ELSEVIER

Carbohydrate Research 306 (1998) 505–515

CARBOHYDRATE RESEARCH

Isoxazolidin-5-one analogs of β-lactam antibiotics

Irma Panfil, Zofia Urbańczyk-Lipkowska, Marek Chmielewski*

Institute of Organic Chemistry of the Polish Academy of Sciences, PL-01-224 Warsaw, Poland

Received 23 June 1997; accepted in revised form 24 November 1997

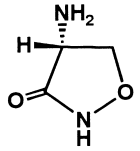
Abstract

Isoxazolidin-5-ones, readily available via conjugate addition–rearrangement of hydroxylamine to α,β-unsaturated sugar 1,5-lactones, react with aldehydes and diethoxymethyl acetate to afford 2,4,5-trisubstituted 1-aza-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonanes. 4,5-Disubstituted 1-aza-2-butoxycarbonyl-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonanes undergo base-catalyzed rearrangement to 4,6-disubstituted butyl 2,3-dideoxy-3-*N*-oxamate-D-ribohexaldono-1,5-lactones. The configuration of representative compounds: (2*S*,4*R*,5*S*,6*S*) 5-acetoxy-4-acetoxymethyl-1-aza-3,9-dioxo-2-methyl-8-oxo-bicyclo[4.3.0]nonane and butyl 4,6-di-*O*-(tert-butyldimethylsilyl)-2,3-dideoxy-3-*N*-oxamate-D-ribohexaldono-1,5-lactone were proved by X-ray crystallography.

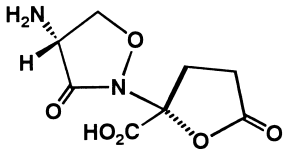
Keywords: Isoxazolidin-5-ones; Analogs of β-lactams; 2,4,5-Trisubstituted 1-aza-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonanes

1. Introduction

The continuing emergence of bacterial resistance has prompted for the search for new antibiotics. There has been much effort focused on the synthesis of non-β-lactam analogs of penicillins and cephalosporins [1–3]. Isoxazolidin-3-one analogs of β-lactam antibiotics like D-cycloserine **1** and lactavicin **2** display interesting and high antibacterial activity [3]. Their properties have been studied extensively [3].



1



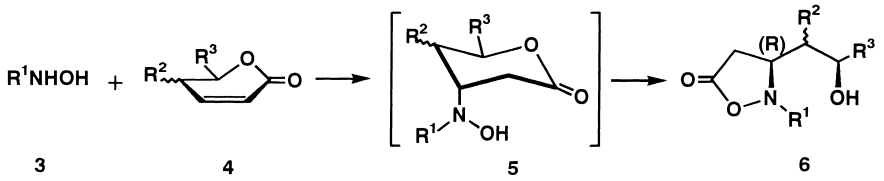
2

Recently, we have reported on the highly stereoselective addition-rearrangement of *N*-substituted hydroxylamines **3** to α,β-unsaturated sugar δ-lactones **4** [4]. The hydroxylamine molecule enters the lactone **4** molecule exclusively *anti* to the terminal C-6 carbon atom. The Michael addition is followed immediately by the opening of the lactone by the *N*-hydroxy group and formation of the isoxazolidin-5-one ring (Scheme 1) [4]. If the starting sugar **4** has the D-erythro or D-threo configuration, then the absolute configuration of the new stereogenic center of compound **6** (C-3 of the isoxazolidin-5-one ring) is (*S*) [4,5].

Several years ago, we have demonstrated that the racemic lactone **4** ($R^2 = H$, $R^3 = CH_2OAc$) added free base hydroxylamine in the presence of formaldehyde to form the bicyclic compound **7** which could be viewed as an isoxazolidin-5-one analog of a bicyclic β-lactam antibiotic (1-dethia-3-

* Corresponding author.

0008-6215/98/$19.00
PII S0008-6215(97)10107-0



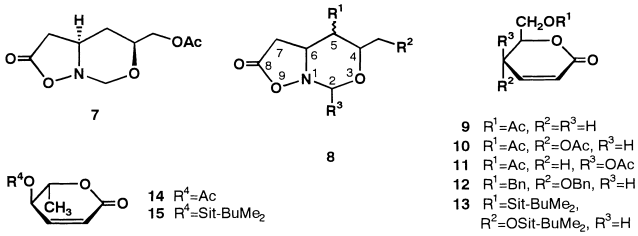
3 4 5 6

R^1 = H, Bn; R^2 = H, OBn, OAc; R^3 = CH_2OR^2

Scheme 1.

oxacepham) [6]. The (*R*) configuration of the bridge-head carbon atom, identical to the configuration of the respective carbon atom in the biologically active β-lactam antibiotics, in a combination with the isoxazolidin-5-one fragment which possess acylating properties [7], might result in biological activity similar to that shown by original β-lactam antibiotics. The use of other aldehydes for condensation with **6** (R^1 = H) would eventually introduce a substituent in the place which is occupied in β-lactam antibiotics by the carboxylic function to afford compounds **8**.

The present paper describes formation of compounds **8** starting from lactones **9**–**15** and formaldehyde, acetaldehyde, benzyloxyacetaldehyde (**16**), diethoxymethyl acetate (**17**), and butyl glyoxylate (**18**). The aim of these investigations was to find whether isoxazolidin-5-ones could exhibit activity similar to isoxazolidin-3-ones **1** and **2**.



7

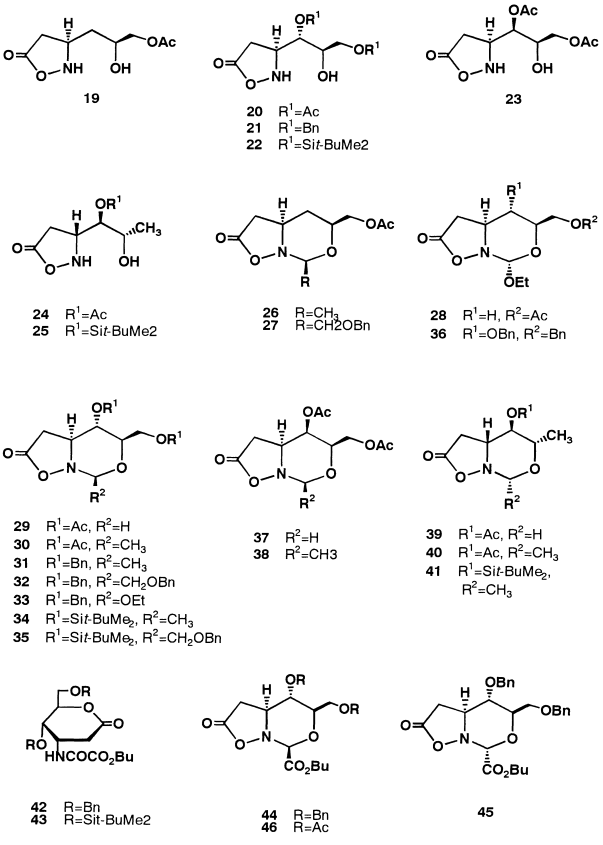
8

9 R^1=Ac, R^2=R^3=H
10 R^1=Ac, R^2=OAc, R^3=H
11 R^1=Ac, R^2=H, R^3=OAc
12 R^1=Bn, R^2=OBn, R^3=H
13 R^1=Sit-$BuMe_2$, R^2=OSit-$BuMe_2$, R^3=H

14 R^4=Ac
15 R^4=Sit-$BuMe_2$

2. Results and discussion

Commercially available hydroxylamine hydrochloride was transformed into the free base by treatment with equimolar amount of sodium methoxide. The addition–rearrangement reaction was performed in methanol solution at room temperature. The crude isoxazolidinones **19**–**25** were used for reaction with aldehydes. Condensations with formaldehyde were performed, as before [6], in aqueous solution whereas condensations with acetaldehyde were carried out without solvent. Reactions of isoxazolidinones **19**–**25** with compounds **16**–**18** were carried out in benzene. The respective 1-aza-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonanes **26**–**32**, **34**, **35**, **37**–**41** were obtained in moderate or good yield as single isomers. The configuration at C-2 of the bicyclic skeleton was assigned assuming that under conditions used, the thermodynamic product having the pseudoequatorial substituent should be formed. This assumption was confirmed by X-ray crystallography of compound **30** (Fig. 1).



