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# Synthesis of the C′D′ disaccharide of aureolic acid *

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## ABSTRACT

Arylbis(arylthio)sulfonium salts have been used to activate glycals towards nucleophilic addition to form principally 2-deoxy-β-glycosides. This method was applied to the synthesis of the 2-(methylphenylthio)-2′-phenylthio derivative (**22**) of methyl *O*-(4-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-(1 → 3)-3,4-di-*O*-benzyl-2,6-dideoxy-2,6-β-D-*arabino*-hexopyranoside, the C′D′ ring analog of an aureolic acid disaccharide. The condensation of 1,5-anhydro-2,6-dideoxy-D-*arabino*-hex-1-enitol with methanol in the presence of the phenylbis(phenylthio)sulfonium salt resulted in formation of the first β-glycoside linkage. The methyl 6-deoxyglucoside obtained was deprotected at HO-3 to give the 2-thiophenyl-substituted 2,6-dideoxy-β-glucoside. This was coupled with 1,5-anhydro-3,4-di-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol in the presence of 4-methylphenyl[bis(4-methylphenyl)thio]sulfonium salt to give the (1 → 3)-linked disaccharide **22**. Finally, desulfurization of **22** using WII Raney nickel generated the required 2,2′-dideoxydisaccharide.

## INTRODUCTION

The aureolic acids are a group of highly toxic antibiotics which also have significant antitumor properties[1]. They include aureolic acid (**1**), the chromomycins (**2**), the olivomycins (**3**), and other related compounds. The structures of the aureolic acid group of compounds are based upon two aglycons, chromomycinone (**4**) and olivin (**5**). The aglycons are linked at their 2- and 6-positions to chains of one, two, or three sugars. This group of antibiotics inhibit DNA-dependent RNA polymerase and are active against Gram-positive bacteria, DNA viruses, and certain tumors[1]. The mode of action of these glycosylated anthracenones has been extensively studied[2]. The sugar chains of the antibiotics are essential for binding in the complex[1]. Analogs in which the saccharides have been partially hydrolyzed bind weakly, with rates of dissociation of their complexes increasing as the number of sugars decreases[1]. At least some sugars must be present since the aglycons do not complex with DNA and are inactive against tumors and microorganisms. Since

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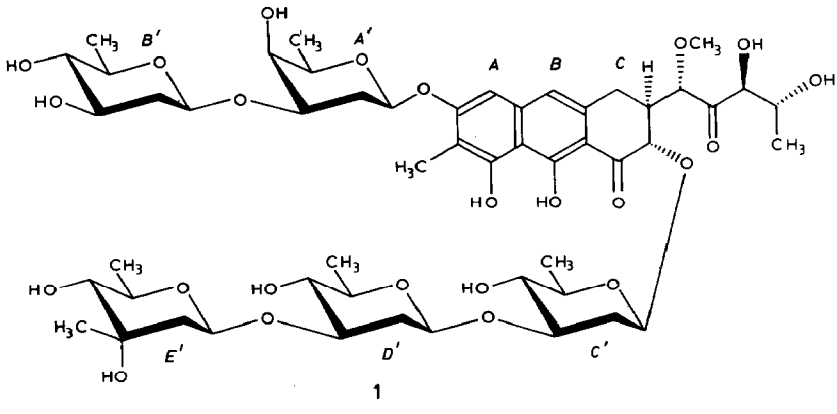
* Dedicated to Professor Serge David.



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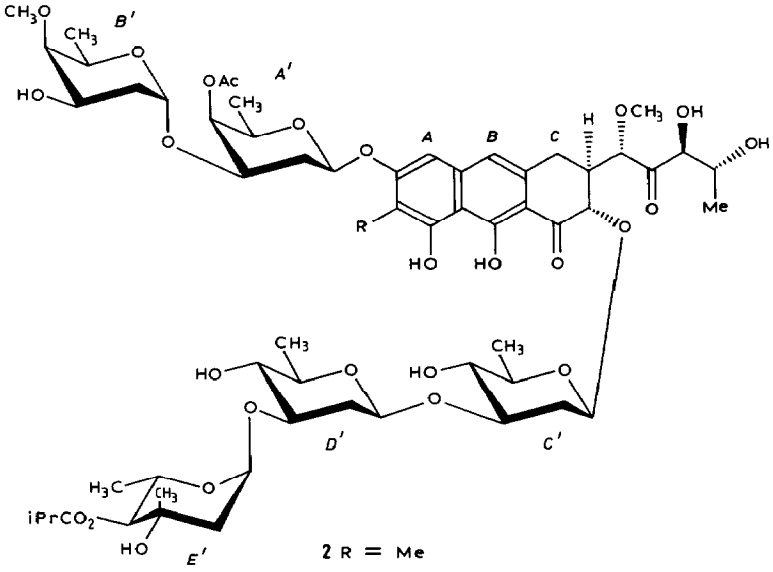
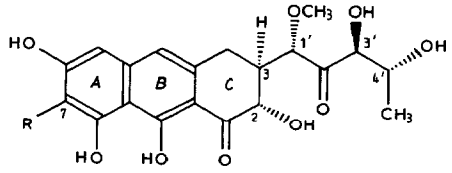
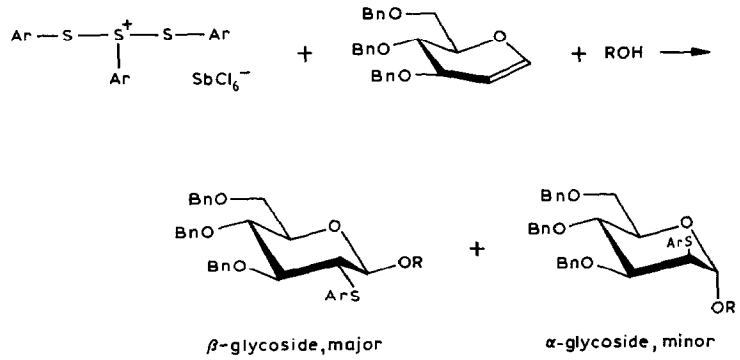


2 R = Me
3 R = H



4 R = $CH_3$
5 R = H

sugars play an important role in binding to DNA, they constitute a "site" where modifications can be done to understand the binding hypothesis as well as to make better drugs. For this reason, synthesis of the aureolic acids and their saccharide




Scheme 1.

derivatives has been a topic of interest among several groups[3], including the synthesis of both the aglycon[4] and carbohydrate portions[5–17]. One type of linkage which is essential for the synthesis of aureolic acid and related compounds is the 2-deoxy-β-D-glycosidic linkage. Several methods leading to stereoselective synthesis of such a linkage have been reported[18]. One of the methods developed in our laboratory, involves the use of arylbis(arylthio)sulfonium salts; these salts have proven to be exceptionally useful reagents for glycosyl transfer of glycals to a variety of hydroxyl donors[19] (see Scheme 1). A substituent effect study showed that the salt with a 4-tolylthio group is the most β-selective. The face selectivity is also dependent on the structure of the nucleophile and the glycal[19].

