225.1, 135.0, 95.0; CIHRMS M + NH_4^+ (calculated for $C_{18}H_{26}O_2Si$) 320.2046, found 320.2046; $[\alpha]^{23}_D$ = +7° (c 0.25, CH_2Cl_2).

(2S,3R)-Methyl 2-Azido-3-(dimethylphenylsilyl)hex-4-enoate (3f). Enolization conditions/electrophile: from (S)-**2b**; 1.04 mg, 0.4 mmol, LDA (1.2 equiv), trisyl azide (1.0 equiv), -78 °C → rt, 10 h, 88 mg, (73%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.57-7.28 (m, 5 H), 5.40 (m, 2 H), 3.88 (d, 1 H, J = 5.6 Hz), 2.29 (dd, 1 H, J = 3.2, 9.2 Hz), 1.68 (d, 3 H, J = 5.4 Hz), 0.43 (s, 3 H), 0.33 (s, 3 H); ^{13}C NMR (60 MHz, $CDCl_3$) δ 170.74, 136.37, 134.00, 129.38, 127.84, 125.13, 63.59, 52.27, 36.26, 18.21, -16.45, -15.78; IR (neat) ν_{max} 3100-2800, 2140, 1760, 1450, 1270, 1130, 990, 860, 780, 720 cm^{-1}, CIMS (NH_3) 321.1, 261.0, 226.0, 152.0, 94.9; CIHRMS M^+ (calcd for $C_{15}H_{21}N_3O_2Si$) 303.4762, found 303.4562; $[\alpha]^{23}_D$ = +7.1° (c 1.4, $CHCl_3$).

(2R,3S)-(E)-Methyl 2-(Cyclohexylmethyl)-3-(dimethylphenylsilyl)hex-4-enoate (3h). Enolization conditions/electrophile: from (R)-**2a**; 1.0 g, 3.80 mmol; LDA (1.3 equiv), THF/20% HMPA, cyclohexylmethyl bromide (2.0 equiv), -78 °C → rt, 10 h, 1.03 g, (76%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49-7.33 (m, 5 H), 5.22-5.14 (m, 2 H), 3.40 (s, 3 H), 2.56-2.52 (m, 1 H), 2.05-2.00 (dd, 1 H, J = 10.0, 9.1 Hz), 1.65 (d, 3 H), J = 5.6 Hz), 1.60-1.45 (m), 1.29-0.55 (m), 0.31 (s, 3 H), 0.25 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.16, 137.62, 134.22, 128.86, 128.44, 127.45, 125.52, 50.99, 50.92, 43.20, 38.97, 36.31, 35.99, 34.22, 32.19, 26.49, 26.27, 26.11, 18.05, -3.26, -4.32; IR (neat) ν_{max} 3060-2850, 1760, 1470, 1450, 1280, 1030, 840 cm^{-1}; CIMS (NH_3) 359.1, 358.1, 282.1, 281.1, 261.0, 152.0, 135.0; CIHRMS M + NH_4^+ (calcd for $C_{22}H_{34}O_2Si_1$) 376.2672, found 376.2679; $[\alpha]^{23}_D$ = +3.3° (c 0.7, CH_2Cl_2).

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Registry No. (R)-**2a**, 136174-52-2; (S)-**2b**, 136314-66-4; **3a**^{anti}, 136824-13-0; **3a**^{syn}, 136824-14-1; **3b**^{anti}, 136824-15-2; **3b**^{syn}, 136824-16-3; **3c**^{anti}, 136824-17-4; **3c**^{syn}, 136824-18-5; **3d**^{anti}, 134451-72-2; **3d**^{syn}, 136235-01-3; **3e**^{anti}, 136824-19-6; **3e**^{syn}, 136824-20-9; **3f**^{anti}, 136824-21-0; **3f**^{syn}, 136824-22-1; **3g**^{anti}, 136824-23-2; **3g**^{syn}, 136824-24-3; **3h**^{anti}, 136824-25-4; **3h**^{syn}, 136824-26-5; allyl bromide, 106-95-6; trisyl azide, 36982-84-0; cyclohexylmethyl bromide, 2550-36-9; 2-bromopropane, 75-26-3.

Supplementary Material Available: Spectral data for all reaction products **3a-h** in the form of ^1H NMR and ^{13}C NMR spectra (16 pages). Ordering information is given on any current masthead page.

