A carbohydrate based approach for the total synthesis of 1,3-polyol/α-pyrone anti-fungal natural products

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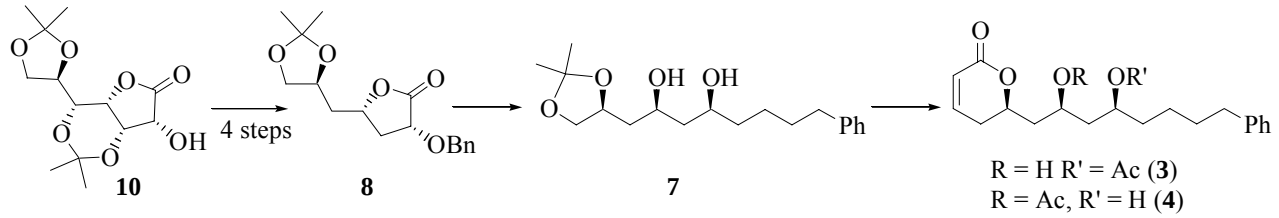


Table of Contents:

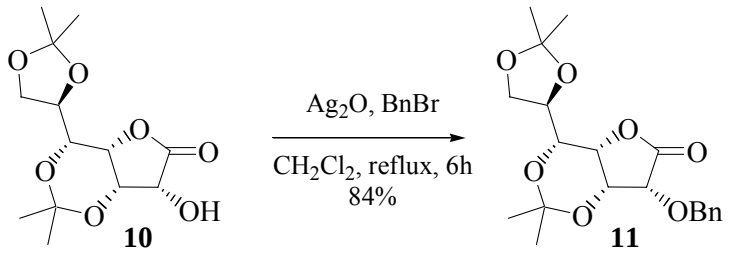
S. No.	Description	Page
1	General Methods	S4
2	**Entry 11**	
	Synthesis and Spectral Data	S4
3	**Entry 9**	
	Synthesis and Spectral Data	S5
4	**Entry 12**	
	Synthesis and Spectral Data	S6
	^{1}H-NMR Spectrum	S7
	^{13}C-NMR Spectrum	S8
	DEPT Spectrum	S9
	X-ray Structures	S10
	Crystallographic Table	S11
6	Entry **12**-Xanthate	
	Synthesis and Spectral Data	S12
7	Entry **8**	
	Synthesis and Spectral Data	S12
	^{1}H-NMR Spectrum	S14
	^{13}C-NMR Spectrum	S15
	DEPT Spectrum	S16
8	**Lactal Derived from 12**	
	Synthesis and Spectral Data	S17
	Entry 13	
	Synthesis and Spectral Data	S17
	^{1}H-NMR Spectrum	S19
	^{13}C-NMR Spectrum	S20
	DEPT Spectrum	S21
9	**Entry 14**	
	Synthesis and Spectral Data	S22
10	**Entry 7-Bz**	
	Synthesis and Spectral Data	S22
11	**Entry 7**	
	Synthesis and Spectral Data	S23
	^{1}H-NMR Spectrum	S24
	^{13}C-NMR Spectrum	S25
	DEPT Spectrum	S26
12	**Entry 7-diPMB**	
	Synthesis and Spectral Data	S27
13	**Entry 15**	
	Synthesis and Spectral Data	S28
14	**Entry 6**	
	Synthesis and Spectral Data	S28
	^{1}H-NMR Spectrum	S30
	^{13}C-NMR Spectrum	S31
	DEPT Spectrum	S32

15	**Entry 16**	
	Synthesis and Spectral Data	S33
16	**Selective Hydrogenation of 16**	S34
	Spectral Data of *Z*-Acrylate Intermediate	S34
17	**Entry 17**	
	Synthesis and Spectral Data	S34
	^{1}H-NMR Spectrum	S36
	^{13}C-NMR Spectrum	S37
	DEPT Spectrum	S38
18	**PMB Deprotection of 17**	S39
19	**Entries 18 and 19**	
	Spectral Data	S39
20	**Entry 20**	
	Spectral Data	S39
	^{1}H-NMR Spectrum	S41
	^{13}C-NMR Spectrum	S42
	DEPT Spectrum	S43
21	**Entries 18-Ac and 19-Ac**	
	Synthesis and Spectral Data	S44
22	**Entry 21**	
	Spectral Data	S45
	^{1}H-NMR Spectrum	S46
	^{13}C-NMR Spectrum	S47
	DEPT Spectrum	S48
23	**Entries 3 and 4**	
	Synthesis and Spectral Data	S49
	HPLC of **3**/**4** Mixture	S51
	^{1}H-NMR Spectrum of **3**	S52
	^{13}C-NMR Spectrum of **3**	S53
	DEPT Spectrum of **3**	S54
	^{1}H-NMR Spectrum of **4**	S55
	^{13}C-NMR Spectrum of **4**/**3**	S56
	DEPT Spectrum of **4**/**3**	S57

Experimental Section

General methods: all air and/or moisture sensitive reactions were carried out in anhydrous solvents under an atmosphere of argon in an oven-dried glassware. All anhydrous solvents were distilled prior to use: THF and diethyl ether from Na and benzophenone; CH_2Cl_2 from CaH_2; MeOH from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using Spectrochem silica gel (60–120 mesh). Specific optical rotations $[\alpha]_D^{25}$ are given in 10^{-1} deg cm^2g^{-1}. Infrared spectra are recorded in $CHCl_3$ and are reported in wave number (cm^{-1}). ^1H and ^{13}C NMR chemical shifts are reported in ppm downfield from tetramethylsilane and coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

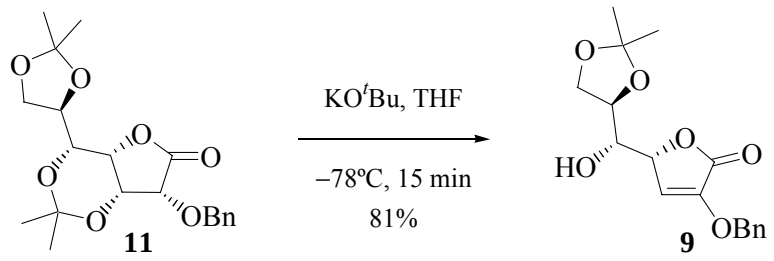
2-*O*-Benzyl-3,5;6,7-di-*O*-isopropylidine-D-glucoheptonic-γ-lactone (11).



To a solution of **10** (5.0 g, 17.3 mmol) in CH_2Cl_2 (50 ml) was added benzyl bromide (2.47 ml, 20.8 mmol), silver oxide (6.02 g, 26 mmol) and the mixture was refluxed for 6 h. The contents were filtered (Celite), concentrated and the resulting white solid was crystallized from ethyl acetate/hexane (1:3) to obtain **11** (5.5 g, 84%) as colourless needles. MP 198 °C. $[\alpha]_D^{25} = -36.9$ (c = 1, $CHCl_3$). IR ($CHCl_3$): υ 3393, 3019, 1797, 1384, 1215, 1149, 1076, 757, 668 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.39–7.36 (m, 5H), 4.86 (d, J = 12.7 Hz, 1H), 4.79 (d, J = 12.7 Hz, 1H),4.51–4.45 (m, 1H), 4.35–4.26 (m, 1H), 4.20–4.17 (m, 2H), 4.08 (dd, J = 8.8, 6.4 Hz, 1H), 3.91 (dd, J = 8.8, 4.0 Hz, 1H), 3.77 (br d, J = 8.8 Hz, 1H), 1.43 (s, 6H), 1.39 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (50 MHz) 19.2 (q), 24.7 (q), 26.8 (q), 28.9 (q),

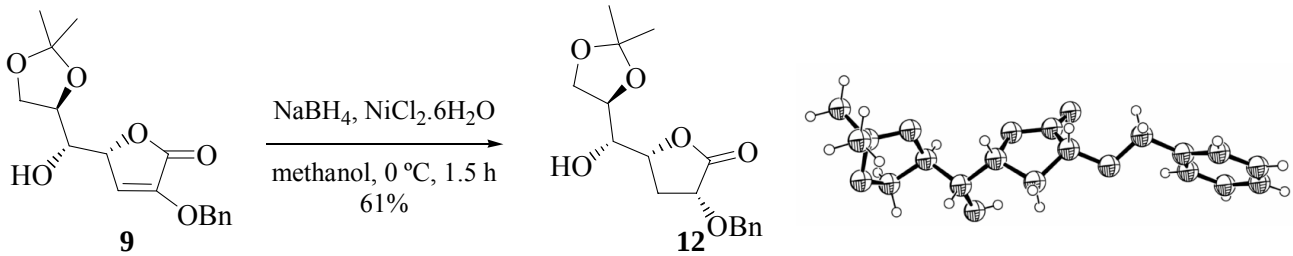
66.8 (t), 67.9 (d), 68.5 (d), 69.4 (d), 72.3 (t), 72.9 (d), 75.5 (d), 98.4 (s), 109.4 (s), 128.3 (d), 128.5 (d), 136.3 (s), 172.8 (s) ppm. Anal. Calcd For $C_{20}H_{26}O_7$: C 63.48, H 6.93%; found: C 63.28, H 7.21%.

2-Benzyloxy-3-deoxy-6,7-*O*-isopropylidine-D-*arabino*hept-2-enoic-γ-lactone (9).



At −78 °C, a suspension of KO^{t}Bu (1.48 gm, 13.2 mmol) in anhydrous THF (50 ml) was treated with a solution of benzylether **11** (5 gm, 13.2 mmol) in anhydrous THF (80 ml) and stirred for 15 min at −78 °C. The reaction mixture was quenched with a solution of AcOH (0.8 ml, 13.2 mmol) in THF (5 ml) and allowed to reach rt. The contents were filtered (Celite), concentrated and the crude product was purified by crystallization from ethyl acetate/hexane (1:3) to procure **9** (3.43 g, 81%) as a colourless solid. mp 162 °C. $[\alpha]_D^{25}$ = +31.7 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3420, 3020, 2400, 1760, 1652, 1381, 1215, 1059, 756, 668 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.40–7.36 (m, 5H), 6.17 (d, *J* = 2.1 Hz, 1H), 5.09 (dd, *J* = 4.1, 2.1 Hz, 1H), 5.02 (s, 2H), 4.16 (dd, *J* = 6.2, 4.1 Hz, 1H), 4.12 (dt, *J* = 6.2, 3.5 Hz, 1H), 3.99 (dd, *J* = 7.6, 3.5 Hz, 1H), 3.55 (dd, *J* = 7.6, 4.1 Hz, 1H), 2.40 (br.s, 1H), 1.37 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (50 MHz) 25.1 (q), 26.7 (q), 67.1 (t), 72.8 (t), 73.1 (d), 75.3 (d), 79.5 (d), 109.7 (s), 115.9 (d), 127.6 (d), 128.5 (d), 128.6 (d), 134.7 (s), 145.9 (s), 167.8 (s) ppm. Anal. Calcd For $C_{17}H_{20}O_6$: C 63.74, H 6.29%; found: C 63.80, H 6.03%.

2-*O*-Benzyl-3-deoxy-6,7-*O*-isopropylidine-D-*gluco*heptoic-γ-lactone (12).



At 0 °C, a solution of **9** (1 gm, 3.1 mmol) in methanol (30 ml) was treated with $NiCl_2.6H_2O$ (220 mg, 0.9 mmol) and stirred for 30 min. To this $NaBH_4$ (342 mg, 9.1 mmol) and AcOH (to maintain pH = 7) were added in three portions with a 10 minutes interval. After completing the addition, stirring was continued for another 30 min at 0 °C. The contents were filtered (Celite), concentrated, dissolved in ethylacetate (25 ml), washed with water, brine, dried (Na_2SO_4) and concentrated to get a white solid. The crude product was purified by crystallization in CH_2Cl_2/hexane to get a white crystalline solid **12** (615 mg, 61%). mp 116 °C. $[\alpha]_D^{25}$ = + 32.4 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3442, 2992, 2881, 1787, 1455, 1370, 1216, 848, 755 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.38–7.32 (m, 5H), 4.96 (d, *J* = 11.8 Hz, 1H), 4.75 (d, *J* = 11.8 Hz, 1H), 4.59 (ddd, *J* = 8.9, 6.4, 2.9 Hz, 1H), 4.24 (dd, *J* = 9.2, 8.4 Hz, 1H), 4.19–3.96 (m, 3H), 3.45 (br.d, *J* = 4.4 Hz, 1H), 2.51 (ddd, *J* = 13.1, 8.3, 6.4 Hz, 1H), 2.30 (dt, *J* = 13.1, 9.1 Hz, 1H),1.38 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (75 MHz) 25.1 (q), 26.7 (q), 31.1 (t), 67.2 (t), 72.1 (t), 72.9 (d), 73.2 (d), 75.3 (d), 76.4 (d), 109.4 (s), 128.0 (d), 128.4 (d), 136.9 (s), 174.5 (s) ppm. Anal. Calcd For $C_{17}H_{22}O_6$: C 63.34, H 6.88%; found: C 63.38, H 7.14%.

Entry_12H

13 May 2005
b srinivas

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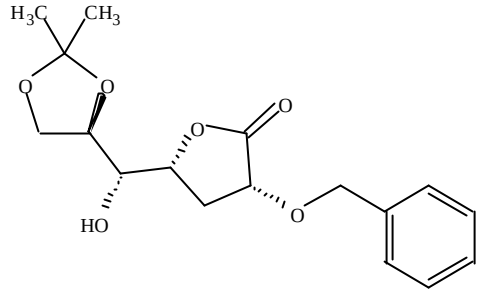

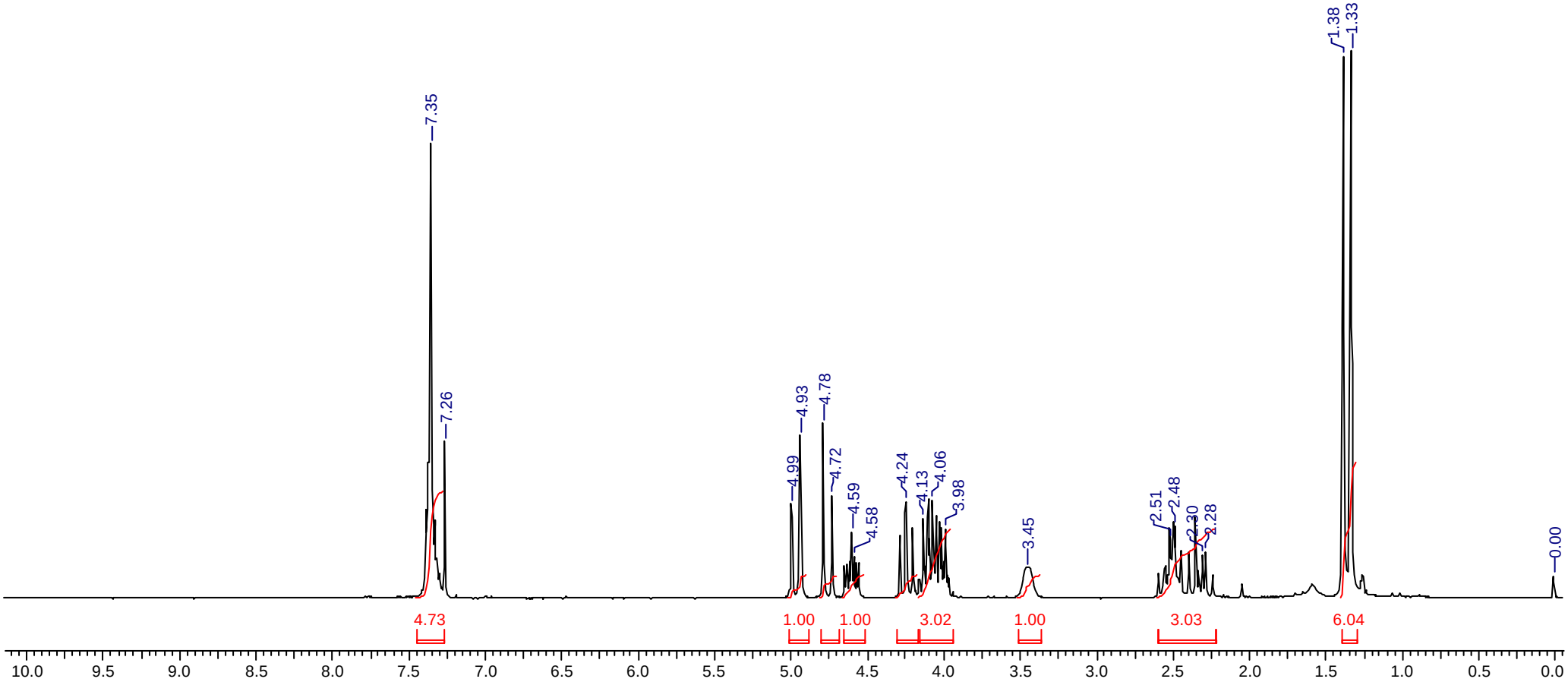

Entry_12

S8

13 May 2005
B SRINIVAS

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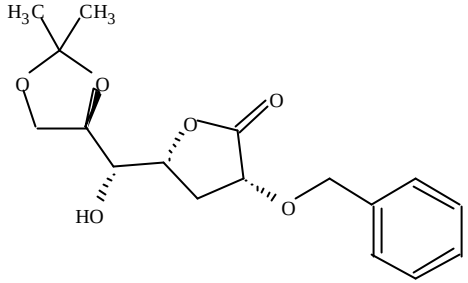

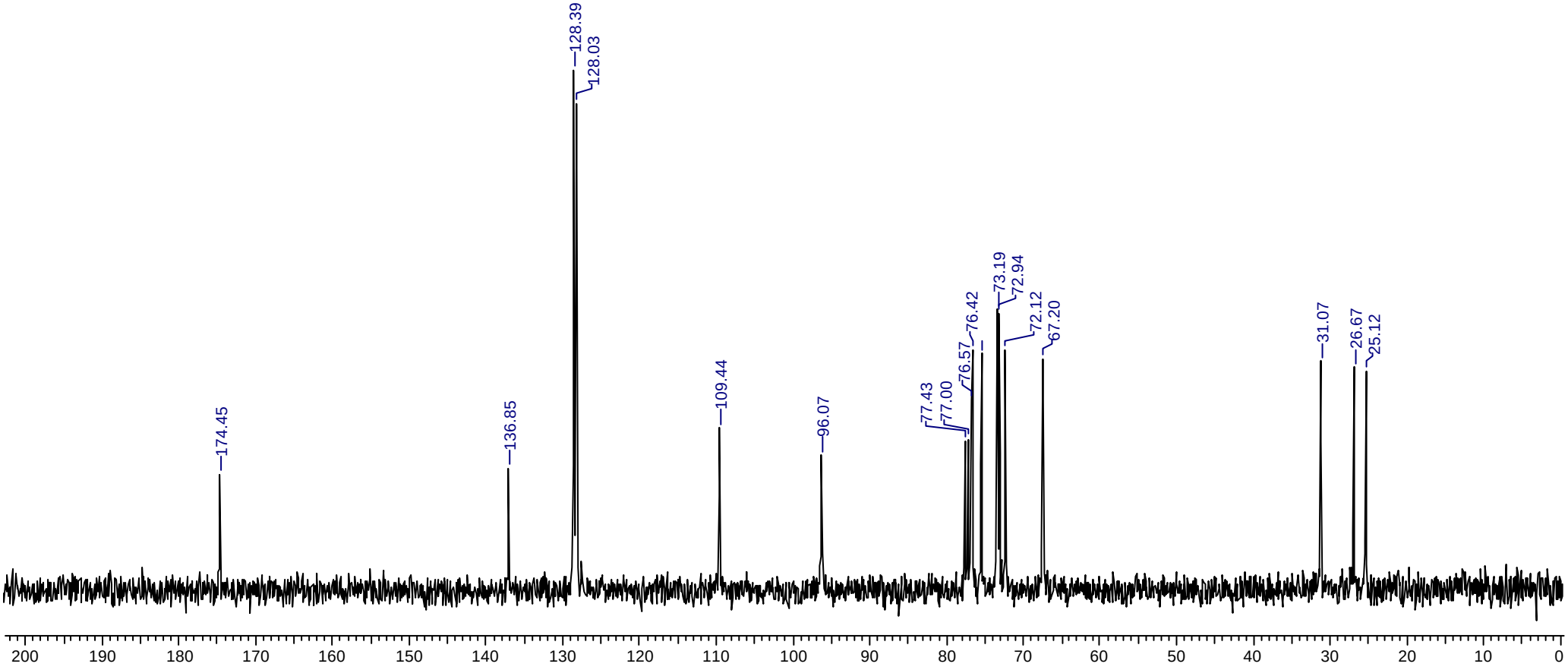

Entry_12

13 May 2005
B SRINIVAS

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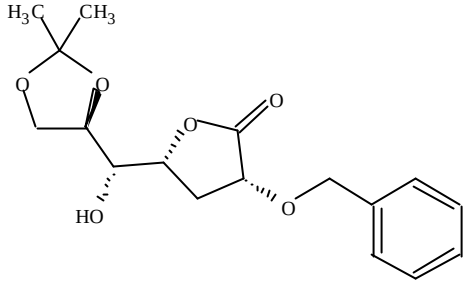
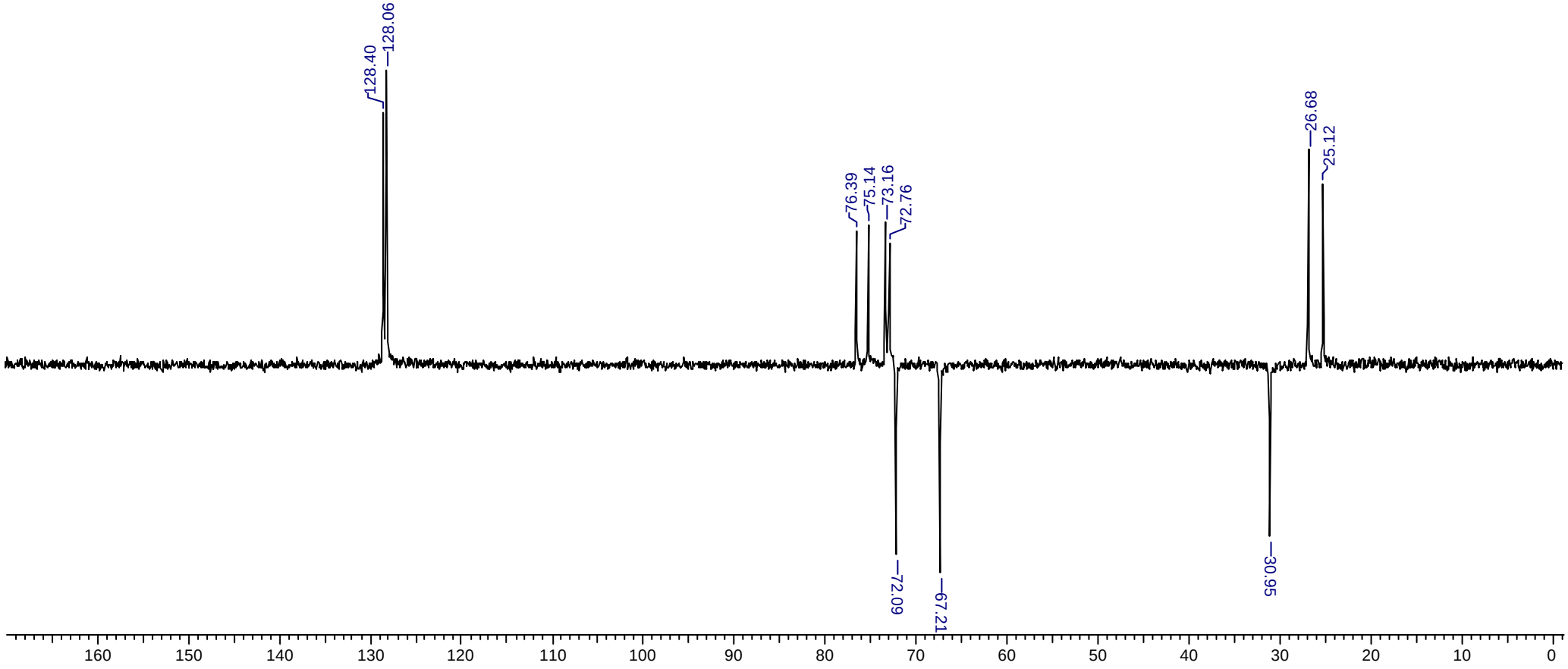
Temperature (grad C) 24.000							





Crystal Data: Single crystals of the compound were grown by slow evaporation of the solution in a solvent mixture of dichloro methane and pet-ether. Colourless plate like crystal of approximate size 0.48 x 0.24 x 0.02 mm, was used for data collection on *Bruker SMART APEX* CCD diffractometer using Mo K_α radiation with fine focus tube with 50kV and 30mA. Crystal to detector distance 6.05 cm, 512 x 512 pixels / frame, multiscan data acquisition. Total scans = 3, total frames = 1212, Oscillation / frame –0.3º, exposure / frame = 10.0 sec / frame, maximum detector swing angle = –30.0º, beam center = (260.2, 252.5), in plane spot width = 1.24, SAINT integration, θ range = 2.52 to 25.00 º, completeness to θ of 23.33 º is 99.2 %. SADABS correction applied , C17 H22 O6, M = 322.35. Crystals belong to monoclinic, space group $P2_1$, a = 9.195(1), b = 6.1777(8), c = 15.004(2) Å, β = 93.846(2)º, V = 850.4 (2) $Å^3$, Z = 2, D_c = 1.259 mg m^{-3}, μ (MoK_α) = 0.095 mm^{-1}, T = 295(2) K, 4283 reflections measured, 2795 unique [I>2σ(I)], R value 0.0594, wR2 = 0.1375. All the data were corrected for Lorentzian, polarisation and absorption effects. SHELX-97 (ShelxTL)[a] was used for structure solution and full matrix least squares refinement on F^2. Hydrogen atoms were included in the refinement as per the riding model. Data collection and refinement parameters are listed in table.

