



Supporting Information

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BINOL-strapped calix[4]pyrrole as a model chirogenic receptor for the enantioselective recognition of carboxylate anions

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Full citation for text reference [14]: D.A. Case, D.A. Pearlman, J.W. Caldwell, T.E. Cheatham III, J. Wang, W.S. Ross, C.L. Simmerling, T.A. Darden, K.M. Merz, R.V. Stanton, A.L. Cheng, J.J. Vincent, M. Crowley, V. Tsui, H. Gohlke, R.J. Radmer, Y. Duan, J. Pitner, I. Massova, G.L. Seibel, U.C. Singh, P.K. Weiner and P.A. Kollman (2002), AMBER 7, University of California, San Francisco.

Full citation for text reference [17]: M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian 98, Revision A.7 Gaussian, Inc., Pittsburgh PA, 1998.

Experimental section

Proton NMR spectra (400 MHz, Bruker DPX-400) were recorded using TMS as the internal standard. High resolution mass spectra were obtained on an Voyager-DE STR MALDI-TOF mass spectrometer. Column chromatography was performed over silica gel (Merck, 230-400 mesh). Pyrrole was distilled at atmospheric pressure from CaH₂. All other reagents were obtained from Aldrich and used as received unless noted otherwise. The experimental procedures and spectroscopic data for the corresponding enantiomeric compounds throughout the synthesis were identical each other. The retained enantiomeric purity was checked by CD spectra for the final receptors and synthetic procedure for only one stereoisomer is reported.

(S)-(-)-6-[2'-(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (4S)

K₂CO₃ (2.0 g, 14.47 mmol) was added to a solution of (S)-(-)-1,1'-bi-2-naphthol (0.5 g, 1.75 mmol) in DMF (15 mL) and stirred for 1 hour at 60 °C, then 6-bromohexan-2-one (1.00 g, 5.56 mmol) was added to the reaction mixture and the stirring continued for an additional 24 h. The mixture was then combined with water (50 mL) and extracted with methylene chloride. The organic layer was dried (Na₂SO₄) and the solvent was removed in vacuo. The resulting viscous solid was purified by column

chromatography on silica gel (CH₂Cl₂: EtOAc = 9:1). Yield 0.82 g (96%); ¹H NMR (CDCl₃) δ 1.17 - 1.21 (m, 4H, CH₂), 1.38 - 1.43 (m, 4H, CH₂), 1.84 (s, 6H, CH₃), 1.94 - 1.98 (m, 4H, CH₂), 3.91 - 4.00 (m, 4H, CH₂), 7.13 - 7.15 (m, 2H, Ar-H), 7.18 - 7.22 (m, 2H, Ar-H), 7.29 - 7.33 (m, 2H, Ar-H), 7.38 - 7.41 (m, 2H, Ar-H), 7.83 - 7.85 (m, 2H, Ar-H), 7.91 - 7.94 (m, 2H, Ar-H); ¹³C NMR: 20.33, 28.66, 29.48, 42.99, 69.48, 115.73, 120.61, 123.59, 125.46, 126.19, 127.86, 129.21, 129.31, 134.14, 154.42, 209.06; MALDI-TOF MS Calcd. For C₃₂H₃₄O₄ 482.25, Found 482.21.

(R)-(+)-6-[2'-(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (4R)

K₂CO₃ (1.93 g, 13.97 mmol), (R)-(+)-1,1'-bi-2-naphthol (0.4 g, 1.40 mmol) and 6-bromohexan-2-one (1.00 g, 5.56 mmol) was treated identically as for the synthesis of (4S). All the spectroscopic data were identical with (4S).

Compound (5S)

(S)-(-)-6-[2'-(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (0.685 g, 1.42 mmol) was dissolved in pyrrole (3 mL, 43.24 mmol) and then TFA (0.11? mL, 1.41 mmol) was added. The mixture was stirred for 2 hr at 60 °C. The reaction was quenched by adding aqueous NaOH (0.1 N, 50 mL) and then extracted with CH₂Cl₂. The organic layer was dried (Na₂SO₄) and the solvent was removed in vacuo. The resulting viscous solid was purified by column chromatography on silica gel (CH₂Cl₂:EtOAc = 19:1). Yield 0.713 g (70%); ¹H NMR (CDCl₃) δ 0.84 - 0.93 (m, 4H, CH₂), 1.20 - 1.28 (m, 4H, CH₂), 1.31 (s, 6H, CH₃), 1.59 - 1.69 (m, 4H, CH₂), 3.78 (t, 4H, CH₂), 5.88 - 5.90 (m, 4H, pyrrolic-H), 6.05 - 6.08 (m, 4H, pyrrolic-H), 6.45 - 6.52 (m, 4H, pyrrolic-H), 7.08 - 7.10 (m, 2H, Ar-H), 7.16 - 7.20 (m, 2H, Ar-H), 7.27 - 7.32 (m, 4H, Ar-H), 7.50 (br s, 2H, NH), 7.61 (br s, 2H, NH), 7.82 - 7.89 (m, 4H, Ar-H); ¹³C NMR: 26.75, 30.26, 39.29, 41.10, 70.25, 105.09, 105.12, 107.91, 107.95, 116.28, 117.42, 117.46, 120.91, 123.97, 126.0, 126.65, 128.41, 129.62, 129.71, 134.62, 138.55, 155.0; MALDI-TOF MS Calcd. For C₄₈H₅₀N₄O₂ 714.39, Found 714.33.

Compound (5R)

(R)-(+)-6-[2'-(5-Oxo-hexyloxy)-[1,1']binaphthalenyl-2-yloxy]-hexan-2-one (0.630 g, 1.31 mmol), pyrrole (3.5 mL, 50.4 mmol) and TFA (0.07? mL, 0.91 mmol) was treated identically as for the synthesis of (5S). All the spectroscopic data were identical with (5S).

