Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Total Synthesis of Tricolorin A *via* Interrupted Pummerer Reaction Mediated Glycosylation and One-pot Relay Glycosylation

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1. General Comments

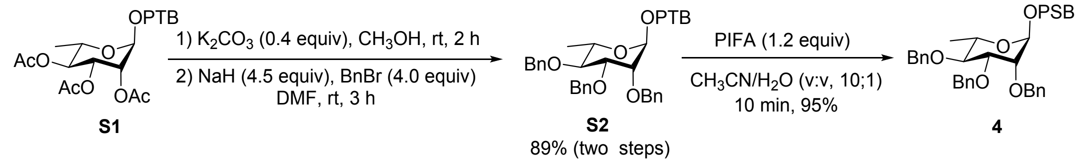
All reactions were monitored by thin-layer chromatography over silica-gel-coated TLC plates (Yantai Chemical Industry Research Institute). The spots on TLC were visualized by warming 10% H_2SO_4 (10% H_2SO_4 in ethanol) sprayed plates on a hot plate. Column chromategraphy was performed using silica gel (Qingdao Marine Chemical Inc., China). NMR spectra were recorded on a Bruker AM-400 spectrometer (400 MHz). The ^{1}H NMR and ^{13}C NMR chemical shifts were referenced to the solvent or solvent impurity peaks for $CDCl_3$ at δ_H 7.24 and δ_C 77.23. Optical rotations were measured at 25 °C with a Rudolph Autopol IV automatic polarimeter using a quartz cell with 1 mL capacity and a 1 dm path length. Concentrations (*c*) are given in g/100 mL. High resolution mass spectra were recorded on a Bruker micrOTOF II spectrometer using electrospray ionization (ESI), HRMS mass analyzer type is TOF. Melting points were tested on a X-5 melting point apparatus (Beijing TECH Instrument CO. LTD) without correction.

2. Materials

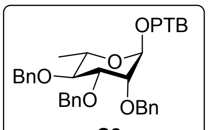
Unless otherwise noted, all reactions were performed under argon atmosphere. Solvents for reactions were dried on an Innovative Technologies Pure Solv400 solvent purifier. Molecular sieves (4Å, powder < 50 μm) for reactions were flame dried immediately before use. 2,6-Di-*tert*-butyl-4-methylpyridine (DTBMP) and trifluoromethanesulfonic anhydride (Tf_2O) were purchased from Acros®. Bis(trifluoroacetoxy)iodobenzene (PIFA), 3-chloroperoxybenzoic acid (*m*-CPBA) and all other commercially available chemicals were purchased from Adamas® and used without further purification. The known compounds **S1**[1], **S3**[3], **S7**[4], **S10**[8] and **7**[7]， **8**[5], **9**[2] were synthesized following literature procedures.

3. Syntheses of disaccharides 2a and 2b

Preparation of OPSB glycoside 4



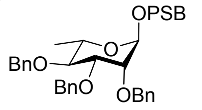
O-2-[(Propan-2-yl)sulfanyl]benzyl 2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranoside (S2)



S2

To a solution of compound **S1**[1] (380.0 mg, 0.83 mmol) in MeOH (2.8 mL) was added K_2CO_3 (46.0 mg, 0.33 mmol), the mixture was stirred at room temperature for 2 h, then filtered and evaporated under reduced pressure to afford the crude deacetylated product. This crude product was dissolved in DMF (2.8 mL) and cooled to 0 °C under an atmosphere of argon. NaH (150.0 mg, 3.76 mmol) was added slowly and stirred over a period of 10 min before benzyl bromide (397.0 µL, 3.34 mmol) was added. The reaction mixture was stirred at room temperature for 3 h and quenched with MeOH, then extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated under reduced pressure and purified by chromatography to give **S2** (445.0 mg, 89%). Colorless syrup. $R_f = 0.30$ (petroleum ether-EtOAc 30:1). $[\alpha]_D^{25} = -48.18$ (c, 1.7 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.12 (19H, m, Ar-H), 4.87 (1H, d, $J = 10.8$ Hz, PhCH), 4.86 (1H, s, H-1), 4.72-4.67 (3H, m, 3 × PhCH), 4.59-4.53 (4H, m, 4 × PhCH) 3.84 (1H, dd, $J = 9.6, 3.2$ Hz, H-3), 3.76 (1H, br s, H-2), 3.72 (1H, m, H-5), 3.57 (1H, t, $J = 9.6$ Hz, H-4), 3.25 (1H, m, $CH(CH_3)_2$), 1.28 (3H, d, $J = 6.4$ Hz, CH_3), 1.18 (6H, d, $J = 6.8$ Hz, $CH(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 138.8, 138.8, 138.5, 134.7, 132.7, 128.6, 128.5, 128.5, 128.2, 128.2, 127.9, 127.9, 127.8, 127.7, 127.1, 97.9, 80.7, 80.3, 75.6, 75.0, 72.9, 72.4, 68.5, 67.6, 38.8, 23.3, 23.2, 18.2. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{37}H_{42}NaO_5S$ 621.2645; found 621.2652.

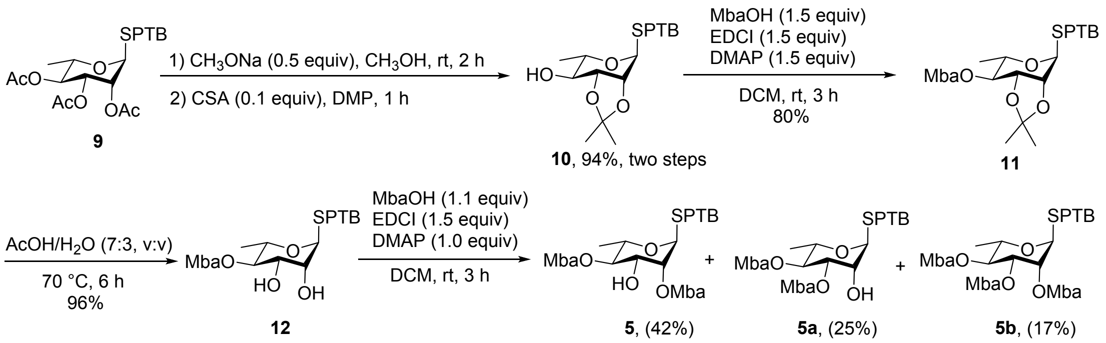
O-2-[(Propan-2-yl)sulfinyl]benzyl 2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranoside (4)



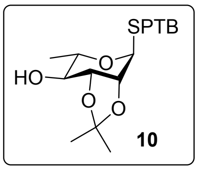
4

To a solution of **S2** (407.0 mg, 0.68 mmol) in CH_3CN/H_2O (0.33 mL, 10:1, v:v) was added PIFA (350.0 mg, 0.82 mmol), the reaction mixture was stirred at room temperature for 10 min, then diluted with water, extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was subjected to flash column chromatography to afford **4** (396.0 mg, 95%). Colorless syrup. $R_f = 0.42$ (petroleum ether-EtOAc 2:1). Analysis by ^1H NMR indicated a mixture of sulfoxide isomers (*R* and *S*, 1:0.5). ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.26 (28.5H, m, Ar-H), 4.93 (1.5H, m), 4.85 (1H, br s, H-1), 4.77 (1.5H, m), 4.74-4.57 (7H, m), 4.54-4.47 (1.5H, m), 3.82-3.60 (6H, m), 2.85- 2.71 (1.5H, m), 1.34 (4.5H, m), 1.19 (1.5H, d, $J = 7.2$ Hz, CH_3), 1.14 (3H, d, $J = 6.8$ Hz, CH_3), 1.04 (4.5H, d, $J = 6.8$ Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 141.5, 138.6, 138.2, 135.0, 134.9, 131.1, 129.7, 129.5, 129.1, 129.0, 128.7, 128.6, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 125.5, 125.5, 98.0, 97.6, 80.6, 80.5, 80.1, 79.9, 75.7, 75.6, 74.7, 74.7, 73.1, 72.5, 72.4, 68.9, 68.7, 65.8, 65.0, 54.0, 53.7, 18.3, 18.2, 17.6, 17.4, 13.2, 12.9. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{37}H_{42}NaO_6S$ 637.2594; found 637.2594.

Preparation of acceptor 5



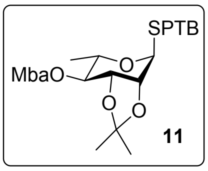
S-2-[(Propan-2-yl)sulfanyl]benzyl 2,3-*O*-isopropylidene-*α*-L-rhamnopyranoside (10)



10

To a solution of compound **9**[2] (1.75 g, 3.72 mmol) in MeOH (7.4 mL) was added CH_3ONa (100.0 mg, 1.86 mmol), the mixture was stirred at room temperature for 2 h. The solution was neutralized with Amberlyst 15, (dry) ion-exchange resin. The mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in 2,2-dimethoxypropane (7.4 mL), and then CSA (36.0 mg, 0.37 mmol) was added. The mixture was stirred for 1 h at room temperature and quenched with Et_3N. Then the mixture was concentrated under reduced pressure and purified by chromatography to give **10** (1.35 g, 94%, two steps). White solid. m.p. 69-71 °C. R_f = 0.48 (petroleum ether-EtOAc 4:1). $[\alpha]_D^{25}$ = -324.63 (c, 1.64 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.11 (4H, m, Ar-H), 5.36 (1H, s, H-1), 4.09 (1H, d, *J* = 5.2 Hz, H-2), 4.06-3.96 (3H, m, H-3, H-4, PhC*H*), 3.86 (1H, d, *J* = 13.2 Hz, PhC*H*), 3.45-3.38 (2H, m, H-5, $C\mathit{H}(\mathit{C}H_3)_2$), 2.35 (1H, m, OH), 1.49 (3H, s, isopropylidene CH_3), 1.32-1.26 (12H, m, $4 \times CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 135.7, 132.5, 130.4, 128.0, 126.8, 109.8, 79.3, 78.6, 76.7, 75.7, 66.2, 38.8, 33.0, 28.4, 26.5, 23.5, 23.2, 17.5. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{28}NaO_4S_2$ 407.1321; found 407.1327.

S-2-[(Propan-2-yl)sulfanyl]benzyl 2,3-*O*-isopropylidene-4-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (11)

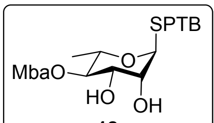


11

To a solution of **10** (1.00 g, 2.87 mmol) in CH_2Cl_2 (9.5 mL) was added (*S*)-(+)-2-methylbutyric acid (MbaOH, 469.0 μL, 4.30 mmol), DMAP (0.52 g, 4.30 mmol) and 3-(3-dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDCI, 0.82 g, 4.30 mmol) , the resulting solution was stirred at room temperature for 3 h then diluted with water, extracted with EtOAc. The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*.

The residue was purified by silica gel column chromatography to give compound **11** (1.07g, 80%). White solid. m.p. 53-56 °C. R_f = 0.30 (petroleum ether-EtOAc 30:1). $[\alpha]_D^{25}$ = -239.73 (c, 2.2 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.12 (4H, m, Ar-H), 5.39 (1H, s, H-1), 4.92 (1H, m, H-4), 4.16-4.07 (3H, m, H-2, H-3, H-5), 3.98 (1H, d, J = 13.2 Hz, PhC*H*), 3.86 (1H, d, J = 13.2 Hz, PhC*H*), 3.42 (1H, m, C*H*(*C*H_3)$_2$), 2.39 (1H, m, COC*H*(CH_3)), 1.74-1.63 (1H, m, COCH(CH_3)C*H*$_2$), 1.52 (3H, s, isopropylidene CH_3), 1.50-1.45 (1H, m, COCH(CH_3)C*H*$_2$), 1.32 (3H, d, J= 6.8 Hz, CH_3), 1.28-1.25 (6H, m, 2 × CH_3), 1.15 (6H, t, J= 6.8 Hz, 2 × CH_3), 0.91 (3H, t, J = 7.2 Hz, CH_3).^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 138.7, 135.7, 132.5, 130.5, 128.1, 126.8, 110.0, 79.4, 76.7, 75.9, 74.6, 65.0, 41.3, 38.8, 33.1, 27.9, 26.9, 26.8, 23.5, 23.2, 17.2, 16.7, 11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{24}H_{36}NaO_5S_2$ 491.1896; found 491.1893.

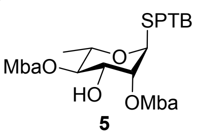
***S*-2-[(Propan-2-yl)sulfanyl]benzyl 4-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (12)**



12

A solution of compound **11** (1.00 g, 2.13 mmol) in AcOH/H_2O (7.0 mL, 7:3, v:v) was stirred at 70 °C for 6 h, then diluted with water, extracted with EtOAc. The organic layer was washed with saturated $NaHCO_3$, brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was subjected to flash column chromatography to afford **12** (0.87 g, 96%). White solid. m.p. 96-100 °C. R_f = 0.24 (petroleum ether-EtOAc 2:1). $[\alpha]_D^{25}$ = -243.23 (c, 1.7 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.13 (4H, m, Ar-H), 5.20 (1H, s, H-1), 4.79 (1H, t, J= 9.6, 9.2 Hz, H-4), 4.22 (1H, m, H-3), 3.99 (1H, d, J= 12.8 Hz, PhC*H*), 3.94 (1H, br s, H-2), 3.88 (1H, d, J= 12.8 Hz, PhC*H*), 3.83-3.78 (1H, m, H-5), 3.40 (1H, m, C*H*(*C*H_3)$_2$), 3.08 (1H, d, J= 6.4 Hz, OH), 2.79 (1H, m, OH), 2.41 (1H, m, COC*H*(CH_3)), 1.71-1.62 (1H, m, COCH(CH_3)C*H*$_2$), 1.53-1.44 (1H, m, COCH(CH_3)C*H*$_2$), 1.30 (3H, d, J= 6.8 Hz, CH_3), 1.27 (3H, d, J= 6.4 Hz, CH_3), 1.20 (3H, d, J= 6.4 Hz, CH_3), 1.15 (3H, d, J= 6.8 Hz, CH_3), 0.91 (3H, t, J= 7.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 138.9, 135.6, 132.7, 130.5, 128.1, 126.9, 83.2, 75.9, 72.3, 71.3, 66.4, 41.5, 38.9, 33.4, 26.9, 23.5, 23.2, 17.6, 16.8, 11.8. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{21}H_{32}NaO_5S_2$ 451.1583; found 451.1569.

***S*-2-[(Propan-2-yl)sulfanyl]benzyl 2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (5)**

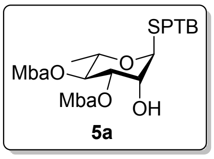


5

To a solution of **12** (0.80 g, 1.87 mmol) in CH_2Cl_2 (18.7 mL) was added (*S*)-(+)-2-methylbutyric acid (MbaOH, 225.0 μL, 2.06 mmol), DMAP (0.23 g, 1.87 mmol) and 3-(3-dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDCI, 0.54 g, 2.82 mmol) , the resulting solution was stirred at room temperature for 3 h then diluted with water, extracted with EtOAc. The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give compound **5** (0.40 g, 42%). Colorless syrup. R_f= 0.25 (petroleum ether-EtOAc 10:1). $[\alpha]_D^{25}$ = -113.38 (c, 2.1 in $CHCl_3$). ^1H

NMR (400 MHz, CDCl$_3$) δ 7.43-7.13 (4H, m, Ar-H), 5.21(1H, s, H-1), 5.13 (1H, d, *J* = 3.6 Hz, H-2), 4.85 (1H, t, *J* = 9.6 Hz, H-4), 4.20 (1H, m, H-5), 4.03 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.97 (1H, dd, *J* = 10.4, 3.2 Hz, H-3), 3.96 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.39 (1H, m, C*H*(CH$_3$)$_2$), 2.49-2.38 (2H, m, COC*H*(CH$_3$)), 2.15 (1H, d, *J* = 7.6 Hz, OH), 1.73-1.65 (2H, m, COCH(CH$_3$)C*H*$_2$), 1.53-1.44 (2H, m, COCH(CH$_3$)C*H*$_2$), 1.28 (6H, t, *J* = 6.4 Hz, 2 × CH$_3$), 1.18-1.14 (9H, m, 3 × CH$_3$), 0.91 (6H, t, *J* = 7.6 Hz, 2 × CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 177.7, 176.2, 139.0, 135.6, 132.9, 130.4, 128.1, 127.1, 82.2, 75.0, 73.9, 69.9, 66.9, 41.4, 41.2, 39.0, 34.1, 26.9, 26.9, 23.4, 23.3, 17.5, 16.8, 16.6, 11.7, 11.7. HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ calcd for $C_{26}H_{40}NaO_6S_2$ 535.2159; found 535.2138.

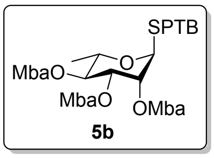
***S*-2-[(Propan-2-yl)sulfanyl]benzyl 3,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (5a)**



5a

5a (0.24 g, 25%). Colorless syrup. R_f = 0.48 (petroleum ether-EtOAc 4:1). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43-7.13 (4H, m, Ar-H), 5.19-5.12 (3H, m, H-1, H-3, H-4), 4.26 (1H, m, H-5), 4.07 (1H, br s, H-2), 4.01 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.90 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.40 (1H, m, C*H*(CH$_3$)$_2$), 2.37-2.25 (2H, m, COC*H*(CH$_3$)), 2.23 (1H, d, *J* = 4.0 Hz, OH), 1.68-1.57 (2H, m, COCH(CH$_3$)C*H*$_2$), 1.44-1.33 (2H, m, COCH(CH$_3$)C*H*$_2$), 1.30 (3H, d, *J* = 6.8 Hz, CH$_3$), 1.27 (3H, d, *J* = 6.4 Hz, CH$_3$), 1.18 (3H, d, *J* = 6.4 Hz, CH$_3$), 1.11 (6H, t, *J* = 6.4 Hz, 2 × CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 175.8, 175.5, 138.9, 135.7, 132.8, 130.5, 128.0, 126.9, 83.4, 71.9, 70.9, 70.9, 67.3, 41.3, 41.2, 38.9, 33.4, 26.6, 26.5, 23.5, 23.2, 17.6, 16.8, 16.7, 11.9, 11.8.

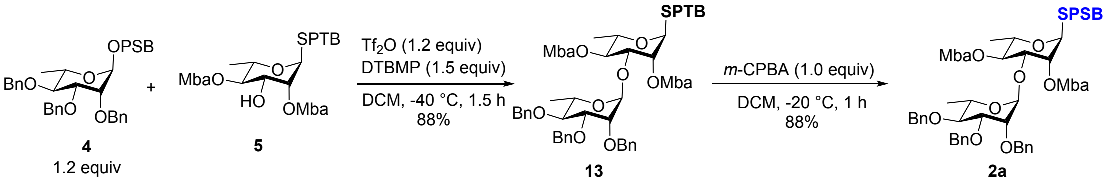
***S*-2-[(Propan-2-yl)sulfanyl]benzyl 2,3,4-tri-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (5b)**



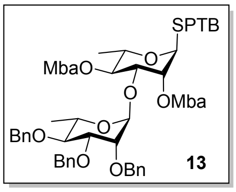
5b

5b (0.19 g, 17%). Colorless syrup. R_f = 0.65 (petroleum ether-EtOAc 10:1). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43-7.14 (4H, m, Ar-H), 5.32 (1H, br s, H-1), 5.25 (1H, dd, *J* = 10.0, 3.2 Hz, H-3), 5.14 (1H, t, *J* = 9.6 Hz, H-4), 5.12 (1H, s, H-2), 4.25 (1H, m, H-5), 4.04 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.94 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.39 (1H, m, C*H*(CH$_3$)$_2$), 2.49-2.40 (1H, m, COC*H*(CH$_3$)), 2.34-2.25 (1H, m, COC*H*(CH$_3$)), 2.23-2.14 (1H, m, COC*H*(CH$_3$)), 1.76-1.47 (4H, m, COCH(CH$_3$)C*H*$_2$), 1.42-1.31 (2H, m, COCH(CH$_3$)C*H*$_2$), 1.28 (6H, t, *J* = 6.8 Hz, 2 × CH$_3$), 1.17 (3H, d, *J* = 6.0 Hz, CH$_3$), 1.14 (3H, d, *J* = 7.2 Hz, CH$_3$), 1.11 (3H, d, *J* = 7.2 Hz, CH$_3$), 1.03 (3H, d, *J* = 7.2 Hz, CH$_3$), 0.93 (3H, t, *J* = 7.6, 7.2 Hz, CH$_3$), 0.87 (3H, t, *J* = 7.6, 7.2 Hz, CH$_3$), 0.80 (3H, t, *J* = 7.6, 7.2 Hz, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) δ 175.7, 175.6, 175.5, 138.9, 135.7, 133.0, 130.4, 128.1, 127.0, 82.2, 71.0, 71.0, 69.8, 67.5, 41.3, 41.2, 41.0, 39.0, 33.8, 26.9, 26.5, 23.4, 23.3, 17.6, 16.8, 16.6, 16.2, 11.9, 11.8.

Synthesis of disaccharide 2a

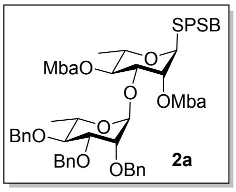


***S*-2-[(Propan-2-yl)sulfanyl]benzyl 3-*O*-(2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl)-2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (13)**



A solution of glycosyl donor **4** (28.7 mg, 0.046 mmol), acceptor **5** (20.0 mg, 0.039 mmol) and DTBMP (12.0 mg, 0.058 mmol) in CH_2Cl_2 (0.78 mL) in the presence of 4 Å MS (100 wt%) was stirred at -40 °C for 10 min, then Tf_2O (8.0 µL, 0.046 mmol) was added. The solution was stirred at -40 °C for 1.5 h and then quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **13** (32.0 mg, 88%). Yellow syrup. R_f = 0.37 (petroleum ether-EtOAc 13:1). $[\alpha]_D^{25}$ = -63.5 (c, 1.43 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.15 (19H, m, Ar-H), 5.18 (2H, m), 5.08 (1H, t, *J* = 9.6 Hz, 10.0 Hz), 4.86-4.82 (2H, m), 4.71 (1H, d, *J* = 12.4 Hz, PhC*H*), 4.61-4.50 (4H, m, 4 × PhC*H*), 4.14 (1H, m), 4.03 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.99 (1H, m), 3.96 (1H, d, *J* = 12.4 Hz, PhC*H*), 3.70-3.66 (2H, m), 3.57-3.49 (2H, m), 3.39 (1H, m), 2.42 (1H, m), 2.20 (1H, m), 1.75-1.61 (2H, m), 1.47-1.40 (1H, m), 1.37-1.32 (1H, m), 1.29 (3H, d, *J* = 6.8 Hz, CH_3), 1.28 (3H, d, *J* = 6.4 Hz, CH_3), 1.21 (3H, d, *J* = 5.6 Hz, CH_3), 1.12 (6H, d, *J* = 7.2 Hz, 2 × CH_3), 1.06 (3H, d, *J* = 7.2 Hz, CH_3), 0.88 (3H, d, *J* = 7.2 Hz, CH_3), 0.80 (3H, d, *J* = 7.2 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 175.4, ,138.9, 138.8, 138.5, 138.4, 135.4, 132.7, 130.2, 128.3, 128.1, 127.9, 127.5, 127.5, 127.5, 127.5, 127.5, 127.3, 126.9, 100.8, 82.1, 80.1, 80.0, 75.6, 75.5, 74.7, 73.1, 72.9, 72.6, 72.4, 69.0, 67.4, 41.2, 41.1, 38.9, 34.0, 26.6, 26.4, 23.2, 23.1, 17.8, 17.5, 16.7, 16.6, 11.8,11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{53}H_{68}NaO_{10}S_2$ 951.4146; found 951.4166.

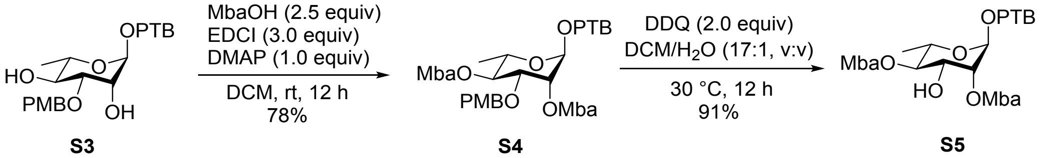
***S*-2-[(Propan-2-yl)sulfinyl]benzyl 3-*O*-(2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl)-2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (2a)**



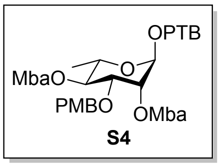
A solution of 3-Chloroperoxybenzoic acid (*m*-CPBA, 52.0 mg, 0.22 mmol) in DCM (2.0 mL) was slowly injected into the solution of **13** (210.0 mg, 0.22 mmol) in DCM (2.5 mL) at -20 °C. The mixture was stirred at -20 °C for 1 h, diluted with EtOAc and then poured into 10% $Na_2S_2O_3$ aqueous solution. The organic layer was washed with saturated $NaHCO_3$, brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography to afford **2a** (189.0 mg, 88%). Colorless syrup. R_f = 0.42 (petroleum ether-EtOAc 2:1). Analysis by ^{1}H NMR indicated a mixture of sulfoxide isomers (*R* and *S*, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.26 (38H, m, Ar-H), 5.30-5.06 (6H, m), 4.92-4.69 (5H, m), 4.62-4.46 (8H, m), 4.20-3.86 (8H, m), 3.69-3.41 (8H, m), 3.02

(1H, m), 2.94 (1H, m), 2.47-2.37 (2H, m), 2.28-2.18 (2H, m), 1.74-1.58 (4H, m), 1.48-1.34 (4H, m), 1.32-1.27 (8H, m), 1.24-1.06 (28H, m), 0.90-0.78 (12H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 175.9, 175.4, 175.3, 141.4, 141.1, 138.8, 138.8, 138.4, 138.3, 138.3, 135.1, 135.0, 131.1, 131.1, 130.7, 130.5, 128.5, 128.5, 128.4, 128.3, 128.2, 128.0, 128.0, 127.6, 127.5, 127.5, 127.4, 125.9, 125.6, 101.0, 82.5, 81.4, 80.1, 80.0, 75.7, 75.6, 75.4, 75.3, 74.7, 74.7, 72.9, 72.9, 72.4, 72.2, 72.1, 69.0, 67.8, 54.2, 54.0, 41.2, 41.2, 41.1, 41.1, 31.5, 31.0, 26.6, 26.5, 26.4, 17.8, 17.6, 17.6, 17.3, 16.7, 16.6, 16.5, 13.4, 13.1, 11.9, 11.7, 11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{53}H_{68}NaO_{11}S_2$ 967.4095; found 967.4090.

Preparation of acceptor S5



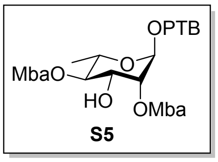
O-2-[(Propan-2-yl)sulfanyl]benzyl 2,4-di-*O*-[2(*S*)-methylbutyryl]-3-*O*-(*p*-methoxybenzyl)-*α*-L-rhamnopyranoside (S4)



S4

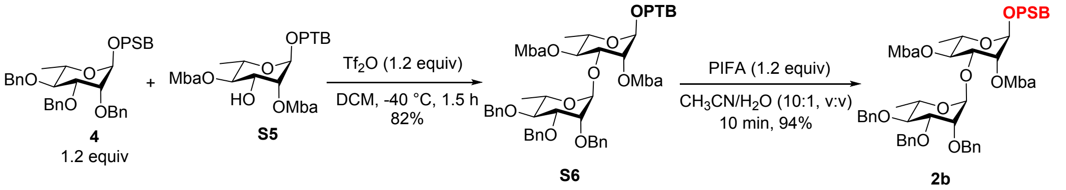
To a solution of **S3**[3] (235.0 mg, 0.52 mmol) in CH_2Cl_2 (5.2 mL) was added (*S*)-(+)-2-methylbutyric acid (MbaOH, 143.0 µL, 1.31 mmol), DMAP (64.0 mg, 0.52 mmol) and 3-(3-dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDCI, 301.0 mg, 1.57 mmol), the resulting solution was stirred at room temperature for 12 h then diluted with water, extracted with EtOAc. The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give compound **S4** (251.0 mg, 78%). Colorless syrup. $R_f = 0.41$ (petroleum ether-EtOAc 10:1). $[\alpha]_D^{25} = -13.79$ (c, 1.4 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-6.78 (8H, m, Ar-H), 5.41(1H, br s, H-2), 5.05 (1H, t, *J*= 9.6, 10.0 Hz, H-4), 4.87 (2H, m, H-1, H-3), 4.60 (1H, d, *J*= 12.0 Hz, PhC*H*), 4.53 (1H, d, *J*= 11.2 Hz, PhC*H*), 4.30 (1H, d, *J*= 10.8 Hz, PhC*H*), 3.91-3.85 (2H, m, H-5, PhC*H*), 3.76 (3H, s, OCH_3), 3.38-3.31 (1H, m, $CH(CH_3)_2$), 2.51-2.42 (1H, m, $COCH(CH_3)$), 2.33-2.26 (1H, m, $COCH(CH_3)$), 1.71-1.61 (2H, m, $COCH(CH_3)CH_2$), 1.51-1.34 (2H, m, $COCH(CH_3)CH_2$), 1.26 (6H, d, *J*= 6.8 Hz, 2 × CH_3), 1.17 (3H, d, *J*= 6.4 Hz, CH_3), 1.13 (3H, d, *J*= 5.2 Hz, CH_3), 1.09 (3H, d, *J*= 7.2 Hz, CH_3), 0.88-0.83 (6H, m, 2 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 175.1, 159.0, 138.6, 134.8, 132.6, 130.0, 129.9, 129.3, 128.7, 128.3, 127.0, 113.6, 113.5, 97.7, 74.6, 72.0, 70.8, 68.0, 67.8, 67.0, 55.2, 41.3, 41.0, 38.7, 26.7, 26.6, 23.2, 23.1, 17.6, 16.7, 16.5, 11.8, 11.4. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{34}H_{48}NaO_8S$ 639.2962; found 639.2952.

O-2-[(Propan-2-yl)sulfanyl]benzyl 2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (S5)

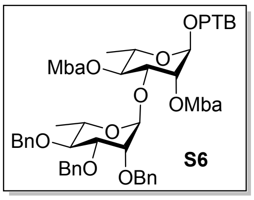


To a solution of **S4** (223.0 mg, 0.36 mmol) in CH_2Cl_2–H_2O (17:1, v/v, 36.0 mL) was added DDQ (164.0 mg, 0.72 mmol), the reaction mixture was stirred at room temperature for 12 h and then quenched with aqueous $NaHCO_3$, extracted with EtOAc. The combined organic layer was washed with aqueous $NaHCO_3$, brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give compound **S5** (163.0 mg, 91%). Colorless syrup. R_f = 0.40 (petroleum ether-EtOAc 7:1). $[\alpha]_D^{25}$ = -35.47 (c, 0.95 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.25 (4H, m, Ar-H), 5.13 (1H, d, J= 3.2 Hz, H-2), 4.91 (1H, s, H-1), 4.90-4.83 (2H, m, H-4, PhC*H*), 4.61 (1H, d, J= 12.0 Hz, PhC*H*), 4.08 (1H, m, H-3), 3.95 (1H, m, H-5), 3.39-3.29 (1H, m, C*H*(CH_3)$_2$), 2.52-2.36 (2H, m, COC*H*(CH_3)), 2.08 (1H, d, J = 8.4 Hz, OH), 1.76-1.63 (2H, m, COCH(CH_3)C*H*$_2$), 1.54-1.44 (2H, m, COCH(CH_3)C*H*$_2$), 1.26 (6H, d, J = 6.4 Hz, 2 × CH_3), 1.19 (3H, d, J= 6.0 Hz, CH_3), 1.16 (6H, t, J= 7.2 Hz, 2 × CH_3), 0.94-0.98 (6H, m, 2 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 176.4, 138.7, 134.9, 132.8, 128.9, 128.5, 127.3, 97.4, 74.7, 72.6, 69.2, 68.2, 66.5, 41.4, 41.3, 38.9, 26.9, 26.9, 23.3, 23.3, 17.6, 16.8, 16.8, 11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{26}H_{40}NaO_7S$ 519.2387; found 519.2362.

