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Stereocontrolled formation of oxacephams from carbohydrates

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Dedicated to Professor Derek Horton on the occasion of his 70th birthday

Abstract

The [2 + 2] cycloaddition of chlorosulfonyl isocyanate to (*Z*)-4-*O*-propenyl ethers **16**, **17**, **29** and **30** proceeds with an excellent stereoselectivity in the case of ether **16** and with moderate stereoselectivity in remaining cases. Adducts were transformed into corresponding oxacephams: **37** in the first case, a mixture of **37**/**40** in the second and third case, and a mixture of **50**/**51** in the last case. In all instances addition to the *si–re* side of the olefin dominates. Oxacephams **41** and **52** with opposite R-configuration at the bridgehead carbon C-5a can be obtained by the alternate methodology based on the alkylation of nitrogen in 4-vinyloxyazetidin-2-one by protected 6-*O*-triflate **24** or **25**, followed by cyclization via intramolecular displacement of the vinyloxy group. Compounds **37**, **40**, **41**, **50**, **51** and **52** constitute a convenient entry leading to polyfunctionalized oxacephams.

Keywords: [2 + 2] Cycloaddition; Chlorosulfonyl isocyanate; 4-*O*-Propenyl-hexopyranosides; 4-*O*-Vinyloxyazetidin-2-one; Oxacephams

1. Introduction

In previous papers,[1–3] we have shown that [2 + 2] cycloaddition of chlorosulfonyl isocyanate (CSI) to 3-*O*-and 5-*O*-vinyl ethers of 1,2-*O*-isopropylidene-α-D-glucofuranose proceeds in many cases with excellent stereoselectivity and allows control of the configuration at C-4 of the 4-alkoxyazetidin-2-one. The cycloadducts offer an entry to clavams and 5-oxacephams via suitable transformation of the sugar fragment.[4,5]

It has been shown by us[6] that the [2 + 2] cycloaddition of chlorosulfonyl isocyanate (CSI) to sugar vinyl ethers is sterically controlled. To assign the spatial array of atoms in the transition state of the cycloaddition, s-trans conformation of the ether fragment should be used. We have shown, in addition, that the alternative to the above cycloaddition method, based on the alkylation of the nitrogen atom in 4-vinyloxyazetidin-2-one (**5**) by a structurally akin sugar fragment, followed by an intramolecular displacement of the vinyloxy group, leads to oxacephams with the opposite configuration at the C-6 carbon atom.[7,8] These two complementary methods are exemplified in Scheme 1 by the transformation of 1,3-*O*-ethylidene-L-erythritol (**1**) into cephams **7**–**9**.[9] In the cycloaddition method, the presence of a large substituent at O-4, such as trityl, promotes the exclusive formation of one stereoisomer **2**, which after N-alkylation yields oxacepham **7**. Whereas, if the less bulky substituent is present, such as mesyl, then both possible diastereomeric products **3** and **4** are formed, which then lead to the mixture of corresponding cephams **7** and **8**.[9] The second methodology provides cepham **9** as a sole reaction product after nucleophilic displacement at C-4 of the azetidin-2-one ring in **6**.

We expected that the presence of the rigid trans trioxadecalin skeleton in compounds **7**–**9** would result in angle strain and influence the geometry of the four-

Abbreviations: PMB, *p*-methoxybenzyl; TBDPS, *tert*-butyldiphenylsilyl; TBS, *tert*-butyldimethylsilyl.

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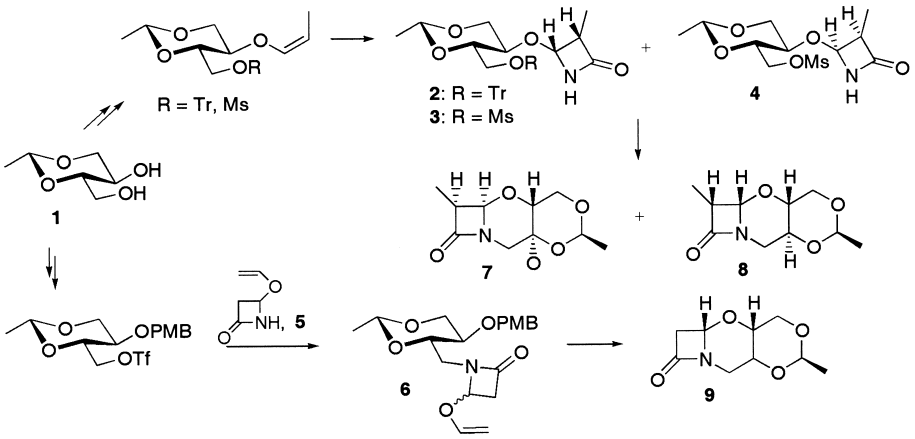
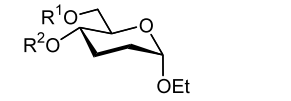


Scheme 1.

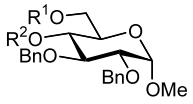
membered β-lactam ring. Bearing in mind that the configuration at C-6 in the cephams is essential for their biological activity,[10] it was of interest to synthesize compounds that would be enantiomerically related to **7**–**9** within the cepham fragment and to examine their potential biological activities.

2. Results and discussion

For the present study, we selected readily available ethyl 2,3-dideoxy-D-*erythro*-hexoside (**10**) and methyl 2,3-di-*O*-benzyl-D-glucoside (**11**). Compounds **10** and **11** were transformed into derivatives **16** and **17**, respectively, by standard methods,[9] while the corresponding tosylate **29** and mesylate **30** were obtained by a similar standard reaction sequence from compound **26**. It is worth noting that rearrangement of the allyl ether **27** in the presence of a large excess of potassium *tert*-butoxide (4 times molar equiv) caused simultaneous 6-*O*-desilylation. The *Z* configuration of propenyl ethers **16**, **17**, and **28**–**30** was assigned on the basis of the vicinal coupling constants between olefinic protons (*J* 6.2 Hz).



10: $R^1 = R^2 = H$
12: R^1 = Tr, $R^2 = H$
14: R^1 = Tr, R^2 = All
16: R^1 = Tr, R^2 = 
18: R^1 = TBDPS, $R^2 = H$
20: R^1 = TBDPS, R^2 = PMB
22: $R^1 = H$, R^2 = PMB
24: R^1 = Tf, R^2 = PMB
26: R^1 = TBS, $R^2 = H$
27: R^1 = TBS, R^2 = All
28: $R^1 = H$, R^2 = 
29: R^1 = Ts, R^2 = 
30: R^1 = Ms, R^2 =



11: $R^1 = R^2 = H$
13: R^1 = Tr, $R^2 = H$
15: R^1 = Tr, R^2 = All
17: R^1 = Tr, R^2 = 
19: R^1 = TBS, $R^2 = H$
21: R^1 = TBS, R^2 = PMB
23: $R^1 = H$, R^2 = PMB
25: R^1 = Tf, R^2 = PMB

The [2 + 2] cycloaddition of CSI to **16**, followed by the reduction of the *N*-chlorosulfonyl group of the adduct with bis-(2-methoxyethoxy)aluminum hydride (Red-Al, Aldrich), led to the β-lactam **33** as a sole product in 54% yield. The trityl protecting group in **33** was then removed cleanly by treatment with sodium in liquid ammonia to give **34** in 85% yield. The hydroxy group in **34** was subsequently tosylated under standard conditions affording **35**. Intramolecular alkylation of the β-lactam nitrogen atom in **35** using a two-phase system led to oxacepham **37** in 86% yield. The molecular structure assignment and 6S-configuration of **37** was proved by NOE measurement between H-4 and H-6. The lack of any spin–spin interaction between both protons indicated their anti arrangement. The NMR assignment has been also supported by CD spectroscopy.[11]

The cycloaddition performed with **29** gave two corresponding azetidin-2-ones **35** and **38** in a ratio of 1.5:1, respectively, in 65% yield. The same reaction carried out using mesylate **30** yielded diastereomers **36** and **39** in a ratio of 1.6:1, respectively. These results indicate the existence of a steric control during cycloaddition. Intramolecular alkylation of the nitrogen atom carried out with either mixtures **35**/**38** or **36**/**39** led to oxacephams **37** and **40**. In both instances, the proportion of isomeric cephams **37** and **40** remained the same as in the substrates **35**/**38** and **36**/**39**. Chromatographic separation of **37** and **40** allowed one to characterize cepham **40**

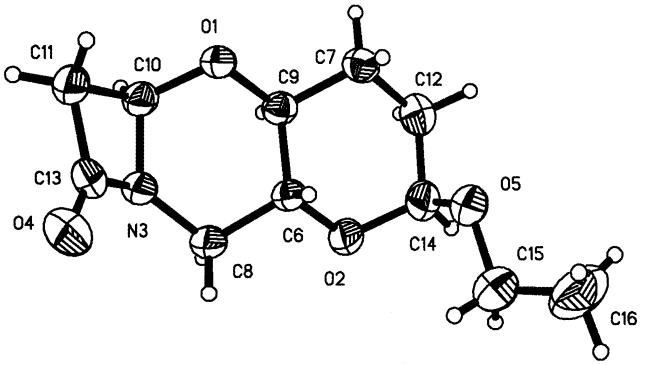
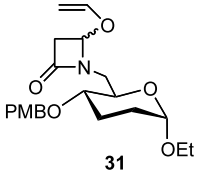


Fig. 1. X-Ray structure of compound **41a** with crystallographical numbering scheme.

in which H-4 and H-6 show NOE effects, indicating presence of the *cis* arrangement of both protons. Analogously to cepham **37**, the NMR assignment made for **40** was also supported by the CD spectroscopy.[11]



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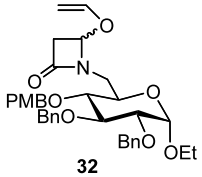

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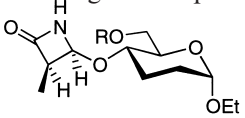
Stereocontrolled formation of the 6R-configuration in the same strained tricyclic skeleton can be achieved by the second methodology as outlined above. Starting triflate **24** was obtained from compound **10** by a standard sequence of reactions involving silylation of the terminal group, protection of the secondary hydroxy group in **18** by a *p*-methoxybenzyl residue, desilylation of **20** leading to **22**, and finally the formation of triflate **24**. Alkylation of 4-vinyloxyazetidin-2-one **5** with the triflate **24** gave mixture of diastereomers **31**, which was treated with a Lewis acid to give cephams **41**. Acidic conditions that were necessary during the intramolecular substitution at C-4′ of the azetidin-2-one ring caused partial epimerization at the acetal center (C-2) of the product. The structure and configuration of crystalline compound **41a** was proved by the single-crystal X-ray analysis (Fig. 1, Table 1).[10] Partial hydrolysis of the acetal moiety in **37**, followed by the oxidation of resulting hemiacetal, yielded lactone **42**, which does offer an entry to the related cephams with a side chain at C-4 (side chains that are located in a related position are present in many natural clavams **43**[12]).