19

20 R^1=Ac
21 R^1=Bn
22 R^1=Sit-BuMe2

23

24 R^1=Ac
25 R^1=Sit-BuMe2

26 R=CH_3
27 R=CH_2OBn

28 R^1=H, R^2=Ac
36 R^1=OBn, R^2=Bn

29 R^1=Ac, R^2=H
30 R^1=Ac, R^2=CH_3
31 R^1=Bn, R^2=CH_3
32 R^1=Bn, R^2=CH_2OBn
33 R^1=Bn, R^2=OEt
34 R^1=Sit-$BuMe_2$, R^2=CH_3
35 R^1=Sit-$BuMe_2$, R^2=CH_2OBn

37 R^2=H
38 R^2=CH3

39 R^1=Ac, R^2=H
40 R^1=Ac, R^2=CH_3
41 R^1=Sit-$BuMe_2$, R^2=CH_3

42 R=Bn
43 R=Sit-BuMe2

44 R=Bn
46 R=Ac

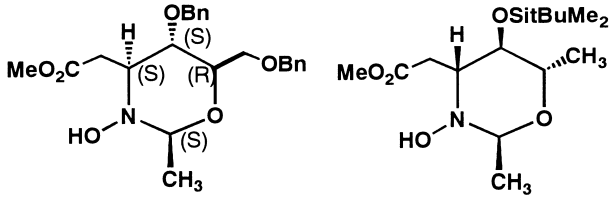
45

When compound **19** was condensed with orthoester **17** in boiling benzene, one stereoisomer **28** was formed, whereas when **21** was reacted with **17**, in boiling dichloromethane, two stereoisomers **33** and **36** were obtained in a ratio of about 2:3, respectively. In boiling toluene, **21** and **17** furnished

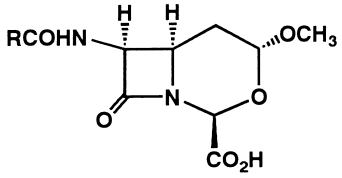
33 as a single product. The stereochemical course of the condensation is controlled by the reaction temperature; low temperature of boiling dichloromethane allows to obtain both epimers. The (*S*) configuration at C-2 was assigned to compounds **28** and **33** on the assumption that the anomeric effect should direct the geometry of the more stable product.

The condensation of isoxazolidinones with freshly prepared butyl glyoxylate (**18**) proceeded in different manner. Under conditions used for other aldehydes, glyoxylate **18** with compound **21** or **22** gave mixtures of hemiacetals, which were not investigated further. In boiling benzene in the presence of anhydrous sodium carbonate, isoxazolidines **21** or **22** and glyoxylate **18** provided amide **42** or **43**, respectively, as the single products. The structure and configuration of **43**, was proved by X-ray crystallography (Fig. 2). In boiling toluene in the presence of catalytic amount of *p*-toluenesulfonic acid, **21** treated with **18** afforded three products: the expected bicyclic compound **44** as the main component, its C-2 epimer **45**, and the amide **42**. Compounds **44** and **45** were unstable; upon standing in solution, they slowly underwent isomerisation to afford **42**. The isomerisation was accelerated by addition of a base. For example, addition of 2 equiv of triethylamine in deuterated chloroform solution transformed **44** into **42** after 2 h. The possible mechanism of isomerisation is depicted in Scheme 2. The isomerisation process is initiated with H-2 proton abstraction which proceeds via the cyclic iminoether intermediates **47** and **49**. The configuration of the final product **42** retains the initial configuration at C-5 of the sugar chain; the proposed reaction pathway might led to the inversion of configuration at that carbon atom via the iminoether **47**. Such a nucleophilic displacement of iminoether against carboxylate should eventually provide the L-*lyxo* configuration of the resulting amide **42**. The X-ray structure determination of **43** shows that this is not the case.

Acylating properties of the isoxazolidin-5-one ring in compounds **7**, **26**–**41** were exemplified by treatment of compounds **31** and **41** with methanol in the presence of catalytic amount of ammonia. As was recently shown, such a low concentration of ammonia caused trans-esterification, whereas the respective amide was not formed [8]. Isoxazolidinones **31** and **41** under these conditions furnished esters **50** and **51**, respectively.

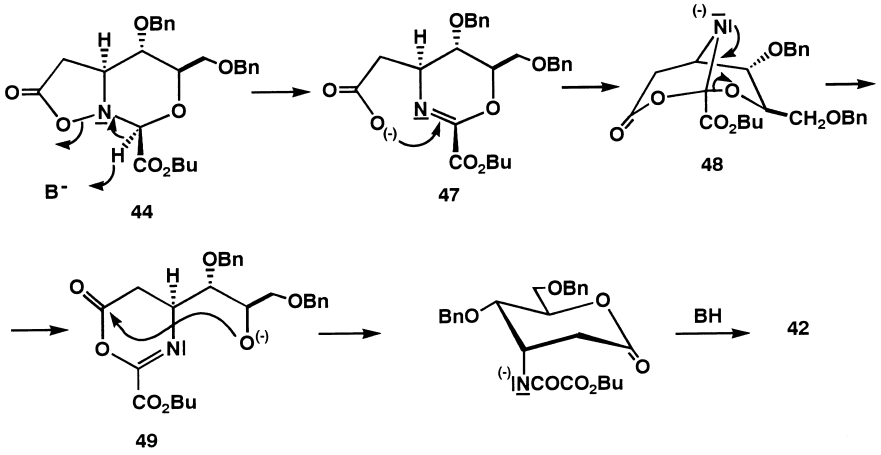


50 **51**



52

Compounds **20**, **30**, and **44** were tested for antibacterial activity. All show a low activity: against *Escherichia coli* and *Staphylococcus aureus*, **20** displays



Scheme 2.

a MIC of 34 mg/mL, compound **30** a MIC of 54 mg/mL, and **44** a MIC of 33 mg/mL. It appears that cyclic hydroxylamine esters, contrary to cyclic hydroxamic acid esters **1** and **2**, do not provide any structural element offering antibacterial activity. However, the low chemical stability of isoxazolidin-5-one rings, particularly in the case of compound **44**, could be responsible for the low biological activity of the tested compounds. It should be noted that β-lactams **52** structurally related to **8** exhibit pronounced biological activity [9].

3. Experimental

Optical rotations were measured with JASCO DIP-360 digital polarimeter. IR spectra were obtained with a FT-IR-1600 Perkin–Elmer spectrophotometer. ^{1}H NMR spectra were recorded using a Bruker AM 500 spectrometer at 500 MHz. Mass spectra were obtained with an AMD 604 spectrometer. Column chromatography was performed on E. Merck Kieselgel (230–400 mesh). Lactones **9**–**15** were obtained according to the

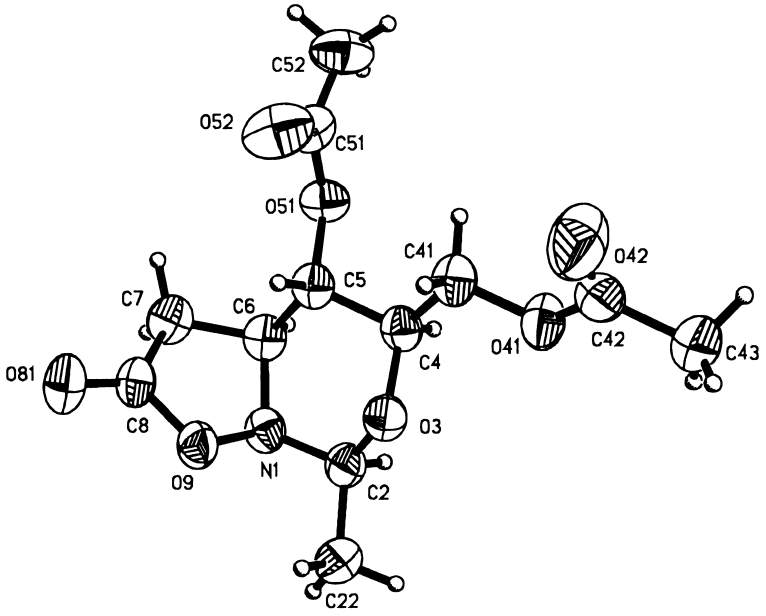


Fig. 1. ORTEP diagram of compound **30**. Thermal ellipsoids at 50% probability level

