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Note

Synthesis of 1,2-anhydro-D-altropyranose and -D-allopyranose benzyl ethers

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1,2-Anhydro-3,4,6-tri-*O*-benzyl-β-D-altropyranose (**11**) and 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-allopyranose (**21**) are useful monomers for stereoregular polymerization to afford α-(1 → 2)-linked D-altropyranan or β-(1 → 2)-linked D-allopyranan, which are valuable model compounds for immunological research [1], and may serve as glycosyl donors in the stereospecific synthesis of oligosaccharides [2] and other biomedical products [3]. According to the literature [4], altrose and allose derivatives occur frequently as components of bioactive natural products. For example, *Epipodophyllotoxin altrosides* were used as antitumor agents to increase the mean survival time of mice inoculated with P388 *leukaemia* cells by 220% [5]. It was also reported that some oligosaccharides containing altropyranose could be used as wound healing agents [6], and some aryl β-D-allopyranosides were observed in the leaves of a higher plant (*Protea rubropilosa*) used in glycosidase-specificity studies [7]. These results have caused us to study the synthesis of the title anhydro sugars via an intramolecular S_N2 reaction [8] of a C-2 alkoxide with a C-1 bearing a leaving group, or an inverse ring closure [9] reaction of a C-1 alkoxide with a C-2 attached to a leaving group. Thus, methyl 4,6-*O*-benzylidene-α-D-altropyranoside (**1**) was prepared from D-glucose [10], and selective 2-*O*-allylation of **1** [11] gave methyl 2-*O*-allyl-4,6-*O*-benzylidene-α-D-altropyranoside (**2**) in satisfactory yield (78.7%). The structure of **2** was established from its ^1H NMR spectrum by single frequency decoupling and further confirmed by the preparation of its derivatives (**3**, **4**). Carefully controlled acid-catalyzed debenzylidenation of **2** furnished methyl 2-*O*-allyl-α-D-altropyranoside (**5**), and benzylation of **5**

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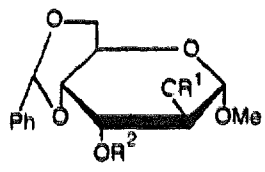
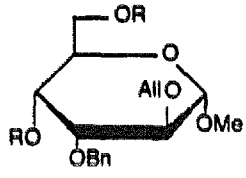
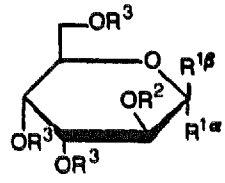
afforded methyl 2-*O*-allyl-3,4,6-tri-*O*-benzyl-α-D-altropyranoside (**6**) in moderate yield. Hydrolysis (**6** → **7**) followed by deallylation of **7** with $PdCl_2$ afforded 3,4,6-tri-*O*-benzyl-D-altropyranose (**8**) as a syrup. An alternative preparation of **8** (i.e., benzylation of **2** at C-3 followed by debenzylidenation, then benzylation at C-4 and C-6) was not successful as decomposition occurred at the debenzylidenation stage. Acetylation of **8** with acetic anhydride in pyridine gave 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-altropyranose (**9**) quantitatively, and treatment of **9** with dry hydrogen chloride in diethyl ether furnished the key intermediate, 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-altropyranosyl chloride (**10**). On treatment with potassium *tert*-butoxide in oxolane, **10** was converted to the target compound, 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-D-altropyranose (**11**) which was identified by TLC and ^1H NMR spectroscopy. The up-field signal at δ 3.40 ($J_{H\text{-}1,H\text{-}2} = J_{H\text{-}2,H\text{-}3} = 4.0$ Hz) is characteristic of the 1,2-epoxide ring [8,9]. Since **11** was not stable, it was not possible to obtain a satisfactory elemental analysis. Further identification was carried out by methanolysis of **11** in absolute MeOH in the absence of a promoter at room temperature, giving the 1,2-*trans* linked product, methyl 3,4,6-tri-*O*-benzyl-α-D-altropyranoside (**12**), in a quantitative yield.



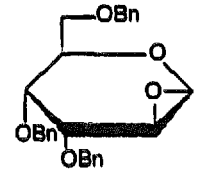
	R^1	R^2
1	H	H
2	All	H
3	All	Ac
4a	All	Bn



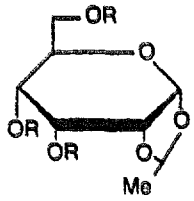
4b R = H
4c R = Ac



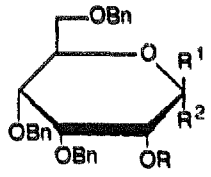
	$R^{1\alpha}$	$R^{1\beta}$	R^2	R^3
5	OMe	H	All	H
6	OMe	H	All	Bn
7	OH,H		All	Bn
8	OH,H		H	Bn
9	OAc	H	Ac	Bn
10	Cl	H	Ac	Bn
12	OMe	H	H	Bn



