Electronic Supplementary Information (ESI)

Regioselective di- and tetra- functionalisation of γ-cyclodextrin using capping methodology

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Content

NMR and mass spectra

NMR spectra of all compounds were recorded in $CDCl_3$ at 25 °C.

$6^A,6^B$-Bis-*O*-bis{benzene-1,3-bis[bis(4-*tert*-butylphenyl)methyl]}-$2^A,2^B,2^C,2^D,2^E,2^F,2^G,2^H,3^A,3^B,3^C,3^D,3^E,3^F,3^G,3^H,6^C,6^D,6^E,6^F,6^G,6^H$-docosa-*O*-methyl-γ-cyclodextrin (6):

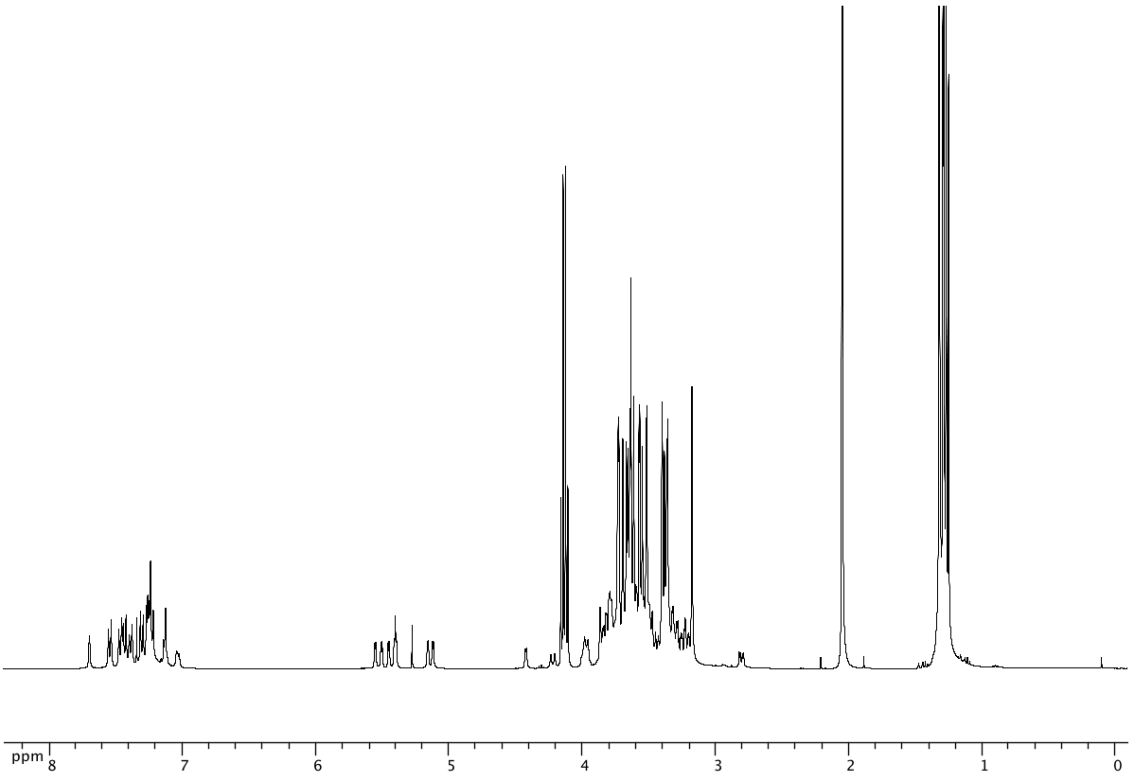
$6^A,6^B$:$6^D,6^E$-Tetra-*O*-bis{benzene-1,3-bis[bis(4-*tert*-butylphenyl)methyl]}$2^A,2^B,2^C,2^D,2^E,2^F,2^G,2^H,3^A,3^B,3^C,3^D,3^E,3^F,3^G,3^H,6^C,6^F,6^G,6^H$-icosa-*O*-methyl-γ-cyclodextrin (7):

$6^A,6^B$:$6^E,6^F$-Tetra-*O*-bis{benzene-1,3-bis[bis(4-*tert*-butylphenyl)methyl]}$2^A,2^B,2^C,2^D,2^E,2^F,2^G,2^H,3^A,3^B,3^C,3^D,3^E,3^F,3^G,3^H,6^C,6^D,6^G,6^H$-icosa-*O*-methyl-γ-cyclodextrin (8):

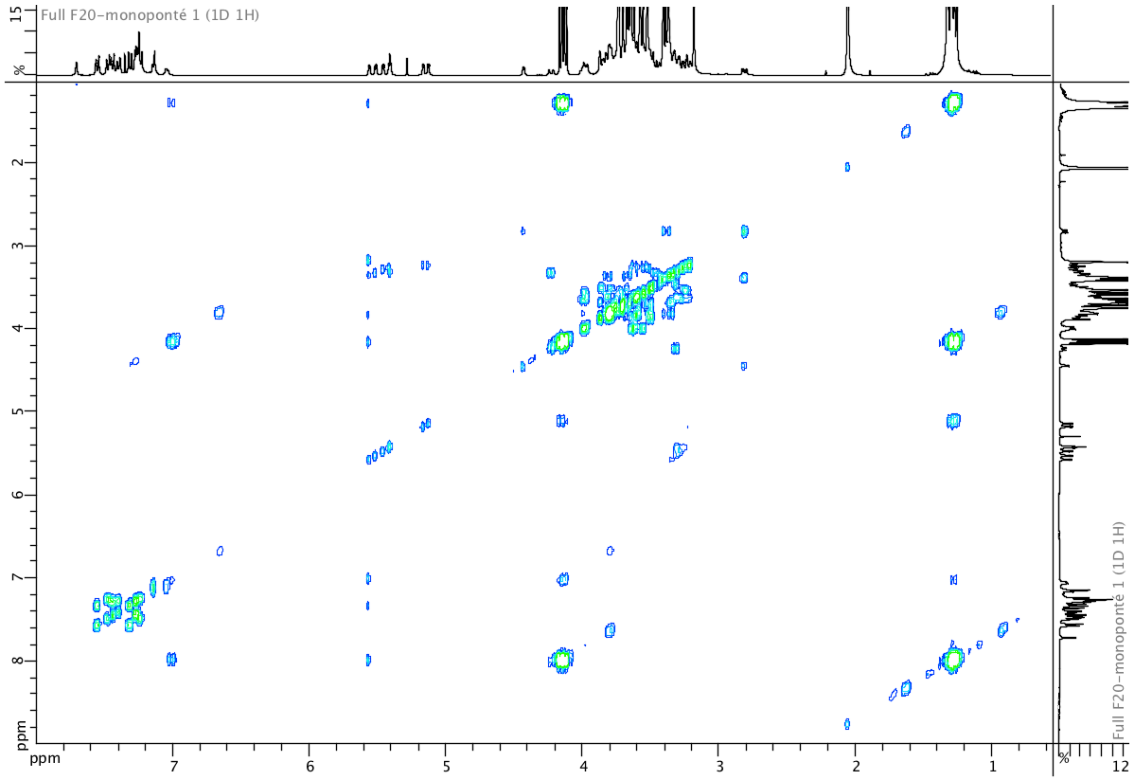
$2^{A},2^{B},2^{C},2^{D},2^{E},2^{F},2^{G},2^{H},3^{A},3^{B},3^{C},3^{D},3^{E},3^{F},3^{G},3^{H},6^{C},6^{D},6^{G},6^{H}$-icosa-*O*-methyl-γ-cyclodextrin (9):

$2^{A},2^{B},2^{C},2^{D},2^{E},2^{F},2^{G},2^{H},3^{A},3^{B},3^{C},3^{D},3^{E},3^{F},3^{G},3^{H},6^{C},6^{D},6^{E},6^{F},6^{G},6^{H}$-docosa-*O*-methyl-γ-cyclodextrin (10).

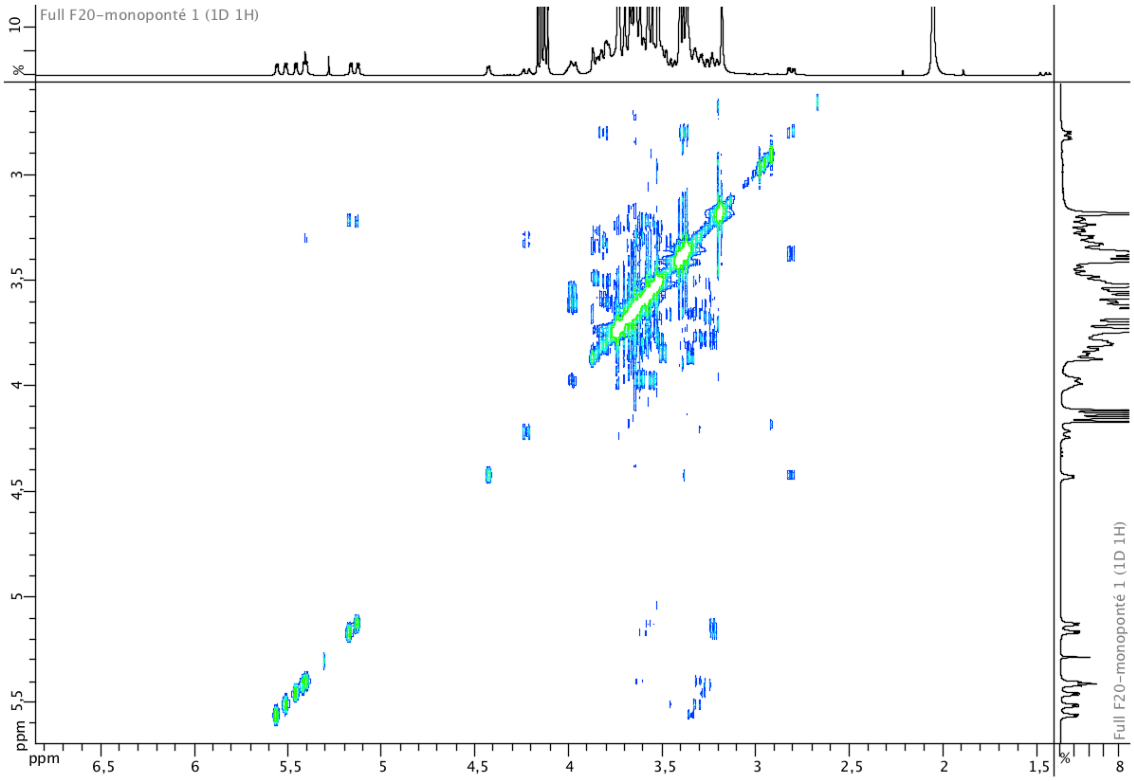
$2^{A},2^{B},2^{C},2^{D},2^{E},2^{F},2^{G},2^{H},3^{A},3^{B},3^{C},3^{D},3^{E},3^{F},3^{G},3^{H},6^{C},6^{F},6^{G},6^{H}$-icosa-*O*-methyl-γ-cyclodextrin (11):



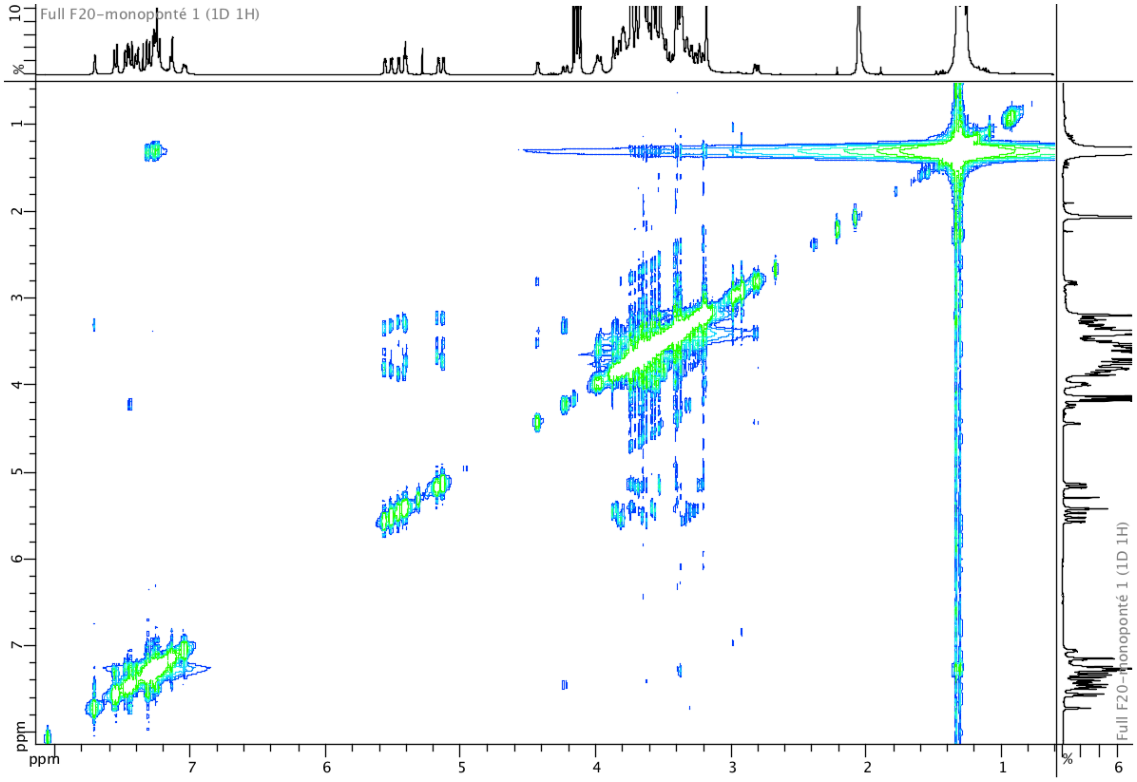
^{1}H NMR spectrum of **6.**



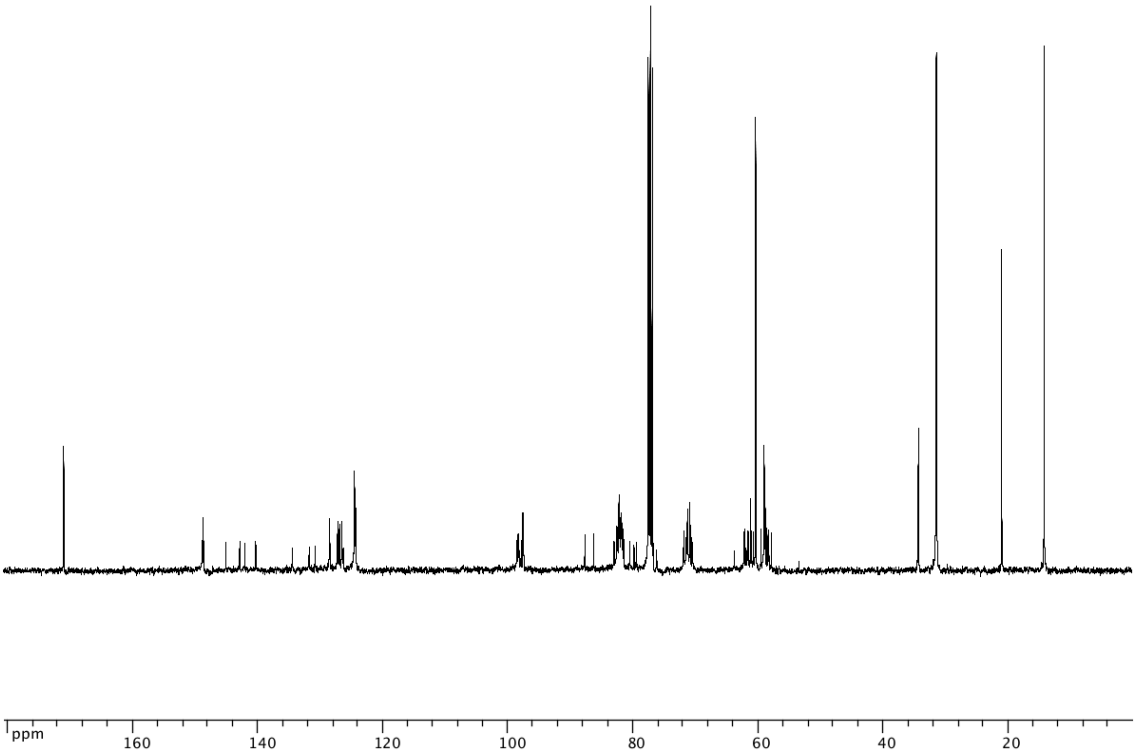
$^{1}H/^{1}H$ COSY spectrum of **6.**



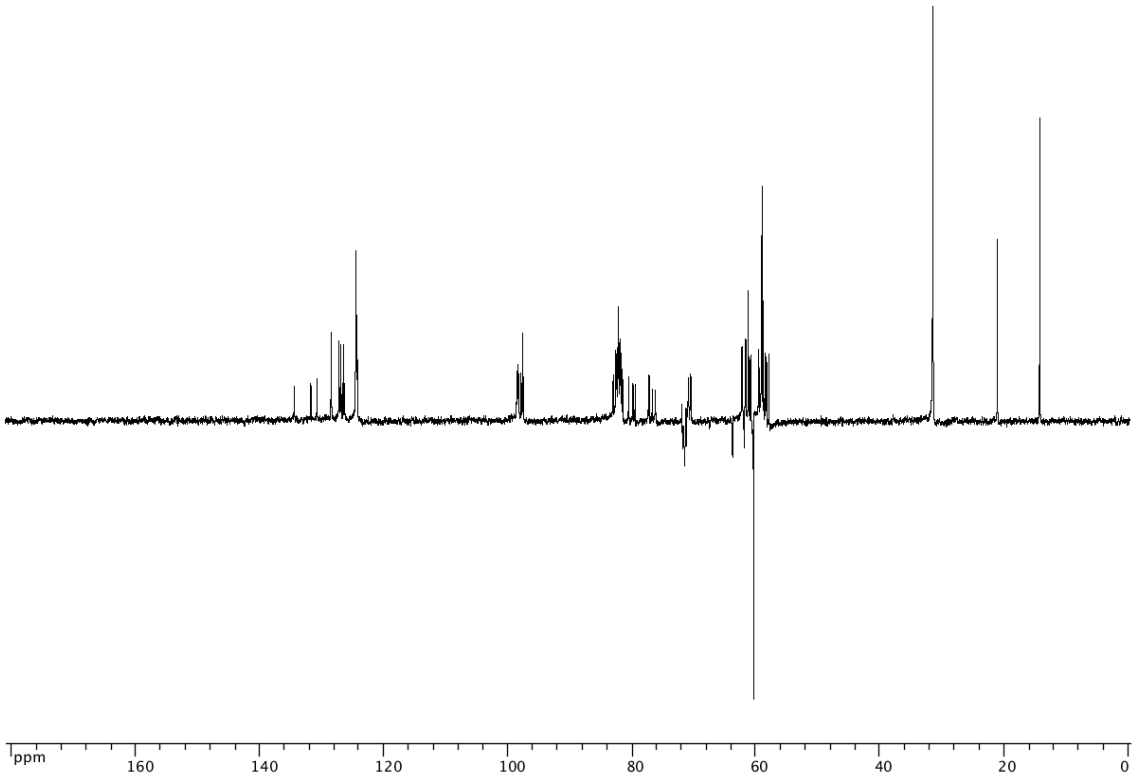
$^{1}H/^{1}H$ TOCSY spectrum of **6**.