Syntheses of Destomic Acid and Anhydrogalantinic Acid from L-Serinal

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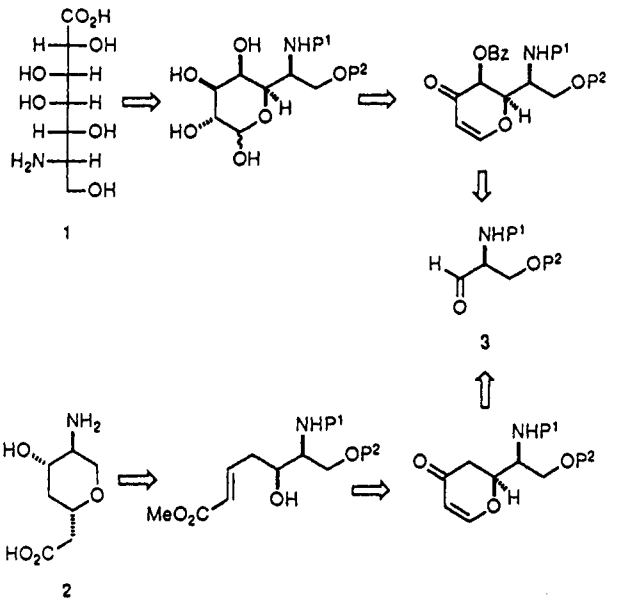
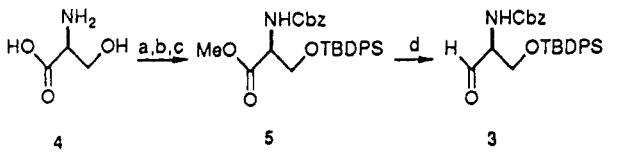
A few years ago we began a program to examine applications of α-amino aldehydes in total syntheses of natural products.[1,2] We found such aldehydes to be very convenient and versatile heterodienophiles under high-pressure[1-5] and/or Lewis acid catalysis[6-9] conditions. [4 + 2] Cycloadditions of 1,3-dienes to N-protected α-amino aldehydes offered an easy access to respective optically active cycloadducts which were readily transformed into several natural products.[10]

Scheme I



Scheme II[a]



[a] (a) MeOH, $SOCl_2$; (b) CbzCl, $NaHCO_3$; (c) TBDPSCl, Imd, DMF; (d) DIBAL, -78 °C, Et_2O.

Now we present in detail the formal syntheses of two natural products: destomic acid[11] and anhydrogalantinic acid,[12] both based on methodology involving [4 + 2] cycloadditions of Danishefsky's type dienes to *N*-protected α-amino aldehydes.[6-9]

Destomic acid (6-amino-6-deoxy-L-*glycero*-D-*galacto*-heptonic acid) (1) is a component of the aminocyclitol antibiotics: destomycin A,[13,14] B,[14,15] C,[16] hygromycin B,[17]

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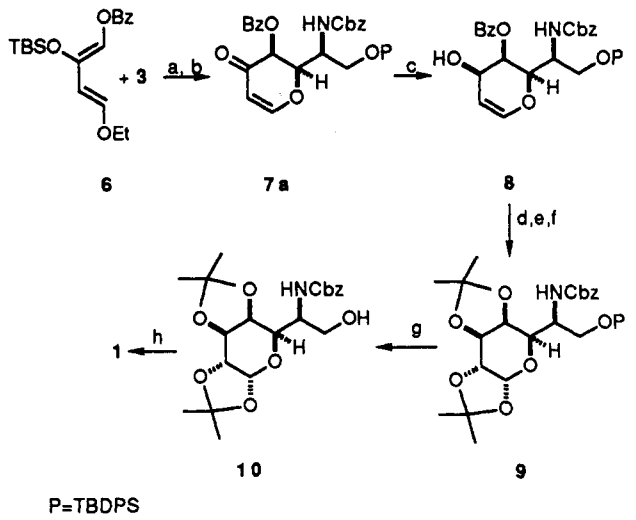
Scheme III[a]



[a] (a) $ZnBr_2$, THF; (b) TFA, CH_2Cl_2; (c) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH; (d) OsO_4, NMO, THF–H_2O; (e) K_2CO_3, MeOH; (f) DMP, *p*-TsOH, Me_2CO; (g) *n*-Bu_4NF, THF; (h) ref 21.

SS-56C,[18] and A-396-I (SS-56D).[19] These antibiotics demonstrate anthelmintic activity and contain a unique structural moiety, namely, that is linked through an orthoester (glycosylidene) linkage to the hexose moiety. The structure of **1** was confirmed by chemical synthesis, starting from D-galactose[20,21] and by X-ray analysis.[22]

(+)-Galantinic acid is a component of galantin I, an antibiotic isolated from a culture broth of *Bacillus pulvifaciens* by Shoji et al.[23] The recent report by Sakai and Ohfune proved that the originally isolated compound **2** (anhydrogalantinic acid) was a product of dehydration of galantinic acid.[24] Transformation of D-methionine into anhydrogalantinic acid (**2**) was reported by Ohfune and Kurokawa.[25] Another approach to the synthesis of anhydrogalantinic acid (**2**) was recently presented by Kano and co-workers.[26]

Results

Retrosynthetic analysis of both natural products reveals a unique opportunity of using L-serine-derived aldehyde **3** as a direct precursor of the side-chain part of each molecule (Scheme I). Obviously high diastereoselectivity of the cycloaddition step is required to make this synthetic plan efficient. Since it has been shown[4-6] that the diastereoselectivity of the [4 + 2] cycloaddition in which α-amino aldehydes are involved highly depends on the type of the N-protection group, we chose for our synthesis the *N*-Cbz blocking group, which strongly promotes the required α-chelation-controlled products. The β-hydroxy function was protected as the *tert*-butyldiphenylsilyl ether to decrease β-chelating interactions.