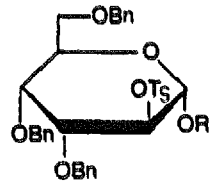
11



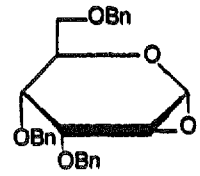
13 R = Ac
14 R = Bn



	R^1	R^2	R
15	H,OH		H
16	H,OAc		Ac
17	H	Cl	Ac
18	H	F	Ac
22	OMe	H	H
23	OMe	H	Ac



19 R = H
20 R = Ac



21

The synthesis of 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-allopyranose (**21**) was accomplished by inverse ring closure. The synthesis of **21** was first attempted via the route used for the synthesis of 1,2-anhydro altrose **11** (i.e., by an intramolecular S_N2 reaction of an C-2 alkoxide with a C-1 bearing a leaving group). Thus, 3,4,6-tri-*O*-acetyl-1,2-*O*-(*R*-ethylidene)-α-D-allopyranose (**13**) containing a trace amount of the *S* isomer was prepared from D-glucose by reported methods [12,13]. Benzylation of **13** with benzyl chloride and KOH in toluene under reflux gave 3,4,6-tri-*O*-benzyl-1,2-*O*-(*R*-ethylidene)-α-D-allopyranose (**14**) whose hydrolysis with M sulfuric acid in dioxane afforded 3,4,6-tri-*O*-benzyl-D-allopyranose (**15**). Subsequent acetylation of **15** with acetic anhydride in pyridine gave the diacetate **16** as an α,β mixture, with the β anomer predominating. Quantitative conversion of **16** to 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-allopyranosyl chloride (**17**) was readily achieved by treating **16** with dry hydrogen chloride in diethyl ether. To prepare the β-halide suitable for the intramolecular S_N2 reaction, fluorination of **17** with silver fluoride in CH_3CN–benzene (2:5) was conducted [8]. However, the fluorination gave the α-linked fluoride (**18**) as the sole product in a satisfactory yield, as indicated from its ^1H NMR spectrum showing H-1 at δ 5.64 (dd, $J_{H\text{-}1,H\text{-}2}$ 6.0, $J_{H\text{-}1,F}$ 54.8 Hz), which is similar to the values observed for α-fluorides (for 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-galactopyranosyl [8b] and 2-*O*-acetyl-3,4-di-*O*-benzyl-6-deoxy-α-D-glucopyranosyl [8c] fluoride, the chemical shifts of H-1 were δ 5.73 and 5.54, while those of H-1 of β anomers were δ 5.12 and 5.17, respectively). Further evidence for its α configuration was provided by the resistance of **18** to ring closure under normal ring closure conditions used for glycopyranosyl β-fluorides [8b,8c]. Since this synthesis of the necessary precursor β-fluoride was unsuccessful, our attention turned to the inverse ring closure [9]. Thus, 3,4,6-tri-*O*-benzyl-D-altropyranose (**8**) was tosylated with TsCl, 5% aq NaOH and Bu_4NHSO_4 in CH_2Cl_2 (phase transfer conditions), or with TsCl in pyridine containing K_2CO_3 (powder, 1 equiv) and 4-dimethylaminopyridine (0.1 equiv). 3,4,6-Tri-*O*-benzyl-2-*O*-*p*-toluenesulfonyl-α-D-altropyranose (**19**) was the sole product (65%, former method; 53%, latter method). In both cases, the unreacted starting material was recovered and could be reused. The structure of **19** was confirmed via the acetylated derivative **20** (only the α anomer was obtained). Ring closure of **19** with potassium *tert*-butoxide in dry oxolane gave the sole product, 1,2-anhydro-3,4,6-tri-*O*-benzyl-α-D-allopyranose (**21**), which was identified by TLC and ^1H NMR spectroscopy. As observed for **11**, the ^1H NMR spectrum of **21** gave a characteristic peak at δ 3.30 ($J_{H\text{-}1,H\text{-}2}$ 2.8, $J_{H\text{-}2,H\text{-}3}$ 3.4 Hz). Quantitative methanolysis, giving methyl 3,4,6-tri-*O*-benzyl-β-D-allopyranoside (**22**), further confirmed the structure of **21**. The structure of **22** was verified by acetylation, since the acetylated compound **23** gave a clearer ^1H NMR spectrum than **22**.

1. Experimental

General methods and materials.—See ref. [8a].