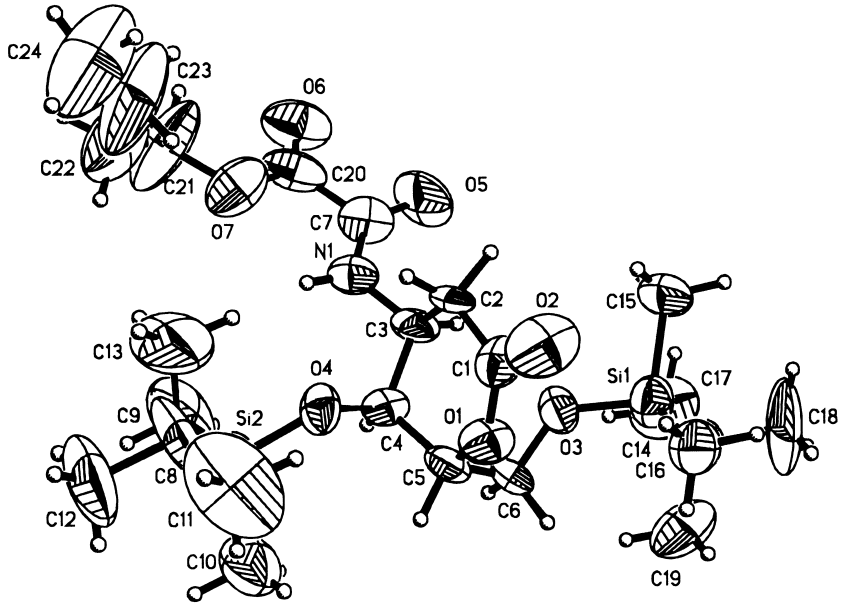


Fig. 2. ORTEP diagram of compound **43**. Thermal ellipsoids at 50% probability level

known procedure [10]. Their spectral data were already reported in ref. [10] for **9**–**11**, **14** and in ref. [5] for **13**, **15**. Spectral data of **12** will be published elsewhere. Additions of hydroxylamine to lactones **9**–**15** were performed according to the general procedure already described before. Isoxazolidin-5-ones **19**–**25** were purified on a silica gel column and after evaporation of the eluent were used directly for the condensation with aldehydes.

Condensation of isoxazolidin-5-ones **19**, **20**, **23** *and* **24** *with formaldehyde*.—The crude isoxazolidin-5-one: **19**, **20**, **23** or **24**, (0.5 mmol) was dissolved in MeOH (1 mL), treated with 37% formalin (3 mol equiv) and stirred for 3 h. Subsequently, the mixture was concentrated and extracted with CH_2Cl_2. The extract was dried, evaporated and purified on a silica gel column to afford 1-aza-3,9-dioxa- 8-oxobicyclo[4.3.0]nonanes **7**, **29**, **37**, and **39**, respectively.

*(4*S*,6*R*)-4-Acetoxymethyl-1-aza-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**7**).—From **19** (0.10 g, 0.5 mmol), 0.05 g (48%); mp 146–150 °C; $[\alpha]_D$ +94.3°; (*c* 1, CH_2Cl_2); Spectral and crystallographical data for racemic **7** were reported in ref. [6].

*(4*R*,5*S*,6*S*)-5-Acetoxy-4-acetoxymethyl-1-aza-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**29**).—From **20** (0.13 g, 0.5 mmol), 0.078 g (58%); mp 158–160 °C; $[\alpha]_D$ +4.4° (*c* 1, CH_2Cl_2); IR (CH_2Cl_2): 1795, 1745 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.99 (t, 1 H, *J* 9.4, 10.0 Hz, H-5), 4.49, 5.16 (2 d, 2 H, *J* 13.4 Hz, H-2, 2′), 4.23 (dd, 1 H, *J* 5.1, 12.4 Hz, CH_AH_BOAc), 4.17 (dd, 1 H, *J* 2.5, 12.4 Hz, CH_AH_BOAc), 3.76 (dd, 1 H, *J* 7.1, 9.4 Hz, H-6), 3.65 (ddd, 1 H, *J* 2.5, 5.1, 10.0 Hz, H-4), 3.08 (dd, 1 H, *J* 7.1, 16.9 Hz, H-7′), 2.75 (d, 1 H, *J* 16.9 Hz, H-7), 2.10, 2.10 (2 s, 6 H, 2 OAc). Anal. Calcd for $C_{11}H_{15}NO_7$: C, 48.35; H, 5.49; N, 5.13. Found: C, 48.1; H, 5.4; N, 4.9.

*(4*R*,5*R*,6*S*)-5-Acetoxy-4-acetoxymethyl-1-aza-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**37**).—From **23** (0.13 g, 0.5 mmol), 0.061 g (45%); mp 104–108 °C; $[\alpha]_D$ + 73.0°; (*c* 1, CH_2Cl_2); IR (CH_2Cl_2): 1795, 1750 cm^{-1}; ^1H NMR (toluene-d_8, 100 °C); δ 4.63 (dd, 1 H, *J* 1.4, 3.7 Hz, H-5), 4.06 (dd, 1 H, *J* 6.4, 11.4 Hz, CH_AH_BOAc), 3.99 (dd, 1 H, *J* 6.6, 11.4 Hz, CH_AH_BOAc), 3.94, 4.87 (2 d, 2 H, *J* 13.3 Hz, H-2, 2′), 3.40 (dt, 1 H, 1.4, 6.4, 6.6 Hz, H-4), 3.05 (dd, 1 H, *J* 3.7, 7.6 Hz, H-6), 2.38 (dd, 1 H, *J* 7.6, 16.2 Hz, H-7′), 2.02 (d, 1 H, *J* 16.2 Hz, H-7), 1.75, 1.79 (2 s, 6 H, 2 OAc). Anal. Calcd for $C_{11}H_{15}NO_7$; C, 48.35; H, 5.49; N, 5.13. Found: C, 48.1; H, 5.6; N, 5.0.

*(4*S*,5*R*,6*R*)-5-Acetoxy-1-aza-3,9-dioxa-4-methyl-8-oxo-bicyclo[4.3.0]nonane* (**39**).—From **24** (0.10 g, 0.5 mmol), 0.052 g (49%); syrup; $[\alpha]_D$ −107.5° (*c* 1, CH_2Cl_2); IR (film): 1795, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.78 (t, 1 H, *J* 9.5, 9.7 Hz, H-5), 4.46, 5.09 (2 d, 2 H, *J* 13.5, Hz, H-2, 2′), 3.70 (dd, 1 H, *J* 7.1, 9.5 Hz, H-6), 3.51 (dq, 1 H, *J* 6.1, 9.7 Hz, H-4), 3.06 (dd, 1 H, *J* 7.1, 16.8 Hz, H-7′), 2.70 (d, 1 H, *J* 16.8 Hz, H-7), 1.25 (d, 3 H, *J* 6.1 Hz, CH_3). Anal. Calcd for $C_9H_{13}NO_5$: C, 50.23; H, 6.04; N, 6.51. Found: C, 49.9; H, 6.1; N, 6.5.

Condensation of isoxazolidin-5-ones **19**–**25** *with acetaldehyde*.—The crude isoxazolidin-5-one **19**–**25** (0.5 mmol) was dissolved in acetaldehyde (1.0 mL) and stirred for 3 h. After standard work up, as above, the product was purified by chromatography.

*(2*S*,4*S*,6*R*)-4-acetoxymethyl-1-aza-3,9-dioxa-2-methyl-8-oxo-bicyclo[4.3.0]nonane* (**26**).—From **19** (0.10 g, 0.5 mmol), 0.056 g (49%); mp 95–97 °C; $[\alpha]_D$ +144.0° (*c* 1, CH_2Cl_2); IR (CH_2Cl_2): 1800, 1755 cm^{-1}; ^1H NMR (C_6D_6); δ 3.97 (q, 1 H, *J* 6.0 Hz, H-2), 3.90 (dd, 1 H, *J* 6.2, 11.6 Hz, CH_AH_BOAc), 3.82 (dd, 1 H, *J* 4.2, 11.6 Hz, CH_AH_BOAc), 3.25 (dddd, 1 H, *J* 2.2, 4.2, 6.2, 11.6 Hz, H-4), 2.92 (bs, 1 H, H-6), 2.41 (dd, 1 H, *J* 6.6, 16.2 Hz, H-7′), 1.75 (d, 1 H, *J* 16.2 Hz, H-7), 1.68 (s, 3 H, OAc), 1.40 (d, 3 H, *J* 6.0 Hz, CH_3), 1.06 (dt, 1 H, *J* 11.5, 11.7, 13.3 Hz, H-5′), 0.61 (bd, 1 H, H-5). Anal. Calcd for $C_{10}H_{15}NO_5$: C, 52.40; H, 6.60; N, 6.11. Found: C, 52.0; H, 6.8; N, 6.0.

