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Improved synthesis of mercapto C-nucleoside possessing *p*-phenyl thiol as base using a lithiated coupling reaction

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ABSTRACT

We have developed a new route for synthesizing mercapto C-nucleoside possessing a phenyl thiol group, using organometallic reagents. Duplexes incorporating redox-active nucleobase analogues display a high melting temperature under oxidation condition. Originally, we had anticipated the production of mercapto C-nucleoside using a Friedel–Crafts coupling reaction via bis(toluoyl) protected ribose and *tert*-butyl phenyl sulfide in the presence of Lewis acid. However, an undesired coupling compound was formed by cleavage of the *S*-*tert*-butyl group of *S*-*tert*-butyl phenyl sulfide by Lewis acids (BF_3 Et_2O, $SnCl_4$). The highly stereoselective synthesis of mercapto C-nucleoside was, however, achieved by the addition of *p*-(*tert*-butyl)thiophenyllithium to a disiloxane-protected 2-deoxyribonolactone. This route showed moderately good yield at all steps. The *tert*-butyl moiety coupled to the sulfur atom at the phenyl group was converted to a 2-nitrophenylsulfenyl (Nps) group, and the Nps group was easily cleaved by ethanethiol to afford the desired compound and its disulfide dimer.

1. Introduction

Recently, there has been considerable interest in the synthesis of nucleoside derivatives bearing a functionalized aromatic moiety at the anomeric position. C-nucleosides bearing aryl groups as an unnatural nucleobase are in high demand due to their use in several important applications such as extending the genetic alphabet,[1] formation of metal arrays[2] and construction of functionalized DNA.[3] Methods for the synthesis of C-nucleosides have been extensively studied. However, synthetic obstacles in terms of low yield and/or poor stereoselectivity have been frequently encountered. There are several synthetic approaches to generating C-nucleosides,[4] including Heck type coupling reaction of aryl iodides with glycals,[5] the addition of organometallic reagents to a protected lactone or ribose derivative[6] and electrophilic substitutions of electron-rich aromatics with ribose under Lewis acids.[7]

We had already carried out the synthesis and characterization of a mercapto C-nucleoside possessing a phenyl thiol group at an anomeric position.[8–10] A duplex containing the unnatural base under oxidizing conditions had a very high T_m. The observed high T_m is due to each unnatural *S*:*S* base pair forming a matching disulfide bond between complementary mercapto C-nucleosides under oxidizing conditions, which markedly stabilizes the resulting duplex by comparison to the control DNA. However, the coupling conversion of the β-anomer of mercapto C-nucleoside with Lewis acid (Friedel–Crafts reaction) had indicated a low yield of only 24% (β/α=2.8). It was therefore important to improve the conversion and stereoselectivity of the coupling reaction between the ribosyl moiety and protected thiophenyl derivatives at the anomeric position.

Herein, we describe an efficient alternative synthetic approach towards generating mercapto C-nucleosides possessing a thiophenyl group. This method utilizes the addition of a *p*-(*tert*-butylthio)phenyl lithium reagent to a disiloxane-protected lactone. We also attempted a Friedel–Crafts type coupling reaction of *tert*-butyl phenyl sulfide[11] and protected deoxyribose in the presence of Lewis acid.

1.1. Synthetic strategy

The synthetic strategy was as follows. Route 1 was a Friedel–Crafts coupling reaction between the oxonium intermediate derived from the bis(toluoyl)-protected deoxyribose and protected thiophenol with Lewis acid (Scheme 1, left). Although this reaction was very convenient and easily performed, the resulting products were a mixture of α- and β-forms at the anomeric position of C-deoxyribose. Because the coupling efficiency was low, we attempted to couple several combinations of protected thiophenol

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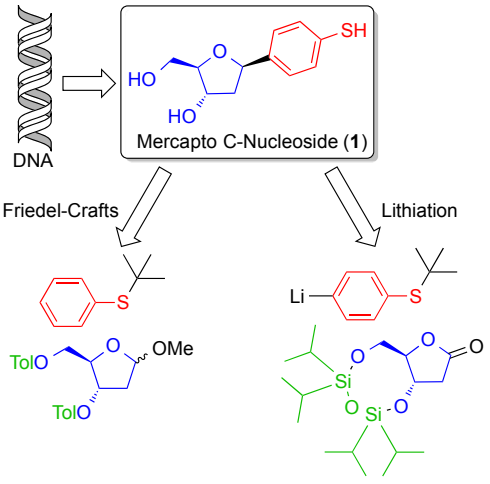
component and 3,5-ditoluoyl-1-α/β-methoxy-2-deoxy-D-ribose.[8] Most of the protected thiophenols did not react with 3,5-ditoluoyl-1-α/β-methoxy-2-deoxy-D-ribose using a variety of Lewis acids. However, benzyl phenyl sulfide did produce the desired Bn protected C-nucleoside in high yield (65%).[8,9] The *S*-benzyl group of benzylthiophenyl C-nucleoside remained uncleaved in the presence of many different reagents, suggesting the *S*-benzyl group was very stable. The tertiary butyl group is a simple hydrocarbon that allows facile deprotection of *tert*-butyl protected compounds. We also anticipated *tert*-butyl phenyl sulfide to be a good starting material for Friedel–Crafts coupling.