Methyl 2-O-allyl-4,6-O-benzylidene-α-D-altropyranoside (**2**).—To a solution of methyl 4,6-*O*-benzylidene-α-D-altropyranoside [10] (**1**, 2.03 g, 7.22 mmol) in

dichloromethane (15 mL) was added tetrabutylammonium iodide (0.2 g, 5.41 mmol), 5% aq sodium hydroxide (6 mL), and allyl bromide (1 mL, 11.7 mmol). The mixture was stirred at room temperature for about 20 h, then diluted with dichloromethane (25 mL) and washed with water (3 × 10 mL). The organic layer was dried (Na_2SO_4) and concentrated to a syrup that was purified by column chromatography with 2:1 petroleum ether-EtOAc to give **2** as a syrup (1.83 g, 78.7%); $[\alpha]_D$ +19.4° (*c* 0.6, $CHCl_3$); ^1H NMR: δ 7.58–7.35 (m, 5 H, Ph*H*), 6.00–5.89 (m, 1 H, CH_2=C*H*-), 5.65 (s, 1 H, PhC*H*), 5.40–5.25 (m, 2 H, *J* 17.1, 1.5, 10.3 Hz, CH_2=CH-), 4.74 (s, 1 H, H-1), 4.31 (dd, 1 H, $J_{5,6}$ 5.0, $J_{6,6'}$ 10.3 Hz, H-6), 4.20–4.15 (m, 2 H, H-2,5), 4.13–4.08 (m, 2 H, CH_2=CH-CH_2), 3.95 (dd, 1 H, $J_{3,4}$ 2.7, $J_{4,5}$ 9.8 Hz, H-4), 3.85 (t, 1 H, $J_{5,6'}$ 10.3, $J_{6,6'}$ 10.3 Hz, H-6'), 3.66 (dd, 1 H, $J_{2,3}$ 1.4, $J_{3,4}$ 2.7 Hz, H-3), 3.49 (s, 3 H, OCH_3). Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.35; H, 6.83. Found: C, 63.63; H, 6.82.

Methyl 3-O-acetyl-2-O-allyl-4,6-O-benzylidene-α-D-altropyranoside (**3**).—Acetylation of **2** (100 mg, 0.27 mmol) with pyridine (2 mL) and acetic anhydride (1.2 mL) at room temperature for 4 h gave compound **3** in quantitative yield as a syrup; $[\alpha]_D$ +4.2° (*c* 1.9, $CHCl_3$); ^1H NMR: δ 7.50–7.31 (m, 5 H, Ph*H*), 6.05–5.80 (m, 1 H, CH_2=C*H*-), 5.60 (s, 1 H, PhC*H*), 5.44–5.20 (m, 3 H, CH_2=CH-, H-3), 4.65 (s, 1 H, H-1), 4.40–4.00 (m, 5 H, H-2,4,5, and CH_2=CH-CH_2), 3.85–3.70 (m, 2 H, H-6,6'), 3.41 (s, 3 H, OCH_3), 2.11 (s, 3 H, COCH_3). Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.64; H, 6.59. Found: C, 62.72; H, 6.38.

Methyl 4,6-di-O-acetyl-2-O-allyl-3-O-benzyl-α-D-altropyranoside (**4c**).—Benzylation [8] of compound **2** (1.5 g, 4.7 mmol) with benzyl bromide (0.9 mL, 6.7 mmol) and sodium hydride (80%, 500 mg, 16.7 mmol) gave methyl 2-*O*-allyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-altropyranoside (**4a**, 1.74 g). Debenzylidenation of **4a** (1.0 g) with 80% aq acetic acid furnished methyl 2-*O*-allyl-3-*O*-benzyl-α-D-altropyranoside (**4b**) in a low yield (0.39 g, 50%). Acetylation of **4b** with pyridine and acetic anhydride gave **4c** as a syrup; $[\alpha]_D$ −3.1° (*c* 0.2, $CHCl_3$); ^1H NMR: δ 7.40–7.28 (m, 5 H, Ph*H*), 5.95–5.78 (m, 1 H, CH_2=C*H*-), 5.30–5.17 (m, 2 H, CH_2=CH-), 5.09 (dd, 1 H, $J_{3,4}$ 2.3, $J_{4,5}$ 7.9 Hz, H-4), 4.68 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.62, 4.56 (2 d, 2 H, *J* 9.9 Hz, PhCH_2), 4.34–4.08 (m, 3 H, H-2,3,5), 4.06–4.00 (m, 2 H, CH_2=CH-CH_2), 3.92–3.85 (m, 2 H, H-6,6'), 3.40 (s, 3 H, OCH_3), 2.03, 2.01 (2 s, 6 H, COCH_3).

