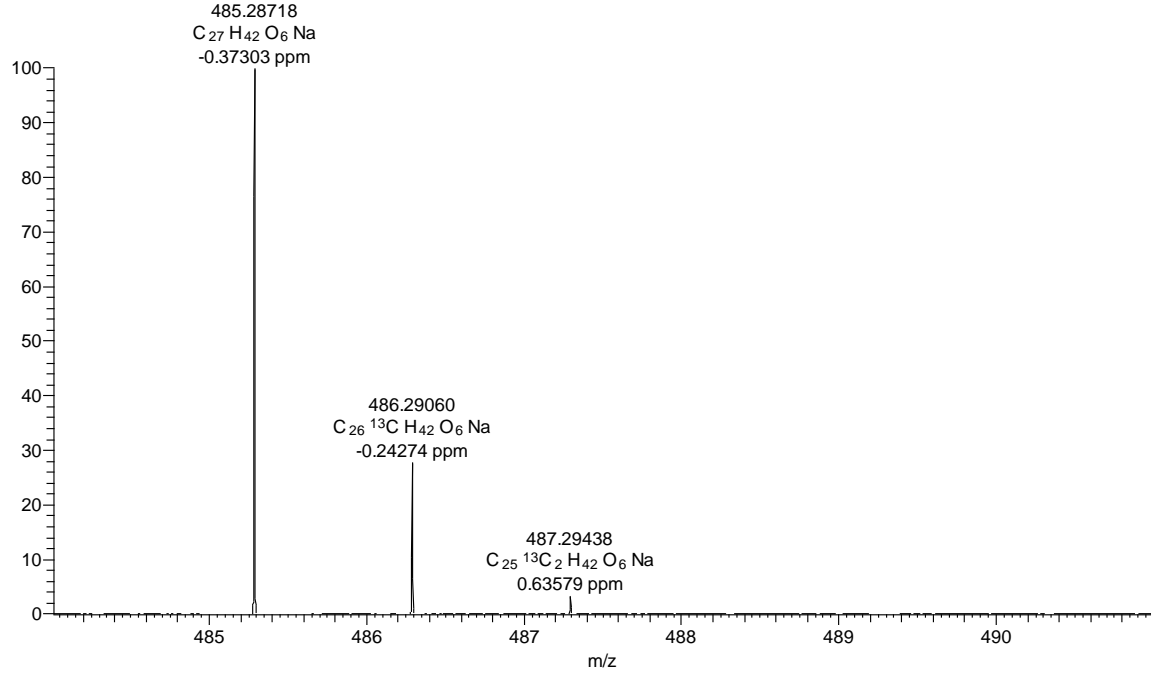


Figure S39. IR and HRMS spectra of 17.

Acquisition Time (sec)	1.6384	Comment	Paula "PKK-102" cd3od/Av500MHz_mar25pkkH2	Date	26 Mar 2014 07:34:36
File Name	\nrmrparc.iqm.unicamp.br/espectros\avance500\2014\mar14\Luiz Carlos\mar25pkkH2_001001r			Frequency (MHz)	499.87
Nucleus	1H	Number of Transients	16	Original Points Count	16384
Pulse Sequence	zg30	Solvent	MeOD	Sweep Width (Hz)	10000.00
				Points Count	65536
				Temperature (degree C)	25.147

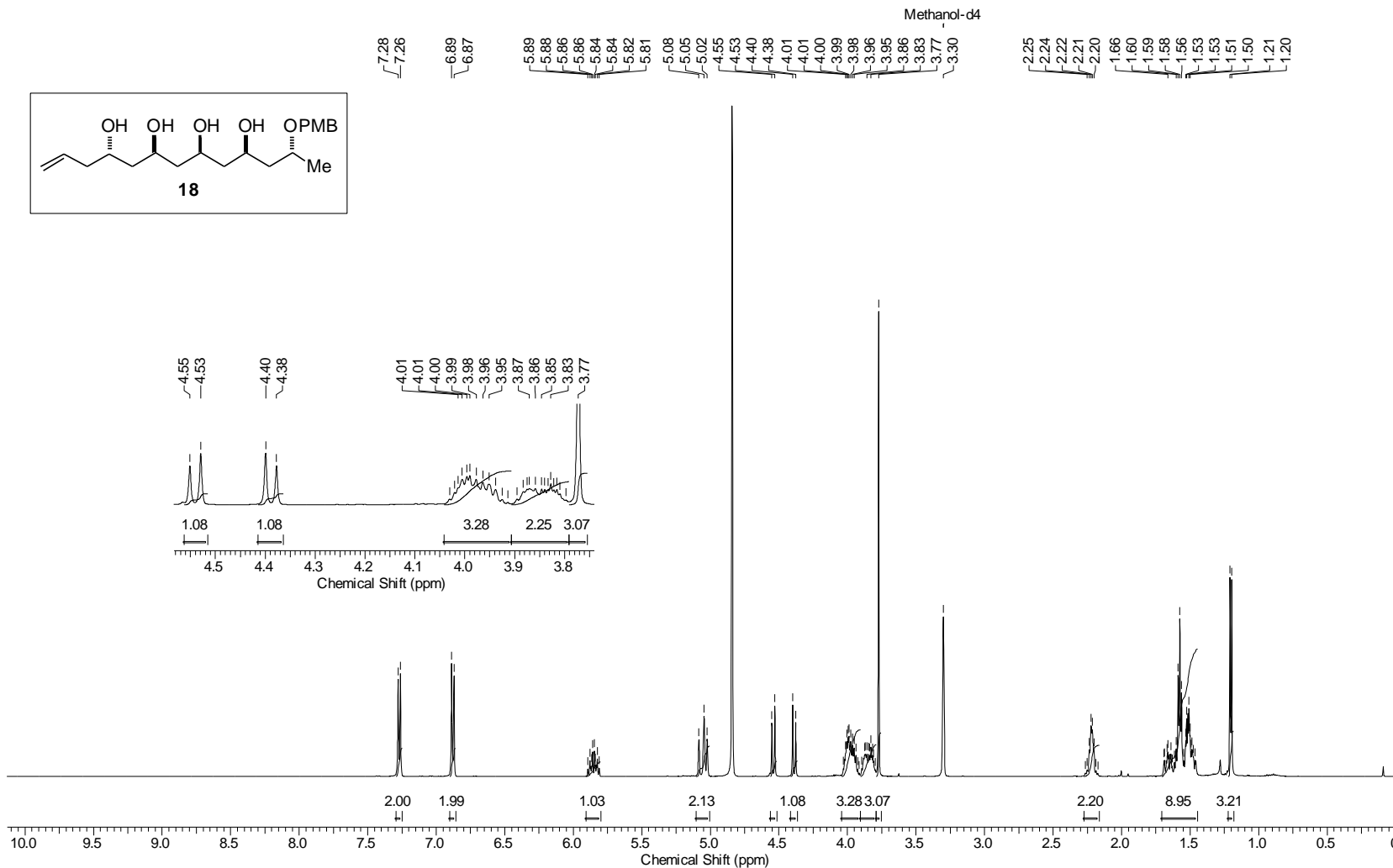


Figure S40. ¹H NMR spectrum of **18** (500 MHz; MeOD).

Acquisition Time (sec)	0.5505	Comment	Paula "PKK-102" cd3od/Av500MHz_mar25pkkH2 - 13C	Date	26 Mar 2014 07:34:48
File Name	\nmr\parc.igim.unicamp.br\espectros\avance500\2014\mar14\Luiz Carlos\mar25pkkH2_002001r	Number of Transients	2048	Frequency (MHz)	125.69
Nucleus	13C	Original Points Count	16384	Points Count	32768
Pulse Sequence	zpgg30	Solvent	MeOD	Sweep Width (Hz)	29761.90
				Temperature (degree C)	25.151

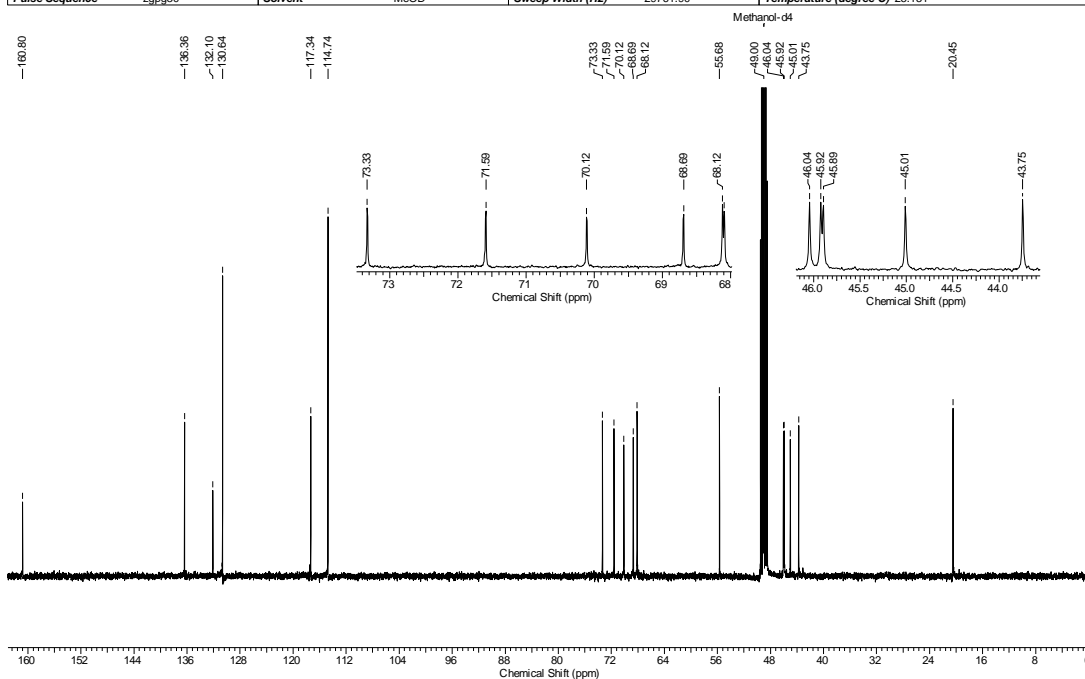


Figure S41. ^{13}C NMR spectrum of **18** (125 MHz; MeOD).

Acquisition Time (sec)	0.5505	Comment	Paula "PKK-102" cd3od/Av500MHz_mar25pkkH2 - Dept135	Date	26 Mar 2014 07:34:58
File Name	\nmr\parc.igim.unicamp.br\espectros\avance500\2014\mar14\Luiz Carlos\mar25pkkH2_003001r	Number of Transients	512	Frequency (MHz)	125.69
Nucleus	13C	Original Points Count	16384	Points Count	32768
Pulse Sequence	dept135	Solvent	MeOD	Sweep Width (Hz)	29761.90
				Temperature (degree C)	25.148

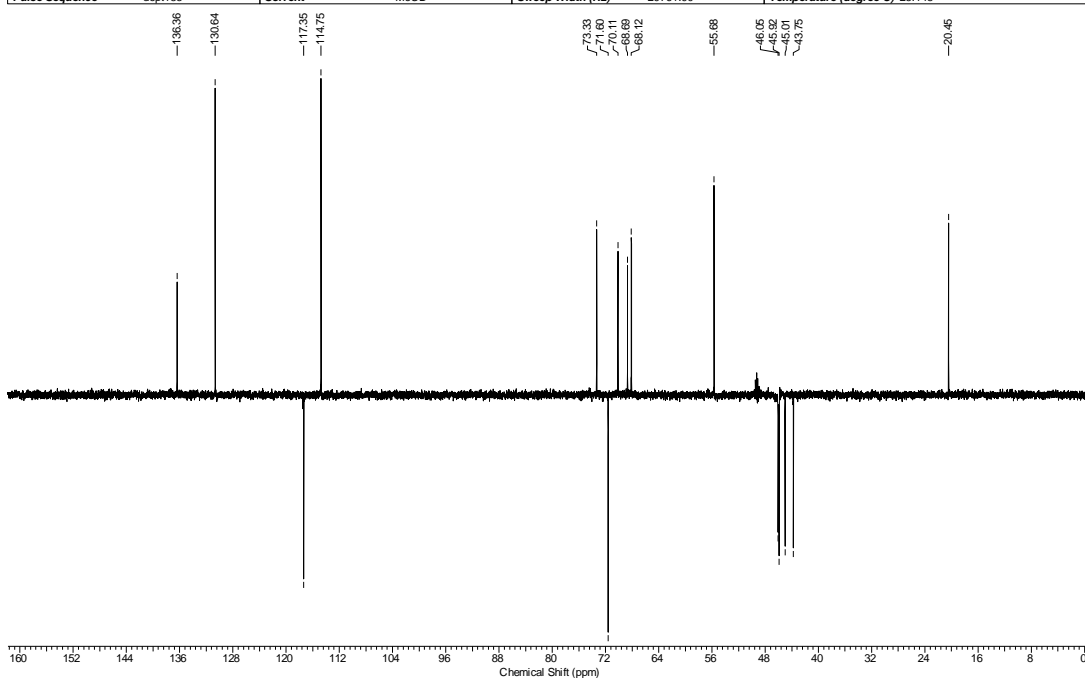


Figure S42. ^{13}C NMR spectrum (DEPT 135) of **18** (125 MHz; MeOD).

Paula - PKK102 - MeOD - Avance 400 MHz - mar28pkkH1 - COSY

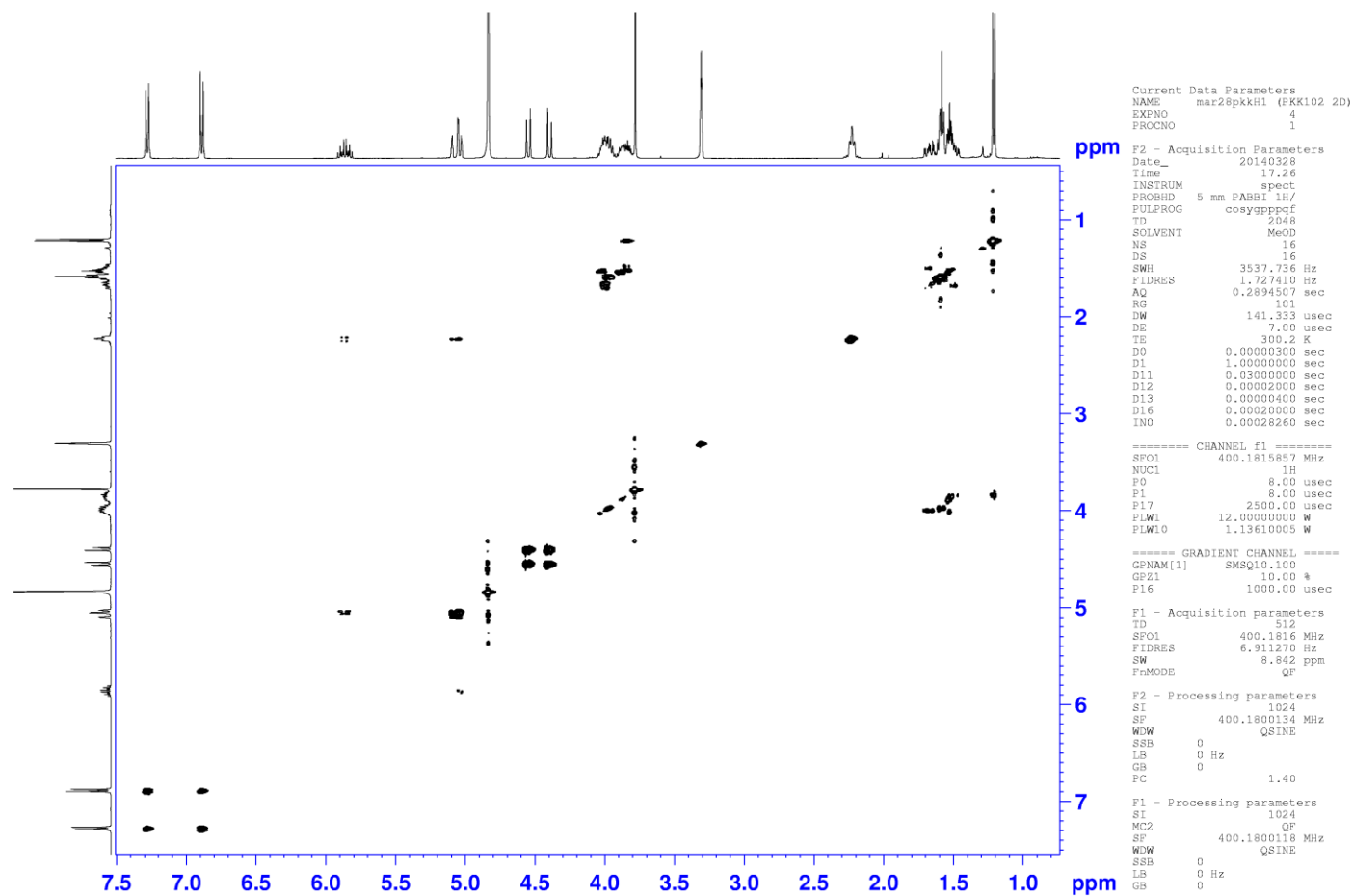


Figure S43. COSY contour map for 18.