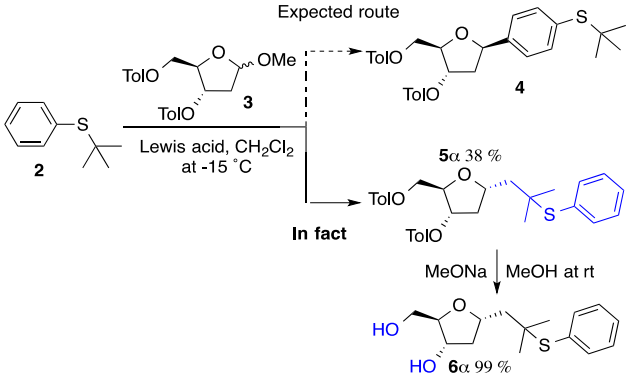
Scheme 1. Synthetic strategy of mercapto C-nucleoside (**1**) possessing a phenyl thiol group as base.

Route 2 involved an organometallic coupling reaction between disiloxane–protected deoxyribonolactone and *tert*-butyl 4-bromophenyl sulfide with *n*-butyllithium at −78 °C (Scheme 1, right).[12] There are several reagents that can be used to protect a thiol group in the presence of *n*-butyllithium.[13] The reduction of the hemiketal coupling product with an excess of Et_3SiH/BF_3 Et_2O provided only the β-epimer C-nucleoside.[6c,12] This route is superior in configuration control at the anomeric position to the route using Friedel–Crafts coupling. However, using this route, available sulfur protective groups for *p*-bromobenzenethiol were somewhat limited due to resistance of the *n*-BuLi to deprotection. As mentioned earlier, we selected the *S*-*tert*-butyl group for protection of *p*-bromobenzenethiol.

2. Result and discussion

2.1. Synthetic approach using Friedel–Crafts alkylation

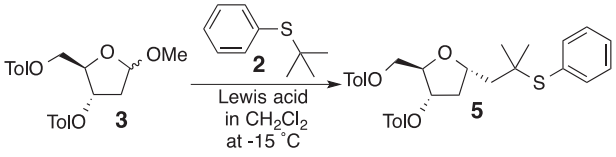
A first approach involved the Friedel–Crafts reaction between 3,5-ditoluoyl-1-α/β-methoxy-2-deoxy-D-ribose **3** and *tert*-butyl phenyl sulfide **2** to give coupling compound **4** (Scheme 2). A new spot corresponding to the coupling product was observed by TLC analysis. The chemical structure of this coupling product was then analyzed using NMR, which indicated the main species to be **5** rather than the anticipated **4**. The chemical structure of the new compound in which the bis(toluoyl)-protective groups had been cleaved by MeONa was investigated by NMR. The ^{1}H NMR spectrum of this deprotected compound **6** showed two features of interest. Firstly, two signals at 1.28 and 1.30 ppm integrated six protons instead of the nine protons one would expect for a *tert*-butyl group (Supplementary data 2, ^{1}H NMR). Secondly, two multiple signals at 1.71 and 1.95 ppm were observed in which each signal showed one proton as an integrated value (Supplementary data 2, ^{1}H NMR, COSY). The signal at 1.71 ppm overlapped with the proton signals of 2′Hα corresponding to the ribosyl moiety and hydroxyl group (HO-). Assuming the new spot obtained by TLC indicated the formation of compound **4** by Friedel–Crafts coupling, we would expect to observe a strong singlet signal derived from the *tert*-butyl group for nine protons at high magnetic field. A COSY spectrum revealed that the 1′H had the new cross-peaks for two protons at 1.71 and 1.95 ppm (Supplementary data 2, COSY). Moreover, these two signals at 1.71 and 1.95 ppm were associated with the same carbon by DEPT135 and HMQC. Therefore, we determined the chemical structure of the new spot as compound **5**. It was clarified that the configuration of the 1′ anomeric position of compound **6** was the α-form by NOESY (Scheme 4; Supplementary data 2, NOESY). NOE of 1′H indicated a cross-peak for the 2″β-proton (at 2.45 ppm), and the 2″β-proton revealed the NOE for the 3′ proton. Therefore, the anomeric proton at the 1′ position faces the β-configuration, and the coupled group faces the α-configuration.