The key compound N,O-protected L-serinal (**3**), was prepared via DIBAL reduction[27] of N,O-protected L-serine methyl ester (**5**) (Scheme II).

Chelation controlled, [4 + 2] cycloaddition of diene **6** to aldehyde **3** gave pyrone **7a** as a major product, which can be easily separated from the mixture of other pyrones (**7b–d**, not shown) by "flash" chromatography. The diastereoisomeric proportion was **7a**:**7b**:**7c**:**7d** = 87:8:4:1 (for a stereochemical model discussion see ref 5). Functionalization of the pyran ring to the *galacto* configuration[28] was achieved via cerium-mediated reduction[29] follwed by cis-hydroxylation (Scheme III). The resultant triol was debenzoylated to afford a tetrol which, after protection, gave diacetonide **9**. Desilylation led to alcohol **10**—the direct precursor of destomic acid in Hashimoto's synthesis.[22]

[4 + 2] Cycloaddition of diene **11** to the same aldehyde **3** afforded pyrone **12** as a single product. Luche-type reduction,[29] followed by acetylation and dihydropyran ring opening reaction[30] gave after Corey-type oxidation[31] an ester **15**, which can be transformed in a manner similar to that previously described[25] into anhydrogalantinic acid (**2**) (Scheme IV).

Experimental Section

^1H NMR spectra were recorded at 500 MHz with a Bruker AM 500 spectrometer in $CDCl_3$ as solvent. ^{13}C NMR spectra were measured at 125 MHz with a Bruker AM 500 spectrometer. Infrared spectra were recorded on a Beckman IR-4240 spectrometer. Optical rotations were determined with a Perkin-Elmer 141 polarimeter.

Column chromatography was carried out with Merck Kieselgel 60 (230–400 mesh). All chromatographic separations were monitored by TLC analyses, performed on Merck DC Alufolien Kieselgel 60F-254. Yields are reported for chromatographically pure compounds.

Dienes **6**[32] and **11**[33] and *N*-(benzyloxycarbonyl)-L-serine methyl ester[34] were prepared according to literature procedures.

***N*-(Benzyloxycarbonyl)-*O*-(*tert*-butyldiphenylsilyl)-L-serine Methyl Ester (5).** To a solution of *N*-(benzyloxycarbonyl)-L-serine methyl ester (2.53 g, 10 mmol) and imidazole (1.36 g, 20 mmol) in anhydrous DMF (20 mL) was added *tert*-butyldiphenylsilyl chloride (2.88 g, 10.5 mmol) dropwise (under argon atmosphere). The reaction mixture was stirred overnight, diluted with diethyl ether (300 mL), washed with water (4 × 200 mL) and brine (100 mL), dried ($MgSO_4$), filtered, and evaporated. The oily residue was chromatographed (hexane–ethyl acetate, 85:15), affording 4.41 g (90% yield) of ester **9**: oil; $[\alpha]^{17}_D$ +5.0° (*c* 1.5, $CHCl_3$); ^1H NMR 7.65–7.52 (m, 5 H), 7.50–7.25 (m, 10 H), 5.68 (bd, *J* = 8.6 Hz, 1 H), 5.12 (s, 2 H), 4.46 (dt, *J* = 8.7, 3.0 Hz, 1 H), 4.10 (dd, *J* = 10.4, 3.0 Hz, 1 H), 3.90 (dd, *J* = 10.3, 3.0 Hz, 1 H), 3.74 (s, 3 H), 1.02 (s, 9 H); ^{13}C NMR 171.09, 156.06, 136.45, 135.61, 132.94, 132.84, 130.02, 128.64, 128.27, 128.19, 127.88, 66.92, 64.39, 55.84, 52.25, 26.51, 19.03; IR (film) 3450, 1740, 1720, 1510, 1260, 1210, 1100, 1070. Anal. Calcd for $C_{28}H_{33}NO_5Si$: C, 68.40; H, 6.76; N, 2.85. Found: C, 68.31; H, 6.67; N, 2.90.

***N*-(Benzyloxycarbonyl)-*O*-(*tert*-butyldiphenylsilyl)-L-serinal (3).** Ester **5** (3.92 g, 8 mmol) was dissolved in dry diethyl ether (25 mL). The reaction mixture was cooled to −78 °C under