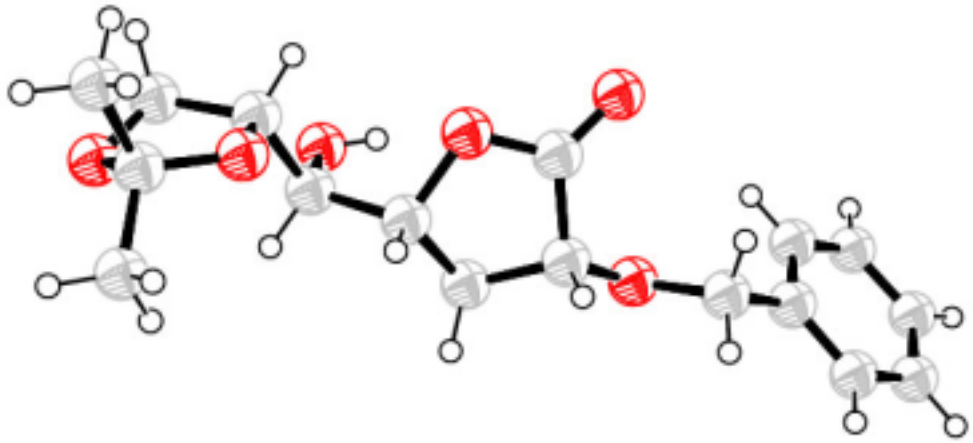


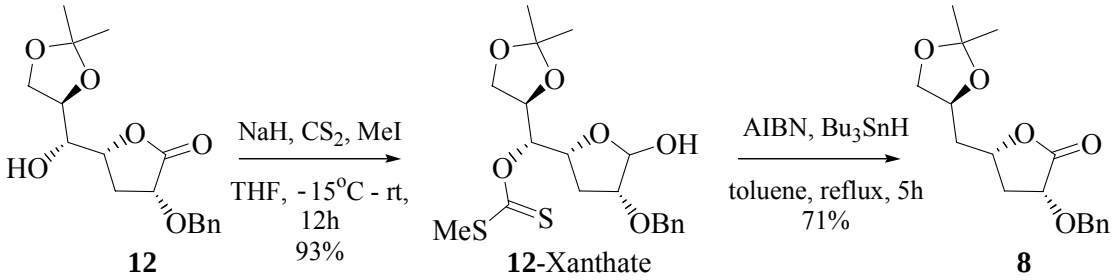
Figure. *ORTEP Diagram of* **12.**

[a]G. M. Sheldrick, SHELX-97 program for crystal structure solution and refinement, University of Gottingen, Germany, 1997

Table. Crystal data and structure refinement for $C_{17}H_{22}O_6$

Empirical formula	$C_{17}H_{22}O_6$
Formula weight	322.35
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic,P21
Unit cell dimensions	a = 9.195(1) Å
	b = 6.1777(8) Åbeta = 93.846(2)º
	c = 15.004(2) Å
Volume	850.38(18) $Å^{-3}$
Z, Calculated density	2,1.259 Mg/m^{-3}
Absorption coefficient	0.095 mm^{-1}
	F(000) 344
Crystal size	0.48 x 0.24 x 0.02 mm
Theta range for data collection	2.52 to 25.00°
Limiting indices	-9<=h<=10, -7<=k<=7, -17<=l<=16
Reflections collected / unique	4283 / 2795 [R_{int} = 0.0334]
Completeness to 2Θ = 25.00	99.2 %
Max. and min. transmission	0.9979 and 0.9556
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2795 / 25 / 211
Goodness-of-fit on F^2	1.017
Final R indices [I>2σ(I)]	R_1 = 0.0594, wR_2 = 0.1375
R indices (all data)	R_1 = 0.0945, wR_2 = 0.1565
Absolute structure parameter	0.8(19)
Largest diff. peak and hole	0.188 and -0.172 e.$Å^{-3}$

2-*O*-Benzyl-3,5-dideoxy-6,7-*O*-isopropylidine-D-*xylo*heptoic-γ-lactone (8).



To a suspension of NaH (771 mg, 19.7 mmol) in anhydrous THF at −15 °C were added CS_2 (3.3 ml, 54 mmol), MeI (3.36 ml, 54 mmol) and stirred for 30 min.To this was added a solution of **12** (5.8 gm, 17.9 mmol) in anhydrous THF and allowed to stirr at rt for 12h. The reaction mixture was poured in cold water and extracted with ethyl acetate.The combined organic extracts were washed with brine, dried (Na_2SO_4), concentrated and the resulting crude product was purified by column chromatography (15% ethyl acetate in petroleum ether) to afford **12**-xanthate (6.89 g, 93%) as an yellow colour solid. mp 124 °C. $[\alpha]_D^{25}$ = +50.7 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3393, 3019, 1788, 1454, 1374, 1215, 1069, 756, 668 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.35–7.29 (m, 5H), 5.99 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.92 (d, *J* = 11.9 Hz, 1H), 4.78–4.69 (m, 1H), 4.73 (d, *J* = 11.8 Hz, 1H), 4.49–4.39 (m, 1H), 4.20 (t, *J* = 9.0, Hz, 1H), 4.04 (dd, *J* = 8.8, 6.2 Hz, 1H), 3.88 (dd, *J* = 8.8, 5.2 Hz, 1H), 2.54 (s, 3H), 2.48 (ddd, *J* = 13.1, 8.0, 6.2 Hz, 1H), 2.05 (ddd, *J* = 13.1, 9.8, 8.8 Hz, 1H), 1.40 (s, 3H), 1.33 (s, 3H). ^{13}CNMR (200 MHz, $CDCl_3$) 19.3 (q), 25.3 (q), 26.8 (q), 31.1 (t), 66.4 (t), 72.1 (t), 72.5 (d), 73.6 (d), 74.5 (d), 79.6 (d), 109.9 (s), 128.1 (d), 128.2 (d), 128.5 (d), 136.8 (s), 173.4 (s), 216.8 (s) ppm. Anal. Calcd For $C_{19}H_{24}O_6S_2$: C 55.32, H 5.86, S 15.54%; found: C 55.48, H 5.62, S 15.19%.

A degassed solution of **12**-xanthate (6.89 gm, 16.7 mmol) in 50 ml of dry toluene, AIBN (10 mg) and tri-*n*-butyltin hydride (6.64 ml, 25.1 mmol) was refluxed for 5 h. After the reaction was complete as monitored by TLC, the reaction mixture was concentrated and the resulting crude product was purified by column chromatography (20% ethylacetate in petroleum ether) to obtain **8** (3.63 g, 71%) as a colorless oil. $[\alpha]_D^{25}$ = +21.0 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3024, 2927, 1783, 1455, 1373, 1216, 757,

667 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.39–7.30 (m, 5H), 4.99 (d, *J* = 11.8 Hz, 1H), 4.75 (d, *J* = 11.8 Hz, 1H), 4.60-4.46 (m, 1H), 4.34–4.21 (m, 1H), 4.22 (dd, *J* = 9.8, 8.1 Hz, 1H), 4.11 (dd, *J* = 8.1, 6.0 Hz, 1H), 3.53 (dd, *J* = 8.1, 7.0 Hz, 1H), 2.61 (ddd, *J* = 12.9, 8.2, 5.7 Hz, 1H), 2.03–1.81 (m, 3H),1.39 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (50 MHz): 25.6 (q), 26.9 (q), 36.0 (t), 40.2 (t), 69.3 (t), 72.1 (t), 72.5 (d), 73.2 (d), 74.1 (d), 108.9 (s), 127.9 (d), 128.0 (d), 128.4 (d), 136.9 (s), 174.2 (s) ppm. Anal. Calcd For $C_{17}H_{22}O_5$: C 66.65, H 7.24%; found: C 66.79, H 7.07%.

Entry_08

13 May 2005
b srinivas

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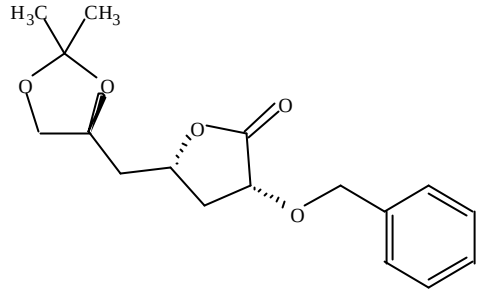

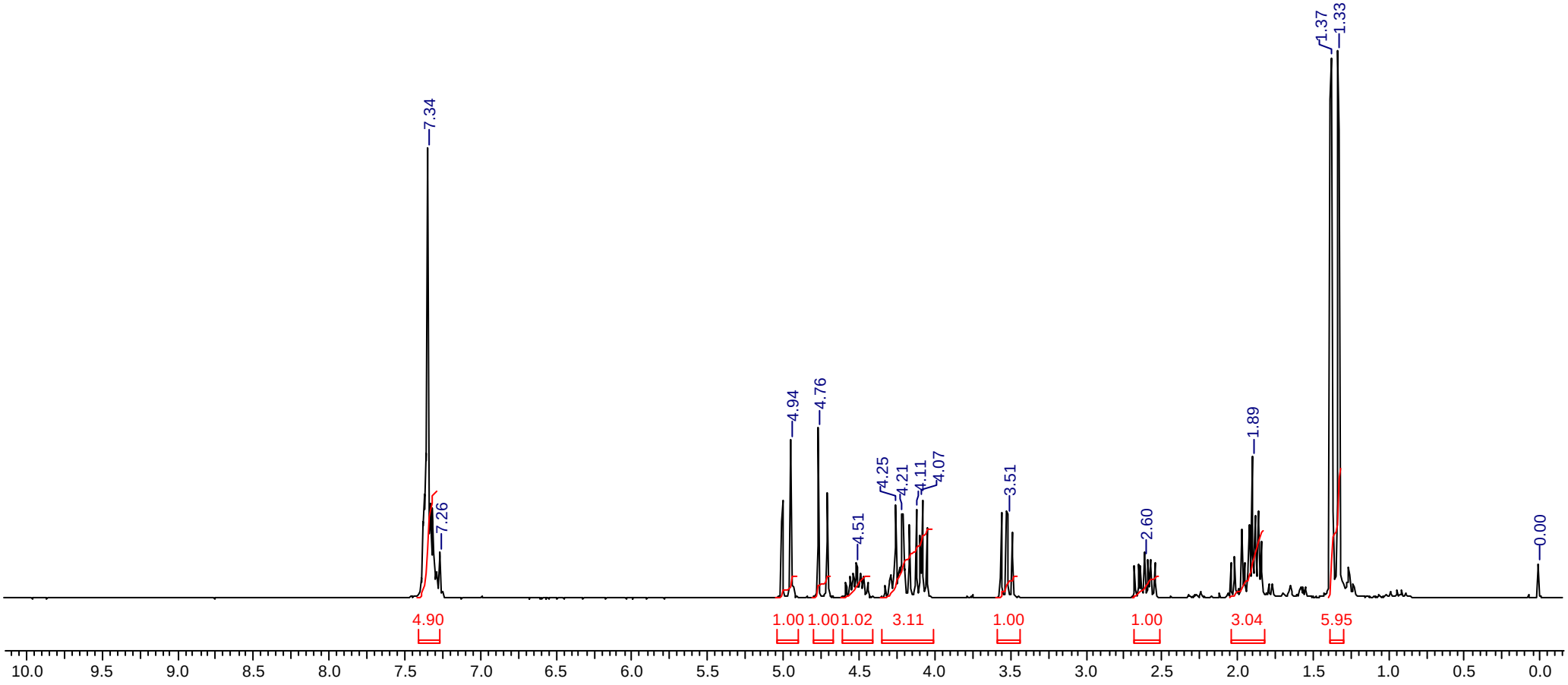

Entry_08

13 May 2005
b srinivas

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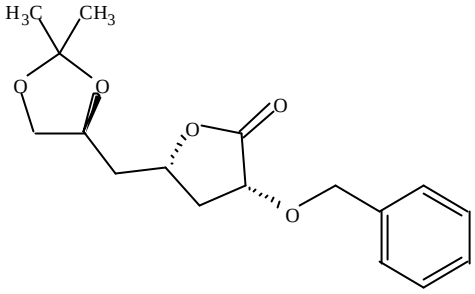

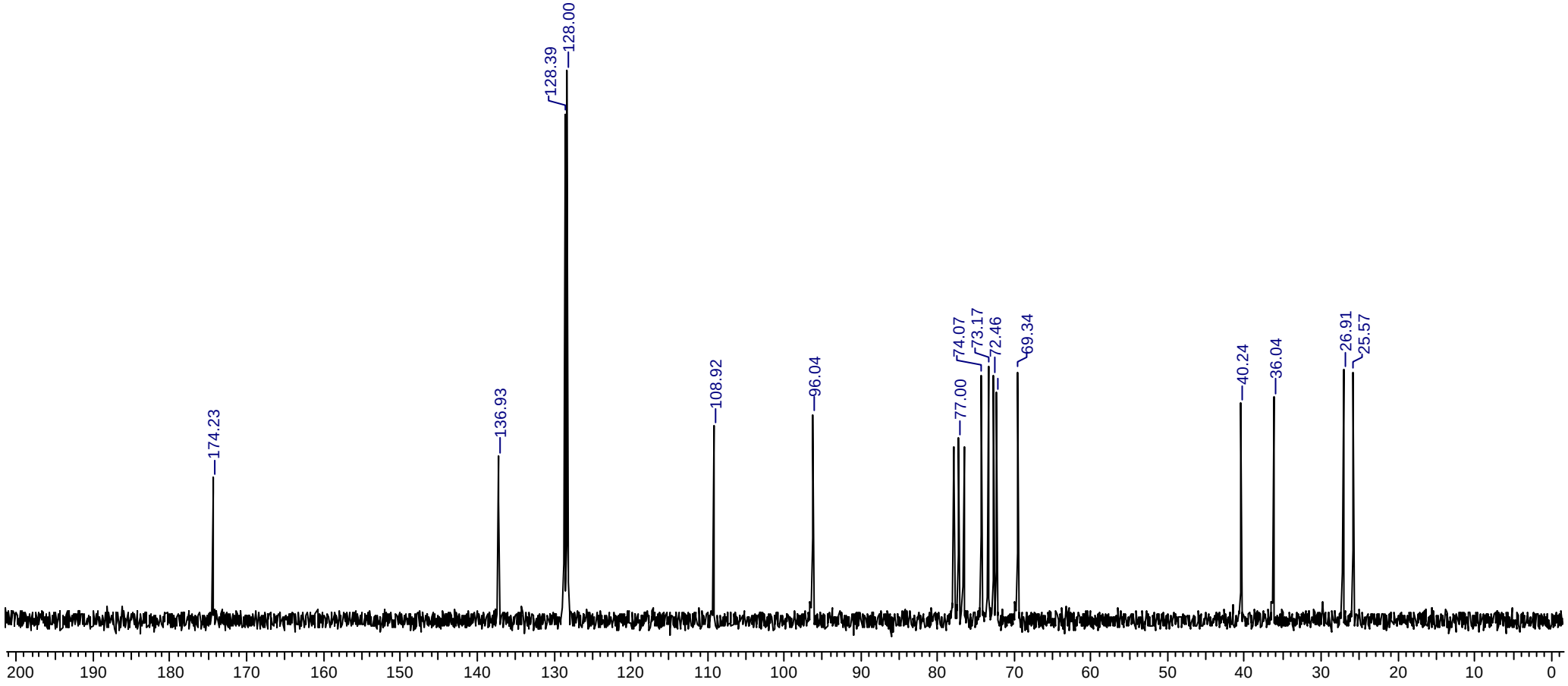

Entry_08

13 May 2005
b srinivas

Acquisition Time (sec)	2.7329	***Comment***	b srinivas	***Date***	03/12/2004 04:09:40	***Frequency (MHz)***	50.32
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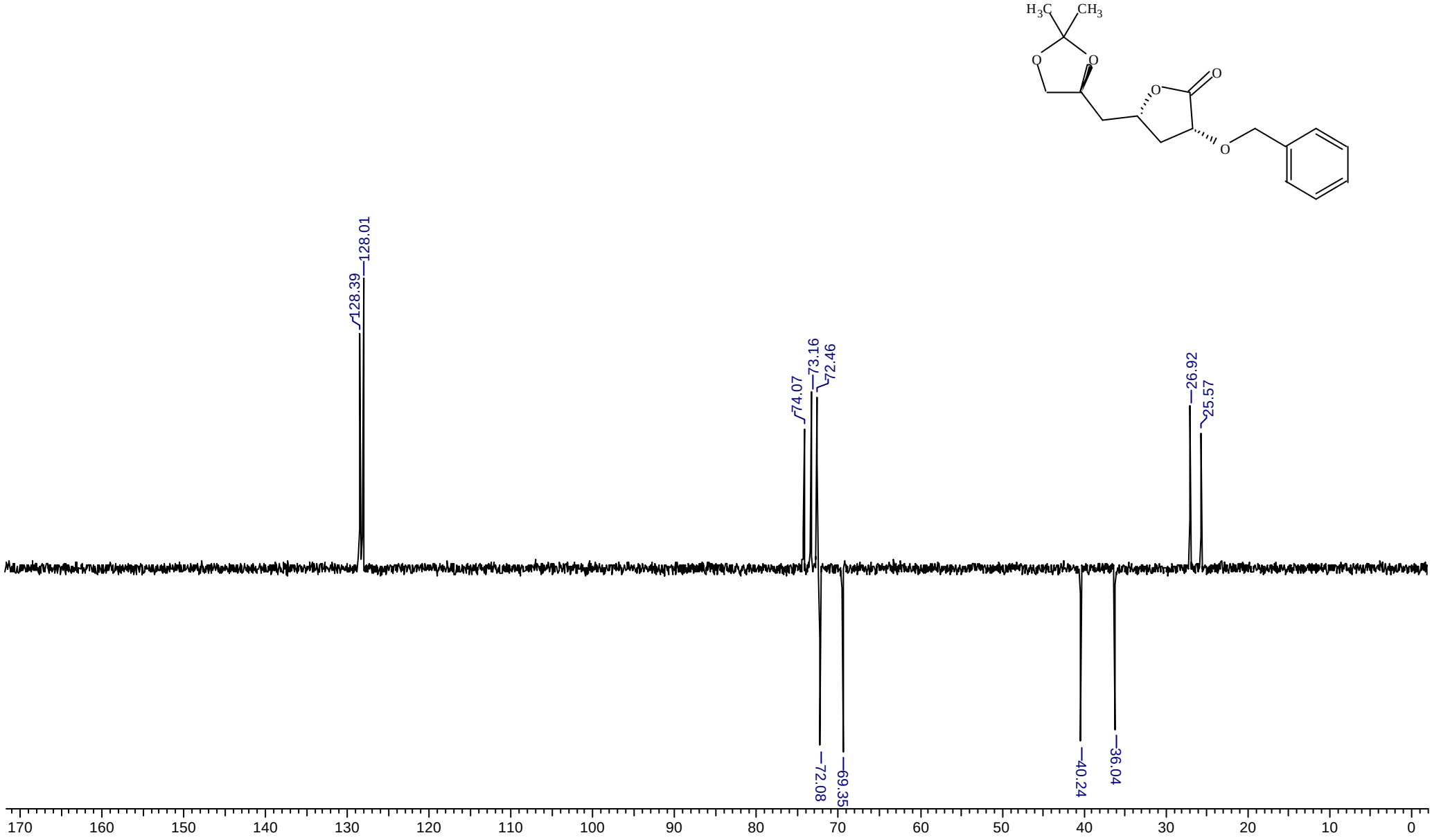
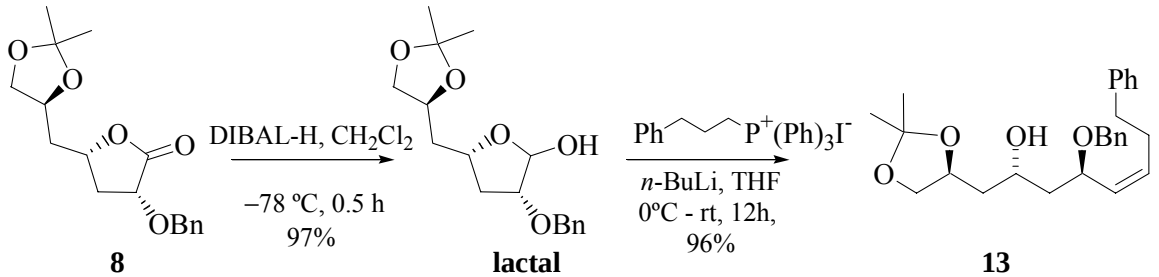


Conversion of Lactone 8 to *Z*-Olefine 13.



The lactone **8** (3.354 gm, 10.947 mmol) was dissolved in dry CH_2Cl_2 (20 ml), cooled to −78 °C and added DIBAL-H (9.71 ml, 19.71 mmol, 2.03 M in toluene) and stirred for 30 min at −78 °C. The reaction mixture was quenched by addition of saturated sodiumpotassium tatrate at −78 °C and the resulting mixture was warmed to room temp.The resulting suspension was filtered, dried (Na_2SO_4) and concentrated. Chromatographic purification (25% ethylacetate in petroleum ether) yielded lactals (3.27 gm, 97%) as colorless oil. IR ($CHCl_3$): υ 3404, 3019, 1731, 1660, 1215, 1067, 765, 669 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.35–7.28 (m, 5H), 5.43 (s, 0.8H), 5.23 (br.d, *J* = 4.2 Hz, 0.2H),4.61–4.50 (m, 2H), 4.45–4.36 (m, 1H), 4.27–4.19 (m, 1H), 4.11–4.07 (m, 1H), 3.99–3.97 (m, 1H), 3.57–3.52 (m, 1H), 2.49–2.26 (m, 1H), 1.89–1.84 (m, 2H), 1.72–1.65 (m, 1H),1.40, 1.32 (2s, 3H), 1.36, 1.28 (2s, 3H). ^{13}C NMR (75 MHz): 25.8 (q), 27.0 (q), 35.3 (t), 36.6 (t), 40.8 (t), 69.9 (t), 71.5 (t), 72.2 (t), 73.7 (d), 73.8 (d), 73.9 (d), 75.6 (d), 78.5 (d), 84.1 (d), 95.8 (d), 101.1 (d), 108.6 (s), 127.6 (d), 127.9 (d), 128.1 (d), 128.4 (d), 128.6 (d), 137.3 (s), 138.0 (s) ppm. Anal. Calcd For $C_{17}H_{24}O_5$: C 66.21, H 7.84%; found: C 66.05, H 8.13%.

