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AN APPROACH TO CARBAPENEMS FROM α,β-UNSATURATED SUGAR LACTONES

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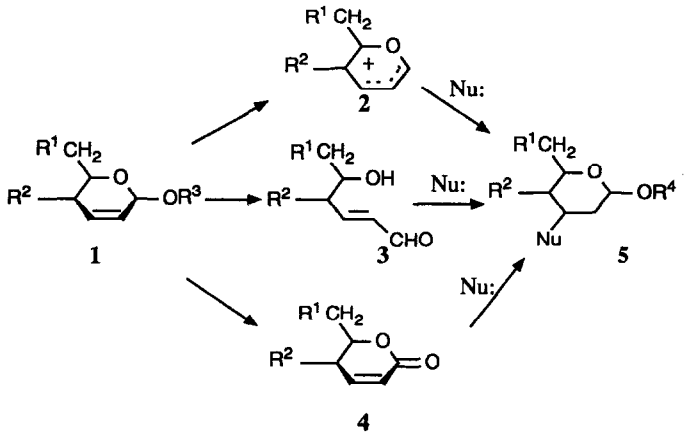
Abstract: Conjugate addition-rearrangement of N-substituted hydroxylamines to α,β-unsaturated D-lactones provides a short and effective route to 3-substituted isoxazolidin-5-ones. These compounds were converted into 4-substituted azetidin-2-ones via a two-step procedure involving hydrogenolysis of the N-O bond followed by cyclization of the resulting β-amino acids. N-Benzyl-4-(3'-acetoxy-2'-tert-butyldimethylsiloxypropyl)azetidin-2-one (37) was transformed into known precursors of carbapenem antibiotics.

Introduction of a substituent on the C-4 carbon atom of the 5,6-dihydro-2H-pyran skeleton **1** can be achieved by three general approaches: (i) addition of a nucleophile to the cation **2** generated from **1** in the presence of acid catalyst[1], (ii) addition of a nucleophile to α,β-unsaturated aldehyde **3** obtained from **1** by hydrolysis[1d,2], (iii) addition of a nucleophile to pyrone **4** obtained from **1** by acetal oxidation (**Scheme 1**).[2a,3] Intermediates **2**, **3**, and **4** can be obtained directly from acetylated glycals *via* a stepwise process involving Ferrier rearrangement to the structure **1** as the first step.[4,5,6] Regarding the relative location of the terminal CH_2R^1 group and of the entering nucleophile, the three approaches shown on **Scheme 1** offer complementary results. Unless the neighboring 4-*O*-acetyl group promotes formation of the *cis* 3,5-arrangement,[4] the first one leads to a mixture of diastereomers with dominance of the *trans* isomer,[1] whereas the second one affords a considerable amount of *cis* isomer.[2] The third approach produces almost exclusively the *trans* isomer, regardless of the presence or absence of a substituent and of the configuration at the C-5 carbon atom.[3]

While working on the synthesis of racemic negamycin (**6**),[7] two groups have reported independently on stereospecific *trans* addition of the azide anion to lactones **7**[2a,3a,3b] (**Scheme 2**). The steric course of addition, although discouraging for the negamycin synthesis, has prompted us to utilize the observed stereospecificity for the synthesis of carbapenem antibiotics for example thienamycin **8**. The general idea is shown on the retrosynthetic scheme (**Scheme 3**).

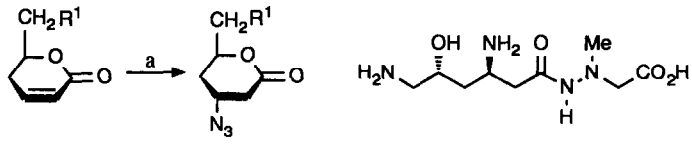
Scheme 1



R^1, R^2 : H, alkoxyl, acyloxyl
R^3 : alkyl

Addition of nitrogen nucleophiles to lactones: D-*glycero* **10**[2a, 3a, 3b, 3c], D-*erythro* **11**[3c], and D-*threo* **12**[3c], derived from D-glucose and D-galactose (the last one), leads to adducts having a hidden β-amino acid fragment with absolute configuration desired for carbapenem antibiotics (**Scheme 3**)[8]. Owing to the axial location of the entering nucleophile, Michael adducts undergo easily *retro* addition upon purification attempts[2a, 3b]. This low stability of the adducts precludes their practical use in the synthesis of β-lactams.

Scheme 2

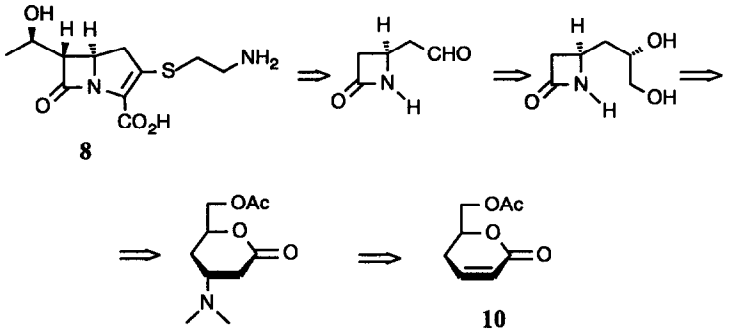


R^1= OAc, NPhtal
a. NaN_3, AcOH

Recently we have found that the room-temperature reaction of hydroxylamine and formaldehyde with lactones **10**, **12** gave bicyclic compounds **13** and **14**, respectively[9], as a result of conjugate *anti*- addition of hydroxylamine, rearrangement of the adduct from a

δ-lactone to the isoxazolidin-5-one ring, and subsequently of formation of a methylene bridge between the nitrogen and oxygen atoms by formaldehyde.[9] The structure of **13**, which was proved by X-ray measurements[10], led us to investigate the addition of *N*-substituted hydroxylamines to lactones **9-12**.

Scheme 3



8 **10**

Our preliminary results[3c] have shown that conjugate addition of *N*-substituted hydroxylamines **15-18** to lactones **9-12** could eliminate all drawbacks involved in our previous attempts at azide anion and *O*-benzylhydroxylamine additions.[2a,3b] These additions proceeded exclusively *anti* to the terminal acetoxymethyl group, but formation of the Michael adduct **19** was never observed. Axial location of the hydroxylamine group induces easy opening of the six-menbered lactone ring by the hydroxyl group to afford the isoxazolidin-5-one skeleton. The formation of isoxazolidin-5-ones, *via* Michael addition of hydroxylamines to unsaturated esters, followed by intramolecular cyclization, of the adduct is a known process; the second step requires, however, a basic catalyst and usually heating.[11] Rapid formation of the isoxazolidin-5-one ring eliminates the problem of the retro Michael addition, affording simultaneously intramolecular protection of both functions, necessary to produce the β-lactam ring.

Lactones **9 - 12** were treated with hydroxylamine (**15**), *N*-methyl- hydroxylamine (**16**), *N*-p-methoxybenzylhydroxylamine (**17**), or *N*-benzylhydroxylamine (**18**) in ethanol solution to afford respective isoxazolidin-5-ones **20-33** in a good yield (**Scheme 4**). Owing to the risk of migration of the acetyl group, the free hydroxyl group in the side chain of isoxazolidin-5-ones was protected with the t-butyldimetylsilyl-, t-butyldiphenylsilyl or acetyl residue to afford compounds **20-33**.