We tested our method by making the C′D′ subunit of the trisaccharide chain of aureolic acid (1). This disaccharide unit has been synthesized by Thiem and assoc.[10–14] and more recently by Binkley and Sivik[17]. Thiem and associates reported the preparation of completely blocked and deblocked methyl and benzyl glycosides of C′D′ disaccharide derivatives, where the key step is the Koenigs–Knorr reaction of 2-bromo-2-deoxy-α-D-glucopyranosyl bromide with the appropriate alcohol. Best results in this glycosidation were obtained when silver triflate was used as a promoter. This glycosidation step gave more favorable results for the preparation of benzyl (β-to-α ratio 13:2, 92% yield) than methyl glycosides (β-to-α ratio 6:1, 61% yield). Subsequent transformations (debromination, etc.) gives the acetyl-protected dideoxy disaccharide in 59% yield. Binkley and associates have synthesized the methyl glycoside of the C′D′ disaccharide. The β linkage between the C′D′ saccharide units was formed by the silver silicate-catalyzed reaction of a 2-deoxy-α-glycosyl halide with a partially protected sugar alcohol in 85% yield (β-to-α ratio 7:2). Thiem and Karl[15] and Binkley and Koholic[16] have also reported the synthesis of a C′D′ disaccharide analog where the glycosidic linkages between the sugars is β and α with the aglycon.

Procedure A

$$3\ Ar{-}S{-}S{-}Ar + 3\ SbCl_5 \xrightarrow[CH_2Cl_2]{-60^\circ C} 2\ Ar{-}S{-}\underset{\displaystyle Ar\quad SbCl_6^-}{\overset{\displaystyle |}{S^+}}{-}S{-}Ar + SbCl_3$$

Procedure B

$$Ar{-}S{-}S{-}Ar + ArSCl + SbCl_5 \xrightarrow[CH_2Cl_2]{-60^\circ C} Ar{-}S{-}\underset{\displaystyle Ar\quad SbCl_6^-}{\overset{\displaystyle |}{S^+}}{-}S{-}Ar$$

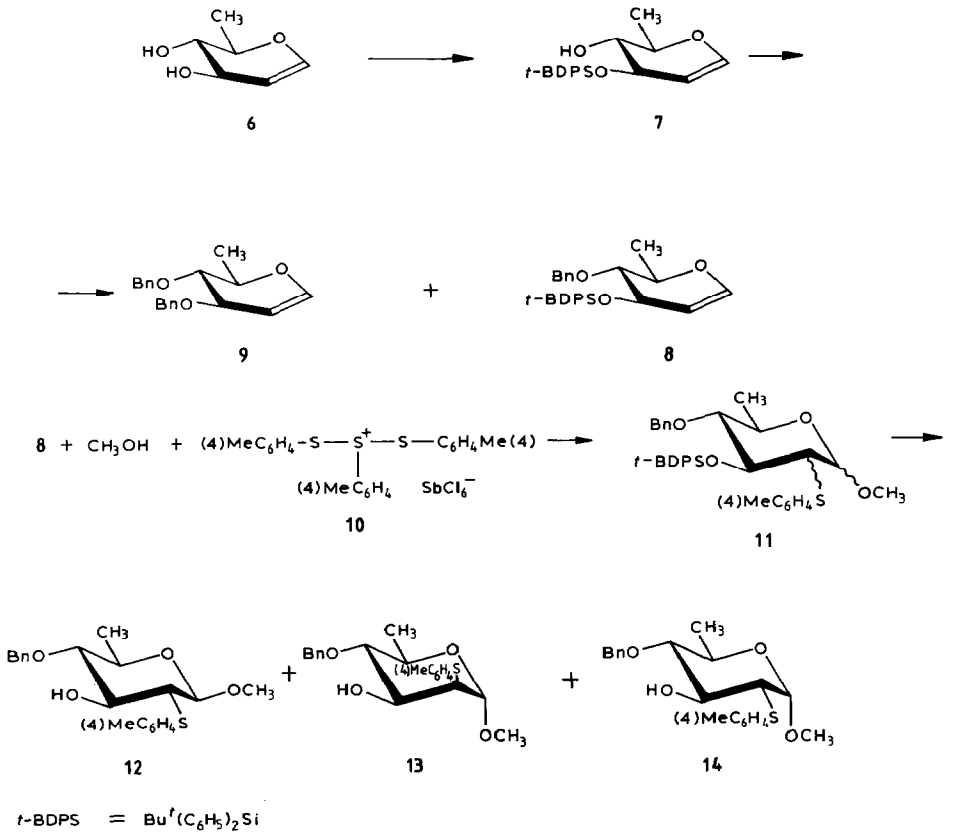
Scheme 2. Methods for the preparation of the aryl(bisarylthio)sulfonium salts.

## RESULTS AND DISCUSSION

The first step in the present glycal-based approach was glycosidation of a protected 1,5-anhydro-2,6-dideoxy-D-*arabino*-hex-1-enitol derivative using methanol as the nucleophile. The requirement was that HO-3 could be deblocked without affecting the protection at HO-4. Thus, a substituted silyl group at O-3 and a benzyl ether at C-4 were used. Treatment of the product from the first glycosidation step, methyl 2-deoxy-2-thiophenyl-β-glycoside, with fluoride will deprotect HO-3 (leaving BnO-4 intact) to give a nucleophile to be used for the second glycosidation.