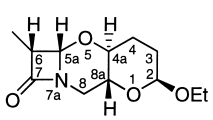
Table 1
Crystal data and structure refinement for compound **41a**

Empirical formula	$C_{11}H_{17}NO_4$
Formula weight	227.26
Crystal system, space group	orthorhombic, $P2_12_12_1$
Unit cell dimensions (Å)	
a	4.9595(2)
b	8.7112(7)
c	27.1774(17)
Volume (Å^3)	1174.15(13)
Z, calculated density (Mg m^{-3})	4, 1.286
Absorption coefficient (mm^{-1})	0.814
F(000)	488
θ range for data collection (°)	3.25–73.86
Reflections collected/unique	1438/1138 [R(int) = 0.0430]
Max. and min. transmission	99.93 and 89.60
Data/restraints/parameters	1138/0/147
Goodness-of-fit on F^2	1.118
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0559$, $wR_2 = 0.1763$
Absolute structure parameter	0.7(6)
Extinction coefficient	0.008(2)
Largest difference peak and hole (e Å^{-3})	0.255 and −0.270

The [2 + 2] cycloaddition of CSI to the propenyl ether **17** proceeded in a high yield (89%) and with a low stereoselectivity to give diastereomer **44** with 50% *de*. Both equatorial substituents in the vicinity of the propenyl ether fragment shield diastereotopic faces of the olefin, but the presence of the bulky trityloxymethyl group played a decisive role in the direction of asymmetric induction.



33: R = Tr
34: R = H
35: R = Ts
36: R = Ms



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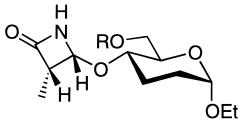
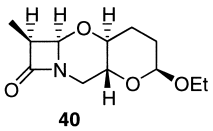


38: R = Ts
39: R = Ms



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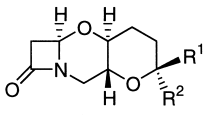
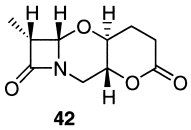


41a: R^1 = OEt, R^2 = H
41b: R^1 = H, R^2 = OEt



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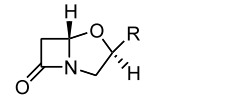
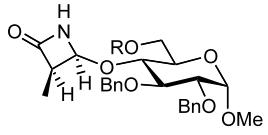
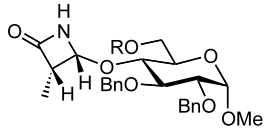


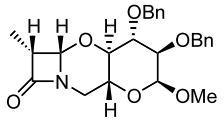
43: R = OH, OH, CO_2H, NH_2



44: R = Tr
46: R = H
48: R = Ts



45: R = Tr
47: R = H
49: R = Ts



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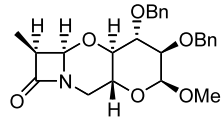

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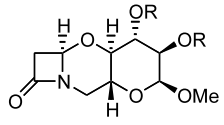

52: R = Bn
53: R = H
54: R = Ac

Mixture **44**/**45** was detritylated, the free terminal hydroxy group was subsequently tosylated, and the resulting tosylates **48**/**49** were in turn subjected to the intramolecular alkylation of the nitrogen atom leading to oxacephams **50**/**51**, which were separated by chromatography into the pure components. The configuration of compounds **51** and **52** was indicated by NOE measurements between the H-4a and H-5a protons. Compound **51** displayed a spin–spin interaction between both protons, whereas diastereomeric compound **50** did not show any interactions.

The second methodology when applied to the β-lactam **33**, which is readily available from glycoside **11**, produced as a sole product compound **52** with the R-configuration at C-6. Benzylic groups in **52** were removed by hydrogenolysis to provide hydrophilic cepham **53** which was characterized as diacetate **54**.

Selected tricyclic β-lactams **7**, **8**, **9**, **37**, **40**, **41a**, and **41b** were evaluated for their biological activities. An inhibition of the DD-carboxypeptidase activity was measured.[13,14] Compounds **9**, **37**, and **40** showed slight activity (20–30% inhibition) at a concentration of 10^{-3} M. We were not able to find any significant differences between the biological activities of tested compounds, and, therefore, at this level of inhibition, structure–activity relationships could not be defined.

3. Conclusions

It was demonstrated that the configuration at the bridgehead carbon atom (C-5a), which is important for the biological activity of β-lactam antibiotics, could be controlled by the selection of strategy used for oxacepham formation. The [2 + 2] cycloaddition method led to diastereomers with the S-configuration at C-5a, whereas the cyclization method provided compounds with an alternative R-configuration at that center. The latter proceeded with better stereoselectivity, particularly for chiral substrates in which diastereotopic faces of the vinyl ether were similarly shielded. The trans-fused ring system provides a rigid template that introduces an alternation of geometry of the β-lactam ring. This, however, was not reflected in the extent of measured biological activity of the products. It was shown that the sugar fragments in the synthesized tricyclic β-lactams can readily be subjected to further transformations.

4. Experimental

Melting points were determined on a Koefler hot-stage apparatus. ^{1}H NMR spectra were recorded using Brucker Avance 500 and Varian Mercury 400 instruments. IR spectra were recorded on a Perkin–Elmer FTIR Spectrum 200 spectrophotometer. Mass spectra were recorded using AMD-604 Inectra GmbH and HPLC–MS with Mariner and API 356 detectors. Optical rotations were measured using a Jasco P 3010 polarimeter at 22 ± 3 °C. Column chromatography was performed using E. Merck Kiesel Gel (230–400 mesh). Compounds **12**,[15] **13**,[16] **15**[17] and **19**[18] were obtained following the indicated literature procedures.

*Methyl 2,3-di-*O*-benzyl-6-*O*-trityl-α-*D*-glucopyranoside* (**13**).—The compound was obtained following the literature procedure[16] (98%). Foam; $[\alpha]_D$ +31.5° (*c* 0.9, CH_2Cl_2); IR (film): ν_{max} 3472 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$): δ 7.46–7.20 (m, 25 H, trityl, benzyl), 4.96,

4.74 (2 d, 2 H, *J* 11.3 Hz, Bn), 4.78, 4.68 (2 d, 2 H, *J* 12.1 Hz, Bn), 4.67 (d, 1 H, *J* 3.6 Hz, H-1), 3.69 (ddd, 1 H, *J* 3.6, 5.2, 9.3 Hz, H-5), 3.77 (t, 1 H, *J* 9.2 Hz, H-3), 3.55 (ddd, 1 H, *J* 2.4, 9.7, 9.7 Hz, H-4), 3.52 (dd, 1 H, *J* 3.6, 9.6, H-2), 3.42 (s, 3 H, OCH_3), 3.35 (dd, 1 H, *J* 3.5, 10.0 Hz, H-6), 3.29 (dd, 1 H, *J* 5.3, 10.0 Hz, H-6′), 2.23 (d, 1 H, *J* 2.5 Hz, OH); ESIHRMS: Calcd for $C_{40}H_{40}NaO_6$: 639.2718; found: *m*/*z* 639.2717 $[M + Na]^+$.

*Ethyl 4-*O*-allyl-2,3-dideoxy-6-*O*-trityl-α-*D*-erythro-hexopyranoside* (**14**).—To a solution of compound **12** (0.97 g, 2.3 mmol) in dry toluene (10 mL) powdered KOH (0.14 g, 2.5 mmol) was added. The suspension was stirred for 20 min, and then allyl bromide (0.17 mL, 2.7 mmol) and 0.02 g Bu_4NBr were added. Stirring was continued for 2 h until disappearance of the substrate was indicated (TLC). The mixture was then filtered through Celite, and the solvent was evaporated. The residue was purified by column chromatography using 9:1 hexane–ethyl acetate as an eluant to give product **14** (0.72 g, 72%). Colorless oil; $[\alpha]_D$ +85.7° (*c* 0.8, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 7.51–7.19 (m, 15 H, trityl), 5.66 (m, 1 H, H-2′), 5.04 (m, 1 H, H-3′a), 5.01 (m, 1 H, H-3′b), 4.87 (bs, 1 H, H-1), 3.94, 3.73 (2 m, 2 H, H-1′a, 1′b), 3.83, 3.51 (2 dq, 2 H, Et), 3.78 (ddd, 1 H, *J* 1.9, 5.2, 9.5 Hz, H-5), 3.39 (bdt, 1 H, *J* 4.9, 9.5, 11.1 Hz, H-6b), 1.98–1.71 (m, 4 H, H-2a, 2b, 3a, 3b), 1.24 (t, 3 H, Et); ESIHRMS: Calcd for $C_{30}H_{34}NaO_4$: 481.2349; found: *m*/*z* 481.2343 $[M + Na]^+$.