Methyl 2-O-allyl-α-D-altropyranoside (**5**).—To a solution of **2** (1.8 g, 5.59 mmol) in acetone (2 mL) was added 80% aq acetic acid (10 mL). The mixture was stirred under reflux for about 4 h. TLC (1:1 petroleum ether–EtOAc) indicated that the starting material had disappeared. MeOH:H_2O:Et_3N (12:5:3, 8 mL) was added, and the mixture was stirred under reflux for another 30 min. Concentration and purification of the product by column chromatography (1:1 petroleum ether–EtOAc) gave **5** as a syrup (1.04 g, 79.5%); $[\alpha]_D$ +2.4° (*c* 0.6, $CHCl_3$); ^1H NMR: δ 6.00–5.80 (m, 1 H, CH_2=C*H*-), 5.40–5.20 (m, 2 H, CH_2=CH-), 4.75 (s, 1 H, H-1), 4.15–3.65 (m, 8 H, H-2,3,4,5,6,6' and CH_2=CH-CH_2), 3.45 (s, 3 H, OCH_3), 2.90–2.75 (bs, 3 H, O*H*). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.28; H, 7.69. Found: C, 50.96; H, 7.70.

Methyl 2-O-allyl-3,4,6-tri-O-benzyl-α-D-altropyranoside (**6**).—To a solution of **5** (1.0 g, 4.27 mmol) in anhydrous oxolane (15 mL) was added, with vigorous stirring in an ice-cold water bath, sodium hydride (80%, 1.25 g, 41.7 mmol) and benzyl bromide (2.4 g, 14 mmol). The mixture was stirred and reflux for 8 h, at which time TLC (3:1

petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was directly subjected to steam distillation to remove the excess benzyl bromide and by-product dibenzyl ether, and then extracted with dichloromethane. The organic layer was concentrated to a syrup that was purified by column chromatography with 4:1 petroleum ether–EtOAc to give **6** (1.86 g, 86.4%) as a syrup; $[\alpha]_D$ +2.7° (*c* 4.8, $CHCl_3$); ^1H NMR: δ 7.40–7.11 (m, 15 H, PhH), 5.89–5.70 (m, 1 H, CH_2=CH-), 5.20–5.05 (m, 2 H, CH_2=CH-), 4.70 (s, 1 H, H-1), 4.68, 4.45 (2 d, 2 H, *J* 10.5 Hz, PhCH_2), 4.46, 4.59 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 4.54, 4.49 (2 d, 2 H, *J* 11.2 Hz, PhCH_2), 4.30–4.21 (m, 1 H, H-5), 4.00–3.90 (m, 2 H, CH_2=CH–CH_2), 3.85–3.60 (m, 5 H, H-2,3,4,6,6′), 3.40 (s, 3 H, OCH_3). Anal. Calcd for $C_{31}H_{36}O_6$: C, 73.81; H, 7.14. Found: C, 73.79; H, 7.18.

2-O-*Allyl-3,4,6-tri*-O-*benzyl*-D-*altropyranose* (**7**).—To a solution of **6** (1.8 g, 3.57 mmol) in 60% aq acetic acid (15 mL) was added 1 N hydrochloric acid (5 mL), and the mixture was stirred at 95 °C for 8 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the starring material had disappeared. The mixture was carefully neutralized with powdered sodium bicarbonate, concentrated and partitioned between water and dichloromethane. The organic layer was dried over sodium sulfate and concentrated. Purification of the residue by column chromatography with 2:1 petroleum ether–EtOAc as solvent furnished syrupy **7** (1.32 g, 75.4%); $[\alpha]_D$ +2.2° (*c* 0.5, $CHCl_3$); ^1H NMR: δ 7.40–7.20 (m, 15 H, PhH), 5.83–5.68 (m, 1 H, CH_2=CH-), 5.20–5.03 (m, 2 H, CH_2=CH-), 4.82–4.42 (m, 7 H, H-1, 3 PhCH_2), 4.00–3.84 (m, 3 H, CH_2=CH–CH_2, H-3), 3.82–3.75 (m, 4 H, H-2,4,5,6), 3.64–3.59 (m, 1 H, H-6′). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.47; H, 6.94. Found: C, 73.14; H, 7.22.

