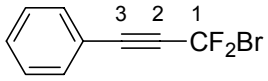
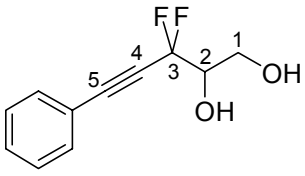
Preparation of 1-bromo-1,1-difluoro-3-phenyl-prop-2-yne 2a



n-Buthyllithium (250.0 mmol, 156.5 mL of a 1.6 N solution in hexanes) was added dropwise to a cold (-78 °C) solution of phenylacetylene (250 mmol, 27.5 mL) in THF (500 mL). After completion of the addition a white precipitate formed and the suspension was stirred at 0 °C for 15 minutes and recooled to -78 °C. A cold (-70 °C) solution of dibromodifluoromethane (275 mmol, 25 mL) in THF (250 mL) was added dropwise through a cold jacketed dropping funnel over 1 hour. After completion of the addition, the brown solution was stirred at -78 °C for 1 hour and at 0 °C for 1 hour. The reaction mixture was quenched with ammonium chloride (500 mL of a saturated aqueous solution). The layers were separated and the aqueous layer further extracted with diethyl ether (3 x 500 mL). The combined organic extracts were washed with brine (250 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to leave a brown oil (52.23 g). Distillation under reduced pressure afforded the desired alkyne **2a** as pale yellow oil (47.37 g, 82 %, 96 % by GC). Bp 60 °C/1.5 mmHg (Lit.[91] 50 °C/1.0 mmHg); ν_{max} (film)/cm^{-1} 3060w (Ar-H); 2253s (C≡C) δ_H (300 MHz, $CDCl_3$) 7.57-7.37 (m, -C_6H_5); δ_C (75 MHz, $CDCl_3$) 132.3 (t, $^5J_{C\text{-}F}$ 2.3), 130.9, 128.7, 118.8 (t, $^4J_{C\text{-}F}$ 2.3), 102.1 (t, $^1J_{C\text{-}F}$ 289.4), 90.0 (t, $^3J_{C\text{-}F}$ 5.7), 81.0 (t, $^2J_{C\text{-}F}$ 38.4); δ_F (282 MHz, $CDCl_3$) -45.4 (s); *m/z* (EI) 232 (27 %, $M^+[^{81}Br]$), 230 (27, $M^+[^{79}Br]$), 213 (17), 211 (18), 151 (80). The spectral data were in agreement with those reported by Wakselman *et al.* (I. Rico, D. Cantacuzene, and C. Wakselman, *J. Chem. Soc. Perkin Trans. 1*, 1982, 1063.)

Preparation of 3,3-difluoro-5-phenyl-pent-4-yne-1,2-diol 1



A mixture of sodium iodide (89.0 mmol, 13.3 g), mercury (II) acetate (4.4 mmol, 1.4 g), glycolaldehyde dimer (89.0 mmol, 10.7 g) and zinc powder (89.0 mmol, 5.79 g) was added in one portion to a solution of alkyne **75** (89.0 mmol, 20.5 g) in THF (350 mL). Upon addition, a gentle reflux was observed and the solution was stirred at room temperature for 18 hours. The reaction mixture was quenched with HCl (350 mL of a

2N solution) and extracted with ethyl acetate (3 x 250 mL). The combined organic extracts were washed with sodium sulfite (200 mL of a saturated aqueous solution), brine (200 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a brown oil (18.90 g). Purification by column chromatography (40 % ethyl acetate in light petroleum) afforded the desired diol **1** as a yellow oil, which solidified on standing (12.98 g, 69 %, 100 % by GC). R_f (40 % ethyl acetate in light petroleum) 0.25; Mp 35-36 °C; (Found C, 62.35; H, 4.85; $C_{11}H_{10}F_2O_2$ requires: C, 62.26; H, 4.75 %); ν_{max} (KBr)/cm^{-1} 3370s br (O-H), 2944m (Ar-H), 2241s (C≡C); δ_H (250 MHz, $CDCl_3$) 7.43-7.20 (5H, m, -C_6H_5), 4.08-3.96 (1H, m, H-2), 3.87 (1H, dd, J_{gem} 11.8, J 3.3, H-1a), 3.79 (1H, dd, J_{gem} 11.8, J 7.6, H-1b), 3.53 (2H, br s, 2 x -O*H*); δ_C (63 MHz, $CDCl_3$) 132.7, 130.6, 128.9, 120.0 (t, $^4J_{C\text{-}F}$ 2.8), 113.9 (t, $^1J_{C\text{-}F}$ 237.0), 89.6 (t, $^3J_{C\text{-}F}$ 6.9), 79.5 (t, $^2J_{C\text{-}F}$ 38.9), 74.8 (t, $^2J_{C\text{-}F}$ 27.7), 61.9; δ_F (235 MHz, $CDCl_3$) -94.0 (1H, dd, first half of an AB quartet, J_{gem} 279.3, $^3J_{F\text{-}H}$ 8.6), -94.8 (1H, dd, second half of an AB quartet, J_{gem} 279.3, $^3J_{F\text{-}H}$ 9.9; *m/z* (ES) 235 (100 %, $[M+Na]^+$).