*Methyl 4-*O*-allyl-2,3-di-*O*-benzyl-6-*O*-trityl-α-*D*-glucopyranoside* (**15**).—The compound was obtained following the literature procedure[17] (94%). Foam; $[\alpha]_D$ +43.1° (*c* 1.2, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 7.46–7.20 (m, 25 H, trityl, benzyl), 5.53 (m, 1 H, H-2′), 4.97 (m, 2 H, H-3′a,b), 4.90, 4.82 (2 d, 2 H, *J* 12.1 Hz, Bn), 4.77, 4.71 (2 d, 2 H, *J* 10.7 Hz, Bn), 4.74 (d, 1 H, *J* 3.6 Hz, H-1), 4.10 (qt, 1 H, *J* 1.4, 5.9 Hz, H-1′a), 3.88 (t, 1 H, *J* 9.3 Hz, H-3), 3.76 (qt, 1 H, *J* 1.4, 5.8 Hz, H-1′b), 3.72 (ddd, 1 H, *J* 2.0, 4.5, 9.5 Hz, H-5), 3.58 (dd, 1 H, *J* 3.6, 9.6, H-2), 3.47 (dd, 1 H, *J* 9.0, 9.9 Hz, H-4), 3.44 (s, 3 H, OCH_3), 3.41 (dd, 1 H, *J* 2.0, 10.1 Hz, H-6), 3.11 (dd, 1 H, *J* 4.6, 10.1 Hz, H-6′); ESIHRMS: Calcd for $C_{43}H_{44}NaO_6$: 679.3035; found: *m*/*z* 679.3069 $[M + Na]^+$.

*Ethyl 2,3-dideoxy-(Z)-4-*O*-propenyl-6-*O*-trityl-α-*D*-erythro-hexopyranoside* (**16**).—The solution of allyl ether **14** (0.7 g, 1.55 mmol) and freshly sublimed *t*-BuOK (1.7 mmol) in DMSO (10 mL) was left standing for 1.5 h (TLC monitoring) at 50 °C. Subsequently, the mixture was poured into satd aq NaCl and extracted with *t*-BuOMe (3 × 25 mL). The organic layer was washed with water, dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography using 95:5 hexane–EtOAc as the eluant to give the product **16** (0.608 g, 86%). Colorless oil; $[\alpha]_D$ +11.3° (*c* 0.2, CH_2Cl_2); IR ($CHCl_3$): ν_{max} 1667 cm^{-1} (C=C-O); ^1H NMR ($CDCl_3$): δ 7.50–7.19 (m, 15 H, trityl), 5.86 (dq, 1 H, *J* 6.2, 1.7 Hz, H-1′), 4.88 (bd, 1 H, *J* 3.2 Hz, H-1), 4.20 (dq, 1 H, *J* 6.2, 6.7 Hz, H-2′), 3.88–3.81 (m, 2 H, H-5, Et), 3.63 (dt, 1 H, *J* 4.9, 9.8 Hz, H-4), 3.52 (dq, 1 H, Et), 3.35 (dd, 1 H, *J* 1.9, 9.9 Hz, H-6a), 3.16 (dd, 1 H, *J* 5.5, 9.9 Hz, H-6b), 1.96–1.73 (m, 4 H, H-2,2a,3,3a), 1.33 (dd, 3 H, *J* 1.6, 6.7 Hz, CH_3), 1.26 (t, 3 H, Et); ESIHRMS: Calcd for $C_{30}H_{34}NaO_4$: 481.2349; found: *m*/*z* 481.2361 $[M + Na]^+$.

*Methyl 2,3-di-*O*-benzyl-(Z)-4-*O*-propenyl-6-*O*-trityl-α-*D*-glucopyranoside* (**17**).—Compound **17** was obtained from **15** following the procedure described for **16** (85%). Colorless foam; $[\alpha]_D$ +42.4° (*c* 0.8, CH_2Cl_2); IR (film): ν_{max} 1668 cm^{-1} (=CH-O-); ^1H NMR ($CDCl_3$): δ 7.46–7.18 (m, 25 H, trityl, benzyl), 5.97 (dq, 1 H, *J* 6.2, 1.7 Hz, H-1′), 4.83, 4.71 (2 d, 2 H, *J* 12.2 Hz, Bn), 4.79, 4.74 (2 d, 2 H, *J* 10.5 Hz, Bn), 4.73 (d, 1 H, *J* 3.6 Hz, H-1), 4.14 (dq, 1 H, *J* 6.2, 6.8 Hz, H-2′), 3.90 (dd, 1 H, *J* 8.6, 9.8 Hz, H-3), 3.79 (ddd, 1 H, *J* 1.7, 4.4, 10.0 Hz, H-5), 3.75 (dd, 1 H, *J* 8.5, 10.0 Hz, H-4), 3.57 (dd, 1 H, *J* 3.6, 9.6 Hz, H-2), 3.44 (s, 3 H, OCH_3), 3.37 (dd, 1 H, *J* 1.7, 10.2 Hz, H-6), 3.26 (dd, 1 H, *J* 4.4, 10.2 Hz, H-6′); ESIHRMS: Calcd for $C_{43}H_{44}NaO_6$: 679.3035; found: *m*/*z* 679.3057 $[M + Na]^+$.

*Ethyl 6-*O*-tert-butyldiphenylsilyl-2,3-dideoxy-α-*D*-erythro-hexopyranoside* (**18**).—Compound **18** was obtained from **10** following standard silylation procedures (98%). Colorless oil; $[\alpha]_D$ +43.8° (*c* 0.6, CH_2Cl_2); IR (film): ν_{max} 3470 cm^{-1} (OH); ^1H NMR ($CDCl_3$): δ 7.71–7.37 (m, 10 H, 2 Ph), 4.71 (bd, 1 H, *J* 2.9 Hz, H-1), 3.83 (dd, 1 H, *J* 4.8, 10.3 Hz, H-6), 3.81 (dd, 1 H, *J* 6.1, 10.3 Hz, H-6′), 3.66 (dt, 1 H, *J* 4.9, 9.2 Hz, H-4), 3.63 (m, 1 H, H-5), 3.59, 3.37 (2 dq, 2 H, Et), 1.90–1.62 (m, 4 H, H-2,2′,3,3′), 1.18 (t, 3 H, Et), 1.07 (s, 9 H, *t*-Bu); ESIHRMS: Calcd for $C_{24}H_{34}NaO_4Si$: 437.2119; found: *m*/*z* 437.2143 $[M + Na]^+$.

*Ethyl 6-*O*-tert-butyldiphenylsilyl-2,3-dideoxy-4-*O*-p-methoxybenzyl-α-*D*-erythro-hexopyranoside* (**20**).—To a solution of compound **18** (0.7 g, 1.7 mmol) in dry toluene (10 mL) powdered KOH (0.114 g, 2.04 mmol) was added. The resulting suspension was stirred for 20 min, and then *p*-$MeOC_6H_4CH_2Cl$ (0.28 mL, 2.04 mmol) and 0.04 g Bu_4NBr was added. Stirring was continued for 2 h until disappearance of the substrate was indicated (TLC). The mixture was then filtered through Celite, and the solvent was evaporated. The residue was purified by column chromatography using 9:1 hexane–EtOAc as the eluant to give the product **20** (0.69 g, 70%). Colorless oil; $[\alpha]_D$ +76.1° (*c* 0.5, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 7.75–7.34 (m, 10 H, 2 Ph), 7.13, 6.81 (2 m, 4 H, -C_6H_4-), 4.83 (bd, 1 H, *J* 3.0 Hz, H-1), 4.54, 4.35 (2 d, 2 H, *J* 11.1 Hz, $ArCH_2$), 3.79 (s, 3 H, OCH_3), 3.77, 3.46 (2 dq, 2 H, Et), 3.74 (m, 1 H, H-5), 3.46 (m, 1 H, H-42.05–1.66 (m, 4 H, H-2,2′,3,3′), 1.21 (t, 3 H, Et), 1.06 (s, 9 H, *t*-Bu); ESIHRMS: Calcd for $C_{32}H_{42}NaO_5Si$: 557.2694; found: *m*/*z* 557.2701 $[M + Na]^+$.

Methyl 2,3-di-O-*benzyl-6*-O-tert-*butyldimethylsilyl-4*-O-p-*methoxybenzyl-α*-D-*glucopyranoside* (**21**).—Compound **21** was obtained from known compound **19**[18] according to the procedure described for **20** (95%). Colorless oil; $[\alpha]_D$ +22.3° (*c* 1.7, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 7.38–7.26 (m, 20 H, 2 Ph, benzyl), 7.20, 6.85 (2 m, 4 H, C_6H_4), 4.97, 4.67 (2 d, 2 H, *J* 10.8 Hz, Bn), 4.80, 4.57 (2 d, 2 H, *J* 10.6 Hz, Bn), 4.78, 4.67 (2 d, 2 H, *J* 12.0 Hz, Bn), 4.60 (d, 1 H, *J* 3.6 Hz, H-1), 3.97 (dd, 1 H, *J* 8.9, 9.6 Hz, H-3), 3.79 (s, 3 H, OCH_3), 3.77 (dd, 1 H, *J* 2.6, 11.3 Hz, H-6), 3.75 (dd, 1 H, *J* 3.8, 11.3 Hz, H-6′), 3.59 (ddd, 1 H, *J* 2.6, 3.8, 9.8 Hz, H-5), 3.49 (dd, 1 H, *J* 8.9, 9.8 Hz, H-4), 3.48 (dd, 1 H, *J* 3.6, 9.6 Hz, H-2), 3.36 (s, 3 H, OCH_3), 0.89, 0.05, 0.04 (3 s, 15 H, *t*-BuMe_2Si); ESIHRMS: Calcd for $C_{35}H_{48}O_7$NaSi: 631.3062; found: *m*/*z* 631.3070 $[M+Na]^+$.