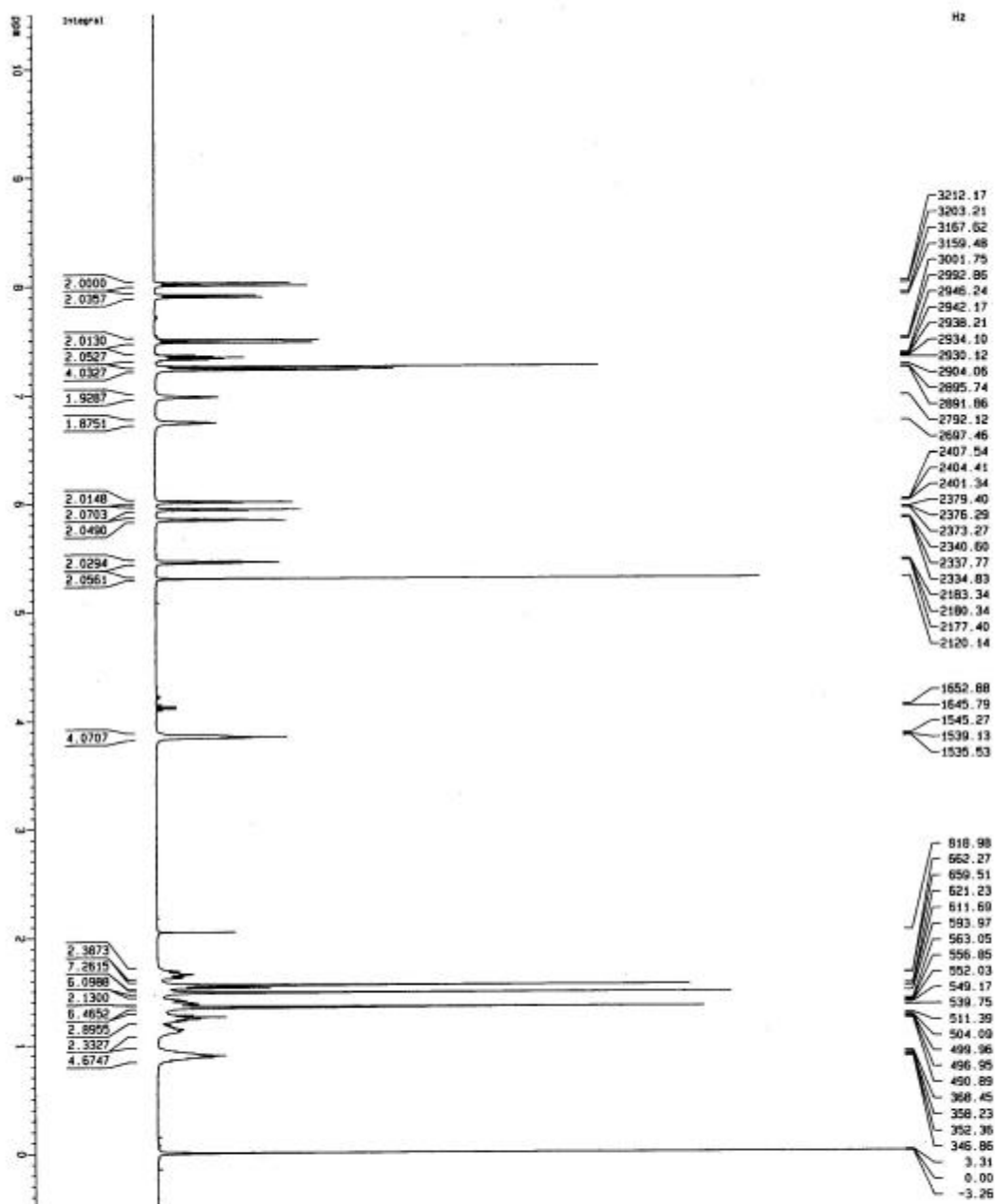
Receptor (1S)

Compound (**5S**) (0.561 g, 0.78 mmol) was dissolved in acetone (200 mL) and then $\text{BF}_3 \cdot \text{OEt}_2$ (0.04 mL, 0.32 mmol) was added. The mixture was stirred for 50 min at room temperature. The reaction was quenched by adding aqueous NaOH (0.1 N, 50 mL) then, extracted with CH_2Cl_2 . The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The resulting dark solid was purified by column chromatography on silica gel (CH_2Cl_2). Yield 67 mg (11 %). ^1H NMR (CDCl_3) δ 0.85 - 0.94 (m, 4H, CH_2), 1.12 - 1.18 (m, 2H, CH_2), 1.22 - 1.28 (m, 2H, CH_2), 1.35 - 1.42 (m, 8H, CH_3 and CH_2), 1.48 (s, 6H, CH_3), 1.55 (s, 6H, CH_3), 1.62 - 1.69 (m, 2H, CH_2), 3.84 - 3.86 (m, 4H, CH_2), 5.45 - 5.46 (m, 2H, pyrrolic-H), 5.83 - 5.85 (m, 2H, pyrrolic-H), 5.93 - 5.94 (m, 2H, pyrrolic-H), 6.00 - 6.02 (m, 2H, pyrrolic-H), 6.73 (br s, 2H, NH), 6.97 (br s, 2H, NH), 7.23 - 7.24 (m, 4H, Ar-H), 7.31 - 7.36 (m, 2H, Ar-H), 7.48 - 7.50 (m, 2H, Ar-H), 7.89 - 7.91 (m, 2H, Ar-H), 8.00 - 8.03 (m, 2H, Ar-H); ^{13}C NMR: 23.55, 27.90, 29.51, 29.83, 30.51, 35.52, 39.27, 40.46, 53.43, 71.20, 101.17, 102.91, 105.13, 105.97, 116.49, 121.12, 123.51, 125.45, 125.95, 127.85, 129.07, 129.47, 133.69, 134.06, 135.08, 138.40, 140.55, 155.08; MALDI-TOF MS Calcd. For $\text{C}_{54}\text{H}_{58}\text{N}_4\text{O}_2$ 794.46, Found 794.01.

Receptor (1R)

Compound (**5R**) (0.438 g, 0.61 mmol), acetone (120 mL) and $\text{BF}_3 \cdot \text{OEt}_2$ (0.04 mL, 0.32 mmol) was treated identically as for the synthesis of (**1S**). All the spectroscopic data were identical with (**1S**).

¹H NMR spectrum of **1S** (CDCl₃)