A suspension of 3-phenylpropyl-triphenylphosphonium iodide (30.3 gm, 59.67 mmol) in anhydrous THF (120 ml) was cooled to 0°C, treated with *n*-BuLi (23 ml, 53.703 mmol, 2.34 M in hexane) and stirred at rt for 1h. The resulting yellow solution was transferred drop wise to a solution of lactal (3.68 gm, 11.93 mmol) in 50 ml of anhydrous THF at 0 °C and the contents were stirred at rt for 12 h. The reaction was quenched by addition of saturated aqueous NH_4Cl, extracted with ethyl acetate, dried (Na_2SO_4) and concentrated. Purification by column chromatography (15% ethyl acetate in petroleum

ether) gave **13** (4.7 g, 96%) as a colorless oil. $[\alpha]_D^{25}$ = +21.9 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ3486, 2985, 2937, 1604, 1454, 1369, 1067, 1028, 736, 698 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.32–7.29 (m, 2H), 7.26–7.22 (m, 5H), 7.17–7.12 (m, 3H), 5.66–5.60 (dt, *J* = 10.9, 7.5 Hz, 1H), 5.48–5.43 (ddt, *J* = 10.9, 9.2, 1.3 Hz, 1H), 4.43 (d, *J* = 11.8 Hz, 1H), 4.35 (br.dt, *J* = 8.5, 3.5 Hz, 1H), 4.25–4.20 (m, 1H), 4.15 (d, *J* = 11.8 Hz, 1H), 4.03 (dd, *J* = 8.2, 6.0 Hz, 1H), 4.01–3.97 (tt, *J* = 9.1, 3.1 Hz, 1H), 3.50–3.47 (t, *J* = 8.0 Hz, 1H), 2.75–2.64 (m, 2H), 2.42–2.32 (m, 2H), 1.65–1.53 (m, 3H), 1.46 (ddd, *J* = 12.3, 8.7, 3.5 Hz, 1H), 1.38 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (75 MHz): 25.7 (q), 26.9 (q), 29.6 (t), 35.7 (t), 40.7 (t), 42.6 (t), 66.0 (d), 69.7 (t), 69.9 (t), 71.9 (d), 73.7 (d), 108.3 (s), 125.9 (d), 127.5 (d), 127.6 (d), 128.2 (d), 128.5 (d), 131.0 (d), 132.1 (d), 138.3 (s), 141.2 (s) ppm. Anal. Calcd For $C_{26}H_{34}O_4$: C 76.06, H 8.34%; found: C 76.17, H 8.53%.

Entry_13

13 May 2005
Imported from UXNMR.

Acquisition Time (sec)	2.0447	***Comment***	Imported from UXNMR.		***Date***	02/02/2005 14:51:24	
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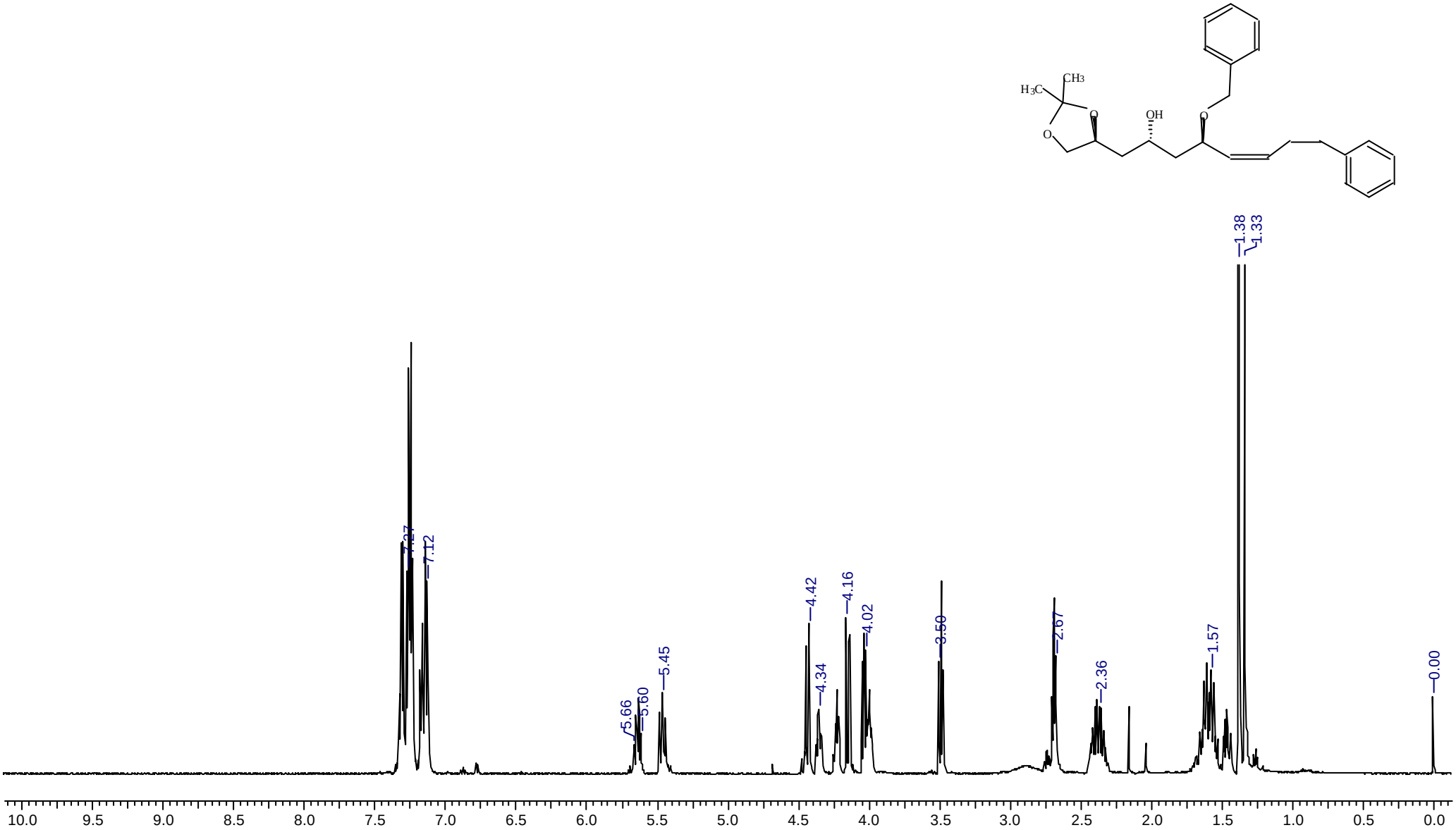
Temperature (grad C)	0.000						



Entry_13

16 May 2005
SRINIVAS

Acquisition Time (sec) 0.4342	***Comment*** SRINIVAS			***Date*** 00/00/00 00:00:00			***Frequency (MHz)*** 75.48
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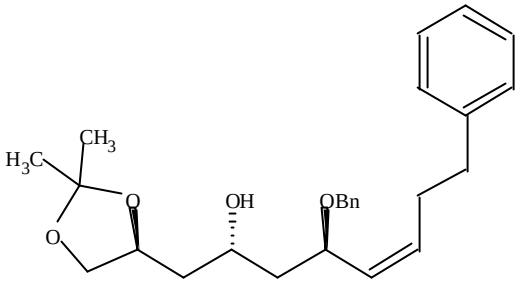
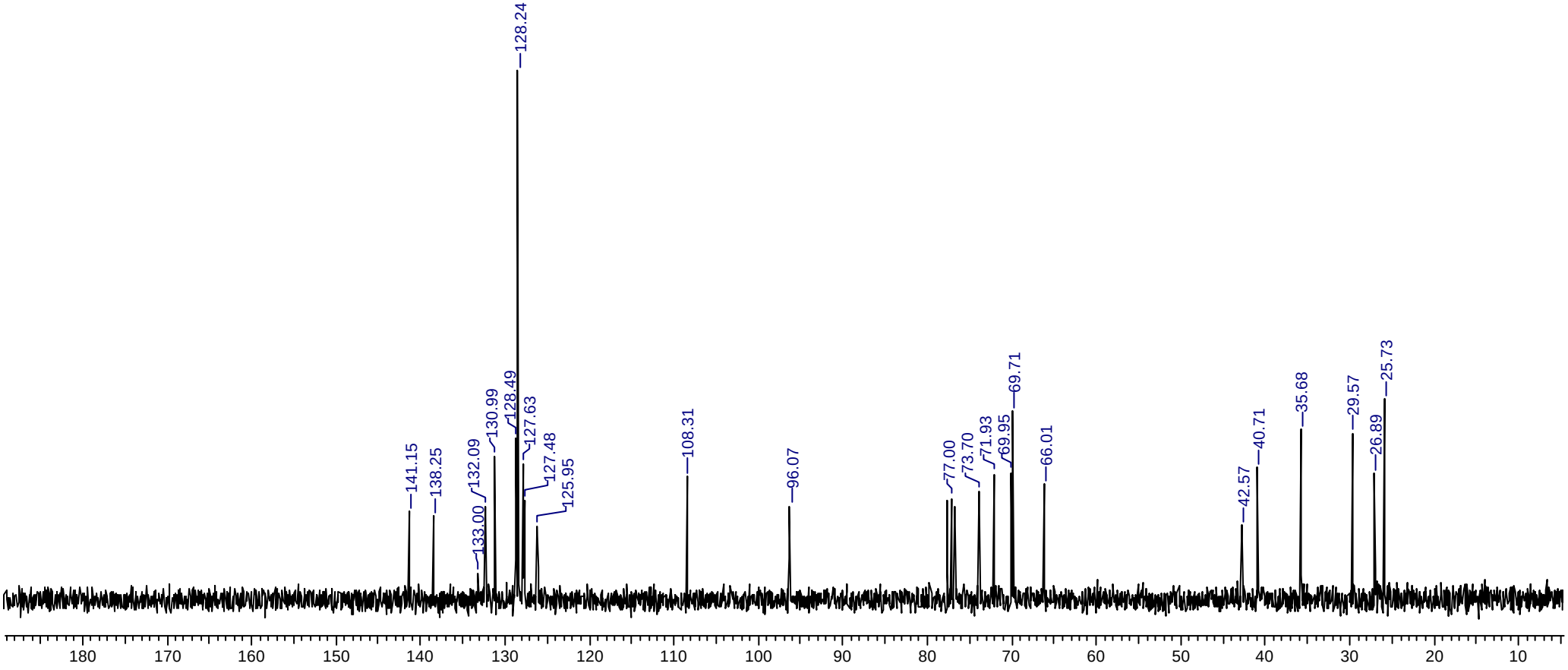
Temperature (grad C) 24.000							





Entry_13

13 May 2005
SRINIVAS

Acquisition Time (sec) 0.4342	***Comment*** SRINIVAS			***Date*** 00/00/00 00:00:00			***Frequency (MHz)*** 75.48
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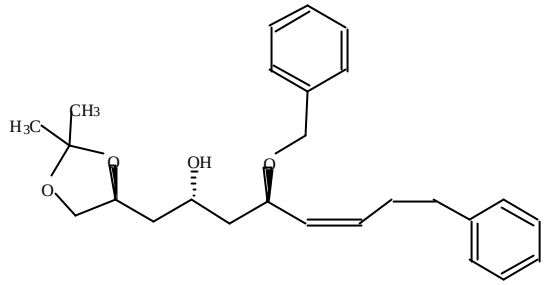
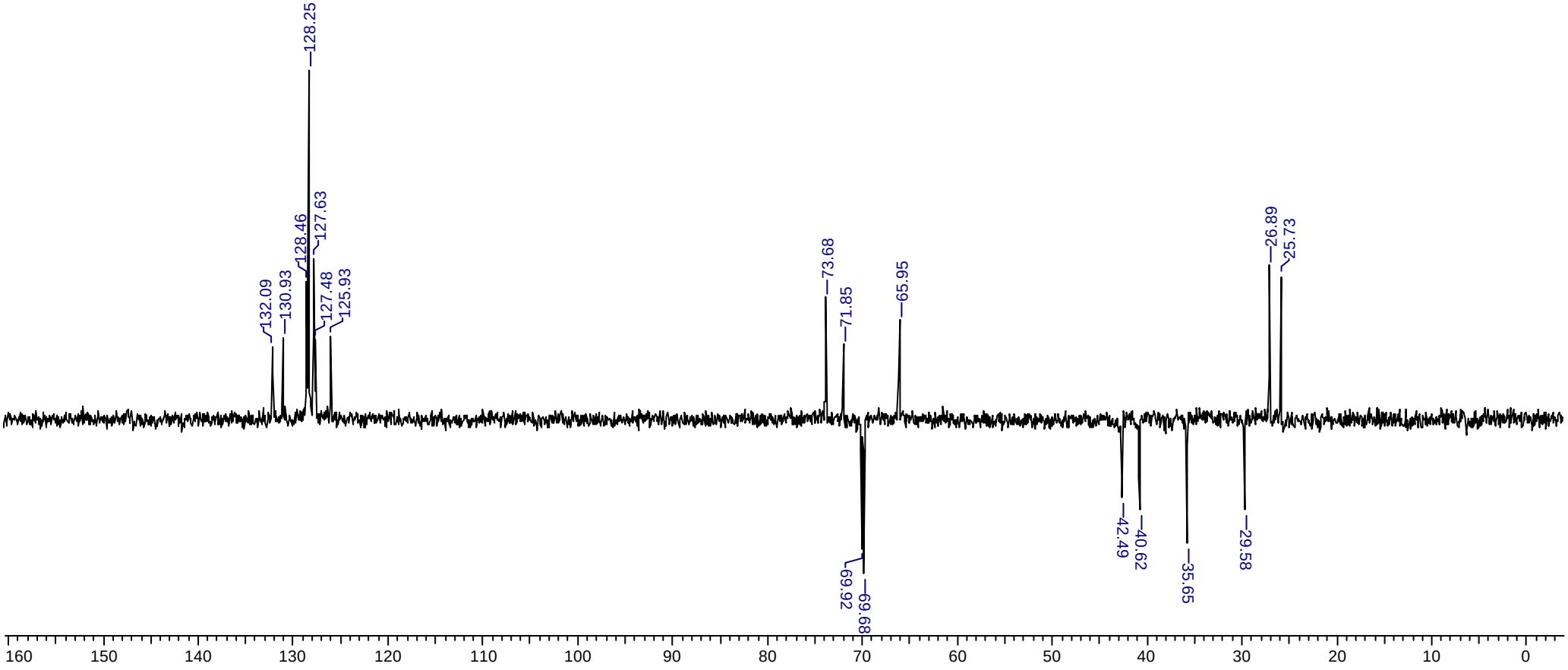
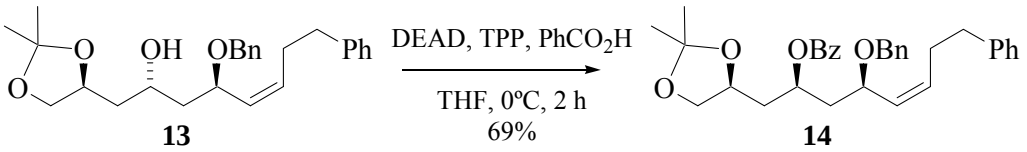
Temperature (grad C) 24.000							



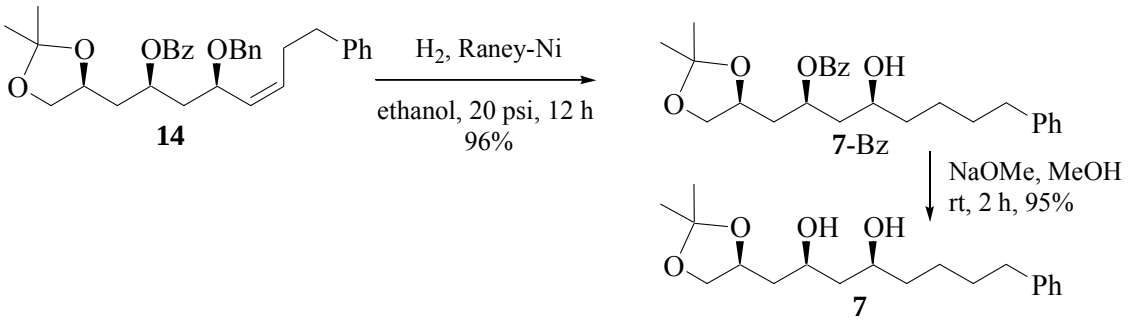


Mitsunobu Reaction of 13 with Benzoic Acid.



At 0 °C, a solution of **13Z** (1 g, 2.43 mmol) in THF (20 ml) was treated with TPP (830 mg, 3.16 mmol), DEAD (0.5 ml, 3.16 mmol) followed by benzoic acid (386 mg, 3.16 mmol) and stirring was continued for 2 h. The reaction mixture was concentrated and the resulting crude product was purified by column chromatography (10% ethyl acetate in petroleum ether) to obtain **14** (864 mg, 69%) as a colorless oil. $[\alpha]_D^{25}$ = +33.1 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3402, 3017, 1715, 1602, 1495, 1371, 1274, 1216.1069.1026, 756, 712, 699, 667 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.96–7.92 (m, 2H), 7.58–7.51 (m, 1H), 7.45–7.35 (m, 2H), 7.24–7.11 (m, 8H), 7.00–6.96 (m, 2H), 5.69 (dt, *J* = 10.9, 7.3 Hz, 1H), 5.37–5.18 (m, 2H), 4.43 (d, *J* = 11.8 Hz, 1H), 4.31–4.10 (m, 2H), 4.10 (d, *J* = 11.8 Hz, 1H), 4.04 (dd, *J* = 7.9, 5.8 Hz, 1H), 3.50 (br.dd, *J* = 7.8, 7.0 Hz, 1H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.29–1.97 (m, 4H), 1.91–1.65 (m, 2H), 1.35 (s, 3H), 1.28 (s, 3H). ^{13}C NMR (50 MHz): 25.7 (q), 26.9 (q), 29.56 (t), 35.6 (t), 37.9 (t), 39.8 (t), 69.4 (t), 69.6 (t), 69.8 (d), 70.9 (d), 72.6 (d), 108.7 (s), 125.8 (d), 127.3 (d), 127.7 (d), 128.2 (d), 129.5 (d), 130.4 (d), 132.7 (d), 133.5 (d), 138.4 (s), 141.1 (s), 165.7 (s) ppm. Anal. Calcd For $C_{33}H_{38}O_5$: C 77.01, H 7.44%; found: C 76.86, H 7.69%.

Preparation of Diol 7 by Hydrogenation and Saponification of 14.



Hydrogenation. A suspension of **14** (1 gm, 1.942 mmol), Raney-Ni (50 mg) in ethanol (20 ml) was flushed with hydrogen gas and stirred under hydrogen (20 psi) atmosphere for 12 h. The reaction

mixture was filtered (Celite), concentrated and purified by column chromatography (25% ethyl acetate in petroleum ether) to obtain the intermediate benzoate **7**-Bz (800 mg, 96%) as acolorless oil. $[\alpha]_D^{25} = +1.5$ (c = 1, $CHCl_3$). IR ($CHCl_3$): υ 3429, 3019, 2935, 1712, 1603, 1495, 1372, 1276, 1216, 1069, 756, 713, 668 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 8.02 (dt, J = 8.1, 1.1 Hz, 2H), 7.59–7.51 (m, 1H), 7.46–7.38 (m, 2H), 7.29–7.10 (m, 5H), 5.44–5.31 (ddd, J = 8.0, 5.9 Hz, 1H), 4.23 (dt, J = 13.1, 6.5 4.6 Hz, 1H), 4.12–4.00 (dd, J = 8.0, 5.9 Hz, 1H), 3.82–3.78 (m, 1H), 3.58 (dd, J = 8.0, 7.2 Hz, 1H), 2.58 (t, J = 7.5 Hz, 2H), 2.20–1.86 (m, 4H), 1.68–1.21 (m, 6H), 1.38 (s, 3H), 1.30 (s, 3H).^{13}CNMR (200 MHz, $CDCl_3$) 25.1 (t), 25.7 (q), 26.9 (q), 31.3 (t), 35.8 (t), 37.5 (t), 37.8 (t), 41.6 (t), 69.1 (d), 69.4 (t), 70.6 (d), 72.7 (d), 108.9 (s), 125.6 (d), 128.2 (d), 128.4 (d), 129.6 (d), 130.2 (s), 133.0 (d), 142.4 (s), 166.0 (s) ppm. Anal. Calcd For $C_{26}H_{34}O_5$: C 73.21, H8.03%; found: C 73.06, H 8.26

Saponification. At 0 °C, a solution of the above benzoate **7**-Bz (500 mg, 1.172 mmol) in dry methanol (15 ml) was treated with Na (40 mg, 1.758 mmol) and the resulting reaction mixture was stirred at rt being monitored by TLC. After 2h, the reaction mixture was neutralized with AcOH at 0 °C, evaporated and purified by column chromatography (40% ethyl acetate in petroleum ether) to obtain diol **7** (359 m, 95%) as a colorless oil. $[\alpha]_D^{25} = -2.9$ (c = 1, $CHCl_3$). IR ($CHCl_3$): υ 3381, 2935, 1603, 1381, 1493, 1452, 1381, 1216, 1056, 756, 699 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.28–7.12 (m, 5H), 4.31–4.18 (m, 1H), 4.12–3.98 (m, 2H), 3.91–3.76 (m, 2H), 3.58–3.49 (m, 1H), 2.61 (t, J = 7.5 Hz, 2H), 1.71–1.46 (m, 8H), 1.40–1.34 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H).^{13}C NMR (50 MHz): 25.0 (t), 25.7 (q), 26.9 (q), 31.5 (t), 35.9 (t), 37.7 (t), 40.9 (t), 43.1 (t), 69.6 (t), 71.8 (d), 72.1 (d), 75.2 (d), 109.3 (s), 125.6 (d), 128.1 (d), 128.3 (d), 142.4 (s) ppm. Anal. Calcd For $C_{19}H_{30}O_4$: C 70.77, H 9.37%; found: C 70.59, H 9.50%.