Synthesis of disaccharide 2b



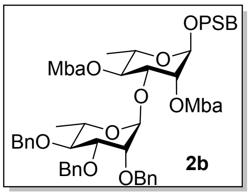
O-2-[(Propan-2-yl)sulfanyl]benzyl 3-*O*-(2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl)-2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (S6)



A solution of glycosyl donor **4** (22.3 mg, 0.036 mmol) and acceptor **S5** (15.0 mg, 0.030 mmol) in CH_2Cl_2 (0.6 mL) in the presence of 4 Å MS (100 wt%) was stirred at -40 °C for 10 min, then Tf_2O (6.1 μL, 0.036 mmol) was added. The solution was stirred at -40 °C for 1.5 h and then quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **S6** (22.5 mg, 82%). Colorless syrup. R_f = 0.39 (petroleum ether-EtOAc 13:1). $[\alpha]_D^{25}$ = -29.21 (c, 1.90 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.20 (19H, m, Ar-H), 5.15 (1H, br s), 5.05 (1H, t, J= 9.6 Hz, 10.0 Hz), 4.88-4.81 (4H, m), 4.69 (1H, d, J= 12.4 Hz, PhC*H*), 5.60-4.51 (5H, m), 4.09 (1H, dd, J= 10.0, 2.8 Hz), 3.84 (1H, m), 3.70-3.66 (2H, m), 3.59-3.49 (2H, m), 3.31 (1H, m), 2.45-2.36 (1H, m, COC*H*(CH_3)), 2.19-2.14 (1H, m, COC*H*(CH_3)), 1.71-1.60 (2H, m, COCH(CH_3)C*H*$_2$), 1.46-1.29 (2H, m, COCH(CH_3)C*H*$_2$), 1.23 (6H, d, J = 6.4 Hz, 2 × CH_3), 1.21 (3H, d, J= 6.0 Hz, CH_3), 1.11 (6H, t, J= 6.0 Hz, 2 × CH_3), 1.02 (3H, d, J= 7.2 Hz, CH_3), 0.86 (3H, t, J = 7.2 Hz, CH_3), 0.77 (3H, t, J = 7.2 Hz, CH_3). ^{13}C

NMR (100 MHz, $CDCl_3$) δ 176.2, 175.6, 139.1, 138.9, 138.7, 138.6, 134.8, 133.0, 128.9, 128.5, 128.5, 128.4, 128.3, 127.7, 127.7, 127.6, 127.5, 127.3, 101.0, 97.1, 80.4, 80.3, 75.7, 75.4, 74.9, 73.1, 72.6, 72.5, 72.0, 69.1, 68.1, 67.1, 41.4, 41.3, 38.9, 26.8, 26.6, 23.3, 23.3, 18.1, 17.8, 16.9, 16.8, 12.0, 11.9. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{53}H_{68}NaO_{11}S$ 935.4375; found 935.4374.

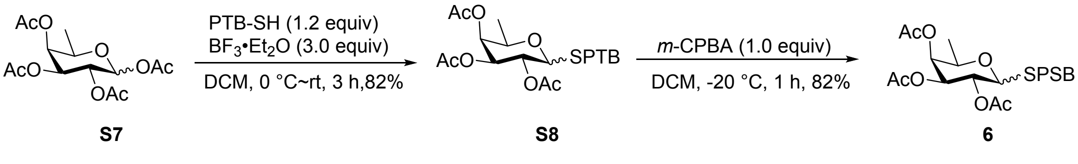
***O*-2-[(Propan-2-yl)sulfinyl]benzyl 3-*O*-(2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl) -2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranoside (2b)**



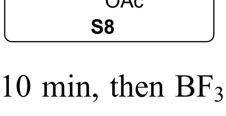
2b

To a solution of **S6** (24.0 mg, 0.026 mmol) in CH_3CN/H_2O (0.5 mL, 10:1, v:v) was added PIFA (13.6 mg, 0.32 mmol), the reaction mixture was stirred at room temperature for 10 min, then diluted with water, extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was subjected to flash column chromatography to afford **2b** (23.0 mg, 94%). Colorless syrup. R_f = 0.24 (petroleum ether-EtOAc 2:1). Analysis by ^1H NMR indicated a mixture of sulfoxide isomers (*R* and *S*, 1:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.93-7.26 (38H, m, Ar-H), 5.12-5.05 (4H, m), 4.88-4.70 (10H, m), 4.62-4.48 (10H, m), 4.04 (1H, dd, *J*= 10.0, 3.2, Hz), 3.98 (1H, dd, *J*= 10.0, 3.2 Hz), 3.82 (1H, m), 3.75-3.67 (5H, m), 3.53 (4H, m), 2.95-2.86 (2H, m), 2.48-2.38 (2H, m), 2.23-2.15 (2H, m), 1.75-1.56 (4H, m), 1.48-1.40 (2H, m), 1.34-1.31 (7H, m), 1.22-1.14 (22H, m), 1.11-1.04 (9H, m), 0.91-0.76 (12H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 176.1, 175.5, 175.5, 142.2, 141.9, 139.0, 139.0, 138.6, 138.6, 138.5, 134.7, 134.2, 131.2, 131.2, 130.3, 129.8, 129.4, 129.4, 128.5, 128.3, 127.8, 127.8, 127.7, 127.7, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 125.9, 125.6, 101.3, 101.3, 97.3, 96.4, 80.2, 80.2, 75.7, 75.6, 75.5, 75.1, 74.9, 74.9, 73.2, 73.1, 72.6, 72.6, 72.2, 72.0, 71.8, 71.7, 69.2, 69.1, 67.5, 67.4, 66.0, 65.9, 54.4, 54.1, 41.4, 41.3, 41.3, 41.2, 26.7, 26.6, 18.1, 17.9, 17.9, 17.8, 17.5, 16.9, 16.9, 16.8, 13.3, 12.0, 12.0, 11.9, 11.9. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{53}H_{68}NaO_{12}S$ 951.4324; found 951.4338.

4. Synthesis of macrolacrone disaccharide 3



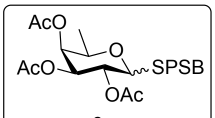
***S*-2-[(Propan-2-yl)sulfanyl]benzyl 2,3,4-tri-*O*-acetyl-D-fucopyranoside (S8)**



S8

A solution of compound **S7**[4] (100.0 mg, 0.30 mmol) and 4 Å MS (100 wt%) in CH_2Cl_2 (0.3 mL) was stirred at 0 °C , then 2-(2-propylthio)benzyl thiol (PTB-SH, 71.4 mg, 0.36 mmol) in CH_2Cl_2 (0.3 mL) was added. The resulting mixture was stirred at 0 °C for 10 min, then $BF_3{\cdot}Et_2O$ (244.0 μL, 0.90 mmol) was added. The reaction mixture was stirred at room temperature for 3 h and then quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **S8** (115.0 mg, 82%, β/α = 3.8:1). Analytical data for ***β* anomer of S8**. Yellow syrup. R_f = 0.55 (petroleum ether-EtOAc 3:1). $[\alpha]_D^{25}$ = -80.03 (c, 3.1 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.43-7.15 (4H, m, Ar-H), 5.22 (1H, d, *J* = 3.6 Hz, H-4), 5.19 (1H, t, *J* = 10.0 Hz, H-2), 4.95 (1H, dd, *J* = 10.0, 3.6 Hz, H-3), 4.33 (1H, d, *J* = 10.0 Hz, H-1), 4.16 (1H, d, *J* = 13.2 Hz, PhC*H*), 4.01 (1H, d, *J* = 13.2 Hz, PhC*H*), 3.73 (1H, m, H-5), 3.35 (1H, m, C*H*(CH_3)$_2$), 2.15 (3H, s, $COCH_3$), 1.96 (3H, s, $COCH_3$), 1.93 (3H, s, $COCH_3$), 1.27 (3H, d, *J* = 5.6 Hz, CH_3), 1.25 (3H, d, *J* = 5.6 Hz, CH_3), 1.19 (3H, d, *J* = 6.4 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.9, 170.3, 169.9, 139.5, 135.6, 133.2, 130.5, 127.9, 127.1, 83.0, 73.3, 72.5, 70.7, 67.5, 39.1, 32.9, 23.4, 23.3, 21.0, 20.9, 20.8, 16.5. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{22}H_{30}NaO_7S_2$ 493.1325; found 493.1314. Analytical data for ***α* anomer of S8**. Yellow syrup. R_f = 0.56 (petroleum ether-EtOAc 3:1). $[\alpha]_D^{25}$ = 217.3 (c, 3.1 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.42-7.12 (4H, m, Ar-H), 5.62 (1H, d, *J* = 5.2 Hz), 5.26-5.16 (3H, m), 4.47 (1H, m, H-5), 3.97 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.83 (1H, d, *J* = 12.8 Hz, PhC*H*), 3.37 (1H, m, C*H*(CH_3)$_2$), 2.13 (3H, s, $COCH_3$), 1.98 (3H, s, $COCH_3$), 1.94 (3H, s, $COCH_3$), 1.28 (3H, d, *J* = 6.4 Hz, CH_3), 1.26 (3H, d, *J* = 6.4 Hz, CH_3), 1.08 (3H, d, *J* = 6.4 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.8, 170.3, 170.1, 139.3, 135.6, 132.9, 130.4, 128.0, 127.0, 82.3, 71.2, 68.9, 68.1, 65.1, 39.0, 33.1, 23.4, 23.3, 21.0, 20.9, 20.8, 16.0. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{22}H_{30}NaO_7S_2$ 493.1325; found 493.1318.

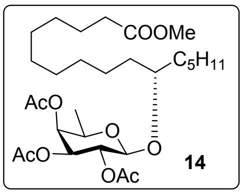
S-2-[(Propan-2-yl)sulfinyl]benzyl 2,3,4-tri-*O*-acetyl-D-fucopyranoside (6)



6

A solution of 3-Chloroperoxybenzoic acid (*m*-CPBA, 552.0 mg, 2.40 mmol) in DCM (12.0 mL) was slowly injected into the solution of **S8** (1.13 g, 2.40 mmol) in DCM (12.0 mL) at -20 °C. The mixture was stirred at -20 °C for 1 h, diluted with EtOAc and then poured into 10% $Na_2S_2O_3$ aqueous solution. The organic layer was washed with saturated $NaHCO_3$, brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography to afford **6** (0.95 g, 82%). White foam. R_f = 0.41 (petroleum ether-EtOAc 1:1). Analysis by ^1H NMR indicated mixture of sulfoxide and α/β anomers. ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.85-7.33 (6.8H, m, Ar-H), 5.26-5.18 (3.4H, m), 5.02-4.95 (1.7H, m), 4.37 (1H, d, *J* = 10.0 Hz), 4.31 (1H, d, *J* = 10.0 Hz), 4.15 (1H, d, *J* = 13.6 Hz, PhC*H*), 4.06 (0.7H, d, *J* = 12.0 Hz, PhC*H*), 3.99 (0.7H, d, *J* = 12.0 Hz, PhC*H*), 3.86 (1H, d, *J* = 13.2 Hz, PhC*H*), 3.78 (1.7H, m), 3.07 (0.7H, m, C*H*(CH_3)$_2$), 2.98 (1H, m, C*H*(CH_3)$_2$), 2.16 (3H, s, $COCH_3$), 2.16 (2.1H, s, $COCH_3$), 2.06 (2.1H, s, $COCH_3$), 1.99 (3H, s, $COCH_3$), 1.96 (2.1H, s, $COCH_3$), 1.94 (3H, s, $COCH_3$), 1.32-1.12 (15.5H, m, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.8, 170.8, 170.3, 170.3, 170.1, 169.9, 141.6, 135.5, 131.2, 131.1, 131.0, 130.9, 128.6, 125.9, 125.6, 83.0, 82.1, 73.6, 73.5, 72.3, 72.3, 70.5, 67.4, 67.0, 54.1, 53.8, 29.5, 29.2, 21.0, 20.9, 20.9, 20.8, 20.8, 17.6, 17.4, 16.6, 13.4, 13.2. HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{31}O_8S_2$ 487.1455; found 487.1456.

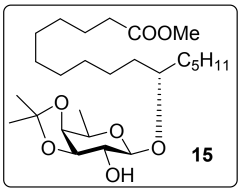
1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2,3,4-tri-*O*-acetyl-*β*-D-fucopyranoside (14)



14

A solution of glycosyl donor **6** (61.0 mg, 0.126 mmol), acceptor **8**[5] (30.0 mg, 0.105 mmol) and DTBMP (32.2 mg, 0.157 mmol) in CH_2Cl_2 (1.0 mL) in the presence of 4 Å MS (100 wt%) was stirred at -20 °C for 10 min, then Tf_2O (21.6 µL, 0.126 mmol) was added. The solution was stirred at -20 °C for 1.5 h and then quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **14** (48.0 mg, 83%). Yellow oil. R_f = 0.32 (petroleum ether-EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (1H, d, J = 3.2 Hz, H-4), 5.13 (1H, dd, J = 10.4, 8.0 Hz, H-2), 4.98 (1H, dd, J = 10.4, 3.2 Hz, H-3), 4.41 (1H, d, J = 8.0 Hz, H-1), 3.73 (1H, m, H-5), 3.64 (3H, s, OCH_3), 3.50 (1H, m, jia-11), 2.31 (2H, t, J = 7.6 Hz, $COCH_2CH_2$), 2.14 (3H, s, $COCH_3$), 2.00 (3H, s, $COCH_3$), 1.95 (3H, s, $COCH_3$), 1.61-1.16 (24H, m), 1.17 (3H, d, J = 6.4 Hz, CH_3), 0.83 (3H, t, J = 7.2 Hz, CH_3). Analytical data for **14** were essentially the same as reported in the literature.[6]

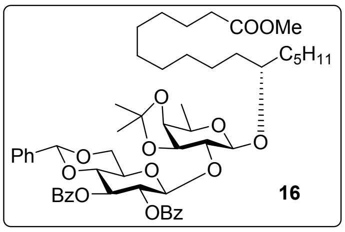
1-(Methoxycarbonyl)pentadec-10(*S*)-yl 3,4-*O*-isopropylidene-*β*-D-fucopyranoside (15)



15

To a solution of compound **14** (187.0 mg, 0.33 mmol) in MeOH (3.3 mL) was added CH_3ONa (7.1 mg, 0.13 mmol), the mixture was stirred for 2 h at room temperature. The solution was neutralized with Amberlyst 15(H). The mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in 2,2-dimethoxypropane (3.3 mL), and CSA (7.7 mg, 0.033 mmol) was added. The mixture was stirred for 1 h at room temperature and quenched with Et_3N. Then the mixture was concentrated under reduced pressure and purified by chromatography to give **15** (129.0 mg, 82%, two steps). Yellow oil. R_f = 0.30 (petroleum ether-EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (1H, d, J = 8.4 Hz), 4.02-3.96 (2H, m), 3.81 (1H, m), 3.64 (3H, s, OCH_3), 3.57 (1H, m), 3.48 (1H, t, J = 7.6 Hz), 2.17 (2H, t, J = 7.6 Hz, $COCH_2CH_2$), 1.51 (3H, s, CH_3), 1.37 (3H, d, J = 6.4 Hz, CH_3), 1.33 (3H, s, CH_3), 1.63-1.24 (24 H, m), 0.86 (3H, t, J = 6.4 Hz, CH_3). Analytical data for **15** were essentially the same as reported in the literature.[6]

1-(Methoxycarbonyl)pentadec-10(*S*)-yl 2-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-3,4-*O*-isopropylidene-*β*-D-fucopyranoside (16)

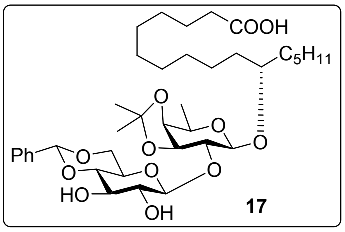


16

A solution of glycosyl donor **7**[7] (183.2 mg, 0.29 mmol), acceptor **15** (115 mg, 0.24 mmol) and DTBMP (74.9 mg, 0.36 mmol) in CH_2Cl_2 (4.8 mL) in the presence of 4 Å MS (100 wt%) was stirred at -20 °C for 10 min, then Tf_2O (50.0 µL, 0.29 mmol) was added. The solution was stirred at -20 °C for 1.5 h then quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **16** (215.0 mg, 95%). Colorless syrup. R_f = 0.41

(petroleum ether-EtOAc 5:1). $[\alpha]_D^{25}$ = 18.77 (c, 1.22 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.00-7.28 (15H, m, Ar-H), 5.74 (1H, t, J= 9.2 Hz), 5.52 (1H, s), 5.42 (1H, t, J= 8.0 Hz), 5.18 (1H, d, J= 7.6 Hz, H''), 4.39 (1H, dd, J= 10.4, 5.2 Hz), 4.20 (1H, d, J= 8.0 Hz, H'), 3.95 (1H, t, J= 6.4 Hz), 3.92 (1H, m), 3.85 (1H, t, J= 10.0 Hz), 3.80 (1H, m), 3.70-3.64 (3H, m), 3.62 (3H, s, OCH_3), 3.55 (1H, m), 2.27 (2H, t, J= 7.2 Hz), 1.55-1.24 (31H, m), 1.14 (3H, s, CH_3), 0.87 (3H, t, J= 6.4 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 165.9, 165.3, 137.1, 133.2, 130.2, 130.0, 130.0, 129.8, 129.2, 128.5, 128.4, 128.4, 126.3, 109.8, 101.7, 101.1, 100.3, 80.6, 80.0, 79.3, 79.1, 76.5, 73.2, 72.6, 69.1, 68.6, 66.8, 51.6, 34.8, 34.3, 34.1, 32.2, 30.2, 30.0, 29.8, 29.6, 29.4, 27.7, 26.2, 25.4, 25.2, 24.9, 22.9, 16.8, 14.3. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{53}H_{70}NaO_{14}$ 953.4658; found 953.4641.

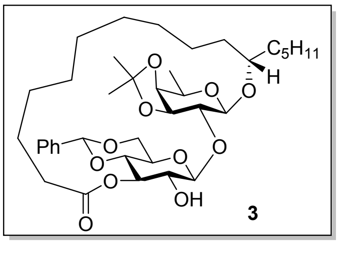
1-(Hydroxycarbonyl)pentadec-10(*S*)-yl 2-*O*-(4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-3,4-*O*-isopropylidene-*β*-D-fucopyranoside (17)



17

A mixture of **16** (209.0 mg, 0.22 mmol) and KOH (125.0 mg, 2.20 mmol) in $CH_3OH–H_2O$ (9:1, v/v, 4.5 mL) was stirred at 60 °C for 6 h. CH_3OH was removed under reduced pressure, then the residue was extracted with EtOAc. The combined organic extracts were washed with brine, dried with Na_2SO_4, and concentrated. The resulting residue was purified by column chromatography to afford **17** (144.0 mg, 91%). Amorphous solid. R_f = 0.41 (DCM:CH_3OH 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.48-7.33 (5H, m, Ar-H), 5.51 (1H, s), 4.63 (1H, d, J= 8.0 Hz), 4.30 (1H, dd, J= 10.4, 4.8 Hz), 4.26 (1H, d, J= 8.4 Hz), 4.13 (1H, dd, J= 6.8, 6.0 Hz), 3.99 (1H, d, J= 5.2 Hz), 3.85-3.42 (7H, m), 2.30 (2H, t, J= 7.2 Hz), 1.60-1.25 (35H, m), 0.87 (3H, t, J = 7.2 Hz, CH_3). Analytical data for **17** were essentially the same as reported in the literature.[6]

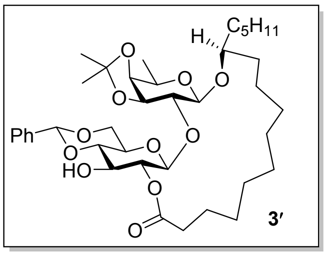
11(*S*)-Hydroxyhexadecanoic acid 11-*O*-4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-(1→3)-3,4-*O*-isopropylidene-*β*-D-fucopyranoside 1,3′-Lactone (3)



3

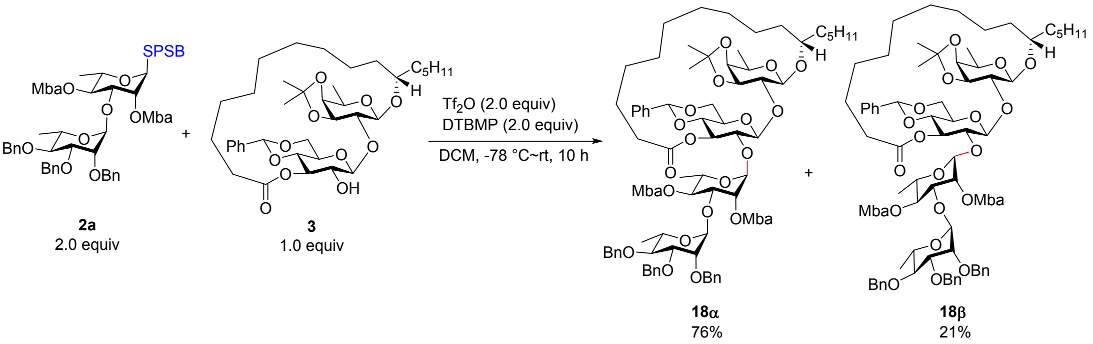
A solution of **17** (74.0 mg, 0.10 mmol), 2,2'-pyridyl disulfide (114.5 mg, 0.52 mmol), triphenylphosphine (136.6 mg, 0.52 mmol) in deoxygenated anhydrous toluene (2.8 mL) was stirred at 25 °C for 5 h. The mixture was diluted with deoxygenated anhydrous toluene (9.5 mL) and then was added dropwise to refluxing dry deoxygenated toluene (131.0 mL) over 10 h. The solution was refluxed under nitrogen for 3 days. After removal of toluene under reduced pressure, the residue was purified by column chromatography to afford **3** (53.5 mg, 74%). White solid. R_f = 0.21 (petroleum ether-EtOAc 4:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.33 (5H, m, Ar-H), 5.50 (1H, s), 5.20 (1H, t, J= 8.8 Hz), 5.04 (1H, d, J= 7.6 Hz, H-1'), 4.25 (1H, dd, J= 10.8, 5.2 Hz), 4.22 (1H, d, J= 8.4 Hz, H-1), 4.15 (1H, dd, J= 6.8, 6.4 Hz), 3.94 (1H, dd, J= 5.2, 1.6 Hz), 3.92 (1H, t, J= 8.0, 7.6 Hz), 4.84 (1H, t, J= 10.4 Hz), 3.78 (1H, dd, J= 7.2, 1.6 Hz), 3.74 (1H, t, J= 9.2 Hz), 3.57-3.48 (2H, m), 3.40 (1H, m), 2.78 (1H, br s), 2.51-2.46 (1H, m), 2.33-2.26 (2H, m), 1.66-1.47 (6H, m), 1.36-1.23 (26H, m), 0.86 (3H, t, *J* = 6.8 Hz, CH_3). Analytical data for **3** were essentially the same as reported in the literature.[6]

11(*S*)-Hydroxyhexadecanoic acid 11-*O*-4,6-*O*-benzylidene-*β*-D-glucopyranosyl)-(1→3)-3,4-*O*-isopropylidene-*β*-D-fucopyranoside 1,2′-Lactone (3')

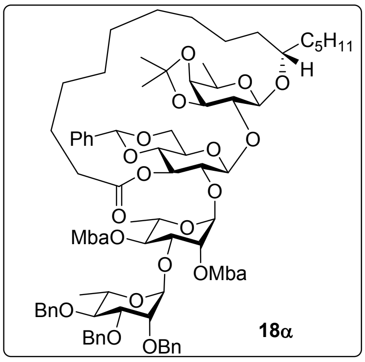


3' (9.9 mg, 14%). White solid. R_f = 0.25 (petroleum ether-EtOAc 4:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.49-7.33 (5H, m, Ar-H), 5.53 (1H, s), 5.21 (1H, d, *J* = 8.8 Hz), 4.89 (1H, t, *J* = 8.0 Hz), 4.26 (1H, dd, *J* = 10.8, 5.2 Hz), 4.14 (1H, d, *J* = 8.0 Hz), 4.05 (1H, m), 3.97 (1H, dd, *J* = 6.4, 1.6 Hz), 3.90-3.66 (5H, m), 3.46 (2H, m), 3.02 (1H, br s), 2.48-2.31 (2H, m), 1.62-1.51 (7H, m), 1.41-1.23 (26H, m), 0.88 (3H, t, *J* = 6.8 Hz, CH_3). Analytical data for **3'** were essentially the same as reported in the literature.[6]

5. Synthesis of tetrasaccharide 18α in a stepwise [2+2] coupling way

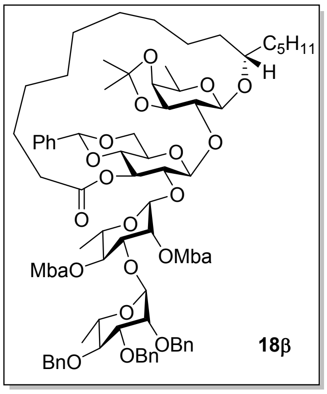


11(*S*)-Hydroxyhexadecanoic acid 11-*O*-2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl) -(1→3)-2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranosyl)-(1→2)-4,6-*O*-benzylidene-*β*-D-glucopyranosyl-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranoside 1,3′-Lactone (18α)



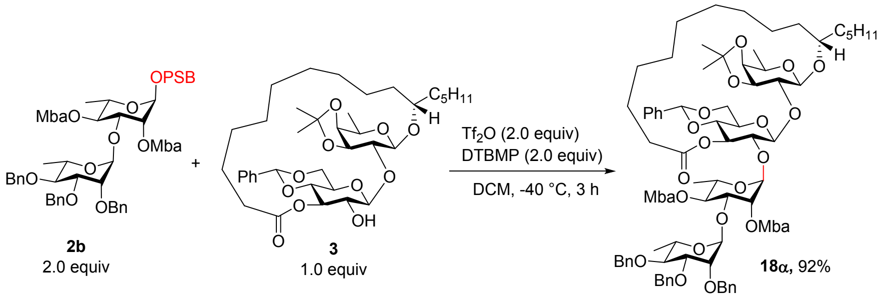
A solution of glycosyl donor **2a** (43.8 mg, 0.046 mmol), acceptor **3** (16.0 mg, 0.023 mmol) and DTBMP (9.5 mg, 0.046 mmol) in CH_2Cl_2 (0.46 mL) in the presence of 4 Å MS (100 wt%) was stirred at -78 °C for 10 min, then Tf_2O (7.9 μL, 0.046 mmol) was added. The reaction mixture was stirred for 10 h during which time it was gradually warmed to ambient temperature. The reaction mixture was quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **18α** (25.0 mg, 76%). White solid. m.p. 55-60 °C. R_f = 0.55 (petroleum ether-EtOAc 5:1). $[\alpha]_D^{19}$ = -13.36 (*c*, 1.1 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.44-7.22 (20H, m, Ar-H), 5.51 (1H, s), 5,31 (1H, dd, *J* = 9.2, 7.2 Hz), 5.18 (1H, d, *J*= 6.4 Hz), 5.11 (1H, t, *J*= 2.8 Hz), 5.07 (1H, d, *J*= 2.0 Hz), 5.03 (1H, t, *J*= 10.0 Hz), 4.96 (1H, d, *J*= 1.2 Hz), 4.86 (1H, d, *J*= 11.6 Hz), 4.72 (1H, d, *J*= 12.8 Hz), 4.68 (1H, d, *J*= 12.8 Hz), 4.58 (1H, d, *J*= 11.6 Hz), 4.52 (1H, d, *J*= 11.6 Hz), 4.48 (1H, d, *J*= 11.6 Hz), 4.39-4.24 (2H, m), 4.12-4.08 (2H, m), 3.99 (1H, m), 3.90-3.44 (11H, m), 2.44 (3H, m), 2.18 (1H, m), 1.70-1.54 (7H, m), 1.47 (3H, s, CH_3), 1.45-1.21(34H, m), 1.13 (3H, m, CH_3), 1.04 (3H, d, *J*= 6.8 Hz, CH_3), 0.87 (6H, m, 2 × CH_3), 0.81 (3H, m, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 175.5, 172.5, 139.2, 138.8, 138.6, 138.6, 137.4, 129.2, 128.5, 128.5, 128.4, 128.3, 127.8, 127.8, 127.7, 127.6, 127.4, 126.3, 109.9, 101.7, 101.5, 100.7, 98.2, 96.5, 82.3, 80.9, 80.4, 80.2, 79.4, 78.4, 75.9, 75.2, 75.1, 74.9, 73.7, 72.6, 72.4, 72.2, 71.9, 69.0, 69.0, 68.5, 67.5, 65.4, 41.5, 41.4, 35.5, 35.0, 34.5, 32.1, 30.6, 29.9, 29.5, 28.1, 28.0, 27.9, 27.1, 26.9, 26.7, 26.6, 25.5, 25.4, 24.2, 22.8, 18.0, 17.6, 17.1, 17.0, 16.9, 14.3, 12.0, 12.0. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{81}H_{112}NaO_{21}$ 1443.7588; found 1443.7603. Analytical data for **18α** were essentially the same as reported in the literature.[6]

11(*S*)-Hydroxyhexadecanoic acid 11-*O*-2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-[2(*S*)-methylbutyryl]-*β*-L-rhamnopyranosyl)-(1→2)-4,6-*O*-benzylidene-*β*-D-glucopyranosyl-(1→2)-3,4-*O*-isopropylidene-*β*-D-fucopyranoside 1,3′-Lactone (18β)



18β

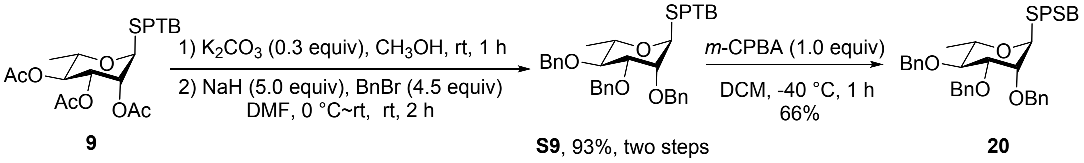
18β (6.8 mg, 21%). White solid. m.p. 54-60 °C. R_f = 0.57 (petroleum ether-EtOAc 5:1). $[\alpha]_D^{19}$ = 18.64 (*c*, 1.1 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43-7.18 (20H, m, Ar-H), 5.50 (1H, s), 5.31 (1H, dd, *J* = 9.2, 7.2 Hz), 5.20 (1H, d, *J*= 6.4 Hz, H-1'), 5.19 (1H, s), 5.04 (1H, t, *J*= 10.0 Hz), 5.02 (1H, s, H-1''), 4.90 (1H, d, *J* = 10.8 Hz), 4.78 (1H, d, *J*= 12.0 Hz), 4.60-4.57 (2H, m), 4.52 (1H, d, *J*= 11.6 Hz), 4.47 (1H, d, *J*= 12.4 Hz), 4.42 (1H, s, H-1'''), 4.33 (1H, dd, *J* = 7.2, 2.8 Hz), 4.27-4.21 (2H, m), 4.19 (1H, d, *J*= 8.0 Hz, H-1), 4.10 (1H, m), 3.92-3.79 (5H, m), 3.72 (1H, d, *J*= 2.4 Hz), 3.69 (1H, t, *J*= 6.8 Hz), 3.56-3.51 (1H, m), 3.49-3.45 (3H, m), 3.36 (1H, m), 2.45-2.40 (2H, m), 2.33-2.25 (2H, m), 1.76-1.64 (4H, m), 1.48 (3H, s, CH_3), 1.45-1.20 (36H, m) 1.14 (3H, d, *J*= 6.8 Hz, CH_3), 1.08 (3H, d, *J*= 6.8 Hz, CH_3), 0.92-0.81 (9H, m, 3 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 175.8, 172.0, 139.9, 139.0, 138.7, 137.3, 129.2, 128.5, 128.5, 128.4, 128.3, 128.1, 127.8, 127.7, 127.6, 127.1, 126.3, 109.9, 101.8, 101.5, 98.4, 98.2, 98.0, 82.5, 82.3, 81.9, 80.5, 79.4, 78.3, 75.7, 75.5, 74.3, 73.8, 72.1, 72.0, 71.4, 71.0, 69.0, 69.0, 68.4, 67.6, 65.3, 41.6, 41.2, 35.8, 32.1, 30.6, 29.5, 28.1, 27.9, 27.4, 27.0, 26.7, 26.6, 25.8, 25.5, 24.4, 22.8, 18.2, 17.6, 16.9, 16.7, 16.3, 14.3, 12.1. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{81}H_{112}NaO_{21}$ 1443.7588; found 1443.7575.



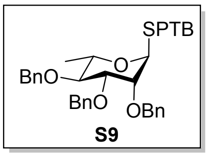
A solution of glycosyl donor **2b** (23.0 mg, 0.024 mmol), acceptor **3** (8.5 mg, 0.012 mmol) and DTBMP (5.0 mg, 0.024 mmol) in CH_2Cl_2 (0.25 mL) in the presence of 4 Å MS (100 wt%) was stirred at -40 °C for 10 min, then Tf_2O (4.2 μL, 0.024 mmol) was added. The reaction mixture was stirred at -40 °C for 3 h. The reaction mixture was quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **18α** (16.0 mg, 92%).