The *N* - *O* bond in compounds **21**, **23**, **25**, **28**, **29**, and **30** can be easily split by hydrogenolysis over palladium catalyst, without affecting the *N*-*p*-methoxybenzyl or *N*-benzyl protections, to give the respective β-amino acids which without characterization were used for the next step in a crude form (**Scheme 5**). In the case of compound **33** many experiments showed, however, that hydrogenolysis of the N-O bond is immediately followed by a shift of the acetyl group from oxygen to the nitrogen atom, and finally by removal of the p-methoxybenzyl protection.

Scheme 4

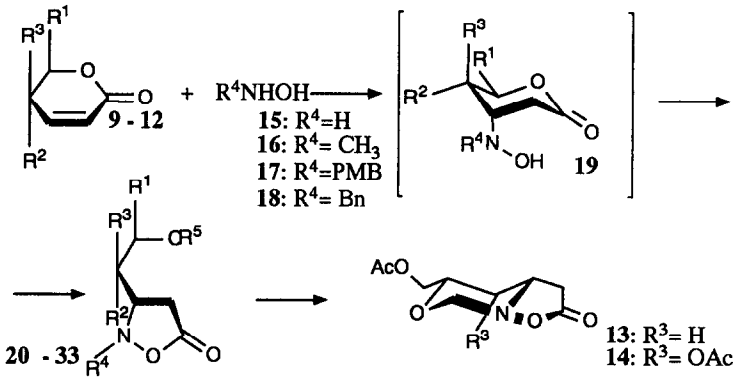
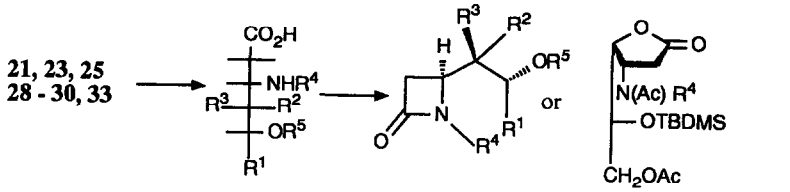


Table 1

	R1	R2	R3	R4	R5
9	H	H	H	-	-
10	CH_2OAc	H	H	-	-
11	CH_2OAc	OAc	H	-	-
12	CH_2OAc	H	OAc	-	-
20	H	H	H	Me	TBDMS
21	H	H	H	PMB	TBDMS
22	CH_2OAc	H	H	Me	TBDMS
23	CH_2OAc	H	H	PMB	Ac
24	CH_2OAc	H	H	PMB	Ac
25	CH_2OAc	H	H	Bn	TBDMS
26	CH_2OAc	OAc	H	Ac	Ac
27	CH_2OAc	OAc	H	Me	TBDMS
28	CH_2OAc	OAc	H	PMB	TBDMS
29	CH_2OAc	OAc	H	PMB	Ac
30	CH_2OAc	OAc	H	Bn	TBDMS
31	CH_2OAc	H	OAc	Me	TBDMS
32	CH_2OAc	H	OAc	Me	Ac
33	CH_2OAc	H	OAc	PMB	TBDMS
35	H	H	H	PMB	TBDMS
36	CH_2OAc	H	H	PMB	TBDMS
37	CH_2OAc	H	H	Bn	TBDMS
38	CH_2OAc	OAc	H	PMB	TBDMS
39	CH_2OAc	OAc	H	PMB	Ac

Scheme 5

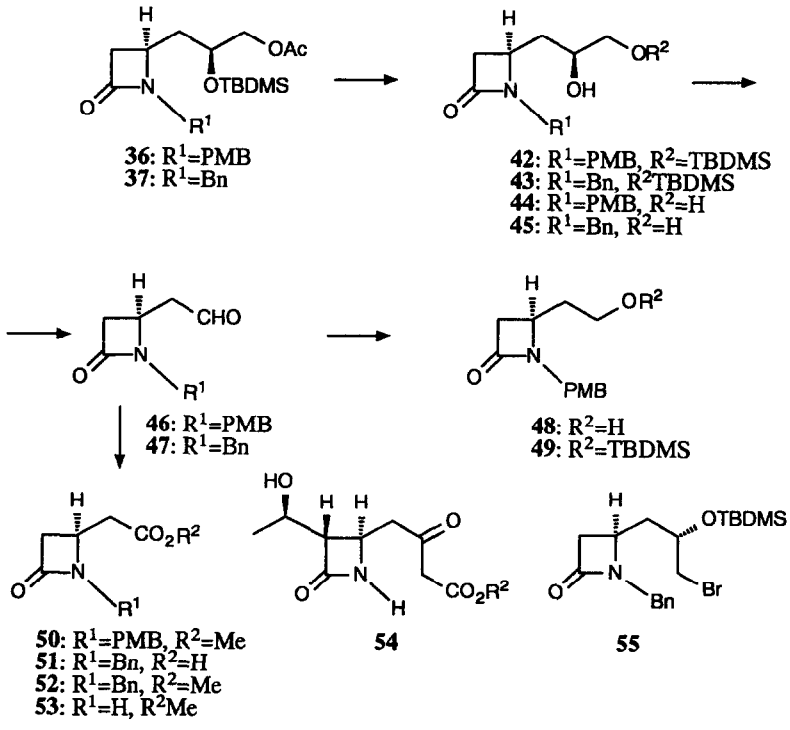


34 **35 - 39**

40: R^4= PMB
41: R^4= H

β-Amino acids **34** were subjected to cyclization using the Mukaiyama[12] regent to from the respective β-lactams **35** - **38**.[13] In the case of compound **33** with the *xylo* configuration, we obtained lactone **41** and traces of lactone **40**. The distinct behaviour of compound **33** during hydrogenolysis remains unclear (**Scheme 5**).

Scheme 6



36: R^1=PMB
37: R^1=Bn

42: R^1=PMB, R^2=TBDMS
43: R^1=Bn, R^2TBDMS
44: R^1=PMB, R^2=H
45: R^1=Bn, R^2=H

46: R^1=PMB
47: R^1=Bn

48: R^2=H
49: R^2=TBDMS

50: R^1=PMB, R^2=Me
51: R^1=Bn, R^2=H
52: R^1=Bn, R^2=Me
53: R^1=H, R^2Me

54

55

Compounds with the *erythro* configuration, with p-methoxybenzyl or benzyl protection at the nitrogen atom (**36** and **37**), were selected for further steps towards carbapenems. Deprotections of the hydroxyl groups in **36** and **37**, followed by glycolic cleavage, gave the respective aldehydes **46** and **47** which could be reduced to alcohols or oxidized to acids. Attempts to remove the p-methoxybenzyl substituent, in order to get the known compound, however, failed. The same sequence of reactions succeeded in the case of N-benzyl protection which could be removed by sodium in liquid ammonia reduction (**Scheme 6**).

The spectroscopic and analytical data of compound **45** were compared with the respective data of the known β-lactam[14] with the same structure, obtained in the past from L-aspartic acid, and used for the total synthesis of carbapenem antibiotics.[15]

The sequence of reactions leading from lactones **10** and **11** to β-lactams **35** - **39** offers easy and regiospecific protections of the hydroxy groups in the side chain. The structural similarities between the side chain of compounds **43** and **45** and the side chain of the crucial intermediate in carbapenem synthesis **54**[16] are striking. Replacement the hydroxyl group in **43** by a bromine atom gave compound **55** which could be utilized in the synthesis of carbapenens as well as in the synthesis of pyrrolidine alkaloids.[17]

Experimental

Melting points are uncorrected. Optical rotations were measured with a JASCO Dip-360 digital polarimetr. IR spectra were taken with a Beckman 4240 spectrophotometr. ^{1}H NMR spectra were recorded with Varian Gemini 200 and Bruker AM 500 spectrometrs. Column chromatography was perfermed on Merck Kieselgel 60 (230-400 mesh).