Ethyl 2,3-dideoxy-4-O-p-*methoxybenzyl-α*-D-erythro-*hexopyranoside* (**22**).—To a solution of **20** (0.6 g, 1.5 mmol) in dry THF (10 mL) TBAF (0.2 g, 1.65 mmol) was added. The reaction was stirred for 20 h (TLC monitoring). The mixture was subsequently evaporated, and the residue was purified by column chromatography using 3:2 hexane–EtOAc as the eluant to give the product **22** (0.36 g, 83%). Colorless oil; $[\alpha]_D$ +116.4° (*c* 0.7, CH_2Cl_2); IR (film): ν_{max} 3470 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$): δ 7.25, 6.87 (2 m, 4 H, -C_6H_4-), 4.78 (bd, 1 H, *J* 3.3 Hz, H-1), 4.58, 4.40 (2 d, 2 H, *J* 11.2 Hz, $ArCH_2$), 3.80 (s, 3 H, OCH_3), 3.78 (dd, 1 H, *J* 3.4, 10.0 Hz, H-6), 3.70 (m, 3 H, H-5,6,O**C**$H_A$$H_B$$CH_3$), 3.42 (m, 2 H, H-5,6,$OCH_A$**H**$_B$$CH_3$), 2.04–1.62 (m, 4 H, H-2,2′,3,3′), 1.20 (t, 3 H, Et), 1.07 (s, 9 H, *t*-Bu); ESIHRMS: Calcd for $C_{16}H_{24}NaO_5$: 319.1516; found: *m*/*z* 319.1521 $[M+Na]^+$.

Methyl 2,3-di-O-*benzyl-4*-O-p-*methoxybenzyl-α*-D-*glucopyranoside* (**23**).—Known compound **23**[19] was obtained from **21** following the procedure described for **22** (98%).

Ethyl 2,3-dideoxy-4-O-p-*methoxybenzyl-6*-O-*triflyl-α*-D-erythro-*hexopyranoside* (**24**).—2,6-Lutidine (0.16 mL, 1.3 mmol) was dissolved under argon in dry CH_2Cl_2 (10 mL). Upon cooling to −20 °C, triflic anhydride (0.21 mL, 1.3 mmol) was added dropwise. Stirring was continued for 5 min, and then solution of compound **22** (0.3 g, 1.0 mmol) in CH_2Cl_2 (1 mL) was added dropwise. Stirring was continued at −20 °C for 5 min, then the solution was warmed up to 0 °C and poured into ice-water (10 mL). The organic phase was separated, washed with cold water (3 × 10 mL), dried ($MgSO_4$) and evaporated. The crude oil was dissolved in *t*-BuOMe (~10 mL) and triturated with hexane (~20 mL). The precipitate was filtered off through Celite, and the filtrate was concentrated to give crude triflate **24**, which was immediately used for the subsequent step without further purification.

Methyl 2,3-di-O-*benzyl-4*-O-p-*methoxybenzyl-6*-O-*triflyl-α*-D-*glucopyranoside* (**25**).—Compound **25** was obtained from **23** following procedure described for **24** (80%) and used in the next step as a crude yellow oil.

Ethyl 6-O-tert-*butyldimethylsilyl-2,3-dideoxy-α*-D-erythro-*hexopyranoside* (**26**).—Compound **26** was obtained form **10** following standard silylation procedure (96%). Colorless oil; $[\alpha]_D$ +183.5° (*c* 1.0, CH_2Cl_2); IR (film): ν_{max} 3451 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$): δ 4.77 (bd, 1 H, *J* 3.1 Hz, H-1), 3.85 (dd, 1 H, *J* 4.4, 10.0 Hz, H-6), 3.73, 3.69 (2 m, 2 H, H-6′, H-4), 3.63 (ddd, 1 H, *J* 1.9, 4.7, 9.1 Hz, H-5), 3.46, 3.43 (2 dq, 2 H, Et), 3.29 (d, 1 H, *J* 1.5, OH), 1.87–1.65 (m, 4 H, H-2,2′,3,3′), 1.22 (t, 3 H, Et), 0.91 (s, 9 H, *t*-Bu), 0.1 (2 s, 6 H, Me); ESIHRMS: Calcd for $C_{14}H_{30}NaO_4Si$: 313.1824; found: *m*/*z* 313.1806 $[M+Na]^+$.

Ethyl 4-O-*allyl-2,3-dideoxy-6*-O-tert-*butyldimethylsilyl-α*-D-erythro-*hexopyranoside* (**27**).—Compound **27** was obtained from **26** following the procedure described for **14** (80%). Colorless oil; $[\alpha]_D$ +109.6° (*c* 2.5, CH_2Cl_2); ^{1}H NMR ($CDCl_3$): δ 5.94 (m, 1 H, H-2′), 5.30 (dq, 1 H, *J* 17.2, 1.7 Hz, H-3′a), 5.18 (dq, 1 H, *J* 10.4, 1.3 Hz, H-3′b), 4.83 (d, 1 H, *J* 3.0 Hz, H-1), 4.14, 3.97 (2 m, 2 H, H-1′a,1′b), 3.87 (dd, 1 H, *J* 2.0, 11.1 Hz, H-6a), 3.83 (dd, 1 H, *J* 5.0, 11.1 Hz, H-6b), 3.77, 3.47 (2 dq, 2 H, Et), 3.64 (ddd, 1 H, *J* 2.0, 3.0, 9.3 Hz, H-5), 3.36 (m, 1 H, H-4), 2.04–1.66 (m, 4 H, H-2,2a,3,3a), 1.24 (t, 3 H, CH_3), 0.95, 0.11 (2 s, 15 H, TBS); ESIHRMS: Calcd for $C_{17}H_{34}NaO_4Si$: 353.2119; found: *m*/*z* 353.2128 $[M+Na]^+$.

Ethyl 2,3-dideoxy-(Z)-4-O-*propenyl-α*-D-erythro-*hexopyranoside* (**28**).—A solution of allyl ether **27** (0.45 g, 1.4 mmol) and freshly sublimed *t*-BuOK (4.8 mmol) in DMSO (10 mL) was left for 2 h (TLC monitoring) at 50 °C. The mixture was poured into satd aq NaCl and extracted with *t*-BuOMe (3 × 10 mL). The organic layer was washed with water, dried ($MgSO_4$) and concentrated. The crude product **28** was used in the next step without any purification.

Ethyl 2,3-dideoxy-(Z)-4-O-*propenyl-6*-O-*tosyl-α*-D-erythro-*hexopyranoside* (**29**).—Compound **29** was obtained from **28** following the procedure described for **35** (70%). Colorless oil; $[\alpha]_D$ +118.5° (*c* 0.9, CH_2Cl_2); IR ($CHCl_3$): ν_{max} 1668 cm^{-1} (=CH-O-); ^{1}H NMR ($CDCl_3$): δ 7.79, 7.32 (2 m, 4 H, C_6H_4), 5.85 (dq, 1 H, *J* 6.1, 1.7 Hz, H-1′), 4.73 (d, 1 H, *J* 3.2 Hz, H-1), 4.36 (dq, 1 H, *J* 6.1, 6.8 Hz, H-2′), 4.23 (dd, 1 H, *J* 2.0, 10.5 Hz, H-6), 4.17 (dd, 1 H, *J* 5.0, 10.5 Hz, H-6′), 3.81 (ddd, 1 H, *J* 2.0, 5.0, 9.7 Hz, H-5), 3.64, 3.40 (2 dq, 2 H, Et), 3.48 (m, 1 H, H-4), 2.44 (s, 3 H, CH_3), 2.0–1.62 (m, 4 H, H-2,2a,3,3a), 1.46 (dd, 1 H, *J* 1.7, 6.8 Hz, CH_3), 1.18 (t, 3 H, CH_3); ESIHRMS: Calcd for $C_{19}H_{26}NaO_6S$: 393.1342; found: *m*/*z* 393.1352 $[M+Na]^+$.

Ethyl 2,3-dideoxy-6-O-*mesyl-(Z)-4*-O-*propenyl-α*-D-erythro-*hexopyranoside* (**30**).—To a solution of compound **28** (0.11 g, 0.5 mmol) in dry pyridine (5 mL),

MsCl (0.04 mL, 0.56 mmol) was added at 0 °C, and mixture was left for 5 h at 20 °C. The reaction mixture was diluted with water (15 mL) and extracted with toluene (3 × 5 mL). Combined organic layers were dried over $MgSO_4$, filtered and concentrated to dryness. The residue was purified by column chromatography on a silica gel using 4:1 hexane–EtOAc as the eluant to give the product **30** (0.1 g, 68%). Colorless oil; $[\alpha]_D$ + 82.0° (*c* 0.4, CH_2Cl_2); IR ($CHCl_3$): ν_{max} 1668 cm^{-1} (=CH-O-); ^1H NMR ($CDCl_3$): δ 5.97 (dq, 1 H, *J* 6.2, 1.7 Hz, H-1′), 4.81 (bd, 1 H, *J* 3.4 Hz, H-1), 4.47 (dq, 1 H, *J* 6.2, 6.8 Hz, H-2′), 4.43 (dd, 1 H, *J* 2.3, 11.1 Hz, H-6), 4.40 (dd, 1 H, *J* 4.6, 11.1 Hz, H-6′), 3.92 (ddd, 1 H, *J* 2.3, 4.6, 9.7 Hz, H-5), 3.72, 3.46 (2 dq, 2 H, Et), 3.56 (m, 1 H, H-4), 3.03 (s, 3 H, CH_3), 2.01–1.67 (m, 4 H, H-2,2a,3,3a), 1.66 (dd, 1 H, *J* 1.7, 6.8 Hz, CH_3), 1.23 (t, 3 H, Et); ESIHRMS: Calcd for $C_{12}H_{22}NaO_6S$: 317.1020; found: *m*/*z* 317.1033 $[M + Na]^+$.