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PROCNO   1

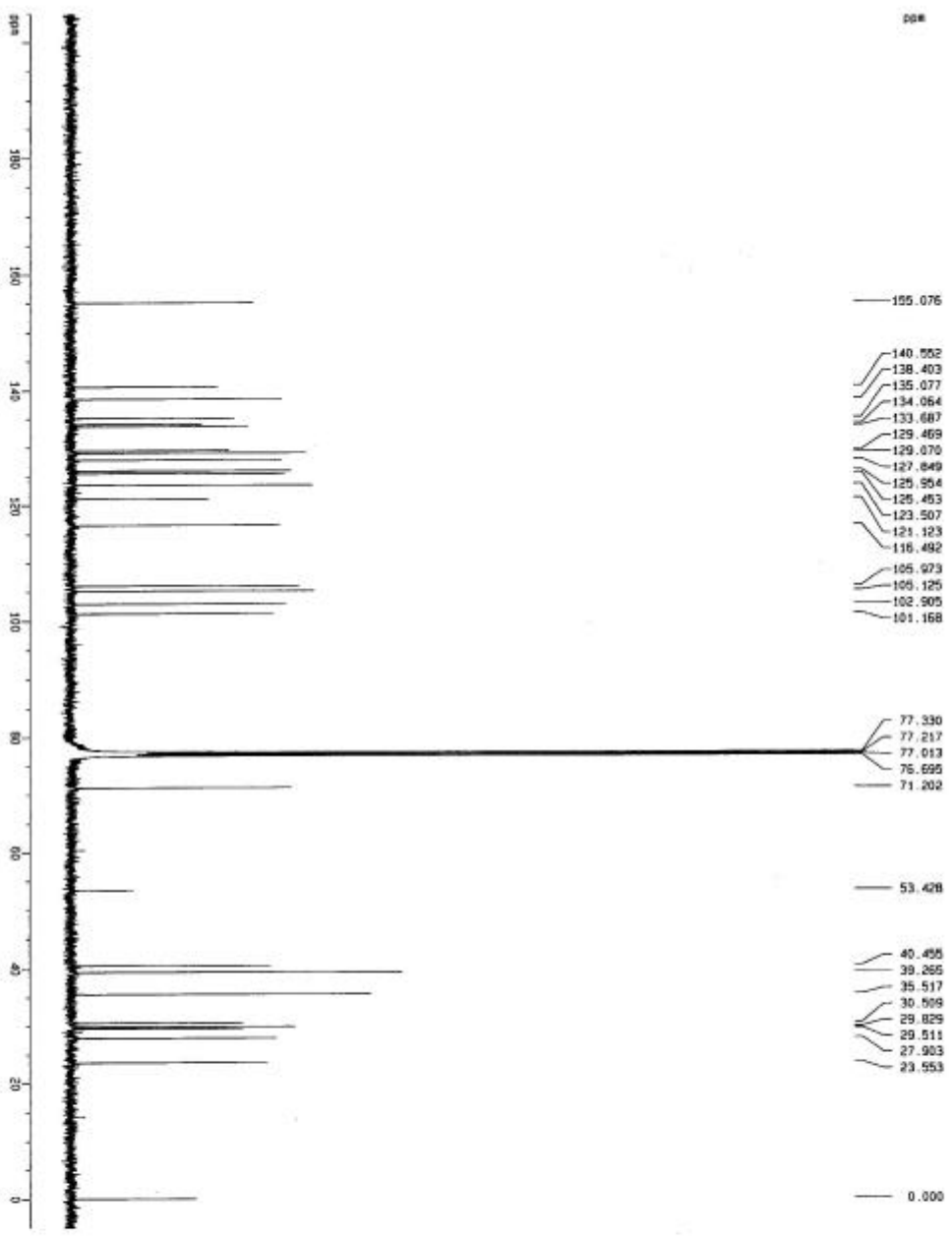
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DM         5.00 us/c
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SI         0

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F2 - Processing parameters
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10 NMR plot parameters
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¹³C NMR spectrum of **1S** (CDCl₃)



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 EXPNO: 264
 PROCNO: 1

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 RG: 3849.1
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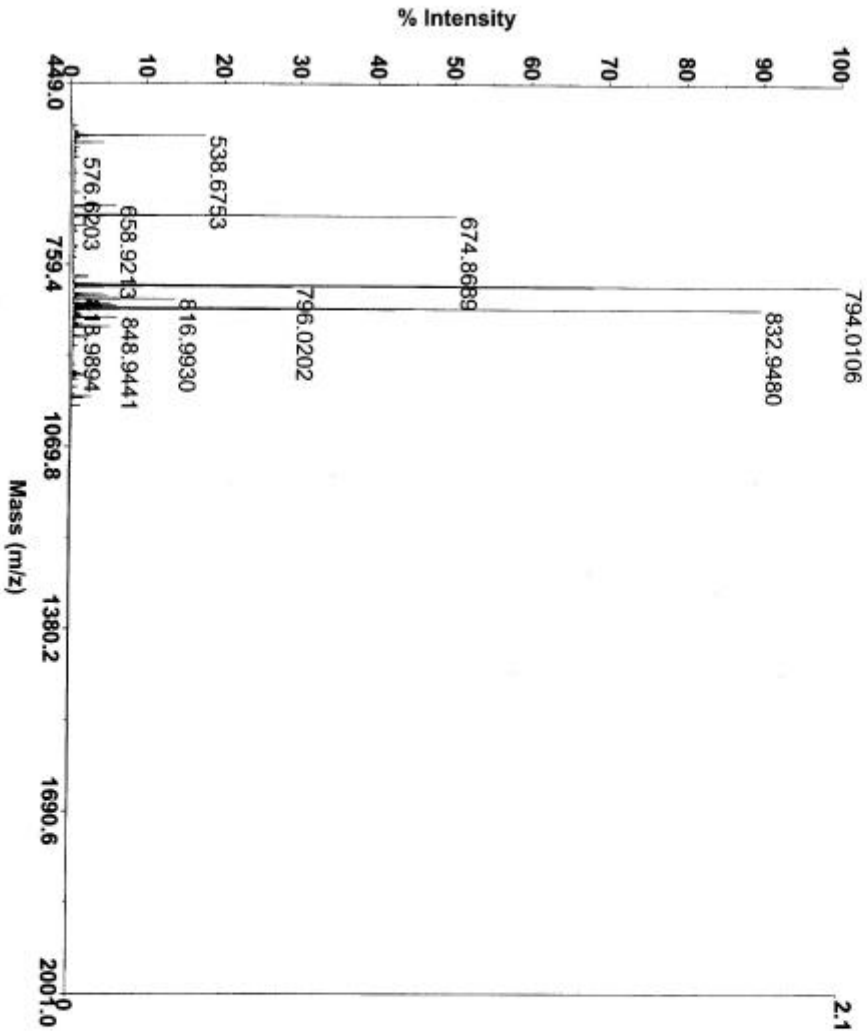
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 F2P: -5.000 DPM
 F2: -503.06 Hz
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High resolution MALDI-TOF Mass spectrum of 1S

Applied Biosystems Voyager System 4372
 Voyager Spec #1=>NR(2.00)=>NF1.0[BP = 794.0, 20820]



Mode of operation: Reflector
 Extraction mode: Delayed
 Polarity: Positive
 Acquisition control: Manual

Accelerating voltage: 20000 V
 Grid voltage: 67%
 Mirror voltage ratio: 1.12
 Guide wire D: 0%
 Extraction delay time: 87 nsec

Acquisition mass range: 450 - 2000 Da
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 Laser intensity: 1829
 Laser Rep Rate: 20.0 Hz
 Calibration type: External - D:\Chem\060628\CM1_0001.c
 Calibration matrix: 2,5-Dihydroxybenzoic acid
 Low mass gate: 500 Da
 Trapped ion selector: Off

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 Vertical offset: -0.1%
 Input bandwidth 0: 500 MHz