6. Synthesis of tetrasaccharide 18α by one-pot relay glycosylation

Preparation of SPSB glycoside 20

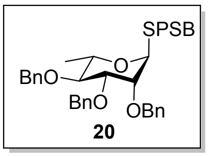


S-2-[(Propan-2-yl)sulfanyl]benzyl 2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranoside (S9)



To a solution of compound **9**[2] (350.0 mg, 0.74 mmol) in MeOH (1.5 mL) was added K_2CO_3 (31.0 mg, 0.22 mmol), the mixture was stirred at room temperature for 1 h, then filtered and evaporated under reduced pressure to afford the crude deacetylated product. This crude product was dissolved in DMF (2.5 mL) and cooled to 0 °C. NaH (149.0 mg, 3.72 mmol) was added slowly and stirred over a period of 10 min before benzyl bromide (397.0 μL, 3.35 mmol) was added. The reaction mixture was stirred at room temperature for 2 h and quenched with MeOH, extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated under reduced pressure and purified by chromatography to give **S9** (427.0 mg, 93%, two steps). Colorless syrup. R_f = 0.26 (petroleum ether-EtOAc 10:1). $[\alpha]_D^{25}$ = -21.15 (c, 1.4 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.44-7.13 (19H, m, Ar-H), 5.24 (1H, br s, H-1), 4,93 (1H, d, J = 10.8 Hz, PhC*H*), 4.66-4.45 (5H, m, PhC*H*), 4.08-4.01 (1H, m, H-3), 3.96 (1H, d, J = 13.2 Hz, PhC*H*), 3.89 (1H, d, J = 13.2 Hz, PhC*H*), 3.78-3.75 (2H, m, H-2, H-3), 3.63 (1H, t, J = 9.2 Hz, H-4), 3.39 (1H, m, $CH(CH_3)_2$), 1.33-1.26 (9H, m, 3 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 138.8, 138.5, 138.1, 135.6, 132.7, 130.4, 128.5, 128.2, 127.9, 127.9, 127.9, 127.8, 127.8, 126.9, 81.5, 80.9, 80.7, 76.3, 75.6, 72.2, 72.1, 68.8, 38.9, 33.7, 23.5, 23.3, 18.2. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{37}H_{42}NaO_4S_2$ 637.2417; found 637.2425.

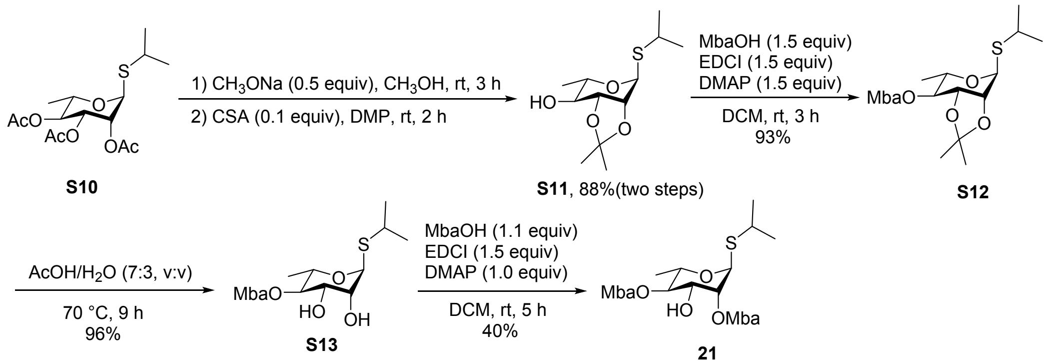
S-2-[(Propan-2-yl)sulfinyl]benzyl 2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranoside (20)



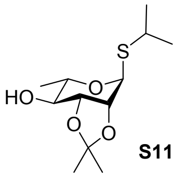
20

A solution of 3-Chloroperoxybenzoic acid (*m*-CPBA, 120.0 mg, 0.52 mmol) in DCM (5.2 mL) was slowly injected into the solution of **S5** (322.0 mg, 0.52 mmol) in DCM (5.2 mL) at -40 °C. The mixture was stirred at -40 °C for 1 h, diluted with EtOAc and then poured into 10% $Na_2S_2O_3$ aqueous solution. The organic layer was washed with saturated $NaHCO_3$, brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography to afford **2a** (216.0 mg, 66%). Colorless syrup. $R_f = 0.48$ (petroleum ether-EtOAc 2:1). Analysis by ^{1}H NMR indicated a mixture of sulfoxide isomers (*R* and *S*, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.21 (19H, m, Ar-H), 5.12 (1H, br s), 4.87 (1H, d, J = 10.8 Hz), 4.61-4.45 (5H, m), 3.93 (1H, m), 3.77 (2H, d, J = 13.6 Hz), 3.70 (1H, s), 3.68-3.66 (1H, m), 3.58 (1H, m), 2.94-2.82 (1H, m), 1.30-1.20 (6H, m, 2 × CH_3), 1.12-1.07 (3H, m, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 141.4, 138.7, 138.3, 138.0, 138.0, 135.9, 135.7, 131.1, 130.8, 130.6, 128.6, 128.4, 128.2, 128.2, 128.0, 128.0, 127.9, 126.0, 125.9, 82.0, 81.8, 80.7, 80.4, 76.4, 76.3, 75.6, 72.5, 72.5, 72.4, 72.4, 69.2, 69.1, 54.2, 53.9, 31.3, 30.9, 18.2, 18.2, 17.8, 17.5, 13.7, 13.1. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{37}H_{42}NaO_5S_2$ 653.2366; found 653.2351.

Preparation of acceptor 21



Isopropyl 2,3-*O*-isopropylidene-1-thio-*α*-L-rhamnopyranoside (S11)

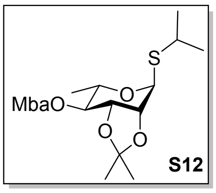


S11

To a solution of compound **S10**[8] (0.90 g, 2.58 mmol) in MeOH (7.4 mL) was added CH_3ONa (70.0 mg, 1.29 mmol), the mixture was stirred at room temperature for 3 h. The solution was neutralized with Amberlyst 15, (dry) ion-exchange resin. The mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in 2,2-dimethoxypropane (5.0 mL), and CSA (65.3 mg, 0.25 mmol) was added. The mixture was stirred at room temperature for 2 h and quenched with Et_3N. Then the mixture was concentrated under reduced pressure and purified by chromatography to give **S11** (0.60 g, 88%, two steps). White solid. $R_f = 0.22$ (petroleum ether-EtOAc 7:1). m.p. 50.2-51.0 °C. $[\alpha]_D^{25} = -159.87$ (*c*, 0.8 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.54 (1H, s, H-1), 4.15 (1H, d, J = 5.6 Hz, H-2), 4.02-3.94 (2H, m, H-3, H-4), 3.44-3.39 (1H, m, H-5), 3.03 (1H, m, $CH(CH_3)_2$), 2.22 (1H, d, J = 4.0 Hz, OH), 1.51 (3H, s, CH_3), 1.33-1.31 (6H, m, 2 × CH_3), 1.28-1.25 (6H, m, 2

× CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.7, 79.4, 78.6, 75.6, 66.2, 34.9, 28.4, 26.6, 23.6, 23.4, 17.4. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{12}H_{22}NaO_4$ 285.1131; found 285.1141.

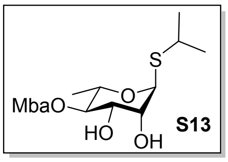
Isopropyl 2,3-*O*-isopropylidene-4-*O*-[2(*S*)-methylbutyryl]-1-thio-*α*-L-rhamnopyranoside (S12)



S12

To a solution of **S11** (0.57 g, 2.18 mmol) in CH_2Cl_2 (7.2 mL) was added (*S*)-(+)-2-methylbutyric acid (MbaOH, 357.0 μL, 3.27 mmol), DMAP (0.40 g, 3.27 mmol) and 3-(3-dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDCI, 0.63 g, 3.27 mmol) , the resulting solution was stirred at room temperature for 3 h then diluted with water, extracted with EtOAc. The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give compound **S12** (0.70 g, 93%). Colorless syrup. R_f = 0.35 (petroleum ether-EtOAc 20:1). $[\alpha]_D^{25}$ = -102.77 (c, 1.66 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.57 (1H, s, H-1), 4.90 (1H, dd, J = 10.0, 8.0 Hz, H-4), 4.15 (1H, d, J = 5.2 Hz, H-3), 4.11-4.06 (2H, m, H-2, H-5), 3.03 (1H, m, $CH(CH_3)_2$), 2.38 (1H, m, $COCH(CH_3)$), 1.71-1.61 (1H, m, $COCH(CH_3)CH_2$), 1.54 (3H, s, CH_3), 1.51-1.44 (1H, m, $COCH(CH_3)CH_2$), 1.33-1.26 (9H, m, 3 × CH_3), 1.14-1.12 (6H, m, 2 × CH_3), 0.90 (3H, t, J = 7.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 109.9, 79.5, 75.9, 74.6, 64.9, 41.3, 35.1, 27.9, 26.9, 26.8, 23.6, 23.5, 17.1, 16.7, 11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{30}NaO_5S$ 369.1706; found 369.1721.

Isopropyl 4-*O*-[2(*S*)-methylbutyryl]-1-thio-*α*-L-rhamnopyranoside (S13)

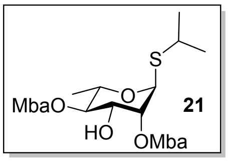


S13

A solution of compound **S12** (0.68 g, 1.97 mmol) in $AcOH/H_2O$ (6.6 mL, 7:3, v:v) was stirred at 70 °C for 9 h, then diluted with water, extracted with EtOAc. The organic layer was washed with saturated $NaHCO_3$, brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was subjected to flash column chromatography to afford **S13** (0.58 g, 96%). White solid. R_f = 0.49 (petroleum ether-EtOAc 2:1). m.p. 58.0-60.2 °C. $[\alpha]_D^{25}$ = -173.6 (*c*, 1.0 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.33 (1H, d, J = 1.6 Hz, H-1), 4.79 (1H, t, J = 9.6 Hz, H-4), 4.22-4.15 (1H, m, H-3), 4.00 (1H, br s, H-2), 3,79 (1H, m, H-5), 3.19 (1H, d, J = 6.8 Hz, OH), 3.07 (1H, m, OH), 3.06-3.00 (1H, m, $CH(CH_3)_2$), 2.41 (1H, m, $COCH(CH_3)$), 1.74-1.63 (1H, m, $COCH(CH_3)CH_2$), 1.53-1.42 (1H, m, $COCH(CH_3)CH_2$), 1.30-1.28 (6H, m, 2 × CH_3), 1.19 (3H, d, J = 6.4 Hz, CH_3) 1.15 (3H, d, J = 7.2 Hz, CH_3), 0.90 (3H, t, J = 7.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 83.4, 75.8, 72.9, 71.2, 66.3, 41.5, 35.9, 26.9, 23.9, 23.8, 17.5, 16.8, 11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{14}H_{26}NaO_5S$ 329.1393; found 329.1382.

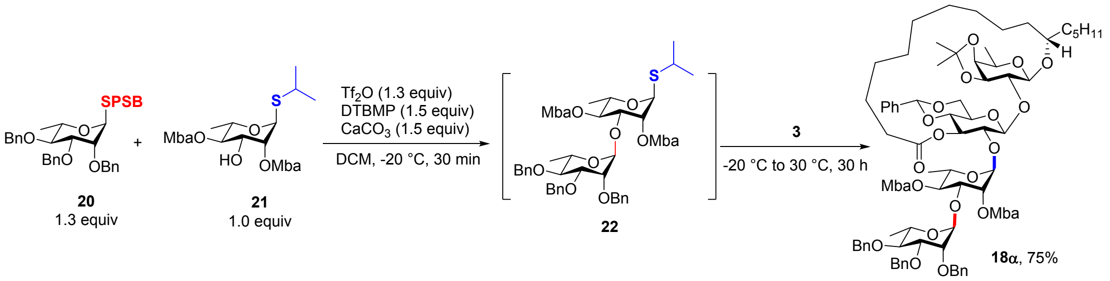
Isopropyl 2,4-di-*O*-[2(*S*)-methylbutyryl]-1-thio-*α*-L-rhamnopyranoside (21)

To a solution of **S13** (0.57 g, 1.86 mmol) in CH_2Cl_2 (18.6 mL) was added (*S*)-(+)-2-methylbutyric acid (MbaOH, 228 μL, 2.05 mmol), DMAP (0.23 g, 1.86 mmol) and 3-



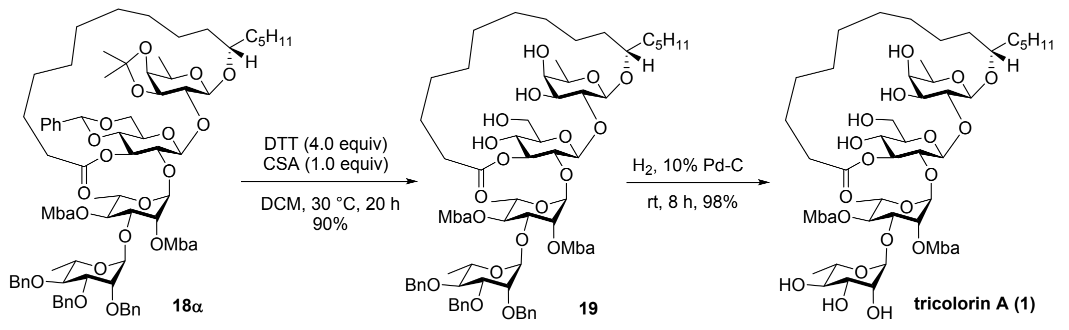
(3-dimethylaminopropyl)-1-ethyl-carbodiimide hydrochloride (EDCI, 0.53 g, 2.80 mmol) , the resulting solution was stirred at room temperature for 3 h then diluted with water, extracted with EtOAc. The combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give compound **21** (0.36 g, 40%). Colorless syrup. R_f = 0.40 (petroleum ether-EtOAc 10:1). $[\alpha]_D^{25}$ = -64.08 (c, 1.37 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.27 (1H, s, H-1), 5.10 (1H, m, H-2), 4.84 (1H, t, J = 9.6 Hz, H-4), 4.20-4.13 (1H, m, H-3), 3.93 (1H, m, H-5), 3.09-2.99 (1H, m, $CH(CH_3)_2$), 2.52-2.37 (2H, m, $COCH(CH_3)$), 2.16 (1H, d, J = 8.4 Hz, OH), 1.74-1.64 (2H, m, $COCH(CH_3)CH_2$), 1.56-1.43 (2H, m, $COCH(CH_3)CH_2$), 1.29 (6H, d, J = 6.4 Hz, 2 × CH_3), 1.19-1.14 (9H, m, 3 × CH_3), 0.91 (6H, m, 2 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 176.4, 81.8, 75.0, 74.9, 69.8, 66.9, 41.4, 41.2, 36.7, 26.9, 24.0, 23.8, 17.6, 16.8, 16.7, 11.7. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{19}H_{34}NaO_6S$ 413.1968; found 413.1977.

Synthesis of tetrasaccharide 18α by one-pot relay glycosylation

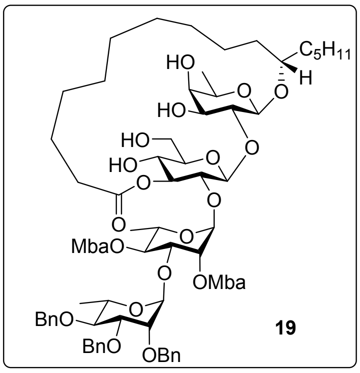


A solution of glycosyl donor **20** (63.0 mg, 0.099 mmol), thioglycoside acceptor **21** (30.0 mg, 0.076 mmol) and DTBMP (23.7 mg, 0.11 mmol) in CH_2Cl_2 (0.55 mL) in the presence of 4 Å MS (100 wt%) and $CaCO_3$ (11.5 mg, 0.11 mmol) was stirred for 10 min at -20 °C. After addition of Tf_2O (16.8 µL, 0.099 mmol), the solution was stirred at -20 °C for 30 min, followed by the addition of acceptor **3** (106.1 mg, 0.15 mmol) in CH_2Cl_2 (0.30 mL). The reaction mixture was stirred at 30 ºC for 30 h. Finally, the reaction system was quenched with Et_3N, filtered through Celite and extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, concentrated, and purified by silica gel column chromatography to give compound **18α** (80.1 mg, 75%). Analytical data for **18α** were essentially the same as reported in the literature.[6]

7. Synthesis of tricolorin A



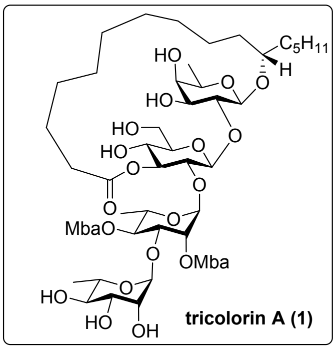
11(*S*)-Hydroxyhexadecanoic acid 11-*O*-2,3,4-tri-*O*-benzyl-*α*-L-rhamnopyranosyl)-(1→3)-2,4-di-*O*-[2(*S*)-methylbutyryl]-*α*-L-rhamnopyranosyl)-(1→2)-*β*-D-glucopyranosyl-(1→2)-*β*-D-fucopyranoside 1,3′-Lactone (19)



19

To a solution of **18α** (22.0 mg, 0.015 mmol) and DL-1,4-dithiothreitol (DTT, 9.5 mg, 0.061 mmol) in CH_2Cl_2 (0.15 mL) was added (+)-camphor-10-sulfonic acid (CSA, 3.6 mg, 0.015 mmol), the resulting solution was stirred at room temperature for 20 h. The solution was extracted with EtOAc, washed with aqueous NaCl, dried with anhydrous Na_2SO_4 and the solvent removed under vacuo. The residue was purified by column chromatography to afford **19** (18.0 mg, 90%). White solid. m.p. 56-64 °C. R_f = 0.51 (DCM:CH_3OH 10:1). $[\alpha]_D^{20}$ = 0.39 (*c*, 1.8 in $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.21(15H, m, Ar-H), 5.10 (1H, d, J = 7.2 Hz), 5.04-4.98 (4H, m), 4.92 (1H, s), 4.86 (1H, d, J = 11.6 Hz), 4.71(1H, d, J = 12.8 Hz), 4.66 (1H, d, J = 12.8 Hz), 4.58-4.49 (3H, m), 4.17-4.12 (2H, m), 4.07 (1H, dd, J = 10.0, J = 2.4 Hz), 3.97 (1H, d, J = 11.6 Hz), 3.89 (2H, m), 3.71-3.47 (14H, m), 2.73 (1H, m), 2.45-2.35 (2H, m), 2.19 (1H, m), 1.71-1.53 (6H, m), 1.45-1.19 (29H, m), 1.13 (3H, d, J = 6.4 Hz, CH_3), 1.11 (3H, d, J = 7.2 Hz, CH_3), 1.03 (3H, d, J = 6.8 Hz, CH_3), 0.88-0.84 (6H, m, 2 × CH_3), 0.79 (3H, t, J = 7.2 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 175.5, 175.3, 139.1, 138.6, 138.5, 128.5, 128.5, 128.3, 127.8, 127.7, 127.6, 127.5, 102.2, 101.1, 98.9, 97.2, 81.9, 80.7, 80.2, 80.2, 79.0, 75.8, 75.5, 75.3, 75.0, 74.6, 72.8, 72.8, 72.5, 72.2, 72.0, 71.2, 70.7, 69.1, 67.2, 62.2, 41.4, 34.6, 34.3, 32.0, 31.5, 29.5, 27.9, 27.7, 26.8, 26.6, 26.4, 25.5, 24.3, 23.5, 22.8, 18.0, 17.0, 17.0, 16.7, 14.3, 12.0, 11.9. HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{71}H_{104}NaO_{21}$ 1315.6962; found 1315.7015. Analytical data for **19** were essentially the same as reported in the literature.[1]

Tricolorin A (1)



The compound **19** (32.0 mg, 0.024 mmol) was subjected to hydrogenation (H_2) with catalytic 10% Pd/C in ethanol (3.0 mL) for 8 h. After being filtered and concentrated, the residue was purified by column chromatography to afford tricolorin A (**1**) (24.8 mg, 98%). White solid. R_f = 0.53 (DCM:CH_3OH 5:1). ^1H NMR (400 MHz, C_5D_5N) δ 5.83-5.76 (3H, m), 5.69 (1H, t, J = 10.0 Hz), 5.55 (1H, s), 5.50 (1H, s), 4.78 (1H, m), 4.72 (1H, m), 4.65 (1H, m), 4.50 (1H, br s), 4.40 (1H, m), 4.34 (1H, t, J = 9.2 Hz), 4.24 (3H, m), 4.11 (2H, m), 4.02 (1H, d, J = 2.4 Hz), 3.90 (1H, m), 3.82 (2H, m), 3.47 (1H, m), 3.0 (1H, m), 2.45(1H, m), 2.38 (1H, m), 2.31 (1H, m), 1.70 (3H, br s), 1.64 (3H, d, J = 6.0 Hz), 1.57 (3H, d, J = 6.4 Hz), 1.16 (3H, d, J = 6.8 Hz), 1.10 (3H, d, J = 6.4 Hz), 0.91 (3H, t, J = 7.2 Hz), 0.82 (6H, m). ^{13}C NMR (100 MHz, C_5D_5N) δ 175.6, 175.4, 172.1, 104.5, 102.9, 99.6, 98.1, 80.6, 80.5, 78.8, 76.1, 76.1, 75.7, 74.5, 73.2, 73.1, 73.0, 72.6, 72.3, 72.2, 71.1, 70.4, 69.3, 67.1, 61.0, 41.4, 41.2, 34.9, 34.2, 31.9, 31.6, 29.4, 28.1, 27.7, 26.8, 26.7, 26.4, 25.5, 24.6, 23.5, 22.7, 18.4, 18.2, 17.2, 16.8, 16.8, 14.0, 11.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{50}H_{86}NaO_{21}$ 1045.5554; found 1045.5512.

Table S1. Comparison of the ^{13}C NMR data of this synthetic and isolated[9] tricolorin A (in C_5D_5N).

	Isolated (*Ref.* 9)	**This Work [a]**	**Δδ**
Entry	**^{13}C-NMR (75.4 MHz, C_5D_5N)**	**^{13}C-NMR (100 MHz, C_5D_5N)**	
1	175.55	175.72	+0.17
2	175.42	175.56	+0.14
3	172.13	172.27	+0.14
4	104.49	104.58	+0.09
5	103.09	103.00	-0.09
6	99.76	99.76	0
7	98.20	98.26	+0.06
8	81.00	80.76	-0.24
9	80.60	80.61	+0.01
10	78.96	78.91	-0.05
11	76.25	76.22	-0.03
12	76.16	76.19	+0.03
13	75.84	75.87	+0.03
14	74.62	74.59	-0.03
15	73.34	73.23	-0.11
16	73.30	73.25	-0.05
17	73.12	72.12	0
18	72.74	72.72	-0.02
19	72.46	72.47	+0.01
20	72.25	72.28	+0.03
21	71.24	71.23	-0.01
22	70.44	70.49	+0.05
23	69.62	69.45	-0.17
24	67.23	67.21	-0.02
25	61.31	61.11	-0.20
26	41.53	41.51	-0.02
27	41.37	41.34	-0.03
28	34.36	34.34	-0.02
29	27.92	27.83	-0.09
30	27.06	26.96	-0.10
31	18.48	18.50	+0.02
32	18.25	18.28	+0.03
33	17.24	17.30	+0.06
34	16.91	16.95	+0.04
35	16.91	16.89	-0.02
36	14.15	14.16	+0.01
37	11.76	11.77	+0.01

a. 99.76 ppm was setted as the reference peak to be consistent with the reported data.

Table S2. Comparison of the ^{13}C NMR data of this synthetic and Yu[10] synthetic tricolorin A (in C_5D_5N).

	Yu (*Ref.* 10)	This Work [a]	$\Delta\delta$
Entry	**^{13}C-NMR (75.6 MHz, C_5D_5N)**	**^{13}C-NMR (100 MHz, C_5D_5N)**	
1	175.6	175.6	0
2	175.5	175.4	-0.1
3	172.1	172.1	0
4	104.5	104.5	0
5	102.9	102.9	0
6	99.7	99.6	-0.1
7	98.2	98.1	-0.1
8	80.8	80.6	-0.2
9	80.5	80.5	0
10	78.8	78.8	0
11	76.2	76.1	-0.1
12	76.1	76.1	0
13	75.8	75.7	-0.1
14	74.5	74.5	0
15	73.23	73.21	-0.02
16	73.18	73.13	-0.05
17	73.0	73.0	0
18	72.6	72.6	0
19	72.4	72.3	-0.1
20	72.2	72.2	0
21	71.1	71.1	0
22	70.4	70.4	0
23	69.4	69.3	-0.1
24	67.1	67.1	0
25	61.1	61.0	-0.1
26	41.4	41.4	0
27	41.3	41.2	-0.1
28	35.0	34.9	-0.1
29	34.3	34.2	-0.1
30	31.9	31.9	0
31	31.6	31.6	0
32	29.4	29.4	0
33	28.1	28.1	0
34	27.8	27.7	-0.1
35	26.9	26.8	-0.1
36	26.7	26.7	0
37	26.5	26.4	-0.1
38	25.5	25.5	0
39	24.6	24.6	0
40	23.5	23.5	0

41	22.7	22.7	0
42	18.4	18.4	0
43	18.2	18.2	0
44	17.2	17.2	0
45	16.83	16.83	0
46	16.78	16.76	-0.02
47	14.1	14.0	-0.1
48	11.7	11.6	-0.1

a. 175.6 ppm was setted as the reference peak to be consistent with the reported data.