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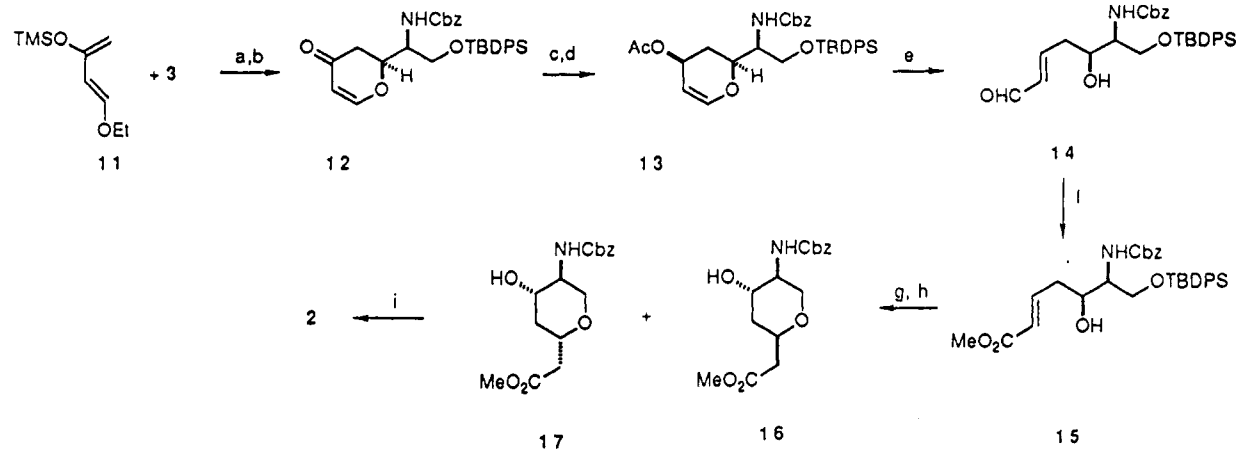
Scheme IV[a]



[a] (a) $ZnBr_2$, THF; (b) TFA, CH_2Cl_2; (c) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH; (d) Ac_2O, Et_3N, CH_2Cl_2; (e) $HgSO_4$, 5 mM H_2SO_4 (aq)–dioxane; (f) NaCN, AcOH, MnO_2, MeOH; (g) *n*-Bu_4NF, THF; (h) K_2CO_3, MeOH; (i) lit. 25.

an argon atmosphere. A solution of diisobutylaluminum hydride (DIBAL) in toluene (1.5 M solution, 10.7 mL, 16 mmol) was added dropwise while maintaining the temperature below −70 °C. After 1 h, methanol (ca. 2 mL) was added dropwise, followed by diethyl ether (150 mL) and saturated aqueous solution of sodium–potassium tartrate (400 mL). Vigorous stirring was continued for ca. 2 h, until all white solids had dissolved. The organic layer was separated, dried ($MgSO_4$), and evaporated. The oily residue was purified by flash chromatography (hexane–ethyl acetate, 85:15) to give 2.58 g of aldehyde **8a** (70% yield): ^1H NMR 9.65 (s, 1 H), 7.70–7.55 (m, 5 H), 7.50–7.28 (m, 10 H), 5.66 (bd, J = 7.5 Hz, 1 H), 5.11 (s, 2 H), 4.37 (dt, J = 7.2, 3.5 Hz, 1 H), 4.21 (dd, J = 10.8, 3.2 Hz, 1 H), 3.92 (dd, 10.8, 3.9 Hz, 1 H), 1.02 (s, 9 H). Since NHCbz α-amino aldehydes are unstable[27] this product was used without any further purification.

[4 + 2] Cycloaddition of 3 with 6 and 11. General Procedure. A mixture of aldehyde **3** (1.99 g, 4.07 mmol), diene **6** (1.39 g, 4.0 mmol) or diene **11** (2 mL, ca. 8 mmol), and a catalytic amount of $ZnBr_2$ in 10 mL of anhydrous THF was stirred at room temperature overnight. The reaction mixture was diluted with diethyl ether (80 mL), washed with saturated aqueous sodium bicarbonate and brine, dried ($MgSO_4$), and evaporated. The resultant oil was then dissolved in 10 mL of methylene chloride and treated with 1.0 mL of trifluoroacetic acid for 5 min. The mixture was then partitioned in separatory funnel between diethyl ether (150 mL) and saturated aqueous $NaHCO_3$ (100 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated to yield a crude product.

2(*R*)-[1′(*S*)-((Benzyloxycarbonyl)amino)-2′-((*tert*-butyldiphenylsilyl)oxy)ethyl]-3(*S*)-(benzoyloxy)-2,3-dihydro-4*H*-pyran-4-one (7a). The main diastereoisomer was separated by column chromatography (hexane to ethyl acetate, 7:3 to 6:4) and crystallized from hexane–diethyl ether to give **7a** as white crystals (1.82 g, 70% yield): mp 114–116 °C; $[\alpha]^{26}_D$ −14.1° (*c* 0.9, $CHCl_3$); ^1H NMR 8.02–7.17 (m, 20 H), 5.67 (d, J = 2.4 Hz, 1 H), 5.58 (dd, J = 6.1, 1.1 Hz, 1 H), 5.02 (d, J = 9.4 Hz, 1 H), 4.94 (d, J = 12.2 Hz, 2 H), 4.82 (dd, J = 10.5, 4.2 Hz, 1 H), 4.63 (d, J = 12.2 Hz, 1 H), 4.33 (m, 1 H), 3.86 (dd, J = 10.5, 4.2 Hz, 1 H), 3.73 (dd, J = 10.6, 6.2 Hz, 1 H), 1.06 (s, 9 H); ^{13}C NMR 185.5, 183.6, 164.7, 162.9, 155.5, 136.0, 135.5, 133.6, 132.7, 132.4, 130.1, 128.8, 128.4, 128.1, 128.0, 127.9, 106.2, 78.8, 69.6, 66.9, 62.4, 52.3, 26.9, 19.2; IR ($CHCl_3$) 1730, 1725, 1700, 1505, 1340, 1340, 1200. Anal. Calcd for $C_{38}H_{39}NO_7Si$: C, 70.24; H, 6.05; N, 2.16. Found: C, 70.14; H, 6.15; N, 2.15.