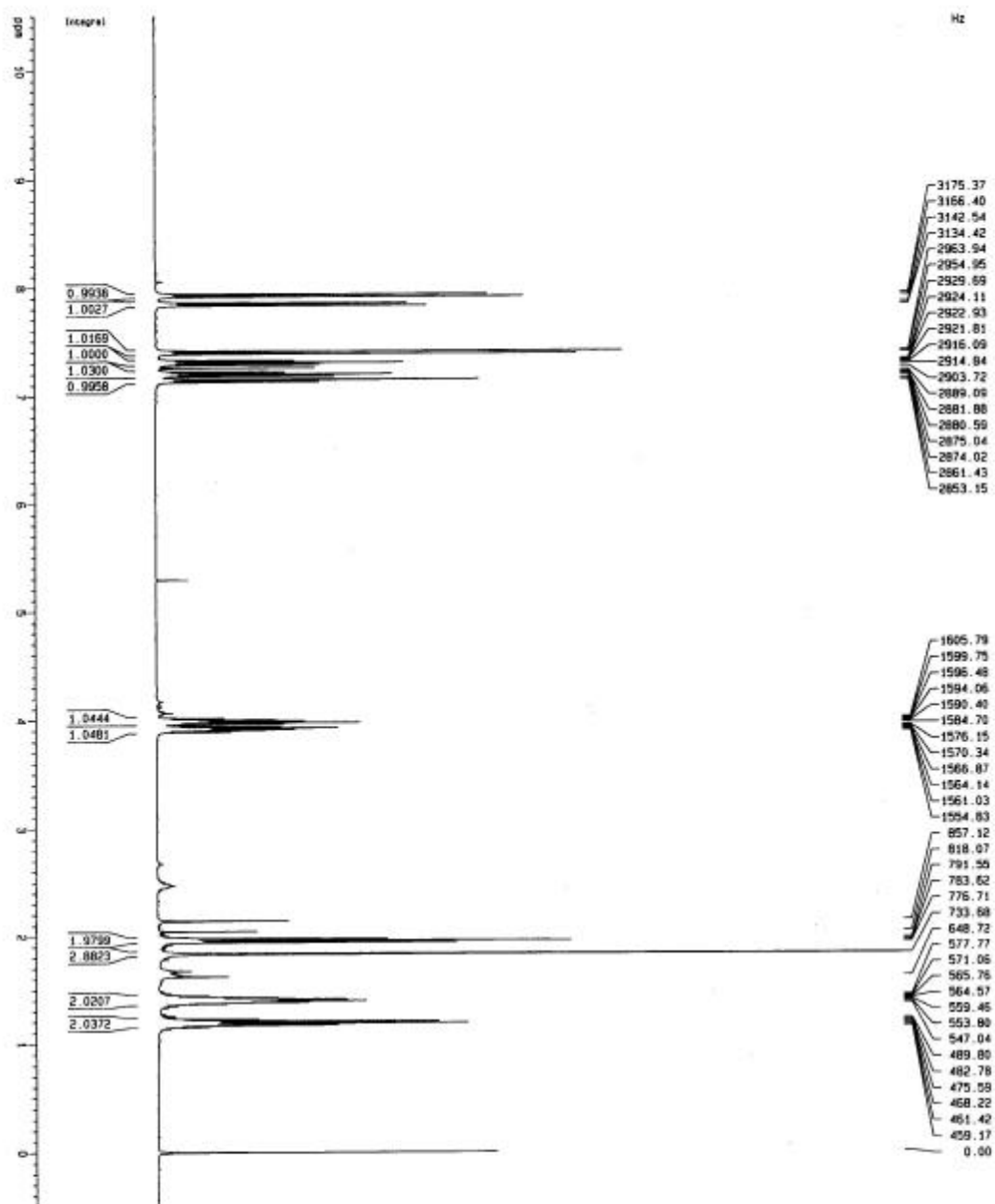
Sample well: 11
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 Serial number: 4372
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 Plate type/Name: C:\VOYAGER\100 well plate.pf
 Lab name: PE Biosystems

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 Relative y-position: 437.435
 Shots in spectrum: 100
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 Mirror pressure: 3.33e-008
 TIC2 pressure: 0.003486
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 TIS flight length: 1187