8. References

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9. NMR Spectra

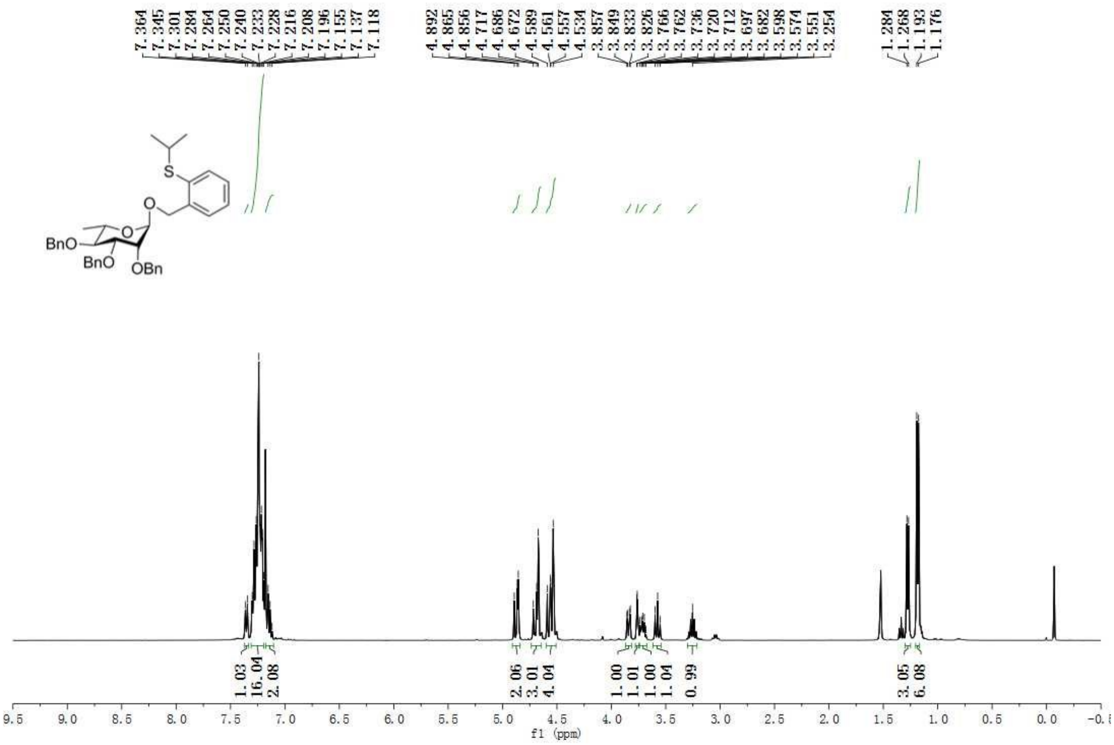

Figure S1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **S2**

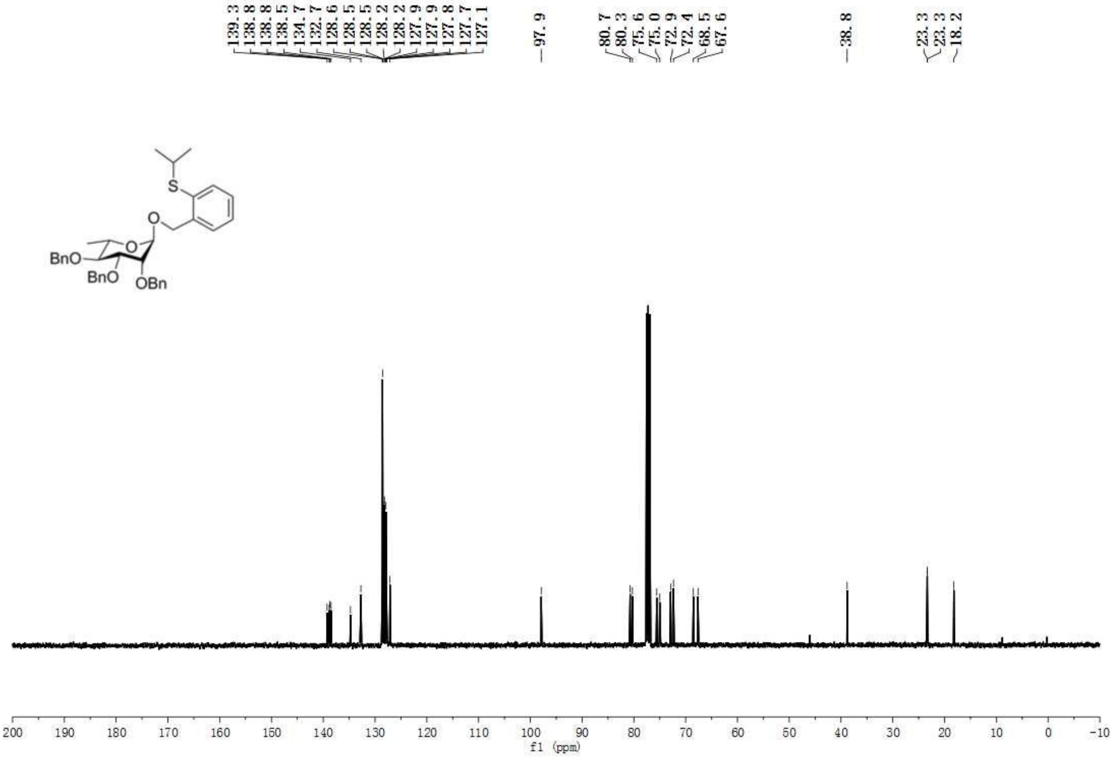

Figure S2. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **S2**

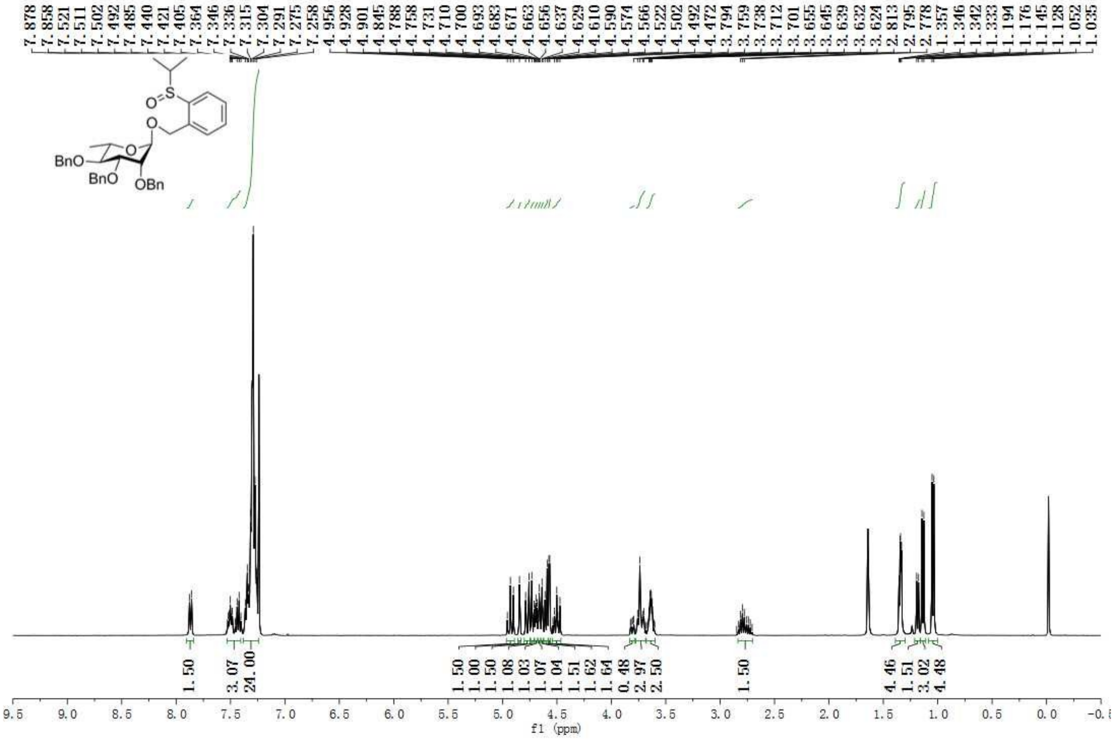

Figure S3. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **4**

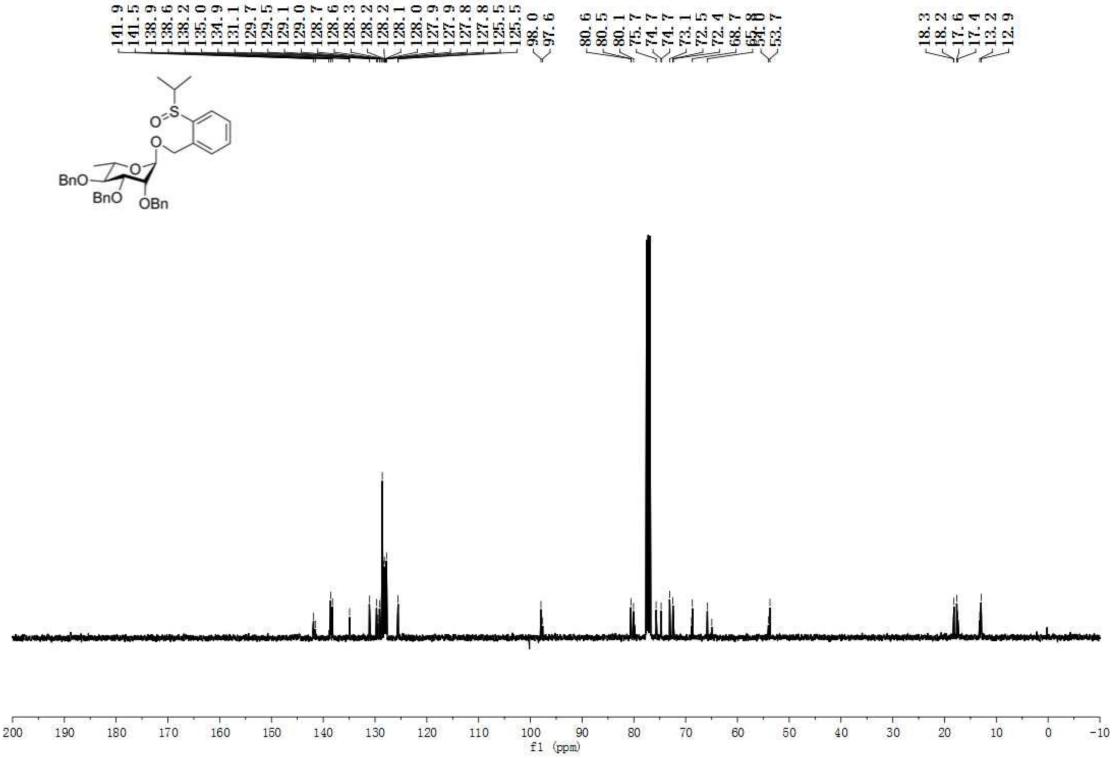

Figure S4. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **4**

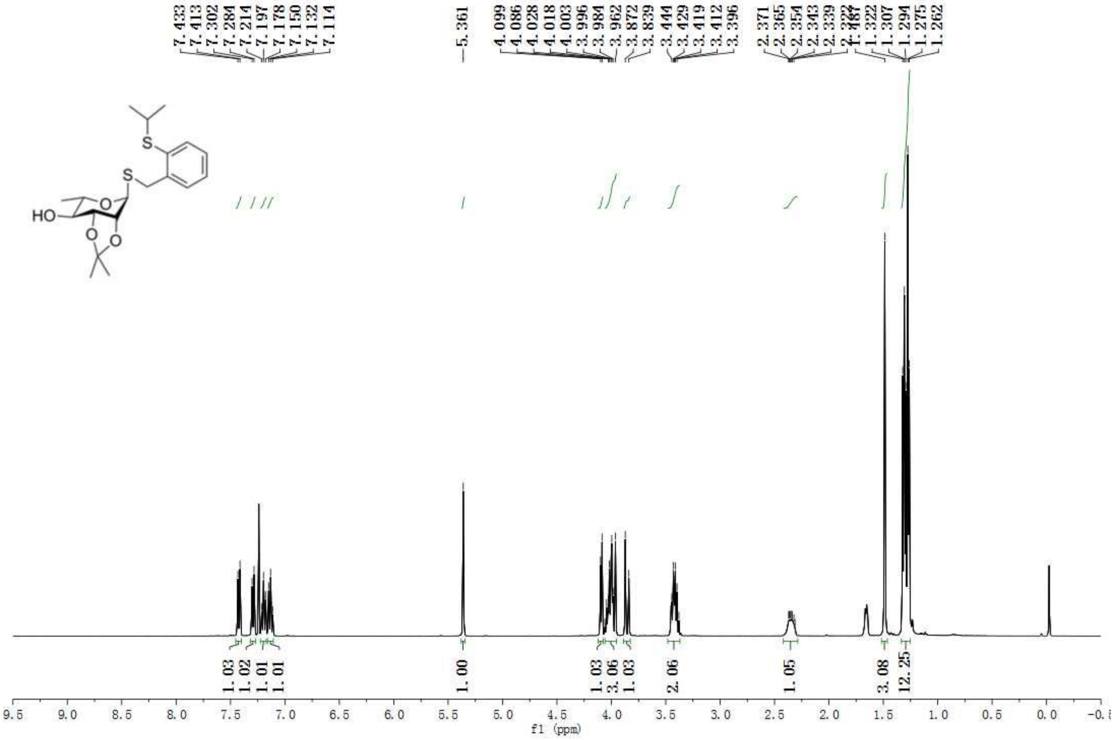

Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **10**

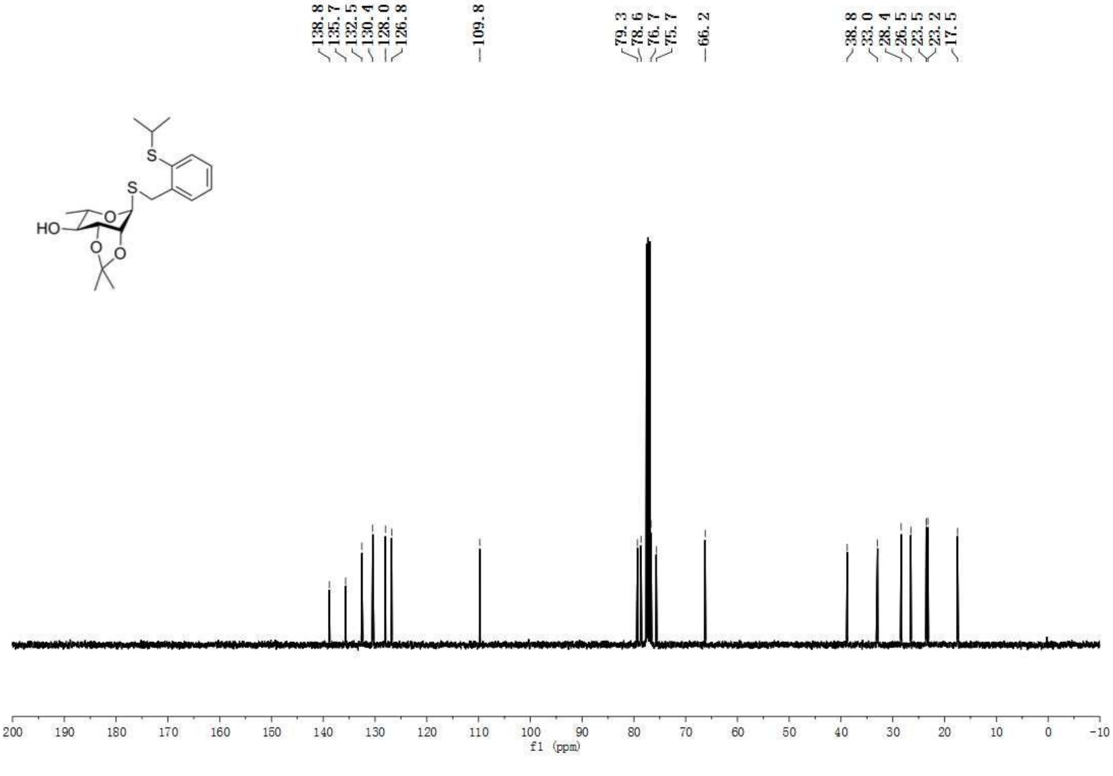

Figure S6. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **10**

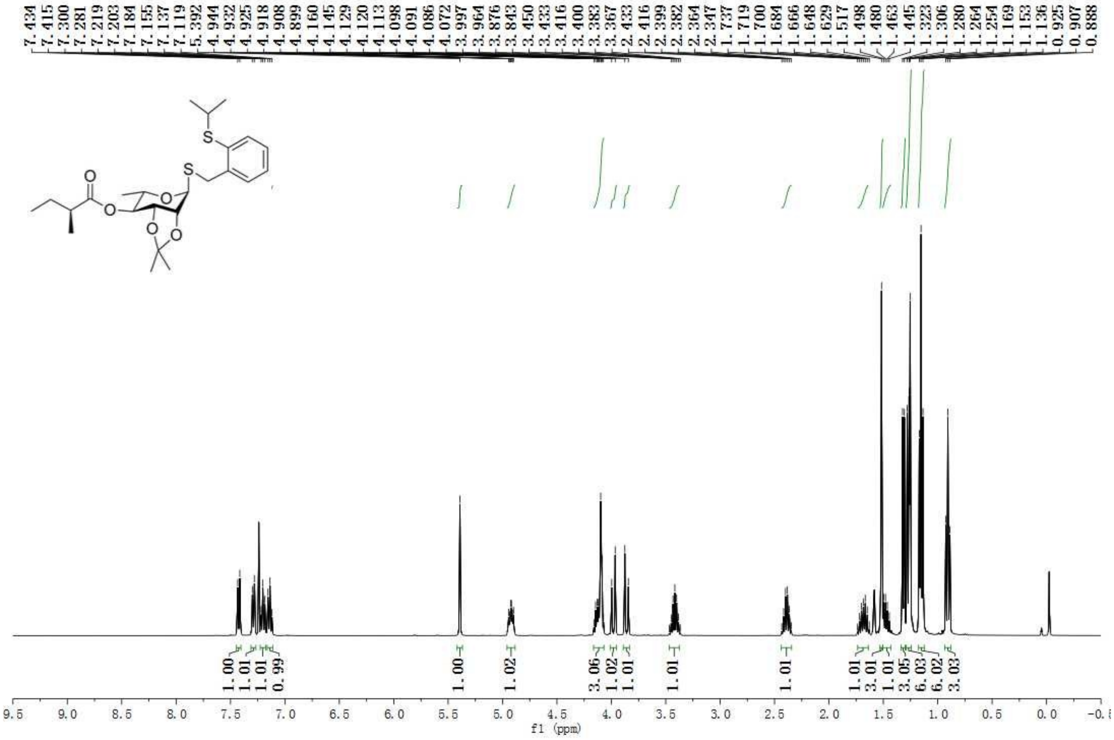

Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **11**

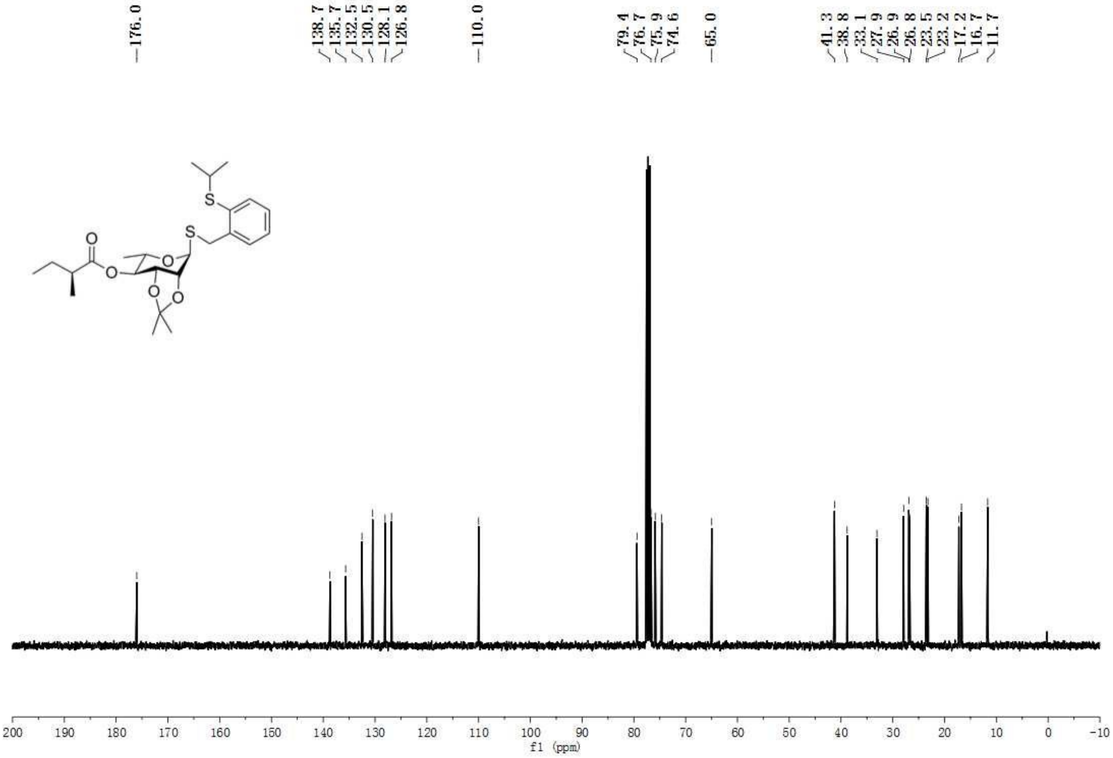

Figure S8. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **11**

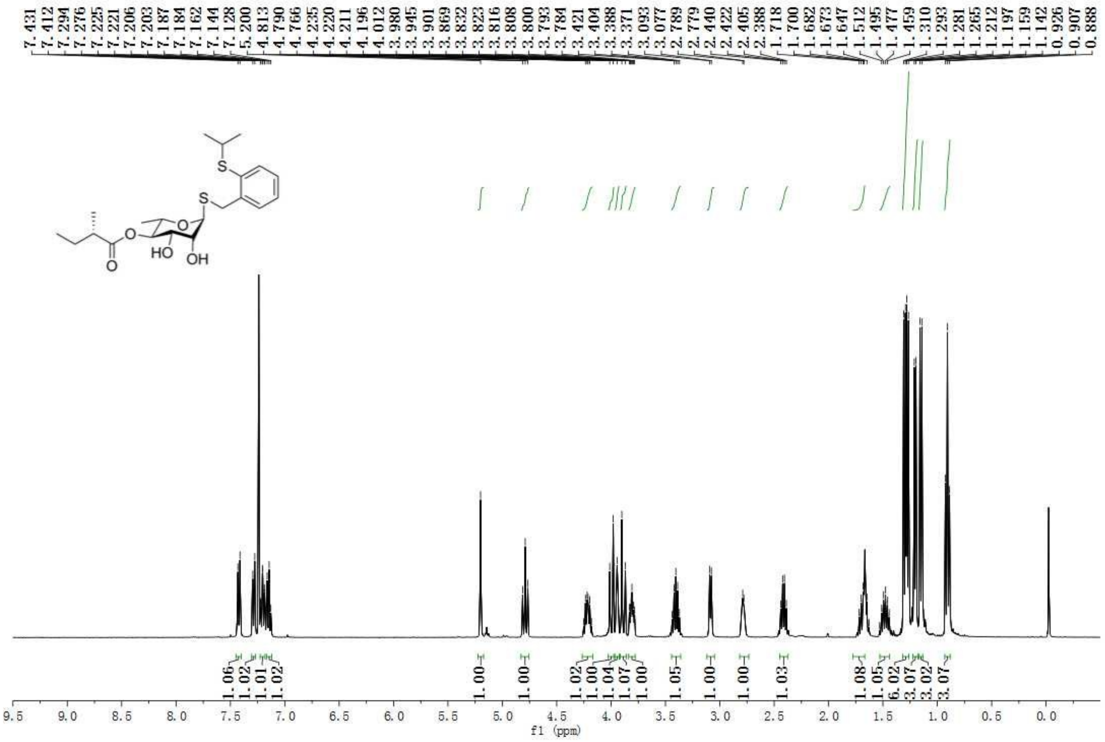

Figure S9. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **12**

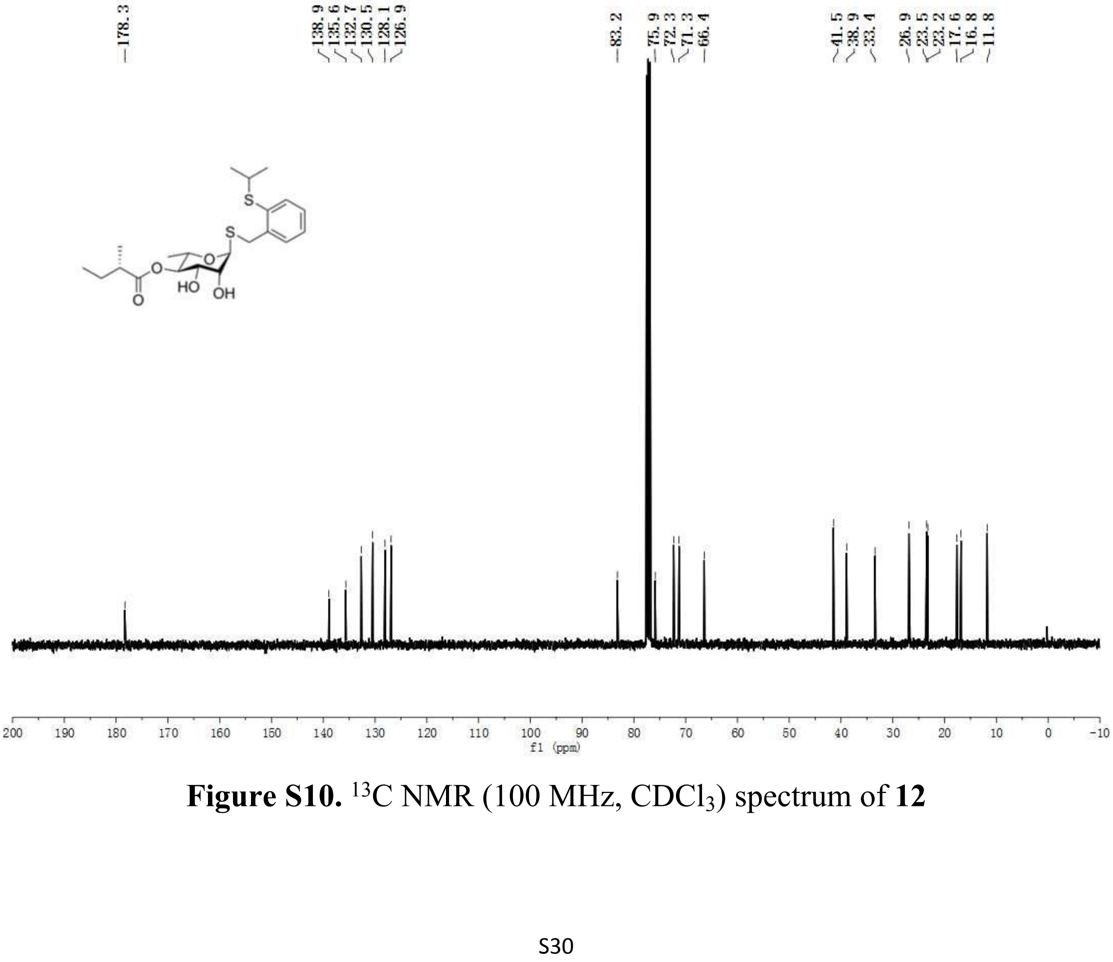

Figure S10. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **12**

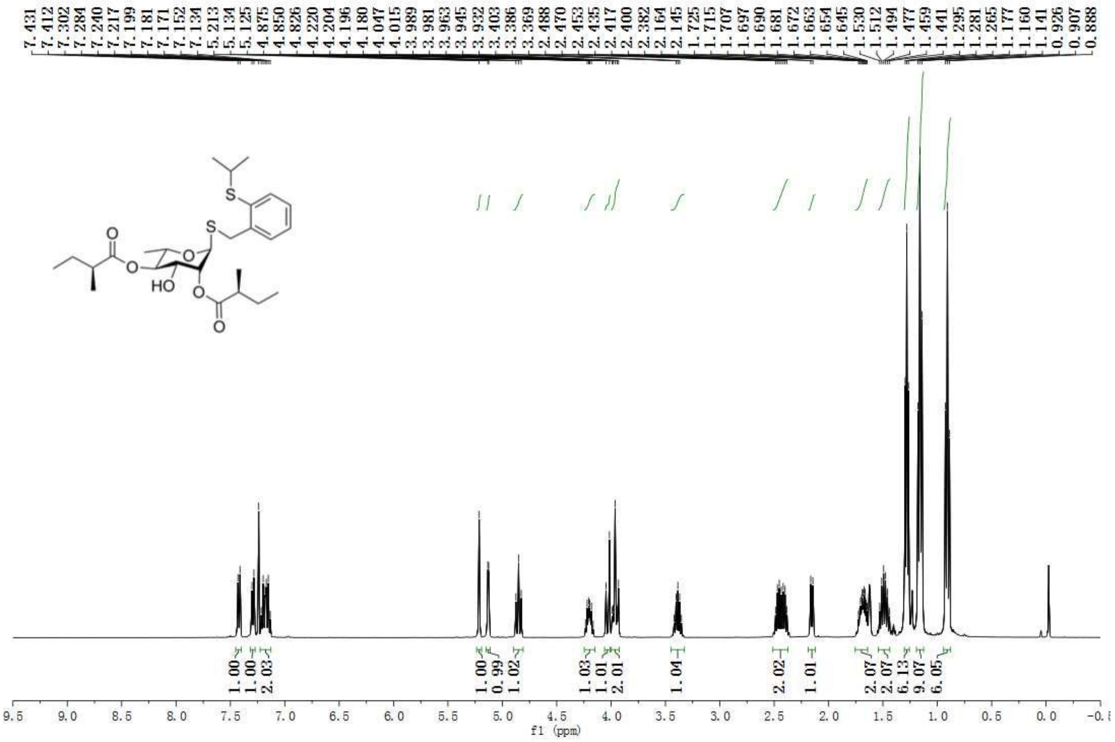

Figure S11. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **5**

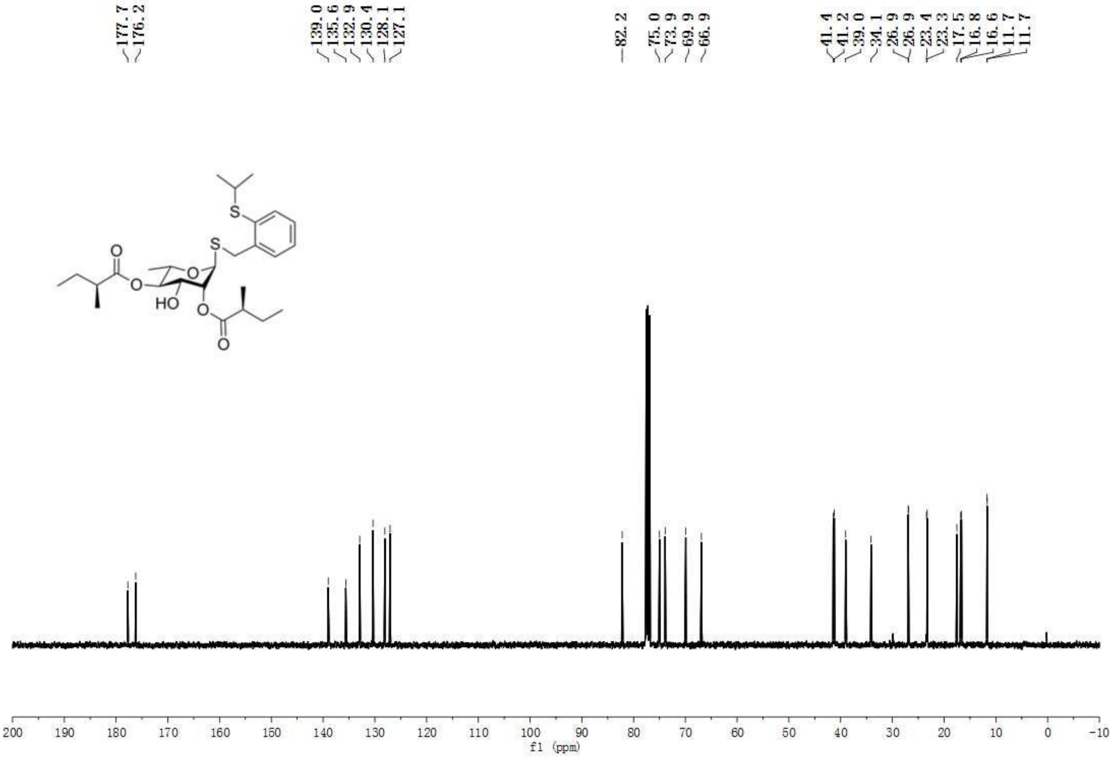

Figure S12. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **5**

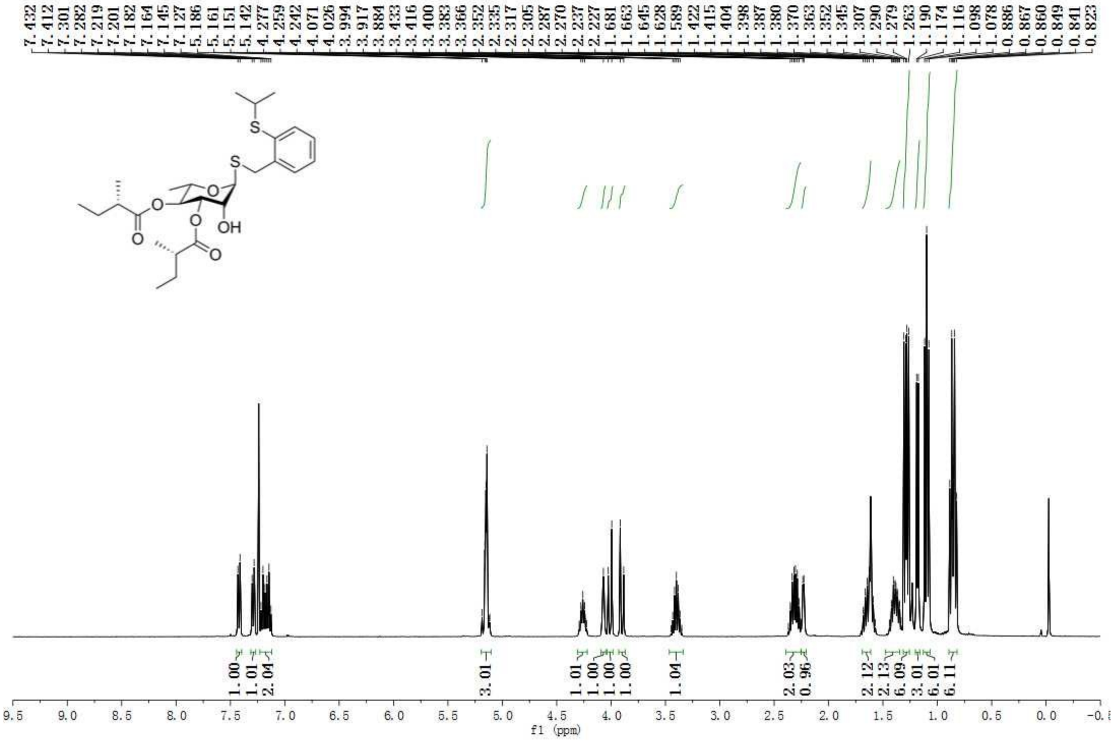