Cerium-Mediated Reductions (7a to 8 and 12 to Pre-13). General Procedure. To a solution of pyrone (1 mmol) and cerium(III) chloride heptahydrate (559 mg, 1.5 mmol) in methanol (10 mL) at −78 °C, under argon, was added sodium borohydride (57 mg, 1.5 mmol) in absolute ethanol (2 mL). After stirring at −78 °C for 1 h, the reaction mixture was allowed to warm to 0 °C, whereupon it was diluted with diethyl ether (40 mL) and quenched with a pH 7 buffer (20 mL). The reaction mixture was transferred to a separatory funnel, and the water layer was extracted with ether (3 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to afford a product.

2(*R*)-[1′(*S*)-((Benzyloxycarbonyl)amino)-2′-((*tert*-butyldiphenylsilyl)oxy)ethyl]-3(*S*)-(benzoyloxy)-4(*R*)-hydroxy-2,3-dihydro-4*H*-pyran (8): 631 mg (97% yield); an oil; $[\alpha]^{20}_D$ +0.5° (*c* 1, $CHCl_3$); ^1H NMR 8.02–7.15 (m, 20 H), 6.46 (d, J = 5.1 Hz, 1 H), 5.56 (d, J = 3.7 Hz, 1 H), 5.03 (d, J = 9.0 Hz, 1 H), 4.87 (d, J = 12.1 Hz, 1 H), 4.76 (dt, J = 6.3, 1.8 Hz, 1 H), 4.63 (bs, 1 H), 4.45 (d, J = 12.2 Hz, 1 H), 4.39 (d, J = 4.3 Hz, 1 H), 4.12 (m, 1 H), 3.82–3.68 (m, 3 H), 1.05 (s, 9 H); ^{13}C NMR 162.4, 155.8, 143.7, 135.6, 132.8, 129.9, 128.4, 128.2, 127.9, 123.8, 104.2, 73.4, 67.4, 66.6, 64.5, 62.9, 53.7, 26.9, 19.4; IR (film) 1730, 1725, 1605, 1510, 1340, 1200. Anal. Calcd for $C_{38}H_{41}NO_7Si$: C, 70.10; H, 6.35; N, 2.15. Found: C, 69.93; H, 6.42; N, 2.13.

1,2:3,4-Di-*O*-isopropylidene-6-(*N*-(benzyloxycarbonyl)-amino)-6-deoxy-7-*O*-(*tert*-butyldiphenylsilyl)-L-*glycero*-α-D-*galacto*-heptopyranose (9). Alcohol **8** (148 mg, 0.227 mmol) and 4-methylmorpholine *N*-oxide monohydrate (62 mg, 0.45 mmol) in 2 mL of THF were treated at room temperature with OsO_4 (0.025 mmol, 0.5 mL of 0.05M solution in *t*-BuOH) for 10 h. Saturated $NaHSO_3$ (ca. 2 mL) was added, and after 2 h of stirring, the reaction mixture was diluted with diethyl ether, washed with water and brine, and dried ($MgSO_4$), yielding 147 mg (94% yield) of a colorless oil. This product was dissolved in 5 mL of methanol and potassium carbonate (31 mg, 0.23 mmol) was added. After 2 h of stirring, the reaction mixture was evaporated. The residue was redissolved in ethyl acetate (20 mL), passed through Celite, and evaporated to yield a pale yellow oil. The crude material was dissolved in a mixture of acetone (2 mL) and 2,2-dimethoxypropane (2 mL), and a catalytic amount of *p*-toluenesulfonic acid was added. After 10 h of stirring the solvents were evaporated and the main product was separated by column chromatography (hexane–ethyl acetate, 8:2 to 7:3), yielding **9** as a colorless oil (110 mg, 72% yield): $[\alpha]^{26}_D$ −16.0° (*c* 0.4, $CHCl_3$); ^1H NMR 7.66–7.26 (m, 15 H), 5.55 (d, J = 5.1 Hz, 1 H), 5.13–5.05 (m, 1 H), 5.10 (s, 2 H), 4.54 (dd, J = 7.7, 2.4 Hz, 1 H), 4.31 (dd, J = 5.1, 2.4 Hz, 1 H), 4.07–4.00 (m, 1 H), 4.06 (d, J = 8.5 Hz, 2 H), 3.94 (d, J = 10.9 Hz, 1 H), 3.82 (d, J = 10.5 Hz, 1 H), 1.50 (s, 3 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.24 (s, 3 H), 1.06 (s, 9 H); ^{13}C NMR 156.2, 136.7, 135.6, 129.8, 128.4, 128.1, 127.7, 127.6, 109.3, 108.5, 96.5, 71.2, 70.9, 70.4, 66.6, 66.2, 63.1, 53.2, 26.9, 26.1, 25.9, 24.9, 24.3, 19.3; IR ($CHCl_3$) 1720, 1505, 1060. Anal. Calcd for $C_{37}H_{47}NO_8Si$: C, 67.14; H, 7.16; N, 2.12. Found: C, 66.98; H, 7.24; N, 1.98.