Entry_07

13 May 2005
b srinivas

Acquisition Time (sec) 7.9167	***Comment*** b srinivas			***Date*** 16/02/2005 17:40:18		***Frequency (MHz)*** 200.13	
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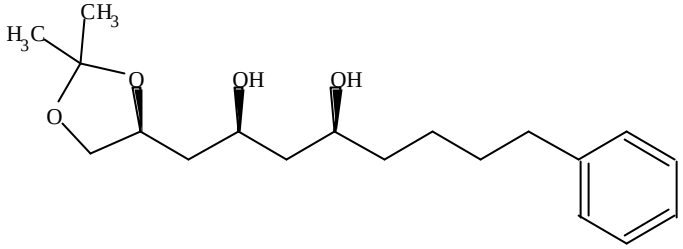
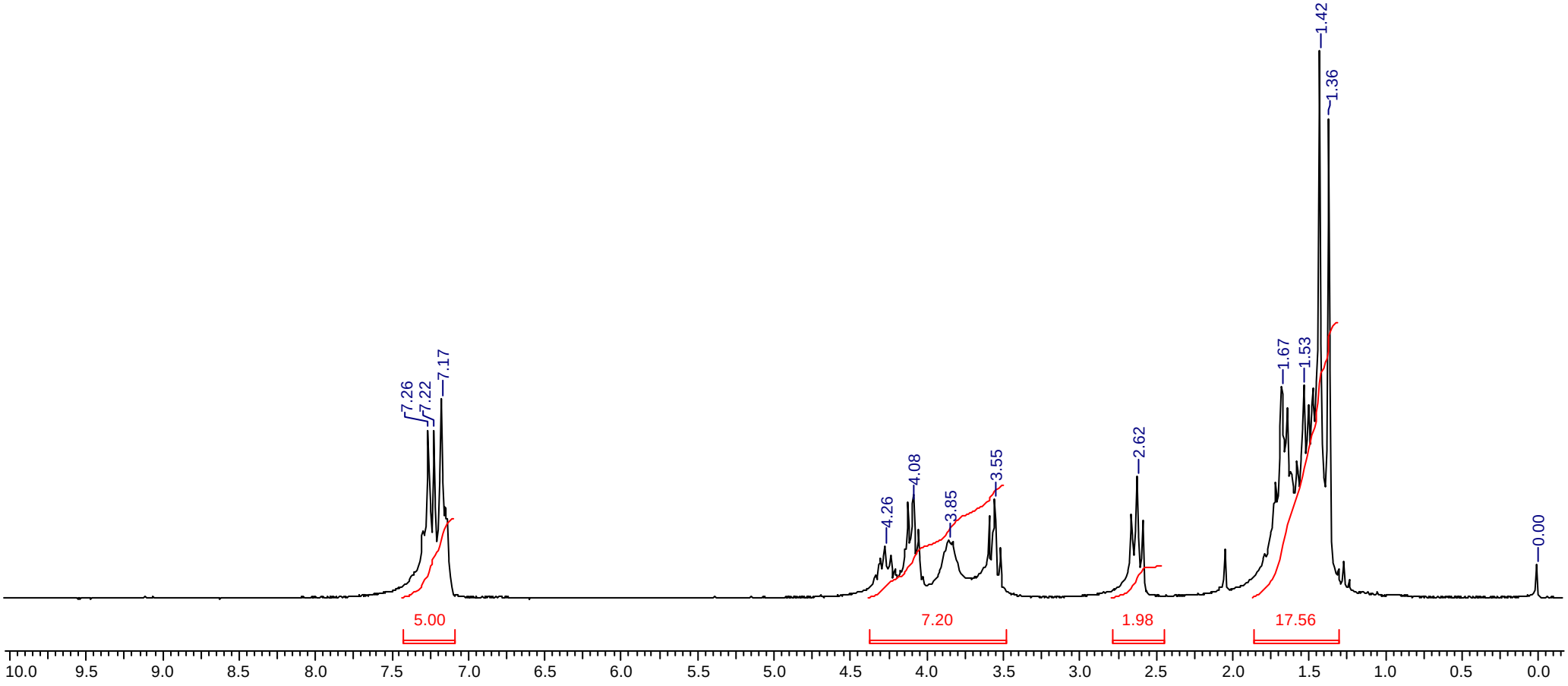
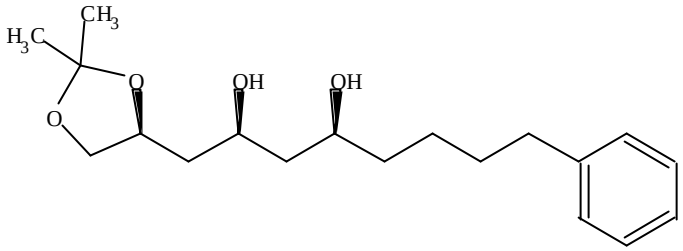


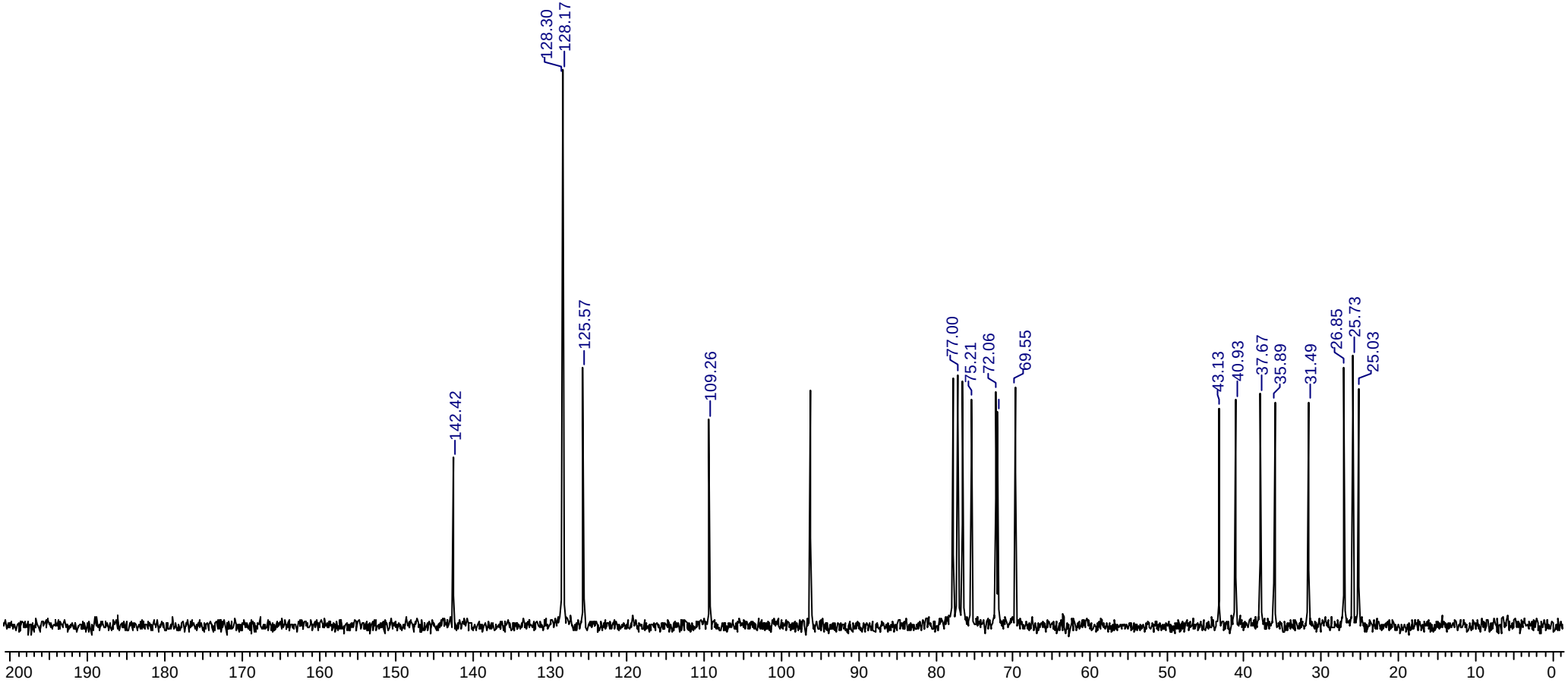


Entry_07

13 May 2005
b srinivas

Acquisition Time (sec) 2.7329	***Comment*** b srinivas			***Date***	03/02/2005 06:09:10	***Frequency (MHz)***	50.32
Nucleus 13C	***Original Points Count*** 32768	***Points Count***	32768	***Sweep Width (Hz)***	11990.41	***Temperature (grad C)***	0.000





Entry_07

S26

13 May 2005
b srinivas

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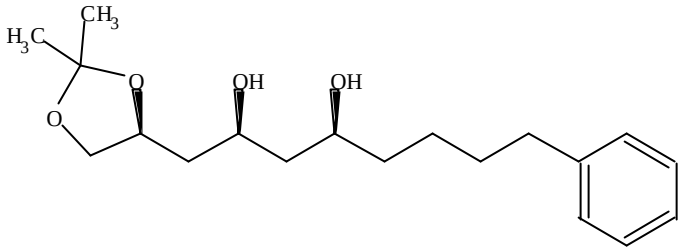
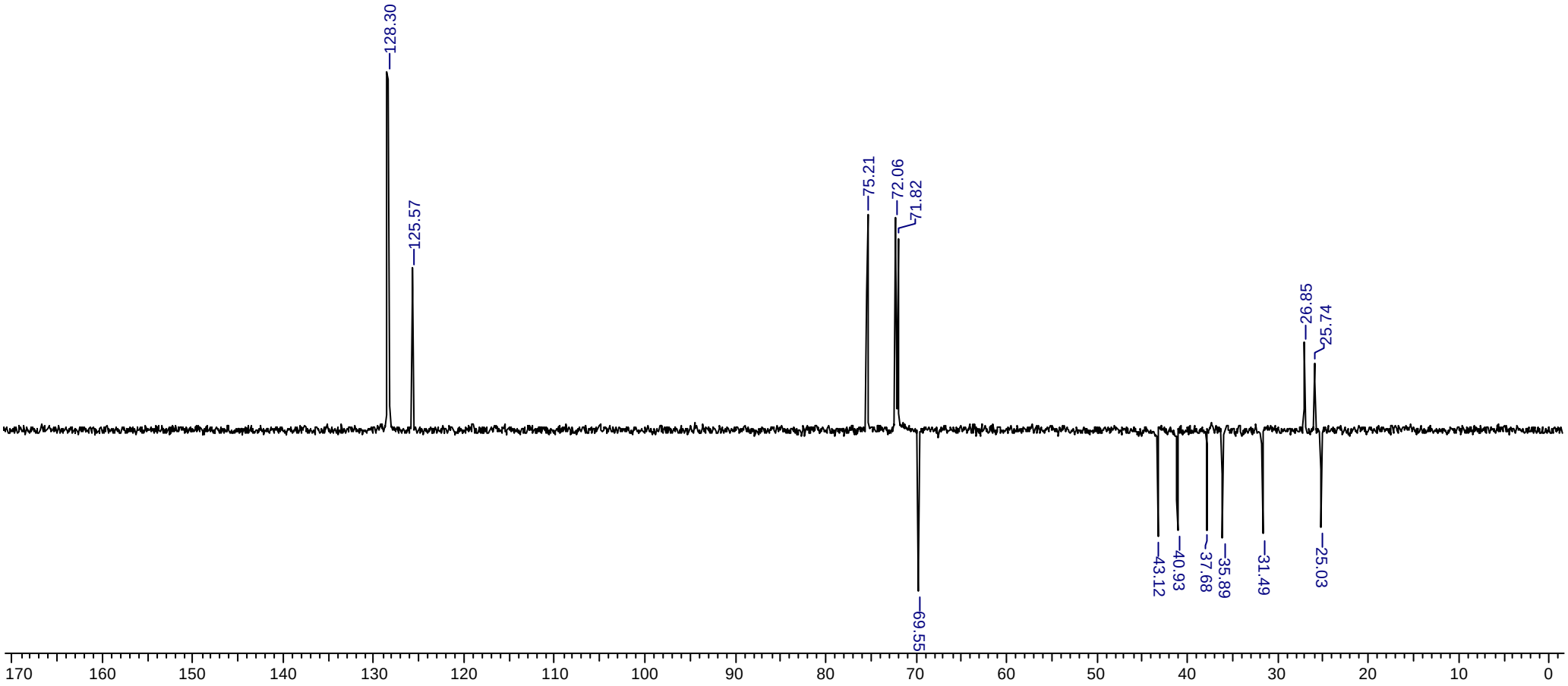
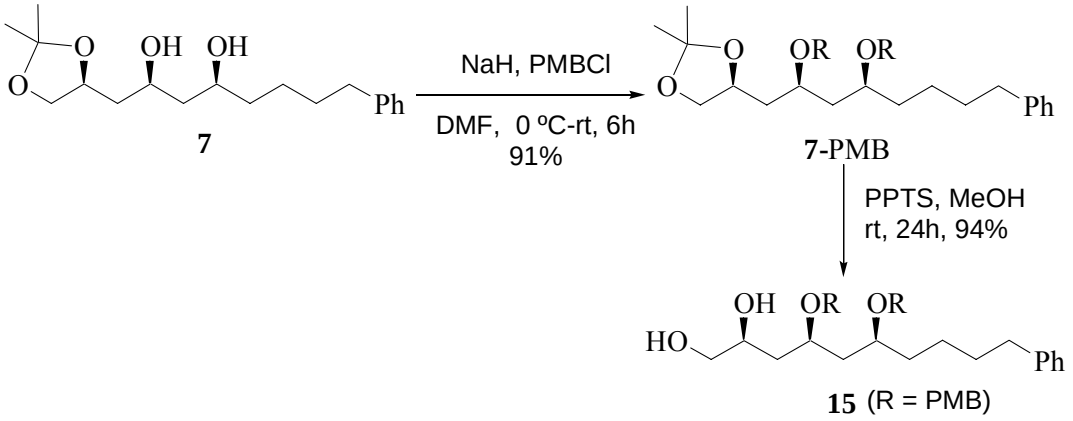




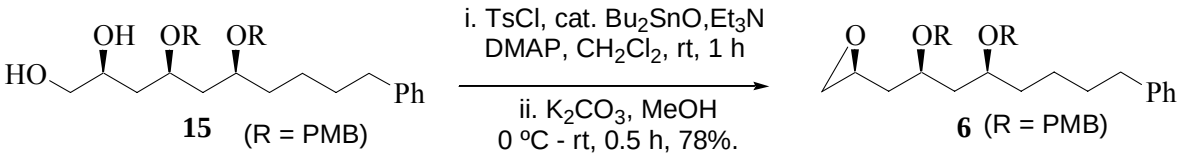
Preparation of Diol 15 from 7.



To a solution of diol **7** (860 mg, 2.66 mmol) in dry DMF (3 ml) was added NaH (533 mg, 13.4 mmol) portions wise at 0 °C and stirred for 30 min. To this, *p*-methoxybenzyl chloride (1.7 ml, 12 mmol) was added at 0°C and stirring was continued for 6 h at rt. The reaction mixture was quenched at 0°C by adding sat.Na_2SO_4 solution, poured into water and extracted with ethyl acetate. The combined organic phases were washed with water, brine, dried (Na_2SO_4) and concentrated. Purification by column chromatography (20% ethyl acetate in petroleum ether) gave **7**-diPMB (1.365 g, 91%) as a colorless oil. $[\alpha]_D^{25}$ = +16.8 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3061, 2984, 2933, 2857, 1612, 1585, 1513, 1463, 1378, 1248, 1172, 1058, 821, 749, 699 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.29–7.11 (m, 5H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 4.41 (d, *J* = 11.2 Hz, 1H), 4.37 (s, 2H), 4.33 (d, *J* = 11.2 Hz, 1H), 4.15 (br.ddd, *J* = 12.4, 7.4, 6.4 Hz, 1H), 3.87 (dd, *J* = 7.8, 5.8 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.55 (t, *J* = 5.8 Hz, 1H), 3.48–3.42 (m, 1H), 3.38 (t, *J* = 7.8 Hz, 1H), 2.62–2.54 (m, 2H), 1.99–1.82 (m, 2H), 1.73–1.47 (m, 6H), 1.43–1.26 (m, 2H), 1.37 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (50 MHz): 24.9 (t), 25.8 (q), 27.1 (q), 31.6 (t), 33.9 (t), 36.0 (t), 37.7 (t), 38.5 (t), 55.2 (q), 69.7 (t), 70.1 (t), 70.3 (t), 72.9 (d), 73.0 (d), 75.5 (d), 108.4 (s), 113.8 (d), 125.7 (d), 128.3 (d), 128.4 (d), 129.3 (d), 129.4 (d), 130.8 (s), 131.1 (s), 142.5 (s), 159.3 (s), 159.3 (s) ppm. Anal. Calcd For $C_{35}H_{46}O_6$: C 74.70, H 8.23%; found: C 74.83, H 8.19%.

A solution of above compound **7**-diPMB (400 mg, 0.7 mmol) and PPTS (267 mg, 1.066 mmol) in methanol (15 ml) was stirred 24 h at rt. After completion of the reaction as indicated by TLC, the reaction mixture was concentrated, dissolved in CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated. Purification by column chromatography (50% ethylacetate in petroleum ether)afforded diol **15** (350 mg, 94%) as colorless oil. $[\alpha]_D^{25}$ = +61.6 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3429, 3012, 2936, 1612, 1513, 1464, 1302, 1249, 1216, 1035, 755, 667 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.29–7.11 (m, 9H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.51 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 11.4 Hz, 1H), 4.32 (d, *J* = 11.4 Hz, 1H), 4.26 (d, *J* = 11.5 Hz, 1H), 3.85–3.61 (m, 2H), 3.77 (2s, 2x 3H), 3.43 (dd, *J* = 11.2, 3.5 Hz, 1H), 3.39–3.32 (m, 1H), 3.28 (dd, *J* = 11.2, 6.0 Hz, 1H), 2.97 (b, 2H), 2.64–2.57 (m, 2H), 1.95 (br.ddd, *J* = 13.2, 8.6, 3.6 Hz, 1H), 1.69–1.48 (m, 6H), 1.42–1.32 (m, 3H). ^{13}C NMR (50 MHz): 24.7 (t), 31.6 (t), 33.8 (t), 35.9 (t), 37.1 (t), 38.4 (t), 55.1 (q), 66.6 (t), 70.0 (t), 70.1 (t), 71.5 (d), 74.5 (d), 76.1 (d), 113.7 (d), 113.9 (d), 125.7 (d), 128.3 (d), 128.4 (d), 129.7 (d), 129.8 (s), 130.5 (s), 142.3 (s), 159.2 (s), 159.3 (s) ppm. Anal. Calcd For $C_{32}H_{42}O_6$: C 73.53, H 8.09%; found: C 73.24, H 8.04%.

Preparation of Key Epoxide 6.



To a solution of diol **15** (500 mg, 0.96 mmol) in dry CH_2Cl_2 (10 ml) and Bu_2SnO (4 mg) were added *p*-TsCl (182 mg, 0.96 mmol) followed by triethylamine (0.266 ml, 1.9 mmol) and DMAP (20 mg).The resulting solution was stirred for 1 h at rt. The reaction mixture was washed with water, brine, dried (Na_2SO_4) and concentrated. The crude tosylate (650 mg) was dissolved in methanol (20 ml) and stirred with anhydrous K_2CO_3 (145 mg) for 30 min. The reaction mixture was concentrated, the crude compound was dissolved in ethyl acetate and subjected for usual work up. Purification by column chromatography (15% ethyl acetate in petroleum ether) gave the epoxide **6** (375 mg, 78% for 2 steps) as

colorless oil. $[\alpha]_D^{25} = -1.8$ (c = 1.5, $CHCl_3$). IR ($CHCl_3$): υ 3026, 2933, 2857, 1612, 1586, 1513, 1463, 1302, 1248, 1173, 1035, 821, 750, 699 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.29–7.12 (m, 9H), 6.82 (br.d, J = 8.4 Hz, 4H), 4.41 (br.s, 2H), 4.40 (d, J = 11.3 Hz, 1H), 4.33 (d, J = 11.3 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.69–3.58 (m, 1H), 3.50–3.39 (m, 1H), 3.03–2.94 (m, 1H), 2.71–2.66 (br.dd, J = 4.4, 5.1 Hz, 1H), 2.58 (t, J = 7.5 Hz, 2H), 2.36 (br.dd, J = 5.1, 2.8 Hz, 1H), 2.01–1.91 (m, 1H), 1.74–1.35 (m, 9H). ^{13}C NMR (50 MHz): 24.9 (t), 31.7 (t), 33.9 (t), 36.0 (t), 36.8 (t), 38.5 (t), 46.6 (t), 49.3 (d), 55.2 (q), 70.2 (t), 73.5 (d), 75.2 (d), 113.7 (d), 125.7 (d), 128.3 (d), 128.4 (d), 129.4 (d), 130.6 (s), 130.9 (s), 142.5 (s), 159.1 (s), 159.2 (s) ppm. Anal. Calcd For $C_{32}H_{40}O_5$: C 76.16, H 7.98%; found: C 76.00, H 7.73%.

ENTRY_06

13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	7.9167	***Comment***	b srinivas	***Date***	10/03/2005 18:49:22		
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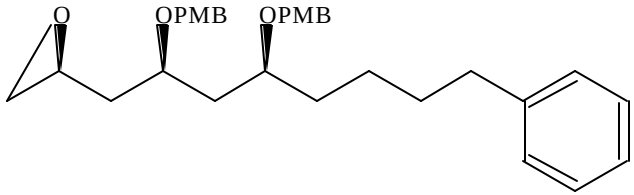
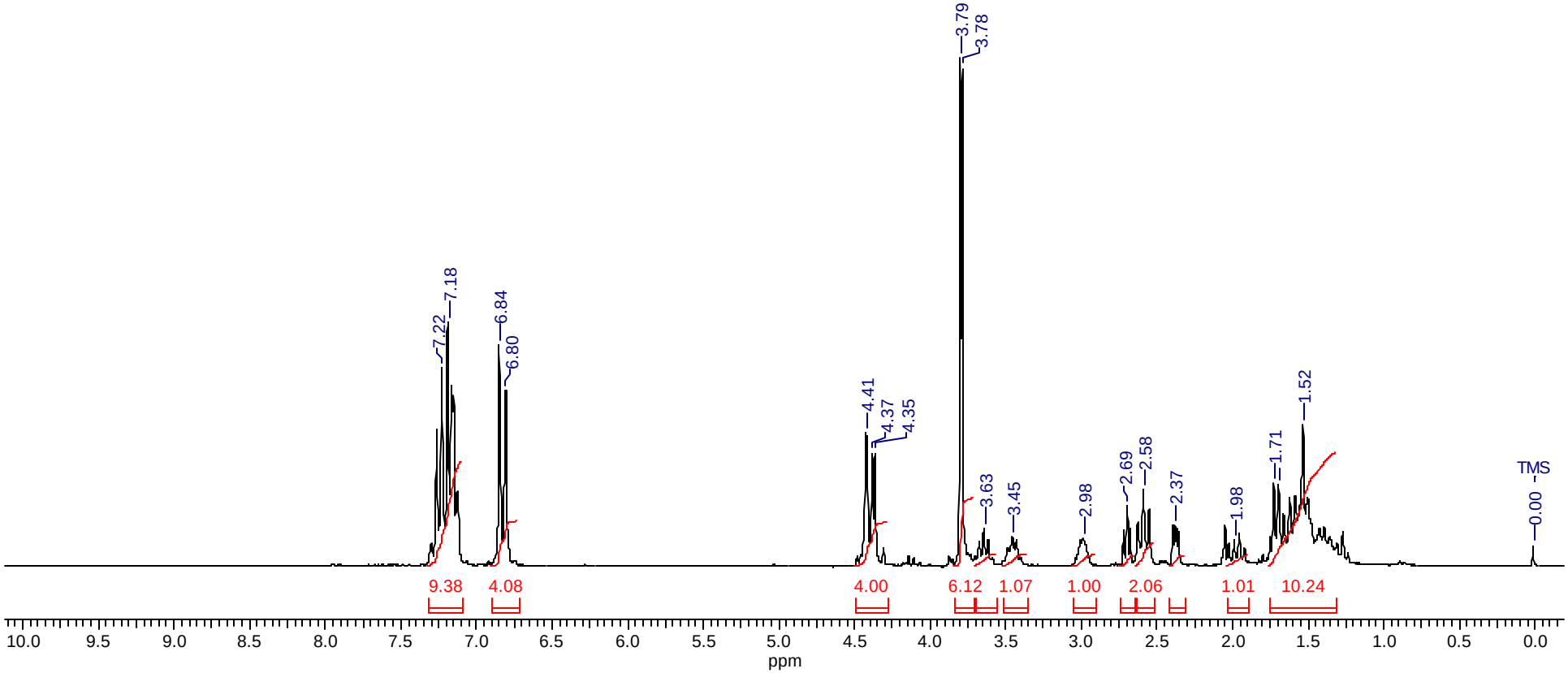
Sweep Width (Hz)	4139.07	***Temperature (degree C)***	0.000				