Figure S13. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **5a**

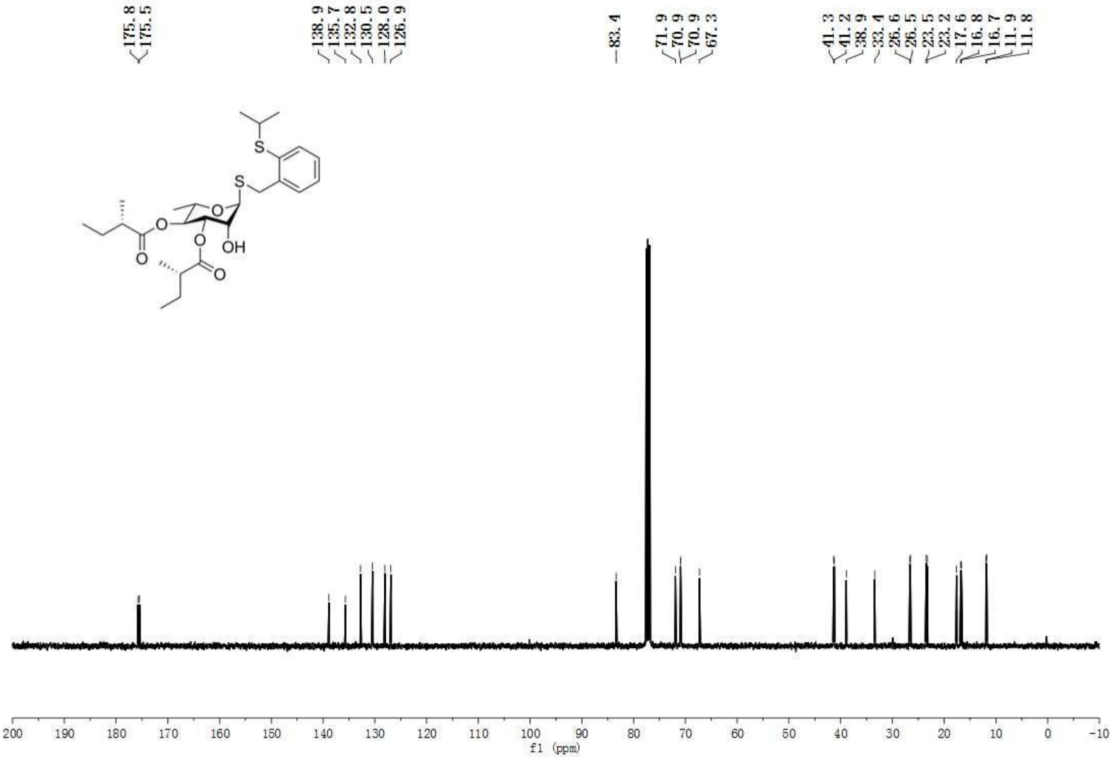

Figure S14. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **5a**

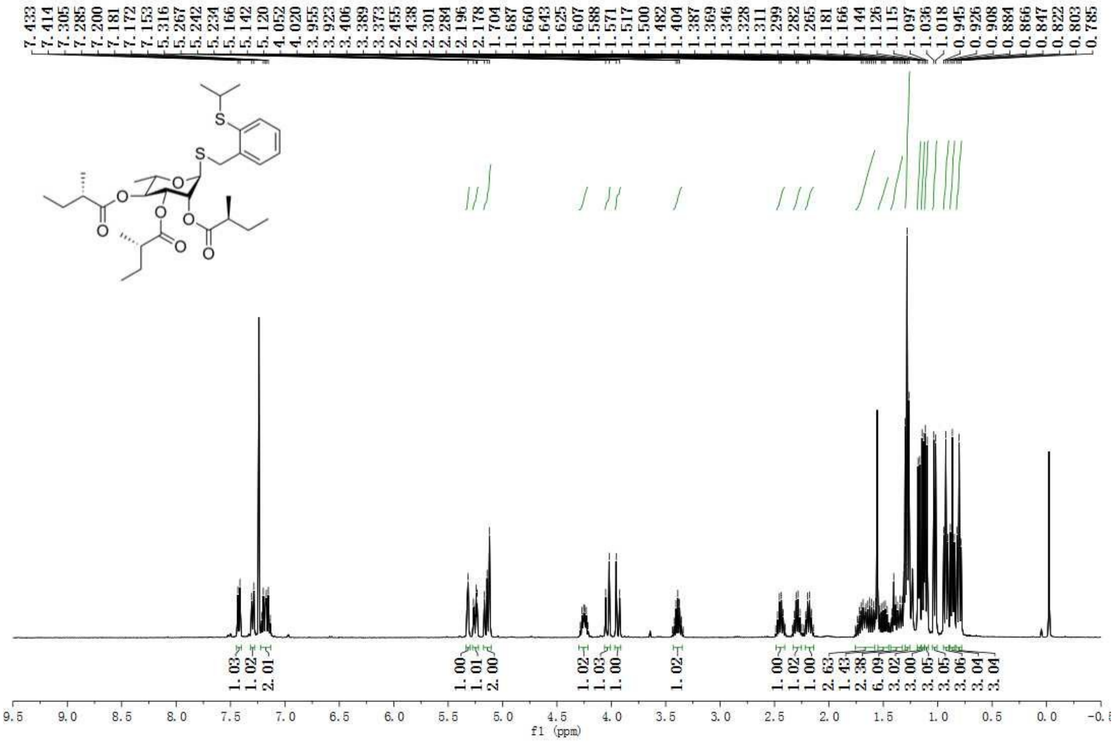

Figure S15. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **5b**

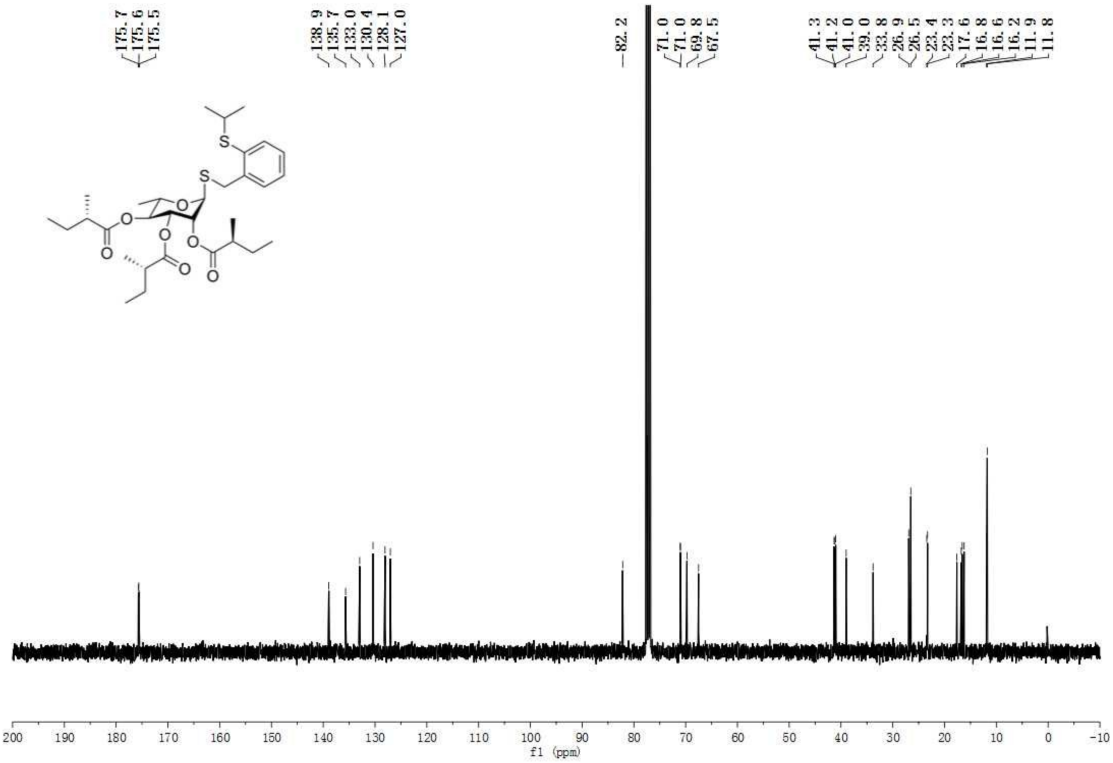

Figure S16. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **5b**

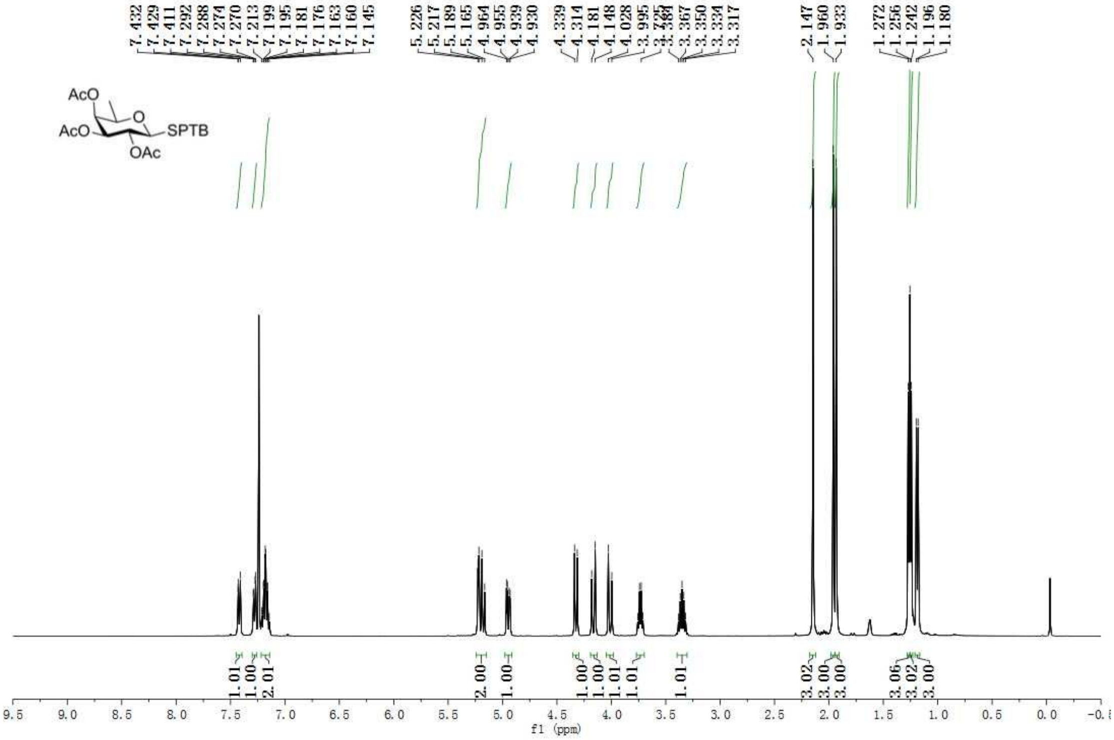

Figure S17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **S8β**

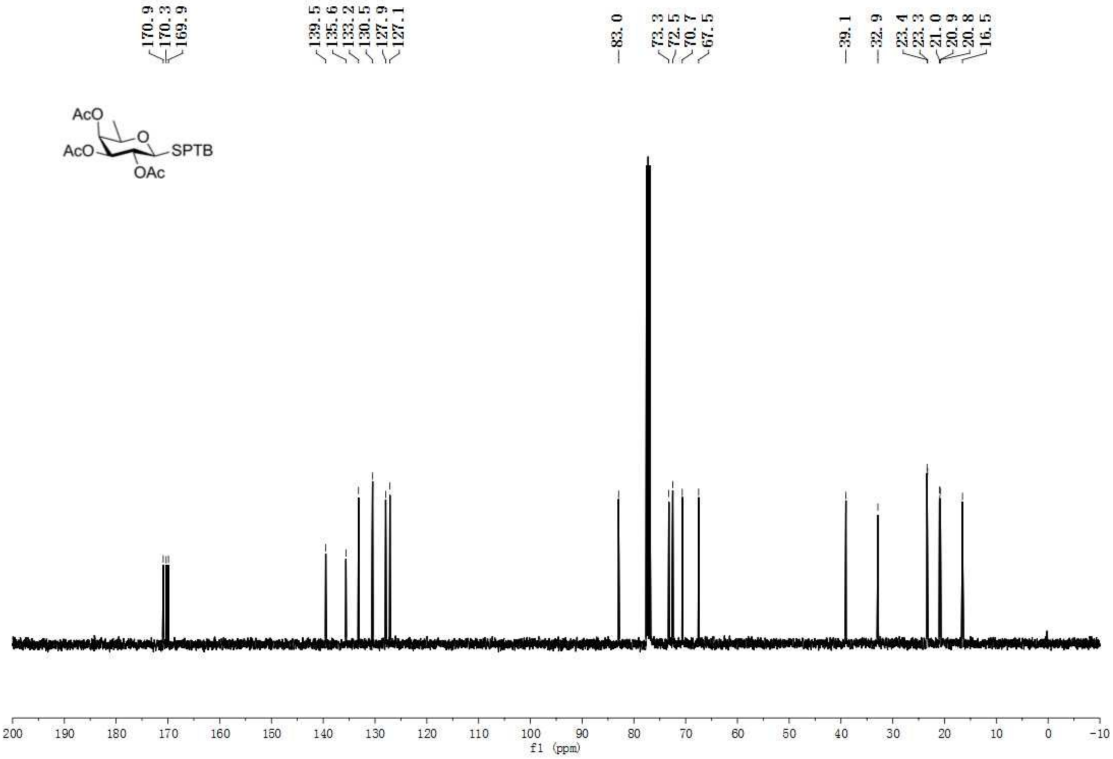

Figure S18. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **S8β**

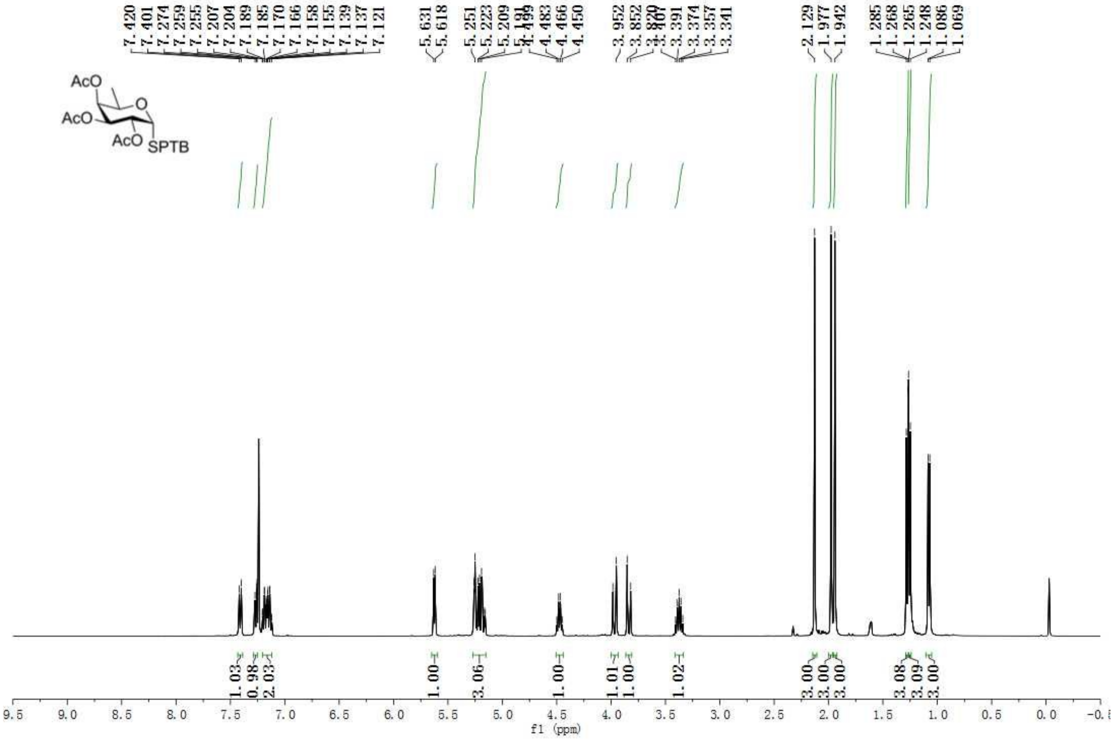

Figure S19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **S8α**

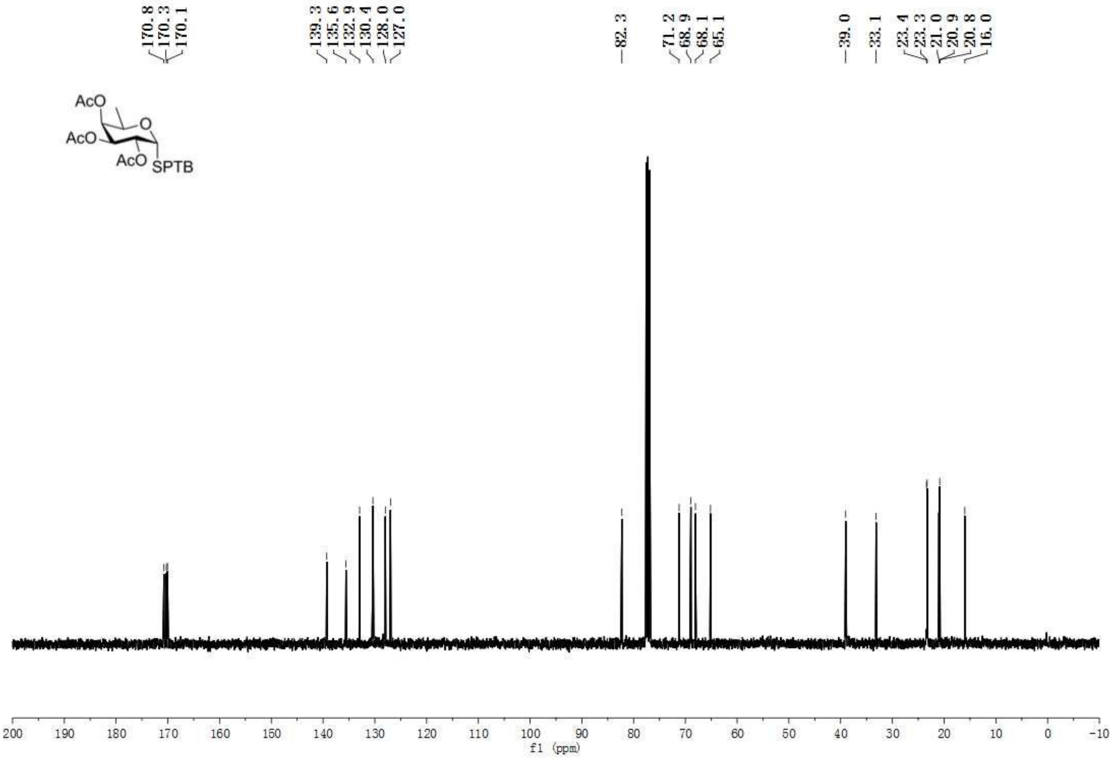

Figure S20. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **S8α**

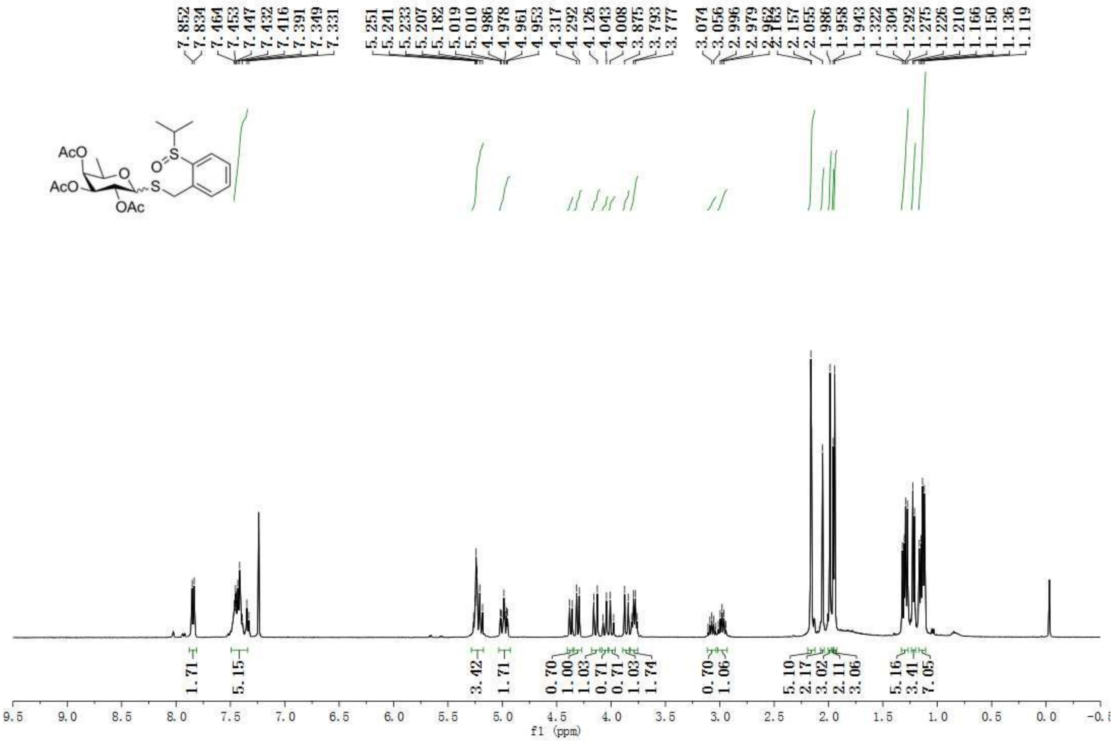

Figure S21. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **6**

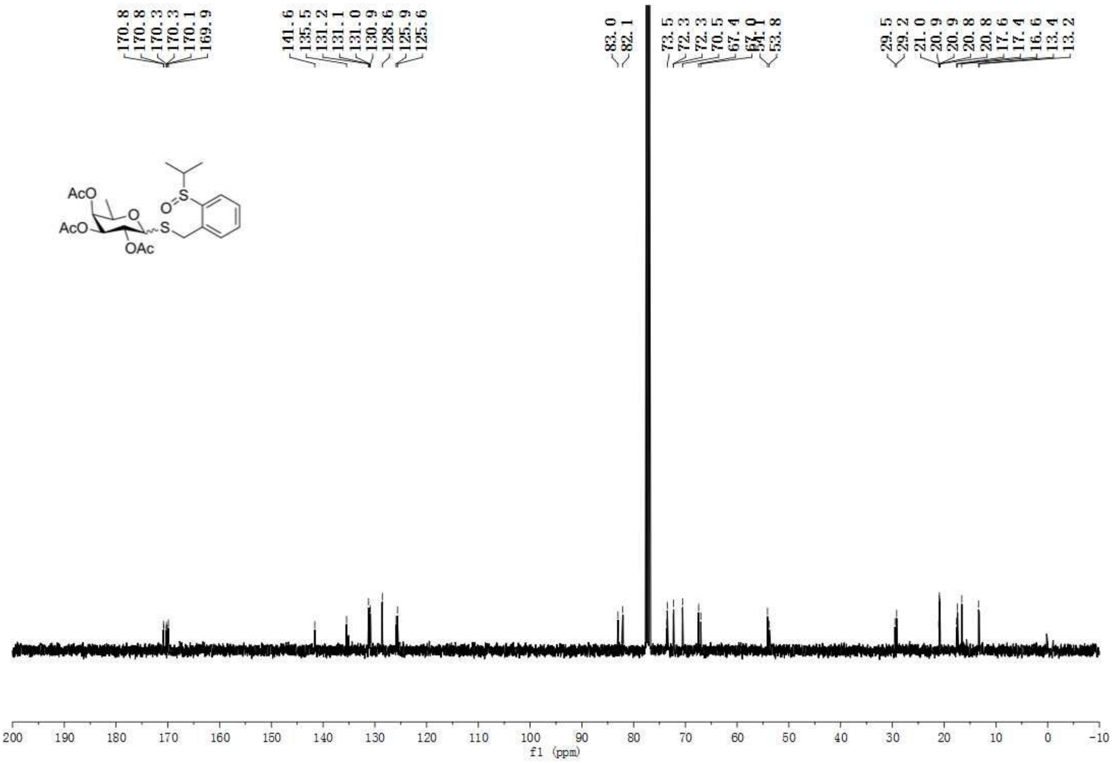

Figure S22. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **6**

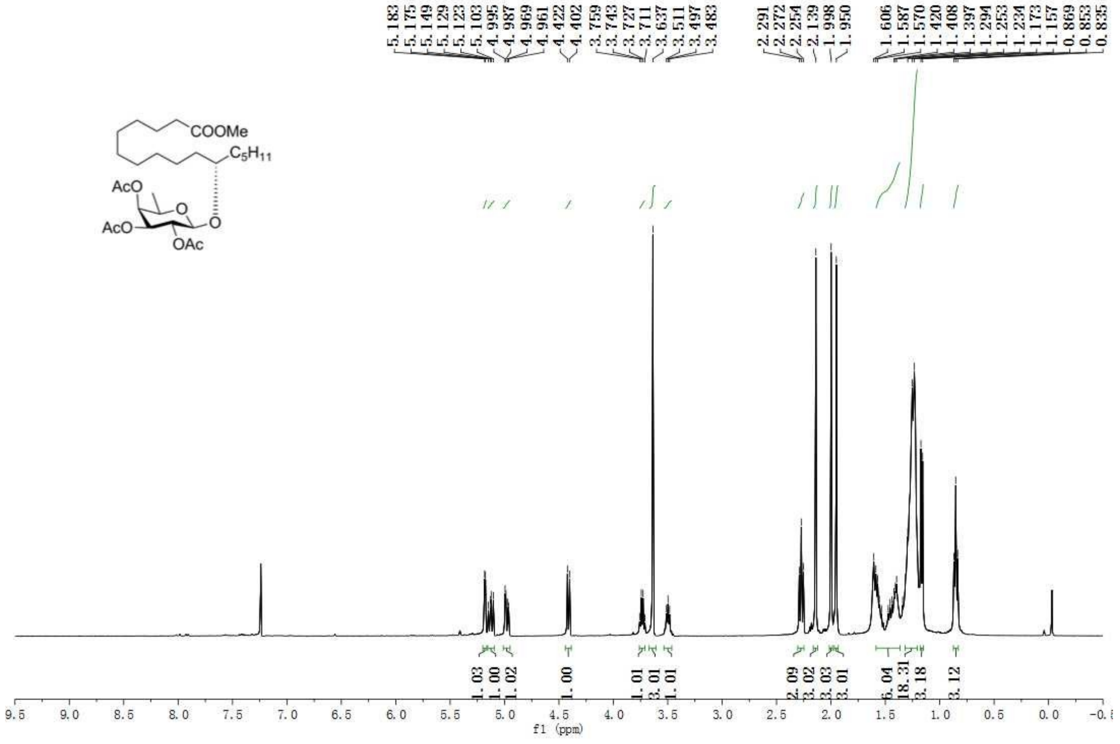

Figure S23. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **14**

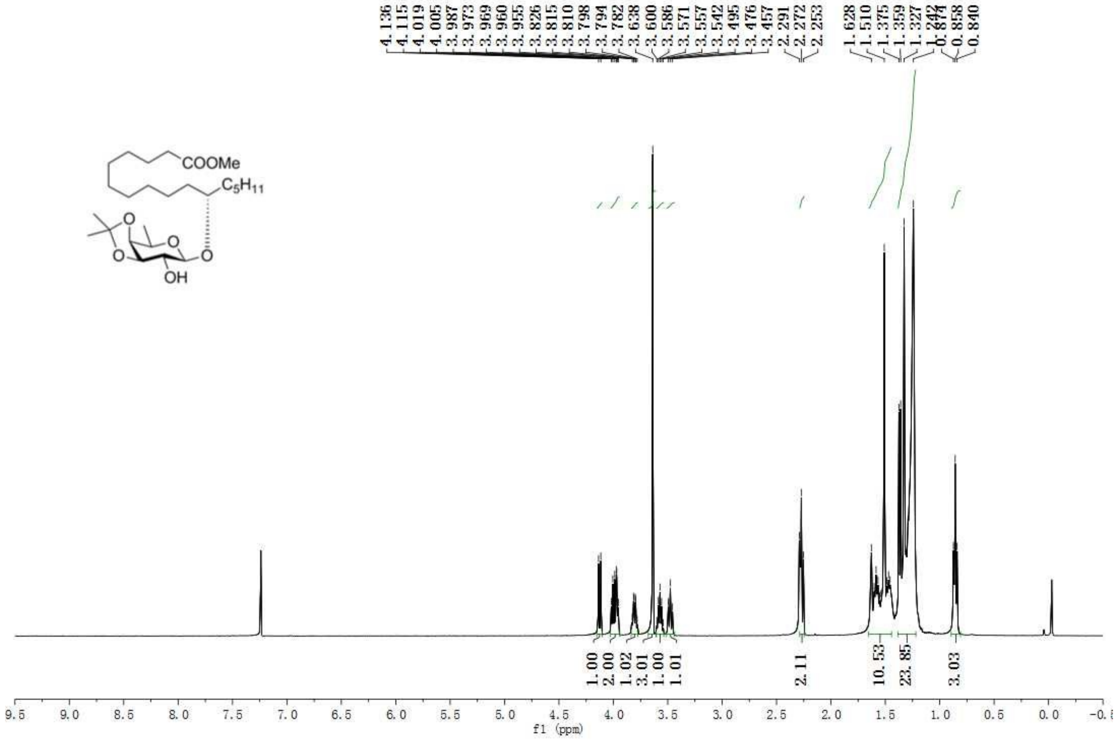

Figure S24. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **15**

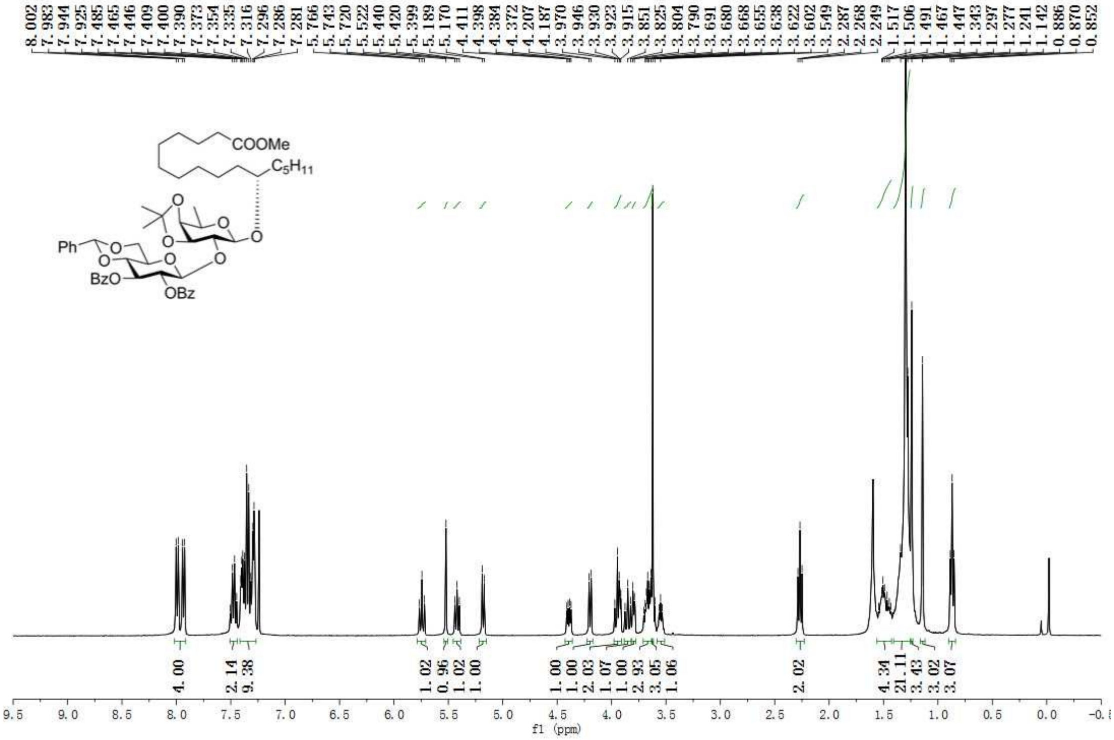

Figure S25. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **16**