Acquired: 06:50:00, August 29, 2006
 D:\Chem\060628\HSJ-1S-BINAP_0002.dsf

Printed: 07:12, August 29, 2006

¹H NMR spectrum of **4S** (CDCl₃)



```

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EXPNO    249
PROCNO   1

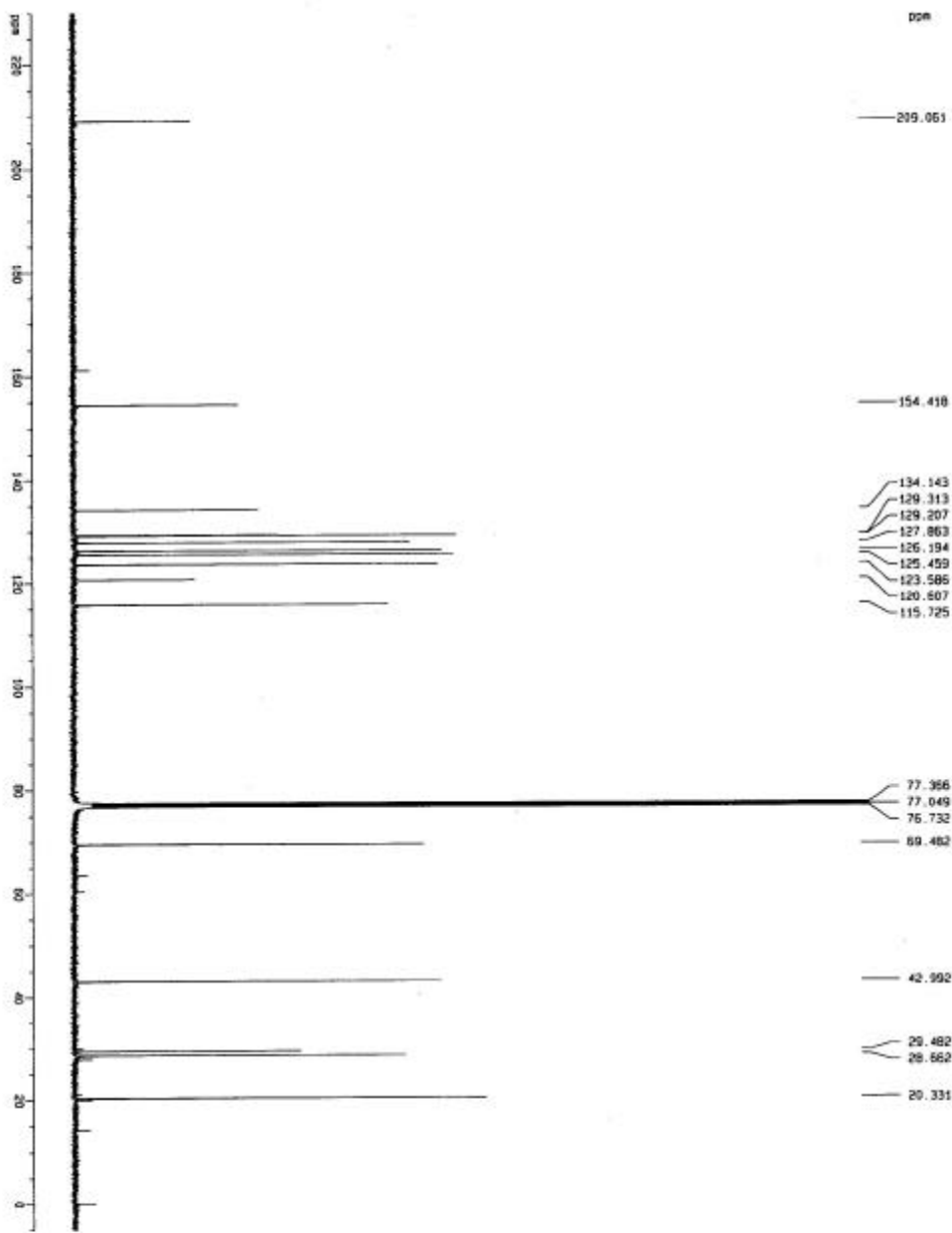
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GB        0
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¹³C NMR spectrum of **4S** (CDCl₃)

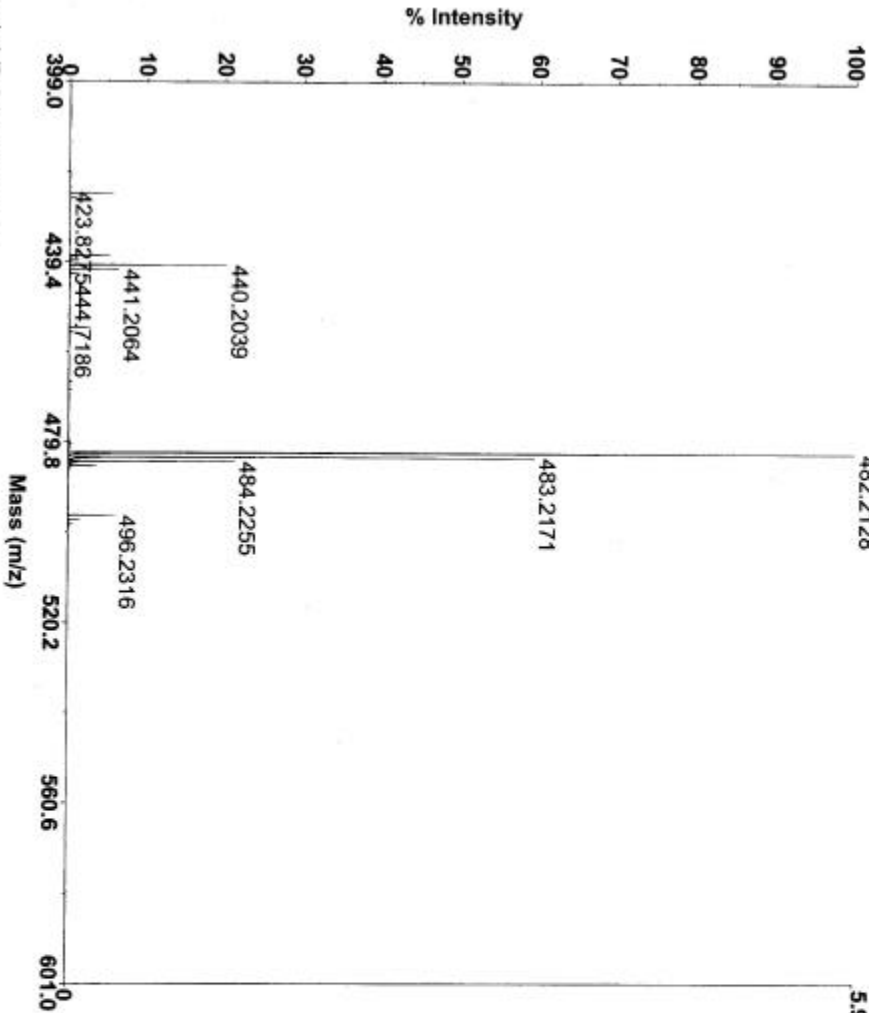


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10 NMR plot parameters
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F2           -5.000 DDM
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HZCM         788.13336 Hz/cm
    
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High resolution MALDI-TOF Mass spectrum of 4S

Applied Biosystems Voyager System 4372
 Voyager Spec #1=>NR(2.00)=>NF1.0[BP = 482.2, 59390]



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 Extraction mode: Delayed Positive
 Polarity: Positive
 Acquisition control: Manual

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 Mirror voltage ratio: 1.12
 Guide wire ID: 0%
 Extraction delay time: 97 nsec

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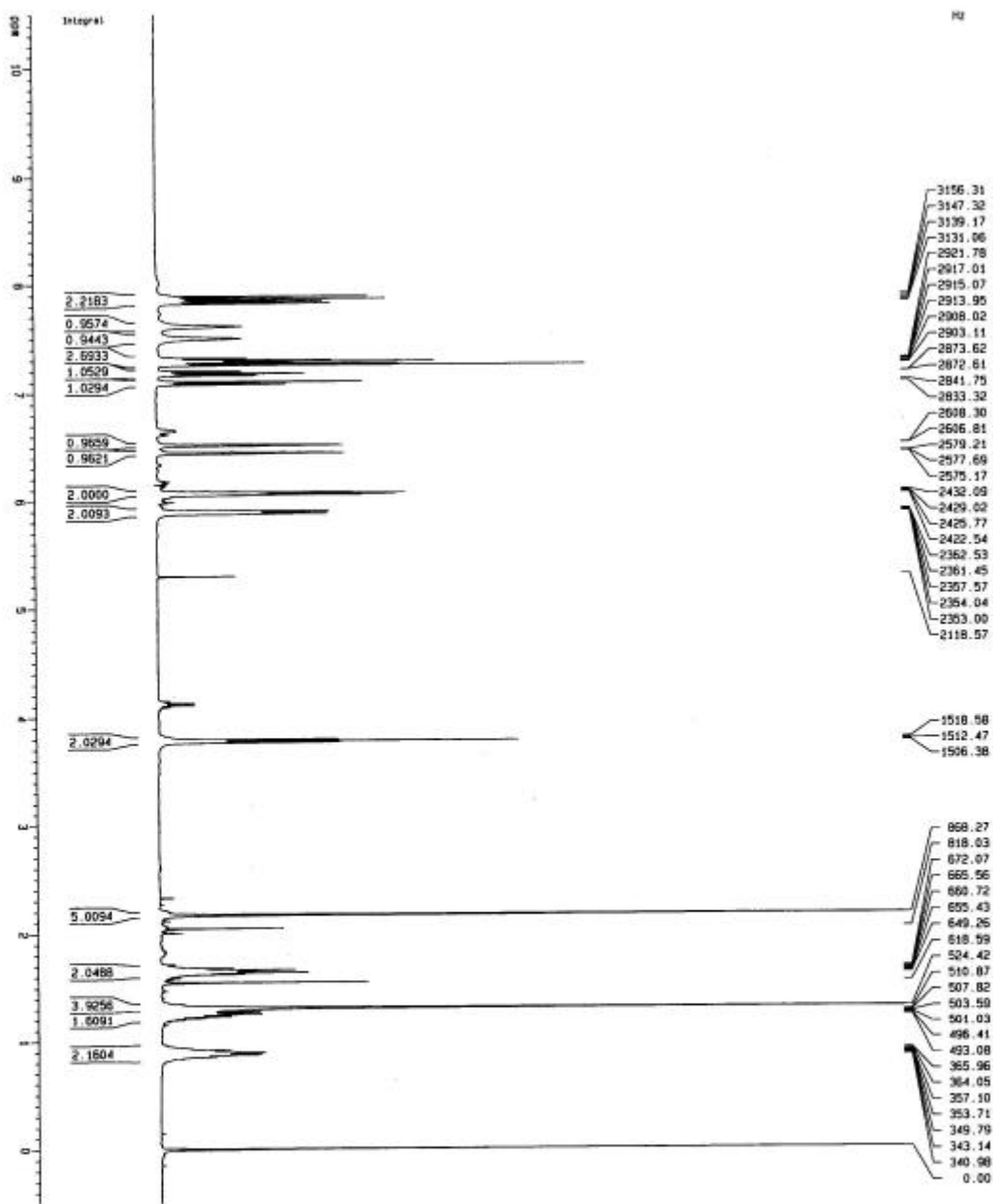
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 Serial number: 4372
