ELECTRONIC SUPPORTING INFORMATION

Mono- and dialdehyde of trehalose: new synthons to prepare trehalose bio-conjugates.

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Section S1. - Experimental Section

Materials

α,α-Trehalose anhydrous and 1,3,5-Trichloro-2,4,6-triazinetrione (trichloroisocyanuric acid) were purchased from Merck co. 2,2,6,6-Tetramethylpiperidine 1-oxyl, L-Carnosine, Sodium hydrogen carbonate, Ammonia, $NaBH_3CN$, Hydrogen peroxide, Methanol and anhydrous Dimethylformammide were purchased from Sigma Aldrich Co. Water was purified with a Milli-Q® system.

Methods

Nuclear Magnetic Resonance Spectroscopy. ^1H and ^{13}C NMR spectra were recorded on a Varian Unity Inova spectrometer at 500 and 125.7 MHz, respectively. The experiments were performed in D_2O at 27°C and the chemical shifts are reported as δ (ppm) referenced to the resonance of residual HOD. Unequivocal assignments of ^1H and ^{13}C resonances were supported by gCOSY, gHSQC and in some cases gHMBC experiments. The VnmrJ v4.0 software was used to process the data.

Mass spectrometry. ESI-LRMS spectra were performed with an Agilent Technologies 6410 Triple Quad LC/MS equipped with a Multimode (ESI/APCI) source. All the newly synthesized compounds were **ESI-HRMS** analysed using a quadrupole-Orbitrap hybrid mass spectrometer (Q Exactive, Thermo Scientific). Nitrogen was used as a sheet gas, capillary temperature and spray voltage were 250 °C and 3.5 kV, respectively. The MS acquisition was performed in Full scan mode (70,000 resolution, scan range 200 to 2000 m/z, maximum injection time 50 ms, AGC target $1 \cdot 10^6$).
The compounds were diluted (not higher than 10 μM) in water containing methanol (10%) and formic acid (0.5 %) and directly injected into the MS spectrometer.

Thin Layer Chromatography. TLC analyses were carried out on silica gel 60 F254 plates (Merck); unless otherwise specified, spots were revealed by spraying the plates with Molybdenum Blue reagent (Sigma).

Section S2. - Synthetic Procedures

Synthesis of the monoaldehyde of trehalose [5-formyl-5-dehydroxymethyl-trehalose] (**2**)**.**

500 mg of Trehalose (1.46 mmol) were dissolved in 250 mL of anhydrous DMF and the solution was added with sodium hydrogencarbonate (3.69 g, 43.95 mmol) and TEMPO (5.7 mg, 36.5 µmol). The mixture was placed in thermostatic bath at 25 °C and then TCCA (339 mg, 1.46 mmol) was added. After 75 min of continuous stirring, the reaction mixture was quenched with 20 mL of methanol and sodium hydrogencarbonate filtered-off. The filtrate was concentrated *in vacuo* to 1/5 of the initial volume and methylene chloride was then added to precipitate sugar components. The precipitate was recovered by filtration and a small aliquot was dissolved in D_2O and analyzed by NMR.

The degree of trehalose conversion was determined from the ratio between the integration value of the signal at 3.55 ppm (H-4') and that of the signal at 3.48 ppm (H-4); trehalose and trehalose *mono*-aldehyde were found in a molar ratio of about 1.25:1.

The remaining precipitate was dissolved in DMF (100 mL) and loaded onto a column of weakly basic anion exchange resin (Lewatit® VP OC 1065) which was washed in sequence with DMF, DMF/H_2O (1:1 v/v) and water. The desired compound was recovered by elution with aqueous 20% CH3COOH. The eluate was lyophilized affording **2** as a white powder (198.6 mg, 40 % yield). TLC, SiO_2, ACN/W (70:30, v/v); Rf 0.45. **ESI(+)-HRMS** *m/z* calcd. for $C_{12}H_{21}O_{11}$ ($[M+H]^+$) 341.1078, found 341.1077.

^{1}H NMR (D_2O): 5.29 (d, J=2, 1 H, H-6'), 5.26 (d, J=4, 1 H, H-1'), 5.25 (d, J=3.5, 1H, H-1) 3.91-3.84 (overlapped multiplets, 4 H, H-3, H-3', H-6a, H-5), 3.82-3.77 (partially overlapped signals, 2 H, H-6b, H-5'), 3.70-3.66 (two overlapped doublet of doublets, 2 H, H-2, H-2'), 3.55 (dd, $J_{4'-5'}$ = 9.5 Hz and $J_{4'-3'}$ = 9.6 Hz, 1 H, H-4'), 3.48 (dd, J_{4-5} = 9.8 Hz and J_{4-3} = 9.2 Hz, 1 H, H-4). **^{13}C- NMR** (D_2O, 125.7 MHz): 93.19 e 93.16 (C1 e C1'), 87.90 (C6'), 72.97 (C5'), 72.45 (C3), 72.28 (C3'), 72.11 (C5), 70.97 e 70.85 (C2 e C2'), 70.40 (C4'), 69.66 (C4), 60.51 (C6).

A colorless aqueous solution of **2**, which gave a positive Tollens's test, turned red-orange in color when treated with the 2,4-dinitrophenylhydrazine reagent. A direct spectrometry analysis [**ESI(+)-LRMS**] of this mixture revealed the presence of an intense peak at m/z 543.2 $(M + Na)^+$ correlated to the molecular ion of the 2,4-dinitrophenylhydrazone of **2**.

Synthesis of the dialdehyde of trehalose [5,5'-diformyl-5,5'-didehydroxymethyl-trehalose] (**3**)**.**

The title compound was prepared following the procedure above described for **2**, but utilizing different molar amounts of TCCA (1.696 g, 7.3 mmol), sodium hydrogencarbonate (18.566 g, 0.221 mol) and TEMPO (17.5 mg, 112 µmol). The reaction time was extended to 3.5 hours. After purification and freeze-drying, 439 mg of pure **3** were obtained (89 % yield) as a white powder. TLC, SiO2, ACN/W (70:30, v/v); Rf 0,35. **ESI(+)-HRMS**: *m/z* calcd. for $C_{12}H_{19}O_{11}$ ($[M+H]^+$) 339.0922, found 339.0921. **^{1}H- NMR** (D_2O): 5.23-5.22 (two overlapped doublets, 4H,H-6, H-1), 3.85 (dd, J_{3-4}= 9.5 Hz, J_{3-2}= 9.5 Hz, 2H, H-3), 3.75 (dd, J_{5-6} = 3.5 Hz and J_{5-4}

= 9.5 Hz, 2H, H-5), 3.62 (dd, J_{1-2} = 3.5 Hz and J_{2-3} = 9.5 Hz, 2H, H-2), 3.49 (dd, J_{4-5} = 9.5 Hz and J_{4-3} = 9.6 Hz, 2 H, H-4'). **^{13}C-NMR** (D_2O, 125.7 MHz): 93.18 (C1), 87.94 (C6), 73.01 (C5), 72.29 (C3), 70.85 (C2), 70.41 (C4).

Synthesis of 6-amino-6-deoxy-trehalose (**4**)**.**

50 mg of **2** (0.147 mmol) were dissolved in 50 mL of methanol and gaseous ammonia was bubbled through this solution for 4 hours at r. t. . Next, $NaBH_3CN$ was added (46.2 mg, 0.735 mmol) and the reaction mixture was allowed to stand for 1 hour at room temperature. The reaction was then quenched by adding 10% HCl up to pH=4 and subsequently neutralized. The resulting mixture was concentrated *in vacuo* and then charged onto a column of strongly acidic cation exchange resin (Dowex® 50X8, H^+). After washing with water, the desired compound was recovered by elution with 2N NH_4OH. The eluate was then freeze dried, affording 48 mg of pure **4** (96 % yield). **^{1}H NMR** (D_2O): 5.26 (d, J=4, 1 H, H-1), 5.23 (d, J=4, 1H, H-1') 3.96 (m, 1 H, H-5') 3.91-3.84 (overlapped multiplets, 4 H, H-3, H-3', H-6a, H-5), 3.79 (dd, J_{5-6b}=5, J_{6a-6b}= 10, 1 H, H-6b), 3.72-3.67 (two overlapped doublet of doublets, 2 H, H-2, H-2'), 3.48 (dd, 1 H, H-4'), 3.42-3.35 (partially overlapped multiplets, 2H, H-4 and H'_{6a}), 3.07 (dd, H'_{6b}). **^{13}C- NMR** (D_2O, 125.7 MHz): 93.2 and 93.1 (C1 e C1'), 72.97 (C5'), 72.45 (C3), 72.28 (C3'), 72.11 (C5), 70.97 e 70.85 (C2 e C2'), 70.41 (C4'), 69.67 (C4), 60.51 (C6). 41.2 (C6').

Synthesis of 6,6'-diamino-6,6'-dideoxy-trehalose (**5**)**.**

Following an experimental procedure similar to that used for preparing compound **4**, compound **5** (47.9 mg) was obtained with a yield of 96%, starting from **3** (50 mg, 0.148 mmol) and using 94.26 mg (1.5 mmol) of $NaBH_3CN$. **^{1}H NMR** (D_2O): 5.23 (d, J=4, 2H, H-1) 3.96 (m, 2 H, H-5) 3.91-3.84 (overlapped multiplets, 4 H, H-3, H-5), 3.72-3.67 (doublet of doublets, 2 H, H-2), 3.48 (dd, 2 H, H-4), 3.42-3.35 (partially overlapped multiplets, 2H, H-4 and H_{6a}), 3.07 (dd, H_{6b}). **^{13}C- NMR** (D_2O, 125.7 MHz): 93.2 (C1), 72.97 (C5), 72.45 (C3), 70.97 (C2), 70.41 (C4), 41.2 (C6).

Synthesis of 5-carboxy-5-dehydroxymethyl-trehalose (**6**) **and 5,5'-dicarboxy-5,5'-didehydroxymethyl-trehalose** (**7**)**.**

Both title compounds **6** and **7** were obtained from compounds **2** (50 mg, 0.147 mmol) and **3** (50 mg, 0.148 mmol) respectively by treating both these with 10% H_2O_2 (25 ml) at r. t. for 12 hours The reaction mixture was concentrated under vacuum and the solution was charged onto a column of a strong basic anion exchange resin (Dowex 1X4), from which the desired compound was recovered by elution with 2N CH_3COOH. The eluate was then freeze dried, affording pure **6** (49.2 mg) or **7** (52 mg).

(6) : 94 % yield; TLC,SiO_2, BuOH/AcOH/W (60:15:25, v/v/v), Rf 0.12). **ESI(-)-HRMS**: *m/z* calcd. for $C_{12}H_{19}O_{12}$ ($[M-H]^-$) 355.0882, found 355.0883. **^{1}H NMR** (D_2O): 5.26 (d, J=3 Hz, 1 H, H-1), 5.21 (d, J=3.5 Hz, 1H, H-1'), 4.28 (d, J=9.5 Hz, 1H, H-5'), 3.92-3.84 (overlapped multiplets, 4 H, H-3, H-3', H-6a, H-5), 3.78 (dd, J_{5-6b}=6 Hz,

J_{6a-6b}= 16 Hz, 1 H, H-6b), 3.73 (dd, $J_{2'-1'}$=3 Hz, $J_{2'-3'}$= 9.5 Hz, 1 H, H-2'), 3.68 (dd, J_{2-1}=3.5 Hz, J_{2-3}= 10 Hz, 1 H, H-2), 3.62 (dd, $J_{4',5'}$ =9.5 Hz, $J_{4',3'}$= 9.2 Hz, 1H, H-4'), 3.48 (dd, $J_{4,5}$ =9.9 Hz, $J_{4,3}$= 9.2 Hz, 1H, H-4). **^{13}C- NMR** (D_2O, 125.7 MHz): 167.1 (C6'), 93.62 e 93.52 (C1 e C1'), 72.41 (C3), 72.22 (C3'), 72.17 (C5), 71.75 (C5'), 70.89 (C2 e C2'), 70.69 (C4'), 69.61 (C4), 60.48 (C6).

(7) : 95% yield. **ESI(-)-HRMS**: *m/*z calcd. for $C_{12}H_{17}O_{13}$ ($[M-H]^-$) 369.0675, found 369.0676. **^{1}H NMR** (D_2O): 5.21 (d, J=3.5 Hz, 2H, H-1), 4.28 (d, J=9.5 Hz, 2H, H-5), 3.88 (m, 2 H, H-3), 3.73 (dd, J_{2-1}=3 Hz, J_{2-3}= 9.5 Hz, 1 H, H-2), 3.62 (dd, $J_{4,5}$ =10 Hz, $J_{4,3}$= 9.2 Hz, 2H, H-4). **^{13}C- NMR** (D_2O, 125.7 MHz): 167.1 (C6), 93.52 (C1), 71.9 (C5), 72.28 (C3), 70.97 (C2), 70.41 (C4).