Measured rotations from polarimetry

7a $[\alpha]_D$ (*c* 1.08 in MeOH) +10.9

7b $[\alpha]_D$ (*c* 1.11 in MeOH) +3.6

7c $[\alpha]_D$ (*c* 0.91 in MeOH) -11.9

7d $[\alpha]_D$ (*c* 1.01 in MeOH) -4.6

Chiral Chromatography

Chiral HPLC was run on a Perkin Elmer 200 series HPLC with Peltier oven column selector fitted with a Chiralcel OJ column. Pre-mixed iPrOH/hexane (0.5:99.5) was used as the eluent. We should also point out that there were co-elution issues with the *pseudo*-racemate made from **7a** and **7b** but that the separation of the enantiomers was

7a

Software Version	: 6.2.1.0.104:0104	Date	: 17/02/2004 11:55:42
Sample Name	: ca562b Hex+iProh	Data Acquisition Time	: 17/02/2004 11:22:51
Instrument Name	: PerkinElmer_HPLC	Channel	: A
Rack/Vial	: 1/3	Operator	: christophe
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 4		

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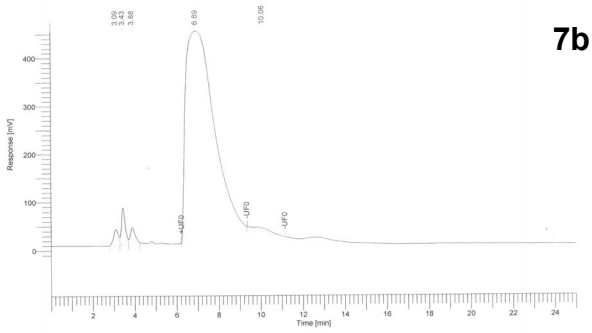

Chiralpak OJ

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	3.09	514228	32864	1.2	BV
2	3.43	956049	74666	2.3	VV
3	3.88	506690	32780	1.2	VB
4	6.89	39652070	430255	95.2	MM
5	10.06	2531	5277	0.0	MM
		41631568	575842	100.0	

7b

Software Version	: 6.2.1.0.104:0104	Date	: 17/02/2004 11:43:01
Sample Name	: ca562a Hex+iProh	Data Acquisition Time	: 17/02/2004 10:56:34
Instrument Name	: PerkinElmer_HPLC	Channel	: A
Rack/Vial	: 1/2	Operator	: christophe
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 3		

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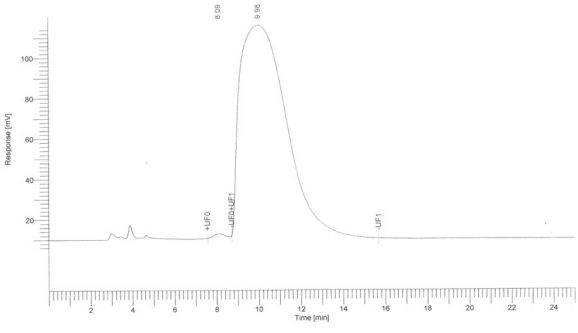

Chiralpak OJ

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	8.09	48536	1623	0.3	MM
2	9.98	15864551	104315	99.7	MM
		15913087	105939	100.0	

Pseudo-racemate
7a + **7b**

Software Version	: 6.2.1.0.104:0104	Date	: 17/02/2004 16:32:12
Reprocess Number	: d7v2km0j: 163		
Sample Name	: ca562a+b mixed from 2/3	Data Acquisition Time	: 17/02/2004 16:07:02
Instrument Name	: PerkinElmer_HPLC	Channel	: A
Rack/Vial	: 1/5	Operator	: christophe
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 1		

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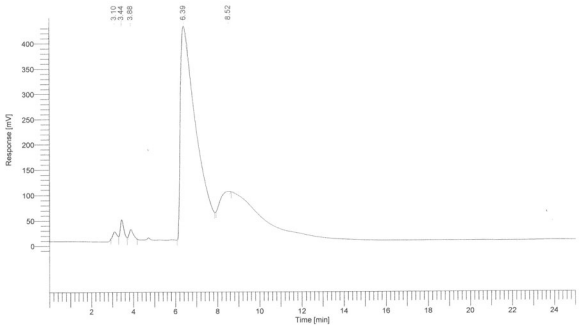


Chiralpak OJ

Peak #	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1	3.10	178890	13996	0.9	BV
2	3.44	439516	38103	2.1	VV
3	3.88	258101	18980	1.3	VB
4	6.39	19217089	412605	93.7	BB
5	8.52	412026	7455	2.0	BB
		20505621	491138	100.0	

clear when injected as single compounds and as the *pseudo*-racemate.