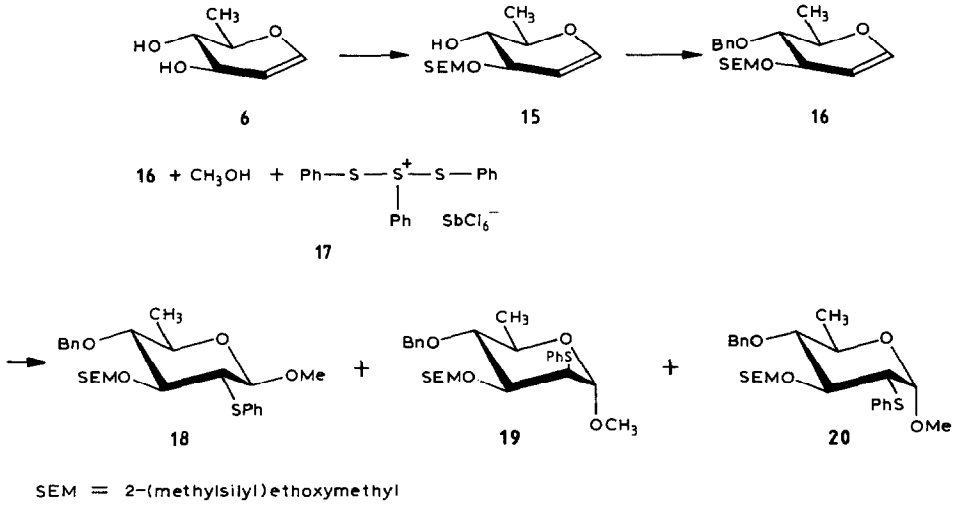
For the synthesis of 1,5-anhydro-4-*O*-benzyl-3-*O*-*tert*-butyldiphenylsilyl-2,6-dideoxy-D-*arabino*-hex-1-enitol (**8**), easily accessible 1,5-anhydro-2,6-dideoxy-D-*arabino*-hex-1-enitol[20] was treated with *tert*-butylchlorodiphenylsilane in the presence of imidazole to give the 3-*O*-*tert*-butyldiphenylsilyl derivative[21] **7**. On benzylation, glycal **7** gave the required product **8** in only 31% yield. Byproduct **9** was isolated in 10% yield; presumably the *tert*-butyldiphenylsilyl protecting group was cleaved during the reaction. Nevertheless, the condensation of glycal **8** and methanol in the presence of 4-methylphenyl[bis(4-methylphenyl)thio]sulfonium salt (**10**), prepared by procedure A (Scheme 2) gave glycosides **11**. These diastereomeric glycosides could be separated only after the *tert*-butyldiphenylsilyl group at O-3 was removed with tetrabutylammonium fluoride. The resultant glycosides **12**, **13**, and **14** were obtained in the ratio 6:1:3. The unwanted glycoside **14** was probably formed as one of the major products since reagent **10** was prepared by procedure A. In this method, the reagent contains a residual one-half equivalent of $SbCl_3$ which causes the epimerization at C-1 of the sensitive 6-deoxy-β-glycoside **12** to afford the corresponding 6-deoxy-α-glycoside **14**.

To improve yields, the process was repeated with the 2-(trimethylsilyl)ethoxymethyl (SEM)[22] group at O-3. The SEM group can be removed under the same conditions as any trialkylsilyl blocking group (treatment with fluoride), but since a Si–C bond in place of a Si–O bond is involved, it is less labile to benzylation conditions (used for blocking O-4). On reaction with SEM chloride, glycal **6** gave the 3-*O*-[2-(trimethylsilyl)ethoxymethyl] derivative **15**. Benzylation of **15** afforded 1,5-anhydro-4-*O*-benzyl-2-deoxy-3-*O*-[2-(trimethylsilyl)ethoxymethyl]-D-*arabino*-hex-1-enitol (**16**) in 72% yield. Glycosidation using the phenylbis(phenylthio)-



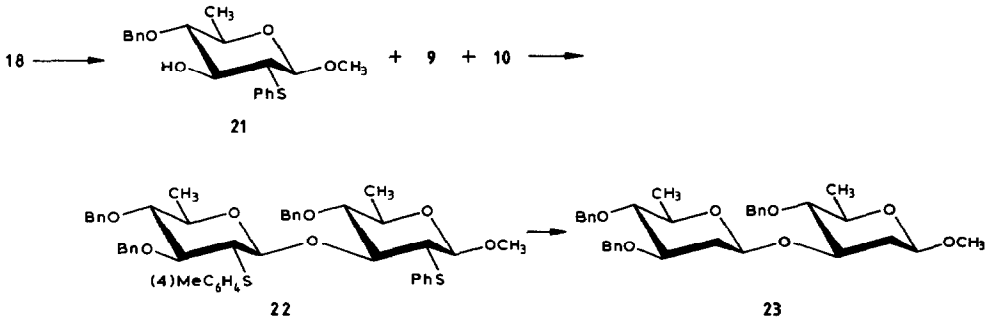

sulfonium reagent (**17**) and methanol resulted in glycosides **18**, **19**, and **20** in a ratio of 23:4:2 (82% yield). The improved yield of the desired product was due to the use of procedure B in preparing reagent **17** (Scheme 2).

The SEM group of methyl 4-*O*-benzyl-2,6-dideoxy-3-*O*-(trimethylsilyl)ethoxymethyl-2-phenylthio-β-D-glucopyranoside (**18**) was cleaved with cesium fluoride in $Me_2SO$ to give methyl 4-*O*-benzyl-2,6-dideoxy-2-phenylthio-β-D-glucopyranoside (**21**) in 80% yield, since tetrabutylammonium fluoride gave poor yields. The use of homonuclear 2D NMR spectroscopy (COSY) permitted assignment of all the proton signals in glycosides **12**–**14** and **21** (the signal of HO-3 was confirmed by $D_2O$ exchange). Coupling of glycal **9** (prepared in 85% yield from **6**) and the tributyltin ether of **21** (prepared in situ) with reagent **10** resulted in methyl *O*-[4-benzyl-2,6-dideoxy-2-(phenylthio)-β-D-glucopyranosyl]-(1 → 3)-3,4-di-*O*-benzyl-2,6-dideoxy-2-(4-methylphenyl)thio-β-D-glucopyranoside (**22**). The stannyl ether of the hydroxyl donor **21** was used to enhance its nucleophilicity[19]. The glycosidation was carried out with the optimal sulfonium reagent **10** prepared by procedure B. The β-D-(1 → 3)-linked disaccharide **22** was obtained in 47.5% yield.