Synthesis of the *mono*-carnosine conjugate of trehalose [6-((3-((1-carboxy-2-(1H-imidazol-4-yl)ethyl)amino)-3-oxopropyl)amino)-6-deoxy-α-α-trehalose] (**8**)**.**

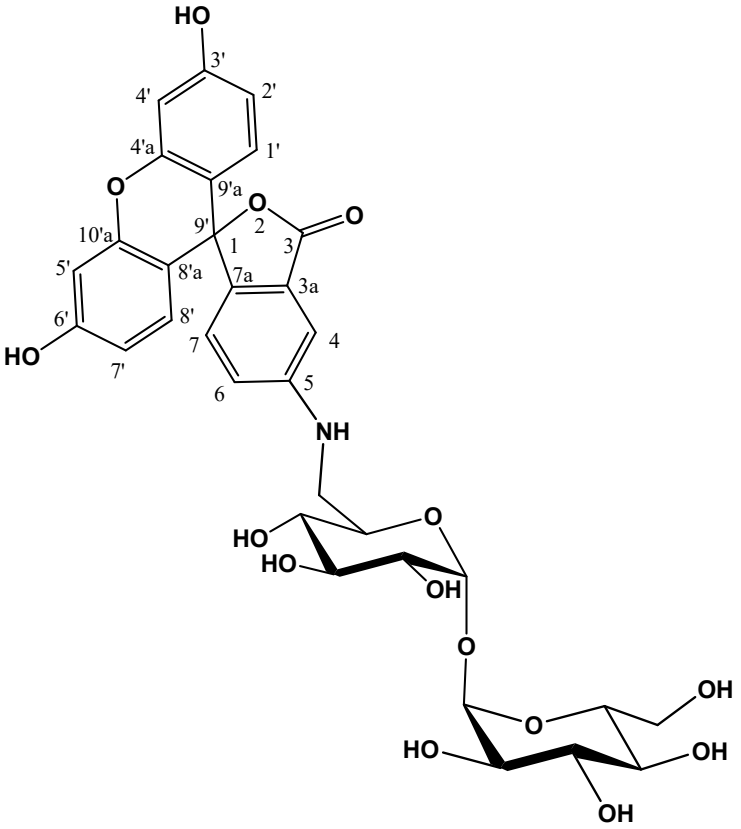
50 mg of **2** (0.147 mmol) were dissolved in 50 mL of methanol and carnosine methyl ester (42.24 mg, 0.176 mmol) was added to this solution. After 4 hours under continuous stirring, $NaBH_3CN$ (46.19 mg, 0.735 mmol) was added and the reaction mixture was allowed to stand for 1 hour at room temperature. After this time, the reaction mixture was cooled to 5 °C and 25 mL of 0.1 N NaOH were added to it, leaving it to stand still for 1 hour. The end of the hydrolysis was checked by TLC/SiO_2[2-PrOH/conc. NH_3 (7:3, v/v)]. Spots were detected by spraying first with "Fast Red B salt" solution and then with 0.1 N NaOH; the Rf value for **8** was 0.2. The mixture was then neutralized, concentrated under vacuum and charged onto a column of a strongly acidic cation exchange resin (Dowex 50X8, H^+). After washing with water, crude **8** was recovered from the column by elution with 2N NH_4OH. The eluate was taken to dryness under vacuum and the residue fractionated by PLC (eluent: 2-Propanol / 0.05 M $(NH_4)_2CO_3$ (7:3, v/v). Fractions containing **8** were collected and lyophilized, affording **8** (58.2 mg, 72% yield). **ESI(+)-LRMS**: *m/z* 551.2 ($[M+H]^+$). **^{1}H- NMR** (D_2O): (ppm) 7.72 (s, 1 H, H-2 of the imidazole ring), 6.88 (s, 1 H, H-5 of imidazole), 5.12 (d, 1H, H-1), 5.07 (d, 1H, H-1'), 3.94 (m, 1 H, CH of the histidine chain), 3.94 (m, 1 H, H-5'), 3.88-3.70 (m, 4 H, H-3,H-3',H-5, H-$6'_b$), 3.66 (dd, 1H, H-6'a), 3.58 (dd, 1H, H-2), 3.52 (dd, 1H, H-2'), 3.34 (dd, 1H, H-4), 3.30 (dd, 1H, H-$6'_b$), 3.25 (m, 2H, H-$6'_a$, H-'4), 3.10 (m, 2 H, β-CH_2 of β-Ala); 3.04 (m, 1 H, Ha of CH_2 of His), 2.87 (dd, 1 H, Hb of CH_2 of His), 2.26 (m, 2H, α-CH_2 of β-Ala). **^{13}C-NMR** (D_2O, 125.7 MHz): 176.9 (-COOH of His), 172.2 (-CONH-), 133.8 (C2 of imidazole ring), 130.1 (C4 of imidazole ring), 117.2 (C5 of imidazole ring), 94.9 (C1), 93.26 (C1'), 72.9 (C6), 72.2 (C3'), 71.9 (C3), 71.6 (C4'), 70.9 (C2), 70.6 (C2'), 70.3 (C4), 67.7 (C5'), 54.4 (CH of His), 48.5 (β-C of β-Ala), 43.4 (C6), 30.5 (α-C of β-Ala), 27.1 (CH_2 of Hys).

Synthesis of the *bis*-carnosine conjugate of trehalose [6,6'-bis((3-((1-carboxy-2-(1H-imidazol-4-yl)ethyl)amino)-3-oxopropyl)amino)-6,6'-dideoxy-α-α-trehalose] (**9**)**.**

The title compound, was prepared following the same synthetic procedure above described for **8**, starting from 50 mg of **3** (0.148 mmol) but utilizing different molar amounts of carnosine methyl ester (85.2 mg,

0.355 mmol) and NaBH4CN (93.0 mg, 1.48 mmol). At the end of the synthesis, **9** (93 mg) was obtained with a yield of 83%. TLC, SiO_2, 2-PrOH/conc. NH_3 (7:3, v/v), detection: "Fast Red B" - 0.1N NaOH, Rf 0.15. **ESI(+)-HRMS**: *m/z* calcd. for $C_{30}H_{47}N_8O_{15}$ ($[M+H]^+$) 759.3155, found 759.3149. **^{1}H- NMR** (D_2O): (ppm) 8.57 (s, 2 H, H-2 of imidazole ring), 7.25 (s, 2 H, H-5 of imidazole), 5.22 (d, 2H, H-1), 4.46 (dd, 2 H, C*H* of the His), 4.07 (m, 2 H, H-5), 3.80 (dd, 2 H, H-3), 3.63 (dd, 2H, H-2), 3.43 (m, 2 H, Ha of β-CH_2 of β-Ala); 3.33 (m, 2 H, H6'a), 3.32 (dd, 2H, H-4), 3.28 (m, 2 H, Hb of β-CH_2 of β-Ala); 3.24 (m, 2 H, H6'b), 3.21 (m, 2 H, Ha of CH_2 of His), 3.04 (m, 2 H, Hb of CH_2 of His), 2.7 (m, 4H, α-CH_2 of β-Ala). **^{13}C-NMR** (D_2O, 125.7 MHz): 176.9 (-COOH of His), 172.2 (-CONH-), 133.8 (C2 of imidazole ring), 130.1 (C4 of imidazole ring), 117.2 (C5 of imidazole ring), 94.9 (C1), 71.9 (C3), 71.6 (C4), 70.6 (C2), 67.7 (C5), 54.4 (CH of His), 48.5 (β-C of β-Ala), 43.4 (C6), 30.5 (α-C of β-Ala), 27.1 (CH_2 of His).

Synthesis of the *mono*-fluorescein conjugate of trehalose [6-((3',6'-dihydroxy-3H-spiro[isobenzofuran-1,9'-xanthen]-3-one-5yl)amino)-6-deoxy-α-α-trehalose] (**10**)**.**



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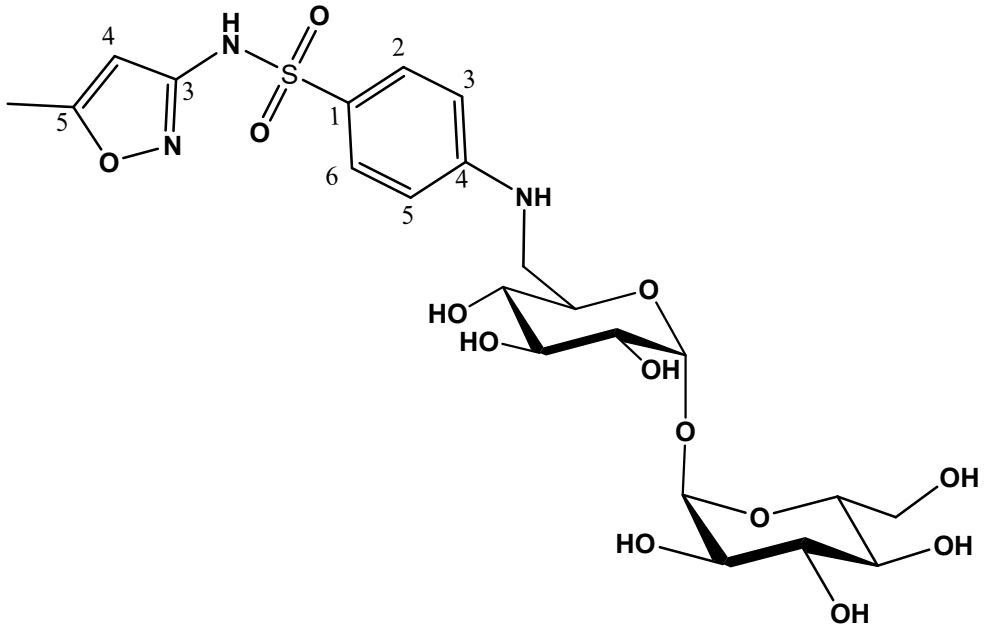
50 mg of **2** (0.147 mmol) were dissolved in 50 mL of methanol and 5-aminofluorescein (61.1 mg, 0.176 mmol, 1.2 eq) was added to this solution. After 1 hours under continuous stirring at r. t., $NaBH_3CN$ (46.19 mg, 0.735 mmol, 5 eq.) was added and the reaction mixture was allowed to stand for 2 hour at r. t.. The end of the reaction was checked by TLC/SiO_2[ACN/H2O (80:20, v/v)], where the Rf value of **10** was 0.63. The

mixture was then concentrated under vacuum and charged onto a column of a strongly acidic cation exchange resin (Dowex 50X8, H^+). After washing with water, crude **10** was recovered from the column by eluting with 2N NH_4OH. The eluate was taken to dryness under vacuum and the residue fractionated by PLC (eluent: H_2O gradient in ACN (from 0 to 20%). Fractions containing **10** were collected and lyophilized, affording **10** (50.35 mg, 51% yield%). **ESI(+)-HRMS**: *m/z* calcd. for $C_{32}H_{34}NO_{15}$ ($[M+H]^+$) 672.1923, found 672.1920. **^{1}H- NMR** (D_2O): (ppm) 7.47 (d, 1H, H-8' of fluorescein), 7.45 (d, 1 H, H-1' of fluorescein), 7.29 (d, 1H, H-4 of fluorescein), 7.18 (d, 1 H, H-7 of fluorescein), 7.06 (d, 1 H, H-6 of fluorescein), 6.80 (d, 2 H, H-2' and H-7' of fluorescein), 6.79 (s, 2 H, H-5' and H-4' of fluorescein), 5.25 (d, 1H, H-1 of trehalose), 5.14 (d, 1H, H-1' of trehalose), 4.10 (m, 1 H, H-5' of trehalose), 3.92-3.75 (m, 6 H, H-3, H-3', H-5, H-6_a, H-6_b, H-$6'_b$ of trehalose), 3.72 (dd, 1H, H-2' of trehalose), 3.58 (dd, 1H, H-2 of trehalose), 3.53-3.40 (overlapped m, 3 H, H-6'a, H-4 and H-'4 of trehalose). **^{13}C-NMR** (D_2O, 125.7 MHz): 158.4 (C3 of fluorescein), 149.4 (C5 of fluorescein), 149.35 (C3' and C6' of fluorescein), 143.4 (C10'a and C4'a of fluorescein), 139.2 (C7a of fluorescein), 132.13 (C8' and C1' of fluorescein), 131.6 (C7 of fluorescein), 128.3 (C3a of fluorescein), 121.4 (C5' and C4' of fluorescein), 114.5 (C6 of fluorescein), 113.9 (C4 of fluorescein), 108.5 (C8'a and C9'a of fluorescein), 103.9 (C7' and C2' of fluorescein), 93.3 (C1 of trehalose), 93.0 (C1' of trehalose), 72.6 (C5 of trehalose), 72.5 (C3' of trehalose), 71.9 (C3 of trehalose), 71.8 (C4 of trehalose), 71.6 (C2' of trehalose), 70.2 (C2 of trehalose), 69.6 (C5' of trehalose), 60.6 (C4 of trehalose), 60.5 (C6 of trehalose), 44.8 (C6' of trehalose).

Synthesis of the *mono*-Sulfamethoxazole conjugate of trehalose [N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide] (**11**).



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50 mg of **2** (0.147 mmol) were dissolved in 50 mL of methanol and sulfamethoxazole (74,5 mg, 0.294 mmol, 2 eq.) was added to this solution. After 6 hours under continuous stirring at 40°C, the mixture was brought to r. t. and then $NaBH_3CN$ (46.19 mg, 0.735 mmol) was added allowing to react for 2 hour. The end of the reaction was checked by TLC/SiO_2[ACN/H2O (80:20, v/v)], where the Rf value of **11** was 0.74. The mixture was then concentrated under vacuum and charged onto a SiO_2 column and, after washing with ACN, a fraction containing crude **11** was recovered by eluting with ACN/H_2O (1:1, v/v). The aqueous eluate, concentrated under reduced pressure, was ~~then~~ charged onto a column of a strongly acidic cation exchange resin (Dowex 50X8, H^+), which was washed with water and by which **11** was recovered by elution with 2N NH_4OH. The ammonia eluate was concentrated under reduced pressure and then lyophilized, affording 61.13 mg of **11** (72% yield%). **ESI(+)-HRMS**: *m/*z calcd. for $C_{22}H_{32}N_3O_{13}S$ ($[M+H]^+$) 578.1650, found 578.1648. **^{1}H- NMR** (D_2O): (ppm) 7.68 (d, J= 10 Hz, 2 H, H-3 and H-5 of benzene ring), 6.79 (d, J= 10 Hz, 2 H, H-2 and H-6 of benzene ring), 6,06 (s, 1H, H-4 of isoxazole ring), 5.17 (d, J=3.7 Hz, 1H, H-1 of trehalose), 5.03 (d, J=3.7 Hz, 1H, H-1' of trehalose), 3.97 (m, 1 H, H-5' of trehalose), 3.89-3.79 (m, 4 H, H-3, H-3',H-5 and H-6_b of trehalose), 3.76 (dd, 1H, H-6a of trehalose), 3.67 (dd, 1H, H-2 of trehalose), 3.61 (d, 1H, H-6'a of trehalose), 3.51 (dd, 1H, H-2' of trehalose), 3.44 (2 overlapped dd, 2H, H-4 and H-4' of trehalose), 3.36 (dd, 1H, H-6'$_b$ of trehalose), 2.31 (s, 3H, CH_3 of isoxazole ring). **^{13}C-NMR** (D_2O, 125.7 MHz): 172.0 (C5 of isoxazole ring), 158.1(C3 of isoxazole ring), 153.1 (C4 of benzene ring), 129.1 (C3 and C5 of benzene ring), 123.5 (C1 of benzene ring), 112.4 (C2 and C6 of benzene ring), 95.4 (C4 of isoxazole ring), 93.2 (C1 of trehalose), 93.1 (C1' of trehalose), 72.6 (C5 of trehalose), 72.5 (C3' of trehalose), 72.1 (C3 of trehalose), 71.4 (C4 of trehalose), 71.0 (C2' of trehalose), 70.9 (C2 of trehalose), 70.3(C5' of trehalose), 60.6 (C4 of trehalose), 60.5 (C6 of trehalose), 43.3 (C6' of trehalose), 11.6 (CH_3 on isoxazole ring).