*(2*S*,4*R*,5*S*,6*S*)-5-Acetoxy-4-acetoxymethyl-1-aza-3,9-dioxa-2-methyl-8-oxo-bicyclo[4.3.0]nonane* (**30**).—From **20** (0.13 g, 0.5 mmol), 0.083 g (59%); mp 148–150 °C; $[\alpha]_D$ +133.3° (*c* 1, CH_2Cl_2); IR (CH_2Cl_2) 1795, 1750 cm^{-1}; ^1H NMR. ($CDCl_3$): δ 4.96 (t, 1 H, *J* 9.5, 10.1 Hz, H-5), 4.57 (q, 1 H, 6.0 Hz, H-2), 4.23 (dd, 1 H, *J* 5.1, 12.4 Hz, CH_AH_BOAc), 4.12 (dd, 1 H, *J* 2.5, 12.4 Hz, CH_AH_BOAc), 3.74 (dd, 1 H, *J* 7.0, 9.5 Hz, H-6), 3.71 (ddd, 1 H, *J* 2.5. 5.1, 10.1 Hz, H-4), 3.04 (dd, 1 H, *J* 7.0, 16.8 Hz, H-7′), 2.71 (d, 1 H, *J* 16.8 Hz, H-7), 2.09, 2.09 (2 s, 6 H, 2 OAc), 1.56 (d, 3 H, *J* 6.0 Hz, CH_3). Anal. Calcd for $C_{12}H_{17}NO_7$: C, 50.17; H, 5.92; N, 4.87. Found: C, 49.8; H, 6.0; N, 4.8.

*(2*S*,4*R*,5*R*,6*S*)-1-Aza-5-benzyloxy-4-benzyloxymethyl-3,9-dioxa-2-methyl-8-oxo-bicyclo[4.3.0]-nonane* (**31**).—From 21 (0.18 g, 0.5 mmol), 0.083 g (68%); mp 90–92 °C; $[\alpha]_D$ + 56.7° (*c* 1, CH_2Cl_2); IR (CH_2Cl_2): 1784 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.57, 4.71 (2 d, 2 H, *J* 12.0 Hz, Bn), 4.45, 4.58 (2 d,

2 H, *J* 11.2 Hz, Bn), 3.80 (dd, 1 H, *J* 8.8, 11.2 Hz, CH_AH_BOBn), 3.76 (dd, 1 H, *J* 2.1, 11.2 Hz, CH_AH_BOBn), 3.53 (m, 1 H, H-4), 3.61 (m, 2 H, H-5, 6), 2.95 (m, 1 H, H-7′), 2.32 (d, 1 H, *J* 16.8 Hz, H-7), 1.53 (d, 1 H, *J* 6.0 Hz, CH_3), Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.92; H, 6.52; N, 3.65. Found: C, 69.0; H, 6.6; N, 3.6.

*(2*S*,4*R*,5*R*,6*S*)-1-Aza-5-*tert*-butyldimethylsiloxy-6-*tert*-butyldimethysiloxymethyl-3,9-dioxa-2-methyl-8-oxo-bicyclo[4.3.0]nonane* (**34**).—From 21 (0.20 g, 0.5 mmol), 0.17 g (78%); mp 51–53 °C; $[\alpha]_D$ + 96.5° (*c* 0.9, CH_2Cl_2); IR (CH_2Cl_2): 1781 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.50 (q, 1 H, *J* 6.0 Hz, H-2), 3.82 (d, 2 H, CH_2OSi), 3.74 (t, 1 H, *J* 9.1, 9.2 Hz, H-5), 3.54 (dd, 1 H, *J* 6.8, 9.1 Hz, H-6), 3.26 (dt, 1 H, *J* 9.2 Hz, H-4), 3.05 (dd, 1 H, *J* 6.8, 16.7 Hz, H-7′), 2.70 (d, 1 H, *J* 16.7 Hz, H-7), 1.48 (d, 3 H, *J* 6.0 Hz, CH_3), 0.06, 0.08, 0.12, 0.13, 0.87 (5s, 3OH, Si*t*-BuMe$_2$); LSIMS (HRMS): *m*/*z*, 432.26023 $[M+H]^+$; Calcd for $C_{20}H_{42}NO_5Si_2$: 432.26015. Anal. Calcd for $C_{20}H_{41}NO_5Si_2$: C, 55.68; H, 9.51; N, 3.24. Found: C, 55.5; H, 9.8; N, 3.1.

*(2*S*,4*R*,5*R*,6*S*)-5-Acetoxy-4-acetoxymethyl-1-aza-3,9-dioxa-2-methyl-8-oxo-bicyclo[4.3.0]nonane* (**38**).—From **23** (0.13 g, 0.5 mmol), 0.066 g (47%); mp 102–106 °C; $[\alpha]_D$ + 89.8° (*c* 1, CH_2Cl_{22}); IR (film): 1800, 1755 cm^{-1}, ^1H NMR ($CDCl_3$): δ 5.05 (dd, 1 H, *J* 1.5, 3.8 Hz, H-5), 4.58 (q, 1 H, *J* 6.1 Hz, H-2), 4.15 (dd, 1 H, *J* 6.3, 11.4 Hz, CH_AH_BOAc), 4.09 (dd, 1 H, *J* 6.7, 11.4 Hz, CH_AH_BOAc), 4.06 (dd, 1 H, *J* 3.8, 7.6 Hz, H-6), 4.02 (dt, 1 H, *J* 1.5, 6.3, 6.7 Hz, H-4), 3.06 (dd, 1 H, *J* 7.6, 16.5 Hz, H-7′), 2.43 (d, 1 H, *J* 16.5 Hz, H-7), 2.06, 2.14 (2 s, 6 H, 2OAc), 1.59 (d, 3 H, *J* 6.1 Hz, CH_3); EI (HRMS): *m*/*z* 287.10053 $[M^{+\bullet}]$; Calcd for $C_{12}H_{17}NO_7$: 287.10050. Anal. Calcd for $C_{12}H_{17}NO_7$: C, 50.17; H, 5.96; N, 4.88. Found: C, 50.1; H, 6.1; N, 5.0.

*(4*S*,5*R*,6*R*)-5-Acetox-1-aza-2,4-dimethyl-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**40**).—From **24** (0.10 g, 0.05 mmol), 0.051 g (45%); mp 139–141 °C; $[\alpha]_D$−186.0° (*c* 0.3, CH_2Cl_2); IR (CH_2Cl_2): 1790, 1745 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.74 (t, 1 H, *J* 9.6, 9.7 Hz, H-5), 4.54 (q, 1 H, *J* 6.1 Hz, H-2), 3.68 (dd, 1 H, *J* 7.1, 9.6 Hz, H-6), 3.57 (dq, 1 H, *J* 6.2, 9.7 Hz, H-4), 3.01 (dd, 1 H, *J* 7.1, 16.8 Hz, H-7′), 2.66 (d, 1H, *J* 16.8 Hz, H-7), 2.10 (s, 3 H, OAc), 1.52 (d, 3 H, *J* 6.1 Hz, CH_3), 1.22 (d, 3 H, *J* 6.2 Hz, CH_3); EI (HRMS): *m*/*z* 229.09488 $[M^{+\bullet}]$; Calcd for $C_{10}H_{15}NO_5$: 229.09502. Anal. Calcd for $C_{10}H_{15}NO_5$: C, 52.40; H, 6.60; N, 6.11. Found: C, 52.4; H, 6.7; N, 5.9.

*(2*S*,4*S*,5*R*,6*R*)-1-Aza-5-*tert*-butyldimethylsiloxy-2,6-dimethyl-3,9-dioxa-8-oxo-bicyclo[4.3.0]no-nane* (**41**).—From **25** (0.14 g, 0.5 mmol), 0.11 g (72%); mp 43–45 °C; $[\alpha]_D$ −128.0° (*c* 1, CH_2Cl_2); IR ($CHCl_3$): 1796, 1780 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.52 (q, 1 H, *J* 6.0 Hz, H-2), 3.52 (dd, 1 H, *J* 6.8, 8.6 Hz, H-6), 3.50 (dd, 1 H, *J* 6.8, 16.9 Hz, H-7′), 3.41 (dq, 1 H, *J* 5.9, 8.9 Hz, H-4), 3.30 (t, 1 H, *J* 8.6, 8.9 Hz, H-5), 2.69 (d, 1 H, *J* 16.9 Hz, H-7), 1.49 (d, 3 H, *J* 6.0 Hz, CH_3), 1.29 (d, 3 H, *J* 5.9 Hz, CH_3), 0.12, 0.88 (2 s, 15 H, Si*t*-BuMe$_2$); EI (MS): *m*/*z* 301 $[M^{+\bullet}]$. Anal. Calcd for $C_{14}H_{27}NO_4S_i$: C, 55.81; H, 8.97; N, 4.67. Found: C, 55.6; H, 9.1; N, 4.6.

