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A Carbohydrate-Based Approach for the Total Synthesis of (−)-Dinemasone B, (+)-4a-*epi*-Dinemasone B, (−)-7-*epi*-Dinemasone B, and (+)-4a,7-Di-*epi*-dinemasone B

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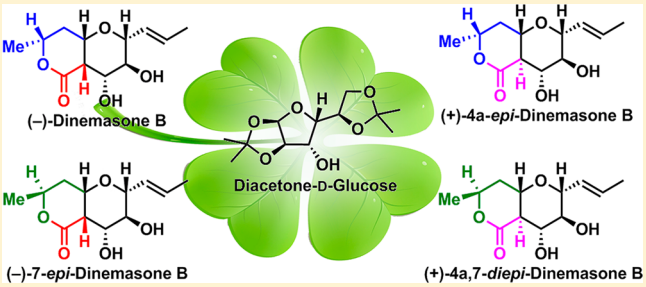
Supporting Information

ABSTRACT: (−)-Dinemasone B was isolated by Krohn and co-workers from a culture of the endophytic fungus *Dinemasporium strigosum* and has shown promising antimicrobial activity. Described herein is the first total synthesis of (−)-dinemasone B, (+)-4a-*epi*-dinemasone B, (−)-7-*epi*-dinemasone B, and (+)-4a,7-di-*epi*-dinemasone B. Their absolute configurations were also determined. The developed synthesis features a stereoselective reduction of *C*-glycosidic ketone, lactonization, and *E*-olefination of aldehyde starting from D-glucose.



INTRODUCTION

(−)-Dinemasone B (**1**) and (−)-dinemasone C (**2**) were first reported by Krohn and co-workers as two naturally occurring antibiotics with biological activities against *Bacillus megaterium* (Gram-positive), *Microbotryum violaceum* (fungus), and *Chlorella fusca* (alga). The compounds were isolated by these researchers from a culture of the endophytic fungus *Dinemasporium strigosum*, which was obtained from the roots of *Calystegia sepium* in 2008 (Figure 1).[1] Because of the presence of the stereogenic hexahydropyrano[4,3-*b*]pyran-5(7*H*)-one structure, these metabolites are challenging targets for synthesis.

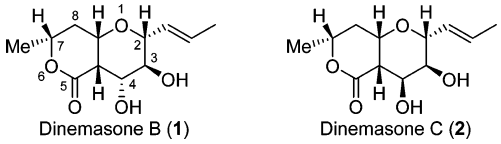


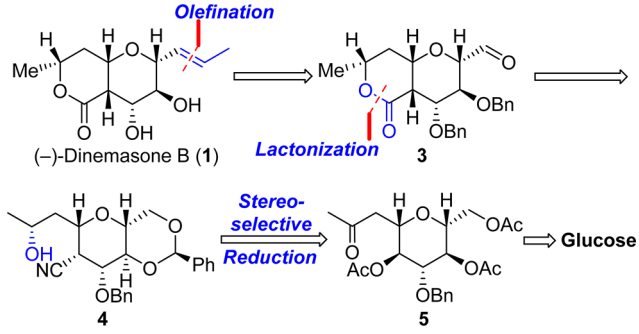
Figure 1. Structures of (−)-dinemasone B (**1**) and (−)-dinemasone C (**2**).

In 2010, Snider and co-workers[2] accomplished the first total synthesis of (±)-dinemasone C (**2**), but studies toward the synthesis of (−)-dinemasone B (**1**) have not been described. Herein, we present the first stereocontrolled total synthesis of **1** utilizing a chiral substrate for the efficient construction of the core structure.

RESULTS AND DISCUSSION

Total Synthesis of (−)-Dinemasone B. Our retrosynthetic analysis of (−)-dinemasone B (**1**) is outlined in Scheme 1. The *E*-alkene would be produced via a Takai−Utimoto reaction with benzyl-protected aldehyde **3**, and δ-lactone **3** could be obtained by intramolecular hydrolysis of the hydroxyl nitrile **4**. The key C7 stereocenter of **4** could be introduced through a stereoselective reduction of *C*-glycosidic ketone **5**, which could be derived from D-glucose.

Scheme 1. Retrosynthetic Analysis of (−)-Dinemasone B (1)



The investigation began with the 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose **6**, which was commercially available or could be easily synthesized from D-glucose.[3] Protection of the hydroxyl group with benzyl bromide in the presence of sodium hydride, followed by cleavage of the isopropylidene groups with Dowex H^+ resin in hot water, afforded **8** in excellent yield.[4] Further treatment of **8** with acetylacetone in $NaHCO_3$ solution[5−7] and acetylization by Ac_2O/pyridine smoothly produced *C*-glycosidic ketone **5** in 78% yield for two steps, as shown in Scheme 2.

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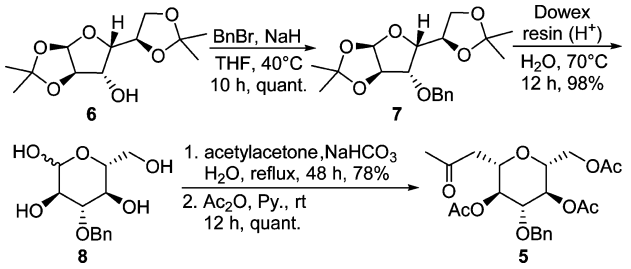
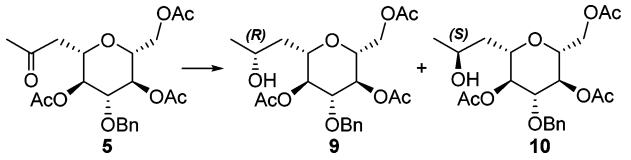
Scheme 2. Synthesis of *C*-Glycosidic Ketone 5



With ketone **5** in hand, a careful survey of conditions for the stereoselective reduction was conducted (Table 1). Reduction

Table 1. Stereoselective Reduction of Ketone 5



entry	reagent	solvent	*T* (°C)	time (h)	yield[a] (%) (**9**/**10** ratio)[b]
1	$NaBH_4$,[c] AcOH[d]	MeOH	0	0.5	98 (33:67)
2	$NaBH_4$,[c] AcOH[d]	CH_2Cl_2	0	0.5	96 (45:55)
3	(*R*)-Me-CBS,[e] BMS[c]	THF	25	1.0	99 (26:74)
4	**(*R*)-Me-CBS,[e] CB[c]**	**toluene**	**25**	**1.0**	**99 (06:94)**
5	(*R*)-Bu-CBS,[e] CB[c]	toluene	25	1.0	98 (10:90)
6	(*S*)-Me-CBS,[e] BMS[c]	THF	25	1.0	99 (64:36)
7	(*S*)-Me-CBS,[e] CB[c]	toluene	25	1.0	98 (36:64)
8	(*S*)-Bu-CBS,[e] CB[c]	toluene	25	1.0	99 (29:71)
9	$LiBH_4$,[c] TarB-H[f]	THF	25	0.5	89 (50:50)
10	DIBAL-H,[c] $Ti(O\text{-}i\text{-}Pr)_4$[f]	toluene	−78	1.0	87 (12:88)
11	L-Selectride,[c] $Ti(O\text{-}i\text{-}Pr)_4$[f]	THF	−78	0.5	91 (50:50)
12	L-Selectride,[c] $Ti(O\text{-}i\text{-}Pr)_4$[f]	CH_2Cl_2	−78	0.5	90 (86:14)
13	**L-Selectride,[c] $Ti(O\text{-}i\text{-}Pr)_4$[f]**	**toluene**	**−78**	**0.5**	**92 (95:05)**

[a]Yield of isolated product. [b]Ratios of **9**/**10** were determined by ^1H NMR analysis. [c]Reductants: $NaBH_4$ (2.0 equiv), BMS (3.0 equiv), CB (3.0 equiv), $LiBH_4$ (2.0 equiv), DIBAL-H (1.1 equiv), L-Selectride (1.1 equiv). [d]Amount of AcOH (2.0 equiv). [e]The CBS catalysts (1.5 equiv). [f]Chelating agent: TarB-H (2.0 equiv), $Ti(O\text{-}i\text{-}Pr)_4$ (4.0 equiv). BMS = borane dimethyl sulfide complex, CB = catecholborane, DIBAL-H = diisobutylaluminum hydride, L-Selectride = lithium tri-*sec*-butylborohydride.

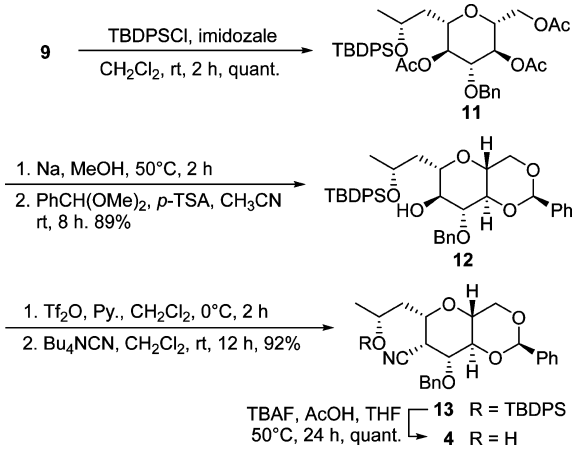
of **5** with sodium borohydride in the presence of AcOH yielded a mixture of alcohols **9** and **10** with poor selectivity (Table 1, entries 1 and 2), which were similar to the results reported in the literature.[8−10] Later, it was found that the major product **10** (*S*-isomer) could be obtained by the Corey−Bakshi−Shibata reduction[11−13] with (*R*)-Me-CBS as the catalyst (Table 1, entries 3 and 4), especially when catecholborane was used as the reductant (ratio **9**/**10** = 06:94) (Table 1, entry 4). According to the literature, the selectivity for the *S*-isomer should be better when (*R*)-Bu-CBS is used.[14] However, a slight decrease in selectivity is observed (Table 1, entry 5).

For the synthesis of the *R*-isomer, the CBS-catalyzed reduction using various reductants provided poor stereoselectivity, affording at best a 2:1 ratio of **9** and **10** (Table 1, entries 6−8). Other bulky reductants, including combinations of lithium borohydride with TarB-H,[15−18] DIBAL-H,[19] and L-Selectride/$Ti(O\text{-}i\text{-}Pr)_4$ in THF,[20−22] gave varying ratios of the two stereoisomers in an unpredictable manner. Under most conditions, poor yields of *R*-isomer **9** were achieved (Table 1, entries 9−12). Serendipitously, changing the solvent to toluene when using L-Selectride/$Ti(O\text{-}i\text{-}Pr)_4$ improved the stereoselective reduction to give the *R*-isomer as the major isomer (Table 1, entry 13).

Both the absolute configurations of alcohols **9** and **10** were determined by NMR studies of the MPA esters.[23,24]

After alcohol **9** was obtained successfully, protection of **9** with TBDPS ether under the condition of TBDPSCl/imidozale afforded **11** in quantitative yield. Removal of the acetate ester followed by acetalization with $PhCH(OMe)_2$ in the presence of *p*-toluenesulfonic acid gave alcohol **12** in 89% yield. Treatment of **12** with trifluoromethanesulfonic anhydride in CH_2Cl_2 at 0 °C, followed by subsequent S_N2 substitution reaction with *n*-tetrabutylammonium cyanide,[25] provided **13**, and deprotection of the TBDPS ether with tetrabutylammonium fluoride produced hydroxyl nitrile **4** in 91% yield over three steps (Scheme 3).

Scheme 3. Synthesis of the Hydroxyl Nitrile 4



To synthesize (−)-dinemasone B (**1**), the δ-lactone must be constructed first. We designed several synthesis pathways (Scheme 4). In the designed path A, reduction of the nitrile **13** to aldehyde **14** with DIBAL-H[26,27] or Red-Al[28] under cold conditions, followed by the removal of the silyl ether, would form the unstable hydroxyl aldehyde **M-1**, which could cyclize automatically to form the hemiacetal **15**. Lactone **16** would be obtained after oxidation, but the cyano group failed to be converted to aldehyde probably due to steric hindrance.

In path B, hydroxyl nitrile **4** was heated with DBU in toluene at 80 °C, allowing for intramolecular condensation of the alcohol with cyanide, to afford the intermediate **M-2**.[29] Following acidolysis, lactone **16** could be obtained. However, when hydroxyl nitrile **4** was treated with DBU, no desired product was observed, and only epimerization product **17** was obtained in 34% yield, along with unreacted substrate. Thus, path B was also abandoned.

Path C converted compound **4** to carboxylic acid **18** by treatment with alkaline hydrogen peroxide in a mixture of water and ethanol at 90 °C,[30] during which epimerization of the carboxylic group occurred. Subsequent lactonization with EDCI

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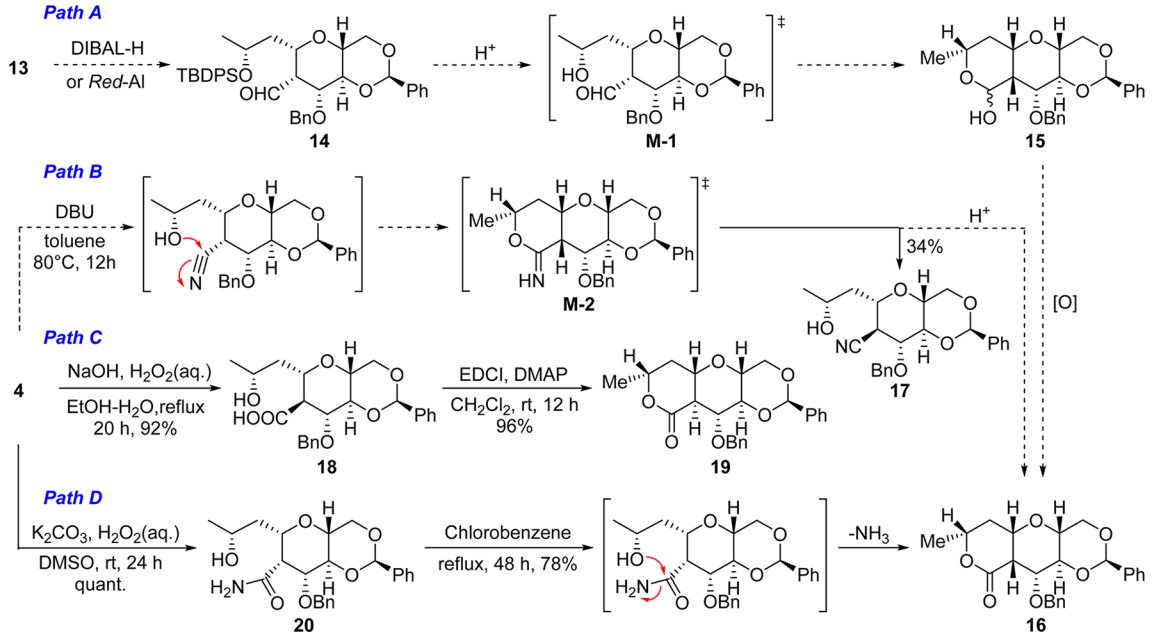
Scheme 4. Construction of Lactones 16 and 19

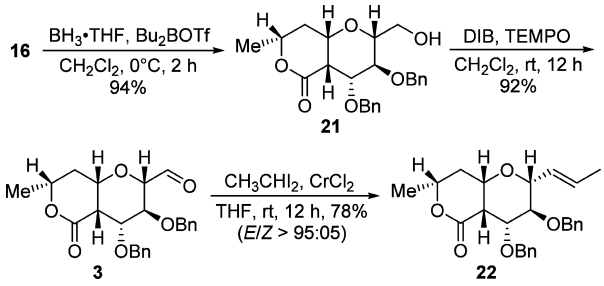


and DMAP afforded the lactone **19** in 88% yield, which was an epimer of lactone **16**.