The following spectra are attached:

^{1}H NMR (600 MHz, D_2O) of **14**

^{19}F NMR (282 MHz, D_2O) of **14**

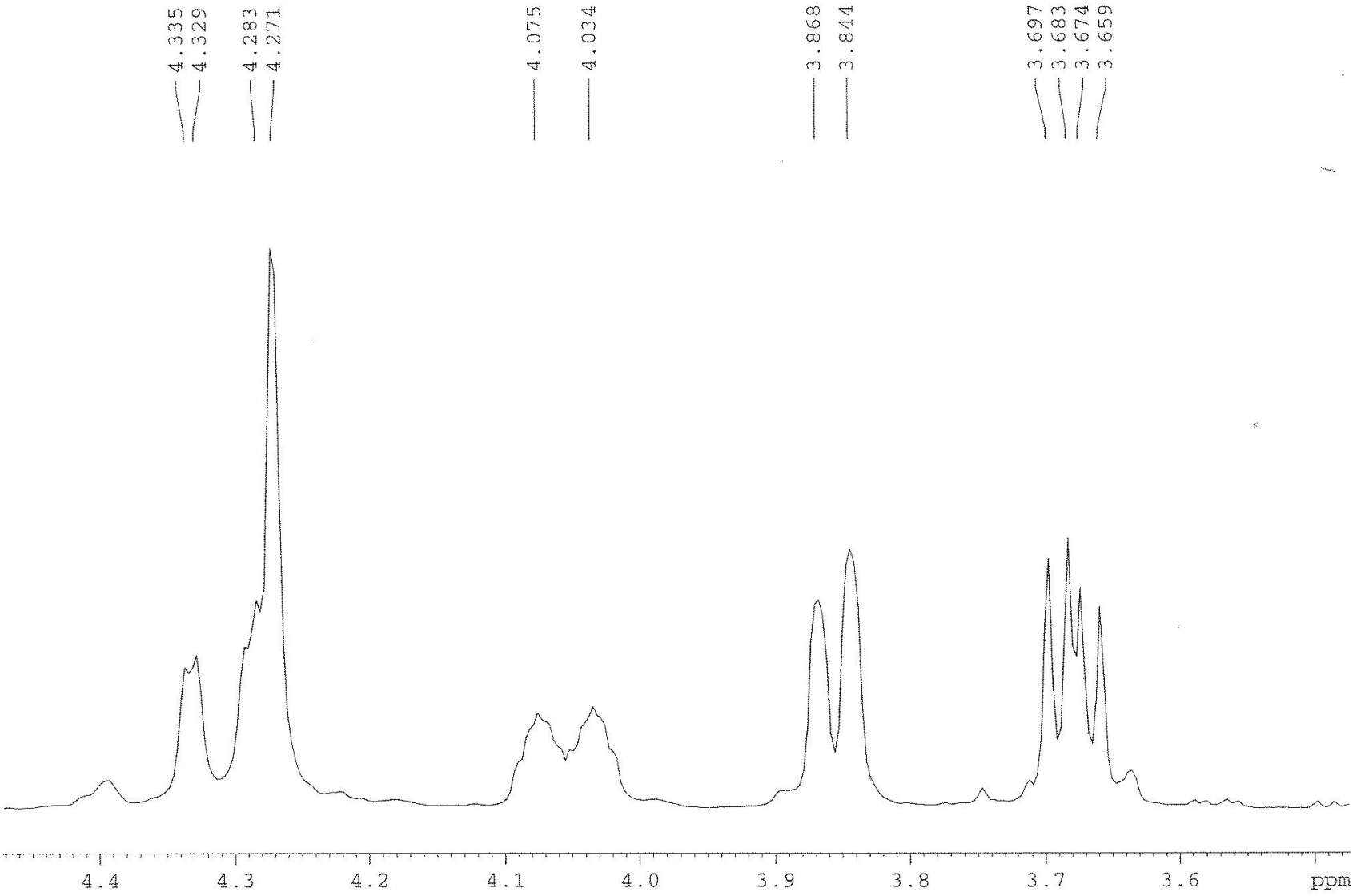
