Practical synthesis of neoponkoranol and its related sulfonium salt, an optimised protocol using isopropylidene as an effective protecting group

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A practical synthesis of neoponkoranol and its related sulfonium salt as potent α-glucosidase inhibitors has been developed in which the key step of coupling reaction was optimised by using isopropylidene as an effective protecting group. The characteristic intramolecular cyclisation of the coupling precursor previously encountered as a side reaction has not been detected and coupling yields were dramatically improved in the present study.

Keywords: neoponkoranol, natural product, synthetic study, *Salacia*, α-glucosidase inhibitor

The inhibition of glucosidases is considered to be one of the most effective therapeutic approach to treat diseases such as diabetes,[1] cancers,[2] viral infections[3] and Gaucher's disease.[4] In the late 1990s, salacinol (**1**) was isolated by Yoshikawa and co-workers as a potent α-glucosidases inhibitor from an Indian Ayurvedic medicinal plant *Salacia reticulate*.[5,6] Shortly thereafter, its related side chain analogues salaprinol[7] (**2**), ponkoranol[7] (**3**) and kotalanol[8] (**4**) as well as the de-*O*-sulfonated sulfonium salts neosalacianol[9] (**5**), neosalaprinol[10] (**6**), neoponkoranol[10] (**7**) and neokotalanol[11] (**8**) were subsequently isolated from the same species of plants. Other than (**2**) and (**6**), the α-glucosidase inhibitory activities of six sulfonium salts were revealed to be as potent as those of acarbose and voglibose which are widely used clinically as antidiabetics. Their intriguing bioactivities as well as unique chemical structures, bearing a 1,4-anhydro-1,4-thio-D-arabinitol core and a polyhydroxylated side chain, (Fig. 1) made them potential lead compounds which could be further developed as a new class of hypoglycaemic drug candidates. Based on structure–activity relationship (SAR) studies[12–17] on this group of natural products, it was recently revealed that the de-*O*-sulfonated versions such as **5**, **6**, **7** and **8** usually present higher inhibitory potency in contrast with their 3′-sulfonates **1**, **2**, **3** and **4** (Fig. 1), making de-*O*-sulfonated salts more attractive as candidates for further structure modification.[10,12–15] The reported synthetic protocol to prepare this type of de-*O*-sulfonated sulfonium salts relies on coupling reaction between protected thiosugar and a corresponding epoxide[15,19–21] or tosylate.[22] The former procedure usually provides a pair of diastereomers at the stereogenic sulfur centre as the coupled product, which is difficult for further purification. On the other hand, it is usually time consuming when tosylate is used as the coupling partner, and the desired product is obtained in poor yield.

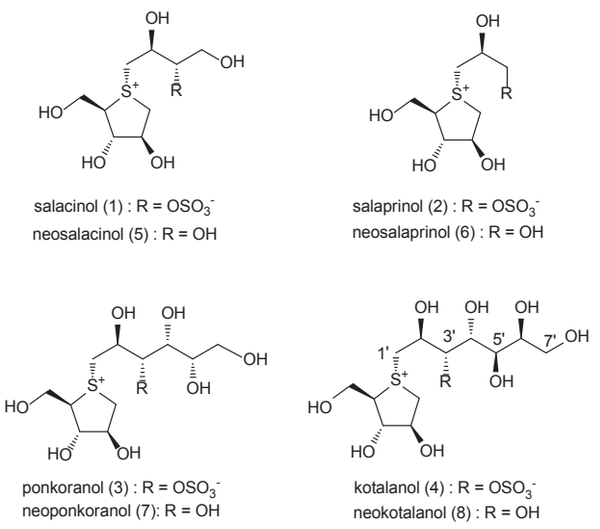

Fig. 1 Sulfonium salts isolated from *Salacia* species as a new class of α-glucosidase inhibitor.