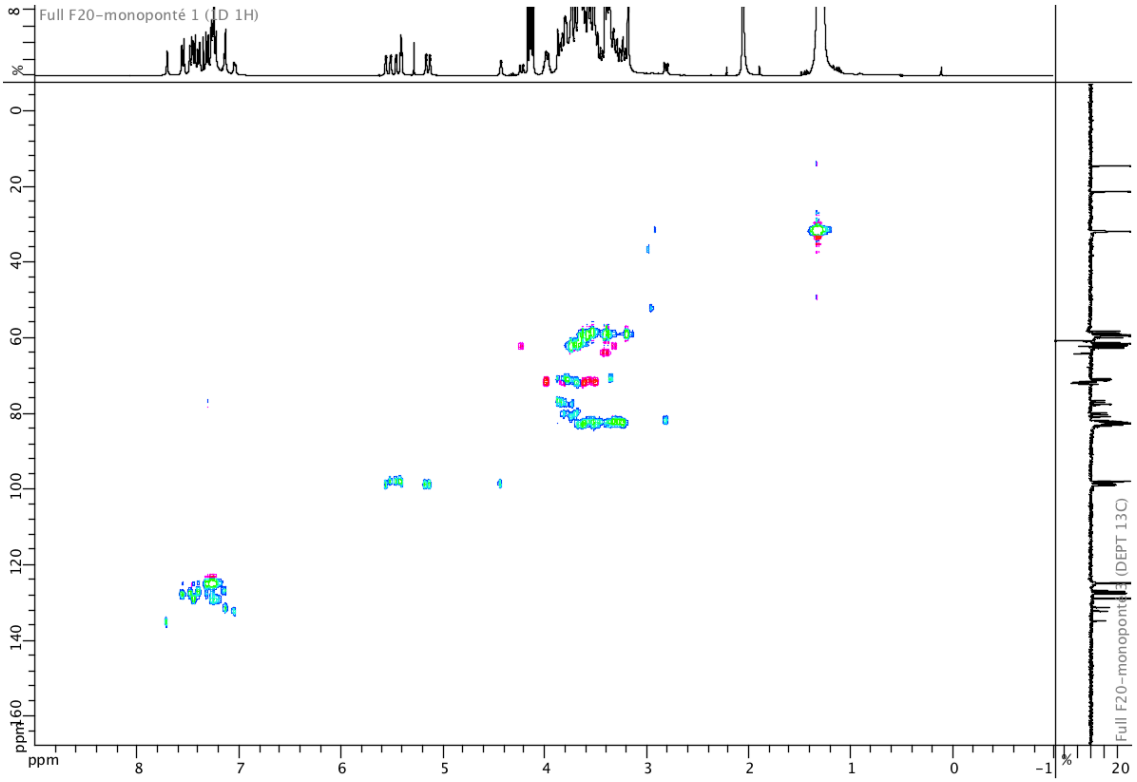
$^{1}H/^{1}H$ ROESY spectrum of **6**.



$^{13}C\{^{1}H\}$ NMR spectrum of **6**.



DEPT 135 spectrum of **6.**



$^{1}H/^{13}C$ HSQC edited spectrum of **6**.

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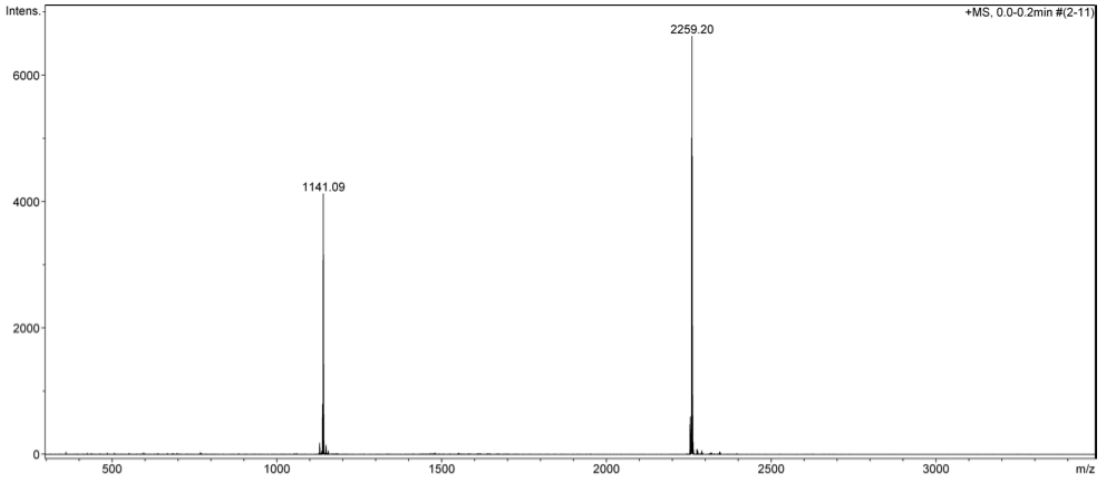
Analysis Info

Analysis Name	O15619ML.d	Acquisition Date	10/14/2011 2:11:43 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ83F20-AB monocap	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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Analysis Info

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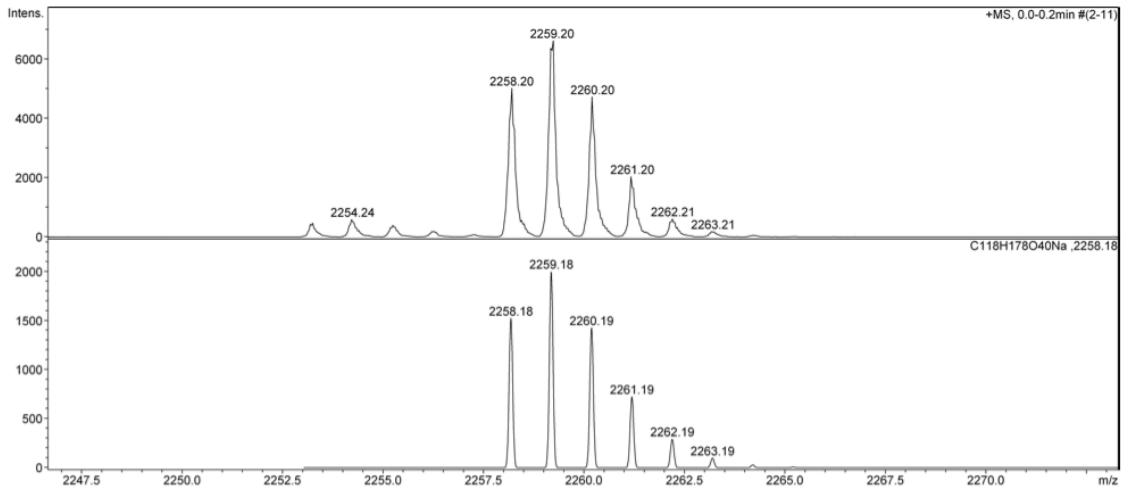
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ83F20-AB monocap	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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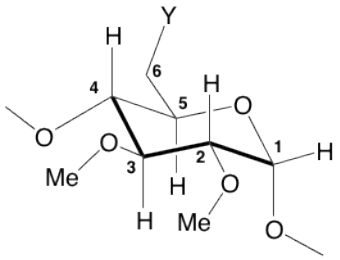
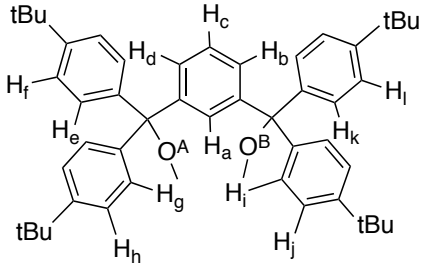
Mass spectrum of **6**, and simulation.

Table 1. Assignment of the sugar protons of **6** (based on TOCSY, COSY, ROESY and HMQC).

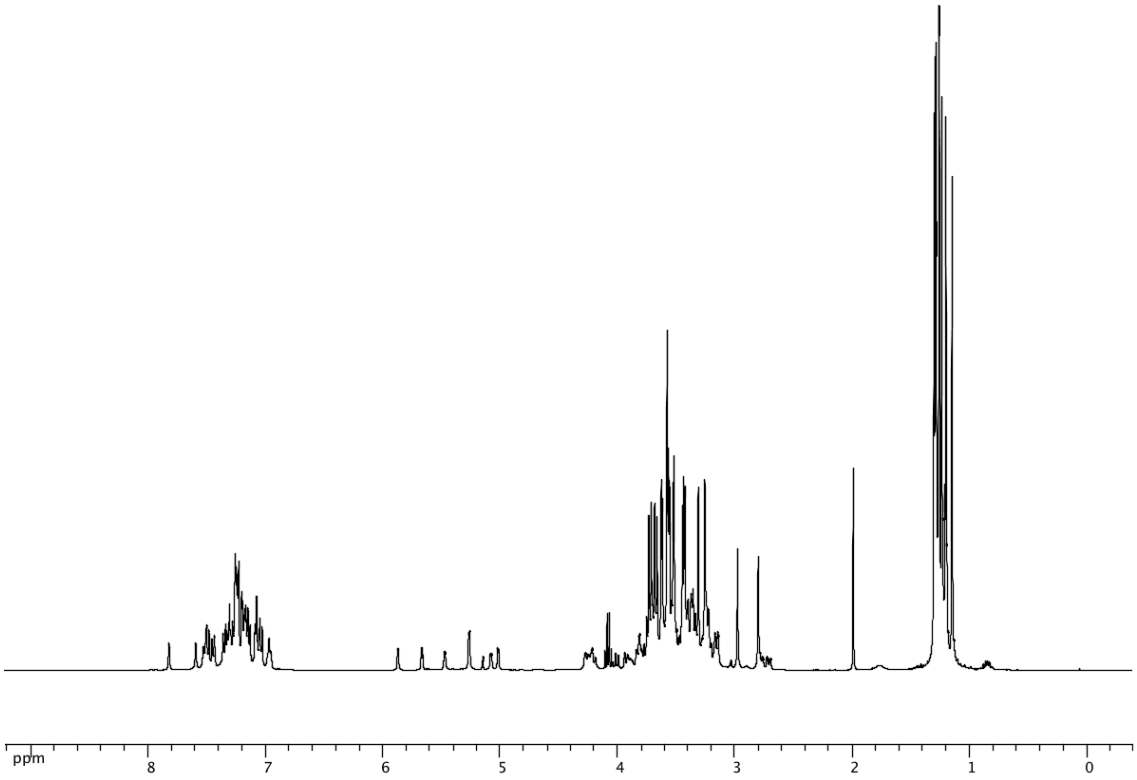


	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**
H-1	5.51	4.42	5.56	5.45	5.41	5.12	5.16	5.40
H-2	3.31	2.81	3.33	3.27	3.25	3.22	3.21	3.30
H-3	3.45	3.37	3.65	3.61	3.51	3.55	3.59	3.60
H-4	3.49	3.81	3.87	3.82	3.71	3.67	3.73	3.81
H-5	3.66	3.33	3.85	3.78	3.68	3.76	3.79	3.76
H-6a	3.37	3.30	3.59	3.62	3.47	3.49	3.55	3.60
H-6b	3.42	4.22	3.61	3.97	3.61	3.63	3.97	3.98
OMe-6	–	–	3.40	3.36	3.18	3.18	3.37	3.41

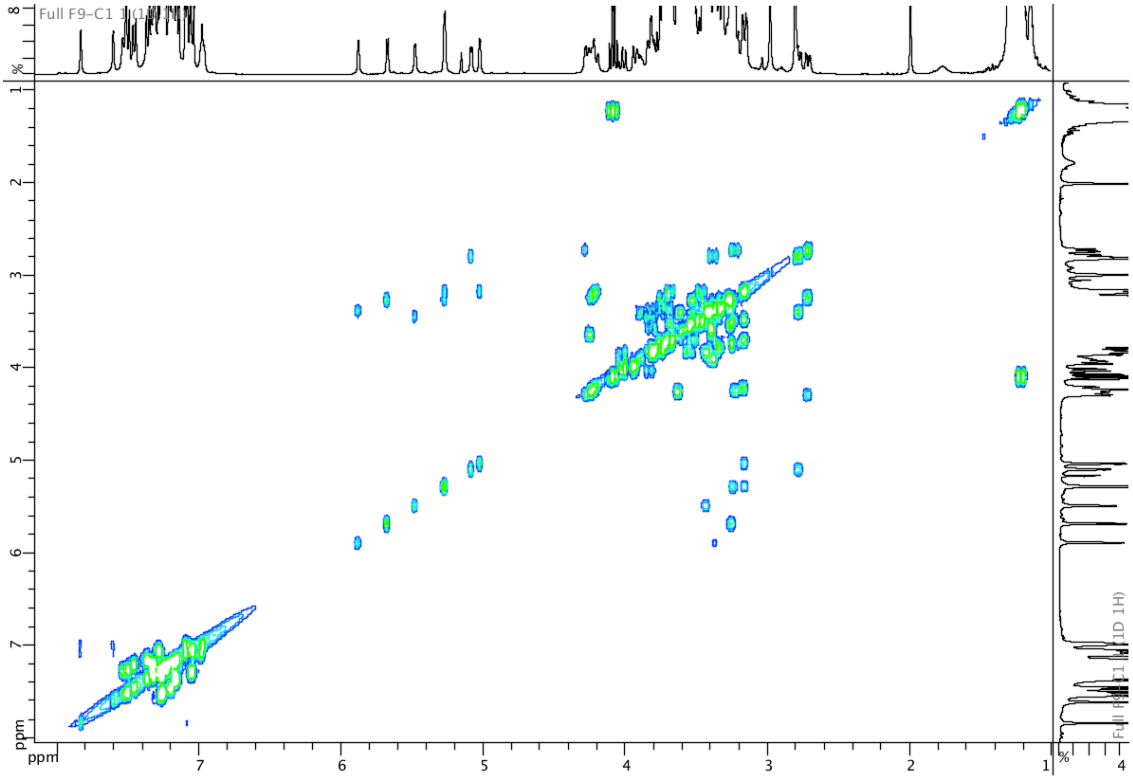
Table 2. Assignment of the aromatic protons of **6** (based on TOCSY, COSY, ROESY and HMQC).