Path D under more mild alkalinity and temperature transformed hydroxyl nitrile **4** into the nonepimerized amide **20** quantitatively.[31] And fortunately, refluxing of **20** in chlorobenzene under a continuous stream of nitrogen afforded the corresponding lactone **16** in 78% yield by elimination of ammonia, as shown in Scheme 4, path D.

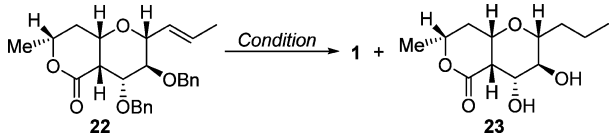
Reductive ring-opening of the cyclic benzyliene acetal of **16** by treatment with BH_3·THF/Bu_2BOTf gave the corresponding primary alcohol **21** in 94% yield.[32] Oxidation of **21** by DIB/TEMPO smoothly furnished benzyl protected aldehyde **3**. Takai–Utimoto reaction[33,34] of **3** led to the desired *E*-alkene **22** in 78% yield with high selectivity (*E*/*Z* > 95:05), as shown in Scheme 5.

Scheme 5. Synthesis of the *E*-Alkene 22



The last step was the deprotection of **22**. Various conditions were tested for the selective removal of benzyl groups (Table 2). When BCl_3 was used,[35] only a trace amount of product was obtained (Table 2, entry 1). Treatment with DDQ at room temperature[36] did not produce any product (Table 2, entry 2). When the mixture was refluxed with DDQ or treatment with Na/naphthalene[37] as a single-electron reductant, only a trace amount of product was observed (Table 2, entries 3 and 4). Hydrogenolysis attempts to selectively remove the benzyl groups also reduced the alkene even when 1-methyl 1,4-cyclohexadiene was used as a hydrogen donor (Table 2, entries 5–8).

Table 2. Results of De-*O*-benzylation of 22



entry	conditions	results
1	BCl_3,[a] CH_2Cl_2, −78 °C, 0.5 h	trace
2	DDQ,[a] CH_2Cl_2–H_2O, rt, 12 h	*b*
3	DDQ,[a] CH_2Cl_2–H_2O, reflux, 6 h	trace
4	Na/naphthalene, THF, −78 °C, 0.5 h	trace
5	Pd/C, H_2 (4.5 atm), THF, rt, 0.5 h	**23** (96%)[c]
6	$Pd(OH)_2$/C, H_2 (4.5 atm), THF, rt, 0.5 h	**23** (97%)[c]
7	$Pd(OH)_2$/C, H_2 (1.0 atm), THF, rt, 0.5 h	**23** (99%)[c]
8	$Pd(OH)_2$/C, 1-methyl-1,4-cyclohexadiene, THF, rt, 0.5 h	**23** (89%)[c]

[a]Amount of agents: BCl_3 (2.5 equiv), DDQ (2.0 equiv). [b]No reaction. [c]Yield of isolated product. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

After the failed deprotection of **22**, we adjusted the protecting groups. Removal of the benzylidene and benzyl group in **16** by hydrogenolysis, followed by protection of **24** with trimethyl chlorosilane, gave lactone **25** in 99% yield over two steps, and the trimethylsilyl group could be removed by hydrolysis under mild conditions.[38] Selective oxidative removal of the TMS group on primary alcohol using Collins oxidation,[39−41] followed by Kocieński–Julia olefination[42−44] with the use of LiHMDS in DMF, afforded the desired *E*-alkene (*E*:*Z* = 94:06) (optimization of *E*-alkene, see below). Removal of the TMS groups in the presence of 2% (v/v) trifluoroacetic acid afforded (−)-dinemasone B (**1**) in 73% yield for three steps (Scheme 6).

The reaction conditions for the olefination of aldehyde **26** were explored, and the results are summarized in Table 3. First, Takai–Utimoto olefination[33,34] of **26** gave a mixture of *E*/*Z*

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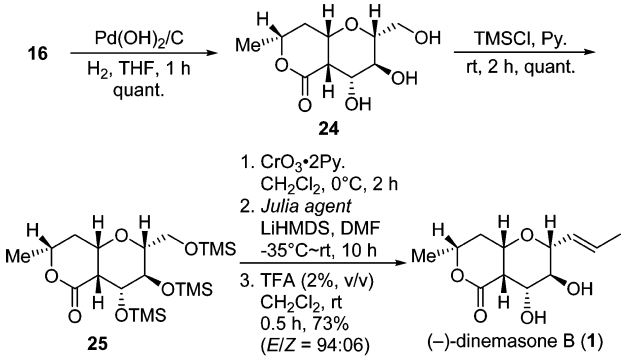
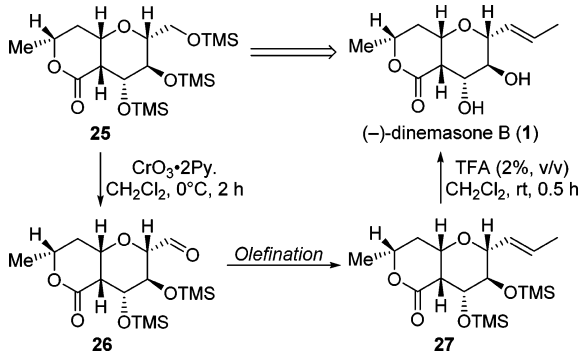
Scheme 6. Total Synthesis of (−)-Dinemasone B (1)



*Julia agent = 5-ethylsulfonyl-1-phenyl-1*H*-tetrazole.

Table 3. Results of the Olefination of Aldehyde 26



entry	reagent and solvent	T (°C)	yield[a] (%)	ratio (E/Z)[b]
1	CH_3CHI_2, $CrCl_2$, THF	25	62	87:13
2	CH_3CHI_2, $CrCl_2$·DMF, THF	25	65	41:59
3	CH_3CHI_2, $CrCl_2$, THF	0	*c*	
4	CH_3CHI_2, $CrCl_2$, THF	65	trace	
5	$Ph_3P{=}CHCH_3$, THF	−78[d]	*c*	
6	$Et_3P{=}CHCH_3$, THF	−78[d]	*c*	
7	Julia agent,[e] LiHMDS, THF	−78[d]	76	55:45
8	Julia agent,[e] LiHMDS, DMF	−60[d]	72	90:10
9	**Julia agent,[e] LiHMDS, DMF**	**−35[d]**	**73**	**94:06**
10	Julia agent,[e] LiHMDS, DMF/HMPA[f]	−35[d]	70	83:17

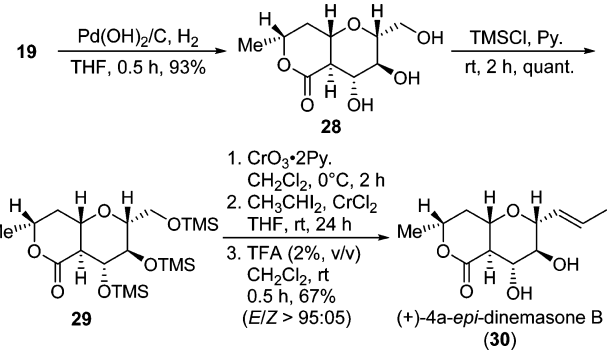
[a]Yield of isolated product. [b]Ratios of E/Z products were determined by ^{1}H NMR analysis. [c]No reaction. [d]Reactions were set up at the indicated temperatures and then allowed to warm to room temperature. [e]Julia agent =5-ethylsulfonyl-1-phenyl-1*H*-tetrazole. [f]A mixture solvent of DMF and HMPA at 4:1 ratio (v/v). LiHMDS = lithium bis(trimethylsilyl)amide, HMPA = hexamethyl phosphoric triamide. Aldehyde **26** was not isolated, made in situ, and then reacted immediately due to its poor stability.

alkene, even when DMF was introduced (Table 3, entries 1 and 2). As the temperature increased (65 °C) or decreased (0 °C), no product was observed (Table 3, entries 3 and 4). The Wittig reaction[45−48] also did not yield the product due to the steric hindrance of the substrate (Table 3, entries 5 and 6). Later, we found that high selectivity for the *E*-double bond could be achieved by the Kocieński−Julia olefination[42−44] (Table 3, entries 7−10), especially with the use of LiHMDS in DMF at −35 °C[43] (Table 3, entry 9).

The ^{1}H NMR and ^{13}C NMR spectra of the synthesized (−)-dinemasone B (**1**) were identical to those reported for the naturally isolated product. The optical rotation was also in good agreement (synthetic **1**: $[\alpha]_D^{25}$ = −28.2 (c = 1.00, CH_2Cl_2); natural **1**: $[\alpha]_D^{25}$ = −27.0 (c = 0.97, CH_2Cl_2)).

Total Synthesis of (+)-4a-*epi*-Dinemasone B. Using a similar approach, catalytic hydrogenolysis of lactone **19** with $Pd(OH)_2$/C in THF and protection of the hydroxyl groups of **28** with TMS gave lactone **29** in 93% yield for two steps. Selective oxidative deprotection of the primary alcohol TMS group,[39−41] Takai−Utimoto olefination[33,34] using CH_3CHI_2 in the presence of $CrCl_2$ in THF, and removal of the remaining TMS groups afforded (+)-4a-*epi*-dinemasone B (**30**) in 67% yield over three steps with an excellent selectivity (E/Z > 95:05) (Scheme 7).

Scheme 7. Total Synthesis of (+)-4a-*epi*-Dinemasone B (30)



Total Synthesis of (−)-7-*epi*-Dinemasone B and (+)-4a,7-Di-*epi*-dinemasone B. Meanwhile, (−)-7-*epi*-dinemasone B (**39**) and (+)-4a,7-di-*epi*-dinemasone B (**44**) were obtained with excellent selectivity from (*S*)-alcohol **10** using the same method described above. The synthetic details are shown in Scheme 8.

All the configurations of (−)-dinemasone B (**1**), (+)-4a-*epi*-dinemasone B (**30**), (−)-7-*epi*-dinemasone B (**39**), and (+)-4a,7-di-*epi*-dinemasone B (**44**) were confirmed by NOESY analysis, which were in agreement with that of the MPA esters,[49] as shown in Figure 2.

CONCLUSION

In summary, we have achieved the stereoselective total syntheses of (−)-dinemasone B, (+)-4a-*epi*-dinemasone B, (−)-7-*epi*-dinemasone B, and (+)-4a,7-di-*epi*-dinemasone B for the first time starting from D-glucose derivative, and the absolute configurations of these compounds were established. The total synthesis of (−)-dinemasone B (**1**) proceeded in 18 steps in 29% overall yield, with the stereoselective reduction of *C*-glycosidic ketone, lactonization, and Kocieński−Julia olefination as the key steps. The stereoselectivity of the process and the high overall yield make the method one of the most practical alternatives to synthesize optically pure hexahydropyrano[4,3-*b*]pyran-5(7*H*)-one systems. Further studies toward the total synthesis of (−)-dinemasone C are currently underway.

