Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Flow chemistry kinetic studies reveal reaction conditions for ready access to unsymmetrical trehalose analogues

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Supplementary Information

Contents

1. General considerations

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker Bruker AVC500 (500MHz) spectrometer. Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded on a Bruker AVC500 (125.6 MHz) and are proton decoupled. Spectra were assigned using COSY, DEPT-135, HMQC, HSQC, and HMBC if required. Phosphorus nuclear magnetic resonance spectra (^{31}P NMR) were recorded on a Bruker AV400 (162 MHz). All chemical shifts are quoted on the δ scale in ppm using residual solvent as an internal standard.

Low resolution mass spectra were recorded on a Micromass Platform 1 spectrometer using electrospray ionization (ES), or on a Bruker Daltronic MicroTOF spectrometrer. High resolution mass spectra were recorded on a Bruker Daltronic MicroTOF spectrometer. m/z values are reported in Daltons. Infrared spectra (FT-IR) were recorded on a Bruker Tensor 27 Fourier Transform spectrophotometer using either KBr discs for solids or as a thin film on NaCl plates. Absorption maxima are reported in wavenumbers (cm^{-1}). Only signals representing functional groups are reported; C-H absorptions and the fingerprint region are not listed. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 589nm (Na D-line) with a path length of 1.0 dm and are reported in units of deg $dm^{-1}cm^{3}g^{-1}$. Concentrations are given in g/100 mL.

Thin Layer Chromatography (TLC) was carried out using Merck aluminium backed sheets coated with Kieselgel $60F_{254}$ silica gel. Visualization of the sheets was achieved using a UV lamp (λ_{max} = 254 or 365 nm) and/or ammonium molybdate (5% in 2M H_2SO_4), or sulfuric acid (0.2M in 1 MeOH : 1 H_2O). Silica gel chromatography was performed on a Biotage SP4 purification system using KP-Sil SNAP cartridges.

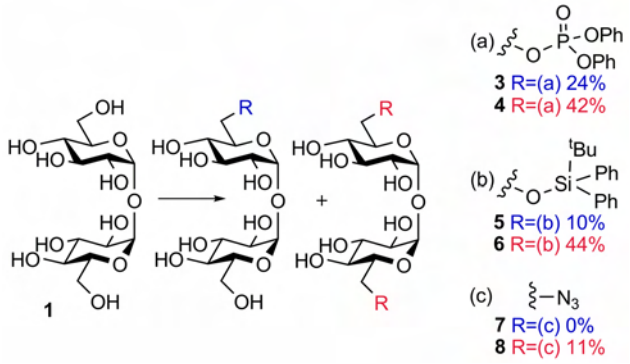
Anhydrous THF, DCM, and diethyl ether were dried under pressure through a column of alumina. Other anhydrous solvents were purchased from Fluka, and stored under

Argon over molecular sieves. All other solvents were used as supplied (analytical or HPLC grade). “Petrol” refers to the fraction of light petroleum ether boiling in the range 40-60°C. “Brine” refers to a saturated aqueous solution of sodium chloride.

Anhydrous D-trehalose was purchased from Fisher Scientific.

2. Synthetic protocols

2.1 Trehalose monofuntionalizations



Phosphorylation

To a suspension of D-trehalose (7.50 g, 21.9 mmol, 1 eq) in anhydrous pyridine (100 mL) was added dropwise diphenylchlorophosphate (4.54 mL, 21.9 mmol, 1 eq). TLC (1 water : 4 isopropanol : 4 ethyl acetate) after 18 hours showed the presence of two products. The reaction was quenched with methanol (10 mL) and the reaction mixture concentrated *in vacuo*. The residue was co-evaporated with toluene to remove pyridine (x3). Silica gel chromatography (1 water : 3 isopropanol : 13 ethyl acetate) allowed separation of the two products. Lyophilization yielded **3** (3.02g, 24%) and **4** (7.41g, 42%) as a white amorphous solids.

Silylation

To a stirred suspension of D-trehalose (0.5g, 1.46mmol, 1eq) and imidazole (0.099g, 1.46mmol, 1eq) in dry DMF (10ml) was added *tert*-butyl diphenylchlorosilane (0.38ml, 1.46mmol, 1eq) at room temperature. After stirring for 26 hours, TLC (1 water : 2 isopropanol : 2 ethyl acetate) indicated the formation of two products. The reaction mixture was concentrated *in vacuo* and purified by silica gel chromatography (2 ethyl acetate : 1 isopropanol) to give **5** (85mg, 10%) and **6** (0.53g, 44%) as white amorphous solids after lyophilization.

Mitsunobu reaction

Synthesis of hydrazoic acid

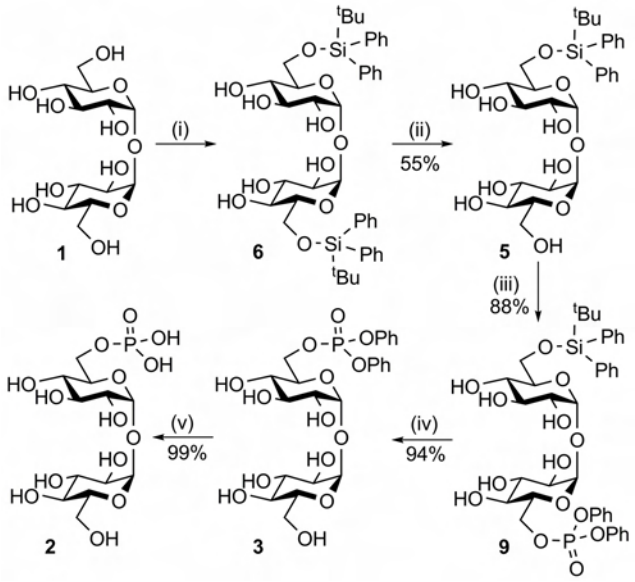
Hydrazoic acid was prepared by the careful addition of concentrated sulphuric acid (0.41ml, 7.7mmol, 0.5eq) to a solution of NaN_3 (1.0g, 15.4mmol, 1eq) in toluene (12ml) and water (1.5ml) at 0 ºC. The toluene layer containing the hydrazoic acid was decanted off via cannula and stored over Na_2SO_4. Titration against a standardized solution of NaOH with phenolphthalein as indicator was used to determine the concentration of HN_3 as 0.75M.

Mitsunobu reaction

Diisopropyl azodicarboxylate (DIAD, 0.057ml, 0.292mmol, 1eq) was added to a stirred solution of D-trehalose (0.10g, 0.292mmol, 1eq) and PPh_3 (0.077g, 0.292mmol, 1eq) in dry 1,4-dioxane (10ml) to form a pale orange solution. After stirring for 30 minutes at room temperature, the solution decolourized and hydrazoic acid (0.750M solution in toluene, 0.39ml, 0.292mmol, 1eq) was added dropwise. TLC (1 water : 2 isopropanol : 2 ethyl acetate) after 66 hours indicated the formation of a product. The reaction was quenched with 2M NaOH (1ml) and the solvent removed *in vacuo*. Silica gel chromatography (1 water : 4 isopropanol : 8 ethyl acetate) followed

by lyophilization allowed isolation of the product as a white amorphous solid (13.3mg, 11%).

2.2 Synthesis of trehalose-6-phosphate



Step (i)and (ii)

To a suspension of D-trehalose (1.0g, 2.92mmol, 1eq) in anhydrous pyridine (50ml) was added *tert*-butyl diphenyl chlorosilane (1.52ml, 5.84mmol, 2eq). TLC (1 water : 4 isopropanol : 10 ethyl acetate) after 14 hours indicated complete consumption of the starting materials. The solvent was removed *in vacuo* and the residue co-evaporated with toluene to remove pyridine (x3). To the crude solid, stirred at 0 ºC in methanol (5ml) and diethyl ether (15ml), was added acetyl chloride (0.40ml, 5.84mmol, 2eq). The reaction mixture was warmed to room temperature, and regularly monitored by TLC and mass spectrometry. After 18 hours, a significant amount of the D-trehalose by-product was seen (~10%) and the reaction quenched with saturated $NaHCO_3$ solution until the mixture was at pH 7 (pH paper), and the solvent removed *in vacuo*. Two separate silica gel columns were required to purify the desired compound (1 water : 4 isopropanol : 10 ethyl acetate followed by 2 isopropanol : 1 ethyl acetate). Lyophilization gave the title compound as a white amorphous solid (0.93g, 55%).

Step (iii)

To a solution of **5** (0.90g, 1.55mmol, 1eq) in anhydrous pyridine (30ml) was added diphenyl chlorophosphate (0.36ml, 1.70mmol, 1.1eq). The reaction mixture was stirred at room temperature for 15 hours, after which TLC (1 water : 4 isopropanol : 10 ethyl acetate) indicated complete consumption of starting material. The reaction was quenched with methanol (2ml), the solvent removed *in vacuo*, and the crude solid co-evaporated with toluene to remove pyridine (x3). Silica gel chromatography (9 ethyl acetate : 1 methanol) followed by lyophilization gave the desired compound as a white solid (1.11g, 88%).

Step (iv)

To a solution of **9** (1.10g, 1.35mmol, 1eq) in methanol (20ml) at room temperature, was added acetyl chloride (0.39ml, 5.41mmol, 4eq). The reaction was stirred at this temperature for 18 hours, after which TLC (1 water : 4 isopropanol : 4 ethyl acetate) indicated completion of the reaction. The reaction mixture was quenched with saturated $NaHCO_3$ solution to pH 7, and the solvent removed *in vacuo*. Silica gel chromatography (1 water : 4 isopropanol : 6 ethyl acetate) followed by lyophilization afforded the desired compound as a white amorphous solid (0.73g, 94%).

Step (v)

A suspension of **3** (0.75g, 1.31mmol, 1eq) and PtO_2 (15 mg, 0.066mmol, 0.05eq) in 75% aqueous ethanol (10 mL) with 0.5% glacial acetic acid (50 μL) was repeatedly degassed under high vacuum and the reaction vessel charged with hydrogen. The reaction was maintained at room temperature with aggressive stirring under an atmospheric pressure of hydrogen for 14 hours after which TLC (5 ethanol : 3 NH_4OH : 1 water) showed the complete consumption of the starting material and the formation of a single product. The reaction mixture was filtered through Celite® and

the solvent was removed *in vacuo*. Lyophilization afforded the title compound as a white amorphous solid (0.55g, 99%).

3. Flow chemistry and kinetic analysis

3.1 General considerations

Reactions were performed using a Syrris Africa flow chemistry system using a 1000µl or 250µl microreactor chip. The flow system was dried by rinsing reagent flasks and microreactor chip with anhydrous DCM (x3). The reagent flasks were subsequently dried over a stream of nitrogen. The flow path was primed with nitrogen, prior to addition of any solvents, or reagents.

High Performance Liquid Chromatography (HPLC) was conducted on a Dionex UltiMate 3000 HPLC system at ambient temperature, with a Varian PLS400 Evaporative Light Scattering detector (ELSD) for eluant detection. Injections were performed by manual injection using a 20µl Rheodyne sample loop as per the manufacturer's instructions.

Quantification of eluants required determination of ELSD response curves as reported previously.[1] 5µl of standardised concentrations of eluants (between 0 – 2.0mg/ml) were injected and the response of the detector measured and fitted to Area = am^b . Values of a and b for the different compounds, chromatographic conditions and ELSD settings are reported below.

