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A formal synthesis of thymine polyoxin C

Kenn E. Harding[a] and Jack M. Southard[b,*]

[a]*Department of Chemistry, Texas A&M University, PO Box 30012, College Station, TX 77842-3012, USA*
[b]*Department of Chemistry and Environmental Sciences, The University of Texas at Brownsville, 80 Ft. Brown, Brownsville, TX 78520, USA*

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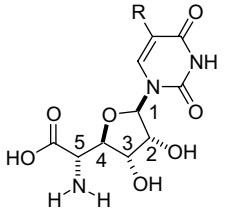
Abstract—A convergent stereoselective synthesis of thymine polyoxin C **1** has been conducted utilizing the benzylimine of D-glyceraldehyde acetonide **7** as a chiral controller and 2-trimethylsilyloxy furan **8** as a four-carbon synthon. In the presence of catalytic $BF_3{\cdot}OEt_2$, **8** has been found to add to **7** with a moderately high level of stereoselectivity. Intermediate 4-(aminoalkyl)-2-butenolide **6** proved to be an ideal candidate for elaboration to **3**.

1. Introduction

From culture broths, Isono and Suzuki[1] isolated a series of pyrimidinyl nucleoside peptide antibiotics that were produced by a streptomycete designated as *Streptomyces cacaoi* var. *asoensis*. This class of antibiotics has been found to be effective toward certain phytopathogenic fungi, which are responsible for sheath-blight disease in rice plants.[1] As agricultural fungicides, these antibiotics have seen widespread use since 1966,[1f] and exhibit no side-effects toward animals.

Polyoxin C **1**, as well as its pyrimidinyl analogues **2** and **3**, have received considerable attention from synthetic chemists.[2] Many of the reported syntheses make use of a carbohydrate-based strategy for the express purpose of building the furanose ring system and the pendant amino acid side chain at C4. Glycosylation of suitably protected glycosyl donor molecules at C1, and persilylated pyrimidine bases, was typically accomplished via the method of Vorbrüggen et al.[3]

Examination of compounds **1**–**3** reveals five contiguous stereogenic carbon atoms. Hence, a suitable framework, such as that found in key intermediate **6**, is essential for facilitating the generation of the *cis*-(2*S*,3*S*)-diol as well as establishment of an (*S*)-absolute configuration at C4. The retrosynthetic analysis of **23**, a formal precursor of **3**,[2m] is shown in Scheme 1. Disconnection between C1 and the nitrogen of the pyrimidine base furnishes the glycosyl acceptor **4**[4] and donor molecules **5α** and **5β**. Further disconnection between C4 and C5 furnishes chiral imine **7**, which can be prepared from D-glyceraldehyde acetonide plus benzylamine (vide infra), and commercially available **8** (2-trimethylsilyloxyfuran, 2-TMSOF). The aforementioned compound can be prepared from furfural[5] and has been used to synthesize numerous 4-substituted 2-buten-4-olides and their corresponding γ-butyrolactones.[6]



1: Polyoxin C, R = CH_2OH
2: Uracil Polyoxin C, R = H
3: Thymine Polyoxin C, R = CH_3

2. Results and discussion

2.1. Preliminary investigation

Condensation of aryl imines or benzyl imines with 2-TMSOF **8** can be promoted by Lewis acids such as BF_3. Our efforts and those of others[6g–x] firmly established the relative stereochemistry for the dominant diastereomer to be 4,5-*anti* for reactions involving achiral as well as chiral imines. For the case involving chiral imine **7**, four diastereomers could, in principle, be generated from this reaction (Scheme 2). The desired 4,5-*anti*:5,6-

* Corresponding author. Tel.: +1 956 574 6691; fax: +1 956 574 6692; e-mail: jmsouthard@utb.edu

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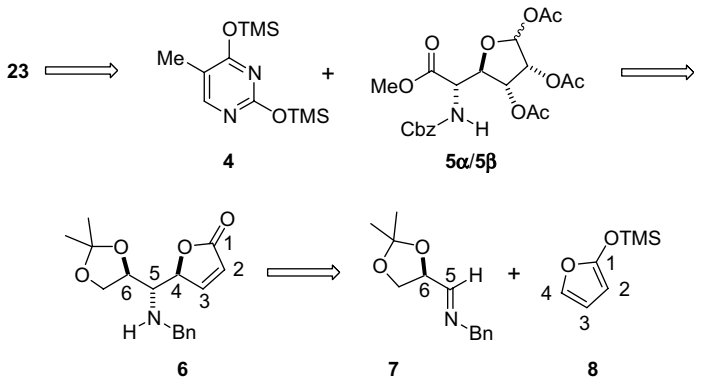
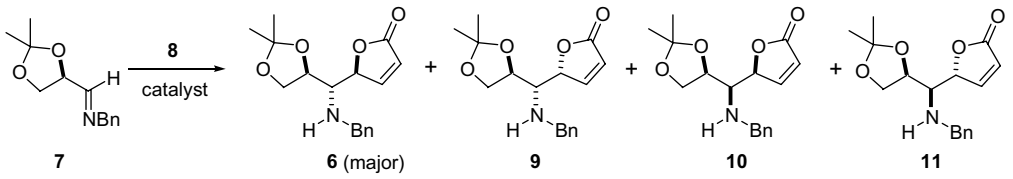


Scheme 1.



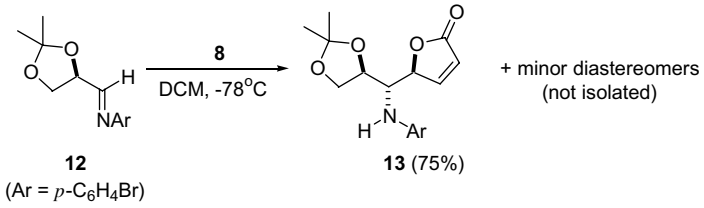
Scheme 2.

anti-diastereomer **6** was produced with moderate-to-high selectivity; minor diastereomers were readily separated using FLC. The choice of **7** as a chiral controller required model studies to prove it was viable for establishing the requisite absolute configuration at C5. One such model study conducted in our laboratory, involved the use of aryl imine **12** (Scheme 3). Product **13** was produced in 75% yield and gave crystals suitable for X-ray analysis.