EXPERIMENTAL SECTION

(2*R*,3*S*,4*R*,4a*S*,7*R*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-[(1*E*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (1). To a solution of Celite (1.88 g, 4g per g(CrO_3)) and pyridine (759 μL, 9.38 mmol) in DCM (5 mL) was added chromium(VI) oxide (469 mg, 4.69 mmol), and the mixture was stirred at rt for 1 h then cooled to 0 °C. Then a solution of lactone **25** (210 mg, 469 μmol) in DCM

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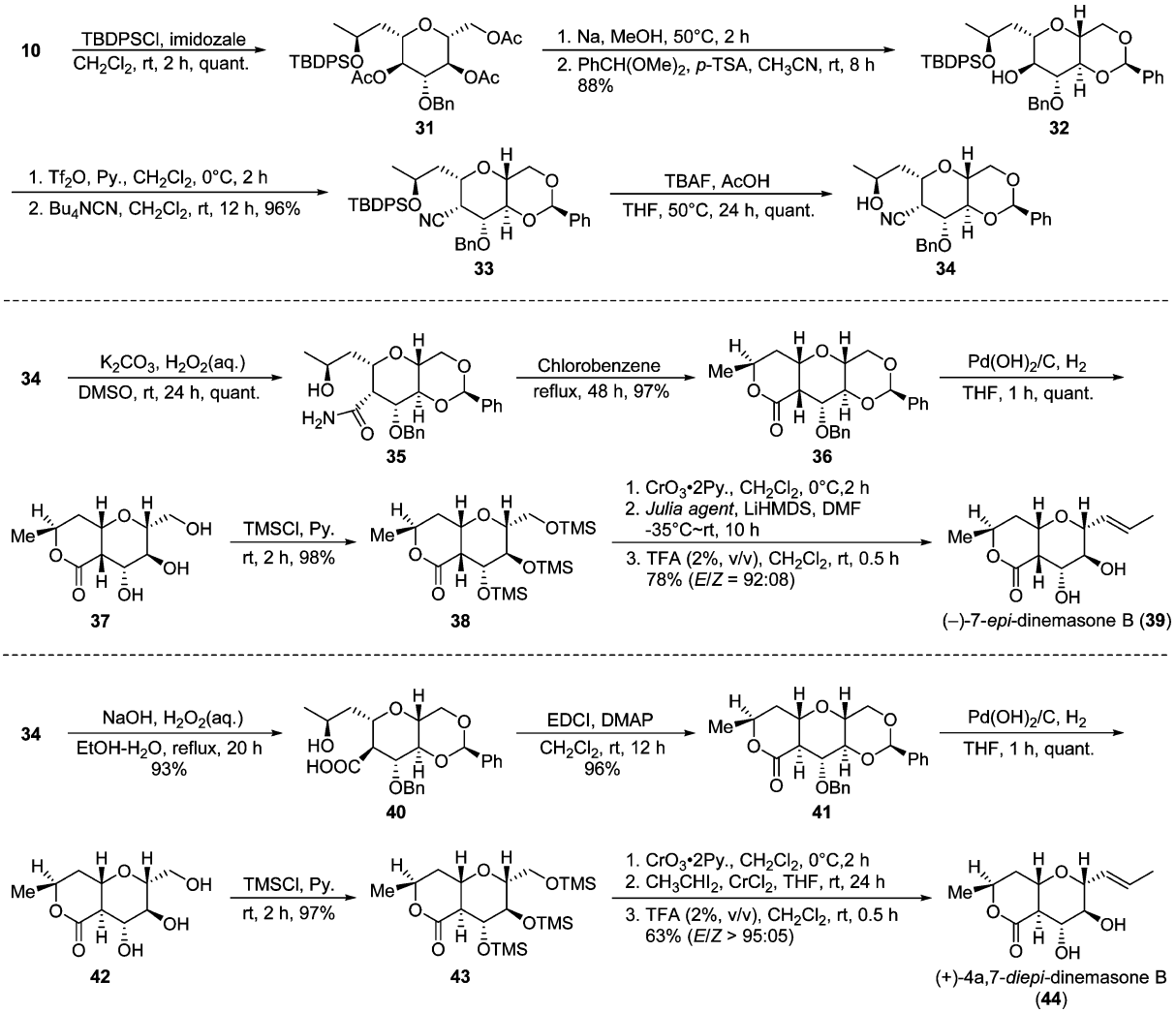
Scheme 8. Total Synthesis of (−)-7-*epi*-Dinemasone B (39) and (+)-4a,7-Di-*epi*-Dinemasone B (44) from (*S*)-Alcohol 10



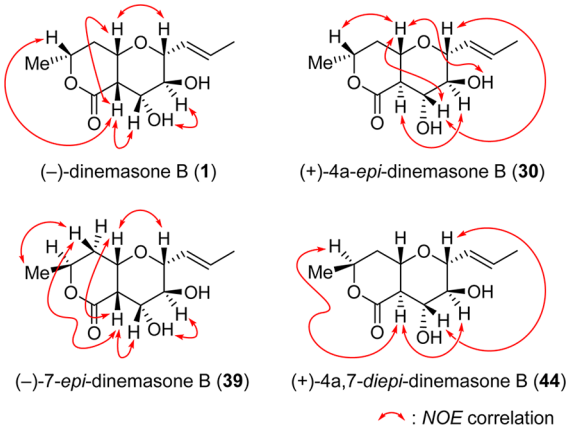


Figure 2. NOESY experiments of (−)-dinemasone B (**1**) and its epimers.

(5 mL) was added and the mixture stirred for 2 h. The reaction mixture was filtered through a pad of silica and concentrated in vacuum to afford an unstable aldehyde, which was used immediately without further purification.

To a solution of 5-(ethylsulfonyl)-1-phenyl-1*H*-tetrazole (134 mg, 563 μmol) in DMF (2 mL) was added LiHMDS (1 M in THF/ethylbenzene, 516 μL, 516 μmol) at −35 °C. This was immediately followed by addition of aldehyde in DMF (3 mL) via cannula. The reaction mixture was allowed to warm slowly to rt and stirred for 10 h before it was diluted with DCM and water. The organic layers were separated, and the aqueous layers were extracted with DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated.

The residue was dissolved in DCM (5 mL), and trifluoroacetic acid (100 μL, 2% v/v) was added dropwise at rt. After being stirred 30 min, the reaction mixture was concentrated and purified by flash column chromatography ($CHCl_3$−acetone, 4:1) to afford **1** (78 mg, 69%) and *Z*-isomer **S3** (5 mg, 4%). Data for **1** (an amorphous solid): R_f = 0.2 ($CHCl_3$−acetone, 4:1); mp 157−158 °C; $[\alpha]_D^{25}$ = −28.2 (*c* = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 (dq, *J* = 15.6 Hz, 6.8 Hz, 1H), 5.50 (dd, *J* = 15.6 Hz, 6.8 Hz, 1H), 4.36 (m, 1H), 4.15 (dt, *J* = 9.2 Hz, 2.8 Hz, 1H), 4.03 (d, *J* = 11.2 Hz, 1H), 3.69 (dt, *J* = 5.2 Hz, 9.2 Hz, 1H), 3.64 (t, *J* = 9.2 Hz, 1H), 3.55 (t, *J* = 8.0 Hz, 1H), 3.00 (t, *J* = 4.0 Hz, 1H), 2.60 (br s, 1H), 2.47 (ddd, *J* = 14.8 Hz, 8.8 Hz, 3.6 Hz, 1H), 1.77 (ddd, *J* = 14.8 Hz, 12.0 Hz, 2.8 Hz, 1H), 1.75 (d, *J* = 6.4 Hz, 3H), 1.42 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 131.7, 127.8, 81.3, 73.5, 72.8, 72.2, 71.4, 44.9, 37.1, 20.6, 18.2 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{12}H_{19}O_5$ $[M + H]^+$ 243.1227, found 243.1228; $C_{12}H_{18}NaO_5$ $[M + Na]^+$ 265.1046, found 265.1046.

(2*R*,3*S*,4*R*,4a*S*,7*R*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-[(1*Z*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (S3). Amorphous solid: R_f = 0.2 ($CHCl_3$−acetone, 4:1); mp 180−181 °C; $[\alpha]_D^{25}$ = −50.0 (*c* = 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (m, 1H),

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5.40 (t, J = 9.6 Hz, 1H), 4.37 (m, 1H), 4.18 (dt, J = 9.2 Hz, 3.2 Hz, 1H), 4.01 (d, J = 13.2 Hz, 1H), 3.97 (t, J = 8.8 Hz, 1H), 3.73 (dt, J = 4.8 Hz, 9.2 Hz, 1H), 3.67 (t, J = 9.2 Hz, 1H), 3.02 (t, J = 4.0 Hz, 1H), 2.47 (ddd, J = 15.2 Hz, 9.2 Hz, 4.0 Hz, 1H), 2.44 (br s, 1H), 1.77 (ddd, J = 15.2 Hz, 12.0 Hz, 2.8 Hz, 1H), 1.75 (d, J = 6.8 Hz, 3H), 1.42 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 131.2, 127.2, 76.0, 73.5, 72.9, 72.5, 71.5, 45.0, 37.1, 20.6, 14.1 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{12}H_{19}O_5$ $[M + H]^+$ 243.1227, found 243.1226; $C_{12}H_{18}NaO_5$ $[M + Na]^+$ 265.1046, found 265.1045.

(2*S*,3*S*,4*R*,4a*R*,7*R*,8a*S*)-Hexahydro-3,4-bis(benzyloxy)-7-methyl-2-(formyl)pyrano[4,3-*b*]pyran-5(7*H*)-one (3). To a stirred solution of **21** (170 mg, 412 μmol) in dry DCM (10 mL) at rt were added $PhI(OAc)_2$ (266 mg, 825 μmol) and TEMPO (65 mg, 412 μmol). The resulting mixture was stirred for 12 h and then quenched with a mixture of saturated aqueous solution of $NaHCO_3$ (5 mL) and $Na_2S_2O_3$ (5 mL). The resulting mixture was extracted with DCM, dried over Na_2SO_4, and concentrated. The crude residue was purified by flash column chromatography (PE−EtOAc, 1:1) to afford aldehyde **3** (156 mg, 92%) as a colorless syrup: R_f = 0.4 (PE−acetone, 1:1); $[\alpha]_D^{25}$ = +4.0 (c = 1.0, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (d, J = 0.4 Hz, 1H), 7.37−7.26 (m, 10H), 4.78 (d, J = 11.2 Hz, 1H), 4.68−4.61 (m, 3H), 4.28 (m, 1H), 4.20 (m, 1H), 4.13 (t, J = 6.7 Hz, 1H), 4.03 (m, 1H), 3.87 (d, J = 6.6 Hz, 1H), 3.00 (dd, J = 4.8 Hz, 4.1 Hz, 1H), 2.30 (ddd, J = 14.5 Hz, 7.5 Hz, 3.0 Hz, 1H), 1.87 (ddd, J = 14.4 Hz, 11.5 Hz, 6.3 Hz, 1H), 1.39 (d, J = 6.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 169.8, 137.8, 137.5, 128.7, 128.6, 128.3, 128.2, 128.1, 81.9, 74.0, 73.6, 72.4, 70.7, 42.5, 37.0, 21.0 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{24}H_{26}NaO_6$ $[M + Na]^+$ 433.1622, found 433.1630.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-5-cyano-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*gluco*-nonitol (4). To a solution of **13** (1.34 g, 2.07 mmol) in THF (50 mL) were added acetic acid (592 μL, 10.35 mmol) and tetrabutylammonium fluoride (1 M in THF, 20.7 mL, 20.70 mmol) at 50 °C, and the resulting solution was stirred for 24 h. The reaction mixture was passed through a short plug of silica gel (PE−EtOAc, 1:1). The filtrate was concentrated, and the residue was subjected to flash column chromatography (PE−EtOAc, 1:1) to afford alcohol **4** (839 mg, quant) as a colorless syrup: R_f = 0.3 (PE−EtOAc, 1:1); $[\alpha]_D^{25}$ = −62.5 (c = 2.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.25 (m, 10H), 5.63 (s, 1H), 4.85 (d, J = 13.1 Hz, 1H), 4.75 (d, J = 12.4 Hz, 1H), 4.29 (dd, J = 10.4 Hz, 4.8 Hz, 1H), 4.03 (m, 1H), 3.99 (t, J = 9.4 Hz, 1H), 3.85−3.77 (m, 3H), 3.41 (dt, J = 4.9 Hz, 9.6 Hz, 1H), 3.19 (dd, J = 5.3 Hz, 2.1 Hz, 1H), 1.99 (ddd, J = 14.3 Hz, 9.3 Hz, 1.8 Hz, 1H), 1.73 (br s, 1H), 1.53 (ddd, J = 13.8 Hz, 10.2 Hz, 3.1 Hz, 1H), 1.22 (d, J = 6.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 137.3, 129.2, 128.6, 128.4, 128.1, 127.9, 126.2, 117.1, 101.7, 80.6, 74.6, 73.4, 72.9, 71.8, 68.5, 64.3, 42.6, 41.0, 24.5 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{24}H_{27}NNaO_5$ $[M + Na]^+$ 432.1781, found 432.1788.

5,7,9-Tri-*O*-acetyl-6-*O*-benzyl-4,8-anhydro-1,3-dideoxy-D-*glycero*-D-*gulo*-non-2-ulose (5). To a solution of **S1** (3.0 g, 9.67 mmol) in pyridine (30 mL) was added acetic anhydride (15 mL). After the solution was stirred at rt for 12 h, the reaction mixture was cooled to 0 °C, methanol was added dropwise, the mixture was concentrated at reduced pressure, and the residue was washed with 1 M HCl (aq) and extracted with DCM. The combined organic layers were washed with saturated $NaHCO_3$ (aq) and brine, dried over Na_2SO_4, concentrated, and purified by flash column chromatography (PE−EtOAc, 3:1) to afford ketone **5** (4.22 g, quant) as an amorphous solid: R_f = 0.5 (PE−EtOAc, 1:1); mp 123−125 °C; $[\alpha]_D^{25}$ = −18.3 (c = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.22 (m, 5H), 5.06 (t, J = 9.6 Hz, 1H), 4.91 (t, J = 9.6 Hz, 1H), 4.61 (s, 2H), 4.17 (dd, J = 12.4 Hz, 5.2 Hz, 1H), 4.02 (dd, J = 12.4 Hz, 2.4 Hz, 1H), 3.89 (ddd, J = 9.6 Hz, 8.8 Hz, 3.2 Hz, 1H), 3.70 (t, J = 9.2 Hz, 1H), 3.57 (ddd, J = 12.4 Hz, 5.2 Hz, 2.4 Hz, 1H), 2.75 (dd, J = 16.8 Hz, 8.8 Hz, 1H), 2.46 (dd, J = 16.8 Hz, 3.2 Hz, 1H), 2.16 (s, 3H), 2.06 (s, 3H), 1.96 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.8, 170.9, 170.0, 169.6, 138.0, 128.6, 128.0, 127.8, 81.8, 76.2, 74.6, 74.2, 73.4, 70.1, 62.5, 45.6, 31.3, 21.0, 20.9 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{22}H_{28}NaO_9$ $[M + Na]^+$ 459.1626, found 459.1616.

3-*O*-Benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (7). Diacetone D-glucose **6** (12.00 g, 46.13 mmol) was dissolved in THF (30 mL), and sodium hydride (5.54 g, 138.4 mmol) was added. After the mixtur was stirred at 0 °C for 30 min, benzyl bromide (6.58 mL, 55.36 mmol) was added, and the resulting mixture was stirred at 40 °C for 10 h. Then the reaction was quenched by addition of methanol dropwise, the solvent was removed under reduced pressure, and the residue was dissolved in DCM and washed with 1 M HCl (aq). The aqueous layers were extracted with DCM, and the combined organic layers were washed with saturated $NaHCO_3$ (aq) and brine, dried over Na_2SO_4, filtered, evaporated, and purified by flash column chromatography (PE−EtOAc, 8:1) to give benzyl ether **7** (16.15 g, quant) as a colorless syrup: R_f = 0.5 (PE−EtOAc, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5H), 5.89 (d, J = 3.6 Hz, 1H), 4.67 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 4.0 Hz, 1H), 4.37 (dt, J = 7.7 Hz, 6.0 Hz, 1H), 4.15 (dd, J = 7.8 Hz, 3.1 Hz, 1H); 4.10 (dd, J = 8.6 Hz, 6.2 Hz, 1H), 4.02 (d, J = 2.9 Hz, 1H), 4.00 (dd, J = 8.5 Hz, 5.8 Hz, 1H), 1.48 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.30 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 128.5, 127.9, 127.7, 111.8, 109.0, 105.4, 82.7, 81.8, 81.4, 72.6, 72.4, 67.5, 26.9, 26.8, 26.3, 25.5 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{19}H_{26}NaO_6$ $[M + Na]^+$ 373.1622, found 373.1628.