Minor side products were observed, but they were not conclusively proven to be the $\alpha$ anomers. Desulfurization of **22** with WII Raney nickel gave the methyl *O*-(4-*O*-benzyl-2,6-dideoxy-$\beta$-D-glucopyranosyl)-(1 → 3)-3,4-di-*O*-benzyl-2,6-dideoxy-$\beta$-D-glucopyranoside (**23**) in 64% yield. The structure assignment of **23** was done by use of 2D NMR spectroscopy (see Fig. 1).

Thus, an efficient synthesis of the protected C′D′ disaccharide using our thiosulfonium salt method of glycosidation was devised. The starting materials can be prepared in a few steps and in good yield, e.g., **9** and **21** were prepared from **6** in one step (86% yield) and four steps (53% yield), respectively.




## EXPERIMENTAL

*Methods.*—Optical rotations were determined with a Rudolph Research Autopol III automatic polarimeter. NMR spectra were recorded on an GE QE 300 instrument with $CDCl_3$ as solvent. TLC were done on precoated TLC sheets of Silica Gel 60 $F_{254}$ (Merck) and short–longwave UV light was used to detect the

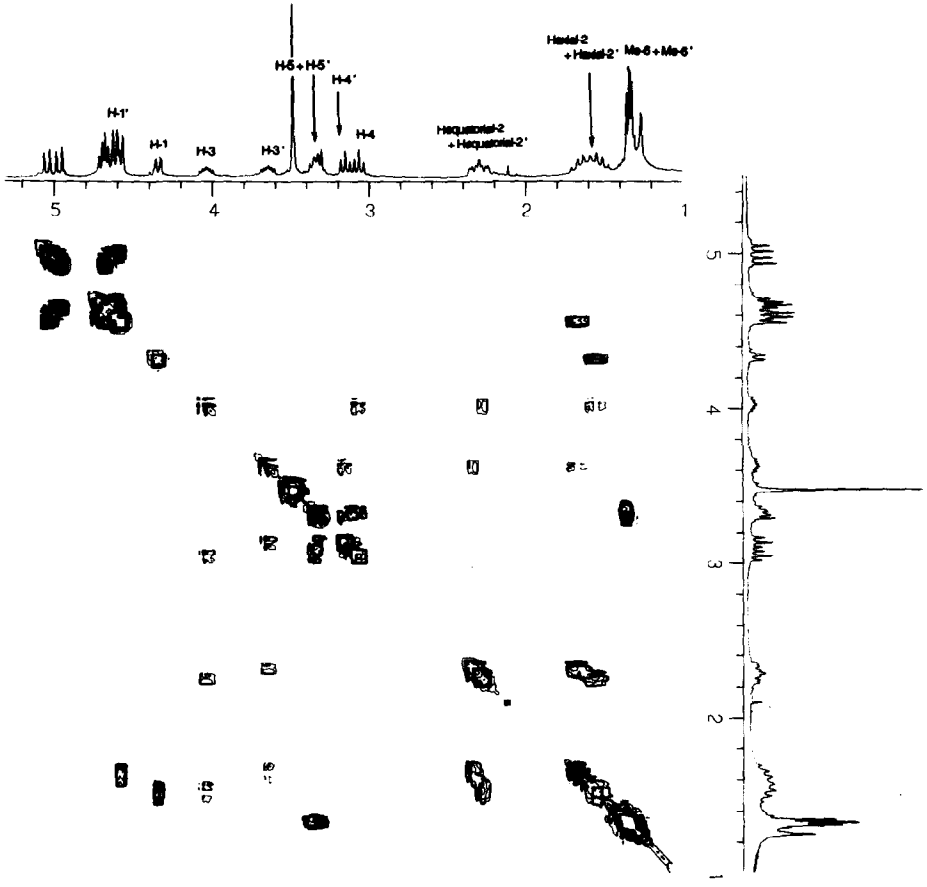



Fig. 1. The 2D NMR spectrum of compound **23**.

spots. PLC plates were prepared with Kieselgel 60 $PF_{254}$ (Merck), and chromatotron (radial chromatography) plates were prepared with Kieselgel 60 $PF_{254}$ gipshaltig (Merck). Methanol was distilled in the presence of Mg and stored over 3A molecular sieves. Dry oxolane was obtained by distillation, under $N_2$, from sodium-benzophenone ketyl. Dichloromethane was distilled in the presence of $P_2O_5$. Other solvents were purified and dried by standard procedures.

*General procedure for preparation of arylbis(arylthio)sulfonium salt reagent.— Procedure A.* A solution of diaryl disulfide (1.5 mmol) in dry $CH_2Cl_2$ (2.5 mL) was added dropwise to $SbCl_5$ (1.5 mL of M solution in $CH_2Cl_2$) at −60°C (under Ar). The mixture was stirred for 30 min at −60°C to give a green 0.25 M solution of the reagent.

*Procedure B.* A solution of diaryl disulfide (1 mmol) and arylsulfenyl chloride (1.1 mmol) in dry $CH_2Cl_2$ (3.0 mL) was added dropwise to $SbCl_5$ (1.0 mL of M

solution in $CH_2Cl_2$; Aldrich) at −60°C (under Ar). The mixture was stirred for 30 min at −60°C to give a green 0.25 M solution of the reagent.

*Treatment of 1,5-anhydro-2-deoxy-*D*-arabino-hex-1-enitol* (**6**) *derivatives with aryl-bis(arylthio)sulfonium salt.*—To a solution of **6** (235 mg, 1.8 mmol)[20] and imidazole (306 mg, 4.5 mmol) in *N*,*N*-dimethylformamide (1 mL) was added *tert*-butylchlorodiphenylsilane (547 mg, 2 mmol). The solution was stirred overnight, and then poured into water and extracted with EtOAc (3 × 10 mL). The organic extract was washed with water, dried ($Na_2SO_4$), and concentrated. The oily residue was purified by flash chromatography with 4:1 EtOAc–hexane to give 1,5-anhydro-3-*O*-*tert*-butyldiphenylsilyl-2-deoxy-D-*arabino*-hex-1-enitol (**7**; 605 mg, 89%) as an oil; $^1$H NMR ($CDCl_3$): δ 1.08 (s, 9 H, $SiCMe_3$) 1.36 (d, 3 H, $CH_3$-5), 1.83 (d, 1 H, OH-4), 3.60 (ddd, 1 H, H-4), 3.78–3.82 (m, 1 H, H-5), 4.23–4.26 (m, 1 H, H-3), 4.56 (dd, 1 H, H-2), 6.24 (dd, 1 H, H-1), 7.32–7.48 (m, 6 H, aryl-H), and 7.68–7.73 (m, 4 H, aryl-H); $J_{1,2}$ 6.1, $J_{1,3}$ 1.1, $J_{2,3}$ 2.4, $J_{4,OH\text{-}4}$ 4.1, and $J_{5,6}$ 6.4 Hz.