Kinetic parameters were estimated by minimisation of the objective function:

$$Q = \sum_i \sum_t \left(x_{i,t,exp} - x_{i,t,theo} \right)^2$$

where $x_{i,t,exp}$ and $x_{i,t,theo}$ are experimental and theoretical concentrations respectively of the different reaction components, i, at different time points t. Theoretical values were determined by computationally solving equations (1)-(4) with Matlab 2009 using a Runge-Kutta algorithm.

$$Tre + R \xrightarrow{k_1} Mono + R \xrightarrow{k_2} Di$$

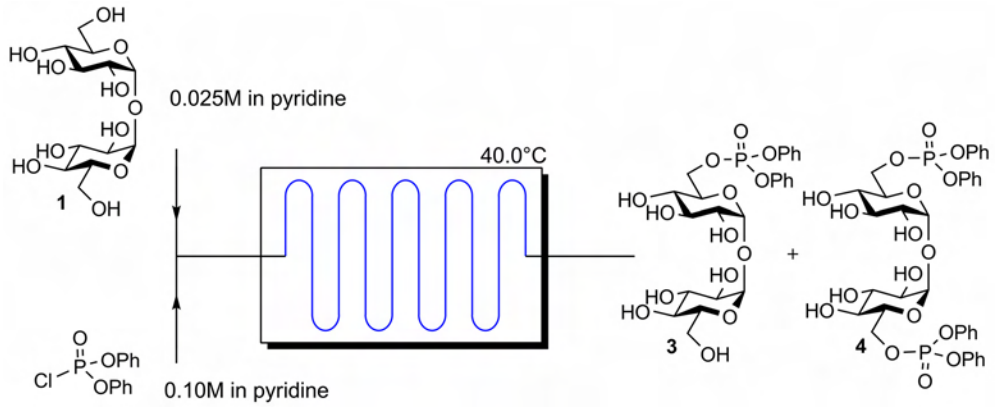
$$d[Tre]/dt = -k_1[Tre][R] \quad (1)$$

$$d[Mono]/dt = k_1[Tre][R] - k_2[Mono][R] \quad (2)$$

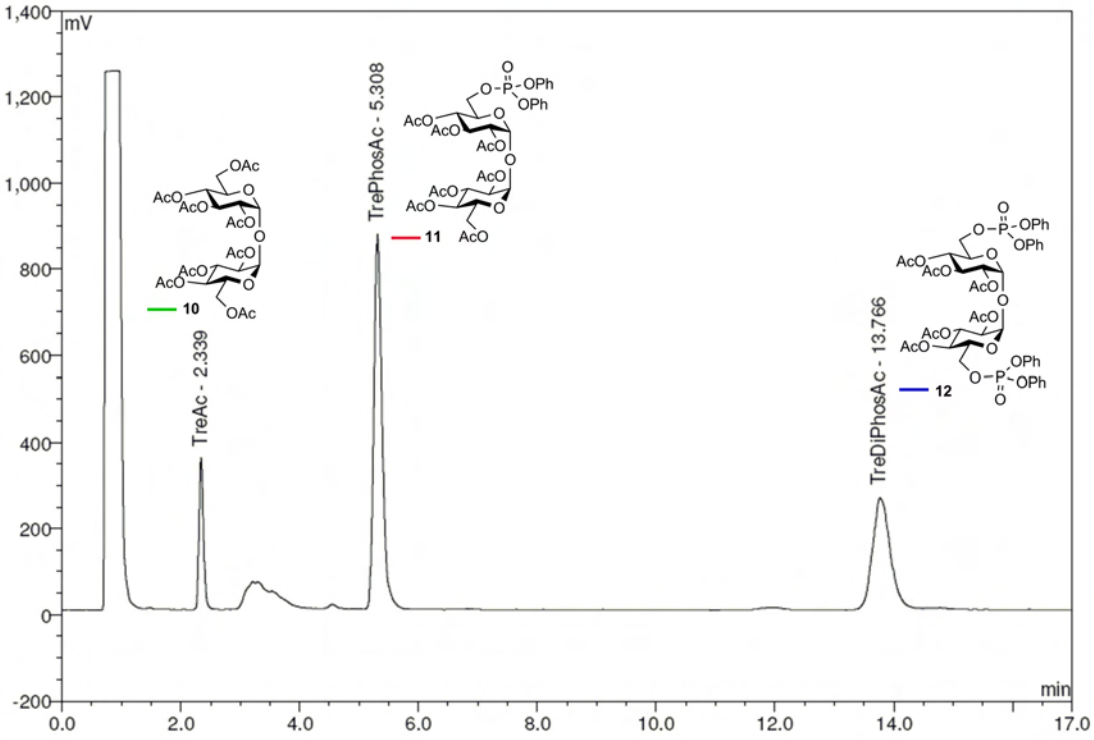
$$d[Di]/dt = k_2[Mono][R] \quad (3)$$

$$d[R]/dt = -k_1[Tre][R] - k_2[Mono][R] \quad (4)$$

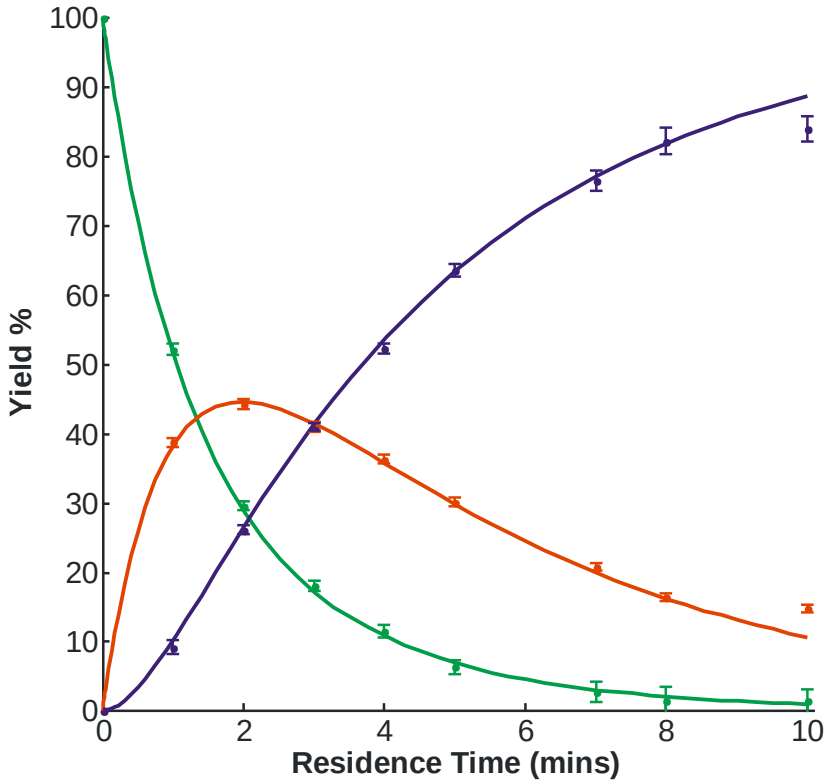
3.2 Trehalose phosphorylation



Reactions were performed using a 1000µl microreactor chip at 40.0 °C. Solutions of D-trehalose (0.025M in pyridine) and diphenylchlorophosphate (0.1M in pyridine) were pumped to the chip at identical flow rates. Reactions were performed with a residence time between 1-10 minutes (1 minute reactions were performed on a 250µl chip). 250µl of the reaction mixture was collected in a vial containing methanol (1ml). The solvents were removed *in vacuo* and the crude residue dissolved in pyridine (0.5ml). Acetic anhydride (0.5ml) was added and the reaction mixture stirred at room temperature for 8 hours. The reactions were quenched with methanol (1ml) and the solvents removed *in vacuo*. The crude products were dissolved in methanol (5ml) and the product distribution analysed by HPLC using 5µl injections into a Phenomenex Synergi Hydro C18 column (250 x 4.8mm, 4µm) with 40 water : 60 acetonitrile as the mobile phase at a flow rate of 1.0 ml/min. Eluants were detected using an in-line ELS detector (gain 5.0, nebulizer 30 °C, drift tube 80 °C, 1.65 Bar N_2).



	a	b
10	261.5	1.435
11	255.8	1.421
12	120.7	1.309



k_1 = 0.157 $mol^{-1}dm^3s^{-1}$, k_2 = 0.133 $mol^{-1}dm^3s^{-1}$, r^2 = 0.986.

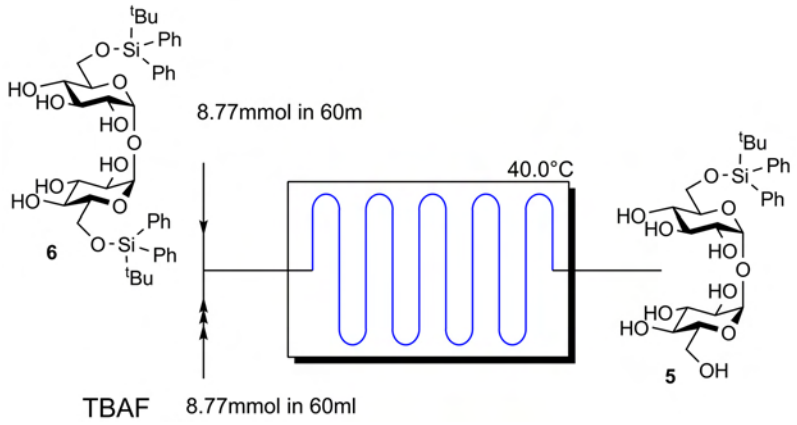
Large Scale Reaction

A 0.025M solution of anhydrous D-trehalose in pyridine was reacted with a 0.10M solution of diphenylchlorophosphate in pyridine at 40.0 °C through a 1000µl microreactor with a residence time of 120 seconds. The effluent from the chip was quenched by addition into water (500ml). 468ml of reaction mixture (equating to 2.0g of trehalose, 5.85mmol) was collected. The solvents were removed *in vacuo* and co-evaporated with toluene to remove pyridine (x3). The desired product was purified by silica gel chromatography (1 water : 4 isopropanol : 6 ethyl acetate + 1% NH_4OH for 4 column volumes, then a gradient to 1 water : 4 isopropanol : 6 ethyl acetate over 6 column volumes) to give **3** as a white amorphous solid (1.31g, 39%).

