Supporting Information

Disodium cromoglycate: exploiting its properties as a NMR weak-aligning medium for small organic molecules

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1. Materials and methods

Cromolyn disodium salt hydrate ($C_{23}H_{14}Na_2O_{11}\cdot H_2O$; MW=512.33 Da as anhydrous) was purchased from TCI Europe (purity >98.0%); 5-norbornen-2-ol ($C_7H_{10}O$; MW=110.15 Da) was purchased from Sigma Aldrich (purity 99%) as a mixture of the *–endo* and *–exo* isomers; methyl-β-D-galactopyranoside ($C_7H_{14}O_6$; MW=194.18 Da) was purchased from Sigma Aldrich; D-(+)-lactose monohydrate ($C_{12}H_{22}O_{11}\cdot H_2O$; MW=343.20 Da as anhydrous) was purchased from Sigma Aldrich; *N*-methyl-codeinium iodide was synthesized following a literature procedure.[1] All reagents were used without further purification.

The DSCG/D_2O phase was formed by dissolving 100 mg of cromolyn in 0.66 mg of D_2O at 70ºC and then letting the solution cool down. The DSCG/D_2O/NaCl nematic phase was formed by dissolving 50 mg of cromolyn and 10 mg of NaCl in 0.66 mg of D_2O at 50ºC and then letting the solution cool down. DSCG hexagonal phase was formed by dissolving 160 mg (in the case of the 21% wt sample) and 200 mg (in the case of the 25% wt sample) at 80ºC. Anisotropic samples were prepared by adding to one of the phases previously described, an amount between 5 and 20 mg of each compound. In the case of *N*-methyl-codeinium iodide in the DSCG/D_2O/NaCl, 60 mg of cromolyn were needed instead of 50 mg, since the ammonium cation stabilizes the isotropic phase in those conditions; therefore more cromolyn was required to form the liquid crystal phase.

2. NMR methodologies

^{1}H and ^{2}H cromolyn studies were performed on a Bruker AVANCE III spectrometer of 400.16 MHz for the

frequency of ^{1}H, 101 MHz for ^{13}C, and 60.38 MHz for ^{2}H. Isotropic samples were shimmed with the TopShim routine present in TopSpin 2.1, while anisotropic samples were heated up to the point were isotropic was recovered, automatically shimmed with TopShim and then, samples were allowed to cool down to the original temperatures.

Pseudo-2D ^{2}H experiments were collected on a Bruker AVANCE I spectrometer of 600.13 MHz for the frequency of ^{1}H, 150.90 MHz for ^{13}C, and 90.56 MHz for ^{2}H, and equipped with a TBI probe. A selective excitation experiment with selective excitation pulse in the presence of a gradient. A gradient strength of 55.5 Gs/cm was used, which corresponds to a spatial frequency gradient in the z-axis of 17974 Hz/cm. A Gaussian cascade selective excitation pulse Q5[2] (shape Q5.1000 from Bruker library) was used with a duration of 6180 µs, corresponding to an excitation bandwidth of 1000 Hz. At a frequency gradient of 17974 Hz/cm, this excitation bandwidth corresponds to a z-slice of 0.55 mm. A total of 31 spatially resolved 1D ^{2}H NMR experiments (one at the center and 15 above and below the center of the coil) were collected sweeping the offset frequency (SPOFFS) from -30000 to +30000 Hz with a phase alignment SPOAL = 1 in steps of 2000 Hz. The automation program popt from the Bruker library was used for this purpose, and the option "store as 2D data" was checked in order to generate the pseudo-2D datasets. Spectra were acquired with 2 scans per slice and experiments were processed in magnitude and baseline correction was applied in the F2 dimension.

^{1}H, ^{13}C, COSY and HSQC needed to assign the signals of each compound and ^{13}C gated-decoupled experiments performed on methyl-β-D-galactopyranoside were performed on a Bruker AVANCE III spectrometer of 400.16 MHz for the frequency of ^{1}H, 101 MHz for ^{13}C, and 60.38 MHz for ^{2}H. *J* Scaled F1 Coupled HSQC and P.E.COSY experiments were performed on a Bruker AVANCE I spectrometer of 600.13 MHz for the frequency of ^{1}H, 150.90 MHz for ^{13}C, and 90.56 MHz for ^{2}H. ^{13}C gated-decoupled experiments were acquired using the zggd pulse sequence of the Bruker catalogue using 64k points (32k complex points) and a relaxation delay d1 of 0.1 s. Spectral window was centered between 20 and 120 ppm (sw=100 ppm, o1p=70 ppm). The respective experiments in the different LC phases were acquired using 8k scans and they were apodized with an exponential window function of 1.00. Lactose *J* Scaled BIRD HSQC experiments in isotropic (D_2O) and anisotropic conditions (cromolyn/NaCl) were acquired at 293K with 12 scans, 640 points in F2 and 2048 in F1 and spectral windows of 6 ppm in the direct dimension and 60 ppm in the indirect dimension, setting the offset in the indirect dimension in 82.5 ppm. In the case of the *J* Scaled BIRD HSQC at 303K in isotropic conditions in the sample with cromolyn/NaCl, 4 scans were acquired with 1024 points in F2 and 2048 points in F1, and spectral windows of 10 ppm and 100 ppm in F2 and F1 respectively, in order to check if signals from cromolyn would appear in the aromatic region of the spectrum. Lactose p.e.COSY experiment in anisotropic conditions was acquired at 293K with 4 scans, 4096 points in F2 and 1024 in F1 and spectral windows of 1.5 ppm in both dimensions. 5-Norbornen-2-ol *J* Scaled BIRD HSQC experiments were acquired at 293K with 24 scans, 896 points in F2 and 2048 in F1 and spectral windows of 8 ppm in the direct dimension and 160 ppm in the indirect dimension, setting the offset in the indirect dimension in 80 ppm. *N*-methyl-codeinium iodide *J* Scaled BIRD HSQC experiments were acquired at 293K with 4 scans for the isotropic sample and 8 for the anisotropic one, 512 points in F2 and 2048 in F1 and spectral windows of 6 ppm in the direct dimension for the isotropic sample and 5.5 for the anisotropic sample, and 160 ppm in the indirect dimension, setting the offset in the indirect dimension in 80 ppm. All *J* Scaled BIRD HSQC were performed using a scaling factor κ=3 for the C-H coupling. An HETCOR experiment was used to try to obtain isotropic and anisotropic peaks from *N*-methyl codeinium iodide in the same experiment at 299K. The experiment was acquired with 65K points in F2 and 128 in F1, with spectral windows of 140.0 and 10.0 ppm in F2 and F1 respectively.

3. Computational methodologies

A D-(+)-lactose molecular dynamics run was provided by Martín-Pastor from a previous study on lactose.[3] The structures from the MD run were optimized at DFT level using the B3LYP[4] functional and the 6-311G* basis set using Gaussian09.[5] We include here only the geometry for the RDC best fit structure, which corresponds to the syn-syn conformation. 5-Norbornen-2-ol 3D structures were generated with OpenBabel-2.3.1[6,7] from 2D ChemDraw structures, and they were DFT optimized using B3LYP/6-311G* as functional and basis set combination. The *N*-methyl-codeinium iodide structure that rendered the best *Q* factor in a previous work in our group[8] was used as a model to fit the RDC data extracted for it. The structures rendered by a MMFF94s[9,10] molecular mechanics (MM) conformational search were then DFT optimized using M06L[11] functional and the 6-31G** basis set. The lowest energy structure named as MCI_1A was the one used to fit the RDC data extracted from the cromolyn/NaCl medium. All calculations were performed using water IEFPCM as solvent model.[12]

4. NMR spectra

4.1 Methyl-β-D-galactopyranoside

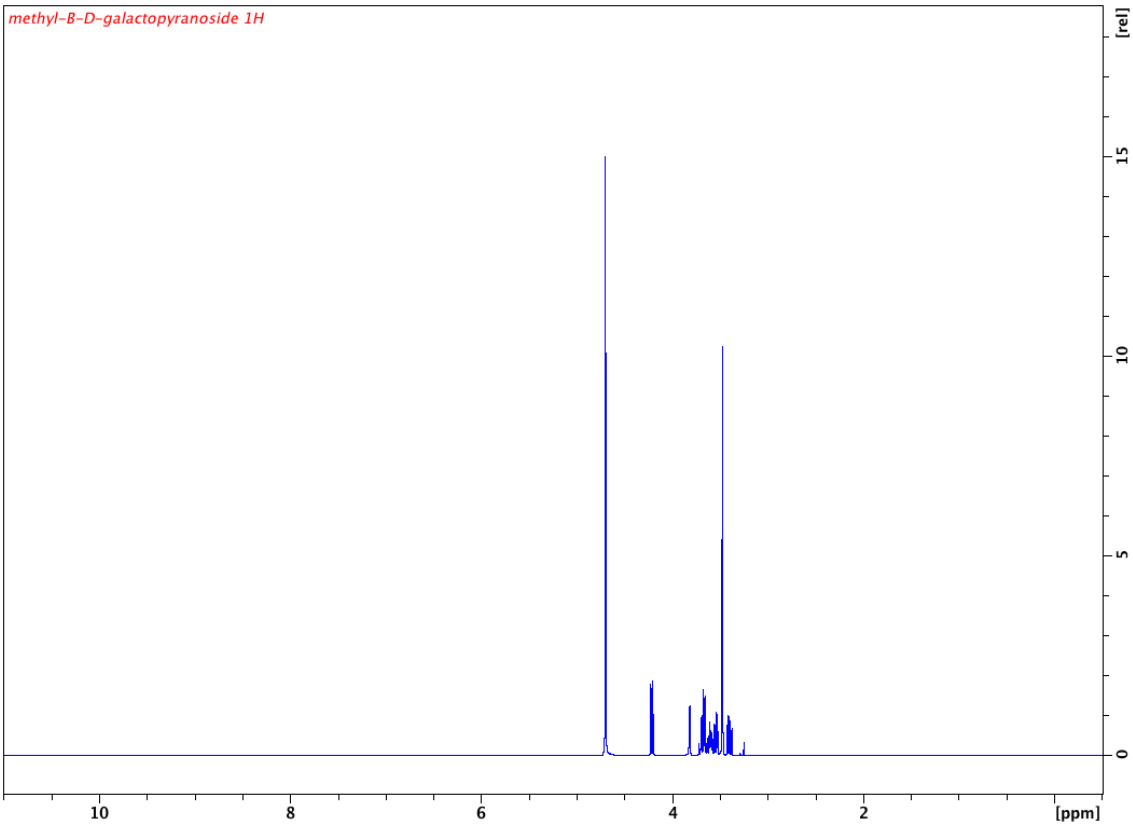

Fig. S1 Methyl-β-D-galactopyranoside ^{1}H 1D spectrum (400 MHz, D_2O, 293K).

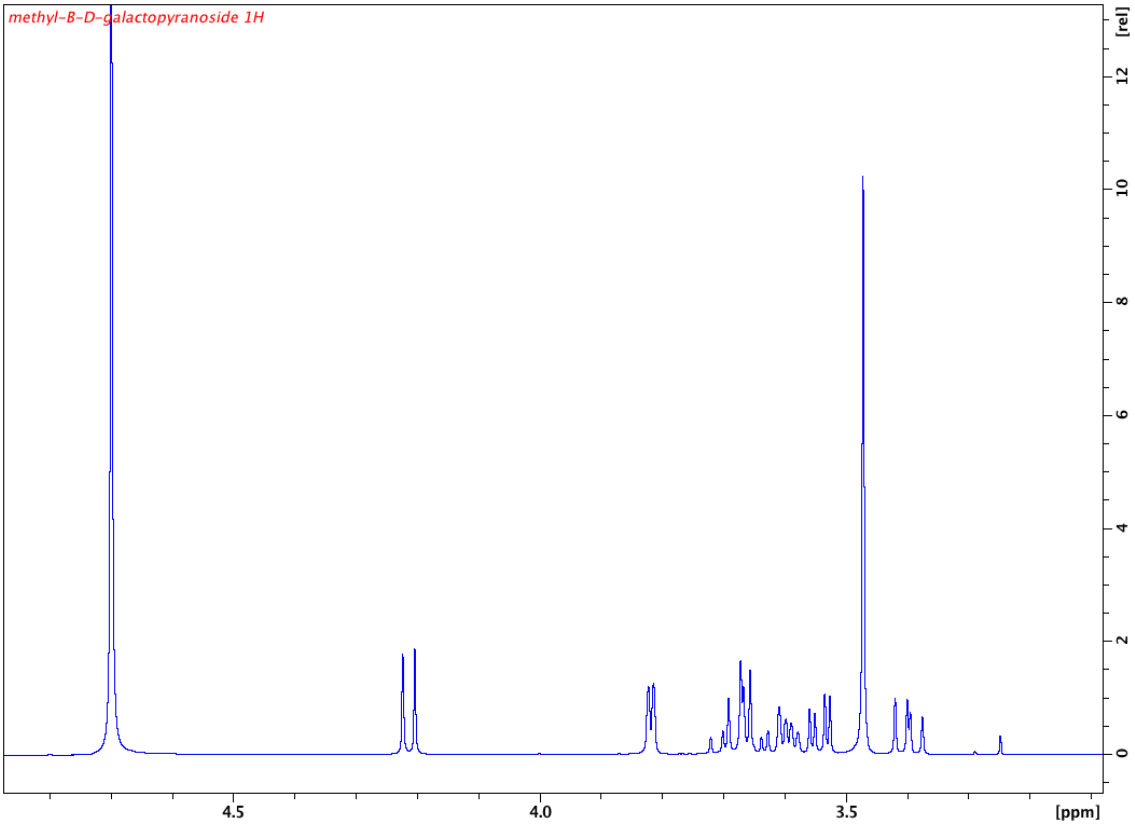

Fig. S2 Amplified methyl-β-D-galactopyranoside ^{1}H 1D spectrum (400 MHz, D_2O, 293K).

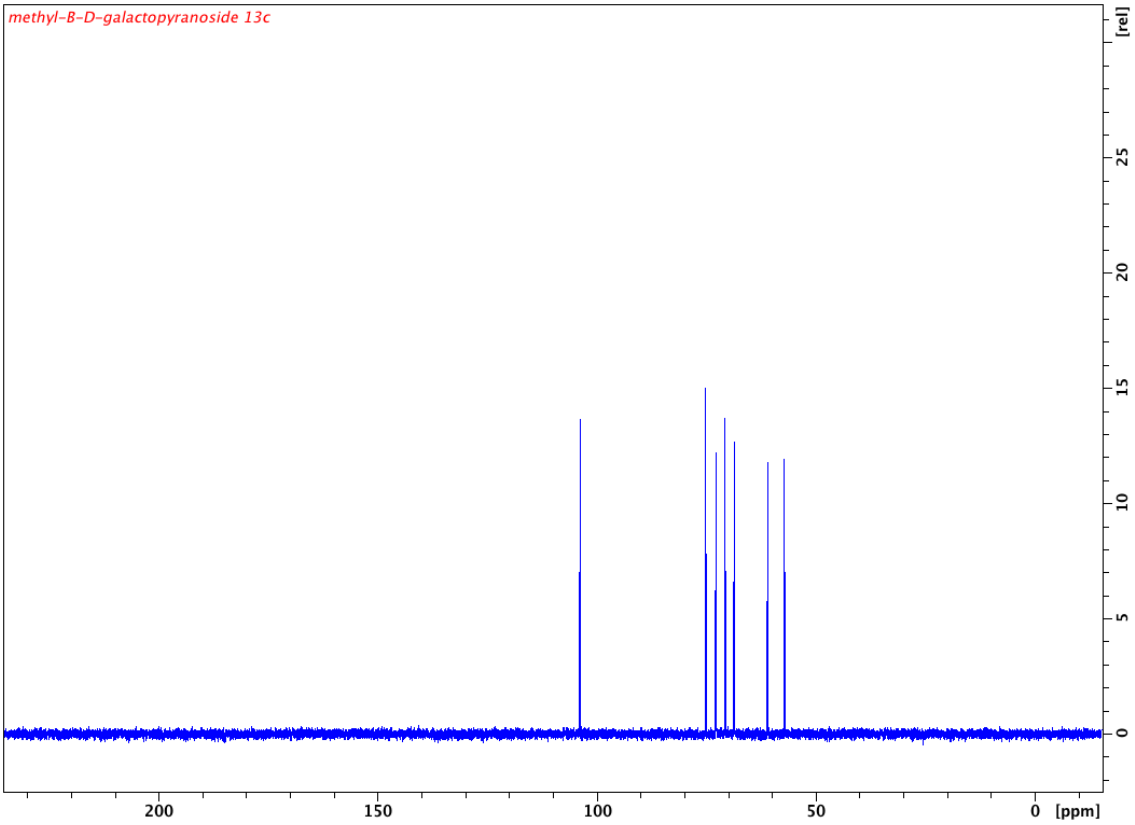

Fig. S3 Methyl-β-D-galactopyranoside ^{13}C 1D spectrum (101 MHz, D_2O, 293K).

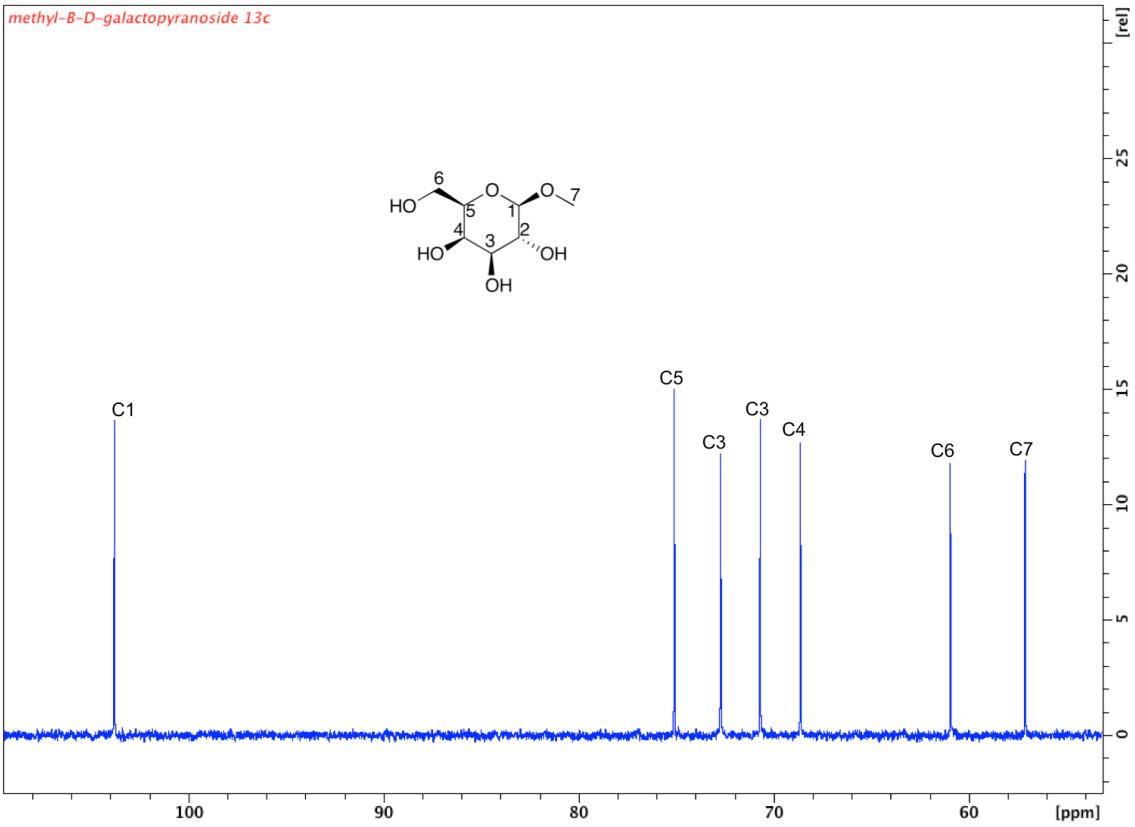

Fig. S4 Annotated methyl-β-D-galactopyranoside ^{13}C 1D spectrum (101 MHz, D_2O, 293K).

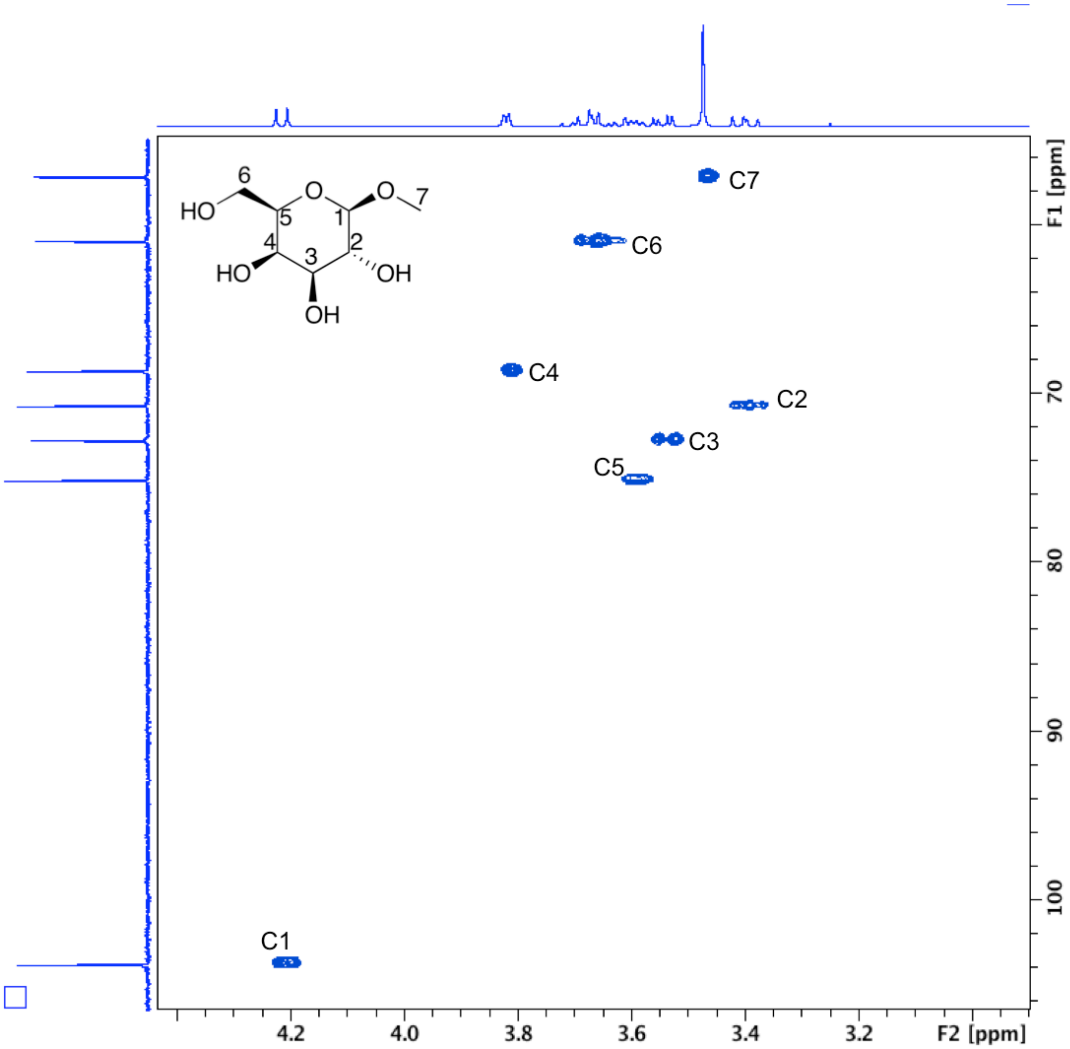

Fig. S5 Annotated methyl-β-D-galactopyranoside HSQC 2D spectrum (400 MHz, D_2O, 293K).