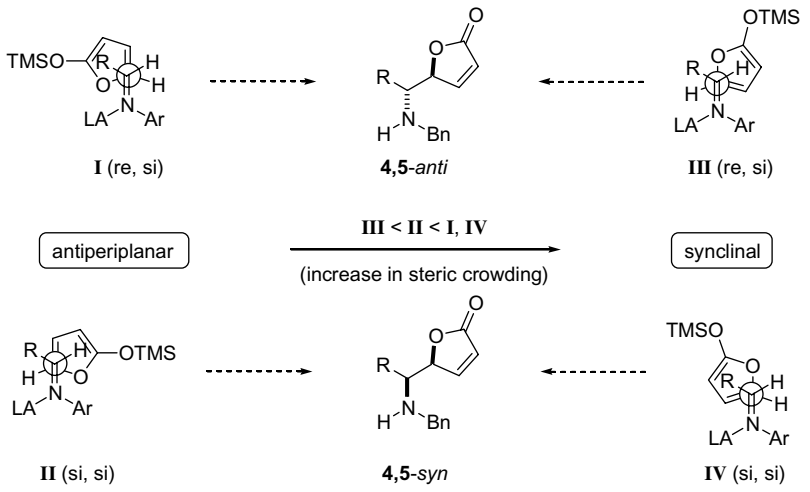
For the general cases, Scheme 4 shows a collection of open transition state structures involving **8** and the Lewis acid-coordinated imine **7**. Competition between these arrangements depends upon a variety of electronic and steric factors. The reactants should be inclined at an angle of ca. 110° consistent with the Bürgi–Dunitz trajectory.[7] Among these four transition states, **I** and **IV** possess a steric hindrance between the R group of the imine and the five-membered ring of **8**. This steric interaction is increased by the non-coplanarity of the two reactants. Examination of transition state structure **II** also reveals steric congestion between the bulky trimethylsilyl group and the aromatic ring. The transition state depicted by **III** was expected to possess the least amount of steric crowding since it does not have any of the interactions mentioned for the other three transition states. Reaction through transition state **III** would result in the formation of the desired 4,5-*anti*-adduct. Thus, steric effects alone provide a rationalization for the predominant formation of 4,5-*anti*-products. Electronic and dipolar factors are much harder to evaluate, and as a result we do not have enough information to include these factors in our evaluation of selectivity in these reactions. It is important to note that the analysis shown in Scheme 4 is contingent upon the configuration of the coordinated imine. In particular, it is essential that the Lewis acid and the R group of the coordinated complex be in a *syn* orientation as shown in each of these cases.

2.2. Synthesis of chiral butenolide

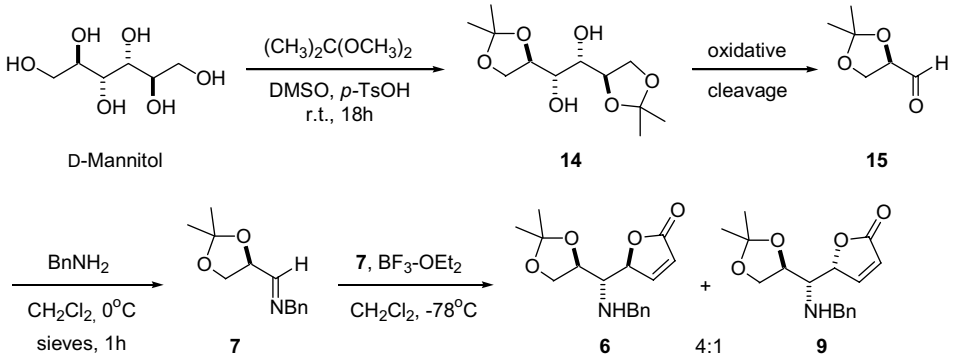
As shown in Scheme 5 our synthesis of **3** began by first generating the diacetonide of D-mannitol **14** using one of the well-documented literature approaches.[8] Oxidative cleavage of **14** by lead(IV) acetate[9] or sodium periodate[10] afforded D-glyceraldehyde acetonide **15**. Imine **7** was prepared by adding 1 equiv of freshly distilled **15** with 1 equiv of benzylamine in the presence of powdered 4 Å molecular sieves. This dichloromethane mixture was cooled to −78 °C whereupon 1.2 equiv of 2-TMSOF **8** was added. Reaction times varied (2–10 h) depending upon the bulk quantity of reactants; once TLC analysis showed reactant consumption, the reactions were



Scheme 3.



Scheme 4.

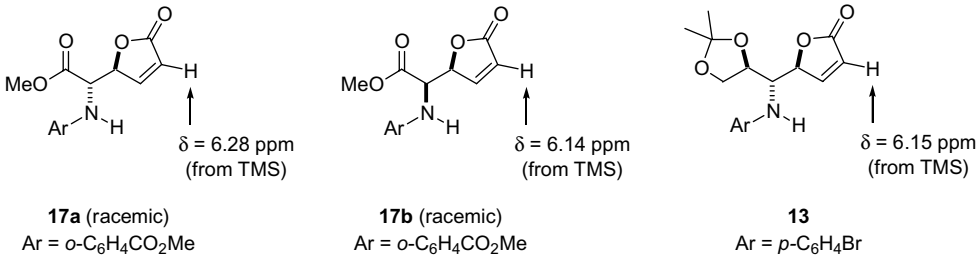


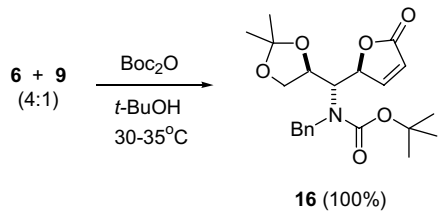
Scheme 5.

quenched using saturated $NaHCO_3$ solution. Product ratios were determined by ^1H NMR analysis of the crude product. The two other possible diastereomers **10** and **11** were not observed.

Although **6** was isolable, it was discovered quite fortuitously that **9** equilibrated under *N*-protection conditions (Scheme 6) to the presumably more stable 4,5-*anti*-diastereomer. Thus, a quantitative yield of **16** was obtained from a 4:1 ratio of **6** and **9**. This indicates that **6** either is more stable or reacts with Boc_2O more rapidly than with **9**. The equilibration would result from enolization of the butenolide either through an enolate or enol tautomer. Base-catalyzed C4 epimerization of this type has previously been reported by Corey and Veukatesawarlu.[11] Unfortunately, we were incapable of isolating **9**; structural assignment of this diastereomer is based exclusively upon the ^1H NMR spectrum of the crude material.

Relative structural assignments were based upon ^1H NMR spectra and supported by single crystal X-ray analysis of related species. The racemic diastereomeric butenolides **17a** and **17b** were isolated in pure form. The α-methine proton at C2 provides a doublet of doublets at $\delta = 6.28$ ($J = 5.8$, 2.0 Hz) for the 4,5-*anti*-diastereomer **17a**. Similarly, the α-methine proton at C2 provides a doublet of doublets at $\delta = 6.14$ ($J = 5.7$, 2.0 Hz) for the 4,5-*syn*-diastereomer **17b**. An approximate 0.14 ppm downfield shift for the H2 proton of the *anti*-isomer from the *syn*-isomer is consistent with several dozens of butenolides that have been prepared in our laboratory.[6b] Single crystal X-ray analysis of **13** offered defining evidence for this claim.





Scheme 6.

2.3. Elaboration of chiral butenolide

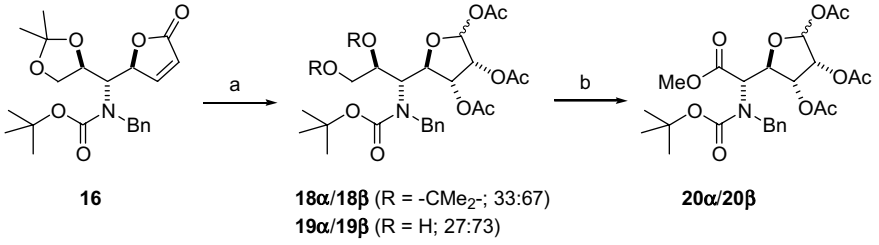
With **16** in hand, a series of functional group transformations, Scheme 7, leads to **23**, a formal equivalent of **3**. Dihydroxylation using catalytic OsO_4/NMO was sluggish. Use of a permanganate ion under phase transfer conditions proved to be more effective. The resulting diol was acetylated using standard conditions. From literature precedence[12] we were confident that dihydroxylation would favor the less hindered α-face of furanone **16**. Subsequent reduction of the furanone to the anomeric hemiacetal was accomplished with DIBAL-H; acetylation of the hemiacetal provided **18** as a mixture of α- and β-anomers (1:2) in an overall yield of 71% for these two steps. The anomeric acetates, **18α** and **18β**, were separable using FLC and thus fully characterized. Acetonide deblocking of **18** was accomplished using warm aqueous acetic acid with a near quantitative yield to provide **19**. Oxidative cleavage of the incipient diol followed by one-pot oxidation and esterification[13] of the crude aldehyde provided **20** in 97% yield in these consecutive steps. Although it was of no consequence, which C1 anomer of **20** was to be used for future glycosylation (vide supra), individual anomers were separated using FLC so that spectral analysis could be clean and that the specific rotation values were more meaningful.