3-*O*-Benzyl-D-glucopyranose (8). To a solution of benzyl ether **7** (10.0 g, 28.56 mmol) in H_2O (50 mL) was added DOWEX 50WX8-400 resin (H^+ form) (20.0 g). The reaction mixture was heated to 70 °C for 12 h, the resin was filtered off, and the filtrate was concentrated, yielding **8** (7.56 g, 98%) as an amorphous solid: R_f = 0.3 ($CHCl_3$−CH_3OH, 6:1); mp 119−120 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41−7.22 (m, 5H), 6.65 (d, J = 3.6 Hz, 1H), 5.04 (s, 2H), 4.81 (d, J = 12.0 Hz, 1H), 4.77 (d, J = 12.0 Hz, 1H), 4.50 (s, 1H), 4.33 (t, J = 7.2 Hz, 1H), 3.68 (ddd, J = 7.6 Hz, 5.2 Hz, 1.2 Hz, 1H), 3.45 (m, 1H), 3.27−3.18 (m, 2H), 3.14−3.05 (m, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.7, 127.9, 127.4, 127.0, 96.9, 85.3, 76.7, 74.8, 73.6, 69.9, 61.1 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{13}H_{18}NaO_6$ $[M + Na]^+$ 293.0996, found 293.1000.

6-*O*-Benzyl-4,8-anhydro-1,3-dideoxy-D-*glycero*-D-*gulo*-non-2-ulose (S1). To a solution of **8** (5.0 g, 18.51 mmol) in H_2O (75 mL) were added sodium bicarbonate (2.33 g, 27.77 mmol) and pentane-2,4-dione (2.29 mL, 22.21 mmol). After being refluxed for 48 h, the reaction mixture was treated with DOWEX 50WX8-400 resin (H^+ form). The resin was filtered off, and the filtrate was concentrated to dryness and purified by flash column chromatography ($CHCl_3$−CH_3OH, 20:1) to afford **S1** (4.48 g, 78%) as an amorphous solid: R_f = 0.5 ($CHCl_3$−CH_3OH, 6:1); mp 87−88 °C; $[\alpha]_D^{25}$ = +10.9 (c = 1.1, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 7.42−7.23 (m, 5H), 4.94 (d, J = 11.6 Hz, 1H), 4.90 (d, J = 11.6 Hz, 1H), 4.45 (d, J = 5.6 Hz, 1H), 4.39 (d, J = 4.8 Hz, 1H), 3.78 (ddd, J = 11.6 Hz, 6.0 Hz, 3.2 Hz, 1H), 3.73 (dt, J = 3.2 Hz, 9.2 Hz, 1H), 3.63 (m, 1H), 3.57 (t, J = 6.4 Hz, 1H), 3.52 (dt, J = 4.8 Hz, 9.2 Hz, 1H), 3.40 (t, J = 8.8 Hz, 1H), 3.30 (ddd, J = 9.6 Hz, 5.2 Hz, 2.8 Hz, 1H), 3.25 (dt, J = 5.6 Hz, 8.8 Hz, 1H), 2.86 (dd, J = 15.6 Hz, 2.8 Hz, 1H), 2.50 (dd, J = 15.6 Hz, 8.8 Hz, 1H), 2.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ 206.8, 140.7, 128.8, 128.4, 127.9, 87.7, 81.3, 77.1, 75.2, 74.8, 72.0, 63.0, 47.0, 30.5 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{16}H_{23}O_6$ $[M + H]^+$ 311.1489, found 311.1489; $C_{16}H_{22}NaO_6$ $[M + Na]^+$ 333.1309, found 333.1307.

5,7,9-Tri-*O*-acetyl-6-*O*-benzyl-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*galacto*-nonitol (9). To a solution of ketone **5** (100 mg, 0.23 mmol) in toluene (30 mL) was added titanium(IV) isopropoxide (274 μL, 0.92 mmol) at rt, and after being stirred for 30 min, the mixture was cooled to −78 °C and L-Selectride (1 M in THF, 253 μL, 253 μmol) added. The reaction was quenched by addition of saturated NH_4Cl (aq) after 30 min, 1 M HCl (aq) was added, the mixture was extracted with DCM, and the combined organic layers were washed with saturated $NaHCO_3$ (aq) and brine, dried over Na_2SO_4, filtered, evaporated, and purified by flash column chromatography (PE−EtOAc, 1:1) to give alcohol **9** (92.43 mg, 92%, R/S > 95:05) as an amorphous solid: R_f = 0.2 (PE−EtOAc, 1:1); mp 72−73 °C; $[\alpha]_D^{25}$ = −22.2 (c = 2.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.22 (m, 5H), 5.08 (t, J = 9.6 Hz, 1H), 4.97 (t, J = 9.6 Hz, 1H), 4.61 (s,

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2H), 4.17 (dd, J = 12.4 Hz, 5.2 Hz, 1H), 4.10 (dd, J = 12.4 Hz, 2.4 Hz, 1H), 4.09 (m, 1H), 3.69 (t, J = 9.2 Hz, 1H), 3.65 (dt, J = 2.8 Hz, 9.2 Hz, 1H), 3.57 (ddd, J = 10.0 Hz, 5.2 Hz, 2.4 Hz, 1H), 2.08 (s, 3H), 1.99 (s, 3H), 1.97 (s, 3H), 1.66−1.51 (m, 3H), 1.20 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 169.8, 169.6, 138.0, 128.6, 127.9, 127.8, 81.8, 76.2, 75.5, 74.4, 73.0, 70.2, 64.2, 62.7, 39.7, 23.9, 21.0, 20.9 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{22}H_{30}NaO_9$ $[M + Na]^+$ 461.1782, found 461.1793.

5,7,9-Tri-*O*-acetyl-6-*O*-benzyl-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*talo*-nonitol (10). To a stirred solution of (*R*)-2-methyl-*CBS*-oxazoborolidine (1 M in toluene, 516 μL, 516 μmol) in toluene (10 mL) was added catecholborane (1 M in THF, 1.03 mL, 1.03 mmol) at 0 °C. The reaction mixture was stirred for 10 min, and then a solution of **5** (150 mg, 344 μmol) in toluene (5 mL) was added. The mixture was warmed to rt, stirred for 1 h, and quenched by the addition of saturated NH_4Cl (aq), 1 M HCl (aq) (10 mL) was added, the mixture was extracted with DCM, and the combined organic layers were washed with saturated $NaHCO_3$ (aq) and brine, dried over Na_2SO_4, filtered, evaporated, and purified by flash column chromatography (PE−EtOAc, 1:1) to give alcohol **10** (149.2 mg, quant, S/R = 94:06) as an amorphous solid: R_f = 0.2 (PE−EtOAc, 1:1); mp 111−112 °C; $[\alpha]_D^{25}$ = −8.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.22 (m, 5H), 5.02 (t, J = 9.6 Hz, 1H), 4.93 (t, J = 9.6 Hz, 1H), 4.61 (s, 2H), 4.20 (d, J = 12.0 Hz, 1H), 4.03 (dd, J = 12.4 Hz, 7.2 Hz, 1H), 3.98 (m, 1H), 3.67 (t, J = 9.6 Hz, 1H), 3.63 (dt, J = 9.6 Hz, 2.4 Hz, 1H), 3.57 (dt, J = 2.4 Hz, 9.2 Hz, 1H), 3.16 (br s, 1H), 2.07 (s, 3H), 1.99 (s, 3H), 1.98 (s, 3H), 1.69−1.56 (m, 2H), 1.18 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 169.7, 169.5, 137.9, 128.6, 128.0, 127.8, 81.5, 79.1, 76.2, 74.4, 73.4, 70.3, 67.8, 62.9, 39.7, 23.5, 21.0, 20.9, 20.8 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{22}H_{31}O_9$ $[M + H]^+$ 439.1963, found 439.1972; $C_{22}H_{30}NaO_9$ $[M + Na]^+$ 461.1782, found 461.1789.

5,7,9-Tri-*O*-acetyl-6-*O*-benzyl-2-*O*-(*tert*-butyldiphenylsilyl)-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*galacto*-nonitol (11). To a solution of alcohol **9** (4.77 g, 10.89 mmol) in DCM (30 mL) were added imidazole (1.85 g, 27.23 mmol) and *tert*-butylchlorodiphenylsilane (3.35 mL, 13.07 mmol). The reaction mixture was stirred at rt for 2 h and then washed with brine, the aqueous layers were extracted with DCM, and the combined organic layers were dried over Na_2SO_4, filtered, evaporated, and purified by flash column chromatography (PE−EtOAc, 5:1) to give **11** (7.36 g, quant) as a colorless syrup: R_f = 0.4 (PE−EtOAc, 3:1); $[\alpha]_D^{25}$ = +1.8 (c = 4.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.22 (m, 15H), 5.04 (t, J = 9.6 Hz, 1H), 4.84 (t, J = 9.6 Hz, 1H), 4.60 (d, J = 11.6 Hz, 1H), 4.56 (d, J = 11.6 Hz, 1H), 4.15 (m, 1H), 4.09 (dd, J = 12.4 Hz, 4.4 Hz, 1H), 3.73 (dd, J = 12.4 Hz, 2.4 Hz, 1H), 3.51 (t, J = 9.2 Hz, 1H), 3.48 (dt, J = 1.6 Hz, 10.0 Hz, 1H), 3.05 (ddd, J = 10.0 Hz, 4.0 Hz, 2.0 Hz, 1H), 2.03 (s, 3H), 2.02 (s, 3H), 1.94 (s, 3H), 1.60 (ddd, J = 14.4 Hz, 9.6 Hz, 1.2 Hz, 1H), 1.49 (ddd, J = 14.4 Hz, 10.4 Hz, 2.4 Hz, 1H), 1.08 (d, J = 6.4 Hz, 3H), 1.06 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 169.9, 169.4, 138.1, 136.0, 134.7, 134.4, 129.8, 129.7, 128.5, 127.9, 127.8, 127.7, 127.6, 82.1, 75.5, 74.9, 74.1, 73.4, 69.7, 66.1, 62.3, 41.8, 27.2, 24.6, 21.1, 20.9, 19.5 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{38}H_{48}NaO_9Si$ $[M + Na]^+$ 699.2960, found 699.2975.

6-*O*-Benzyl-2-*O*-(*tert*-butyldiphenylsilyl)-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*galacto*-nonitol (S2). To a solution of **11** (6.97 g, 10.31 mmol) in methanol (50 mL) was added catalytic sodium, and the reaction mixture was stirred at 50 °C for 2 h. The solution was neutralized with DOWEX 50WX8-400 resin (H^+ form). The resin was filtered off and the filtrate concentrated to afford **S2** (5.67 g, quant) as a colorless syrup, which was directly used without further purification: R_f = 0.2 ($CHCl_3$−CH_3OH, 30:1); $[\alpha]_D^{25}$ = +5.2 (c = 2.3, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.73−7.26 (m, 15H), 4.89 (s, 2H), 4.25 (m, 1H), 3.65 (d, J = 3.3 Hz, 2H), 3.56−3.47 (m, 2H), 3.28 (t, J = 8.9 Hz, 1H), 3.14 (t, J = 9.2 Hz, 1H), 3.00 (dt, J = 9.7 Hz, 3.3 Hz, 1H), 2.16 (ddd, J = 14.0 Hz, 9.7 Hz, 1.4 Hz, 1H), 1.38 (ddd, J = 14.0 Hz, 10.4 Hz, 2.6 Hz, 1H), 1.05 (s, 9H), 1.02 (d, J = 6.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 140.4, 137.0, 136.9, 135.9, 135.3, 130.7, 130.6, 129.1, 129.0, 128.6, 128.4, 128.3, 88.1, 80.8, 77.5, 76.0, 75.5, 71.3, 67.4, 62.4, 43.2, 27.7, 25.1, 20.2 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{32}H_{42}NaO_6Si$ $[M + Na]^+$ 573.2643, found 573.2653.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-2-*O*-(*tert*-butyldiphenylsilyl)-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*galacto*-nonitol (12). To a solution of **S2** (5.15 g, 9.36 mmol) and benzaldehyde dimethyl acetal (2.11 mL, 14.04 mmol) in CH_3CN (50 mL) was added *p*-toluenesulfonic acid monohydrate (89.02 mg, 468 μmol) at rt. After being stirred for 8 h, the reaction mixture was quenched by addition of triethylamine, and the reaction mixture was concentrated and purified by flash column chromatography (PE−EtOAc, 5:1) to give alcohol **12** (5.32g, 89%) as a colorless syrup: R_f = 0.2 (PE−EtOAc, 5:1); $[\alpha]_D^{25}$ = +8.0 (c = 2.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.31 (m, 20H), 5.53 (s, 1H), 5.02 (d, J = 11.6 Hz, 1H), 4.70 (d, J = 11.6 Hz, 1H), 4.12 (m, 1H), 4.10 (dd, J = 10.4 Hz, 4.8 Hz, 1H), 3.60 (dd, J = 10.4 Hz, 9.2 Hz, 1H), 3.59 (ddd, J = 9.6 Hz, 8.8 Hz, 2.4 Hz, 1H), 3.57 (t, J = 8.8 Hz, 1H), 3.52 (t, J = 8.8 Hz, 1H), 3.27 (t, J = 8.8 Hz, 1H), 3.16 (ddd, J = 9.2 Hz, 8.8 Hz, 4.8 Hz, 1H), 2.32 (br s, 1H), 2.13 (ddd, J = 14.0 Hz, 9.6 Hz, 1.6 Hz, 1H), 1.38 (ddd, J = 14.0 Hz, 10.4 Hz, 2.4 Hz, 1H), 1.05 (s, 9H), 1.04 (d, J = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 137.6, 136.1, 134.9, 134.3, 129.7, 129.6, 129.1, 128.7, 128.4, 128.2, 128.1, 127.6, 127.5, 126.1, 101.2, 82.7, 82.4, 76.7, 74.8, 74.3, 70.2, 69.0, 66.0, 42.5, 27.2, 24.6, 19.5 ppm; HRMS (ESI-FT-ICR) m/z Calcd for $C_{39}H_{46}NaO_6Si$ $[M + Na]^+$ 661.2956, found 661.2969.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-2-*O*-(*tert*-butyldiphenylsilyl)-5-cyano-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*gluco*-nonitol (13). To a solution of compound **12** (628 mg, 984 μmol) and pyridine (199 μL, 2.46 mmol) in DCM (10 mL) was added trifluoromethanesulfonic anhydride (194 μL, 1.18 mmol) dropwise at 0 °C. The reaction mixture was stirred for 2 h, after which time it was concentrated and passed through a short plug of silica gel (PE−EtOAc, 20:1) to give triflate as an unstable, colorless syrup that was used immediately without characterization. To a solution of the triflate in DCM (20 mL) was added tetrabutylammonium cyanide (0.44 M in THF, 11.18 mL, 4.92 mmol) dropwise at rt. The solution was allowed to stir for 12 h, and then the mixture was concentrated to dryness, and the residue was subjected to flash column chromatography (PE−EtOAc, 10:1) to afford **13** (586 mg, 92%) as a colorless syrup: R_f = 0.4 (PE−EtOAc, 5:1); $[\alpha]_D^{25}$ = −29.3 (c = 4.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.31 (m, 20H), 5.57 (s, 1H), 4.82 (d, J = 12.4 Hz, 1H), 4.72 (d, J = 12.4 Hz, 1H), 4.11 (ddq, J = 10.0 Hz, 2.0 Hz, 6.4 Hz, 1H), 4.04 (dd, J = 10.4 Hz, 4.8 Hz, 1H), 3.88 (t, J = 9.6 Hz, 1H), 3.67 (t, J = 10.4 Hz, 1H), 3.65 (dt, J = 10.0 Hz, 2.0 Hz, 1H), 3.56 (dd, J = 9.6 Hz, 5.2 Hz, 1H), 3.01 (dd, J = 5.2 Hz, 2.0 Hz, 1H), 2.94 (ddd, J = 10.4 Hz, 9.6 Hz, 4.8 Hz, 1H), 1.90 (ddd, J = 14.4 Hz, 10.0 Hz, 2.0 Hz, 1H), 1.62 (ddd, J = 14.4 Hz, 10.0 Hz, 2.0 Hz, 1H), 1.11 (d, J = 6.4 Hz, 3H), 1.03 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 137.3, 136.0, 135.8, 134.3, 134.1, 130.0, 129.9, 129.2, 128.6, 128.4, 128.1, 127.8, 127.8, 127.7, 126.2, 116.9, 101.6, 80.4, 74.7, 72.9, 72.9, 71.3, 68.4, 66.3, 43.9, 40.9, 27.2, 24.5, 19.5 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{40}H_{45}NNaO_5Si$ $[M + Na]^+$ 670.2959, found 670.2973.