3.3 Desilylation reactions

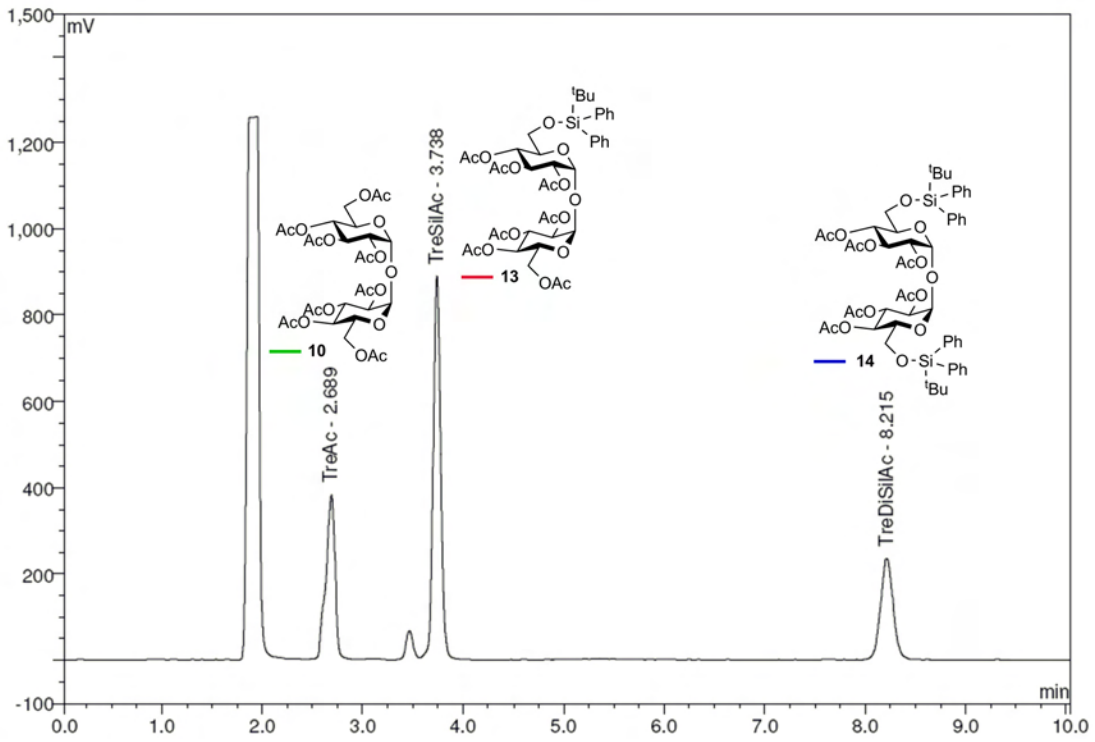
6,6'-*O*-diterbutyldiphenylsilyl-D-trehalose (6)

To a stirred suspension of D-trehalose (3.00g, 8.77mmol, 1eq) in dry pyridine (60ml) was added *tert*-butyl diphenylchlorosilane (4.79ml, 18.4mmol, 2.1eq) at room temperature. After stirring for 12 hours, TLC (1 water : 2 isopropanol : 2 ethyl acetate) indicated the complete consumption of starting. The reaction mixture was concentrated *in vacuo* and co-evaporated with toluene to remove pyridine(x3). The product was purified by silica gel chromatography (9 THF : 1 methanol) to give the desired compound as a white amorphous solid after lyophilization (6.82g, 95%).



Reactions were performed using a Syrris Africa flow chemistry system using a 1000µl microreactor chip at 25.0°C. TBAF (8.77mmol in 60ml of solvent) was pumped through the chip at a flow rate three times that of **6** (8.77mmol in 60ml of solvent). Reactions were performed with a residence time between 0-70 minutes. 250µl of the reaction mixture was collected and diluted with pyridine (1ml). To this mixture was added acetic anhydride (1ml) and the reaction mixtures maintained at room temperature for 10 hours. The reactions were quenched with methanol (1ml) and the solvents removed *in vacuo*. The crude products were dissolved in methanol (5ml) and the product distribution analysed by HPLC using 5µl injections into a Pheneomenex Jupiter Proteo C12 column (300 x 4.8mm, 5µm) with acetonitrile as the

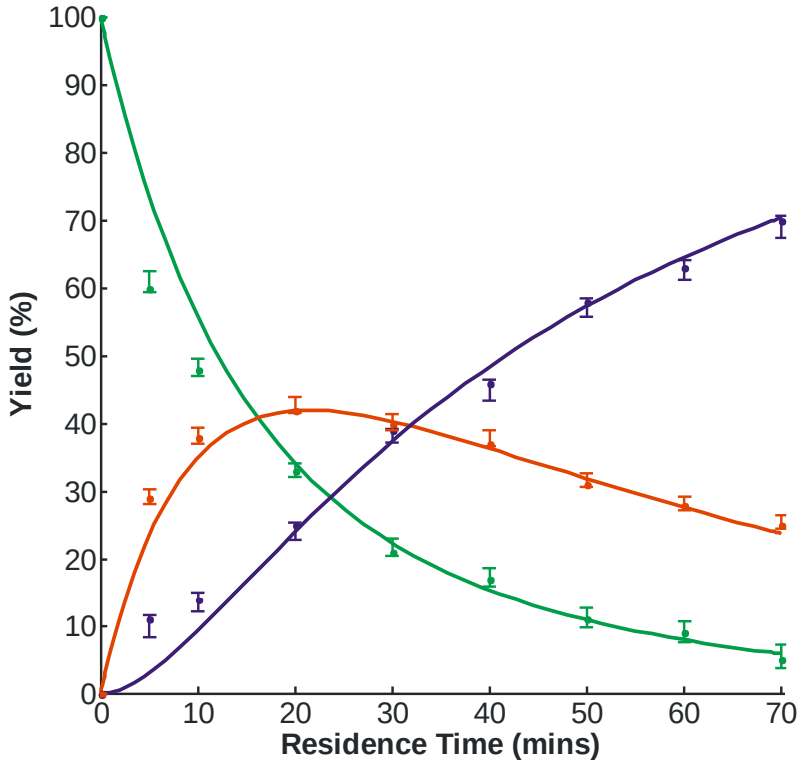
mobile phase at a flow rate of 1.0 ml/min. Eluants were detected using an in-line ELS detector (gain 2.0, nebulizer 30°C, drift tube 80°C, 1.65 Bar N_2)



	a	b
10	175.3	1.361
13	175.5	1.360
14	112.7	1.288

High solubility system

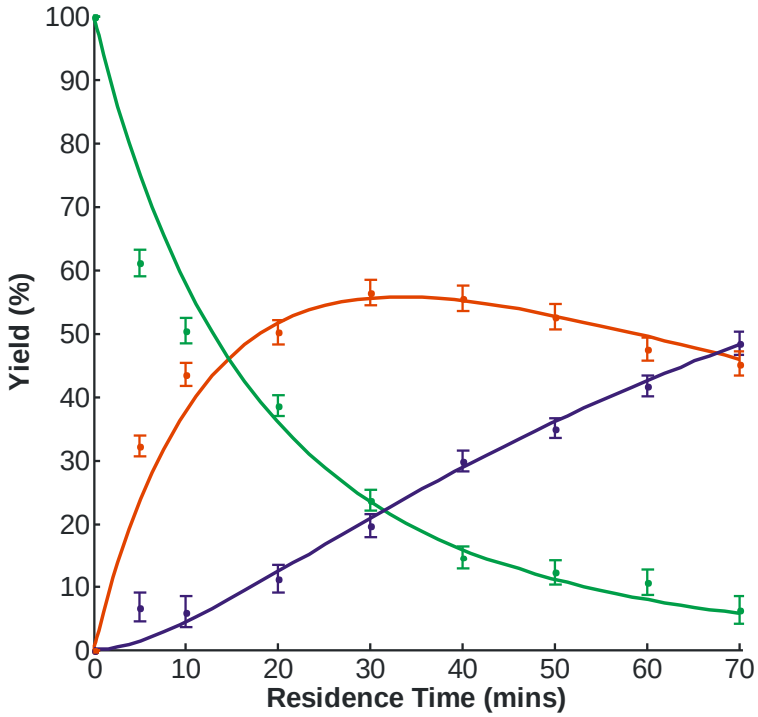
6 was dissolved in pyridine and TBAF dissolved in methanol. The reaction was performed as described above and kinetic parameters estimated by minimization of *Q*.



k_1 = 21.9 x 10^{-3} $mol^{-1}dm^3s^{-1}$; k_2 = 17.9 x 10^{-3} $mol^{-1}dm^3s^{-1}$; r^2 = 0.9651

Low solubility system

6 was dissolved in THF and TBAF dissolved in petrol with 1% methanol. The reaction was performed as described above and kinetic parameters estimated by minimization of *Q*.



k_1 = 21.6 x 10^{-3} $mol^{-1}dm^3s^{-1}$; k_2 = 7.67 x 10^{-3} $mol^{-1}dm^3s^{-1}$; r^2 = 0.9691

4. Compound characterization data

Trehalose-6-phosphate (2)

R_f 0.2 (5 ethanol : 3 NH_4OH : 1 water), $[\alpha]_D^{18}$ + 150.3 (c = 1.0, H_2O) lit.[2] $[\alpha]_D^{21}$ +151.2 (c = 0.8, H_2O); ^{1}H NMR (500MHz, D_2O) δ ppm 3.36 (1H, t, $J_{H3'\text{-}H4'}$ 9.5Hz, $J_{H4'\text{-}H5'}$ 9.5Hz, H4'), 3.50 (1H, t, $J_{H3\text{-}H4}$ 9.6Hz, $J_{H4\text{-}H5}$ 9.6Hz, H4), 3.56 (1H, dd, $J_{H2\text{-}H3}$ 10.1Hz, $J_{H1\text{-}H2}$ 3.8Hz, H2), 3.59 (1H, dd, $J_{H2'\text{-}H3'}$ 9.8Hz, $J_{H1'\text{-}H2'}$ 3.8Hz, H2'), 3.67 (1H, dd, $J_{H6'a\text{-}H6'b}$ 11.8Hz, $J_{H5'\text{-}H6'b}$ 5.4Hz, H6'b), 3.71-3.79 (4H, m, H3, H3', H5', H6'a), 3.82 (1H, d, $J_{H4\text{-}H5}$ 10.1Hz, H5), 3.86 (ddd, $J_{H6a\text{-}H6b}$ 12.1Hz, $J_{H6b\text{-}31P}$ 5.4Hz, $J_{H5\text{-}H6b}$ 1.7Hz, H6b), 3.94 (1H, ddd, $J_{H6a\text{-}H6b}$ 11.9Hz, $J_{H6a\text{-}31P}$ 7.7Hz, $J_{H5\text{-}H6a}$ 4.1Hz, H6a), 5.09 (1H, d, $J_{H1'\text{-}H2'}$ 4.1Hz, H1'), 5.12 (1H, d, $J_{H1\text{-}H2}$ 3.8Hz, H1); ^{13}C NMR (126MHz, D_2O) δ ppm 60.5 (1C, C6'), 63.0 (1C, d, $J_{C6\text{-}31P}$ 4.8Hz, C6), 69.1 (C1, C4'), 69.7 (1C, C4), 70.9 (1C, C2), 71.1 (1C, C2'), 71.6 (1C, d, $J_{C5\text{-}31P}$ 6.7Hz, C5), 72.1 (1C, C5'), 72.2 (1C, C3), 72.4 (1C, C3'), 93.3 (1C, C1), 93.4 (1C, C1'); ^{31}P{^{1}H} NMR (162MHz, D_2O) δ ppm 3.6 (1P, $ROP(O)(OH)_2$); m/z (ES^-) 421.5 $[M - H]^-$.