2.4. Completion of the formal synthesis

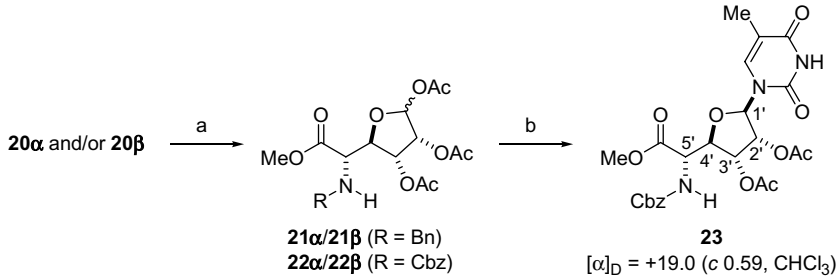
Debenzylation of **20** under catalytic hydrogenation conditions proved difficult (Scheme 8). This was most likely due to steric crowding imparted by the Boc group. Removal of the Boc group using the method of Boger et al.[14] gave the *N*-benzyl hydrochloride, which was subsequently free-based with bicarbonate to provide **21** as an expected pair of anomeric C1 acetates. With the Boc group removed, debenzylation proceeded relatively smoothly. The resulting primary amine was protected with a carbobenzoxy (Cbz) group to provide a 1:2 mixture of **22α** and **22β**, respectively. Using the method described by Vorbrüggen et al.,[3] this mixture served as glycosyl donors to the persilylated thymine base **4**[4] to provide **23** with a 74% yield. The product nucleoside **23** was a white foam, which gave ^1H and ^{13}C NMR data the same as that of Garner.[2m,15] Thus, a formal synthesis of **3** was accomplished. Garner completed the synthesis of **3** from **23** by ester hydrolysis (aq LiOH) followed by *N*-debenzylation (H_2, Pd/C).[2m]

3. Conclusion

Starting from **15**, the overall yield for this 12-step synthesis of **23** was 15%. This shows the utility of 4-(aminoalkyl)-2-butenolides of thymine polyoxins as templates in synthesis.[16] Such butenolides are quite versatile, proving to be amenable to a broad range of well-known reactions. In addition, the importance of 2-(trimethylsilyloxy)-furan **8** as an alkylating agent has been made



Scheme 7. Reagents and yields: (a) (i) $KMnO_4$, DCH-18-C6, DCM, −10 °C, 23 h, 70%; (ii) Ac_2O, py, rt, 15 min (74%); (iii) DIBAL-H, $PhCH_3$, −78 °C, 1 h, 81%; (iv) Ac_2O, py, rt, 5 h (88%); (b) (i) 70% AcOH·H_2O, 45 °C, 100 min (98%); (ii) $Pb(OAc)_4$, K_2CO_3, DCM, 0 °C, 10 min; (iii) Br_2, H_2O, MeOH, $NaHCO_3$, rt, 5 h, 97% over two steps.



Scheme 8. Reagents and yields: (a) (i) 2.2 M HCl–EtOAc, then HCl(g) 20 s, then satd aq $NaHCO_3$, dioxane, rt, 10 min, 87%; (ii) 10% Pd–C, H_2 (1 atm), THF, NaOAc, rt, 12 h (76%); (iii) CbzCl, dioxane, 7% aq $NaHCO_3$, 12 °C, 2 h 45 min (87–93%); (b) **4**, TMSOTf, DCE, reflux, 25 min, 74%.

increasingly apparent as a result of this work and by the work of other researchers.

4. Experimental

4.1. General

Unless noted otherwise, reagents available commercially were used without further purification. Glassware used in non-aqueous reactions was oven-dried (150 °C) for extended periods. All reactions were conducted under anhydrous nitrogen (>1 atm). Solvents were dried using standard procedures; dichloromethane (DCM) was distilled from phosphorus pentoxide or calcium hydride immediately prior to use. Flash liquid chromatography (FLC) was performed using 60 Å silica gel (Merck, 230–400 mesh) as a stationary phase. Gradient elution was conducted using various proportions of ethyl acetate and hexanes under positive nitrogen pressure. Samples were concentrated using a Büchi® rotary evaporator, which was connected to a water aspirator at a pressure of ca. 40 mmHg. Thin layer chromatography (TLC) was performed using glass-backed plates precoated with 0.20 mm of silica (silica gel 60 F_{254}, EM Separations Technology). After development (closed chamber), visualization was effected for non-UV-active species by dipping in aqueous $KMnO_4$/K_2CO_3 (Char A) or 5% PMA/EtOH (Char B, phosphomolybdic acid). Amines were detected by wetting with ninhydrin/EtOH solution. All stains required heating for a few seconds. Infrared spectra were measured on a Nicolet Impact 410 spectrometer. ^{1}H NMR spectra were obtained on a Varian Associates Model XL-200 operating at 200 MHz or XL 400 spectrometer operating at 400 MHz. ^{13}C NMR spectra were obtained on a Varian Associates Model XL-200 operating at 50 MHz. Chemical shifts are reported using the δ (delta) scale for ^{1}H and ^{13}C spectra. TMS (tetramethylsilane) was used as an internal standard (0.00 ppm) for all ^{1}H spectra. Unless indicated otherwise, $CDCl_3$ (deuterochloroform) served as an internal standard (77.0 ppm) for all ^{13}C spectra. Choices of deuterated solvents ($CDCl_3$, acetone-d_6, DMSO-d_6, CD_3OD, D_2O, Cambridge Scientific; C_6D_6, Aldrich) are indicated below. Select ^{13}C spectral assignments were obtained with the aid of APT (attached proton test) experiments. For the APT experiments, a positive phase (+) implies the presence of a methyl or methine carbon atom; a negative phase (−) implies the presence of a methylene or a quaternary carbon atom. Optical rotations were determined using a Jasco Digital Polarimeter. Optical measurements were made at ambient temperature utilizing a 10 mm cell (length) and anhydrous solvents ($CHCl_3$, EtOH, MeOH, or benzene). Melting points of solid compounds were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. Diastereomeric excess (% de) values were determined by integration of suitable sets of peaks on the ^{1}H NMR spectra. For cases in which diastereomers were inseparable by FLC, ^{1}H NMR, and ^{13}C NMR data is that of the major diastereomer unless otherwise noted.