Section S3. - NMR Spectra

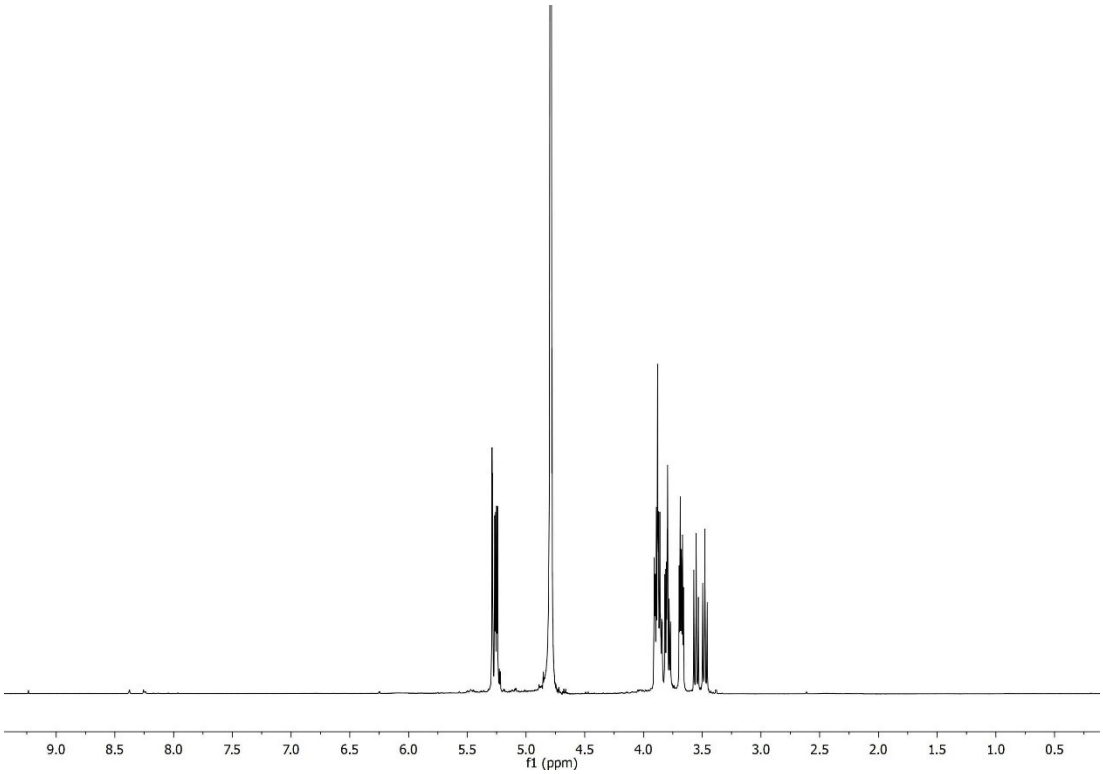

Figure S1: ^{1}H-NMR spectrum of 5-formyl-5-dehydroxymethyl-trehalose **(2)**

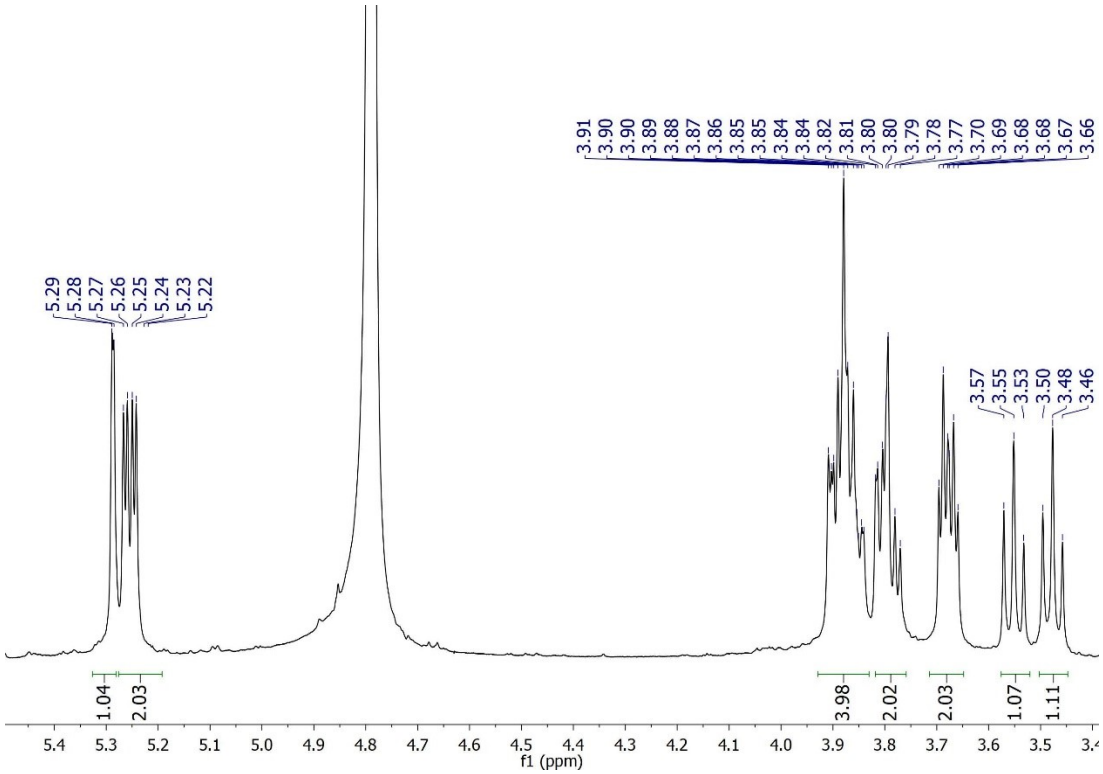

Figure S2: ^{1}H-NMR spectrum of 5-formyl-5-dehydroxymethyl-trehalose **(2)**; magnification between 3.4 and 5.5 ppm.