3,4,6-Tri-O-*benzyl*-D-*altropyranose* (**8**) *and 1,2-di*-O-*acetyl-3,4,6-tri*-O-*benzyl*-α-D-*altropyranose* (**9**).—To a solution of **7** (520 mg, 1.06 mmol) in anhydrous methanol (15 mL) was added palladium chloride (20 mg, 0.11 mmol). The mixture was stirred at room temperature for 4 h. Filtration and concentration of the filtrate gave a residue that was purified by column chromatography with 2:1 petroleum ether–EtOAc as the solvent furnishing syrupy **8** (440 mg, 92.1%); $[\alpha]_D$ +4.8° (*c* 1.9, $CHCl_3$). Acetylation of **8** (510 mg, 1.13 mmol) with pyridine (5 mL) and acetic anhydride (3 mL) at room temperature for 5 h gave compound **9** in quantitative yield as a syrup; $[\alpha]_D$ +1.2° (*c* 1.2, $CHCl_3$); ^1H NMR: δ 7.40–7.10 (m, 15 H, PhH), 6.18 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1), 5.20 (dd, 1 H, $J_{1,2}$ 1.2, $J_{2,3}$ 2.4 Hz, H-2), 4.70–4.40 (m, 6 H, 3 PhCH_2), 4.25–4.15 (m, 1 H, H-5), 3.90–3.70 (m, 4 H, H-3,4,6,6′), 2.15, 2.05 (2 s, 6 H, COCH_3). Anal. Calcd for $C_{31}H_{34}O_8$: C, 69.66; H, 6.37. Found: C, 69.53; H, 6.36.

2-O-*Acetyl-3,4,6-tri*-O-*benzyl*-α-D-*altropyranosyl chloride* (**10**).—A solution of **9** (50 mg, 0.09 mmol) in dry diethyl ether (10 mL) was saturated at 0 °C with hydrogen chloride gas under a nitrogen atmosphere. The solution was kept at room temperature in a sealed bottle for 2 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The solution was concentrated under reduced pressure to a syrupy residue which was dissolved in dichloromethane (1 mL) and concentrated. This procedure was repeated several times to remove the hydrogen chloride. Purification of the product by column chromatography (3:1 petroleum ether–EtOAc) gave **10** as a syrup (43 mg, 90%); $[\alpha]_D$ +121° (*c* 2.1, $CHCl_3$); ^1H NMR: δ 7.40–7.10 (m, 15 H, PhH), 6.01 (bs, 1 H, H-1), 5.34 (d, 1 H, $J_{2,3}$ 2.9 Hz, H-2), 4.86,

4.61 (2 d, 2 H, *J* 12.2 Hz, PhCH_2), 4.67, 4.53 (2 d, 2 H, *J* 12.2 Hz, PhCH_2), 4.40, 4.39 (2 d, 2 H, *J* 11.0 Hz, PhCH_2), 3.95–3.70 (m, 5 H, H-3,4,5,6,6'), 2.05 (s, 3 H, COCH_3). Anal. Calcd for $C_{29}H_{31}ClO_6$: C, 68.17; H, 6.07. Found: C, 68.00; H, 6.03.

1,2-Anhydro-3,4,6-tri-O-*benzyl*-β-D-*altropyranose* (**11**).—To a solution of **10** (40 mg, 0.078 mmol) in dry oxolane was added potassium *tert*-butoxide (12 mg, 0.1 mmol), and the mixture was stirred at room temperature for 45 min, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the starting material had disappeared. The mixture was concentrated to dryness, and the residue was repeatedly extracted with 3:1 petroleum ether–EtOAc. Concentration of the combined extracts yielded **11** as a syrup (31.5 mg, 93%); ^{1}H NMR: δ 7.45–7.15 (m, 15 H, Ph*H*), 4.82–4.44 (m, 7 H, H-1, 3 PhCH_2), 4.30–4.26 (m, 1 H), 4.00–3.92 (m, 1 H), 3.88–3.82 (m, 1 H), 3.80–3.72 (m, 1 H), 3.68 (m, 1 H), 3.40 (t, 1 H, $J_{1,2} = J_{2,3} = 4.0$ Hz, H-2).

Methyl 3,4,6-tri-O-*benzyl*-α-D-*altropyranoside* (**12**).—Compound **11** (20 mg, 0.046 mmol) was dissolved in anhyd methanol (2 mL) and kept for 1 h at room temperature. TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The solution was concentrated to afford **12** quantitatively as a syrup; $[\alpha]_D$ +2.1° (*c* 0.6, $CHCl_3$); ^{1}H NMR: δ 7.36–7.24 (m, 15 H, Ph*H*), 4.62 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.61, 4.46 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 4.60, 4.58 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.53, 4.51 (2 d, 2 H, *J* 11.1 Hz, PhCH_2), 4.24–4.20 (dd, 1 H, $J_{2,3}$ 2.6, $J_{3,4}$ 3.1 Hz, H-3), 4.01–3.99 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 2.6 Hz, H-2), 3.90–3.78 (m, 1 H, H-5), 3.76 (dd, 1 H, $J_{3,4}$ 3.1, $J_{4,5}$ 7.0 Hz, H-4), 3.66–3.62 (m, 2 H, H-6,6'), 3.42 (s, 3 H, OCH_3). Anal. Calcd for $C_{28}H_{32}O_6$: C, 72.41; H, 6.90. Found: C, 72.05; H, 7.08.