4.2. *N*-Benzylimine-D-glyceraldehyde 7

Two approaches were used for the synthesis of **7**. In one case, freshly distilled D-glyceraldehyde acetonide **15** was diluted with anhyd DCM to a concentration of ca. 1.0 M. At this point, crushed 4 Å molecular sieves were added (ca. 50 mg sieves per 1 mmol aldehyde). The aldehyde/sieve mixture was then cooled to 0 °C while stirring under anhyd N_2. One equivalent of distilled benzylamine ($BnNH_2$) was added dropwise, and the mixture stirred briskly for 1–2 h. The resulting imine was then subjected to the conditions outlined below for the synthesis of **6**. In a separate case, anhyd ether was substituted for DCM. Anhydrous Na_2SO_4 was also used in place of 4 Å molecular sieves (ca. 3 mmol Na_2SO_4 per 1 mmol aldehyde). As with the 'molecular sieve strategy,' benzylamine was added dropwise, and the mixture stirred very briskly for 1–2 h at 0 °C. In this case, the resulting imine was isolated by filtration followed by removal of solvent in vacuo, which provided a solid, white wax. A small aliquot was removed for spectral analysis. IR (neat) 3030, 2984, 2876, 2250, 1674, 1496, 1373 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.41, 1.47 (s, 2 × 3H, $C(CH_3)_2$), 3.97 (dd, J = 9, 6 Hz, 1H, H-3a). 4.21 (dd, J = 9, 7 Hz, 1H, H-3b), 4.62 (d, J = 1 Hz, 2H, CH_2Ph), 4.63 (approx. q, J = 6 Hz, 1H, H-2), 7.2–7.4 (br m, 5H, Ph), 7.77 (dt, J = 5, 1 Hz, 1H, H-1); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.4, 26.5 ($C(CH_3)_2$), 60.1 (CH_2Ph), 64.6 (C-3), 67.4 (C-2) 110.4 ($C(CH_3)_2$), 127.2, 127.9, 128.5, 138.3 (Ph), 164.1 (C-1).

4.3. (4*S*,5*S*,6*S*)-5-(*N*-Benzylamino)-6,7-*O*-isopropylidene-2,3,5-trideoxy-D-*ribo*-hept-2-enono-1,4-lactone 6

To a flask containing 10.36 g (47.2 mmol) of **7** was added 425 mL anhyd DCM. The mixture was stirred until it became homogeneous, whereupon the clear solution was cooled to −78 °C. At this point, 7.38 g (47.2 mmol) of **8**[17] was added, and the solution left to cool for 15 min while stirring briskly. Using a syringe, 5.81 mL (47.2 mmol) of $BF_3{\cdot}OEt_2$ was slowly added (15 min). The solution was allowed to stir under anhyd N_2 at −78 °C for 9 h. The reaction was quenched by the addition of 50 mL of saturated, aqueous $NaHCO_3$. Once the aqueous phase had thawed, the layers were separated, and the remaining aqueous phase extracted with DCM (2 × 100 mL). The combined organic phases were rinsed with 100 mL of brine, and then dried with anhyd Na_2SO_4. TLC of the crude material showed a major spot at R_f = 0.43, and a minor spot at R_f = 0.50 (UV and Char B; 50% EtOAc/hexanes). ^{1}H NMR analysis of the crude material showed a 79:21 ratio for **6** and **9**, respectively. Flash liquid chromatography on 60 Å silica gel, using 40% EtOAc/hexanes, gave 12.46 g (87%) of **6** plus **9**. A second chromatography provided pure **6** (**9** was not preparatively isolable). Mp 61–63 °C, $[\alpha]_D^{27} = -49.0$ (c 1.00, $CHCl_3$); IR (KBr) 3334, 2995, 2884, 1960, 1736, 1594 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.31, 1.40 (s, 2 × 3H, $C(CH_3)_2$), 1.46 (br s, 1H, NH), 3.10 (dd, J = 7, 4 Hz, 1H, H-5), 3.77–4.02 (m, 2H, H-7b, H-6), 3.87 (d, J = 11 Hz, 2H, CH_2Ph), 4.10 (dd, J = 6, 3 Hz, 1H, H-7a), 5.37 (dt, J = 4, 2 Hz, 1H, H-4), 6.18 (dd, J = 6, 2 Hz, 1H, H-2), 7.30 (m,

5H, CH_2Ph), 7.55 (dd, $J = 6$, 2 Hz, 1H, H-3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.1 (+, $C(CH_3)_2$), 26.6 (+, $C(CH_3)_2$), 53.0 (−, NCH_2Ph), 61.2 (+, C-5), 67.6 (−, C-7), 75.5 (+, C-6), 83.7 (+, C-4), 109.7 (−, $C(CH_3)_2$), 122.3 (+, C-2), 127.3, 128.2, 128.4 (+, CH_2Ph), 139.6 (−, CH_2Ph), 154.4 (+, C-3), 172.8 (−, CO_2). Characteristic signals for presumed 4,5-*syn*:5,6-*anti*-isomer **9** (data obtained from spectrum of crude product mixture): ^1H NMR (200 MHz, $CDCl_3$) δ 6.05 (dd, $J = 5.82$ and 2.09 Hz, 0.21H, H-2), 7.65 (dd, $J = 5.75$ and 1.51 Hz, 0.21H, H-3). FABHRMS (NBA) *m/e*, found: 304.1547; calcd for $C_{21}H_{17}NO_4$: 304.1549 $[M+H]^+$.

4.4. (4*S*,5*S*,6*S*)-5-[*N*-Benzyl-*N*-[(1,1-dimethylethoxy)carbonyl]amino]-6,7-*O*-isopropylidene-2,3,5-trideoxy-D-*ribo*-hept-2-enono-1,4-lactone 16

Butenolide **6** (1.18 g, 3.89 mmol) was dissolved in 9.0 mL *t*-BuOH under anhydrous N_2 at ca. 30–35 °C (oil bath). Upon dissolution, 1.79 mL (2.0 equiv, 7.78 mmol) molten di-*tert*-butyl dicarbonate (Boc_2O) was added at once via syringe. The reaction was monitored via TLC (Char A) until **6** had been consumed (24 h). The product carbamate gave an $R_f = 0.60$ (50% EtOAc/hexanes). Residual solvent was removed in vacuo. Flash liquid chromatography on 60 Å silica gel, using 30% EtOAc/hexanes as the mobile phase, gave **16** (1.57 g, 100%) as a white solid. Mp 91.5–93 °C, $[\alpha]_D^{27} = -124.8$ (*c* 1.05, $CHCl_3$); IR 3079, 2979, 1748, 1711 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.26 (s, $2 \times 3H$, $C(CH_3)_2$), 1.44 (s, $3 \times 3H$, $C(CH_3)_3$), 3.33 (t, $J = 6$ Hz, 1H, H-5), 3.73 (d, $J = 6$ Hz, 1H, H-7a), 3.77 (d, $J = 6$ Hz, H-7b), 4.19 (br d, $J = 15$ Hz, 1H, CH(*H*a)Ph), 4.67 (br d, $J = 15$ Hz, 2H, CH(*H*b)Ph and H-6), 5.43 (dt, $J = 3$, 2 Hz, 1H, H-4), 5.99 (dd, $J = 5$, 2 Hz, 1H, H-2), 7.28 (m, 5H, Ph), 7.63 (dd, $J = 6$, 2 Hz, 1H, H-3); ^{13}C NMR (50 MHz, $CDCl_3$) d 25.5, 26.5 (+, $C(CH_3)_2$), 28.1 (+, $C(CH_3)_3$), 53.7 (−, NCH_2Ph), 62.7 (+, C-5), 66.7 (−, C-7), 73.5 (+, C-6), 80.9 (−, $C(CH_3)_3$), 84.2 (+, C-4), 109.8 (−, $C(CH_3)_2$), 120.1 (+, C-2), 127.8, 128.3, 128.6 (+, Ph), 137.8 (−, Ph), 154.3 (+, C-3), 155.0 (−, OCON), 172.7 (−, CO_2); FABHRMS (NBA) *m/e*, found: 404.2071; calcd for $C_{22}H_{29}NO_6$: 404.2073, $[M+H]^+$.