Recently, the chemical synthesis of neoponkoranol (**7**) and its side chain epimers as potent α-glucosidase inhibitors has been reported.[10] The key synthetic procedure addressed was the coupling reaction between a protected thiosugar (**9**) and a triflate, during which process, the desired coupled products were obtained in relatively low yield. (Fig. 2, part I) After carefully analysing the structures of side products **14** and **15** isolated from the coupling reaction, the formation of the two compounds could be explained by a characteristic intramolecular cyclisation of triflate (**11**), which was triggered by nucleophilic attack from the sulfur atom of thiosugar (**9**) to the methylene carbon at the C3-benzyloxy moiety of **11** (conformation B) as shown in Fig. 2 part II. On the other hand, the direct attack from the sulfur atom of thiosugar (**9**) to the methylene at C6 bearing leaving group (TfO^-) in **11** (conformation A) provided the desired coupled product (**13**) in low yield. Due to the unique structure features and excellent bioactivities, it is necessary to develop an efficient protocol to construct the de-*O*-sulfonated sulfonium salt moiety which is the characteristic structure of these series of natural inhibitors. As a continuous synthetic study on this group of sulfonium salts, we now present our latest efforts to optimise the coupling reaction between thiosugar and triflate, which would greatly facilitate the subsequent structure modification of this group of natural products.

Based on our proposed mechanism of the previously reported coupling reaction (Fig. 2, part II), it was speculated that protection with appropriate group which could tightly fix the C3 hydroxy moiety of the monosaccharide structure could be an effective way to prevent the undesired intramolecular cyclisation reaction of the corresponding triflate. Thus, benzyl 2,3-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranoside (**16**)[23] which was prepared from D-mannose through four steps with the overall yield of 65%