3,4,6-Tri-O-*benzyl-1,2*-O-(R-*ethylidene*)-α-D-*allopyranose* (**14**).—To a solution of 3,4,6-tri-*O*-acetyl-1,2-*O*-(*R*-ethylidene)-α-D-allopyranose (**13**) [14] (3.8 g, 11.4 mmol) in toluene (30 mL) was added, with vigorous stirring, finely powdered potassium hydroxide (12 g). The mixture was boiled under reflux, and benzyl chloride (18 g, 142 mmol) was added dropwise over a 15 min period. The mixture was stirred and boiled under reflux for 2 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was directly subjected to steam distillation to remove the excess benzyl chloride and the by-product dibenzyl ether, and then extracted with dichloromethane. The organic layer was concentrated to a syrup that was purified by column chromatography with 4:1 petroleum ether–EtOAc as the eluent to give **14** (4.9 g, 90%); $[\alpha]_D$ −31° (*c* 1.1, $CHCl_3$); ^{1}H NMR: δ 7.42–7.20 (m, 15 H, Ph*H*), 5.49 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.07 (q, 1 H, *J* 4.9 Hz, C*H*CH$_3$), 4.88, 4.45 (2 d, 2 H, *J* 10.6 Hz, PhCH_2), 4.78, 4.66 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.42, 4.34 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.28–4.22 (m, 1 H, H-3), 4.06–3.92 (m, 2 H, $J_{1,2}$ 4.0 Hz, H-2, H-5), 3.68 (dd, 1 H, $J_{3,4}$ 2.3, $J_{4,5}$ 7.8 Hz, H-4), 3.48 (dd, 1 H, $J_{5,6}$ 2.1, $J_{6,6'}$ 10.6 Hz, H-6), 3.32 (dd, 1 H, $J_{5,6'}$ 3.7, $J_{6,6'}$ 10.6 Hz, H-6), 1.52 (d, 3 H, *J* 4.9 Hz, CHCH_3). Anal. Calcd for $C_{29}H_{32}O_6$: C, 73.10; H, 6.72. Found: C, 73.28; H, 6.67.

3,4,6-Tri-O-*benzyl*-D-*allopyranose* (**15**) *and 1,2-di*-O-*acetyl-3,4,6-tri*-O-*benzyl*-D-*allopyranose* (**16**).—To a solution of **14** (2.8 g, 5.88 mmol) in dioxane (42 mL) was added 1 M sulfuric acid (8 mL), and the mixture was boiled under reflux with stirring for 6 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The mixture was carefully neutralized with powdered sodium bicarbonate, concentrated, and partitioned between water and dichloromethane. The

organic layer was dried over sodium sulfate and concentrated. Purification of the residue by column chromatography with 2:1 petroleum ether–EtOAc as the eluent furnished syrupy **15** (2.14 g, 81%) as an α,β mixture in a ratio of 3:2; $[\alpha]_D$ −26° (*c* 0.9, $CHCl_3$); ^1H NMR: δ 7.40–7.20 (m, 15 H, PhH), 5.01 (d, 0.6 H, $J_{1,2}$ 3.1 Hz, H-1α), 4.99–4.42 (m, 6.4 H, 3 PhCH_2, $J_{1,2}$ 8.9 Hz, H-1β), 4.22–4.01 (m, 2 H, H-2,3), 3.90–3.58 (m, 4 H, H-4,5,6,6′).

Acetylation of **15** (1 g, 2.22 mmol) with pyridine (5 mL) and acetic anhydride (3 mL) at room temperature for 4 h gave compound **16** in a quantitative yield as a syrup consisting of α and β anomers in a ratio of 1:8, $[\alpha]_D$ +87° (mixture, *c* 1.1, $CHCl_3$). For the β anomer, ^1H NMR: δ 7.35–7.20 (m, 15 H, PhH), 6.08 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.77, 4.59 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.72 (dd, 1 H, $J_{1,2}$ 9.6, $J_{2,3}$ 2.7 Hz, H-2), 4.64, 4.47 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 4.57, 4.45 (2 d, 2 H, *J* 11.4 Hz, PhCH_2), 4.28 (t, 1 H, $J_{2,3} = J_{3,4}$ = 2.7 Hz, H-3), 4.23–4.13 (m, 1 H, H-5), 3.77 (dd, 1 H, $J_{3,4}$ 2.7, $J_{4,5}$ 9.8 Hz, H-4), 3.76–3.70 (m, 2 H, H-6,6′), 2.05, 1.98 (2 s, 6 H, COCH_3). Anal. Calcd for $C_{31}H_{34}O_8$ (mixture): C, 69.66; H, 6.37. Found: C, 69.57; H, 6.30.