4.5. (2*R*,3*S*,4*S*,5*S*)-5-[*N*-Benzyl-*N*-[(1,1-dimethylethoxy)carbonyl]amino]-6,7-*O*-isopropylidene-5-deoxy-D-glycero-D-alloheptofuranose, 1,2,3-triacetate 18

Butenolide **16** (6.11 g, 15.1 mmol), along with 1.01 g of dicyclohexano-18-crown-6, were dissolved in 94 mL of DCM, and cooled to −10 °C (glycerol/CO_2) under N_2. At this point 1.44 g (9.1 mmol) of powdered $KMnO_4$ was added in one portion and the dark mixture was stirred briskly. After 3 h, an additional 1.44 g (9.1 mmol, 18.2 mmol total) of powdered $KMnO_4$ was added in one portion. After 17 h reaction time, TLC showed the continued presence of **16**. An additional 0.48 g (3.0 mmol, 21.3 mmol total) of powdered $KMnO_4$ was added, and brisk stirring continued for 5.5 h (22.5 h total), after which TLC (Char A) showed essentially only one product at $R_f = 0.19$ (50% EtOAc/hexanes). The reaction was quenched at −10 °C by the addition of 55 mL of saturated aqueous Na_2SO_3 while stirring briskly. The cold bath was removed, and the saturated aqueous citric acid added dropwise until the brown color disappeared (required 32 mL). The two phase yellow mixture was diluted with 50 mL of DCM and separated. The remaining aqueous phase was extracted with DCM (3×50 mL). The combined organic extracts were dried with anhyd Na_2SO_4. After gravity filtration, the solvent was removed in vacuo. Flash liquid chromatography on 60 Å silica gel, using 70% EtOAc/hexanes as the mobile phase, gave unreacted **16** (0.16 g), followed by the desired diol (4.54 g, 70.4%) as a white foam. The diol was fully characterized (data not shown). Under anhyd N_2, 188 mg (0.43 mmol) of the diol was dissolved with 1.5 mL of DCM and cooled to −78 °C (acetone/CO_2). To this solution was added freshly prepared DIBAL-H (1.5 M in toluene, 950 μL, 1.43 mmol) over the course of 8 min. After 1 h, the reaction was quenched by the addition of 0.52 mL (12.8 mmol) of MeOH. The cold reaction mixture was poured onto 1 M HCl (5 °C, 20 mL) and stirred briskly for 5 min. The mixture was extracted with EtOAc (4×20 mL). The combined organic phases were rinsed with brine (17 mL), and the brine phase back-extracted with Et_2O (20 mL). The organic phases were combined, dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. Flash liquid chromatography on 60 Å silica gel, initially using 50% EtOAc/hexanes as the mobile phase followed by 100% EtOAc, gave a forerun of the unreacted diol (44 mg), followed by the desired triol (117 mg, 80.7% based on recovered diol, $R_f = 0.50$ in 100% EtOAc). The triol was immediately protected as triacetate **18**. The entire quantity of triol was dissolved with 215 mL (2.65 mmol) of pyridine followed by the dropwise addition of 215 mL (2.28 mmol) of acetic anhydride. The yellow solution was stirred at ambient temperature for 5 h, at which time TLC showed complete product formation (two products; $R_f = 0.55$ and 0.50 in 50% EtOAc/hexanes). Excess pyr- idine and acetic anhydride were removed using a Kügelrohr (bulb-to-bulb) apparatus at 3.0 mmHg. Flash liquid chromatography on 60 Å silica gel (25×40 mm), using 30% EtOAc/hexanes as the mobile phase gave **18** (133 mg, 88.1%) as a 67:31 (β/α) inseparable mixture of C1 anomers. White foam; $[\alpha]_D^{25} = -5.0$ (*c* 7.66, $CHCl_3$); IR ($CHCl_3$) 1752, 1689 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 60 °C) δ 1.22, 1.25 (s, $2 \times 3H$, $C(CH_3)_2$), 1.47 (s, 9H, $C(CH_3)_3$), 2.01, 2.03, 2.08 (s, $3 \times 3H$, $OCOCH_3$), 3.43–3.76 (br s, 2H, H-4 and H-7a), 4.11 (m, 1H, H-7b), 4.38 (br s, 1H, H-6), 4.47 (br s, 2H, CH_2Ph), 4.55 (br s, 1H, H-4), 5.32 (d, $J = 5$ Hz, 1H, H-2), 5.53 (dd, $J = 7$, 4 Hz, 1H, H-3), 6.13 (d, $J = 1$ Hz, 0.67H, H-1a), 6.43 (d, $J = 5$ Hz, 0.33H, H-1b), 7.27 (br s, 5H, Ph); ^{13}C NMR (50 MHz, $CDCl_3$, 60 °C) d 20.1, 20.3, 20.8 ($OCOCH_3$), 25.7, 26.5 ($C(CH_3)_2$), 28.3 ($C(CH_3)_3$), 56.5 (CH_2Ph), 67.2 (C-7), 69.5 (C-5), 71.8, 74.0, 74.6 (C-2, C-3, and C-6), 81.0 ($C(CH_3)_3$), 82.4 (C-4), 98.4 (C-1), 109.6 ($C(CH_3)_2$), 127.3, 128.4, 128.6, 139.1 (Ph), 155.6 (NCO_2), 168.8, 169.1, 169.3 ($OCOCH_3$); FABHRMS (NBA-NaI) *m/e*, found: 588.2438, calcd for $C_{28}H_{39}NO_{11}$: 588.2421 $[M+Na]^+$.

4.6. (2*R*,3*S*,4*S*,5*R*,6*S*)-5-[*N*-Benzyl-*N*-[(1,1-dimethylethoxy)carbonyl]amino]-5-deoxy-D-glycero-β-D-allofuranose, 1,2,3-triacetate, and α-D-allofuranose, 1,2,3-triacetate 19β and 19α