Scheme 2. Anticipated (top) and actual (bottom) synthetic route towards mercapto C-nucleoside (**1**).

We carried out the Friedel–Crafts coupling reaction on compounds **2** and **3** with three different Lewis acids at −15 °C (Table 1). In all cases, we obtained only **5**α, rather than the desired 4-*S*-protected aryl C-nucleoside **4**. BF_3 and $SnCl_4$ as Lewis acids afforded compound **5**, but we could not generate both **4** and **5** in the presence of TMSOTf as Lewis acid.

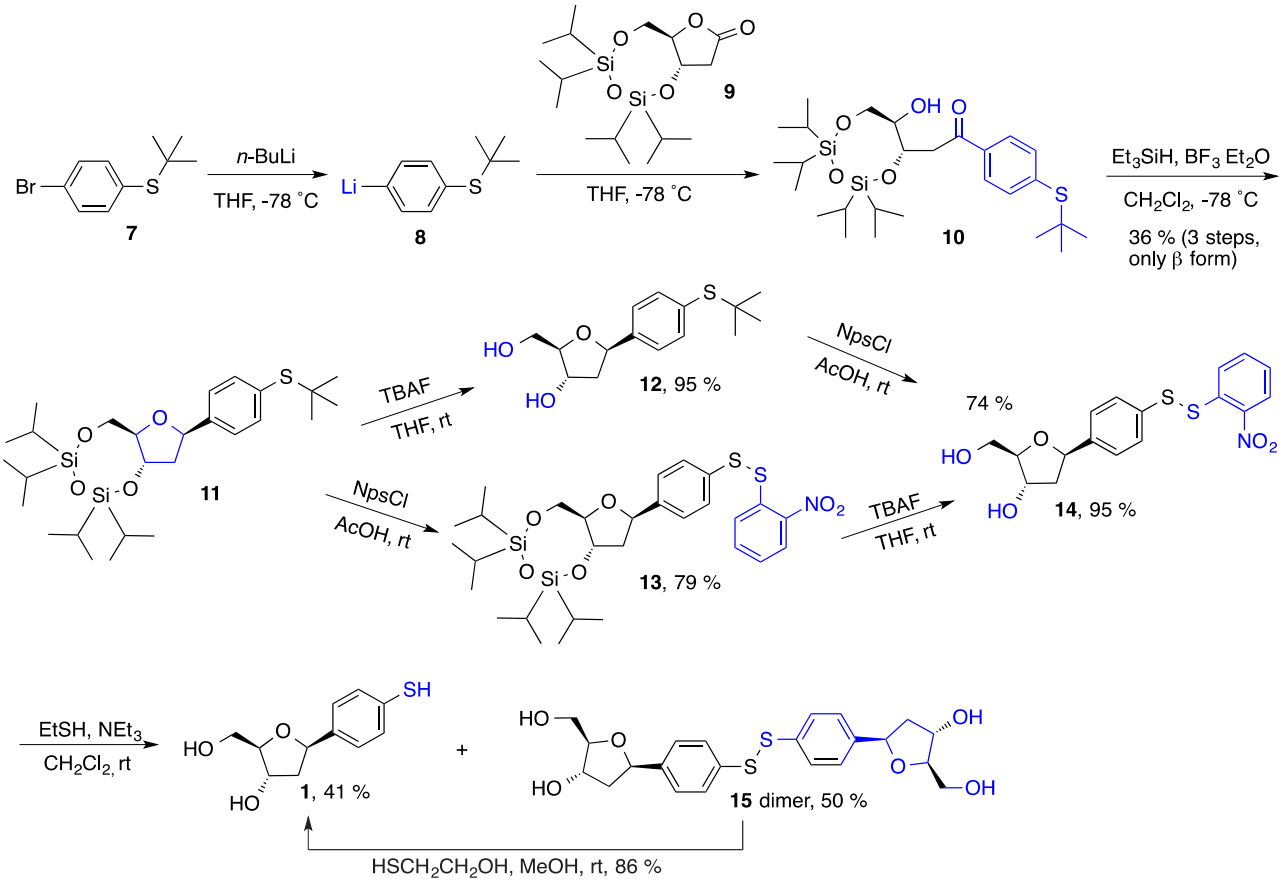
Table 1
Effect of different Lewis acids on Friedel–Crafts coupling between compound **2** and **3**