Condensation of isoxazolidin-5-ones **19**, **21**, *and* **22** *with benzyloxyacetalaldehyde* (**16**).—The crude isoxazolidin-5-one **19**, **21**, or **22** (0.5 mmol) was dissolved in benzene (5 mL) and treated with benzyloxyacetaldehyde **16** (3 molar equiv). The reaction was stirred for 1 h. After standard work up, as above, the product was purified by chromatography.

*(2*S*,4*S*,6*R*)-4-Acetoxymethyl-1-aza-2-benzyloxymethyl-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**27**).—From **19** (0.10 g, 0.5 mmol), 0.13 g (57%); syrup; $[\alpha]_D$ + 122.0° (*c* 0.2, CH_2Cl_2); IR ($CHCl_3$): 1785, 1740 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.62 (s, 2 H, Bn), 4.61 (t, 1 H, *J* 5.5 Hz, H-2), 4.11 (d, 2 H, CH_2OBn), 3.96 (ddd, 1 H, *J* 5.3, 6.9, 11.5 Hz, H-6), 3.85 (m, 1 H, *J* 2.6, 5.3, 5.8, 11.3 Hz, H-4), 3.82 (dd, 1 H, *J* 5.3, 10.5 Hz, CH_AH_BOAc), 3.72 (dd, 1 H, *J* 5.8, 10.5 Hz, CH_AH_BOAc), 3.14 (dd, 1 H, *J* 6.9, 16.4 Hz, H-7′), 2.43 (d, 1 H, *J* 16.4 Hz, H-7), 2.08 (s, 3 H, OAc), 1.60 (dt, 1 H, *J* 11.3, 11.5, 13.6 Hz, H-5′), 1.53 (ddd, 1 H, *J* 2.6, 5.3, 13.6 Hz, H-5); LSIMS (HRMS): *m*/*z* 336.144806 $[M+H]^+$; Calcd for $C_{17}H_{22}NO_6$: 336.14471. Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.89; H, 6.26; N, 4.18. Found: C, 61.0; H, 6.4; N, 4.2.

*(2*S*,4*R*,5*R*,6*R*)-1-Aza-5-benzyloxy-2,4-di(benzyloxymethyl)-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**32**).—From **21** (0.18 g, 0.5 mmol), 0.19 g (77%); mp 92–94 °C; $[\alpha]_D$ + 53.8° (*c* 1, CH_2Cl_2); IR ($CHCl_3$): 1787 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.61 (s, 2H, OBn), 4.58 (t, 1H, *J* 5.2, 5.8 Hz, H-2), 4.56, 4.70 (2d, 2H, *J* 12.0 Hz, Bn), 4.45, 4.59 (2 d, 2 H, *J* 11.3 Hz, Bn), 3.83 (dd, 1 H, *J* 3.4, 11.4 Hz, C-4 CH_AH_BOBn), 3.81 (dd, 1 H, *J* 5.2, 10.4 Hz, C-2 CH_AH_BOBn), 3.78 (dd, 1 H, *J* 2.0, 11.4 Hz, C-4 CH_AH_BOBn), 3.73 (dd, 1 H, *J* 5.8, 10.4 Hz, C-2 CH_AH_BOBn), 3.66 (t, 1 H, *J* 9.1, 9.2 Hz, H-5), 3.62 (dd, 1 H, *J* 6.6, 9.2 Hz, H-6), 3.53 (ddd, 1 H, *J* 2.0,

3.4, 9.1 Hz, H-4), 2.97 (dd, 1 H, *J* 6.6, 16.8 Hz, H-7′), 2.28 (d, 1 H, *J* 16.8 Hz, H-7); EI (MS): *m/z* 489 ($M^{+\bullet}$). Anal. Calcd for $C_{29}H_{31}NO_6$: C, 71.16; H, 6.33; N, 2.86. Found: C, 70.9; H, 6.3; N, 2.9.

*(2*S*,4*R*,5*R*,6*R*)-1-Aza-2-benzyloxymethyl-5-(*tert*-butyldimethylsiloxy)-4-(*tert*-butyldimethylsiloxy)-methyl-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane* (**35**).—From **22** (0.20 g, 0.5 mmol) 0.13 g (49%); mp 53–55 °C; $[\alpha]_D$ + 83.0° (*c* 0.6, CH_2Cl_2); IR ($CHCl_3$): 1784 cm^{-1}; H NMR ($CDCl_3$): δ 4.61 (t, 1 H, *J* 4.9, 6.0 Hz, H-2), 4.59, 4.63 (2 d, 2 H, *J* 12.1 Hz, Bn), 3.85 (d, 2 H, CH_2OSi), 3.82 (dd, 1 H, *J* 4.9, 10.4 Hz, CH_AH_BOBn), 3.81 (t, 1 H, *J* 9.1, 9.2, Hz, H-5), 3.69 (ddd, 1 H, *J* 6.0, 10.4 Hz, CH_AH_BOBn), 3.56 (dd, 1 H, *J* 6.8, 9.1 Hz, H-6), 3.29 (dt, 1 H, *J* 2.3, 2.3, 9.2 Hz, H-4), 3.08 (dd, 1 H *J* 6.8, 16.8 Hz, H-7′), 2.69 (d, 1 H, *J* 16.8 Hz, H-7), 0.06, 0.13, 0.87, 0.88 (4 s, 30 H, 2 Si*t*-BuMe_2); LSIMS (MS): *m/z* 538 $[M+H]^+$. Anal. Calcd for $C_{27}H_{47}NO_6Si_2$: C, 60.33; H, 8.75; N, 2.60. Found: C, 60.0; H, 8.7; N, 2.4.

*(2*S*,4*S*,6*R*)-4-Acetoxymethyl-1-aza-3,9-dioxa-2-ethoxy-8-oxo-bicyclo[4.3.0]nonane* (**28**).—Compound **19** (0.04 g, 0.25 mmol) and diethoxymethyl acetate (**17**; 0.04 g, 0.25 mmol) in C_6H_6 (5 mL) were refluxed for 15 min. Subsequently, the solvent was evaporated and the residue was purified by chromatography to afford **28** (0.043 g, 84%); mp 88–90 °C; $[\alpha]_D$ + 95.5° (*c* 0.3, CH_2Cl_2); IR ($CHCl_3$): 1790, 1741 cm^{-1}, ^1H NMR ($CDCl_3$): δ 5.62 (s, 1 H, H-2), 4.26 (m, 1 H, H-4), 4.16 (ddd, 1 H, *J* 5.0, 6.8, 11.9 Hz, H-6), 4.13 (dd, 1 H, *J* 3.9, 11.8 Hz, CH_AH_BOAc), 4.09 (dd, 1 H, *J* 6.0, 11.8 Hz, CH_AH_BOAc), 3.66–3.80 (m, 2 H, OCH_2), 3.09 (dd, 1 H, *J* 6.8, 16.4 Hz, H-7′), 2.43 (d, 1 H, *J* 16.4 Hz, H-7), 2.10 (s, 3 H, OAc), 1.63 (dt, 1 H, *J* 11.8, 11.9, 13.5 Hz, H-5′), 1.51 (bd, 1 H, H-5), 1.28 (t, 3 H, CH_3); LSIMS (HRMS): *m/z* 260.11426, $[M+H]^+$; Calcd for $C_{11}H_{17}NO_6$: 260.11341. Anal. Calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.56; N, 5.46. Found: C, 51.2; H, 6.6; N, 5.4.