ENTRY_06

13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	2.7329	***Comment***	b srinivas	***Date***	13/03/2005 12:01:18
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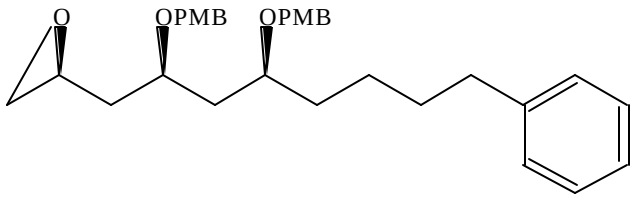
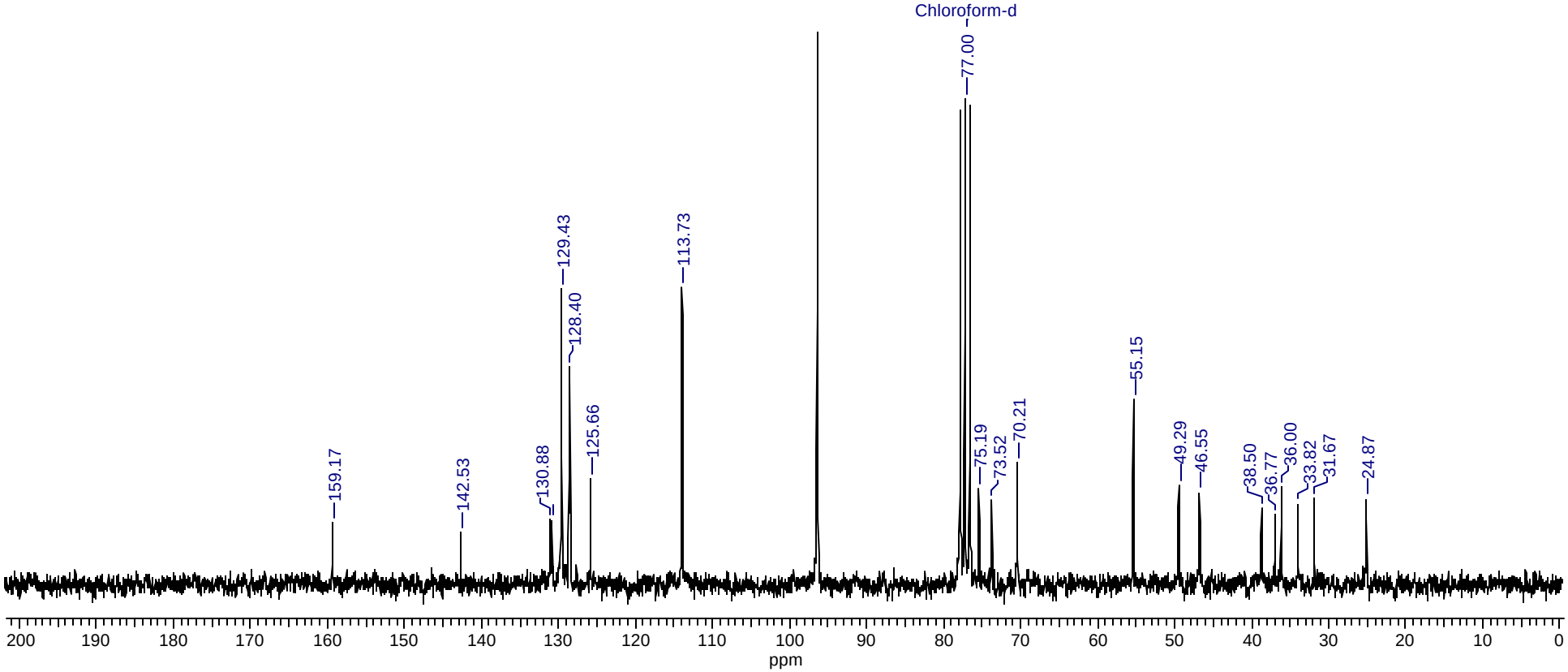
Points Count	32768	***Solvent***	BENZENE-D6	***Sweep Width (Hz)***	11990.41
Temperature (degree C)	0.000				





ENTRY_6

16 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	2.7329	***Comment***	b srinivas	***Date***	13/03/2005 12:24:34		
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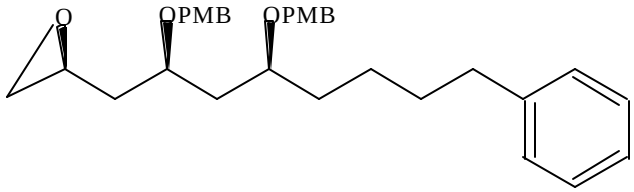
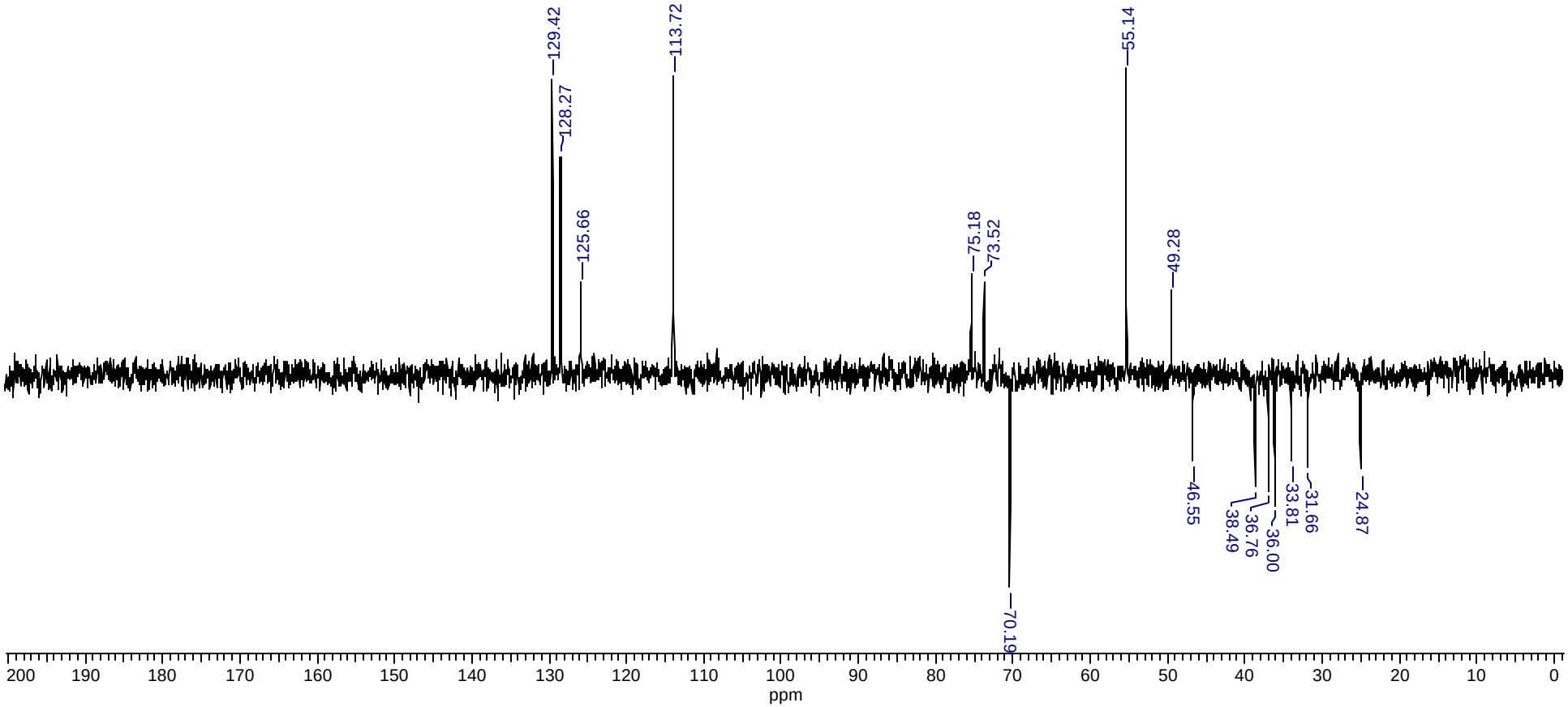
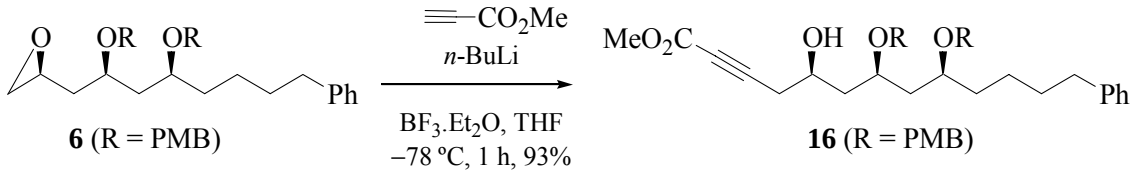
Solvent	BENZENE-D6	***Sweep Width (Hz)***	11990.41	***Temperature (degree C)***	0.000		



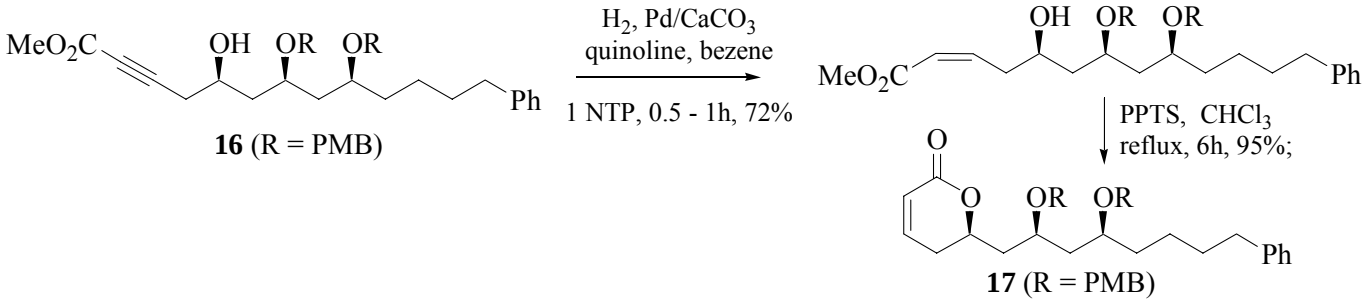


Coupling of Epoxide 6 and Methyl Propiolate.



Methyl propiolate (590 µl, 6.6 mmol) was taken in a flame dried two neck round bottom flask (50 ml) and dissolved in anhydrous THF (15 ml). The reaction mixture was cooled to −78 °C, treated with *n*-BuLi (4.2 ml, 6.64 mmol, 1.6M in hexane) drop wise and stirred for 15 min, treated with $BF_3.Et_2O$ (0.84 ml, 6.6 mmol) and continued stirring for an additional 15 minutes. Once the formation of dark block alkyne borane was observed, a solution of epoxide **6** (335 mg, 0.66 mmol) in anhydrous THF (10 ml) was added and stirred for 30 min at −78 °C. The reaction was quenched at −78 °C by addition of sat.Na_2SO_4 (20 ml), taken in ethyl acetate water and the aqueous phase was extracted with ethyl acetate. Combined organic phase was washed with brine, dried (Na_2SO_4) and concentrated. Purification by column chromatography (20% ethyl acetate in petroleum ether) gave **16** (365 mg, 93%). $[\alpha]_D^{25}$ = +56.7 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3457, 3011, 2936, 2859, 2238, 1714, 1612, 1586, 1513, 1454, 1435, 1302, 1250, 1075, 1035, 822, 755, 667 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.31–7.14 (m, 9H), 6.83 (br.d, *J* = 8.4 Hz, 4H), 4.52 (d, *J* = 11.2 Hz, 1H), 4.47 (d, *J* = 11.2 Hz, 1H), 4.30 (d, *J* = 11.2 Hz, 1H), 4.27 (d, *J* = 11.2 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.90–3.73 (m, 2H), 3.71 (s, 3H), 3.44–3.33 (m, 1H), 2.66–2.58 (t, *J* = 7.5 Hz, 2H), 2.47–2.26 (m, 2H), 2.03–1.90 (m, 1H), 1.71–1.33 (m, 10H). ^{13}C NMR (50 MHz): 24.6 (t), 27.3 (t), 31.6 (t), 33.9 (t), 35.9 (t), 38.3 (t), 39.9 (t), 52.4 (q), 55.1 (q), 69.3 (d), 70.0 (t), 70.5 (t), 74.5 (s), 74.8 (d), 76.4 (d), 86.2 (s), 113.7 (d), 113.9 (d), 125.7 (d), 128.3 (d), 128.4 (d), 129.6 (d), 129.7 (d), 130.5 (s), 142.3 (s), 153.8 (s), 159.2 (s), 159.4 (s) ppm. Anal. Calcd For $C_{36}H_{44}O_7$: C 73.44, H 7.53%; found: C 73.14, H 7.80%.

Preparation of α-Pyrone 17.



A suspension of compound **16** (120 mg, 0.2 mmol), quinoline (50 μl) and $Pd/CaCO_3$ (50 mg) in benzene (15 ml) was flushed with hydrogen gas and stirred for 0.5 to 1h under hydrogen atmosphere being the progress of reaction monitored by TLC. After completion, the reaction mixture was filtered (Celite), concentrated and purified by column chromatography (20% ethyl acetate in petroleum ether) to get *Z*-acrylate (87 mg, 72%) as an oil. $[\alpha]_D^{25}$ = +51.4 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3449, 3019, 1717, 1647, 1612, 1514, 1440, 1249, 1215, 1035, 757, 668 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.30–7.14 (m, 9H), 6.83 (br.d, *J* = 8.6 Hz, 2H), 6.81 (br.d, *J* = 8.6 Hz, 2H), 6.34 (dt, *J* = 11.6, 7.3 Hz, 1H), 5.85 (dt, *J* = 11.6, 1.6 Hz, 1H), 4.51 (d, *J* = 11.2 Hz, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 4.33 (d, *J* = 11.2 Hz, 1H), 4.27 (d, *J* = 11.2 Hz, 1H), 3.78 (s, 6H), 3.78–3.68 (m, 2H), 3.68 (s, 3H), 3.43–3.31 (m, 1H), 2.71 (dt, *J* = 8.9, 6.2, 1.6 Hz, 1H 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 1.95 (ddd, *J* = 13.8, 8.7, 3.7 Hz, 1H), 1.70–1.34 (m, 9H). ^{13}C NMR (50 MHz): 24.7 (t), 31.6 (t), 33.8 (t), 35.9 (t), 36.8 (t), 38.4 (t), 40.9 (t), 50.9 (q), 55.1 (q), 70.0 (t), 70.3 (t), 70.7 (d), 74.7 (d), 76.8 (d), 113.7 (d), 113.9 (d), 120.6 (d), 125.7 (d), 128.3 (d), 128.4 (d), 129.5 (d), 129.6 (d), 129.9 (s), 130.5 (s), 142.4 (s), 146.8 (d), 159.2 (s), 159.3 (s), 166.8 (s) ppm. Anal. Calcd For $C_{36}H_{46}O_7$: C 73.19, H 7.84%; found: C 72.96, H 7.69%.

A solution of above *Z*-acrylate (100 mg, 0.17 mmol) and PPTS (85 mg, 0.34 mmol) in $CHCl_3$ (5 ml) was refluxed for 6 h and partitioned between $CHCl_3$ and water. The combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The resulting crude product was purified by column chromatography (25% ethylacetate in petroleum ether) to afford the α-pyrone **17** (90 mg, 95%) as an yellow color oil. $[\alpha]_D^{25}$ = +60.8(*c* = 1.4, $CHCl_3$). IR ($CHCl_3$): υ 3015, 2933, 2857, 1721, 1612, 1513,

1464, 1386, 1302, 1249, 1217, 1036, 818, 754, 666 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.30–7.13 (m, 9H), 6.86–6.79 (m, 4H), 6.74–6.65 (ddd, *J* = 9.8, 5.7, 2.9 Hz, 1H), 5.95 (ddd, *J* = 9.8, 2.4, 1.0 Hz, 1H), 4.55–4.45 (m, 1H), 4.45 (d, *J* = 11.2 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.31 (d, *J* = 11.5 Hz, 1H), 4.29 (d, *J* = 11.2 Hz, 1H), 3.79 (s, 6H), 3.71–3.59 (m, 1H), 3.52–3.41 (m, 1H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.01–1.86 (m, 3H), 1.81–1.51 (m, 7H), 1.44–1.32 (m, 2H). ^{13}C NMR (50 MHz): 24.6 (t), 29.0 (t), 31.6 (t), 33.7 (t), 35.9 (t), 37.9 (t), 38.9 (t), 55.1 (q), 69.8 (t), 70.2 (t), 71.5 (d), 75.1 (d), 75.2 (d), 113.7 (d), 121.3 (d), 125.6 (d), 128.2 (d), 128.4 (d), 129.4 (d), 129.6 (d), 130.4 (s), 130.8 (s), 142.4 (s), 144.8 (d), 159.1 (s), 159.2 (s), 164.1 (s) ppm. Anal. Calcd For $C_{35}H_{42}O_6$: C 75.24, H 7.57%; found: C 75.53, H 7.49%.

ENTRY_17

13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	7.9167	***Comment***	b srinivas	***Date***	06/04/2005 15:29:58
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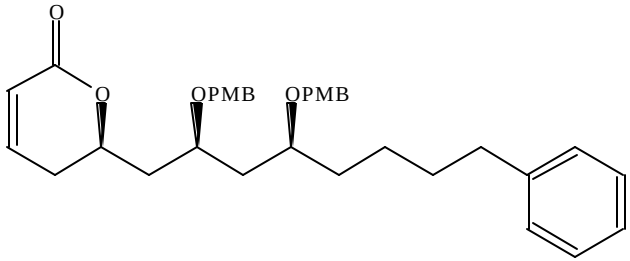
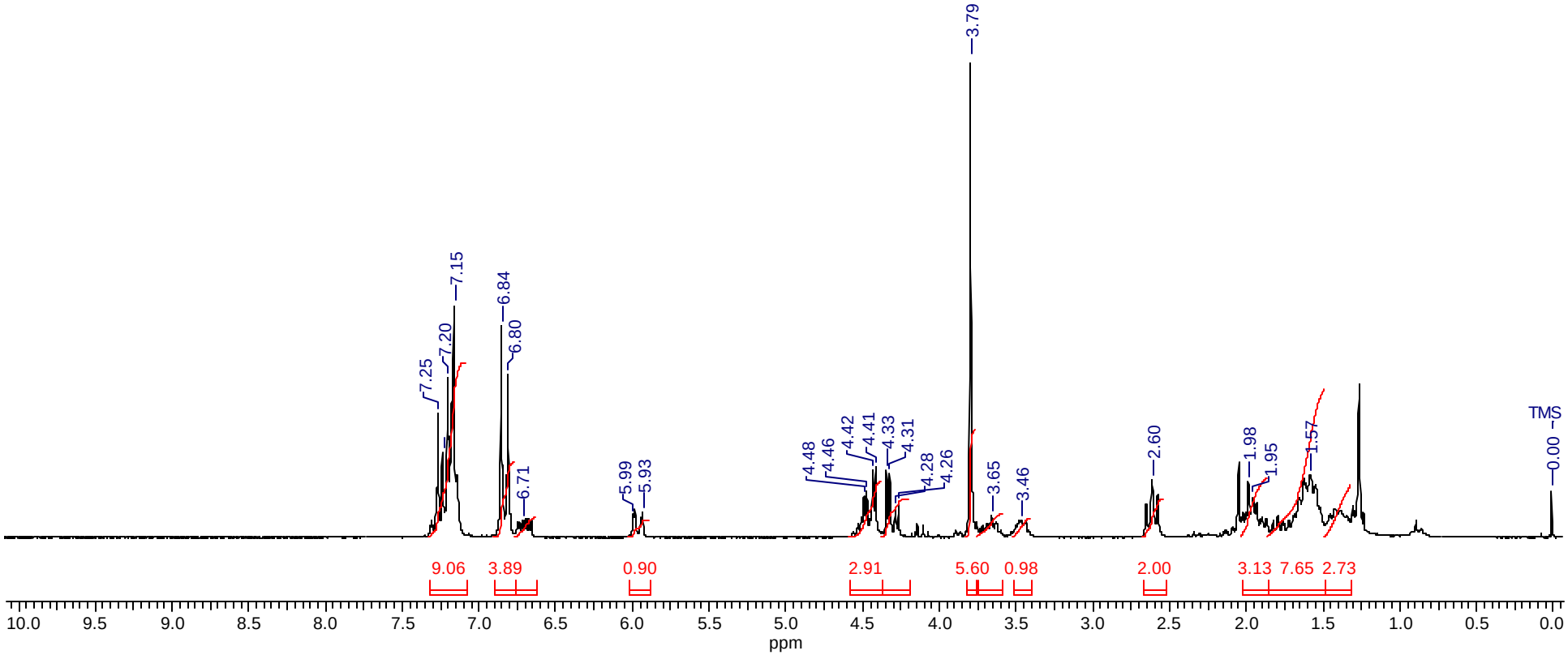
Points Count	32768	***Solvent***	BENZENE-D6	***Sweep Width (Hz)***	4139.07
Temperature (degree C)	0.000				





ENTRY_17

13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	2.7329	***Comment***	b srinivas	***Date***	07/04/2005 04:43:12
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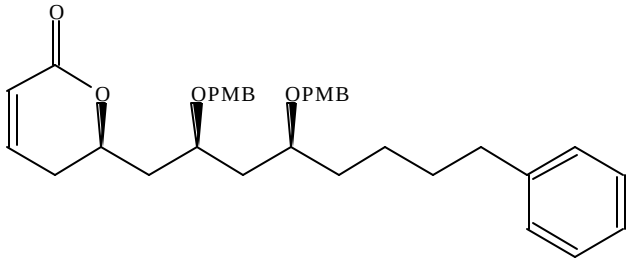
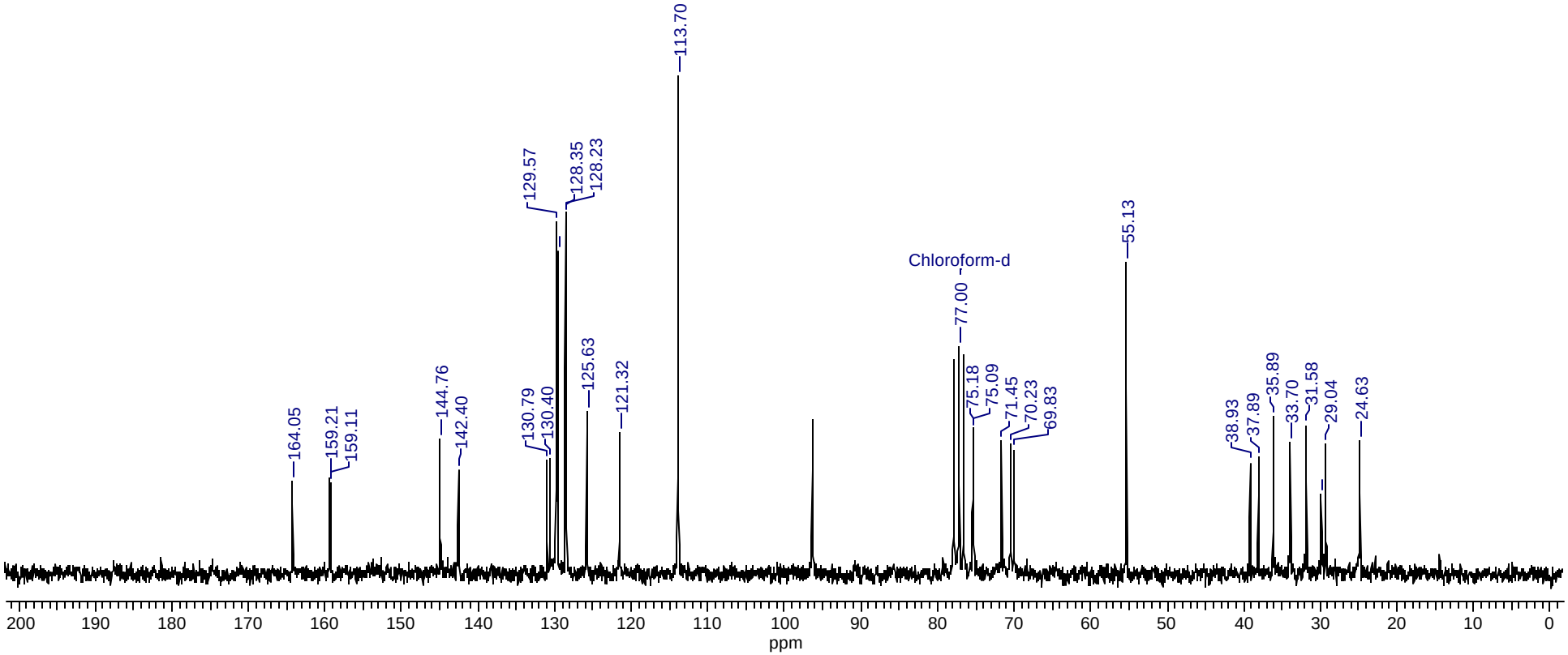
Points Count	32768	***Solvent***	BENZENE-D6	***Sweep Width (Hz)***	11990.41
Temperature (degree C)	0.000				