2-O-Acetyl-3,4,6-tri-O-benzyl-α-D-allopyranosyl chloride (**17**).—The same chlorination and purification conditions (**9** → **10**) were used and compound **17** was obtained as a syrup (249 mg, 87% starting from 300 mg of **16**); $[\alpha]_D$ +153° (*c* 1.3, $CHCl_3$); ^1H NMR: δ 7.40–7.20 (m, 15 H, PhH), 6.19 (d, 1 H, $J_{1,2}$ 4.7 Hz, H-1), 4.90–4.86 (m, 1 H, H-2), 4.80 (t, 2 H, *J* 10.0 Hz, PhCH_2), 4.63–4.42 (m, 5 H, H-3, 2 PhCH_2), 4.17–4.10 (m, 2 H, H-4,5), 3.90–3.60 (m, 2 H, H-6,6′), 2.05 (s, 3 H, COCH_3). Anal. Calcd for $C_{29}H_{31}ClO_6$: C, 68.17; H, 6.07. Found: C, 67.83; H, 6.17.

2-O-Acetyl-3,4,6-tri-O-benzyl-α-D-allopyranosyl fluoride (**18**).—To a solution of **17** (350 mg, 0.69 mmol) in 2:5 acetonitrile–benzene (10 mL) was added silver fluoride (200 mg, 1.6 mmol). The mixture was stirred vigorously for 16 h in the dark at room temperature, centrifuged, and the filter cake was washed repeatedly with dichloromethane. The supernatant liquor and combined washings were concentrated. Purification of the syrup by column chromatography (3:1 petroleum ether–EtOAc) yielded **18** as a syrup (287 mg, 85%); $[\alpha]_D$ +58.1° (*c* 0.9, $CHCl_3$); ^1H NMR: δ 7.45–7.20 (m, 15 H, PhH), 5.64 (dd, 1 H, $J_{1,F}$ 54.8, $J_{1,2}$ 6.0 Hz, H-1), 4.79, 4.50 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.75–4.70 (m, 1 H, H-2), 4.65–4.53 (m, 5 H, H-3, 2 PhCH_2), 4.30–4.21 (m, 2 H, H-4,5), 3.78–3.75 (m, 2 H, H-6,6′), 2.09 (s, 3 H, COCH_3). Anal. Calcd for $C_{29}H_{31}FO_6$: C, 70.59; H, 6.28. Found: C, 70.45; H, 6.23.

3,4,6-Tri-O-benzyl-2-O-p-toluenesulfonyl-α-D-altropyranose (**19**).—To a solution of **8** (431 mg, 0.96 mmol) in pyridine (5 mL) was added TsCl (450 mg, 2.4 mmol), 4-dimethylaminopyridine (DMAP, 12.2 mg, 0.1 mmol), and powdered K_2CO_3 (138 mg, 1 mmol). The mixture was stirred at room temperature for 24 h, poured into ice-cold water, and extracted with dichloromethane (30 mL). The organic layer was washed with cold water (30 mL) and 1 N HCl (3 × 20 mL), and dried over Na_2SO_4. The solution was concentrated and the resulting residue was purified by column chromatography (3:1 petroleum ether–EtOAc) to give **19** (306 mg, 53%) as a syrup; $[\alpha]_D$ +68° (*c* 0.1); ^1H NMR: δ 7.81 (d, 2 H, *J* 7.8 Hz, PhH of Ts), 7.38–7.12 (m, 17 H, PhH), 5.51 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.76, 4.65 (2 × 2 d, 4 H, *J* 12.5 Hz, 2 PhCH_2), 4.69 (dd, 1 H, $J_{1,2}$ 1.6, $J_{2,3}$ 6.0 Hz, H-2), 4.56–4.52 (m, 1 H, H-3), 4.45 (s, 2 H, PhCH_2), 3.74–3.68 (m, 2

H, H-5, H-6), 3.64–3.60 (m, 1 H, H-4), 3.56 (dd, 1 H, $J_{5,6}$ 1, $J_{6,6'}$ 9.4 Hz, H-6'). Anal. Calcd for $C_{34}H_{36}O_8S \cdot 0.5H_2O$: C, 66.56; H, 6.04. Found: C, 66.50; H, 6.13.