6-*O*-(diphenoxyphosphoryl)-D -trehalose (3)

R_f 0.68 (1 water : 4 isopropanol : 4 ethyl acetate), $[\alpha]_D^{22}$ +63.9 (c = 1.0, MeOH); ^{1}H NMR (500MHz, MeOD) δ ppm 3.34 (1H, t, $J_{H3'-H4'}$ 9.1Hz, $J_{H4'-H5'}$ 9.1Hz, H4'), 3.38 (1H, t, J_{H3-H4} 9.1Hz, J_{H4-H5} 9.1Hz, H4), 3.43 (1H, dd, $J_{H2'-H3'}$ 9.8Hz, $J_{H1'-H2'}$ 3.5Hz, H2'), 3.48 (1H, dd, J_{H2-H3} 9.8Hz, J_{H1-H2} 3.8Hz, H2), 3.70 (1H, dd, $J_{H6'a-H6'b}$ 12.0Hz, $J_{H5'-H6'b}$ 5.4Hz, H6'b), 3.80 (1H, t, $J_{H2'-H3'}$ 9.5Hz, $J_{H3'-H4'}$ 9.5Hz, H3'), 3.81 (1H, t, J_{H2-H3} 9.1Hz, J_{H3-H4} 9.1Hz, H3), 3.80-3.83 (1H, m, H6'a), 3.84 (1H, m, $J_{H5'-H6'b}$ 4.1Hz, $J_{H5'-H6'a}$ 2.2Hz, H5'), 4.09 (1H, dt, J_{H4-H5} 10.1Hz, J_{H5-H6a} 2.1Hz, J_{H5-H6b} 2.1Hz, H5), 4.48 (1H, ddd, $J_{H6a-H6b}$ 11.5Hz, $J_{H6b-31P}$ 7.1Hz, J_{H5-H6b} 3.5Hz, H6b), 4.55 (1H, ddd, $J_{H6a-H6b}$ 11.5Hz, $J_{H6a-31P}$ 6.8Hz, J_{H5-H6a} 1.9Hz, H6a), 5.09 (1H, d, $J_{H1'-H2'}$ 3.8Hz, H1'), 5.10 (1H, d, J_{H1-H2} 3.8Hz, H1), 7.21-7.31 (3H, m, ArH_{ortho}, ArH_{para}), 7.40-7.43 (2H, m, ArH_{meta}); ^{13}C NMR (126MHz, MeOD) δ ppm 62.6 (1C, C6'), 69.8 (1C, d, J_{C6-31P} 6.7Hz, C6), 71.2 (1C, C4'), 71.9 (1C, C4), 72.0 (1C, d, J_{C5-31P} 6.7Hz, C5), 73.0 (1C, C5'), 73.2 (1C, C2'), 73.9 (1C, C2), 74.4 (1C, C3'), 74.6 (1C, C3), 95.2 (1C, C1'), 95.3 (1C, C1), 121.4 (2C, d, J_{C-31P} 4.8Hz, ArC_{ortho}), 126.8 (1C, ArC_{para}), 131.1 (2C, ArC_{meta}), 151.9 (1C, d, J_{C-31P} 7.6Hz, ArC_{ipso}), 151.9 (1C, d, J_{C-31P} 7.6Hz, ArC_{ipso}); ^{31}P{^{1}H} NMR (162MHz, MeOD) δ ppm -12.0 (1P, $P(O)(OPh)_2$); FT-IR (KBr disc) υ 1287 (P=O), 3271 br (OH); HRMS m/z (ES^+) 596.1357 $[M + Na]^+$ required (596.1344); elemental C (49.87%) H (5.19%), required C (50.18%) H (5.44%).

6,6'-*O*-di(diphenoxyphosphoryl)-D-trehalose (4)

R_f 0.71 (1 water : 4 isopropanol : 4 ethyl acetate), $[\alpha]_D^{22}$ +63.8 (c = 1.0, MeOH); ^{1}H NMR (500MHz, MeOD) δ ppm 3.37 (2H, t, J_{H3-H4} 9.1Hz, J_{H4-H5} 9.1Hz, H4), 3.40 (2H, dd, J_{H2-H3} 9.9Hz, J_{H1-H2} 3.6Hz, H2), 3.79 (2H, t, J_{H2-H3} 9.3Hz, J_{H3-H4} 9.3Hz, H3), 4.07 (2H, ddd, J_{H4-H5} 9.9Hz, J_{H5-H6b} 4.7Hz, J_{H5-H6a} 2.0Hz, H5), 4.48 (2H, ddd, $J_{H6a-H6b}$

11.1Hz, $J_{H6b-31P}$ 7.6Hz, J_{H5-H6b} 4.7Hz, H6b), 4.55 (2H, ddd, $J_{H6-H6'}$ 11.1Hz, $J_{H6a-31P}$ 6.6Hz, J_{H5-H6a} 1.9Hz, H6a), 5.00 (2H, d, J_{H1-H2} 3.8Hz, H1), 7.21-7.29 (6H, m, ArH_{ortho}, ArH_{para}), 7.37-7.43 (4H, m, ArH_{meta}); ^{13}C NMR (126MHz, MeOD) δ ppm 69.8 (2C, d, J_{C6-31P} 6.7Hz, C6), 51.3 (2C, C4), 72.1 (2C, d, J_{C5-31P} 6.7Hz, C5), 73.0 (2C, C2), 74.5 (2C, C3,), 95.3 (2C, C1), 121.2 (8C, d, J_{C-31P} 4.8Hz, ArC_{ortho}), 126.9 (4C, ArC_{para}), 131.1 (8C, d, J_{C-31P} 2.9Hz, ArC_{meta}), 151.9 (2C, d, J_{C-31P} 1.9Hz, ArC_{ipso}), 151.9 (2C, d, J_{C-31P} 2.9Hz, ArC_{ipso}); $^{31}P\{^{1}H\}$ NMR (162MHz, MeOD) δ ppm -11.9 (1P, $P(O)(OPh)_2$); FT-IR (KBr disc) υ 1271 (P=O), 3364 br (OH); HRMS m/z (ES^+) 829.1629 $[M + Na]^+$ required (829.1633).

6-*O*-terbutyldiphenylsilyl-D-trehalose (5)

R_f 0.29 (1 water : 4 isopropanol : 4 ethyl acetate), $[\alpha]_D^{18}$ +20.3 (c = 1.0, dioxane); ^1H NMR (500 MHz, DMSO-d_6) δ ppm 1.00 (9H, s, ^{t}Bu), 3.15 (1H, td, $J_{H3'-H4'}$ 9.3Hz, $J_{H4'-H5'}$ 9.3Hz, $J_{H4'-OH}$ 5.7Hz, H4'), 3.25 (1H, td, J_{H3-H4} 9.5Hz, J_{H4-H5} 9.5Hz, J_{H4-OH} 5.0Hz, H4), 3.26 (1H, m, H2'), 3.29 (1H, dt, J_{H2-H3} 10.7Hz, J_{H1-H2} 4.4Hz, J_{H2-OH} 4.4Hz, H2), 3.49 (1H, dt, $J_{H6'a-H6'b}$ 11.4Hz, $J_{H5'-H6'b}$ 5.5Hz, $J_{H6'b-OH}$ 5.5Hz, H6'b), 3.55-3.64 (3H, m, H3', H5', H6'a), 3.68 (1H, ddd, J_{H3-H4} 9.9Hz, J_{H3-OH} 4.7Hz, J_{H2-H3} 1.9Hz, H3), 3.79 (1H, dd, $J_{H6a-H6b}$ 10.7Hz, J_{H5-H6b} 5.4Hz, H6b), 3.83 (1H, dd, $J_{H6a-H6b}$ 10.7Hz, J_{H5-H6a} 1.3Hz, H6a), 3.87 (1H, ddd, J_{H4-H5} 9.9Hz, J_{H5-H6b} 5.0Hz, J_{H5-H6a} 1.3Hz, H5), 4.39 (1H, t, J_{H6a-OH} 5.8Hz, J_{H6b-OH} 5.8Hz, 6'-OH), 4.58 (1H, d, J_{H2-OH} 6.3Hz, 2-OH), 4.66 (1H, d, $J_{H2'-OH}$ 6.3Hz, 2'-OH), 4.75 (1H, d, $J_{H3'-OH}$ 4.7Hz, 3'-OH), 4.78 (1H, d, $J_{H4'-OH}$ 5.4Hz, 4'-OH), 4.84 (1H, d, J_{H3-OH} 5.0Hz, 3-OH), 4.86 (1H, d, J_{H4-OH} 5.4Hz, 4-OH), 4.95 (1H, d, $J_{H1'-H2'}$ 3.5Hz, H1'), 4.97 (1H, d, J_{H1-H2} 3.8Hz, H1), 7.40-7.46 (6H, m, ArH_{ortho}, ArH_{para}), 7.67 (4H, ad, J 6.9Hz, ArH_{meta}); ^{13}C NMR (126 MHz, DMSO-d_6) δ ppm 19.0 (1C, $\underline{C}(CH_3)_3$), 26.6 (1C, $C(\underline{C}H_3)_3$), 60.7 (1C, C6'), 63.4 (1C, C6), 69.9 (1C, C4), 70.1 (1C, C4'), 71.6 (1C, C2), 71.7 (1C, C2'), 72.3 (1C, C5), 72.5

(1C, C3), 73.0 (1C, C5'), 73.0 (1C, C3'), 93.0 (1C, C1), 93.1 (1C, C1'), 127.8 (4C, ArC_{ortho}), 129.6 (1C, ArC_{para}), 129.7 (1C, ArC_{para}), 133.3 (2C, ArC_{ipso}), 133.5 (2C, ArC_{ipso}), 135.1 (1C, ArC_{meta}), 135.2 (1C, ArC_{meta}); FT-IR (KBr disc) υ 3400 br (OH); m/z (ES^+) 603.2221 $[M + Na]^+$ (required 603.2232); elemental C (58.00%) H (6.97%), required C (57.91%) H (6.94%).

6,6'-*O*-diterbutyldiphenylsilyl-D-trehalose (6)

R_f 0.35 (1 water : 2 isopropanol : 2 ethyl acetate), $[\alpha]_D^{17}$ +71.5 (c = 1.0, dioxane), ^1H NMR (500MHz, DMSO) δ ppm 1.00 (18H, s, 2 x ^tBu), 3.26 (2H, td, J_{H3-H4} 9.5Hz, J_{H4-H5} 9.5Hz, J_{H4-OH} 5.4Hz, H4), 3.30 (2H, ddd, J_{H2-H3} 9.8Hz, J_{H2-OH} 6.3Hz, J_{H1-H2} 3.8Hz, H2), 3.63 (2H, td, J_{H2-H3} 9.1Hz, J_{H3-H4} 9.1Hz, J_{H3-OH} 5.0Hz, H3), 3.80 (2H, dd, $J_{H6a-H6b}$ 11.0Hz, J_{H5-H6b} 5.7Hz, H6b), 3.86 (4H, m, H5, H6a), 4.62 (2H, d, J_{H2-OH} 6.3Hz, 2-OH), 4.84 (2H, d, J_{H3-OH} 4.7Hz, 3-OH), 4.91 (2H, d, J_{H2-OH} 5.4Hz, 4-OH), 5.06 (1H, d, J_{H1-H2} 3.5Hz, H1), 7.36-7.46 (12H, ArH_{ortho}, ArH_{para}), 7.70 (8H, m, ArH_{meta}); ^{13}C NMR (126MHz, DMSO) δ ppm 19.0 (2C, 2 x $\underline{C}(CH_3)_3$), 26.6 (6C, 2 x $C(\underline{C}H_3)_3$), 63.4 (2C, C6), 70.0 (2C, C4), 71.8 (2C, C2), 72.3 (2C, C5), 73.2 (2C, C3), 92.8 (2C, C1), 127.5 (4C, ArC_{ortho}), 127.7 (4C, ArC_{ortho}), 129.2 (2C, ArC_{para}), 129.6 (2C, ArC_{para}), 134.5 (4C, ArC_{ipso}), 135.2 (4C, ArC_{ipso}), 133.3 (2C, ArC_{meta}), 133.5 (2C, ArC_{meta}); FT-IR (KBr disc) υ 3350 br (OH); m/z (ES^+) 841.3410 $[M + Na^+]$ (required 841.3410).

6,6'-diazido-D-trehalose (8)

R_f 0.69 (1 water : 2 isopropanol : 2 ethyl acetate), $[\alpha]_D^{17}$ +154.8 (c = 0.5, H_2O), lit.[3] $[\alpha]_D^{20}$ +156 (c = 1.0, H_2O); ^1H NMR (500MHz, D_2O) δ ppm 3.37 (2H, t, J_{H3-H4} 9.1Hz, J_{H4-H5} 9.1Hz, H4), 3.47 (2H, dd, $J_{H6a-H6b}$ 13.7Hz, J_{H5-H6b} 5.8Hz, H6b), 3.58 (2H, as, H2), 3.58 (2H, dd, $J_{H6a-H6b}$ 10.4Hz, J_{H5-H6a} 3.8Hz, H6a), 3.74 (2H, t, J_{H2-H3} 9.5Hz, J_{H3-H4} 9.5Hz, H3), 3.89 (2H, ddd, J_{H4-H5} 10.0Hz, J_{H5-H6b} 5.9Hz, J_{H5-H6a} 2.4Hz, H5), 5.11 (2H, d, J_{H1-H2} 3.8Hz, H1); ^{13}C NMR (126MHz, D_2O) δ ppm 50.8 (2C, C6), 70.4

(2C, C4), 70.9 (2C, C2), 71.1 (2C, C5), 72.3 (2C, C3), 93.8 (2C, C1); FT-IR (KBr disc) υ 2106 (N_3), 3428 br (OH); HRMS m/z (ES^-) 391.1218 $[M - H]^-$ required (391.1219).