Paula - PKK102 - MeOD - Avance 400 MHz - mar28pkkH1 HSQC

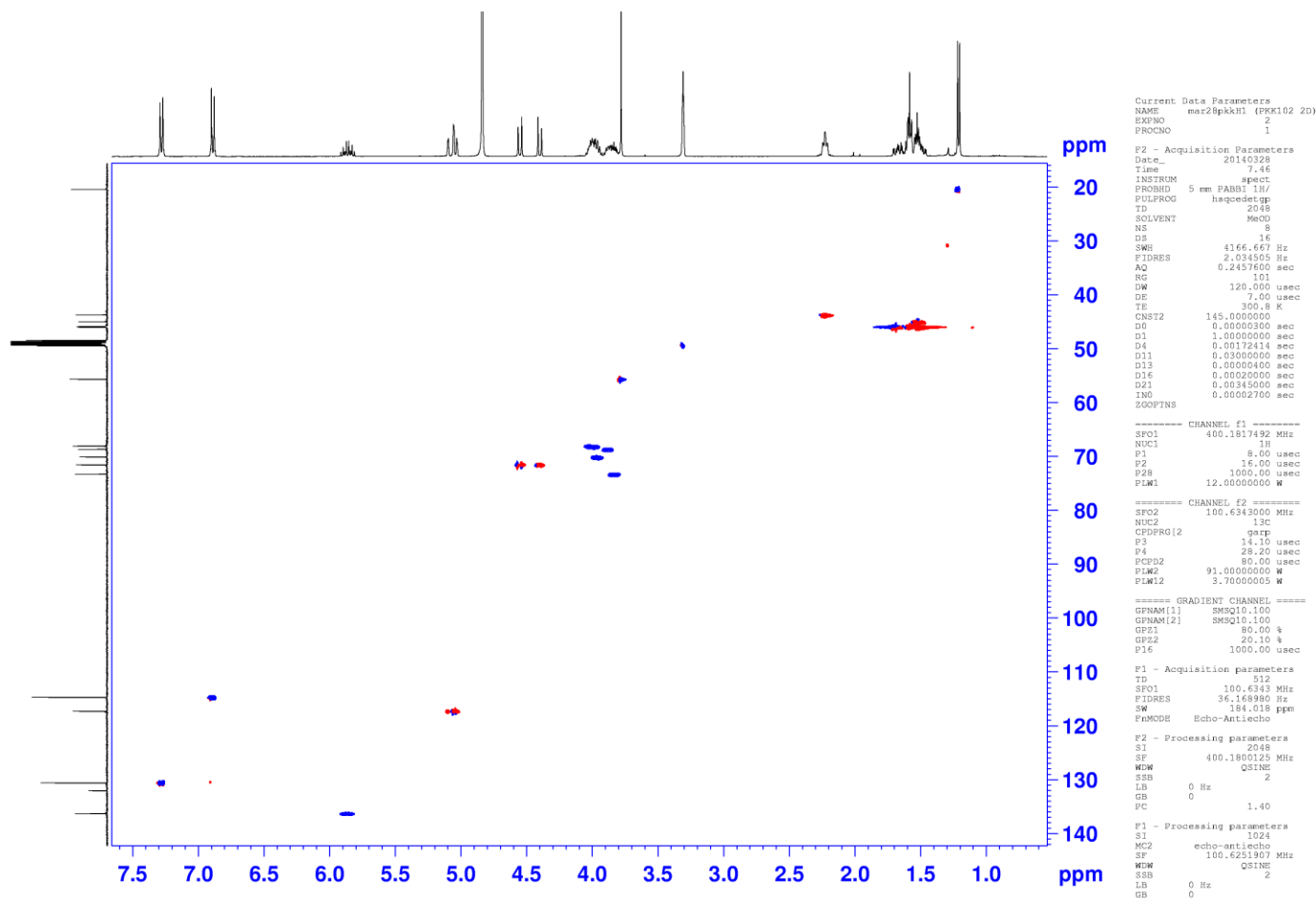


Figure S44. HSQC contour map for 18.

Paula - PKK102 - MeOD - Avance 400 MHz - mar28pkkH1 HMBC

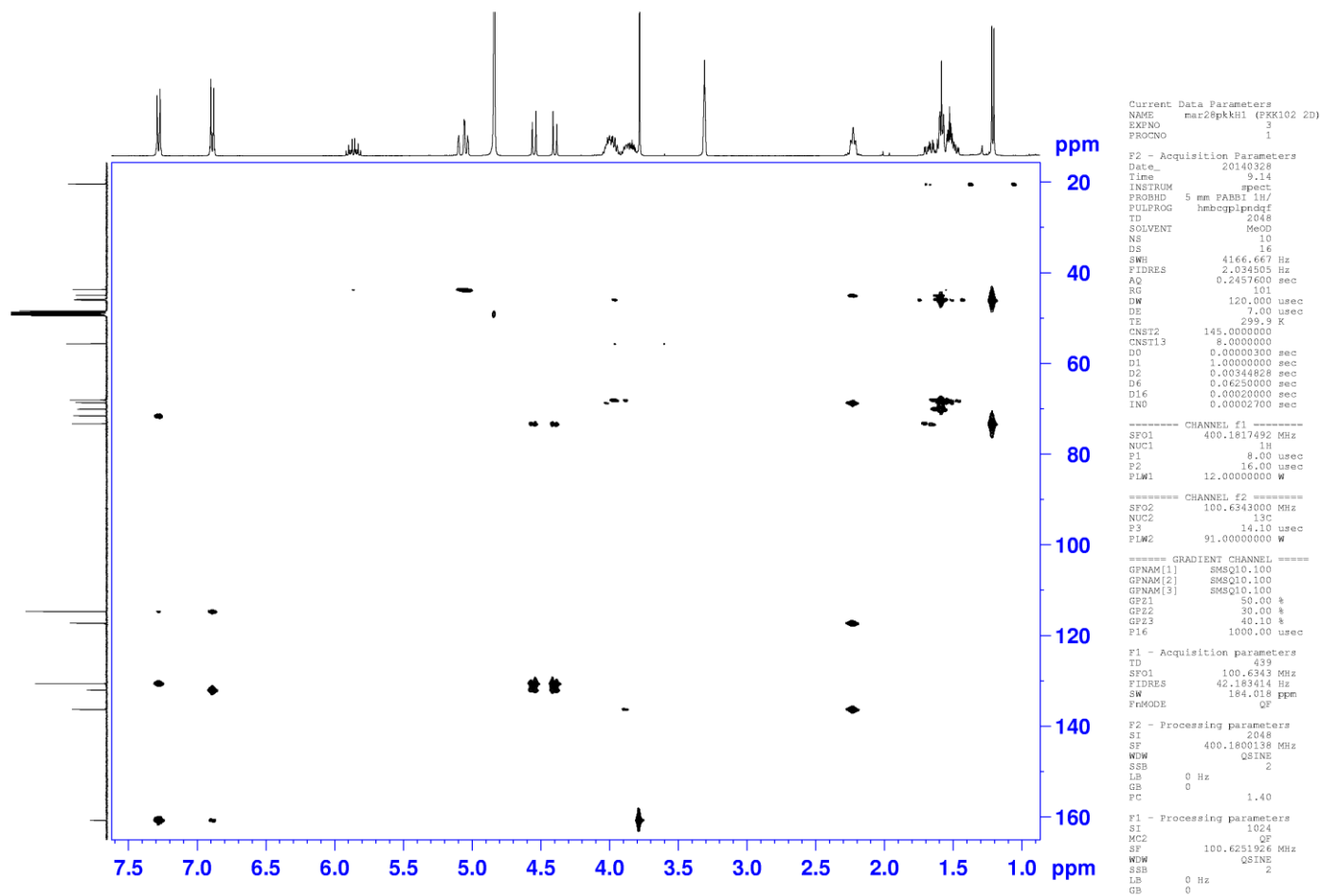
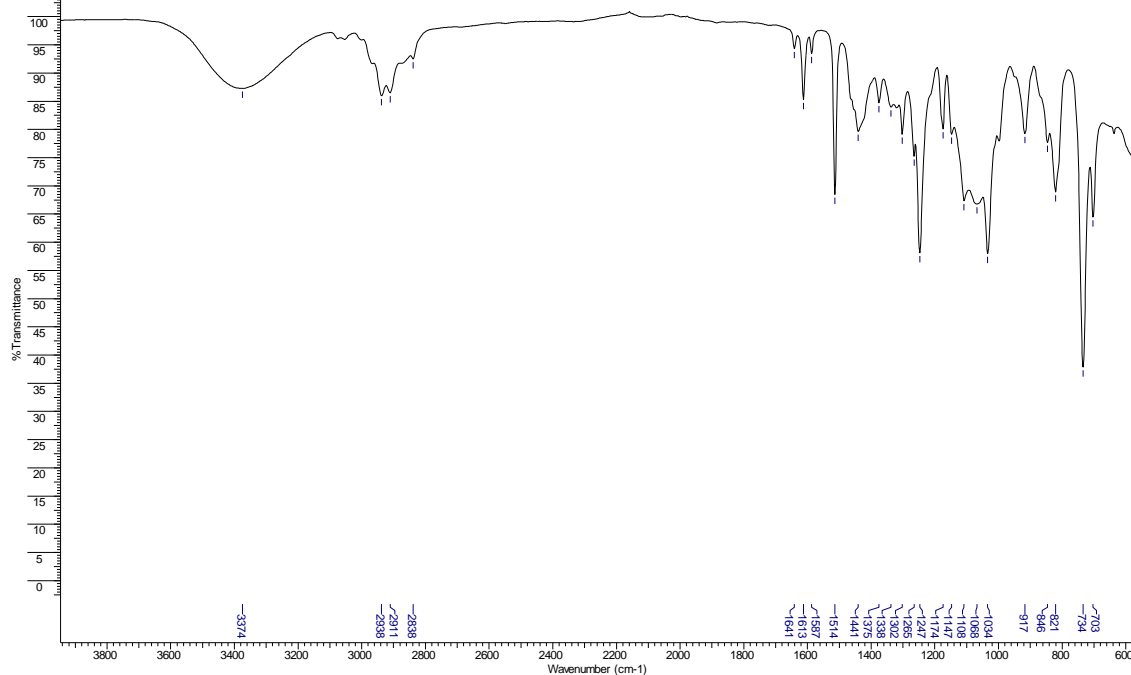


Figure S45. HMBC contour map for 18.

Title	cial do Brasil (GMT-3:00)	Comment	Amostra 001 por LOOS data sexta-feira, outubro 17 2014	Origin	cial do Brasil (GMT-3:00)
File Name	E:\MESTRADO\IV PAULA\PKK102.SP	Date Stamp	fri oct 17 17:06:12 2014 Hora oficial do Brasil (GMT-3:00)	Instrument	Spectrum Two
Date	fri oct 17 17:06:12 2014 Hora oficial do Brasil (GMT-3:00)	Technique	Infrared	Y Axis	%Transmittance
Spectral Region	IR	X Axis	Wavenumber (cm-1)	Spectrum Range	550.0000 - 4000.0000
Points Count	3451	Data Spacing	1.0000		



C008 #33 RT: 0.50 AV: 1 NL: 1.50E8
T: FTMS + p ESI Full ms [150.00-1500.00]

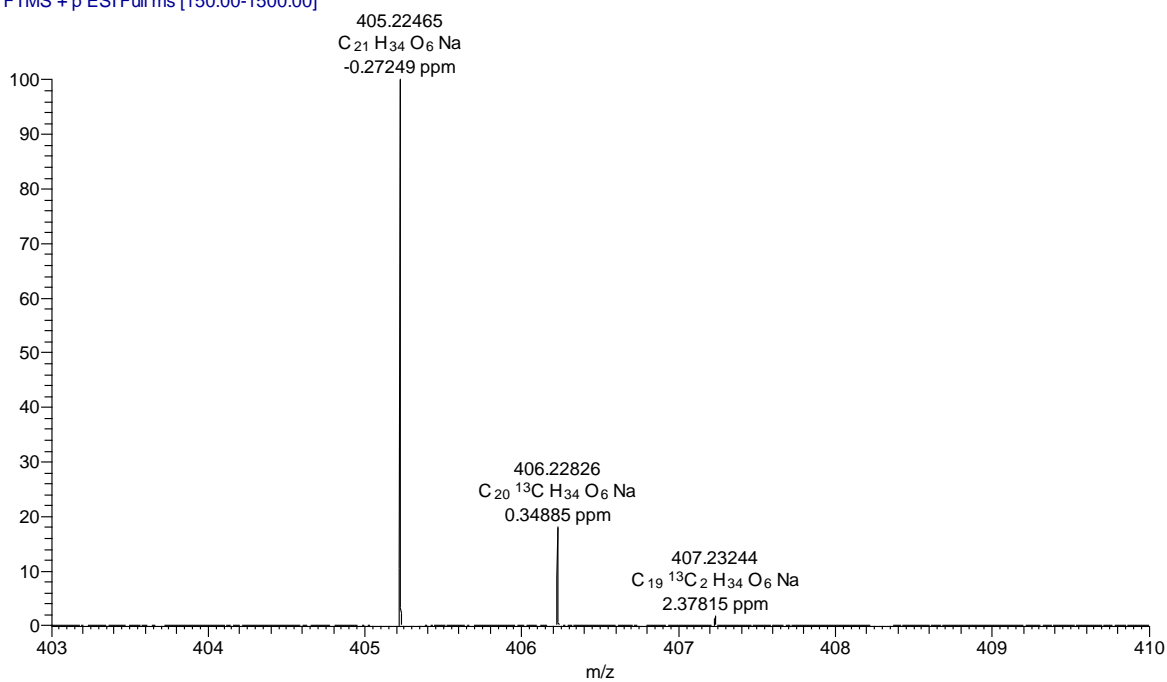


Figure S46. IR and HRMS spectra of 18.