ENTRY_17

13 May 2005
Dr. C.V. RAMANA
b srinivas

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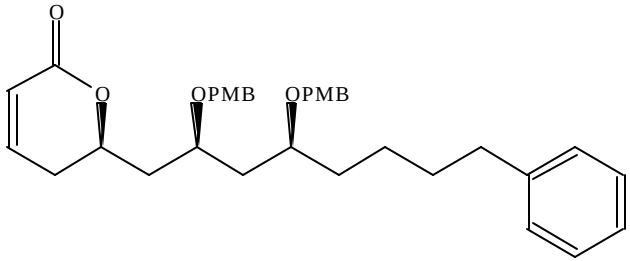
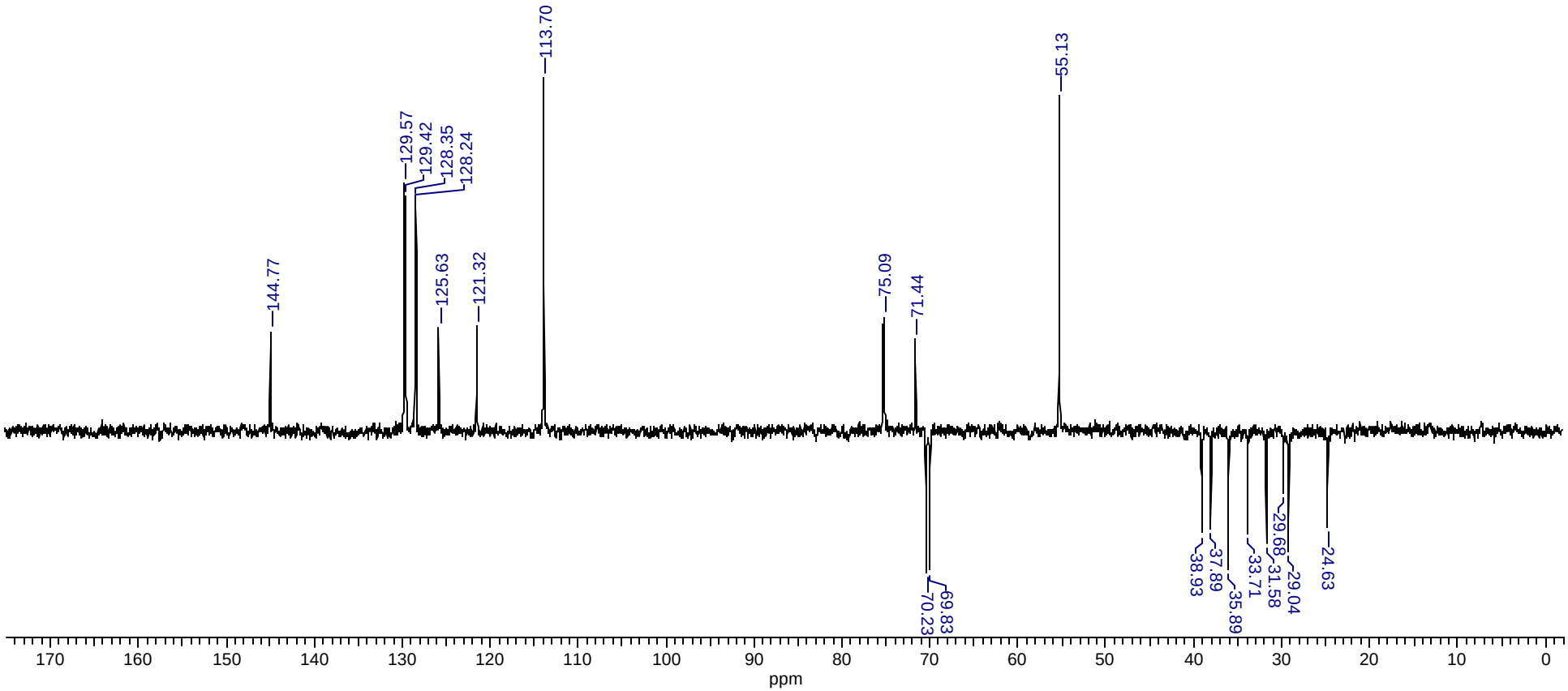
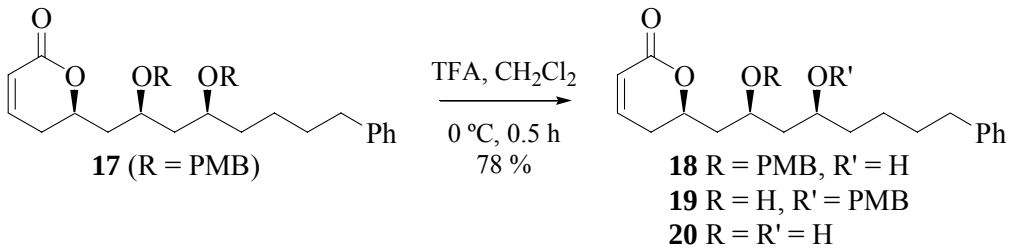
Points Count	32768	***Solvent***	BENZENE-D6	***Sweep Width (Hz)***	11990.41
Temperature (degree C)	0.000				





PMB deprotection of 17.



A solution of compound **17** (145 mg, 0.26 mmol) in CH_2Cl_2 (10 ml) at 0 °C, was treated with TFA (50 µl) and stirred for 30 min at 0 °C. The reaction was quenched by addition of saturated bicarbonate solution and the aqueous layer was extracted with CH_2Cl_2. Combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (40%→50% ethyl acetate in petroleum ether) to afford a 1:1 mixture of alcohols **18** and **19** (61 mg, 54%) and diol **20** (20 mg, 24%).

Data of 18 and 19: $[\alpha]_D^{25}$ = +54.8 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3462, 3019, 2937, 2860, 1719, 1612, 1514, 1454, 1390, 1251, 1215, 1035, 757, 668 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.19–7.07 (m, 7H), 6.82–6.70 (m, 3H), 5.96–5.88 (m, 1H), 4.59–4.21 (m, 3H), 3.92–3.77 (m, 1H), 3.71 (s, 3H), 3.68–3.54 (m, 1H), 2.59–2.49 (m, 2H), 2.33–2.18 (m, 2H), 2.14–1.67 (m, 2H), 1.67–1.45 (m,6H), 1.41–1.28 (m, 3H).^{13}C NMR (50 MHz): 24.1 (t), 25.1 (t), 29.1 (t), 29.7 (t), 31.5 (t), 31.6 (t), 33.1 (t), 35.8 (t), 35.9 (t), 37.6 (t), 38.8 (t), 40.7 (t), 41.8 (t), 55.1 (q), 68.0 (d), 70.2 (t), 70.4 (t), 70.6 (d), 74.7 (d), 75.2 (d), 75.5 (d), 79.5 (d), 113.9 (d), 121.2 (d), 121.4 (d), 125.6 (d), 125.7 (d), 128.2 (d), 128.3 (d), 129.5 (d), 129.6 (d), 129.8 (s), 142.2 (s), 142.5 (s), 144.8 (d), 145.2 (d), 159.3 (s), 159.4 (s), 163.9 (s), 164.3 (s) ppm. Anal. Calcd For $C_{27}H_{34}O_5$: C 73.94, H 7.81%; found: C 74.05, H 7.63%.

Data of Diol 20: $[\alpha]_D^{25}$ = +62.1 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3684, 3020, 2934, 1725, 1522, 1476, 1215, 1055, 759, 669 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.30–7.11 (m, 5H), 6.89 (dt, *J* = 9.8, 4.5, 3.8 Hz, 1H), 6.02 (dt, *J* = 9.8, 1.8 Hz, 1H), 4.72–4.57 (br.ddt, *J* = 8.9, 7.5, 5.5 Hz, 1H), 4.15–4.03 (m, 1H), 3.90–3.79 (m, 1H), 3.50 (b, 2H), 2.62 (t, *J* = 7.5 Hz, 2H), 2.45–2.39 (m, 2H), 2.08–1.94 (m, 1H),

1.81−1.32 (m, 9H). ^{13}C NMR (50 MHz): 24.9 (t), 29.4 (t), 31.4 (t), 35.8 (t), 38.1 (t), 42.3 (t), 42.7 (t), 69.5 (d), 72.7 (d), 76.2 (d), 121.2 (d), 125.7 (d), 128.2 (d), 128.3 (d), 142.4 (s), 145.4 (d), 164.2 (s) ppm. Anal. Calcd For $C_{19}H_{26}O_4$: C 71.66, H 8.23%; found: C 71.39, H 8.81%.

ENTRY_20

13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	7.9167	***Comment***	b srinivas	***Date***	19/04/2005 02:55:14
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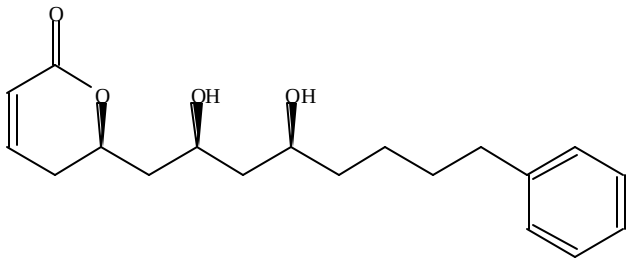
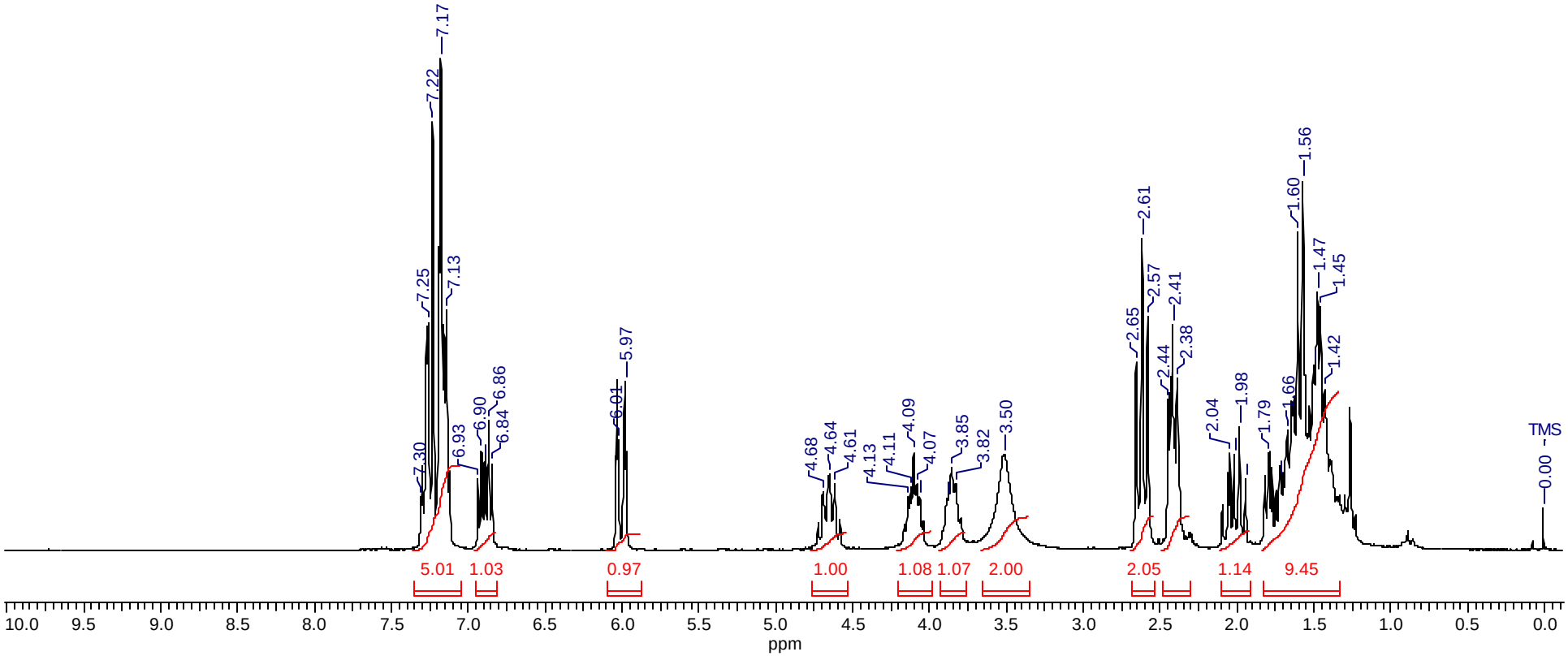
Points Count	32768	***Solvent***	BENZENE-D6	***Sweep Width (Hz)***	4139.07
Temperature (degree C)	0.000				





ENTRY_20

13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	2.7329	***Comment***	b srinivas	***Date***	19/04/2005 03:59:02
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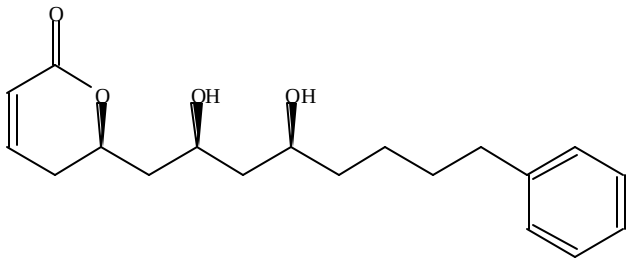
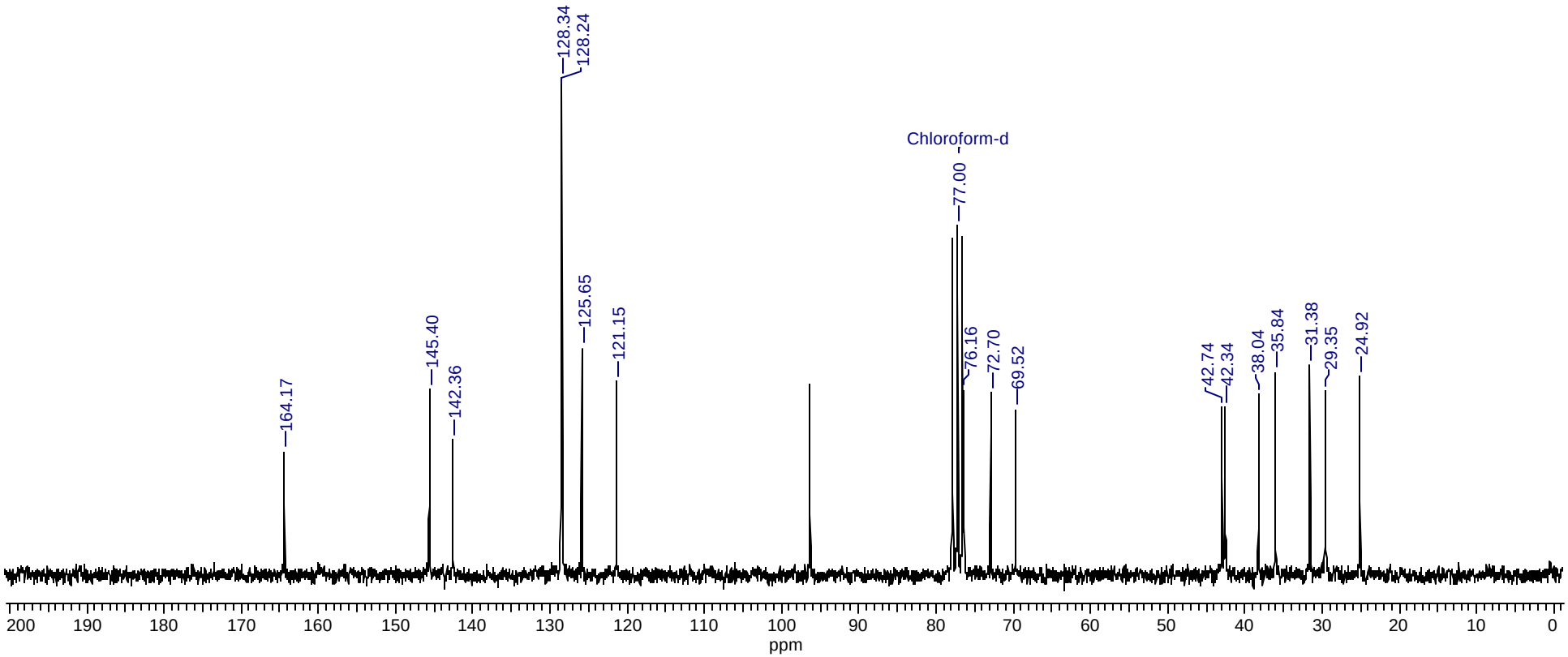
Frequency (MHz)	50.32	***Nucleus***	13C	***Original Points Count***	32768
Points Count	32768	***Solvent***	BENZENE-D6	***Sweep Width (Hz)***	11990.41
Temperature (degree C)	0.000				

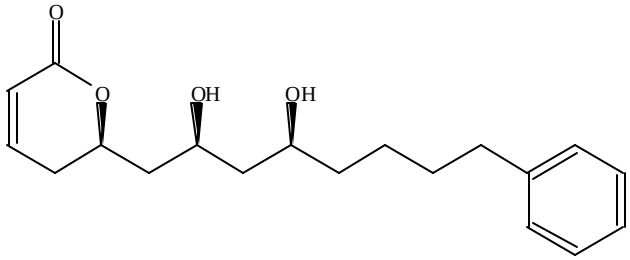


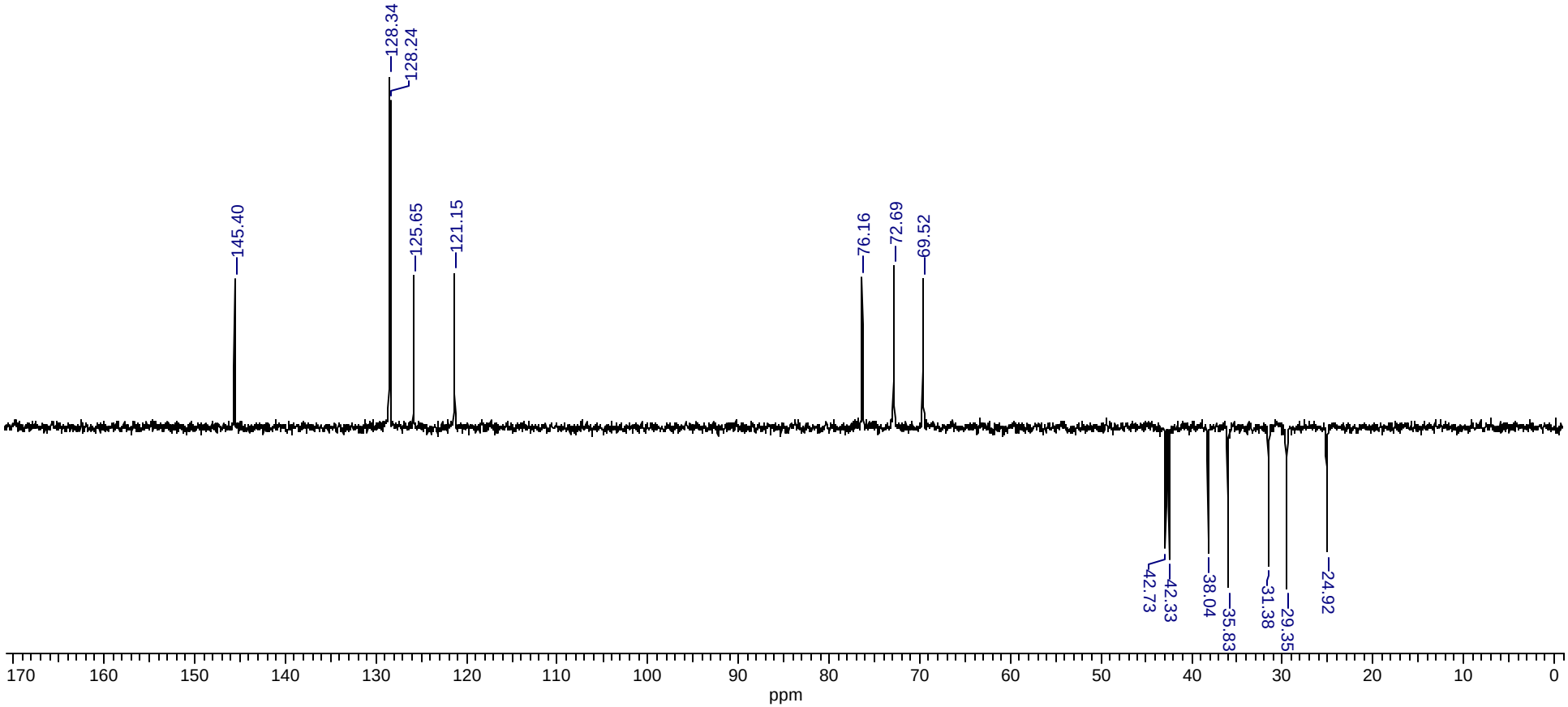


ENTRY_20

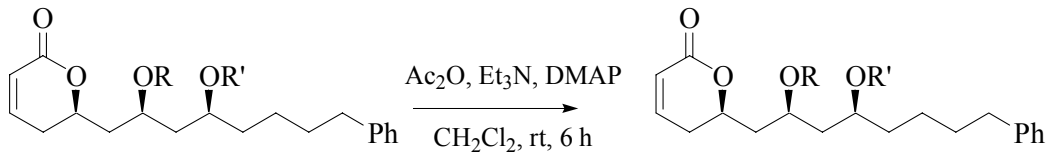
13 May 2005
Dr. C.V. RAMANA
b srinivas

Acquisition Time (sec)	2.7329	***Comment***	b srinivas	***Date***	19/04/2005 03:17:04		
File Name	C:\Documents and Settings\CVR\My Documents\UGADHI_05\PAPERS\SREENU\SRINIVAS_01\Entry_20\LAC_DIOL_DEPT.ESP						
Frequency (MHz)	50.32	***Nucleus***	13C	***Original Points Count***	32768	***Points Count***	32768
Solvent	BENZENE-D6	***Sweep Width (Hz)***	11990.41	***Temperature (degree C)***	0.000		





Acetylation of 18 and 19.

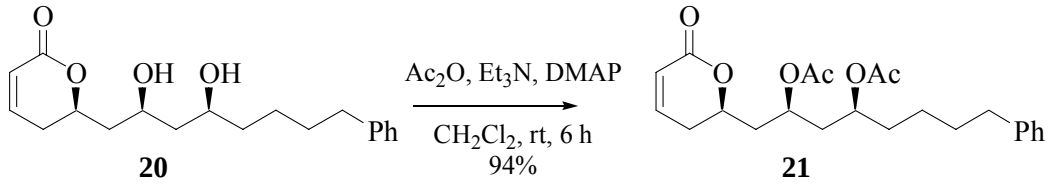


18 R = PMB, R' = H
19 R = H, R' = PMB

18-Ac R = PMB, R' = Ac
19-Ac R = Ac, R' = PMB

To a solution of regioisomeric mixture of **18** and **19** (54 mg, 0.12 mmol) in CH_2Cl_2 (5 ml) was added acetic anhydride (60 µl, 0.62 mmol), triethylamine (85 µl, 0.61 mmol), DMAP (5 mg) and stirred for 6 h at rt. The reaction mixture was added to CH_2Cl_2/water and the organic layer was separated, dried (Na_2SO_4) and concentrated. The resulting crude product was purified by column chromatography (30% ethyl acetate in petroleum ether) to yield 1:1 regioisomeric mixture of **18**-Ac and **19**-Ac (55 mg, 94%) as an yellow color oil. $[\alpha]_D^{25}$ = +48.9(*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3020, 2936, 2860, 1726, 1612, 1513, 1464, 1375, 1249, 1216, 1037, 757, 668 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ: 7.30–7.11 (m, 7H), 6.88–6.81 (m, 2H), 6.80–6.71 (m, 1H), 6.00–5.94 (m, 1H), 5.21–4.89 (2m, 1H), 4.59–4.33 (m, 3H), 3.78 (2s,3H), 3.59–3.37 (m, 1H), 2.64–2.54 (m, 2H), 2.39–2.03 (m, 3H), 1.99, 1.98 (2s, 3H), 1.92–1.51 (m, 7H),1.45–1.29 (m, 2H). ^{13}C NMR (50 MHz): 21.1 (q), 24.5 (t), 24.8 (t), 29.1 (t), 29.1 (t), 31.1 (t), 31.5 (t), 33.3 (t), 34.4 (t), 35.7 (t), 35.8 (t), 38.1 (t), 38.4 (t), 38.6 (t), 39.3 (t), 55.2 (q), 68.3 (d), 69.8 (t), 69.9 (t), 71.2 (d), 71.3 (d), 74.9 (d), 74.9 (d), 75.1 (d), 113.7 (d), 121.4 (d), 125.6 (d), 128.2 (d), 128.3 (d), 129.4 (d), 129.6 (d), 130.1 (s), 130.6 (s), 142.3 (s), 142.4 (s), 144.6 (d), 144.8 (d), 159.2 (s), 159.3 (s), 163.7 (s), 164.0 (s), 170.5 (s) ppm. Anal. Calcd For $C_{29}H_{36}O_6$: C 72.47, H 7.55%; found: C 72.39, H 7.26%.