^{13}C NMR (? MHz, D_2O) of **14**

dqfCOSY (600MHz, D_2O) of **14**

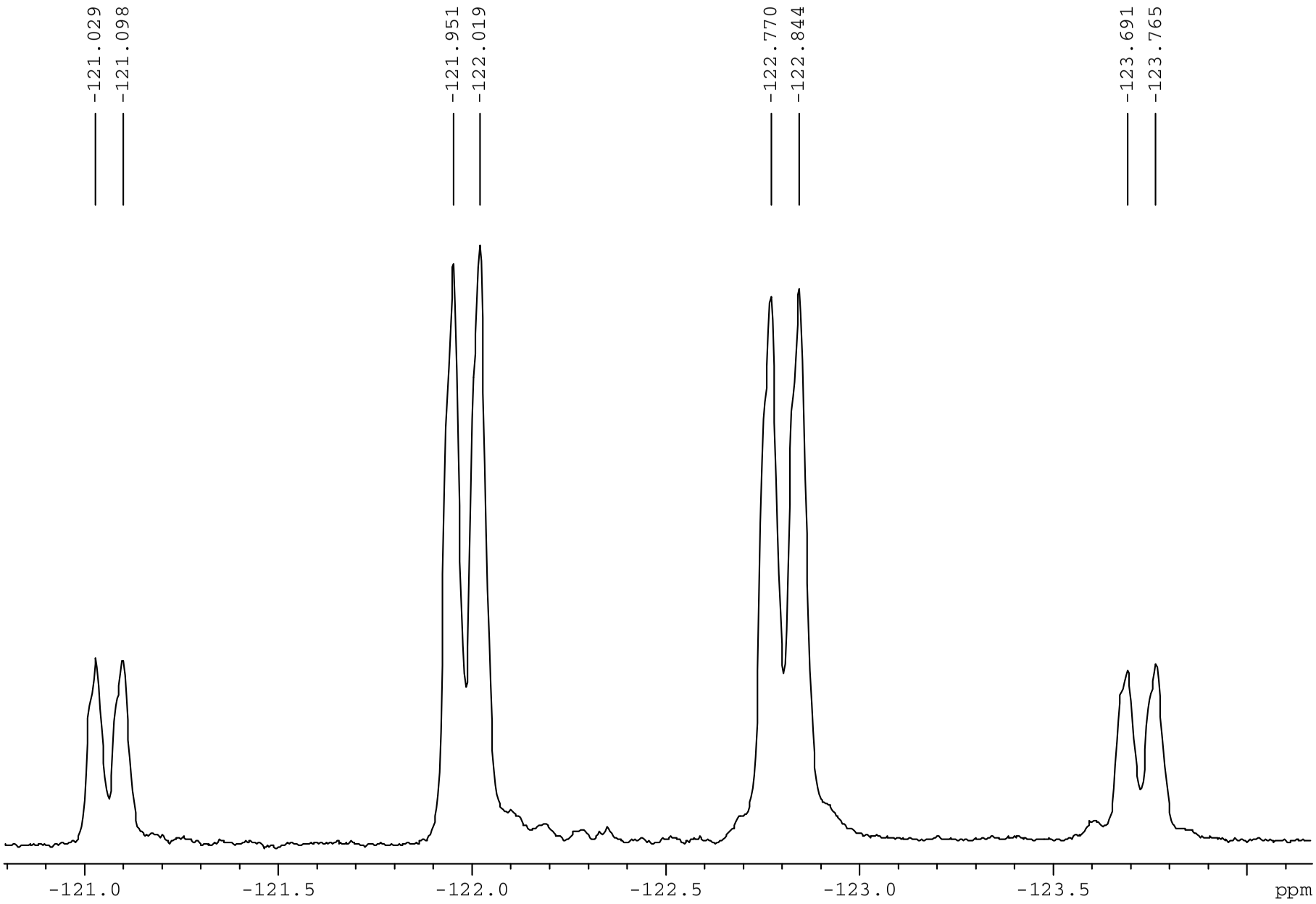
HMQC (D_2O) of **14**

HMBC (D_2O) of **14**