Acquisition Time (sec)	1.6384	Comment	Paula "PKK-100" cdcl3/Av500MHz_mar25pkkH1	Date	26 Mar 2014 07:34:24
File Name	\\nmrparc.iqm.unicamp.br/espectros\avance500\2014\mar14\Luiz Carlos\mar25pkkH1_001001r			Frequency (MHz)	499.87
Nucleus	1H	Number of Transients	16	Original Points Count	16384
Pulse Sequence	zg30	Solvent	CHLOROFORM-D	Sweep Width (Hz)	10000.00
				Points Count	65536
				Temperature (degree C)	25.150

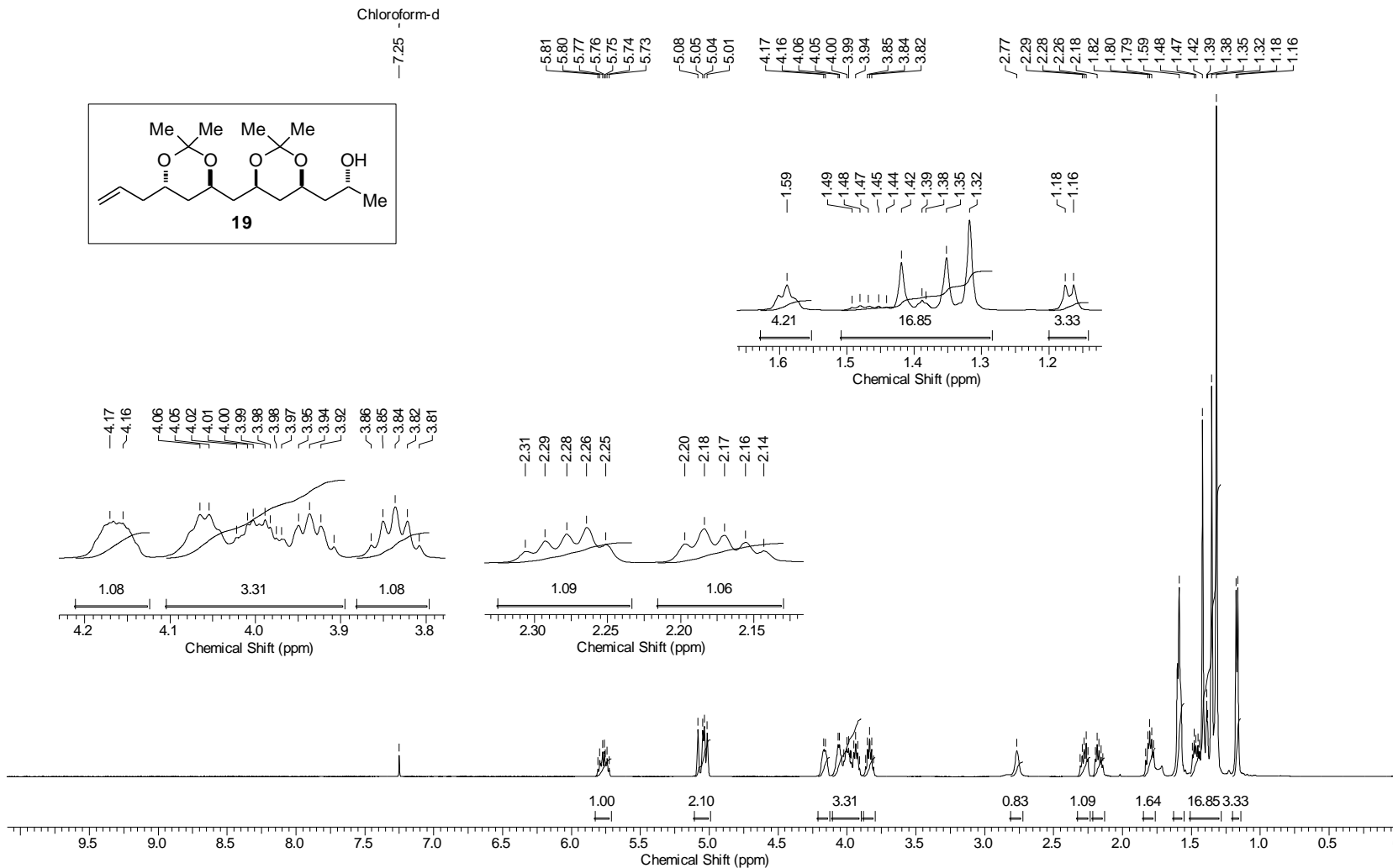


Figure S47. ^1H NMR spectrum of **19** (500 MHz; CDCl_3).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK100 - CDCl ₃ - Av 500 MHz - mar20pkkH1 13C	Date	20 Mar 2014 10:53:58		
File Name	F:\Mestrado\Espectros	RMN500\mar20pkkH1 (PKK100) 002001r	Frequency (MHz)	125.69	Nucleus	13C	
Number of Transients	512	Original Points Count	16384	Points Count	32768	Pulse Sequence	zgpg30
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.191		

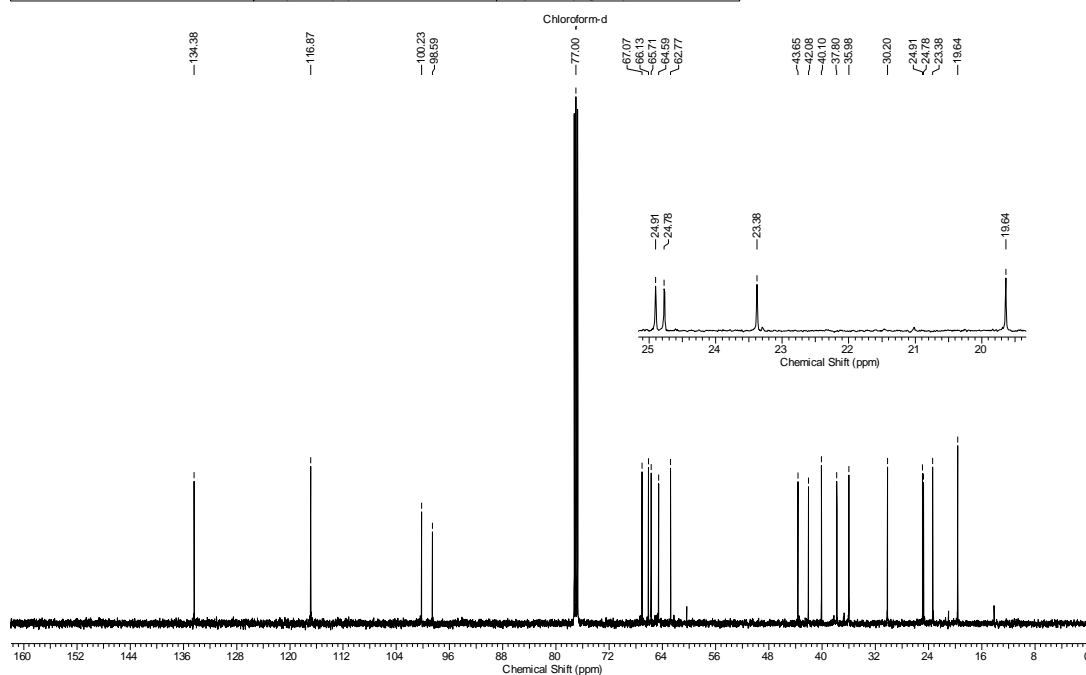


Figure S48. ¹³C NMR spectrum of **19** (125 MHz; CDCl₃).

Acquisition Time (sec)	0.5505	Comment	Paula - PKK100 - CDCl ₃ - Av 500 MHz - mar20pkkH1 DEPT135	Date	20 Mar 2014 10:54:10		
File Name	F:\Mestrado\Espectros	RMN500\mar20pkkH1 (PKK100) 003001r	Frequency (MHz)	125.69	Nucleus	13C	
Number of Transients	128	Original Points Count	16384	Points Count	32768	Pulse Sequence	dept135
Solvent	CHLOROFORM-D	Sweep Width (Hz)	29761.90	Temperature (degree C)	25.151		

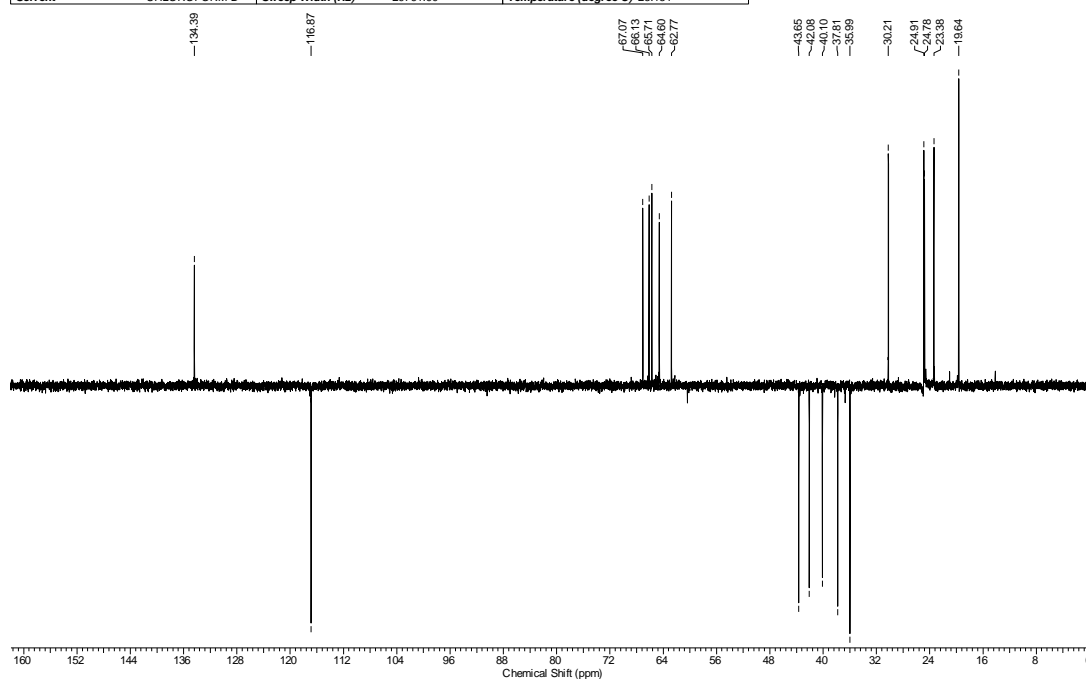
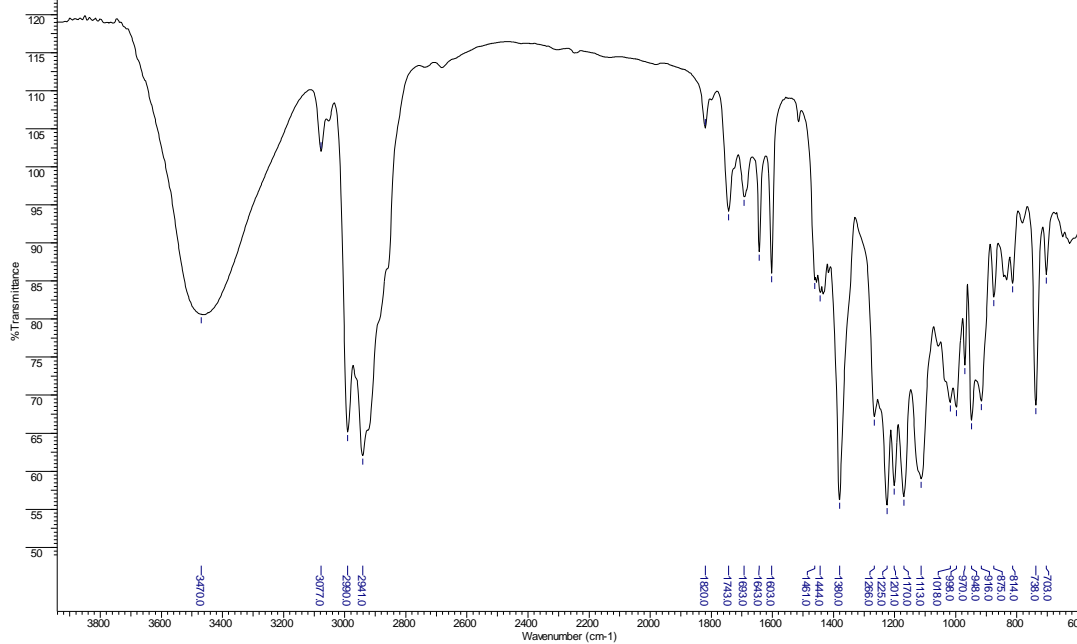


Figure S49. ¹³C NMR spectrum (DEPT 135) of **19** (125 MHz; CDCl₃).

Title	brasileiro de verão (GMT-2:00)	Comment	recuperado de PKK77	Origin	brasileiro de verão (GMT-2:00)
File Name	F:\MESTRADO\IV PAULA\PKK76.SP	Date Stamp	fri dec 20 09:38:31 2013 Horário brasileiro de verão (GMT-2:00)		
Date	fri dec 20 09:38:31 2013 Horário brasileiro de verão (GMT-2:00)	Technique	Infrared	Instrument	Spectrum Two
Spectral Region	IR	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Points Count	3451	Data Spacing	1.0000		Spectrum Range 550.0000 - 4000.0000



C006 #24 RT: 0.36 AV: 1 NL: 3.39E7
T: FTMS + p ESI Full ms [150.00-1500.00]

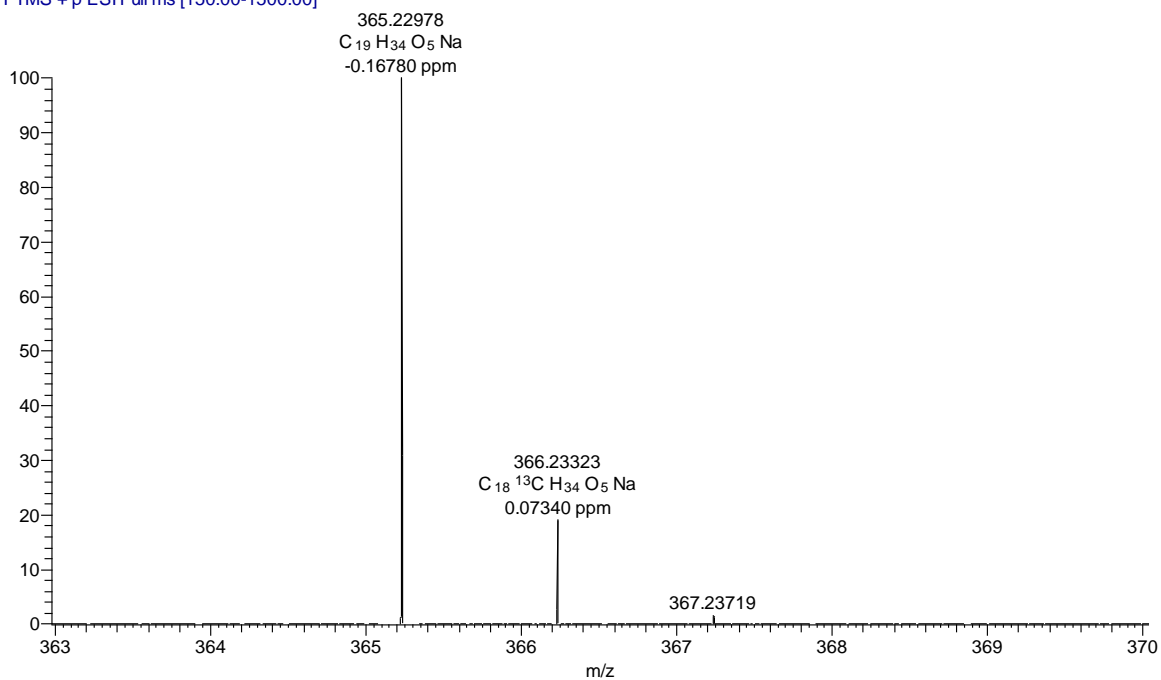


Figure S50. IR and HRMS spectra of 19.