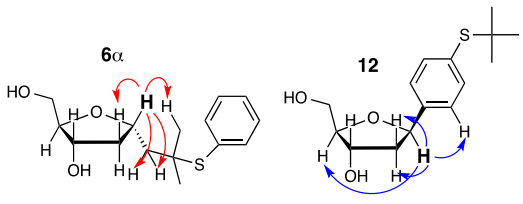
Lewis acid	Equivalent	Time/h	Isolated yield of **5**α/%
BF_3	2	24	20
	4	6	11
	4	4	18
$SnCl_4$	4	4	38
	4	16	31
TMSOTf	4	24	0 (No reaction)

2.2. Synthetic approach using a lithiated coupling reaction

Next, our efforts were devoted to the synthesis of the mercapto C-nucleoside (**1**) by a lithiated route. The coupling reaction by lithiation essentially followed the syntheses of *C*-glycosides by Woski et al.[6c,12,14] As starting material for the synthesis of mercapto C-nucleoside (**1**), the readily available 3,5-*O*-[(1,1,3,3,-



Scheme 3. Synthetic route of mercapto C-nucleoside using lithiated organometallic reagent.



Scheme 4. Important correlation in NOESY deriverd from **6**α and **12**.

tetraisopropyl)disiloxanediyl]-2-deoxy-D-ribono-1,4-lactone **9** and the *tert*-butyl 4-bromophenyl sulfide **7** were used (Scheme 3). Bromide-lithium exchange in **8** with *n*-BuLi at −78 °C and in situ reaction with ribonolactone **9** protected 1,1,3,3-tetraisopropyldisiloxane furnished a mixture of hemiketal **10**, which was subsequently reduced with an excess of Et_3SiH/BF_3 Et_2O to provide only isomer **11** in the β-configuration in 36% yield for all three steps. The deprotection of disiloxane of compound **11** could be carried out using tetrabutylammonium fluoride (TBAF) in THF to afford compound **12** in a good yield (95%). The anomeric configurations in **12** were assigned by NOESY experiments (Scheme 4; Supplementary data 4, NOESY). The NOE of 1′H was observed in 4′αH and 2″H (2.28 ppm, medium), and 2′H (2.03 ppm) indicated the NOE for 3′βH (medium). The anomeric proton at the 1′ position faces on the α-configuration, and the coupled aromatic group faced the β-configuration. Therefore, we determined that compound **12** has a β-configuration.

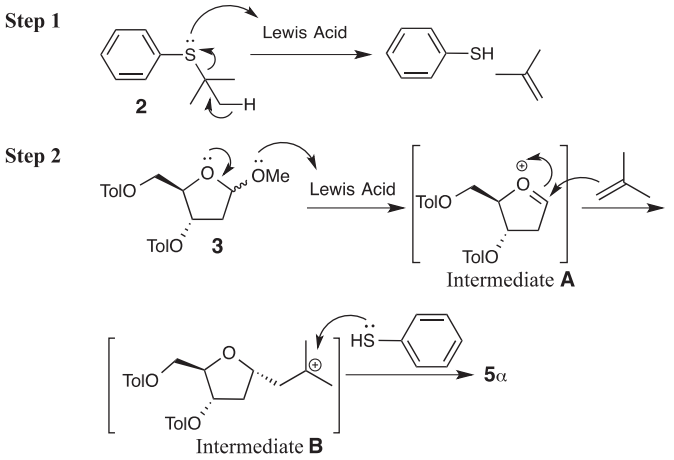
The *S*-*tert*-butyl group was very stable in the presence of normal acids, bases and many electrophilic reagents. Treatment of *tert*-butyl thioether protected compound **11** with 2-nitrophenylsulfenyl chloride (NpsCl)[15] in acetic acid resulted in exchange of the *tert*-butyl group for a Nps group to afford compound **13**.[16] Compound **12**, which also possesses an *S*-*tert*-butyl group, underwent a similar exchange reaction in the presence of NpsCl to yield compound **14**. The compound **14** was reduced with ethanethiol containing triethylamine in methanol at room temperature to give compound **1**. We found that *S*-Nps nucleoside **14** could easily be converted into mercapto C-nucleoside **1** (41%) and disulfide dimer product **15** (50%; total 91%). Dimer **15** was easily converted to target compound **1** using the reducing agent mercaptoethanol (86%).

2.3. Mechanism

A possible mechanism for the production of compound **5**α is proposed in Scheme 5. The lone pair derived from the sulfur atom of *tert*-butyl phenyl sulfide **2** attacks the Lewis acid, and the proton of the *tert*-butyl group is simultaneously eliminated to produce 2-methylpropene (isobutene) and phenyl thiol (step 1).[17] 3,5-Ditoluoyl-1-α/β-methoxy-2-deoxy-D-ribose **3** can form the carbocation intermediate **A** with Lewis acid. Oxonium intermediate **A** reacts with 2-methylpropene to produce tertiary carbocation intermediate **B**. The final step occurs via nucleophilic attack of phenyl thiol to the tertiary carbocation of intermediate **B** to produce compound **5**α (step2).