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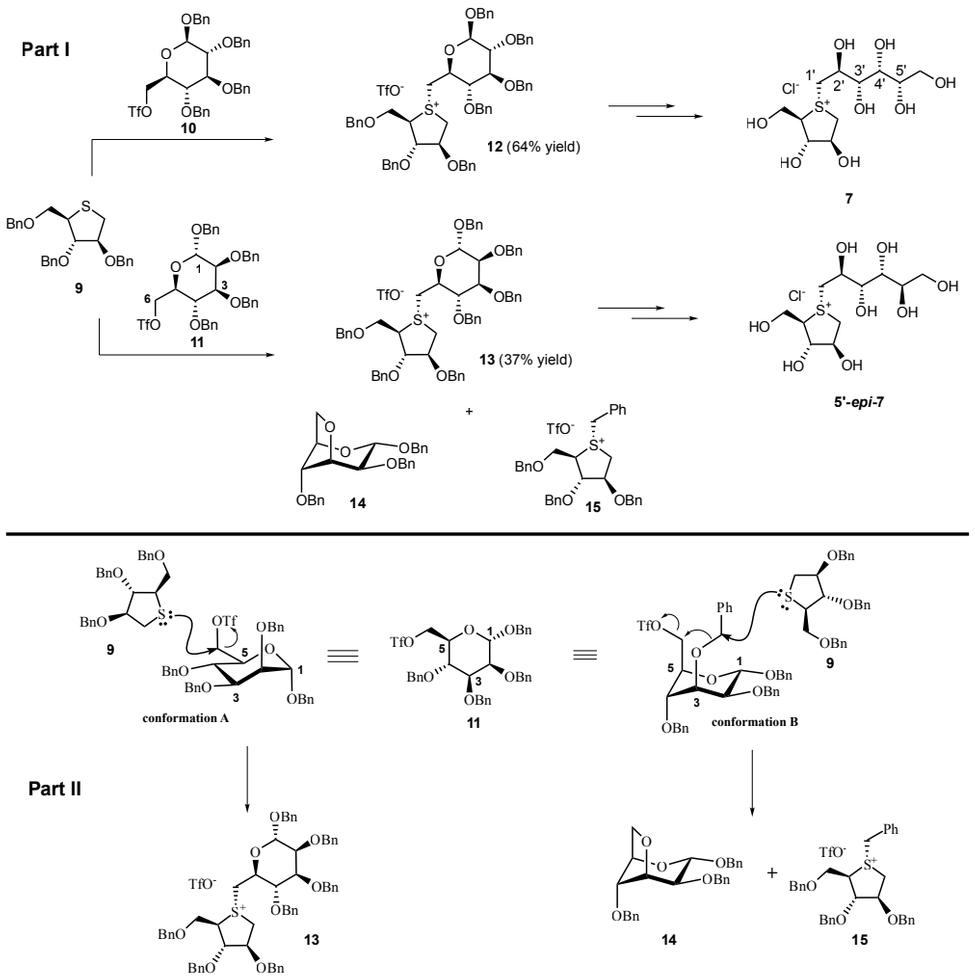
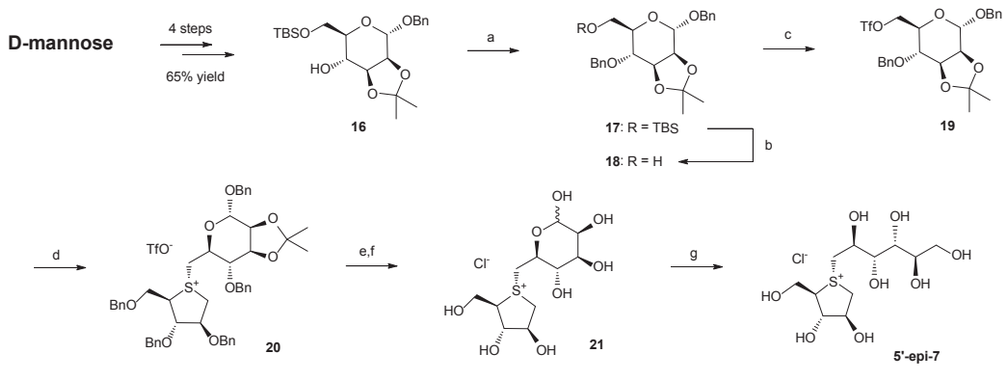
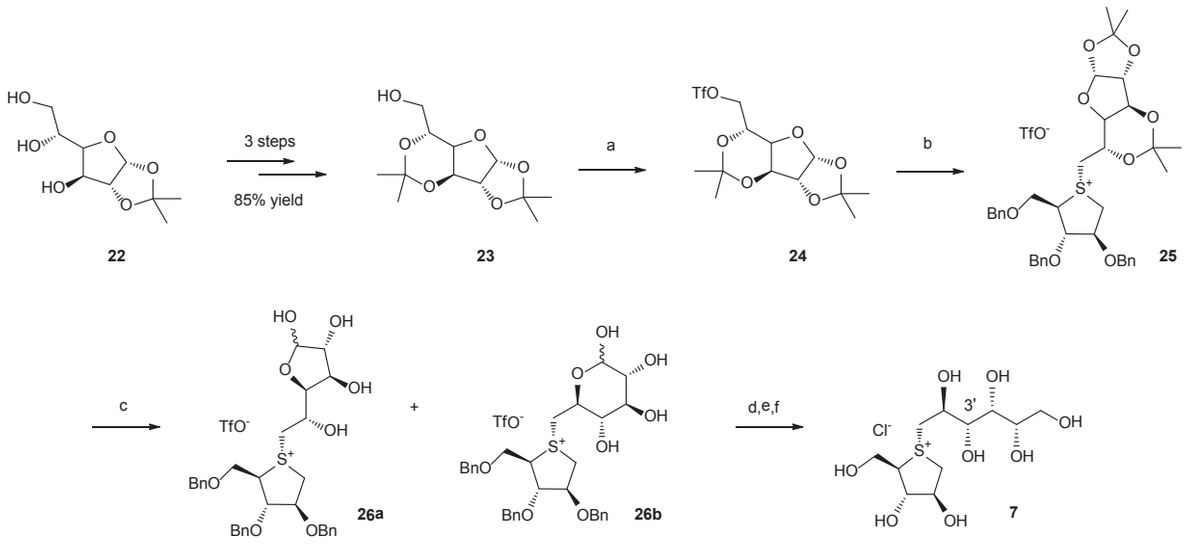


Fig. 2 Previously reported synthesis of **7** and its side chain epimer and plausible mechanism of coupling reaction between triflate (**11**) and thiosugar (**9**).