Acquisition Time (sec)	2.6564	Date	07 Jan 2014 14:25:18		Frequency (MHz)	600.17	
File Name	\nmrsparc.iqm.unicamp.br/espectros\avance600\2014\jan14\Luz Carlos\jan07pkh1_001001r				Points Count	65536	
Nucleus	1H	Number of Transients	16	Original Points Count	32768	Sweep Width (Hz)	12335.53
Pulse Sequence	zg30	Solvent	CHLOROFORM-D				
Temperature (degree C)	25.150						

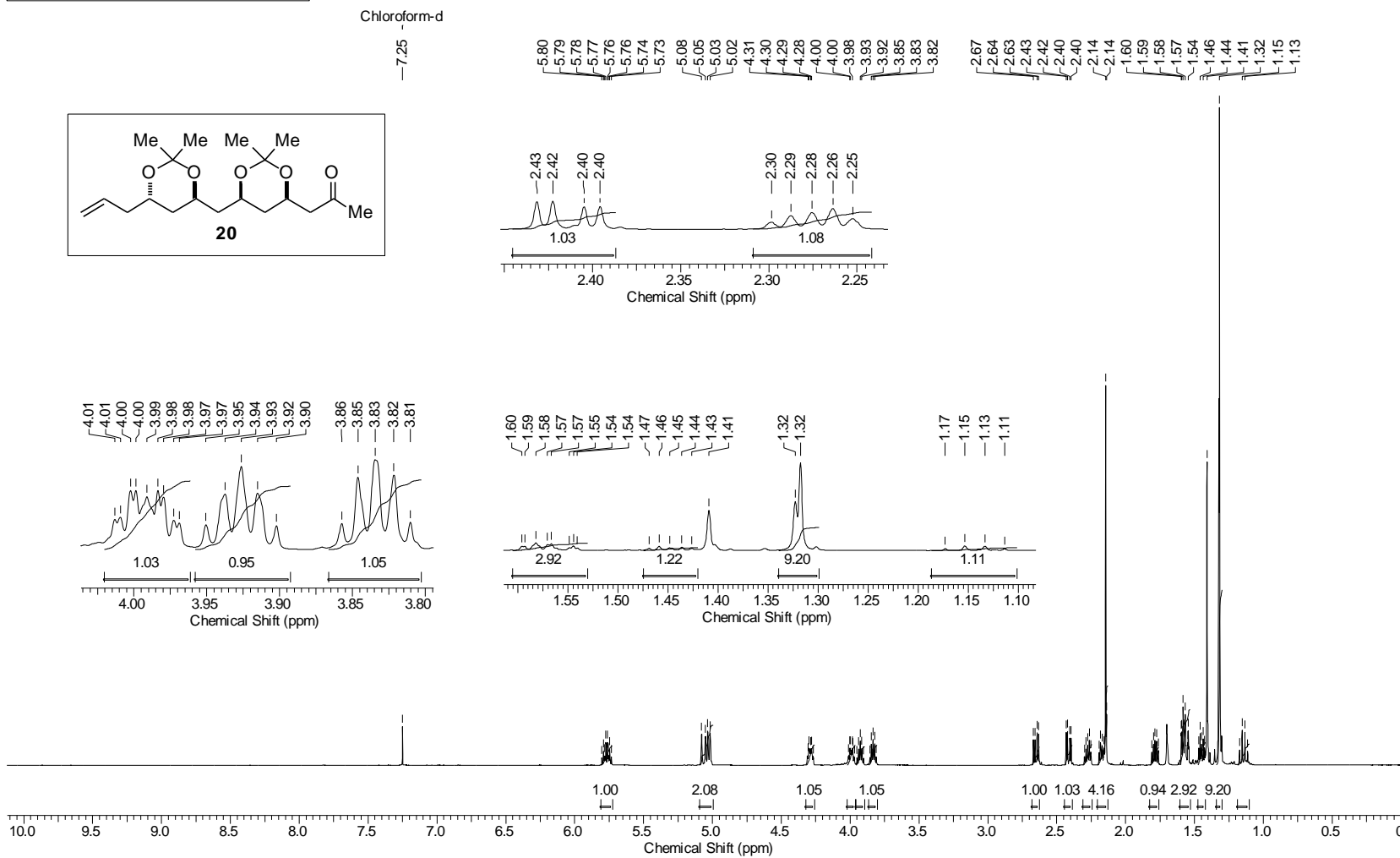


Figure S51. ^1H NMR spectrum of **20** (600 MHz; CDCl_3).

Acquisition Time (sec)	0.4544	Date	07 Jan 2014 15:58:08	Frequency (MHz)	150.91
File Name	\nmr\parc.igim.unicamp.br\espectros\avance600\2014\jan14\Luiz Carlos\jan07pkkH1_002001r			Points Count	32768
Nucleus	13C	Number of Transients	1877	Original Points Count	16384
Pulse Sequence	zpgp30	Solvent	CHLOROFORM-D	Sweep Width (Hz)	36057.69
				Temperature (degree C)	25.150

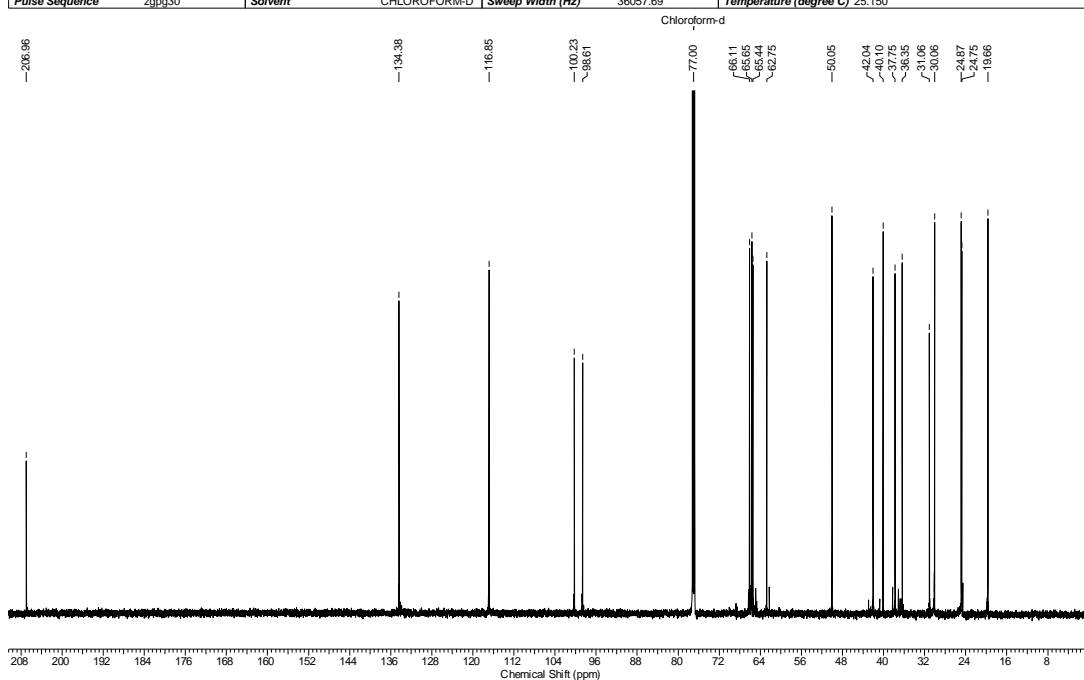


Figure S52. ^{13}C NMR spectrum of **20** (150 MHz; CDCl_3).

Acquisition Time (sec)	0.6816	Date	07 Jan 2014 16:42:42	Frequency (MHz)	150.91
File Name	\nmr\parc.igim.unicamp.br\espectros\avance600\2014\jan14\Luiz Carlos\jan07pkkH1_003001r			Points Count	65536
Nucleus	13C	Number of Transients	1024	Original Points Count	16384
Pulse Sequence	depts135	Solvent	CHLOROFORM-D	Sweep Width (Hz)	24038.46
				Temperature (degree C)	25.151

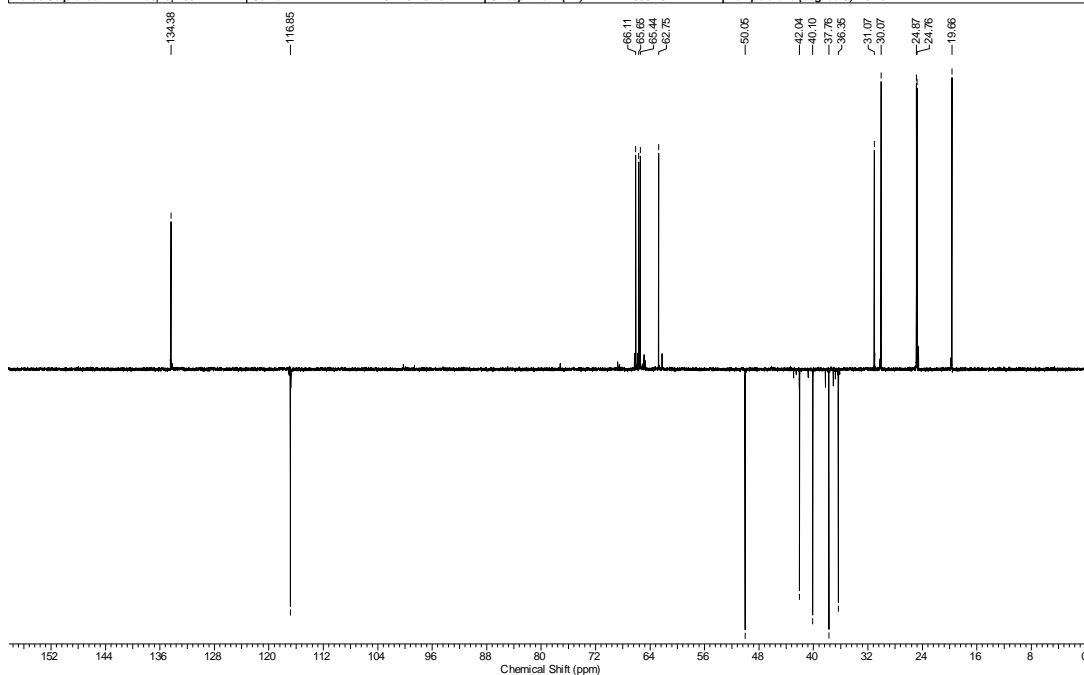
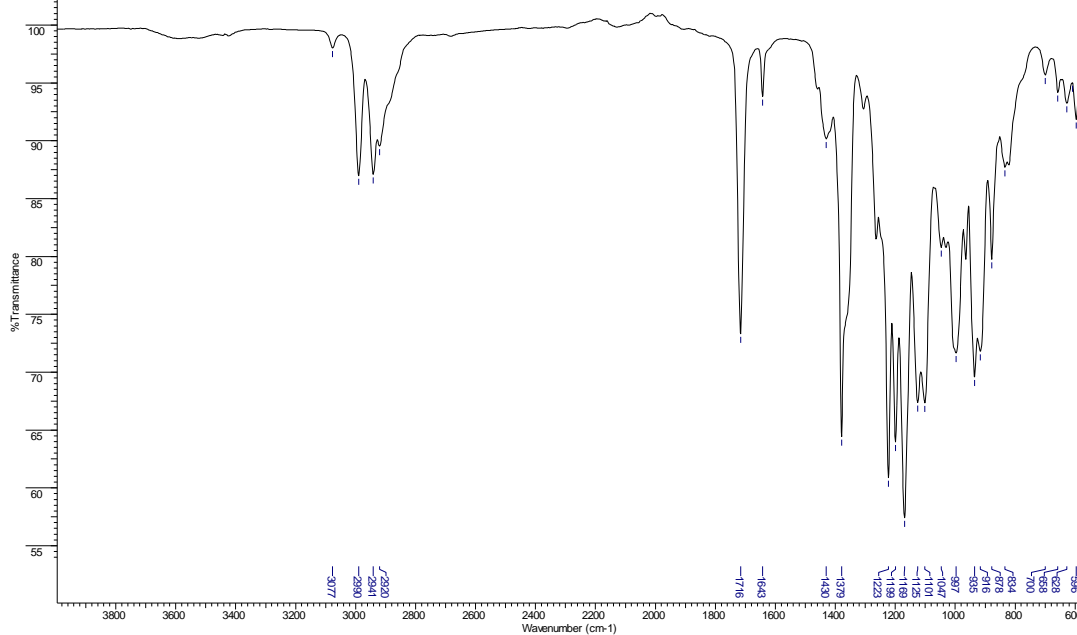


Figure S53. ^{13}C NMR spectrum (DEPT 135) of **20** (150 MHz; CDCl_3).

Title	brasileiro de verão (GMT-2:00)	Comment	Amostra 001 por LQOS data sexta-feira, janeiro 24 2014	Origin	brasileiro de verão (GMT-2:00)
File Name	E:\MESTRADO\IV PAULA\PKK77.SP	Date Stamp	fri jan 24 10:40:35 2014 Horário brasileiro de verão (GMT-2:00)	Technique	Infrared
Date	fri jan 24 10:40:35 2014 Horário brasileiro de verão (GMT-2:00)	X Axis	Wavenumber (cm-1)	Y Axis	% Transmittance
Spectral Region	IR	Data Spacing	1.0000	Instrument	Spectrum Two
Points Count	3451			Spectrum Range	550.0000 - 4000.0000



C007 #8 RT: 0.12 AV: 1 NL: 5.81E7
T: FTMS + p ESI Full ms [150.00-1500.00]

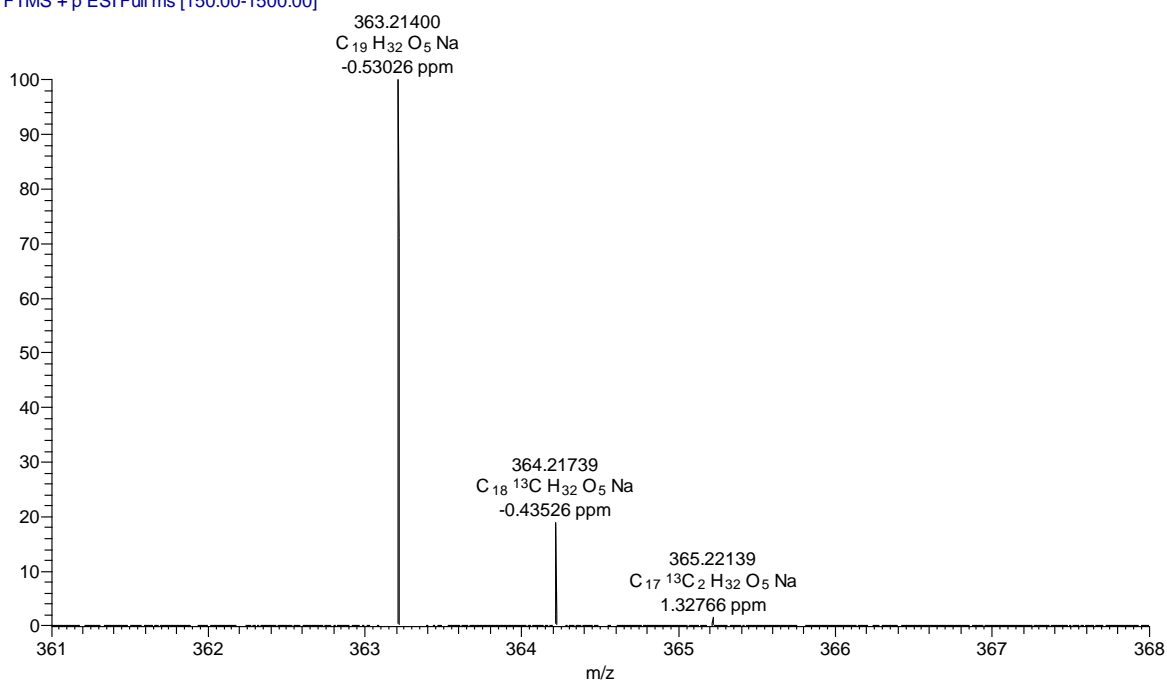


Figure S54. IR and HRMS spectra of 20.