3. Conclusion

In conclusion, a practical synthetic approach for the preparation of mercapto C-nucleoside (**1**) has been developed. Originally, we had anticipated the production of mercapto C-nucleoside (**1**) using Friedel–Crafts coupling involving 3,5-ditoluoyl-1-α/β-methoxy-2-deoxy-D-ribose **3** and *tert*-butyl phenyl sulfide **2** with Lewis acid. Unfortunately, an undesired coupling compound **5**α



Scheme 5. Proposed mechanism for the unexpected coupling reaction between ribose **3** and *tert*-butyl phenyl sulfide **2** with Lewis acid.

was generated using this route. However, mercapto C-nucleoside (**1**) was successfully produced via a lithiated route by preparing the coupling compound **11**, which was afforded from *tert*-butyl 4-bromophenyl sulfide **7** and disiloxane-protected deoxy-ribonolactone **9**. This route showed moderately good yield at all steps. The *tert*-butyl group coupled to a sulfur atom was converted to an *o*-nitrophenylsulfenyl (Nps) group by NpsCl in acetic acid. The Nps group was then readily cleaved by ethanethiol under basic conditions in CH_2Cl_2 to afford compound **1** and the disulfide dimer **15**.

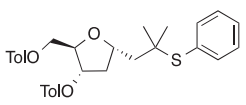
4. Experimental section

4.1. General

All solvents and reagents were of reagent-grade quality, and used without further purification. The TLC analysis was carried out on silica gel 60 F_{254} 1.05554 (Merck). Column chromatography was performed using Wakogel C-300 (silica gel, Wako) or Silica gel 60 N (Kanto Chemical Co.). The NMR spectra were recorded on a JEOL ECS 400 (400.0 MHz for ^{1}H; 100.4 MHz for ^{13}C) spectrometer. The spectra were referenced to TMS in $CDCl_3$ or CD_3OD (internal standard). Complete assignment of all NMR signals was performed using a combination of ^{1}H, ^{13}C, COSY, HMQC, DEPT135 and NOESY experiments. The chemical shifts (δ) are reported in parts per million; multiplicity is indicated by: s (singlet), d (doublet), t (triplet), q (quintet), m (multiplet), and br (broad). The coupling constants, *J*, are reported in Hertz. Mass spectra were measured using ESI on a JEOL AccuTOF by direct analysis in real time method (DART). Optical rotations were measured at 25 °C. $[\alpha]_D^{25}$ values are given in 10^{-1} deg cm^2 g^{-1}.

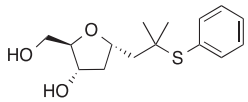
4.2. Syntheses

*4.2.1. 1′,2′-Dideoxy-1′α-[(2-methyl-2-thiophneyl)propyl]-3,5-di-O-(4-toluoyl)-D-ribose (**5**α).*



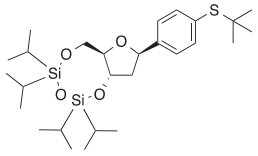
A mixture of *tert*-butyl phenyl sulfide (0.332 g, 1.5 mmol) and 3,5-ditoluoyl-1-α/β-methoxy-2-deoxy-D-ribose (0.384 g, 1.0 mmol) was stirred in 5.0 mL of anhydrous CH_2Cl_2 at −15 °C under an argon atmosphere. 1 mol/L of $SnCl_4$ (4 equiv, 4 mmol, 639 mL) was then added to the reaction mixture for 10 min. The solution was stirred at −15 °C for 12 h, and then the reaction was quenched by addition of MeOH and 50 mL of saturated $NaHCO_3$ in H_2O. The mixture was extracted twice with 50 mL of CH_2Cl_2. The organic layers were combined and washed with brine and water before being dried over anhydrous $MgSO_4$. The solution was filtered, concentrated and purified by silica gel chromatography. The desired compound was eluted with hexane–diethyl ether (9:1) to afford **5**α as a pale yellow oil (197 mg, 38%). ^{1}H NMR ($CDCl_3$): δ 7.93 (4H, *J*=8.2, 16.8 Hz, dd), 7.48 (2H, m), 7.20–7.24 (7H, m), 5.45 (1H, m), 4.62 (1H, m), 4.55 (1H, m), 4.46 (1H, m), 2.71 (1H, *J*=6.4, 6.8, 7.2 Hz, ddd), 2.42 (3H, s), 2.39 (3H, s), 1.99 (1H, *J*=7.8, 14.4 Hz, dd), 1.89 (1H, *J*=5.2, 7.7, 15.4 Hz, ddd), 1.76 (1H, *J*=3.6, 14.8 Hz, dd), 1.68 (1H, br), 1.31 (3H, s), 1.29 (3H, s). ^{13}C NMR ($CDCl_3$): δ 166.5, 166.4, 144.1, 143.9, 137.7, 132.0, 129.8, 129.8, 129.2, 128.9, 128.6, 127.3, 127.0, 81.1, 76.4, 64.7, 48.6, 47.8, 39.8, 30.0, 28.3, 21.8, 21.7. ESIMS *m*/*e* 541 $[M+Na]^+$. HRMS (ESI) calcd for $C_{31}H_{34}O_5SNa$: 541.2025, found: 541.2044. $[\alpha]_D^{25}$ +36.1 (*c* 0.41, $CHCl_3$).