1,2:3,4-Di-*O*-isopropylidene-6-(*N*-(carbobenzyloxy)-amino)-6-deoxy-L-*glycero*-α-D-*galacto*-heptopyranose (10). Compound **9** (110 mg, 0.166 mmol) was dissolved in THF (1 mL) and treated with tetrabutylammonium fluoride (0.3 mmol, 0.3 mL of 1.0M solution in THF) for 15 min. The reaction mixture was then diluted with diethyl ether, washed with water and brine, dried with $MgSO_4$, and evaporated. The oily residue was purified by column chromatography (hexane–ethyl acetate, 7:3), affording alcohol **10** as an oil (60 mg, 86% yield): $[\alpha]^{24}_D$ −47.3° (*c* 0.2, $CHCl_3$)

[lit.[21] $[\alpha]^{25}_D$ -48.8° (c 2, $CHCl_3$)]; ^1H NMR 7.42-7.27 (m, 5 H), 5.52 (d, J = 4.9 Hz, 1 H), 5.50-5.40 (m, 1 H), 5.11 (s, 2 H), 4.63 (dd, J = 8.1, 2.3 Hz, 1 H), 4.36 (dd, J = 8.1, 1.6 Hz, 1 H), 4.31 (dd, J = 4.9, 2.3 Hz, 1 H), 4.11 (bd, J = 6.0 Hz, 1 H), 3.90-3.70 (m, 3 H), 1.58 (s, 3 H), 1.51 (s, 3 H), 1.43 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR 156.8, 136.8, 128.9, 128.5, 109.9, 109.3, 96.9, 71.4, 71.2, 67.1, 66.0, 61.7, 54.0, 26.0, 25.1, 24.3; IR ($CHCl_3$) 1730, 1515, 1060. Anal. Calcd for $C_{21}H_{29}NO_8$: C, 59.56; H, 6.90; N, 3.31. Found: C, 59.48; H, 6.75; N, 3.28.

For additional comparison with literature data alcohol **10** was acetylated in standard way (Ac_2O, Et_3N, DMAP cat., CH_2Cl_2, rt, 1 h), to give 1,2:3,4-di-*O*-isopropylidene-6-*N*-((carbobenzyloxy)-amino)-6-deoxy-7-*O*-acetyl-L-*glycero*-α-D-*galacto*-heptopyranose as an oil: $[\alpha]^{25}_D$ -46.9° (c 0.5, $CHCl_3$) [lit.[21] $[\alpha]^{25}_D$ -47.8° (c 2.0, $CHCl_3$)]; ^1H NMR 7.36-7.29 (m, 5 H), 5.53 (d, J = 5.0 Hz, 1 H), 5.14 (d, J = 6.04 Hz, 1 H), 5.11 (s, 2 H), 4.59 (dd, J = 7.9, 2.4 Hz, 1 H), 4.31 (dd, J = 5.0, 2.4 Hz, 1 H), 4.28-4.15 (m, 3 H), 4.25 (dd, J = 7.9, 1.7 Hz, 1 H), 3.90 (d, J = 4.3 Hz, 1 H), 2.03 (s, 3 H), 1.49 (s, 3 H), 1.38 (s, 3 H), 1.32 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR 171.0, 156.8, 137.3, 128.9, 128.5, 128.4, 110.1, 109.1, 97.0, 72.2, 71.5, 67.0, 65.9, 63.7, 51.5, 26.1, 25.1, 24.5, 20.8. IR ($CHCl_3$): 1740, 1730, 1520, 1260, 1210, 1075. Anal. Calcd for $C_{23}H_{31}NO_9$: C, 59.35; H, 6.71; N, 3.01. Found: C, 59.53; H, 6.90; N, 3.04.