*(2*S*,4*R*,5*R*,6*R*)-1-Aza-5-benzyloxy-4-methyl-3,9-dioxa-2-ethoxy-8-oxo-bicyclo[4.3.0]nonane* (**33**) *and (2*R*,4*R*,5*R*,6*S*)-1-aza-5-benzyloxy-4-benzyloxymethyl-3,9-dioxa-2-ethoxy-8-oxo-bicyclo[4.3.0]nonane* (**36**).—Compound **21** (0.089 g, 0.25 mmol) and diethoxymethyl acetate **17** (0.04 g, 0.25 mmol) in CH_2Cl_2 (5 mL) were refluxed for 0.5 h. Subsequently, the solvent was evaporated and the residue was separated on a silica gel column using 7:3 hexane–EtOAc as an eluent to afford the more polar compound **33** (0.037 g, 36%) and the less polar compound **36** (0.045 g, 54%). The same reaction performed in boiling toluene gave compound **33** (0.092 g, 90%) as a single product. **33**: syrup; $[\alpha]_D$ + 11.4° (*c* 0.3, CH_2Cl_2); IR ($CHCl_3$): 1793 cm^{-1}; ^1H NMR ($CDCl_3$, 55 °C): δ 5.24 (bs, 1 H, H-2), 4.57, 4.66 (2 d, 2 H, *J* 11.9 Hz, OBn), 4.47, 4.60, (2 d, 2 H, *J* 11.5 Hz, OBn), 3.92 (bt, 1 H, H-5), 3.72–3.88 (m, 5 H, H-4, CH_2OAc, OCH_2), 3.67 (bm, 1 H, H-6), 2.67 (dd, 1 H, *J* 7.4, 16.8 Hz, H-7′), 2.40 (dd, 1 H, *J* 7.0, 16.8 Hz, H-7), 1.21 (t, 3 H, CH_3); MS (EI): *m/z* 413 ($M^{+\bullet}$). Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.82; H, 6.53; N, 3.38. Found: C, 67.0; H, 6.5; N, 3.4. **36**: syrup; $[\alpha]_D$ −23.8° (*c*, 0.4, CH_2Cl_2); IR ($CHCl_3$): 1792 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.58 (s, 1 H, H-2), 4.56, 4.72 (2 d, 2 H, *J* 12.0 Hz, OBn), 4.44, 4.57 (2 d, 2 H, *J* 11.3 Hz, OBn), 4.02 (m, 1 H, H-4), 3.63–3.86 (m, 6 H, H-5, 6, OCH_2, CH_2OBn), 2.90 (dd, 1 H, *J* 6.8, 16.8 Hz, H-7′), 2.31 (d, 1 H, *J* 16.8 Hz, H-7), 1.25 (t, 3 H, CH_3); EI (HRMS): *m/z* 414.192269, $[M+H]^+$; Calcd for $C_{23}H_{27}NO_6$: 414.191663.

*Butyl 4,6-di-*O*-benzyl-2,3-dideoxy-3-*N*-oxamate-*D*-ribo–hexaldono-1,5-lactone* (**42**).—Compound **21** (0.178 g, 0.5 mmol) and butyl glyoxylate **18** (0.09 g, 0.7 mmol) were dissolved in benzene (5 mL), treated with anhydrous Na_2CO_3 (0.075 g, 0.7 mmol) and refluxed for 4 h. Subsequently, the mixture was filtered, evaporated and purified on a silica gel column using–hexane 9:1 EtOAc as an eluent to afford **42** (0.105 g) in 45% yield; syrup, $[\alpha]_D$ − 6.2° (*c* 0.4, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 7.40 (d, 1 H, *J* 8.8 Hz, NH), 4.73 (m, 1 H, *J* 3.4, 6.2, 8.8, 10.4 Hz, H-3), 4.69 (quintet, 1 H, *J* 2.5, 3.2, 5.2 Hz, H-5), 4.51, 4.68 (2 d, 2 H, *J* 12.0 Hz, OBn), 4.51, 4.57 (2 d, 2 H, *J* 11.9 Hz, OBn), 3.87 (t, 1 H, *J* 2.5, 3.4 Hz, H-4), 3.66 (dd, 1 H, *J* 5.2, 10.5 Hz, CH_AH_BOBn), 3.63 (dd, 1 H, *J* 3.2, 10.5 Hz, CH_AH_BOBn), 2.79 (dd, 1 H, *J* 6.2, 17.4 Hz, H-2′), 2.71 (dd, 1 H, *J* 10.4, 17.4 Hz, H-2), 0.96, 1.42, 1.73, 4.29 (4 m, 9 H, Bu); EI (HRMS): *m/z* 469.21012, $[M^{+\bullet}]$; Calcd for $C_{26}H_{31}NO_7$: 469.21005. Anal. Calcd for $C_{26}H_{31}NO_7$: C, 66.52; H, 6.60; N, 2.98; Found: C, 66.7; H, 6.6; N, 3.0.

*Butyl 4,6-di-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-3-*N*-oxamate-*D*-ribo-hexaldono-1,5-lactone* (**43**).—Compound **43** was obtained from **22** (0.20 g. 0.5 mmol) according to the procedure described above. Yield 0.116 g (45%); mp 82–84 °C; $[\alpha]_D$ − 4.7° (*c* 0.1, CH_2Cl_2); IR ($CHCl_3$): 1729, 1624 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.24 (d, 1 H, NH), 4.76 (m, 1 H, H-3), 4.38 (dt, 1 H, *J* 2.2, 2.5, 5.4 Hz, H-5), 4.12 (t, 1 H, 2.2, 2.7 Hz, H-4), 3.83

(dd, 1 H, *J* 5.4, 11.1 Hz, CH_AH_BOSi), 3.79 (dd, 1 H, *J* 2.5, 11.1 Hz, CH_AH_BOSi), 2.77 (dd, 1H, *J* 6.1, 17.3 Hz, H-2′), 2.65 (dd, 1 H, *J* 10.9, 17.3 Hz, H-2), 0.95, 1.42, 1.73, 4.30 (4 m, 9 H, Bu), 0.09, 0.10, 0.13, 0.90, 0.93 (5 s, 30 H, 2 Si*t*-BuMe_2); LSIMS (MS): *m/z* 518, $[M+H]^+$. Anal. Calcd for $C_{24}H_{47}NO_7Si_2$: C, 55.70; H, 9.09; N, 2.70. Found: C, 56.0; H, 9.3; N, 2.7.

*(2S,4R,5R,6S)- and (2R,4R,5R,6S)-1-Aza-5-benzyloxy-4-benzyloxymethyl-2-butoxycarbonyl-3,9-dioxa-8-oxo-bicyclo[4.3.0]nonane (**44** and **45**).*—Compound **21** (0.357 g, 1.0 mmol), freshly distilled butyl glyoxylate (0.195 g, 1.5 mmol) and *p*-TsOH (6 mg) in toluene (25 mL) were refluxed for 0.5 h. Subsequently, the solvent was evaporated and the residue was separated on a silica gel column using 9:1 toluene–EtOAc as an eluent to afford **44** (0.234 g, 50%) yield and **45** (0.023 g, 5%).

44: mp 117–119 °C; $[\alpha]_D$ + 71.2° (*c* 0.5, CH_2Cl_2); IR ($CHCl_3$): 1797, 1760 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.96 (s, 1 H, H-2), 4.64, 4.75 (2 d, 2 H, *J* 11.9 Hz, OBn), 4.47, 4.64 (2 d, 2 H, *J* 11.3 Hz, OBn), 3.88 (dd, 1 H, *J* 3.5, 11.7 Hz, CH_AH_BOBn), 3.86 (dd, 1 H, *J* 2.2, 11.7 Hz, CH_AH_BOBn), 3.71 (dd, 1 H, *J* 6.6, 9.1 Hz, H-6), 3.68 (t, 1 H, *J* 8.7, 9.1 Hz, H-5), 3.61 (dt, 1 H, *J* 2.2, 3.5, 8.7 Hz, H-4), 3.00 (dd, 1 H, *J* 6.6, 16.9 Hz, H-7′), 2.28 (d, 1 H, *J* 16.9 Hz, H-7), 0.93, 1.40, 1.69, 4.27 (4 m, 9 H, Bu), LSIMS (HRMS): *m/z* 470.21831, $[M+H]^+$; Calcd for $C_{26}H_{32}NO_7$: 470.21788. Anal. Calcd for $C_{26}H_{31}NO_7$: C, 66.52; H, 6.60; N, 2.98. Found: C, 66.6; H, 6.7; N, 2.9.

45: mp 55–57 °C; $[\alpha]_D$ + 41.8° (*c* 0.5, CH_2Cl_2); ^1H NMR ($CDCl_3$): δ 5.51 (s, 1 H, H-2), 4.57, 4.73 (2 d, 2 H, *J* 12.0 Hz, OBn), 4.45, 4.59 (2 d, 2 H, *J* 11.4 Hz, OBn), 4.01 (ddd, 1 H, *J* 2.0, 3.3, 9.7 Hz, H-4), 3.88 (dd, 1 H, *J* 7.0, 9.7 Hz, H-6), 3.84 (dd, 1 H, *J* 3.3, 11.4 Hz, CH_AH_BOBn), 3.76 (dd, 1 H, *J* 2.0, 11.4 Hz, CH_AH_BOBn), 3.72 (t, 1 H, *J* 9.7, 9.7 Hz, H-5), 3.00 (dd, 1 H, *J* 7.0, 17.0, H-7′), 2.34 (d, 1 H, *J* 17.0 Hz, H-7), 0.93, 1.38, 1.66, 4.20 (4 m, 9 H, Bu); LSIMS (HRMS): *m/z* 470.21739, $[M+H]^+$; Calcd for $C_{26}H_{32}NO_7$: 470.21788.