To a 25 mL flask was added **18** (0.135g, 0.24 mmol), followed by 6.75 mL of 70% aqueous acetic acid. With brisk stirring, the transparent reaction solution was heated to 45 °C (oil bath). The reaction was monitored via TLC (Char A) until **18** had been consumed (100 min). The product gave an $R_f = 0.16$ (50% EtOAc/hexanes). The heat source was removed and the solution cooled to ambient temperature. The clear reaction solution was then added dropwise to 13.5 mL of cold, saturated aqueous $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 25 mL). The combined organic phases were dried over anhyd Na_2SO_4, filtered, and concentrated in vacuo. Residual acetic acid was removed by azeotropic distillation with *n*-heptane (100 mL) using the rotary evaporator. Flash liquid chromatography on 60 Å silica gel (15 × 110 mm), using 70% EtOAc/hexanes as the mobile phase, gave **19** (0.123 g, 98%) as a white foam. ^{1}H NMR of this product showed a 73:27 ratio of β- and α-anomers, respectively. $[\alpha]_D^{24} = -36.0$ (*c* 0.67, $CHCl_3$); IR ($CHCl_3$) 3477, 3005, 2979, 1784, 1686, 1457, 1369, 1218 cm^{-1}; ^{1}H NMR (200 MHz, acetone-d_6, 57 °C) δ 1.44 (br s, 9H, $C(CH_3)_3$), 2.01 (s, 3H, $OCOCH_3$), 2.02 (s, 3H, $OCOCH_3$), 2.06 (s, 3H, $OCOCH_3$), 2.58 (s, 1H, CH_2OH), 3.33 (br s, 1H, $CH(OH)CH_2$), 3.45 (br s, 2H, H-7a and H-7b), 4.06 (m, 1H, H-6), 4.49 (m, 1H, H-5), 4.62 (d, $J = 15$ Hz, 2H, CH_2Ph), 4.83 (br s, 1H, H-4), 5.28 (m, 1H, H-3), 5.38 (br s, 1H, H-2), 6.06 (d, $J = 1$ Hz, 0.73H, H-1b), 6.35 (d, $J = 4$ Hz, 0.27H, H-1a), 7.34 (m, 5H, $C_6H_5CH_2$); ^{13}C NMR (50 MHz, $CDCl_3$, 60 °C) δ 20.3, 20.4, 20.7 ($OCOCH_3$), 28.4 ($C(CH_3)_3$), 52.1 (CH_2Ph), 63.3 (C-7), 63.9 (C-5), 69.6 (C-6), 72.7 (C-2, or C-3), 74.0 (C-3 or C-2), 81.5 ($C(CH_3)_3$), 84.1 (C-4), 98.6 (C-1), 128.2, 128.5, 128.7, 138.0 (Ph), 159.9 (NCO_2), 168.8, 169.2, 169.7 ($OCOCH_3$); FABHRMS (NBA-NaI) *m/e*, found: 548.2111 calcd for $C_{25}H_{35}NO_{11}$: 548.2108, $[M+Na]^+$.

4.7. (1*S*,2*R*,3*S*,4*S*,5*S*)-5-[*N*-Benzyl-*N*-[(1,1-dimethylethoxy)carbonyl]amino]-5-deoxy-β-D-allofuranuronate, 1,2,3-triacetate 20β

To a 10 mL flask was added **19** (0.109 g, 0.21 mmol; as a mixture of α- and β-anomers). Under anhyd N_2 with stirring, the foam was dissolved with 2.5 mL of DCM and cooled to 0 °C with the aid of an ice-bath. The septum was momentarily removed and 96 mg (0.22 mmol) of $Pb(OAc)_4$ and 0.285 g (2.06 mmol) of K_2CO_3 were added at once. Analysis via TLC showed the absence of **19** after 10 min. The contents of the flask were filtered over a bed of Celite®/Na_2SO_4 (9:1, 2 × 2 cm) and rinsed with DCM (20 mL). The solvent was removed in vacuo (rotary evaporator, bath at ambient temp) leaving 0.116 g of crude aldehyde as a yellow oil. The crude aldehyde was dissolved in 1.14 mL of 9:1 MeOH/water. At this point solid $NaHCO_3$ (0.347 g, 4.13 mmol) was added, followed by 0.46 mL (0.91 mmol) of 2.0 M Br_2 (in 9:1 MeOH/water). The reaction was monitored via TLC (Char A) every hour for the absence of aldehyde, which gave a streak beginning near the baseline when developed with 50% EtOAc/hexanes. After stirring the orange mixture briskly at ambient temperature for 5 h, the contents of the flask were cooled to 0 °C (external ice-bath) and 5.0 mL of 0.10 M $Na_2S_2O_3$ was added to quench the reaction. The resulting mixture was extracted with DCM (6 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and then filtered. Flash liquid chromatography on 60 Å silica gel (15 × 150 mm), using 30% EtOAc/hexanes as the mobile phase, gave **20β** ($R_f = 0.50$ in 50% EtOAc/hexanes) and **20α** ($R_f = 0.45$ in 50% EtOAc/hexanes) in good yield (0.101 g, 92.7% over two steps) as white foams. $[\alpha]_D^{25} = -42.1$ (*c* 0.97, $CHCl_3$); IR ($CHCl_3$) 3031, 2975, 2950, 1762, 1695, 1405, 1369, 1231, 1159 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 60 °C) δ 1.44 (s, 9H, $C(CH_3)_3$), 2.01, 2.03, 2.06 (s, 3 × 3H, $OCOCH_3$), 3.56 (s, 3H, CO_2CH_3), 4.44 (br s, 1H, H-5), 4.74 (t, $J = 7$ Hz, 1H, H-4), 4.52 (s, 2H, CH_2Ph), 5.27 (dd, $J = 5$, 1 Hz, 1H, H-2), 5.38 (m, 1H, H-3), 6.12 (d, $J = 1$ Hz, H-1), 7.28 (br s, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$, 60 °C) δ 20.3, 20.4, 20.9 ($OCOCH_3$), 28.2 ($C(CH_3)_3$), 49.4 (CH_2Ph), 51.9 (CO_2CH_3), 60.8 (C-5), 71.8 (C-3 or C-2), 74.3 (C-2 or C-3), 79.7 (C-4), 81.6 ($C(CH_3)_3$), 98.6 (C-1), 127.4, 128.1, 128.4, 137.8 (Ph), 156.5 (NCO_2), 168.6, 169.1, 169.2 ($OCOCH_3$), 171.8 (CO_2CH_3); FABHRMS (NBA-NaI) *m/e*, found: 546.1957, calcd for $C_{25}H_{33}NO_{11}$: 546.1951 $[M+Na]^+$.

4.8. (1*R*,2*R*,3*S*,4*S*,5*S*)-Methyl 5-[*N*-benzyl-*N*-[(1,1-dimethylethoxy)carbonyl]amino]-5-deoxy-α-D-allofuranuronate, 1,2,3-triacetate 20α

For **20α**: $[\alpha]_D^{25} = +12.2$ (*c* 0.90, $CHCl_3$); IR ($CHCl_3$) 3019, 2981, 2953, 1753, 1692, 1365, 1211, 1160 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, 60 °C) δ 1.45 (s, 9H, $C(CH_3)_3$), 1.98, 1.99, 2.04 (s, 3 × 3H, $OCOCH_3$), 3.64 (s, 3H, CO_2CH_3), 4.41 (d, $J = 16$ Hz, 1H, CH(*H*a)Ph), 4.52 (m, 1H, H-5), 4.57 (dd, $J = 5$, 3 Hz, 1H, H-4), 4.66 (d, $J = 16$ Hz, 1H, CH(C*H*b)Ph), 5.09 (dd, $J = 6$, 5 Hz, 1H, H-2), 5.48 (m, 1H, H-3), 6.32 (d, $J = 5$ Hz, 1H, H-1), 7.27 (br s, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$, 60 °C) δ 20.1, 20.4, 20.7 ($OCOCH_3$), 28.2 ($C(CH_3)_3$), 50.7 (CH_2Ph), 52.1 (CO_2CH_3), 60.5 (C-5), 69.7 (C-3 or C-2), 70.6 (C-2 or C-3), 81.6 ($C(CH_3)_3$), 83.1 (C-4), 94.0 (C-1), 127.1, 127.9, 128.3, 138.4 (Ph), 155.9 (NCO_2), 168.8, 168.9, 169.2 ($OCOCH_3$), 169.5 (CO_2CH_3); FABHRMS (NBA-NaI) *m/e*, found: 546.1956; calcd for $C_{25}H_{33}NO_{11}$: 546.1951 $[M+Na]^+$.