2(*S*)-[1′(*S*)-((Benzyloxycarbonyl)amino)-2′-((*tert*-butyldiphenylsilyl)oxy)ethyl]-2,3-dihydro-4*H*-pyran-4-one (12). The crude adduct (see general procedure) was purified by flash chromatography (hexane–ethyl acetate, 95:5) and then treated with trifluoroacetic acid, etc. The product was crystallized (hexane–ethyl ether), affording **12** as white crystals (1.89 g, 70% yield): mp 137-139 °C; $[\alpha]^{26}_D$ -14.9° (c 1.0, $CHCl_3$); ^1H NMR 7.65-7.30 (m, 15 H), 7.21 (d, J = 6.0 Hz, 1 H), 5.41 (dd, J = 6.0, 1.0 Hz, 1 H), 5.09 (bs, 2 H), 4.87 (d, J = 9.7 Hz, 1 H), 4.76 (bd, J = 14.9 Hz, 1 H), 4.03 (m, 1 H), 3.78 (m, 2 H), 2.74 (dd, J = 16.8, 15.2 Hz, 1 H), 2.38 (dd, J = 16.8, 2.3 Hz, 1 H), 1.05 (s, 9 H); ^{13}C NMR 162.2, 135.5, 132.7, 130.0, 129.9, 128.6, 128.6, 128.3, 128.2, 127.9, 127.8, 107.5, 67.2, 62.1, 54.2, 38.8, 26.8, 19.2; IR ($CHCl_3$) 1740, 1690, 1610, 1515. Anal. Calcd for $C_{31}H_{35}NO_5Si$: C, 70.29; H, 6.66; N, 2.64. Found: C, 70.37; H, 6.64; N, 2.87.

2(*S*)-[1′(*S*)-((Benzyloxycarbonyl)amino)-2′-((*tert*-butyldiphenylsilyl)oxy)ethyl]-4(*R*)-acetoxy-2,3-dihydro-4*H*-pyran (13). Reduction of pyrone **12** (654 mg, 1.24 mmol) was accomplished in a similar manner to **7a**, yielding 656 mg (100% yield) of the crude alcohol. This oily product was dissolved in methylene chloride (10 mL). Triethylamine (0.70 mL, 505 mg, 5 mmol) followed by acetic anhydride (204 mg, 188 μL, 2 mmol) and catalytic amount of DMAP were added. After 5 min solvents were removed in vacuo. Product was purified by column chromatography (hexane–ethyl acetate, 8:2), and crystallized from hexane–ethyl ether, yielding 602 mg (85% yield) of **13** as white crystals: mp 131-132 °C; $[\alpha]^{26}_D$ -14.4° (c 1.0, $CHCl_3$); ^1H NMR 7.75-7.20 (m, 15 H), 6.36 (d, J = 6.1 Hz, 1 H), 5.58-5.38 (m, 1 H), 5.21-5.00 (m, 2 H), 4.90 (d, J = 9.7 Hz, 1 H), 4.76 (d, J = 6.1 Hz, 1 H), 4.36 (bd, J = 12.1 Hz, 1 H), 4.05-3.90 (m, 1 H), 3.75-3.60 (m, 2 H), 2.25-2.15 (m, 1 H), 2.04 (s, 3 H), 2.00-1.80 (m, 1 H), 1.06 (s, 9 H); ^{13}C NMR 145.9, 135.5, 133.0, 129.8, 129.7, 128.4, 128.0, 127.7, 127.6, 101.8, 72.2, 66.9, 65.4, 62.4, 54.6, 30.3, 26.7, 21.1, 19.1; IR ($CHCl_3$) 1740, 1730, 1655, 1510, 1250-1200. Anal. Calcd for $C_{33}H_{39}NO_6Si$: C, 69.08; H, 6.85; N, 2.44. Found: C, 69.15; H, 6.83; N, 2.43.

7-((*tert*-Butyldiphenylsilyl)oxy)-6(*S*)-((benzyloxycarbonyl)amino)-5(*S*)-hydroxy-2-heptenal (14). Acetate **13** (571 mg, 1.0 mmol) was dissolved in dioxane (50 mL). Sulfuric acid (200 mL, 0.005 M aqueous H_2SO_4) and mercury(II) sulfate (592 mg, 2 mmol) were added, and the reaction mixture was virogously stirred for 48 h. Then sodium bicarbonate (252 mg, 3 mmol) was added, and after 10 min the product was extracted with diethyl ether (3 × 200 mL). Combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to give 475 mg (90% yield) of the crude unstable aldehyde **14**, which was immediately used in the next transformation: ^1H NMR 9.51 (d, J = 7.9 Hz, 1 H), 7.67-7.28 (m, 15 H), 6.88 (dt, J = 15.9, 6.8 Hz, 1 H), 6.16 (dd, J = 15.9, 7.9 Hz, 1 H), 5.14 (d, J = 9.4 Hz, 1 H), 5.09 (m, 2 H), 4.16 (bt, J = 5.6 Hz, 1 H), 3.89-3.80 (m, 2 H), 3.72-3.67 (m, 1 H), 3.12 (bs, 1 H), 2.58-2.42 (m, 2 H), 1.06 (s, 9 H).