*Ethyl 2,3,6-trideoxy-4-*O-p-*methoxybenzyl-6-*C-*(4′*R,*4′*S)-(4′-vinyloxyazetidin-2′-on-1′-yl)-α-*D-erythro-*hexopyranoside* (**31**).—To a stirred suspension of finely powdered Bu_4NHSO_4 (0.19 g, 0.55 mmol) in dry THF (10 mL) under argon was added 4-vinyloxyazetidin-2-one (0.057 g, 0.5 mmol). Subsequently, upon cooling to − 78 °C, BuLi (0.56 mL of 2 M in hexane, 1.13 mmol) was added, followed after 20 min by crude triflate **24** (∼ 0.7 mmol) in dry THF (3 mL). Stirring was continued at − 78 °C for 15 min. Subsequently, the mixture was allowed to slowly warm up to room temperature and stand for an additional 15 min. The reaction mixture was poured into water (15 mL) and extracted with *t*-BuOMe (3 × 10 mL). The combined organic extracts were washed with water, dried ($MgSO_4$) and evaporated. The crude product was purified on silica gel using 4:1 hexane–EtOAc as the eluant to give a mixture **31** (0.15 g, 52%). Colorless oil; IR (film): ν_{max} 1768 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) selected signals of both diastereomers: δ 6.45 and 6.40 (2 dd, 1 H, *J* 6.6, 14.2 Hz, =CHO- of both diastereomers), 5.38 and 5.34 (2 dd, 1 H, *J* 1.1, 3.6 Hz, H-4′ of both diastereomers), 4.76 and 4.75 (2 dd, 1 H, *J* 2.9 Hz, H-1 of both diastereomers), 3.80, 3.79 (2 s, 3 H, OCH_3 of both diastereomers); ESIHRMS: Calcd for $C_{21}H_{29}NNaO_6$: 414.1887; found: *m*/*z* 414.1898 $[M + Na]^+$.

*Methyl 2,3-di-*O-*benzyl-6-deoxy-4-*O-p-*methoxybenzyl-6-*C-*(4′*R,*4′*S)-(4′-vinyloxyazetidin-2′-on-1′-yl)-α-*D-glucopyranoside* (**32**).—A mixture **32** was obtained from **25** according to the procedure described for **31** (72%). Colorless oil; IR (film): ν_{max} 1769 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) selected signals of both diastereomers: δ 6.42 and 6.34 (2 dd, 1 H, *J* 6.6, 14.2 Hz, =CHO- of both diastereomers), 5.34 and 5.30 (2 dd, 1 H, *J* 1.0, 3.6 Hz, H-4′ of both diastereomers), 3.80, 3.79 (2 s, 3 H, OCH_3 of both diastereomers); ESIHRMS: Calcd for $C_{34}H_{39}NNaO_8$: 612.2568; found: *m*/*z* 612.2555 $[M + Na]^+$.

*Ethyl 2,3-dideoxy-4-*O-*(3′*R,*4′*S)-(3′-methylazetidin-2′-on-4′-yl)-6-*O-*trityl-α-*D-erythro-*hexopyranoside* (**33**).—To a suspension of anhyd Na_2CO_3 (0.26 g, 2.4 mmol) in dry toluene (2.5 mL) chlorosulfonyl isocyanate (0.17 g, 1.95 mmol) was added. The mixture was stirred, and upon cooling to − 78 °C a solution of vinyl ether **16** (0.45 g, 0.98 mmol) in toluene (0.5 mL) was added dropwise. Stirring was continued for 1.5 h, then the mixture was diluted with toluene (3 mL), treated with $[(MeOCH_2CH_2O)_2AlH_2]Na$ (Red-Al, 1 M in toluene, 1.95 mL), and left for 30 min, continuously maintaining a temperature of − 78 °C. Subsequently, the temperature was allowed to rise to 0 °C, water (0.1 mL) was added, and the solution was stirred for 15 min. The mixture was filtered through Celite, and the solvent was evaporated. The residue was purified by silica gel column chromatography using 3:2 hexane–EtOAc. Obtained **33** (0.26 g, 54%). Colorless crystals; mp 118–120 °C; $[\alpha]_D$ + 51.0° (*c* 0.7, CH_2Cl_2); IR ($CHCl_3$): ν_{max} 3411 (NH), 1770 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 7.50–7.20 (m, 15 H, trityl), 6.03 (bs, 1 H, NH), 4.90 (bd, 1 H, *J* 2.4 Hz, H-1), 4.85 (d, 1 H, *J* 4.4 Hz, H-4′), 3.83, 3.53 (2 dq, 2 H, Et), 3.78 (ddd, 1 H, *J* 1.8, 4.8, 9.5 Hz, H-5), 3.58 (m, 1 H, H-4), 3.38 (dd, 1 H, *J* 1.8, 9.9 Hz, H-6a), 3.09 (dd, 1 H, *J* 4.9, 9.9 Hz, H-6b), 2.93 (qdd, 1 H, *J* 7.6, 2.3, 4.4 Hz, H-3′), 2.0–1.75 (m, 4 H, H-2,2a,3,3a), 1.26 (t, 3 H, Et), 1.04 (d, 1 H, *J* 7.6 Hz, CH_3); ESIHRMS: Calcd for $C_{31}H_{35}NNaO_5$: 524.2407; found: *m*/*z* 524.2406 $[M + Na]^+$.

*Ethyl 2,3-dideoxy-4-*O-*(3′*R,*4′*S)-(3′-methylazetidin-2′-on-4′-yl)-α-*D-erythro-*hexopyranoside* (**34**).—Compound **33** (0.23 g, 0.46 mmol) in dry THF (1 mL) was added to a stirred solution of sodium metal (0.106 g, 4.6 mmol) in NH_3 (liq, 20 mL). The mixture was stirred for 25 min at − 70 °C, then solid NH_4Cl (0.2 g) was added to destroy excess $NaNH_2$. After removing the cooling bath, the solvent was evaporated, and the residue was partitioned between water and THF. The aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated to dryness to give **34** (0.1 g, 85%) as a light-yellow oil. The product was used for the next step without any further purification.

*Ethyl 2,3-dideoxy-4-*O-*(3′*R,*4′*S)-(3′-methylazetidin-2′-on-4′-yl)-6-*O-*tosyl-α-*D-erythro-*hexopyranoside* (**35**).—To a solution of compound **34** (0.1 g, 0.39 mmol) in dry pyridine (3 mL) TsCl (0.46 mmol) was added at 0 °C. After 20 h at 20 °C the reaction mixture was diluted with water (5 mL) and extracted with toluene (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to dryness. The residue was purified by column chromatography on a silica gel using 1:1 hexane–EtOAc as the eluant to give **35** (0.12 g, 75%). Colorless oil; $[\alpha]_D$ + 96.8° (*c* 0.4, CH_2Cl_2); IR (film): ν_{max} 3264 (NH), 1765 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 7.79, 7.34 (2 m, 4 H, C_6H_4), 6.11

(bs, 1 H, NH), 5.03 (d, 1 H, *J* 4.4 Hz, H-4′), 4.73 (bd, 1 H, *J* 3.0 Hz, H-1), 4.32 (dd, 1 H, *J* 3.9, 10.5 Hz, H-6a), 4.09 (dd, 1 H, *J* 1.8, 10.5 Hz, H-6b), 3.78 (ddd, 1 H, *J* 1.8, 3.9, 9.5 Hz, H-5), 3.52 (m, 1 H, H-4), 3.62, 3.40 (2 dq, 2 H, Et), 3.28 (qdd, 1 H, *J* 7.6, 2.3, 4.4 Hz, H-3′), 2.45 (s, 3 H, CH_3), 2.0–1.64 (m, 4 H, H-2,2a,3,3a), 1.18 (t, 3 H, Et), 1.12 (d, 3 H, CH_3); ESIHRMS: Calcd for $C_{19}H_{27}NNaO_7S$: 436.1400; found: *m*/*z* 436.1407 $[M + Na]^+$.

*(2*S,*4a*S,*5a*S,*6*R,*8a*R*) 1,5-Dioxa-2-ethoxy-6-methyl-7a-aza-cyclobuta[*b*]decalin-7-one* (**37**).—To a solution of **35** (0.105 g, 0.25 mmol) in dry acetonitrile (10 mL) was added Bu_4NBr (0.1 g, 0.3 mmol) and K_2CO_3 (0.35 g). The mixture was heated under reflux for 3 h, cooled, diluted with toluene (10 mL) and filtered. The solution was washed with water (5 mL), dried over $MgSO_4$, filtered and concentrated to dryness. The residue was purified by column chromatography on silica gel using 3:2 hexane–EtOAc as the eluant to give **37** (0.05 g, 77%). Oil; $[\alpha]_D$ +26.8° (*c* 1.9, CH_2Cl_2); IR (film): ν_{max} 1771 cm^{-1} (C=O); ^1H NMR (C_6D_6): δ 4.69 (d, 1 H, *J* 3.3 Hz, H-5a), 4.44 (bd, 1 H, *J* 3.2 Hz, H-2), 3.77 (m, 1 H, *J* 7.6, 9.0, 9.5 Hz, H-8a), 3.65 (dd, 1 H, *J* 9.0, 12.1 Hz, H-8), 3.47, 3.13 (2 dq, 2 H, Et), 3.31 (ddd, 1 H, *J* 4.8, 9.5, 11.1 Hz, H-4a), 3.02 (ddd, 1 H, *J* 1.8, 7.6, 12.1 Hz, H-8′), 2.77 (qdd, 1 H, *J* 1.8, 3.3, 7.6 Hz, H-6), 1.94-1.23 (m, 4 H, H-3,3′,4,4′), 1.07 (d, 1 H, *J* 7.6 Hz, CH_3), 1.03 (t, 3 H, Et); ESIHRMS: Calcd for $C_{12}H_{19}NNaO_4$: 264.1206; found: *m*/*z* 264.1222 $[M + Na]^+$.