Acquisition Time (sec)	3.1654	Comment	PKK82 CDCl3 250MHz jan16pkkH1	Date	16 Jan 2014 20:02:30
File Name	F:\Mestrado\Espectros RMN\250\jan16pkkH1 (PKK82)_001001r	Frequency (MHz)	250.13	Nucleus	1H
Number of Transients	16	Original Points Count	16384	Points Count	32768
Solvent	CHLOROFORM-D	Sweep Width (Hz)	5175.98	Pulse Sequence	zg30
				Temperature (degree C)	24.060

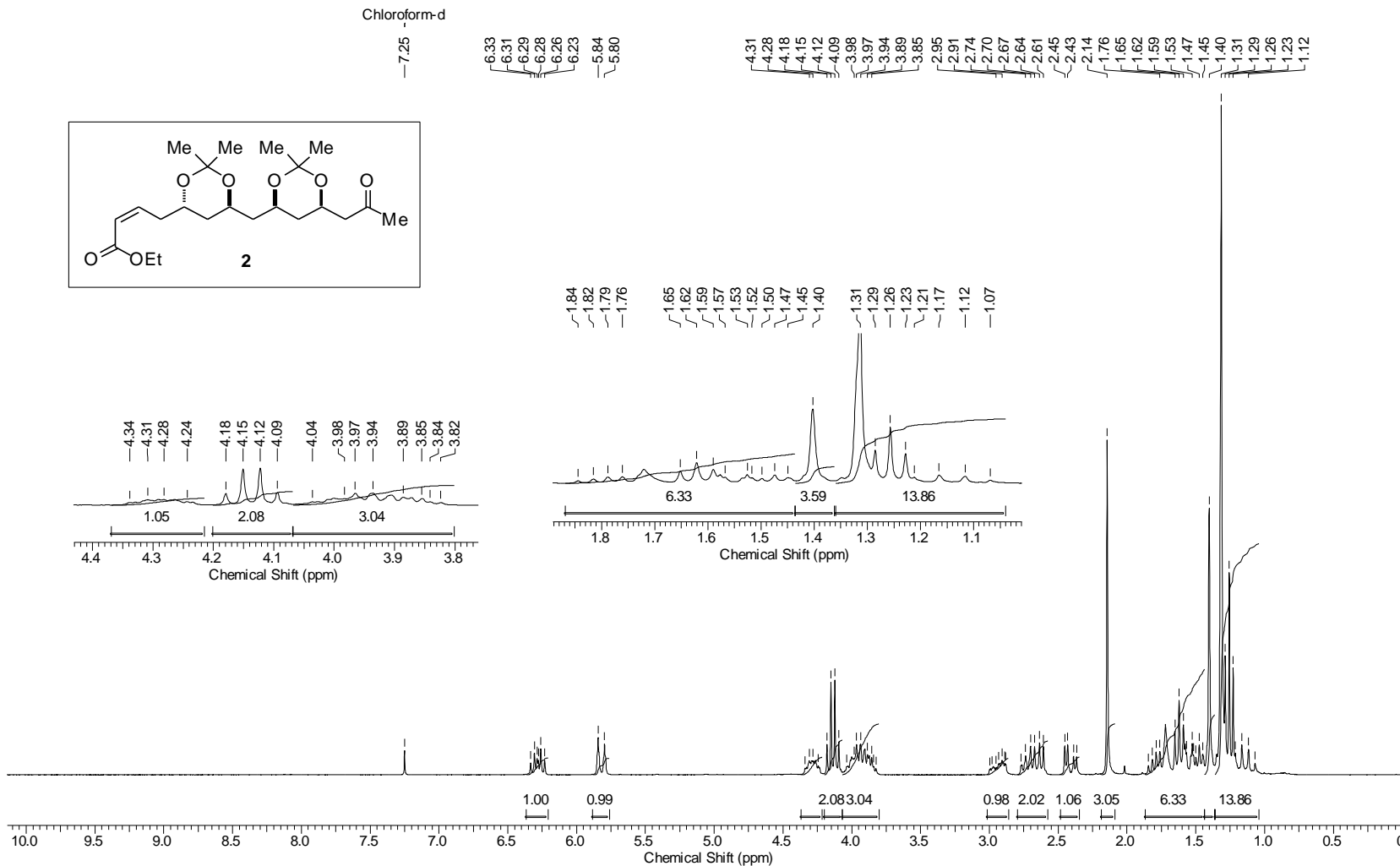


Figure S55. ¹H NMR spectrum of **2** (250 MHz; CDCl₃).

Acquisition Time (sec)	0.5439	Comment	PKK82 CDCl3 250MHz jan16pkkC1	Date	24 Jan 2014 11:16:36
File Name	F:\Mestrado\Espectros RMN\250\jan16pkkC1 (PKK82)\correto_002001r	Number of Transients	18863	Original Points Count	8192
Nucleus	13C	Solvent	CHLOROFORM-D	Frequency (MHz)	62.90
Pulse Sequence	zpgg30	Number of Points	32768	Points Count	32768
Temperature (degree C)	25.060	Sweep Width (Hz)	15060.24		

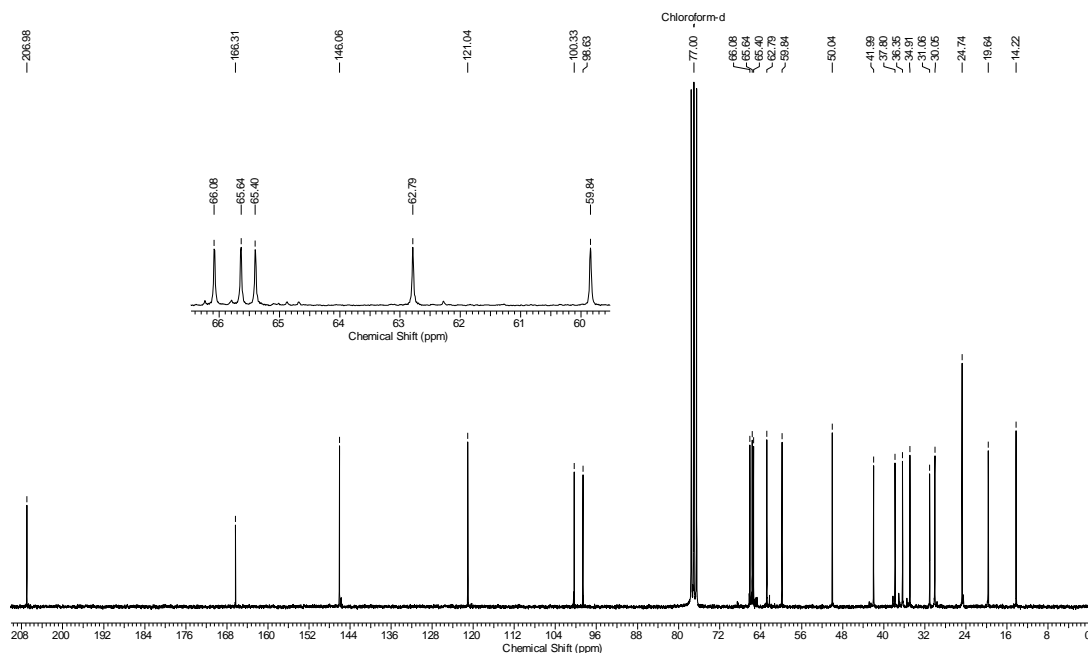


Figure S56. ^{13}C NMR spectrum of **2** (62.5 MHz; CDCl_3).

Acquisition Time (sec)	0.5439	Comment	PKK82 CDCl3 250MHz jan16pkkC1 dept135	Date	24 Jan 2014 11:16:18
File Name	F:\Mestrado\Espectros RMN\250\jan16pkkC1 (PKK82)\correto_001001r	Number of Transients	1024	Original Points Count	8192
Nucleus	13C	Solvent	CHLOROFORM-D	Frequency (MHz)	62.90
Pulse Sequence	dept135	Sweep Width (Hz)	15060.24	Points Count	32768
Temperature (degree C)	24.160			Temperature (degree C)	24.160

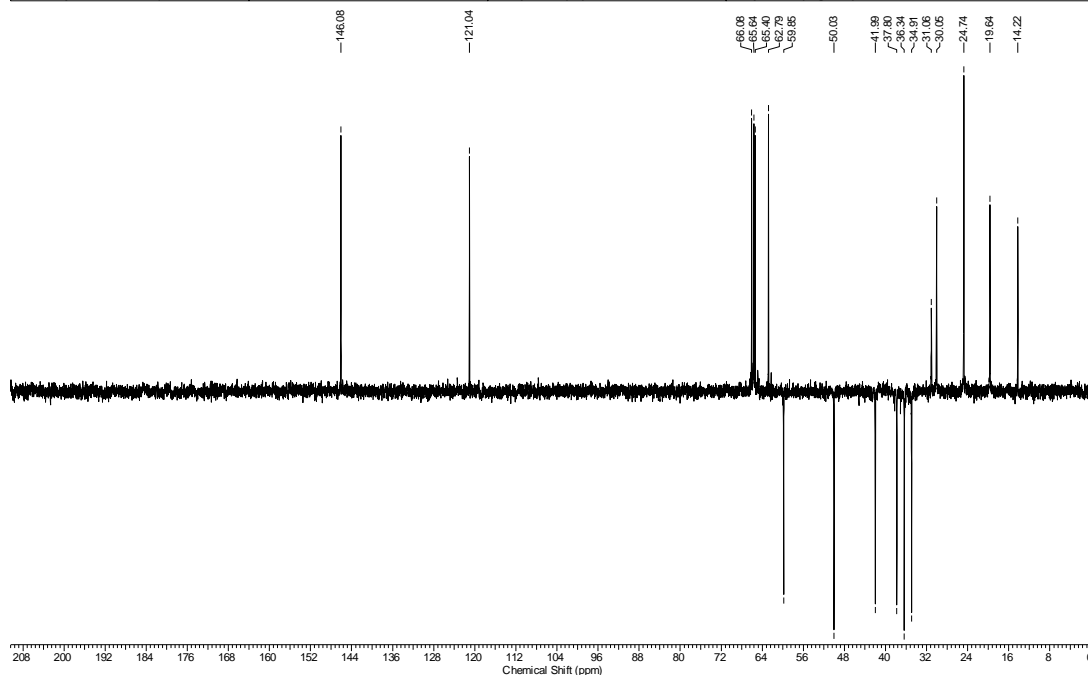
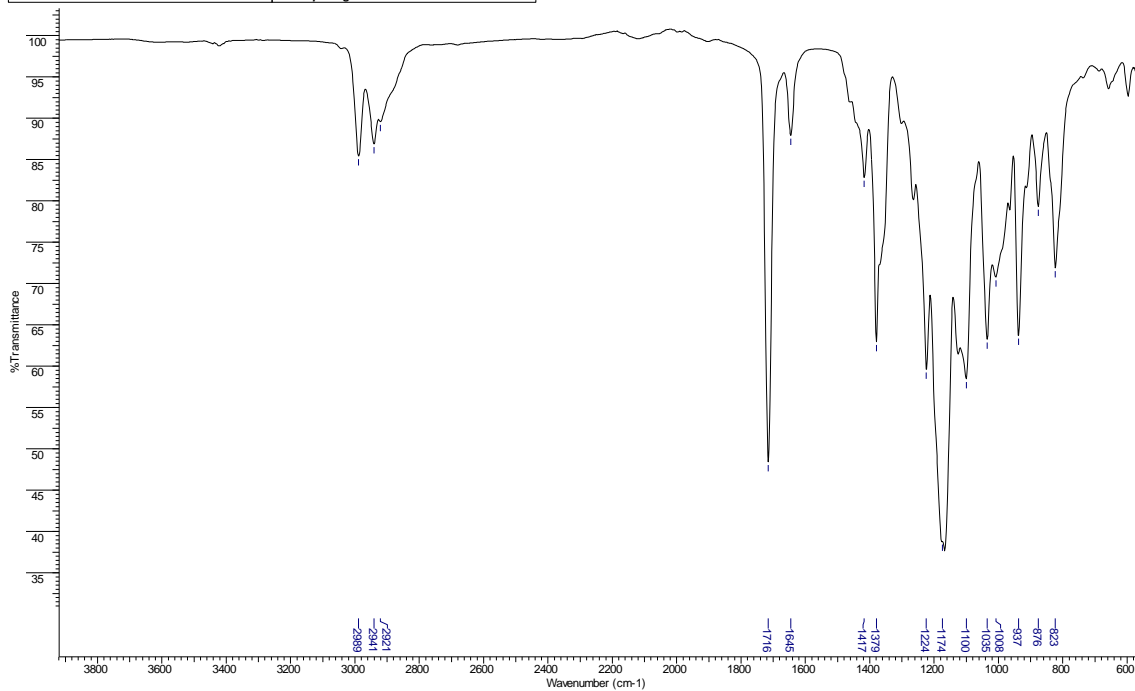


Figure S57. ^{13}C NMR spectrum (DEPT 135) of **2** (62.5 MHz; CDCl_3).

Title	cial do Brasil (GMT-3:00)	Comment	Amostra 002 por LQOS data sexta-feira, outubro 17 2014	Origin	cial do Brasil (GMT-3:00)
File Name	E:\MESTRADO\IV PAULA\PKK112.SP	Date Stamp	fri oct 17 17:12:21 2014 Hora oficial do Brasil (GMT-3:00)		
Date	fri oct 17 17:12:21 2014 Hora oficial do Brasil (GMT-3:00)	Technique	Infrared	Instrument	Spectrum Two
Spectral Region	IR	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Points Count	3451	Data Spacing	1.0000	Spectrum Range	550.0000 - 4000.0000



C009 #7 RT: 0.10 AV: 1 NL: 2.37E6
T: FTMS + p ESI Full ms [150.00-1500.00]

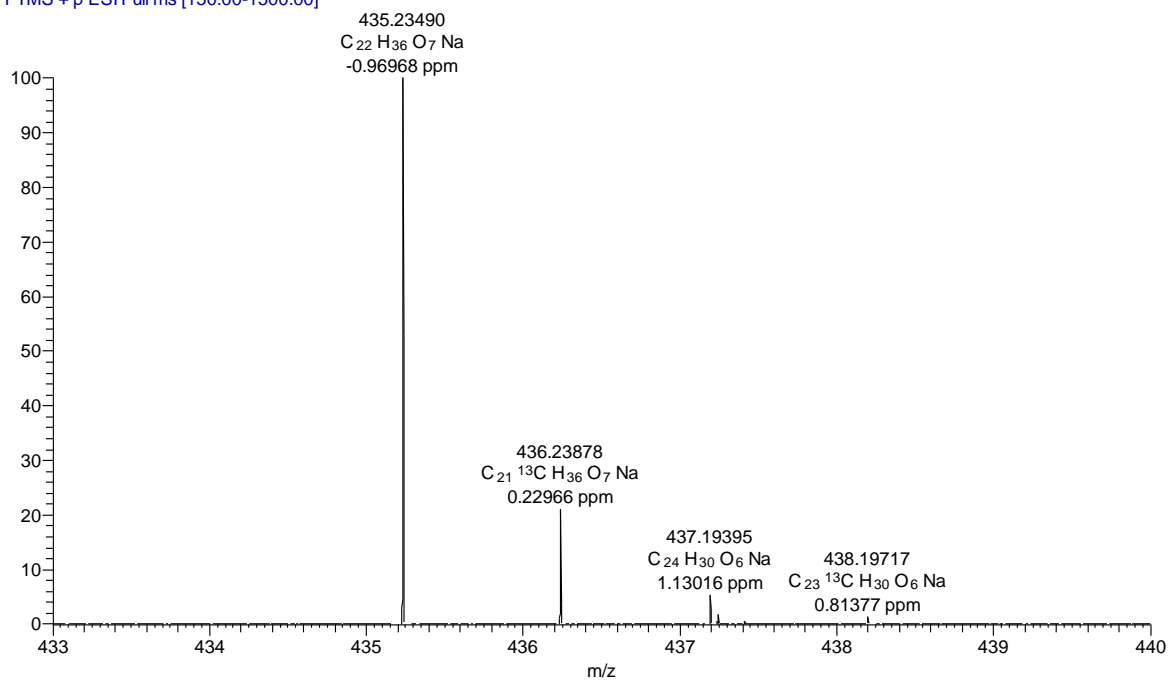


Figure S58. IR and HRMS spectra of 2.