Lactone **10** was obtained from **11** according to the known procedure[17] which consisted in reductive removal of the 4-OAc group followed by a base catalyzed shift of the double bond from β,γ- to α,β-position; as a base DBU was used insted of Et_3N proposed in the original paper.[18] Lactones **11** and **12** were obtained using known method.[19]

Addition of N-substituted hydroxylamines 15-18 to lactones 9-12. General procedure. To a solution of lactone (1.0 mmol) in anhydrous ethyl alcohol (10 mL) N-substituted hydroxylamine (freshly prepared from respective hydrochloride by the sodium ethoxide titration in ethanol solution in the presence of phenolophthalein; 1.0 mmol in 3 mL of ethanol) was added. A mixture was stirred at room temp. for 3 h. Subsequently the solvent was evaporated and the crude product was acetylated with acetic anhydride - pyridine mixture, or was silylated with *tert*-butyldimethylsilylchloride, or with *tert*-butylchlorodiphenylsilane (1.2 mmol) in DMF (20 mL) in the presence of DMAP (2.0 mmol), at room temp. during 3 h. The mixture was then poured into water and extracted with ethyl ether. The extract was washed with brine, dried, and evaporated. The crude residue was purified on a silica gel column using hexane - ethyl acetate as an eluent to afford respective compounds **20** - **33**.

N-Methyl-3-(2'-*tert*-butyldiphenylsiloxyethyl)-isoxazolidin-5-one (20): from **9** and **16**: 78%: mp. 70-72°C: IR (film): 1795 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.05 (s, 9H, t-Bu), 1.69 (m,

1H, H-1'a), 1.89 (m, 1H, H-1'b), 2.57 (dd, 1H, *J* 17.1 and 10.6 Hz, H-4a), 2.78 (dd, 1H, *J* 17.1 and 6.9 Hz, H-4b), 2.85 (s, 3H, N-CH_3), 3.31 (bs, 1H, H-3), 3.71 (m, 1H, H-2'a), 3.78 (m, 1H, H-2'b); MS m/z: M^+ 383. Anal. Calcd for $C_{22}H_{29}NO_3Si$: C, 68.9; H, 7.6; N, 3.7. Found: C, 69.3; H, 7.6; N, 3.6.

N-(p-Methoxybenzyl)-3-(2'-*tert*-butyldiphenylsiloxyethyl)-isoxazolidin-5-one (21); from **9** and **18**; 87%, syrup; IR (film): 1795 cm^{-1}; ^1H NMR ($CDCl_3$): 1.04 (s, 9H, t-Bu), 1.69 (m, 1H, H-1'a), 1.90 (m, 1H, H-1'b), 2.51 (dd, 1H, *J* 17.2 and 9.0 Hz, H-4a), 2.69 (dd, 1H, *J* 17.2 and 7.4 Hz, H-4b), 3.58 (m, 1H, H-3), 3.68 (m, 1H, H-2'a), 3.77 (m, 1H, H-2'b), 3.78 (s, 3H, OCH_3), 3.99, 4.11 (2d, 2H, *J* 14.0 Hz, benzyl); MS m/z: M^+ 489. Anal. Calcd for $C_{29}H_{35}NO_4Si$: C, 71.2; H, 7.2; N, 2.9. Found: C, 71.2; H, 7.3; N, 3.0.

(3R,2'S) N-Methyl-3-(3'-acetoxy-2'-*tert*-butyl-dimethylsiloxypropyl)-isoxazolidin-5-one (22); from **10** and **16**; 52%, mp. 54-55°C; $[\alpha]_D$ -114° (*c* 0.88, CH_2Cl_2); IR (KBr): 1800, 1745 cm^{-1}; ^1H NMR ($CDCl_3$): 0.03, 0.10, 0.89 (3s, 15H, t-BuMe_2Si), 1.71 (m, 1H, H-1'a), 1.86 (m, 1H, H-1'b), 2.08 (s, 3H, OAc), 2.60 (dd, 1H, *J* 16.7 and 10.5 Hz, H-4a), 2.88 (dd, 1H, *J* 16.7 and 6.9 Hz, H-4b), 2.89 (s, 3H, N-CH_3), 3.30 (m, 1H, H-3), 3.96 (m, 1H, H-2'), 4.00 (m, 2H, H-3'a, 3'b); MS m/z: M^+ 331. Anal. Calcd for $C_{15}H_{29}NO_5Si$: C, 54.3; H, 8.8; N, 4.2. Found: C, 54.1; H, 8.7; N, 3.9.

(3R,2'S) N-(p-Methoxybenzyl)-3-(3'-acetoxy-2'-*tert*-butyldimethylsiloxypropyl)-isoxazolidin-5-one (23): from **10** and **18**; 69%; syrup; $[\alpha]_D$ -137° (*c* 0.9, CH_2Cl_2); IR (film): 1800, 1735 cm^{-1}; ^1H NMR ($CDCl_3$): 0.05, 0.08, 0.87 (3s, 15H, t-BuMe_2Si), 1.69 (m, 1H, H-1'a), 1.83 (m, 1H, H-1'b), 2.06 (s, 3H, OAc), 2.51 (dd, 1H, *J* 17.2 and 8.4 Hz, H-4a), 2.81 (dd, 1H, *J* 17.2 and 7.4 Hz, H-4b), 3.54 (m, 1H, H-3), 3.80 (s, 3H, OCH_3), 3.90 (m, 3H, H-2', 3'a, 3'b), 4.05, (2d, 2H, *J* 13.8 Hz, benzyl); MS m/z: M^+ 437. Anal. Calcd for $C_{22}H_{35}NO_6Si$: C, 60.4; H, 8.1; N, 3.2. Found: C, 60.6; H, 8.0; N, 3.0.

(3R,2'S) N-(p-Methoxybenzyl)-3-(2',3'-diacetoxypropyl)-isoxazolidin-5-one (24); from **10** and **18**; 79%; mp. 89-90°C; $[\alpha]_D$ -129° (*c* 1.1, CH_2Cl_2); IR ($CHCl_3$): 1790, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 2.05, 2.06 (2s, 6H, 2 OAc), 1.76 (m, 1H, H-1'a) 1.97 (m, 1H, H-1'b), 2.53 (dd, 1H, *J* 17.2 and 8.3 Hz, H-4a), 2.86 (dd, 1H, *J* 17.2 and 7.4 Hz, H-4b), 3.43 (m, 1H, H-3), 3.81 (s, 3H, OCH_3), 3.96 (dd, 1H, *J* 12.0 and 5.9 Hz, H-3'a), 4.07, 4.11 (2d, 2H, *J* 13.7 Hz, benzyl), 4.16 (dd, 1H, *J* 12.0 and 3.8 Hz, H-3'b), 5.11 (m, 1H, H-2'); MS m/z: M^+ 365. Anal Calcd. for $C_{18}H_{23}NO_7$: C, 59.2; H, 6.4; N, 3.8. Found: C, 59.2; H, 6.5; N, 3.6.