*Ethyl 2,3-dideoxy-4-*O*-(3′*S*,4′*R*)- and (3′*R*,4′*S*)-(3′-methylazetidin-2′-on-4′-yl)-6-*O*-tosyl-α-*D*-*erythro*-hexo-pyranoside* (**35**) *and* (**38**).—A mixture **35** and **38** in a ratio of 1.5:1, respectively, was obtained by addition of CSI to **29** following procedure described for **33** (65%).

Spectral data taken for the mixture **35** and **38**: IR (film): ν_{max} 3278 (NH), 1768 cm^{-1} (C=O); **35**: ^1H NMR ($CDCl_3$) selected signals: δ 6.10 (bs, 1 H, NH), 5.04 (d, 1 H, *J* 4.5 Hz, H-4′), 4.81 (bd, 1 H, *J* 3.1 Hz, H-1), 4.32 (dd, 1 H, *J* 3.9, 10.5 Hz, H-6a), 4.10 (dd, 1 H, *J* 1.9, 10.5 Hz, H-6b), 1.19 (d, 3 H, *J* 7.5 Hz, CH_3).

Compound **38**: ^1H NMR ($CDCl_3$) selected signals: δ 6.27 (bs, 1 H, NH), 4.91 (d, 1 H, *J* 4.3 Hz, H-4′), 4.81 (bd, 1 H, *J* 3.2 Hz, H-1), 4.46 (dd, 1 H, *J* 3.1, 10.5 Hz, H-6a), 3.99 (dd, 1 H, *J* 1.9, 10.4 Hz, H-6b), 1.12 (d, 3 H, *J* 7.5 Hz, CH_3); ESIHRMS: Calcd for $C_{19}H_{27}NNaO_7S$: 436.1420; found: *m*/*z* 436.1408 $[M + Na]^+$.

*Ethyl 2,3-dideoxy-6-*O*-mesyl-4-*O*-(3′*S*,4′*R*)- and (3′*R*,4′*S*)-(3′-methylazetidin-2′-on-4′-yl)-6-α-*D*-erythro-hexopyranoside* (**36**) *and* (**39**).—A mixture **36** and **39** in a ratio of 1.6:1, respectively, was obtained by addition of CSI to **30** following procedure described for **33** (42%).

Spectral data taken for the mixture **36** and **39**: IR (film): ν_{max} 3274 (NH), 1768 cm^{-1} (C=O); **36**: ^1H NMR ($CDCl_3$) selected signals: δ 6.18 (bs, 1 H, NH), 5.12 (d, 1 H, *J* 4.5 Hz, H-4′), 4.81 (bd, 1 H, *J* 3.2 Hz, H-1), 4.52 (dd, 1 H, *J* 3.8, 11.1 Hz, H-6a), 4.33 (dd, 1 H, *J* 1.9, 11.1 Hz, H-6b), 3.37 (qdd, 1 H, *J* 7.6, 2.4, 4.5 Hz, H-3′).

Compound **39**: ^1H NMR ($CDCl_3$) selected signals: δ 6.55 (bs, 1 H, NH), 5.13 (d, 1 H, *J* 4.2 Hz, H-4′), 4.82 (bd, 1 H, *J* 4.0 Hz, H-1), 4.65 (dd, 1 H, *J* 3.0, 11.0 Hz, H-6a), 4.26 (dd, 1 H, *J* 1.9, 11.0 Hz, H-6b), 3.28 (qdd, 1 H, *J* 7.6, 2.2, 4.2 Hz, H-3′); ESIHRMS: Calcd for $C_{13}H_{23}NNaO_7S$: 360.1087; found: *m*/*z* 360.1105 $[M + Na]^+$.

*(2*S,*4a*S,*5a*S,*6*R,*8a*R*) and (2*S,*4a*S,*5a*R,*6*S,*8a*R*) 2-Ethoxy-1,5-dioxa-6-methyl-7a-azacyclobuta[*b*]decalin-7-one* (**37**) *and* (**40**).—A mixture of **37** and **40** was obtained from **35** and **38** or from **36** and **39** following procedure described for **37**. Proportions of **37**/**40** were the same as in the substrate used.

Compound **40**: Oil; $[\alpha]_D$ +10.0° (*c* 2.1, CH_2Cl_2); IR (film): ν_{max} 1770 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 4.46 (bd, 1 H, *J* 3.2 Hz, H-2), 4.36 (d, 1 H, *J* 3.8 Hz, H-5a), 4.03 (dd, 1 H, *J* 6.1, 12.8 Hz, H-8), 3.66 (m, 1 H, *J* 6.1, 9.2, 10.1 Hz, H-8a), 3.42, 3.08 (2 dq, 2 H, Et), 2.90 (ddd, 1 H, *J* 4.3, 9.2, 11.4 Hz, H-4a), 2.84 (qdd, 1 H, *J* 1.6, 3.8, 7.5 Hz, H-6), 2.53 (ddd, 1 H, *J* 1.6, 10.1, 12.8 Hz, H-8′), 2.03–1.32 (m, 4 H, H-3,3′,4,4′), 1.11 (d, 1 H, *J* 7.5 Hz, CH_3), 0.95 (t, 3 H, Et); ESIHRMS: Calcd for $C_{12}H_{19}NNaO_4$: 264.1206; found: *m*/*z* 264.1215 $[M + Na]^+$.

*(2*S,*4a*S,*5a*R,*8a*R*) and (2*R,*4a*S,*5a*R,*8a*R*) 2-Ethoxy-1,5-dioxa-7a-azacyclobuta[*b*]decalin-7-one* (**41a**) *and* (**41b**).—To a stirred solution of **31** (0.1 g, 0.25 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C was added $BF_3{\cdot}Et_2O$ (0.032 g, 0.25 mmol). The mixture was allowed to warm up to room temperature and then maintained at this temperature for 15 min (TLC control). Subsequently, satd aq $NaHCO_3$ (2 mL) was added, and stirring was continued for 10 min. The organic phase was separated, washed with water, and dried ($MgSO_4$) and the solvent was evaporated. The crude products were separated on a silica gel column using 1:7:2 acetone–hexane–CH_2Cl_2 as the eluant to afford **41a** (0.033 g, 41%) and **41b** (0.006 g, 7%).

Compound **41a**: colorless crystals, mp 87–88 °C; $[\alpha]_D$ +139.6° (*c* 0.2, CH_2Cl_2); IR (film): ν_{max} 1762 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): δ 5.01 (d, 1 H, *J* 3.3 Hz, H-5a), 4.76 (d, 1 H, *J* 3.2 Hz, H-2), 3.98 (dd, 1 H, *J* 6.0, 12.8 Hz, H-8), 3.69, 3.43 (2 dq, 2 H, Et), 3.63 (dt, 1 H, *J* 6.0, 9.3, 10.0 Hz, H-8a), 3.33 (ddd, 1 H, *J* 4.7, 9.3, 10.6 Hz, H-4a), 3.13 (ddd, 1 H, *J* 1.7, 3.3, 15.0 Hz, H-6), 2.83 (dd, 1 H, *J* 0.5, 15.0 Hz, H-6′), 2.77 (ddd, 1 H, *J* 1.7, 10.2, 12.8 Hz, H-8′), 1.96–1.75 (m, 4 H, H-3,3′,4,4′), 1.22 (t, 3 H, Et); ESIHRMS: Calcd for $C_{11}H_{17}NNaO_4$: 250.1050; found: *m*/*z* 250.1089 $[M + Na]^+$.

Compound **41b**: colorless crystals, mp 135–137 °C; $[\alpha]_D$ +7.8° (*c* 0.3, CH_2Cl_2); IR (film): ν_{max} 1762 cm^{-1}

(C=O); ^{1}H NMR ($CDCl_3$): δ 5.01 (d, 1 H, *J* 3.3 Hz, H-5a), 4.51 (dd, 1 H, *J* 2.2, 9.0 Hz, H-2), 4.06 (dd, 1 H, *J* 5.7, 13.0 Hz, H-8), 3.90, 3.53 (2 dq, 2 H, Et), 3.29 (dt, 1 H, *J* 5.05, 9.1, 9.1 Hz, H-4a), 3.26 (dt, 1 H, *J* 5.7, 9.1, 9.5 Hz, H-8a), 3.14 (ddd, 1 H, *J* 1.7, 3.3, 15.0 Hz, H-6), 2.87 (ddd, 1 H, *J* 1.7, 9.5, 13.0 Hz, H-8′), 2.80 (dd, 1 H, *J* 0.5, 15.0 Hz, H-6′), 2.10–1.55 (m, 4 H, H-3,3′,4,4′), 1.22 (t, 3 H, Et); ESIHRMS: Calcd for $C_{11}H_{17}NNaO_4$: 250.1050; found: *m*/*z* 250.1076 $[M + Na]^+$.