Acquisition Time (sec)	1.5903	Date	07 Mar 2014 13:39:24	Frequency (MHz)	499.87	Nucleus	¹ H
File Name	F:\Mestrado\Espectros RMN\500\mar07pkkH1 (PKK96)_001001r			Pulse Sequence	zg30	Solvent	MeOD
Number of Transients	32	Original Points Count	16384	Points Count	65536		
Sweep Width (Hz)	10302.20	Temperature (degree C)	25.139				

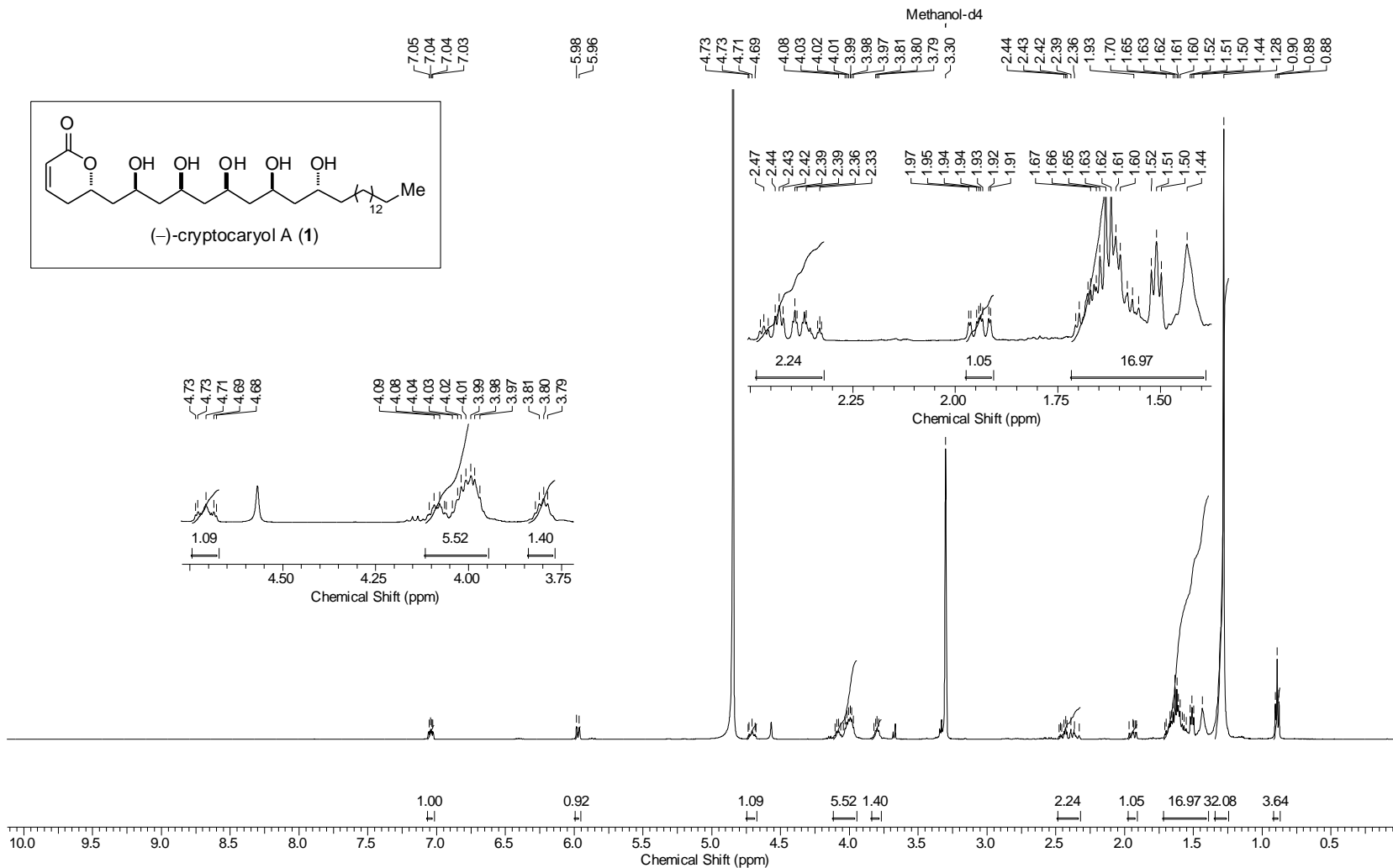


Figure S59. ¹H NMR spectrum of 1 (500 MHz; MeOD).

Acquisition Time (sec)	0.5505	Comment	mar05pkkC1 2014 500MHz PKK 96	Date	06 Mar 2014 08:43:50
File Name	\nmr\sparc.igq.unicamp.br\espectros\lavance500\2014\mar14\Luz Carlos\mar05pkkC1_001001r			Frequency (MHz)	125.69
Nucleus	13C	Number of Transients	18432	Original Points Count	16384
Pulse Sequence	zpgg30	Solvent	MeOD	Sweep Width (Hz)	29761.90
				Temperature (degree C)	25.156

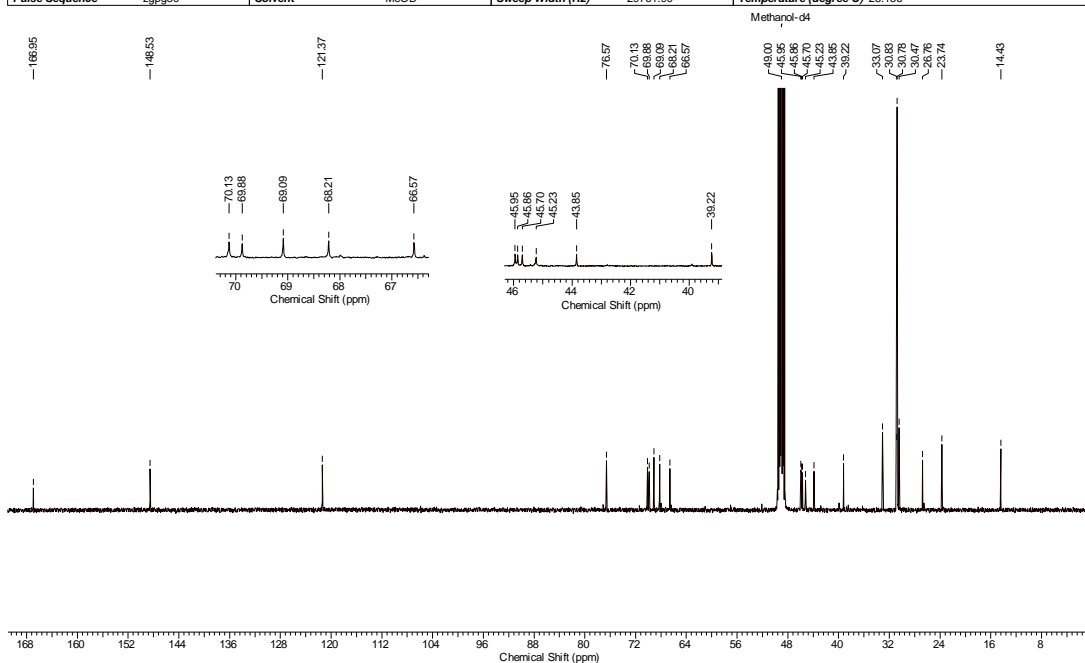


Figure S60. ^{13}C NMR spectrum of **1** (125 MHz; MeOD).

Acquisition Time (sec)	0.5505	Comment	Paula "PKK-96" cd3od / Av500MHz mar06pkkD1 - dept135	Date	07 Mar 2014 09:10:30
File Name	\nmr\sparc.igq.unicamp.br\espectros\lavance500\2014\mar14\Luz Carlos\mar06pkkD1_001001r			Frequency (MHz)	125.69
Nucleus	13C	Number of Transients	2847	Original Points Count	16384
Pulse Sequence	dept135	Solvent	MeOD	Sweep Width (Hz)	29761.90
				Temperature (degree C)	25.155

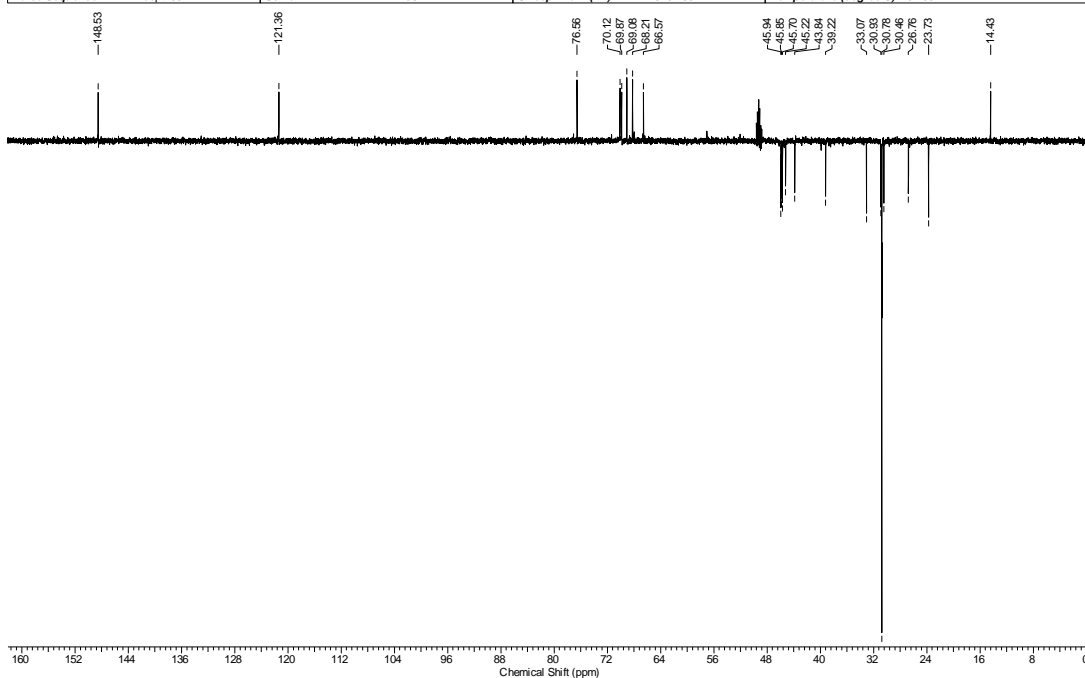
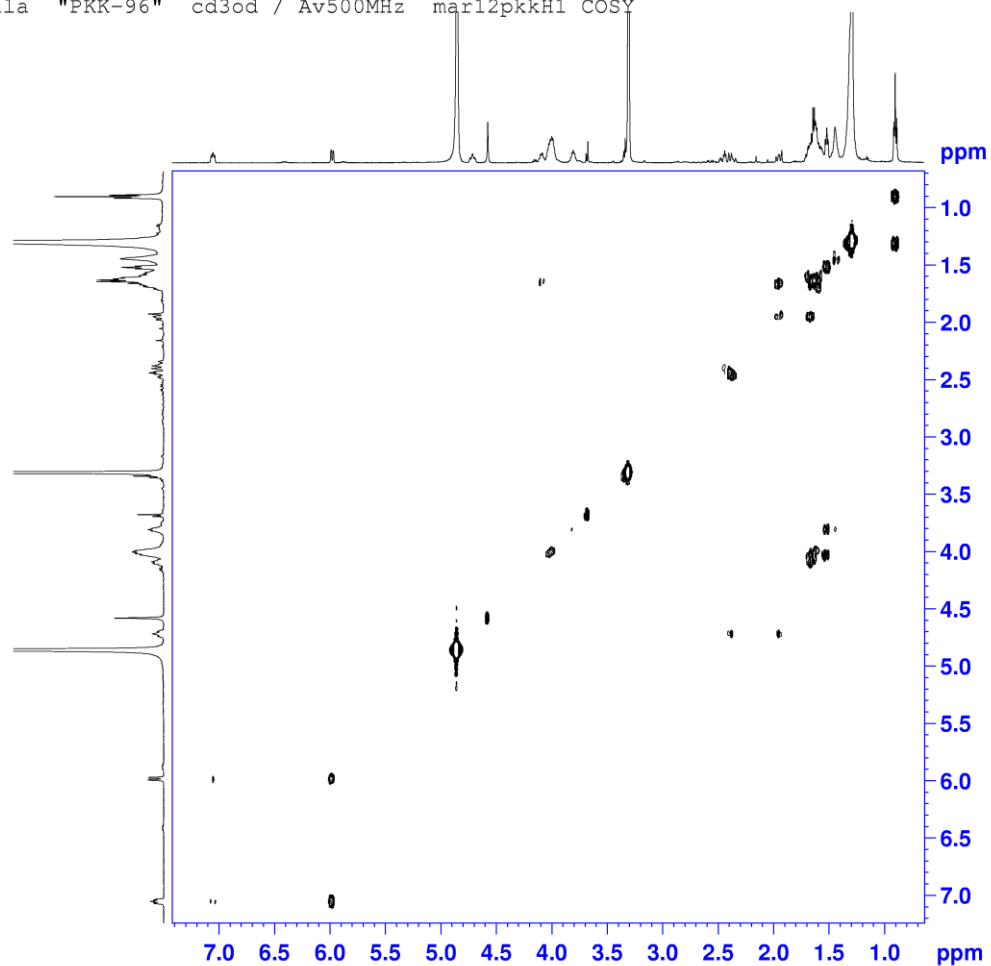


Figure S61. ^{13}C NMR spectrum (DEPT 135) of **1** (125 MHz; MeOD).

Paula "PKK-96" cd3od / Av500MHz mar12pkkH1 COSY



```
Current Data Parameters
NAME      mar12pkkH1 (PKK96)
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20140312
Time      7.53
INSTRUM   spect
PROBHD    5 mm PABBO BB/
PULPROG   cosygpppqf
TD         2048
SOLVENT   MeOD
NS         6
DS         16
SWH        5450.582 Hz
FIDRES     2.661417 Hz
AQ         0.1878699 sec
RG         128
DW         91.733 usec
DE         6.50 usec
TE         298.1 K
D0         0.00000300 sec
D1         2.00000000 sec
D11        0.03000000 sec
D12        0.00002000 sec
D13        0.00000400 sec
D16        0.00020000 sec
IN0        0.00018340 sec

===== CHANNEL f1 =====
SFO1      499.8720486 MHz
NUC1      1H
PQ        11.75 usec
F1        11.75 usec
P17       2500.00 usec
PLW1      25.00000000 W
PLW10     5.10589981 W

===== GRADIENT CHANNEL =====
GPNAM[1]  SMSQ10.100
GP21      10.00 %
P16       1000.00 usec

F1 - Acquisition parameters
TD         139
SFO1      499.872 MHz
FIDRES     39.227070 Hz
SW         10.908 ppm
FnMODE     QF

F2 - Processing parameters
SI         1024
SF         499.8700113 MHz
WDW        QSINE
SSB        0
LB         0 Hz
GB         0
PC         1.40

F1 - Processing parameters
SI         1024
MC2        QF
SF         499.8700138 MHz
WDW        QSINE
SSB        0
LB         0 Hz
GB         0
```

Figure S62. COSY contour map for 1.