Electrospray MS of **14**

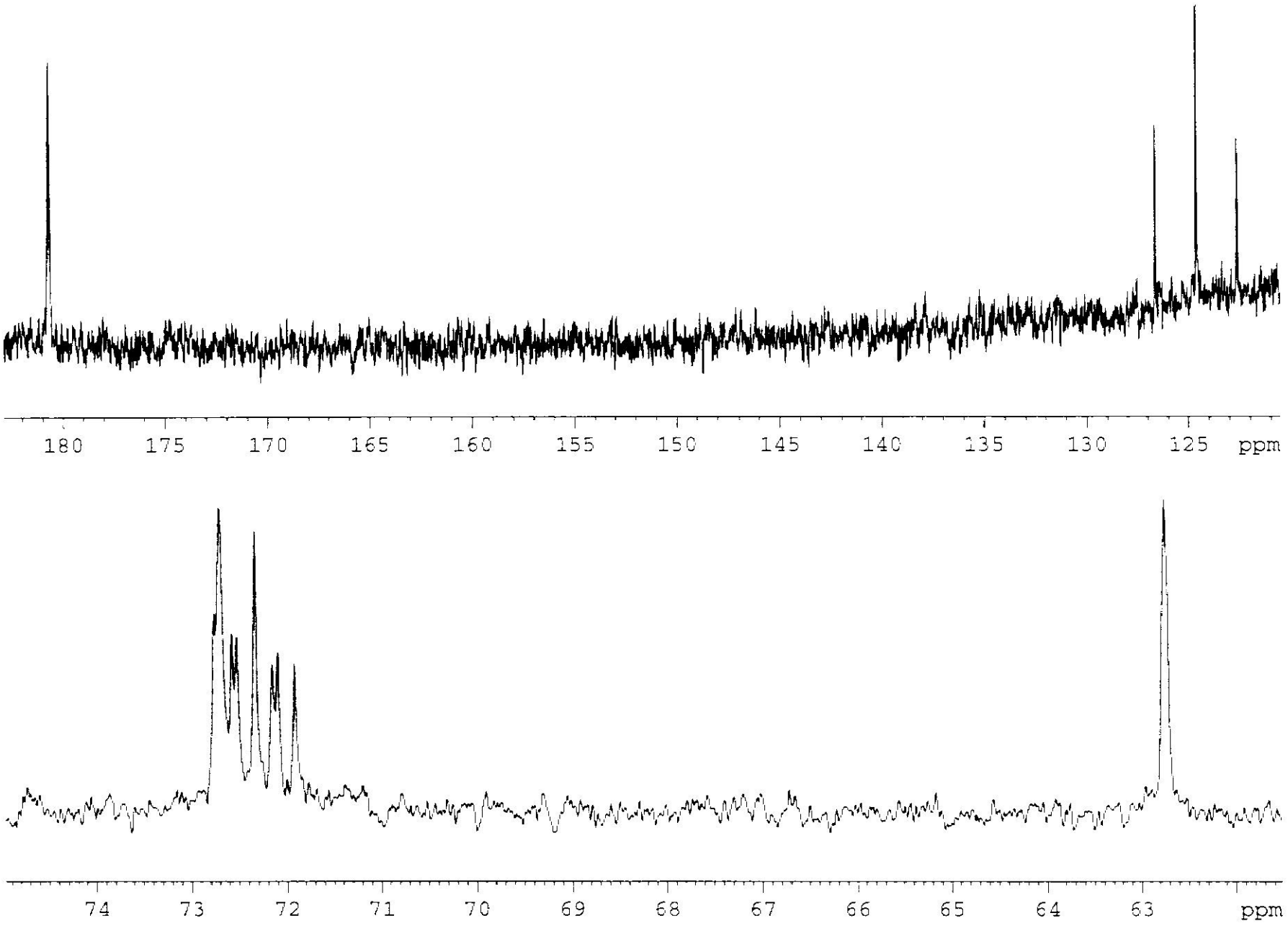


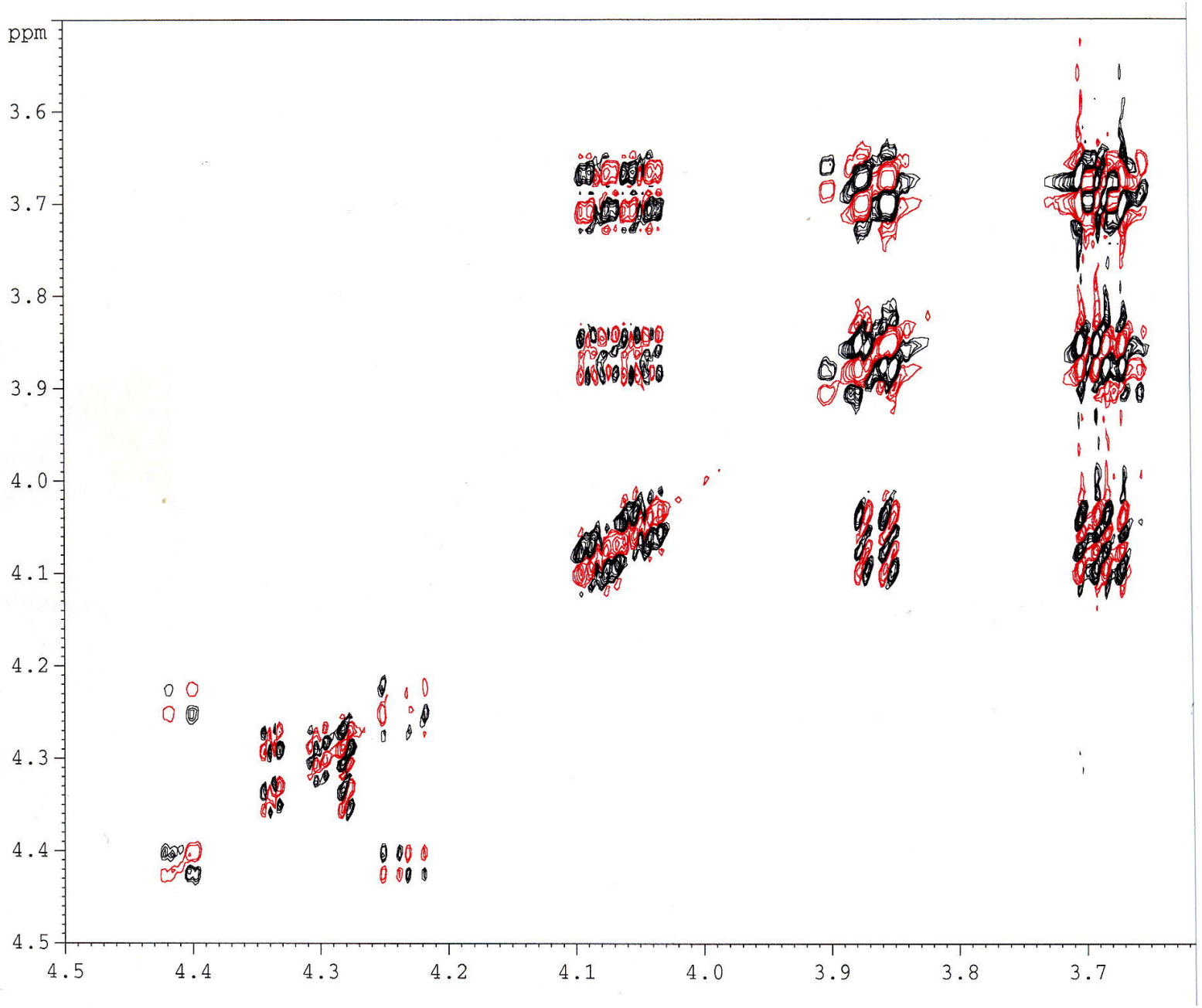
^{1}H NMR (600 MHz, D_2O) of **14**