6-*O*-ditertbutyldiphenylsilyl-6'-*O*-diphenoxyphosphoryl-D-trehalose (9)

R_f 0.9 (1 water : 4 isopropanol : 10 ethyl acetate), $[\alpha]_D^{22}$ +31.4 (c = 1.0, MeOH), ^1H NMR (500MHz, MeOD) δ ppm 3.34 (2H, t, J_{H3-H4} 9.7Hz, J_{H4-H5} 9.7Hz, H4, H4'), 3.38 (1H, dd, J_{H2-H3} 9.7Hz, J_{H1-H2} 3.5Hz, H2), 3.46 (1H, dd, $J_{H2'-H3'}$ 9.9Hz, $J_{H1'-H2'}$ 3.9Hz, H2'), 3.78 (1H, t, $J_{H2'-H3'}$ 9.4Hz, $J_{H3'-H4'}$ 9.4Hz, H3'), 3.80 (1H, t, J_{H2-H3} 9.4Hz, J_{H3-H4} 9.4Hz, H3), 4.05 (2H, m, H5, H5'), 4.45 (1H, dd, J_{H5-H6b} 4.1Hz, $J_{H6a-H6b}$ 7.3Hz, H6b), 4.47 (1H, dd, $J_{H6a-H6b}$ 7.1Hz, J_{H5-H6a} 3.9Hz, H6a), 4.52 (1H, m, H6'b), 4.55 (1H, ddd, $J_{H6'a-H6'b}$ 11.2Hz, $J_{H6'b-31P}$ 6.6Hz, $J_{H5'-H6'b}$ 2.0Hz, H6'b), 7.19-7.26 (6H, m, P-OPh ArH_{ortho}, P-OPh ArH_{para}), 7.35-7.41 (10H, m, P-OPh ArH_{ortho}, P-OPh ArH_{meta}, Si-Ph Ar_{ortho}, Si-Ph Ar_{para}), 7.71-7.74 (4H, m, Si-Ph ArH_{meta}); ^{13}C NMR (126MHz, MeOD) δ ppm 20.3 (1C, $\underline{C}(CH_3)_3$), 27.4 (3C, $C(\underline{C}H_3)_3$), 69.9 (1C, d, $J_{C6'-31P}$ 6.7Hz, C6'), 69.9 (1C, C6), 71.3 (1C, C5), 71.7 (1C, C4), 72.0 (1C, d, $J_{C5'-31P}$ 6.7Hz, C5'), 73.1 (1C, C4'), 73.3 (1C, C2), 74.3 (1C, C2'), 74.6 (1C, C3), 74.9 (1C, C3'), 94.9 (1C, C1), 95.0 (1C, C1'), 121.2 (4C, d, J_{C-31P} 4.7Hz, P-OPh ArC_{ortho}), 126.8 (2C, Si-Ph ArC_{para}) 128.7 (2C, d, J_{C-31P} 4.8Hz, P-OPh ArC_{para}), 130.8 (4C, Si-Ph ArC_{ortho}), 131.1 (4C, d, J_{C-31P} 2.9Hz, P-OPh ArC_{meta}), 134.8, 135.0 (2 x 1C, 2 x Si-Ph ArC_{ipso}), 136.8, 137.9 (2 x 2C, 4 x Si-Ph ArC_{meta}), 151.9 (2C, d, J_{C-31P} 6.7Hz, P-OPh ArC_{ipso}); $^{31}P\{^1H\}$ NMR (162MHz, $CDCl_3$) δ ppm -12.1 (1P, $P(O)(OPh)_2$); FT-IR (KBr disc) υ 3369 br (OH); HRMS m/z (ES^-) 811.2556 $[M - H]^-$ required (811.2556).

2,2',3,3',4,4',5,5',6,6'-O-acetyl-D-trehalose (10)

R_f 0.02 (2 petrol : 1 ethyl acetate); $[\alpha]_D^{25}$ +160 (c = 1.0, $CHCl_3$), lit.[4] $[\alpha]_D^{22}$ +160 (c = 1.0, $CHCl_3$), m.p. 97-98°C (methanol), lit.[4] m.p. 98-100°C; ^{1}H NMR (500MHz, $CDCl_3$) δ ppm 2.02, 2.04, 2.07, 2.07 (4 x 6H, 4 x s, 8 x OAc), 4.00 (2H, dd, $J_{H6a-H6b}$ 12.1, J_{H5-H6b} 2.0Hz, H6b), 4.04 (2H, ddd, J_{H4-H5} 10.1Hz, J_{H5-H6a} 5.4Hz, J_{H5-H6b} 2.7Hz, H5), 4.23 (1H, dd, $J_{H6a-H6b}$ 12.0Hz, J_{H5-H6a} 5.7Hz, H6a), 5.03 (1H, dd, J_{H2-H3} 10.4Hz, J_{H1-H2} 3.8Hz, H2), 5.03 (1H, t, J_{H3-H4} 9.9Hz, J_{H4-H5} 9.9Hz, H4), 5.28 (1H, d, J_{H1-H2} 3.8Hz, H1), 5.48 (1H, t, J_{H2-H3} 9.8Hz, J_{H3-H4} 9.8Hz, H3); ^{13}C NMR (126MHz, $CDCl_3$) δ ppm 20.5, 20.6, 20.6, 20.6 (4 x 2C, 8 x CO<u>C</u>H_3), 61.7 (2C, C6), 68.1 (2C, C5), 68.5 (2C, C4), 69.8 (2C, C2), 69.9 (2C, C3), 92.2 (2C, C1), 169.5, 169.6, 169.9, 170.5 (4 x 2C, 8 x C=O); m/z 696.6 $[M + NH_4]^+$, 701.6 $[M + Na]^+$, 737.6 $[M + CH_3CN + NH_4]^+$.

6-*O*-(diphenoxyphosphoryl)-2,2',3,3',4,4',6'-*O*-acetyl-D-trehalose (11)

R_f 0.8 (ethyl acetate), $[\alpha]_D^{25}$ +50.7 (c = 0.71, $CHCl_3$); ^{1}H NMR (500MHz, $CDCl_3$) δ ppm 2.03, 2.05, 2.06, 2.06, 2.09, 2.10, 2.11 (7 x 3H, 7 x s, 7 x OAc), 4.01 (1H, dd, $J_{H6'a-H6'b}$ 12.1Hz, $J_{H5-H6'b}$ 2.0Hz, H6'b), 4.06 (1H, ddd, $J_{H4'-H5'}$ 10.2Hz, $J_{H5'-H6'a}$ 5.5Hz, $J_{H5'-H6'b}$ 1.9Hz, H5'), 4.14 (1H, ddd, J_{H4-H5} 10.2Hz, J_{H5-H6a} 5.1Hz, J_{H5-H6b} 2.1Hz, H5), 4.24 (1H, dd, $J_{H6'a-H6'b}$ 12.3Hz, $J_{H5'-H6'a}$ 5.7Hz, H6'a), 4.25 (1H, add, $J_{H6a-H6b}$ 11.0Hz, $J_{H6b-31P}$ 6.3Hz, H6b), 4.31 (1H, ddd, $J_{H6a-H6b}$ 11.4Hz, $J_{H6a-31P}$ 6.6Hz, J_{H5-H6a} 5.7Hz, H6a), 4.96 (1H, dd, J_{H2-H3} 10.2Hz, J_{H1-H2} 3.9Hz, H2), 5.05 (1H, t, J_{H3-H4} 9.3Hz, J_{H4-H5} 9.3Hz, H4), 5.05 (1H, dd, $J_{H2'-H3'}$ 10.1Hz, $J_{H1'-H2'}$ 4.7Hz, H2'), 5.06 (1H, t, $J_{H3'-H4'}$ 9.6Hz, $J_{H4'-H5'}$ 9.6Hz, H4'), 5.13 (1H, d, J_{H1-H2} 3.8Hz, H1), 5.21 (1H, d, $J_{H1'-H2'}$ 4.1Hz, H1'), 5.46 (1H, t, $J_{H2'-H3'}$ 9.8Hz, $J_{H3'-H4'}$ 9.8Hz, H3'), 5.49 (1H, t, J_{H2-H3} 9.8Hz, J_{H3-H4} 9.8Hz, H3), 7.20-7.26 (6H, m, ArH_{ortho}, ArH_{para}), 7.35 (2H, t, $J_{ortho-meta}$ 7.9Hz, $J_{meta-para}$ 7.9Hz, ArH_{meta}), 7.36 (2H, t, $J_{ortho-meta}$ 7.9Hz, $J_{meta-para}$ 7.9Hz, ArH_{meta}); ^{13}C NMR (126MHz, $CDCl_3$) δ ppm 20.5, 20.5, 20.6 (x3), 20.7, 20.7 (7 x 1C, 7 x CO<u>C</u>H_3), 61.7

(1C, C6'), 66.6 (1C, d, $J_{C\text{-}31P}$ 4.8Hz, C6), 68.2 (1C, C5'), 68.4 (1C, C4'), 68.4 (1C, C4), 68.7 (1C, d, $J_{C\text{-}31P}$ 7.6Hz, C5), 69.5 (1C, C2'), 69.7 (1C, C2), 69.9 (1C, C3'), 70.1 (1C, C3), 92.5 (1C, C1'), 92.8 (1C, C1), 120.0 (2C, d, $J_{C\text{-}31P}$ 2.9Hz, ArC_{ortho}), 120.0 (2C, d, $J_{C\text{-}31P}$ 2.9Hz, ArC_{ortho}), 125.5 (2C, ArC_{para}), 129.8 (4C, ArC_{meta}), 150.3 (1C, d, $J_{C\text{-}31P}$ 5.7Hz, ArC_{ipso}), 150.4 (1C, d, $J_{C\text{-}31P}$ 4.8Hz, ArC_{ipso}), 169.3, 169.5, 169.5, 169.6, 170.0, 170.0, 170.6 (7 x 1C, 7 x C=O); $^{31}P\{^{1}H\}$ NMR (162MHz, $CDCl_3$) δ ppm -11.8 (1P, $P(O)(OPh)_2$); FT-IR (thin film) υ 1241 (P=O), 1723 (C=O); HRMS (ES^+) m/z 891.2083 $[M + Na]^+$ (required 891.2083).