An 80% NaH oil suspension (53 mg, 1.76 mmol) was washed with dry hexane and suspended in dry 1:1 DMF–oxolane (3 mL). To this suspension was added a solution of **7** (604 mg, 1.6 mmol) in the same solvent (3 mL), dropwise with stirring at room temperature. After the addition was complete, the mixture was stirred for 1 h and then tetrabutylammonium iodide (10 mg) and benzyl bromide (300 mg, 1.76 mmol) were added. After stirring for 6 h, the mixture was poured into water and extracted three times with EtOAc (10 mL). The combined organic extracts were dried ($Na_2SO_4$) and evaporation of the solvent gave a crude product that was subjected to radial chromatography (1:9 EtOAc–hexane) to yield **8** (235 mg, 31%) and **9** (47 mg, 10%).

1,5-Anhydro-4-*O*-benzyl-3-*O*-*tert*-butyldiphenylsilyl-2-deoxy-D-*arabino*-hex-1-enitol (**8**). Oil; $^1$H NMR ($CDCl_3$): δ 1.07 (s, 9 H, $SiCMe_3$), 1.41 (d, 3 H, Me-5), 3.5 (t, 1 H), 4.01 (t, 1 H), 4.40–4.45 (m, 2 H), 4.65 (AB, 2 H, PhC$H_2$), 6.17 (d, 1 H, H-1), and 7.25–7.74 (m, 15 H, aryl-H); $J_{1,2}$ 9.3, $J_{5,6}$ 6.9, and $J_{AB,CH_2Ph}$ 11.6 Hz.

Compound **9**. Oil; $^1$H NMR ($CDCl_3$): δ 1.43 (d, 3 H, $CH_3$-5), 3.54 (dd, 1 H), 3.95–4.06 (m, 1 H, H-5), 4.24–4.30 (m, 1 H), 4.67 (AB, 2 H, PhC$H_2$), 4.85 (AB, 2 H, PhC$H_2$), 6.41 (dd, 1 H, H-1), and 7.30–7.48 (m, 10 H, aryl-H); $J_{1,2}$ 6.1, $J_{1,3}$ 0.8, $J_{5,6}$ 6.4, $J_{AB,CH_2PH}$ 11.3, and $J_{AB,CH_2PH}$ 11.6 Hz.

To a solution of glycal **8** (234 mg, 0.51 mmol) and MeOH (100 μL) in dry $CH_2Cl_2$ at −60°C (under Ar) was added by a syringe technique 4-methylphenyl[bis(4-methylphenyl)thio]sulfonium salt solution (**10**; 2.2 mL, 0.55 mmol, prepared by procedure A). After the reaction was complete (~10 min), satd aq $NaHCO_3$ (30 mL) was added and the mixture was stirred for 30 min at room temperature. The mixture was extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic extracts were dried ($Na_2SO_4$) and evaporation of the solvent gave a crude mixture that was subjected to radial chromatography (1:9 EtOAc–hexane to give a diastereomeric mixture of the methyl glycosides (187.5 mg, 60%, 0.31 mmol). Without purification, this was dissolved in dry oxolane (1.6 mL) and added to a solution of tetrabutylammonium fluoride (243 mg, 0.77 mmol) in

oxolane (1 mL). The mixture was stirred at room temperature for 30 min, and then poured into water and extracted three times with EtOAc (20 mL). The combined organic extracts were dried ($Na_2SO_4$) and evaporation of the solvent gave a crude product which was subjected to radial chromatography (1:3 EtOAc–hexane) to yield methyl 4-*O*-benzyl-2,6-dideoxy-2-(4-methylphenyl)thio-β-D-glucopyranoside (**12**), methyl 4-*O*-benzyl-2,6-dideoxy-2-(4-methylphenyl)thio-α-D-mannopyranoside (**13**), and methyl 4-*O*-benzyl-2,6-dideoxy-2-(4-methylphenyl)thio-α-D-glucopyranoside (**14**).

Compound **12**. Yield 56.9 mg, oil; $^1H$ NMR ($CDCl_3$): δ 1.26 (d, 3 H, $CH_3$-5), 2.30 (s, 3 H, aryl-$CH_3$), 2.63 (d, 1 H, OH-3), 3.05 (dd, 1 H, H-2), 3.10 (dd, 1 H, H-4), 3.34 (s, 3 H, $OCH_3$), 3.76 (dq, 1 H, H-5), 3.97 (dt, 1 H, H-3), 4.73 (d, 1 H, H-1), 4.79 (AB, 2 H, PhC$H_2$), 7.08 (d, 2 H, aryl-H), 7.23–7.33 (m, 5 H, aryl-H), and 7.38 (d, 2 H, aryl-H); $J_{1,2}$ 3.2, $J_{2,3}$ 10.7, $J_{3,OH-3}$ 1.5, $J_{3,4}$ 10.7, $J_{4,5}$ 9.4, $J_{5,6}$ 6.0, and $J_{AB,CH_2Ph}$ 11.2 Hz.

Compound **13**. Yield, 9.5 mg, oil; $^1H$ NMR ($CDCl_3$): δ 1.25 (d, 3 H, $CH_3$-5), 2.29 (s, 3 H, aryl-$CH_3$), 2.73 (dd, 1 H, H-2), 3.00 (d, 1 H, OH-3), 3.10 (t, 1 H, H-4), 3.19–3.22 (m, 1 H, H-5), 3.46 (ddd, 1 H, H-3), 3.48 (s, 3 H, $OCH_3$), 4.02 (d, 1 H, H-1), 4.78 (AB, 2 H, PhC$H_2$), 7.07 (d, 2 H, aryl-H), 7.21–7.34 (m, 5 H, aryl-H), and 7.39 (d, 2 H, aryl-H); $J_{1,2}$ 8.3, $J_{2,3}$ 10.8, $J_{3,OH-3}$ 1.5, $J_{3,4}$ 8.8, $J_{4,5}$ 8.8, $J_{5,6}$ 6.0, and $J_{AB,CH_2Ph}$ 11.1 Hz.