*(4a*S,*5a*S,*6*R,*8a*R*) 1,5-Dioxa-6-methyl-7a-aza-cyclobuta[*b*]decalin-2,7-one* (**42**).—Compound **37** (0.05 g, 0.2 mmol) was dissolved in 50% aq dioxane, and *p*-TsOH (0.002 g) was added. This mixture was heated under reflux for 2.5 h, then extracted with EtOAc (3 × 5 mL) and dried over anhyd $MgSO_4$, and the solvent was evaporated to give syrup. This residue was dissolved in water (5 mL), bromine (0.05 mL) and calcium carbonate powder (0.1 g) were added, and the mixture was stirred for 0.5 h. The excess of bromine was removed with sodium bisulfite, and the product was extracted with CH_2Cl_2. The extract was dried over anhyd $MgSO_4$, and the solvent was evaporated. The residue was purified by column chromatography on silica gel using 2:3 hexane–EtOAc as the eluant to give **42** (0.02 g, 50%); oil; $[\alpha]_D$ +7.6° (*c* 0.1, CH_2Cl_2); IR (film): ν_{max} 3475 (NH), 1750 cm^{-1} (2 × C=O); ^{1}H NMR ($CDCl_3$): δ 5.03 (d, 1 H, *J* 3.7 Hz, H-5a), 4.24 (dd, 1 H, *J* 6.1, 13.2 Hz, H-8), 4.03 (dt, 1 H, *J* 6.1, 9.5, 9.8 Hz, H-8a), 3.67 (dt, 1 H, *J* 6.03, 9.5, 9.7 Hz, H-4a), 3.41 (ddq, 1 H, *J* 1.6, 3.7, 7.6 Hz, H-6), 2.95 (ddd, 1 H, *J* 1.6, 9.8, 13.2 Hz, H-8′), 2.84 (ddd, 1 H, *J* 4.9, 8.8, 17.9 Hz, H-3), 2.67 (dt, 1 H, *J* 17.9, 8.1, 8.1 Hz, H-3′), 2.27 (m, 1 H, H-4), 1.96 (m, 1 H, H-4′), 1.22 (d, 3 H, *J* 7.6 Hz, CH_3); ESIHRMS: Calcd for $C_{10}H_{13}NNaO_4$: 234.0737; found: *m*/*z* 234.0722 $[M + Na]^+$.

Methyl 2,3-di-O-*benzyl-4*-O-*(3′*R,*4′*S*)- and (3′*S,*4′*R*)-(3′-methylazetidin-2′-on-4′-yl)-6*-O-*trityl-α*-D-*glucopyranosides* (**44**) *and* (**45**).—Cycloaddition of CSI to the vinyl ether **17** was performed according to the procedure described for **33**. A mixture **44** and **45** in a ratio of 3:1, respectively, was obtained in 89% yield. Foam; IR (film) taken for the mixture: ν_{max} 3374, 3296 (NH), 1776 cm^{-1} (C=O); ^{1}H NMR (C_6D_6) taken for the mixture: **44**, δ 5.20 (bd, 1 H, NH), 5.00 (d, 1 H, 4.5 Hz, H-4′), 4.79 (d, 1 H, *J* 3.4 Hz, H-1), 4.03 (t, 1 H, *J* 8.8, 9.5 Hz, H-3), 3.88 (ddd, 1-H, *J* 1.6, 5.0, 10.0 Hz, H-5), 3.60 (dd, 1 H, *J* 3.4, 9.5 Hz, H-2), 3.52 (dd, 1 H, *J* 1.6, 10.0 Hz, H-6), 3.47 (t, 1 H, *J* 8.8, 10.0 Hz, H-4), 3.29 (dd, 1 H, *J* 5.0, 10.0 Hz, H-6′), 3.22 (s, 3 H, OCH_3), 2.70 (qdd, 1 H, *J* 7.5, 2.6, 4.5 Hz, H-3′), 0.91 (d, 3 H, *J* 7.5 Hz, CH_3); **45**: δ 5.74 (bs, 1 H, NH), 4.78 (d, 1 H, *J* 3.4 Hz, H-1), 4.47 (d, 3 H, *J* 4.5 Hz, H-4′), 4.03 (t, 1 H, *J* 8.5, 10.0 Hz, H-3), 3.80 (m, 1 H, H-5), 3.65 (dd, 1 H, *J* 3.4, 9.6 Hz, H-2), 3.62 (t, 1 H, *J* 8.5, 9.9 Hz, H-4), 3.45 (dd, 1 H, *J* 1.7, 10.0 Hz, H-6), 3.17 (s, 3 H, OCH_3), 3.10 (dd, 1 H, *J* 3.8, 10.0 Hz, H-6′), 2.57 (qdd, 1 H, *J* 7.5, 1.3, 4.5 Hz, H-3′), 0.86 (d, 3 H, *J* 7.5 Hz, CH_3). LSIHRMS taken for the mixture: Calcd for $C_{44}H_{45}NNaO_7$: 722.3094; found: *m*/*z* 722.3143 $[M + Na]^+$.

Methyl 2,3-di-O-*benzyl-4*-O-*(3′*R,*4′*S*)- and (3′*S,*4′*R*)-(3′-methylazetidin-2′-on-4′-yl)-α*-D-*glucopyranosides* (**46**) *and* (**47**).—A mixture of compounds **44**/**45** was detritylated using 0.4% of *p*-TsOH in MeOH at room temperature (yield 83%). Mixture **46**/**47** was used for the next step without any purification.

Methyl 2,3-di-O-*benzyl-4*-O-*(3′*R,*4′*S*)- and (3′*S,*4′*R*)-(3′-methylazetidin-2′-on-4′-yl)-6*-O-*tosyl-α*-D-*glucopyranosides* (**48**) *and* (**49**).—A mixture **48**/**49** was obtained according to the procedure described for **35** (70%). Colorless oil; spectral data taken for the mixture; IR (film): ν_{max} 1771 cm^{-1} (C=O); **48**: ^{1}H NMR ($CDCl_3$) selected signals: δ 5.87 (bs, 1 H, NH), 5.06 (d, 1 H, *J* 4.6 Hz, H-4′), 4.2 (t, 1 H, *J* 9.2 Hz, H-3), 3.11 (s, 3 H, OCH_3), 1.16 (d, 3 H, *J* 7.6 Hz, CH_3); **49**: ^{1}H NMR ($CDCl_3$) selected signals: δ 5.76 (bs, 1 H, NH), 4.66 (d, 1 H, *J* 4.1 Hz, H-4′), 4.3 (t, 1 H, *J* 9.3 Hz, H-3), 3.15 (s, 3 H, OCH_3), 1.15 (d, 3 H, *J* 7.6 Hz, CH_3); ESIHRMS: Calcd for $C_{32}H_{37}NNaO_9S$: 634.086; found: *m*/*z* 634.050 $[M + Na]^+$.

*(2*S,*3*R,*4*S,*4a*R,*5a*S,*6*R,*8a*R*) and (2*S,*3*R,*4*S,*4a*R,*5a*R,*6*S,*8a*R*) 3,4-Dibenzyloxy-1,5-dioxa-2-methoxy-6-methyl-7a-aza-cyclobuta[*b*]decalin-7-one* (**50**) *and* (**51**).—A mixture **50**/**51** was obtained from **48**/**49** according to the procedure described earlier (60%). Compounds **50** and **51** were separated on a silica gel column using 60:35:5 toluene–CH_2Cl_2–acetone as the eluant.

Compound **50**: Oil; $[\alpha]_D$ +17.7° (*c* 0.3, CH_2Cl_2); IR (film): ν_{max} 1771 cm^{-1} (C=O); ^{1}H NMR (C_6D_6): δ 7.30, 7.05 (m, 10 H, Bn), 4.92, 4.79 (2 d, 2 H, *J* 11.5 Hz, Bn), 4.65 (d, 1 H, *J* 3.3 Hz, H-5a), 4.61, 4.42 (2 d, 2 H, *J* 12.0 Hz, Bn), 4.42 (d, 1 H, *J* 3.6 Hz, H-2), 4.02 (t, 1 H, *J* 9.1 Hz, H-4), 3.68 (m, 2 H, H-8, H-8a), 3.52 (t, 1 H, *J* 9.3 Hz, H-4a), 3.25 (dd, 1 H, *J* 3.6, 9.5 Hz, H-3), 3.05 (s, 3 H, OCH_3), 2.95 (m, 1 H, H-8′), 2.78 (qdd, 1 H, *J* 1.7, 3.3, 7.6 Hz, H-6), 1.17 (d, 3 H, *J* 7.7 Hz, CH_3); ESIHRMS: Calcd for $C_{25}H_{29}NNaO_6$: 462.1887; found: *m*/*z* 462.1869 $[M + Na]^+$.

Compound **51**: Oil; $[\alpha]_D$ +18.9° (*c* 0.2, CH_2Cl_2); IR (film): ν_{max} 1771 cm^{-1} (C=O); ^{1}H NMR (C_6D_6): δ 7.38, 7.08 (m, 10 H, Bn), 4.87, 4.80 (2 d, 2 H, *J* 11.8 Hz, Bn), 4.61, 4.47 (2 d, 2 H, *J* 12.1 Hz, Bn), 4.48 (d, 1 H, *J* 3.5 Hz, H-2), 4.30 (d, 1 H, *J* 3.8 Hz, H-5a), 4.03 (t, 2 H, *J* 9.2 Hz, H-4), 3.99 (dd, 1 H, *J* 6.0, 12.7 Hz, H-8), 3.57 (ddd, 1 H, *J* 6.0, 9.3, 10.1 Hz, H-8a), 3.43 (dd, 1 H, *J* 3.6, 9.4 Hz, H-3), 3.09 (t, 1 H, *J* 9.3 Hz, H-4a), 2.90 (s, 3 H, OCH_3), 2.82 (qdd, 1 H, *J* 1.5, 3.8, 7.4 Hz, H-6), 2.48 (ddd, 1 H, *J* 1.5, 10.1, 12.7 Hz, H-8), 1.06 (d, 3 H, *J* 7.5 Hz, CH_3); ESIHRMS: Calcd for $C_{25}H_{29}NNaO_6$: 462.1887; found: *m*/*z* 462.1910 $[M + Na]^+$.