*4.2.2. 1′,2′-Dideoxy-1′α-[(2-methyl-2-thiophneyl)propyl]-D-ribose (**6**).*



To a solution of compound **5**α (100 mg, 0.193 mmol) in MeOH (3 mL) was added MeONa (156 mg, 1 mmol). The reaction mixture was stirred for 2 h at room temperature, and then neutralized with a saturated aqueous NH_4Cl solution and extracted three times with CH_2Cl_2. The organic layers were combined, washed twice with H_2O, and dried over anhydrous $MgSO_4$. The solution was filtered, concentrated and purified by silica gel chromatography. The desired compound was eluted with $CHCl_3$–MeOH (10:1) to afford **6** as a colorless oil (53 mg, 99%). ^{1}H NMR ($CDCl_3$) δ 7.50 (2H, m), 7.34 (3H, m), 4.43 (1H, m), 4.30 (1H, m), 3.83 (1H, *J*=5.4, 9.2 Hz, dd), 3.69 (2H, m), 2.45 (1H, *J*=6.6, 6.8, 12.4 Hz, ddd), 1.98 (3H, m), 1.71 (4H, m), 1.30 (3H, s), 1.29 (3H, s). ^{13}C NMR ($CDCl_3$) δ 137.7, 132.0, 128.9, 128.6, 86.9, 75.6, 72.9, 62.6, 48.6, 48.4, 42.7, 30.1, 28.6. ESIMS *m*/*e* 305 $[M+Na]^+$. HRMS (ESI) calcd for $C_{15}H_{22}O_3SNa$: 305.1187, found: 305.1176. $[\alpha]_D^{25}$ +40.9 (*c* 0.45, $CHCl_3$).

*4.2.3. 1′,2′-Dideoxy-3′,5′-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-1′β-[4-(tert-butylthio)phenyl]-D-ribose (**11**).*

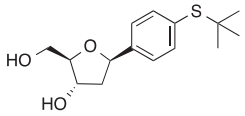


To a solution the *tert*-butyl 4-bromophenyl sulfide **7** (3.07 mmol, 0.754 g) in anhydrous THF (4.0 mL) under Ar and at −78 °C was added *n*-BuLi (1.5 M in hexane, 1.0 equiv 2.25 mL). The mixture was stirred at −78 °C for 1 h and then added via cannula to a solution of 3,5-*O*-[(1,1,3,3,-tetraisopropyl)disiloxanediyl]-2-deoxy-D-ribono-1,4-lactone **9** (3.07 mmol, 1.15 g) in anhydrous THF (4.0 mL) at −78 °C. After 1 h, the reaction mixture was quenched at −78 °C with saturated aqueous NH_4Cl and then extracted with EtOAc. The combined EtOAc phases were washed with saturated aqueous NH_4Cl and twice with water, before being dried over anhydrous Na_2SO_4. The resulting solution was concentrated in vacuo and then subjected to silica gel chromatography. The desired compound was eluted with hexane–diethyl ether (10:1) to afford hemiketal **10** as a pale yellow oil (0.982 g).