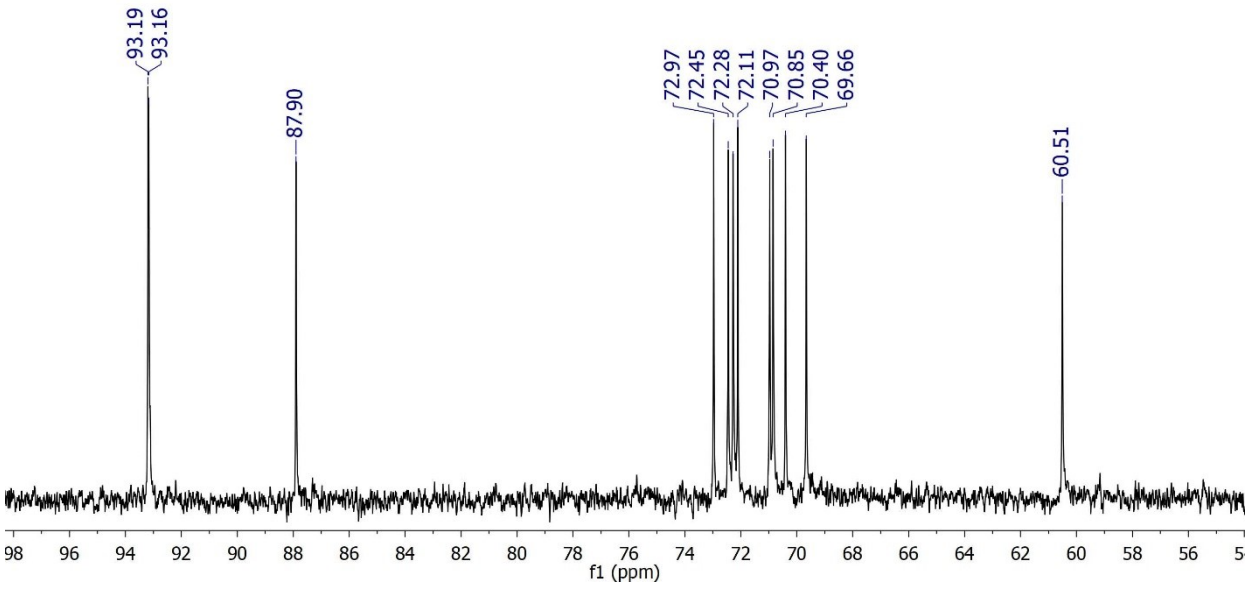

Figure S3: ^{13}C-NMR spectrum of 5-formyl-5-dehydroxymethyl-trehalose **(2)**

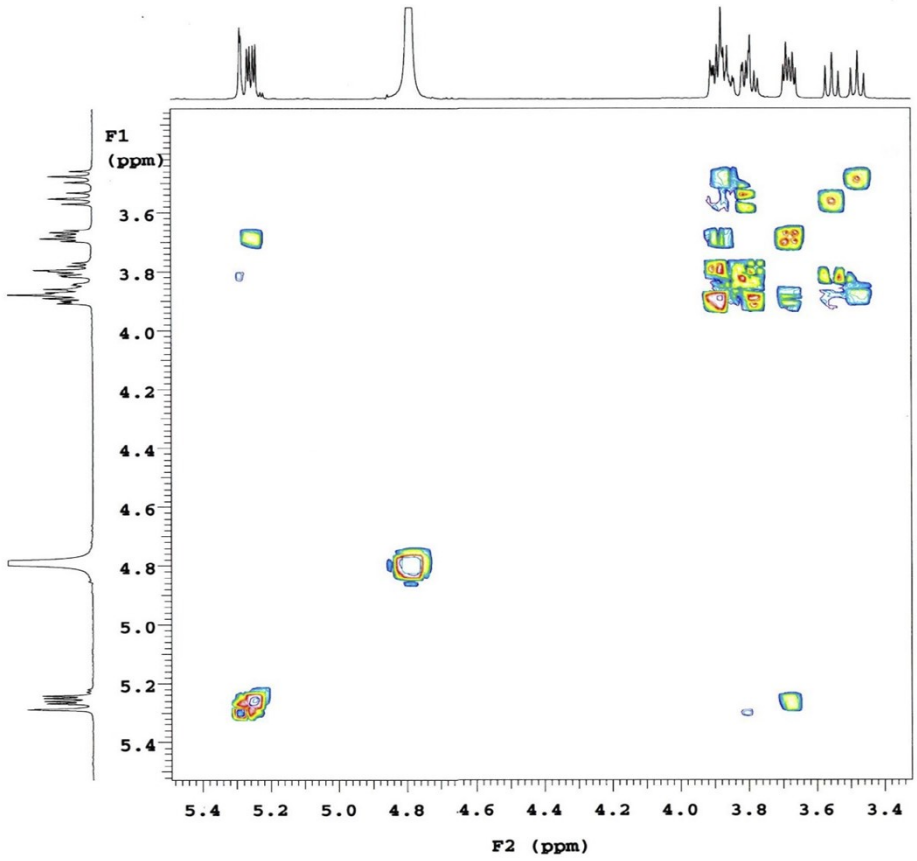

Figure S4: gCOSY NMR spectrum of 5-formyl-5-dehydroxymethyl-trehalose **(2)**

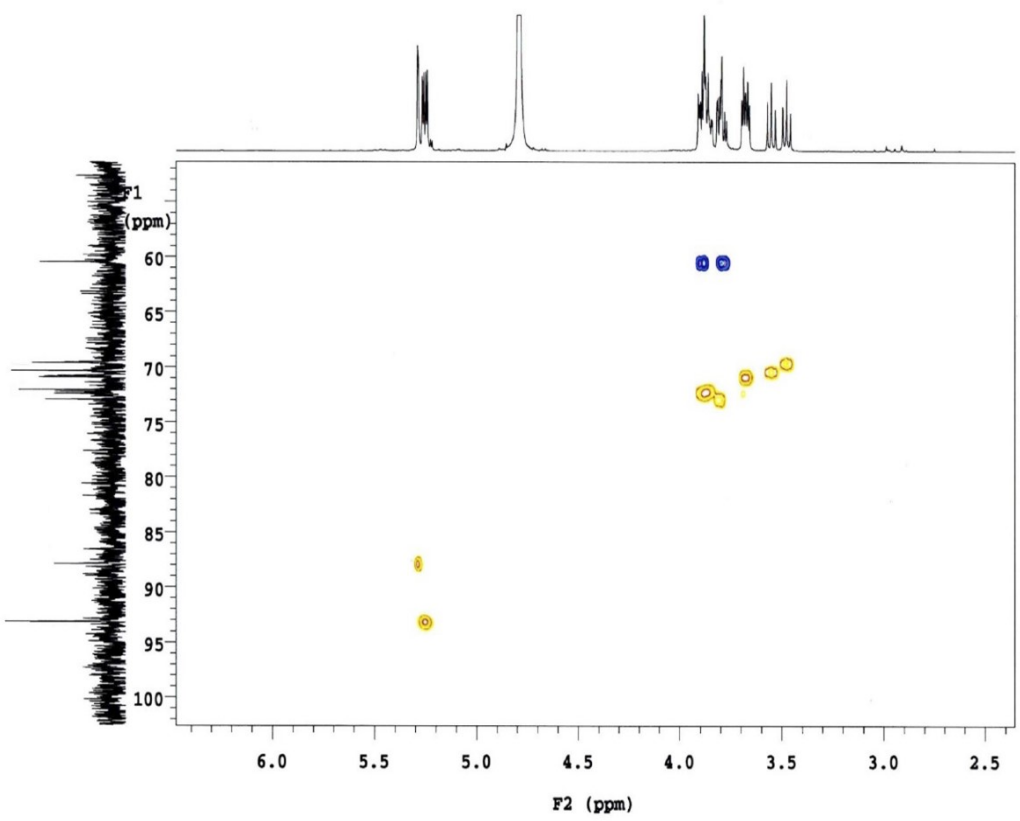

Figure S5: gHSQC NMR spectrum of 5-formyl-5-dehydroxymethyl-trehalose **(2)**

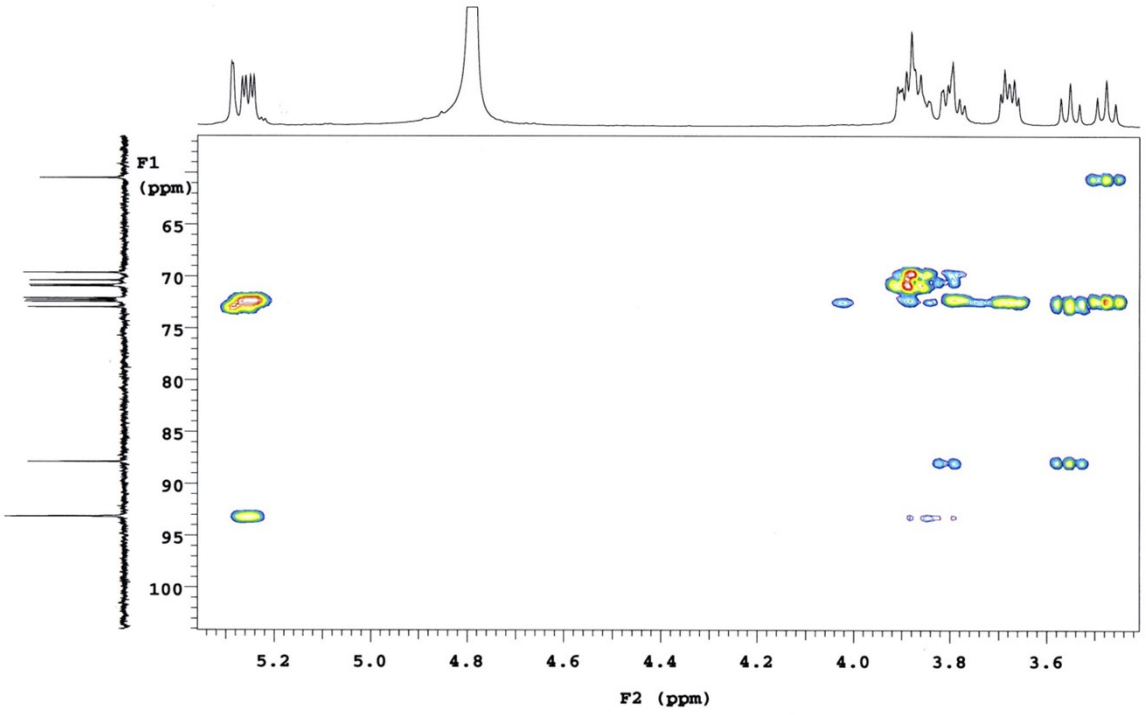

Figure S6: gHMBC NMR spectrum of 5-formyl-5-dehydroxymethyl-trehalose **(2)**

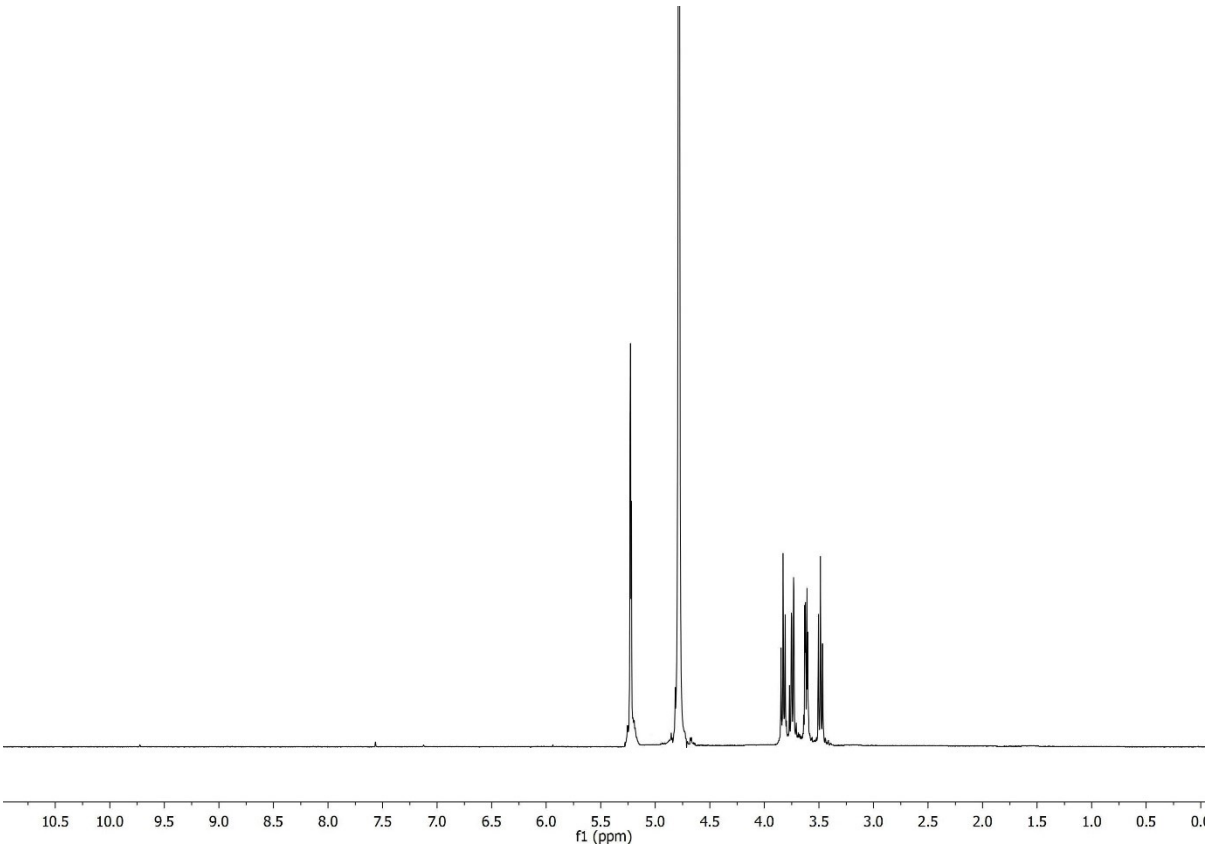

Figure S7: ^{1}H-NMR spectrum of 5,5'-diformyl-5,5'-didehydroxymethyl-trehalose **(3)**

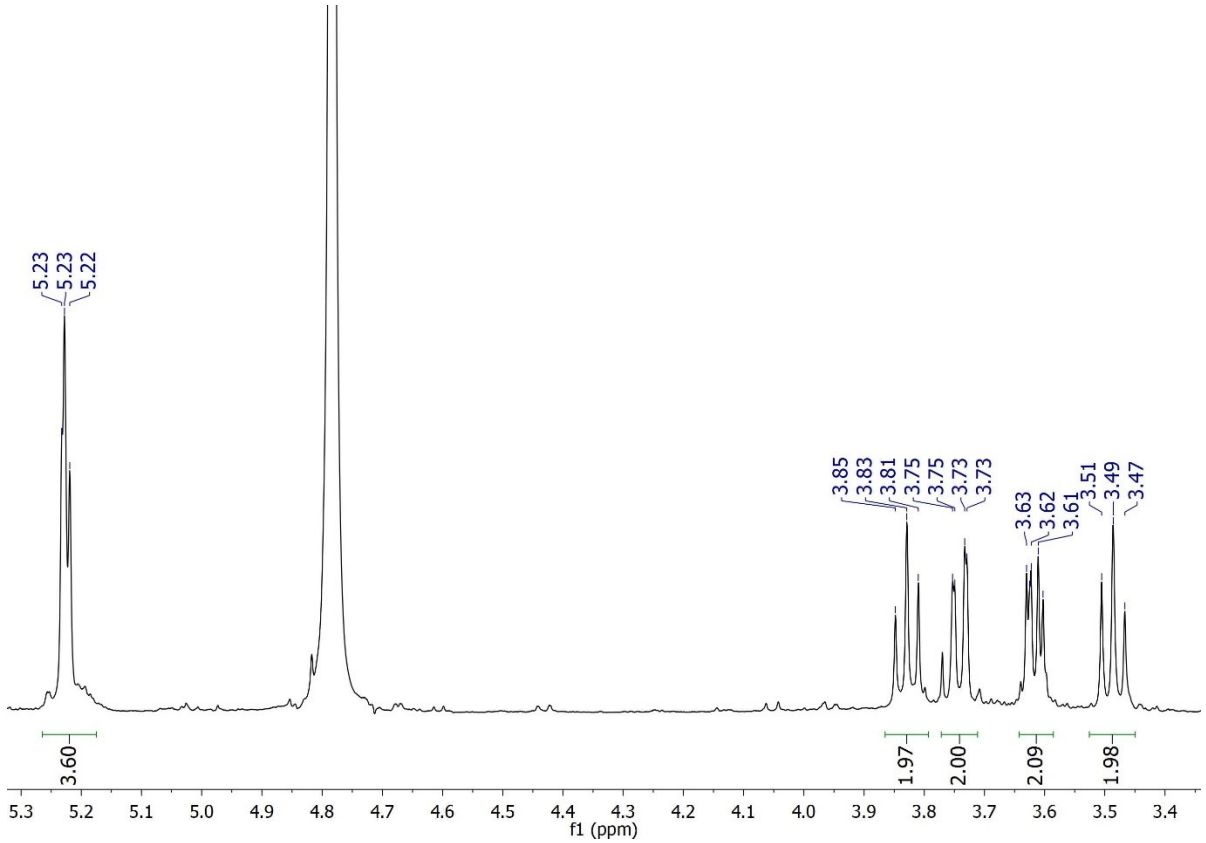

Figure S8: ^{1}H-NMR spectrum of 5,5'-diformyl-5,5'-didehydroxymethyl-trehalose **(3)**; magnification between 3.4 and 5.3 ppm.

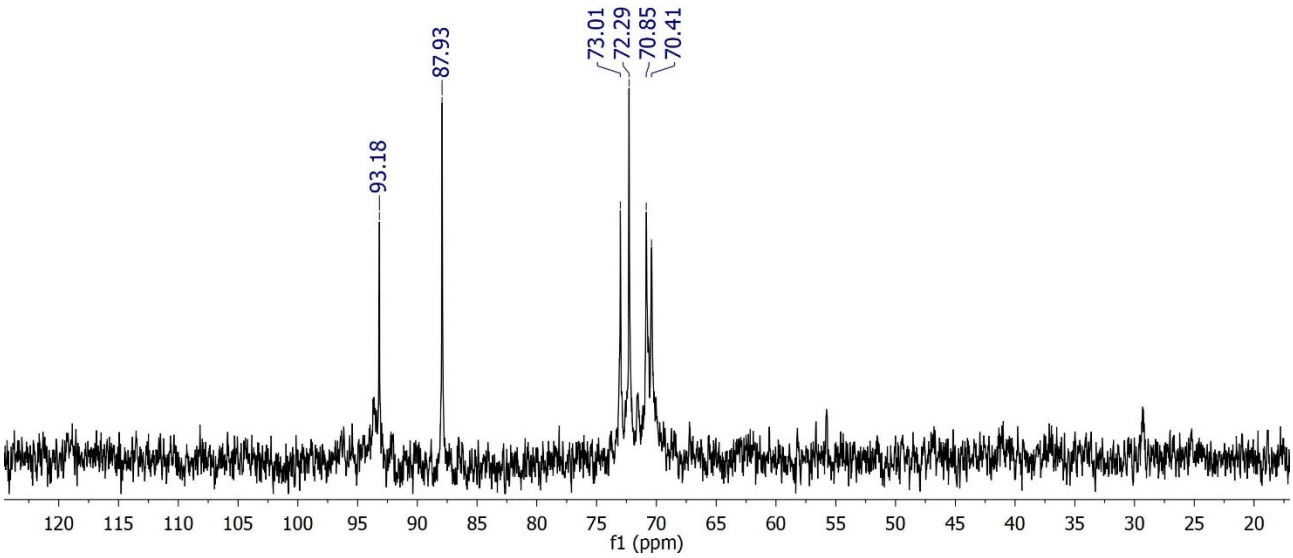

Figure S9: ^{13}C-NMR spectrum of 5,5’-diformyl-5,5’-didehydroxymethyl-trehalose **(3)**

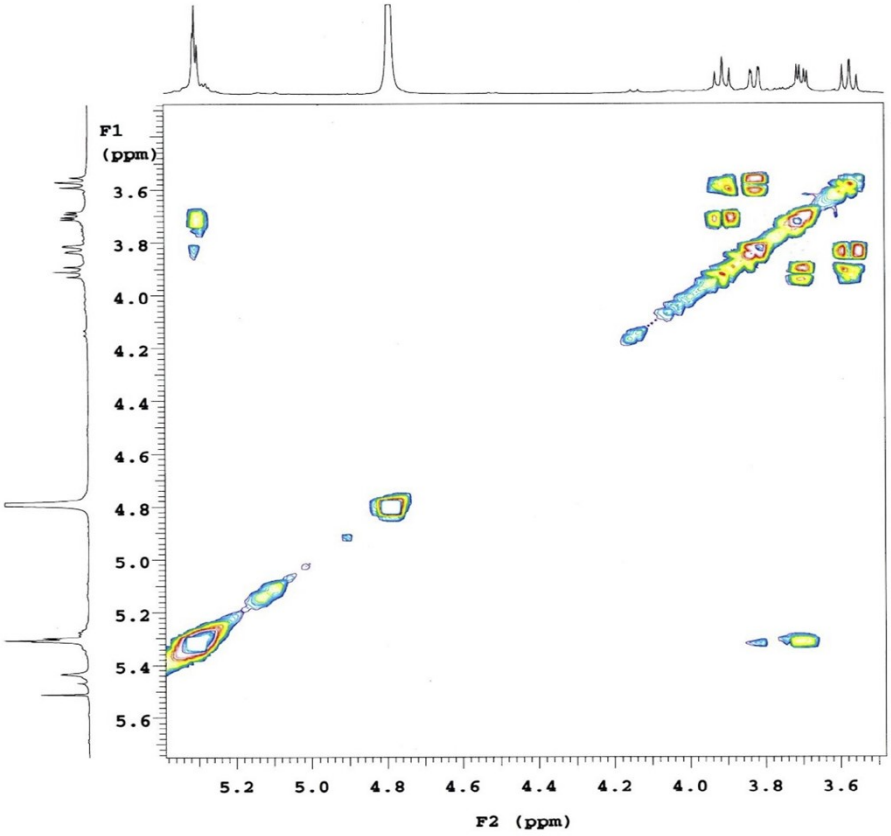

Figure S10: gCOSY spectrum of 5,5’-diformyl-5,5’-didehydroxymethyl-trehalose **(3)**