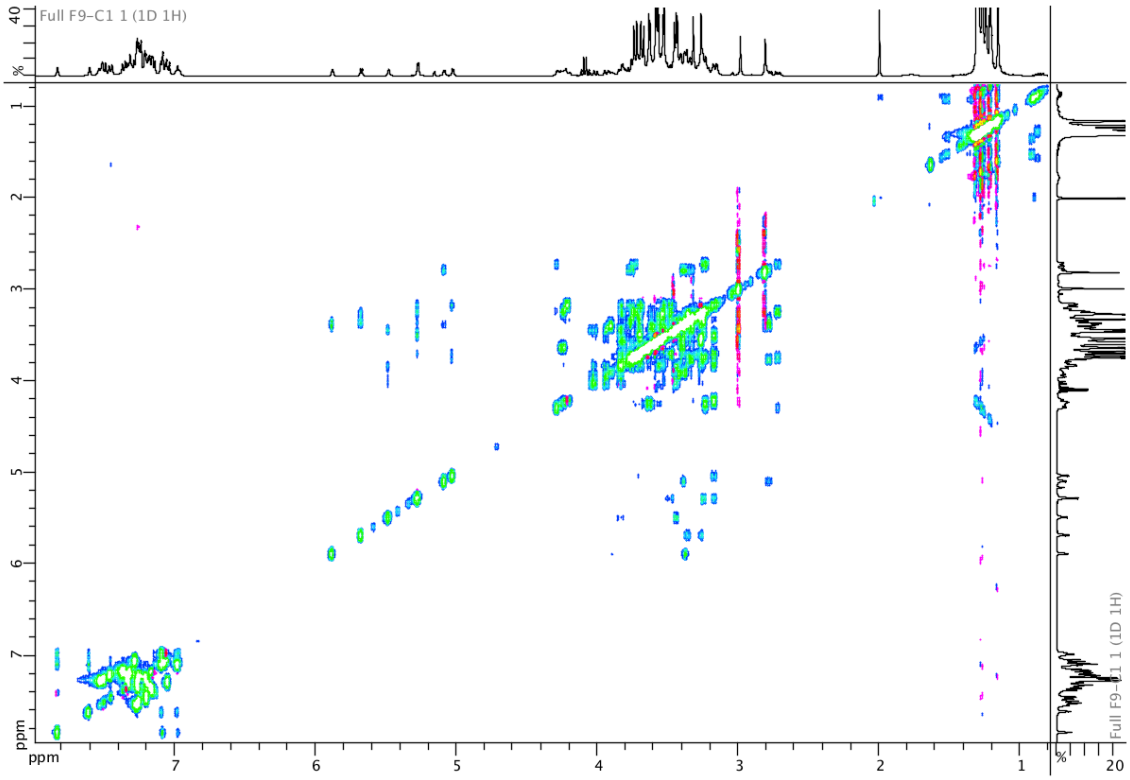
	A,B bridge
H_a	7.70
H_b	7.12
H_c	7.04
H_d	7.14
H_e	7.47
H_f	7.23
H_g	7.55
H_h	7.31
H_i	7.44
H_j	7.27
H_k	7.39
H_l	7.25



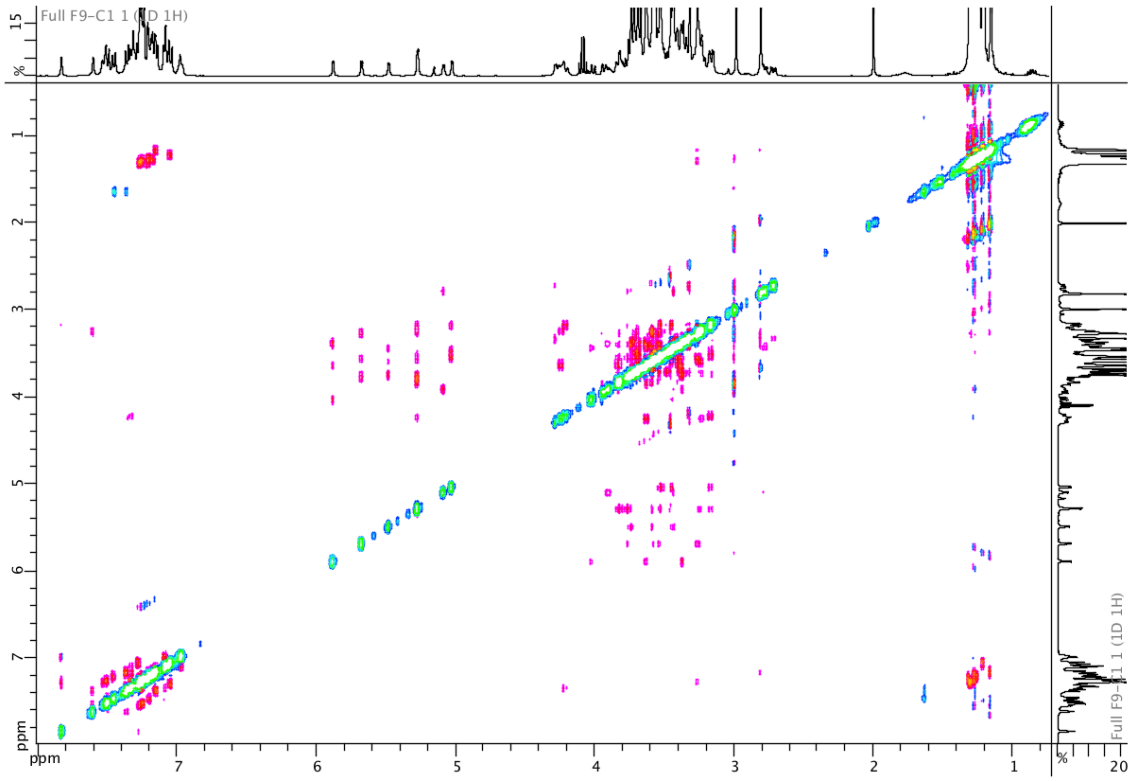
^{1}H NMR spectrum of **7**.



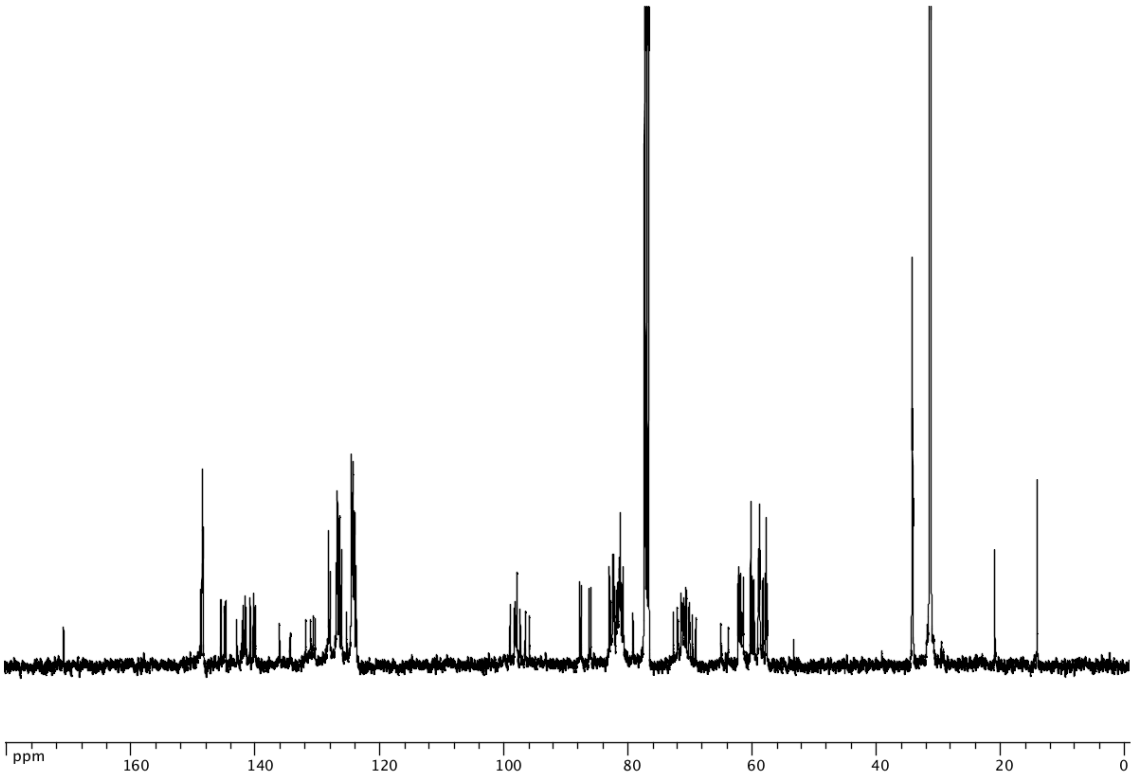
^{1}H/^{1}H COSY spectrum of **7**.



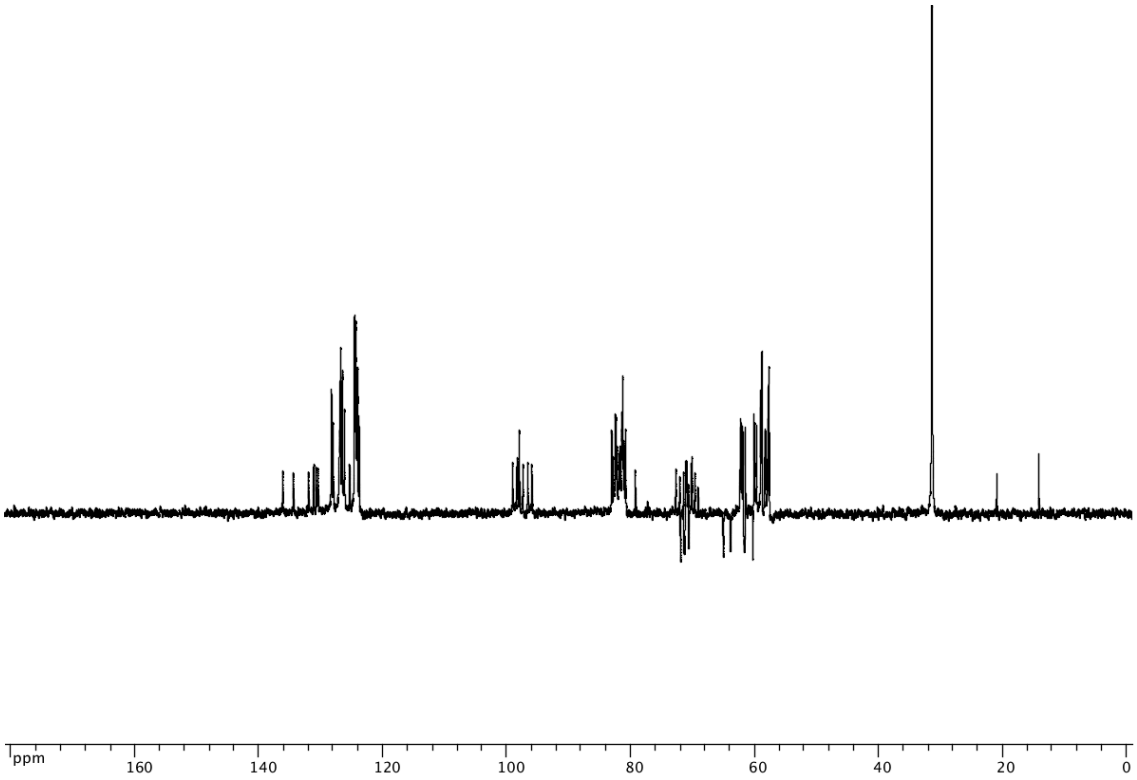
$^{1}H/^{1}H$ TOCSY spectrum of **7**.



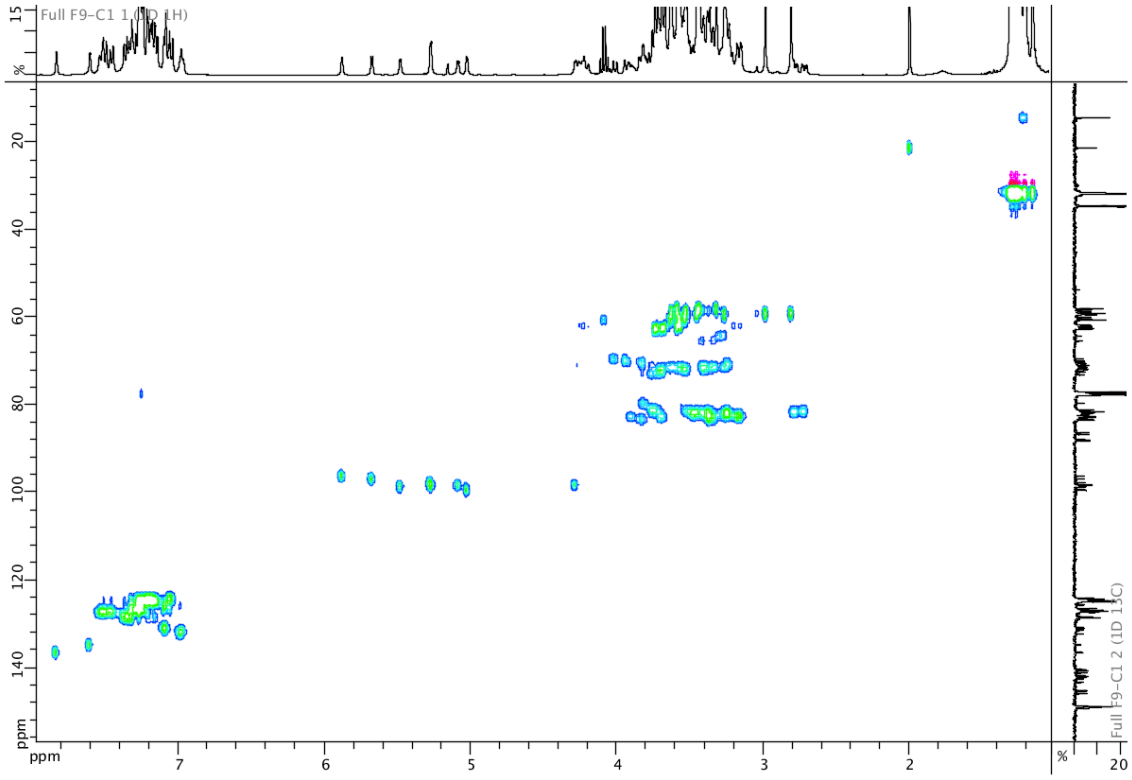
$^{1}H/^{1}H$ ROESY spectrum of **7**.



$^{13}C\{^{1}H\}$ NMR spectrum of **7**.



DEPT 135 spectrum of **7**.



$^{1}H/^{13}C$ HSQC edited spectrum of **7**.

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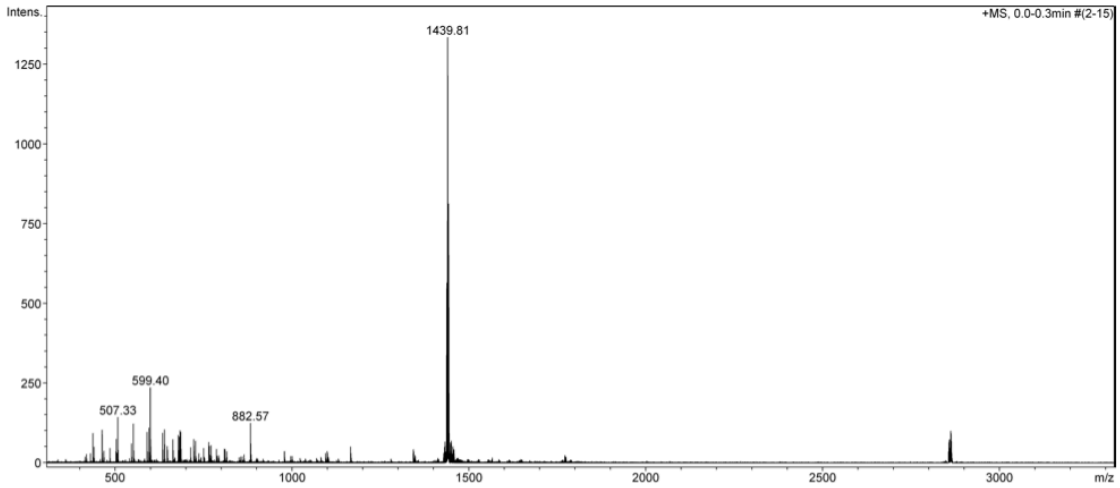
Analysis Info

Analysis Name	O15618ML.d	Acquisition Date	10/14/2011 2:06:47 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ83-F9-C1	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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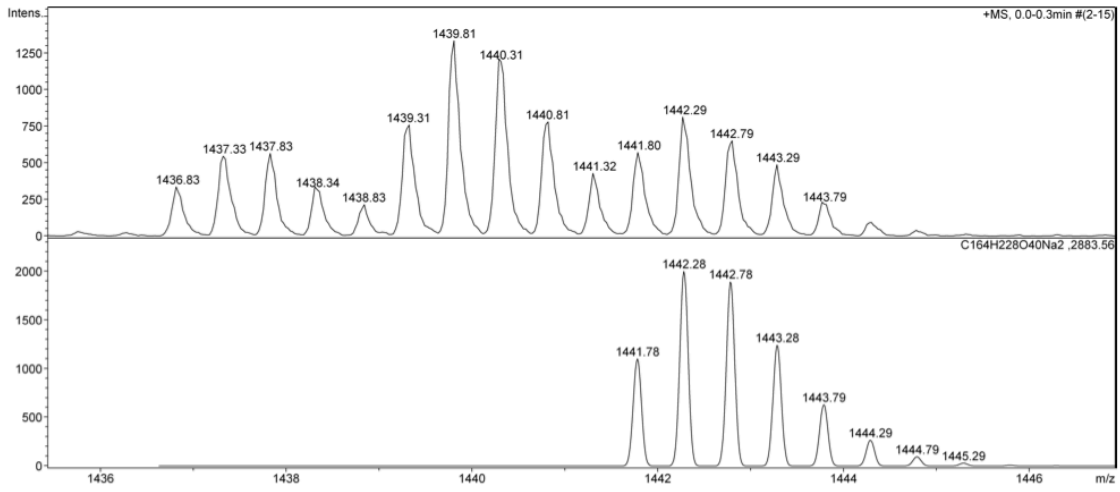
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15618ML.d	Acquisition Date	10/14/2011 2:06:47 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ83-F9-C1	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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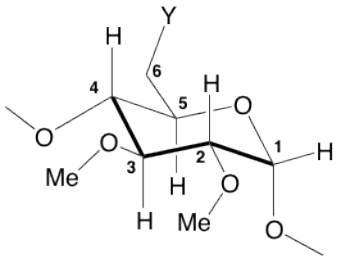
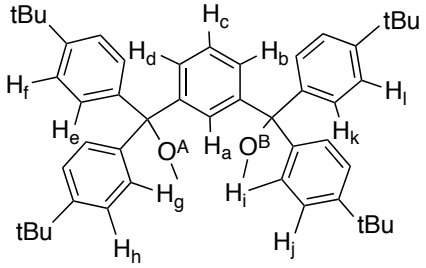
Mass spectrum of **7** and simulation.