1-O-Acetyl-3,4,6-tri-O-benzyl-2-O-p-toluenesulfonyl-α-D-altropyranose (**20**).—Acetylation of **19** (100 mg, 0.17 mmol) with pyridine (3 mL) and acetic anhydride (2 mL) at room temperature for 4 h gave **20** in a quantitative yield as a syrup; $[\alpha]_D$ −8.6° (*c* 0.3); ^{1}H NMR: δ 7.69 (d, 2 H, *J* 8.0 Hz, PhH of Ts), 7.40–7.10 (m, 17 H, PhH), 6.00 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 4.64, 4.48 (2 d, 2 H, *J* 11.8 Hz, PhCH_2), 4.60, 4.58 (2 d, 2 H, *J* 11.8 Hz, PhCH_2), 4.55 (dd, 1 H, $J_{1,2}$ 1.4, $J_{2,3}$ 4.6 Hz, H-2), 4.35 (s, 2 H, PhCH_2), 4.16–4.10 (m, 1 H, H-5), 4.01 (dd, 1 H, $J_{2,3}$ 4.6, $J_{3,4}$ 2.9 Hz, H-3), 3.86 (dd, 1 H, $J_{3,4}$ 2.9, $J_{4,5}$ 9.2 Hz, H-4), 3.71–3.66 (m, 2 H, H-6,6'), 2.42 (s, 3 H, PhCH_3), 1.82 (s, 3 H, COCH_3). Anal. Calcd for $C_{36}H_{38}O_9S$: C, 66.87; H, 5.88. Found: C, 66.91; H, 5.80.

1,2-Anhydro-3,4,6-tri-O-benzyl-α-D-allopyranose (**21**).—Ring closure of **19** (130 mg, 0.21 mmol) under the same conditions used for the preparation of **11** from **10** yielded **21** as a syrup (88 mg, 95%); ^{1}H NMR: δ 7.40–7.15 (m, 15 H, PhH), 5.00 (d, 1 H, $J_{1,2}$ 2.8 Hz, H-1), 4.80, 4.78 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.60, 4.52 (2 d, 2 H, *J* 10.6 Hz, PhCH_2), 4.59, 4.55 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 3.95–3.90 (m, 2 H, H-3,5), 3.70 (dd, 1 H, $J_{3,4}$ 3.0, $J_{4,5}$ 7.9 Hz, H-4), 3.65 (dd, 1 H, $J_{5,6}$ 2.5, $J_{6,6'}$ 9.9 Hz), 3.60 (dd, 1 H, $J_{5,6'}$ 5.1, $J_{6,6'}$ 9.9 Hz, H-6'), 3.30 (dd, 1 H, $J_{1,2}$ 2.8, $J_{2,3}$ 3.4 Hz, H-2). *m/z*: 432 (M^+, 6%), 385 (20%), 342 (20%), 309 (20%), 253 (60%), 203 (34%), 91 (basic peak, off scale).

Methyl 3,4,6-tri-O-benzyl-β-D-allopyranoside (**22**) *and methyl 2-O-acetyl-3,4,6-tri-O-benzyl-β-D-allopyranoside* (**23**).—Methanolysis of **21** under the same condition (**11** → **12**) afforded **22** quantitatively as a syrup; $[\alpha]_D$ −40.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR: δ 7.34–7.24 (m, 10 H, 2 Ph-H), 4.68, 4.60 (2 d, 2 H, *J* 12.3 Hz, PhCH_2), 4.63, 4.46 (2 d, 2 H, *J* 12.3 Hz, PhCH_2), 4.12 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.10 (dd, 1 H, $J_{4,5}$ 2.2, $J_{5,5'}$ 12.7 Hz, H-5), 3.95 (dd, 1 H, $J_{1,2}$ 7.3, $J_{2,3}$ 9.1 Hz, H-2), 3.73–3.69 (m, 1 H, H-4), 3.56 (s, 3 H, CH_3O), 3.40 (dd, 1 H, $J_{2,3}$ 9.1, $J_{3,4}$ 2.2 Hz, H-3), 3.31 (d, 1 H, $J_{5,5'}$ 12.7 Hz, H-5'). Acetylation of **22** afforded **23**; $[\alpha]_D$ −20° (*c* 0.7); ^{1}H NMR: δ 7.40–7.10 (m, 15 H, PhH), 4.85, 4.63 (2 d, 2 H, *J* 10.9 Hz, PhCH_2), 4.81 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.67 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 2.7 Hz, H-2), 4.60 (s, 2 H, PhCH_2), 4.58, 4.56 (2 d, 2 H, *J* 12.1 Hz, PhCH_2), 4.30 (t, 1 H, $J_{2,3} = J_{3,4}$ = 2.7 Hz, H-3), 4.10 (ddd, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 2.0, $J_{5,6'}$ 4.5 Hz, H-5), 3.80 (dd, 1 H, $J_{5,6}$ 2.0, $J_{6,6'}$ 10.9 Hz, H-6), 3.70 (dd, 1 H, $J_{5,6'}$ 4.5, $J_{6,6'}$ 10.9 Hz, H-6'), 3.68 (dd, 1 H, $J_{3,4}$ 2.7, $J_{4,5}$ 9.5 Hz, H-4), 3.48 (s, 3 H, OCH_3), 2.01 (s, 3 H, COCH_3). Anal. Calcd for $C_{30}H_{34}O_7$: C, 71.15; H, 6.72. Found: C, 71.23; H, 6.70.

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