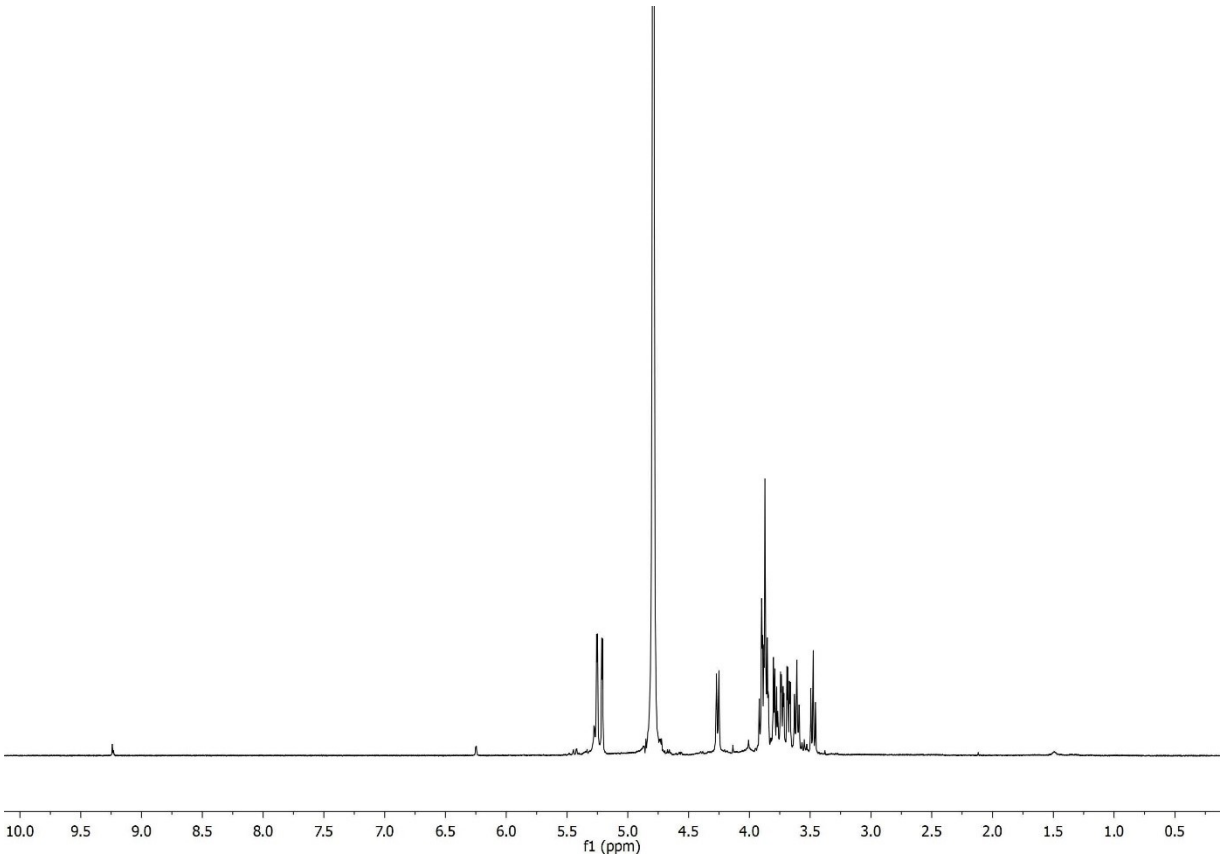

Figure S11: ^{1}H-NMR spectrum of 5-carboxy-5-dehydroxymethyl-trehalose **(6)**

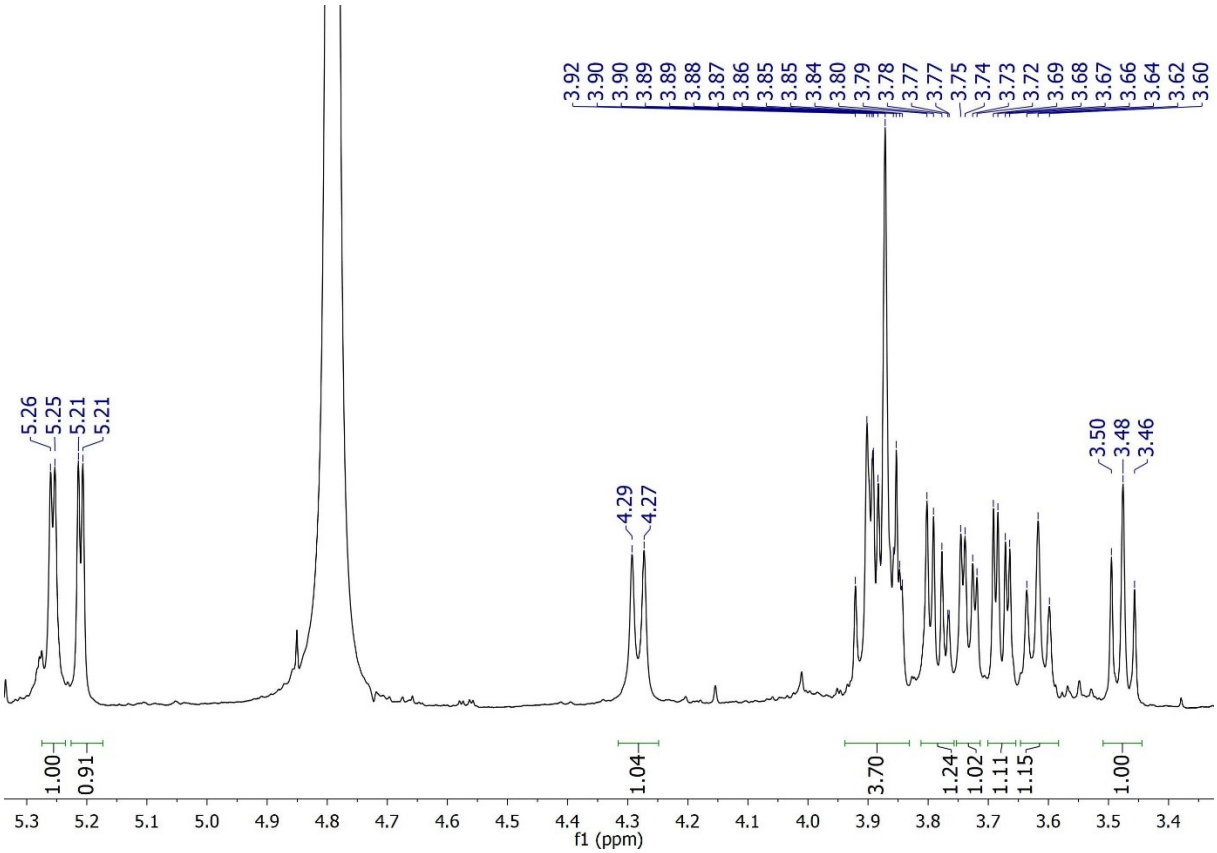

Figure S12: ^{1}H-NMR spectrum of 5-carboxy-5-dehydroxymethyl-trehalose **(6)**; magnification of area between 3.3 and 5.3 ppm.