(2*R*,4a*R*,5a*S*,7*R*,9a*R*,10*R*,10a*S*)-10-Benzyloxy-7-methyl-2-phenylhexahydro-4*H*-pyrano[3′,4′:5,6]pyrano[3,2-*d*][1,3]-dioxin-9(4a*H*)-one (16). A solution of amide **20** (200 mg, 468 μmol) in chlorobenzene (10 mL) was refluxed for 48 h, while a continuous stream of nitrogen was bubbled through the solution. After evaporation, the residue was purified by flash column chromatography (PE−EtOAc, 2:1) to afford lactone **16** (150 mg, 78%) as an amorphous solid: R_f = 0.2 (PE−EtOAc, 2:1); mp 201−203 °C; $[\alpha]_D^{25}$ = +32.6 (c = 3.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.19 (m, 10H), 5.60 (s, 1H), 4.91 (d, J = 12.8 Hz, 1H), 4.67 (d, J = 12.8 Hz, 1H), 4.37 (t, J = 9.4 Hz, 1H), 4.19 (m, 1H), 4.15 (dd, J = 10.4 Hz, 4.8 Hz, 1H), 4.07 (dt, J = 9.4 Hz, 3.2 Hz, 1H), 3.75 (dd, J = 9.7 Hz, 4.9 Hz, 1H), 3.69 (t, J = 10.2 Hz, 1H), 3.28 (dt, J = 4.8 Hz, 9.9 Hz, 1H), 2.87 (t, J = 3.9 Hz, 1H), 2.32 (ddd, J = 15.2 Hz, 9.5 Hz, 3.4 Hz, 1H), 1.58 (ddd, J = 15.2 Hz, 12.3 Hz, 3.2 Hz, 1H), 1.30 (s, J = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 138.7, 137.7, 129.0, 128.6, 128.4, 128.0, 127.8, 126.2, 101.5, 79.0, 75.7, 73.7, 73.4, 72.8, 71.8, 68.5, 45.7, 37.4, 20.5 ppm; HRMS (ESI-FT-ICR) m/z calcd for

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$C_{24}H_{27}O_6$ [M + H]$^+$ 411.1802, found 411.1811; $C_{24}H_{26}NaO_6$ [M + Na]$^+$ 433.1622, found 433.1622.

(*R*)-7,9-*O*-Benzylidene-6-*O*-benzyl-5-cyano-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*galacto*-nonitol (17). 1.8-Diazabicyclo-[5.4.0]undec-7-ene (87.3 μL, 586 μmol) was added to a solution of alcohol **4** (120 mg, 293 μmol) and toluene (5 mL). The reaction mixture was heated to 80 °C for 12 h, cooled to rt, diluted with DCM (5 mL), and quenched with a saturated aqueous $NaHCO_3$ (10 mL). The organic layer was separated, and the aqueous phase was extracted with DCM. The combined organic layers were dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (PE−EtOAc, 4:1) to afford **17** (41 mg, 34%) as an amorphous solid (76 mg of compound **4** was recovered): R_f = 0.7 (PE−EtOAc, 1:1); mp 138−139 °C; $[\alpha]_D^{25}$ = −28.6 (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.26 (m, 10H), 5.59 (s, 1H), 4.96 (d, *J* = 11.1 Hz, 1H), 4.86 (d, *J* = 11.0 Hz, 1H), 4.32 (dd, *J* = 10.5 Hz, 4.9 Hz, 1H), 4.06 (m, 1H), 3.99 (td, *J* = 10.2 Hz, 2.2 Hz, 1H), 3.93 (dd, *J* = 10.4 Hz, 9.0 Hz, 1H), 3.70 (t, *J* = 10.2 Hz, 1H), 3.60 (t, *J* = 9.2 Hz, 1H), 3.48 (td, *J* = 9.8 Hz, 4.9 Hz, 1H), 2.70 (t, *J* = 10.5 Hz, 1H), 1.93 (ddd, *J* = 14.6 Hz, 9.7 Hz, 2.2 Hz, 1H), 1.71 (ddd, *J* = 14.5 Hz, 9.5 Hz, 2.3 Hz, 1H), 1.66 (br s, 1H), 1.25 (d, *J* = 6.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 137.1, 129.3, 128.6, 128.5, 128.4, 128.3, 126.1, 117.7, 101.7, 82.7, 75.3, 74.7, 70.9, 68.6, 64.0, 42.6, 40.9, 24.1 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{24}H_{28}NO_5$ [M + H]$^+$ 410.1962, found 410.1957.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-5-carboxy-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*galacto*-nonitol (18). Nitrile **4** (500 mg, 1.22 mmol) was dissolved in a mixture of ethanol (5.0 mL) and H_2O (2.5 mL), followed by addition of aqueous hydrogen peroxide (35%, 2.5 mL) and sodium hydroxide (488 mg, 12.2 mmol) at 0 °C. After being stirred at rt for 2 h, the solution was heated to reflux for 20 h and cooled to rt, ethanol was removed under reduced pressure, and the residue was diluted with H_2O, acidified (pH = 2) with 1 M HCl (aq) at 0 °C, and then extracted with DCM immediately. The combined organic layers were dried over Na_2SO_4 and concentrated, and the crude residue was purified by flash column chromatography (DCM−CH_3OH, 10:1) to afford carboxylic acid **18** (481 mg, 92%) as an amorphous solid: R_f = 0.3 ($CHCl_3$−CH_3OH, 10:1); mp 151−152 °C; $[\alpha]_D^{25}$ = −40.0 (*c* = 1.0, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.8 (br s, 1H), 7.45−7.25 (m, 10H), 5.72 (s, 1H), 4.80 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.48 (m, 1H), 4.19 (dd, *J* = 10.4 Hz, 5.2 Hz, 1H), 3.97 (t, *J* = 9.6 Hz, 1H), 3.84−3.70 (m, 4H), 3.41 (dt, *J* = 4.8 Hz, 9.6 Hz, 1H), 2.38 (t, *J* = 10.0 Hz, 1H), 1.48−1.35 (m, 2H), 1.03 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.2, 138.6, 137.7, 128.7, 128.1, 128.0, 127.4, 127.3, 125.9, 100.3, 82.2, 78.9, 74.5, 73.4, 70.1, 67.9, 61.7, 55.7, 43.1, 24.3 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{24}H_{28}NaO_7$ [M + Na]$^+$ 451.1727, found 451.1731.

(2*R*,4a*R*,5a*S*,7*R*,9a*S*,10*R*,10a*S*)-10-(Benzyloxy)-7-methyl-2-phenylhexahydro-4*H*-pyrano[3′,4′:5,6]pyrano[3,2-*d*][1,3]-dioxin-9(4a*H*)-one (19). To a stirred solution of carboxylic acid **18** (620 mg, 1.45 mmol) in DCM (20 mL) were added EDCI (418 mg, 2.18 mmol) and DMAP (8.9 mg, 72.5 μmol) at rt. The resulting mixture was stirred for 12 h and then solvent evaporated under vacuum. The crude residue was purified by flash column chromatography (PE−EtOAc, 3:1) to afford lactone **19** (570 mg, 96%) as an amorphous solid: R_f = 0.3 (PE−EtOAc, 2:1); mp 123−124 °C; $[\alpha]_D^{25}$ = −25.4 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.17 (m, 10H), 5.55 (s, 1H), 4.96 (d, *J* = 10.0 Hz, 1H), 4.81 (d, *J* = 10.0 Hz, 1H), 4.42 (m, 1H), 4.26 (dd, *J* = 10.4 Hz, 5.2 Hz, 1H), 3.92 (t, *J* = 9.6 Hz, 1H), 3.71−3.62 (m, 3H), 3.42 (dt, *J* = 4.8 Hz, 9.6 Hz, 1H), 2.45 (dd, *J* = 11.6 Hz, 10.0 Hz, 1H), 2.28 (dt, *J* = 12.8 Hz, 4.4 Hz, 1H), 1.70 (m, 1H), 1.37 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 138.6, 137.4, 129.1, 128.6, 128.4, 128.3, 127.8, 126.0, 101.6, 83.9, 76.2, 75.7, 74.1, 73.2, 70.8, 68.7, 52.0, 38.0, 22.5 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{24}H_{26}NaO_6$ [M + Na]$^+$ 433.1622, found 433.1627.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-5-carbamoyl-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*gluco*-nonitol (20). To a solution of **4** (100 mg, 244 μmol) in DMSO (2 mL) were added potassium carbonate (135 mg, 976 μmol) and aqueous hydrogen peroxide (35%, 500 μL, 4.88 mmol) at 0 °C. The solution was stirred at rt for 24 h, diluted with water, and extracted with DCM, and the organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated to afford amide **20** (104 mg, quant) as an amorphous solid, which was directly used without further purification: R_f = 0.3 (PE−acetone, 1:1); mp 84−85 °C; $[\alpha]_D^{25}$ = −47.2 (*c* = 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.26 (m, 10H), 6.06 (br s, 1H), 5.65 (s, 1H), 5.50 (br s, 1H), 4.84 (d, *J* = 12.3 Hz, 1H), 4.80 (d, *J* = 12.3 Hz, 1H), 4.39 (t, *J* = 9.5 Hz, 1H), 4.31 (dd, *J* = 10.4 Hz, 4.8 Hz, 1H), 4.04 (m, 1H), 3.93−3.87 (m, 2H), 3.84 (t, *J* = 10.3 Hz, 1H), 3.45 (dt, *J* = 4.7 Hz, 9.8 Hz, 1H), 2.98 (dd, *J* = 6.1 Hz, 2.4 Hz, 1H), 1.97 (ddd, *J* = 14.5 Hz, 9.2 Hz, 2.3 Hz, 1H), 1.59 (m, 2H), 1.22 (d, *J* = 6.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 138.4, 137.6, 129.0, 128.5, 128.3, 127.8, 127.7, 126.2, 101.6, 79.4, 76.5, 75.1, 72.6, 72.3, 68.9, 64.9, 51.7, 41.7, 24.6 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{24}H_{29}NNaO_6$ [M + Na]$^+$ 450.1887, found 450.1890.

(2*R*,3*S*,4*R*,4a*R*,7*R*,8a*S*)-Hexahydro-3,4-bis(benzyloxy)-7-methyl-2-(hydroxymethyl)pyrano[4,3-*b*]pyran-5(7*H*)-one (21). To a solution of compound **16** (300 mg, 731 μmol) in dry DCM (50 mL) was added BH_3·THF (1 M in THF, 7.31 mL, 7.31 mmol) at 0 °C, and the mixture was stirred for 5 min. Then Bu_2BOTf (1 M in DCM, 2.19 mL, 2.19 mmol) was added to the mixture slowly. After the mixture was stirred at 0 °C for 2 h, TLC showed that the starting material had disappeared. Triethylamine (366 μL) was then added to the reaction flash followed by careful addition of methanol until the evolution of H_2 had ceased. After evaporation, the residue was purified by flash column chromatography (PE−EtOAc, 1:1) to afford **21** (283 mg, 94%) as a colorless syrup: R_f = 0.2 (PE−acetone, 2:1); $[\alpha]_D^{25}$ = +20.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.26 (m, 10H), 4.96 (d, *J* = 10.8 Hz, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 12.0 Hz, 1H), 4.63 (d, *J* = 10.8 Hz, 1H), 4.21 (m, 1H), 4.03 (m, 2H), 3.82 (m, 1H), 3.78 (dd, *J* = 11.6 Hz, 2.8 Hz, 1H), 3.61 (dd, *J* = 11.6 Hz, 5.6 Hz, 1H), 3.31 (ddd, *J* = 8.4 Hz, 5.6 Hz, 2.4 Hz, 1H), 2.87 (t, *J* = 3.6 Hz, 1H), 2.32 (ddd, *J* = 14.8 Hz, 8.8 Hz, 3.2 Hz, 1H), 1.90 (br s, 1H), 1.69 (ddd, *J* = 14.8 Hz, 12.0 Hz, 3.6 Hz, 1H), 1.36 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 138.4, 138.2, 128.6, 128.5, 128.2, 128.0, 127.9, 80.2, 74.9, 74.6, 73.1, 72.0, 71.9, 62.9, 43.7, 37.3, 20.6 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{24}H_{28}NaO_6$ [M + Na]$^+$ 435.1778, found 435.1783.