(3R,2'S) N-Benzyl-3-(3'-acetoxy-2'-*tert*-butyldimethylsiloxypropyl)-isoxazolidin-5-one (25), from **10** and **17**; 73%; syrup; $[\alpha]_D$ -114° (*c* 1.35, CH_2Cl_2); IR (film): 1800, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 0.05, 0.06, 0.87 (3s, 15H, t-BuMe_2Si), 1.73 (m, 1H, H-1'a), 1.87 (m, 1H, H-1'b), 2.06 (s, 3H, OAc), 2.56 (dd, 1H, *J* 17.2 and 8.8 Hz, H-4a), 2.84 (dd, 1H, *J* 17.2 and 7.3 Hz, H-4b), 3.56 (m, 1H, H-3), 3.92 (m, 3H, H-2', 3'a, 3'b), 4.09, 4.19 (2d, 2H, *J* 13.9 Hz, benzyl); MS m/z: M^+ 349. Anal. Calcd for $C_{21}H_{35}NO_5Si$: C, 61.9; H, 8.2; N, 3.4. Found: C, 61.8; H, 8.2; N, 3.2.

(3S,1'S,2'R) N-Methyl-3-(1',3'-diacetoxy-2'-*tert*-butyldimethylsiloxypropyl)-isoxazolidin-5-one (27), from **11** and **16**; 56%; syrup; $[\alpha]_D$ -89° (*c* 1.1, CH_2Cl_2); IR (film): 1795, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 0.06, 0.08, 0.90 (3s, 15H, t-BuMe_2Si), 2.09, 2.11 (2s, 6H, 2

OAc), 2.90 (s, 3H, N-CH_3), 2.83 (dd, 1H, *J* 17.5, and 7.9 Hz, H-4a), 2.98 (dd, 1H, *J* 17.5 and 9.1 Hz, H-4b), 3.52 (m, 1H, *J* 2.9, 7.9, and 9.1 Hz, H-3) 3.99 (q, 1H, H-2'), 4.07 (dd, 1H, *J* 12.9 and 5.1 Hz, H-3'a), 4.08 (dd, 1H, *J* 12.9 and 5.8 Hz, H-3'b), 5.14 (dd, 1H, *J* 2.9 and 4.4 Hz, H-1); MS m/z: M^+ 389. Anal. Calcd for $C_{17}H_{31}NO_7Si$: C, 52.4; H, 8.0; N, 3.6. Found: C, 53.2; H, 8.0; N, 3.6.

(3s,1'S,2'R) N-(p-Methoxybenzyl)-3-(1',3'-diacetoxy-2'-*tert*-butyldimethylsiloxypropyl)-isoxazolidin-5-one (28), from **11** and **18**; 61%; mp. 96-97°C; $[\alpha]_D$ -83° (*c* 0.74, CH_2Cl_2); IR (film): 1785, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 0.07, 0.09, 0.88 (3s, 15H, t-BuMe_2Si), 2.06, 2.11 (2s, 6H,2 OAc), 2.62 (dd, 1H, *J* 17.6 and 8.3 Hz, H-4a), 2.85 (dd, 1H, *J* 17.6 and 7.6 Hz, H-4b), 3.75 (ddd, 1H, *J* 3.4, 8.3, and 7.6 Hz, H-3), 3.80 (s, 3H, OCH_3), 3.98 (m, 3H, H-2', H-3'a, 3'b), 4.01, 4.02 (2d, 2H, *J* 13.7 Hz, benzyl), 5.18 (dd, 1H, *J* 3.4 and 4.3 Hz, H-1'); MS m/z: M^+ 495. Anal Calcd. for $C_{24}H_{37}NO_8Si$: C, 58.2; H, 7.5; N, 2.8. Found: C, 57.9; H, 7.7; N, 2.7.

(3s,1'S,2'R) N-(p-Methoxybenzyl)-3-(1',2',3'-triacetoxypropyl)-isoxazolidin-5-one (29), from **11** and **18**; 76%; syrup, $[\alpha]_D$ -81° (*c* 0.58, CH_2Cl_2); IR (film): 1795, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 2.05, 2.06 (2s, 9H, 3 OAc), 2.71 (dd, 1H, *J* 17.5 and 8.5 Hz, H-4a), 2.81 (dd, 1H, *J* 17.5 and 7.2 Hz, H-4b), 3.6 (ddd, 1H, *J* 3.1, 8.5, and 7.2 Hz, H-3), 3.81 (s, 3H, OCH_3), 4.12, 4.22 (2d, 2H, *J* 13.5 Hz, benzyl), 4.16 (dd, 1H, *J* 12.4 and 3.4 Hz, H-3'a), 4.18 (dd, 1H, *J* 12.4 and 5.0 Hz, H-3'b), 5.18 (ddd, 1H, *J* 7.0, 3.4, and 5.0 Hz, H-2'), 5.23 (dd, 1H, *J* 3.1 and 7.0 Hz, H-1'); MS m/z: M^+ 423. Anal. Calcd for $C_{20}H_{25}NO_9$: C, 56.7; H, 6.0; N, 3.3. Found: C, 56.4; H, 5.9; N, 3.3.

(3S,1'S,2'R) N-Benzyl-3-(1',3'-diacetoxy-2'-*tert*-butyldimethylsiloxypropyl)-isoxazolidin-5-one (30), from **11** and **17**; 64%, syrup, $[\alpha]_D$ -102° (*c* 0.35, CH_2Cl_2), IR (film): 1805, 1760 cm^{-1}; ^1H NMR ($CDCl_3$): 0.08, 0.09, 088 (3s, 15H, t-BuMe_2Si), 2.06, 2.12, (2s, 6H, 2 OAc), 2.65 (dd, 1H, *J* 17.6 and 8.2 Hz, H-4a), 2.89 (dd, 1H, *J* 17.6 and 8.0 Hz, H-4b), 3.78 (dt, 1H, *J* 3.9, 8.2, and 8.0 Hz, H-3), 3.99 (m, 3H, H-2', 3'a, 3'b), 4.05, 4.30 (2d, 2H, *J* 13.8 Hz, benzyl), 5.20 (dd, 1H, *J* 2.9 and 7.1 Hz, H-1'); MS m/z: M^+-56= 408. Anal. Calcd for $C_{23}H_{34}NO_7Si$: C, 59.5; H, 7.4; N, 3.0. Found: C, 59.2; H, 7.5; N, 3.3.

(3S,1'R,2'R) N-Methyl-3-(1',3'-diacetoxy-2'-*tert*-butyldiphenylsiloxypropyl)-isoxazolidin-5-one (31), from **12** and **16**; 30%; syrup; $[\alpha]_D$ -17.3° (*c* 1, CH_2Cl_2); IR (film): 1795, 1755 cm^{-1}; ^1H NMR ($CDCl_3$), 1.07 (s, 9H, t-Bu), 1.76 2.05 (2s, 6H, 2 OAc), 2.42 (dd, 1H, *J* 17.8 and 5.8 Hz, H-4a), 2.67 (dd, 1H, *J* 17.8 and 8.7 Hz, H-4b), 2.86 (s, 3H, N-CH_3), 3.57 (m, 1H, H-3), 4.1 (m, 3H, H-2', 3a', 3'b), 5.01 (dd, 1H, *J* 4.0 and 6.8 Hz, H-1'); MS m/z: M^+- 56= 456. Anal. Calcd for $C_{27}H_{35}NO_7Si$: C, 63.2; H, 6.8; N, 2.7. Found: C, 63.2; H, 6.9; N, 2.9.