Table 3. Assignment of the sugar protons of **7** (based on TOCSY, COSY, ROESY and HMQC).

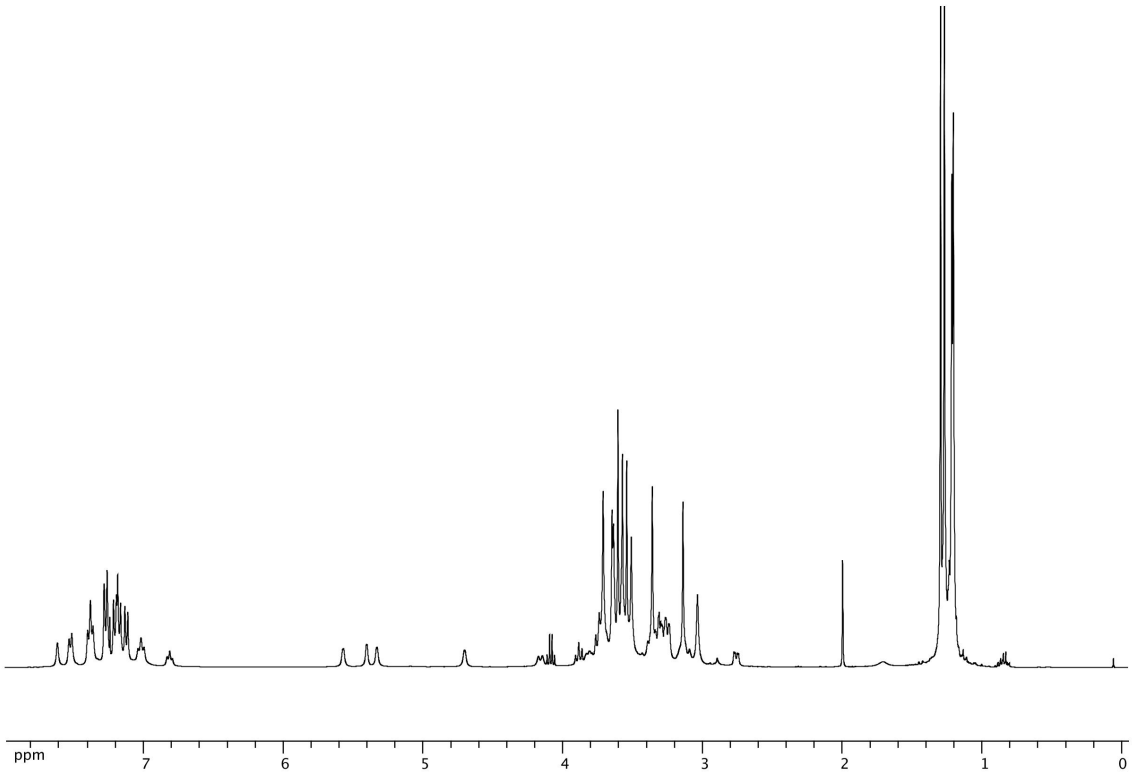


	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**
H-1	5.26	4.27	5.48	5.87	5.08	5.67	5.02	5.27
H-2	3.15	2.71	3.42	3.36	2.78	3.24	3.16	3.23
H-3	3.46	3.22	3.82	3.41	3.38	3.35	3.76	3.81
H-4	3.34	3.73	4.02	3.89	3.76	3.52	3.83	3.68
H-5	3.40	3.23	3.94	3.68	3.32	3.82	3.69	3.55
H-6a	3.26	3.24	3.25	3.33	3.17	3.62	3.39	3.38
H-6b	3.30	4.23	3.52	3.41	4.20	4.23	3.53	3.60
OMe-6	–	–	3.26	–	–	2.80	2.98	3.31

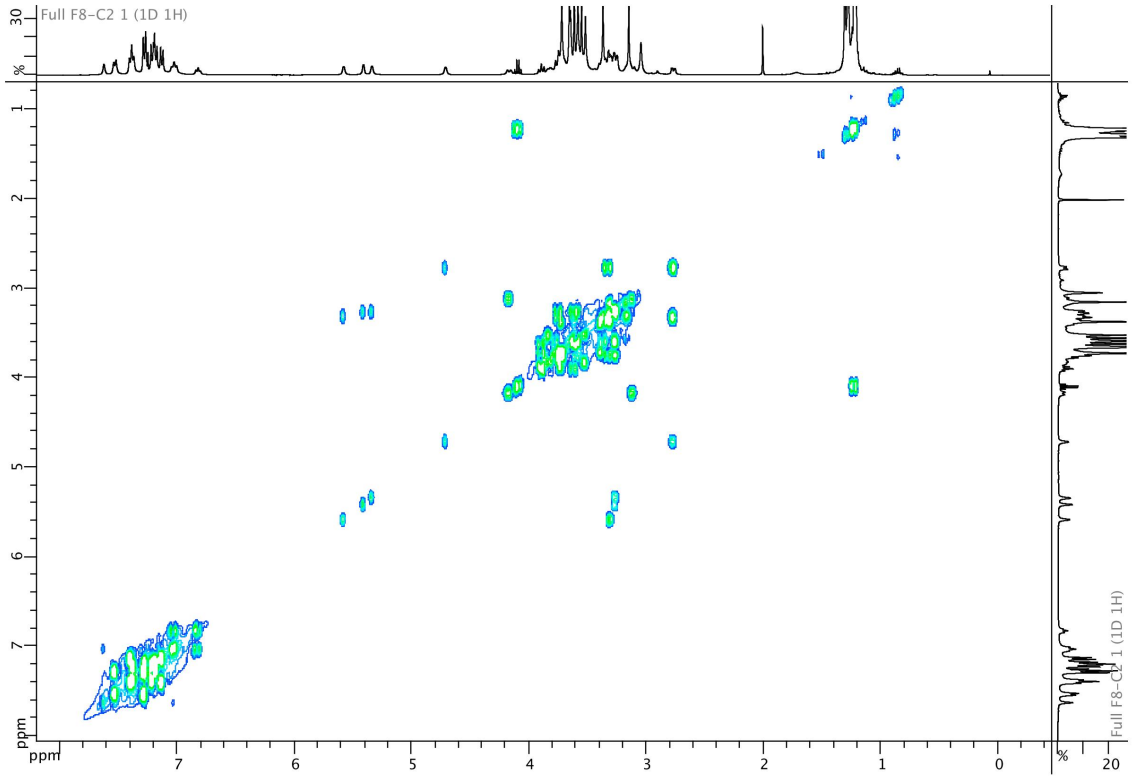
Table 4. Assignment of the aromatic protons of **7** (based on TOCSY, COSY, ROESY and HMQC).



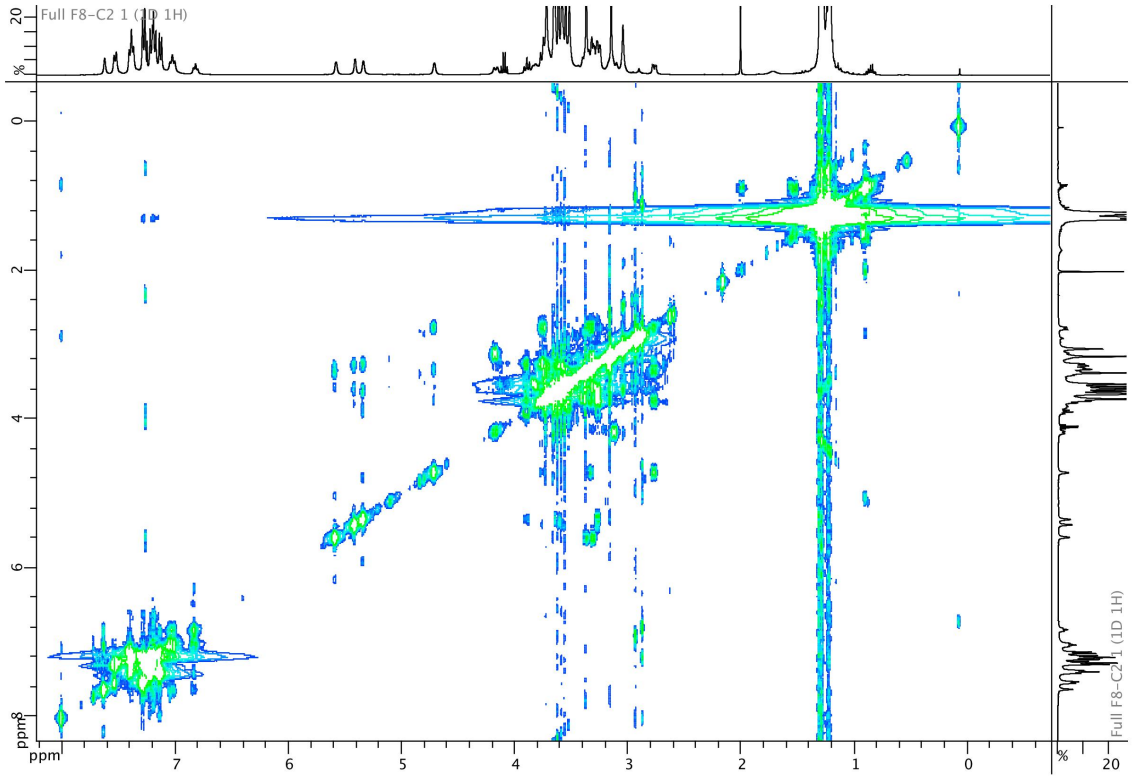
	A,B bridge		D,E bridge
H_a	7.60	$H_{a'}$	7.83
H_b	7.08	$H_{b'}$	7.09
H_c	7.04	$H_{c'}$	7.05
H_d	6.99	$H_{d'}$	6.97
H_e	7.27	$H_{e'}$	7.32
H_f	7.26	$H_{f'}$	7.16
H_g	7.36	$H_{g'}$	7.27
H_h	7.16	$H_{h'}$	7.05
H_i	7.52	$H_{i'}$	7.32
H_j	7.27	$H_{j'}$	7.23
H_k	7.45	$H_{k'}$	7.50
H_l	7.19	$H_{l'}$	7.26



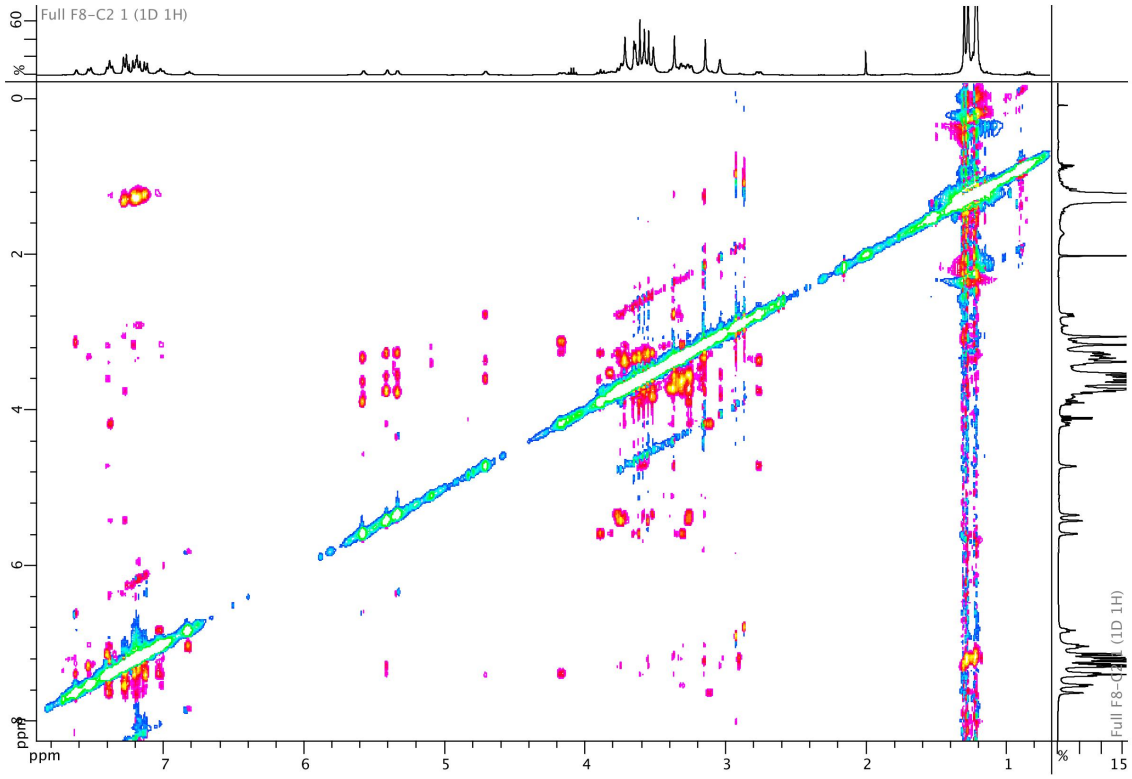
^{1}H NMR spectrum of **8**.



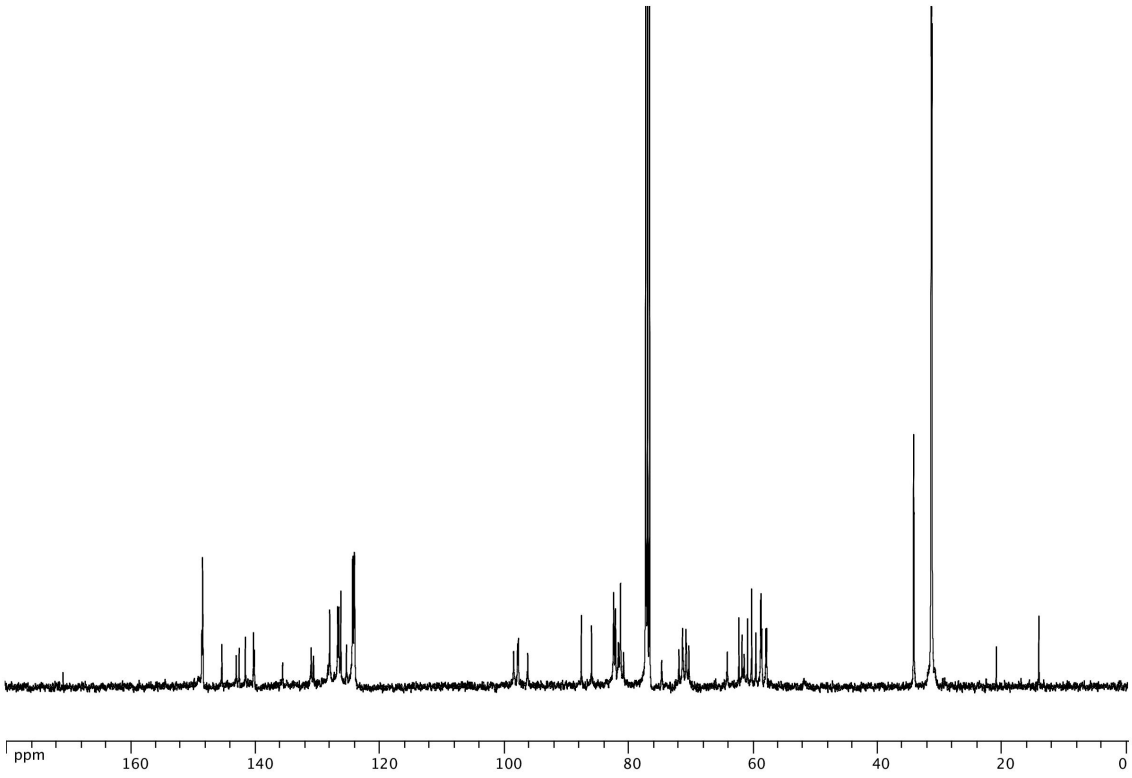
$^{1}H/^{1}H$ COSY spectrum of **8.**



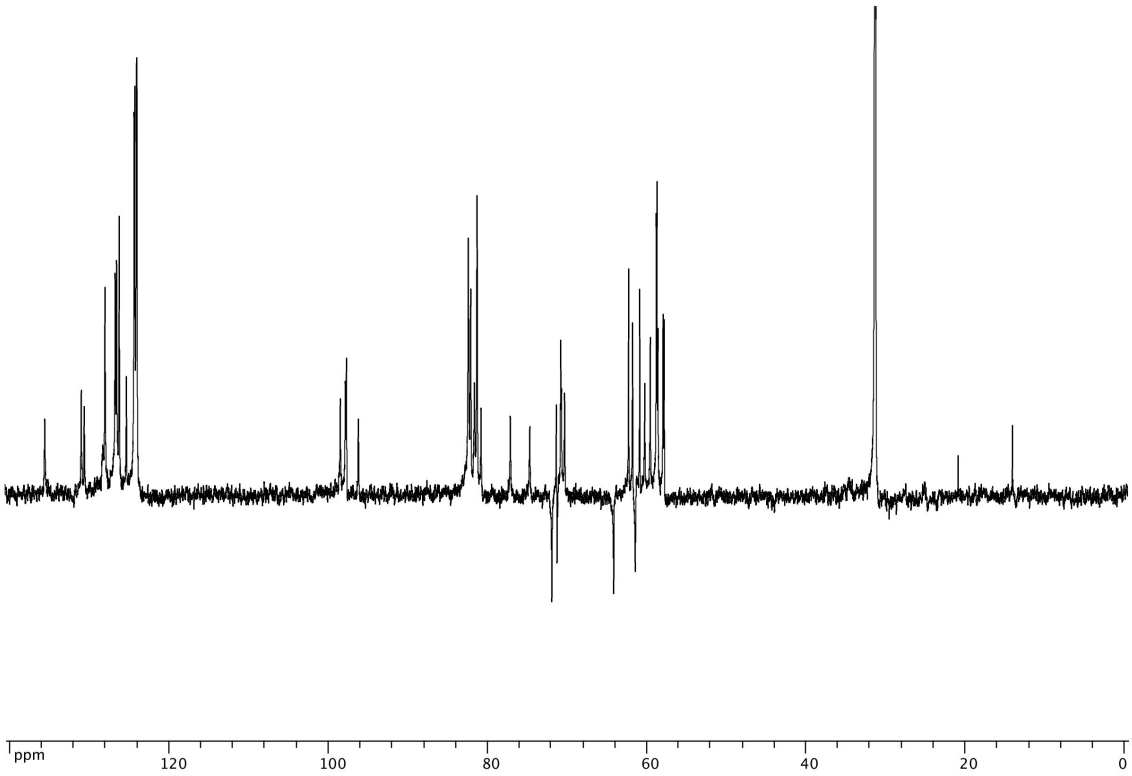
$^{1}H/^{1}H$ TOCSY spectrum of **8**.