 Instrument name: Voyager-DE STR
 Plate type filename: C:\VOYAGER\100 well plate.pl
 Lab name: PE Biosystems

Absolute x-position: 16827.3
 Absolute y-position: 42228.9
 Relative x-position: -0.186407
 Relative y-position: 1.39827
 Shots in spectrum: 100
 Source pressure: 2.833e-008
 Minor pressure: 2.994e-008
 TCF pressure: 0.003213
 TIS gate width: B
 TIS flight length: 1187

Printed: 07:24, August 28, 2006

¹H NMR spectrum of **5S** (CDCl₃)



Current Data Parameters
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 EXPNO 295
 PROCNO 1

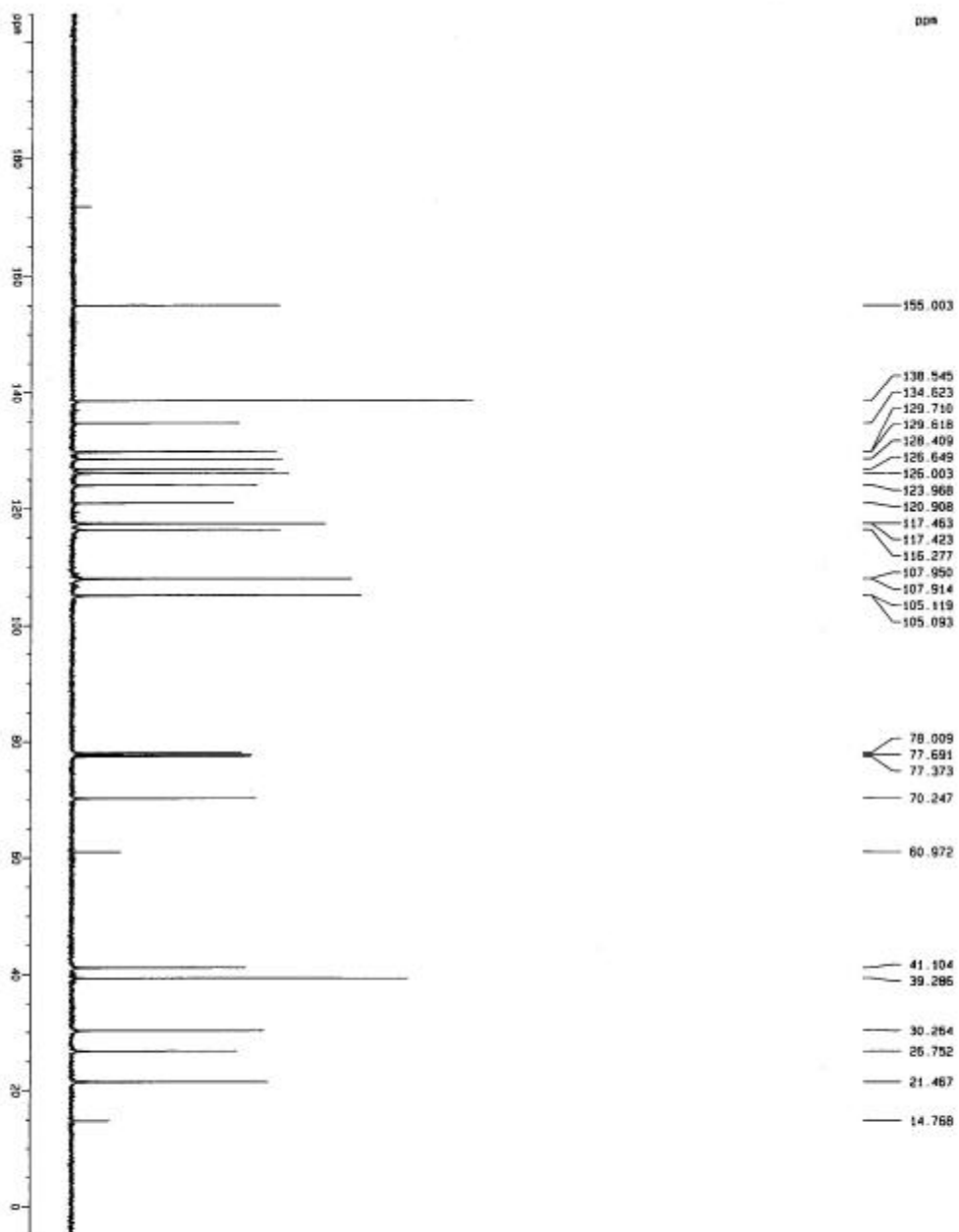
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***** CHANNEL f1 *****
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F2 - Processing parameters
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 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
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 F1 4201.37 Hz
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 F2 -200.07 Hz
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 HZCM 146.71434 Hz/cm

¹³C NMR spectrum of **5S** (CDCl₃)

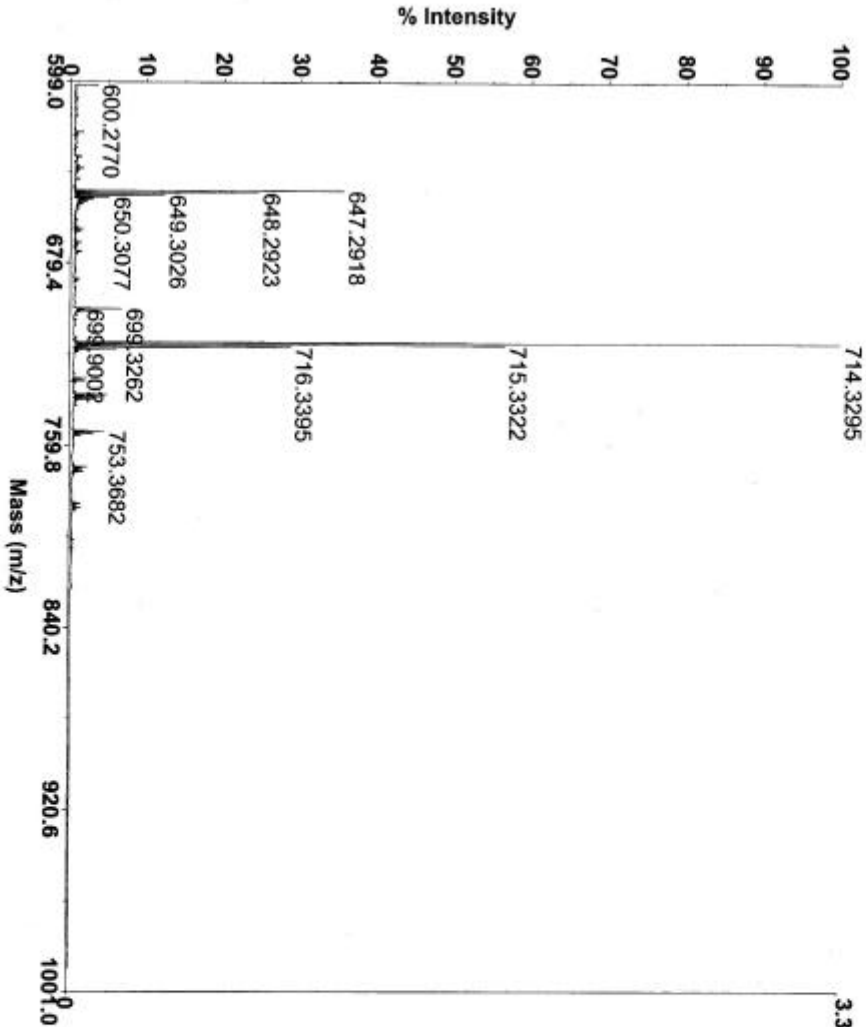


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FIDRES   0.485048 Hz
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RG       7298.2