was selected as the starting material to synthesise 5′-***epi***-7. The secondary alcohol of compound **16** was first benzylated with benzyl bromide in the presence of sodium hydroxide in DMF to give benzyl 2,3-*O*-isopropylidene-4-benzyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranoside (**17**) in 97% yield. Selective deprotection of the TBS group in **17** was accomplished by using TBAF to give benzyl 2,3-*O*-isopropyridene-4-benzyl-α-D-mannopyranoside (**18**) with the yield of 95% (Scheme 1). The subsequent sulfonation of **18** with trifluoromethanesulfonic anhydride in the presence of 2,6-lutidine in dry dichloromethane afforded benzyl 2,3-*O*-isopropylidene-4-benzyl-6-*O*-trifluoromethanesulfonyl-α-D-mannopyranoside (**19**) in 85% yield, which was directly coupled with **9** in dry THF for 3 days to give the desired sulfonium salt (*S*)-2,3,5-tri-*O*-benzyl-1-deoxy-*S*-(1,4-di-*O*-benzyl-2,3-*O*-isopropylidene-6-deoxy-α-D-mannopyrananos-6-yl)-4-thio-D-arabinofuranose trifluoromethanesulfonate (**20**) in 87% yield while no other side product was isolated. Thus, by applying isopropylidene as



Scheme 1 Reagents and conditions: (a) BnBr, NaH, DMF, rt, 1 h (97%); (b) TBAF, THF, rt, 12 h (95%); (c) Tf_2O, 2,6-lutidine, –20–0 °C, 30 min (85%); (d) thiosugar (**9**), THF, rt, 72 h (87%); (e) H_2, 10% Pd–C, 50% aq. TFA, 50 °C, 48 h; (f) IRA 400J (Cl^- form), CH_3OH, rt, 3 h; (g) $NaBH_4$, H_2O, 0 °C, 20min (51% from **20**).



Scheme 2 Reagents and conditions: (a) Tf_2O, 2,6-lutidine, –20–0 °C, 30 min (91%); (b) thiosugar, THF, rt, 72 h (85%); (c) 50% aq. TFA, 50 °C, 1.5 h; (d) H_2, 10%Pd–C, 80% aq. AcOH, 50 °C, 48 h; (e) IRA 400J(Cl^- form), CH_3OH, rt, 3 h; (f) $NaBH_4$, H_2O, 0 °C, 20 min (50% from **25**).

the protecting group on C3 hydroxyl moiety, the yield of the key coupling reaction was improved from previously reported 37% to 87% in the present study, which clearly confirmed our former assumption that locking hydroxy group on C3 position would effectively prevent the intramolecular cyclisation of the corresponding triflate as side reaction. Sulfonium salt (**20**) was then converted to the target compound 5′-***epi***-7 by hydrogenolysis over Pd–C under acidic condition followed by ion exchange reaction using IRA 400J (Cl^- form) and finally by $NaBH_4$ reduction in 51% overall yield from **20**.

In view of this result, a similar strategy was used for the synthesis of natural product neoponkoranol (**7**). Hence, 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (**23**)[24], which could be easily prepared from commercially available 1,2-*O*-isopropylidene-α-D-glucofuranose (**22**) through three steps with the overall yield of 85% was subjected to sulfonation reaction to give the corresponding triflate (**24**) in 91% yield (Scheme 2). Coupling reaction between **24** and thiosugar **9** was then immediately conducted in dry THF at room temperature for 3 days to afford the desired coupled product (*S*)-2,3,5-tri-*O*-benzyl-1-deoxy-*S*-(1,2:3,5-di-*O*-isopropylidene-6-deoxy-α-D-glucofuranos-6-yl)-4-thio-D-arabinofuranose trifluoromethanesulfonate (**25**) with the yield of 85%. Acid catalysed hydrolysis of **25** was then performed through treatment with 50% trifluoroacetic acid leading to the almost quantitative formation of intermediate (**26**) as a mixture of both furanose and pyranose form anomers[24]. Finally, compound **26** was converted to the target compound neoponkoranol (**7**) in 50% overall yield in a similar procedure as discussed above for the preparation of 5′-***epi***-7.

Conclusions

Based on our former synthetic studies on a naturally occurring potent α-glucosidase inhibitor neoponkoranol (**7**), we have developed an efficient strategy to optimise the coupling reaction as the key protocol to synthesise this series of sulfonium salts. Compared with the previously reported route, triflates (**19**) and (**24**) selected in the present study as coupling precursors could be more easily and economically prepared from commercially available materials. In addition, coupling yields were dramatically improved from 37% to 87% (in D-mannose derived trial) and from 64% to 85% (in D-glucose derived trial), respectively, indicating that isopropylidene protection of C3 and its adjacent hydroxy group on monosaccharide moiety could effectively prevent the side reaction which was encountered in our previous investigation. It is highly commented that the present findings would greatly facilitate the further structure modification of this group of natural products, which is now underway in our laboratory.