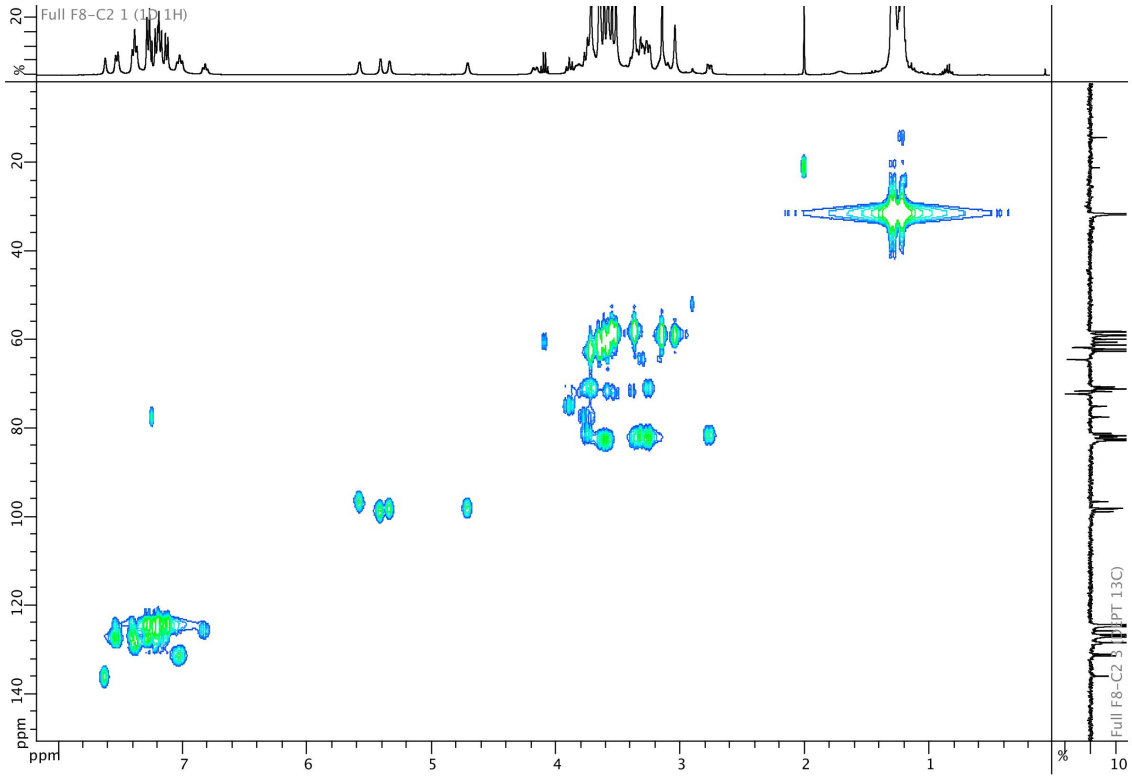
$^{1}H/^{1}H$ ROESY spectrum of **8**.



$^{13}C\{^{1}H\}$ NMR spectrum of **8**.



DEPT 135 spectrum of **8.**



$^{1}H/^{13}C$ HMQC spectrum of **8.**

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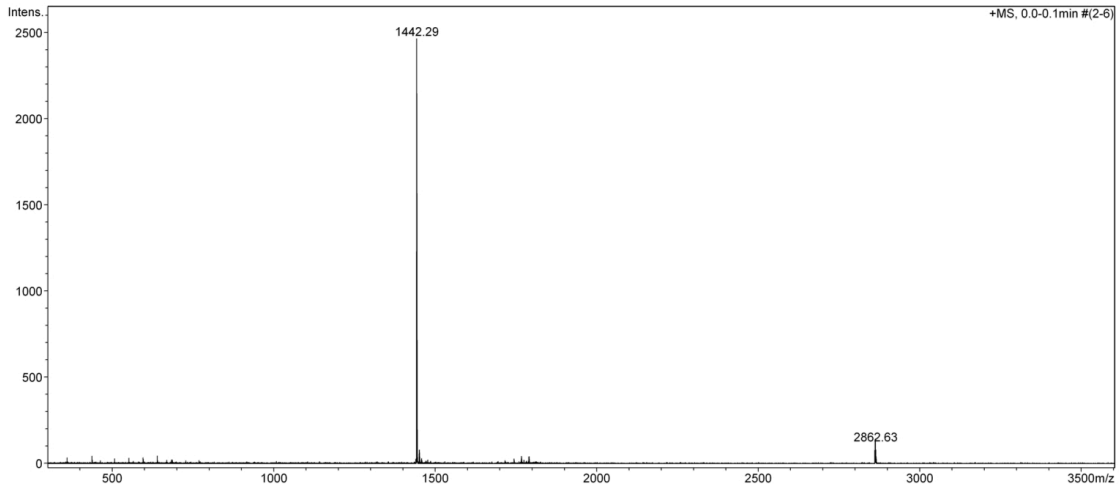
Analysis Info

Analysis Name	O15620ML.d	Acquisition Date	10/14/2011 2:14:20 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ83-F8-C2	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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Analysis Info

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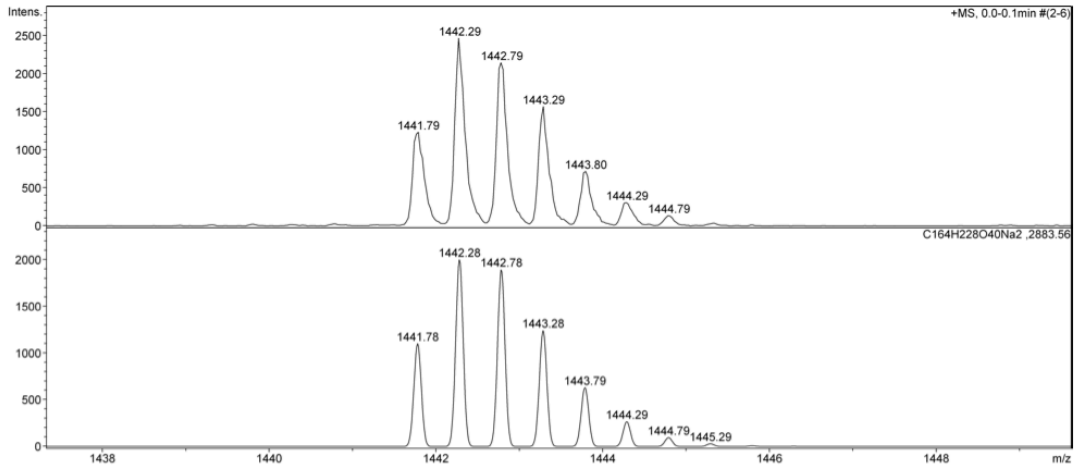
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ83-F8-C2	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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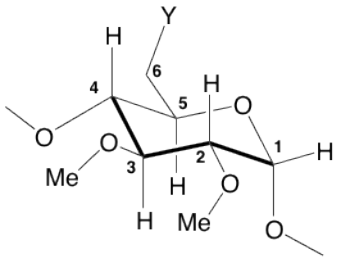
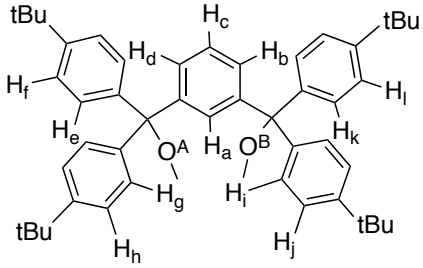
Mass spectrum of **8** and simulation.

Table 5. Assignment of the sugar protons of **8** (based on TOCSY, COSY, ROESY and HMQC).

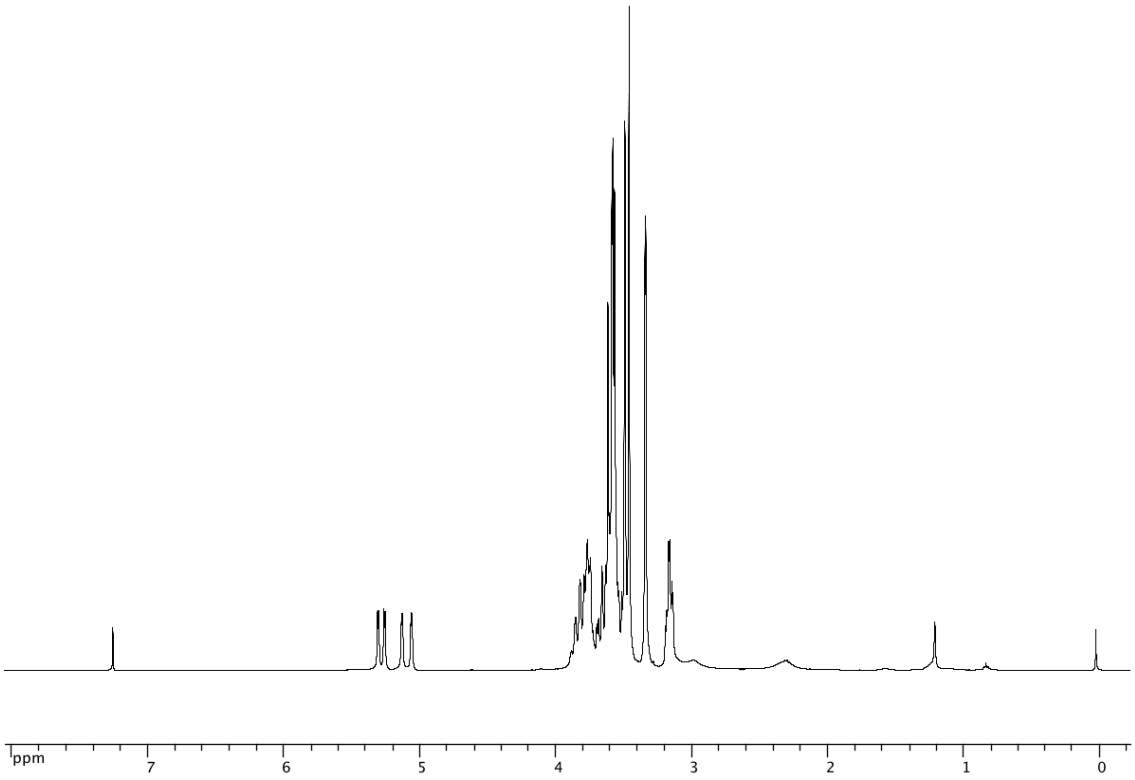


	A	B	C	D
H-1	5.57	4.70	5.40	5.33
H-2	3.29	2.76	3.25	3.26
H-3	3.35	3.32	3.59	3.63
H-4	3.57	3.75	3.77	3.89
H-5	3.56	3.23	3.70	3.73
H-6a	3.15	3.10	3.24	3.59
H-6b	3.30	4.16	3.33	3.61
OMe-6	–	–	3.14	3.03

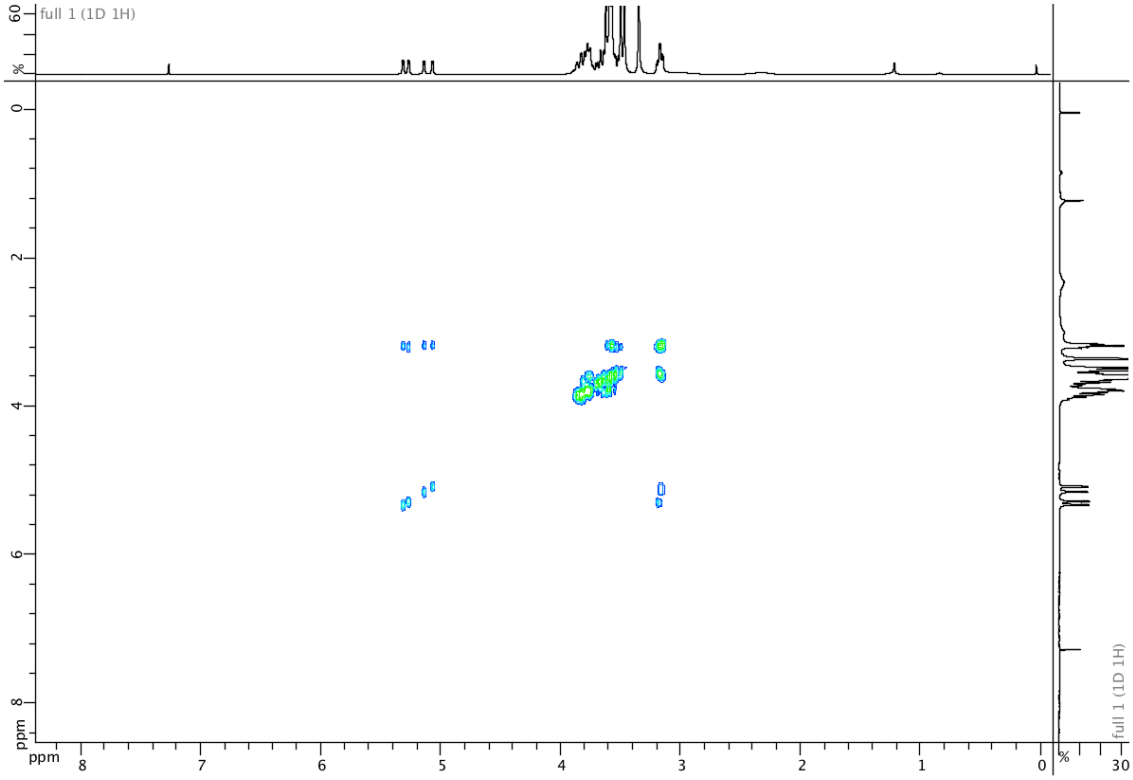
Table 6. Assignment of the aromatic protons of **8** (based on TOCSY, COSY, ROESY and HMQC).