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TE       5.00 usec
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D11      0.03000000 sec
D12      0.00000000 sec
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PL1      -2.00 dB
SFO1     100.6254388 MHz
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PL2      -2.00 dB
SFO2     400.1524706 MHz
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GB       0
PC       1.40
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1D NMR list parameters
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F2       -53.000 MHz
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HDCM     704.28995 Hz/cm
  
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High resolution MALDI-TOF Mass spectrum of 5S

Applied Biosystems Voyager System 4372 Voyager Spec #1=>NF1.0=>NR(2.00)[BP = 714.3, 32877]

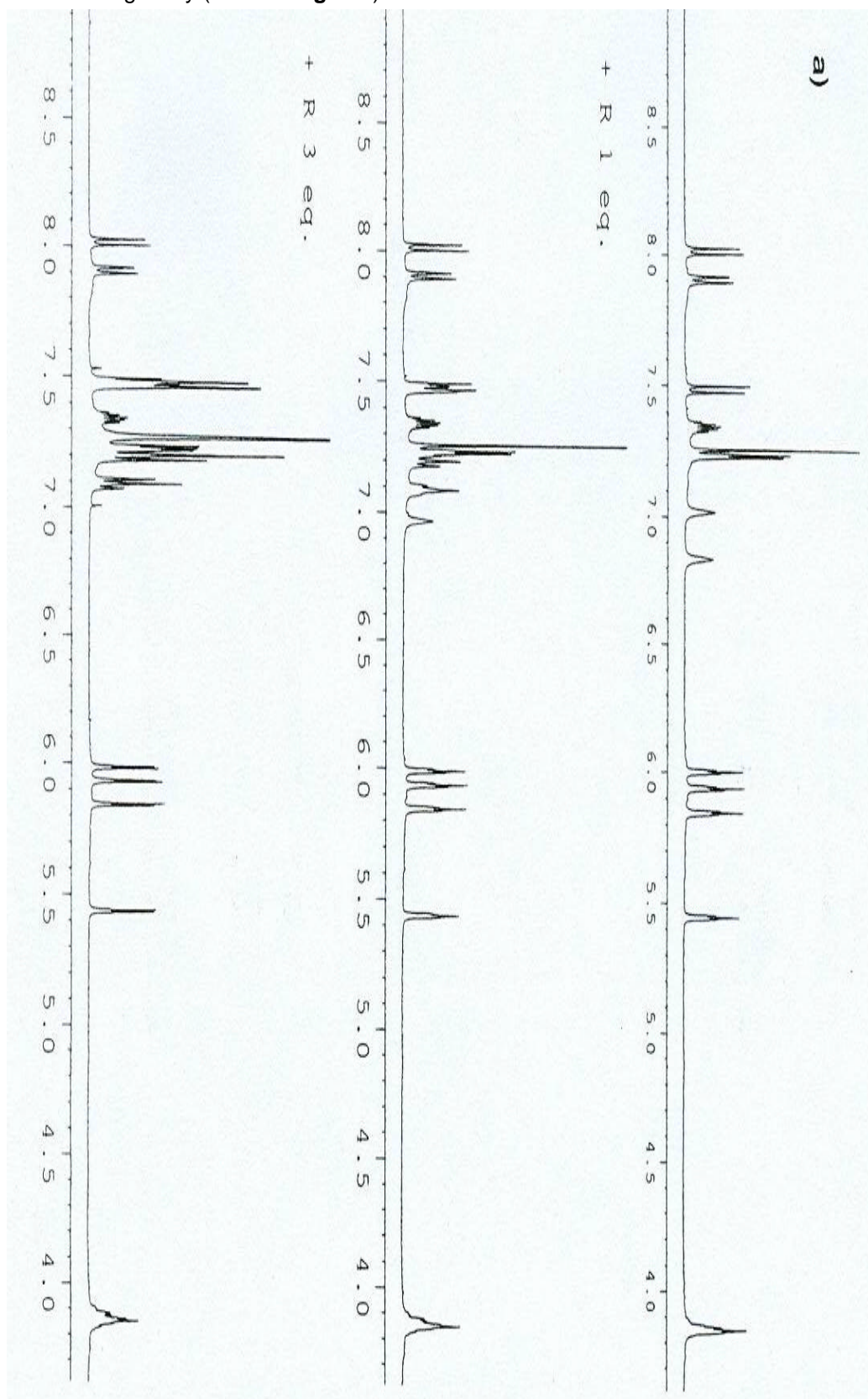


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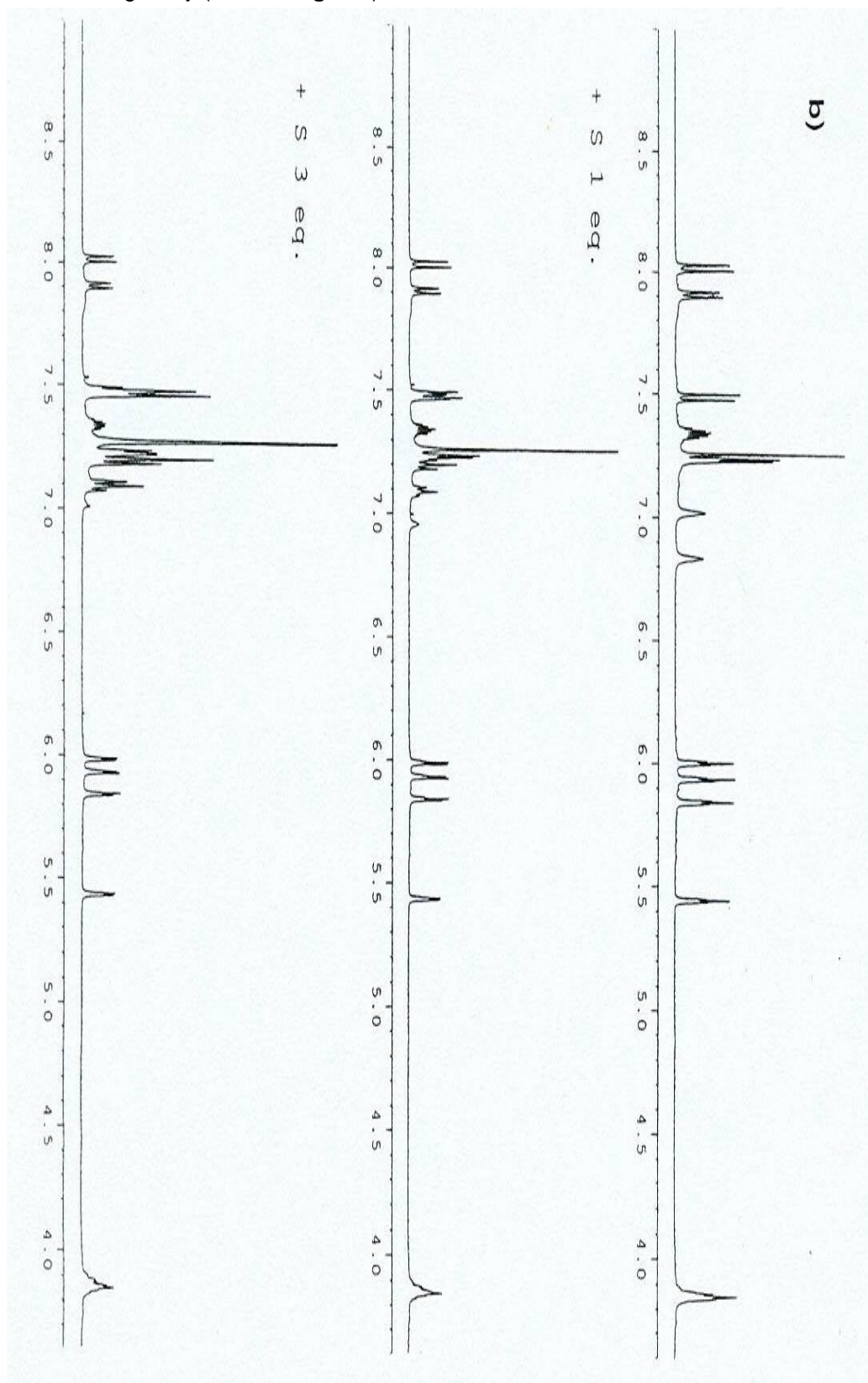
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Minor voltage ratio:	1.12
Guide wire 0:	0%
Extraction delay time:	87 nsec
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Laser Rep Rate:	20.0 Hz
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Calibration matrix:	2,5-Dihydroxybenzoic acid
Low mass gate:	550 Da
Trimod ion selector:	Off