Experimental

Melting points were taken on XT-4 micro melting point apparatus and are uncorrected. NMR spectra were recorded for ^{1}H NMR at 300, 500or 700 MHz and for ^{13}C NMR at 75, 125 or 175 MHz. For ^{1}H NMR, tetramethylsilane (TMS) served as internal standard (δ=0) for $CDCl_3$ and no internal standard was added for D_2O. ^{1}H NMR data are reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), and coupling constant in Hz. For ^{13}C NMR, TMS (δ=0) or $CDCl_3$ (δ=77.25) was used as internal standard for $CDCl_3$ and no internal standard was used for D_2O. Mass spectra were obtained using Agilent 1100-LCMSD-Trap/SL and HRMS were obtained using Agilent QTOF 6520. Low-resolution MS and HRMS data were obtained using ESI ionisation. Column chromatography was carried out over Fuji Silysia silica gel BW-200. All the organic extracts were dried over anhydrous sodium sulfate prior to evaporation.

Benzyl-2,3-O-isopropylidene-4-benzyl-6-O-tert-butyldimethylsilyl-β-D-mannopyranoside (**17**): A solution of **16**[23] (1.2 g, 2.8 mmol) in dry DMF (5 mL) was added to a mixture of sodium hydride (NaH, 240 mg, 6 mmol, 60% in liquid paraffin) and benzyl bromide (BnBr, 0.5 mL, 4.1 mmol) in dry DMF (10 mL) at 0 °C. After stirring at room temperature for 2 h, the resulting mixture was poured into ice-water, then extracted with ether. The extract was washed with brine, and condensed under reduced pressure to give a yellow oil (1.68 g), which on column chromatography (hexane/AcOEt, 40/1) gave the title compound (**17**, 1.4 g, 97%) as a pale yellow oil. $[\alpha]^{D}_{25}$=+47.4 (c=1, CH_3OH) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.12 (m, 10H), 5.00 (s, 1H), 4.80 (d, J=11.5 Hz, 1H), 4.65 (d, J=11.5 Hz, 1H), 4.52 (d, J=11.5 Hz, 1H), 4.41 (d, J=11.5 Hz, 1H), 4.25 (t, J=6.5 Hz, 1H), 4.09 (d, J=5.5 Hz, 1H), 3.80 (dd, J=11.0 Hz, 1.5 Hz, 1H), 3.69 (dd, J=11.0 Hz, 5.5 Hz, 1H), 3.61 (ddd, J=10.0 Hz, 5.5 Hz, 1.5 Hz, 1H), 3.46 (dd, J=10.0 Hz, 6.5 Hz, 1H), 1.40 (s, 3H), 1.26 (s, 3H), 0.83 (s, 9H), 0.001 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 137.1, 128.4, 128.23, 128.19, 127.9, 127.8, 127.5, 109.1, 96.1, 78.9, 75.9, 75.7, 72.9, 69.8, 68.6, 62.7, 27.8, 26.3, 25.9, 18.3. HRMS(ESI M+H) *m/z*

calcd for $C_{29}H_{43}O_6Si$: 515.2829; found:515.2841.