6,6'-*O*-di(diphenoxyphosphoryl), 2,2',3,3',4,4'-*O*-acetyl-D-trehalose (12)

R_f 0.33 (2 ethyl acetate : 1 petrol), $[\alpha]_D^{19}$ +80.4 (c = 1.0, $CHCl_3$); ^{1}H NMR (500MHz, $CDCl_3$) δ ppm 2.02, 2.03, 2.04 (3 x 6H, 3 x s, 6 x CH_3), 4.12 (2H, ddd, $J_{H4\text{-}H5}$ 10.1Hz, $J_{H5\text{-}H6a}$ 6.6Hz, $J_{H5\text{-}H6b}$ 2.0Hz, H5), 4.22 (2H, ddd, $J_{H6a\text{-}H6b}$ 11.1Hz, $J_{H6b\text{-}31P}$ 6.6Hz, $J_{H5\text{-}H6b}$ 2.2Hz, H6b), 4.29 (2H, ddd, $J_{H6a\text{-}H6b}$ 11.4Hz, $J_{H6a\text{-}31P}$ 6.6Hz, $J_{H5\text{-}H6a}$ 5.4Hz, H6a), 4.96 (2H, dd, $J_{H2\text{-}H3}$ 10.2Hz, $J_{H1\text{-}H2}$ 3.9Hz, H2), 5.00 (2H, d, $J_{H1\text{-}H2}$ 3.8Hz, H1), 5.03 (2H, dd, $J_{H4\text{-}H5}$ 10.2, $J_{H3\text{-}H4}$ 9.3Hz, H4), 5.43 (2H, dd, $J_{H2\text{-}H3}$ 10.1Hz, $J_{H3\text{-}H4}$ 9.5Hz, H3), 7.16-7.22 (12H, m, ArH_{ortho}, ArH_{para}), 7.32-7.36 (8H, m, ArH_{meta}); ^{13}C NMR (126MHz, $CDCl_3$) δ ppm 20.5, 20.6, 20.7 (3 x 2C, CH_3), 66.6 (2C, d, $J_{C6\text{-}31P}$ 5.7Hz, C6), 68.3 (2C, C4), 68.7 (2C, d, $J_{C5\text{-}31P}$ 8.6Hz, C5), 69.3 (2C, C2), 70.1 (2C, C3), 93.0 (2C, C1), 120.0 (8C, d, $J_{C\text{-}31P}$ 4.8Hz, ArC_{ortho}), 125.5 (4C, ArC_{para}), 129.8 (8C, ArC_{meta}), 150.3 (2C, d, $J_{C\text{-}31P}$ 6.7Hz, ArC_{ipso}), 150.4 (2C, d, $J_{C\text{-}31P}$ 7.6Hz, ArC_{ipso}), 169.3, 169.4, 170.0 (3 x 2C, C=O); $^{31}P\{^{1}H\}$ NMR (162MHz, $CDCl_3$) δ ppm -11.9 (1P, $P(O)(OPh)_2$); FT-IR (thin film) υ 1248 (P=O), 1755 (C=O); HRMS m/z (ES^+) 1081.23 (100%), 1082.23 (52%), 1083.24 (17%), 1084.24 (4%) required 1081.23 (100%), 1082.23 (53%), 1083.23 (19%), 1084.24 (5%).

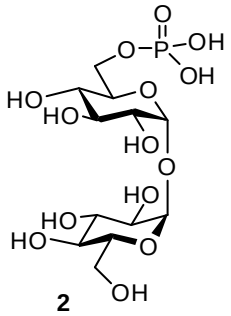
6-*O*-ditertbutyldiphenylsilyl, 2,2',3,3',4,4',6'-acetyl-D-trehalose (13)

R_f 0.17 (2 petrol : 1 ethyl acetate), $[\alpha]_D^{25}$ +119.4 (c = 1.0, $CHCl_3$), m.p. 154-156°C (ethyl acetate/petrol); ^{1}H NMR (500MHz, $CDCl_3$) δ ppm 1.03 (9H, s, ^{t}Bu), 1.92, 1.96, 2.01, 2.04, 2.05, 2.10, 2.10 (7 x 3H, 7 x s, 7 x OAc), 3.65 (2H, ad, *J* 3.2Hz, H6'a, H6'b), 3.94 (1H, dt, $J_{H4'-H5'}$ 10.2Hz, $J_{H5'-H6'a}$ 3.0Hz, $J_{H5'-H6'b}$ 3.0Hz, H5'), 4.04 (1H, dd, $J_{H6a-H6b}$ 12.0Hz, J_{H5-H6b} 1.9Hz, H6b), 4.07 (1H, ddd, J_{H4-H5} 10.4Hz, J_{H5-H6a} 5.5Hz, J_{H5-H6b} 2.0Hz, H5), 4.24 (1H, dd, $J_{H6a-H6b}$ 11.8Hz, J_{H5-H6a} 5.2Hz, H6a), 5.03 (1H, dd, J_{H2-H3} 10.2Hz, J_{H1-H2} 3.9Hz, H2), 5.06 (1H, t, J_{H3-H4} 8.7Hz, J_{H4-H5} 8.7Hz, H4), 5.06 (1H, dd, $J_{H2'-H3'}$ 10.7Hz, $J_{H1'-H2'}$ 3.5Hz, H2'), 5.26 (1H, t, $J_{H3'-H4'}$ 9.8Hz, $J_{H4'-H5'}$ 9.8Hz, H4'), 5.25 (1H, d, $J_{H1'-H2'}$ 3.8Hz, H1'), 5.32 (1H, d, J_{H1-H2} 4.1Hz, H1), 5.47 (1H, t, J_{H2-H3} 9.8Hz, J_{H3-H4} 9.8Hz, H3), 5.49 (1H, t, $J_{H2'-H3'}$ 10.1Hz, $J_{H3'-H4'}$ 10.1Hz, H3'), 7.31-7.47 (6H, m, ArH_{ortho}, ArH_{para}), 7.62 (4H, ddd, ^3J 10.9Hz, ^3J 8.0Hz, ^4J 1.3Hz, ArH_{meta}); ^{13}C NMR (126MHz, $CDCl_3$) δ ppm 19.1 (1C, $\underline{C}(CH_3)_3$), 20.4, 20.6, 20.7 (3 x 1C, 3 x CO$\underline{C}H_3$), 20.6, 20.6 (2 x 2C, 4 x CO$\underline{C}H_3$), 26.7 (3C, C($\underline{C}H_3)_3$), 61.8 (1C, C6), 61.8 (1C, C6'), 68.1 (1C, C5), 68.4 (1C, C4'), 68.4 (1C, C4), 69.6 (1C, C2'), 70.1 (1C, C2), 70.2 (1C, C3), 70.4 (1C, C3'), 70.6 (1C, C5'), 92.4 (1C, C1'), 92.5 (1C, C1), 127.7 (4C, ArC_{ortho}), 129.8 (2C, ArC_{para}), 129.8 (2C, ArC_{para}), 132.8 (2C, ArC_{ipso}), 132.8 (2C, ArC_{ipso}), 135.6 (2C, ArC_{meta}), 135.6 (2C, ArC_{meta}), 169.3, 169.4, 169.5, 169.7, 169.9, 170.2, 170.6 (7 x 1C, 7 x C=O); FT-IR (KBr disc) υ 1754 (C=O); HRMS m/z (ES^+) 897.2980 $[M + Na]^+$ (required 897.2972).

6,6'-*O*-ditertbutyldiphenylsilyl, 2,2',3,3',4,4'-acetyl-D-trehalose (14)

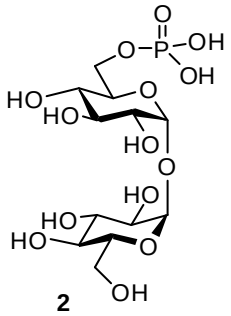
R_f 0.35 (2 petrol : 1 ethyl acetate), $[\alpha]_D^{25}$ +94.6 (c = 1.4, $CHCl_3$); ^{1}H NMR (500MHz, $CDCl_3$) δ ppm 1.06 (18H, s, 2 x ^{t}Bu), 1.92, 1.96, 2.01 (3 x 6H, 3 x s, 6 x OAc), 3.67 (4H, ad, *J* 3.2Hz, H6a, H6b), 3.93 (2H, dt, $J_{H4\text{-}H5}$ 10.3Hz, $J_{H5\text{-}H6a}$ 2.3Hz, $J_{H5\text{-}H6b}$ 2.3Hz, H5), 5.04 (2H, dd, $J_{H2\text{-}H3}$ 10.4Hz, $J_{H1\text{-}H2}$ 3.8Hz, H2), 5.28 (2H, t, $J_{H3\text{-}H4}$ 9.8Hz, $J_{H4\text{-}H5}$ 9.8Hz, H4), 5.27 (2H, d, $J_{H1\text{-}H2}$ 4.1Hz, H1), 5.46 (2H, t, $J_{H2\text{-}H3}$ 10.1Hz, $J_{H3\text{-}H4}$ 10.1Hz, H3), 7.34-7.47 (12H, m, ArH_{ortho}, ArH_{para}), 7.64 (8H, ddd, ^3J 13.7Hz, ^3J 7.9Hz, ^4J 1.4Hz, ArH_{meta}); ^{13}C NMR (126MHz, $CDCl_3$) δ ppm 19.2 (2C, $\underline{C}(CH_3)_3$), 20.5, 20.6, 20.7 (3 x 2C, 6 x CO$\underline{C}H_3$), 26.7 (6C, C($\underline{C}H_3$)$_3$), 61.8 (2C, C6), 68.4 (2C, C4), 69.9 (2C, C2), 70.5 (2C, C5), 70.8 (2C, C3), 92.6 (2C, C1), 127.7 (8C, ArC_{ortho}), 129.8 (2C, ArC_{para}), 129.8 (2C, ArC_{para}), 132.8 (2C, ArC_{ipso}), 132.9 (2C, ArC_{ipso}), 135.6 (4C, ArC_{meta}), 135.6 (4C, ArC_{meta}), 169.3, 169.6, 170.2 (3 x 2C, 6 x C=O); FT-IR (KBr disc) υ 1756 (C=O); HRMS m/z (ES^+) $[M + Na]^+$ peaks 1790.55 (100%), 1791.56 (88%), 1792.55 (41%), 1793.54 (13%), 1794.57 (5.0%), required, 1790.55 (100%), 1791.56 (84%), 1792.56 (44%), 1793.56 (18%), 1794.57 (6%); elemental C (57.72%) H (6.25%), required C (57.65%) H (6.22%).

5. NMR spectra



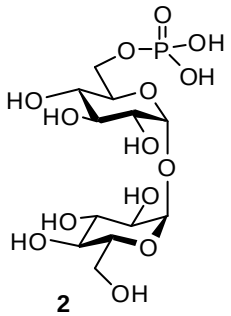
2

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	128
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	DEUTERIUM OXIDE
Spectrum Offset (Hz)	3089.5557
Sweep Width (Hz)	10330.26
Temperature (degree C)	27.000



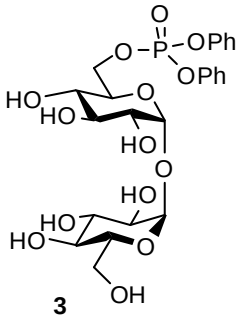
2

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	1024
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1820.00
SW(cyclical) (Hz)	31250.00
Solvent	DEUTERIUM OXIDE
Spectrum Offset (Hz)	12580.1094
Sweep Width (Hz)	31249.05
Temperature (degree C)	27.000



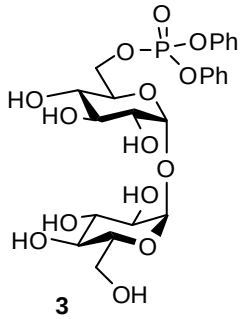
2

Frequency (MHz)	162.00
Nucleus	31P
Number of Transients	32
Origin	av400
Pulse Sequence	zgpg30
Receiver Gain	26008.00
SW(cyclical) (Hz)	64935.07
Solvent	DEUTERIUM OXIDE
Spectrum Offset (Hz)	-7274.8262
Sweep Width (Hz)	64933.09
Temperature (degree C)	27.000