Compound **14**. Yield 28.4 mg, oil; $^1H$ NMR ($CDCl_3$): δ 1.32 (d, 3 H, $CH_3$-5), 2.31 (s, 3 H, aryl-$CH_3$), 2.60 (d, 1 H, *J* 9.0 Hz, OH-3), 3.12 (t, 1 H, H-4), 3.28 (s, 3 H, $OCH_3$), 3.53 (dd, 1 H, H-2), 3.70 (dq, 1 H, H-5), 4.26 (ddd, 1 H, H-3), 4.80 (AB, 2 H, PhC$H_2$), 4.90 (s, 1 H, H-1), 7.10 (d, 2 H, aryl-H), and 7.24–7.39 (m, 7 H, aryl-H); $J_{1,2}$ 1.3, $J_{2,3}$ 4.9, $J_{3,OH-3}$ 9.2, $J_{3,4}$ 9.0, $J_{4,5}$ 9.0, $J_{5,6}$ 6.2, and $J_{AB,CH_2Ph}$ 11.1 Hz.

*Methyl O-(4-O-benzyl-2,6-dideoxy-2-phenylthio)-β-D-mannopyranosyl-(1 → 3)-3,4-di-O-benzyl-2,6-dideoxy-2-(4-methylphenyl)thio-β-D-mannopyranoside* (**22**).—A solution of **6** (250 mg, 1.92 mmol) in $CH_2Cl_2$ (2 mL) under Ar was stirred overnight at room temperature with diisopropylethylamine (676 μL, 3.84 mmol) and chloro-2-(trimethylsilyl)ethoxymethane (394 μL, 2.11 mmol). The mixture was then poured into water and extracted with EtOAc (3 × 10 mL). The organic extract was washed with water, dried ($Na_2SO_4$), and concentrated. The oily residue was purified by flash chromatography with 1:1 EtOAc–hexane to give 1,5-anhydro-2-deoxy-3-*O*-[2-(trimethylsilyl)ethoxymethyl]-D-*arabino*-hex-1-enitol (**15**) (360 mg, 72%), oil; $^1H$ NMR ($CDCl_3$) δ 0.02 (s, 9 H, $SiMe_3$), 0.95–1.60 (m, 2 H, $SiCH_2$), 1.35 (d, 1 H, OH-4), 1.41 (d, 3 H, $CH_3$-5), 3.40 (ddd, 1 H, H-4), 3.52–3.61 (m, 1 H), 3.81–3.97 (m, 3 H), 4.63–4.65 (m, 1 H), 4.79 (AB, 2 H, PhC$H_2$), and 6.34 (dd, 1 H, H-1); $J_{1,2}$ 6.1, $J_{1,3}$ 1.5, $J_{4,OH-4}$ 7.0, $J_{5,6}$ 6.3, and $J_{AB,CH_2Ph}$ 7.4 Hz.

An 80% NaH oil suspension (41 mg, 1.37 mmol) was washed with dry hexane and suspended in dry 1:1 DMF–oxolane (2 mL). To this suspension was added a solution of glycal **15** (300 mg, 1.14 mmol) in the same solvent (2 mL) dropwise with stirring at room temperature. After the addition was complete, the mixture was

stirred for 1 h and then tetrabutylammonium iodide (10 mg) and benzyl bromide (163 μL, 1.37 mmol) were added. After stirring for 6 h the mixture was poured into water and extracted three times with EtOAc (10 mL). The combined organic extracts were dried ($Na_2SO_4$) and evaporation of the solvent gave a crude product which was subjected to radial chromatography (1:9 EtOAc–hexane) to yield 1,5-anhydro-4-*O*-benzyl-2,6-dideoxy-3-*O*[2-(trimethylsilyl)ethoxymethyl]-D-*arabino*-hex-1-enitol (**16**) (289 mg 72%), oil; $^1$H NMR ($CDCl_3$): $^1$H, δ 0.01 (s, 9 H, $SiMe_3$), 0.93 (t, 2 H, $SiCH_2$), 1.35 (d, 3 H, $CH_3$-5), 3.43 (dd, 1 H, H-4), 3.58–3.71 (m, 2 H, $OCH_2CH_2Si$), 3.94–4.00 (m, 1 H), 4.27–4.30 (m, 1 H), 4.73–4.82 (m, 3 H, H-2, $OCH_2O$), 4.76 (AB, 2 H, $PhCH_2$), 6.33 (d, 1 H, H-1), and 7.27–7.35 (m, 5 H, aryl-H); $J_{SiCH_2,SiCH_2CH_2O}$ 8.5, $J_{1,2}$ 6.1, $J_{5,6}$ 6.5, and $J_{AB,CH_2Ph}$ 11.5 Hz; $^{13}$C, δ −1.57, 17.24, 17.98, 65.24, 73.88, 74.50, 79.92, 93.97, 100.91, 127.60, 127.70, 128.27, 138.19, and 144.34.

To a solution of **16** (175 mg, 0.5 mmol) and MeOH (100 μL) in dry $CH_2Cl_2$ (6 mL) at −60°C (under Ar) was added by a syringe technique the phenyl(bisphenylthio)sulfonium salt (**17**) solution (2.2 mL, 0.55 mmol, prepared by procedure B). After the reaction was complete (~ 10 min), satd aq $NaHCO_3$ (30 mL) was added, and the mixture was stirred for 30 min at room temperature. The mixture was extracted with $CH_2Cl_2$ (3 × 50 mL) and the combined organic extracts were dried ($Na_2SO_4$). Evaporation of the solvent gave a crude product mixture which was subjected to radial chromatography (1:9 EtOAc–hexane) to give methyl 4-*O*-benzyl-2,6-dideoxy-3-*O*-[2-(trimethylsilyl)ethoxymethyl]-2-phenylthio-β-D-glucopyranoside (**18**), methyl 4-*O*-benzyl-2,6-dideoxy-3-*O*-[2-(trimethylsilyl)ethoxymethyl]-2-phenylthio-α-D-mannopyranoside (**19**), and methyl 4-*O*-benzyl-2,6-dideoxy-3-*O*-[2-(trimethylsilyl)ethoxymethyl]-2-phenylthio-α-D-glucopyranoside (**20**) (total yield 82%).