Paula "PKK-96" cd3od / Av500MHz mar07pkkh1 HSQC

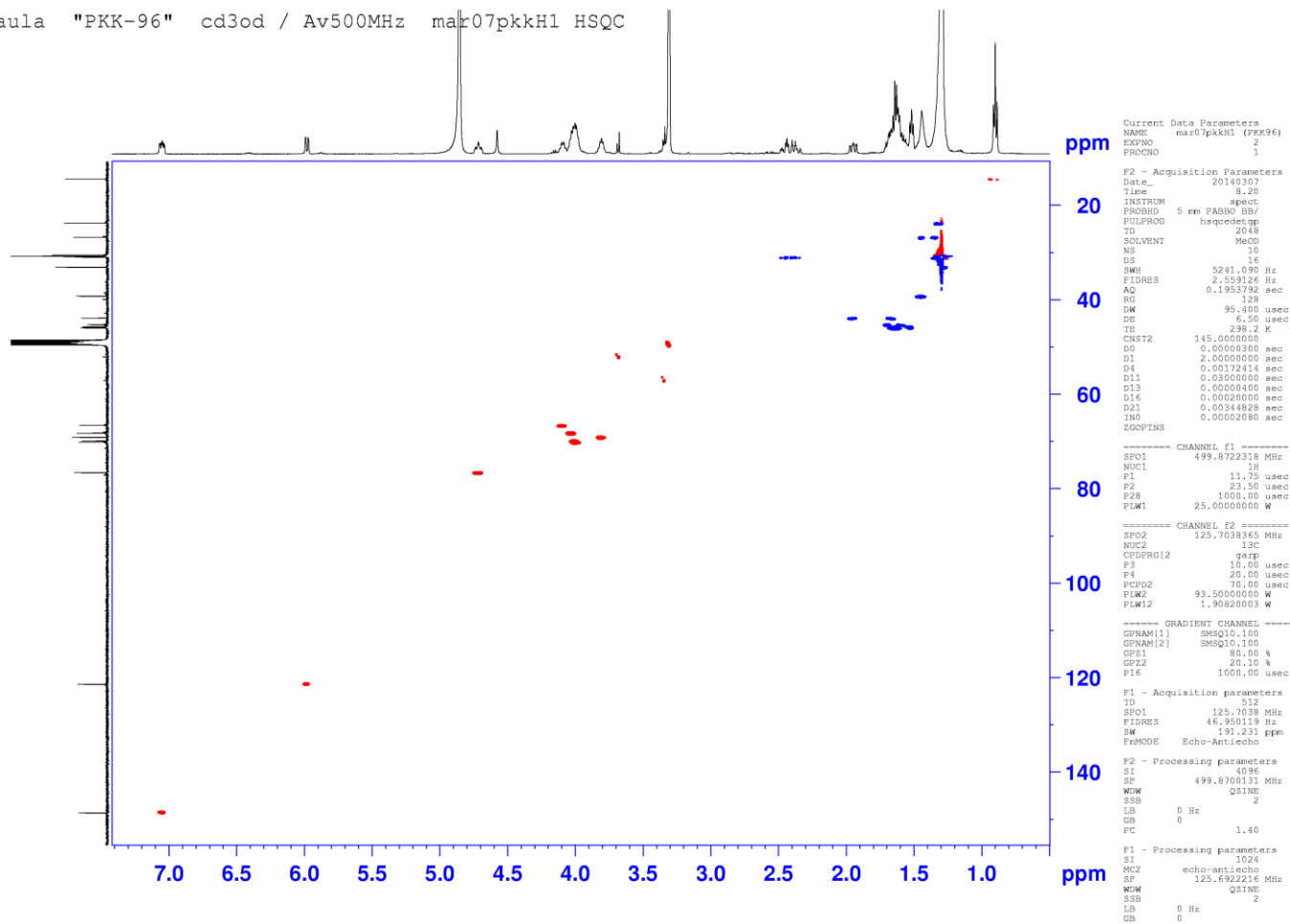


Figure S63. HSQC contour map for 1.

Paula - PKK96 - MeOD / Av600 MHz - out23pkkH1 - HMBC

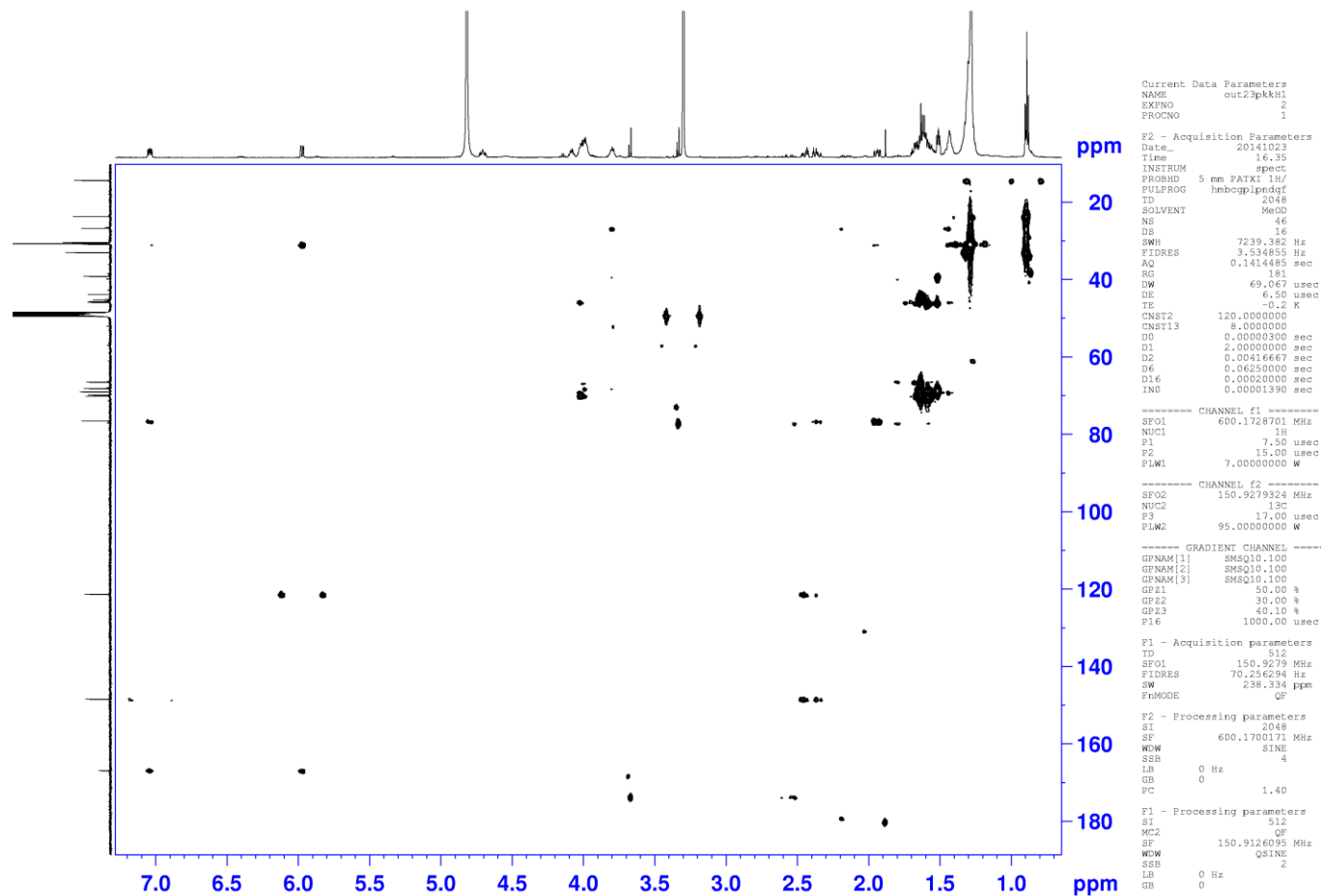
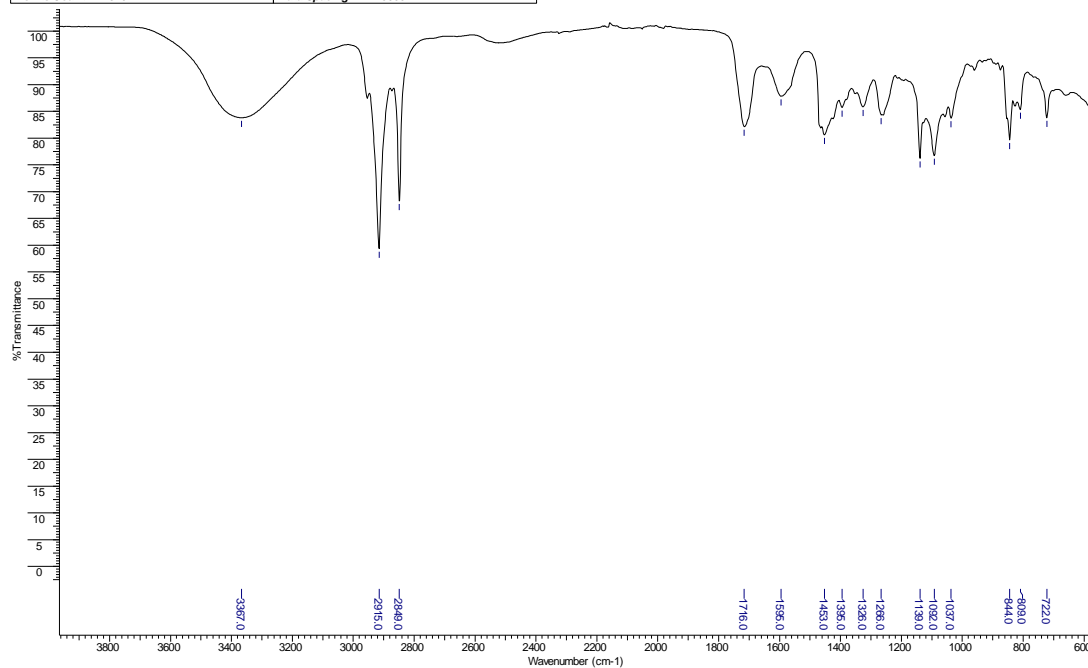


Figure S64. HMBC contour map for 1.

Title	brasileiro de verão (GMT-2:00)	Comment	Amostra 001 por LQOS data terça-feira, outubro 28 2014	Origin	brasileiro de verão (GMT-2:00)
File Name	F:\MESTRADO\IV PAULA\PKK96.SP	Date Stamp	tue oct 28 13:13:49 2014 Horário brasileiro de verão (GMT-2:00)	Technique	Infrared
Date	tue oct 28 13:13:49 2014 Horário brasileiro de verão (GMT-2:00)	X Axis	Wavenumber (cm-1)	Y Axis	%Transmittance
Spectral Region	IR	Data Spacing	1.0000	Instrument	Spectrum Two
Points Count	3451			Spectrum Range	550.0000 - 4000.0000



C010 #27 RT: 0.41 AV: 1 NL: 4.43E6
T: FTMS + p ESI Full ms [150.00-1500.00]

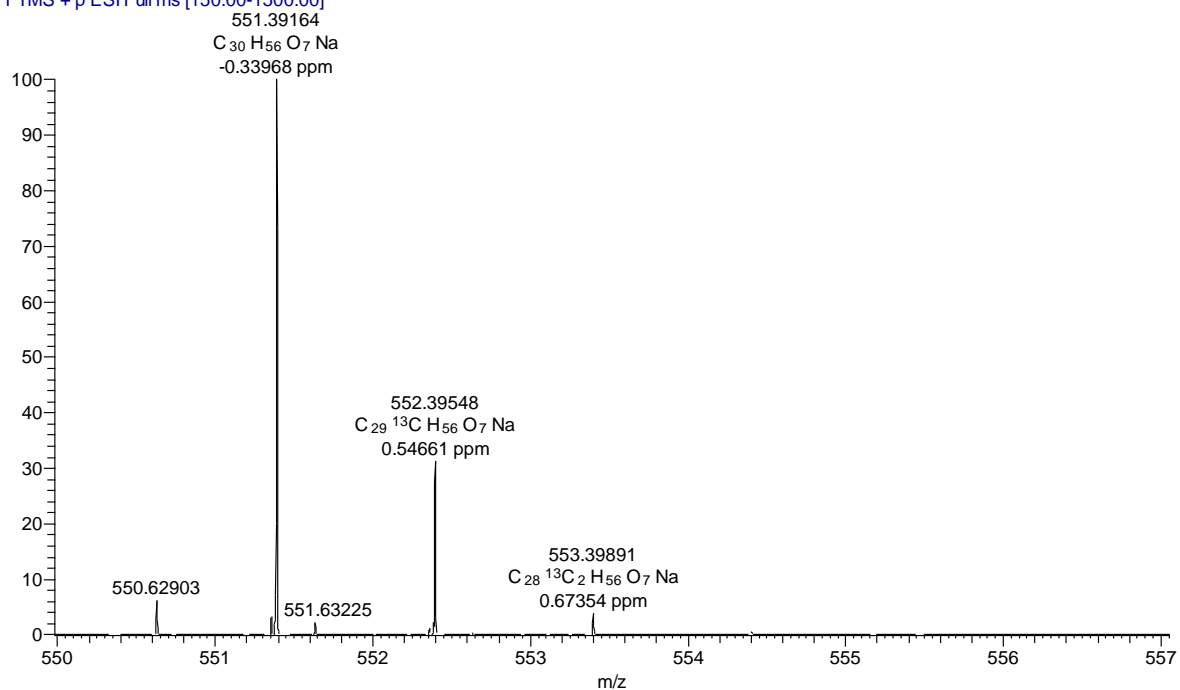


Figure S65. IR and HRMS spectra of 1.

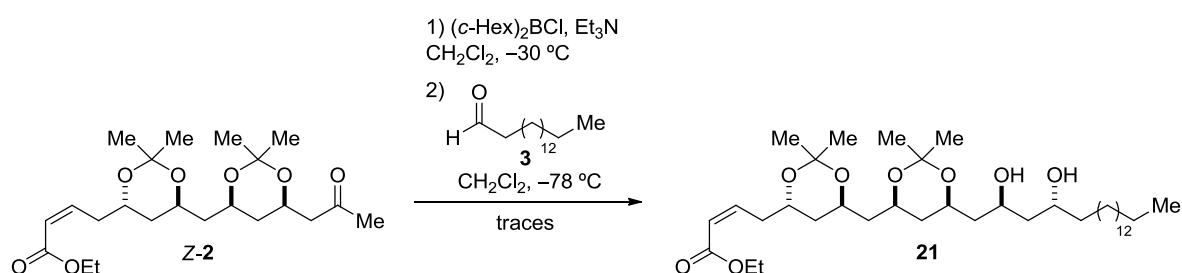
Table S1. ^1H and ^{13}C NMR chemical shifts for natural and synthetic cryptocaryol A.

Position	Natural Product			Dias Synthetic Product			O'Doherty Synthetic Product		
	$\delta^{13}\text{C}$	$\delta^1\text{H}$	multiplicity (J in Hz)	$\delta^{13}\text{C}^c$	$\delta^1\text{H}^a$	multiplicity (J in Hz)	$\delta^{13}\text{C}$	$\delta^1\text{H}$	multiplicity (J in Hz)
2	167.0			167.0			167.0		
3	121.4	5.97	dd (9.8, 1.9)	121.4	5.97	dd (9.6, 1.9)	121.4	5.97	dd (9.6, 2.5)
4	148.6	7.04	ddd (9.8, 6.0, 2.3)	148.5	7.05	ddd (9.6, 5.9, 2.4)	148.6	7.04	ddd (9.6, 6.0, 2.8)
5a	31.0	2.45	m	30.9	2.45	m	31.0	2.45	ddd (19.2, 5.2, 5.2)
5b		2.36	ddt (18.5, 11.8, 2.6)		2.36	ddt (18.5, 11.7, 2.5)		2.36	dddd (19.2, 11.6, 2.8, 2.8)
6	76.6	4.71	m	76.6	4.71	m	76.6	4.67-4.74	m
7a	43.9	1.94	ddd (14.5, 9.7, 2.3)	43.9	1.94	ddd (14.4, 9.9, 2.5)	43.9	1.94	ddd (14.8, 9.6, 2.8)
7b		1.67	m		1.66	m		1.55-1.71	m
8	66.6	4.08	m	66.6	4.08	m	66.6	4.09	(dddd, 8.8, 6.4, 6.4, 2.4)
9	46.0	1.68	m	46.0	1.63	m	46.0	1.55-1.71	m
10	69.9	3.97	m	69.9	4.00	m	69.9	3.96-4.04	m
11a	45.3	1.64	m	45.2	1.67	m	45.3	1.55-1.71	m
11b					1.60	m			
12	70.2	4.00	m	70.1	4.00	m	70.2	3.96-4.04	m
13	45.9	1.59	m	45.9	1.63	m	45.9	1.55-1.71	m
14	68.3	4.02	m	68.2	4.02	m	68.2	3.96-4.04	m
15	45.8	1.50	m	45.7	1.51	m	45.8	1.49-1.52	m
16	69.1	3.79	m	69.1	3.80	m	69.1	3.77-3.82	m
17	39.3	1.43	m	39.2	1.44	m	39.3	1.40-1.46	m
18a	26.8	1.32	m	26.8	1.43	m	26.8	1.25-1.32	m
18b					1.33	m			
19-28	30.5-31.0	1.27-1.29	br s	30.5-30.9	1.24-1.36	br s	30.5-31.0	1.25-1.32	br s
29	33.2	1.29	m	33.1	1.28	m	33.1	1.25-1.32	m
30	23.8	1.27	m	23.7	1.31	m	23.8	1.25-1.32	m
31	14.5	0.89	t (6.9)	14.4	0.89	t (7.0)	14.5	0.89	t (6.8)

^a Assignment based on COSY, HSQC, and HMBC experiments.