(2S,4R,5R,6S)-5-Acetoxy-4-acetoxymethyl-1-aza-2-butoxycarbonyl-3,9-dioxa-8-oxo-bicyclo-[4.3.0]-nonane (**46**).—Compound **46** was obtained from **20** (0.26 g, 1 mmol) according to the procedure described above (0.216 g, 58%); mp 108–110 °C; $[\alpha]_D$ + 138.6° (*c* 0.5, CH_2Cl_2): IR ($CHCl_3$): 1801, 1763, 1741 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.03 (s, 1 H, H-2), 5.02 (t, 1 H, *J* 9.3, 10.1 Hz, H-5), 4.32 (dd, 1 H, *J* 5.2, 12.5 Hz, CH_AH_BOAc), 4.22 (dd, 1 H, *J* 2.5, 12.5 Hz, CH_AH_BOAc), 3.88 (dd, 1 H, *J* 7.0, 9.3 Hz, H-6), 3.81 (ddd, 1 H, *J* 2.5, 5.2, 10.1 Hz, H-4), 3.13 (dd, 1 H, *J* 7.0, 16.9 Hz, H-7′), 2.78 (d, 1 H, *J* 16.9 Hz, H-7), 2.09, 2.11 (2 s, 6 H, 2 OAc), 0.95, 1.41, 1.70, 4.29 (4 m, 9 H, Bu); LSIMS (HRMS): *m/z* 374.14488, $[M+H]^+$; Calcd for $C_{16}H_{24}NO_9$: 374.14510. Anal. Calcd for $C_{16}H_{23}NO_9$: C, 51.47; H, 6.17; N, 3.75. Found: C, 51.3; H, 6.1; N, 3.6.

(2S,4S,5S,6R)-5-Benzyloxy-6-benzyloxymethyl-3-hydroxy-4-methoxycarbonylmethyl-2-methyl-1,3-oxazine (**50**).—Compound **31** (0.383 g, 1.0 mmol) was dissolved in 0.1% soln of ammonia in MeOH (2.0 mL) and left for 0.5 h. Subsequently, the solvent was evaporated and the residue was purified by chromatography to afford **50** (0.344 g, 83%); syrup; $[\alpha]_D$ −15.9° (*c* 0.4, CH_2Cl_2); IR ($CHCl_3$): 3575, 1730 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.57, 4.68 (2 d, 2 H, *J* 12.2 Hz, OBn), 4.35–4.60 (m, 3 H, H-2, OBn), 3.64 (s, 3 H, OCH_3), 3.54–3.76 (m, 4 H, H-5, 6, CH_2OBn), 3.33 (bs, 1 H, H-4), 2.76 (dd, 1 H, *J* 4.4, 14.1 Hz, $CH_AH_BCO_2Me$), 2.67 (dd, 1 H, *J* 8.9, 14.1 Hz, $CH_AH_BCO_2Me$), 1.40 (d, 1 H, *J* 5.8 Hz, CH_3); EI (MS): *m/z* 415 ($M^{+\bullet}$). Anal. Calcd for $C_{23}H_{29}NO_6$: C, 66.50; H, 6.98; N, 3.37. Found: C, 66.3; H, 7.0; N, 3.4.

*(2R,4R,5R,6S)-5-*Tert*-butyldimethylsiloxy-2,6-dimethyl-3-hydroxy-4-methoxycarbonylmethyl-1,3-oxazine* (**51**).—Compound **51** was obtained from 41 (0.30 g, 1 mmol) according to the procedure described above (0.283 g, 85%); syrup; $[\alpha]_D$ + 35.2° (*c* 0.4, CH_2Cl_2); IR ($CHCl_3$): 3576, 1730 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.36 (bs, 1 H, H-2), 3.70 (s, 3 H, OCH_3), 3.55 (bt, 1 H, *J* 8.4, 9.4 Hz, H-5), 3.19 (bm, 1 H, H-4), 3.18 (dq, 1 H, *J* 6.0, 8.4 Hz, H-6), 2.78 (dd, 1 H, *J* 3.9, 13.5 Hz, $CH_AH_BCO_2Me$), 2.63 (bdd, 1 H, *J* 10.8, 13.5 Hz, $CH_AH_BCO_2Me$), 1.36 (d, 1 H, *J* 5.8 Hz, C-2 CH_3), 1.27 (d, 1 H, *J* 6.0 Hz, C-6 CH_3), 0.08, 0.10, 0.89 (3 s, 15 H, Si*t*-BuMe_2); MS (EI): *m/z* 333 ($M^{+\bullet}$). Anal. Calcd for $C_{15}H_{31}NO_5Si$: C, 54.05; H, 9.30; N, 4.20. Found: C, 54.1; H, 9.4; N 4.2.

X-ray crystallography of compounds **30** *and* **43**.—X-ray diffraction measurements of crystals of **30** and **43** were performed on an MACH3 diffractometer with graphite monochromated CuK_α radiation. Unit cell parameters were obtained by least-squares fit of the setting angles of 15 reflections in the θ-range between 22.3 and 43.5, and 22.3 and 38.7°, for compounds **30** and **43**, respectively. The data were collected at room temperature using the ω–2θ scan technique and were corrected for the Lorentz and polarization effects.

Table 1
Crystal data and structure refinement for **30** and **43**

Compound	**30**	**43**
Formula	$C_{12}H_{17}NO_7$	$C_{24}H_{47}NO_7Si_2$
Temperature (K)	293(2)	293(2)
Wavelength (Å)	1.54178	1.54178
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	C2
Unit cell dimensions (Å,°):	a = 5.1139(2)	a = 27.560(9)
	b = 14.8867(5)	b = 6.930(2)
	c = 18.5455(8)	c = 16.394(4)
		β = 90.97(2)
Volume (Å)	1411.85(9)	3131(2)
Z	4	4
Density$_{calc.}$ (Mg m^{-3})	1.351	1.099
Absorption coefficient (mm^{-1})	0.961	1.333
F(000)	608	1128
θ range for data collection (°)	3.81–73.02	4.16–57.13
Reflections collected	1444	1242
Independent reflections	1444	1242
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	1440/0/199	1242/0/307
Goodness-of-fit on F^2	1.040	1.095
Final R indices [$I > \sigma(I)$]	$R_1 = 0.0380, wR_2 = 0.1044$	$R_1 = 0.0756, wR_2 = 0.1662$
R indices (all data)	$R_1 = 0.0391, wR_2 = 0.1103$	$R_1 = 0.0948, wR_2 = 0.1794$
Absolute structure parameter	−0.1(4)	0.1(2)
Extinction coefficient	0.0027(6)	0.0000(2)
Largest diff. peak and hole (e. Å^{-3})	0.218 and −0.142	0.213 and −0.224

Intensity of the three control reflections measured every 200 reflections showed no crystal decomposition. The structures were solved by the direct methods [11] and refined using SHELXL93 [12][1]. During refinement procedure function minimized was $\Sigma w(|F_o| - |F_c|)^2$, conventional R indices were denoted R_1 and those based on F^2 were denoted R_2. Weighting scheme adopted during refinement was: $w = 1/[\sigma^2(F_o)^2 + 0.07\,P)^2 + 0.1781\,P]$, and $w = 1/[\sigma^2(F_o)^2 + 0.12\,P)^2 + 0.138\,P]$, respectively, for compounds **30** and **43**, where $P = (F_o^2 + 2F_c^2)/3$. The non-hydrogen atoms were refined anisotropically, whereas the H-atoms were placed in the calculated positions and their thermal parameters were refined isotropically. Due to the lack of sufficient number of reflections and high thermal motions of terminal groups in compound **43**, isotropic thermal parameters for H-atoms were set at value 50% higher then for the parent atoms. Extinction parameters were allowed to vary during refinement procedure in order to verify correct absolute structure. High thermal parameters observed in molecule of compound **43** might be corellated with weak packing forces (compare crystal densities for **30** and **43**). To our own experience, such bulky or flexible residues as $(Me)_2$t-BuSi and n-Bu very often show static or dynamic disorder in the crystals. The atomic scattering factors were taken from the International

[1] Tables of atomic coordinates, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained, on request from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, UK, CB2 IEZ.