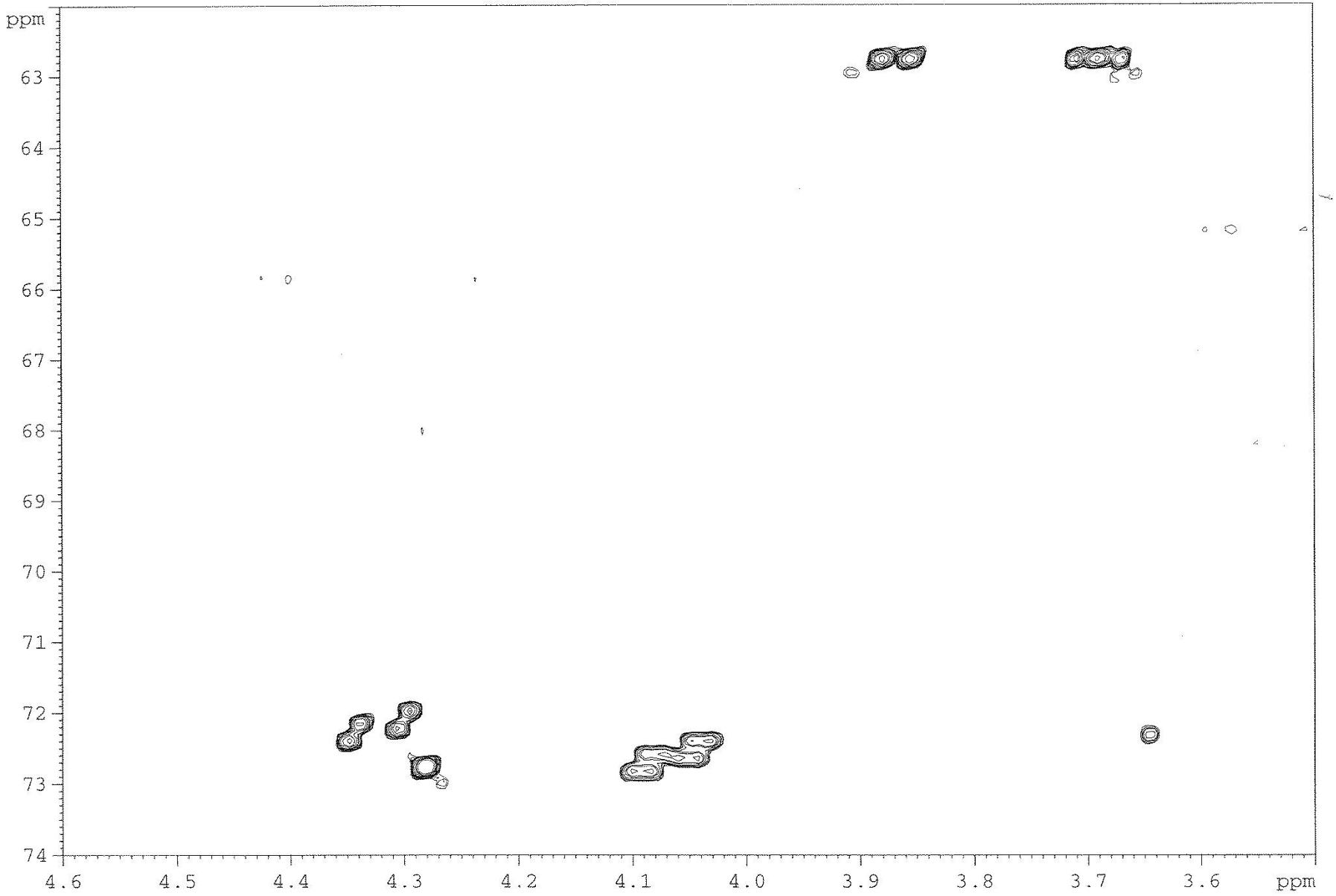
^{19}F NMR (282 MHz, D_2O) of **14**

^{13}C NMR (? MHz, D_2O) of **14**

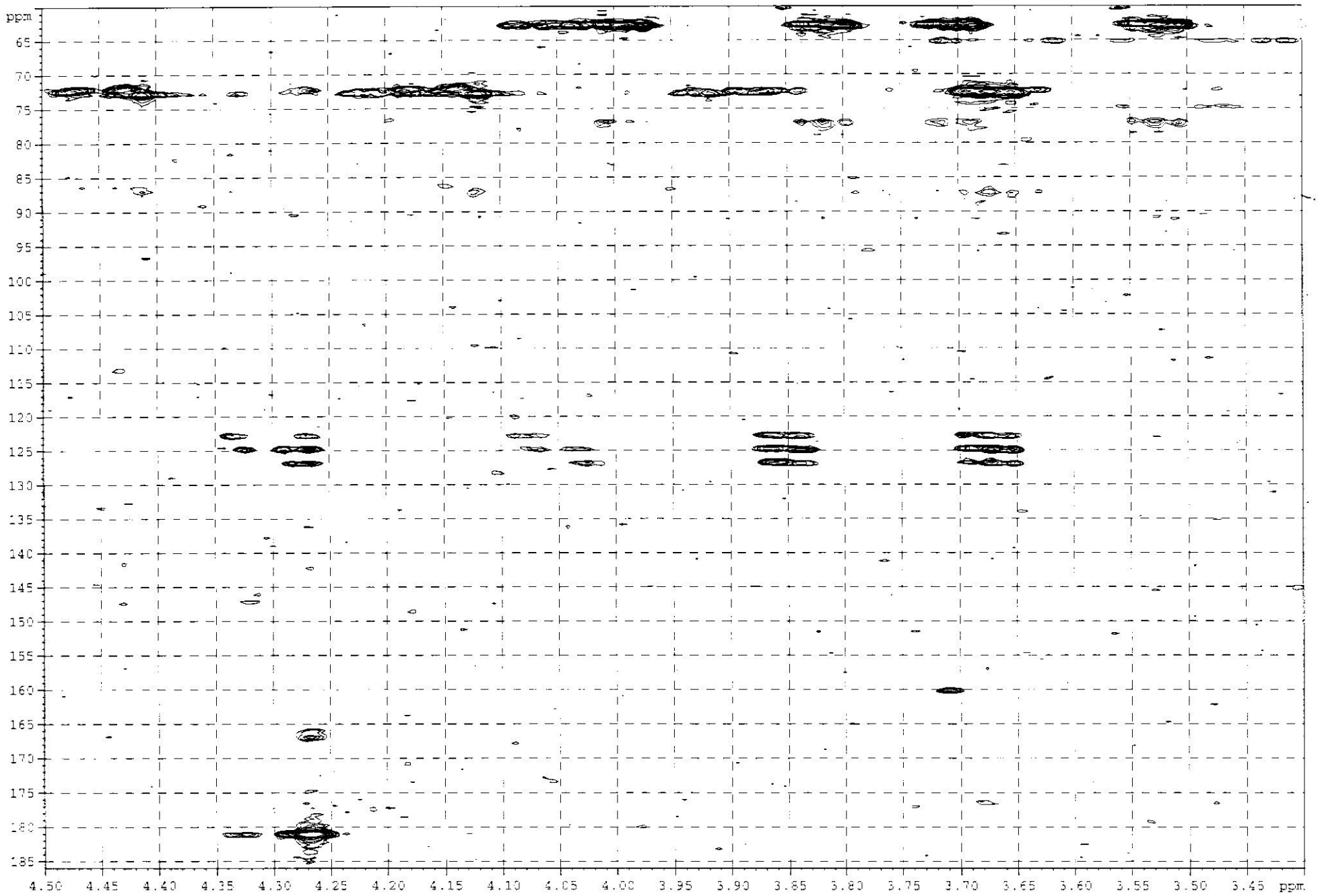