Benzyl 2,3-O-isopropylidene-4-benzyl-β-D-mannopyranoside (**18**): A mixture of compound **17** (1.03 mg, 2 mmol), 1 M solution of tetrabutylammonium fluoride in THF (2.1 mL, 2.1 mmol), THF (10 mL) was stirred at room temperature for 12 h. After the total consumption of the starting material, the mixture was poured into ice-water (50 mL) and extracted with AcOEt. The extract was washed with brine and condensed to give a pale yellow oil (852 mg), which on column chromatography (*n*-hexane/ethyl acetate, 20/1) gave the title compound (**18**, 761 mg, 95%) as a white solid, m.p. 126–128 °C, $[\alpha]^{D}_{25}$=+63.3 (*c*=1, CH_3OH) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.22 (m, 10H), 5.12 (s, 1H), 4.88 (d, *J*=11.5 Hz, 1H), 4.70 (d, *J*=11.5 Hz, 1H), 4.63 (d, *J*=11.5 Hz, 1H), 4.49 (d, *J*=11.5 Hz, 1H), 4.35 (t, *J*=6.5 Hz, 1H), 4.19 (d, *J*=5.5 Hz, 1H), 3.83 (dd, *J*=11.5 Hz,2.5 Hz, 1H), 3.73–3.70 (m, 2H), 3.56 (dd, *J*=10.0 Hz,6.5 Hz, 1H), 1.48 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 136.8, 128.4, 128.3, 128.1, 128.0, 127.7, 109.3, 96.4, 78.6, 75.9, 75.8, 72.8, 69.2, 68.7, 62.4, 27.9, 26.3.HRMS(ESIM+H) *m/z* calcd for $C_{23}H_{29}O_6$: 401.1964; found:401.1953.

(S)-2,3,5-Tri-O-benzyl-1-deoxy-S-(1,4-di-O-benzyl-2,3-O-isopropylidene-6-deoxy-α-D-mannopyrananos-6-yl)-4-thio-D-arabinofuranose trifluoromethanesulfonate (**20**): Under argon atmosphere, to a solution of 2,6-lutidine (200 μL, 2.25 mmol) in 12 mL dry dichloromethane was added trifluoromethanesulfonic anhydride (Tf_2O, 430 μL, 2.25 mmol) at –20 °C. After 5 min, a solution of **18** (600 mg, 1.5 mmol) in dry dichloromethane (12 mL) was added dropwise to the solution at –20 °C. The resulting mixture was stirred at –20 °C for 5 min, and then at 0 °C for another 30 min. The mixture was poured into ice-cooled water and extracted with dichloromethane. The extract was condensed under reduced pressure to give a pale yellow oil (825 mg). After column chromatography (*n*-hexane/AcOEt, 20/1), the target triflate benzyl 2,3-*O*-isopropyridene-4-benzyl-6-*O*-trifluoro-methanesulfonyl-α-D-mannopyranoside (**19**, 679mg, 85%) was obtained as a pale yellow oil, which was then directly coupled with thiosugar (**9**). A solution of thiosugar (**9**, 630 mg, 1.5 mmol) in THF (1.5 mL) at room temperature was added under argon atmosphere to a solution of **19** (533 mg, 1.0 mmol) in THF (1.5 mL). The resultant mixture was then stirred at room temperature for 72 h. After the total consumption of the triflates, the reaction mixture was condensed under reduced pressure to give a pale yellow oil (1.1 g), which on column chromatography ($CHCl_3$/MeOH, 200/1) gave the title compound (**20**, 826 mg, 87%) as a pale yellow oil. $[\alpha]^{D}_{25}$=+70.5 (*c*=1, CH_3OH) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.10 (m, 25H), 5.04 (s, 1H), 4.79 (d, *J*=11.5 Hz, 1H), 4.57–4.32 (m, 10H), 4.25 (t, *J*=6.5 Hz, 1H), 4.20 (s-like, 1H), 4.13–4.05 (m, 2H), 3.95 (m, 1H), 3.79–3.70 (m, 3H), 3.67–3.51 (m,3H), 3.34 (dd, *J*=9.5, 6.5 Hz, 1H), 1.42 (s, 3H), 1.28(s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 136.7, 136.4, 136.1 (C×2), 128.9, 128.79, 128.75, 128.7, 128.64, 128.58, 128.52, 128.44, 128.43, 128.39, 128.34, 128.32, 128.28, 128.24, 128.21, 128.14, 128.10, 128.06, 128.00, 127.95, 127.9, 109.9, 96.9, 82.7, 77.7, 76.5, 75.5, 73.6, 72.6, 72.44, 72.35 (C×2), 70.4, 66.7, 66.5, 65.6, 48.3, 47.9, 27.9, 26.2. HRMS(ESI) *m/z* calcd for $C_{49}H_{55}O_8S^+$: 803.3618; found:803.3626.