4.9. (1*R*,2*R*,3*S*,4*S*,5*S*)-Methyl 5-*N*-benzylamino-5-deoxy-α-D-allofuranuronate, 1,2,3-triacetate 21α[18]

To a 25 mL flask was added **20α** (30 mg, 0.057 mmol) along with 2.40 mL of 2.2 M HCl–EtOAc,[19] which was delivered via syringe. Gaseous HCl was bubbled into the reaction solution (ca. 20 s) via a lecture bottle, which was attached to a 10 cm × 22 gauge needle. Note: TLC analysis (Char A) showed **20α** and baseline material (i.e., $R_f = 0$) after 15 s of bubbling, and only baseline material when developed with 50% EtOAc/hexanes after 20 s of bubbling. At this point, all volatiles were

removed in vacuo (rotary evaporator, bath at ambient temp) leaving a viscous, amber oil. A Teflon-coated stir bar was added along with 0.50 mL of 1,4-dioxane and 4.80 mL of saturated aqueous $NaHCO_3$. The turbid suspension became clear after 10 min, at which point TLC showed free amine formation ($R_f = 0.38$ in 50% EtOAc/hexanes; ninhydrin). The aqueous phase was extracted with EtOAc (5×10 mL) and then dried over anhydrous Na_2SO_4. After filtration, the solvents were removed in vacuo. Flash liquid chromatography using 60 Å silica gel (15×130 mm), 40% EtOAc/hexanes as the mobile phase, gave **21α** (21 mg, 86.6%) as a pale yellow oil. $[\alpha]_D^{27} = +31.2$ (*c* 1.30, $CHCl_3$); IR ($CHCl_3$) 3332, 3023, 2956, 2919, 2851, 1738 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 60 °C) δ 1.45 (br s, 1H, NH), 2.03, 2.06, 2.07 (s, $3 \times 3H$, $OCOCH_3$), 3.54 (d, $J = 4$ Hz, 1H, H-5), 3.74 (s, CO_2CH_3, 3H), 3.80 (d, $J = 9$ Hz, CH_2Ph, 2H), 4.49 (dd, $J = 4$, 3 Hz, 1H, H-4), 5.26 (dd, $J = 7$, 4 Hz, 1H, H-2), 5.37 (dd, $J = 7$, 4 Hz, 1H, H-3), 6.38 (d, $J = 4$ Hz, 1H, H-1), 7.28 (br s, C_6H_5, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.3, 20.7, 21.0 ($3OCOCH_3$), 52.4 (CO_2CH_3), 53.1 (CH_2Ph), 61.7 (C-5), 70.0 (C-2 or C-3), 70.3 (C-3 or C-2), 85.9 (C-4), 93.9 (C-1), 127.1, 128.2, 128.5, 139.3 (Ph), 169.3, 169.7, 169.9 ($OCOCH_3$), 171.8 (CO_2CH_3); FABHRMS (NBA-NaI) *m/e*, found: 446.1431; calcd for $C_{20}H_{25}NO_9$: 446.1427, $[M+Na]^+$.

4.10. (1*S*,2*R*,3*S*,4*S*,5*S*)-Methyl 5-*N*-benzylamino-5-deoxy-β-D-allofuranuronate, 1,2,3-triacetate 21β

The method outlined for **21α** was adopted. In this effort, 97 mg of **20β** yielded 60 mg (76.5%) as a viscous yellow oil ($R_f = 0.49$ in 50% EtOAc). $[\alpha]_D^{24} = -14.3$ (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 3332, 3027, 2947, 1747, 1454, 1366 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 60 °C) δ 1.98, 2.01, 2.08 (s, $OCOCH_3$, $3 \times 3H$), 3.45 (d, $J = 3$ Hz, 1H, H-5), 3.68 (d, $J = 13$ Hz, 1H, CH(*H*a)Ph), 3.72 (s, CO_2CH_3, 3H), 3.84 (d, $J = 13$ Hz, 1H, CH(*H*b)Ph), 4.34 (t, $J = 6$ Hz, 1H, H-3), 5.32 (dd, $J = 5$, 1 Hz, 1H, H-2), 5.55 (t, $J = 6$ Hz, 1H, H-3), 6.10 (d, $J = 1$ Hz, 1H, H-1), 7.28 (br s, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.5 (+, $2 \times OCOCH_3$), 20.9 (+, $OCOCH_3$), 52.0 (+, CO_2CH_3), 52.3 (−, CH_2Ph), 62.8 (+, C-5), 71.6 (+, C-3), 74.2 (+, C-2), 82.4 (+, C-4), 98.2 (+, C-1), 127.2, 128.1, 128.4 (+, Ph), 139.2 (−, Ph), 168.9 (−, $OCOCH_3$), 169.4 (−, $2 \times OCOCH_3$), 172.4 (−, CO_2CH_3); FABHRMS (NBA-NaI) *m/e*, found: 446.1427; calcd for $C_{20}H_{25}NO_9$: 446.1419 $[M+Na]^+$.

4.11. (1*R*,2*R*,3*S*,4*S*,5*S*)-Methyl 5-deoxy-5-[[(phenylmethoxy)carbonyl]amino]-β-D-allofuranuronate 1,2,3-triacetate 22β[20]

To a 10 mL flask containing a Teflon-coated stirrer bar was added **21β** (42 mg, 0.10 mmol). Solid NaOAc (4 mg, 0.05 mmol) was added along with 2.5 mL of THF and 23 mg of 10% Pd–C. The flask was fitted with a septum, aspirated three times, each time being purged with N_2. The flask was again aspirated with H_2, which was introduced with a rubber balloon (ca. 1 atm.). The mixture was stirred briskly overnight. Analysis of the debenzylation via TLC showed the complete absence of **21β** after 13.5 h. The contents of the flask were diluted with THF (6 mL) and filtered through fluted paper using copious amounts of THF (ca. 50 mL). TLC indicated the presence of a 1° amine (ninhydrin) at $R_f = 0.36$ (100% EtOAc). Flash liquid chromatography on 60 Å silica gel (15×95 mm), using 80% EtOAc/hexanes as the mobile phase, gave the 1° amine (25 mg, 75.6%) as a pale yellow foam, which was immediately protected. The entire quantity of the 1° amine was dissolved with 1.0 mL of 1,4-dioxane, and cooled to 12 °C. To the flask was added 0.25 mL of 7% aqueous $NaHCO_3$, followed by 26 mL (0.18 mmol, 2.5 equiv) of benzyl chloroformate (Cbz-Cl). TLC analysis after 2 h 45 min showed the complete absence of the 1° amine and product formation at $R_f = 0.30$ (50% EtOAc/hexanes). Flash liquid chromatography on 60 Å silica gel (15×110 mm), using 40% EtOAc/hexanes as the mobile phase, gave **22β** (32 mg, 92.8%) as a clear oil. $[\alpha]_D^{25} = +8.2$ (*c* 1.10, $CHCl_3$); IR ($CHCl_3$) 3357, 3020, 2954, 2921, 2846, 1754, 1526 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 60 °C), δ 2.01, 2.02, 2.10 (s, $3 \times 3H$, $OCOCH_3$), 3.75 (s, 3H, CO_2CH_3), 4.45 (dd, $J = 7$, 5 Hz, 1H, H-4), 4.67 (dd, $J = 9$, 4 Hz, 1H, H-5), 5.11 (s, CH_2Ph), 5.30 (dd, $J = 5$, 0.5 Hz, 1H, H-2), 5.46 (br s, 1H, NH), 5.55 (dd, $J = 8$, 5 Hz, 1H, H-3), 6.11 (d, $J = 0.5$ Hz, 1H, H-1), 7.33 (br s, 5H, C_6H_5); ^{13}C (50 MHz, benzene-d_6) δ 19.8, 20.3 (−, $OCOCH_3$), 52.0 (−, C-5), 56.0 (−, CO_2CH_3), 67.3 (+, CH_2Ph), 71.0 (−, C-2 or C-3), 74.5 (−, C-3 or C-2), 81.9 (−, C-4), 98.1 (−, C-1), 128.2 128.3, 128.8 (−, Ph), 136.7 (+, Ph), 156.0 (+, NCO_2), 168.2, 168.9, 169.2 (+, $OCOCH_3$), 169.3 (+, CO_2CH_3); FABHRMS (NBA-NaI) *m/e*, found: 490.1334: calcd for $C_{21}H_{25}NO_{11}$: 490.1325 $[M+Na]^+$.