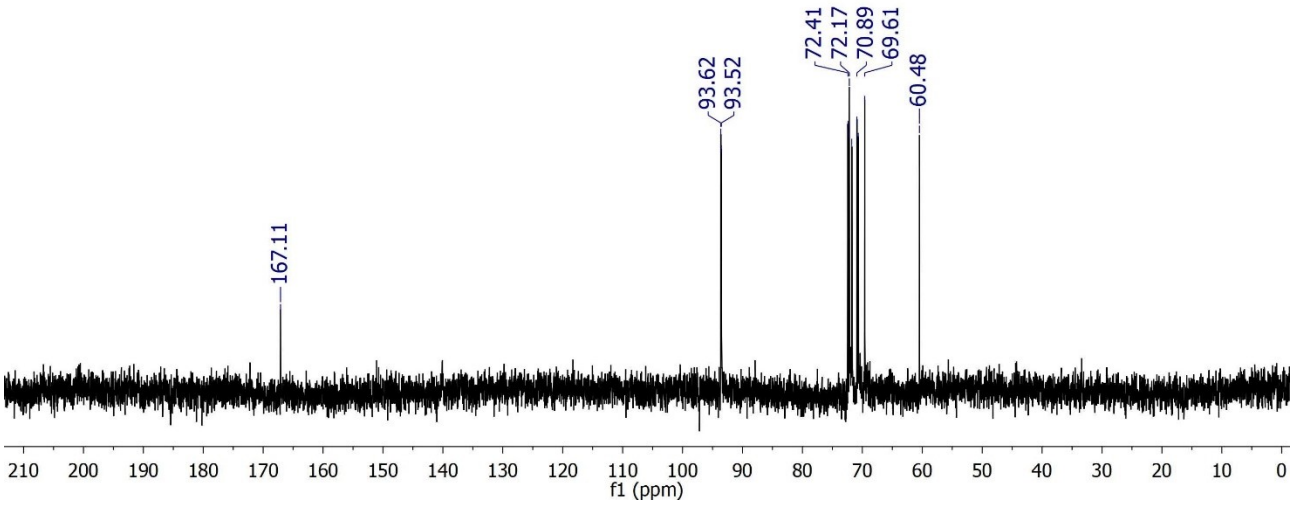

Figure S13: ^{13}C-NMR spectrum of 5-carboxy-5-dehydroxymethyl-trehalose **(6)**

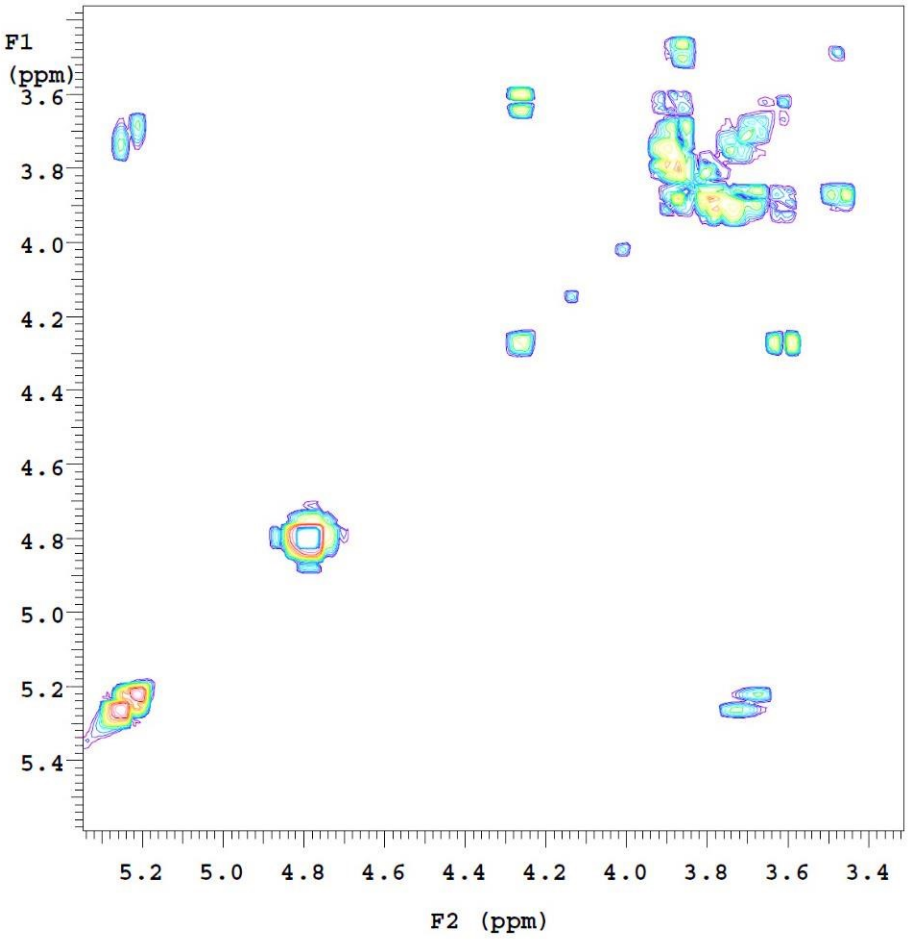

Figure S14: gCOSY NMR spectrum of 5-carboxy-5-dehydroxymethyl-trehalose **(6)**

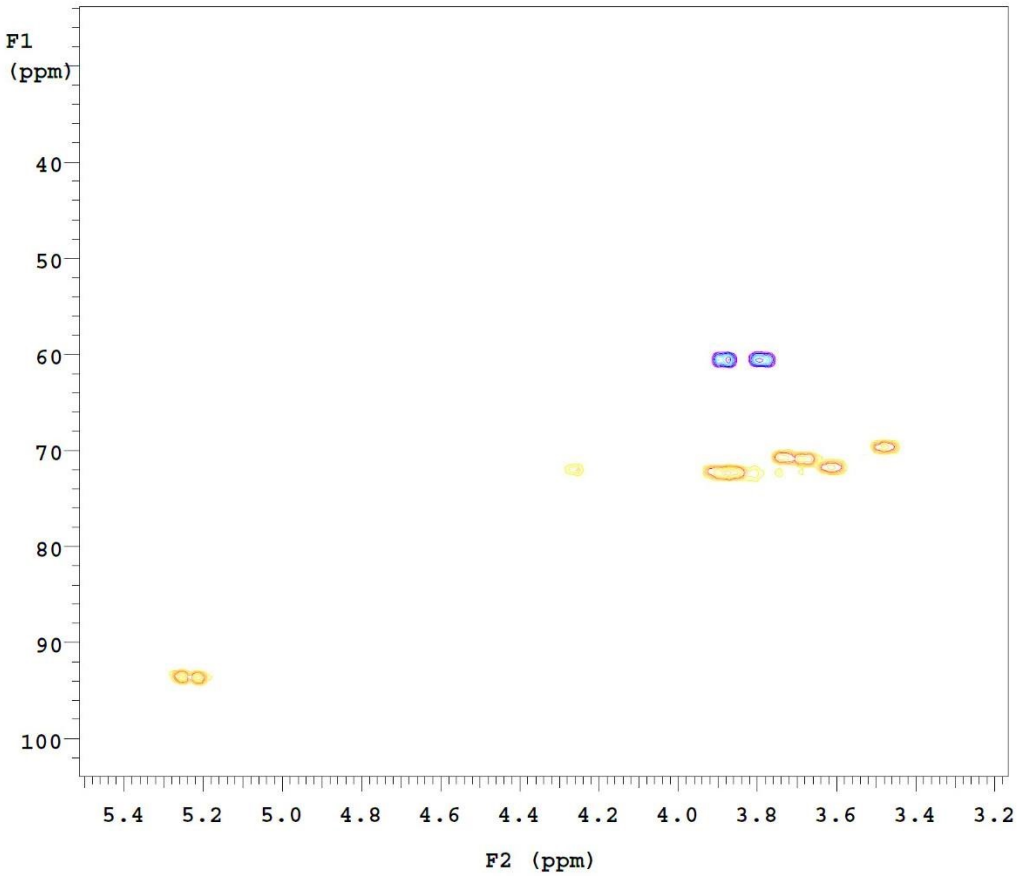

Figure S15: gHSQC NMR spectrum of 5-carboxy-5-dehydroxymethyl-trehalose **(6)**

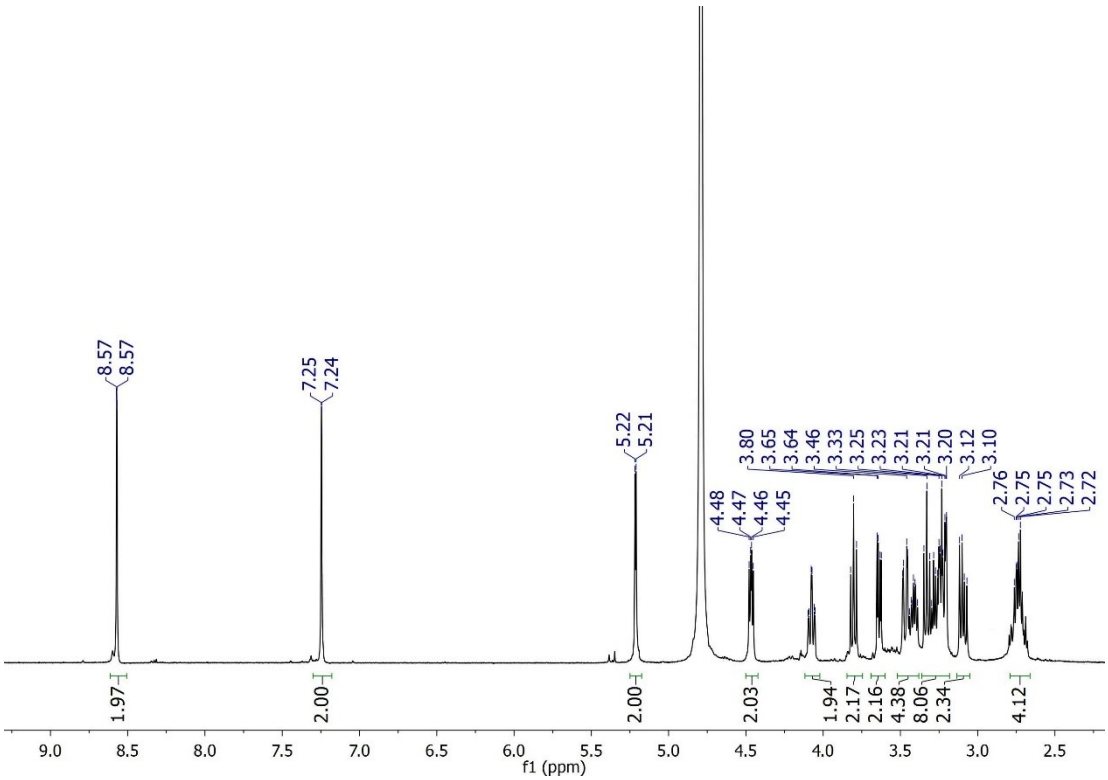

Figure S16: ^{1}H-NMR spectrum of 6,6'-bis((3-((1-carboxy-2-(1H-imidazol-4-yl)ethyl)amino)-3-oxopropyl)amino)-6,6'-dideoxy-α-α-trehalose **(9)**

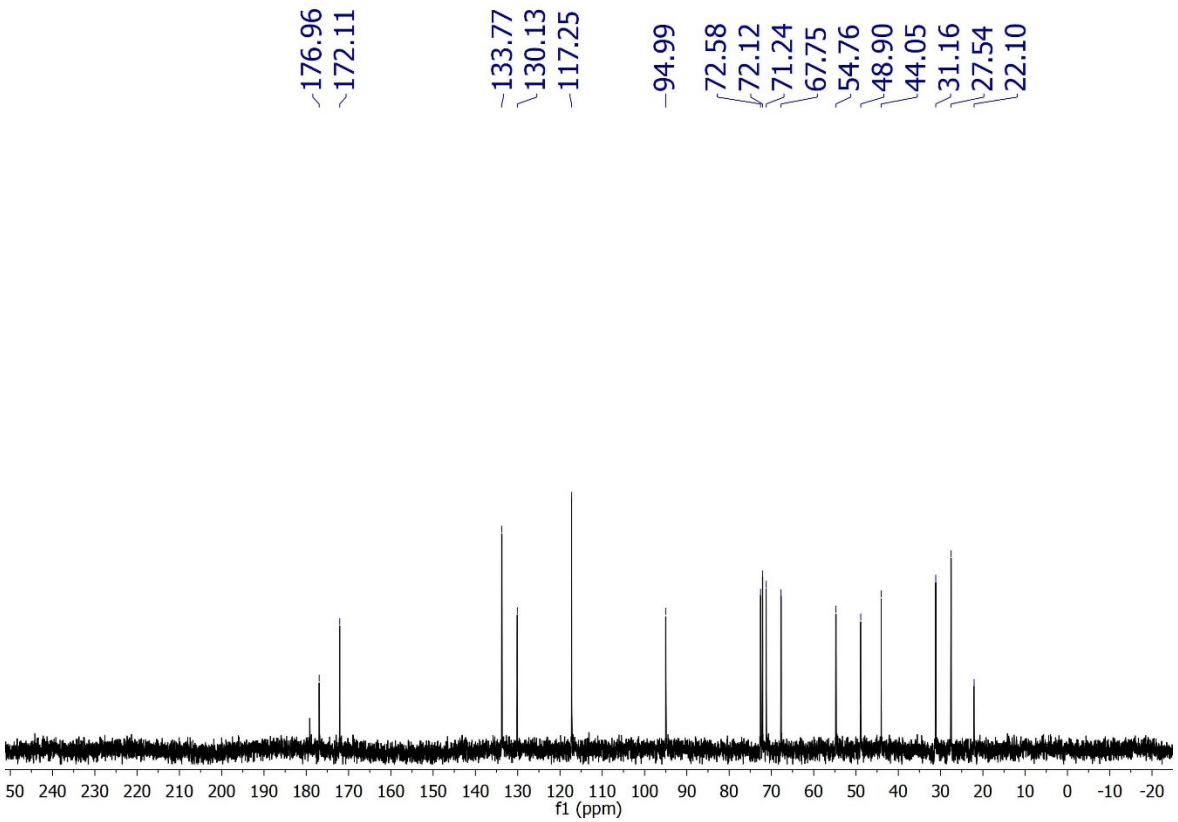

Figure S17: ^{13}C-NMR spectrum of 6,6'-bis((3-((1-carboxy-2-(1H-imidazol-4-yl)ethyl)amino)-3-oxopropyl)amino)-6,6'-dideoxy-α-α-trehalose **(9)**

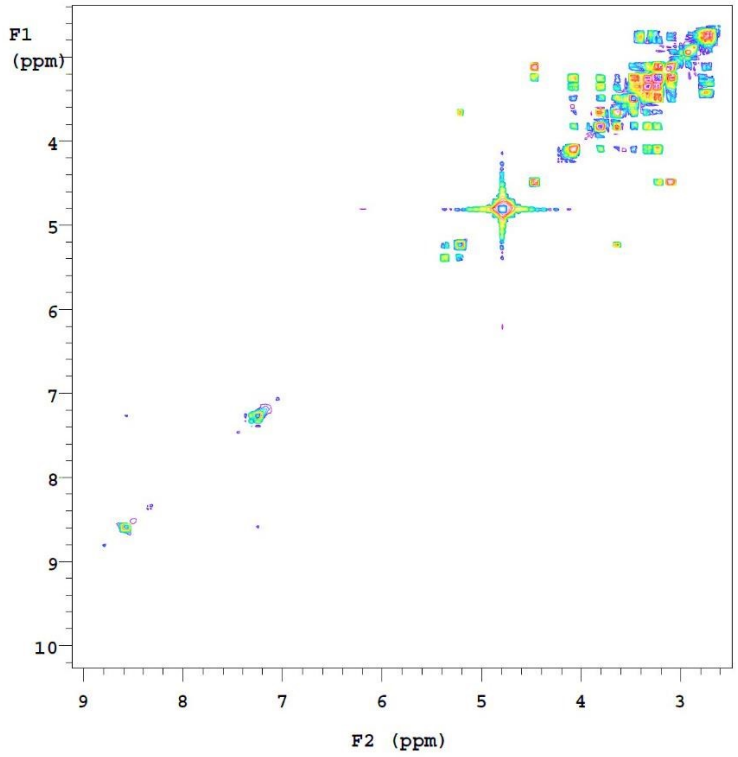

Figure S18: gCOSY spectrum of 6,6'-bis((3-((1-carboxy-2-(1H-imidazol-4-yl)ethyl)amino)-3-oxopropyl)amino)-6,6'-dideoxy-α-α-trehalose **(9)**

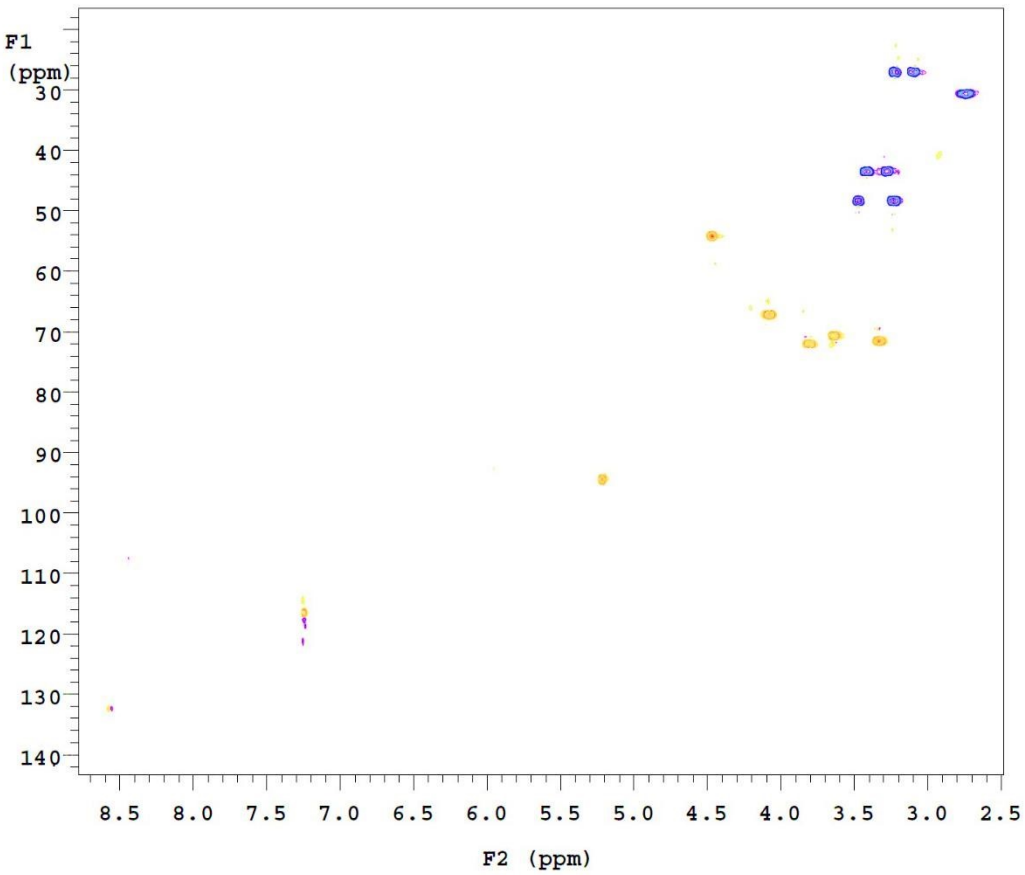

Figure S19: gHSQC spectrum of 6,6'-bis((3-((1-carboxy-2-(1H-imidazol-4-yl)ethyl)amino)-3-oxopropyl)amino)-6,6'-dideoxy-α-α-trehalose **(9).**

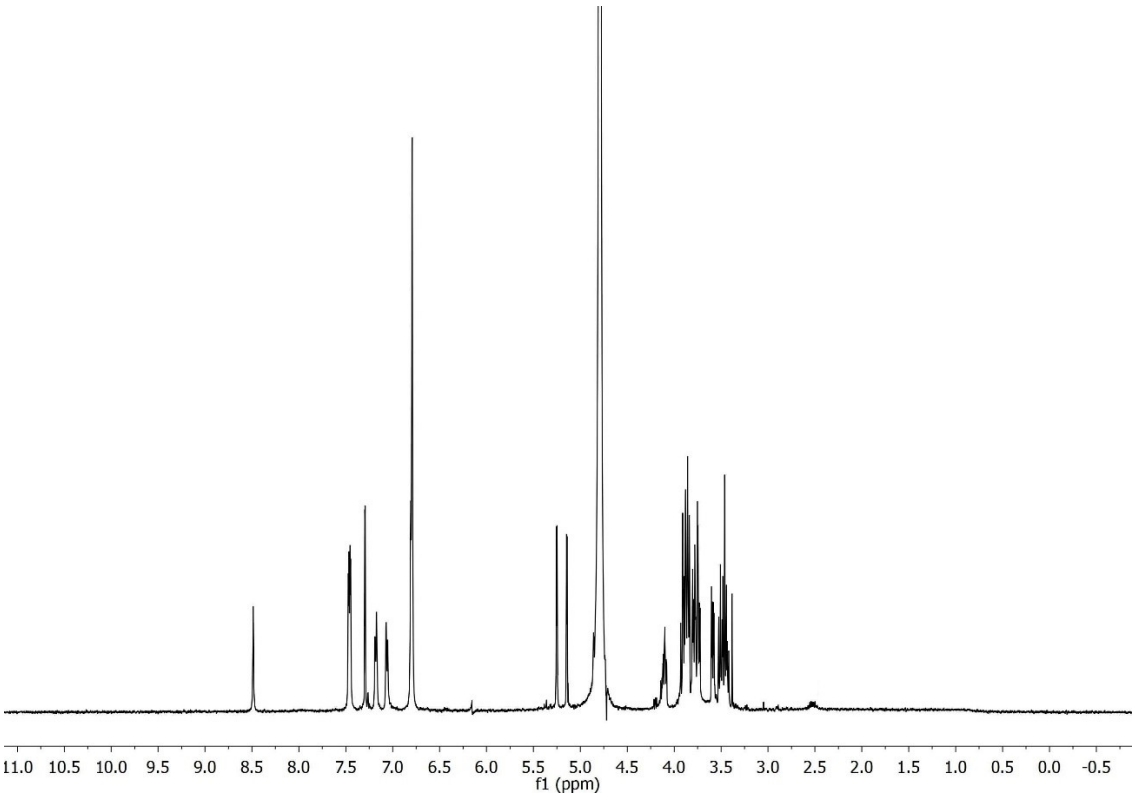

Figure S20: ^{1}H-NMR spectrum of 6-((3',6'-dihydroxy-3H-spiro[isobenzofuran-1,9'-xanthen]-3-one-5yl)amino)-6-deoxy-α-α-trehalose **(10)**.