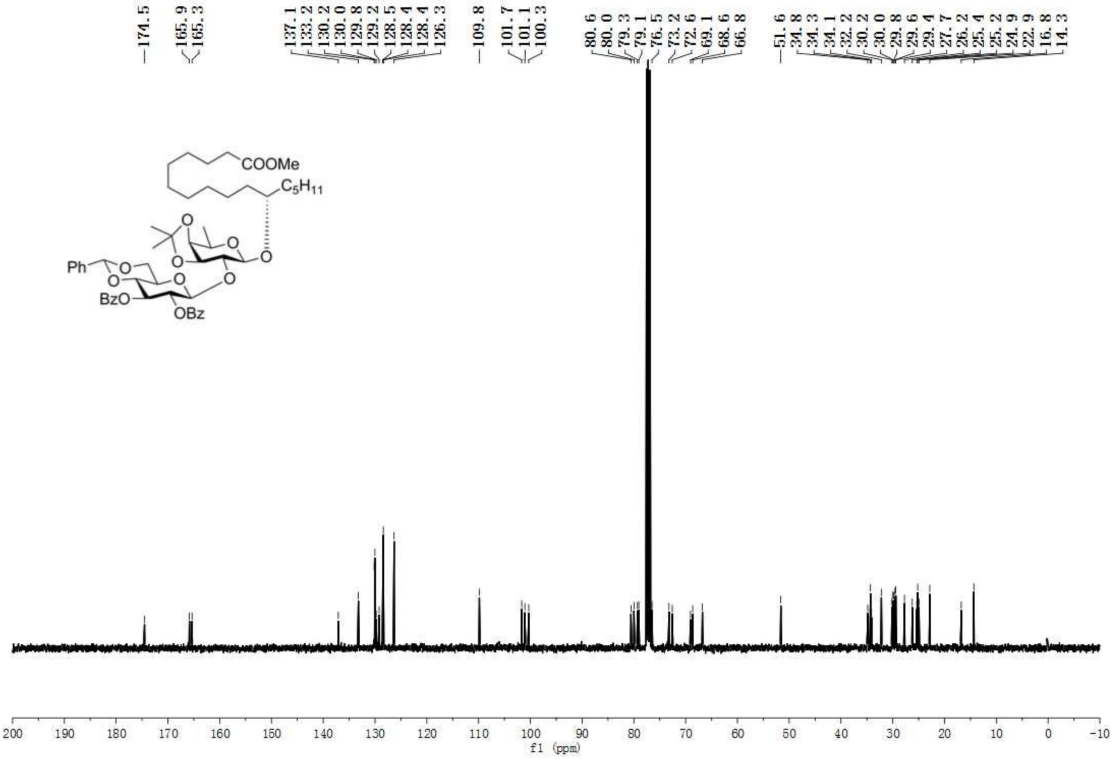

Figure S26. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **16**

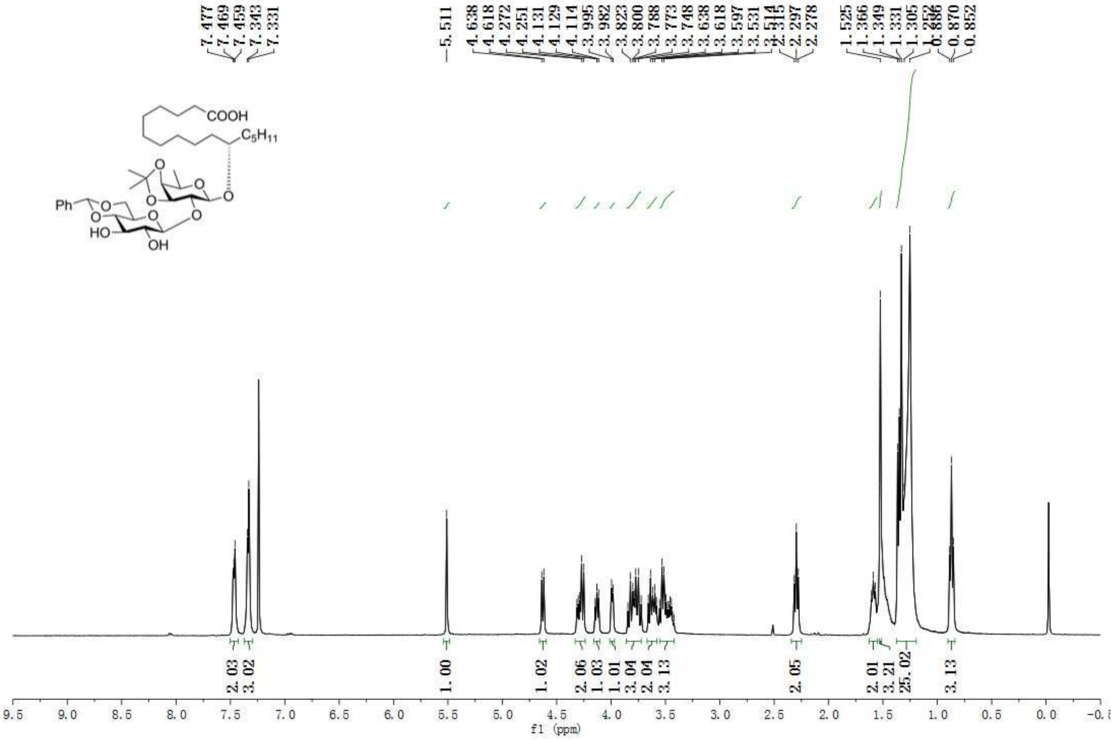

Figure S27. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **17**

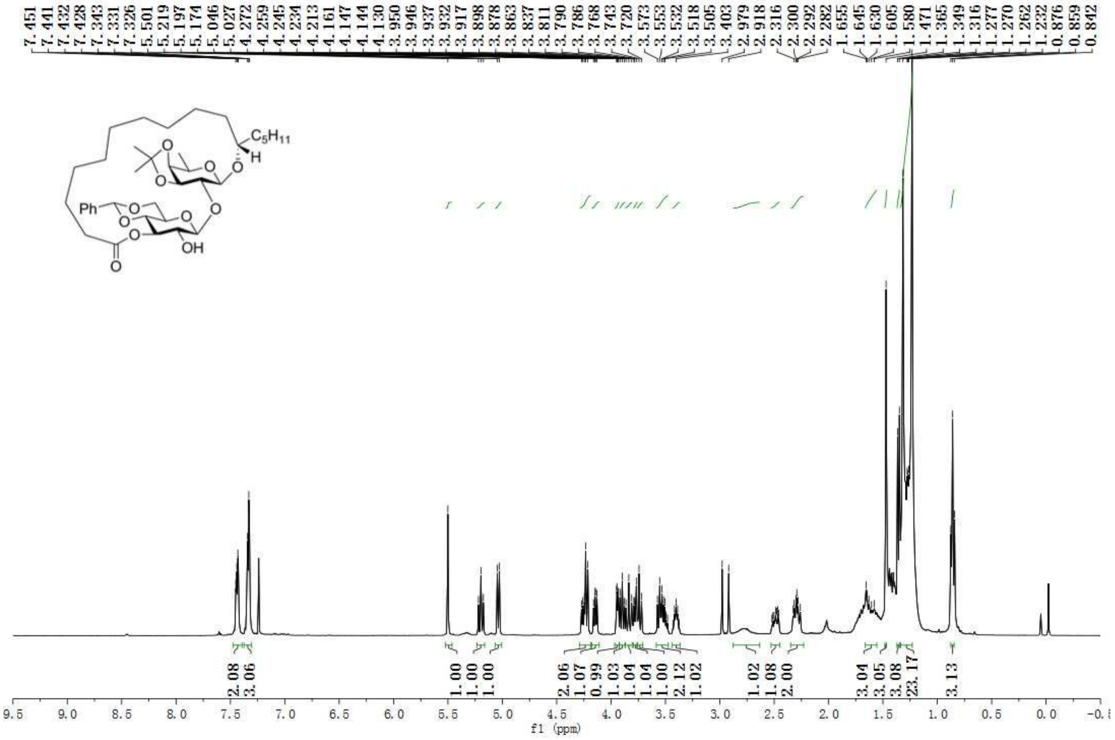

Figure S28. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **3**

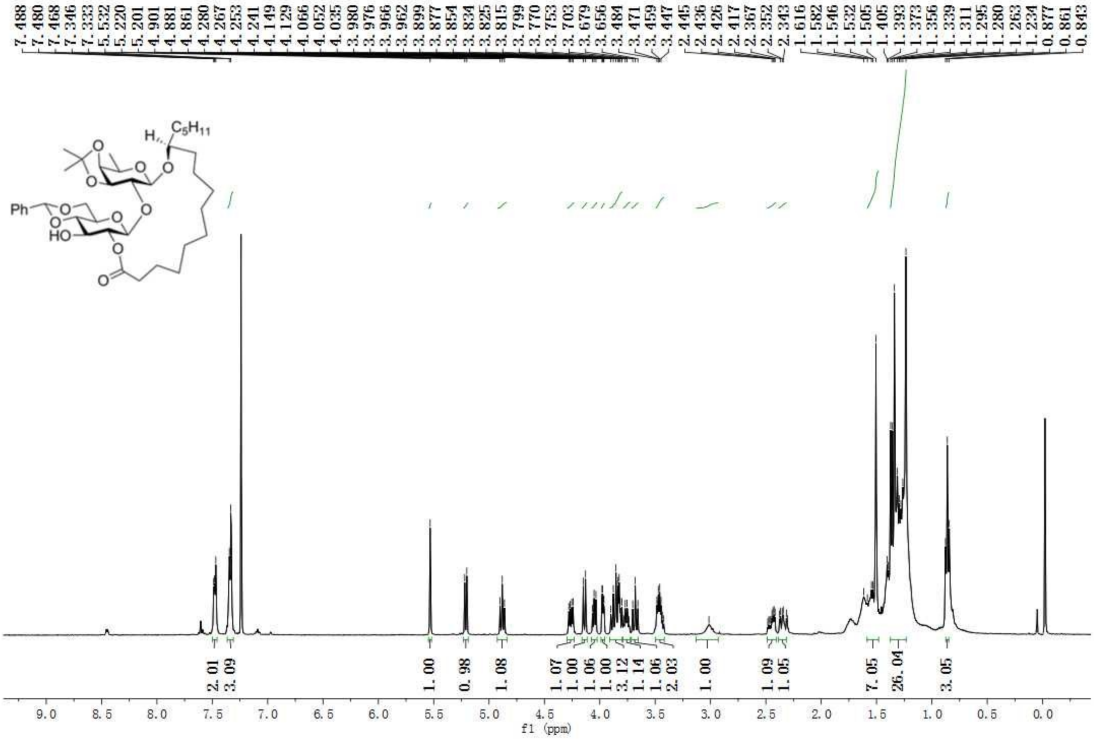

Figure S29. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **3'**

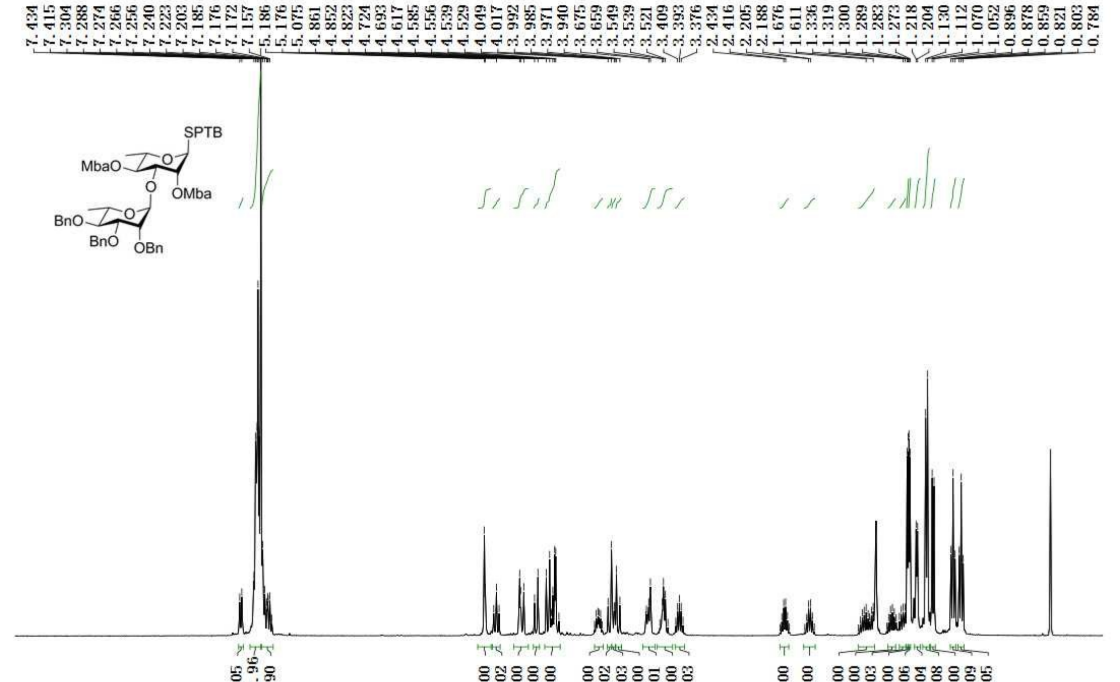

Figure S30. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **13**

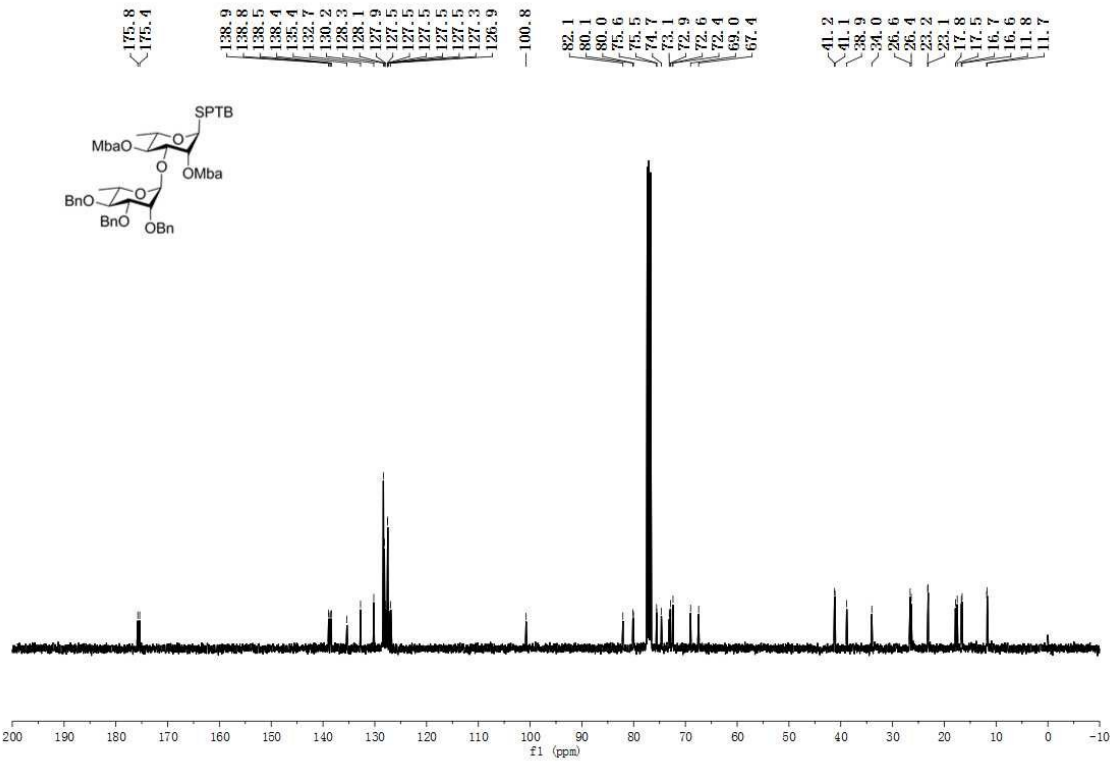

Figure S31. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **13**

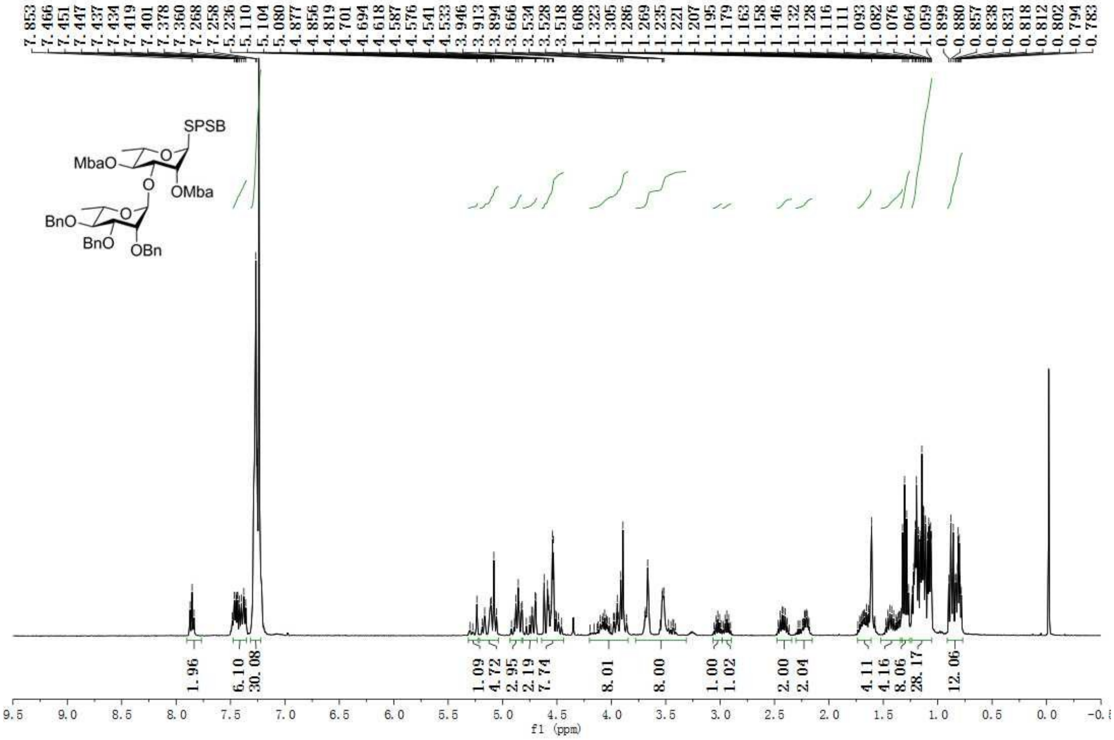

Figure S32. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **2a**

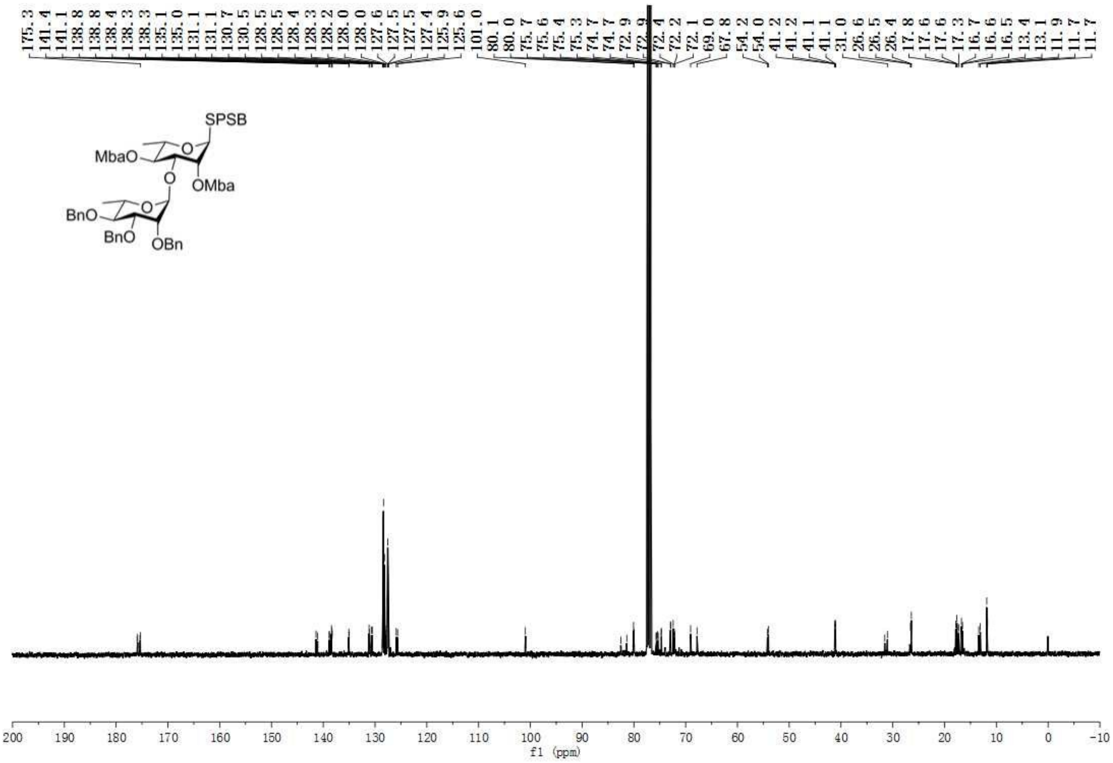

Figure S33. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **2a**

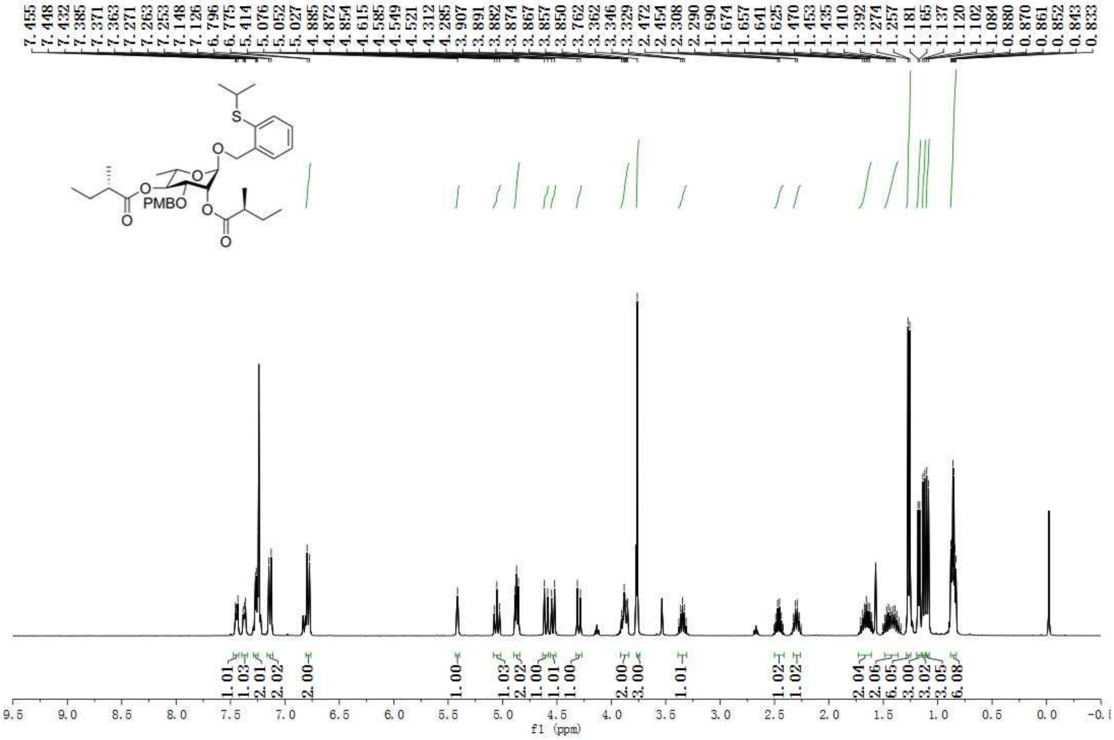

Figure S34. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **S4**

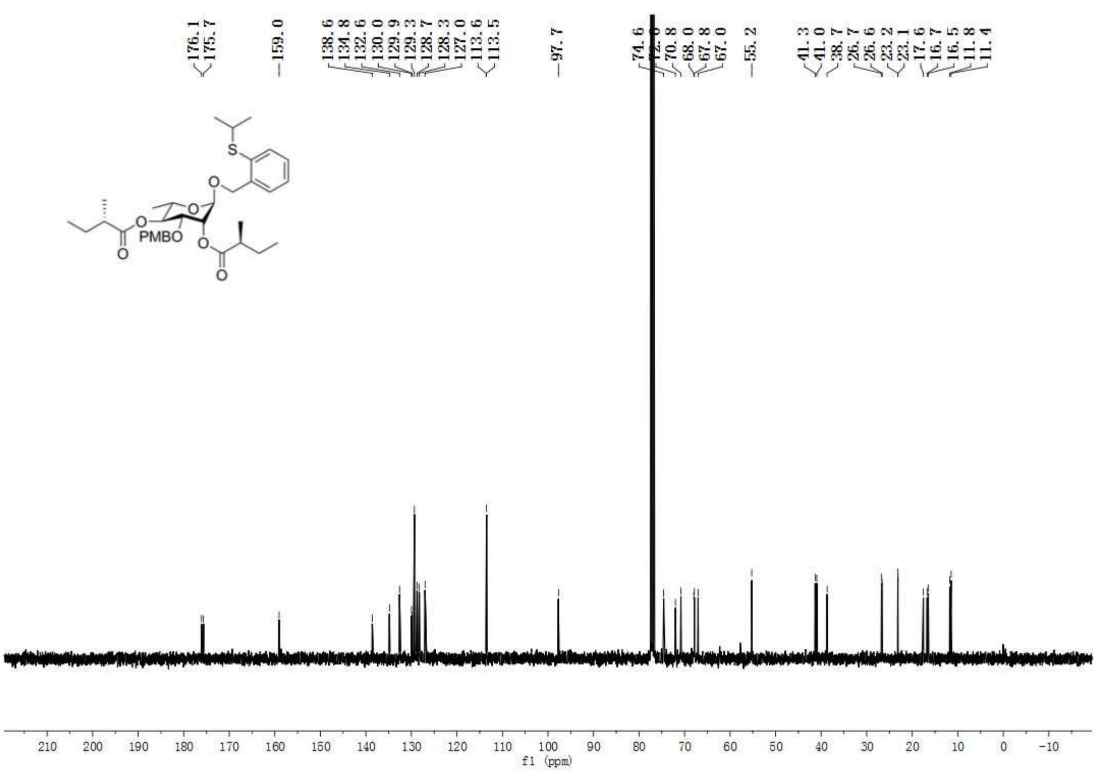

Figure S35. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **S4**

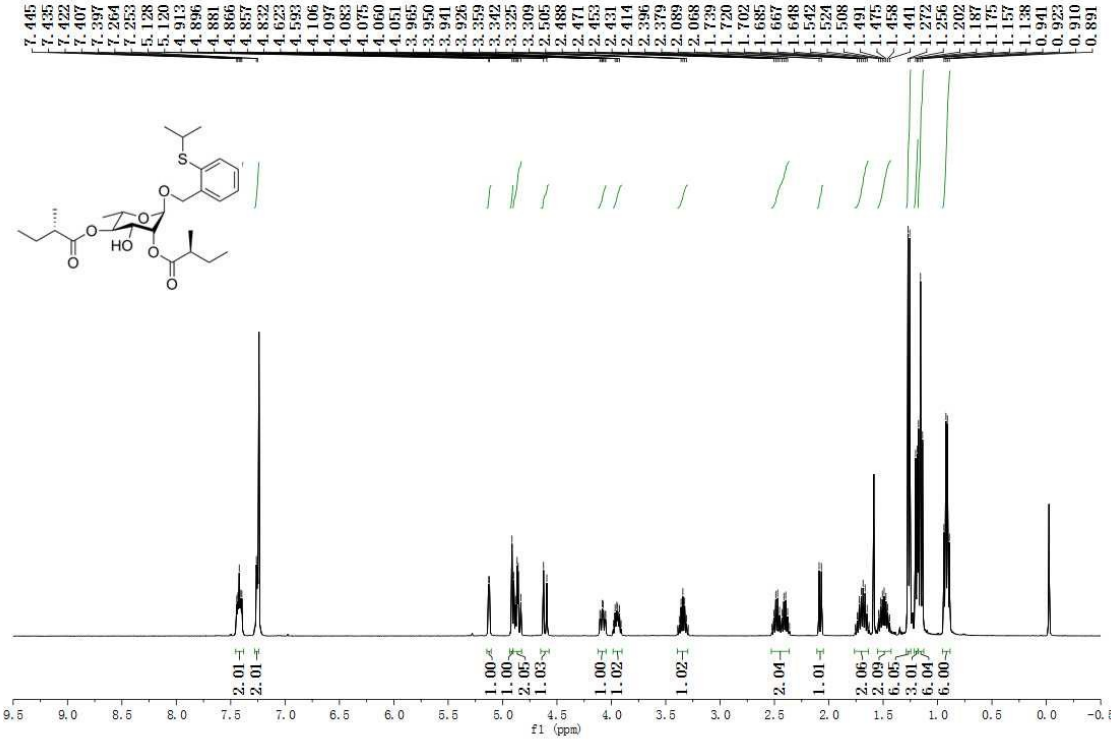

Figure S36. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **S5**

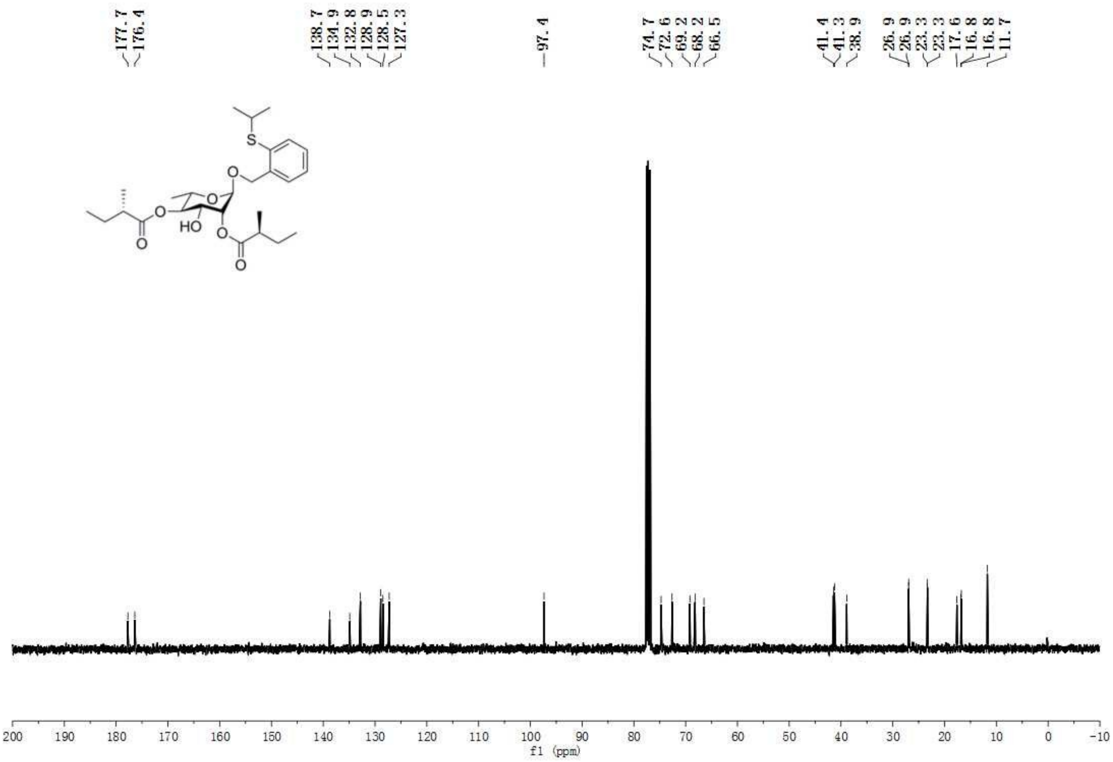

Figure S37. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **S5**

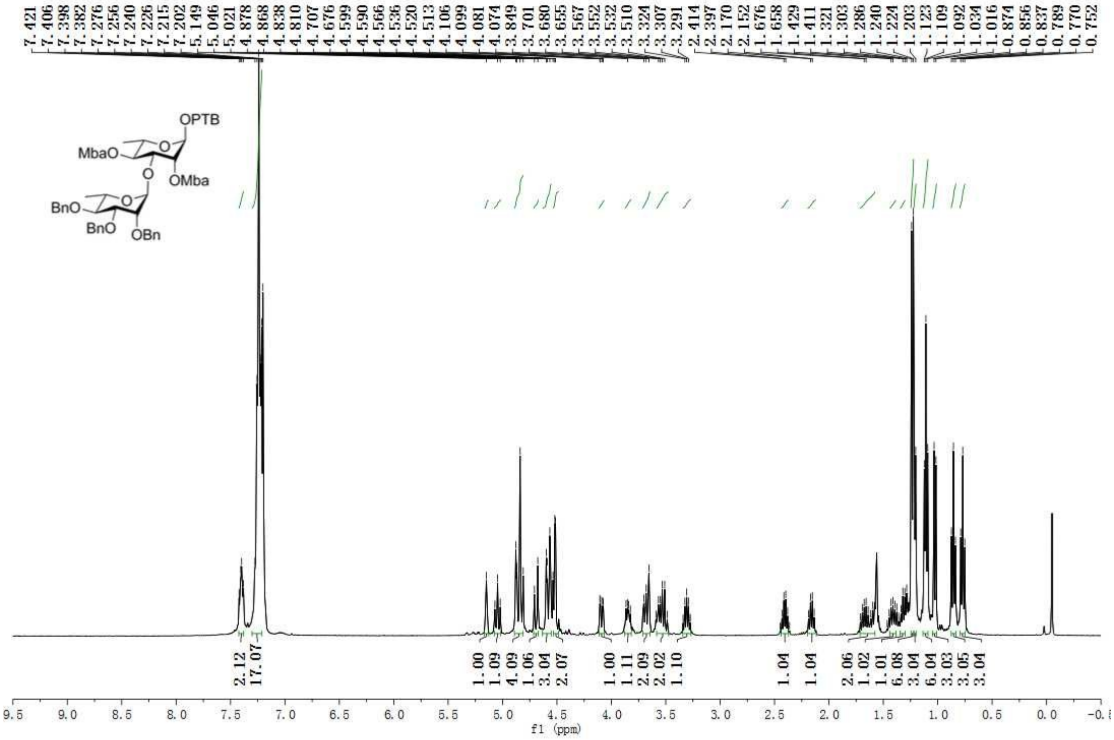

Figure S38. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **S6**