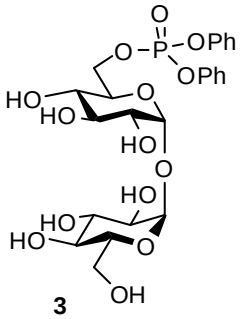
3

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	MeOD
Spectrum Offset (Hz)	3089.5557
Sweep Width (Hz)	10330.26
Temperature (degree C)	27.000



3

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	512
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1820.00
SW(cyclical) (Hz)	31250.00
Solvent	MeOD
Spectrum Offset (Hz)	12758.7549
Sweep Width (Hz)	31249.05
Temperature (degree C)	27.000



3

Frequency (MHz)	162.00
Nucleus	31P
Number of Transients	32
Origin	av400
Pulse Sequence	zgpg30
Receiver Gain	18390.40
SW(cyclical) (Hz)	64935.07
Solvent	MeOD
Spectrum Offset (Hz)	-8126.5610
Sweep Width (Hz)	64933.09
Temperature (degree C)	27.000

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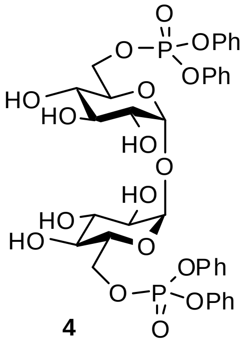

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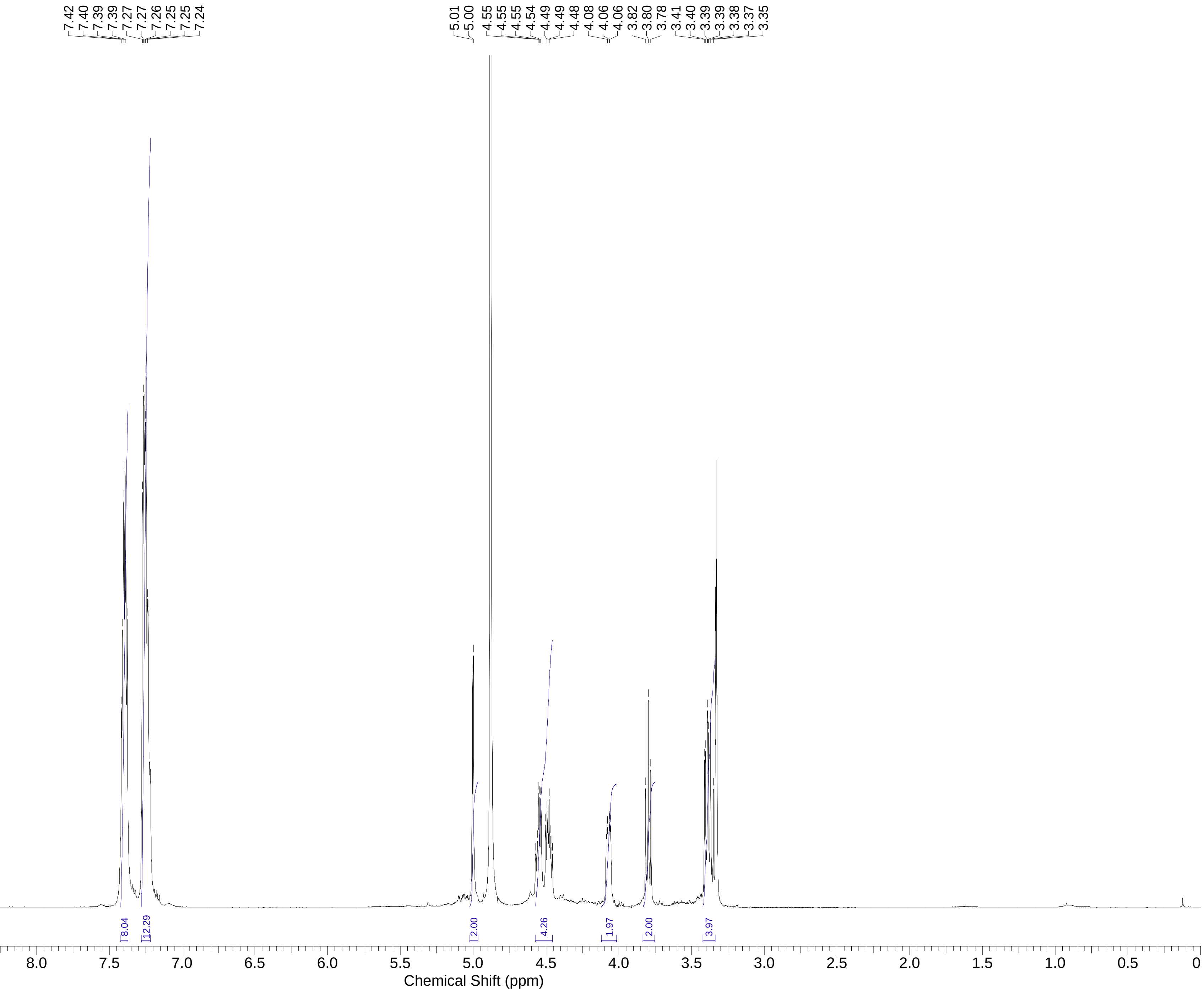
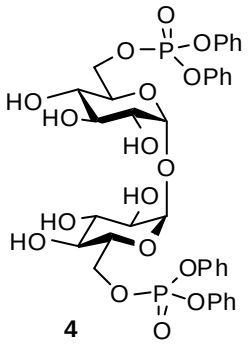
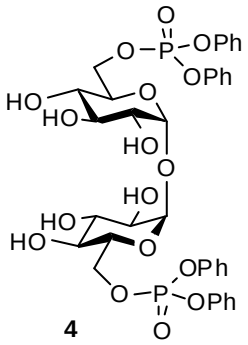


Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	MeOD
Spectrum Offset (Hz)	3089.5557
Sweep Width (Hz)	10330.26
Temperature (degree C)	27.000



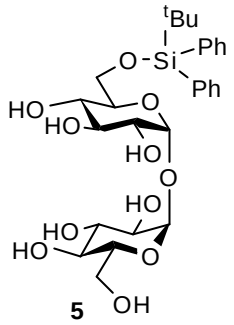
4

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	512
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1030.00
SW(cyclical) (Hz)	31250.00
Solvent	MeOD
Spectrum Offset (Hz)	12758.7549
Sweep Width (Hz)	31249.05
Temperature (degree C)	27.000



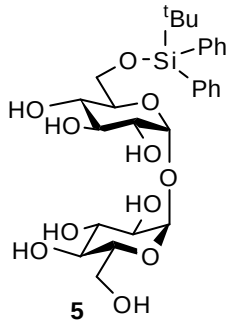
4

Frequency (MHz)	162.00
Nucleus	31P
Number of Transients	32
Origin	av400
Pulse Sequence	zgpg30
Receiver Gain	20642.50
SW(cyclical) (Hz)	64935.07
Solvent	MeOD
Spectrum Offset (Hz)	-8099.8774
Sweep Width (Hz)	64933.09
Temperature (degree C)	27.000



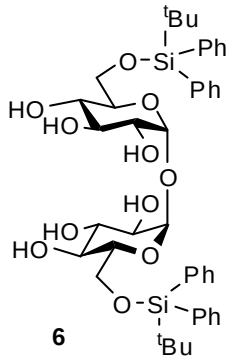
5

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	DMSO-d6
Spectrum Offset (Hz)	3089.5557
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



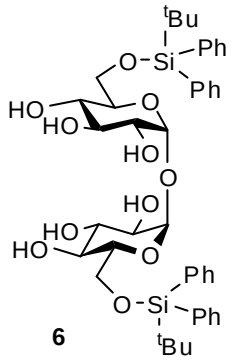
5

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	1024
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1820.00
SW(cyclical) (Hz)	31250.00
Solvent	DMSO-d6
Spectrum Offset (Hz)	12519.7266
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



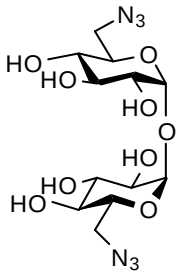
6

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	DMSO-d6
Spectrum Offset (Hz)	3089.5557
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



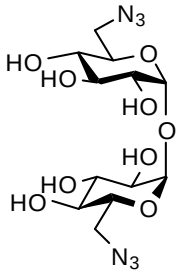
6

Frequency (MHz)	125.81
Nucleus	13C
Number of Transients	256
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1150.00
SW(cyclical) (Hz)	31250.00
Solvent	DMSO-d6
Spectrum Offset (Hz)	12522.5273
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



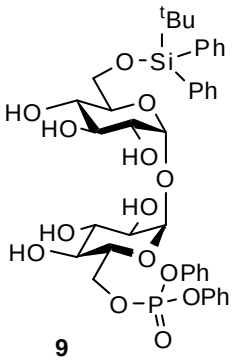
8

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	DEUTERIUM OXIDE
Spectrum Offset (Hz)	3089.5557
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



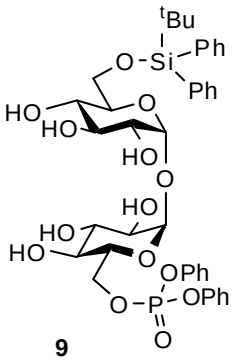
8

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	512
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1290.00
SW(cyclical) (Hz)	31250.00
Solvent	DEUTERIUM OXIDE
Spectrum Offset (Hz)	12580.1094
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



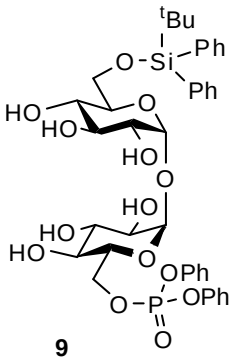
9

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	MeOD
Spectrum Offset (Hz)	3844.8057
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



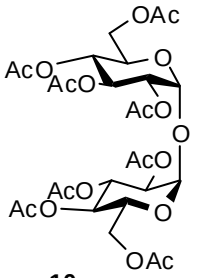
9

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	1024
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1030.00
SW(cyclical) (Hz)	31250.00
Solvent	MeOD
Spectrum Offset (Hz)	12758.7549
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



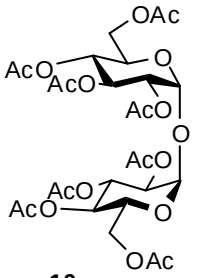
9

Frequency (MHz)	162.00
Nucleus	31P
Number of Transients	32
Origin	av400
Pulse Sequence	zgpg30
Receiver Gain	23170.50
SW(cyclical) (Hz)	64935.07
Solvent	MeOD
Spectrum Offset (Hz)	-9296.6221
Sweep Width (Hz)	64933.09
Temperature (degree C)	27.000



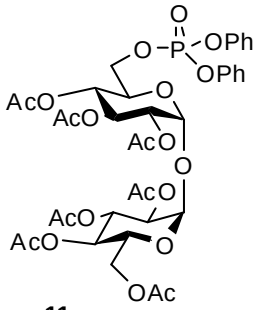
10

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	3065.5417
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



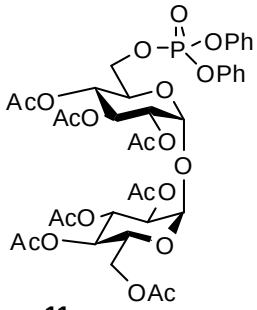
10

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	256
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1290.00
SW(cyclical) (Hz)	31250.00
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	12571.3047
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



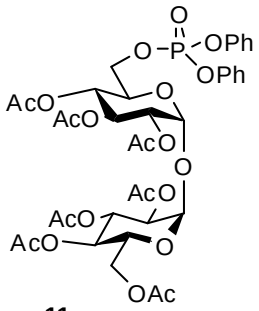
11

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	3065.5417
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