(3S,1'R,2'R) N-Methyl-3-(1',2',3'-triacetoxypropyl)-isoxazolidin-5-one (32), from **12** and **16**, 77%; mp. 65-66°C; $[\alpha]_D$ -52.0° (*c* 1, CH_2Cl_2); IR (film): 1795, 1755 cm^{-1}; ^1H NMR ($CDCl_3$): 2.07, 2.10, 2.13 (3s, 9H, 3 OAc), 2.67, (dd, 1H, *J* 17.9 and 4.9 Hz, H-4a). 2.91 (s, 3H, N-CH_3), 3.03 (dd, 1H, *J* 17.9 and 8.9 Hz, H-4b), 3.54 (m, 1H, H-3), 4.04 (dd, 1H, *J* 12.0 and 5.9 Hz, H-3a'), 4.31 (dd, 1H, *J* 12.0 and 5.0 Hz, H-3b'), 5.23 (dd, 1H, *J* 4.2 and 6.2 Hz, H-1'), 5.39 (m, 1H, H-2'); MS m/z: M^+ 317. Anal. Calcd for $C_{13}H_{19}NO_8$: C,

49.2; H, 6.0; N, 4.4. Found: C, 49.0; H, 6.1; N, 4.3.

(3S,1'R,2'R) N-(p-Methoxybenzyl)-3-(1',3'-diacetoxy-2'-*tert*-butyldimethylsiloxypropyl)-isoxazolidin-5-one (33), from **12** and **18**, 75%; mp. 81-82°; $[\alpha]_D$ -48.5 (*c* 1, CH_2Cl_2); IR (film): 1790, 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 0.08, 0.09, 0.87 (3s, 15H, t-BuMe_2Si), 2.04, 2.08 (2s, 6H, 2 OAc), 2.52 (dd, 1H, *J* 17.9 and 3.7 Hz, H-4a), 2.71 (dd, 1H, *J* 17.9 and 9.2 Hz, H-4b), 3.80 (s, 3H, OCH_3), 3.82 (m, 2H, H-3, H-3'a), 4.05 (m, 1H, *J* 6.5, 3.4, and 5.3 Hz, H-2'), 4.11 (dd, 1H, *J* 11.5 and 3.4 Hz, H-3'b), 4.10, 4.14 (2d, 1H, *J* 13.5 Hz, benzyl), 4.92 (t, 1H, *J* 5.6 and 5.3 Hz, H-1'); MS m/z: M^+ 495. Anal. Calcd for $C_{24}H_{38}NO_8Si$: C, 58.2; H, 7.7; N, 2.8. Found: C, 58.3; H, 7,7; N, 3.0.

(3S,1'S,2'R) N-Acetyl-(1',2',3'-triacetoxypropyl)-isoxazolidin-5-one (26). Addition of hydroxylamine (**15**) to lactone **11** was performed according to the general procedure described above. The post-reaction mixture was evaporated and acetylated with acetic anhydride-piridine mixture. After standard work up the crude product was purified by chromatography to afford **26**, 80%; syrup: $[\alpha]_D$ +60° (*c* 1, CH_2Cl_2); IR (film): 1680, 1740, 1790 cm^{-1}; ^1H NMR (CD_3OD): 2.04, 2.10, 2.12, 2.25 (4s, 12H, N-Ac, 3 OAc), 2.64 (dd, 1H, *J* 18.5 and 3.1 Hz, H-4a), 2.92 (dd, 1H, *J* 18.5 and 9.2 Hz, H-4b), 4.16 (dd, 1H, H-3'a), 4.42 (dd, 1H, H-3'b), 4.51 (dd, 1H, H-1'), 5.18 (dt, 1H, H-2'), 5.34 (dt, 1H, H-1'); MS m/z: M^+ 345. Anal. Calcd for $C_{14}H_{19}NO_9$: C, 48.7; H, 5.5; N, 4.1. Found: C, 48.2; H, 5.6; N, 3.9.

Hydrogenolysis of isoxazolidin-5-ones and formation of azetidin-2-ones 35-38. General procedure. Isoxazolidin-5-one **21**, **23**,**25**, and **28** (1 mmol) was dissolved in methanol (100 mL) and hydrogenated over 10% Pd/C (0.35 g), at room temperature, under atmospheric pressure, for 3 hs, 40 min, 8 min, and 20 min respectively. Subsequently the catalyst was filtered off, and methanol was evaporated. The crude residue was suspended in dichloromethane (20 ml) and treated with 2-chloro-1-methylpyridinium iodide (1.1 mmol) and triethylamine (2.2 mmol). The reaction mixture was stirred for 2 h at room temperature. Subsequently the solvent was evaporated and the residue was purified on a silica gel column to afford corres ponding β-lactam in about 60-70% yield.

N-(p-Methoxybenzyl)-4-(2'-*tert*-butyldiphenylsiloxyethyl)-azetidin-2-one (35); syrup; IR (film): 1760 cm^{-1}; ^1H NMR ($CDCl_3$): 1.01 (s, 9H, t-Bu), 1.57 (m, 1H, H-1'a), 1.92 (m, 1H, H-1'b), 2.64 (dd, 1H, *J* 14.6 and 2.0 Hz, H-3a), 2.95 (dd, 1H, *J* 14.6 and 5.0 Hz, H-3b), 3.58 (m, 1H, H-4), 3.62 (m, 2H, H-2'a, 2'b), 3.79 (s, 3H, OCH_3), 4.04, 4.47 (2d, 2H, *J* 15.1 Hz, benzyl); MS m/z: M^+ 473. Anal. Calcd for $C_{29}H_{35}NO_3Si$: C, 73.6; H, 7.4; N, 2.9. Found: C, 73.4; H, 7.4; N, 3.0.

(4R,2'S) N-(p-Methoxybenzyl)-4-(3'-acetoxy-2'-*tert*-butyldimethylsiloxypropyl)-azetidin-2-one (36); syrup; $[\alpha]_D$ -10.6° (*c* 0.53, CH_2Cl_2); IR (film): 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 0.04, 0.05, 0.81 (3s, 15H, t-BuMe_2Si), 1.47 (m, 1H, H-1'a), 1.91 (m, 1H, H-1'b), 2.04 (s, 3H, OAc), 2.61 (dd, 1H, *J* 14.6 and 1.9 Hz, H-3a), 3.01 (dd, 1H, *J* 14.6 and 4.9 Hz, H-3b), 3.58 (m, 1H, H-4), 3.80 (s, 3H, OCH_3), 3.88 (m, 3H, H-2', 3'a, 3'b), 4.07, 4.52 (2d, 2H, *J* 15.0 Hz, benzyl); MS m/z: M^+-57 = 364. Anal. Calcd for $C_{22}H_{35}NO_5Si$: C, 62.7; H, 8.4; N, 3.3. Found: C, 62.5; H, 8.6; N, 3.2.

(4R,2'S) N-Benzyl-4-(3'-acetoxy-2'-*tert*-butyldimethylsiloxypropyl)-azetidin-2-one (37);

syrup; $[\alpha]_D$ -34.7° (*c* 0.34, CH_2Cl_2); IR (film): 1755 cm^{-1}; ^1H NMR ($CDCl_3$): 0.05, 0.07, 0.81 (3s, 15H, t-BuMe_2Si), 1.47 (m, 1H, H-1'a), 1.90 (m, 1H, H-1'b), 2.04 (s, 3H, OAc), 2.64 (dd, 1H, *J* 14.5 and 1.9 Hz, H-3a), 3.04 (dd, 1H, *J* 14.5 and 4.9 Hz, H-3b), 3.61 (m, 1H, H-4), 3.82 (m, 1H, H-2'), 3.82 (m, 2H, H-3'a, 3'b), 4.13, 4.58 (2d, 2H, *J* 15.2 Hz, benzyl); MS m/z: M^+ 391. Anal. Calcd for $C_{21}H_{33}NO_4Si$: C, 64.4; H, 8.5; N, 3.6. Found: C, 64.1; H, 8.7; N, 3.3.