Diactetate 21.

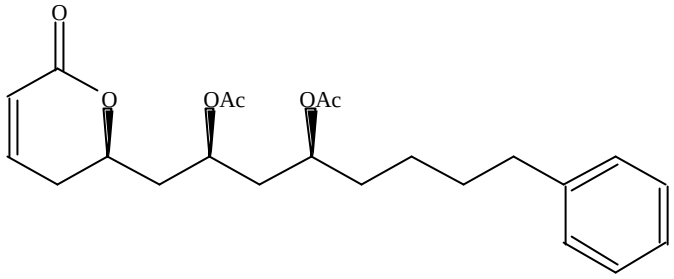


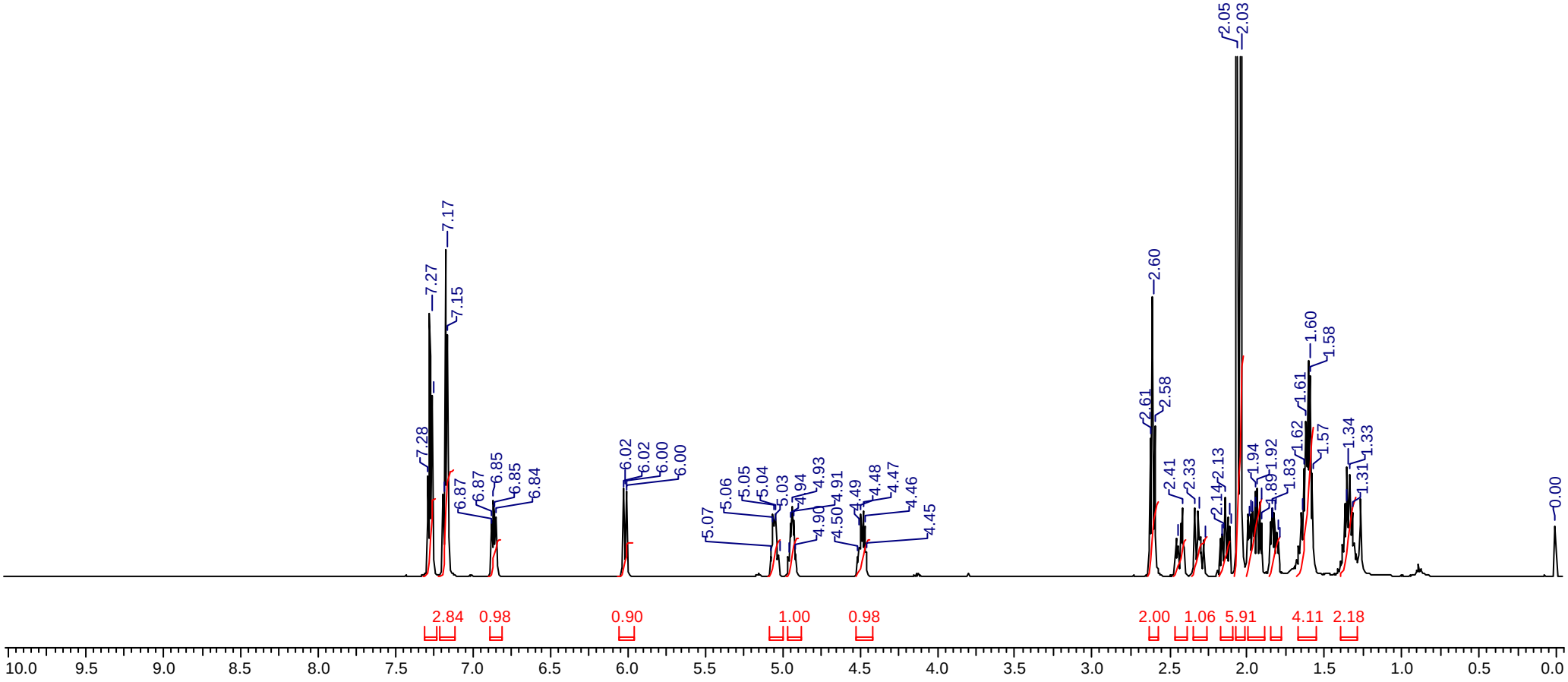
In a manner similar to that used in the preparation of **18**-Ac/**19**-Ac, treatment of **20** (29 mg, 0.09 mmol) in CH_2Cl_2 (6 ml) with Ac_2O (85 µl, 0.91 mmol), triethylamine (126 µl, 0.91 mmol) and DMAP (5 mg) and usual work up after 6 h stirring followed by purification by column chromatography (30% ethyl acetate in petroleum ether) gave **21** (34 mg, 94%) as an yellow color oil. $[\alpha]_D^{25}$ = +48.6 (*c* = 1, $CHCl_3$). IR ($CHCl_3$): υ 3020, 2936, 2861, 1730, 1496, 1374, 1242, 1216, 1152, 1038, 758, 668 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.28–7.25 (m, 2H), 7.18–7.15 (m, 3H), 6.87–6.84 (m, 1H), 6.02–6.00 (dd, *J* = 9.7, 1.9 Hz, 1H), 5.07–5.02 (m, 1H), 4.95–4.90 (m, 1H), 4.50–4.45 (m, 1H), 2.61–2.58 (t, *J* = 7.5 Hz, 2H), 2.46–2.40 (m, 1H), 2.33–2.27 (m, 1H), 2.16–2.10 (m, 1H), 2.05 (s, 3H), 2.03 (s, 3H), 1.99–1.89 (m, 2H), 1.84–1.79 (m, 1H), 1.66–1.57 (m, 4H), 1.39–1.28 (m, 2H). ^{13}CNMR (125 MHz, $CDCl_3$) δ 21.1 (q), 24.6 (t), 29.1 (t), 31.0 (t), 34.1 (t), 35.6 (t), 38.9 (t), 38.9 (t), 67.8 (d), 70.8 (d), 74.9 (d), 121.3 (d), 125.7 (d), 128.2 (d), 128.4 (d), 142.3 (s), 144.7 (d), 163.7 (s), 170.6 (s), 170.8 (s) ppm. MALDI-TOF (MS) calcd for $C_{23}H_{30}O_6Na$ 425.19, found 425.19 (M + Na). Anal. Calcd. for $C_{23}H_{30}O_6$: C 68.64, H 7.51; found: C 68.89, H 7.61.

Entry_21

16 May 2005

Acquisition Time (sec) 2.1823	***Comment***	Imported from UXNMR.		***Date***	20/04/2005 10:59:52		
Frequency (MHz) 500.13	***Nucleus***	1H	***Original Points Count*** 16384	***Points Count***	16384	***Sweep Width (Hz)***	7507.51
Temperature (grad C) 0.000							

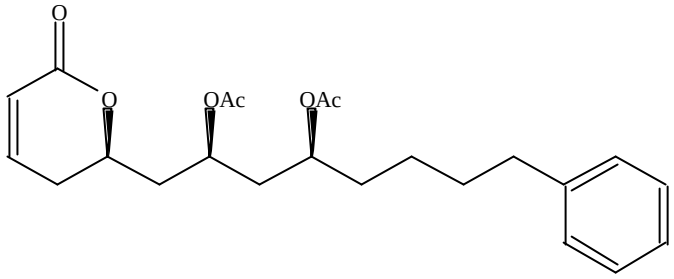


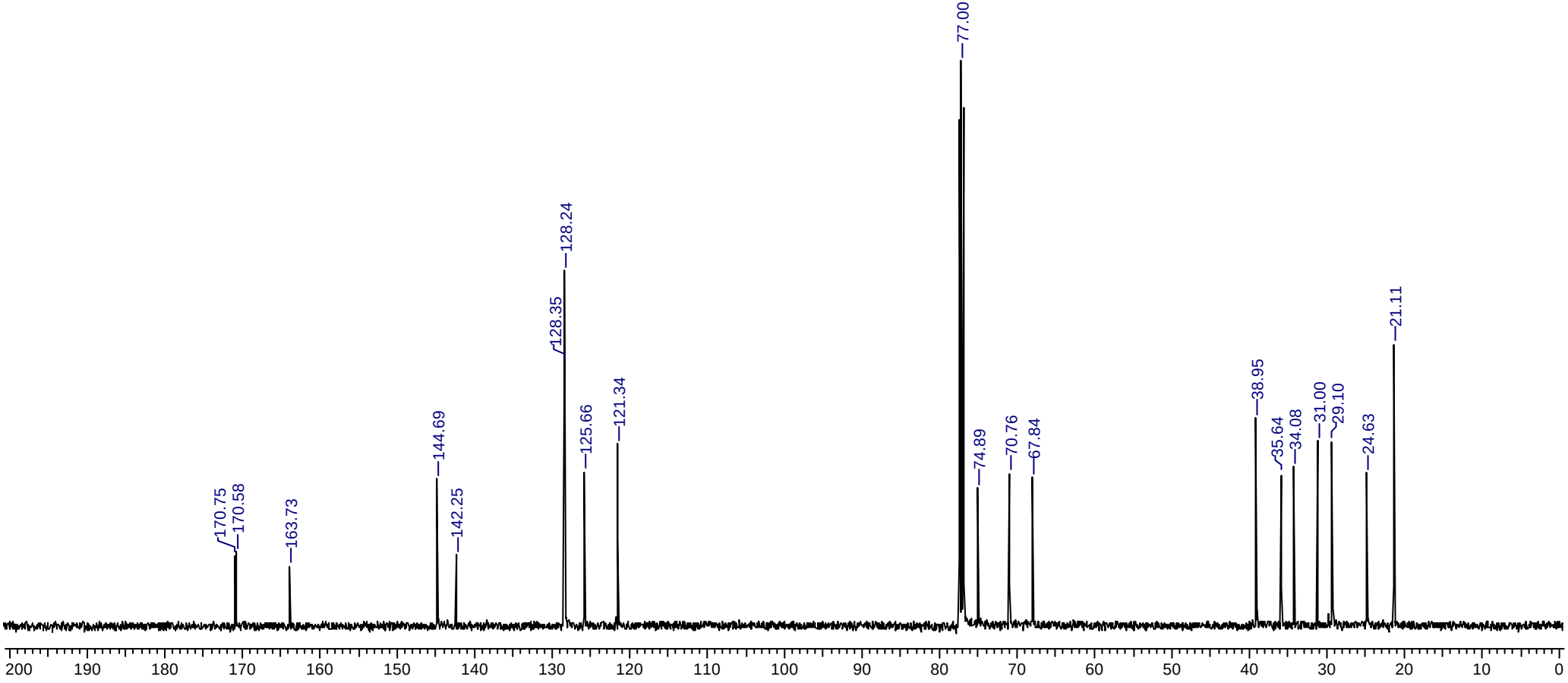


Entry_21

16 May 2005

Acquisition Time (sec)	0.5210	***Comment***	Imported from UXNMR.		***Date***	20/04/2005 12:15:24	
Frequency (MHz)	125.76	***Nucleus***	13C	***Original Points Count*** 16384	***Points Count***	16384	***Sweep Width (Hz)*** 31446.54
Temperature (grad C)	0.000						

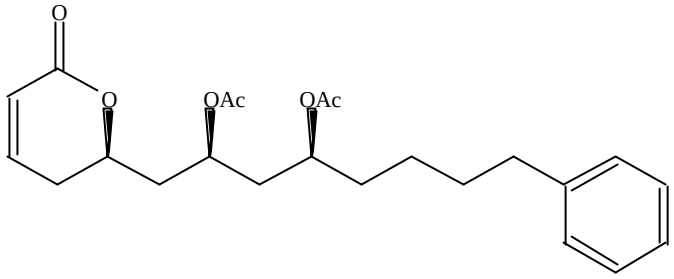


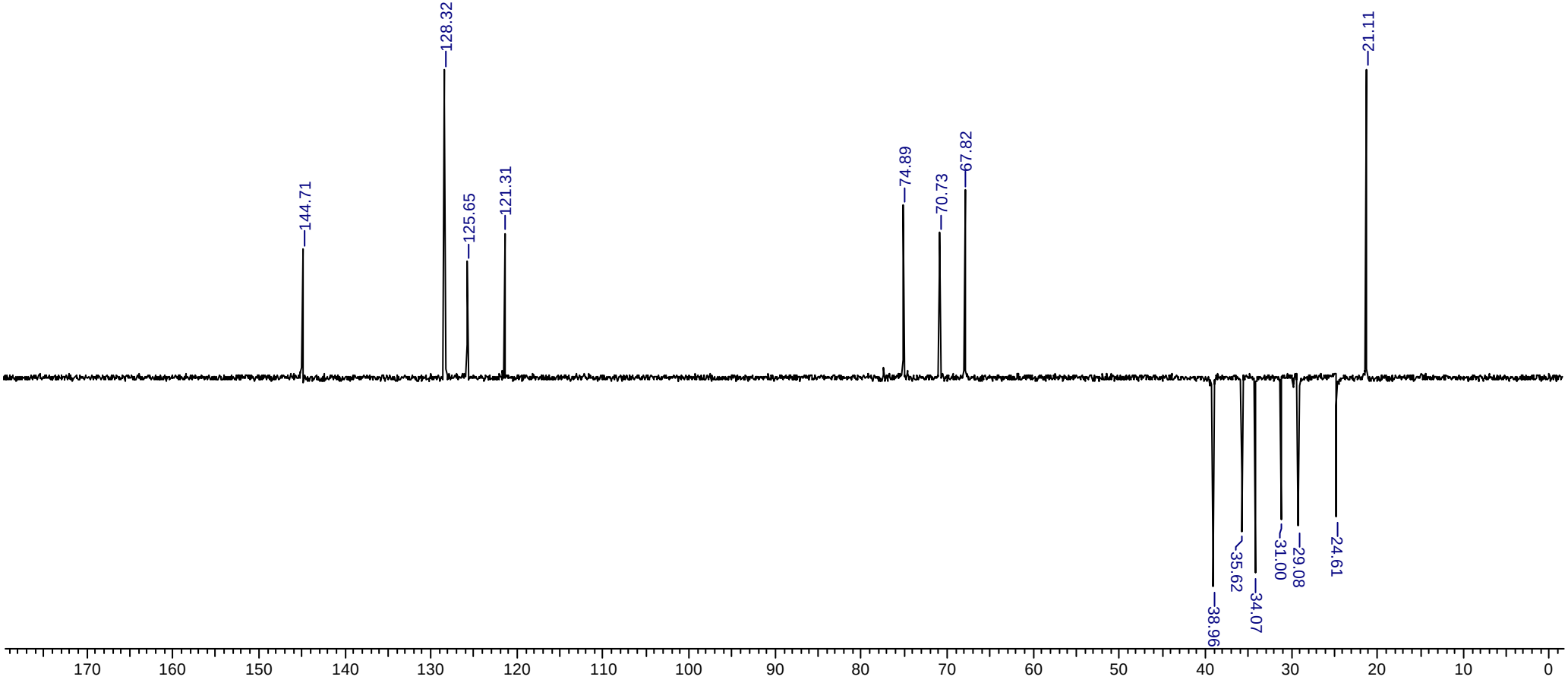


Entry_21

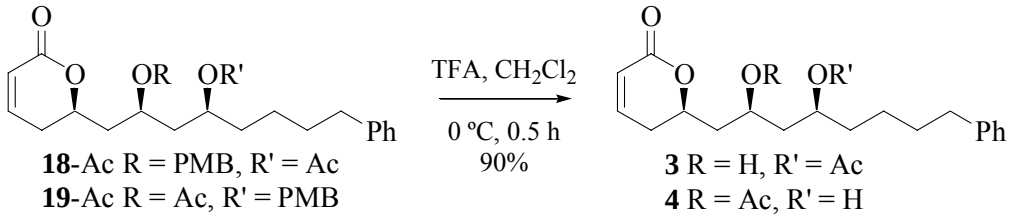
16 May 2005

Acquisition Time (sec)	1.0420	***Comment***	Imported from UXNMR.		***Date***	20/04/2005 12:02:32	
Frequency (MHz)	125.76	***Nucleus***	13C	***Original Points Count*** 32768	***Points Count***	32768	***Sweep Width (Hz)*** 31446.54
Temperature (grad C)	0.000						





Synthesis of α-pyrone Natural Products 3 and 4.



In a manner similar to that used in the deprotection of **17**, treatment of **18**-Ac/**19**-Ac (58 mg, 0.12 mmol) in CH_2Cl_2 (6 ml) with TFA (20 μl) and stirring at 0 °C 30 min, usual workup and purification by column chromatography (40% ethyl acetate in petroleum ether) gave an equilibrium mixture of natural regioisomers **3** and **4** (39 mg, 90%) as an yellow color oil.

$[\alpha]_D^{25}$ = +39 (*c* = 0.4, MeOH), Lit.$[\alpha]_D^{25}$ = +35 (*c* = 0.05, MeOH).[4] IR ($CHCl_3$): υ 3440, 3019, 2934, 2859, 1724, 1513, 1496, 1384, 1250, 1216, 1043, 757, 668 cm^{-1}. MALDI-TOF (MS) calcd for $C_{21}H_{28}O_5Na$ 383.18, found 383.17 (M + Na). Anal. Calcd For $C_{21}H_{28}O_5$: C 69.98, H, 7.83; found: C 69.79, H 7.96%.

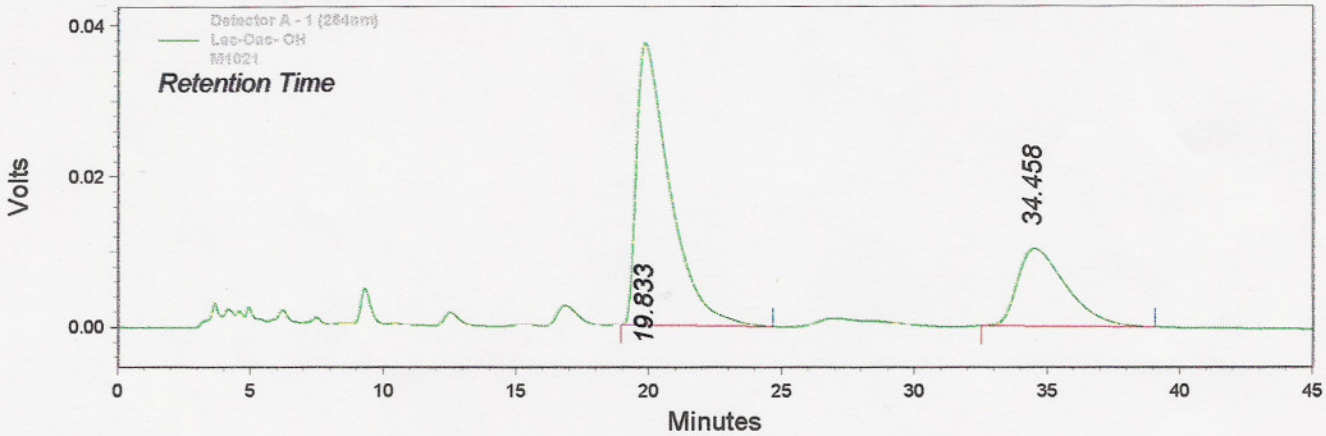
A portion of **3**/**4** mixture was subjected to preparative HPLC separation and the ^{1}H and ^{13}C NMR of the separated **3** and **4** were recorded. In case of the minor isomer **4**, we found the equilibration is facile and the difference in the ratio of **4** : **3** changed from 1 : 0.14 (^{1}H NMR) to 1 : 0.75 (^{13}C NMR), the later being recorded for over night.

Major Isomer 3: $[\alpha]_D^{25}$ = +33 (*c* = 0.3, MeOH) {Lit.$[\alpha]_D^{25}$ = +35 (*c* = 0.05, MeOH)}.[4] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.24 (m, 2H), 7.18-7.14 (m, 3H), 6.87 (dt, *J* = 9.8, 4.2 Hz, 1H), 6.01 (br.dt, *J* = 9.5, 1.7 Hz, 1H), 4.97–4.92 (m, 1H), 4.66–4.60 (m, 1H), 3.90–3.86 (m, 1H), 2.59 (t, *J* = 7.5 Hz, 2H), 2.40–2.37 (m, 2H), 2.02 (s, 3H),1.95–1.41 (m, 10H). ^{13}C NMR (125 MHz): 21.3 (q), 24.8 (t), 29.4 (t), 31.1 (t), 34.5 (t), 35.7 (t), 41.7 (t), 42.3 (t), 67.0 (d), 72.3 (d), 76.6 (d), 121.2 (d), 125.7 (d), 128.3 (d), 128.4 (d), 142.3 (s), 145.2 (d), 163.9 (s), 171.3 (s) ppm.

Minor Isomer 4: ^{1}H NMR (500 MHz, $CDCl_3$): δ δ 7.27–7.24 (m, 2H), 7.18–7.14 (m, 3H), 6.87–6.84 (ddd, *J* = 9.7, 6.1, 2.4 Hz, 1H), 6.01 (ddd, *J* = 9.7, 2.6, 0.7 Hz, 1H), 5.24–5.19 (m, 1H), 4.54–4.48 (m, 1H), 3.72–3.67 (m, 1H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.48–2.43 (m, 1H), 2.34–2.26 (m, 1H), 2.18 (ddd, *J* = 14.6, 8.4, 6.3 Hz, 1H), 2.05 (s, 3H), 1.95 (ddd, *J* = 14.6, 6.8, 4 Hz, 1H), 1.82–1.71 (m, 2H), 1.66–1.42 (m, 6H). ^{13}C NMR (125 MHz): 21.3 (q), 25.0 (t), 29.2 (t), 31.3 (t), 35.8 (t), 37.7 (t), 39.3 (t), 41.7 (t), 69.0 (d), 69.2 (d), 75.1 (d), 121.4 (d), 125.7 (d), 128.3 (d), 128.4(d), 142.4(s), 144.7 (d), 163.9 (s), 170.9(s).