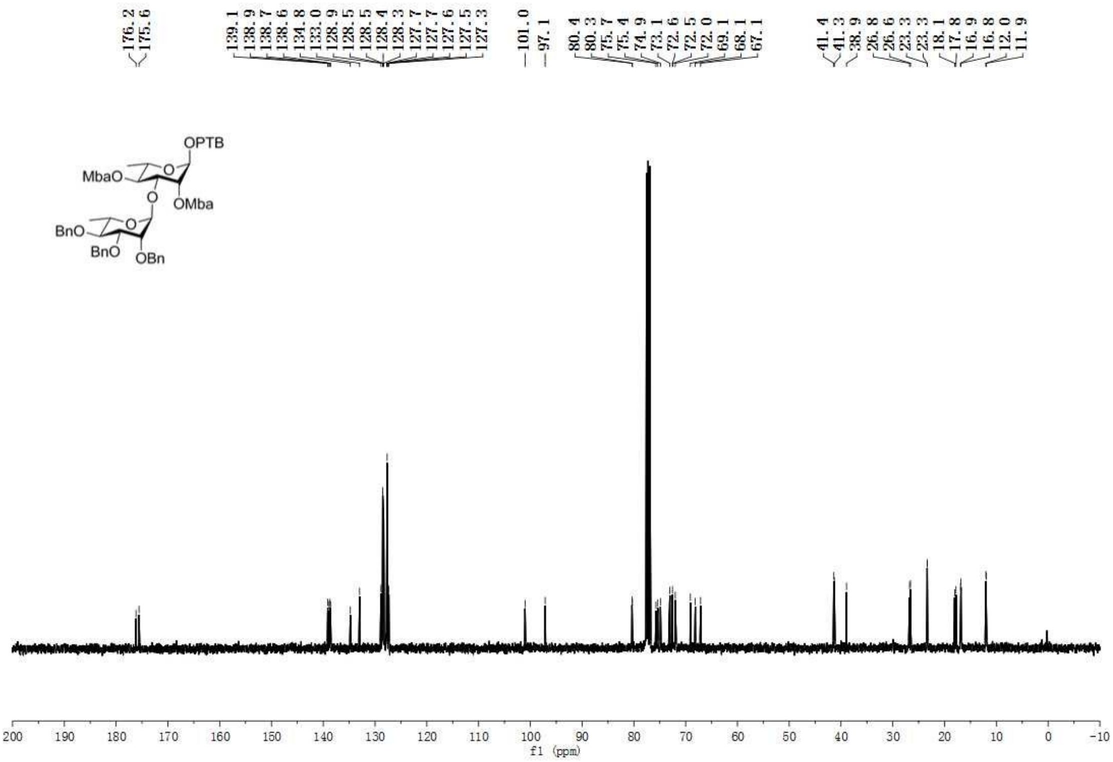

Figure S39. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **S6**

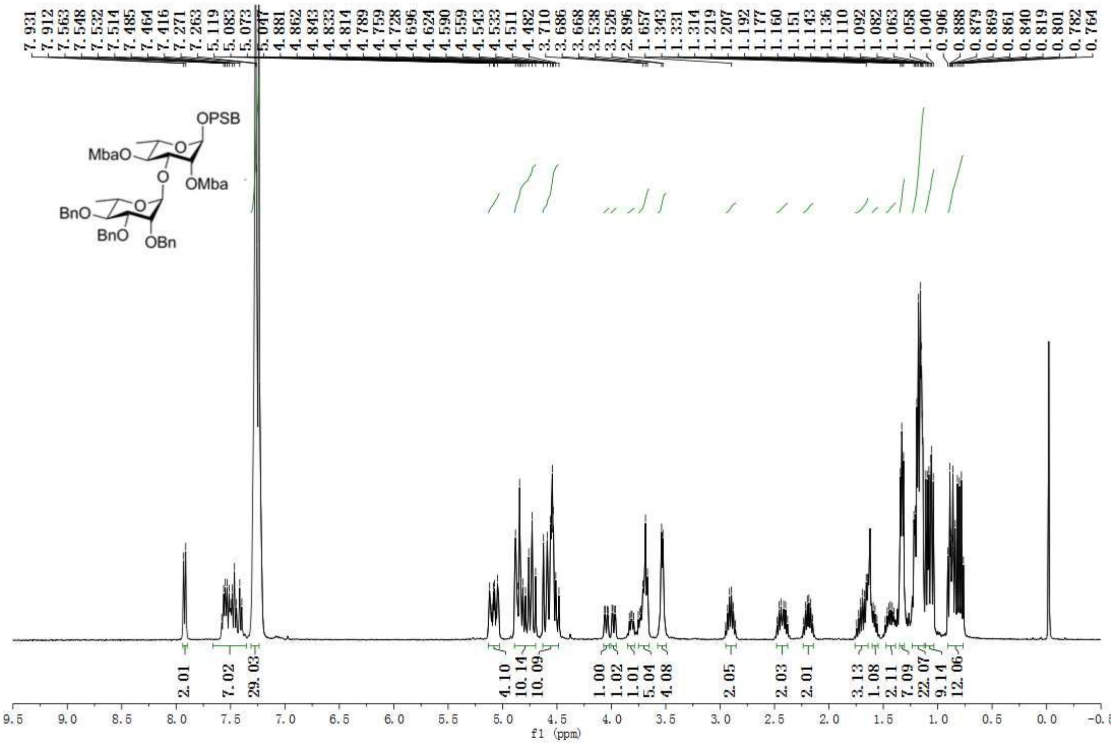

Figure S40. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **2b**

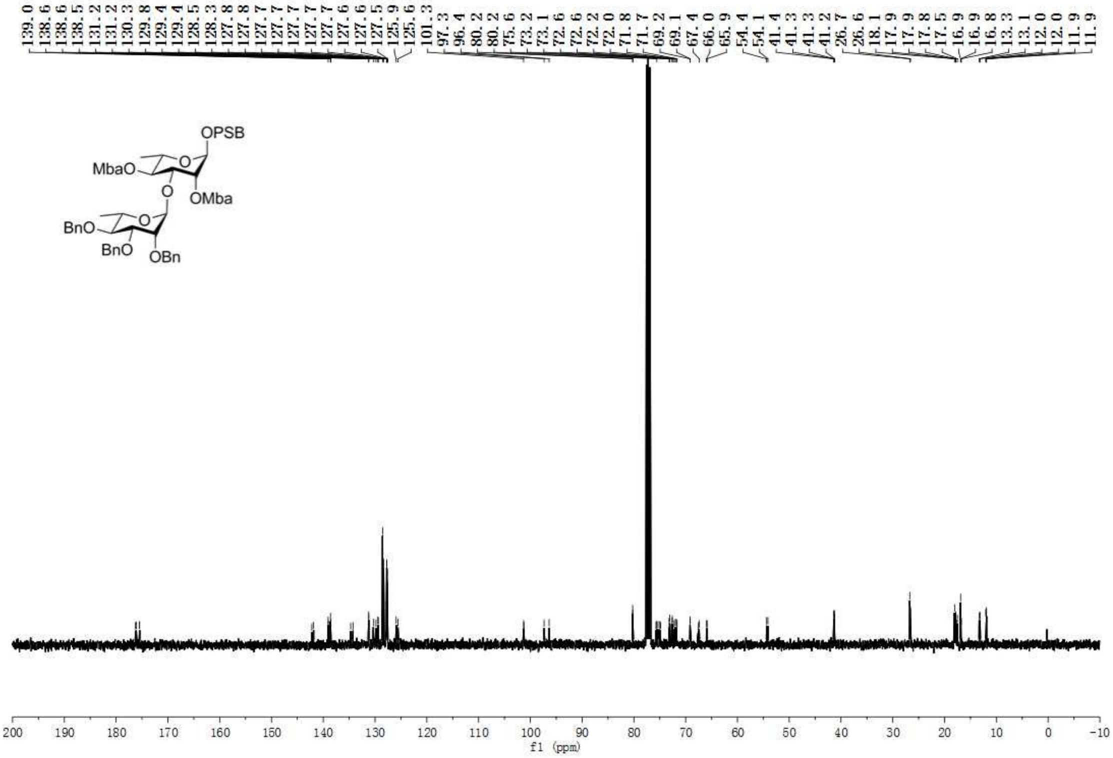

Figure S41. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **2b**

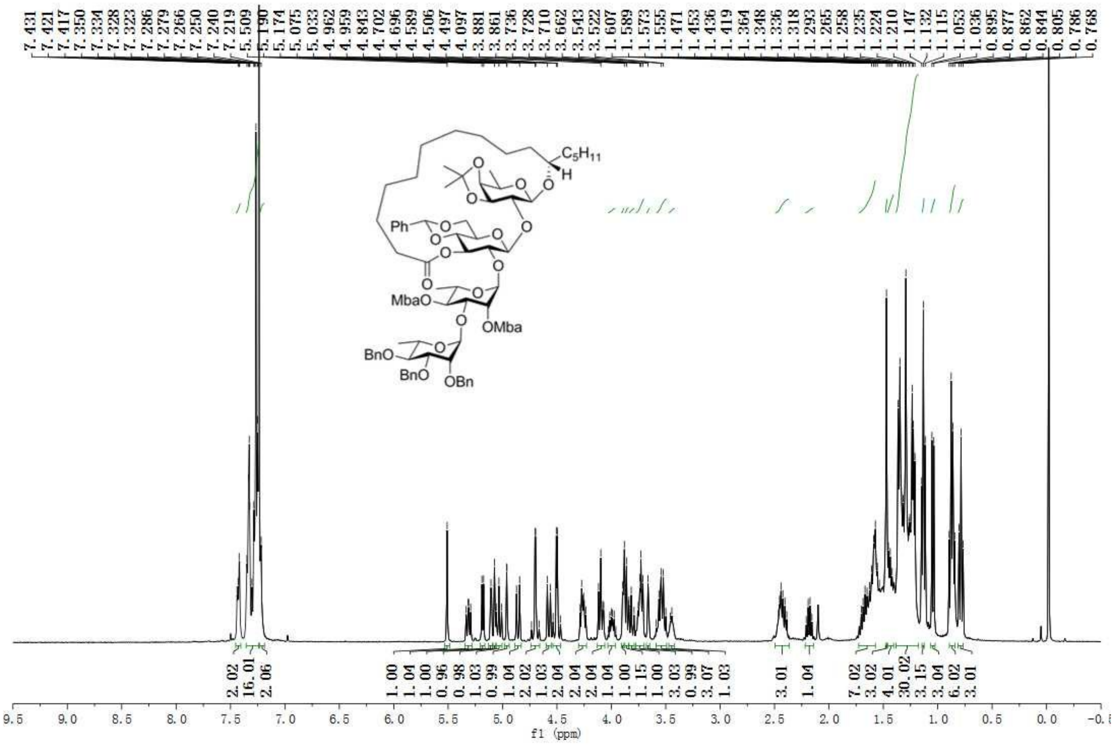

Figure S42. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **18α**

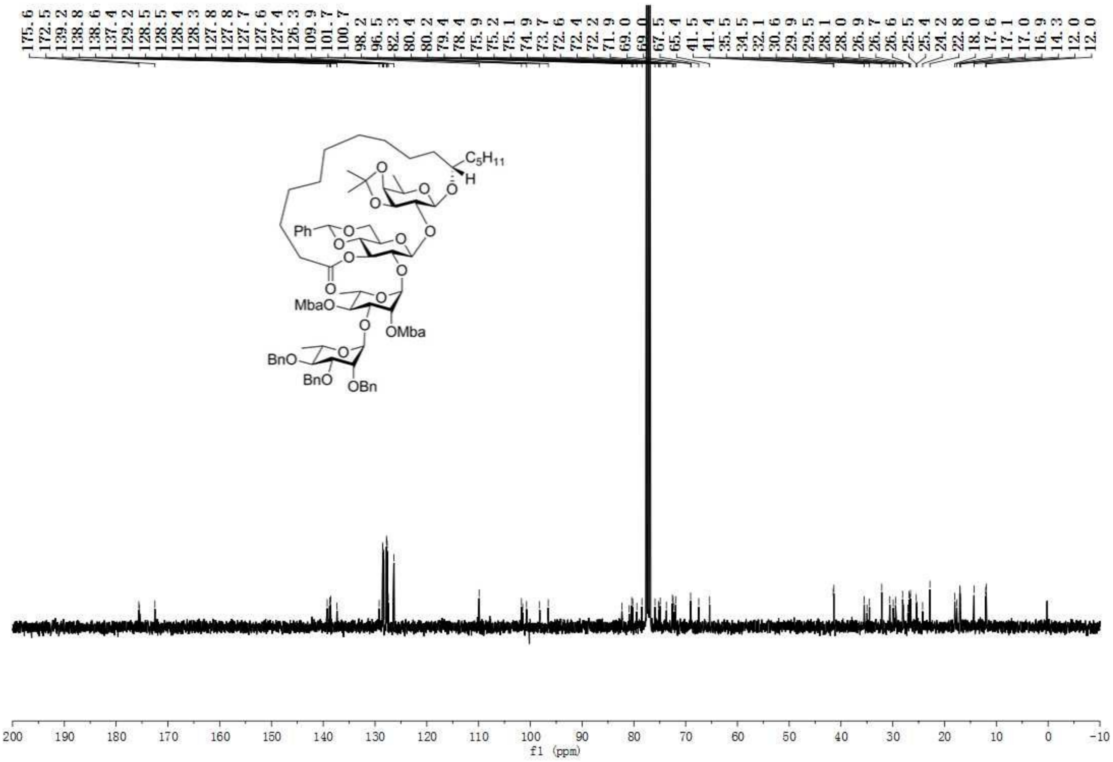

Figure S43. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **18α**

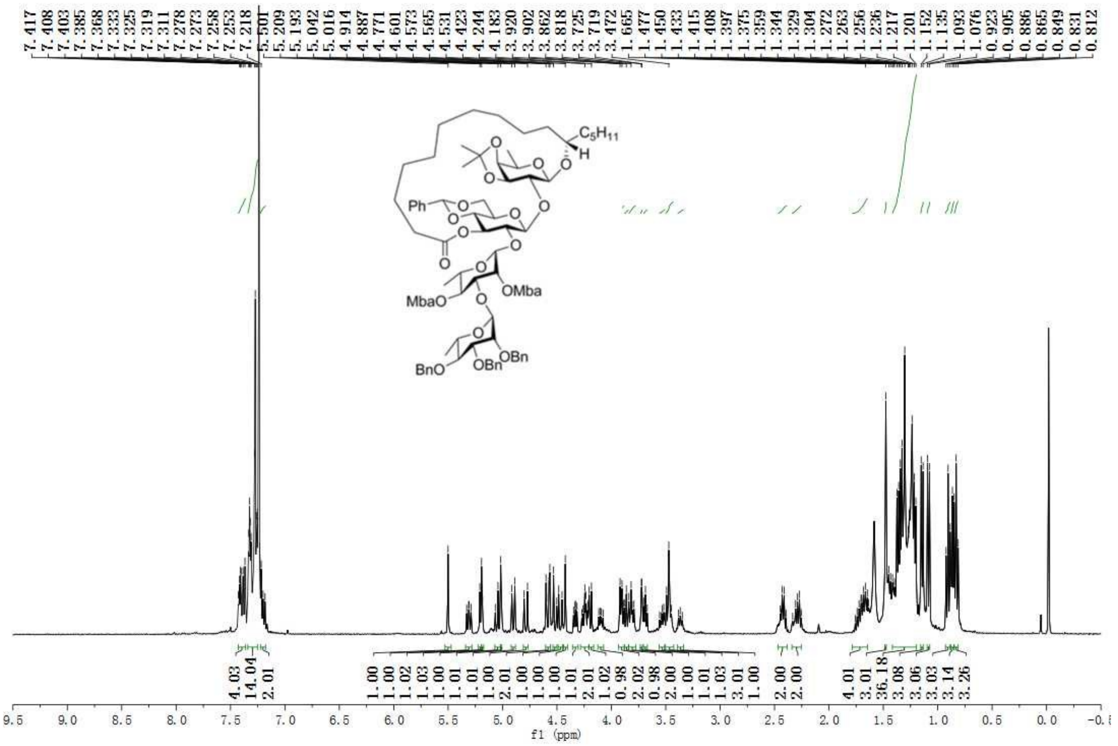

Figure S44. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **18β**

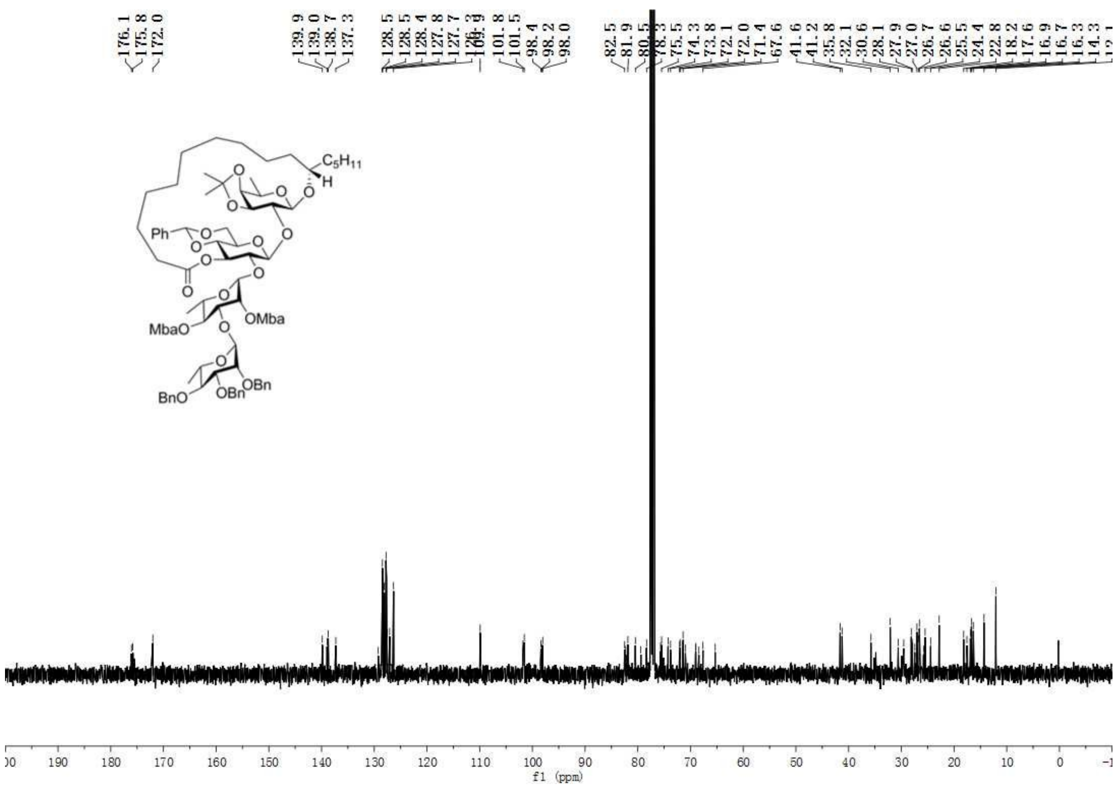

Figure S45. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **18β**

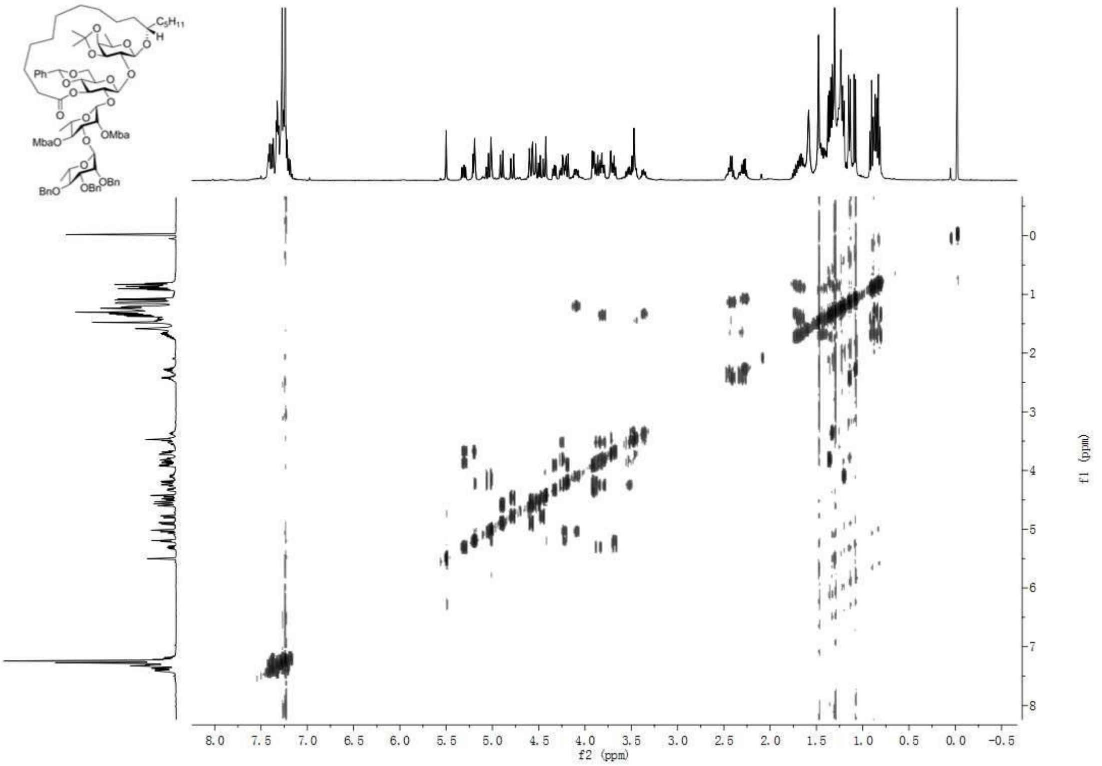

Figure S46. ^{1}H-^{1}H COSY spectrum of **18β**

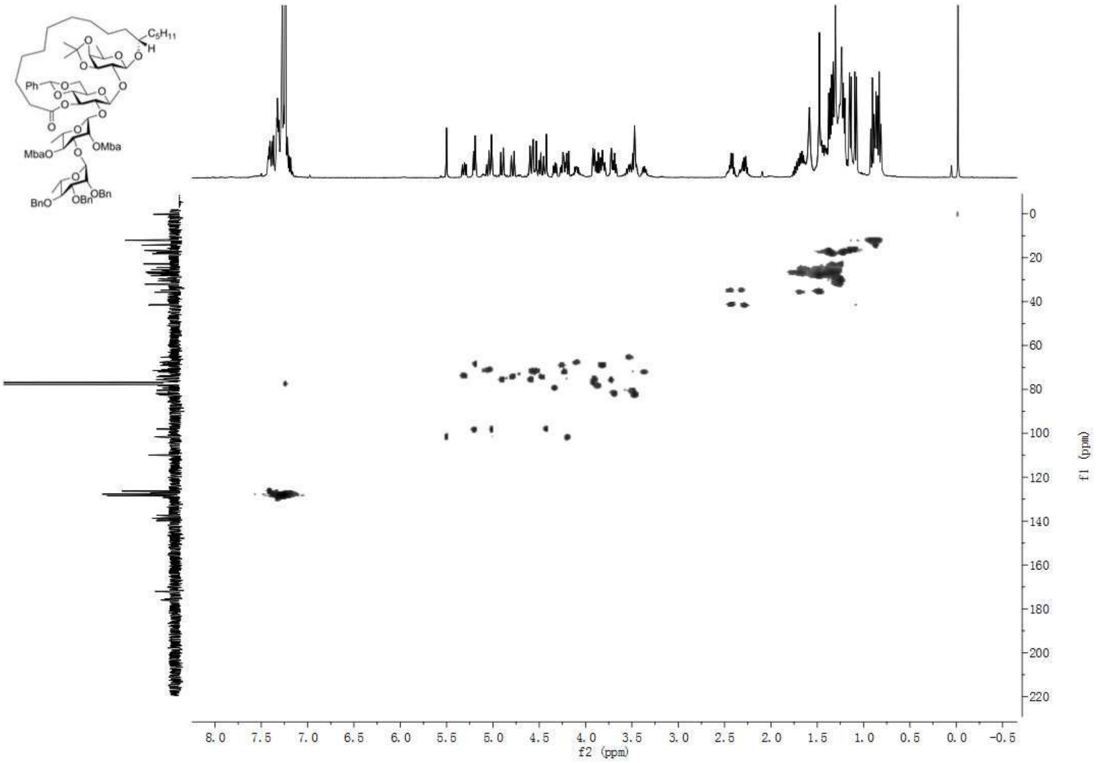

Figure S47. HSQC spectrum of **18β**

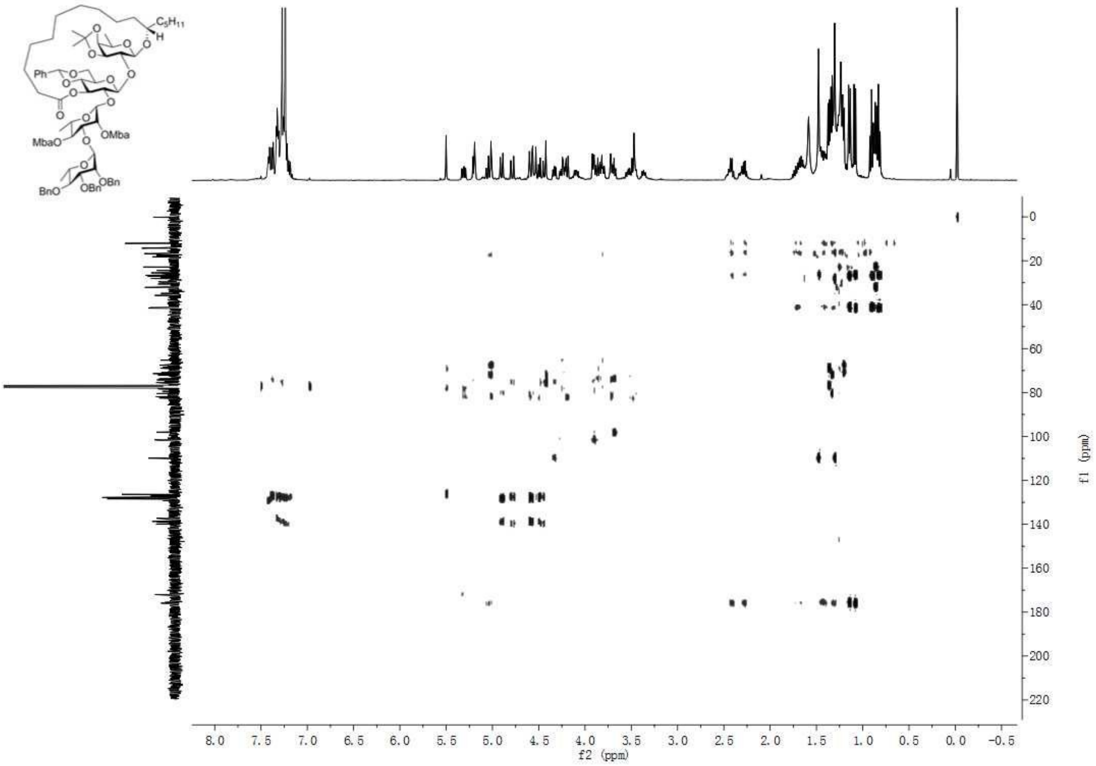

Figure S48. HMBC spectrum of **18β**

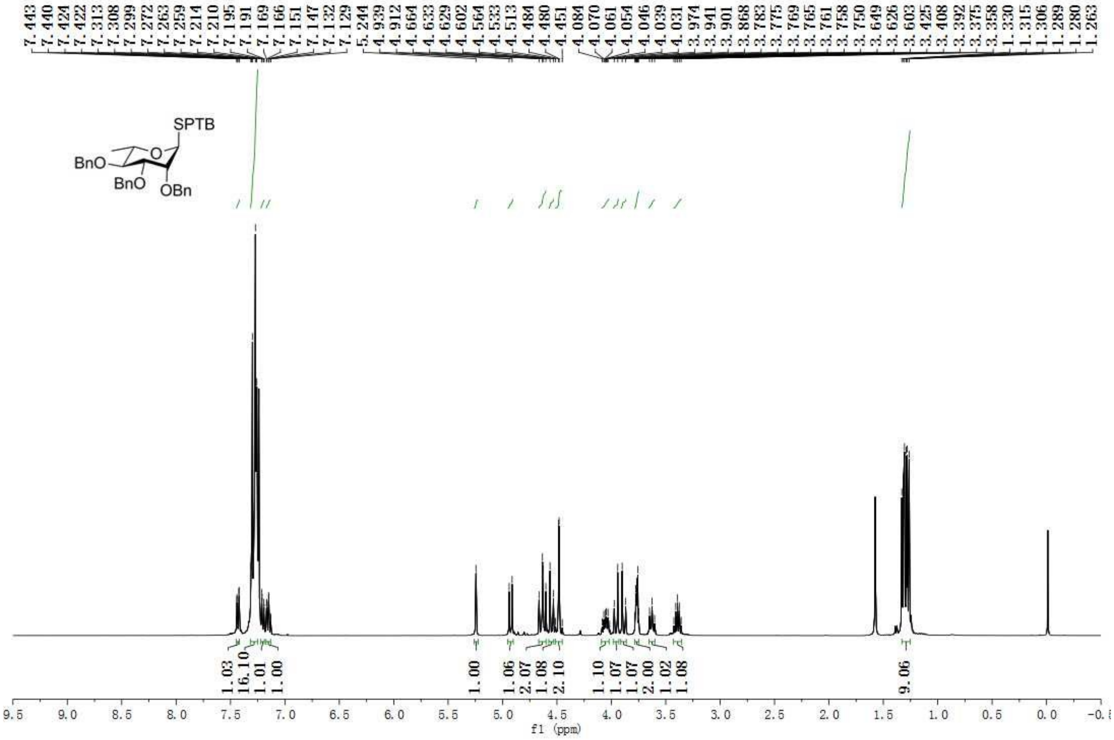

Figure S49. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **S9**

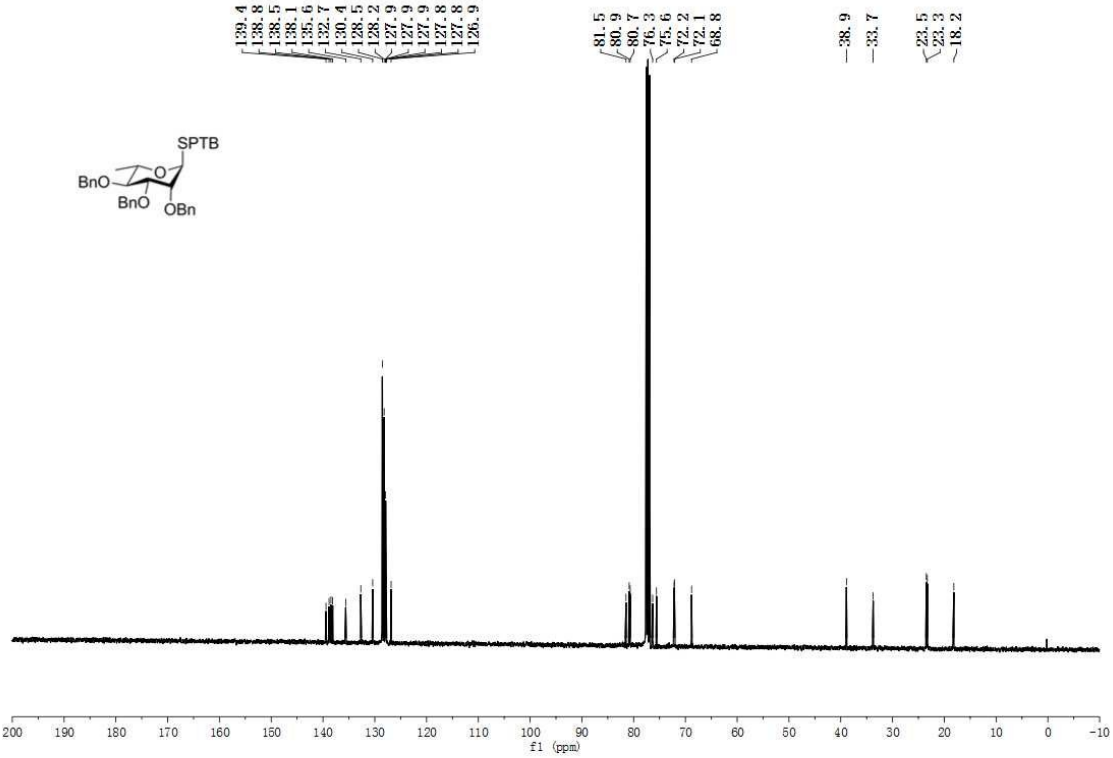

Figure S50. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **S9**

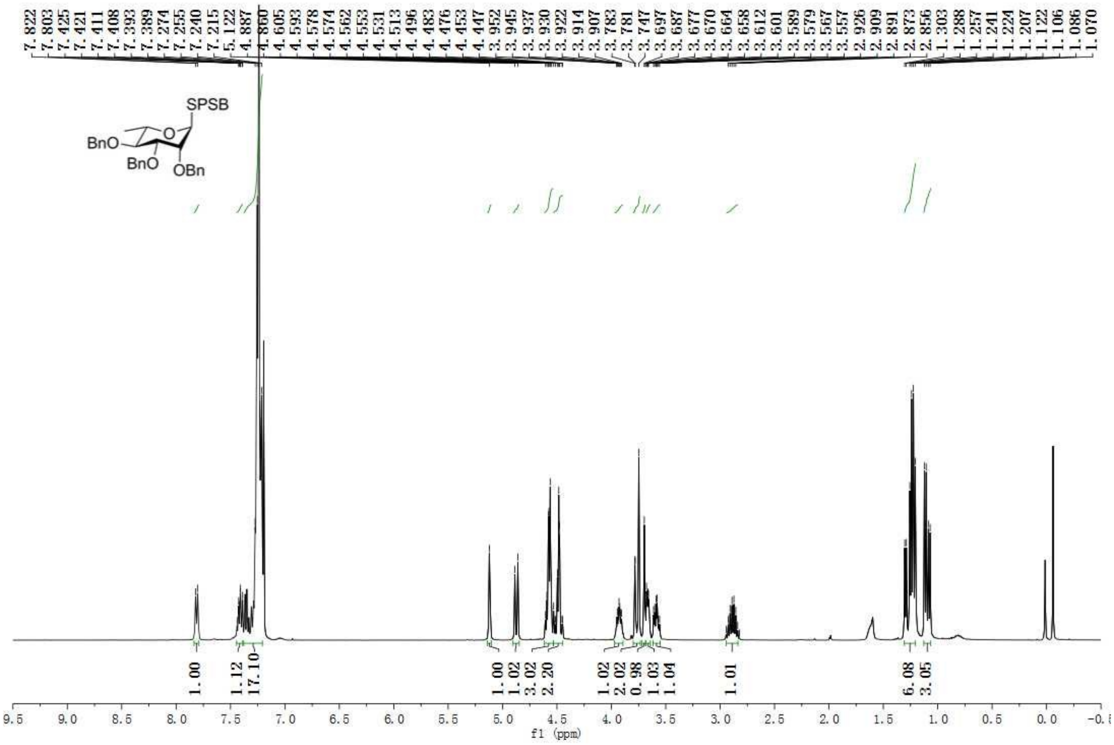

Figure S51. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **20**