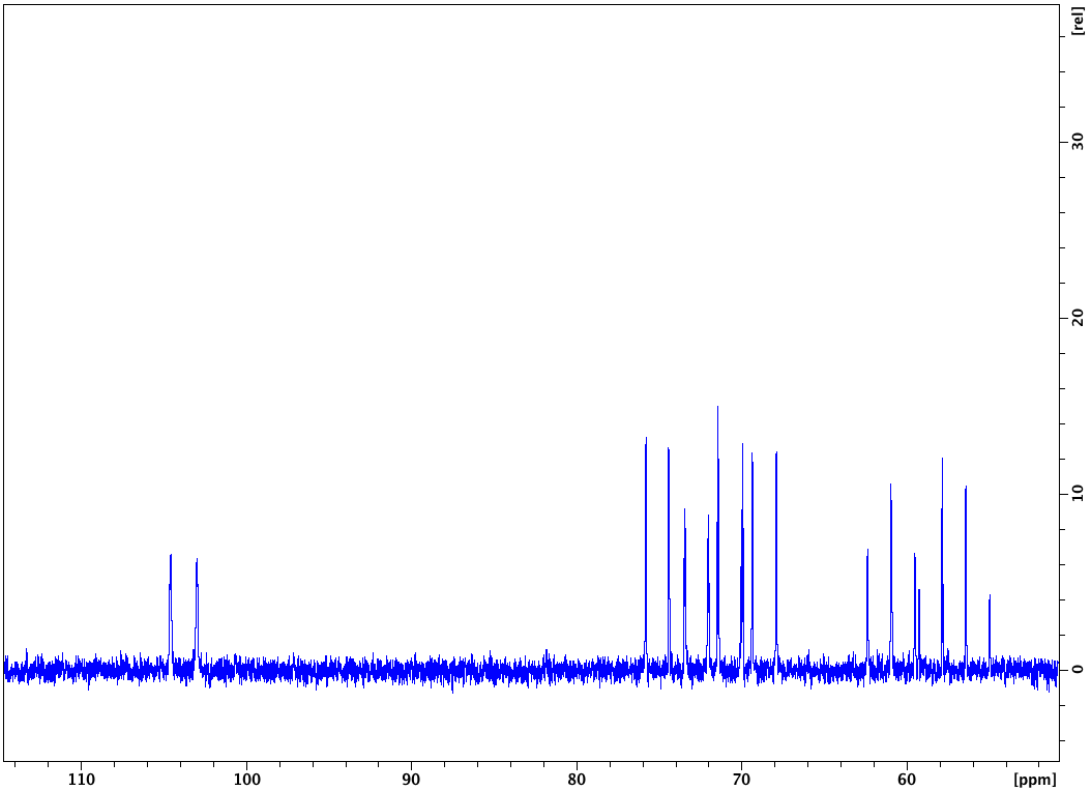

Fig. S6 Methyl-β-D-galactopyranoside ^{13}C gated decoupled 1D spectrum (101 MHz, D_2O, 293K).

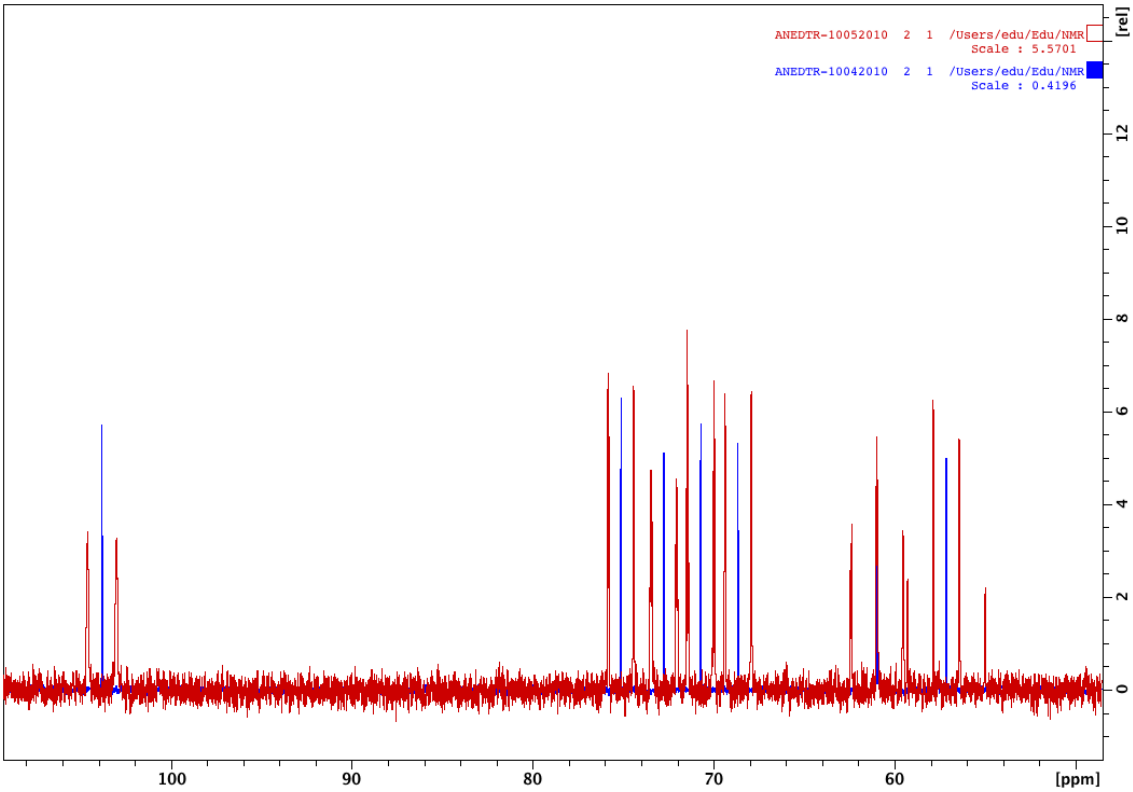

Fig. S7 Superimposed ^{13}C and isotropic ^{13}C gated decoupled methyl-β-D-galactopyranoside 1D spectra (101 MHz, D_2O, 293K).

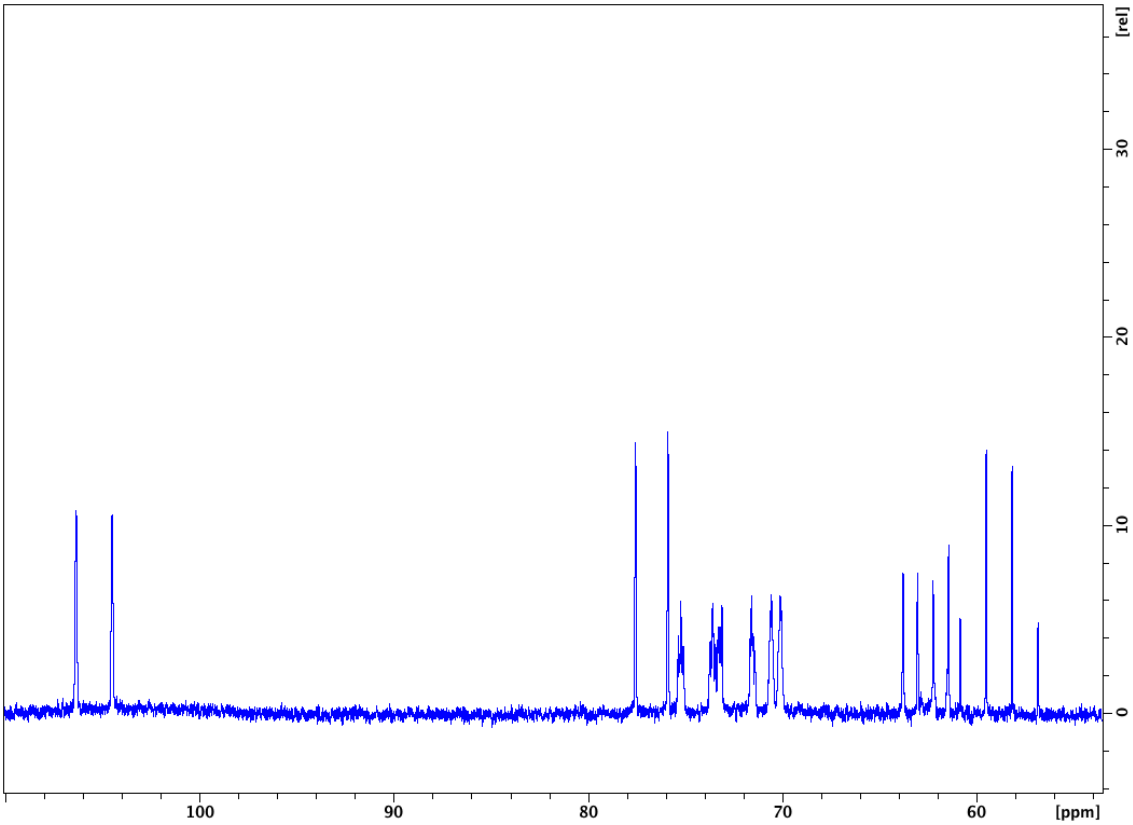

Fig. S8 Anisotropic methyl-β-D-galactopyranoside ^{13}C gated decoupled 1D spectrum (101 MHz, DSCG (13 wt. %), D_2O, 293K).

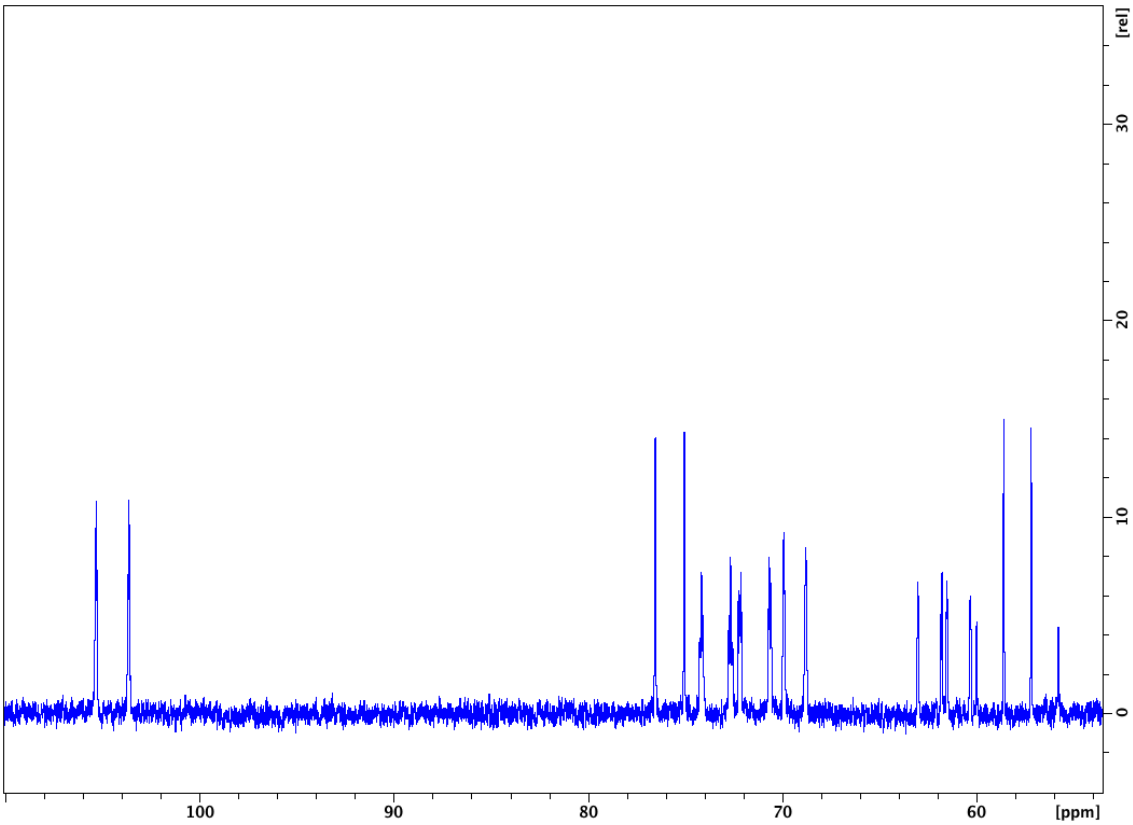

Fig. S9 Anisotropic methyl-β-D-galactopyranoside ^{13}C gated decoupled 1D spectrum (101 MHz, DSCG (7 wt. %)/NaCl, D_2O, 293K).

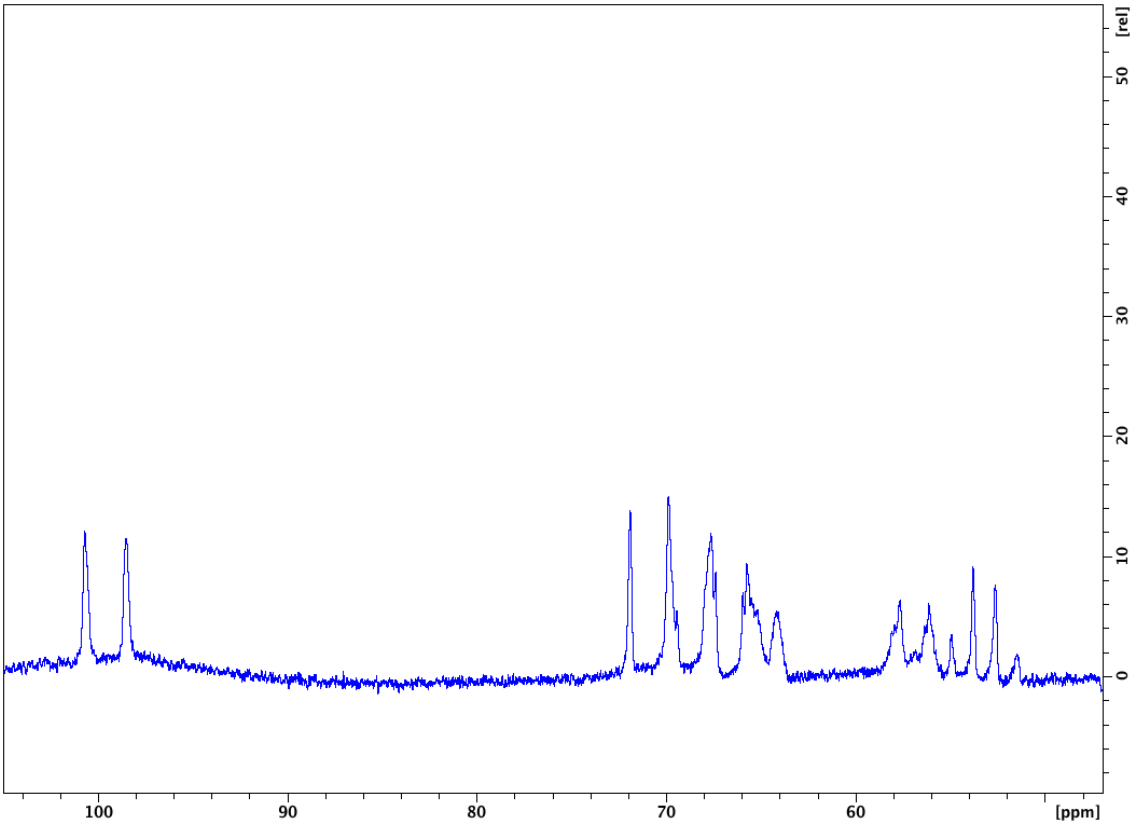

Fig. S10 Anisotropic methyl-β-D-galactopyranoside ^{13}C gated decoupled 1D spectrum (101 MHz, DSCG (25 wt. %), D_2O, 293K).

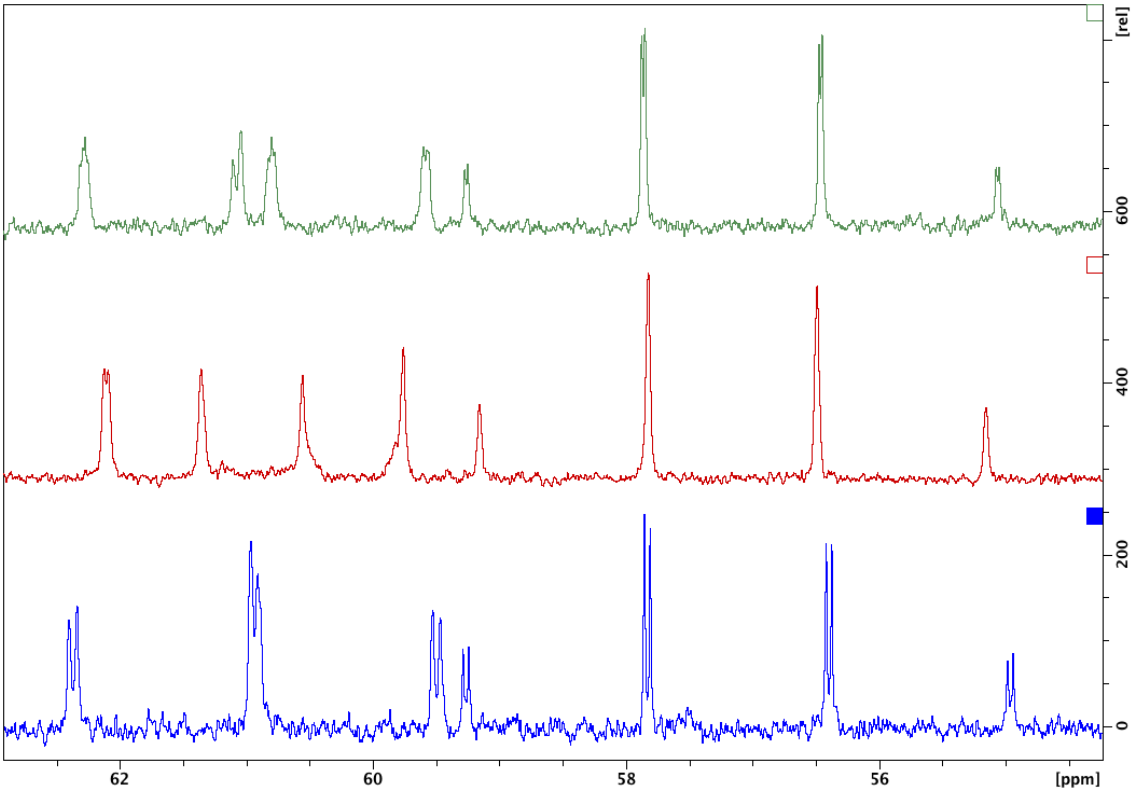

Fig. S11 Amplified stacked ^{13}C gated decoupled 1D isotropic (blue), anisotropic in the DSCG/D_2O (red) phase and anisotropic in DSCG/D_2O/NaCl phase (green) methyl-β-D-galactopyranoside spectra (101 MHz).

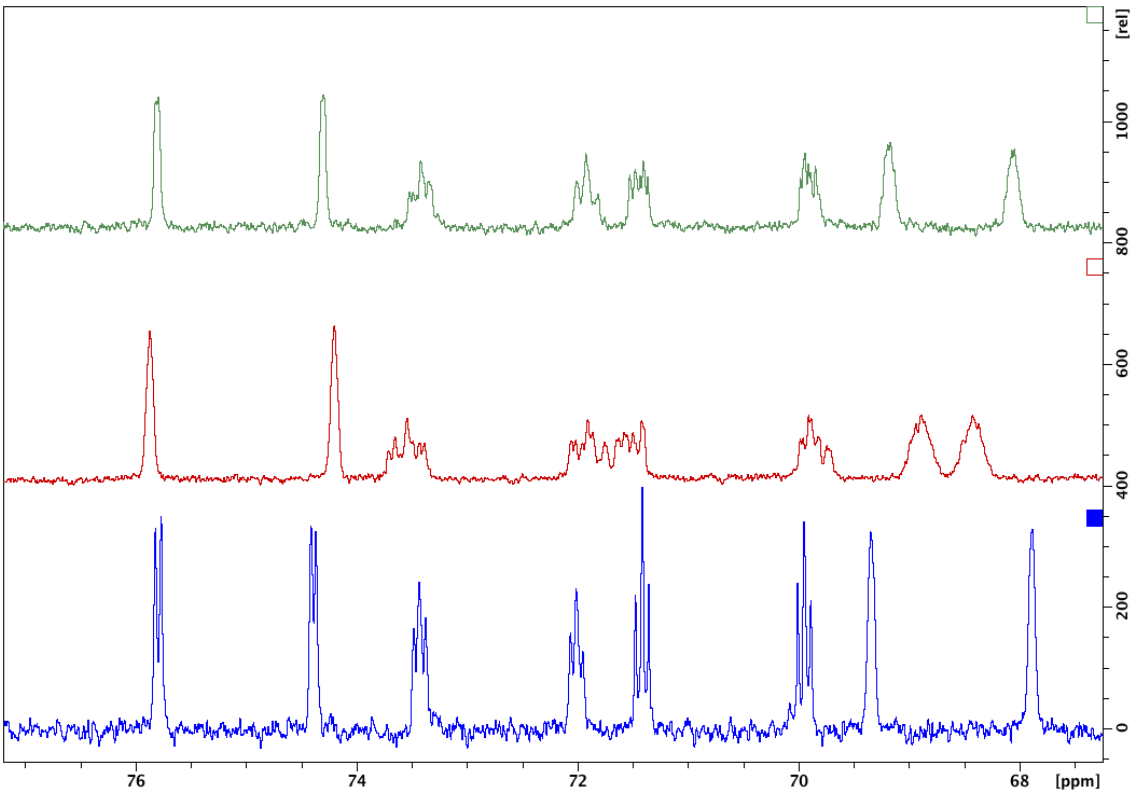

Fig. S12 Amplified stacked ^{13}C gated decoupled 1D isotropic (blue), anisotropic in the DSCG/D_2O (red) phase and anisotropic in DSCG/D_2O/NaCl phase (green) methyl-β-D-galactopyranoside spectra (101 MHz).

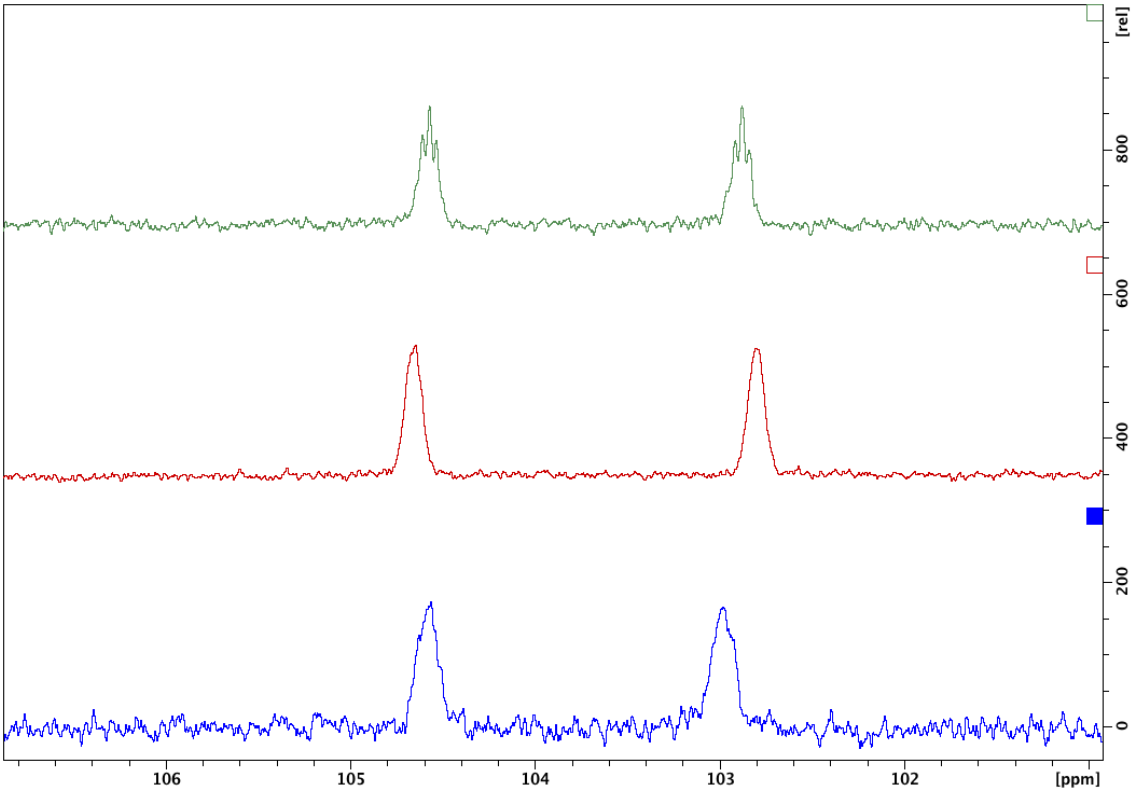

Fig. S13 Amplified stacked ^{13}C gated decoupled 1D isotropic (blue), anisotropic in the DSCG/D_2O (red) phase and anisotropic in DSCG/D_2O/NaCl phase (green) methyl-β-D-galactopyranoside spectra (101 MHz).