(4S,1'S,2'S) N-(p-Methoxybenzyl)-4-(1',3'-diacetoxy-2'-*tert*-butyldimethysiloxypropyl)-azetidin-2-one (38); syrup; $[\alpha]_D$ +2.3° (*c* 0.53, CH_2CL_2); IR (film): 1760 cm^{-1}; ^1H NMR ($CDCl_3$): 0.11, 0.4, 0.8 (3s, 15H, t-BuMe_2Si), 2.04, 2.10 (2s, 6H, 2 OAc), 2.81 (dd, 1H, *J* 14.5 and 5.1 Hz, H-3a), 3.03 (dd, 1H, *J* 14.5 and 2.2 Hz, H-3b), 3.67 (ddd, 1H, *J* 5.1, 2.2, and 1.4 Hz, H-4), 3.81 (s, 3H, OCH_3), 3.88 (m, 1H, H-2'), 3.93 (dd, 1H, *J* 11.5 and 4.7 Hz, H-3'a), 3.97 (dd, 1H, *J* 11.5 and 5.9 Hz, H-3'b), 3.86, 4.63 (2d, 2H, *J* 15.9 Hz, benzyl), 5.16 (dd, 1H, *J* 1.4 and 4.8 Hz, H-1'); MS m/z: M^+-57 = 422. Anal. Calcd for $C_{24}H_{37}NO_7Si$: C, 60.1; H, 7.8; N, 2.9. Found: C, 60.1; H, 7.8; N, 2.7.

3-Acetamido-6-O-acetyl-5-O-*tert*-butyldimethylsilyl-2,3-dideoxy-D-xyloaldono-1,4-lactone (40). Compound **33** hydrogenated for 3 h according to the procedure described above gave respective amino acid **34** which was purified on a silica gel using ethyl acetate as on eluent; 79%; mp. 114-116°C, IR (CH_2Cl_2); 3440, 1745, 1680 cm^{-1}; MS m/z: M^+-57 = 320. Anal. Calcd for $C_{16}H_{31}NO_7Si$: C, 50.9; H, 8.2; N, 3.7. Found: C, 51.3; H, 8.0; N, 3.7. Compound **34** (R^1=CH_2OAc, R^2=OAc, R^3=R^4=H, R^5=TBDMS), treated with Mukaiyama reagent - according to the general procedure described, above gave lactone **40**; 67%; mp. 151-152°C; $[\alpha]_D$ -71.2° (*c* 1, CH_2Cl_2); IR (CH_2Cl_2): 3460, 1795, 1750, 1690 cm^{-1}; ^1H NMR ($CDCl_3$): 0.19, 0.20, 0.93 (3s, 15H, t-BuMe_2Si), 2.02. 2.08 (2s, 6H, OAc, NAc), 2.52 (dd, 1H, *J* 17.4 and 9.1 Hz, H-2), 2.83 (dd, 1H, *J* 17.4 and 9.5 Hz, H-2'), 4.06 (ddd, 1H, *J* 7.2 Hz, H-6), 4.26 (dd, 1H, *J* 10.6 and 5.3 Hz, H-6'), 4.72 (dd, 1H, *J* 7.9 and 2.2 Hz, H-4), 5.02 (m, 1H, H-3), 5.98 (bd, 1H, *J* 8.0 Hz, NH); MS m/z: M^+-57 = 302. Anal. Calcd for $C_{16}H_{29}NO_6Si$: C, 53.5; H, 8.1; N, 3.9. Found: C, 53.2; H, 8.3; N, 3.9.

Hydrogenolysis of compound **33** for 10 min allowed to isolate a side product **41**; - syrup, IR (film): 1790, 1755 cm^{-1}; ^1H NMR ($CDCl_3$): 0.07, 0.10, 0.85 (3s, 15H, t-BuMe_2Si), 2.06, 2.19 (2s, 6H, OAc, NAc), 2.56 (dd, 1H, *J* 18.1 and 9.5 Hz, H-2), 2.61 (dd, 1H, *J* 18.1 and 4.5 Hz, H-2'), 3.82 (s, 3H, OCH_3), 3.88 (dd, 1H, *J* 11.5 and 7.3 Hz, H-6), 3.93 (dd, 1H, *J* 11.5 and 6.0 Hz, H-6'), 4.08 (ddd, 1H, *J* 7.3, 6.0, and 1.8 Hz, H-5), 4.39, 4.57 (2d, 2H, *J* 16.6 Hz, benzyl), 4.46 (m, 1H, H-3), 4.62 (dd, 1H, *J* 3.3 and 1.8 Hz, H-4); MS m/z: M^+ 479, high mass Calcd for $C_{10}H_{12}NO_2$ ($CH_3OC_6H_4CH_2NCOCH_3^+$): - 178.0868. Found: 178.0868.

(4R,2'S) N-(p-Methoxybenzyl)-4-(2'-*tert*-butyldimethylsiloxy-3'-hydroxypropyl)-azetidin-2-one (42). Compound **36** (0.23 g, 0.27 mmol) was dissolved in a solution of ammonia in methanol (15 mL; 7.6 mol/dm^3) and left overnight. Subsequently methanol was evaporated under vacuum, and the residue was purified on a silica gel column to give **42** (0.18 g, 86%); mp. 75-76°C; $[\alpha]_D$ -9.6° (*c* 0.62, CH_2Cl_2); IR ($CDCl_3$): 1740 cm^{-1}; ^1H NMR ($CDCl_3$ + D_2O); 0.05, 0.07, 0.89 (3s, 15H, t-BuMe_2Si), 1.38 (ddd, 1H, *J* 13.9, 3.1, and 9.0 Hz, H-1'a), 1.81 (ddd, 1H, *J* 3.9, 9.4, and 4.3 Hz, H-1'b), 2.67 (dd, 1H, *J* 14.6 and 2.2 Hz,

H-3a), 3.06 (dd, 1H, *J* 4.6 and 5.0 Hz, H-3b), 3.32 (dd, 1H, J 9.9 and 7.1 Hz, H-3'a), 3.51 (dd, 1H, *J* 9.9 and 3.5 Hz, H-3'b),3.61 (m, 1H, H-2'), 3.72 (m, 1H, H-4), 3.80 (s, 3H, OCH_3), 4.17, 4.48 (2d, 2H, *J* 15.1 Hz, benzyl). Anal. Calcd for $C_{20}H_{33}NO_4Si$: C, 63.3; H, 8.8; N, 3.7. Found: C, 63.1; H, 8.7; N, 3.7.