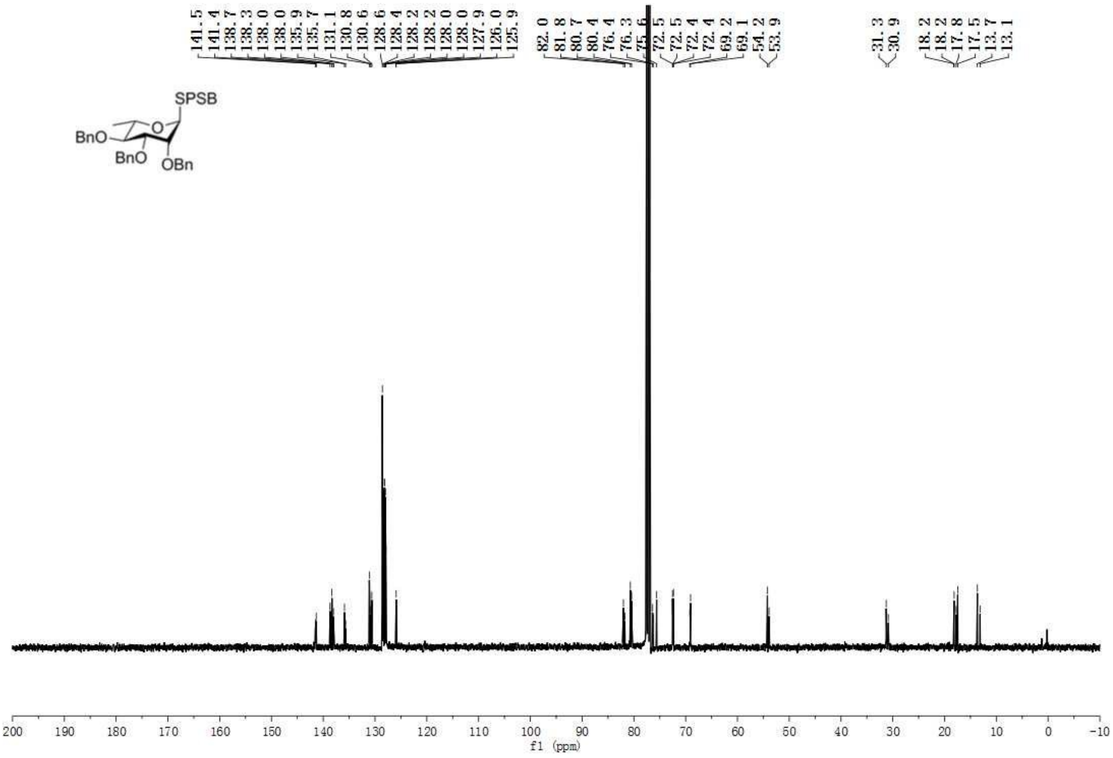

Figure S52. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **20**

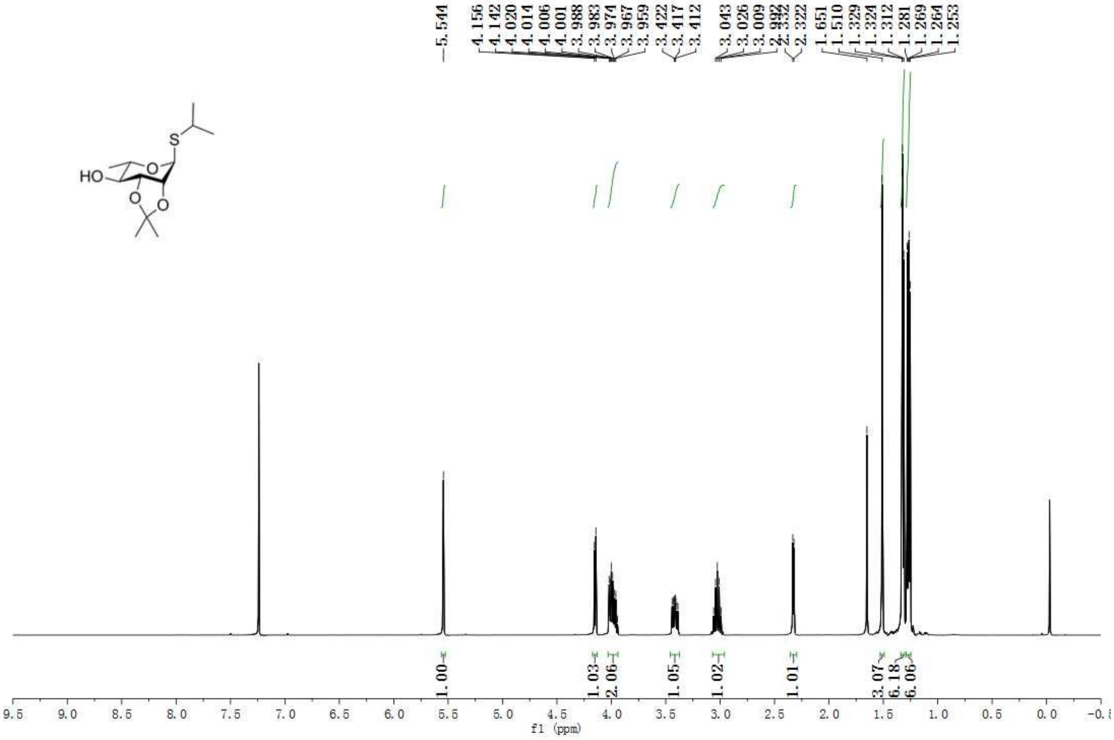

Figure S53. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **S11**

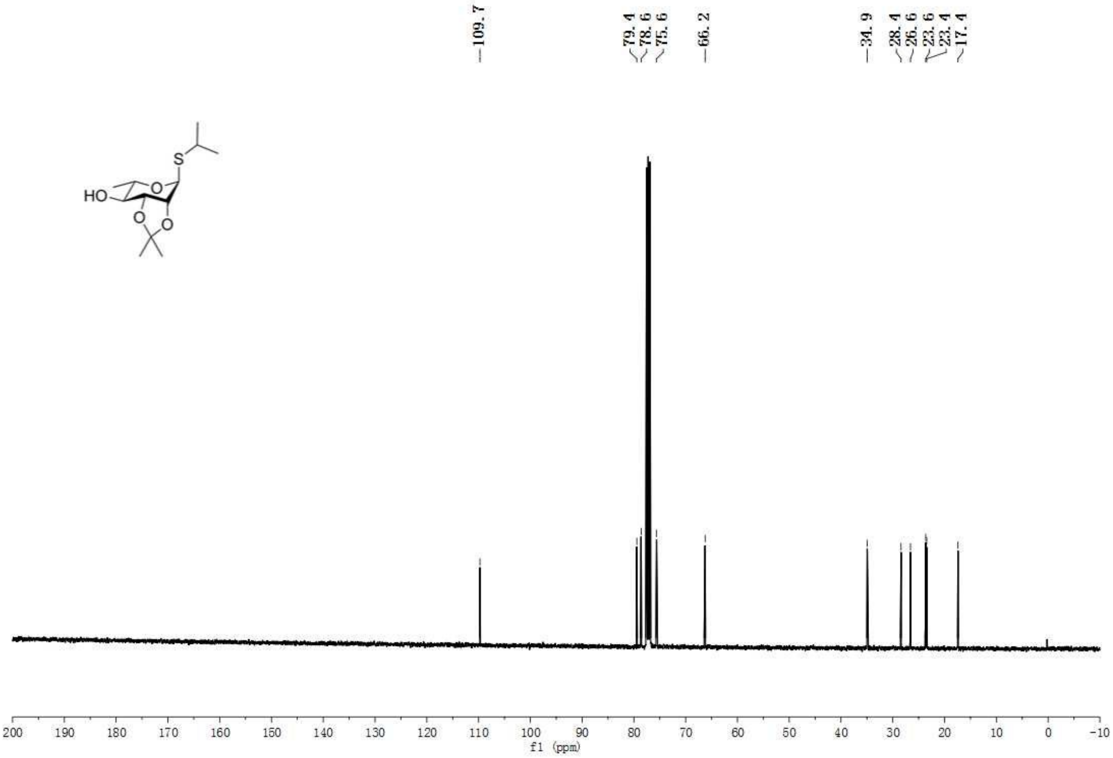

Figure S54. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **S11**

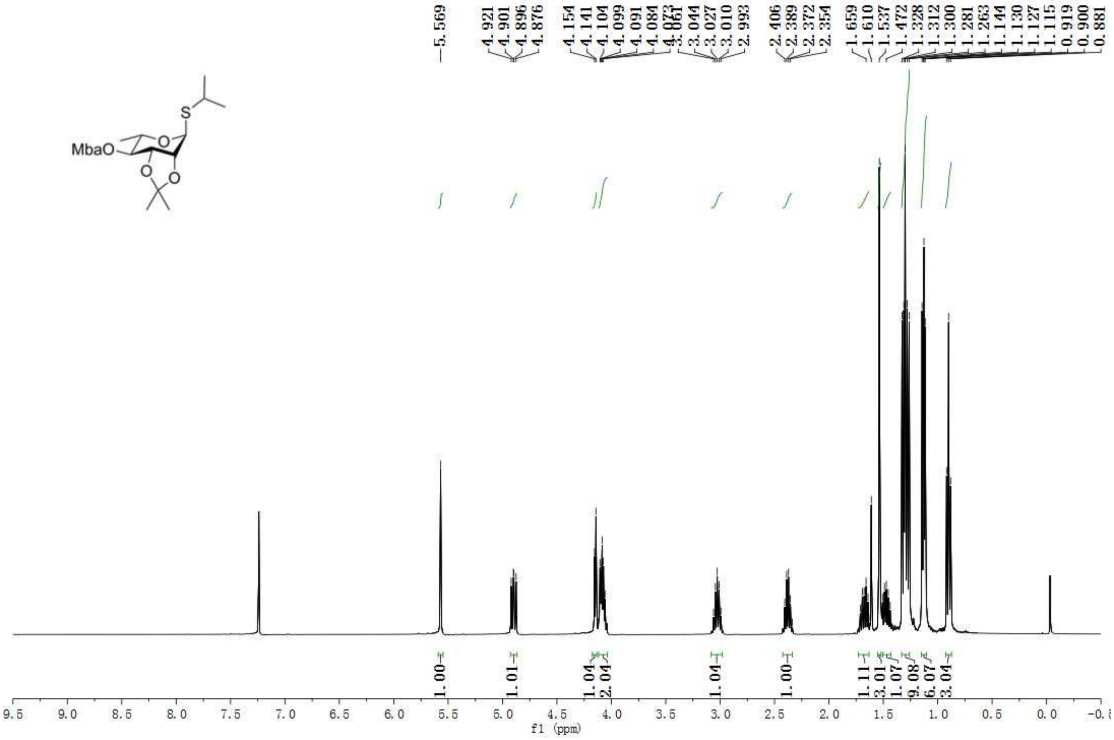

Figure S55. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **S12**

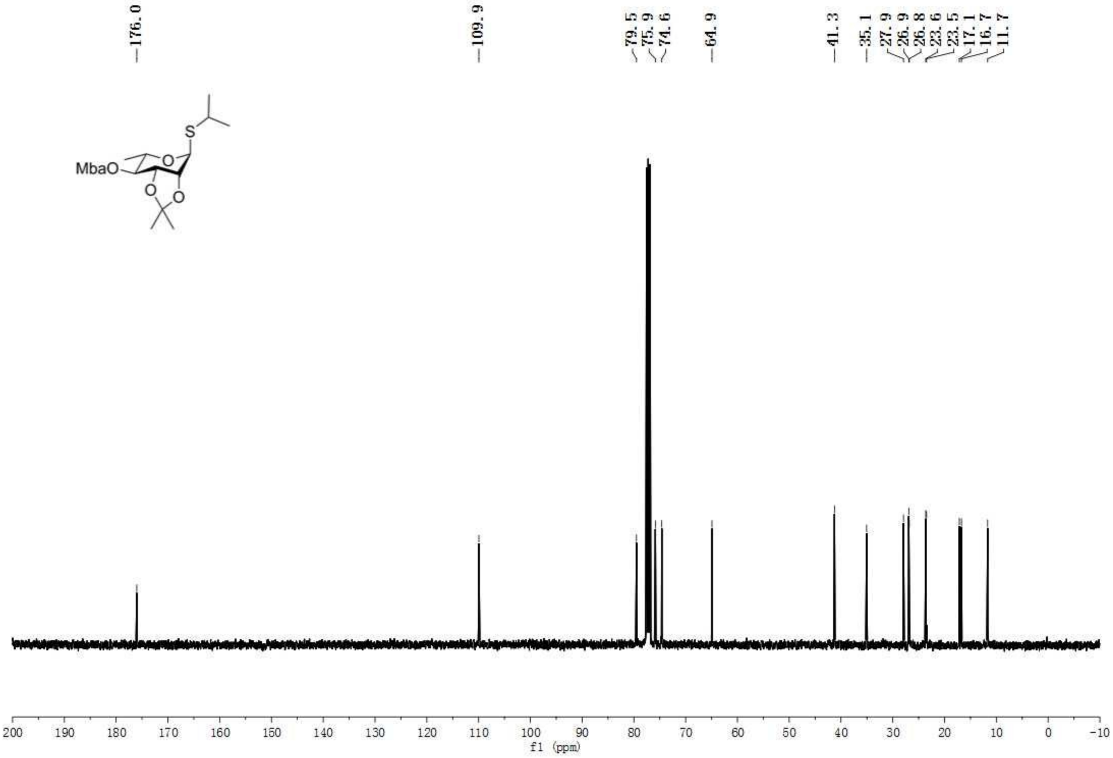

Figure S56. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **S12**

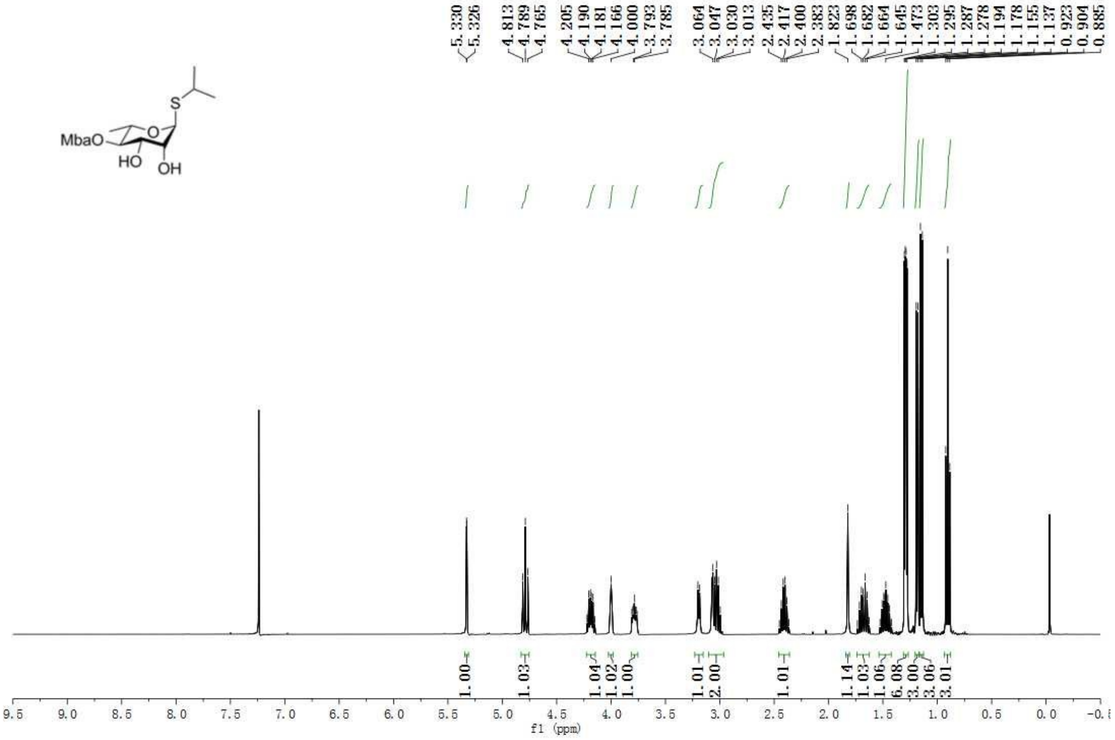

Figure S57. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **S13**

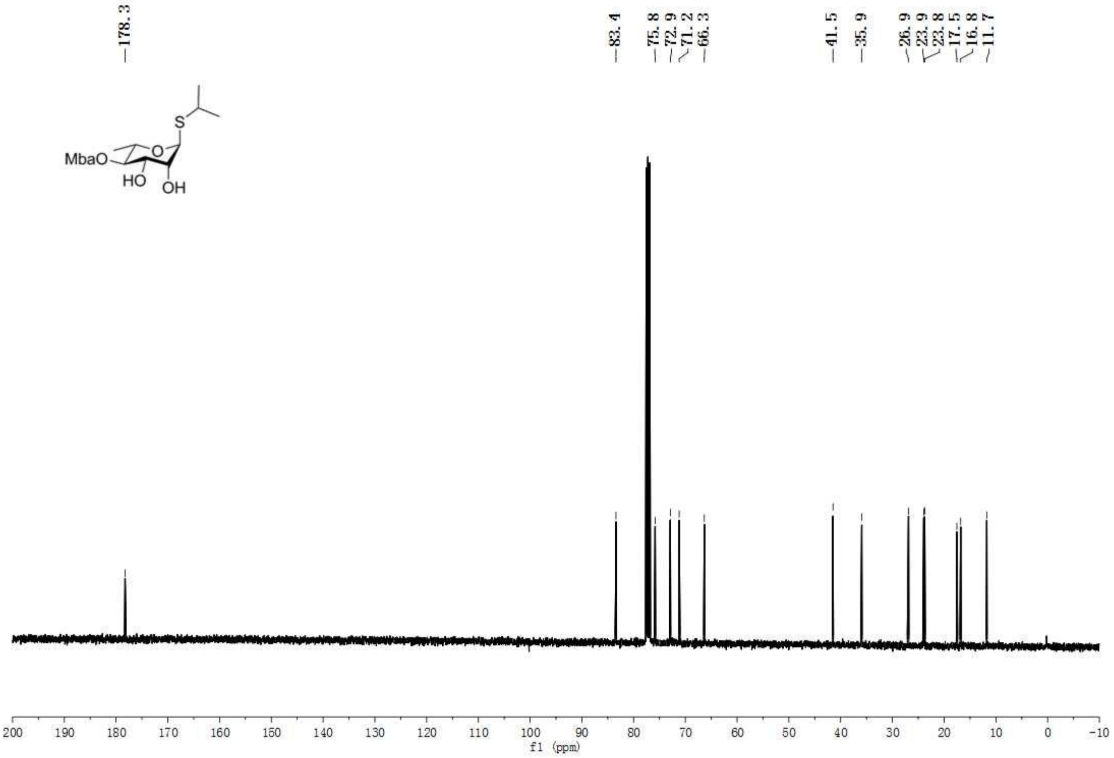

Figure S58. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **S13**

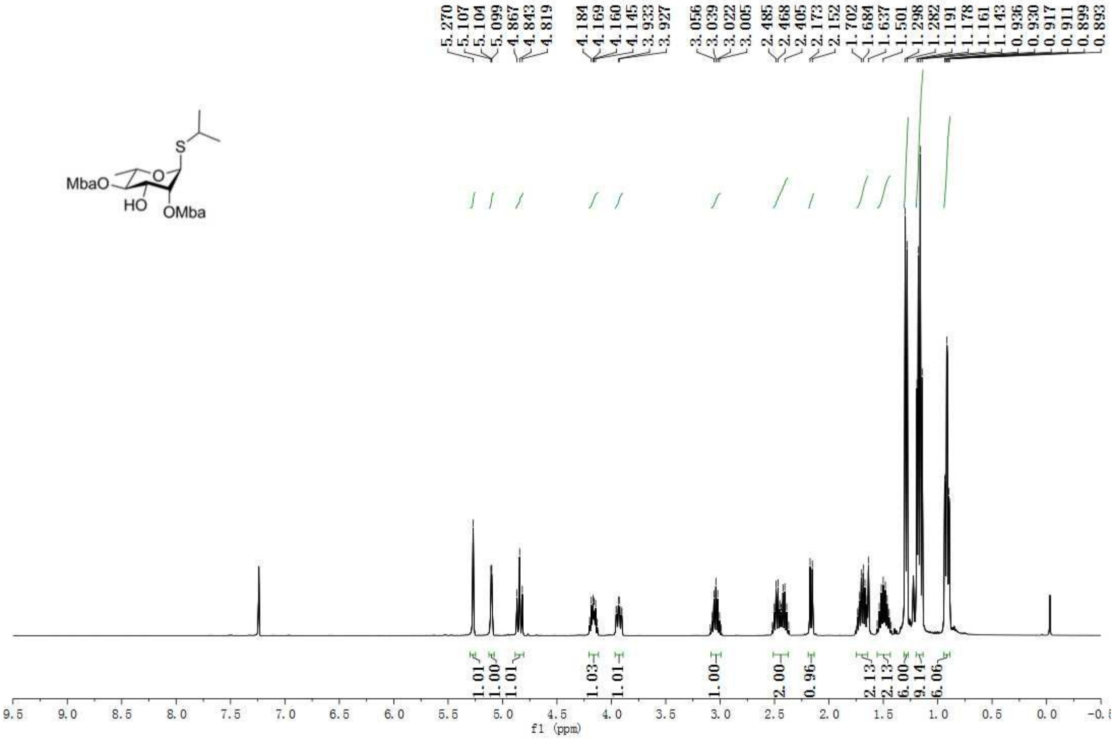

Figure S59. ^{1}H NMR (400 MHz, CDCl$_3$) spectrum of **21**

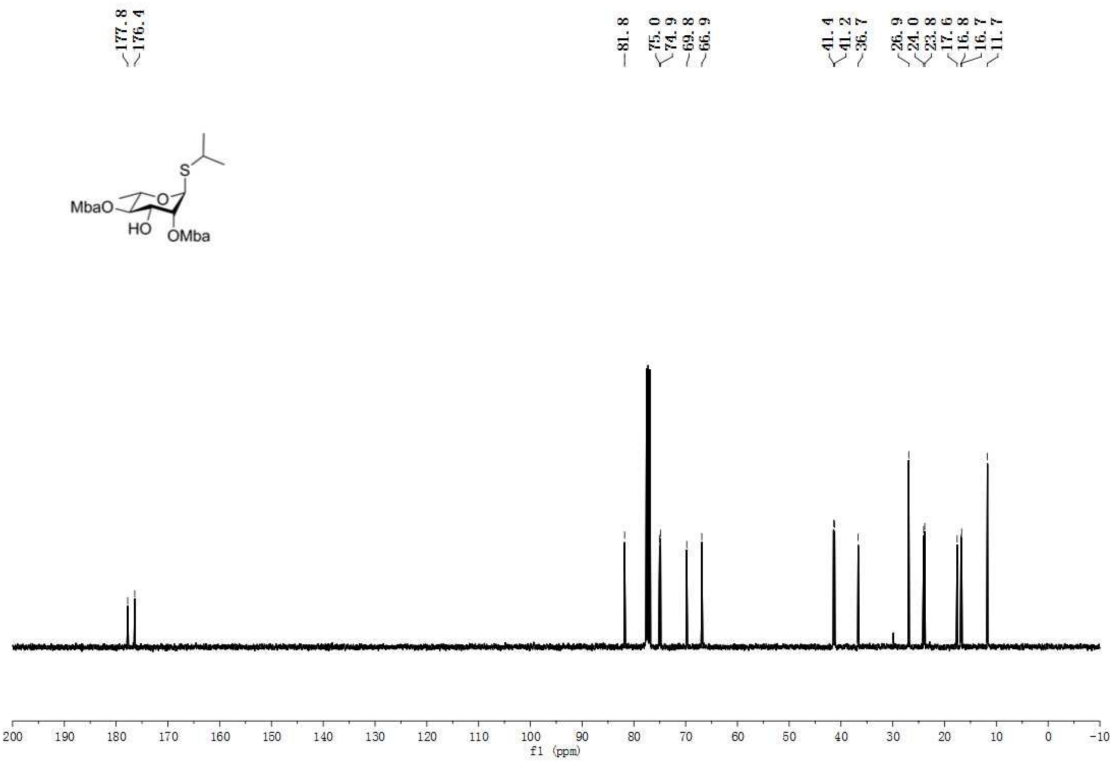

Figure S60. ^{13}C NMR (100 MHz, CDCl$_3$) spectrum of **21**

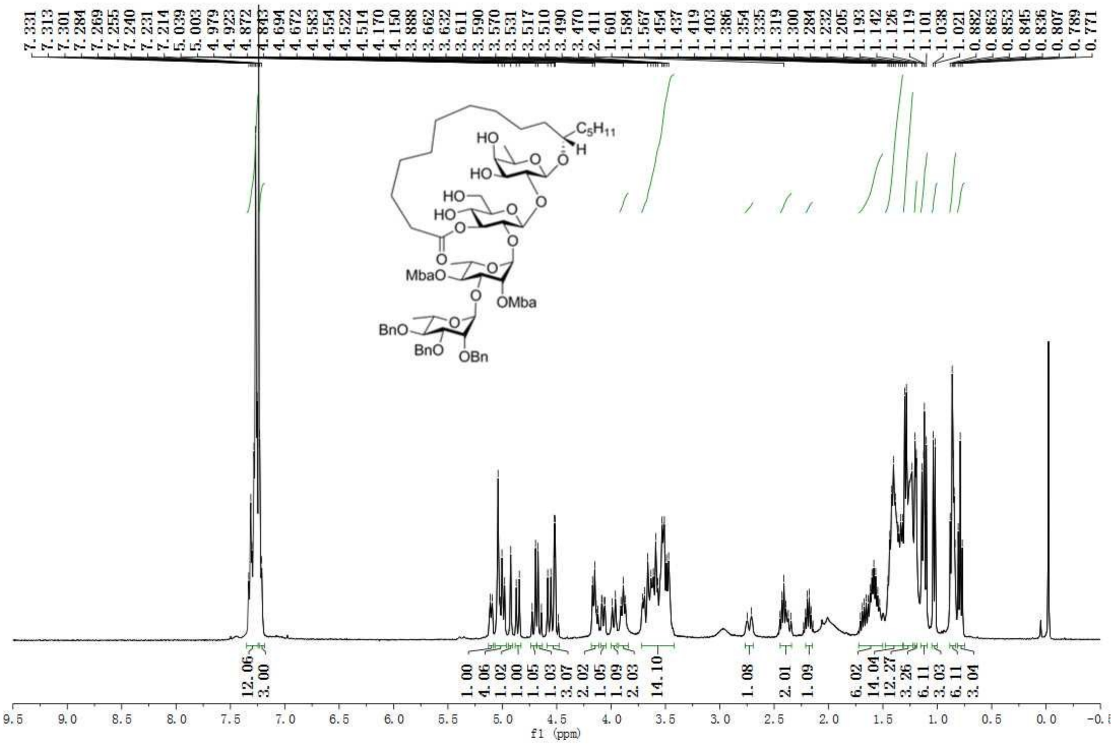

Figure S61. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **19**

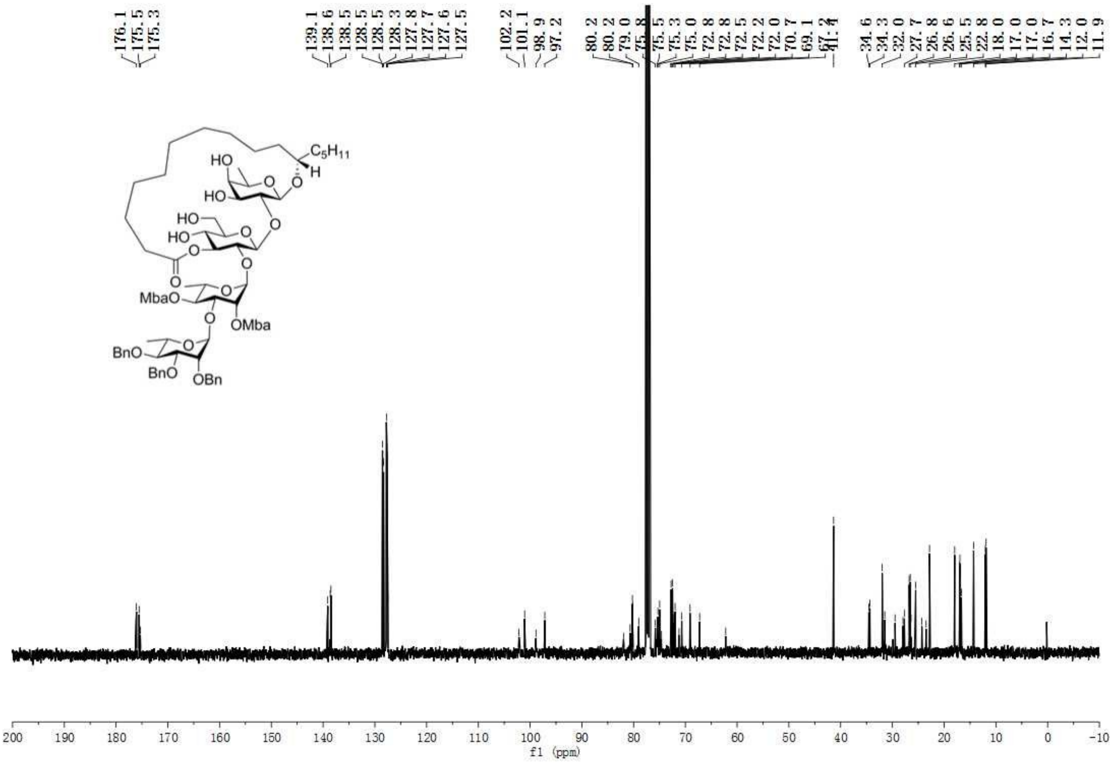

Figure S62. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **19**

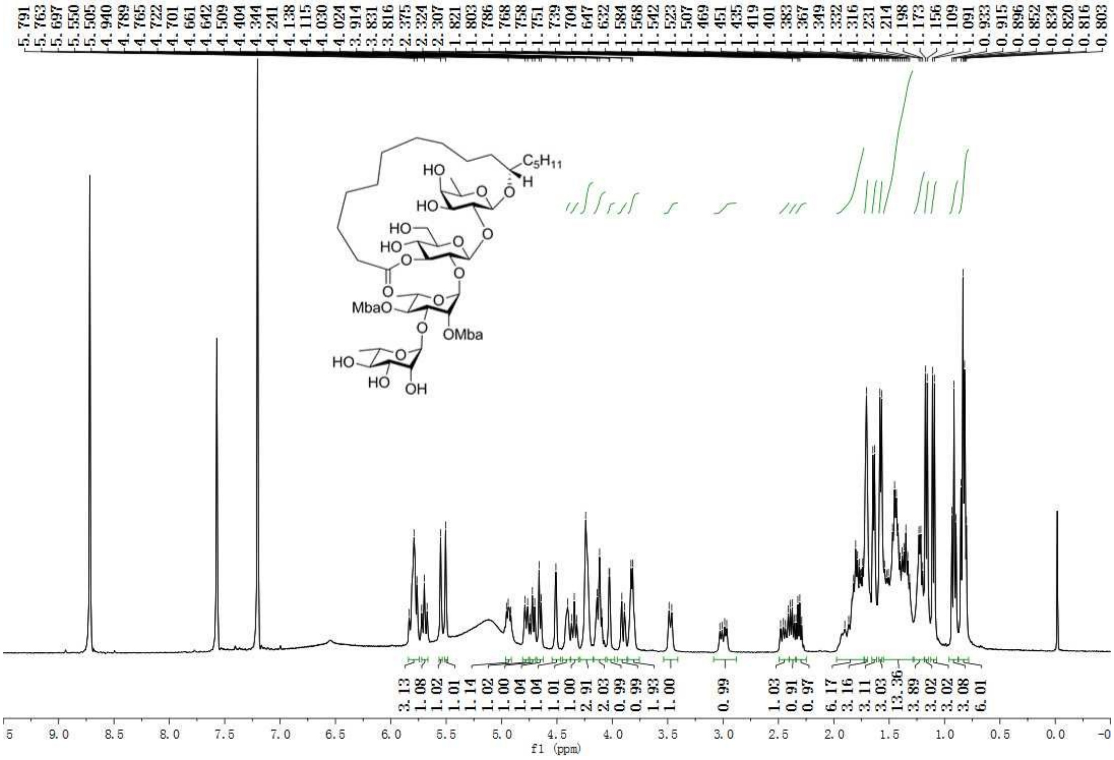

Figure S63. ^{1}H NMR (400 MHz, C_5D_5N) spectrum of **tricolorin A**

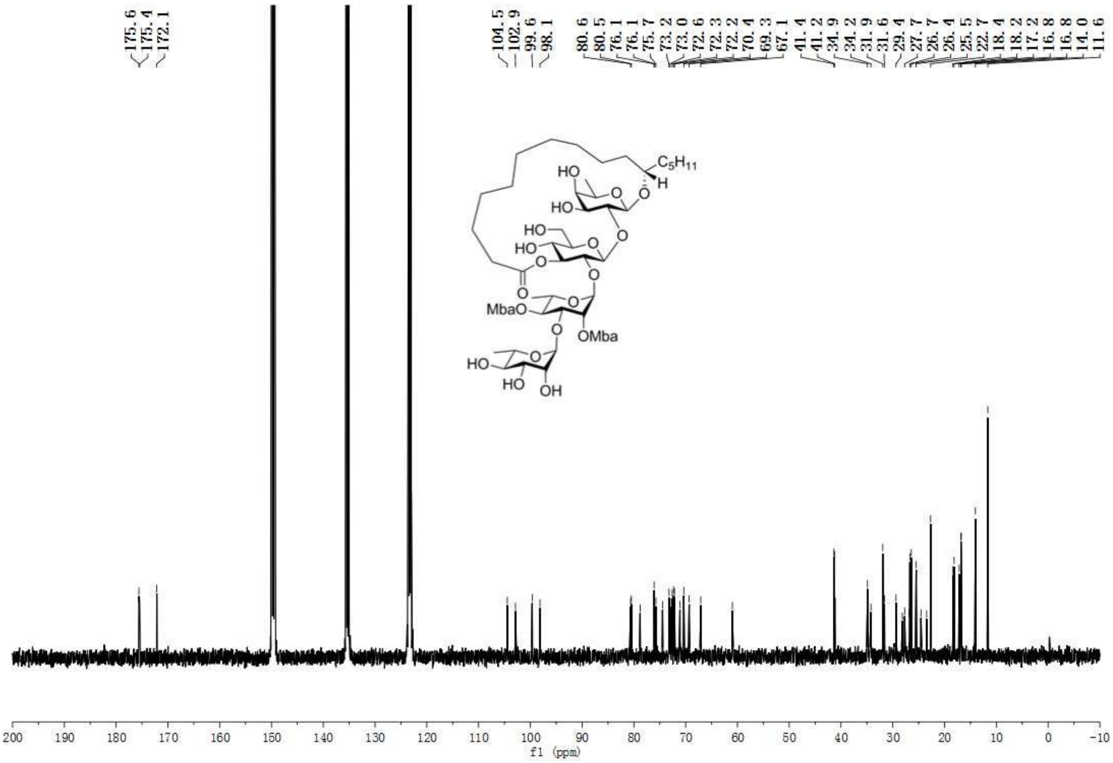

Figure S64. ^{13}C NMR (100 MHz, C_5D_5N) spectrum of **tricolorin A**