Compound **18**. Yield 158.6 mg, oil; $^1$H NMR ($CDCl_3$): δ −0.13 (s, 9 H, $SiMe_3$), 0.83–0.90 (m, 2 H, $SiCH_2$), 1.26 (d, 3 H, $CH_3$-5), 3.17 (t, 1 H, H-4), 3.26 (dd, 1 H, H-2), 3.36 (s, 3 H, $OCH_3$), 3.52–3.61 (m, 1 H, $OCH_2CH_2Si$), 3.50–3.82 (m, 2 H, H-5, $OCH_2CH_2Si$), 3.95 (dd, 1 H, H-3), 4.68 (d, 1 H, H-1), 4.77 (AB, 2 H, $PhCH_2$), 4.96 (s, 2 H, $OCH_2O$), and 7.16–7.51 (m, 10 H, aryl-H); $J_{1,2}$ 3.7, $J_{2,3}$ 11.0, $J_{3,4}$ 9.0, $J_{4,5}$ 9.0, $J_{5,6}$ 6.3, and $J_{AB,CH_2Ph}$ 11.1 Hz.

Compound **19**. Yield 27.6 mg, oil; $^1$H NMR ($CDCl_3$): δ 0.08 (s, 9 H, $SiMe_3$), 0.82 (m, 2 H, $SiCH_2$), 1.30 (d, 3 H, $CH_3$-5), 3.28 (s, 3 H, $OCH_3$), 3.38 (t, 1 H, H-4), 3.53–3.62 (m, 1 H, $OCH_2CH_2Si$), 3.65–3.78 (m, 3 H, H-2, 5, $OCH_2CH_2Si$), 4.33 (dd, 1 H, H-3), 4.70 (s, 1 H, H-1), 4.75 (s, 2 H, $OCH_2O$), 4.75 (AB, 2 H, $PhCH_2$), and 7.18–7.49 (m, 10 H, aryl-H); $J_{2,3}$ 4.8, $J_{3,4}$ 9.0, $J_{4,5}$ 9.0, $J_{5,6}$ 6.2, and $J_{AB,CH_2Ph}$ 11.1 Hz.

Compound **20**. Yield 13.8 mg, oil; $^1$H NMR ($CDCl_3$): δ 0.01 (s, 9 H, $SiMe_3$), 0.93–1.04 (m, 2 H, $SiCH_2$), 1.36 (d, 3 H, $CH_3$-5), 3.07 (dd, 1 H, H-2), 3.26 (t, 1 H, H-4), 3.35–3.48 (m, 1 H), 3.51 (s, 3 H, $OCH_3$), 3.61–3.73 (m, 2 H), 4.03–4.10 (m, 1 H), 4.18 (d, 1 H, H-1), 4.81 (AB, 2 H), 5.09 (AB, 2 H), and 7.27–7.68 (m, 10 H, aryl-H); $J_{1,2}$ 8.7, $J_{2,3}$ 10.7, $J_{3,4}$ 8.6, $J_{4,5}$ 8.6, and $J_{5,6}$ 6.0 Hz.

A solution of **18** (382 mg, 0.78 mmol) in $Me_2SO$ (5 mL) was added to CsF (3.5 g, 23 mmol) and 18-Crown-6 (20 mg) in $Me_2SO$ (6 mL). The mixture was stirred and heated to 105°C for 12 h, and then poured into water and extracted three times with EtOAc (30 mL). The combined organic extracts were dried ($Na_2SO_4$) and evaporation of the solvent gave a crude product which was subjected to radial chromatography (1:3 EtOAc–hexane) to give methyl-4-*O*-benzyl-2,6-dideoxy-2-phenylthio-β-D-glucopyranoside (**21**) (225 mg, 80%), oil, $[\alpha]_D^{25}$ +59° ($CHCl_3$); NMR ($CDCl_3$): $^1H$, δ 1.22 (d, 3 H, $CH_3$-5), 2.79 (dd, 1 H, H-2), 2.96 (br s, 1 H, OH-3), 3.07 (t, 1 H, H-4), 3.19–3.24 (m, 1 H, H-5), 3.43 (s, 3 H, $OCH_3$), 3.42–3.48 (m, 1 H, H-3), 4.02 (d, 1 H, H-1), 4.72 (AB, 2 H, PhC$H_2$), and 7.16–7.49 (m, 10 H, aryl-H); $J_{1,2}$ 8.7, $J_{2,3}$ 10.8, $J_{3,4}$ 8.8, $J_{4,5}$ 8.8, $J_{5,6}$ 6.1, and $J_{AB,CH_2Ph}$ 11.1 Hz; $^{13}C$, δ 17.83 (C-6), 56.79, 57.18, 70.76, 74.12, 74.82, 83.81, 102.72 (C-1), 127.71, 127.96, 128.02, 128.32, 128.84, 128.95, 133.81 and 138.23.

An 80% suspension of NaH in oil (53 mg, 1.76 mmol) was washed with dry hexane and suspended in dry 1:1 DMF–oxolane (3 mL). To this suspension a solution of **6** (104 mg, 0.8 mmol) in the same solvent (1.5 mL) was added dropwise with stirring at room temperature. After the addition was complete, the mixture was stirred for 1 h and then tetrabutylammonium iodide (10 mg) and benzyl bromide (300 mg, 1.76 mmol) were added. After stirring for 6 h, the mixture was poured into water and extracted three times with EtOAc (10 mL). The combined organic extracts were dried ($Na_2SO_4$), and evaporation of the solvent gave a crude product which was subjected to radial chromatography (1:9 EtOAc–hexane) to yield 1,5-anhydro-3,4-di-*O*-benzyl-2,6-dideoxy-D-*arabino*-hex-1-enitol (**9**) (211 mg, 85%), oil; $^1H$ NMR data ($CDCl_3$): δ 1.43 (d, 3 H, $CH_3$-5), 3.54 (dd, 1 H), 3.95–4.06 (m, 1 H, H-5), 4.24–4.30 (m, 1 H), 4.67 (AB, 2 H, PhC$H_2$), 4.85 (AB, 2 H, PhC$H_2$), 6.41 (dd, 1 H, H-1), and 7.30–7.48 (m, 10 H, aryl-H); $J_{1,2}$ 6.1, $J_{1,3}$ 0.8, $J_{5,6}$ 6.4, $J_{AB,CH_2Ph}$ 11.3, and $J_{AB,CH_2Ph}$ 11.6 Hz.