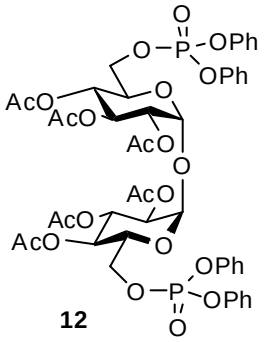
11

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	512
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	912.00
SW(cyclical) (Hz)	31250.00
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	12571.3047
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



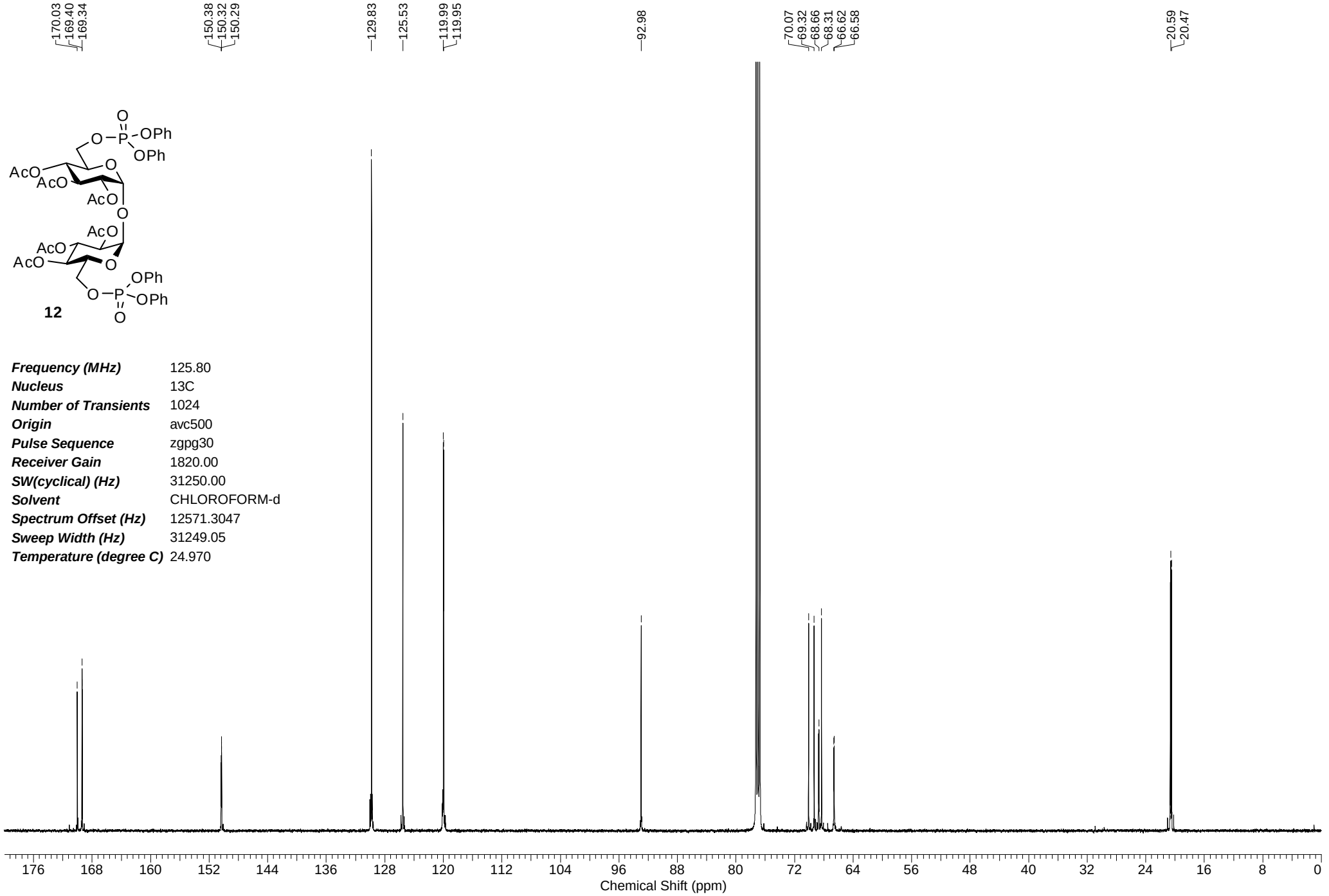
11

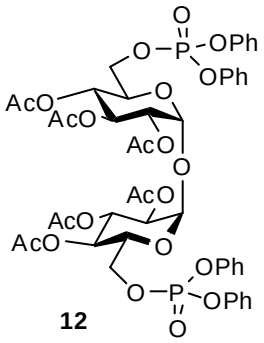
Frequency (MHz)	162.00
Nucleus	31P
Number of Transients	32
Origin	av400
Pulse Sequence	zgpg30
Receiver Gain	23170.50
SW(cyclical) (Hz)	64935.07
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	-8099.8774
Sweep Width (Hz)	64933.09
Temperature (degree C)	27.000



12

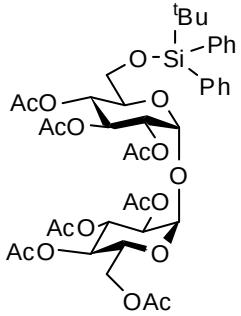
Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	3065.5417
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970


170.03
169.40
169.34
150.38
150.32
150.29
129.83
125.53
119.99
119.95
92.98
70.07
69.32
68.66
68.31
66.62
66.58
20.59
20.47
12
Frequency (MHz) 125.80
Nucleus 13C
Number of Transients 1024
Origin avc500
Pulse Sequence zgpg30
Receiver Gain 1820.00
SW(cyclical) (Hz) 31250.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 12571.3047
Sweep Width (Hz) 31249.05
Temperature (degree C) 24.970
176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)



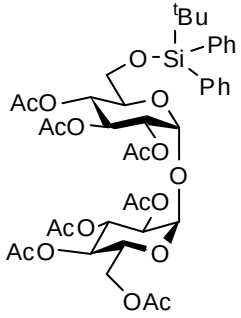
12

Frequency (MHz)	162.00
Nucleus	31P
Number of Transients	32
Origin	av400
Pulse Sequence	zgpg30
Receiver Gain	18390.40
SW(cyclical) (Hz)	64935.07
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	-8099.8774
Sweep Width (Hz)	64933.09
Temperature (degree C)	27.000



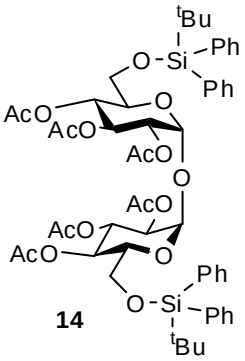
13

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	3065.5417
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970



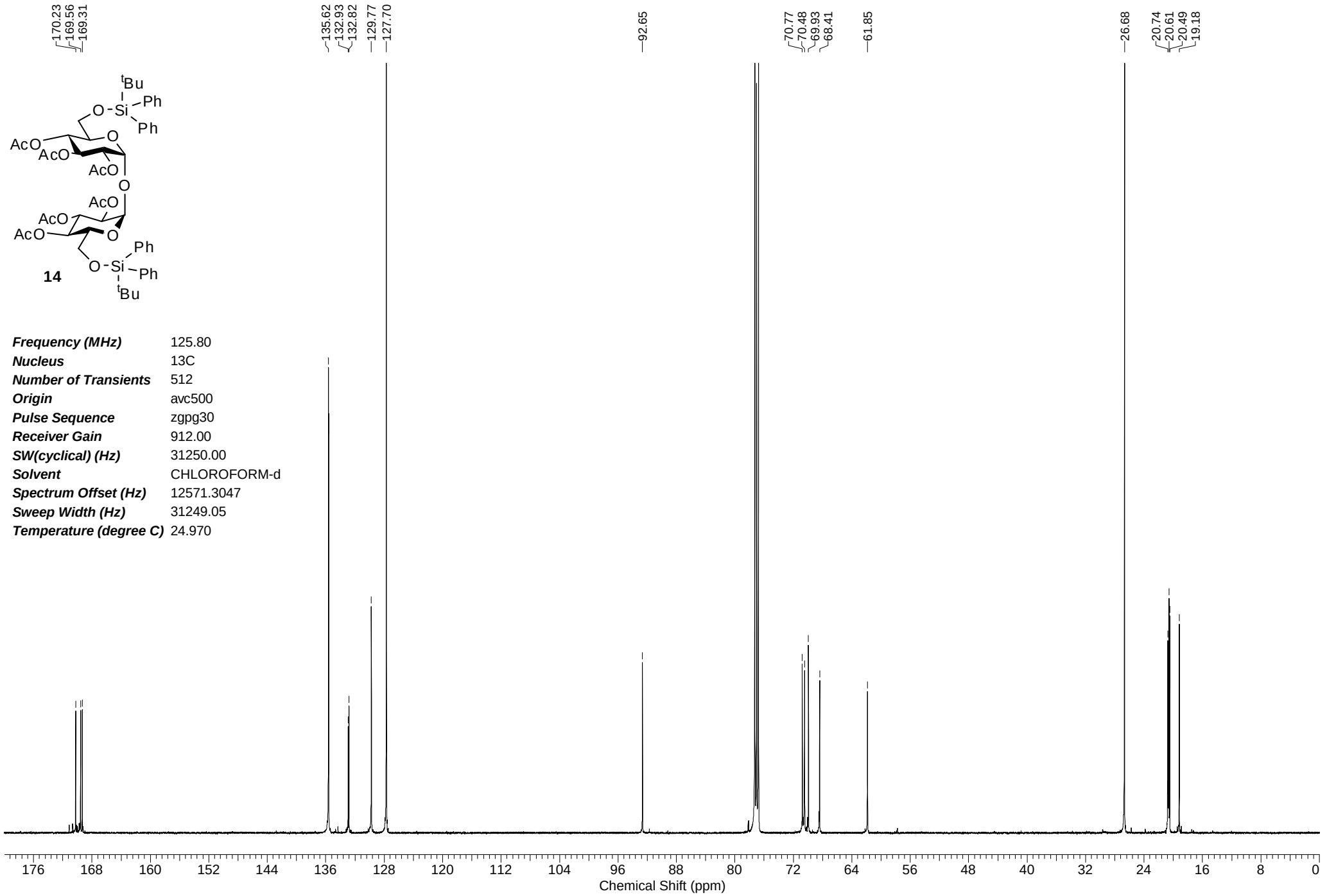
13

Frequency (MHz)	125.80
Nucleus	13C
Number of Transients	256
Origin	avc500
Pulse Sequence	zgpg30
Receiver Gain	1820.00
SW(cyclical) (Hz)	31250.00
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	12571.3047
Sweep Width (Hz)	31249.05
Temperature (degree C)	24.970



14

Frequency (MHz)	500.30
Nucleus	1H
Number of Transients	16
Origin	avc500
Pulse Sequence	zg30
Receiver Gain	4.00
SW(cyclical) (Hz)	10330.58
Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	3065.5417
Sweep Width (Hz)	10330.26
Temperature (degree C)	24.970


170.23
169.56
169.31
135.62
132.93
132.82
129.77
127.70
92.65
70.77
70.48
69.93
68.41
61.85
26.68
20.74
20.61
20.49
19.18
tBu
Ph
Ph
O
Si
AcO
AcO
AcO
O
AcO
AcO
AcO
O
Ph
Ph
O
Si
tBu
14
Frequency (MHz) 125.80
Nucleus 13C
Number of Transients 512
Origin avc500
Pulse Sequence zgpg30
Receiver Gain 912.00
SW(cyclical) (Hz) 31250.00
Solvent CHLOROFORM-d
Spectrum Offset (Hz) 12571.3047
Sweep Width (Hz) 31249.05
Temperature (degree C) 24.970
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

6. References

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