*(2*S,*3*R,*4*S,*4a*R,*6*R,*8a*R*) 3,4-Dibenzyloxy-1,5-dioxa-2-methoxy-7a-aza-cyclobuta[*b*]-decalin-7-one* (**52**).—Compound **52** was obtained from mixture **32** following

the procedure described for **41** (20%). Colorless oil; $[\alpha]_D$ +48.4° (*c* 0.2, CH_2Cl_2); IR (film): ν_{max} 1772 cm^{-1} (C=O); ^1H NMR (C_6D_6)): δ 7.38–7.05 (m, 10 H, 2 Ph), 4.88, 4.81 (2 d, 2 H, *J* 11.5 Hz, Bn), 4.59, 4.45 (2 d, 2 H, *J* 12.1 Hz, Bn), 4.47 (d, 1 H, *J* 3.7 Hz, H-2), 4.3 (t, 1 H, *J* 2.2 Hz, H-5a), 4.0 (t, 1 H, *J* 9.4 Hz, H-4), 3.98 (dd, 1 H, *J* 6.0, 12.7 Hz, H-8), 3.57 (ddd, 1 H, *J* 6.0, 9.4, 9.8 Hz, H-8a), 3.41 (dd, 1 H, *J* 3.7, 9.4 Hz, H-3), 3.03 (t, 1 H, *J* 9.4 Hz, H-4a), 2.94 (s, 3 H, OCH_3), 2.5 (m, 2 H, H-6,6′), 2.45 (dd, 1 H, *J* 9.8, 12.7 Hz, H-8); ESIHRMS: Calcd for $C_{24}H_{27}NNaO_6$: 448.1731; found: *m*/*z* 448.1733 $[M+Na]^+$.

*(2*S*,3*R*,4*S*,4a*R*,6*R*,8a*R*) 3,4-Diacetoxy-1,5-dioxa-2-methoxy-7a-aza-cyclobuta[*b*]-decalin-7-one* (**53**).—To a solution of **52** (0.05 g, 0.12 mmol) in MeOH (0.5 mL) was added 5% Pd/C (0.005 g). (**Caution!** Extreme fire hazard.) The mixture was stirred for 2 h under H_2 at room temperature. The catalyst was filtered through Celite, and the filtrate was concentrated. The residue **53** was acetylated with Ac_2O–pyridine, and the product obtained after standard workup was purified by column chromatography on silica gel using 2:3 hexane–EtOAc as the eluant to afford **54** (0.025 g, 65%). Colorless crystals; mp 149.3–150.5 °C; $[\alpha]_D$ +83.8° (*c* 0.4, CH_2Cl_2); IR (film): ν_{max} 1773 cm^{-1} (C=O), 1750 cm^{-1} (Ac); ^1H NMR ($CDCl_3$): δ 5.45 (t, 1 H, *J* 9.5, 10.0 Hz, H-4), 4.99 (dd, 1 H, *J* 0.5, 3.3 Hz, H-5a), 4.88 (d, 1 H, *J* 3.7 Hz, H-2), 4.84 (dd, 1 H, *J* 3.7, 10.0 Hz, H-3), 4.10 (dd, 1 H, *J* 6.0, 12.9 Hz, H-8), 3.72 (ddd, 1 H, *J* 6.0, 9.9, 9.9 Hz, H-8a), 3.40 (s, 3 H, OCH_3), 3.39 (t, 1 H, *J* 9.5, 10.2 Hz, H-4a), 3.15 (ddd, 1 H, *J* 1.6, 3.3, 15.1 Hz, H-6), 2.90 (dd, 1 H, *J* 0.5, 15.1 Hz, H-6′), 2.86 (ddd, 1 H, *J* 1.6, 10.2, 12.9 Hz, H-8′), 2.07 (2 s, 6 H, CH_3); ESIHRMS: Calcd for $C_{14}H_{19}NNaO_8$: 352.1003; found: *m*/*z* 352.0996 $[M+Na]^+$.

Assay of DD-carboxypeptidase activity.—The enzyme activity was measured as described previously.[13,14] Samples for assay of the DD-carboxypeptidase activity consisted of 10 μL of DD-carboxypeptidase from *Saccharopolyspora erythraea* PZH TZ 64-575 (40 units/mg), 20 μL of substrate solution containing 4.52 mg/mL Nα, Nε-diacetyl-L-lysyl-D-alanyl-D-alanine in 0.1 M phosphate buffer, pH 8.0, and 10 μL of 0.1 M phosphate buffer, pH 8.0. A standard sample contained 20 μL of D-alanine in distilled water.

The reaction mixture for assay of the DD-carboxypeptidase activity consisted of 60 μL of 0.05 mg/mL flavin adenine dinucleotide in 0.1 M phosphate buffer, pH 8.0, 10 μL of 0.05 mg/mL horseradish peroxidase (1230 U/mg) in distilled water, 5 μL of 5 mg/mL *o*-dianisidine in MeOH, and 2 μL of 11.77 mg/mL D-amino acid oxidase from porcine kidney (6.7 U/mg) in 0.1 M phosphate buffer, pH 8.0.

Samples were incubated for 30 min at 37 °C and then boiled for 2 min. After cooling, 77 μL of the reaction mixture was added, and all samples were incubated for 10 min at 37 °C. Next, to each sample was added 350 μL of 5:5:6 MeOH–distilled water–H_2SO_4. The extinction of the resulting solution was measured at 540 nm.

The inhibition of DD-peptidase 64-575 by the oxacephams discussed above was evaluated.[20] Mixtures of 10 μL of DD-peptidase 64-575 (40 U/mg), 5 μL solution of a cepham in MeOH and 5 μL of 0.1 M phosphate buffer, pH 8.0 were incubated for 45 min at 37 °C. The concentration of a cepham in the mixture was from 0.1 to 0.000055 M. After incubation 20 μL of substrate solution was added to 20 μL of each sample, and the resulting mixtures were incubated again. The following oxacephams were tested: **7**, **8**, **9**, **37**, **40**, **41a**, and **41b**.

5. Supplementary material

Full crystallographic details, excluding structure features for compound **41a**, have been deposited (accession no. CCDC 184078) with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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References

1. Kałuża, Z.; Furman, B.; Chmielewski, M. *Tetrahedron: Asymmetry* **1994**, *5*, 2179–2186.
2. Kałuża, Z.; Furman, B.; Chmielewski, M. *Tetrahedron: Asymmetry* **1995**, *65*, 1719–1730.
3. Furman, B.; Kałuża, Z.; Chmielewski, M. *J. Org. Chem.* **1997**, *62*, 3135–3139.
4. Neuß, O.; Furman, B.; Kałuża, Z.; Chmielewski, M. *Heterocycles* **1997**, *45*, 265–270.
5. Furman, B.; Molotov, S.; Thürmer, R.; Kałuża, Z.; Voelter, W.; Chmielewski, M. *Tetrahedron* **1997**, *53*, 5883–5890.
6. Furman, B.; Krajewski, P.; Kałuża, Z.; Thürmer, R.; Voelter, W.; Kozerski, L.; Williamson, M. P.; Chmielewski, M. *J. Chem. Soc., Perkin Trans. 2* **1999**, 217–224.
7. (a) Kałuża, Z.; Park, S.-H. *Synlett* **1996**, 895–896;
   (b) Kałuża, Z.; Łysek, R. *Tetrahedron: Asymmetry* **1997**, *8*, 2553–2560;
   (c) Kałuża, Z. *Tetrahedron Lett.* **1998**, *39*, 8349–8352.
8. Kałuża, Z.; Furman, B.; Krajewski, P.; Chmielewski, M. *Tetrahedron* **2000**, *56*, 5553–5562.
9. Borsuk, K.; Suwińska, K.; Chmielewski, M. *Tetrahedron: Asymmetry* **2001**, *12*, 979–981.

10. (a) *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R. B.; Gorman, M., Eds.; Academic Press: New York, 1982; Vols. 1–3;
(b) *The Chemistry of β-Lactams*; Georg, G. J., Ed.; VCH: New York, 1993;
(c) *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Elks, J., Ed., First International Symposium; Royal Soc. Chem.: London, 1976;
(d) *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Gregory, G. I., Ed.; Second International Symposium; Royal Soc. Chem.: London, 1980;
(e) *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Brown, A. G.; Roberts, S. M., Eds.; Third International Symposium; Royal Soc. Chem.: London, 1984;
(f) *Recent Advances in the Chemistry of β-Lactam Antibiotics*; Bentley, P. H.; Southgate, R., Eds.; Fourth International Symposium; Royal Soc. Chem.: London, 1988.
11. Łysek, R.; Borsuk, K.; Chmielewski, M.; Kałuża, Z.; Urbańczyk-Lipkowska, Z.; Klimek, A.; Frelek, J. *J. Org. Chem.* **2002**, *67*, 1472–1479.
12. Baggaley, K. H.; Brown, A. G.; Schofield, Ch. *J. Nat. Prod. Rep.* **1997**, 309–333 and references cited therein.
13. Frère, J.-M.; Leyh-Bouille, M.; Ghuysen, J.-M.; Nieto, M.; Perkins, H. R. *Methods Enzymol.* **1976**, *45*, 610–636.
14. Kurzątkowski, W.; Solecka, J.; Filipek, J.; Kurzątkowski, J. D.; Kuryłowicz, W. *Appl. Microbiol. Biotechnol.* **1990**, *33*, 452–454.
15. Shiozaki, H.; Kobayashi, Y.; Akai, H. *Tetrahedron* **1991**, *47*, 7021–7028.
16. Kenner, J.; Richards, G. N. *J. Chem. Soc.* **1955**, 1810–1812.
17. Eby, R.; Schuerch, C. *Carbohydr. Res.* **1980**, *79*, 53–62.
18. (a) Molino, B. F.; Fraser-Reid, B. *Can. J. Chem.* **1987**, *65*, 2834–2842;
(b) Klaffke, W.; Warren, Ch. D.; Jeanloz, R. W. *Carbohydr. Res.* **1992**, *244*, 171–179.
19. Johansson, R.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2371–2374.
20. Solecka, J.; Kurzątkowski, W. *Med. Doś. Mikrobiol.* **1999**, *51*, 151–165.