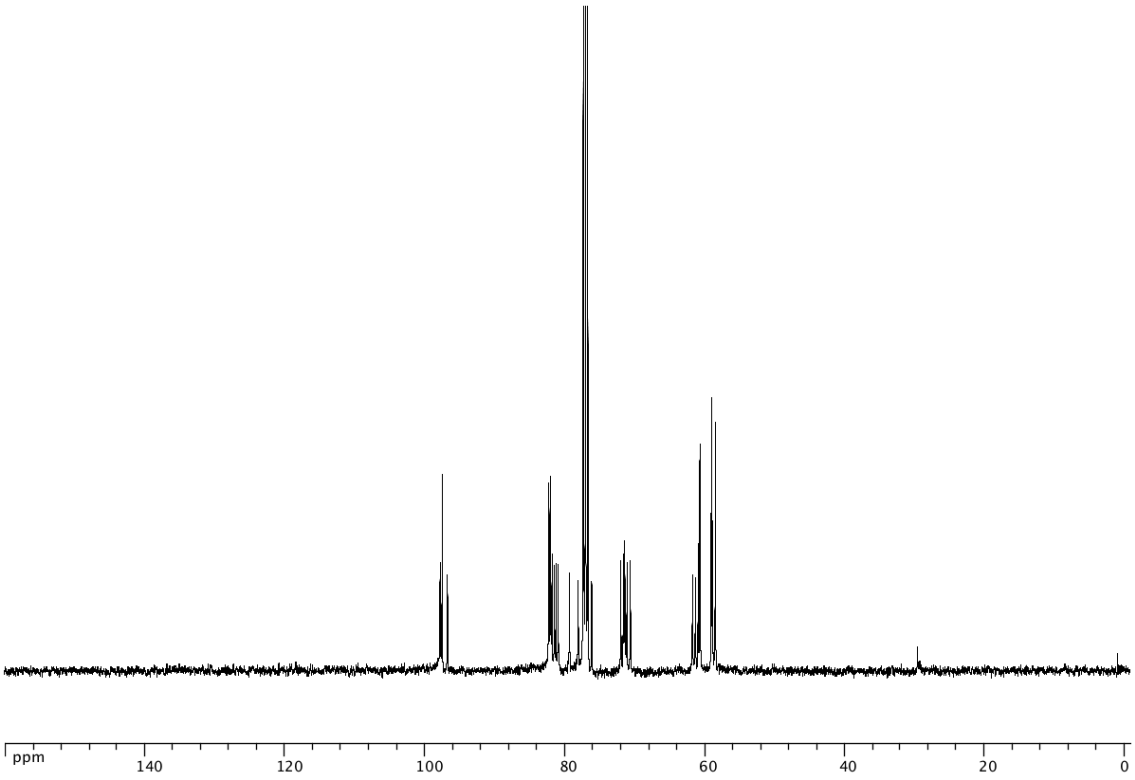
	A,B (or E,F) bridge
H_a	7.62
H_b	7.03
H_c	7.02
H_d	7.00
H_e	7.27
H_f	7.17
H_g	7.52
H_h	7.27
H_i	7.37
H_j	7.20
H_k	7.39
H_l	7.12



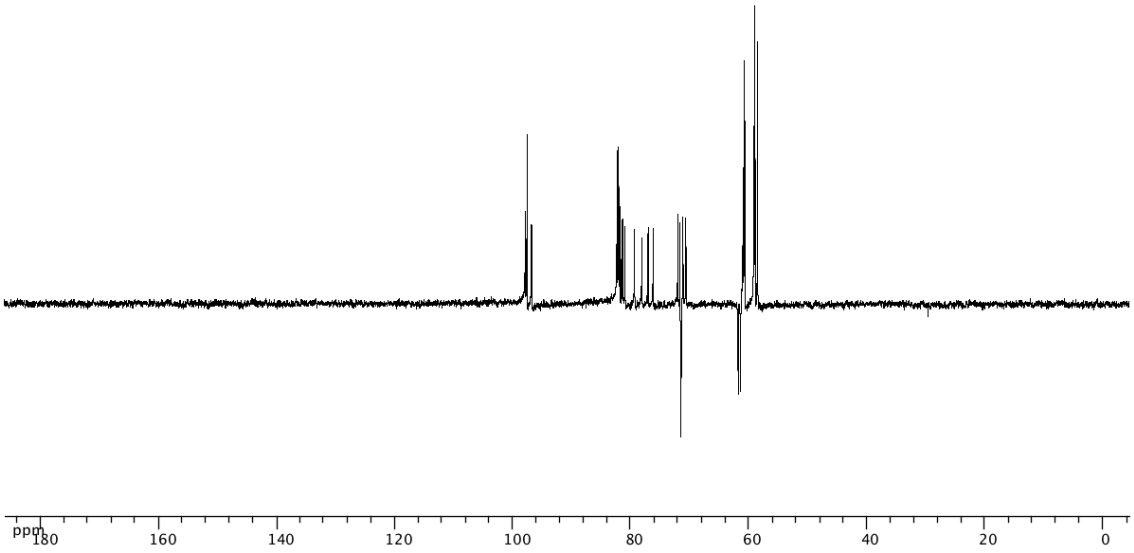
^{1}H NMR spectrum of **9**.



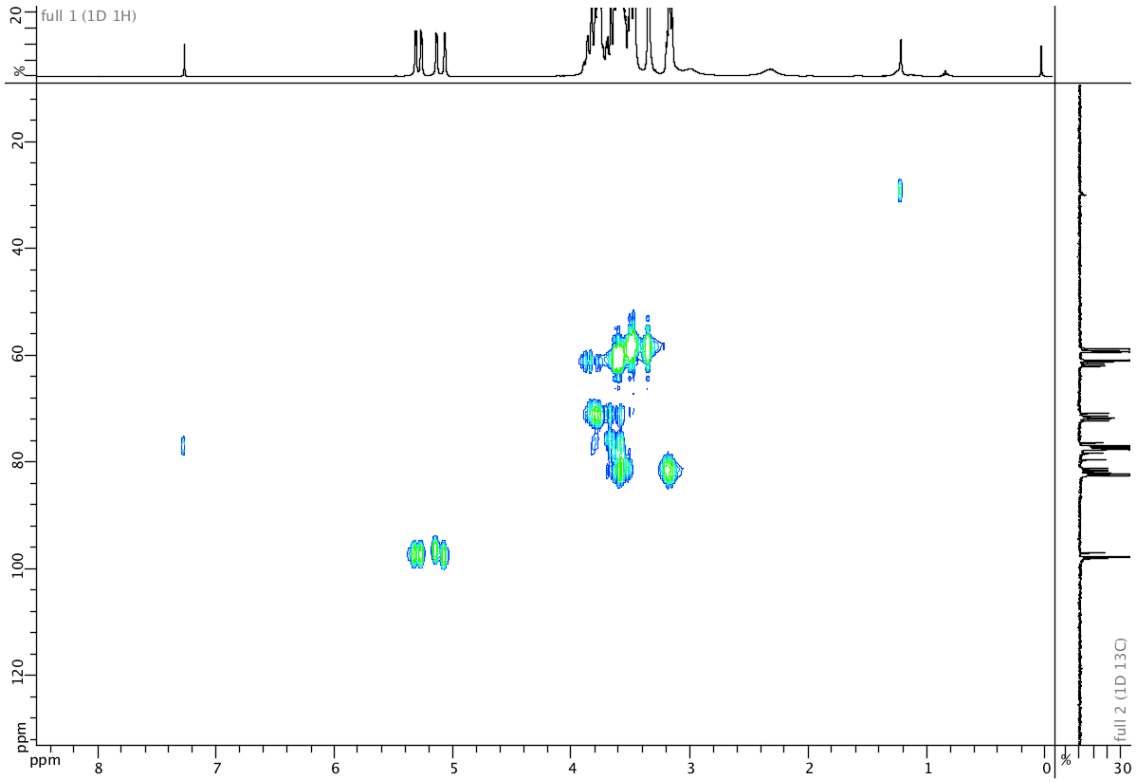
$^{1}H/^{1}H$ COSY spectrum of **9**.



$^{13}C\{^{1}H\}$ NMR spectrum of **9**.



DEPT 135 spectrum of **9**.



$^{1}H/^{13}C$ HMQC spectrum of **9**.

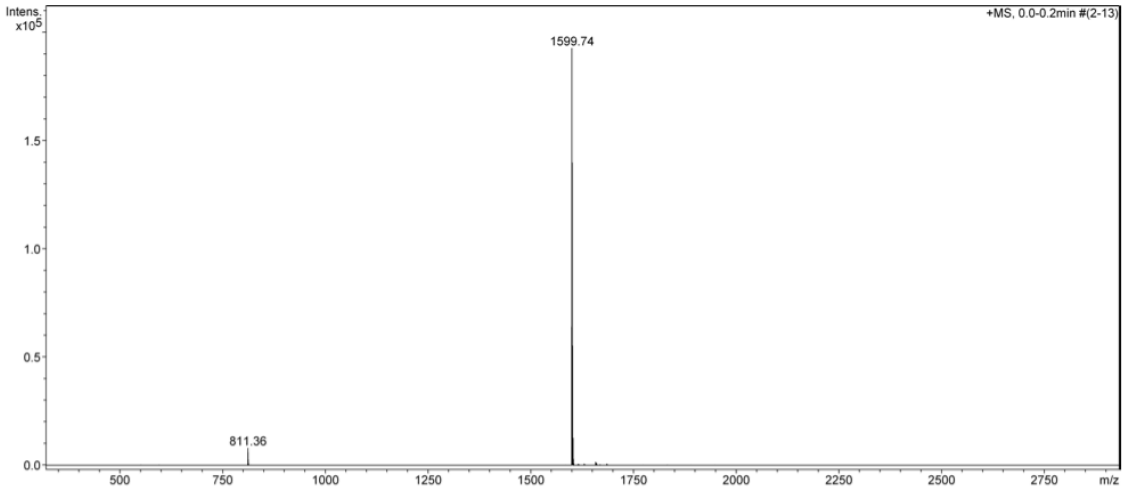
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15805ML.d	Acquisition Date	11/10/2011 3:46:33 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ85 C2	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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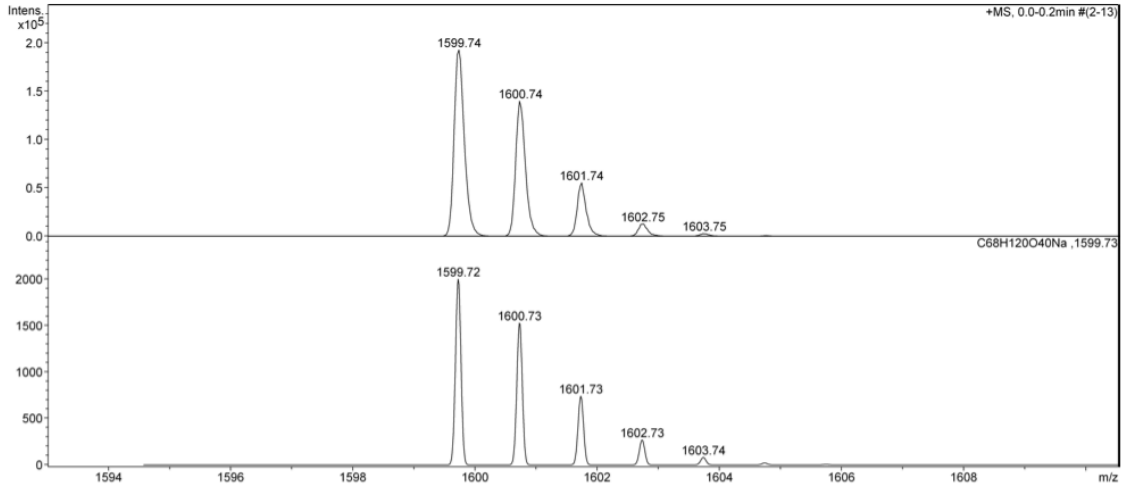
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15805ML.d	Acquisition Date	11/10/2011 3:46:33 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ85 C2	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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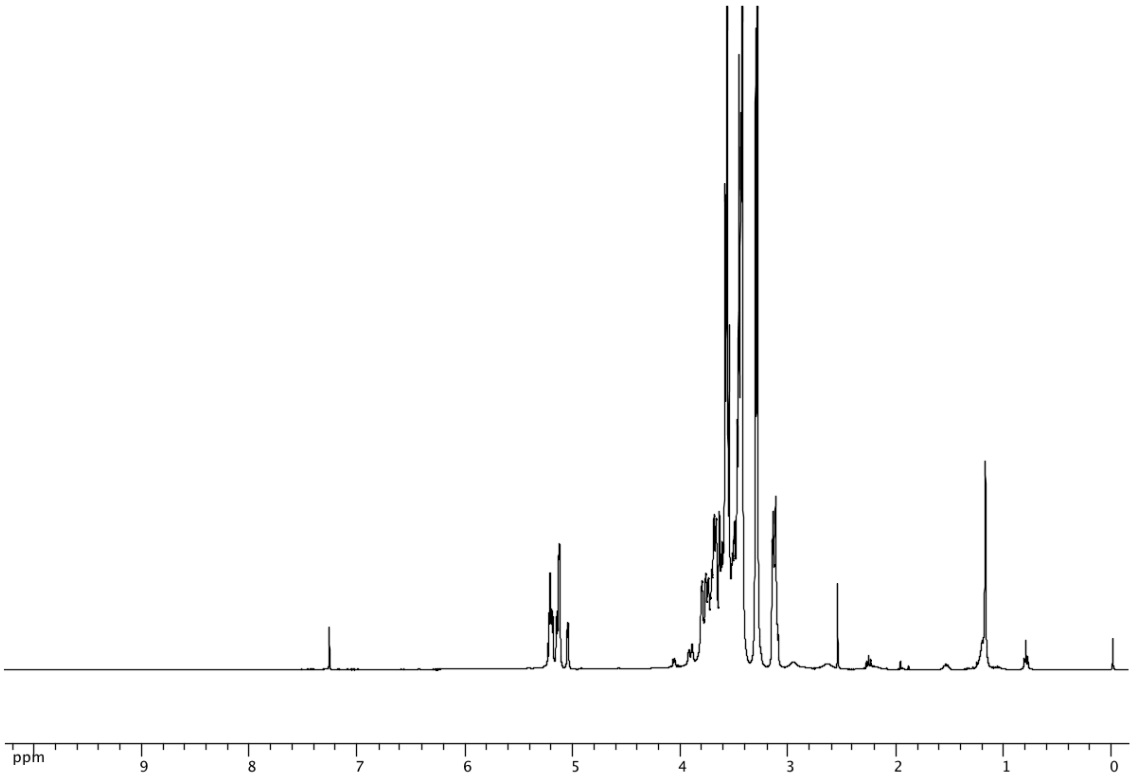
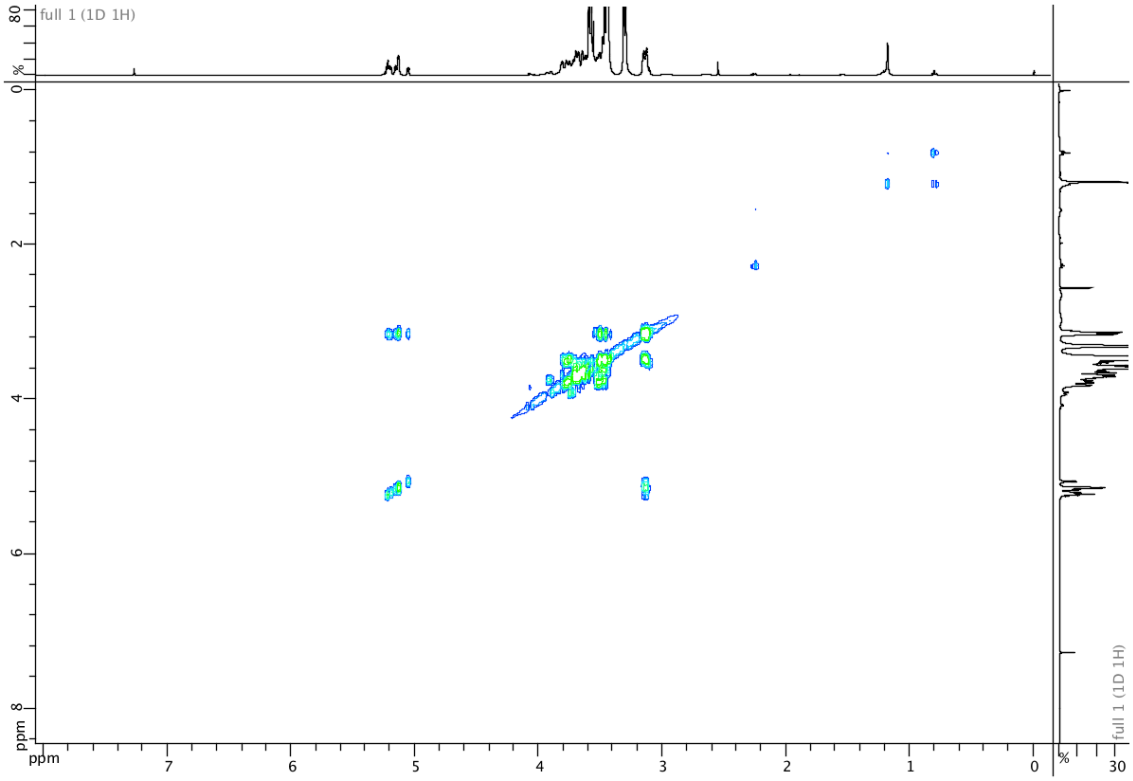
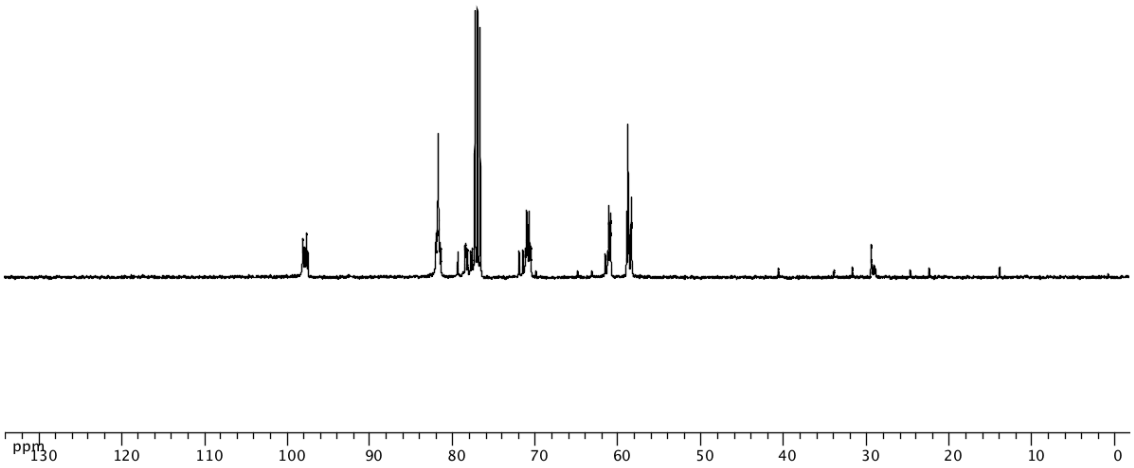
Mass spectrum of **9** and simulation.