(2*R*,3*S*,4*R*,4a*R*,7*R*,8a*S*)-Hexahydro-3,4-dibenzyloxy-7-methyl-2-[(1*E*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (22). In the glovebox, chromium(II) chloride (324 mg, 2.63 mmol) was loaded in a three-neck flask. On the Schlenk line, THF (2 mL) was transferred via cannula and the mixture stirred for 1 h to break up the aggregated chromium. In a round-bottom flask, aldehyde **3** (180 mg, 439 μmol) was combined with 1,1-diiodoethane (88 μL, 878 μmol) and THF (2 mL). Then the aldehyde solution was cannulated onto the chromium slurry. The reaction mixture was stirred at rt for 12 h and then poured into brine (50 mL), and the aqueous layer was extracted with DCM. The combined organics were washed with brine, dried over Na_2SO_4, and concentrated. The crude residue was purified by flash column chromatography (PE−EtOAc, 4:1) to afford compound **22** (145 mg, 78%, *E*/*Z* > 95:05) as a colorless syrup: R_f = 0.4 (PE−acetone, 2:1); $[\alpha]_D^{25}$ = +35.6 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.26 (m, 10H), 5.81 (dq, *J* = 15.2 Hz, 6.4 Hz, 1H), 5.46 (ddd, *J* = 15.2 Hz, 7.2 Hz, 1.6 Hz, 1H), 4.88 (d, *J* = 10.4 Hz, 1H), 4.85 (d, *J* = 12.0 Hz, 1H), 4.69 (d, *J* = 12.0 Hz, 1H), 4.63 (d, *J* = 10.8 Hz, 1H), 4.21 (m, 1H), 3.99 (dt, *J* = 8.8 Hz, 3.6 Hz, 1H), 3.89 (t, *J* = 8.8 Hz, 1H), 3.72 (m, 1H), 3.61 (t, *J* = 8.4 Hz, 1H), 2.82 (t, *J* = 3.6 Hz, 1H), 2.31 (ddd, *J* = 14.8 Hz, 8.4 Hz, 3.2 Hz, 1H), 1.72 (dd, *J* = 6.8 Hz, 1.2 Hz, 3H), 1.68 (ddd, *J* = 11.2 Hz, 9.6 Hz, 3.2 Hz, 1H), 1.35 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 138.7, 138.5, 130.8, 128.6, 128.5, 128.4, 128.0, 127.9, 127.8, 81.2, 79.9, 78.6, 75.1, 73.3, 72.0, 71.7, 44.3, 37.5, 20.6, 18.1 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{26}H_{31}O_5$ [M + H]$^+$ 423.2166, found 423.2171; $C_{26}H_{30}NaO_6$ [M + Na]$^+$ 455.1986, found 445.1988.

(2*R*,3*S*,4*R*,4a*S*,7*R*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-propylpyrano[4,3-*b*]pyran-5(7*H*)-one (23). A solution of **22** (10 mg, 41.3 μmol) in THF (1.0 mL) was treated with 20% $Pd(OH)_2$/C

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(20 mg) and placed under an H_2 atmosphere (4.5 atm). After 30 min at rt, the reaction mixture was filtered through Celite and then concentrated to afford **23** (9.8 mg, 97%) as an amorphous solid without further purification: R_f = 0.2 ($CHCl_3$−acetone, 4:1); mp 142−143 °C; $[\alpha]_D^{25}$ = −13.3 (*c* = 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (m, 1H), 4.06 (dt, *J* = 9.2 Hz, 3.2 Hz, 1H), 4.01 (d, *J* = 11.6 Hz, 1H), 3.62 (dt, *J* = 5.2 Hz, 9.6 Hz, 1H), 3.55 (t, *J* = 9.2 Hz, 1H), 3.11 (dt, *J* = 2.0 Hz, 8.4 Hz, 1H), 2.97 (t, *J* = 4.4 Hz, 1H), 2.65 (br s, 1H), 2.44 (ddd, *J* = 14.0 Hz, 9.2 Hz, 4.0 Hz, 1H), 1.83−1.71 (m, 2H), 1.56−1.29 (m, 6H), 0.91 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 80.1, 74.0, 72.9, 72.5, 71.4, 44.9, 37.0, 33.9, 20.6, 18.6, 14.2 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{12}H_{21}O_5$ $[M + H]^+$ 245.1384, found 245.1381; $C_{12}H_{20}NaO_5$ $[M + Na]^+$ 267.1203, found 267.1205.

(2*R*,3*S*,4*R*,4a*S*,7*R*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-hydroxymethylpyrano[4,3-*b*]pyran-5(7*H*)-one (24). To a solution of lactone **16** (100 mg, 244 μmol) in THF (5 mL) was added $Pd(OH)_2$/C (200 mg), and the mixture was stirred under H_2 atmosphere (4.5 atm) at rt for 1 h, filtered through Celite, and concentrated to afford **24** (56.5 mg, quant) as an amorphous solid without further purification: R_f = 0.3 ($CHCl_3$−acetone, 1:5); mp 171−172 °C; $[\alpha]_D^{25}$ = −40.0 (*c* = 0.2, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 4.99 (d, *J* = 5.2 Hz, 1H), 4.47 (t, *J* = 5.6 Hz, 1H), 4.44 (m, 1H), 4.31 (d, *J* = 8.0 Hz, 1H), 4.04 (dt, *J* = 9.6 Hz, 2.8 Hz, 1H), 3.64 (ddd, *J* = 11.6 Hz, 5.6 Hz, 2.0 Hz, 1H), 3.51 (dt, *J* = 4.8 Hz, 8.8 Hz, 1H), 3.44 (dt, *J* = 5.2 Hz, 8.8 Hz, 1H), 3.31 (dd, *J* = 11.6 Hz, 6.0 Hz, 1H), 3.16 (t, *J* = 3.6 Hz, 1H), 3.01 (ddd, *J* = 8.8 Hz, 6.4 Hz, 1.6 Hz, 1H), 2.42 (ddd, *J* = 14.8 Hz, 9.2 Hz, 3.6 Hz, 1H), 1.42 (ddd, *J* = 14.8 Hz, 12.0 Hz, 2.4 Hz, 1H), 1.24 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ 171.8, 81.9, 72.5, 71.5, 71.3, 67.5, 61.4, 45.4, 36.8, 20.1 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{10}H_{17}O_6$ $[M + H]^+$ 233.1020, found 233.1019.

(2*R*,3*R*,4*R*,4a*R*,7*R*,8a*S*)-Hexahydro-3,4-bis[(trimethylsilyl)oxy]-7-methyl-2-[(trimethylsilyl)oxy]methylpyrano[4,3-*b*]pyran-5(7*H*)-one (25). Trimethylsilyl chloride (164 μL, 1.29 mmol) was added to a solution of **24** (50 mg, 215 μmol) in pyridine (3 mL). The mixture was stirred at rt for 2 h and then diluted with ether. The organic layers were washed with water, dried over Na_2SO_4, filtered, and concentrated in vacuum. The pyridine was coevaporated with toluene to give the expected persilylated lactone **25** (95.5 mg, quant) as a colorless syrup, which was directly used without further purification: R_f = 0.4 (PE−EtOAc, 5:1); $[\alpha]_D^{25}$ = +15.0 (*c* = 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (m, 1H), 4.10 (dt, *J* = 8.0 Hz, 4.4 Hz, 1H), 3.93 (t, *J* = 6.8 Hz, 1H), 3.86 (s, 1H), 3.77 (d, *J* = 11.2 Hz, 1H), 3.59 (dd, *J* = 11.2 Hz, 6.8 Hz, 1H), 3.20 (t, *J* = 6.4 Hz, 1H), 2.86 (s, 1H), 2.32 (m, 1H), 1.75 (ddd, *J* = 15.6 Hz, 11.2 Hz, 4.4 Hz, 1H), 1.37 (d, *J* = 6.4 Hz, 3H), 0.16 (s, 9H), 0.14 (s, 9H), 0.10 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 82.3, 74.3, 71.8, 71.3, 68.9, 63.3, 45.8, 37.4, 20.7, 0.7, 0.5, −0.2 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{19}H_{41}O_6Si_3$ $[M + H]^+$ 449.2206, found 449.2218.

(2*R*,3*S*,4*R*,4a*S*,7*R*,8a*S*)-Hexahydro-3,4-bis[(trimethylsilyl)oxy]-7-methyl-2-[(1*E*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (27). Alkene **27** is a synthetic intermediate of **1**, and the synthesis of compound **1** was followed; purification with flash column chromatography (PE−EtOAc, 5:1) afforded compound **27** as a colorless syrup (decomposition of a part on silica gel): R_f = 0.3 (PE−EtOAc, 4:1); $[\alpha]_D^{25}$ = +13.3 (*c* = 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (dq, *J* = 15.2 Hz, 6.4 Hz, 1H), 5.40 (ddq, *J* = 15.2 Hz, 7.6 Hz, 1.6 Hz, 1H), 4.29 (m, 1H), 4.12 (dt, *J* = 8.4 Hz, 4.0 Hz, 1H), 3.92 (t, *J* = 8.0 Hz, 1H), 3.79 (br s, 1H), 3.52 (t, *J* = 8.0 Hz, 1H), 2.84 (t, *J* = 3.6 Hz, 1H), 2.35 (ddd, *J* = 3.2 Hz, 8.8 Hz, 14.8 Hz, 1H), 1.75−1.70 (m, 4H), 1.37 (d, *J* = 6.0 Hz, 3H), 0.15 (s, 9H), 0.12 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.6, 129.4, 82.7, 74.2, 71.9, 71.6, 37.7, 20.7, 18.0, 1.0, 0.6 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{18}H_{35}O_5Si_2$ $[M + H]^+$ 387.2018, found 387.2015.

(2*R*,3*S*,4*R*,4a*R*,7*R*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-(hydroxymethyl)pyrano[4,3-*b*]pyran-5(7*H*)-one (28). To a solution of **19** (200 mg, 488 μmol) in THF (10 mL) was added $Pd(OH)_2$/C (400 mg), and the mixture was stirred under H_2 atmosphere (1.0 atm) at rt for 30 min. The solution was filtered through Celite and concentrated to afford lactone **28** (105 mg, 93%) as a colorless syrup without further purification: R_f = 0.3 ($CHCl_3$−acetone, 1:5); $[\alpha]_D^{25}$ = +60.0 (*c* = 1.0, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 4.58 (m, 1H), 4.47 (s, 1H), 4.31 (m, 1H), 3.86−3.77 (m, 3H), 3.66 (m, 1H), 3.56 (dt, *J* = 1.2 Hz, 6.2 Hz, 1H), 3.42−3.32 (m, 2H), 2.30 (dt, *J* = 12.8 Hz, 3.6 Hz, 1H), 2.23 (t, *J* = 10.6 Hz, 1H), 1.78 (q, *J* = 11.9 Hz, 1H), 1.38 (d, *J* = 6.3 Hz, 3H) ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ 173.5, 81.6, 76.0, 73.9, 72.6, 72.0, 63.1, 51.3, 37.6, 22.0 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{10}H_{17}O_6$ $[M + H]^+$ 233.1020, found 233.1018; $C_{10}H_{16}NaO_6$ $[M + Na]^+$ 255.0839, found 255.0837.

(2*R*,3*R*,4*R*,4a*S*,7*R*,8a*S*)-Hexahydro-3,4-bis[(trimethylsilyl)oxy]-7-methyl-2-[(trimethylsilyl)oxy]methylpyrano[4,3-*b*]pyran-5(7*H*)-one (29). Following the procedure described for the synthesis of **25** from **24**, compound **29** was prepared from **28** (150 mg, 646 μmol). The reaction gave persilylated lactone **29** (289 mg, quant) as a colorless syrup: R_f = 0.5 (PE−EtOAc, 5:1); $[\alpha]_D^{25}$ = +37.1 (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.43 (m, 1H), 3.92 (dd, *J* = 9.2 Hz, 7.6 Hz, 1H), 3.78 (dd, *J* = 11.6 Hz, 2.0 Hz, 1H), 3.73 (dd, *J* = 11.6 Hz, 4.4 Hz, 1H), 3.61 (dd, *J* = 9.2 Hz, 7.6 Hz, 1H), 3.57 (dt, *J* = 3.6 Hz, 11.2 Hz, 1H), 3.18 (ddd, *J* = 9.2 Hz, 4.0 Hz, 2.0 Hz, 1H), 2.35 (dt, *J* = 12.8 Hz, 4.4 Hz, 1H), 2.28 (dd, *J* = 11.6 Hz, 9.6 Hz, 1H), 1.73 (q, *J* = 11.2 Hz, 1H), 1.42 (d, *J* = 6.0 Hz, 3H), 0.19 (s, 18H), 0.11 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 80.8, 74.2, 73.8, 73.4, 71.9, 62.5, 53.5, 38.3, 22.7, 1.6, 1.0, 0.0 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{19}H_{41}O_6Si_3$ $[M + H]^+$ 449.2206, found 449.2205.

(2*R*,3*S*,4*R*,4a*R*,7*R*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-[(1*E*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (30). To a solution of Celite (1.03 g, 4g per g(CrO_3)) and pyridine (416 μL, 5.14 mmol) in DCM (3 mL) was added chromium(VI) oxide (257 mg, 2.57 mmol), and the mixture was stirred at rt for 1 h. The mixture was cooled to 0 °C, and a solution of lactone **29** (115 mg, 257 μmol) in DCM (4 mL) was added. After being stirred for 2 h, the reaction mixture was filtered through a pad of silica and concentrated in vacuum to afford an unstable aldehyde, which used immediately without further purification.