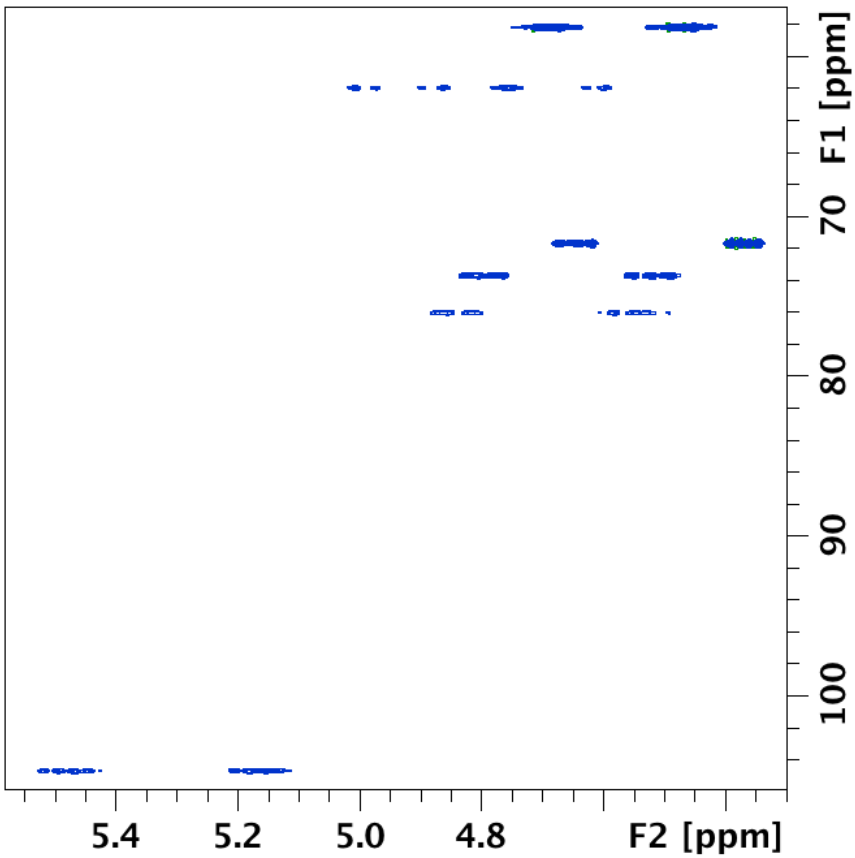

Fig. S14 Methyl-β-D-galactopyranoside F2 coupled HSQC spectrum in the DSCG N phase (400 MHz, D_2O, 293K).

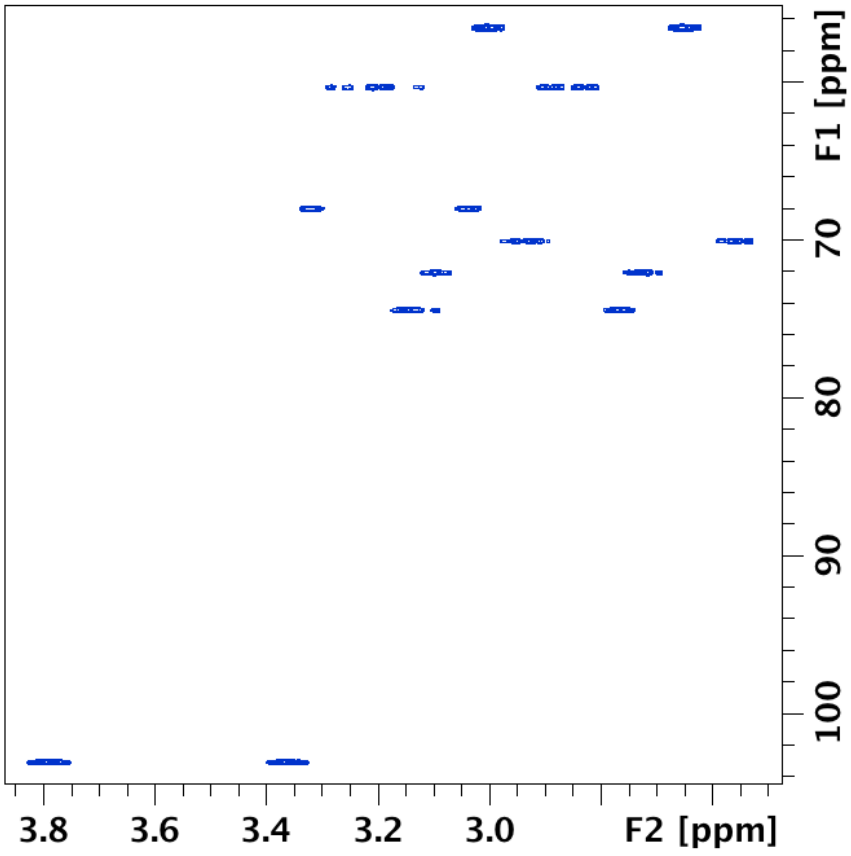

Fig. S15 Methyl-β-D-galactopyranoside F2 coupled HSQC spectrum in the DSCG N phase (600 MHz, D_2O, 293K).

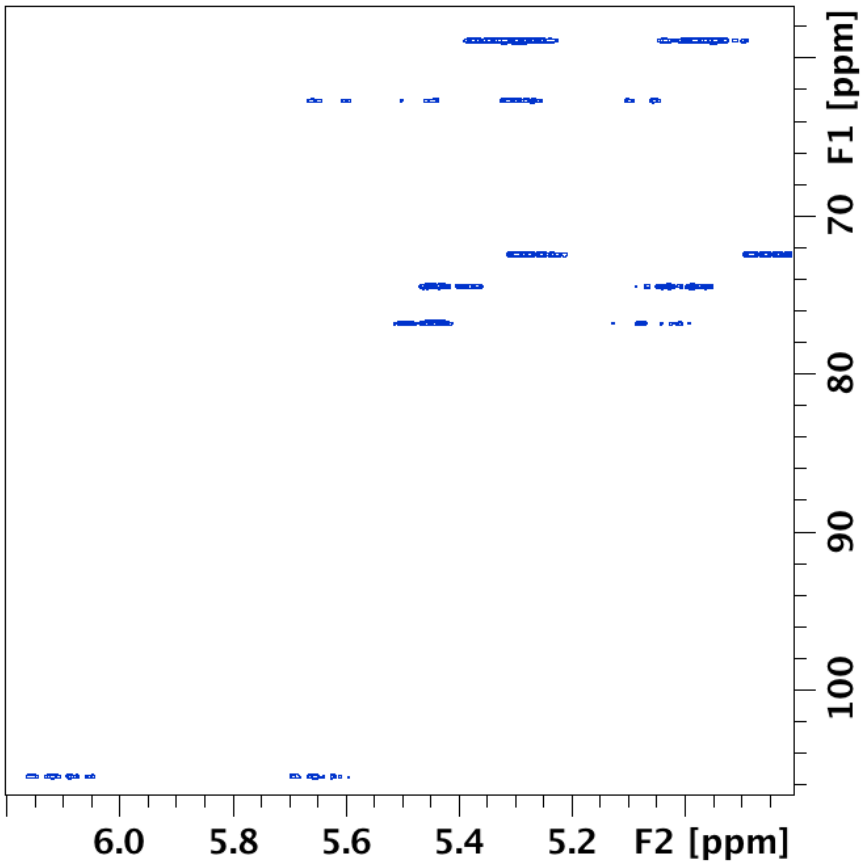

Fig. S16 Methyl-β-D-galactopyranoside F2 coupled HSQC spectrum in the DSCG N^d phase (400 MHz, D_2O, 293K).

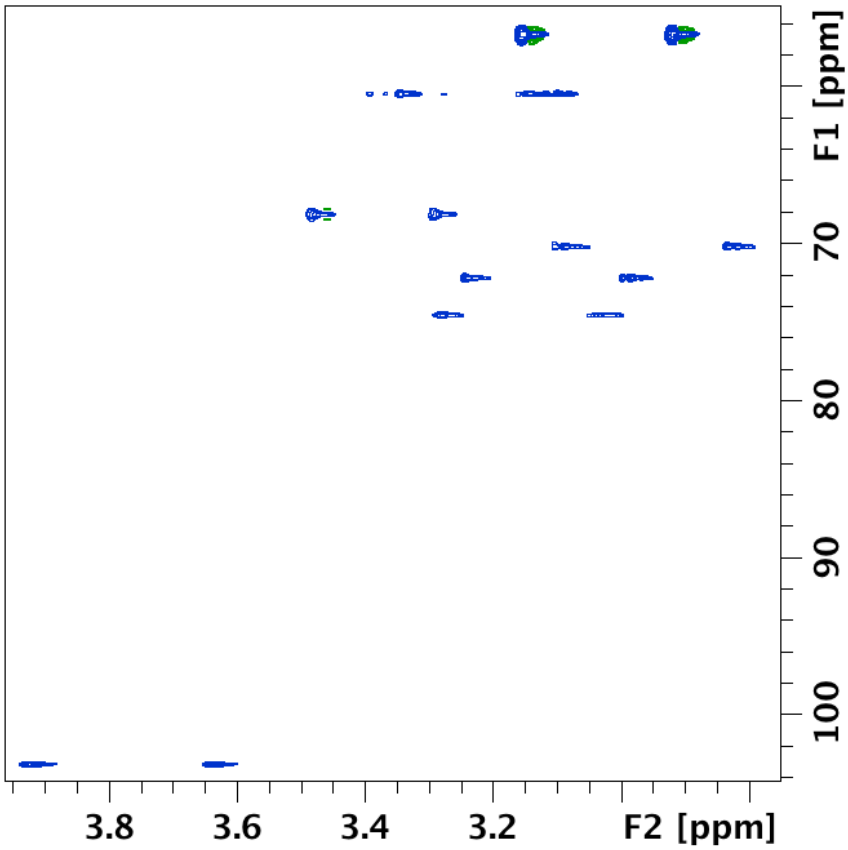

Fig. S17 Methyl-β-D-galactopyranoside F2 coupled HSQC spectrum in the DSCG N^d phase (600 MHz, D_2O, 293K).

4.2 Lactose

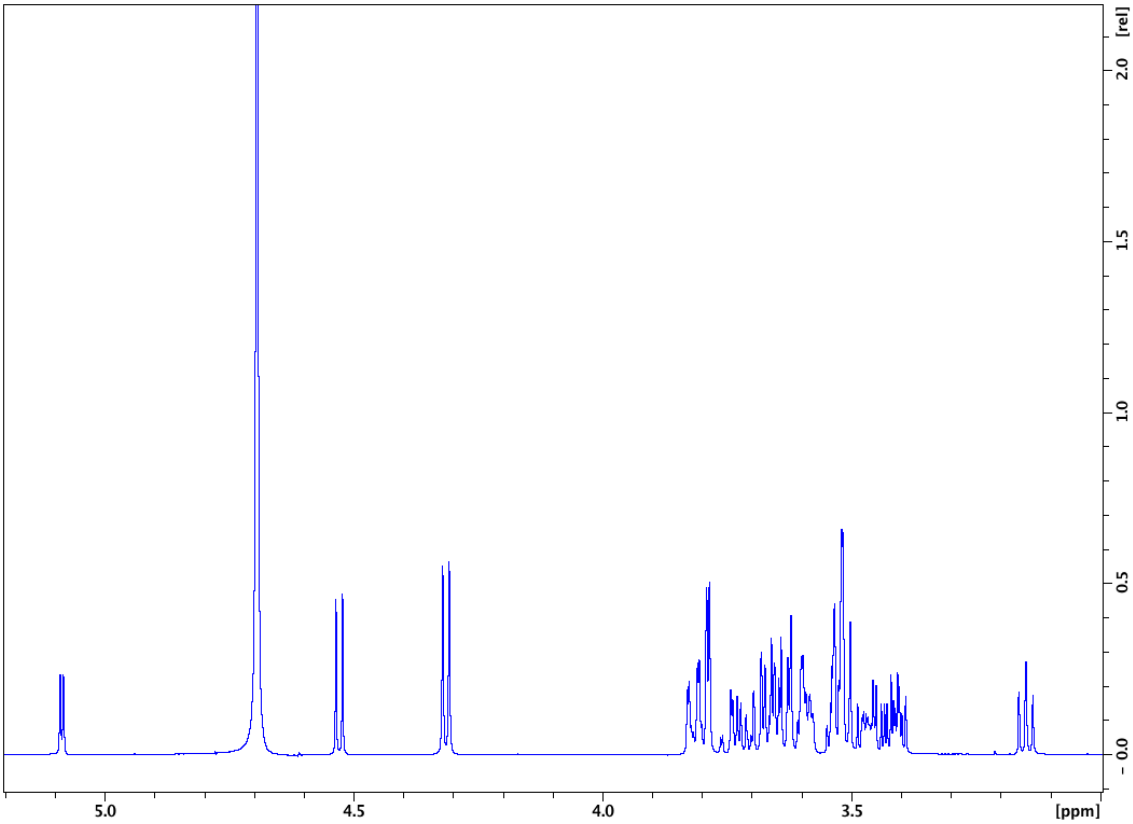

Fig. S18 D-(+)-Lactose ^{1}H 1D spectrum (400 MHz, D_2O, 293K).

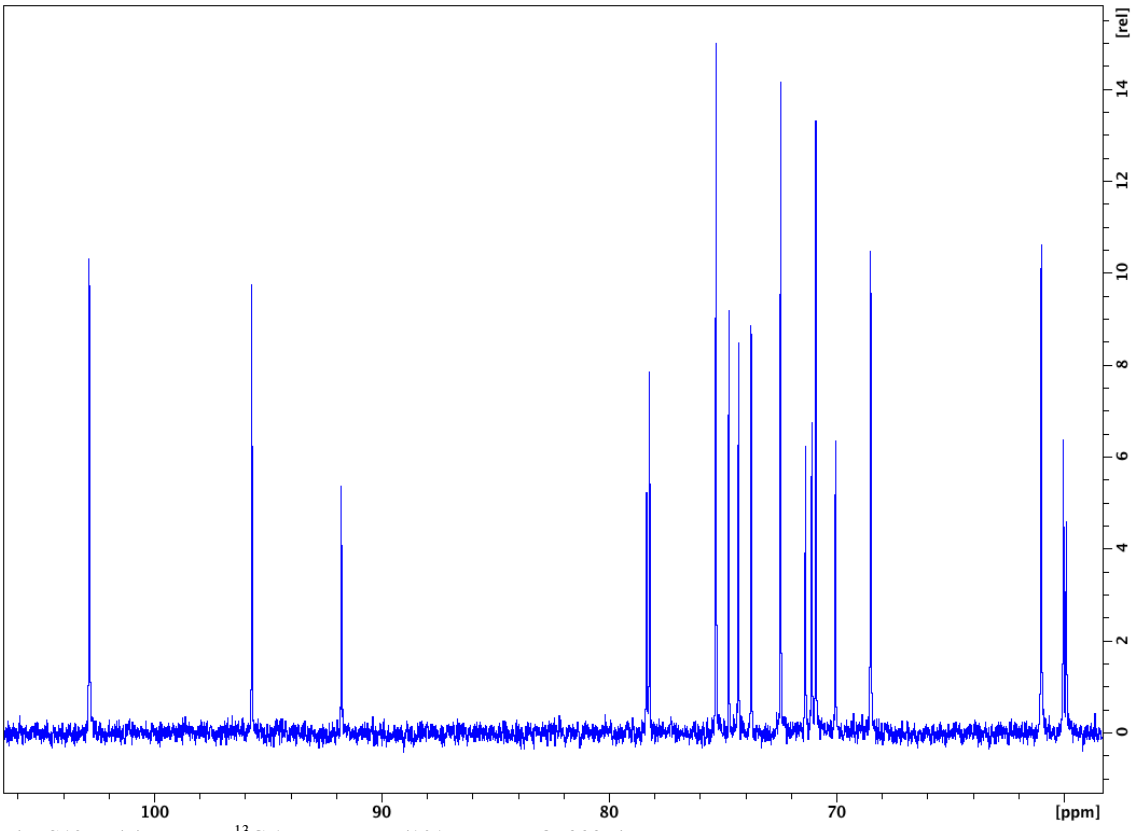

Fig. S19 D-(+)-Lactose ^{13}C 1D spectrum (101 MHz, D_2O, 293K).

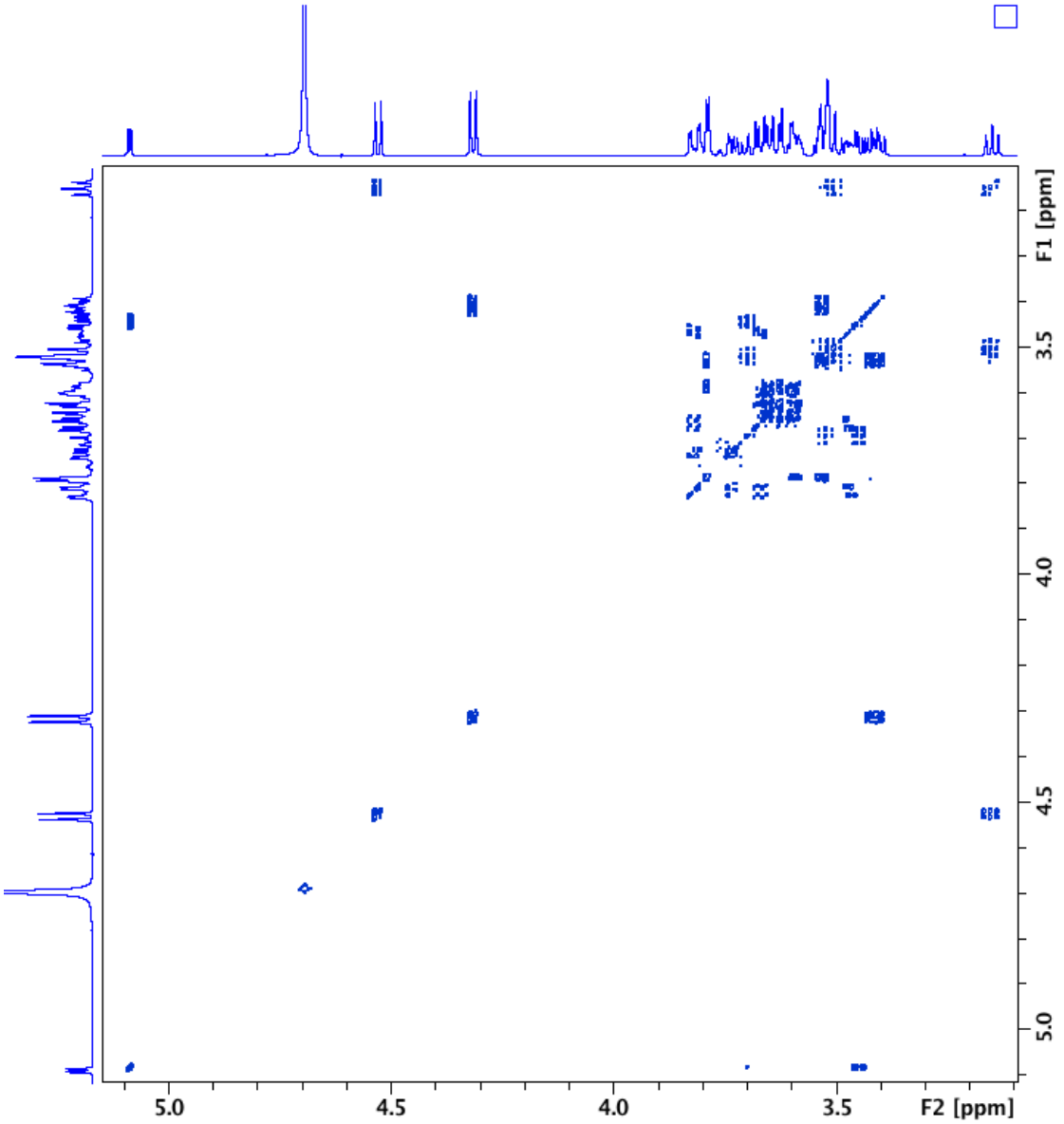

Fig. S20 D-(+)-Lactose COSY 2D spectrum (600 MHz, D_2O, 293K).

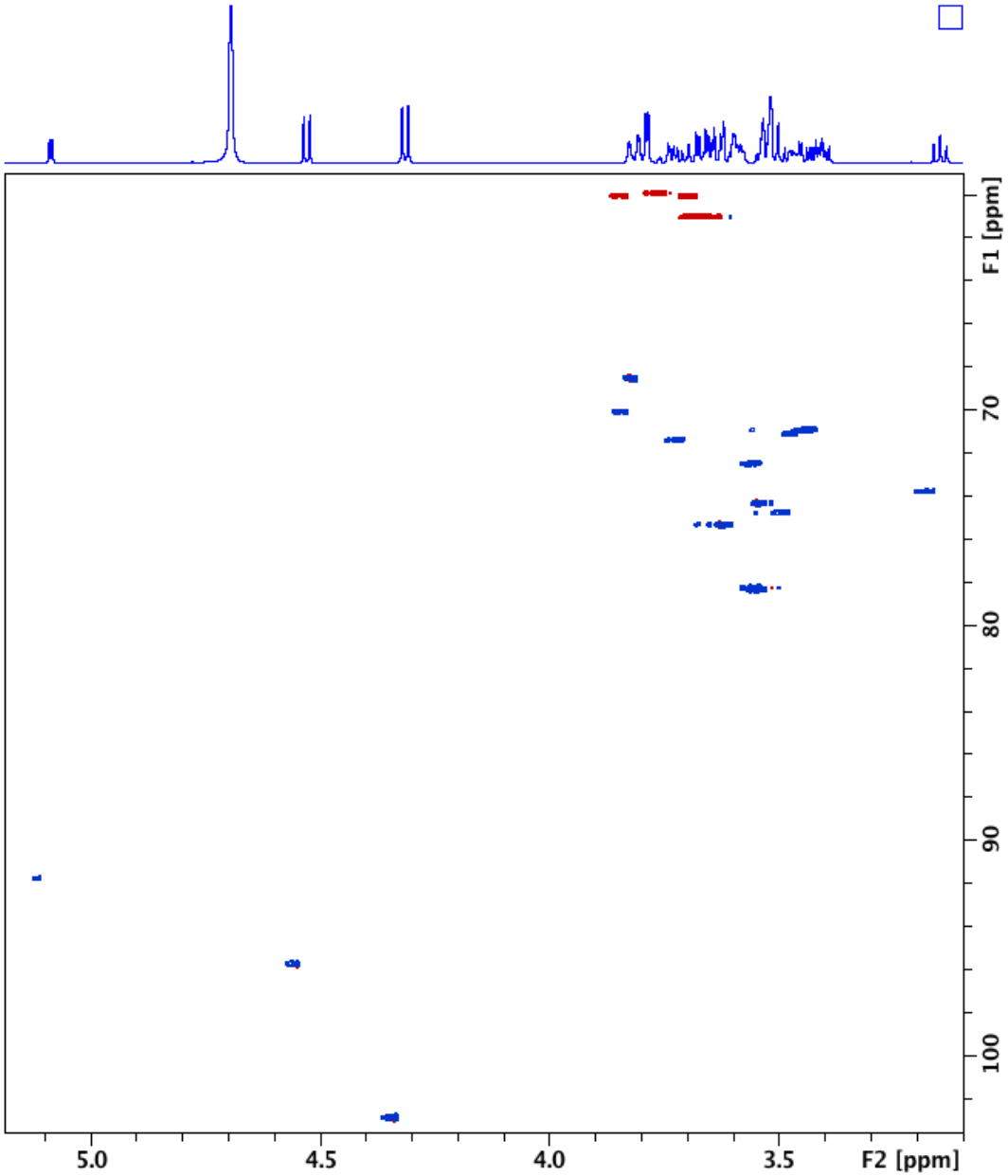

Fig. S21 D-(+)-Lactose HSQC 2D spectrum (600 MHz, D_2O, 293K).