Attempts to optimize de aldol reaction

To improve the yields in the last three steps of the (-)-cryptocaryol A synthesis, we first investigated the influence of the solvents in the aldol coupling. In the original procedure, Et₂O was used for enolization of methyl ketone **Z-2**, and a solution of hexadecanal in CH₂Cl₂ was added to the pre-formed enolate. We envisioned that using CH₂Cl₂ for both the enolization and aldehyde addition may improve the yield; however, only traces of the desired product were observed (Scheme S1).



Scheme S1.

Analysis of the byproducts from the aldol reaction in CH₂Cl₂ by ¹H NMR revealed a new signal at 6.77 ppm (doublet of triplets, *J* = 16.1, 7.1 Hz) corresponding to an *E* alkene. Unfortunately, the new peak corresponds to the isomerization product of compound **Z-2** under the reaction conditions (Figure S66).

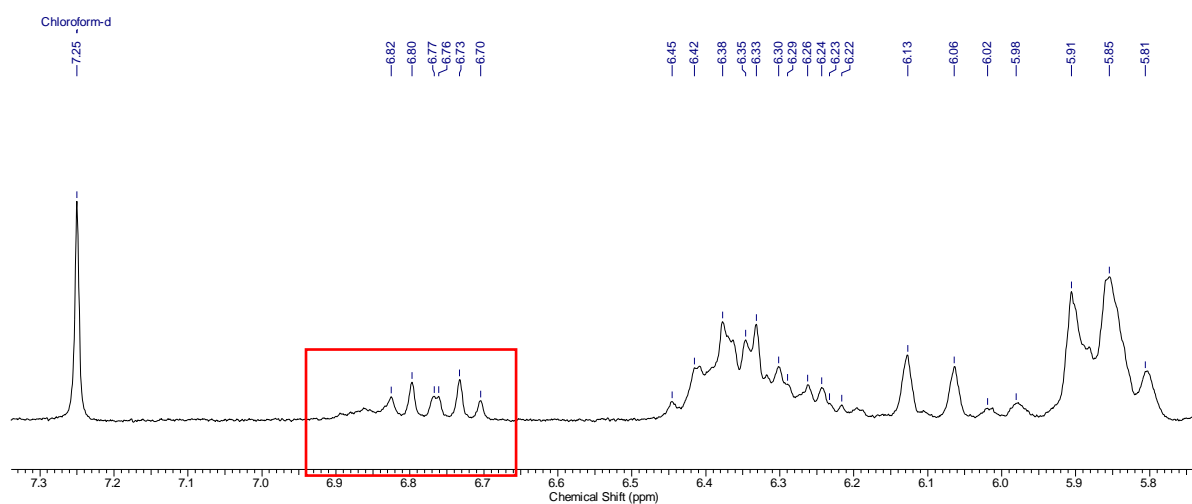
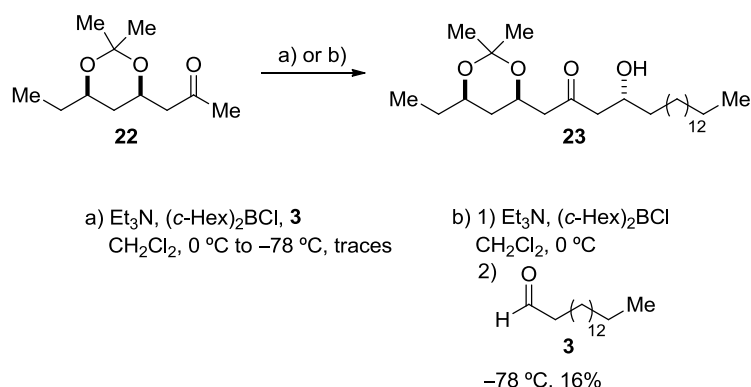


Figure S66.

We attributed the isomerization of methyl ketone **Z-2** to the complexation of the Lewis acid, (c-Hex)₂BCl, to the ester carbonyl. Thus, we began by investigating milder

enolization conditions to reduce the degradation of the starting material. Under the standard enolization conditions, (c-Hex)₂BCl is added to a solution of the methyl ketone at 0 °C, followed by addition of Et₃N. After 30 minutes, the reaction mixture is cooled to -78 °C, and a solution of the aldehyde is added. Therefore, we envisioned that reducing the enolization time or adding the Lewis acid to a mixture of the ketone and aldehyde in the aldol coupling may improve the yield. To investigate the effect of time and the order of addition of reagents, we used model methyl ketone **22**.

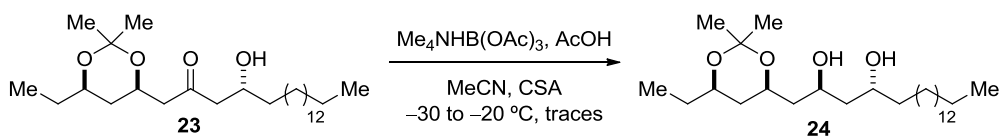
First, we performed the enolization of methyl ketone **22** in the presence of aldehyde **3**. However, only traces of the desired product were obtained. Next, (c-Hex)₂BCl was added to a solution of Et₃N and methyl ketone, and the enolate was allowed to form over 5 min before addition of the aldehyde. Under these conditions, the aldol adduct **23** was obtained in 16% yield (Scheme S2). However, the low yield in this reaction is inconsistent with the reaction progress observed on TLC. Therefore, we believe that the product degraded during purification on column chromatography.



Scheme S2.

To avoid potential degradation of aldol adduct **23**, the crude product was used in the subsequent step without purification by column chromatography. Therefore, the aldol reaction was accomplished according to Scheme S2b. After quenching the excess Lewis acid with MeOH, the volatiles were removed under reduced pressure, and the residue was diluted with CH₂Cl₂ and washed with H₂O to remove excess Et₃N•HCl formed during the reaction. The organic layer was concentrated and the crude product was submitted to a 1,3-*anti* reduction using the Evans method.¹ However, the crude aldol adduct **23** was insoluble in the solvent mixture (MeCN and AcOH) used for this reaction. Only a small amount of diol **24** was obtained and 10% of compound **23** was recovered (Scheme S3).

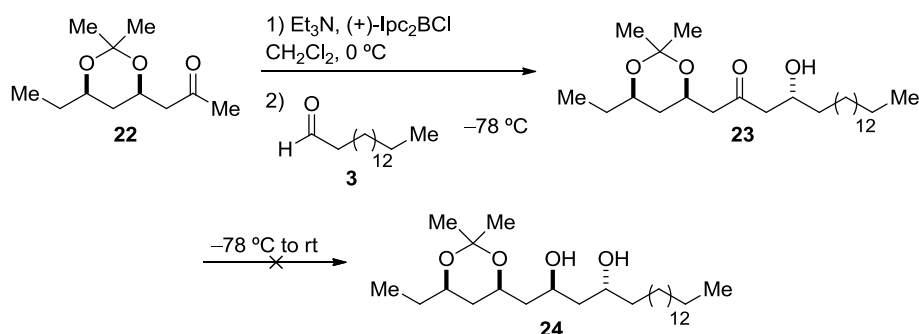
¹ a) Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, 27, 5939. b) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, 110, 3560.



Scheme S3.

Based on the poor solubility and yield for the 1,3-*anti* reduction, we decided to use an alternative method described by Dieckmann and Menche to effect the aldol reaction and subsequent reduction.² This method uses Ipc_2BCl as a Lewis acid in the initial aldol coupling between a methyl ketone and an aldehyde followed by a subsequent asymmetric reduction of the ketone carbonyl upon warming. The aldol reaction and tandem reduction affords products with 1,5-*anti* and 1,3-*syn* stereochemistry.

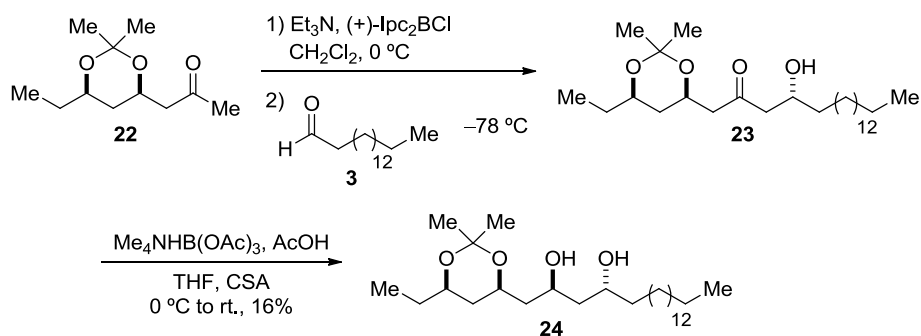
Application of the Dieckmann and Menche methodology to ketone **22** afforded the desired aldol product; however, no reduction of the ketone carbonyl was observed after 24 hours at room temperature by TLC (Scheme S4).



Scheme S4.

As an alternative, the aldol reaction was performed using (+)- Ipc_2BCl , and the corresponding product was reduced using the Evans method with THF as solvent. However, the solubility of compound **23** in THF was low and only 16% of diol **24** was obtained (Scheme S5).

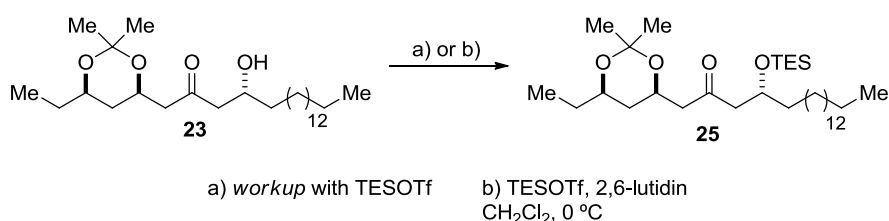
² Dieckmann, M.; Menche, D. *Org.Lett.* **2013**, *15*, 228.



Scheme S5.

Since optimization of both the aldol coupling between **22** and **3** and the reduction of **23** were difficult, we decided to protect the hydroxyl of **23** as the TES ether with TESOTf to improve its solubility for a stereoselective carbonyl reduction. Therefore, the aldol reaction involving methyl ketone **22** and aldehyde **3** was quenched by addition of TESOTf at $-78\text{ }^\circ\text{C}$, and gradually warmed to room temperature (Scheme S6a). However, the TLC of aldol reaction after the addition of TESOTf remained the same and the desired silyl ether was not isolated.

We envisioned that the silyl protection failed because the Lewis acid was still coordinated to the secondary alcohol. Therefore, the aldol reaction was accomplished again, and after the reaction was complete the excess Lewis acid was quenched with MeOH and the reaction medium was washed with H_2O . The crude product was then treated with TESOTf and 2,6-lutidine, but only a complex mixture of byproducts was observed (Scheme S6b).³



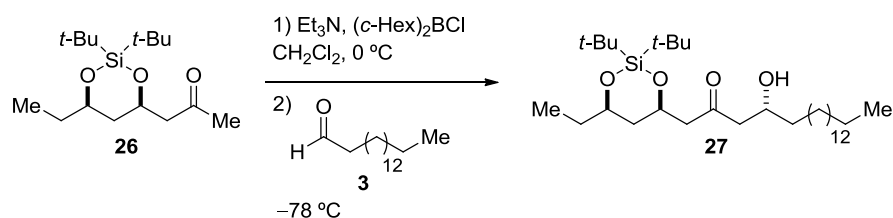
Scheme S6.

Finally, we decided to investigate the influence of eluents used during purification of the aldol adduct by column chromatography. Model substrate **26** was submitted twice to the aldol reaction conditions shown in Scheme S7. Purification of **27** was first performed by loading the crude product on the column with CH_2Cl_2 , followed by using a mixture of

³ Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 4th ed.; John Wiley & Sons; Nova York, 2007.

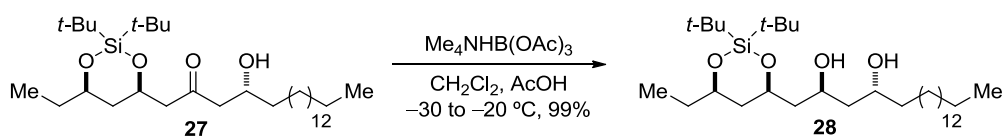
hexane and ethyl acetate as eluent. With these conditions, only traces of the desired product were isolated.

For the second purification, the crude product was loaded on the column with CH_2Cl_2 and this solvent was also used as eluent. In this case, the aldol adduct **27** was obtained in 44% yield, which is a superior yield to those observed for reactions involving aldehyde **3**.



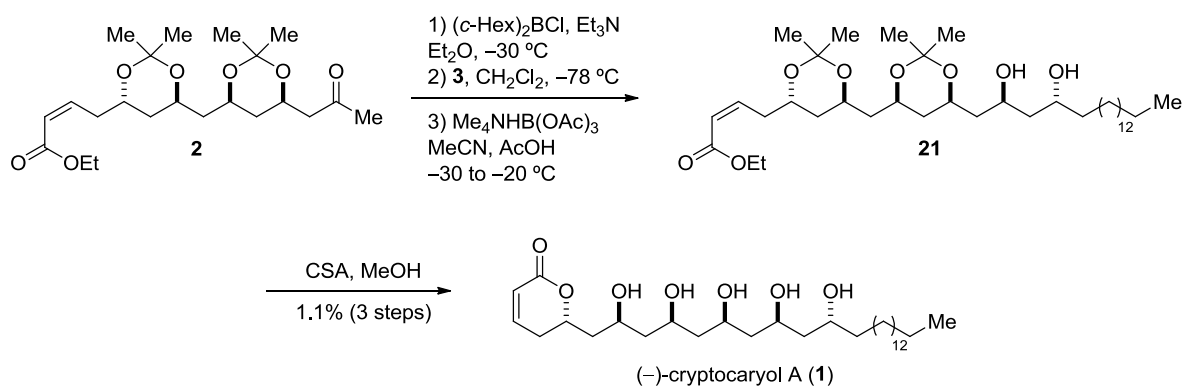
Scheme S7.

The reduction step was then optimized by substituting MeCN , used in the Evans methodology, for CH_2Cl_2 , which can solubilize both the starting material and reducing agent. Reaction of aldol adduct **27** with $\text{Me}_4\text{NHB}(\text{OAc})_3$ in CH_2Cl_2 and AcOH afforded diol **28** in 99% yield, which demonstrates that CH_2Cl_2 is the ideal solvent for substrate **27** (Scheme S8). Furthermore, aldol adduct **27** could be reduced to diol **28** under the optimized conditions, albeit in poor yield.



Scheme S8.

With the optimized conditions for the model substrate in hand, we next applied them to the actual substrate. Since the solvent mixture did not influence the yields in the aldol reaction, Et_2O was used for enolization of methyl ketone **2** (Scheme S8). The aldol adduct was then purified with a mixture of CH_2Cl_2 : AcOEt (9:1) as eluent. Subsequent reduction of the aldol adduct under the Evans conditions using CH_2Cl_2 afforded compound **21**. The crude product was partially purified by column chromatography and then treated with CSA in MeOH to give (-)-cryptocaryol A in 1.1% yield over 3 steps (Scheme S9).



Scheme S9.