*(R)-1-Deoxy-R-(6-deoxy-D-mannitol-6-yl)-4-thio-D-arabinofuranose chloride (**5′-epi-7**):* A suspension of 10% Pd–C (500 mg) in 60% aqueous TFA solution (10 mL) was pre-equilibrated with hydrogen. A solution of compound **20** (476 mg, 0.5 mmol) in 1,4-dioxane (2 mL) was added to the suspension and the mixture was hydrogenated at 50 °C under atmospheric pressure until uptake of hydrogen ceased. The catalyst was filtered off and washed with a mixture of methanol and water. After the combined filtrate and the washings were condensed under reduced pressure, the residue (245 mg) was washed with dichloromethane to give a colourless oil (228 mg), which was treated with IRA 400J (Cl^- form, 2.50 g) in methanol (3 mL) at room temperature for 3 h. The resins were filtered off and washed with methanol. The filtrate and the washings were combined and condensed under reduced pressure to give a colourless oil (200 mg), which was treated with $NaBH_4$ (130 mg, 3.4 mmol) in water (15 mL) at 0 °C for 20 min. The mixture was acidified with 2M hydrochloric acid to pH *ca* 4, and condensed under reduced pressure to give a white solid (320 mg), which on column chromatography ($CHCl_3$/MeOH, 10/1 → 4/1) gave the title compound (**5′-epi-7**, 89 mg, 51%). ^{1}H NMR (700 MHz, D_2O): 3.67 (1H, dd, *J*=11.8, 6.0 Hz, H-6'a), 3.74 (1H, ddd, *J*=*ca* 8.8, 6.0, 2.7 Hz, H-5′), 3.77 (1H, dd, *J*=8.8, 1.2 Hz, H-4'), 3.80 (1H, dd, *J*=13.2, 9.0 Hz, H-1'a), 3.85 (1H, dd, *J*=*ca* 11.8, 2.7 Hz, H-6'b), 3.88 (1H, dd, *J*=8.2, 1.2 Hz, H-3'), 3.90 (1H, dd, *J*=13.0, 4.0 Hz, H-1a), 3.93 (1H, dd, *J*=13.0, 3.0 Hz, H-1b), 3.95 (1H, dd, *J*=11.2, 8.2 Hz, H-5a), 3.98 (1H, dd, *J*=*ca* 13.2, 3.2 Hz, H-1'b), 4.13 (1H, ddd, *J*=*ca* 8.2, 5.0, 2.6 Hz, H-4), 4.15 (1H, dd, *J*=11.2, 5.0 Hz, H-5b), 4.23 (1H, ddd, *J*=9.0, 8.2, 3.2 Hz, H-2'), 4.45 (1H, dd, *J*=*ca* 2.9, 2.6 Hz, H-3), 4.76 (1H, ddd, *J*=*ca* 4.0, 2.9, 2.9 Hz, H-2);^{13}C NMR (175 MHz, D_2O) δ: 50.8 (C-1), 53.1 (C-1'), 61.9 (C-5), 65.7 (C-6'), 70.0 (C-2'), 71.6 (C-4'), 72.7 (C-4), 73.3 (C-5′), 74.3 (C-3'), 79.7 (C-2), 80.2 (C-3). HRMS(ESI) *m/z* calcd for $C_{11}H_{23}O_8S^+$: 315.1114; found: 315.1134.