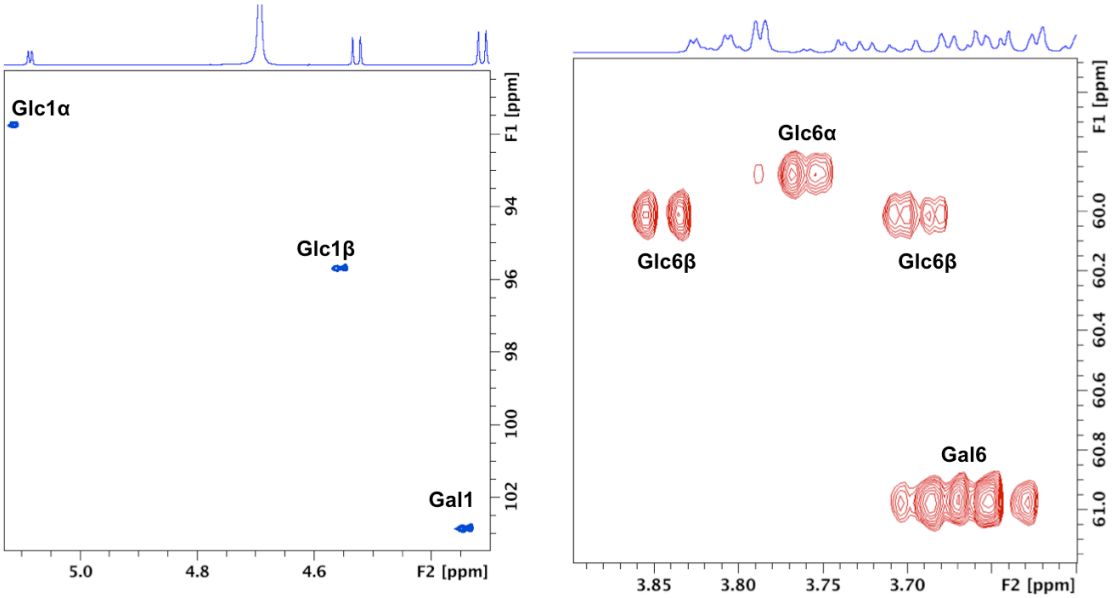

Fig. S22 Annotated D-(+)-Lactose HSQC 2D spectrum (600 MHz, D_2O, 293K).

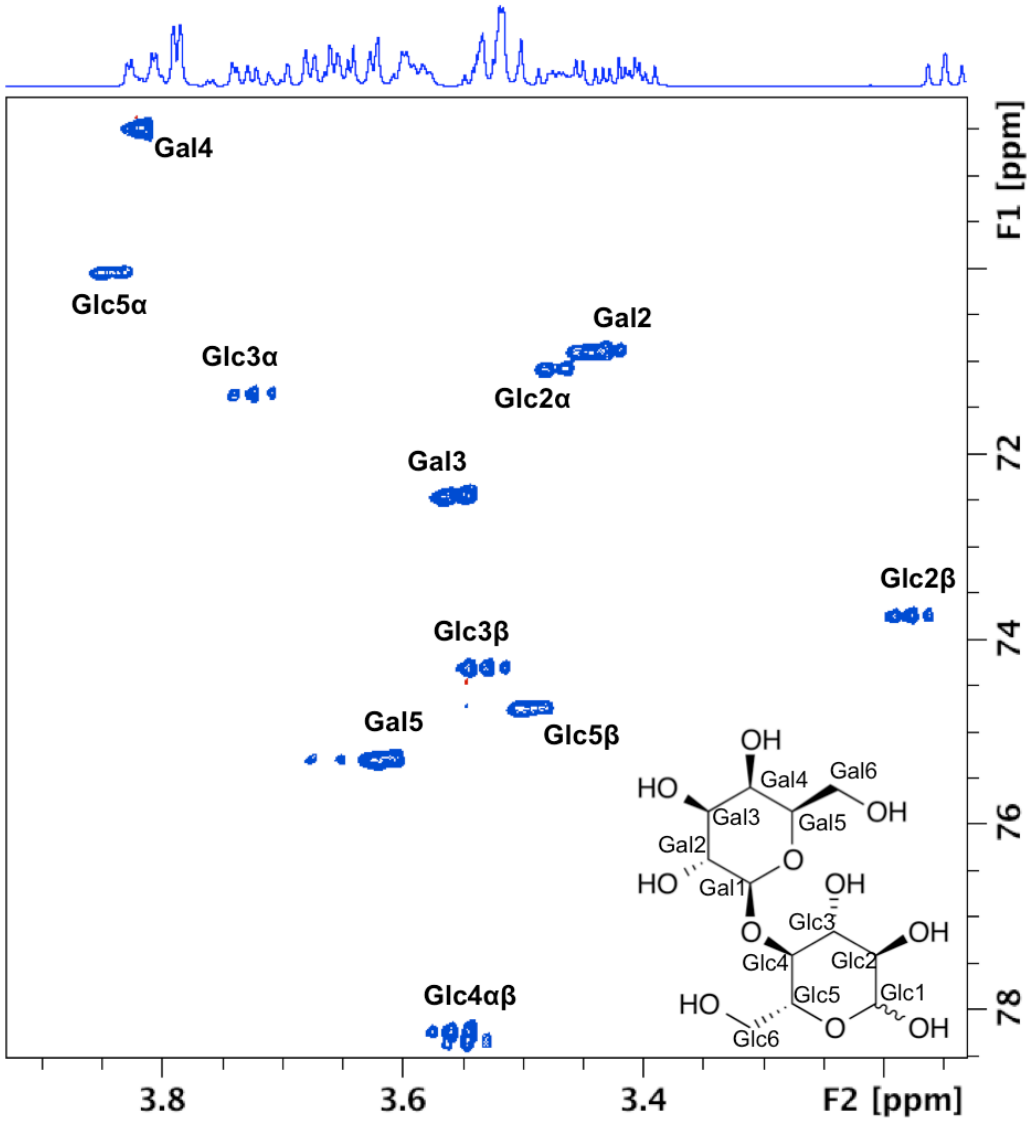

Fig. S23 Annotated D-(+)-Lactose HSQC 2D spectrum (600 MHz, D_2O, 293K).

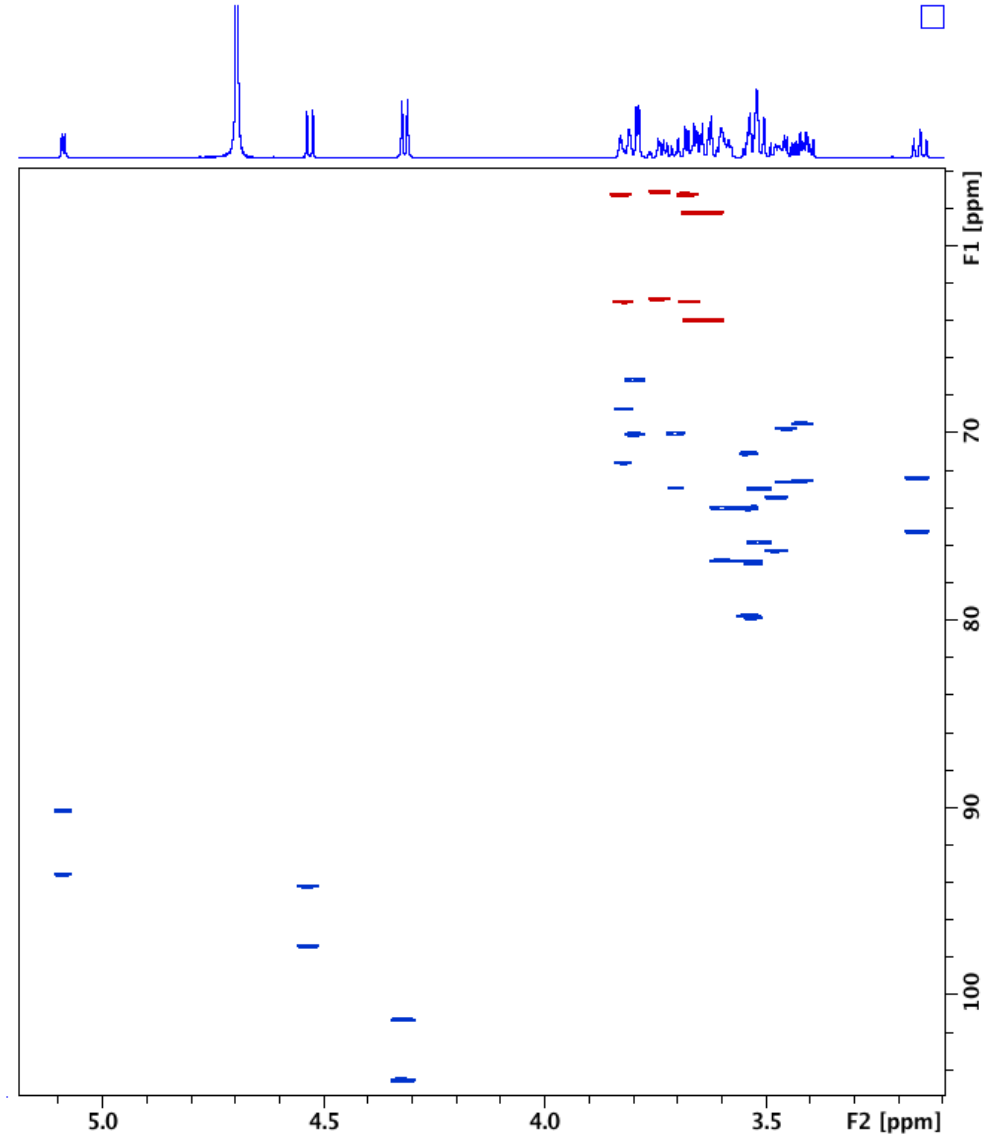

Fig. S24 D-(+)-Lactose isotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum (600 MHz, D_2O, 293K).

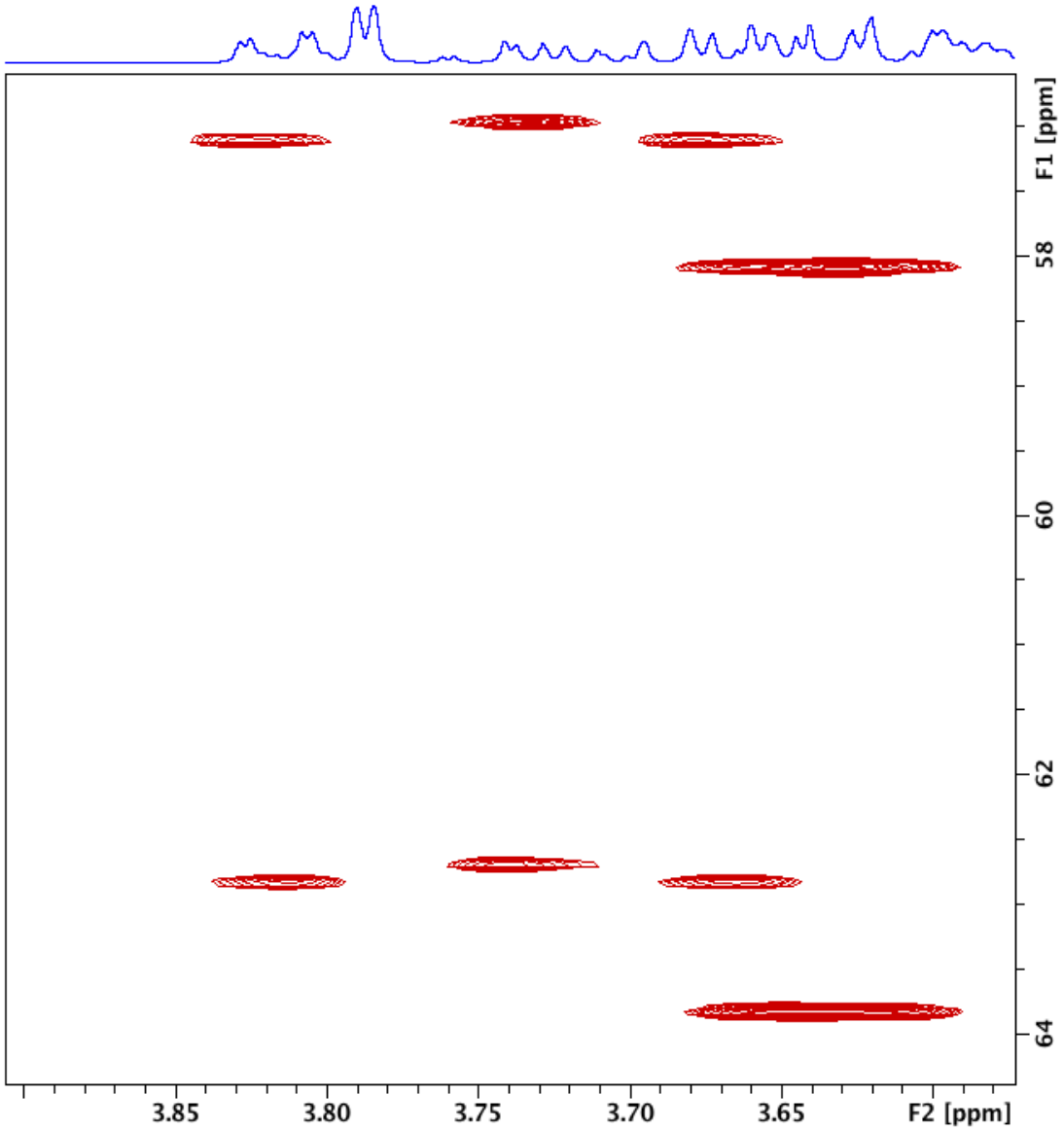

Fig. S25 Amplified methylene D-(+)-lactose region in the isotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum (600 MHz, D_2O, 293K).

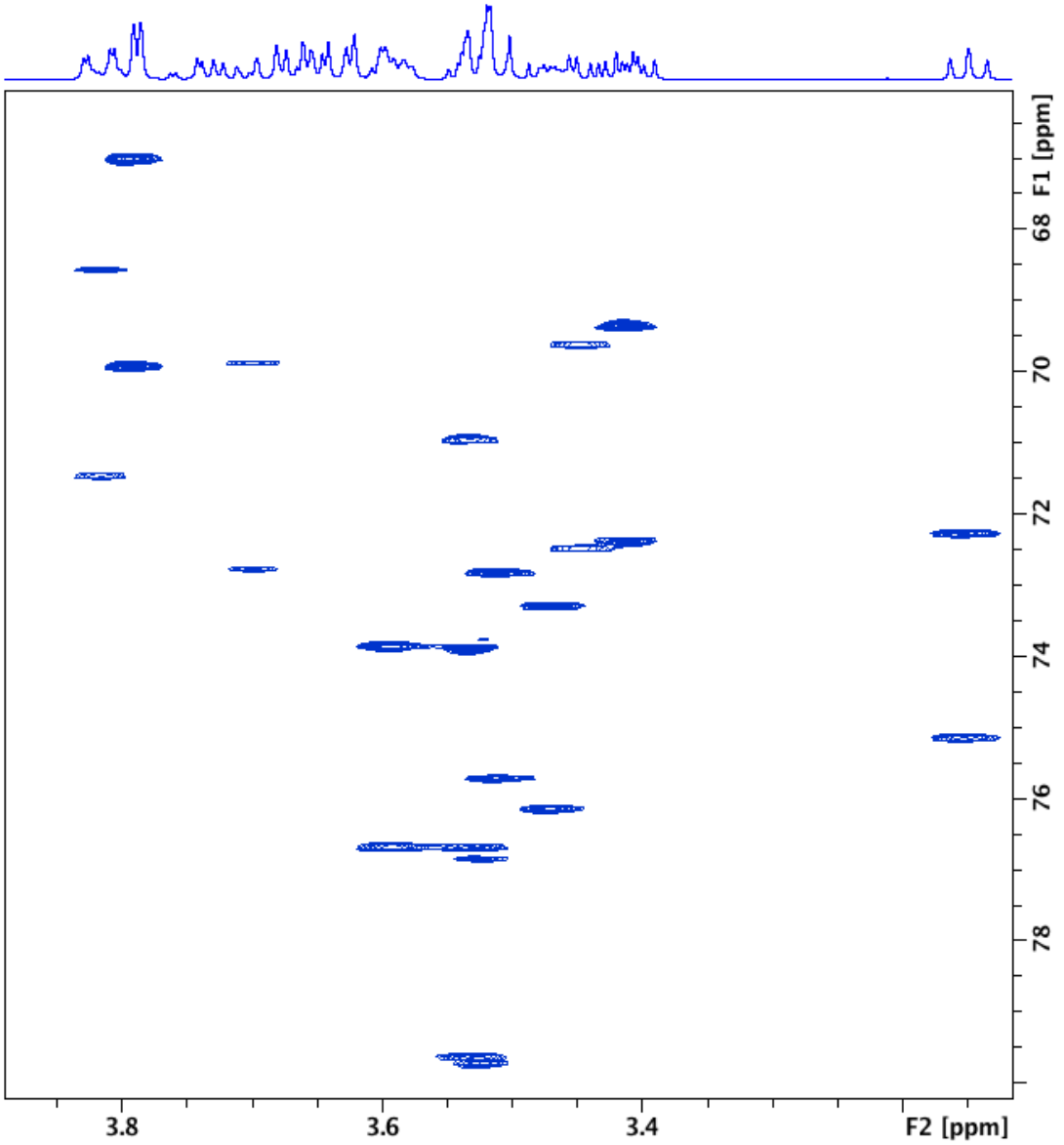

Fig. S26 Amplified D-(+)-lactose isotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum (600 MHz, D_2O, 293K).

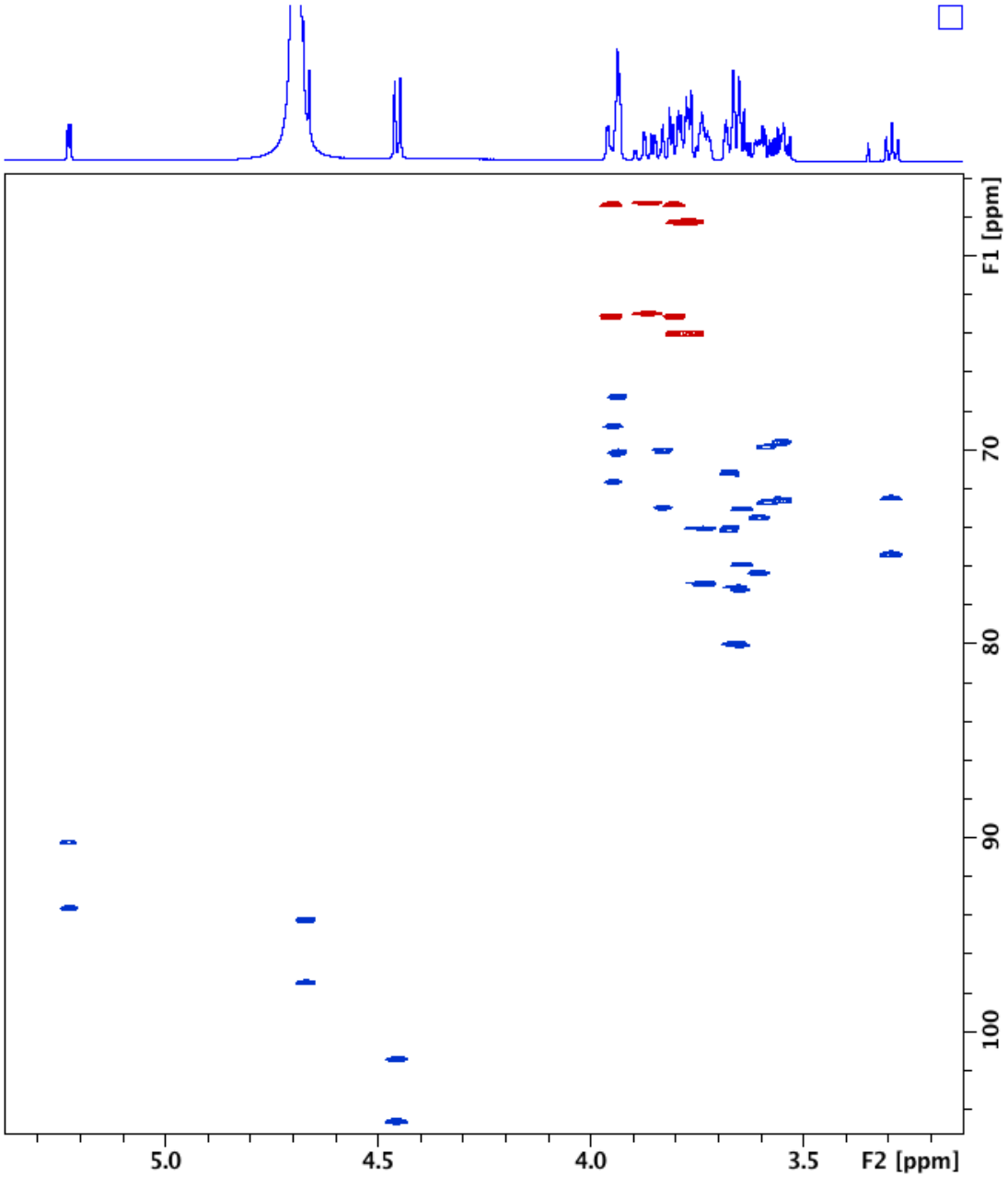

Fig. S27 D-(+)-Lactose isotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum in the N^d phase at 303K (600 MHz, cromolyn/NaCl/D_2O, 303K).