Table 2
Atomic coordinates (×10^4) and equivalent isotropic displacement parameters (Å^2×10^3) for **30**. U(equiv) is defined as one third of the trace of the orthogonalized U_{ij} tensor

	x	y	z	U(equiv)
N-1	20644(4)	−3745(1)	−7691(1)	45(1)
C-2	19406(6)	−4620(2)	−7752(1)	47(1)
C-22	17592(8)	−4683(2)	−8395(2)	62(1)
O-3	17938(4)	−4878(1)	−7133(10)	47(1)
C-4	19552(5)	−4920(2)	−6506(1)	44(1)
C-41	17929(6)	−5289(2)	−5900(2)	52(1)
O-41	17341(4)	−6214(1)	−6065(1)	59(1)
C-42	15537(7)	−6589(2)	−5652(2)	60(1)
O-42	14451(8)	−6196(2)	−5177(2)	102(1)
C-43	15084(10)	−7558(2)	−5850(2)	80(1)
C-5	20455(5)	−3963(2)	−6352(1)	41(1)
O-51	22209(3)	−3953(1)	−5748(1)	49(1)
C-51	21292(6)	−3661(2)	−5101(2)	52(1)
O-52	19199(5)	−3318(2)	−5035(1)	79(1)
C-52	23152(8)	−3859(3)	−4518(2)	76(1)
C-6	21958(5)	−3582(2)	−6998(1)	45(1)
C-7	22029(5)	−2559(2)	−6985(2)	53(1)
C-8	19446(6)	−2332(2)	−7326(2)	48(1)
O-81	18191(5)	−1653(1)	−7305(1)	65(1)
O-9	18527(4)	−3057(1)	−7686(1)	50(1)

Table 3
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **43**. U(equiv) is defined as one third of the trace of the orthogonalized U_{ij} tensor

	x	y	z	U(equiv)
Si-1	1523(2)	44	8758(3)	73(2)
Si-2	3890(2)	2954(12)	7258(3)	80(")
O-1	2878(4)	−155(26)	8697(6)	68(3)
O-2	2781(6)	−3203(27)	8617(8)	115(6)
O-3	1942(3)	1135(19)	8258(6)	64(3)
O-4	3441(3)	1464(18)	7368(5)	62(3)
O-5	2086(5)	−300(31)	5547(7)	121(6)
O-6	2515(5)	10(29)	4049(7)	116(5)
O-7	3223(5)	121(28)	4729(6)	105(5)
N-1	2813(4)	396(24)	6122(8)	66(4)
C-1	2779(6)	−1744(44)	8264(13)	65(6)
C-2	2704(6)	−1617(28)	7347(10)	67(6)
C-3	2657(5)	371(26)	6963(10)	59(5)
C-4	2931(6)	1855(25)	7447(9)	48(5)
C-5	2818(6)	1749(33)	8347(11)	65(6)
C-6	2312(6)	2383(27)	8563(9)	67(5)
C-7	2513(7)	99(33)	5541(10)	68(5)
C-8	4430(7)	1357(47)	1357(47)	141(10)
C-9	3832(8)	4203(43)	6232(11)	176(14)
C-10	3919(7)	4758(36)	8059(12)	125(8)
C-11	4443(9)	523(47)	8192(19)	201(15)
C-12	4886(6)	2602(44)	7157(16)	173(12)
C-13	4389(9)	−255(50)	6657(19)	218(19)
C-14	1007(7)	1748(37)	9012(12)	93(7)
C-15	1308(6)	−1826(34)	8013(9)	98(7)
C-16	1775(6)	−1089(31)	9694(9)	87(6)
C-17	806(7)	2586(39)	8252(14)	129(9)
C-18	596(6)	501(53)	9425(13)	186(15)
C-19	1205(8)	3243(43)	9615(12)	129(8)
C-20	2750(8)	105(39)	4658(12)	83(6)
C-21	3475(9)	3475(9)	233(57)	174(16)
C-22	3922(13)	−471(55)	4033(16)	160(13)
C-23	4031(13)	−2555(65)	4300(20)	219(20)
C-24	4387(12)	−3836(64)	4244(20)	252(21)

Tables [13]. Crystal data, details of data collection and structure refinement for compounds **30** and **43** are given in Table 1. The final atomic parameters and their equivalent isotropic temperature factors for non-hydrogen atoms are shown in Table 2 and Table 3[1].

Acknowledgement

This work was supported by the State Committee for Scientific Research (Grant 3T 09A 13112).

References

[1] E.C. Taylor, R.J. Clemens, H.M.L. Davies, and N.F. Haley, *J. Am. Chem. Soc.*, 103 (1981) 7659–7660; E.C. Taylor, N.F. Haley, and R.J. Clemens, *J. Am. Chem. Soc.*, 103 (1981) 7743–7752; E.C. Taylor, H.M.L. Davies, and J.S. Hinkle, *J. Org. Chem.*, 51 (1986) 1530–1536; J.E. Baldwin, M.F. Chan, G. Gallacher, P. Monk, and K. Prout, *J. Chem. Soc., Chem. Commun.*, (1983) 250–252; J.E. Baldwin, M.F. Chan, G. Gallacher, P. Monk, and K. Prout, *Tetrahedron*, 40 (1984) 4513–4525; J.E. Baldwin, R.M. Adlington, R.H. Jones, C.J. Schofield, C. Zarocostas, and C.W. Greengrass, *J. Chem. Soc., Chem. Commun.*, (1985) 194–196; L.N. Jungheim, S.K. Sigmund, N.D. Jones, and J.K. Swartzendruber, *Tetrahedron Lett.*, 28 (1987) 289–292; D.B. Boyd, B.J. Foster, L.D. Hatfield, W.J. Hornback, N.D. Jones, J.F. Munroe, and J.K. Swartzendruber, *Tetrahedron Lett.*, 27 (1986) 3457–3460; N.E. Allen, J.N. Hobbs, D.A. Preston, J.R. Turner, and C.Y.E. Wu, *J. Antibiotics*, 43 (1990) 92–99; J. Marchand-Brynaert and L. Ghosez, *Bull. Soc. Chim. Belg.* 94 (1985) 1021–1031; J.P. Declercq, M. van Meerssche, and J. Marchand-Brynaert, *Bull. Soc. Chim. Belg.*, 95 (1986) 241–245.

[2] E.F. Galc, E. Cuncliffe, P.E. Reynolds, and M.J. Waring, *The Molecular Basis of Antibiotics Action*, John Wiley, New York, 1981; J. Marchand-Brynaert, and L. Ghosez, *Non β-Lactum Analogs of Penicillin and Cephalosporins*, in G. Lukacs, and M. Ohno (Eds.), *Recent Progress in the Chemical Synthesis of Antibiotics* Springer–Verlag Berlin, 1990, pp. 727–797; J. Marchand-Brynaert, Z. Bounkhala-Khrouz, J.C. Carretero, J. Davies, D. Ferrond, B.J. van Keulen, B. Serckx-Poncin, and L. Ghoses, in *Recent advances in the chemistry of β-lactam antibiotics*, *Chem. Soc.* (special public.), 70 (1998) 157–170.

[3] Y. Nozaki, N. Katayama, H. Ono, S. Tsubotani, S. Harada, H. Okazaki, and Y. Nakao, *Nature*, 325 (1987) 179–180. Y. Nakao in *Recent advances in the chemistry of β-lactam antibiotics*, *Chem. Soc.* (special public.), 70 (1998) 119–138; J.E. Baldwin, C. Ng Si, and A.J. Pratt, *Tetrahedron Lett.*, 28 (1987) 4319–4320; S. Harada, S. Tsubotani, T. Hida, K. Kogama, M. Kondo, and H. Ono, *Tetrahedron*, 44 (1988) 6589–6606.

[4] S. Maciejewski, I. Panfil, C. Bełzecki, and M. Chmielewski, *Tetrahedron*, 48 (1992) 10363–10376.

[5] J. Frelek, I. Panfil, P. Gluziński, and M. Chmielewski, *Tetrahedron Asymm.*, 7 (1996) 3415–3426.

[6] I. Panfil, C. Bełzecki, M. Chmielewski, and K. Suwińska, *Tetrahedron*, 45 (1989) 233–238.

[7] M. Jurczak, D. Socha, and M. Chmielewski, *Tetrahedron*, 52 (1996) 1411–1424; G.W. Anderson, J.E. Zimmerman, and F.M. Callahan, *J. Am. Chem. Soc.*, 86 (1964) 1839–1842.

[8] W. Abramski and M. Chmielewski, *J. Carbohydr. Chem.*, 15 (1996) 109–113.

[9] M. Chmielewski, J. Jurczak, and S. Maciejewski, *Carbohydr. Res.*, 165 (1987) 111–115.
[10] J.G. Gleason, T.F. Buckley, K.G. Holden, D. Boles Bryan, and P. Siler, *J. Am. Chem. Soc.*, 101 (1979) 4730–4732.
[11] G.M. Sheldrick, *Acta Cryst.*, A46 (1990) 467.
[12] G.M. Sheldrick, SHELXL93: Program for refinement of crystal structure, University of Gottingen, Germany, 1993.
[13] *International Tables for X-Ray Crystallography*, Vol. IV, Kynoch Press, Birmingham, UK, 1974.