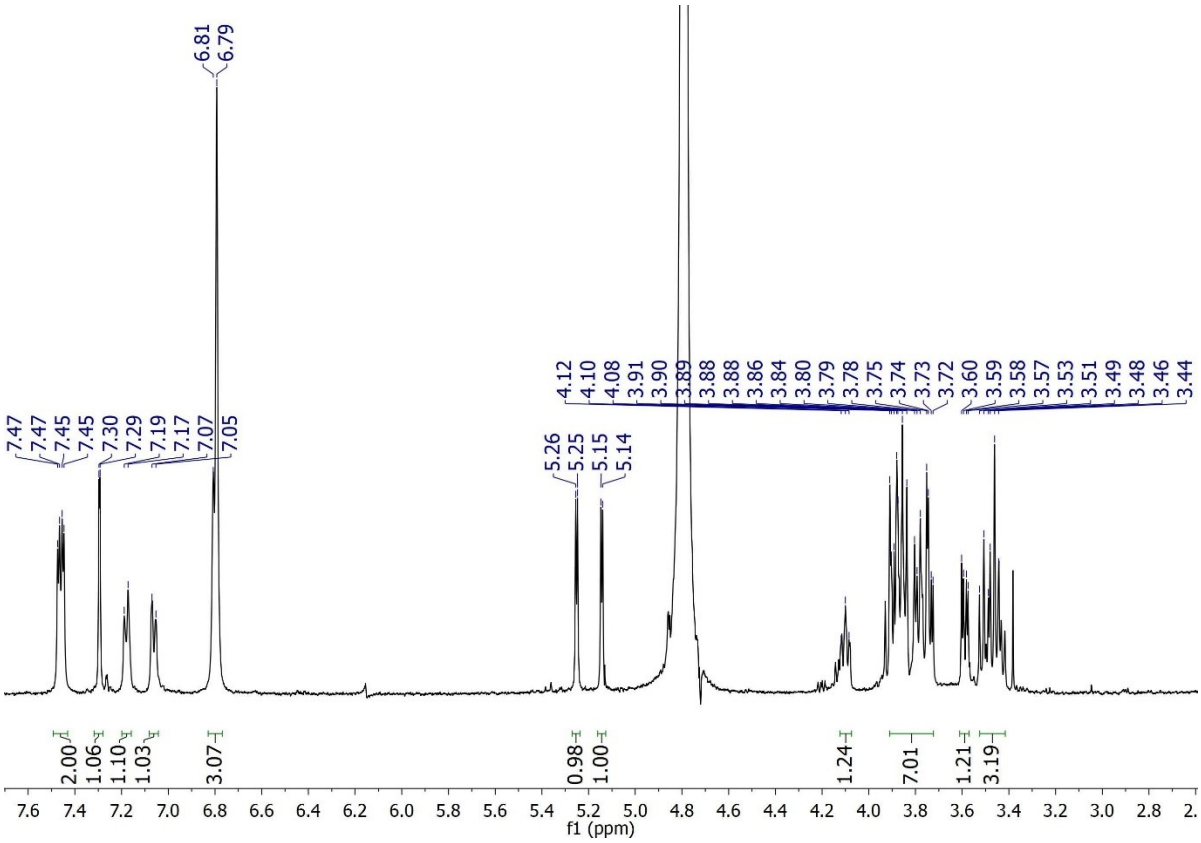

Figure S21: ^{1}H-NMR spectrum of 6-((3',6'-dihydroxy-3H-spiro[isobenzofuran-1,9'-xanthen]-3-one-5yl)amino)-6-deoxy-α-α-trehalose **(10)**; magnification of area between 2.7 and 7.7 ppm.

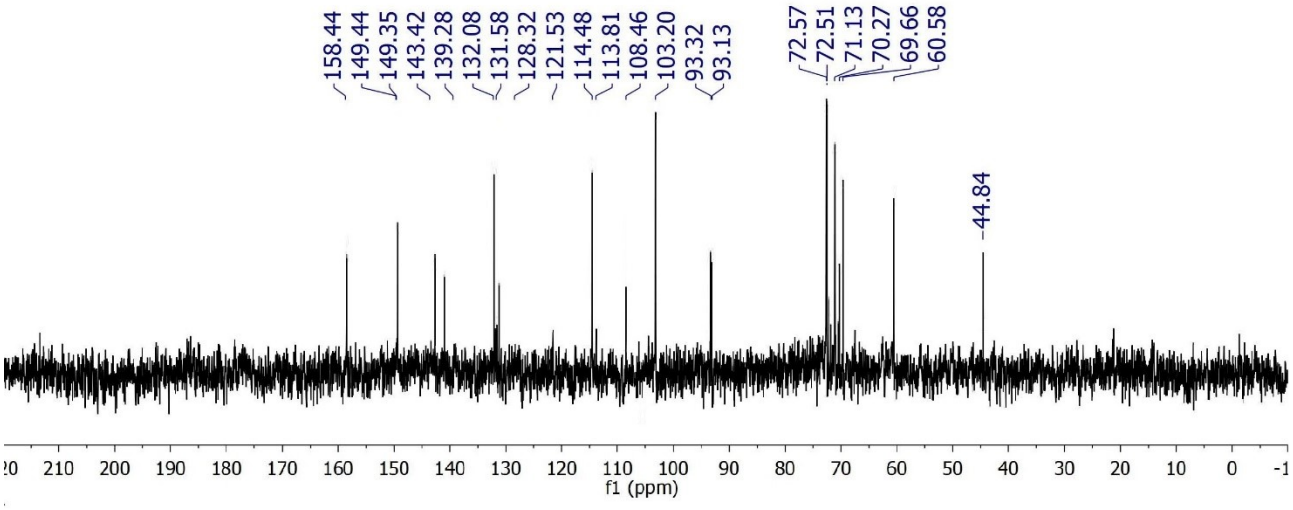

Figure S22: ^{13}C-NMR spectrum of 6-((3',6'-dihydroxy-3H-spiro[isobenzofuran-1,9'-xanthen]-3-one-5yl)amino)-6-deoxy-α-α-trehalose **(10)**.

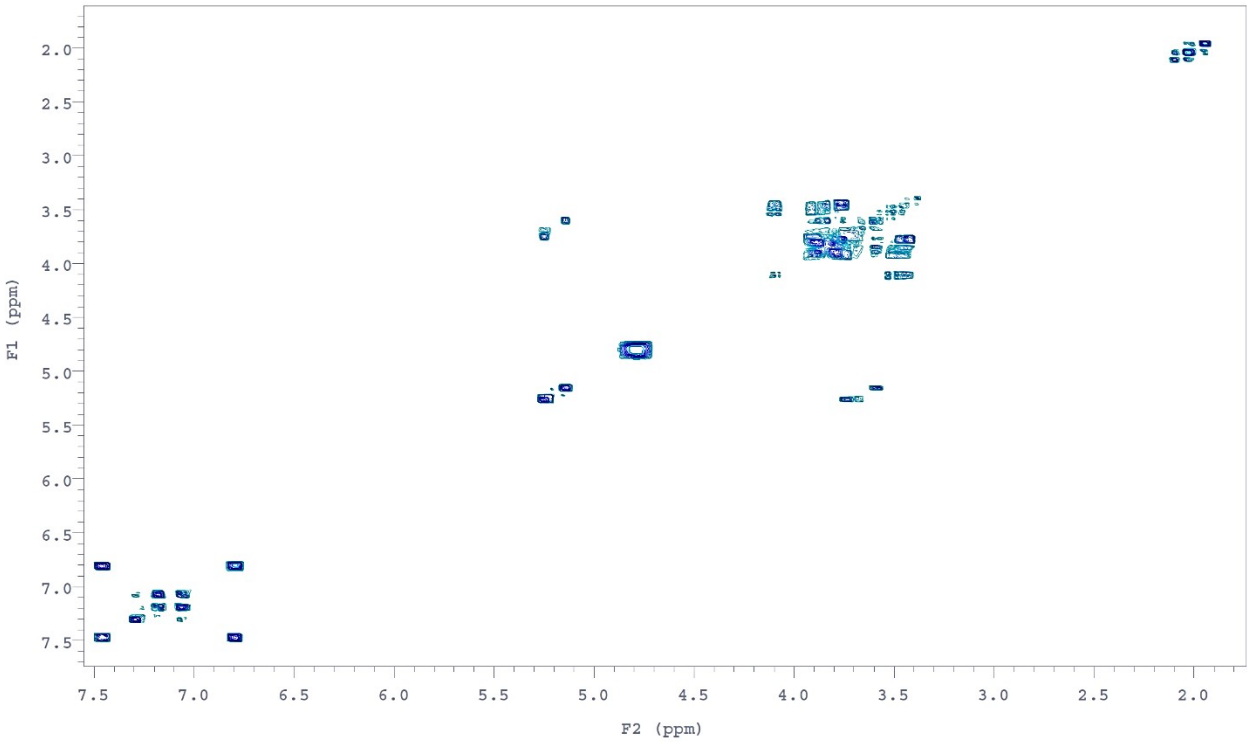

Figure S23: gCOSY spectrum of 6-((3',6'-dihydroxy-3H-spiro[isobenzofuran-1,9'-xanthen]-3-one-5yl)amino)-6-deoxy-α-α-trehalose **(10)**.

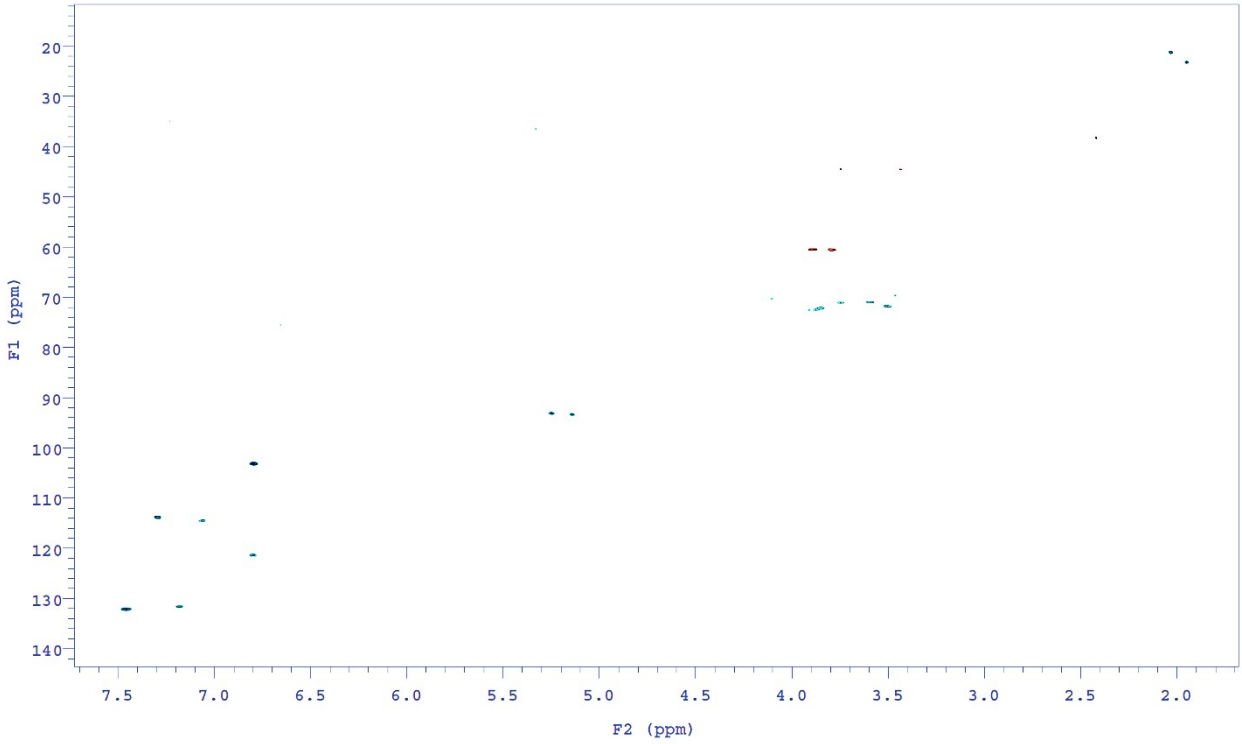

Figure S24: gHSQC spectrum of 6-((3',6'-dihydroxy-3H-spiro[isobenzofuran-1,9'-xanthen]-3-one-5yl)amino)-6-deoxy-α-α-trehalose **(10)**.

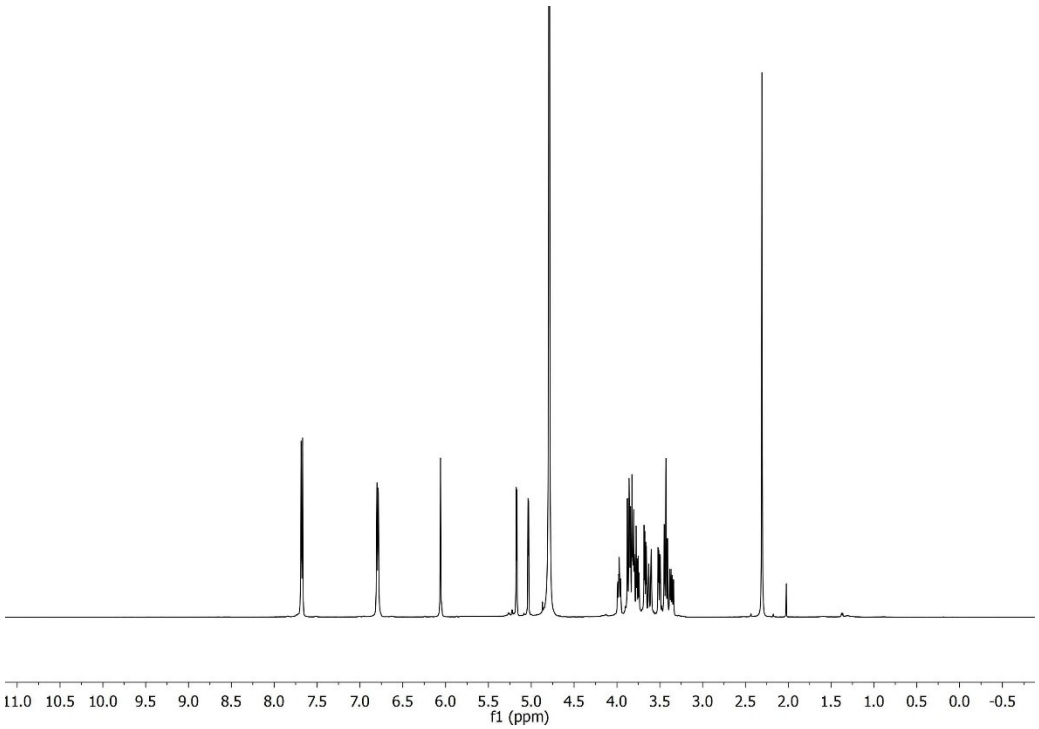

Figure S25: ^{1}H-NMR spectrum of N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide (**11**).