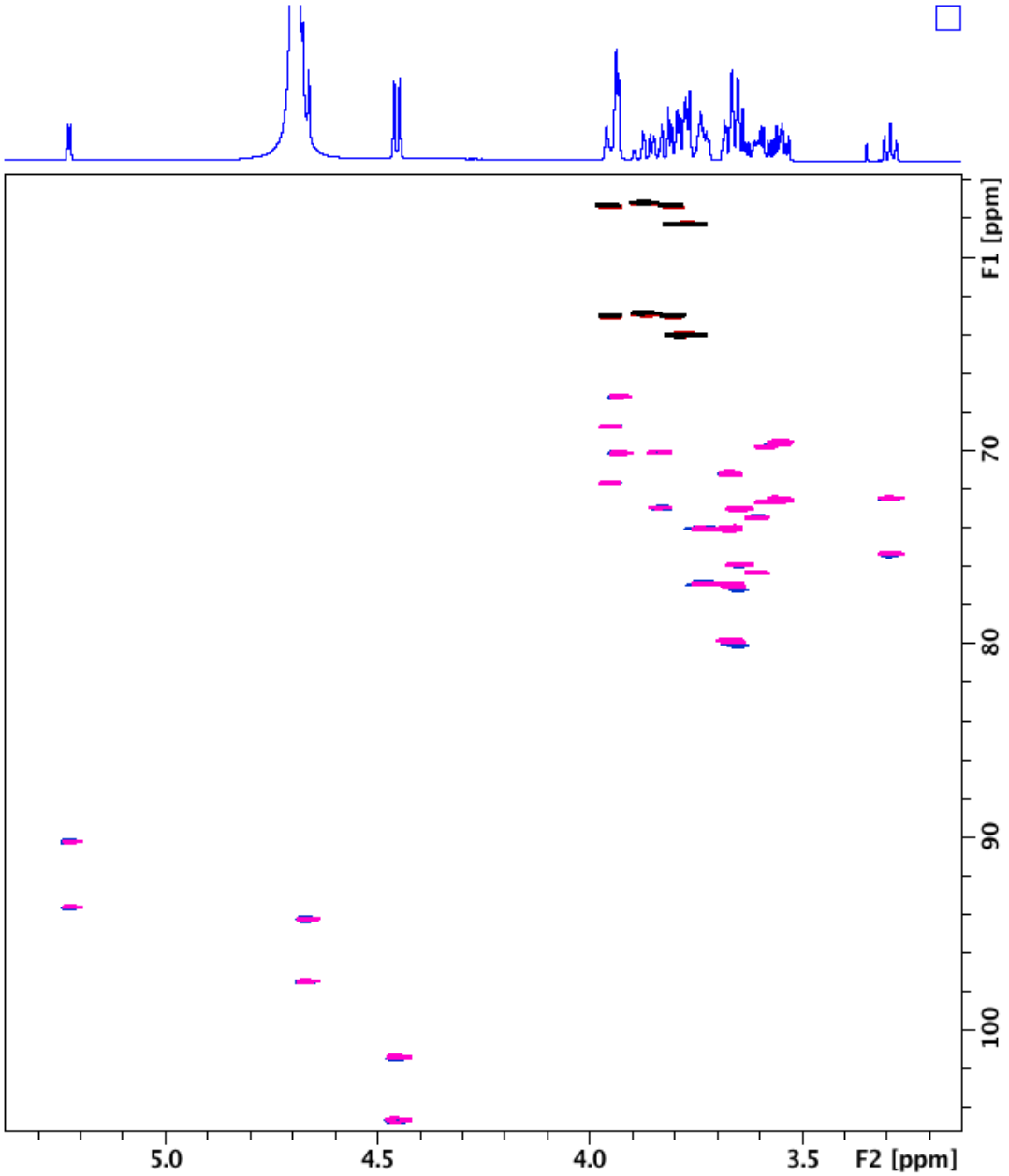

Fig. S28 Superimposed D-(+)-lactose *J* Scaled F1 coupled BIRD HSQC 2D spectrum in D_2O at 293K (blue peaks: positive, red peaks: negative) and in the cromolyn/NaCl/D_2O phase at 303K (pink peaks: positive, black peaks: negative) (600 MHz).

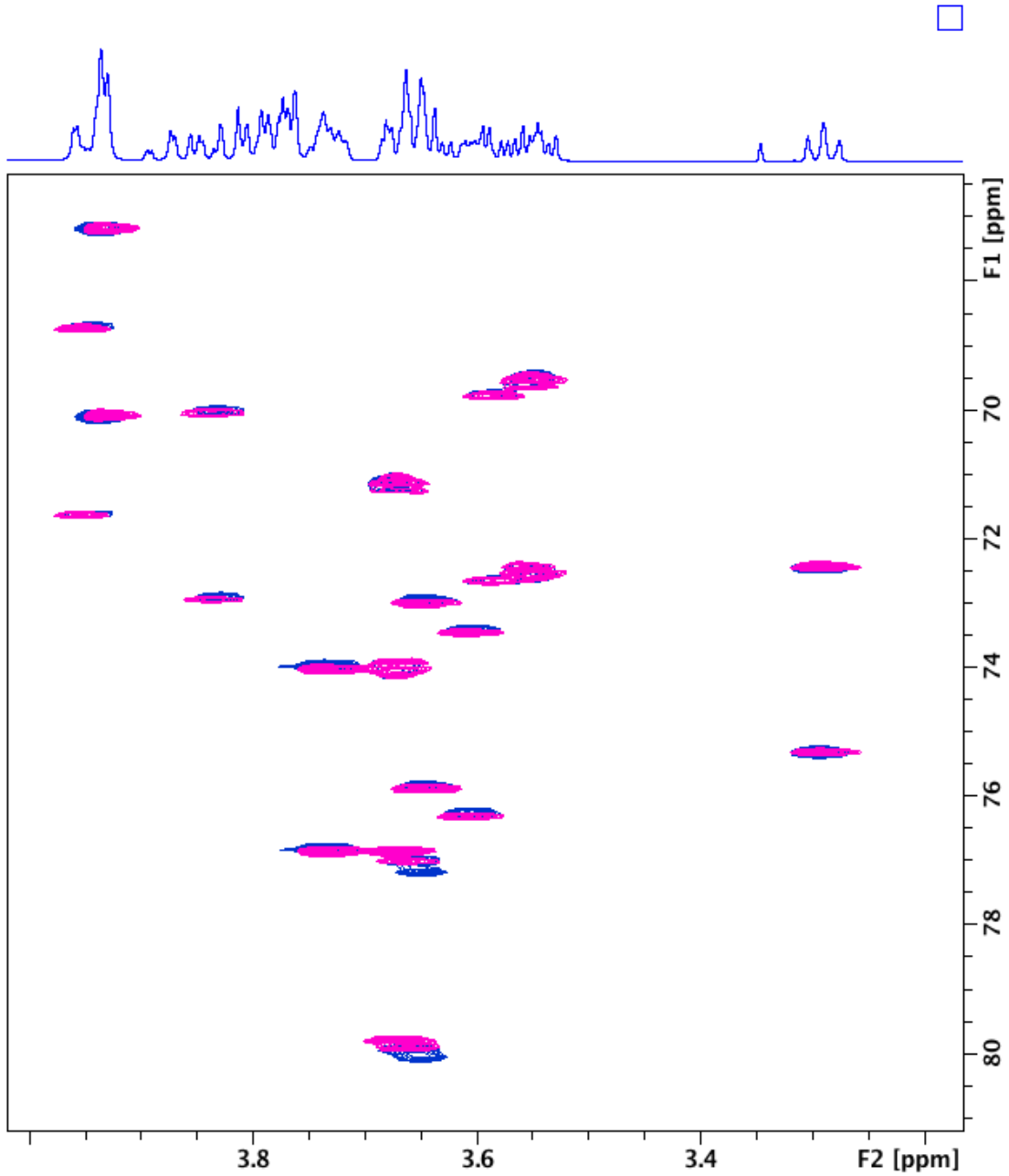

Fig. S29 Amplified superimposed D-(+)-lactose *J* Scaled F1 coupled BIRD HSQC 2D spectrum in D_2O at 293K (blue peaks: positive, red peaks: negative) and in the cromolyn/NaCl/D_2O phase at 303K (pink peaks: positive, black peaks: negative) (600 MHz).

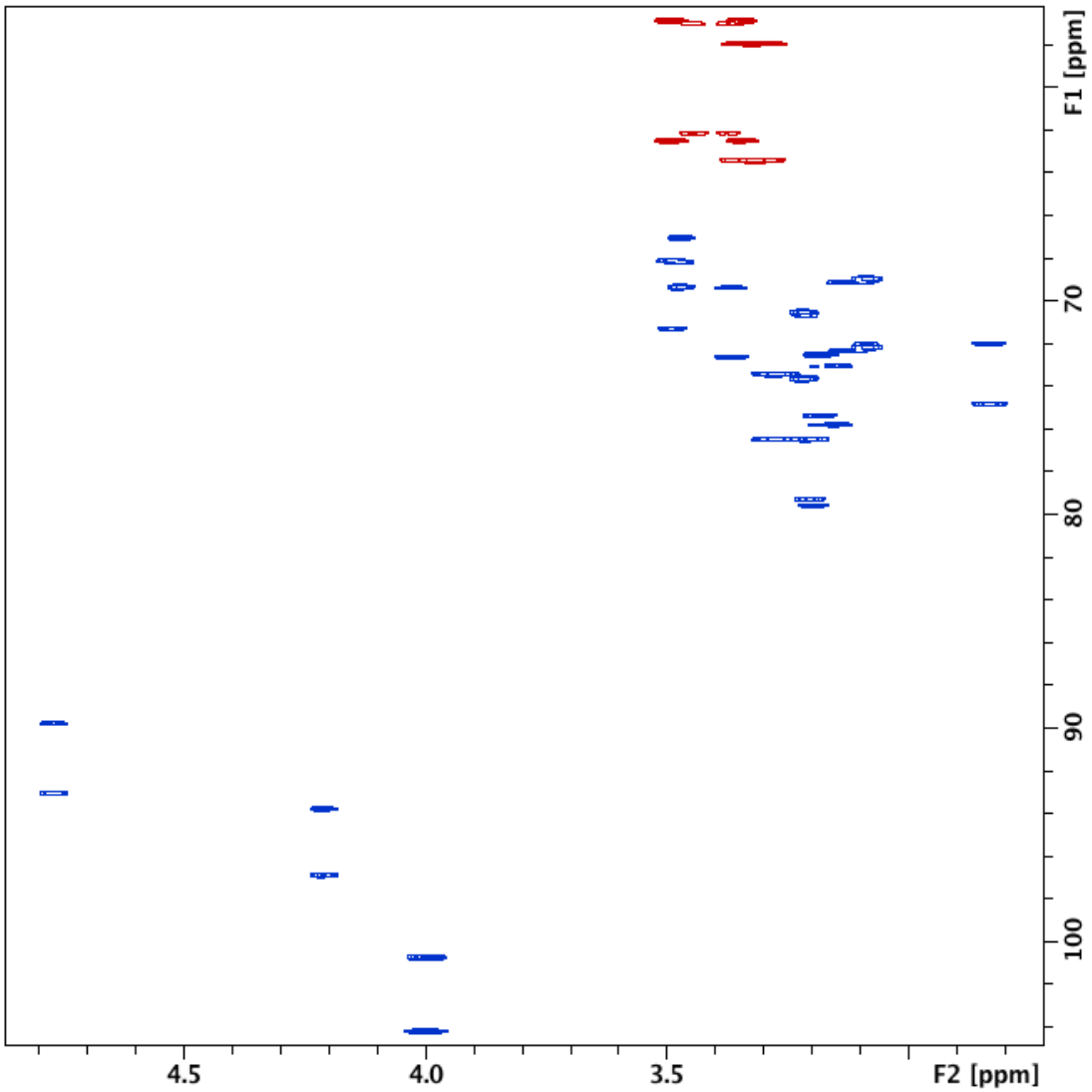

Fig. S30 D-(+)-Lactose anisotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum (600 MHz, cromolyn/NaCl/D_2O, 293K).

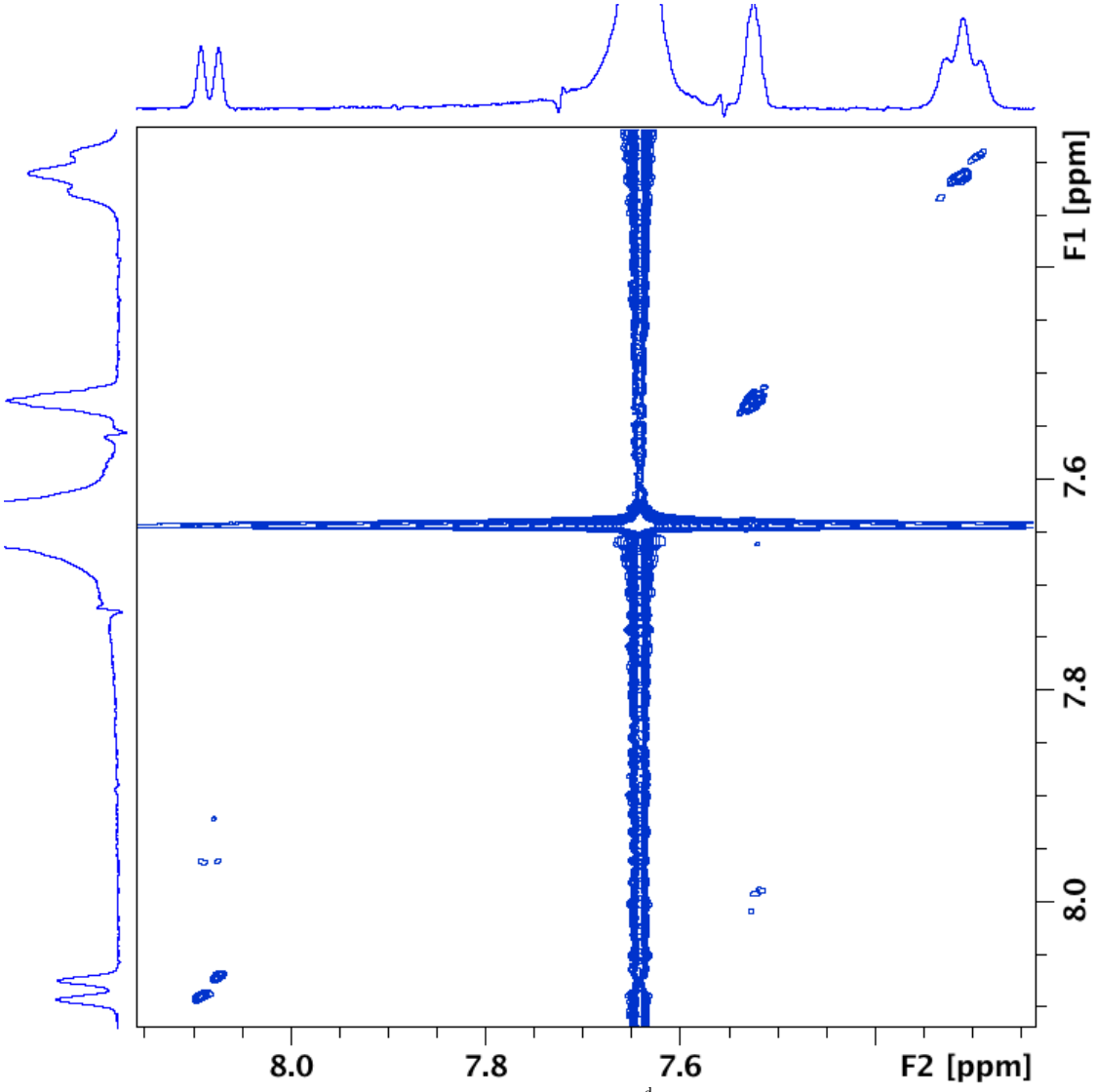

Fig. S31 D-(+)-Lactose anisotropic p.e.COSY 2D spectrum in the N^d phase (600 MHz, cromolyn/NaCl/D_2O, 293K).

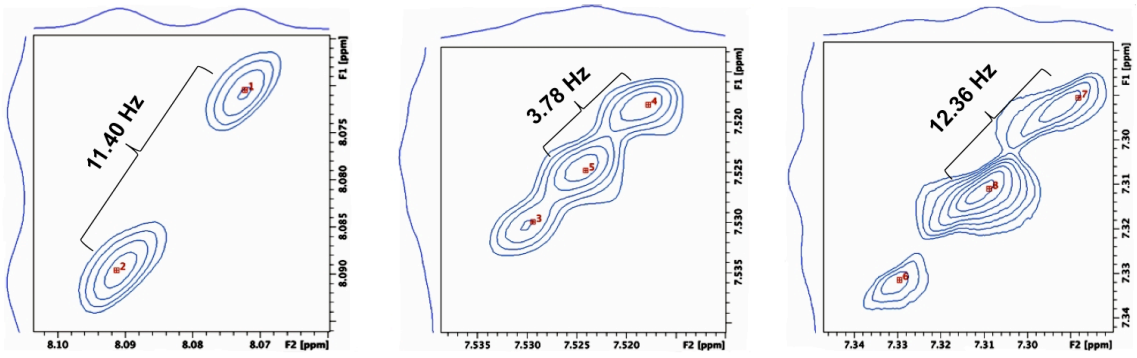

Fig. S32 Amplified D-(+)-lactose anisotropic p.e.COSY 2D spectrumin the N^d phase. a) Glucose-H1α region, b) Glucose-H1β region and c) Galactose-H1 region.

4.3 Norbornenol

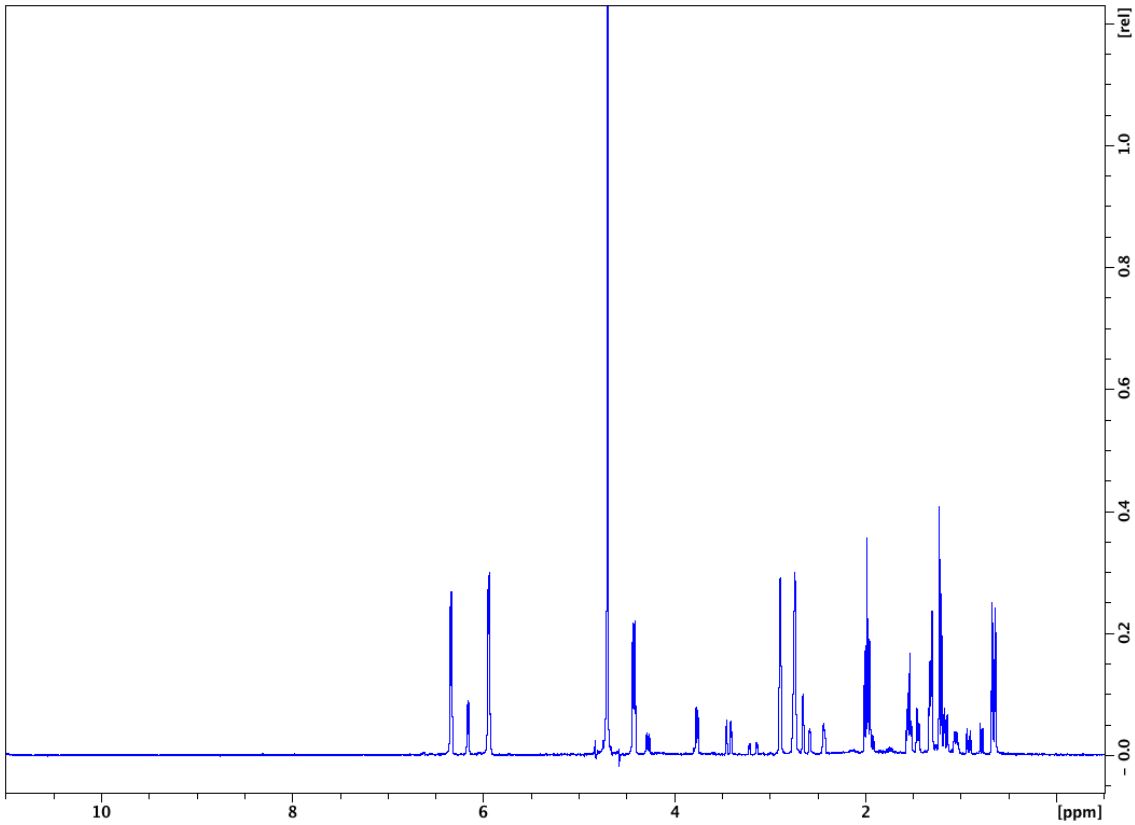

Fig. S33 5-Norbornen-2-ol ^{1}H 1D spectrum (400 MHz, D_2O, 293K).

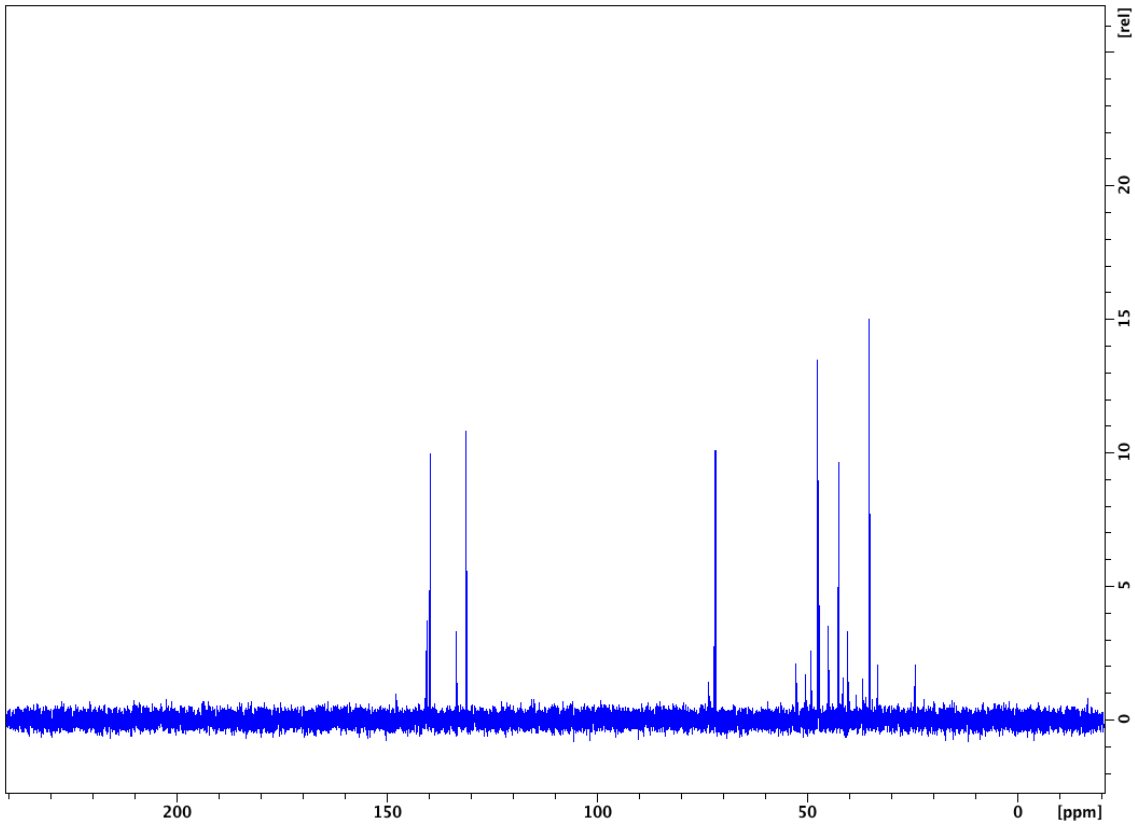

Fig. S34 5-Norbornen-2-ol ^{13}C 1D spectrum (101 MHz, D_2O, 293K).