A solution of chromium(II) chloride (189 mg, 1.54 mmol) in THF (1 mL) was stirred violently at rt for 1 h, followed by addition of aldehyde and 1,1-diiodoethane (52 μL, 514 μmol) in THF (3 mL) via cannula. The reaction mixture was stirred for 24 h before it was diluted with DCM and water. The organic layers were separated, and the aqueous layers were extracted with DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated.

The residue was dissolved in DCM (5 mL), and trifluoroacetic acid (100 μL, 2% v/v) was added dropwise at rt. After stirred 30 min, the reaction mixture was concentrated, which was purified by flash column chromatography ($CHCl_3$−acetone, 4:1) to afford **30** (42 mg, 67%, *E*/*Z* > 95:05) as a colorless syrup: R_f = 0.2 ($CHCl_3$−acetone, 4:1); $[\alpha]_D^{25}$ = +35.0 (*c* = 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (m, 1H), 5.54 (dd, *J* = 15.2 Hz, 7.2 Hz, 1H), 4.52 (m, 1H), 4.48 (br s, 1H), 3.89 (t, *J* = 9.2 Hz, 1H), 3.74 (t, *J* = 8.4 Hz, 1H), 3.65 (dt, *J* = 3.2 Hz, 11.2 Hz, 1H), 3.40 (t, *J* = 9.2 Hz, 1H), 2.65 (br s, 1H), 2.33 (dt, *J* = 13.2 Hz, 3.6 Hz, 1H), 2.28 (t, *J* = 10.4 Hz, 1H), 1.82−1.73 (m, 4H), 1.46 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 132.3, 127.8, 80.8, 75.8, 74.7, 72.8, 71.3, 50.5, 37.2, 22.1, 18.2 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{12}H_{19}O_5$ $[M + H]^+$ 243.1227, found 243.1228; $C_{12}H_{18}NaO_5$ $[M + Na]^+$ 265.1046, found 265.1046.

5,7,9-Tri-*O*-acetyl-6-*O*-benzyl-2-*O*-(*tert*-butyldiphenylsilyl)-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*talo*-nonitol (31). Following the procedure described for the synthesis of **11** from **9**, compound **31** was prepared from **10** (200 mg, 456 μmol). The reaction gave **31** (308 mg, quant) as an amorphous solid: R_f = 0.4 (PE−EtOAc, 3:1); mp 113−114 °C; $[\alpha]_D^{25}$ = −26.7 (*c* = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.21 (m, 15H), 5.01 (t, *J* = 10.0 Hz, 1H), 4.87 (t, *J* = 9.6 Hz, 1H), 4.58 (s, 2H), 4.09 (dd, *J* = 12.4 Hz, 6.0 Hz, 1H), 4.06 (m, 1H), 3.98 (dd, *J* = 12.4 Hz, 2.0 Hz, 1H), 3.62 (t, *J* = 9.2 Hz, 1H), 3.50−3.44 (m, 2H), 1.99 (s, 3H), 1.96 (s, 3H), 1.91 (s, 3H), 1.73 (ddd, *J* = 14.0 Hz, 8.8 Hz, 4.0 Hz, 1H), 1.58 (ddd, *J* = 14.0 Hz, 6.8 Hz,

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1.6 Hz, 1H), 1.07 (d, J = 6.4 Hz, 3H), 1.06 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 169.8, 169.6, 138.2, 136.0, 135.9, 134.7, 134.3, 129.7, 129.6, 128.6, 127.9, 127.8, 127.7, 127.6, 82.1, 75.9, 75.1, 74.1, 73.6, 70.4, 66.7, 63.1, 40.7, 27.2, 23.0, 21.0, 20.9, 20.8, 19.4 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{38}H_{48}NaO_9Si$ $[M + Na]^+$ 699.2960, found 699.2947.

6-*O*-Benzyl-2-*O*-(*tert*-butyldiphenylsilyl)-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*talo*-nonitol (S4). Following the procedure described for the synthesis of **S2** from **11**, compound **S4** was prepared from **31** (300 mg, 444 μmol). The reaction gave **S4** (239 mg, 98%) as a colorless syrup: R_f = 0.2 ($CHCl_3$–CH_3OH, 30:1); $[\alpha]_D^{25}$ = −36.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.70–7.23 (m, 15H), 4.88 (s, 2H), 4.23 (m, 1H), 3.74 (dd, J = 12.0 Hz, 2.0 Hz, 1H), 3.58 (dd, J = 12.0 Hz, 5.2 Hz, 1H), 3.40 (t, J = 9.2 Hz, 1H), 3.29 (t, J = 8.8 Hz, 1H), 3.22 (dt, J = 2.0 Hz, 9.2 Hz, 1H), 3.13 (t, J = 9.2 Hz, 1H), 3.11 (m, 1H), 2.02 (ddd, J = 13.6 Hz, 8.8 Hz, 2.0 Hz, 1H), 1.76 (ddd, J = 13.6 Hz, 9.2 Hz, 4.0 Hz, 1H), 1.11 (d, J = 6.0 Hz, 3H), 1.05 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 140.5, 137.0, 135.9, 135.6, 130.7, 129.2, 129.1, 128.6, 128.5, 128.4, 88.1, 81.5, 78.4, 76.1, 75.8, 71.8, 68.5, 63.0, 43.0, 27.5, 23.3, 20.0 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{32}H_{43}O_6Si$ $[M + H]^+$ 551.2823, found 511.2811; $C_{32}H_{42}NaO_6Si$ $[M + Na]^+$ 573.2643, found 573.2630.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-2-*O*-(*tert*-butyldiphenylsilyl)-4,8-anhydro-1,3-dideoxy-D-*erythro*-L-*talo*-nonitol (32). Following the procedure described for the synthesis of **12** from **S2**, compound **32** was prepared from **S4** (220 mg, 400 μmol). The reaction gave **32** (229 mg, 90%) as a colorless syrup: R_f = 0.2 (PE–EtOAc, 5:1); $[\alpha]_D^{25}$ = −9.4 (c = 2.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.21 (m. 20H), 5.54 (s, 1H), 4.99 (d, J = 11.6 Hz, 1H), 4.74 (d, J = 11.6 Hz, 1H), 4.21 (dd, J = 10.6 Hz, 5.2 Hz, 1H), 4.12 (m, 1H), 3.61 (dd, J = 10.6 Hz, 9.2 Hz, 1H), 3.58 (t, J = 9.6 Hz, 1H), 3.56 (t, J = 9.6 Hz, 1H), 3.39 (ddd, J = 9.6 Hz, 9.2 Hz, 3.6 Hz, 1H), 3.34 (t, J = 9.6 Hz, 1H), 3.32 (ddd, J = 9.6 Hz, 9.2 Hz, 5.2 Hz, 1H), 2.81 (d, J = 2.0 Hz, 1H), 1.97 (ddd, J = 14.0 Hz, 7.2 Hz, 3.6 Hz, 1H), 1.74 (ddd, J = 14.0 Hz, 9.2 Hz, 2.0 Hz, 1H), 1.11 (d, J = 6.4 Hz, 3H), 1.06 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 137.6, 136.0, 134.6, 134.3, 129.7, 129.6, 129.0, 128.6, 128.4, 128.1, 127.9, 127.7, 127.6, 126.1, 101.2, 82.5, 82.2, 77.5, 74.7, 74.6, 70.4, 69.1, 67.3, 42.4, 27.1, 23.1, 19.3 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{39}H_{46}NaO_6Si$ $[M + Na]^+$ 661.2956, found 661.2970.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-2-*O*-(*tert*-butyldiphenylsilyl)-5-cyano-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*manno*-nonitol (33). Following the procedure described for the synthesis of **13** from **12**, compound **33** was prepared from **32** (225 mg, 352 μmol). The reaction gave **33** (219 mg, 96%) as a colorless syrup: R_f = 0.4 (PE–EtOAc, 5:1); $[\alpha]_D^{25}$ = −49.2 (c = 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.30 (m, 20H), 5.60 (s, 1H), 4.78 (d, J = 12.4 Hz, 1H), 4.66 (d, J = 12.4 Hz, 1H), 4.25 (dd, J = 10.8 Hz, 5.2 Hz, 1H), 3.94 (m, 1H), 3.93 (t, J = 9.6 Hz, 1H), 3.76 (dd, J = 10.8 Hz, 9.2 Hz, 1H), 3.74 (dt, J = 7.2 Hz, 2.4 Hz, 1H), 3.59 (dd, J = 9.6 Hz, 5.2 Hz, 1H), 3.31 (ddd, J = 9.6 Hz, 9.2 Hz, 5.2 Hz, 1H), 2.90 (dd, J = 5.2 Hz, 2.4 Hz, 1H), 2.03 (ddd, J = 14.0 Hz, 7.2 Hz, 6.0 Hz, 1H), 1.79 (ddd, J = 14.0 Hz, 7.2 Hz, 4.0 Hz, 1H), 1.13 (d, J = 6.0 Hz, 3H), 1.02 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 137.3, 135.9, 135.8, 134.1, 133.7, 130.2, 130.0, 129.2, 128.6, 128.4, 180.0, 127.8, 127.7, 126.1, 116.7, 101.6, 80.6, 74.8, 73.5, 72.8, 71.8, 68.5, 66.3, 42.2, 39.7, 27.1, 23.9, 19.3 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{40}H_{46}NO_5Si$ $[M + H]^+$ 648.3140, found 648.3146.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-5-cyano-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*manno*-nonitol (34). Following the procedure described for the synthesis of **4** from **13**, compound **34** was prepared from **33** (210 mg, 324 μmol). The reaction gave **34** (133 mg, quant) as a colorless syrup: R_f = 0.3 (PE–EtOAc, 1:1); $[\alpha]_D^{25}$ = −43.3 (c = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.28 (m, 10H), 5.64 (s, 1H), 4.88 (d, J = 12.4 Hz, 1H), 4.76 (d, J = 12.4 Hz, 1H), 4.30 (dd, J = 4.8 Hz, 10.4 Hz, 1H), 4.02 (t, J = 9.2 Hz, 1H), 3.97 (m, 1H), 3.86–3.78 (m, 3H), 3.45 (dt, J = 4.8 Hz, 9.6 Hz, 1H), 3.23 (dd, J = 2.4 Hz, 5.6 Hz, 1H), 2.04 (dt, J = 15.0 Hz, 7.2 Hz, 1H), 1.75 (ddd, J = 3.2 Hz, 5.6 Hz, 15.0 Hz, 1H), 1.58 (br s, 1H), 1.24 (d, J = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 137.2, 129.2, 128.7, 128.4, 128.1, 127.7, 126.2, 116.7, 101.8, 80.5, 75.3, 74.5, 73.1, 72.0, 68.5, 65.9, 41.6, 40.2, 23.9 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{24}H_{28}NO_5$ $[M + H]^+$ 410.1962, found 410.1970.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-5-carbamoyl-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*manno*-nonitol (35). Following the procedure described for the synthesis of **20** from **4**, compound **35** was prepared from **34** (175 mg, 428 μmol). The reaction gave **35** (183 mg, quant) as an amorphous solid: R_f = 0.3 (PE–acetone, 1:1); mp 165–166 °C; $[\alpha]_D^{25}$ = −36.4 (c = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.25 (m, 10H), 6.07 (br s, 1H), 5.97 (br s, 1H), 5.64 (s, 1H), 4.83 (d, J = 12.8 Hz, 1H), 4.79 (d, J = 12.8 Hz, 1H), 4.36 (t, J = 9.6 Hz, 1H), 4.30 (dd, J = 4.8 Hz, 10.4 Hz, 1H), 3.99 (m, 1H), 3.90–3.81 (m, 3H), 3.46 (dt, J = 4.8 Hz, 10.0 Hz, 1H), 2.99 (dd, J = 2.4 Hz, 6.0 Hz, 1H), 2.63 (br s, 1H), 1.98 (dt, J = 14.4 Hz, 8.8 Hz, 1H), 1.68 (dt, J = 14.4 Hz, 4.0 Hz, 1H), 1.19 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 138.2, 137.5, 129.1, 128.5, 128.3, 127.8, 126.2, 101.6, 79.2, 77.5, 76.2, 72.6, 72.5, 68.7, 66.8, 51.4, 41.1, 23.6 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{24}H_{30}NO_6$ $[M + H]^+$ 428.2068, found 428.2075.

(2*R*,4a*R*,5a*S*,7*S*,9a*R*,10*R*,10a*S*)-10-(Benzyloxy)-7-methyl-2-phenylhexahydro-4*H*-pyrano[3′,4′:5,6]pyrano[3,2-*d*][1,3]-dioxin-9(4a*H*)-one (36). Following the procedure described for the synthesis of **16** from **20**, compound **36** was prepared from **35** (180 mg, 421 μmol). The reaction gave **36** (168 mg, 97%) as an amorphous solid: R_f = 0.2 (PE–EtOAc, 2:1); mp 187–188 °C; $[\alpha]_D^{25}$ = −3.1 (c = 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.25 (m, 10H), 5.61 (s, 1H), 4.88 (d, J = 12.8 Hz, 1H), 4.80 (d, J = 12.8 Hz, 1H), 4.75 (m, 1H), 4.25 (dd, J = 4.8 Hz, 10.4 Hz, 1H), 3.96 (m, 1H), 3.95 (t, J = 9.2 Hz, 1H), 3.80 (dd, J = 4.8 Hz, 10.0 Hz, 1H), 3.74 (t, J = 10.0 Hz, 1H), 3.47 (dt, J = 4.8 Hz, 10.0 Hz, 1H), 2.91 (dd, J = 2.4 Hz, 4.8 Hz, 1H), 2.15 (dt, J = 14.4 Hz, 3.6 Hz, 1H), 1.69 (m, 1H), 1.37 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 138.4, 137.5, 129.0, 128.5, 128.3, 127.9, 127.8, 126.2, 101.6, 79.4, 77.1, 73.4, 72.9, 72.7, 68.6, 45.8, 35.9, 21.8 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{24}H_{27}O_6$ $[M + H]^+$ 411.1802, found 411.1798; $C_{24}H_{26}NaO_6$ $[M + Na]^+$ 433.1622, found 433.1617.