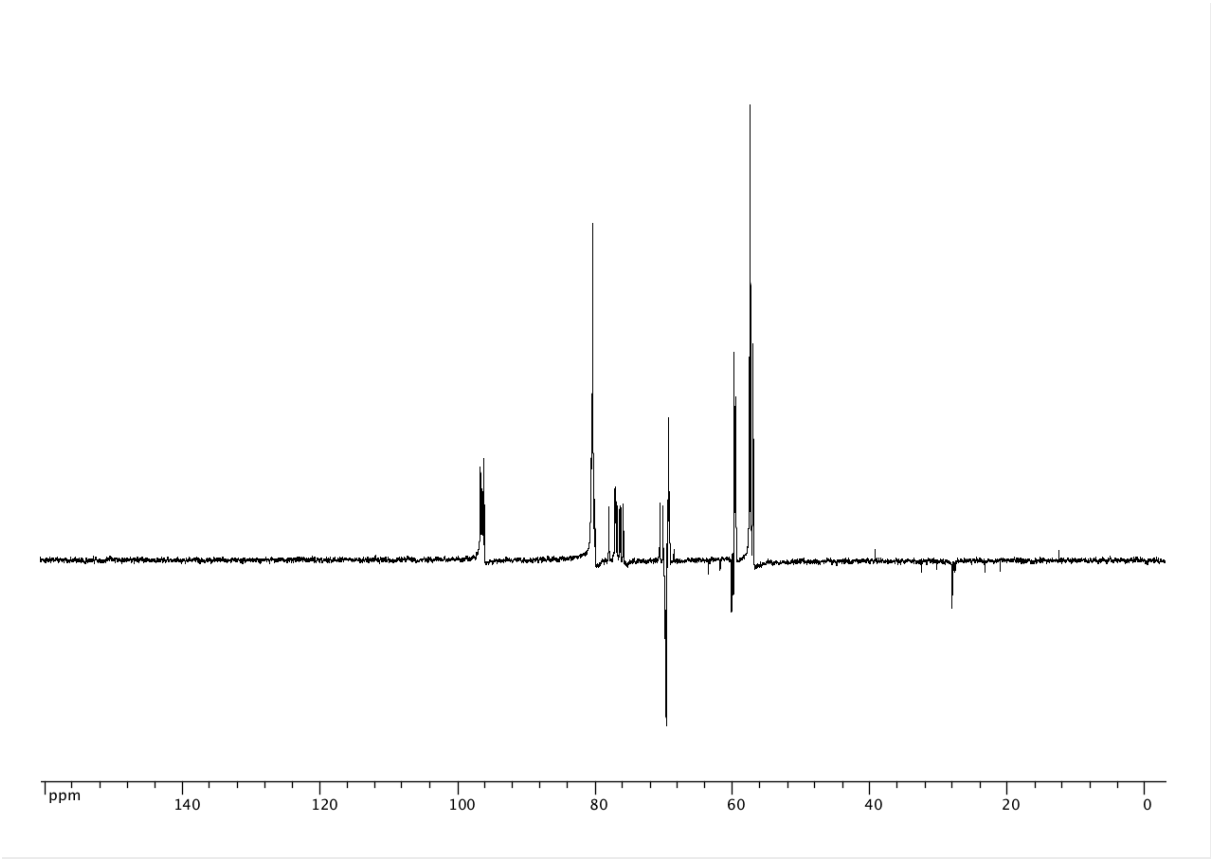
^{1}H NMR spectrum of **10**.



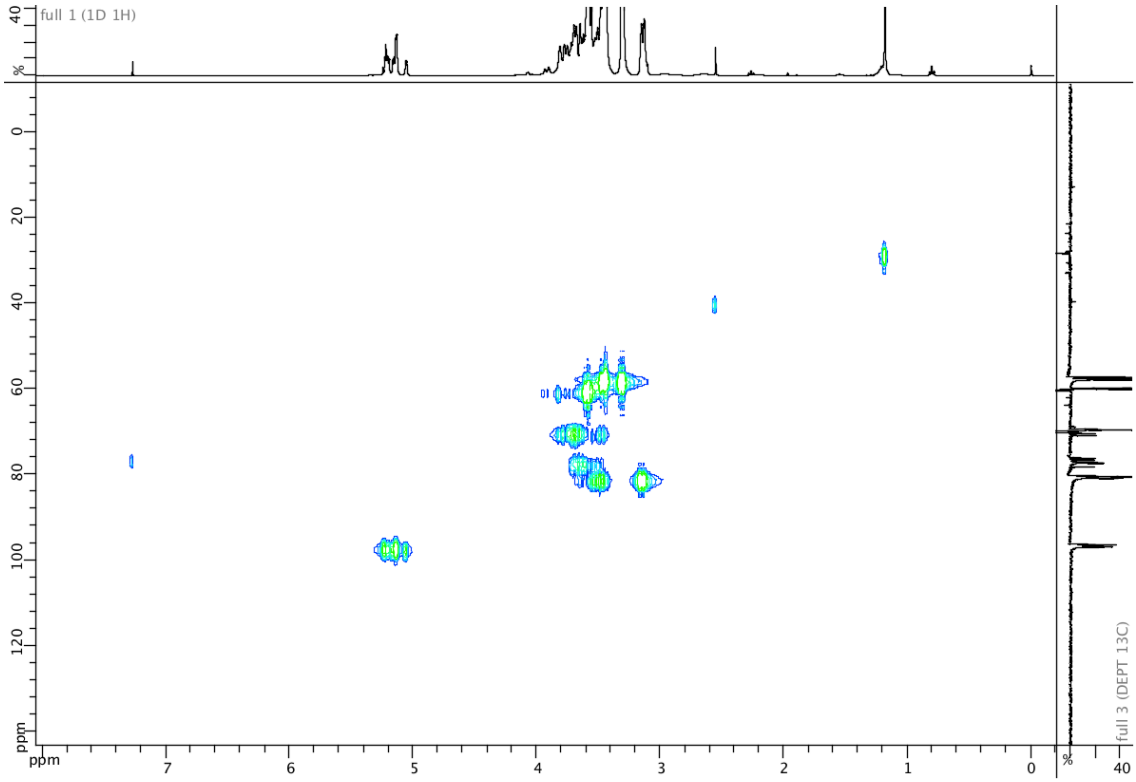
$^{1}H/^{1}H$ COSY spectrum of **10**.



$^{13}C\{^{1}H\}$ NMR spectrum of **10**.



DEPT 135 spectrum of **10**.



$^{1}H/^{13}C$ HMQC spectrum of **10**.

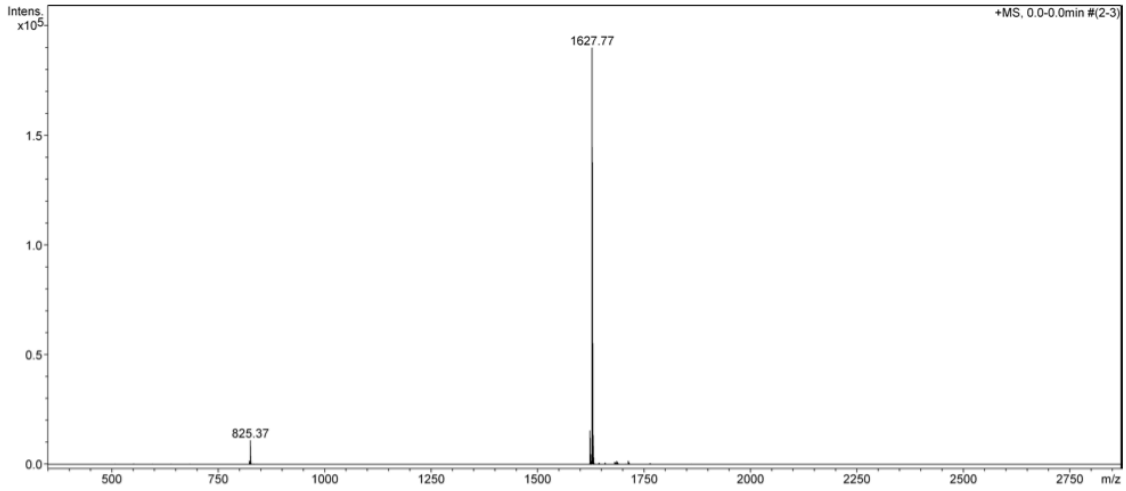
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15803ML.d	Acquisition Date	11/10/2011 3:39:03 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ85 diol	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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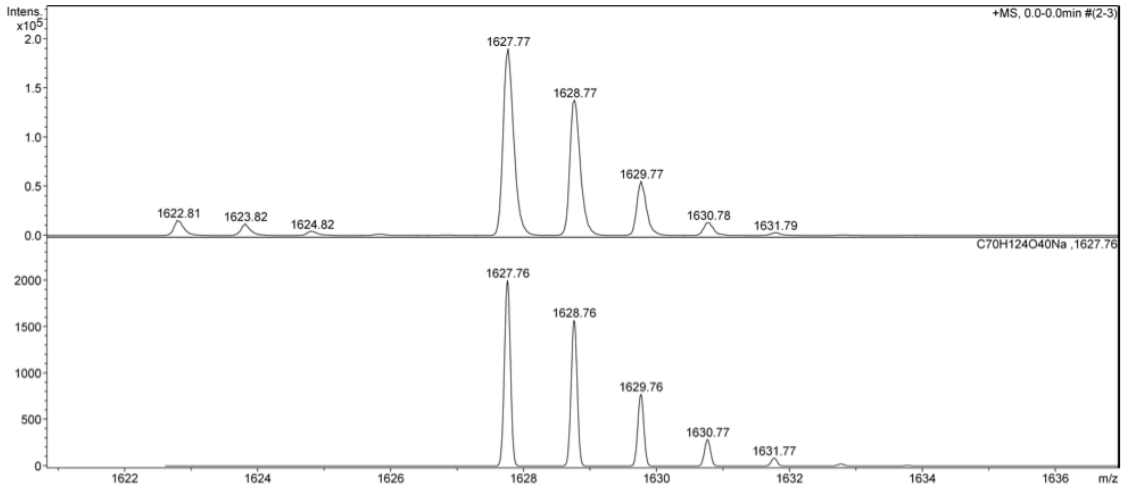
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15803ML.d	Acquisition Date	11/10/2011 3:39:03 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ85 diol	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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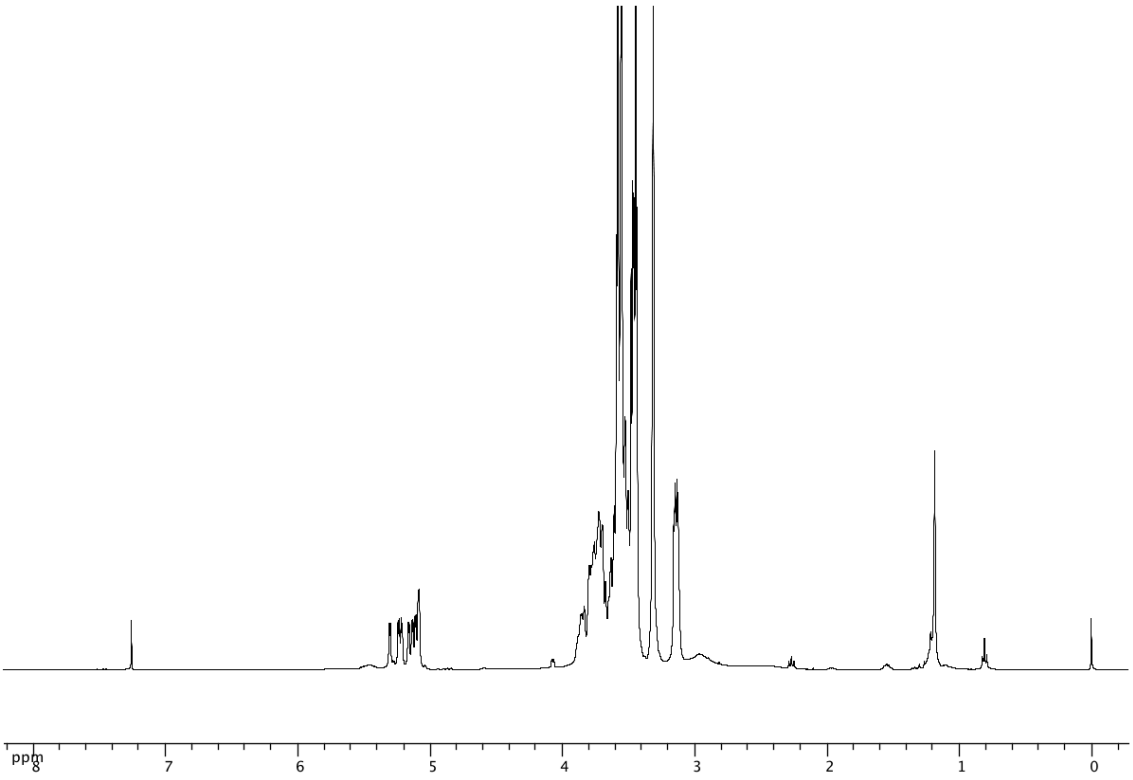
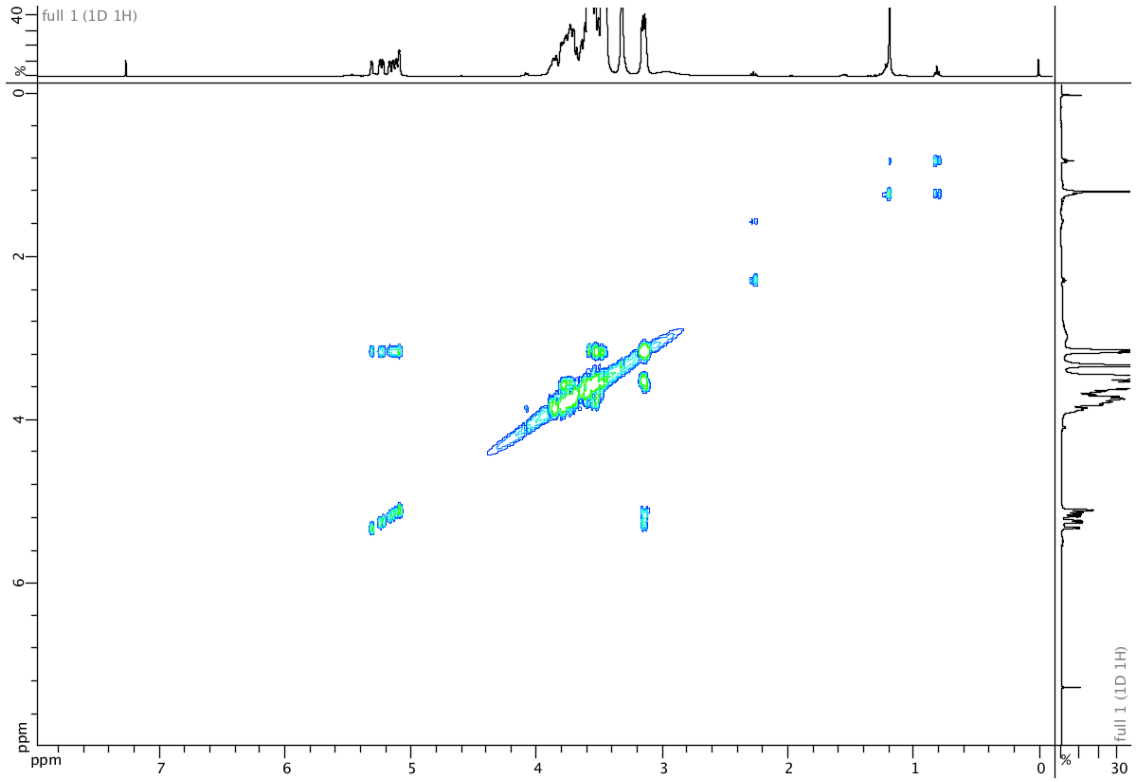
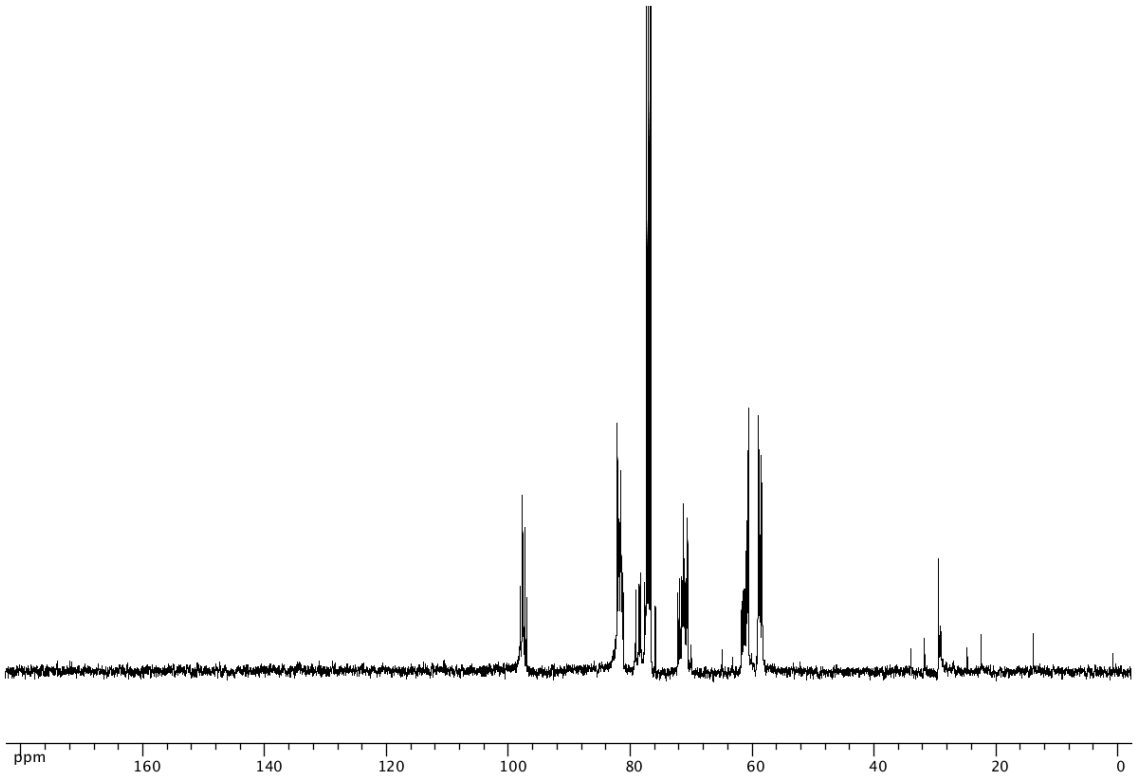
Mass spectrum of **10** and simulation.