A solution of hemiketal **10** in CH_2Cl_2 (6.0 mL) under Ar and at −78 °C was treated with Et_3SiH (5.46 mmol, 0.636 g) and BF_3 Et_2O

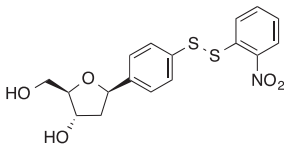
(5.46 mmol, 0.775 g). The resulting solution was stirred at −78 °C for 1 h, and then the reaction was quenched at −78 °C with saturated aqueous Na_2CO_3 solution. The organic phase was washed twice with water and then dried over anhydrous Na_2SO_4. The solution was filtered, concentrated and purified by silica gel chromatography. The desired compound was eluted with hexane–diethyl ether (10:1) to afford **11** as a pale yellow oil (0.578 g, 36% yield for all three steps). ^{1}H NMR ($CDCl_3$): δ 7.49 (2H, J=8.4 Hz, d), 7.31 (2H, J=8.4 Hz, d), 5.10 (1H, J=7.2 Hz, t), 4.55 (1H, m), 4.14 (1H, m), 3.91 (1H, m), 2.39 (1H, J=6.23, 10.3, 18.5, ddd), 2.07 (1H, J=1.89, 5.60, 16.2 Hz, ddd), 1.27 (9H, s), 1.07 (28H, m). ^{13}C NMR ($CDCl_3$): δ 142.9, 137.6, 131.7, 126.0, 86.5, 78.7, 73.1, 63.6, 46.0, 43.2, 31.0, 17.7, 17.5, 17.5, 17.5, 17.4, 17.3, 17.2, 17.1, 13.6, 13.5, 13.1, 12.6. ESIMS m/e 524 $[M+Na]^+$. HRMS (ESI) calcd for $C_{27}H_{48}O_4SSi_2Na$: 547.2710, found: 547.2724. $[\alpha]_D^{25}$ −8.06 (c 0.40, $CHCl_3$).

*4.2.4. 1′,2′-Dideoxy-1′β-[4-(tert-butylthio)phenyl]-D-ribose (**12**).*



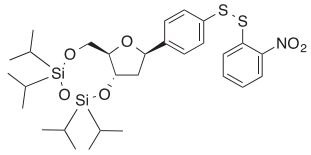
To a solution of the disiloxane compound **11** (0.157 g, 0.30 mmol) in anhydrous THF (2 mL) was added TBAF (1.2 mL, 1 mol/L in THF, 4.0 equiv). The reaction mixture was stirred for 5 h at room temperature, and then a saturated aqueous NH_4Cl solution was added to quench the reaction. The mixture was extracted with EtOAc and the organic layer was then washed twice with H_2O, before being dried over anhydrous Na_2SO_4. The solution was filtered, concentrated and purified by silica gel chromatography. The desired compound was eluted with hexane–EtOAc (1:1) to afford **12** as a pale yellow foam (0.080 g, 95%). ^{1}H NMR ($CDCl_3$): δ 7.52 (2H, J=8.3 Hz, d), 7.31 (2H, J=7.6 Hz, d), 5.19 (1H, J=5.6, 10.8 Hz, dd), 4.46 (1H, m), 4.03 (1H, m), 3.81 (1H, J=4.5, 11.6 Hz, qd), 2.28 (1H, J=2.0, 5.6, 13.2 Hz, ddd), 2.03 (1H, J=6.2, 10.4, 13.4 Hz, ddd), 1.56 (2H, br), 1.28 (9H, s). ^{13}C NMR ($CDCl_3$): δ 141.4, 137.1, 131.7, 125.5, 87.2, 79.6, 73.3, 63.1, 45.9, 43.5, 30.8, 16.9. EIMS m/e 282 $[M]^+$. HRMS (ESI) calcd for $C_{15}H_{22}O_3SNa$: 305.1187, found: 305.1199. $[\alpha]_D^{25}$ +30.7 (c 0.20, $CHCl_3$).

*4.2.5. 1′,2′-Dideoxy-1′β-[(4-(2-nitrophenyl)disulfide) phenyl]-D-ribose (**14**).*