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Bin size:	1 trace
Number of data points:	10455
Vertical scale 0:	500 mV
Vertical offset:	-0.1%
Input bandwidth 0:	500 MHz
Sample well:	19
Plate ID:	PLATE1
Serial number:	4372
Instrument name:	Voyager-DE STR
Plate type/Manufacturer:	CAVOY/ALGER/100 well plate.glt
Lab name:	PE Biosystems
Absolute x-position:	41801
Absolute y-position:	42036.3
Relative x-position:	-426.505
Relative y-position:	-191.243
Shots in spectrum:	100
Source pressure:	3.547e-008
Mirror pressure:	2.941e-008
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TIS flight length:	1187

Printed: 07/33, August 29, 2006

NMR binding study (1S with R-guest)



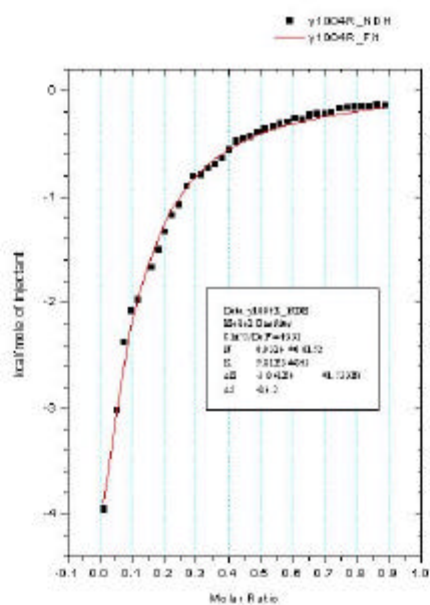
NMR binding study (1S with S-guest)



ITC

Isothermal Titration Calorimetry (ITC) measurements were performed as follows: Solutions of the chosen receptor in rigorously dry acetonitrile were made up so as to provide a receptor concentration range of 0.1–1 mM. These solutions were then individually titrated with the appropriate alkylammonium salts at 30 ± 0.01 °C. The original heat pulses were normalized using reference titrations carried out using the same salt solution but pure solvent, as opposed to a solution containing the receptor.

ITC plot (1S with R-guest)



ITC plot (1S with S-guest)