(S)-2,3,5-Tri-O-benzyl-1-deoxy-S-(1,2:3,5-di-O-isopropylidene-6-deoxy-α-D-glucofuranos-6-yl)-4-thio-D-arabinofuranose trifluoromethanesulfonate (**25**): In a manner similar to that used for the synthesis of triflate (**19**), diacetonide (**23**[24], 390 mg, 1.5 mmol) was subjected to sulfonation reaction to afford **24** (536 mg, 91%) as a colourless oil, which was directly coupled with thiosugar (**9**). A solution of thiosugar (**9**, 630 mg, 1.5 mmol) in THF (1.5 mL) at room temperature under argon atmosphere was added to a solution of **24** (392 mg, 1.0 mmol) in THF (1.5 mL). The resultant mixture was then stirred at room temperature for 72 h. After the total consumption of the triflates, the reaction mixture was condensed under reduced pressure to give a pale yellow oil (1.05 g), which on column chromatography ($CHCl_3$/MeOH, 200/1) gave the title compound (**25**, 690 mg, 85%) as a pale yellow oil. $[\alpha]^{D}_{25}$=+28.6 (*c*=1, CH_3OH) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.15 (m, 15H), 5.98 (d, *J*=3.6 Hz, 1H), 4.67–4,45 (m, 7H), 4.36 (dd, *J*=6.3, 3.6 Hz, 2H), 4.30 (s-like, 1H), 4.25–4.17 (m, 2H), 4.08 (dd, *J*=9.3, 6.3 1H), 3.92–3.72 (m, 5H), 3.41 (m, 1H), 1.48 (s, 3H), 1.313 (s, 3H), 1.307 (s, 3H), 1.28(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 135.97, 135.94, 128.8, 128.7, 128.63, 128.60, 128.52, 128.5, 128.4, 128.31, 128.27, 128.10, 128.07, 112.9, 106.5, 102.0, 83.8, 82.9, 82.6, 80.9, 74.8, 73.6, 72.6, 72.2, 68.8, 67.1, 66.5, 48.9, 48.7, 27.1, 26.6, 24.2, 23.4. HRMS(ESI) *m/z* calcd for $C_{38}H_{47}O_8S^+$: 663.2992; found: 663.2979.

(R)-1-Deoxy-R-(6-deoxy-D-glucitol-6-yl)-4-thio-D-arabinofuranose chloride (neoponkoranol **7***):* A solution of sulfonium salt **25** (406mg, 0.5 mmol) in 50% aqueous TFA solution (5 mL) was stirred at room temperature for 2 h. Concentration of the mixture gave compound **26** (329 mg) as a mixture of both furanose and pyranose form anomers.[12] Without purification, the mixture was then subjected to hydrogenolysis over 10% Pd–C followed by ion exchange reactions using IRA 400J (Cl^- form) and finally by $NaBH_4$ reduction in a similar procedure discussed above to give the title compound (neoponkoranol **7**[10], 78 mg) with the overall yield of 50% from **25**. $[\alpha]_D^{23}$ +4.3 (*c*=0.6, H_2O), lit[10] $[\alpha]_D^{23}$ +4.1 (*c*=0.7, H_2O). ^{1}H NMR (700 MHz, D_2O): 3.61 (1H, dd, *J*=*ca* 11.8, 5.6 Hz, H-6'a), 3.71 (1H, dd, *J*=11.8, 3.6 Hz, H-6'b), 3.73 (1H, dd, *J*=7.8, 1.8 Hz, H-3'), 3.78 (1H, dd, *J*=13.2, 9.2 Hz, H-1'a), 3.80 (1H, ddd, *J*=*ca* 5.6, 5.6, 3.6 Hz, H-5′), 3.82 (1H, dd, *J*=*ca* 5.6, 1.8 Hz, H-4'), 3.88 (1H, dd, *J*=13.0, 4.0 Hz, H-1a), 3.92 (1H, dd, *J*=13.0, 3.0 Hz, H-1b), 3.95 (1H, dd, *J*=11.0, 8.2 Hz, H-5a), 3.97 (1H, dd, *J*=13.2, 3.2 Hz, H-1'b), 4.12 (1H, ddd, *J*=*ca* 8.2, 4.8, 3.0 Hz, H-4), 4.14 (1H, dd, *J*=11.0, 4.8 Hz, H-5b), 4.25 (1H, ddd, *J*=9.2, 7.8, 3.2 Hz, H-2'), 4.45 (1H, dd, *J*=*ca* 3.0, 3.0 Hz, H-3), 4.76 (1H, ddd, *J*=*ca* 4.0, 3.0, 3.0 Hz, H-2); ^{13}C NMR (175 MHz, D_2O): 50.9 (C-1), 52.8 (C-1'), 62.0 (C-5), 65.0 (C-6'), 70.2 (C-2'), 72.0 (C-4'), 72.6 (C-4), 75.5 (C-5′), 75.8 (C-3'), 79.7 (C-2), 80.3 (C-3). HRMS(ESI) *m/z* calcd for $C_{11}H_{23}O_8S^+$: 315.1114; found: 315.1128.

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