(4R,2'S) N-Benzyl-4-(2'-*tert*-butyldimethylsiloxy-3'-hydroxypropyl)-azetidin-2-one (43). Compound was obtained from **37** according to the procedure described above; 83%; mp. 67-68°C; $[\alpha]_D$ -18.5° (*c* 0.2, CH_2Cl_2); IR (film): 1750 cm^{-1}; ^1H NMR ($CDCl_3$ + D_2O); 0.05, 0.08, 0.88 (3s, 15H, t-BuMe_2Si), 1.37 (ddd, 1H, *J* 13.9, 8.9, and 3.0 Hz, H-1'a), 1.82 (ddd, 1H, *J* 13.9, 4.2, and 9.6 Hz, H-1'b), 2.69 (dd, 1H, *J* 14.6 and 2.3 Hz, H-3a), 3.09 (dd, 1H, *J* 14.6 and 5.0 Hz, H-3b), 3.31 (dd, 1H, *J* 9.9 and 7.2 Hz, H-3'a), 3.51 (dd, 1H, *J* 9.9 and 3.5 Hz, H-3'b), 3.61 (m, 1H, H-2'), 3.74 (m, 1H, H-4), 4.23, 4.54 (2d, 2H, *J* 15.3 Hz, benzyl). Anal. Calcd for $C_{19}H_{31}NO_3Si$: C, 65.3; H, 9.0; N, 4.0. Found: C, 65.3; H, 9.1; N, 4.0.

(4R,2'S) N-(p-Methoxybenzyl)-4-(2',3'-dihydroxypropyl)-azetidin-2-one (44). Compound **42** was desilylated using tetrabutylammonium fluoride in tetrahydrofuran to give **44**; 91%; mp. 85-86°C; $[\alpha]_D$ -4.5° (*c* 0.73, CH_2Cl_2); IR ($CHCl_3$): 1760 cm^{-1} ; ^1H NMR ($CDCl_3$ + D_2O): 1.44 (ddd, 1H, *J* 14.0, 3.4, and 8.8 Hz, H-1'a), 1.86 (ddd, 1H, *J* 14.0, 9.3, and 4.2 Hz, H-1'b), 2.69 (dd, 1H, *J* 14.6 and 2.2 Hz, H-3a), 3.07 (dd, 1H, *J* 14.6 and 5.0 Hz, H-3b), 3.38 (dd, 1H, *J* 10.7 and 7.5 Hz, H-3'a), 3.57 (dd, 1H, *J* 10.7 and 3.1 Hz, H-3'b), 3.68 (m, 2H, H-2', H-4), 3.80 (s, 3H, OCH_3), 4.14, 4.51 (2d, 2H, *J* 15.1 Hz, benzyl); MS m/z: M^+ 265. Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.4; H, 7.2; N, 5.3. Found: C, 63.2; H, 7.4; N, 5.1. **2',3'-Diacetoxy compound 39**: syrup; $[\alpha]_D$ + 12.5° (*c* 0.36, CH_2Cl_2); IR (film): 1770 cm^{-1}; ^1H NMR ($CDCl_2$): 2.02, 2.03, 2.10 (3s, 9H, 3 OAc), 286 (dd, 1H, *J* 14.5 and 5.2 Hz, H-3a), 2.98 (dd, 1H, *J* 14.5 and 1.8 Hz, H-3b), 3.58 (ddd, 1H, *J* 5.2, 1.8, and 1.7 Hz, H-4), 3.81 (s, 3H, OCH_3), 4.11 (dd, 1H, *J* 12.3 and 5.9 Hz, H-3'a), 4.15 (dd, 1H, *J* 12.3 and 3.5 Hz, H-3'b), 3.84, 3.65 (2d, 2H, *J* 15.1 Hz, benzyl), 5.09 (m, 1H, H-2'), 5.34 (dd, 1H, *J* 1.7 and 5.9 Hz, H-1); Ms m/z: M^+ 407; Anal. Calcd for $C_{20}H_{25}NO_8$: C, 59.0; H, 6.2; N, 3.4. Found: C, 58.7; H, 6.0; N, 3.5.

(4R,2'S) N-Benzyl-4-(2',3'-dihydroxypropyl)-azetidin-2-one (45). Compound **43** was desilylated using tetrabutyloammonium fluoride in tetrahydrofuran to give **45** ; 86%; mp. 86-87°C; $[\alpha]_D$ -15.4° (*c* 0.66, CH_2Cl_2); IR ($CHCl_3$): 3400, 1740 cm^{-1}; ^1H NMR ($CDCl_3$ + D_2O): 1.46 (ddd, 1H, *J* 14.0, 8.8, and 3.4 Hz, H-1'a), 1.86 (ddd, 1H, *J* 14.0, 4.2, and 9.2 Hz, H-1'b), 2.71 (dd, 1H, *J* 14.6 and 2.3 Hz, H-3a), 3.09 (dd, 1H, *J* 14.6 and 5.0 Hz, H-3b), 3.36 (dd, 1H, *J* 10.9 and 7.4 Hz, H-3'a), 3.54 (dd, 1H, *J* 10.9 and 3.3 Hz, H-3'b), 3.67 (m, 1H, H-2'), 3.73 (m, 1H, H-4), 4.21, 4.57 (2d, 2H, *J* 15.3 Hz, benzyl). Anal. Calcd for $C_{13}H_{17}NO_3$ C, 66.4; H, 7.3; N, 6.0. Found: C, 66.3; H, 7.5; N, 6.1.

(4R) N-(p-Methoxybenzyl)-4-formylmethylazetidin-2-one (46). Silica gel (230-400 mesh; 0.4 g) was suspended in dichloromethane (3.3 mL) and treated with a 0.65 M sodium meta-periodate water solution (0.6 mL).[20] Subsequently compound (0.058 g, 0.3 mmol) in dichloromethane (0.4 mL) was added, and the mixture was stirred for 15 min. The precipitate was filtred off, washed with dichloromethane, and solutions were combined. The solvent was evaporated and the residue was purified on a silica gel column to afford

46 (0.043 g, 92%); syrup; $[\alpha]_D$ -4.0° (*c* 0.43, CH_2Cl_2); IR (film): 2920, 1730 cm^{-1}; ^1H NMR ($CDCl_3$): 2.62 (ddd, 1H, *J* 18.1, 0.8, and 6.6 Hz, H-1'a), 2.64 (dd, 1H, *J* 14.8 and 2.4 Hz, H-3a), 2.73 (ddd, 1H, *J* 18.1, 1.1, and 6.3 Hz, H-1'b), 3.19 (dd, 1H, *J* 14.8 and 5.1 Hz, H-3b), 3.94 (m, 1H, H-4), 4.21 (2d, 2H, *J* 15.1, benzyl), 9.63 (dd, 1H, *J* 0.8 and 1.1 Hz, H-2'); MS m/z: M^+ 233. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.9; H, 6.5; N, 6.0. - Found: C, 66.6; H, 6.4; N, 5.9.

(4R) N-(p-Methoxybenzyl)-4-(2'-hydroxyethyl)-azetidin-2-one (48). Compound **46** (0.023 g, 0.1 mmol) was dissolved in 75% ethanol (2 mL) and treated with $NaBH_4$ (0.01 g). - Subsequently ethanol was evaporated and the remaining solution was treated with - saturated ammonium sulfate (2 mL), and extracted with dichloromethane. The extract was dried and evaporated. The residue was evaporated to give **48** ; 64%, syrup, $[\alpha]_D$ +20.8° (*c* 0.25, CH_2Cl_2); IR (film) 1730 cm^{-1}; ^1H NMR ($CDCl_3$); 1.64 (m, 1H, H-1'a), 1.94 (m, 1H, H-1'b), 2.68 (dd, 1H, *J* 14.6 and 1.9 Hz, H-3a), 3.05 (dd, 1H, *J* 14.6 and 5.0 Hz, H-3b), 3.61 (m, 1H, H-4), 3.65 (t, 2H, H-2'a, 2'b), 3.80 (s, 3H, OCH_3), 4.13, 4.53 (2d, 2H, benzyl); MS m/z: M^+ 235. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.4; H, 7.3; N, 6.0. Found: C, 66.2; H, 17.5; N, 5.9.