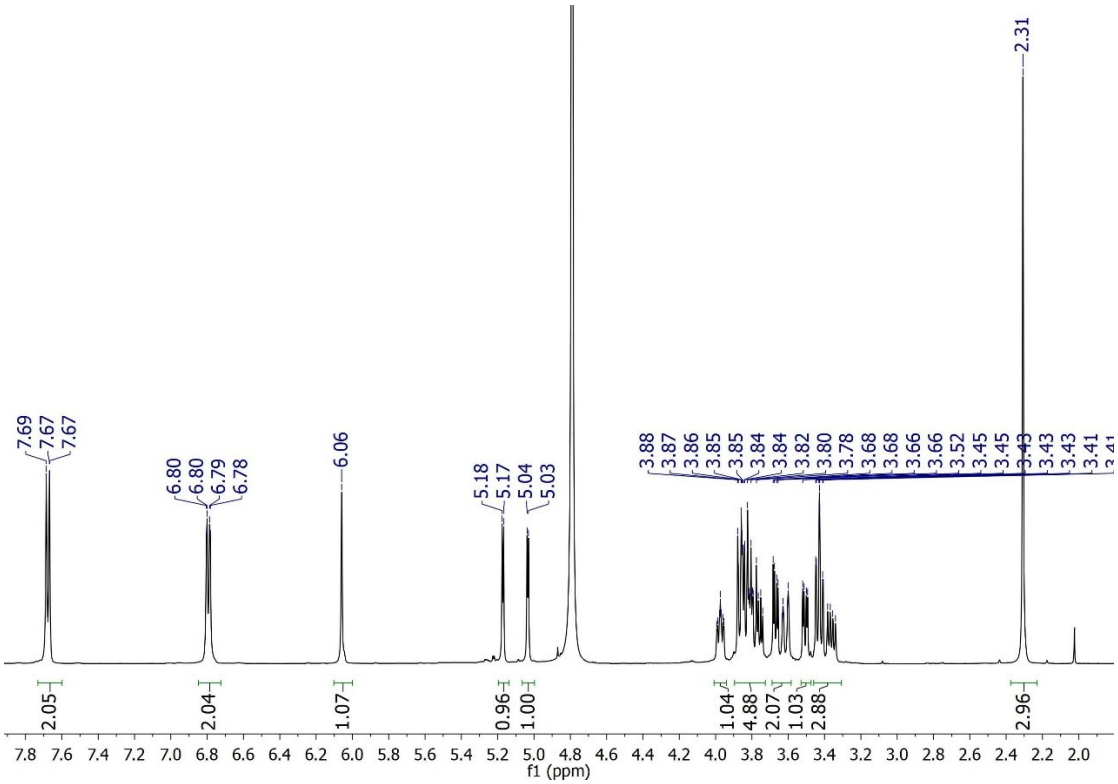

Figure S26: ^{1}H-NMR spectrum of [N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide] (**11**)**;** magnification of area between 2.0 and 7.8 ppm

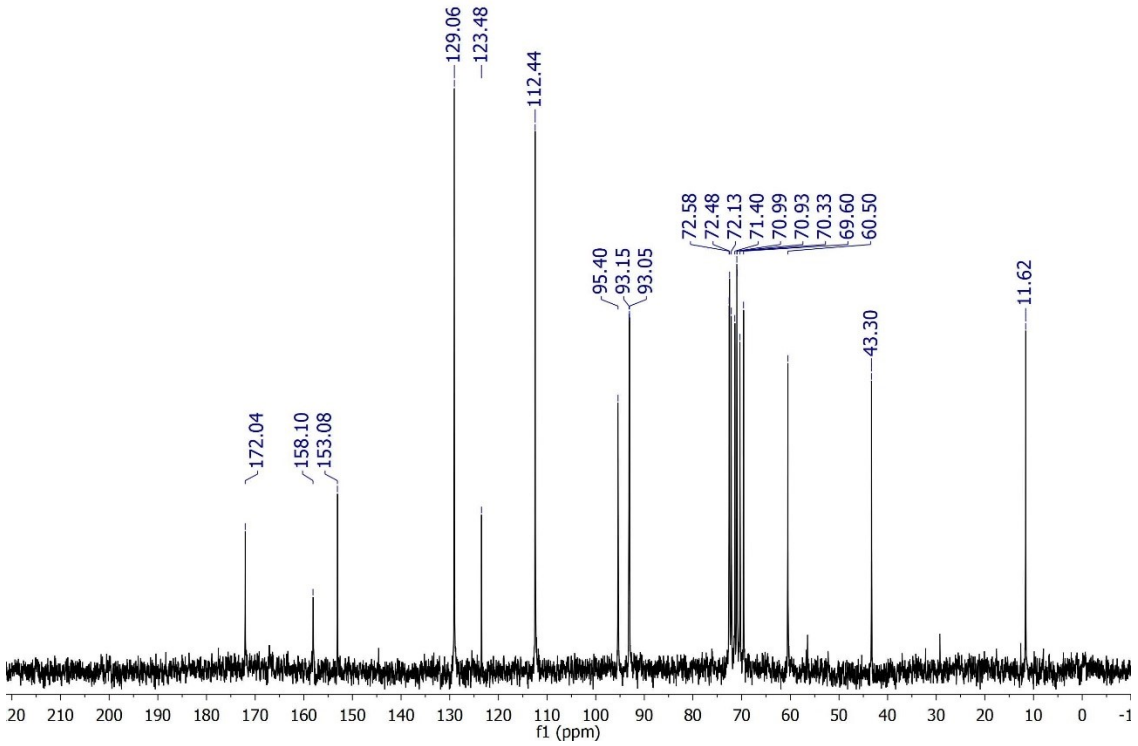

Figure S27: ^{13}C-NMR spectrum of [N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide] (**11**).

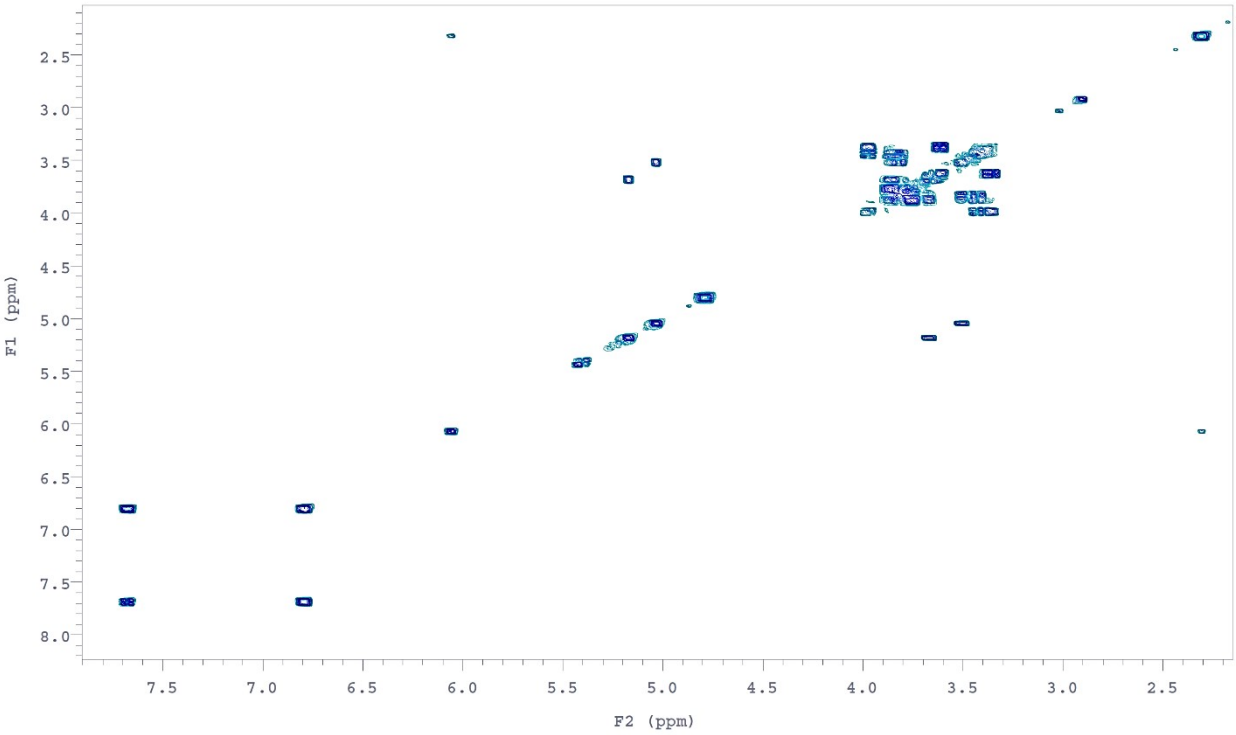

Figure S28: gCOSY spectrum of [N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide] (**11**).

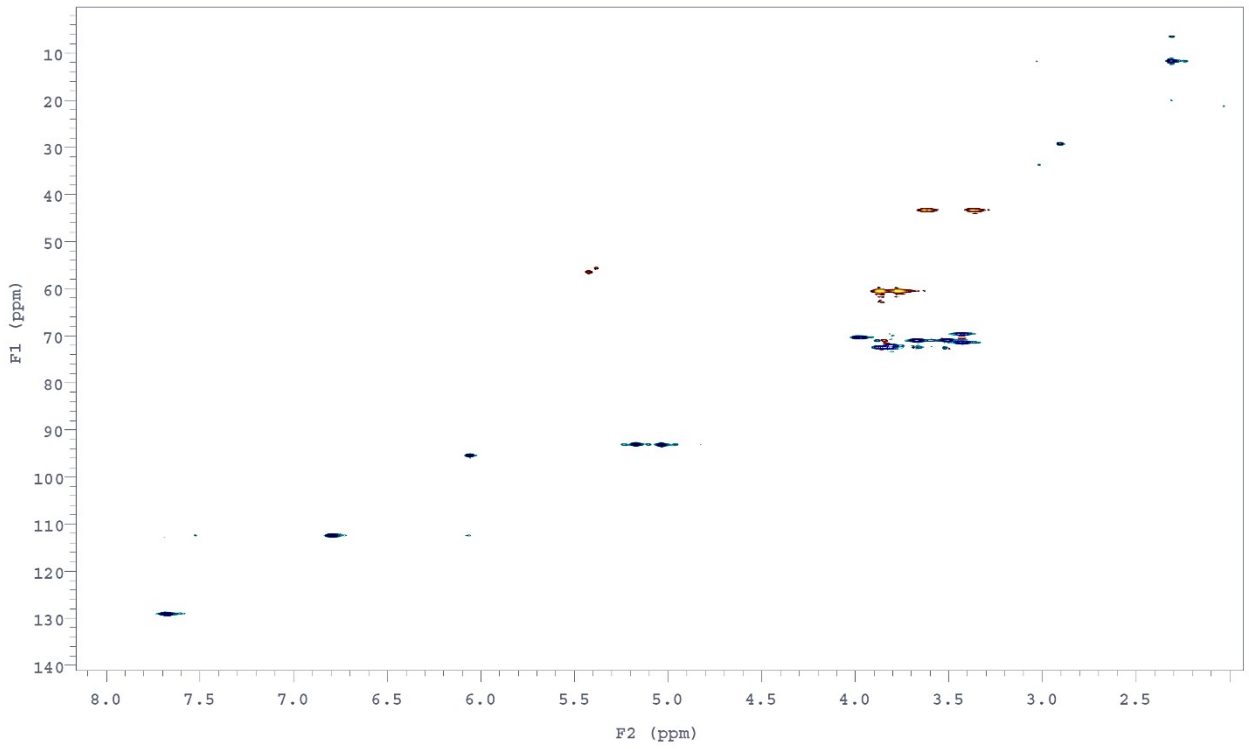

Figure S29: gHSQC spectrum of[N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide] (**11**).

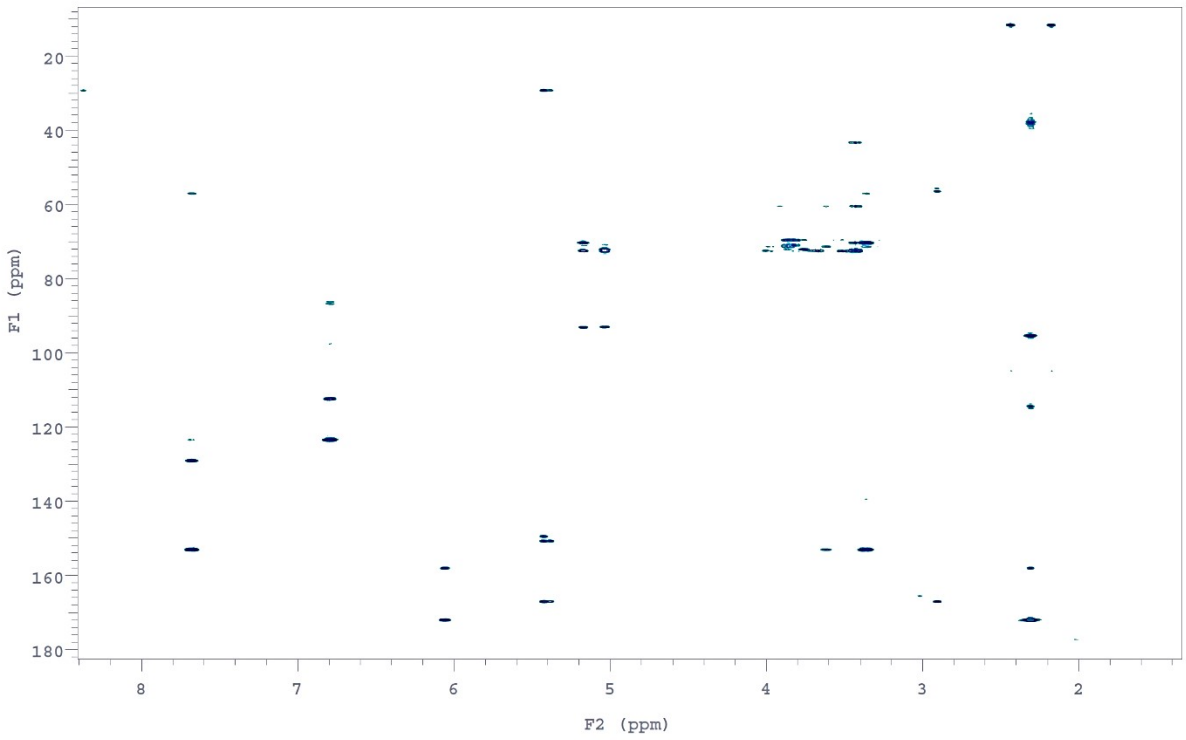

Figure S30: gHMBC spectrum of [N-(5-methylisoxazol-3-yl)-4-((6-deoxy-α-α-trehalose-6-yl)amino)benzenesulfonamide] (**11**).