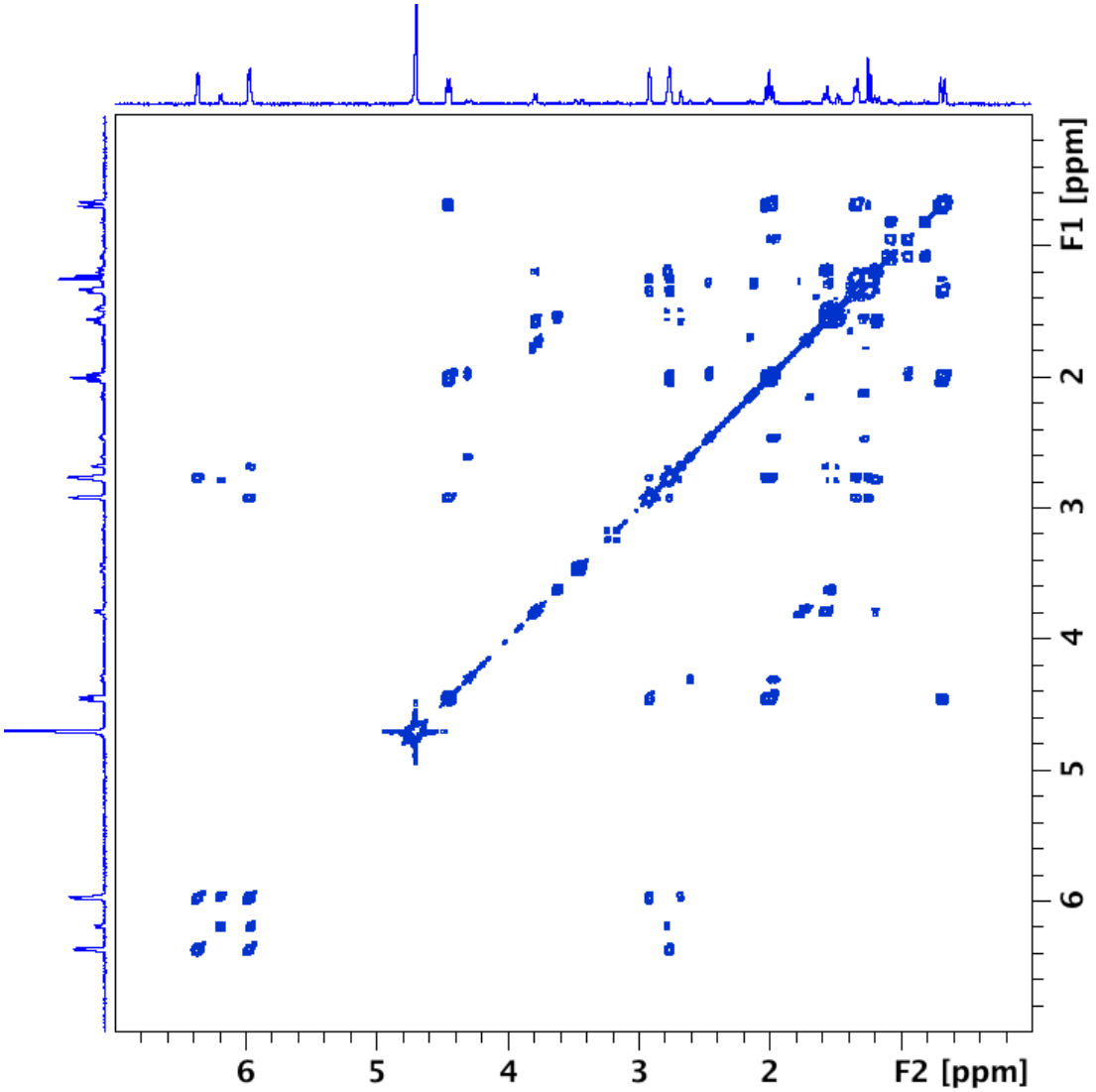

Fig. S35 5-Norbornen-2-ol 2D COSY spectrum (400 MHz, D_2O, 293K).

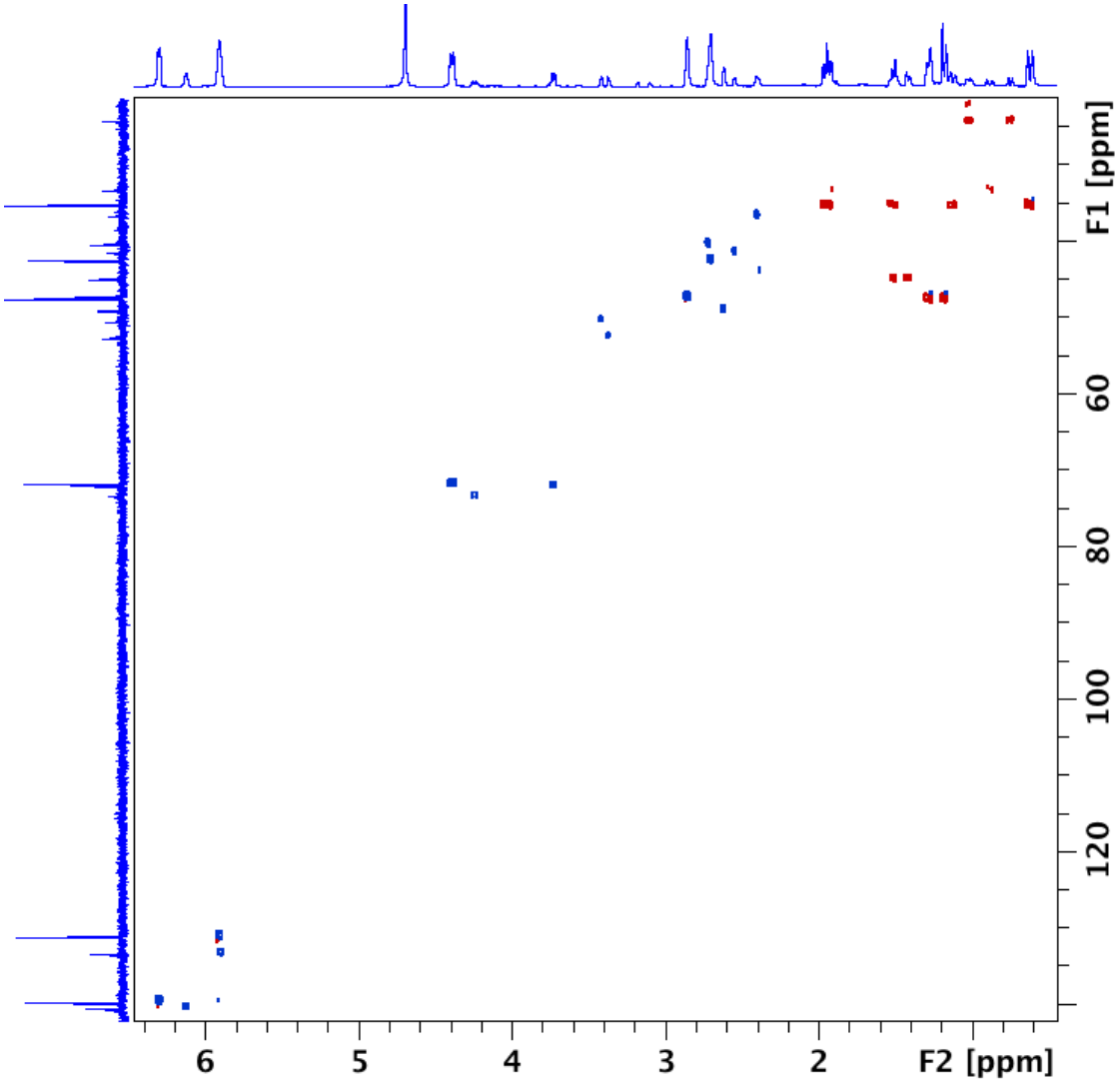

Fig. S36 5-Norbornen-2-ol 2D HSQC spectrum (400 MHz, D_2O, 293K).

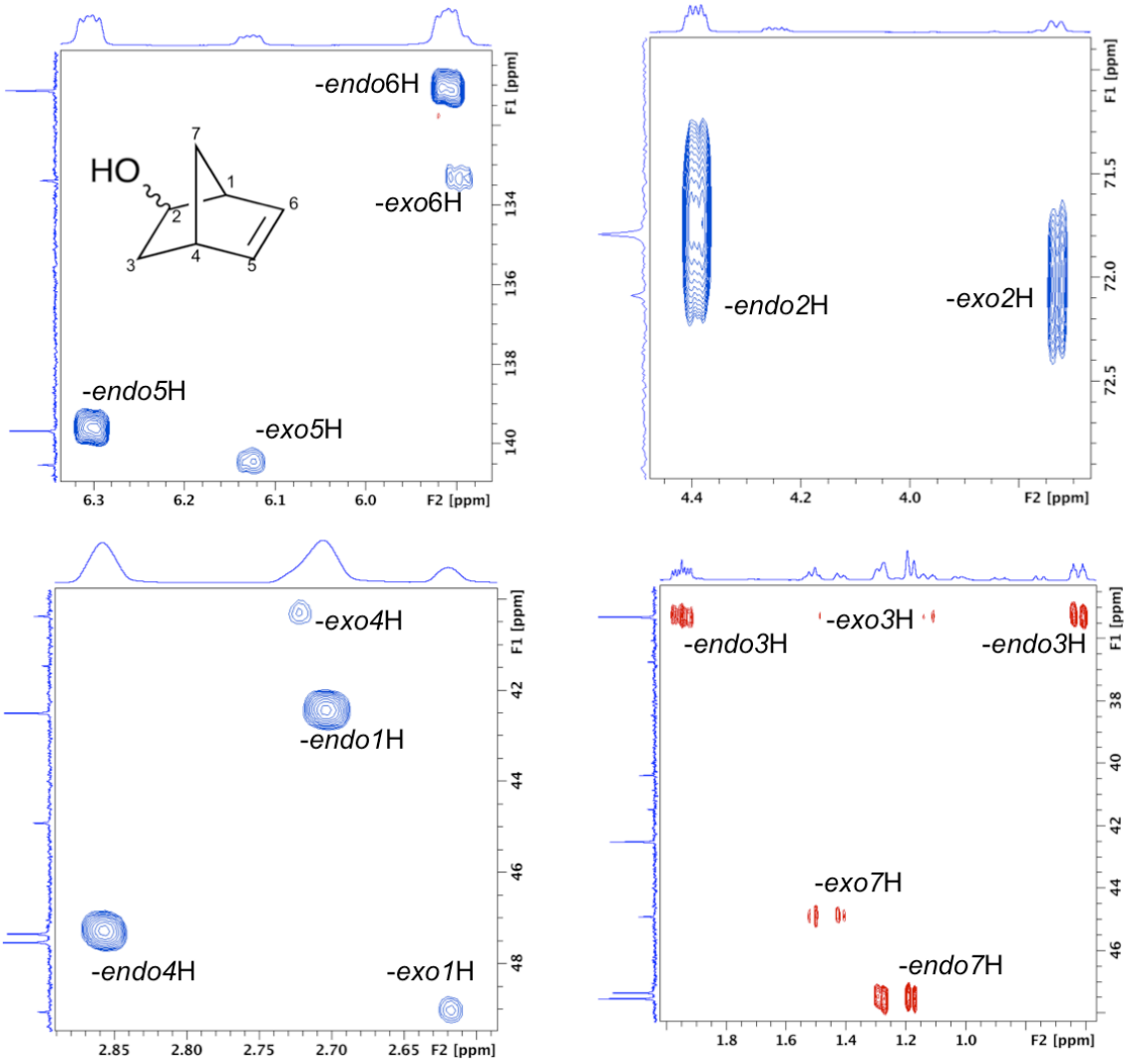

Fig. S37 Amplified and annotated 2D HSQC regions of 5-norbornen-2-ol.

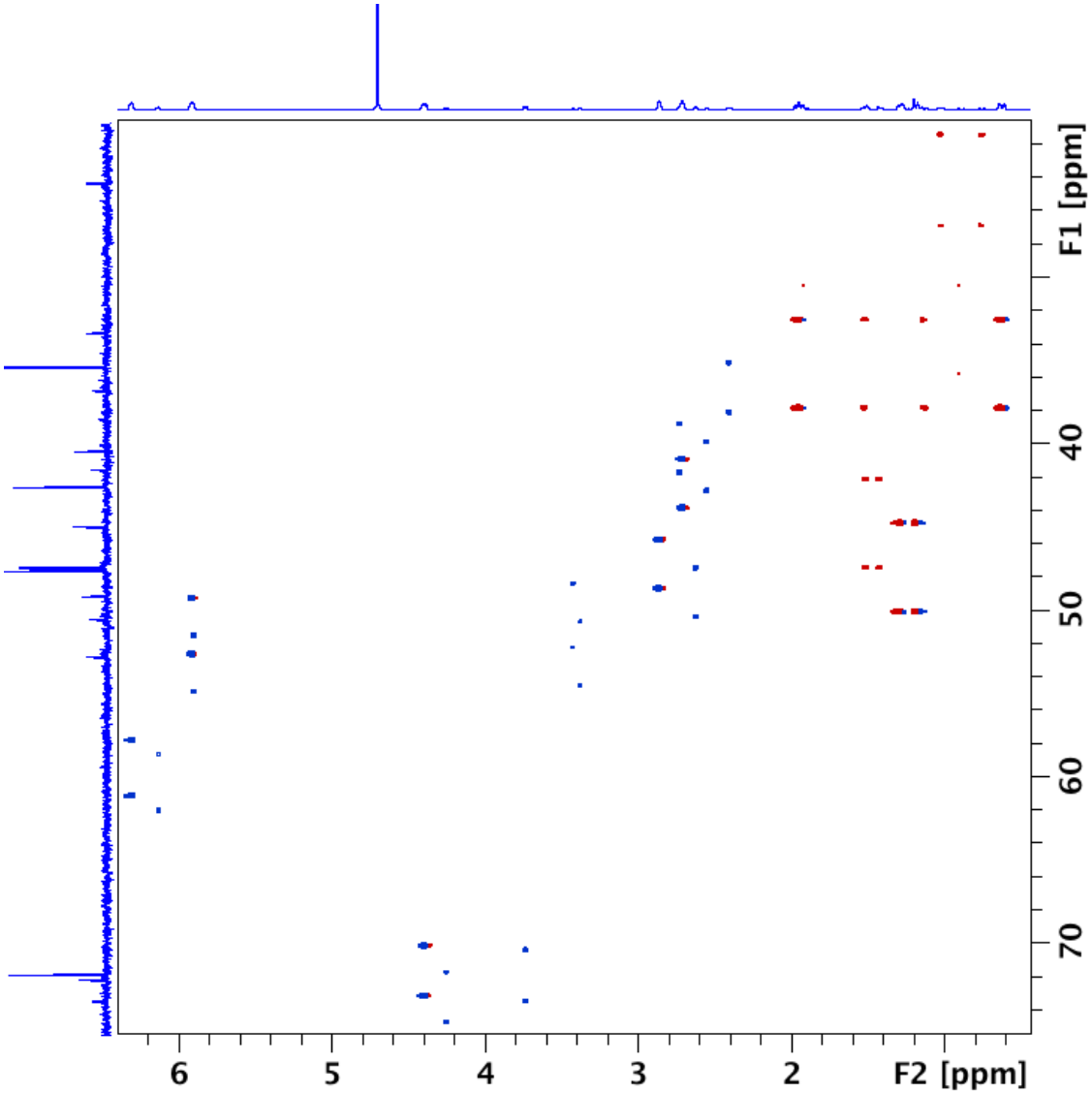

Fig. S38 5-Norbornen-2-ol isotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum (600 MHz, D_2O, 293K).

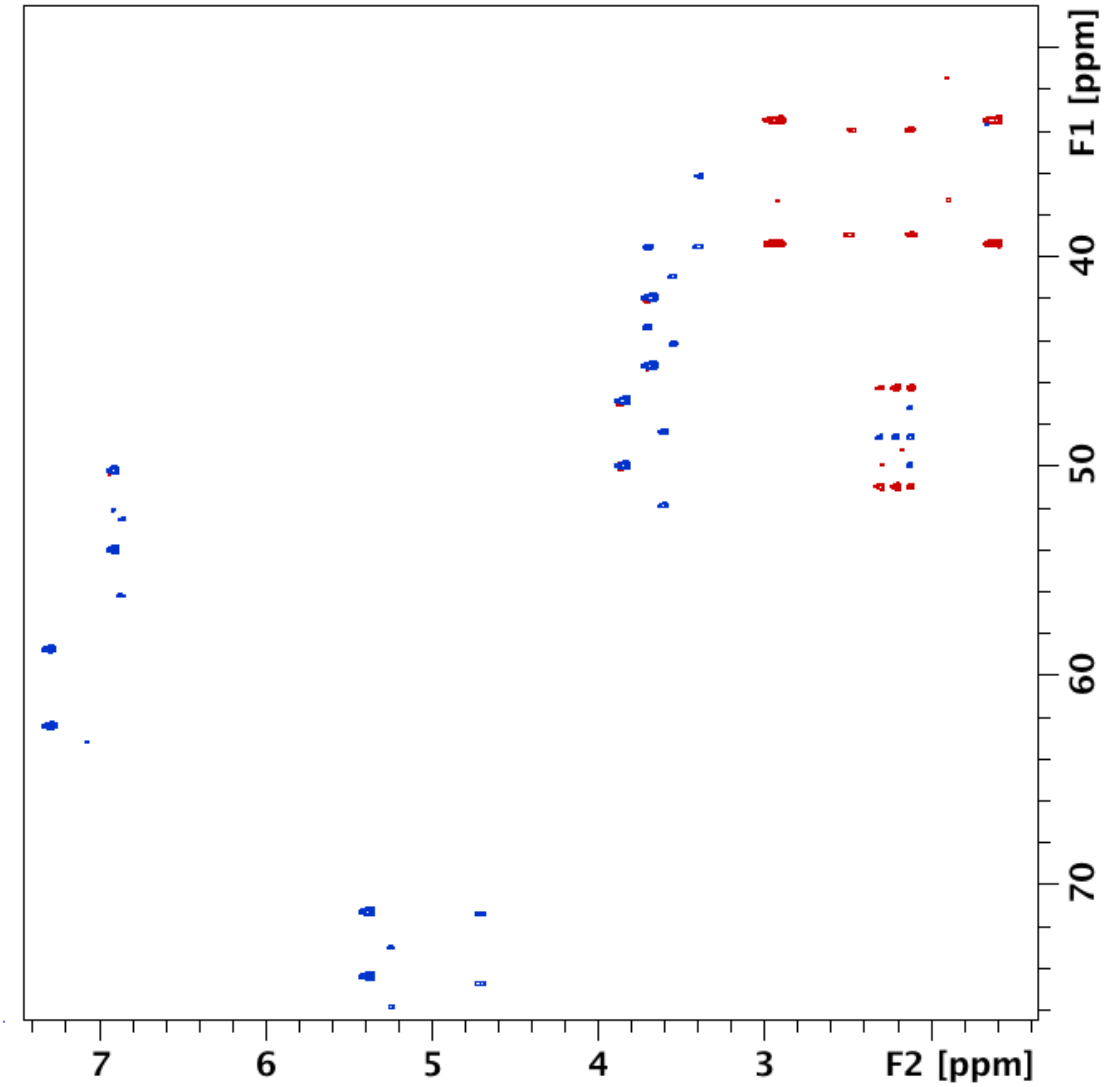

Fig. S39 5-Norbornen-2-ol anisotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum in the N phase (600 MHz, cromolyn/D_2O, 293K).

4.4 *N*-methyl-codeinium iodide

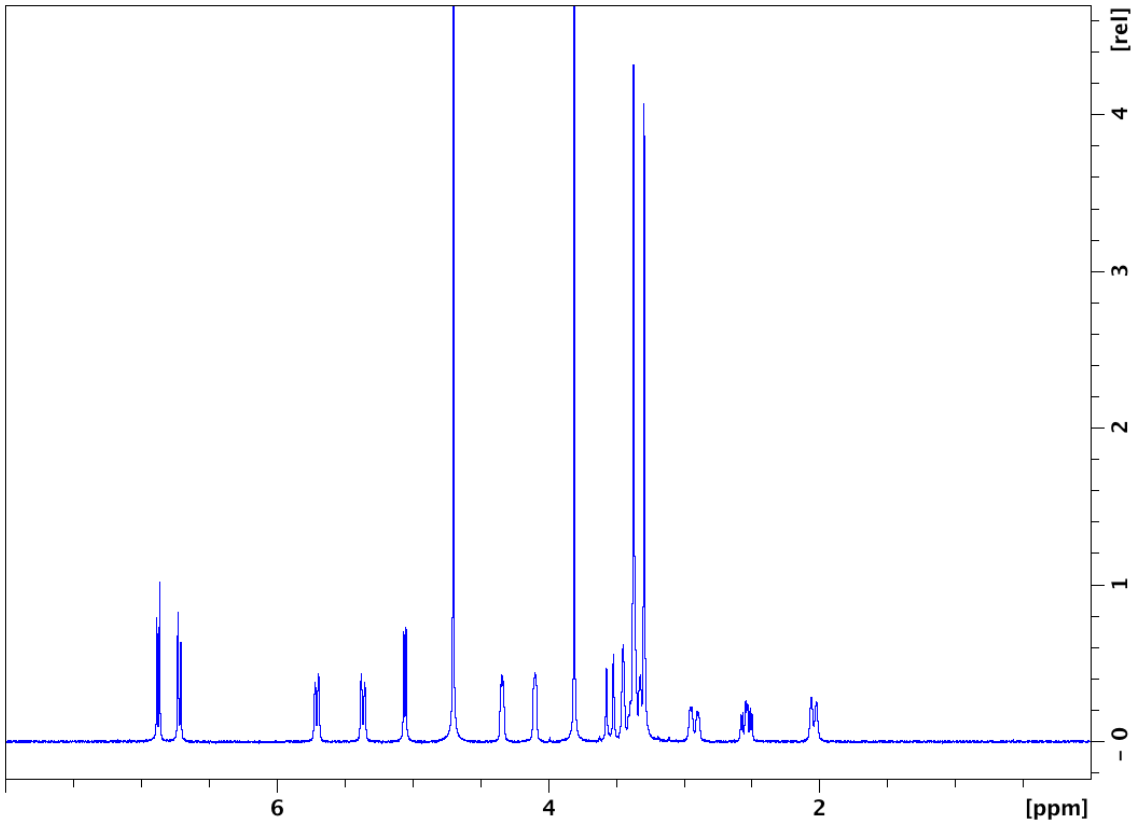

Fig. S40 *N*-Methyl codeinium iodide ^{1}H 1D spectrum (400 MHz, D_2O, 293K).

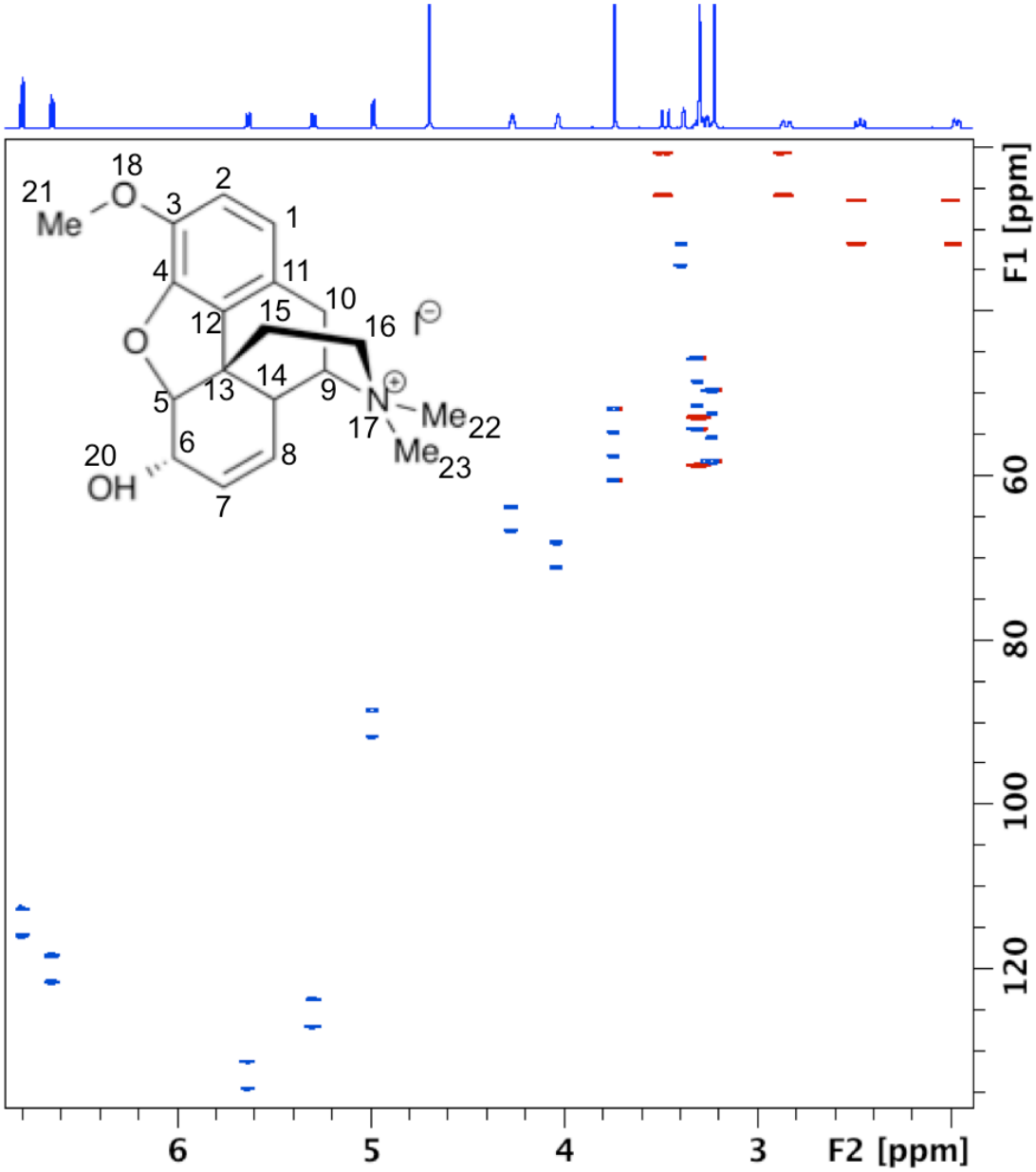

Fig. S41 *N*-Methyl codeinium iodide isotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum (600 MHz, D_2O, 293K).