7-((*tert*-Butyldiphenylsilyl)oxy)-6(*S*)-((benzyloxycarbonyl)amino)-5(*S*)-hydroxy-2-heptenoic Acid, Methyl Ester (15). Aldehyde **14** (475 mg, 0.9 mmol) was dissolved in methanol (100 mL), and sodium cyanide (220.5 mg, 4.5 mmol) was added. When the salt dissolved, acetic acid (120 mg, 114 μL, 2 mmol) and active manganese(IV) oxide (2.0 g, 23 mmol) were added. Oxidation was carried out for 2 days. Then the reaction mixture was filtered through Celite (solid washed with methanol) and evaporated. The oily residue was partitioned between water (50 mL) and ethyl ether (150 mL). The organic layer was washed with brine (50 mL), dried ($MgSO_4$), and evaporated. The main product was separated by column chromatography (hexane–ethyl acetate, 7:3), affording 280-393 mg (50-70% yield, depending on MnO_2 activity) of ester **15** as an oil: $[\alpha]_D^{25}$ +2.5° (c 1.0, $CHCl_3$); ^1H NMR 7.70-7.25 (m, 15 H), 6.97 (dt, J = 15.6, 7.2 Hz, 1 H), 5.89 (d, J = 15.7 Hz, 1 H), 5.40 (d, J = 9.1 Hz, 1 H), 5.09 (s, 2 H), 4.12 (bt, J = 5.9 Hz, 1 H), 3.87-3.79 (m, 2 H), 3.72 (s, 3 H), 3.72-3.65 (m, 1 H), 3.01 (bs, 1 H), 2.46-2.29 (m, 2 H), 1.05 (s, 9 H); ^{13}C NMR 170.3, 156.4, 144.8, 136.4, 135.5, 132.4, 130.2, 128.6, 128.2, 128.1, 128.0, 123.6, 71.4, 67.0, 66.4, 54.3, 51.5, 36.9, 26.9, 19.2; IR ($CHCl_3$) 1730, 1715, 1660, 1500, 1200. Anal. Calcd for $C_{32}H_{39}NO_6Si$: C, 68.42; H, 7.00; N, 2.49. Found: C, 68.32; H, 7.03; N, 2.44.

***N*-(Benzyloxycarbonyl)anhydrogalantinic Acid Methyl Ester (17) and C3 Epimer 16.** Ester **15** (143 mg, 0.255 mmol) was dissolved in 4 mL of THF, and then tetrabutylammonium fluoride (0.5 mL of 1.0 M solution in THF, 0.5 mmol) was added. After 15 min of stirring the solvent was evaporated and the residue was dissolved in 25 mL of methanol. Then anhydrous potassium carbonate (7 mg, 0.05 mmol) was added, and after 15 h of stirring, solvent was evaporated and two diastereoisomers were separated giving 31 mg of ester **17** and 30 mg of C3 epimer (75% total yield).

16: mp 123-124 °C; $[\alpha]^{20}_D$ +12.4° (c 2.5, $CHCl_3$); ^1H NMR 7.40-7.30 (m, 5 H), 5.43 (bd, J = 7.3 Hz, 1 H), 5.13-5.05 (m, 2 H), 4.21-4.15 (m, 1 H), 4.07 (bs, 1 H), 3.68 (s, 3 H), 3.67 (m, 1 H), 3.55 (bd, J = 6.7 Hz, 1 H), 2.58 (m, 1 H), 2.47 (dd, J = 15.2, 8.1 Hz, 1 H), 2.38 (dd, J = 15.5, 4.8 Hz, 1 H), 1.80-1.60 (m, 2 H); ^{13}C NMR 171.4, 156.0, 136.2, 128.6, 128.2, 69.1, 67.0, 66.2, 65.5, 51.9, 50.3, 40.9, 33.8; IR ($CHCl_3$) 1730, 1510, 1205, 1060. Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.43; H, 6.67; N, 4.23.

17: mp 126-127 °C; $[\alpha]^{22}_D$ +2.6° (c 1.1, $CHCl_3$); ^1H NMR 7.40-7.30 (m, 5 H), 5.11 (s, 2 H), 4.65 (bs, 1 H), 4.05 (dd, J = 11.3, 4.6 Hz, 1 H), 3.84-3.78 (m, 1 H), 3.69 (s, 3 H), 3.50-3.60 (m, 2 H), 3.11 (bt, J = 10.5 Hz, 1 H), 2.80 (bs, 1 H), 2.60 (dd, J = 15.6, 7.9 Hz, 1 H), 2.45 (dd, J = 15.5, 5.1 Hz, 1 H), 2.12 (ddd, J = 12.8, 4.4, 1.9 Hz, 1 H), 1.44 (dd, J = 23.8, 11.2 Hz, 2 H); ^{13}C NMR 171.3, 157.1, 136.0, 128.7, 128.4, 128.3, 72.9, 71.9, 68.4, 67.4, 54.6, 51.9, 40.4, 39.2; IR ($CHCl_3$) 1735, 1510, 1210, 1065. Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.51; H, 6.52; N, 4.39.

For correlation reason compound **17** was transformed into NH-BOC form: mp 108-109 °C; $[\alpha]^{26}_D$ -5.4° (c 0.8, $CHCl_3$) [lit.[25] mp 104.5-106 °C; $[\alpha]^{26}_D$ -4.4° (c 1.2, $CHCl_3$)].

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Mild Fluorofunctionalization of Side Chains in Alkyl-Substituted Aromatics by Cesium Fluoroxysulfate

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The side-chain functionalization of alkyl groups, observed in a variety of reactions involving alkyl-substituted aromatic derivatives, has remained so far an open problem from the synthetic as well as mechanistic point of view,[1-6]

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