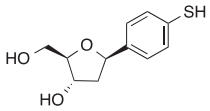
To a solution of the compound **12** (0.305 g, 1.08 mmol) in acetic acid (5 mL) was added 2-nitrophenylsulfenyl chloride (0.225 g, 1.19 mmol). The reaction mixture was stirred at room temperature for 2 h and then the pH of the resulting solution was adjusted to neutrality by adding a saturated aqueous Na_2CO_3. The mixture was extracted with EtOAc and the organic layer washed twice with water, before being dried over anhydrous Na_2SO_4. The solution was filtered, concentrated, and purified by silica gel chromatography. The desired compound was eluted with $CHCl_3$–MeOH (12:1) to afford **14** as a pale yellow foam (0.304 g, 74%). ^{1}H NMR ($CDCl_3$): δ 8.27 (1H, J=1.2, 8.0 Hz, dd), 8.12 (1H, J=1.4, 8.0 Hz, dd), 7.61 (1H, J=1.6, 7.8 Hz, td), 7.44 (2H, J=8.8 Hz, d), 7.34 (1H, J=1.6, 7.8 Hz, td), 7.44 (2H, J=8.4 Hz, d), 5.12 (1H, J=5.6, 10.4 Hz, dd), 4.43 (1H, m), 3.99 (2H, J=4.6, 6.8 Hz, dd), 3.75 (2H, m), 2.23 (2H, J=2.1, 6.0, 16.2 Hz, ddd), 1.97 (2H, J=6.2, 10.0, 18.2 Hz, ddd), 1.83 (1H, J=3.6 Hz, d), 1.78 (1H, J=6.0 Hz, t). ^{13}C NMR ($CDCl_3$): δ 145.6, 141.0, 137.1, 134.6, 134.3, 128.0, 127.5, 127.1, 126.8, 126.6, 126.2, 87.4, 79.6, 73.9, 63.5, 44.1. ESIMS m/e 402 $[M+Na]^+$. HRMS (ESI) calcd for $C_{17}H_{17}NO_5SNa$: 402.0446, found: 402.0417. $[\alpha]_D^{25}$ +24.3 (c 0.21, $CHCl_3$).

*4.2.6. 1′,2′-Dideoxy-3′,5′-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-1′β-[4-((2-nitrophenyl)disulfide)phenyl]-D-ribose(**13**).*



To a solution of the compound **11** (0.573 g, 1.10 mmol) in acetic acid (6 mL) was added 2-nitrophenylsulfenyl chloride (0.219 g, 1.16 mmol). The mixture was stirred at room temperature for 4 h and then the pH of the resulting solution was adjusted to neutrality by adding a saturated aqueous Na_2CO_3. The mixture was extracted with EtOAc and the organic layer washed twice with water, before being dried over anhydrous Na_2SO_4. The solution was filtered, concentrated and purified by silica gel chromatography. The desired compound was eluted with $CHCl_3$–MeOH (12:1) to afford **13** as a pale yellow foam (0.537 g, 79%). ESI mass spectra showed **13** as the deprotected form with a cleaved TIPDS group. ^{1}H NMR ($CDCl_3$): δ 8.26 (1H, J=1.2, 8.3 Hz, dd), 8.12 (1H, J=1.3, 8.3 Hz, dd), 7.60 (1H, J=1.2, 7.7 Hz, td), 7.34 (1H, J=1.2, 7.7 Hz, td), 7.35 (1H, J=7.6, 62 Hz, dd), 5.02 (1H, J=7.2 Hz, t), 4.50 (1H, J=4.6 Hz, t), 4.48 (1H, J=4.5 Hz, t), 3.97 (2H, m), 3.87 (1H, m), 2.33 (1H, J=4.6, 7.1, 16 Hz, ddd), 2.01 (1H, J=7.7, 7.7, 13 Hz, ddd), 1.03 (28H, m). ^{13}C NMR ($CDCl_3$): δ 12.5, 13.0, 13.3, 13.5, 16.9, 17.0, 17.1, 17.2, 17.3, 17.4, 17.5, 42.9, 63.4, 72.9, 76.5, 76.8, 77.0, 77.1, 78.2, 86.2, 125.7, 126.1, 126.6, 127.1, 127.5, 133.7, 133.8, 136.7, 141.5, 145.1. $[\alpha]_D^{25}$ −15.5 (c 0.20, $CHCl_3$).

*4.2.7. 1′,2′-Dideoxy-1′β-(4-mercaptophenyl)-D-ribose (**1**).*



(a) To a solution of the compound **14** (0.309 g, 0.815 mmol) in methanol (10 mL) was added triethylamine (0.412 g, 4.08 mmol) and ethanethiol (1.01 g, 1.22 mL, 16.3 mmol). The mixture was stirred at room temperature for 2 h under Ar and then concentrated and purified by silica gel chromatography. The target compound was eluted with $CHCl_3$–MeOH (12:1) to afford **1** as a white solid (75 mg, 41%) and **15** as a white solid (92.2 mg, 50%). Spectral data for **1** and **15** were identical to those given in Refs. 8 and 9, respectively (see Supplementary data).

(b) To a solution of the compound **15** (57 mg, 0.126 mmol) in methanol (5 mL) was added mercaptoethanol (400 μL, 0.360 mg, 4.61 mmol). The mixture was stirred at room temperature for 6 h under Ar and then concentrated and purified by silica gel chromatography. The target compound was eluted with $CHCl_3$–MeOH (15:1), and then recrystallized from toluene to afford **1** as a colorless solid (49 mg, 86%). $[\alpha]_D^{25}$ +37.0 (c 0.20, CH_3OH).

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Supplementary data

NMR spectra for all new compounds are shown. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.12.085.

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