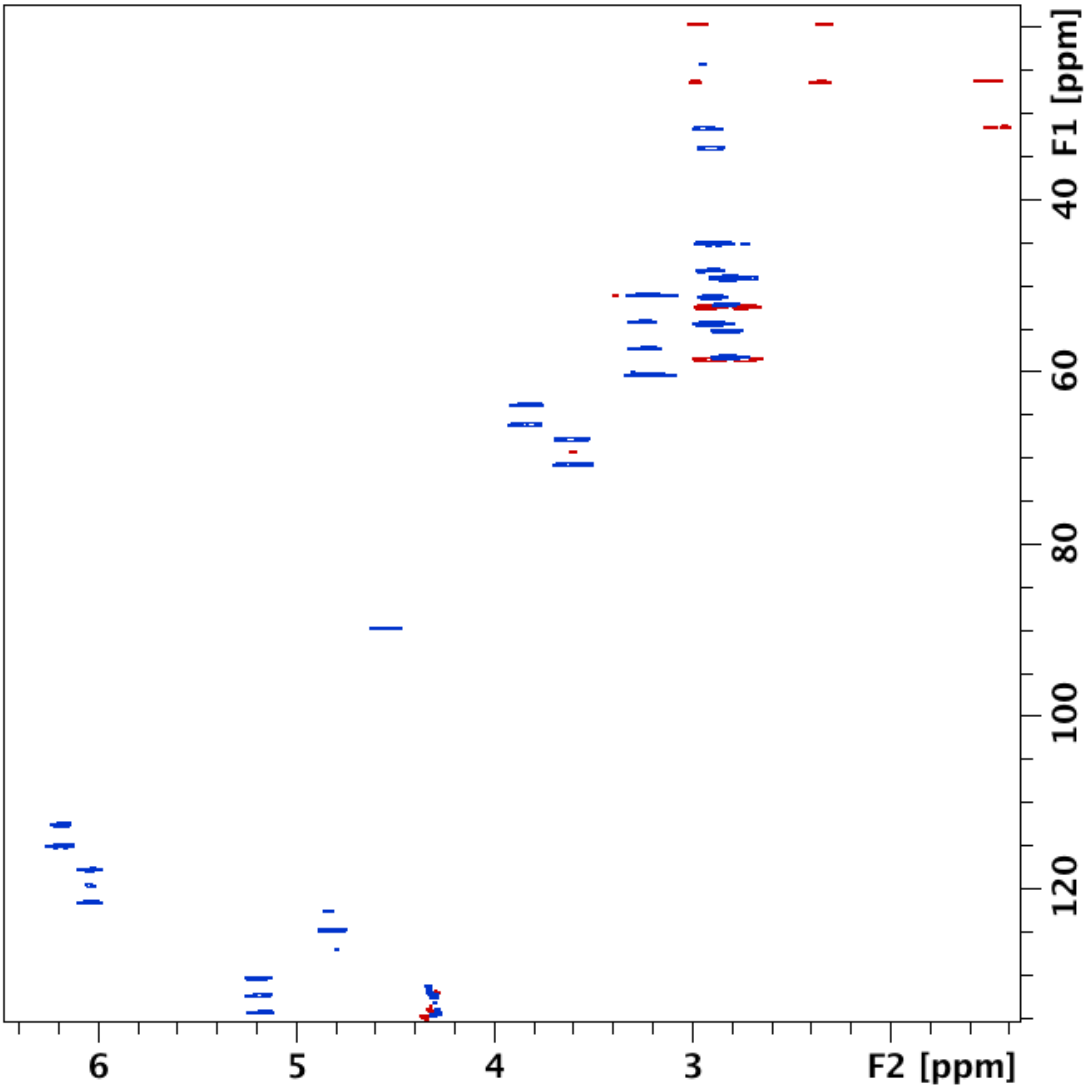

Fig. S42 *N*-Methyl codeinium iodide anisotropic *J* Scaled F1 coupled BIRD HSQC 2D spectrum in the N^d phase (600 MHz, cromolyn/NaCl/D_2O, 293K).

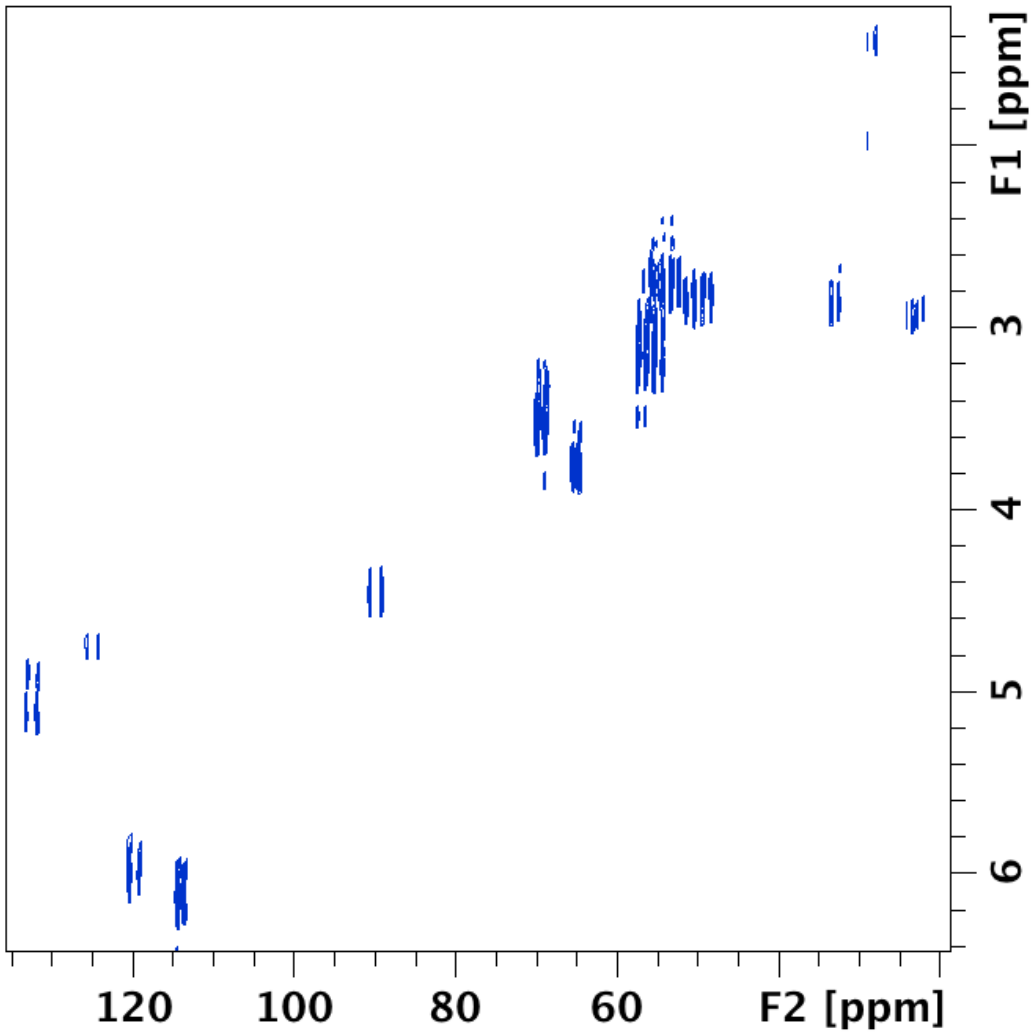

Fig. S43 *N*-Methyl codeinium iodide HETCOR 2D spectrum in the N^d phase at 299K (600 MHz). The experiment was used to try to obtain isotropic and anisotropic peaks in the same spectrum.

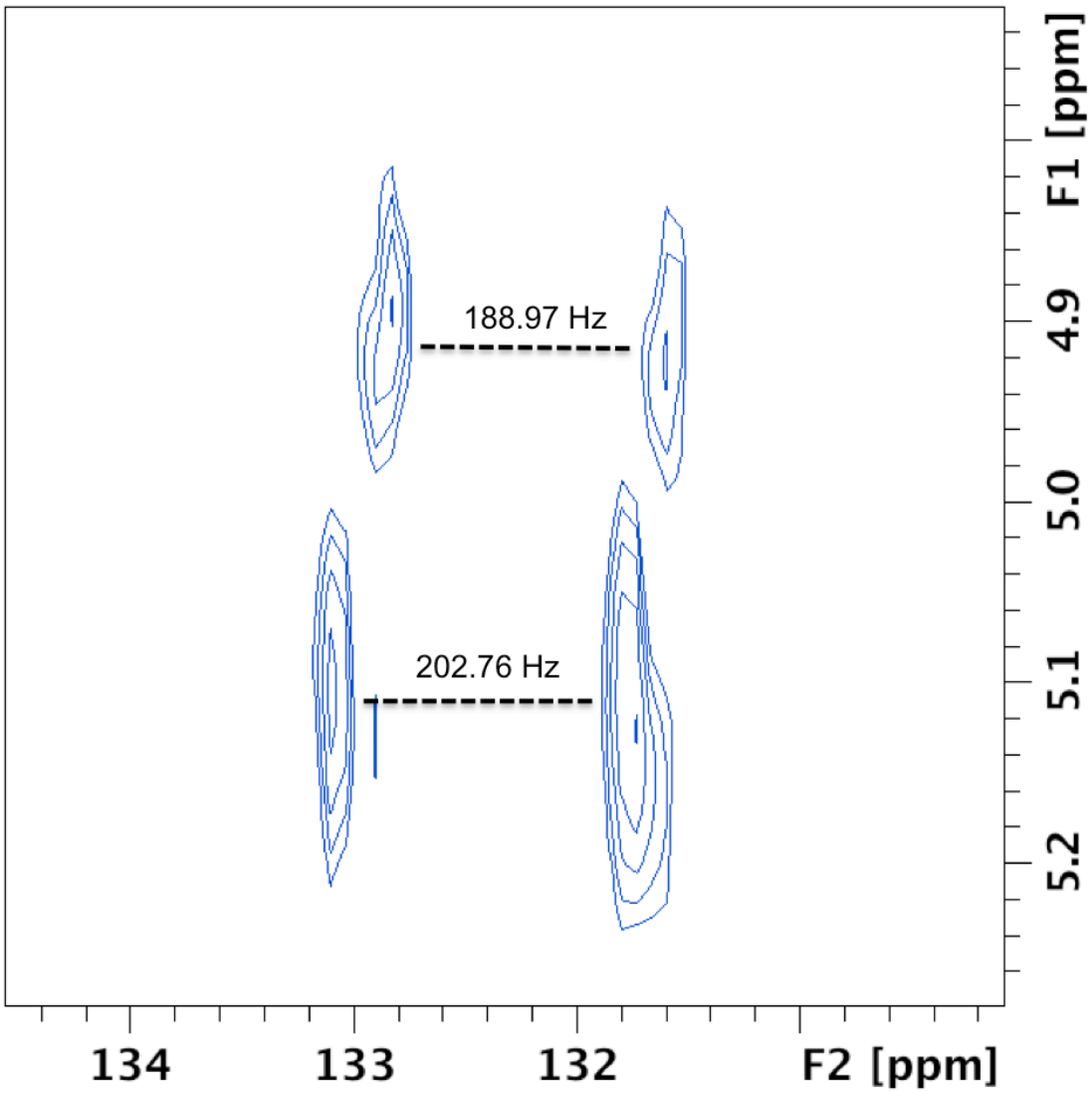

Fig. S44 Amplified C7-H7 region of the *N*-methyl codeinium iodide HETCOR 2D spectrum in the N^d phase at 299K (600 MHz).

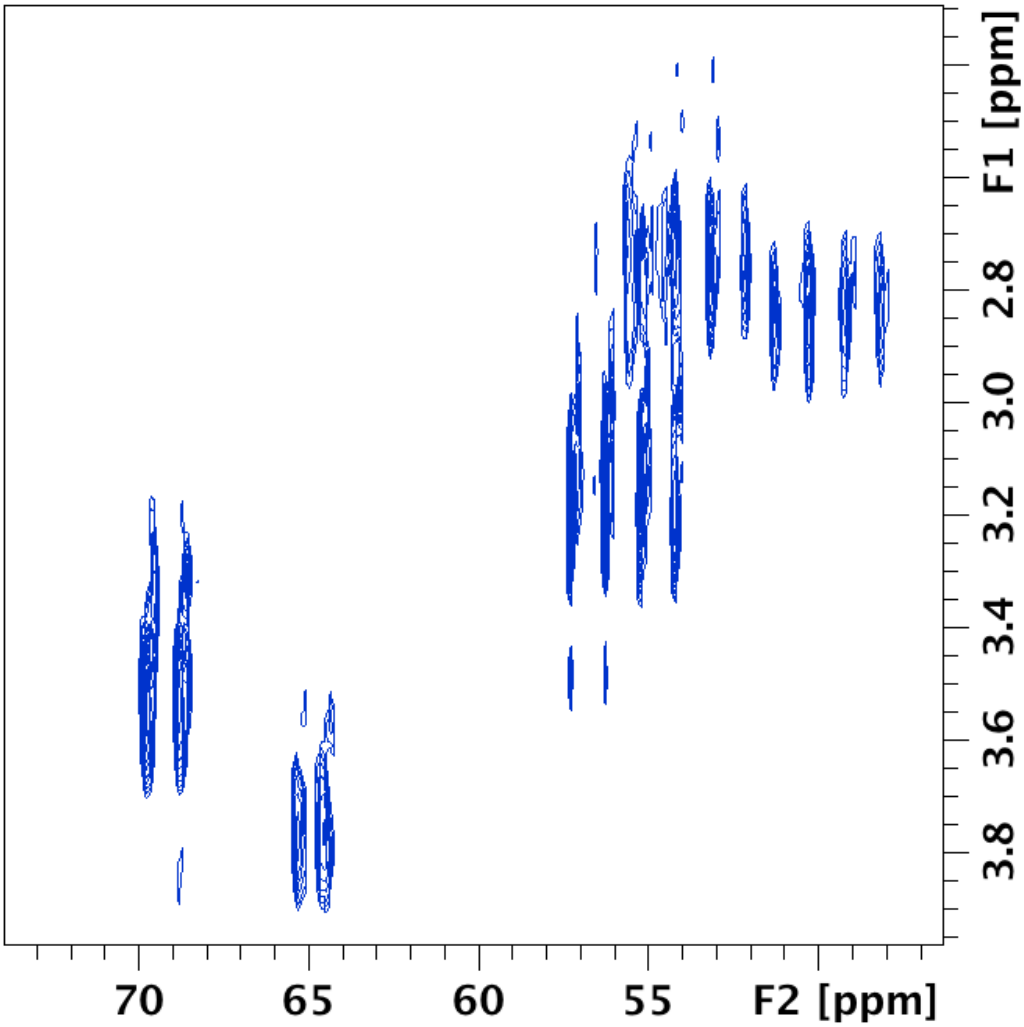

Fig. S45 Amplified aliphatic region of the *N*-methyl codeinium iodide HETCOR 2D spectrum in the N^d phase at 299K (600 MHz).

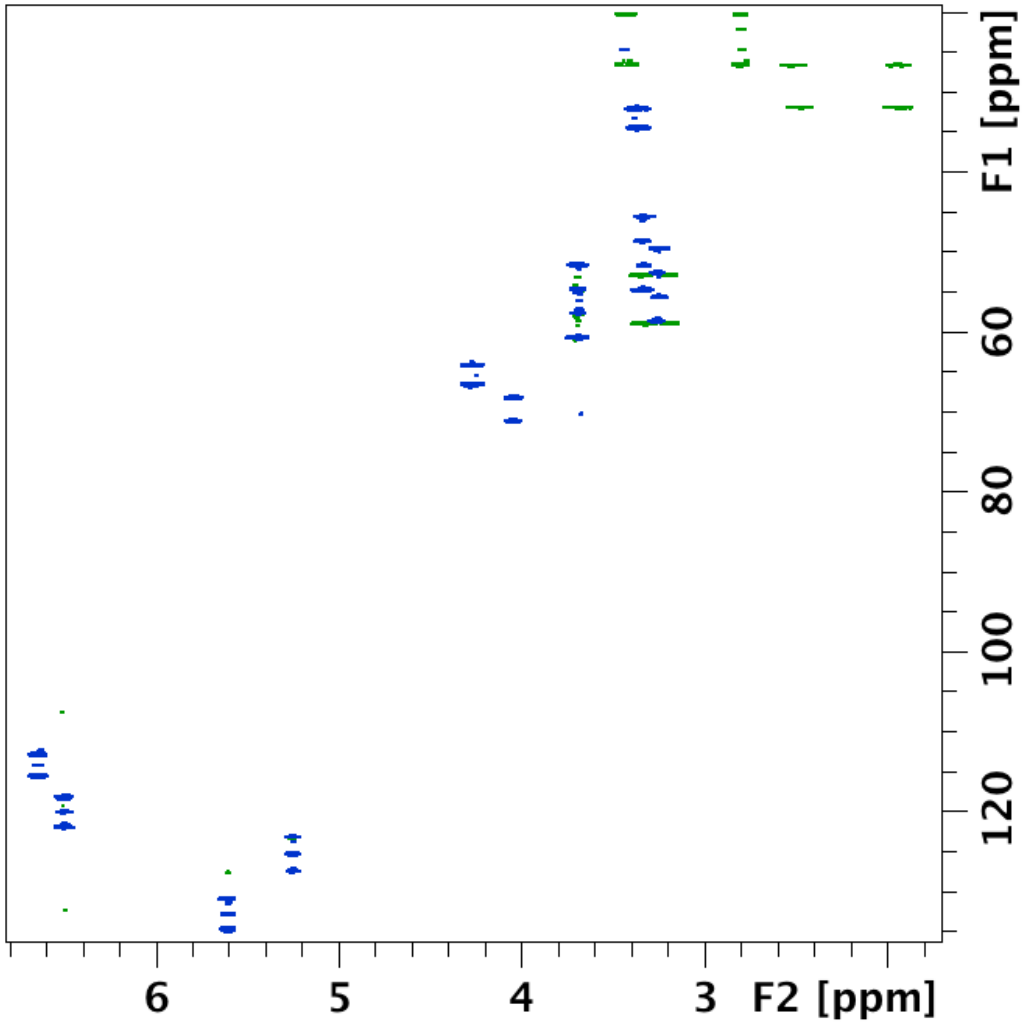

Fig. S46 *N*-Methyl codeinium iodide *J* Scaled BIRD HSQC 2D spectrum in the N^d phase at 299K (600 MHz), performed in order to obtain isotropic and anisotropic peaks in the same spectrum.

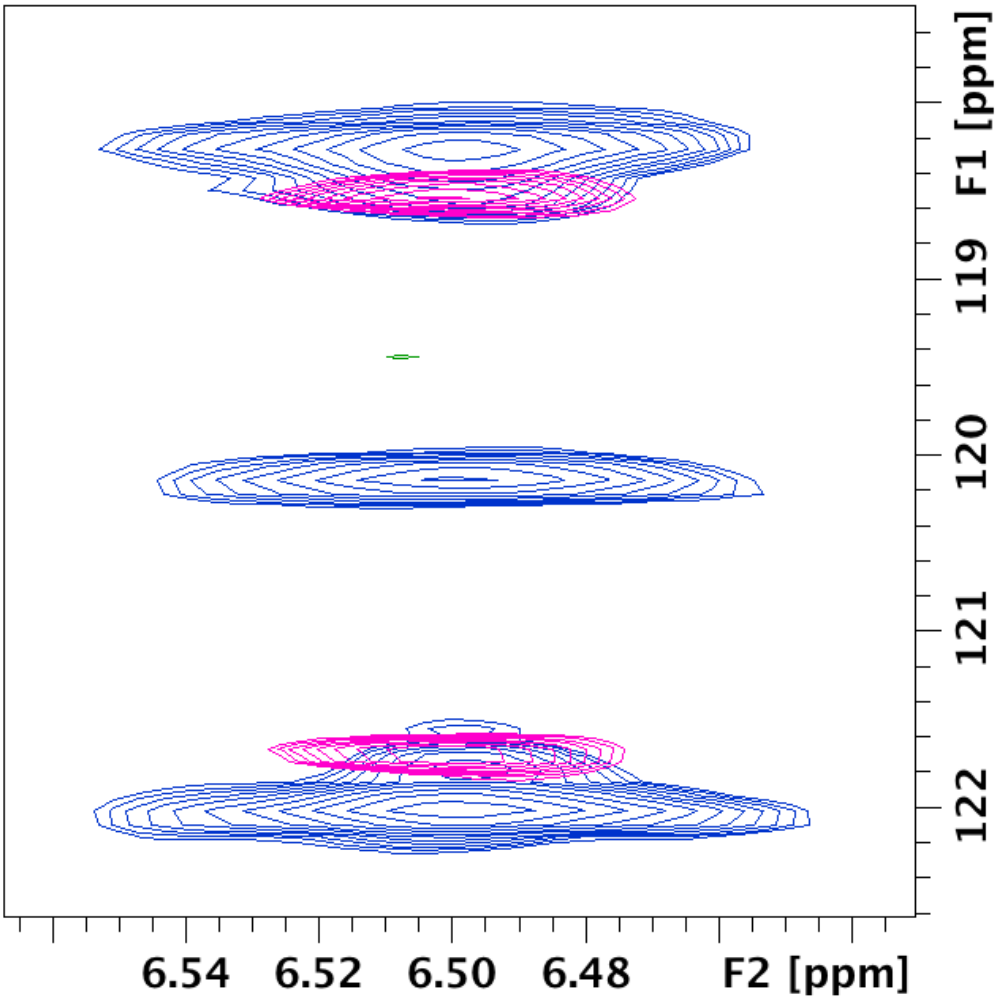

Fig. S47 Amplified C1-H1 *N*-methyl codeinium iodide region in the *J* Scaled BIRD HSQC 2D spectrum in the N^d phase at 299K (600 MHz), performed in order to obtain isotropic and anisotropic peaks in the same spectrum. Pink peaks correspond to the *J* Scaled BIRD HSQC of the same molecule in isotropic (D_2O) conditions.

5. NMR data

5.1 Methyl-β-D-galactopyranoside

Table S1 Comparison of the total couplings $^{1}T_{CH}$ extracted for the N and the Nd phases at 400 and 600 MHz to check for dependency of the couplings with the magnetic field. *Strong coupling effects made not possible the extraction of all the couplings from the F2-coupled HSQC.

^{13}C	$^{1}T_{CH}$ N phase 400 MHz (a)[a]	$^{1}T_{CH}$ N phase 600 MHz (b)[b]	|b-a| (Hz)	$^{1}T_{CH}$ N^{d} phase 400 MHz (c)[c]	$^{1}T_{CH}$ N^{d} phase 600 MHz (d)[d]	|d-c| (Hz)
57.12	135.83	132.21	3.62	141.06	141.03	-0.03
60.94*	-	-	-	-	-	-
68.63	45.18	46.18	1.00	114.12	112.88	-1.24
70.69	167.05	166.00	-1.05	153.46	154.94	1.48
72.73	162.72	163.41	0.69	144.94	146.37	1.43
75.10	-	165.03	-	150.16	149.19	-0.97
103.79	187.31	188.20	0.89	169.73	170.32	0.59

a) ^{2}H $|\Delta_Q|$=199.8 Hz b) ^{2}H $|\Delta_Q|$=200.0 Hz c) 2H $|\Delta_Q|$=85.0 Hz d) ^{2}H $|\Delta_Q|$=89.4 Hz

Table S2 Scalar and experimental dipolar couplings extracted from the two phases used (DSCG/D_2O and DSCG/D_2O/NaCl), along with the calculated ones after the fitting.