Acquisition time : 7/13/05 1:57:13 PM

Data Graph



Run Report

Detector A - 1 (254nm)

Pk #	Retention Time	Area	Area Percent
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2	34.458	1298628	28.51
Totals		4554460	100.00

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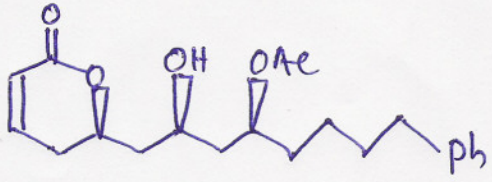
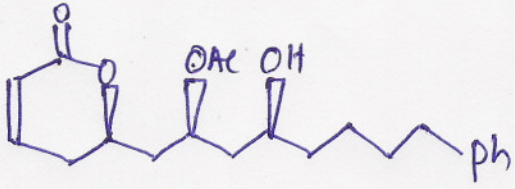
Mobile phase :-IPA:PET 10:90
Wavelength :- 254 nm
Flow rate :- 1.0 ml/min

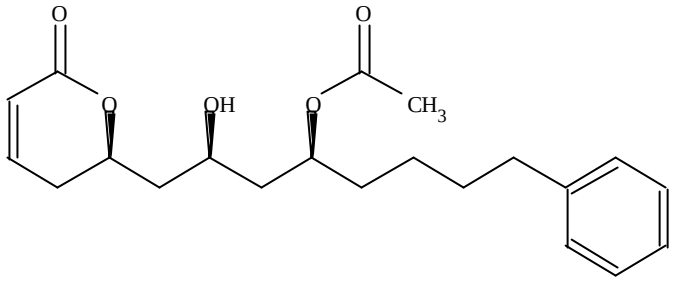


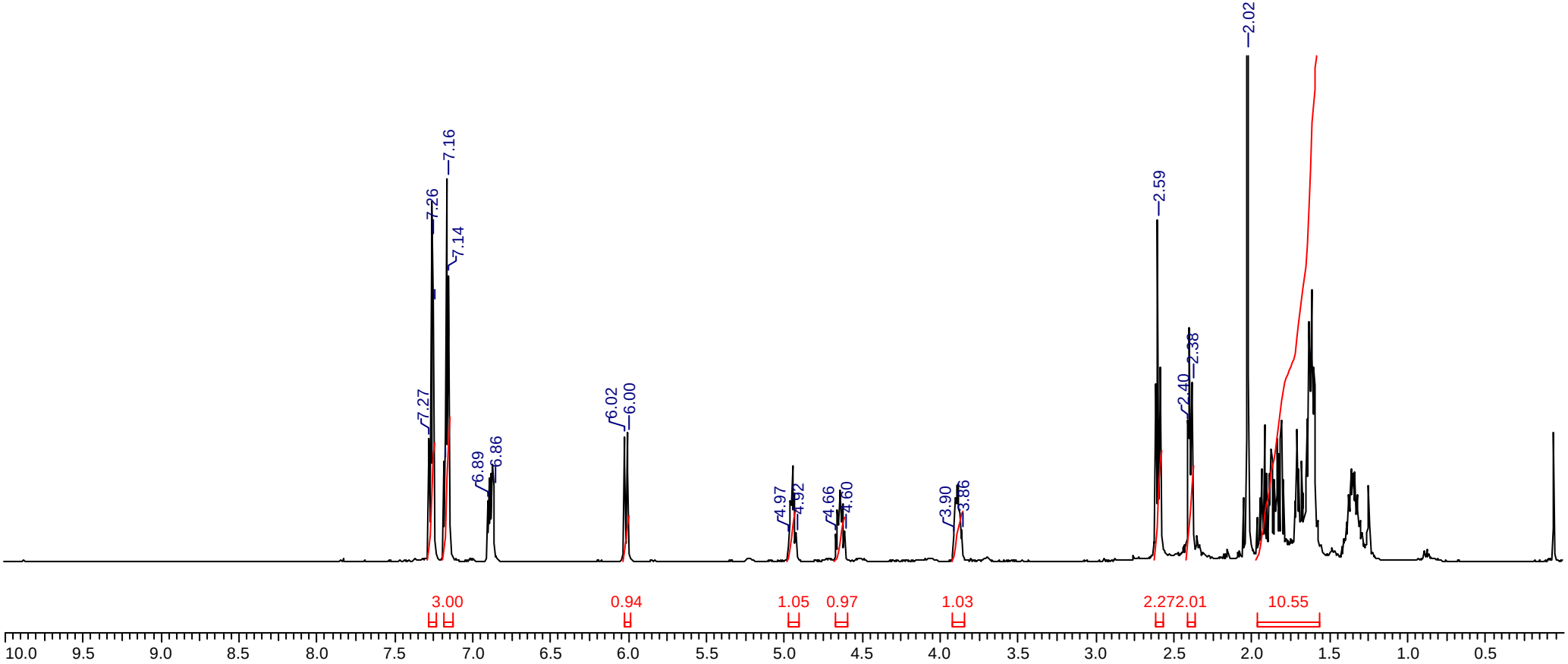


ENTRY_03

20 Jul 2005
Dr C.V. Ramana

Acquisition Time (sec)	2.1823	***Comment***	Dr C.V. Ramana		***Date***	15/07/2005 02:44:08	
Frequency (MHz)	500.13	***Nucleus***	1H	***Original Points Count*** 16384	***Points Count***	16384	***Sweep Width (Hz)*** 7507.51
Temperature (grad C)	0.000						

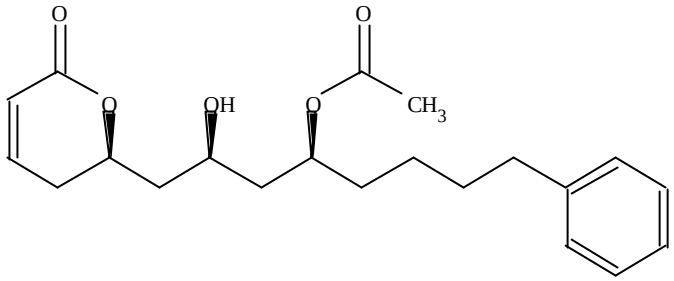


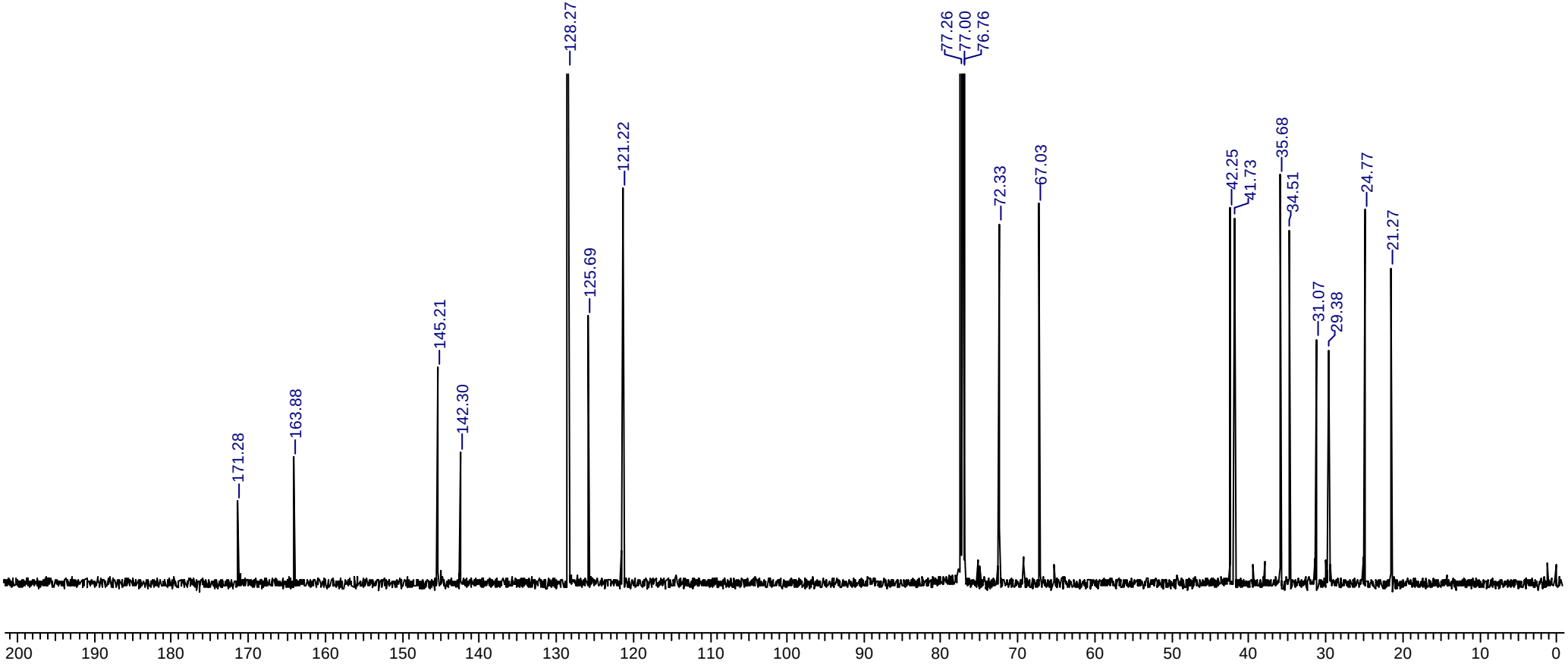


ENTRY_03

19 Jul 2005
CVRAMANA

Acquisition Time (sec) 0.5210	***Comment***	B Srinivas;BSR-1 major;13C		***Date***	15/07/2005 23:28:50		
Frequency (MHz) 125.76	***Nucleus***	13C	***Original Points Count*** 16384	***Points Count***	16384	***Sweep Width (Hz)***	31446.54
Temperature (grad C) 0.000							





ENTRY_03

19 Jul 2005
CVRAMANA

Acquisition Time (sec) 1.0420	***Comment***	B Srinivas;BSR-1 major;13C DEPT		***Date***	15/07/2005 21:40:14		
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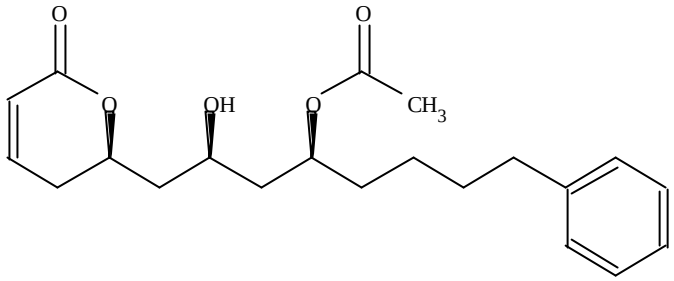
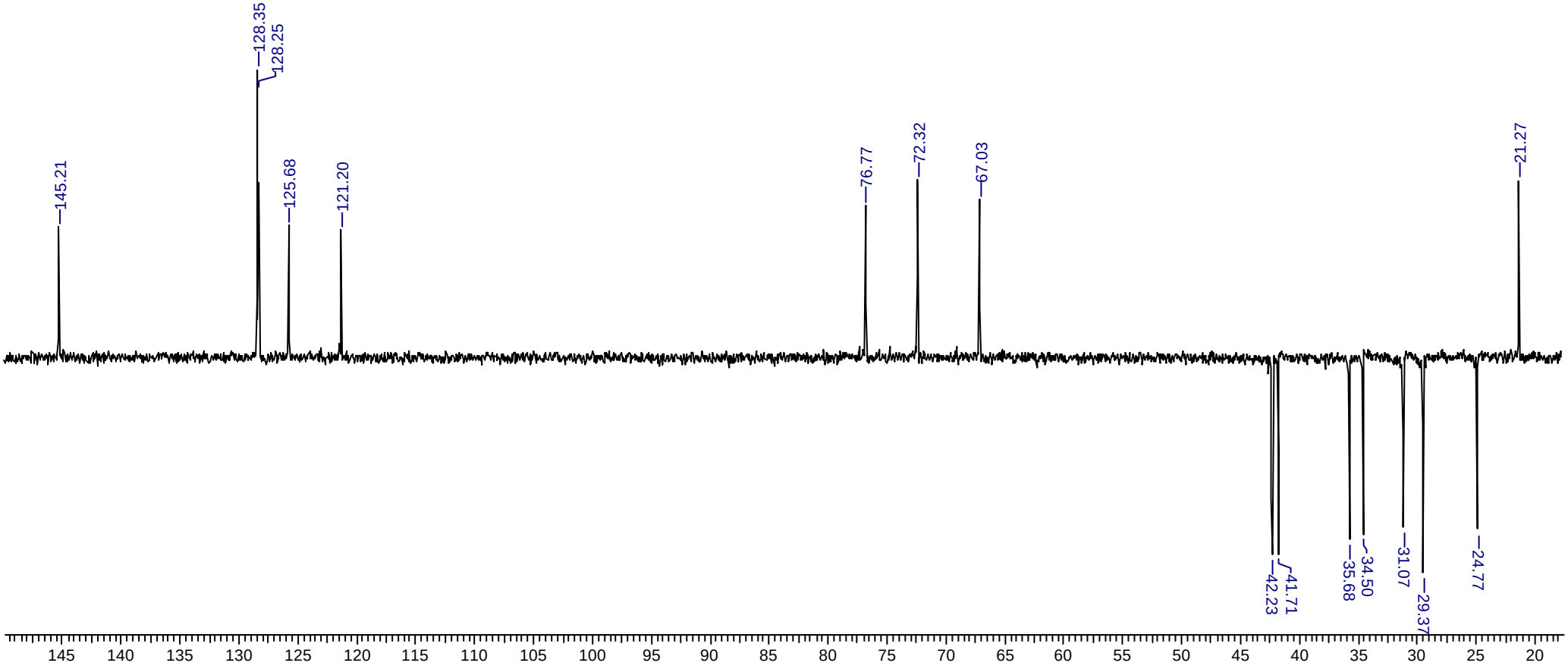
Temperature (grad C) 0.000							

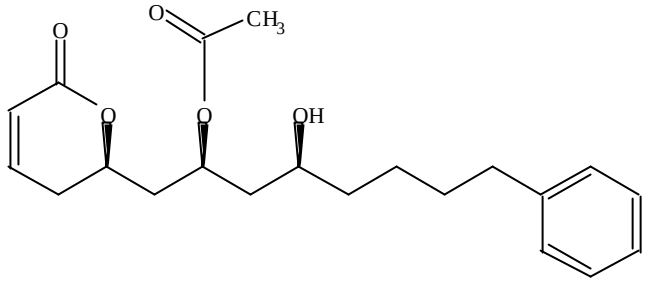


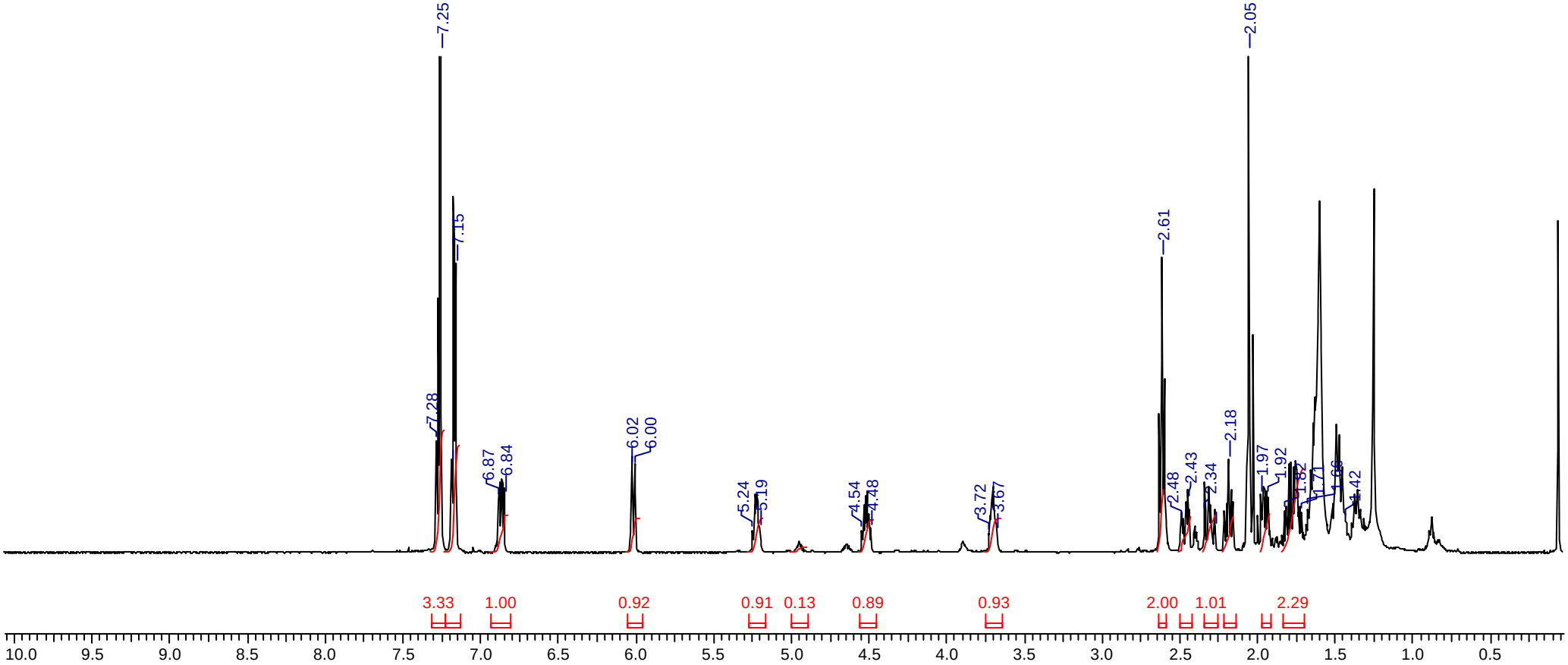


ENTRY_04

20 Jul 2005
Dr C.V.Ramana

Acquisition Time (sec)	2.1823	***Comment***	Dr C.V.Ramana		***Date***	15/07/2005 02:36:00	
Frequency (MHz)	500.13	***Nucleus***	1H	***Original Points Count*** 16384	***Points Count***	16384	***Sweep Width (Hz)*** 7507.51
Temperature (grad C)	0.000						

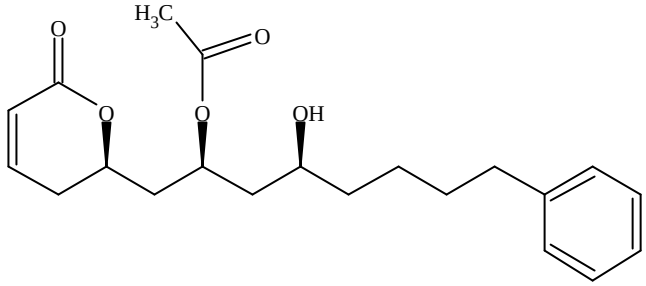


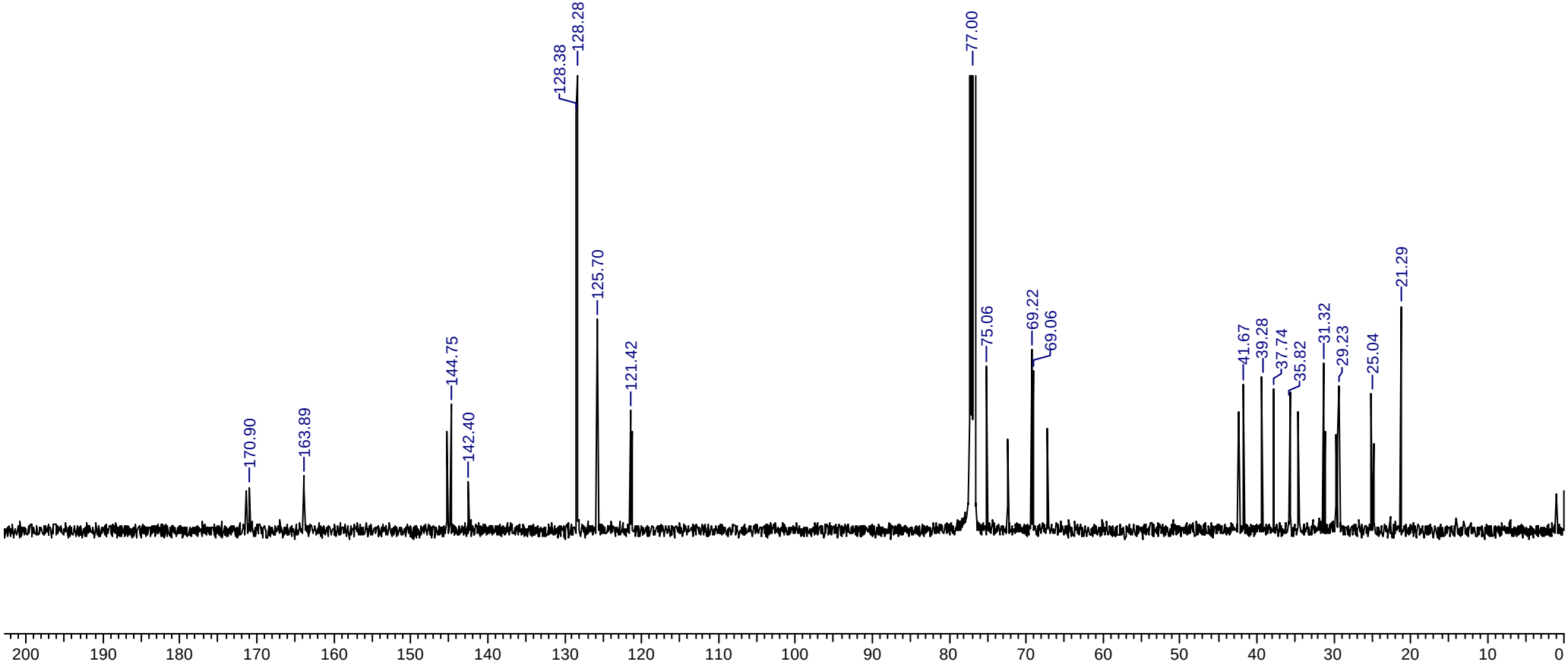


ENTRY_04

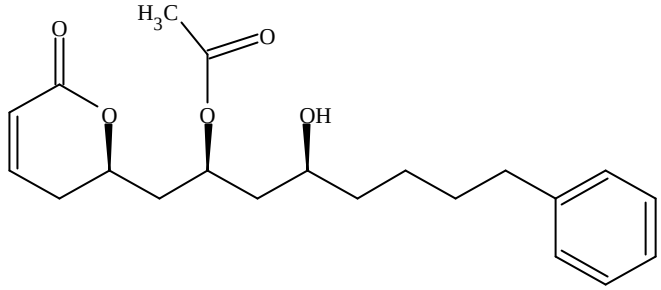
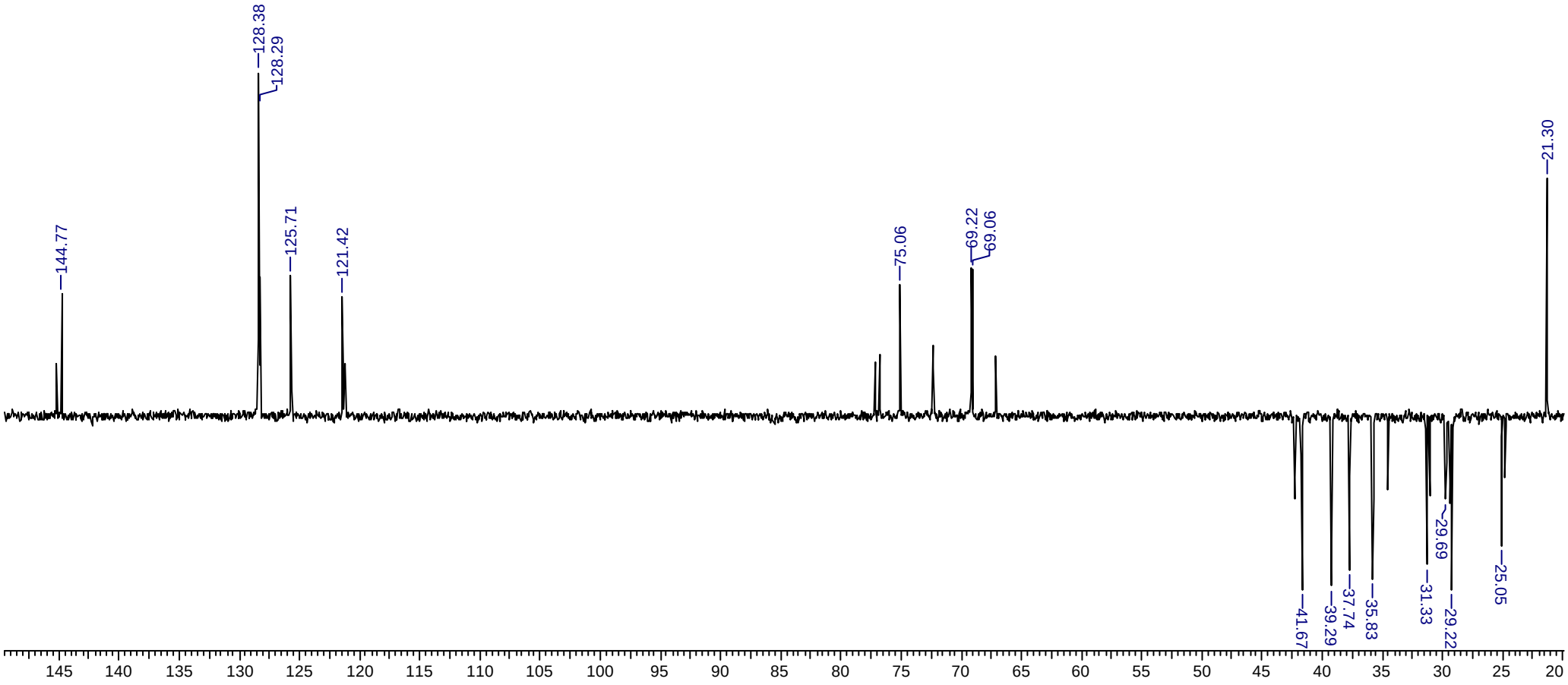
20 Jul 2005
B Srinivas;BSR-2 minor;13C

Acquisition Time (sec)	0.5210	***Comment***	B Srinivas;BSR-2 minor;13C		***Date***	15/07/2005 21:08:36	
Frequency (MHz)	125.76	***Nucleus***	13C	***Original Points Count*** 16384	***Points Count***	16384	***Sweep Width (Hz)*** 31446.54
Temperature (grad C)	0.000						





ENTRY_04

20 Jul 2005

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Frequency (MHz)	125.76	***Nucleus***	13C	***Original Points Count*** 32768	***Points Count***	32768	***Sweep Width (Hz)*** 31446.54
Temperature (grad C)	0.000