(2*R*,3*S*,4*R*,4a*S*,7*S*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-(hydroxymethyl)pyrano[4,3-*b*]pyran-5(7*H*)-one (37). Following the procedure described for the synthesis of **24** from **16**, compound **37** was prepared from **36** (160 mg, 390 μmol). The reaction gave **37** (91 mg, quant) as an amorphous solid: R_f = 0.3 ($CHCl_3$–acetone, 1:5); mp 157–158 °C; $[\alpha]_D^{25}$ = −53.3 (c = 0.3, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 4.83 (m, 1H), 4.67 (d, J = 10.8 Hz, 1H), 4.17 (d, J = 3.2 Hz, 1H), 4.03 (m, 1H), 3.82 (ddd, J = 2.8 Hz, 6.0 Hz, 11.6 Hz, 1H), 3.66 (ddd, J = 5.2 Hz, 6.8 Hz, 12.0 Hz, 1H), 3.60 (ddd, J = 5.2 Hz, 9.2 Hz, 10.8 Hz, 1H), 3.55 (dd, J = 6.0 Hz, 6.8 Hz, 1H), 3.34 (dt, J = 3.2 Hz, 9.2 Hz, 1H), 3.27 (ddd, J = 2.4 Hz, 4.8 Hz, 9.2 Hz, 1H), 3.02 (dd, J = 2.4 Hz, 5.2 Hz, 1H), 2.18 (dt, J = 14.0 Hz, 3.6 Hz, 1H), 1.88 (ddd, J = 1.6 Hz, 11.6 Hz, 14.0 Hz, 1H), 1.34 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ 174.7, 81.9, 75.2, 74.3, 71.7, 70.5, 62.8, 45.9, 35.9, 21.6 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{10}H_{17}O_6$ $[M + H]^+$ 233.1020, found 233.1018.

(2*R*,3*R*,4*R*,4a*R*,7*S*,8a*S*)-Hexahydro-3,4-bis[(trimethylsilyl)-oxy]-7-methyl-2-[(trimethylsilyl)oxy]methylpyrano[4,3-*b*]-pyran-5(7*H*)-one (38). Following the procedure described for the synthesis of **25** from **24**, compound **38** was prepared from **37** (90 mg, 388 μmol). The reaction gave **38** (170 mg, 98%) as a colorless syrup: R_f = 0.5 (PE–EtOAc, 5:1); $[\alpha]_D^{25}$ = +3.3 (c = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.76 (m, 1H), 4.20 (t, J = 4.4 Hz, 1H), 4.06 (m, 1H), 3.71–3.66 (m, 2H), 3.59 (t, J = 10.0 Hz, 1H), 3.53 (dt, J = 2.4 Hz, 6.4 Hz, 1H), 3.05 (dd, J = 4.8 Hz, 6.8 Hz, 1H), 1.98 (dt, J = 14.4 Hz, 2.0 Hz, 1H), 1.65 (ddd, J = 3.6 Hz, 11.6 Hz, 14.8 Hz, 1H), 1.33 (d, J = 6.4 Hz, 3H), 0.13 (s, 9H), 0.12 (s, 18H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 82.4, 72.7, 71.8, 68.6, 67.5, 64.6, 43.2, 37.0, 21.2, 0.3, 0.2, −0.3 ppm; HRMS (ESI-FT-ICR) m/z calcd for $C_{19}H_{41}O_6Si_3$ $[M + H]^+$ 449.2206, found 449.2215.

(2*R*,3*S*,4*R*,4a*S*,7*S*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-[(1*E*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (39). Following the procedure described for the synthesis of **1** from **25**, compound **39** was prepared from **38** (160 mg, 357 μmol). The reaction gave **39** (62

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mg, 72%) and *Z*-isomer **S5** (5.4 mg, 6%). Data for **39** (an amorphous solid): R_f = 0.2 ($CHCl_3$–acetone, 4:1); mp 138–139 °C; $[\alpha]_D^{25}$ = −35.6 (*c* = 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (m, 1H), 5.52 (ddd, *J* = 15.2 Hz, 7.2 Hz, 1.6 Hz, 1H), 4.96 (d, *J* = 10.8 Hz, 1H), 4.89 (m, 1H), 3.97 (m, 1H), 3.69–3.63 (m, 2H), 3.30 (t, *J* = 9.2 Hz, 1H), 2.87 (dd, *J* = 5.6 Hz, 2.4 Hz, 1H), 2.72 (br s, 1H), 2.25 (dt, *J* = 14.4 Hz, 3.6 Hz, 1H), 1.76 (dt, *J* = 6.4 Hz, 1.2 Hz, 3H), 1.74 (ddd, *J* = 14.4 Hz, 12.0 Hz, 1.6 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 131.5, 127.8, 81.0, 74.3, 74.1, 73.1, 70.8, 45.0, 35.8, 21.5, 18.2 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{12}H_{18}NaO_5$ $[M + Na]^+$ 265.1046, found 265.1046.

(2*R*,3*S*,4*R*,4a*S*,7*S*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-[(1*Z*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (S5). Amorphous solid: R_f = 0.2 ($CHCl_3$–acetone, 4:1); mp 147–149 °C; $[\alpha]_D^{25}$ = −40.0 (*c* = 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (m, 1H), 5.40 (dt, *J* = 1.2 Hz, 9.4 Hz, 1H), 4.96 (d, *J* = 10.4 Hz, 1H), 4.89 (m, 1H), 4.08 (t, *J* = 9.2 Hz, 1H), 4.01 (m, 1H), 3.70 (dt, *J* = 5.2 Hz, 10.0 Hz, 1H), 3.33 (t, *J* = 9.2 Hz, 1H), 2.89 (dd, *J* = 5.2 Hz, 2.4 Hz, 1H), 2.60 (br s, 1H), 2.24 (dt, *J* = 14.4 Hz, 3.6 Hz, 1H), 1.77–1.71 (m, 4H), 1.40 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 131.3, 127.1, 75.8, 74.3, 74.1, 73.4, 71.0, 45.1, 35.8, 21.5, 14.1 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{12}H_{18}NaO_5$ $[M + Na]^+$ 265.1046, found 265.1044.

(*R*)-6-*O*-Benzyl-7,9-*O*-benzylidene-5-carboxy-4,8-anhydro-1,3,5-trideoxy-D-*erythro*-L-*talo*-nonitol (40). Following the procedure described for the synthesis of **18** from **4**, compound **40** was prepared from **34** (120 mg, 293 μmol). The reaction gave **40** (117 mg, 93%) as an amorphous solid: R_f = 0.3 ($CHCl_3$–CH_3OH, 10:1); mp 77–78 °C; $[\alpha]_D^{25}$ = −8.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.21 (m, 10H), 5.59 (s, 1H), 5.24 (br s, 1H), 4.90 (d, *J* = 11.2 Hz, 1H), 4.68 (d, *J* = 11.2 Hz, 1H), 4.31 (dd, *J* = 4.8 Hz, 10.2 Hz, 1H) 4.11–4.06 (m, 2H), 3.87 (dt, *J* = 2.6 Hz, 9.3 Hz, 1H), 3.76–3.68 (m, 2H), 3.53 (dt, *J* = 4.8 Hz, 9.6 Hz, 1H), 2.74 (t, *J* = 10.0 Hz, 1H), 1.80–1.67 (m, 2H), 1.17 (d, *J* = 6.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 138.1, 137.3, 129.2, 128.4, 128.1, 127.9, 126.1, 101.6, 82.7, 78.1, 74.9, 70.9, 68.7, 67.0, 55.1, 41.8, 29.8, 23.4 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{24}H_{29}O_7$ $[M + H]^+$ 429.1908, found 429.1918.

(2*R*,4a*R*,5a*S*,7*S*,9a*S*,10*R*,10a*S*)-10-Benzyloxy-7-methyl-2-phenylhexahydro-4*H*-pyrano[3′,4′:5,6]pyrano[3,2-*d*][1,3]-dioxin-9(4a*H*)-one (41). Following the procedure described for the synthesis of **19** from **18**, compound **41** was prepared from **40** (115 mg, 269 μmol). The reaction gave **41** (106 mg, 96%) as an amorphous solid: R_f = 0.4 (PE–EtOAc, 2:1); mp 116–117 °C; $[\alpha]_D^{25}$ = −87.3 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.25 (m, 10H), 5.61 (s, 1H), 4.98 (d, *J* = 10.0 Hz, 1H), 4.92 (d, *J* = 10.0 Hz, 1H), 4.64 (m, 1H), 4.32 (dd, *J* = 10.2 Hz, 4.5 Hz, 1H), 4.08 (t, *J* = 9.4 Hz, 1H), 3.79–3.71 (m, 3H), 3.49 (dt, *J* = 4.6 Hz, 9.4 Hz, 1H), 2.83 (t, *J* = 10.4 Hz, 1H), 2.18 (m, 1H), 1.97 (dt, *J* = 14.6 Hz, 4.5 Hz, 1H), 1.39 (d, *J* = 6.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 138.5, 137.4, 129.1, 128.7, 128.4, 127.9, 126.1, 101.6, 83.8, 76.1, 75.9, 73.1, 72.0, 71.5, 68.7, 49.0, 36.2, 20.6 ppm; HRMS (ESI-FT-ICR) *m*/*z* Calcd for $C_{24}H_{27}O_6$ $[M + H]^+$ 411.1802, found 411.1799; $C_{24}H_{26}NaO_6$ $[M + Na]^+$ 433.1622, found 433.1620.

(2*R*,3*S*,4*R*,4a*R*,7*S*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-(hydroxymethyl)pyrano[4,3-*b*]pyran-5(7*H*)-one (42). Following the procedure described for the synthesis of **24** from **16**, compound **42** was prepared from **41** (105 mg, 256 μmol). The reaction gave **42** (59 mg, quant) as an amorphous solid: R_f = 0.3 ($CHCl_3$–acetone, 1:5); mp 125–126 °C; $[\alpha]_D^{25}$ = +26.7 (*c* = 0.6, acetone); ^{1}H NMR (400 MHz, Acetone-d_6) δ 4.80 (m, 1H), 4.32 (d, *J* = 4.0 Hz, 1H), 4.12 (d, *J* = 3.2 Hz, 1H), 3.86–3.78 (m, 2H), 3.74–3.64 (m, 2H), 3.61 (t, *J* = 6.0 Hz, 1H), 3.41 (dt, *J* = 4.0 Hz, 9.6 Hz, 1H), 3.32 (ddd, *J* = 2.4 Hz, 5.2 Hz, 9.6 Hz, 1H), 2.59 (t, *J* = 10.4 Hz, 1H), 2.12 (dt, *J* = 14.4 Hz, 9.6 Hz, 1H), 1.98 (dt, *J* = 14.4 Hz, 5.2 Hz, 1H), 1.33 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, acetone-d_6) δ 172.7, 82.0, 73.6, 73.1, 72.2, 71.8, 63.1, 49.5, 36.4, 20.9 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{10}H_{16}NaO_6$ $[M + Na]^+$ 255.0839, found 255.0840.

(2*R*,3*R*,4*R*,4a*S*,7*S*,8a*S*)-Hexahydro-3,4-bis[(trimethylsilyl)-oxy]-7-methyl-2-[(trimethylsilyl)oxy]methylpyrano[4,3-*b*]-pyran-5(7*H*)-one (43). Following the procedure described for the synthesis of **25** from **24**, compound **43** was prepared from **42** (55 mg, 237 μmol). The reaction gave **43** (103 mg, 97%) as a colorless syrup: R_f = 0.5 (PE–EtOAc, 5:1); $[\alpha]_D^{25}$ = +32.7 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.63 (m, 1H), 3.97 (dd, *J* = 8.2 Hz, 9.2 Hz, 1H), 3.78–3.72 (m, 2H), 3.63 (dd, *J* = 8.2 Hz, 9.4 Hz, 1H), 3.55 (ddd, *J* = 5.3 Hz, 9.8 Hz, 11.4 Hz, 1H), 3.15 (dt, *J* = 9.5 Hz, 3.2 Hz, 1H), 2.63 (dd, *J* = 9.5 Hz, 11.4 Hz, 1H), 2.16 (dt, *J* = 10.7 Hz, 14.6 Hz, 1H), 1.95 (dt, *J* = 5.2 Hz, 14.5 Hz, 1H), 1.37 (d, *J* = 6.2 Hz, 3H), 0.19 (s, 9H), 0.18 (s, 9H), 0.11 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 81.2, 73.8, 73.0, 72.0, 71.9, 62.3, 50.3, 36.8, 20.6, 1.4, 0.9, 0.0 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{19}H_{40}NaO_6Si_3$ $[M + Na]^+$ 471.2025, found 471.2030.

(2*R*,3*S*,4*R*,4a*R*,7*S*,8a*S*)-Hexahydro-3,4-dihydroxy-7-methyl-2-[(1*E*)-prop-1-enyl]pyrano[4,3-*b*]pyran-5(7*H*)-one (44). Following the procedure described for the synthesis of **30** from **29**, compound **44** was prepared from **43** (100 mg, 223 μmol). The reaction gave **44** (34 mg, 63%, *E*/*Z* > 95:05) as a colorless syrup: R_f = 0.2 ($CHCl_3$–acetone, 4:1); $[\alpha]_D^{25}$ = +40.0 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (m, 1H), 5.54 (dd, *J* = 15.2 Hz, 7.2 Hz, 1H), 4.67 (m, 1H), 3.94 (t, *J* = 9.6 Hz, 1H), 3.75–3.67 (m, 3H), 3.42 (t, *J* = 8.8 Hz, 1H), 2.55 (t, *J* = 10.4 Hz, 1H), 2.49 (br s, 1H), 2.16 (dt, *J* = 14.4 Hz, 9.6 Hz, 1H), 2.03 (dt, *J* = 14.4 Hz, 5.6 Hz, 1H), 1.78 (d, *J* = 6.4 Hz, 3H), 1.41 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 132.4, 127.8, 81.3, 74.2, 73.4, 72.8, 70.8, 48.8, 35.6, 20.9, 18.2 ppm; HRMS (ESI-FT-ICR) *m*/*z* calcd for $C_{12}H_{18}NaO_5$ $[M + Na]^+$ 265.1046, found 265.1047.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General procedures, results of the MPA esters of **9** and **10**, and characterization data (^{1}H and ^{13}C NMR spectra). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(49) The results of the MPA esters using ^1H NMR spectra are shown in the Supporting Information.