4.12. (1*S*,2*R*,3*S*,4*S*,5*S*)-Methyl 5-deoxy-5-[[(phenylmethoxy)carbonyl]amino]-α-D-allofuranuronate 1,2,3-triacetate 22α[20]

The method outlined for **22β** was adopted: 30 mg **21α** yielded 15.2 mg of the 1° amine (64.4%) as a viscous yellow oil. As in the previous case, the entire quantity of this material was immediately protected affording 16.5 mg (77.5%) of **22α** ($R_f = 0.23$ in 50% EtOAc/hexanes). $[\alpha]_D^{26} = +62.4$ (*c* 0.88, $CHCl_3$); IR ($CHCl_3$) 3346, 3028, 2958, 2921, 2851, 1729, 1519 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 60 °C) δ 2.04, 2.08, 2.09 ($OCOCH_3$, $3 \times 3H$), 3.78 (s, CO_2CH_3, 3H), 4.48 (t, $J = 3$ Hz, 1H, H-4), 4.78 (dd, $J = 8$, 3 Hz, 1H, H-5), 5.13 (s, 2H, CH_2Ph), 5.16 (m, 1H, H-2), 5.38 (dd, $J = 7$, 3 Hz, 1H, H-3), 5.53 (m, 1H, NH), 6.37 (d, $J = 4$ Hz, 1H, H-1), 7.33 (br s, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.8, 20.1, 20.5 ($OCOCH_3$), 52.2 (C-5), 56.0 (CO_2CH_3), 67.3 (CH_2Ph), 70.0 (C-2 or C-3), 70.2 (C-3 or C-2), 85.3 (C-4), 94.2 (C-1), 128.3, 129.0, 129.1, 136.8 (Ph), 156.0 (CO_2N), 169.8 (CO_2CH_3); FABHRMS (NBA-NaI) *m/e*, found: 490.1331; calcd for $C_{21}H_{25}NO_{11}$: 490.1325 $[M+Na]^+$.

4.13. Methyl 1,5-dideoxy-1-(3,4-dihydro-5-methyl-2,4-dioxo-1-(2H)-pyrimidinyl)-5 [[(phenylmethoxy)carbonyl]amino]-β-D-allofuranuronate, 2,3-diacetate 23

The method outlined by Garner and Park[2m] was adopted: 69 mg (0.15 mmol) of **22** gave 58 mg (73.4%)

of **23** as a white foam. $[\alpha]_D^{26} = +19.0$ (*c* 0.59, $CHCl_3$), lit.[2m] $[\alpha]_D = +19.8$ (*c* 0.56, $CHCl_3$); IR ($CHCl_3$) 3392, 1759, 1715, 1695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, 60 °C) δ 1.89 (d, $J = 1$ Hz, 3H, 5-CH_3), 2.07, 2.08 (s, $2 \times 3H$, $OCOCH_3$), 3.80 (s, 3H, CO_2CH_3), 4.37 (dd, $J = 5$, 4 Hz, 1H, H-4′), 4.81 (dd, $J = 9$, 4 Hz, 1H, H-5′), 5.14 (s, 2H, CH_2Ph), 5.27 (t, $J = 6$ Hz, 1H, H-2′), 5.52 (t, $J = 6$ Hz, 1H, H-3′), 5.80 (m, 1H, NH), 5.93 (d, $J = 6$ Hz, 1H, H-1′), 7.05 (d, $J = 0.6$ Hz, 1H, H-6), 7.33 (br s, 5H, C_6H_5), 7.85 (br s, 1H, N^3H); ^1H NMR (400 MHz, $CDCl_3$) δ 1.90 (s, 3H, 5-CH_3), 2.09, 2.10 (s, $2 \times 3H$, $OCOCH_3$), 3.81 (s, 3H, CO_2CH_3), 4.39 (approx. t, $J = 4.3$ Hz, 1H, H-4′), 4.83 (dd, $J = 8.3$, 3.5 Hz, 1H, H-5′), 5.12 (d, $J = 12.2$ Hz, 1H, CH(*H*a)Ph), 5.16 (d, $J = 12.2$ Hz, 1H, CH(*H*b)Ph), 5.27 (t, $J = 6.0$ Hz, 1H, H-2′), 5.52 (t, $J = 5.7$ Hz, 1H, H-3′), 5.80 (br d, 1H, NH), 5.93 (d, $J = 5.8$ Hz, 1H, H-1′), 7.05 (br s, 1H, H-6), 7.36 (br s, 5H, C_6H_5), 8.36 (br d, 1H, N^3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.8 (5-CH_3), 18.7 (2OCO*C*H_3), 51.2 (CO_2CH_3), 54.5 (C-5′), 65.5 (CH_2Ph), 69.1 (C-3′ or C-4′), 71.4 (C-4′ or C-3′), 80.2 (C-2′), 87.7 (C-1′), 110.0 (C-5), 127.0, 127.1, 127.6 (Ph), 135.7 (C-6), 136.2 (Ph), 49.8 (C-2), 155.4 (NCO_2), 162.5 (C-4), 168.3, 168.4 (2O*C*OCH$_3$), 168.6 (CO_2CH_3); FABHRMS (NBA) *m*/*e*, found: 534.1727; calcd for $C_{24}H_{27}N_3O_{11}$: 534.1723 (M+).

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15. Rotation data was as follows: lit.[2m] $[\alpha]_D = +19.8$ (*c* 0.56, $CHCl_3$); this work, $[\alpha]_D = +19.0$ (*c* 0.59, $CHCl_3$).

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18. After the development of the procedure for the deprotection and free-basing of the independent α-anomer **20α**, and the β-anomer **20β** to produce **21α** and **21β**, a 193 mg (0.37 mmol) mixture (54:46 α/β) was subject to the same tandem of reactions affording 100 mg (64.1%) of **21α/21β** as a mixture. Separation of these diastereomers using FLC proved difficult.
19. 2.2 M HCl–EtOAc (concentrated) was prepared by bubbling gaseous HCl (lecture bottle) into anhydrous EtOAc for an extended period (about 3 min for 25 mL).
20. After the procedure for the preparation of carbamates **22α** and **22β** had been developed, an approximate 50/50 mixture of deprotected (i.e., Boc group removed) **21α/21β** were subject to the same sequence of transformations (i.e., debenzylation, and Cbz-protection). A 91 mg (0.21 mmol) sample of **21** gave 62 mg (86.6%) of the 1° amine; the entire quantity of the 1° amine was protected as carbamate **22** as an inseparable mixture of C1 anomers (69.2 mg, 79.6%).