To compound **21** (130.5 mg, 0.36 mmol), dissolved in dry toluene (10 mL) under an Ar atmosphere, was added activated powdered 4A molecular sieves (2.3 g) and bis(tributyl)tin oxide (139 μL, 0.27 mmol). The mixture was refluxed for 12 h and thereafter toluene was distilled off. To the residue a solution of glycal **9** (0.18 mmol) in dry $CH_2Cl_2$ (2.2 ml) was added, and the mixture was cooled to −60°C, and the reagent solution **10** (800 μL, 0.20 mmol, prepared by procedure B) was added by a syringe technique. After the reaction was complete (~ 10 min), it was quenched with satd aq $NaHCO_3$ (15 ml) and the mixture was stirred for 30 min at room temperature. It was filtered through Celite (the Celite was washed with 50 mL of $CH_2Cl_2$), and the organic layer of the filtrate was dried ($Na_2SO_4$). Evaporation of the solvent gave a crude product mixture which was subjected to radial chromatography (1:4 EtOAc–hexane) to give **22** (68.5 mg, 47.5%), oil; $[\alpha]_D^{25}$ −24° ($CHCl_3$); NMR* ($CDCl_3$): $^1H$, δ 1.18 (d, 3 H, $CH_3$-5), 1.28 (d, 3 H, $CH_3$-5′),

* For the NMR assignment of disaccharides **22** and **23**, we were not able to distinguish between the C′ and D′ rings. The assignments of the proton signals for each ring were grouped on the basis of 2D NMR data but they could be reversed.

2.29 (s, 3 H, aryl-$CH_3$), 2.85 (t, 1 H, H-4), 3.00–3.31 (m, 2 H, H-2,2′), 3.19–3.35 (m, 2 H, H-4′,5), 3.40 (s, 3 H, $OCH_3$), 3.40–3.56 (m, 2 H, H-5′,3′), 4.05 (dd, 1 H, H-3), 4.08 (d, 1 H, H-1), 4.52 (AB, 2 H, PhC$H_2$), 4.76 (AB, 2 H, PhC$H_2$), 4.91 (AB, 2 H, PhC$H_2$), 5.52 (d, 1 H, H-1′), 6.99 (d, 2 H, aryl-H), 7.21–7.33 (m, 20 H, aryl-H), and 7.61 (d, 2 H, aryl-H); $J_{1',2'}$ 8.5, $J_{1,2}$ 8.4, $J_{2,3}$ 10.8, $J_{3,4}$ 8.6, $J_{4,5}$ 8.6, $J_{5,6}$ 5.8, $J_{5',6'}$ 5.9, $J_{AB,CH_2Ph}$ 10.2, $J_{AB,CH_2PH}$ 10.6, and $J_{AB,CH_2Ph}$ 11.0 Hz; $^{13}C$, $\delta$ 18.07 (C-6 or -6′), 18.15 (C-6 or -6′), 21.08, 55.76, 56.88, 58.38, 70.64, 71.03, 75.00, 75.23, 76.32, 77.28, 82.77, 83.16, 85.34, 102.25 (C-1 or -1′), 103.93 (C-1 or -1′), 127.44, 127.63, 127.70, 127.83, 127.90, 128.17, 128.34, 128.45, 128.47, 128.71, 129.37, 132.36, 133.00, 133.11, 134.22, 136.57, 138.26, 138.40, and 138.49. Anal. Calcd for $C_{47}H_{52}O_7S_2$ (793.1): C, 71.18; H, 6.61; S, 8.09. Found: C, 71.19; H, 6.71; S, 8.14.

A solution of **22** (15.8 mg, 0.02 mmol) in dry oxolane (1.0 mL) was added to a stirred suspension of Raney nickel WII (160 mg) in oxolane (1.0 mL) at room temperature. The reaction was complete (monitored by TLC) in 60 min. The mixture was then filtered through Celite and removal of the solvent gave a colorless residue. Purification by radial chromatography (1 : 4 EtOAc–hexane) gave methyl *O*-(4-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-(1 → 3)-3,4-di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (**23**) (11.2 mg, 64%), oil; $[\alpha]_D^{25}$ −20° ($CHCl_3$); NMR ($CDCl_3$): $^1H$, $\delta$ 1.31 (d, 3 H, $CH_3$-5 or $CH_3$-5′), 1.33 (d, 3 H, $CH_3$-5 or $CH_3$-5′), 1.49–1.69 (m, 2 H, H-2*a*,2′*a*), 2.21–2.34 (m, 2 H, H-2*e*,2′*e*), 3.04 (t, 1 H, H-4), 3.13 (t, 1 H, H-4′), 3.28–3.36 (m, 2 H, H-5,5′), 3.47 (s, 3 H, $OCH_3$), 3.58–3.68 (m, 1 H, H-3′), 3.92–4.04 (m, 1 H, H-3), 4.32 (dd, 1 H, H-1), 4.54–4.69 (m, 4 H, H-1′, 1.5 PhC$H_3$), 4.80 (AB, 2 H, PhC$H_2$), 5.02 (d, 1 H, 0.5 PhC$H_2$), and 7.25–7.41 (m, 15 H, aryl-H); $J_{1,2a}$ 9.7, $J_{1,2e}$ 1.3, $J_{3,4}$ 8.9, $J_{3',4'}$ 8.9, $J_{4,5}$ 8.9, $J_{4',5'}$ 8.9, $J_{aB,CH_2Ph}$ 10.9, and $J_{d,CH_2Ph}$ 10.5 Hz; $^{13}C$, $\delta$ 18.14 (C-6 or -6′), 18.19 (C-6 or -6′), 36.31, 37.39, 56.45, 71.16, 71.31, 74.73, 75.20, 75.79, 79.18, 82.25, 83.71, 95.73 (C-1 or -1′), 100.24 (C-1 or -1′), 127.51, 127.57, 127.64, 127.76, 128.01, 128.11, 128.32, 138.23, 138.33, and 138.59; MS ($CH_4/Cl^+$): 561 $(M - H)^+$.

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