		DSCG (N phase)		DSCG (N^{d} phase)		DSCG (M phase)
^{13}C	$^{1}J_{CH}$	$^{1}D_{CH}$ exp	$^{1}D_{CH}$ calc	$^{1}D_{CH}$ exp	$^{1}D_{CH}$ calc	$^{1}D_{CH}$ exp
1	159.08	27.73	27.97	11.32	11.29	57.2
2	147.62	17.44	17.26	7.57	7.60	-
3	142.94	21.52	21.66	7.67	7.65	-
4	146.74	-99.51	-99.53	-33.66	-33.66	-
5	141.85	26.16	25.94	9.53	9.56	62.63
6	144.27	-68.42	-68.89	-23.14	-23.34	14.80
7	144.61	-10.39	-	-3.59	-	129.39

5.2 D-(+)-Lactose

Table S3 Lactose proton and carbon assignment, $^{1}J_{CH}$ and $^{3}J_{HH}$ couplings in D_2O and in the nematic doped phase (N^{d}) at 303K, $^{1}T_{CH}$ and $^{3}J_{HH}$ couplings in the N^{d} phase at 293K, $^{1}D_{CH}$ and $^{3}D_{HH}$ couplings and difference between the two sets of scalar coupling values, i.e. in D_2O and in the N^{d} phase and $^{1}D_{CH}$ and $^{3}D_{HH}$ calculated for the β-anomer.

Atom	^{1}H (ppm)	^{13}C (ppm)	*J* D_2O (Hz)	*J* N^{d} 303K (Hz)	*T* (Hz)	*D* (Hz)	*D* calc (Hz)	*D* N^{d} (Hz)
Gal1	4.31	102.83	162.33	162.80	173.81	11.48	10.90	11.01
Gal2	3.41	70.88	152.03	151.80	158.82	6.79	8.88	7.02
Gal3	3.53	72.43	147.48	148.59	156.82	9.34	8.21	8.23
Gal4	3.79	68.47	146.45	146.28	116.03	-30.42	-30.37	-30.25
Gal5	3.58	75.26	142.08	142.24	153.76	11.68	11.47	11.52
Gal6	3.62	60.97	144.47	144.50	137.25	-7.22	-	-7.25
Glc1β	4.53	95.68	161.85	161.85	156.33	-5.52	-6.03	-5.52
Glc2β	3.14	73.73	144.66	144.95	142.75	-1.91	-1.70	-2.20
Glc3β	3.51	74.71	145.14	145.01	143.57	-1.57	-1.10	-1.44
Glc4β	3.55	78.19	147.90	148.39	140.23	-7.67	-8.24	-8.16
Glc5β	3.47	74.28	143.48	143.40	139.07	-4.41	-4.27	-4.33
Glc6β	3.67-3.81	60.00	143.99	144.23	141.39	-2.6	-	-2.84
Glc1α	5.08	91.74	170.18	170.18	163.68	-6.5	-	-6.50
Glc2α	3.44	71.06	144.23	144.70	160.56	16.33	-	15.86
Glc3α	3.69	71.33	145.99	146.51	163.07	17.08	-	16.56

Glc4α	3.55	78.32	145.14	144.80	155.10	9.96	-	10.30
Glc5α	3.81	70.02	145.70	146.36	160.72	14.86	-	14.20
Glc6α	3.73	59.86	144.26	144.36	129.31	-14.95	-	-15.05
Gal1-2	-	-	7.80	7.92	12.36	4.56	4.55	-4.44
Glc1β-2β	-	-	7.96	8.14	3.78	-4.18	-4.15	-4.36
Glc1α-2α	-	-	3.76	3.66	11.40	7.64	-	7.74

5.3 5-Norbornen-2-ol

Table S4 5-Norbornen-2-ol proton and carbon assignment, $^{1}J_{CH}$ couplings in D_2O, $^{1}T_{CH}$ couplings in the N phase at 293K and experimental and calculated $^{1}D_{CH}$ couplings.

Atom	^{1}H (ppm)	^{13}C (ppm)	$^{1}J_{CH}$ (Hz)	$^{1}T_{CH}$ (Hz)	$^{1}D_{CH}$ (Hz)	$^{1}D_{CH}$ calc (Hz)
H1-*endo*	2.7	42.51	148.09	162.97	14.88	13.59
H2-*endo*	4.39	71.79	150.92	154.29	3.37	4.36
H3-*endo*	1.95-0.62	35.30	133.33	149.03	15.70	17.11
H4-*endo*	2.85	47.35	147.38	155.70	8.32	8.72
H5-*endo*	6.30	139.63	168.77	183.47	14.70	15.07
H6-*endo*	5.91	131.10	169.71	191.58	21.87	21.25
H7-*endo*	1.51-1.42	47.51	133.98	118.51	-15.47	-16.11
H1-*exo*	2.61	49.05	147.50	176.76	30.50	29.26
H2-*exo*	3.72	72.09	166.75	156.80	-9.10	-9.95
H3-*exo*	1.52-1.12	35.30	133.21	119.09	-16.36	-14.12
H4-*exo*	2.72	40.38	147.83	191.93	43.65	44.10
H5-*exo*	6.12	140.50	169.38	178.71	9.52	9.33
H6-*exo*	5.89	133.37	170.15	184.38	14.72	14.23
H7-*exo*	1.28-1.18	44.90	133.98	114.19	-16.55	-19.79

5.4 *N*-Methyl codeinium iodide

Table S5 *N*-Methyl codeinium iodide proton and carbon assignment, $^{1}J_{CH}$ couplings in D_2O, $^{1}T_{CH}$ couplings in the N[d] phase at 293K, $^{1}D_{CH}$ couplings and averaged $^{1}D_{CH}$ couplings for each methylene group, and calculated $^{1}D_{CH}$.

Atom	^{1}H (ppm)	^{13}C (ppm)	$^{1}J_{CH}$ (Hz)	$^{1}T_{CH}$ (Hz)	$^{1}D_{CH}$ (Hz)	$^{1}D_{CH}$-*av* (Hz)	$^{1}D_{CH}$ calc
15	1.86	29.80	132.55	134.34	1.8	1.5	1.63
15	2.55	29.80	132.52	133.68	1.2	1.5	1.63
10	2.83	23.89	130.32	168.44	38.1	37.8	36.59
16	3.12	55.43	146.23	152.70	6.5	6.5	5.06
22	3.29	54.06	144.93	154.26	9.3	9.3	12.65
16	3.37	55.43	146.23	152.70	6.5	6.5	5.06
23	3.39	50.08	144.82	157.00	12.2	12.2	8.19
14	3.40	33.54	134.64	114.94	-19.7	-19.7	-24.31
10	3.50	23.89	130.35	167.74	37.8	37.8	36.59
21	3.74	56.56	145.93	154.44	8.5	8.5	14.85
9	4.11	69.13	151.36	144.86	-6.5	-6.5	-9.06
6	4.28	66.28	139.60	114.24	-25.4	-25.4	-22.35
5	4.81	91.44	160.66	226.92	66.3	66.3	65.37
8	5.28	125.56	166.27	224.74	58.5	58.5	61.44
7	5.64	135.30	165.26	199.49	34.2	34.2	33.39
1	6.57	119.51	160.65	191.33	30.7	30.7	28.47
2	6.73	114.63	158.69	120.10	-38.6	-38.6	-35.20

6. XYZ coordinates of the tested DFT optimized molecules and MSpin output

6.1 Methyl-β-D-galactopyranoside

```
27
title
C     -1.075708   -0.785917   -0.470083
C      0.104310   -1.708881   -0.160887
C      1.410831   -0.994501   -0.527993
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C	1.498183	0.407978	0.094190
C	0.227088	1.205895	-0.178620
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C	-0.728629	3.340730	0.164668
O	2.614795	1.107907	-0.433147
O	0.140475	-2.105419	1.215886
O	-3.477265	-0.424161	-0.422166
O	2.549111	-1.759393	-0.143500
O	0.268339	2.386582	0.538930
O	-0.902571	0.437433	0.267593
H	-2.457844	-1.568989	0.989028
H	-2.634453	-2.256595	-0.634661
H	-0.530844	4.238506	0.747654
H	-1.732925	2.974454	0.388816
H	-0.657659	3.577330	-0.902593
H	-3.268189	0.411585	0.013563
H	-0.086029	-1.337475	1.758535
H	3.368537	0.506534	-0.365334
H	2.358724	-2.100148	0.743351
H	0.114312	1.402945	-1.257082
H	1.592180	0.316584	1.185543
H	1.474071	-0.888769	-1.615229
H	0.027359	-2.636044	-0.733258
H	-1.084882	-0.560670	-1.545385

Alignment tensor in the DSCG/D_2O phase
A'x=-3.193e-04
A'y=-4.745e-03
A'z= 5.064e-03
Saupe tensor
S'x=-4.789e-04
S'y=-7.117e-03
S'z= 7.596e-03
Alignment tensor eigenvectors
e[x]=(-0.077,-0.125, 0.989)
e[y]=(0.744,-0.668,-0.027)
e[z]=(0.664, 0.733, 0.144)
Alignment tensor in laboratory coordinates:
[-3.914e-04,4.821e-03,6.047e-04]
[4.821e-03,6.017e-04,4.903e-04]
[6.047e-04,4.903e-04,-2.103e-04]
SVD condition number is 3.120e+01
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Rhombic component Ar = 4.425e-03
rhombicity R = 5.826e-01
Asimmetry parameter etha =8.739e-01
GDO = 1.031e-02
Euler Angles (degrees)
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Set 2
(-101.1,221.6,-84.1)

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A'x=-1.098e-04
A'y=-1.678e-03
A'z= 1.788e-03
Saupe tensor
S'x=-1.646e-04
S'y=-2.517e-03

S'z= 2.681e-03
Alignment tensor eigenvectors
e[x]=(-0.075,-0.081, 0.994)
e[y]=(0.742,-0.671, 0.001)
e[z]=(0.667, 0.737, 0.110)
Alignment tensor in laboratory coordinates:
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[1.712e-03,2.153e-04,1.554e-04]
[1.386e-04,1.554e-04,-8.661e-05]
SVD condition number is 3.120e+01
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Rhombic component Ar = 1.568e-03
rhombicity R = 5.848e-01
Asimmetry parameter etha =8.772e-01
GDO = 3.643e-03
Euler Angles (degrees)
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Set 2
(-98.5,221.8,-84.2)

6.2 D-(+)-Lactose

```
45
beta-lactose
C       2.287940   -1.318920   -0.641790
O       2.132300   -2.733710   -0.647690
C       3.585840   -1.028350    0.110620
O       4.705490   -1.547050   -0.600060
C       3.821460    0.478180    0.279490
O       4.128900    1.073060   -0.974900
C       2.596190    2.650310    0.927230
O       1.426840    3.158240    1.561960
C       2.568660    1.130750    0.862270
O       1.415630    0.795720    0.068120
C       1.128070   -0.601280    0.042480
O      -0.030270   -0.791810   -0.704220
C      -1.256900   -0.366950   -0.077590
C      -3.189430    1.243810   -0.309950
O      -3.725750    2.292050   -1.103350
C      -1.790420    0.872530   -0.793790
O      -0.977740    2.029570   -0.604130
C      -1.895030   -2.728690    0.653770
O      -1.762360   -2.412880    2.035110
C      -2.274830   -1.510750   -0.177740
O      -3.533230   -1.056430    0.331270
C      -4.110840    0.033210   -0.395770
O      -5.324440    0.349210    0.199190
H       2.366840   -0.928630   -1.661880
H       1.481080   -2.968540   -1.318850
H       3.520870   -1.495530    1.102860
H       4.468690   -2.433710   -0.902750
H       4.653430    0.623000    0.982510
H       4.740980    0.467790   -1.416920
H       3.446660    2.978220    1.527480
H       2.709010    3.055230   -0.083900
H       0.657980    2.826410    1.078650
H       2.415920    0.742950    1.878470
H       0.991620   -0.961970    1.072720
H      -1.073390   -0.142290    0.975970
```

H	-3.134790	1.545640	0.745160
H	-3.046750	2.977600	-1.151310
H	-1.846590	0.643590	-1.867520
H	-0.059700	1.778960	-0.792170
H	-2.652280	-3.506780	0.500560
H	-0.930810	-3.116550	0.324590
H	-2.598140	-2.019120	2.317070
H	-2.375690	-1.814040	-1.229910
H	-4.243080	-0.273700	-1.443960
H	-5.958990	-0.349290	-0.002640

Alignment tensor RDC set 1
A'x=-4.242e-05
A'y=-4.364e-04
A'z= 4.788e-04
Saupe tensor
S'x=-6.364e-05
S'y=-6.546e-04
S'z= 7.182e-04
Alignment tensor eigenvectors
e[x]=(-0.140, 0.901,-0.410)
e[y]=(-0.684, 0.211, 0.699)
e[z]=(0.716, 0.378, 0.587)
Alignment tensor in laboratory coordinates:
[4.075e-05,1.981e-04,4.071e-04]
[1.981e-04,1.460e-05,5.754e-05]
[4.071e-04,5.754e-05,-5.535e-05]
SVD condition number is 7.837e+00
Axial component Aa = 7.182e-04
Rhombic component Ar = 3.940e-04
rhombicity R = 5.485e-01
Asimmetry parameter etha =8.228e-01
GDO = 9.595e-04
Euler Angles (degrees)
Set 1
(32.8,-45.7,-101.6)
Set 2
(-147.2,225.7,78.4)

Alignment tensor RDC set 2 (N^d)
A'x=-4.949e-05
A'y=-4.434e-04
A'z= 4.929e-04
Saupe tensor
S'x=-7.424e-05
S'y=-6.651e-04
S'z= 7.393e-04
Alignment tensor eigenvectors
e[x]=(-0.130, 0.864,-0.486)
e[y]=(-0.692, 0.272, 0.669)
e[z]=(0.710, 0.423, 0.563)
Alignment tensor in laboratory coordinates:
[3.581e-05,2.371e-04,3.990e-04]
[2.371e-04,1.823e-05,5.726e-05]
[3.990e-04,5.726e-05,-5.404e-05]
SVD condition number is 7.837e+00
Axial component Aa = 7.393e-04
Rhombic component Ar = 3.939e-04
rhombicity R = 5.328e-01

Asimmetry parameter etha =7.992e-01
GDO = 9.805e-04
Euler Angles (degrees)
Set 1
(36.9,-45.3,-100.6)
Set 2
(-143.1,225.3,79.4)

6.3 5-Norbornen-2-ol-*endo*

```
18
title
C       0.274432   -1.261212   -0.615966
C      -1.187967   -0.735636   -0.417159
C      -1.210886    0.675460   -0.985951
C      -0.489950    1.452942   -0.170844
C       1.099445   -0.366368    0.362245
C       0.018440    0.578117    0.967757
C      -1.155960   -0.419308    1.098703
O       2.132084    0.402953   -0.253161
H       0.623205   -1.144130   -1.644226
H       0.350516   -2.319087   -0.349542
H      -1.965592   -1.412955   -0.771415
H      -1.632226    0.946463   -1.947883
H      -0.205141    2.485848   -0.331788
H       1.532789   -0.976191    1.164031
H       0.346693    1.095378    1.869760
H      -0.925934   -1.290130    1.720968
H      -2.071969    0.053812    1.458674
H       2.805665   -0.206606   -0.576001
```

Alignment tensor with the endo RDC data set
A'x=-1.813e-04
A'y=-5.187e-04
A'z= 7.000e-04
Saupe tensor
S'x=-2.720e-04
S'y=-7.780e-04
S'z= 1.050e-03
Alignment tensor eigenvectors
e[x]=(0.407, 0.685, 0.605)
e[y]=(-0.282,-0.536, 0.796)
e[z]=(0.869,-0.494,-0.025)
Alignment tensor in laboratory coordinates:
[4.575e-04,-4.293e-04,5.663e-05]
[-4.293e-04,-6.302e-05,1.547e-04]
[5.663e-05,1.547e-04,-3.945e-04]
SVD condition number is 6.287e+00
Axial component Aa = 1.050e-03
Rhombic component Ar = 3.373e-04
rhombicity R = 3.213e-01
Asimmetry parameter etha =4.819e-01
GDO = 1.281e-03
Euler Angles (degrees)
Set 1
(-92.9,-60.4,-34.7)
Set 2
(87.1,240.4,145.3)

Alignment tensor with the exo RDC data set
A'x= 1.553e-04

A'y= 5.241e-04
A'z=-6.794e-04
Saupe tensor
S'x= 2.329e-04
S'y= 7.861e-04
S'z=-1.019e-03
Alignment tensor eigenvectors
e[x]=(-0.286, 0.792,-0.540)
e[y]=(-0.722, 0.193, 0.665)
e[z]=(0.630, 0.580, 0.516)
Alignment tensor in laboratory coordinates:
[1.574e-05,-3.563e-04,-4.486e-04]
[-3.563e-04,-1.116e-04,-2.026e-04]
[-4.486e-04,-2.026e-04,9.582e-05]
SVD condition number is 6.292e+00
Axial component Aa = -1.019e-03
Rhombic component Ar = -3.688e-04
rhombicity R = 3.619e-01
Asimmetry parameter etha =5.429e-01
GDO = 1.260e-03
Euler Angles (degrees)
Set 1
(48.3,-39.1,-111.6)
Set 2
(-131.7,219.1,68.4)

6.4 5-norbornen-2-ol-*exo*

```
18
title
C       0.373171    1.235764   -0.520525
C      -0.902775    1.016985    0.356276
C      -1.826980    0.123538   -0.465745
C      -1.274596   -1.093224   -0.512729
C       1.015635   -0.188065   -0.565091
C       0.023074   -1.038166    0.282771
C      -0.362998   -0.013746    1.376530
O       2.296321   -0.246492    0.073594
H       1.066047    1.928889   -0.035318
H       0.135421    1.630660   -1.510057
H      -1.342516    1.932534    0.752843
H      -2.706184    0.467680   -0.999153
H      -1.607059   -1.945666   -1.094176
H       1.101105   -0.572674   -1.586758
H       0.445553   -1.992020    0.598901
H      -1.132288   -0.388080    2.055458
H       0.494547    0.347151    1.949292
H       2.907616    0.304942   -0.428707
```

Alignment tensor with the endo RDC data set
A'x=-2.323e-04
A'y=-3.503e-04
A'z= 5.826e-04
Saupe tensor
S'x=-3.484e-04
S'y=-5.255e-04
S'z= 8.739e-04
Alignment tensor eigenvectors
e[x]=(-0.315, 0.930,-0.189)
e[y]=(0.512, 0.334, 0.792)
e[z]=(0.800, 0.153,-0.581)

Alignment tensor in laboratory coordinates:
[2.578e-04,7.928e-05,-4.263e-04]
[7.928e-05,-2.264e-04,-1.034e-04]
[-4.263e-04,-1.034e-04,-3.133e-05]
SVD condition number is 2.594e+00
Axial component Aa = 8.739e-04
Rhombic component Ar = 1.181e-04
rhombicity R = 1.351e-01
Asimmetry parameter etha =2.027e-01
GDO = 1.019e-03
Euler Angles (degrees)
Set 1
(165.3,-53.1,121.6)
Set 2
(-14.7,233.1,-58.4)

Alignment tensor with the exo data set
A'x= 9.119e-05
A'y= 5.827e-04
A'z=-6.739e-04
Saupe tensor
S'x= 1.368e-04
S'y= 8.741e-04
S'z=-1.011e-03
Alignment tensor eigenvectors
e[x]=(-0.257, 0.809,-0.528)
e[y]=(-0.702, 0.219, 0.677)
e[z]=(0.664, 0.545, 0.512)
Alignment tensor in laboratory coordinates:
[-3.301e-06,-3.522e-04,-4.940e-04]
[-3.522e-04,-1.127e-04,-1.409e-04]
[-4.940e-04,-1.409e-04,1.160e-04]
SVD condition number is 2.640e+00
Axial component Aa = -1.011e-03
Rhombic component Ar = -4.915e-04
rhombicity R = 4.862e-01
Asimmetry parameter etha =7.294e-01
GDO = 1.313e-03
Euler Angles (degrees)
Set 1
(46.8,-41.6,-110.1)
Set 2
(-133.2,221.6,69.9)

6.5 *N*-methyl codeinium iodide

```
48
C      -2.657000   -1.077000   -0.215000
C      -1.638000   -0.165000   -0.497000
C      -0.342000   -0.411000   -0.111000
C       0.018000   -1.470000    0.707000
C      -0.989000   -2.393000    1.004000
C      -2.289000   -2.213000    0.522000
C       0.534000    0.723000   -0.552000
C       1.483000    1.025000    0.625000
C       2.273000   -0.267000    0.917000
C       1.370000   -1.423000    1.370000
C      -0.530000    1.792000   -0.870000
C      -0.739000    2.817000    0.264000
C      -0.367000    2.288000    1.625000
C       0.690000    1.495000    1.813000
O      -3.909000   -0.774000   -0.645000
```

N	3.139000	-0.632000	-0.322000
C	1.355000	0.355000	-1.795000
C	2.259000	-0.829000	-1.543000
C	3.910000	-1.893000	-0.075000
O	-1.789000	1.064000	-1.086000
O	-2.041000	3.361000	0.211000
H	-0.777000	-3.248000	1.639000
H	-3.046000	-2.950000	0.774000
H	2.186000	1.821000	0.349000
H	3.020000	-0.079000	1.694000
H	1.212000	-1.255000	2.443000
H	1.894000	-2.381000	1.335000
H	-0.341000	2.314000	-1.811000
H	-0.058000	3.655000	0.046000
H	-0.953000	2.658000	2.463000
H	0.993000	1.184000	2.810000
C	-4.934000	-1.698000	-0.310000
C	4.153000	0.445000	-0.578000
H	0.687000	0.085000	-2.619000
H	1.926000	1.227000	-2.136000
H	1.676000	-1.734000	-1.348000
H	2.928000	-1.030000	-2.382000
H	4.627000	-2.019000	-0.885000
H	3.238000	-2.746000	-0.061000
H	4.437000	-1.805000	0.875000
H	-2.629000	2.611000	0.042000
H	-5.854000	-1.293000	-0.729000
H	-5.042000	-1.799000	0.776000
H	-4.741000	-2.686000	-0.743000
H	3.667000	1.377000	-0.852000
H	4.792000	0.121000	-1.398000
H	4.747000	0.585000	0.324000
I	7.176000	-0.218000	3.411000

Alignment tensor
A'x=-2.575e-04
A'y=-1.323e-03
A'z= 1.580e-03
Saupe tensor
S'x=-3.862e-04
S'y=-1.984e-03
S'z= 2.371e-03
Alignment tensor eigenvectors
e[x]=(0.048, 0.994,-0.097)
e[y]=(-0.036, 0.099, 0.994)
e[z]=(0.998,-0.044, 0.041)
Alignment tensor in laboratory coordinates:
[1.572e-03,-7.667e-05,1.132e-04]
[-7.667e-05,-2.644e-04,-1.084e-04]
[1.132e-04,-1.084e-04,-1.308e-03]
SVD condition number is 7.574e+00
Axial component Aa = 2.371e-03
Rhombic component Ar = 1.065e-03
rhombicity R = 4.494e-01
Asimmetry parameter etha =6.742e-01
GDO = 3.032e-03
Euler Angles (degrees)
Set 1
(-47.1,-86.6,-37.3)
Set 2
(132.9,266.6,142.7)

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