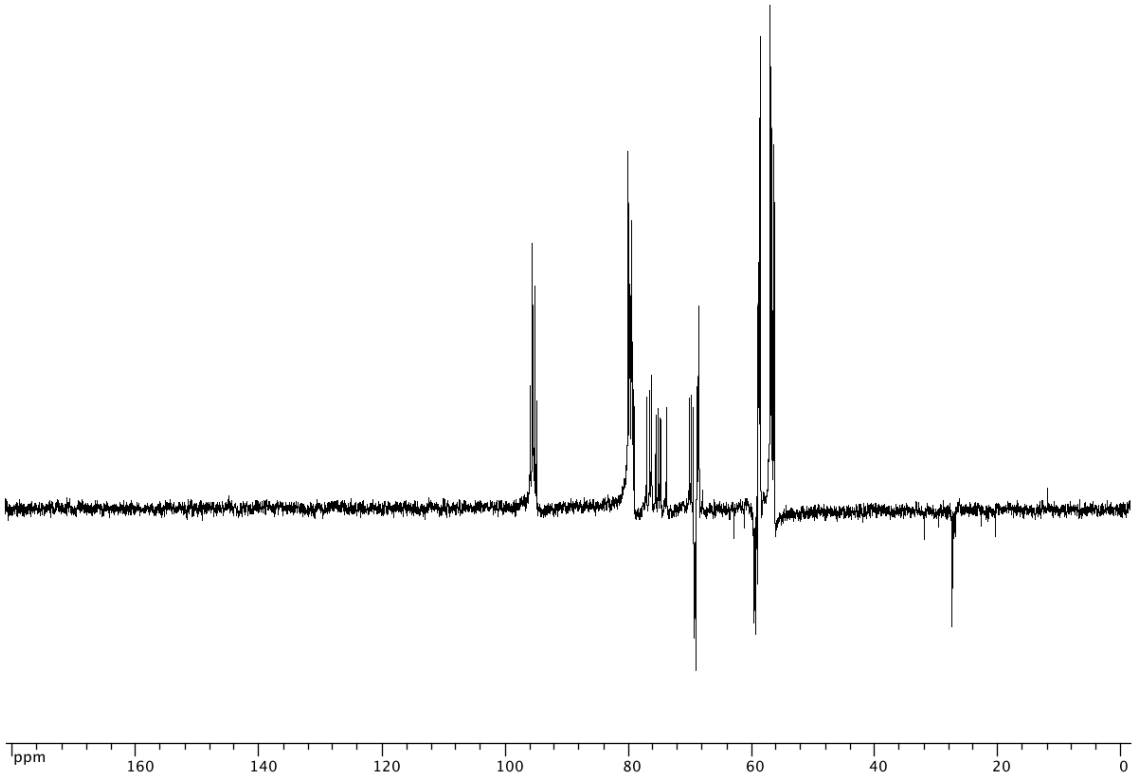
^{1}H NMR spectrum of **11**.



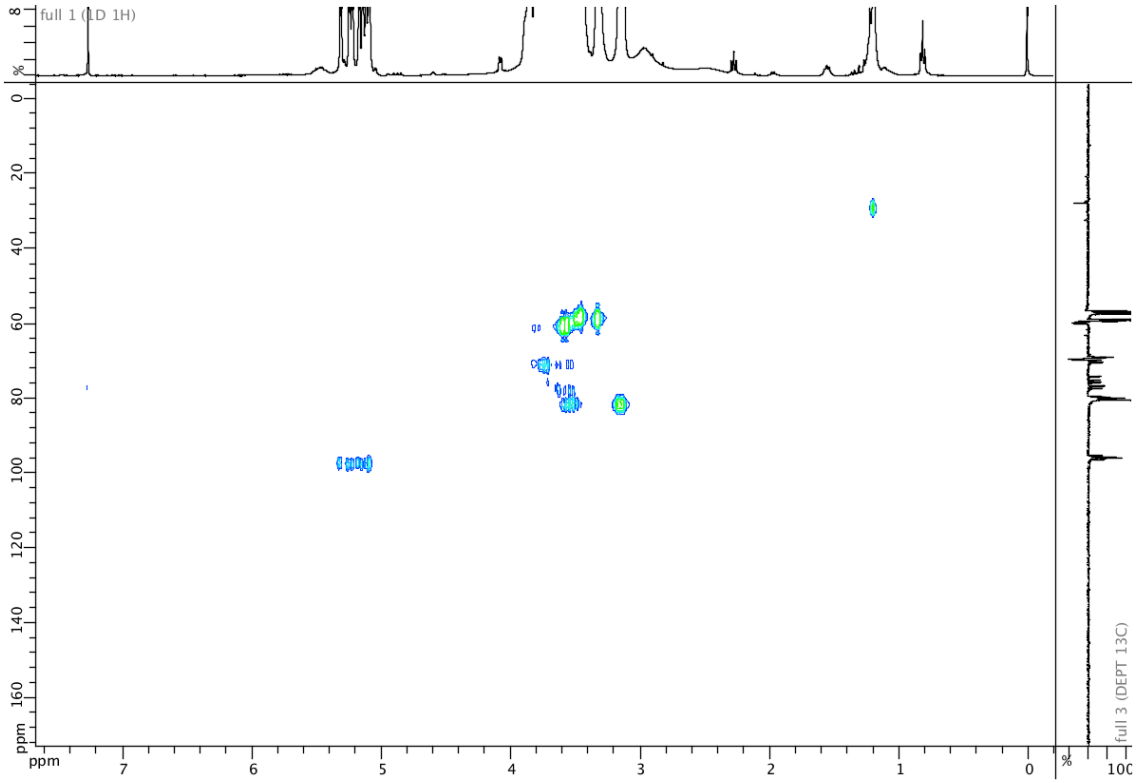
$^{1}H/^{1}H$ COSY spectrum of **11**.



$^{13}C\{^{1}H\}$ NMR spectrum of **11**.



DEPT 135 spectrum of **11**.



$^{1}H/^{13}C$ HMQC spectrum of **11**.

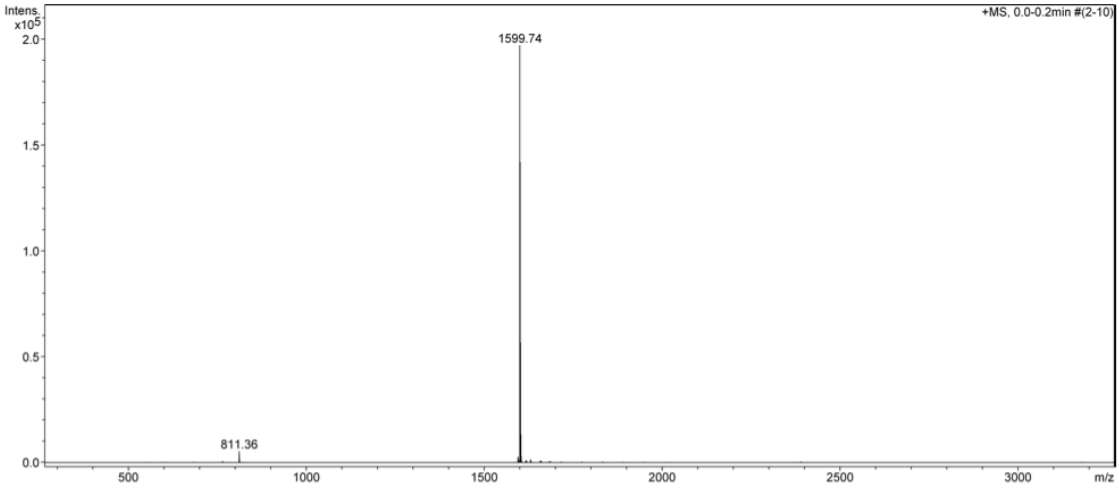
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15804ML.d	Acquisition Date	11/10/2011 3:42:37 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ85 C1	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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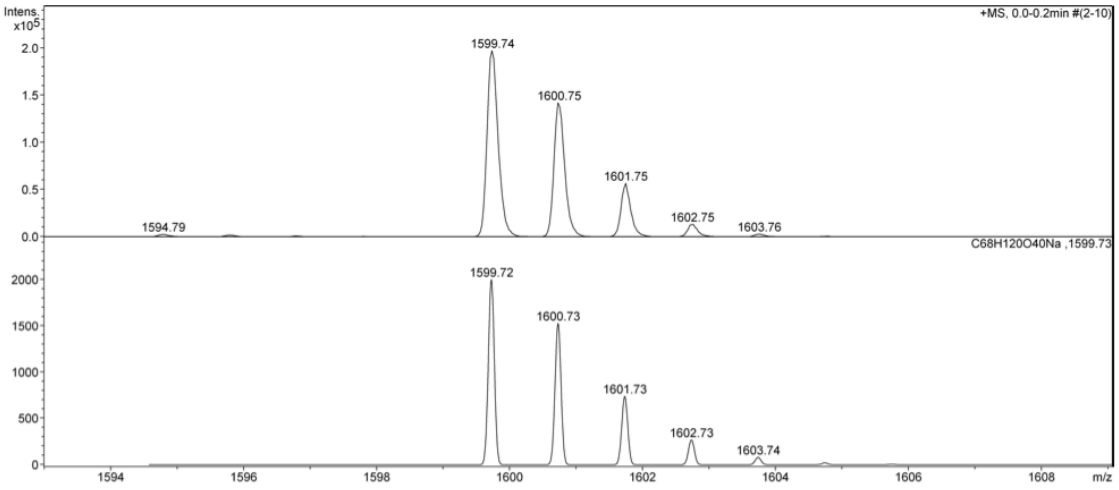
Service de spectrometrie de masse - Institut de Chimie - Strasbourg - UMR 7177 CNRS / ULP

Analysis Info

Analysis Name	O15804ML.d	Acquisition Date	11/10/2011 3:42:37 PM
Method	esi wide pos.m	Operator	Administrator
Sample Name	MJ85 C1	Instrument	micrOTOF
Comment			

Acquisition Parameter

Source Type	ESI	Capillary	4500 V	Nebulizer	0.4 Bar	Corona	219 nA
Ion Polarity	Positive	Set Capillary Exit	150.0 V	Dry Gas	4.0 l/min	Set Hexapole RF	300.0 V
Scan Range	n/a	Set Skimmer 1	50.0 V	Dry Heater	180 °C	APCI Heater	517 °C



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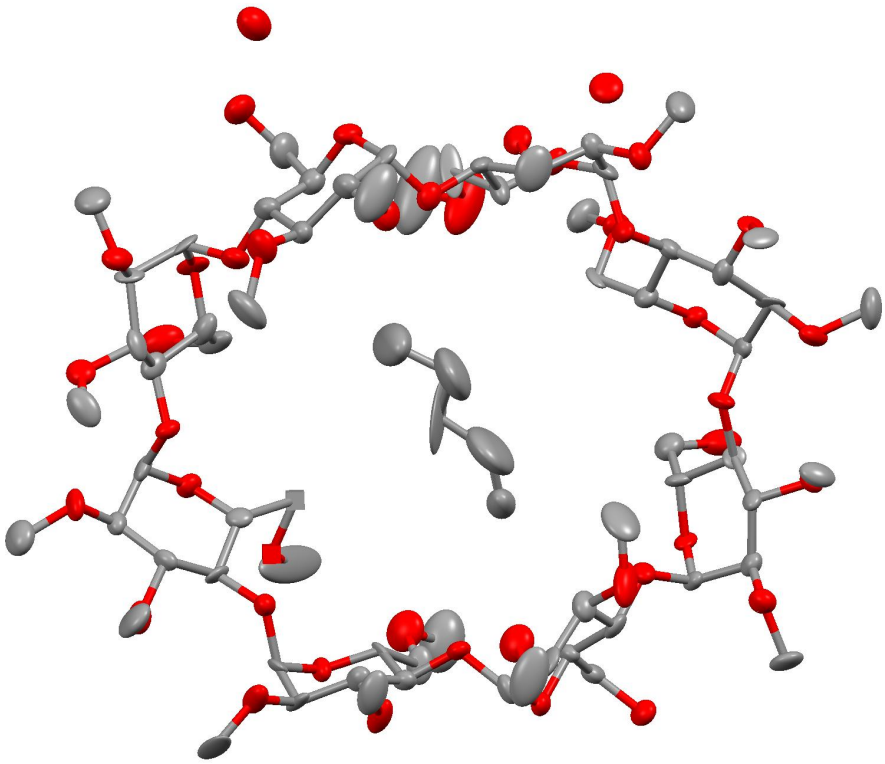
Mass spectrum of **11** and simulation.

Crystal structure analysis



X-ray crystallographic data of 9: Single crystals of **9** were obtained by slow diffusion of pentane into a dichloromethane solution of the compound. Crystal data for $C_{70.5}H_{130}O_{42}$ (**9**·$2H_2O$·$0.5C_5H_{12}$), M_r = 1649.74, orthorhombic, space group $P2_12_12_1$, a = 15.485(1), b = 23.254(1), c = 27.718(1) Å, V = 9981.2(8) Å^3, Z = 4, ρ_{calcd} = 1.098 g cm^{-3}, $\lambda(Mo_{K\alpha})$ = 0.71073 Å, μ = 0.090 mm^{-1}, $F(000)$ = 3556, T = 100(2) K. The sample (0.32 × 0.25 × 0.07 mm) was studied with an Oxford Diffraction Xcalibur Saphir 3 CCD with graphite monochromatised $Mo_{K\alpha}$ radiation. The structure was solved with SIR-97,[16] which revealed the non-hydrogen atoms of the molecule. After anisotropic refinement, many hydrogen atoms were found with a Fourier difference analysis. The whole structure was refined with SHELX-97[17] and full-matrix least-square techniques. Use of F^2 magnitude; x, y, z, β_{ij} for C, O atoms, x, y, z, in riding mode for H atoms, 982 variables and 5983 observations with [$I > 2.0\sigma(I)$], calcd $w = 1/[\sigma^2(F_o^2) + (0.1186\ P)^2]$ where $P = (F_o^2 + 2\ F_o^2)/3$ with the resulting R = 0.0700, R_W = 0.2129, and S_w = 0.691, $\Delta\rho$ < 0.409 e Å^{-3}. CCDC 862358 (**9**) contain the supplementary crystallographic data for this report. These data can be obtained free of charge from The Cambridge Christallographic Data Centre via www.ccdc.cam. ac.uk/data_request/cif.

General procedure for assignment of the glucose units linked by a given capping unit.[3]

Our strategy for full structural assignment began with the differentiation between capped and non-capped C-6 carbon atoms by DEPT 135. These appear as two distinct sets of signals. The H-6 protons were then identified using ^{1}H-^{13}C HMQC (Heteronuclear Multiple Quantum Coherence spectroscopy). By using TOCSY (TOtal Correlation SpectroscopY) and COSY (COrrelated SpectroscopY), each H-6 proton was correlated to the set of protons belonging to the same glucose residue. The connectivity between individual glucose units was then established via a ROESY (Rotating frame Overhause Effect SpectroscopY) experiment showing the proximity between H-4$_N$ and H-1$_{N+1}$ protons (N and N+1 standing for neighbouring glucose moieties labelled in the alphabetical order).

References

1. A. Altomare, J. Foadi, C. Giacovazzo, A. G. G. Moliterni, M. C. Burla and G. Polidori, *J. Appl. Crystallogr.*, 1998, **31**, 74-77.
2. G. M. Sheldrick, SHELXL-97, *Program for Crystal Structure Refinement*, 1997, University of Göttingen, Göttingen (Germany).
3. H.-J. Schneider, F. Hacket and V. Rüdiger, *Chem. Rev.*, 1998, **98**, 1755-1785.