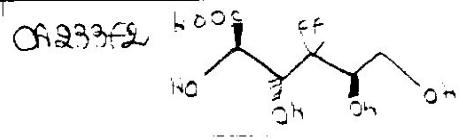
dqfCOSY (600MHz, D_2O) of **14**



HMQC (D_2O) of **14**



HMBC (D_2O) of **14**



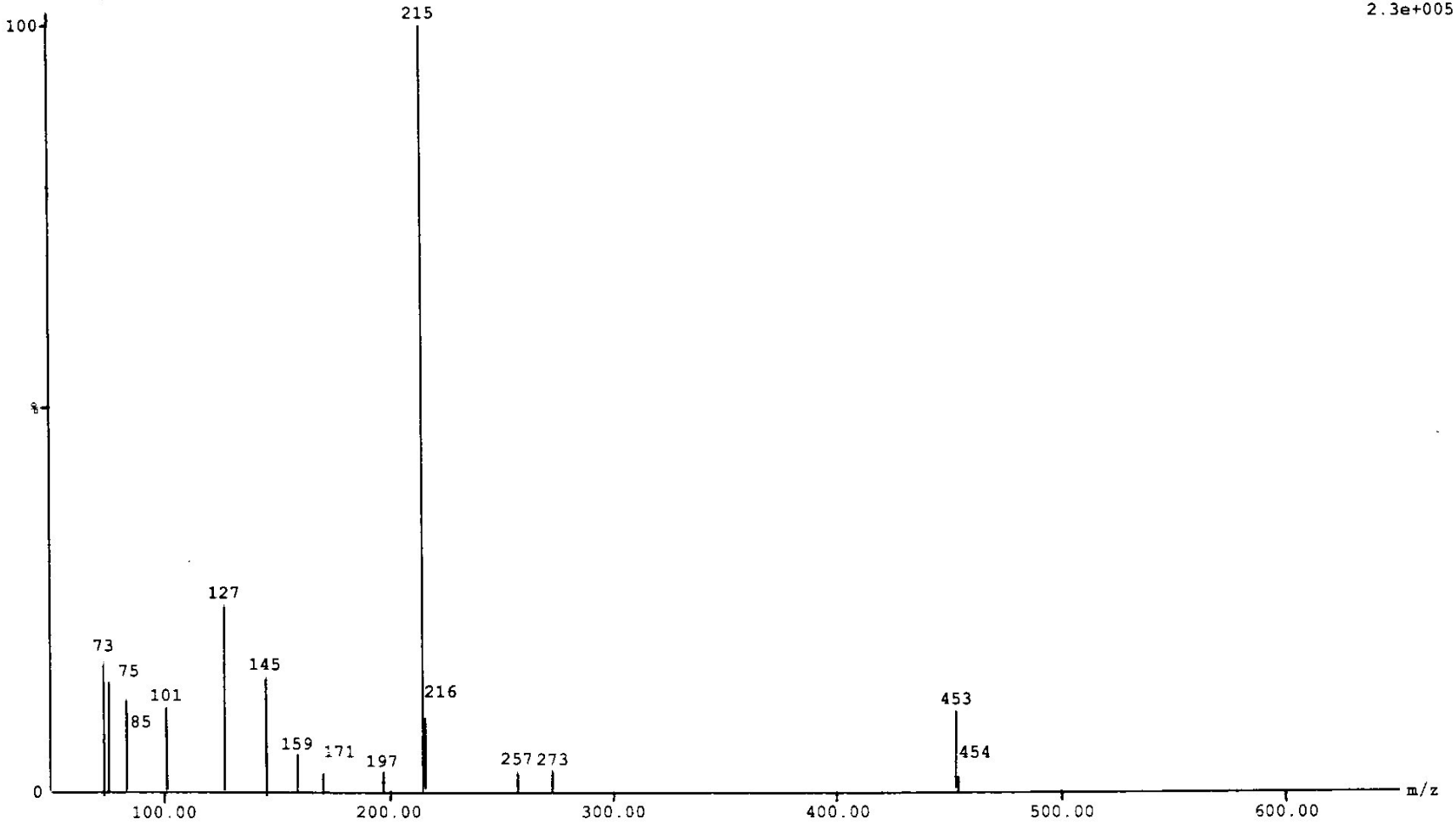
Openlynx Report - Christophe
Sample: 1
Date:24-Feb-2004

Via :1:67
Description:

File:Christophe6-1

Combine (41:47)

2:MS ES-
2.3e+005



Electrospray MS of **14**