Tert-**Butyldimethylsilyl derivative (49)** , syrup; $[\alpha]_D$ +2.0° (*c* 0.85, CH_2Cl_2); IR (film): 1760 cm^{-1}; ^1H NMR ($CDCl_3$): 0.05, 0.78 (2s, 15H, t-BuMe_2Si), 1.50 (m, 1H, H-1'a), 1.87 (m, 1H, H-1'b), 2.63 (ddd, 1H, *J* 14.6, 1.8, and 0.9 Hz, H-3a), 2.94 (dd, 1H, *J* 14.6 and 5.0 Hz, H-3b), 3.51 (m, 3H, H-4, 2'a, 2'b), 3.73 (s, 3H, OCH_3), 4.03, 4.44 (2d, 2H, *J* 15.1 Hz, benzyl). Anal. Calcd for $C_{19}H_{31}NO_3$: C, 65.3; H, 8.9; N, 4.0. Found: C, 65.3; H, 9.2; N, 4.0.

(4R) N-(p-Methoxybenzyl)-4-methoxycarbonylmethyl-azetidin-2-one (50). Compound **44** (0.027 g, 0.1 mmol) was dissolved in tert-butanol (0.5 mL), cooled to 0°C, and treated with a solution of ammonium dihydrogen phosphate (0.16 g in 2 mL of water). Subsequently sodium metaperiodate (0.02 g, 0.11 mmol) in water (0.5 mL) was added. The mixture was then - treated with 30% hydrogen peroxide (0.05 mL) and sodium chlorite (0.024 g) in water (0.5 mL).[21] After 0.5 h, saturated ammonium sulfate (5 mL) was added and the solution was - extracted with ethyl acetate. The extract was dried and evaporated. The residue was - dissolved in methanol and estrified with diazomethane. Subsequently methanol was - evaporated and the crude product was purified by chromatography to give **50** (0.022 g, 83%), mp. 44-46°C; $[\alpha]_D$ +20.5° (*c* 0.4, benzene); IR ($CHCl_3$): 1750 cm^{-1}; ^1H NMR ($CDCl_3$): 2.46 (dd, 1H, *J* 16.2 and 7.1 Hz, H-1'a), 2.58 (dd, 1H, *J* 16.2 and 6.2 Hz, H-1'b), 2.69 (dd, 1H, *J* 14.8 and 2.3 Hz, H-3a), 3.14 (dd, 1H, *J* 14.8 and 5.1 Hz, H-3b), 3.63 (s, 3H, CO_2CH_3), 3.80 (s, 3H, OCH_3), 3.86 (m, 1H, H-4), 4.17, 4.44 (2d, 2H, *J* 15.1 Hz, benzyl); MS m/z M^+ 263. Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.9; H, 6.5; N, 5.3. Found: C, 63.8; H, 6.4; N, 5.1.

(4R) N-Benzyl-4-methoxycarbonylmethyl-azetidin-2-one (52). Compound was obtained - according to the procedure described above; mp. 42-43 °C (lit. Ref. 22; 43.5-44.5°C); $[\alpha]_D$ +22.9° (c 0.6, benzene), [(lit. Ref. 22; $[\alpha]_D$ +23.8° (c 1, benzene)]; IR (film): 1770 and 1735 cm^{-1}; ^1H NMR ($CDCl_3$): 2.49 (dd, 1H, *J* 16.2 and 6.3 Hz, H-1'a), 2.58 (dd, 1H, *J* 16.2 and 6.9 Hz, H-1'b), 2.72 (dd, 1H, *J* 14.8 and 2.4 Hz, H-3a), 3.17 (dd, 1H, *J*

14.8 and 5.1 Hz, H-3b), 3.61 (s, 3H, CO_2CH_3), 3.89 (m, 1H, H-4), 4.25, 4.50 (2d, 2H, *J* 15.3 Hz, benzyl). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.9; H, 6.5; N, 6.0. Found: C, 66.7; H, 6.5; N, 6.1.

(4R) 4-Methoxycarbonylmethyl-azetidin-2-one (53). Compound **45** (0.023 g, 0.1 mmol) was oxidized with sodium metaperiodate followed by oxidation of the resulting aldehyde with sodium chlorite according to the procedure described for compound **50** , to afford crude acid **50** (0.018 g). The acid **51** was dissolved in liquid ammonia (5 mL) and treated with sodium (0.02 g). After 45 min, the solution was treated with ammonium chloride (0.06 g) and left untill ammonia evaporated. Subsequently the mixture was dissolved in methanol (2 mL) and estrified with diazomethane. Methanol was evaporated and the residue was - purified on a silica gel column to give **53** (0.007 g); syrup; $[\alpha]_D$ +64.9° (*c* 0.3, $CHCl_3$); [(lit. Ref 23; $[\alpha]_D$ +63.3° (*c* 1.11, $CHCl_3$); Ref. 24; $[\alpha]_D$+ 64.5° (*c* 0.2, $CHCl_3$)]; IR (film): 3420 and 1760 cm^{-1}; ^1H NMR ($CDCl_3$+D_2O): 2.51 (dd, 1H, *J* 16.2 and 6.3 Hz, H-1'a), 2.60 (dd, 1H, *J* 16.2 and 7.0 Hz, H-1'b), 2.71 (dd, 1H, *J* 14.5 and 2.5 Hz, H-3a), 3.21 (dd, 1H, *J* 14.5 and 5.0 Hz, H-3b), 3.68 (s, 3H, OCH_3), 3.87 (m, 1H, H-4). Anal. Calcd for $C_6H_9NO_3$: C, 50.3; H, 6.4; N, 9.8. Found: C, 50.2; H, 6.4; N, 9.6.

(4R,2'S) N-Benzyl-4-(3'-bromo-2'-*tert*-butyldimethylsiloxypropyl)-azetidin-2-one (55). Compound **43** (0.01 g, 0.03 mmol) was dissolved in pyridine (1 mL) and treated with triphenylphosphine (0.03 g) and carbon tetrabromide (0.02 g). After disappearance of the substrate (2 h; TLC: hexane-ethyl acetate 3:1 v/v), methanol (3 mL) was added into the reaction mixture. Subsequently the solvent was evaporated, and the crude product was purified on a silica gel column using hexane-ethyl acetate 9:1 v/v as an eluent to - afford **55** (0.006 g), syrup; $[\alpha]_D$ +6.9° (*c* 0.35, CH_2Cl_2); IR (film): 1765 cm^{-1}; ^1H NMR ($CDCl_3$): 0.05, 0.08, 0.87 (3s, 15H, t-$BuMe_2Si$), 1.86 (ddd, 1H, *J* 14.7, 4.7, and 3.4 Hz, H1'b), 2.82 (dd, 1H, *J* 14.8 and 2.3 Hz, H-3a), 3.15 (dd, 1H, *J* 14.8 and 5.0 Hz, H-3b), 3.58 (m, 1H, H-4), 3.69 (m, 1H, H-2'), 3.77 (dd, 1H, *J* 12.0 and 4.7 Hz, H-3'a), 3.78 (dd, 1H, *J* 12.0 and 7.8 Hz, H-3'b), 4.23, 4.56 (2d, 2H, *J* 15.4 Hz, Bn). Anal. Calcd for $C_{19}H_{30}BrNO_2Si$: C, 55.3; H, 7.3; N, 3.4. Found: C, 55.2; H, 7.6; N, 3.6.

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